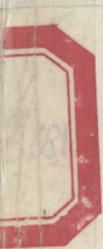


The Medical Management of AIDS

Second Edition



一九九五年十月九日



The Medical Management of AIDS

Second Edition

MERLE A. SANDE, M.D.

Professor and Vice-Chairman, Department of Medicine,
University of California, San Francisco;
Chief, Medical Service, San Francisco General Hospital,
San Francisco, California

PAUL A. VOLBERDING, M.D.

Associate Professor, Department of Medicine,
University of California, San Francisco;
Director, AIDS Program, San Francisco General Hospital,
San Francisco, California



W.B. SAUNDERS COMPANY

Harcourt Brace Jovanovich, Inc.

Philadelphia, London, Toronto, Montreal, Sydney, Tokyo

W. B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.
The Curtis Center
Independence Square West
Philadelphia, PA 19106

Library of Congress Cataloging-in-Publication Data

The Medical management of AIDS / edited by Merle A. Sande, Paul A. Volberding. —2nd ed.

p. cm.

Includes bibliographical references.

Includes index.

ISBN 0-7216-3505-9

I. AIDS (Disease)—Treatment. I. Sande, Merle A.

II. Volberding, Paul.

[DNLM: 1. Acquired Immunodeficiency Syndrome. 2. HIV. WD308 M489]

RC607.A26M43 1990

616.97'92—dc20

DNLM/DLC

for Library of Congress

90-8584
CIP

Listed here is the latest translated edition of this book together with the language of the translation and the publisher.

Spanish—*first edition*—NEISA Cedro 512 06450 Mexico D.F., Mexico

Sponsoring Editor: Martin Wonsiewicz

The Medical Management of AIDS

ISBN 0-7216-3505-9

Copyright © 1990, 1988 by W. B. Saunders Company.

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher.

Printed in the United States of America.

Last digit is the print number: 9 8 7 6 5 4 3

CONTRIBUTORS

DONALD I. ABRAMS, M.D.

Associate Professor of Clinical Medicine,
University of California, San Francisco;
Assistant Director, AIDS Activities Division,
San Francisco General Hospital, San Francisco, California
Hematologic Manifestations of HIV Infection

DONALD ARMSTRONG, M.D.

Professor of Medicine, Cornell University Medical College, Ithaca, New York;
Chief, Infectious Disease Service, and Director,
Microbiology Laboratory, Memorial Sloan-Kettering Cancer Center,
New York, New York
Fungal Infections in AIDS: Histoplasmosis and Coccidioidomycosis

TIMOTHY G. BERGER, M.D.

Assistant Clinical Professor,
University of California, San Francisco;
Chief, Department of Dermatology,
San Francisco General Hospital, San Francisco, California
Dermatologic Care in the AIDS Patient: A 1990 Update

BRUCE BREW, M.B., B.S.

Senior Lecturer in Medicine,
University of New South Wales;
Staff Specialist Neurologist,
St. Vincent's Hospital,
Sydney, Australia
Management of the Neurologic Complications of HIV-1 Infection and AIDS

WILLIAM BUHLES, D.V.M., Ph.D.

Department Head, Department of Immunology and Antiviral Therapy,
Institute of Clinical Medicine,
Division of Syntex, Inc.,
Palo Alto, California
Management of Herpes Virus Infections (CMV, HSV, VZV)

JOHN P. CELLO, M.D.

Professor of Medicine,
University of California, San Francisco;
Chief, Gastroenterology, San Francisco General Hospital,
San Francisco, California
AIDS-Associated Gastrointestinal Disease

RICHARD E. CHAISSON, M.D.

Director, AIDS Services,
Assistant Professor of International Health, and
Assistant Professor of Epidemiology,
Johns Hopkins University School of Hygiene and Public Health,
Baltimore, Maryland

Infections Due to Encapsulated Bacteria, Salmonella, Shigella, and Campylobacter

DAVID A. COOPER, B.Sc. (Med), M.D., F.R.A.C.P., F.R.C.P.A.

Associate Professor of Medicine and Director,
National Centre in HIV Epidemiology and Clinical Research,
University of New South Wales;
Senior Staff Specialist in Immunology,
Centre of Immunology, St. Vincent's Hospital,
Sydney, Australia

Primary HIV Infection: Clinical, Immunologic and Serologic Aspects

BRIAN R. DANNEMANN, M.D.

Postdoctoral Fellow, Division of Infectious Diseases,
Stanford University School of Medicine,
Stanford, California

Toxoplasmosis in Patients with AIDS

BASIL DONOVAN, M.B., B.S., Dip. Ven. (Lond.), F.A.C.Ven.

Senior Staff Specialist and Director,
Sydney STD Centre, Sydney Hospital,
Sydney, Australia

Primary HIV Infection: Clinical, Immunologic and Serologic Aspects •

W. LAWRENCE DREW, M.D., Ph.D.

Associate Professor, Medicine and Laboratory Medicine,
University of California, San Francisco;
Director, Clinical Microbiology and Infectious Diseases, and
Director, Biskind Pathology Research Laboratory,
Mount Zion Hospital and Medical Center,
San Francisco, California

Management of Herpes Virus Infections (CMV, HSV, VZV)

RONALD J. DWORKIN, M.D.

Fellow, Infectious Diseases,
Mount Zion Hospital and Medical Center,
San Francisco, California

Management of Herpes Virus Infections (CMV, HSV, VZV)

KIM S. ERLICH, M.D.

Infectious Disease Consultant,
Seton Medical Center,
Daly City, California

Management of Herpes Virus Infections (CMV, HSV, VZV)

MARGARET A. FISCHL, M.D.

Professor of Medicine,

University of Miami School of Medicine;

Director, Special Immunology, Jackson Memorial Hospital,
Miami, Florida

Treatment of HIV Infection

JULIE LOUISE GERBERDING, M.D.

Assistant Professor of Medicine, Infectious Diseases,

University of California, San Francisco, School of Medicine;

Physician Specialist and Director, HIV Counseling and Testing Service,

San Francisco General Hospital,

San Francisco, California

Occupational HIV Transmission: Issues for Health Care Providers

PHILIP C. GOODMAN, M.D.

Professor of Clinical Radiology and Medicine,

University of California, San Francisco,

San Francisco, California

The Chest Film in AIDS

DEBORAH GREENSPAN, B.D.S.

Clinical Professor, Department of Stomatology,

School of Dentistry,

University of California, San Francisco;

Clinical Director, Oral AIDS Center,

San Francisco, California

Diagnosis and Management of the Oral Manifestations of HIV Infection and AIDS

JOHN S. GREENSPAN, B.Sc., B.D.S., Ph.D., F.R.C.Path.

Professor and Chairman, Department of Stomatology,

School of Dentistry, and Professor of Pathology,

School of Medicine,

University of California, San Francisco;

Director, Oral AIDS Center,

San Francisco, California

Diagnosis and Management of the Oral Manifestations of HIV Infection and AIDS

MOSES GROSSMAN, M.D.

Professor and Vice Chairman of Pediatrics,

University of California, San Francisco;

Chief, Pediatric Services, San Francisco General Hospital,

San Francisco, California

Special Problems in the Child with AIDS

JULIE HAMBLETON, M.D.

Chief Medical Resident,

San Francisco General Hospital,

University of California, San Francisco,

San Francisco, California

Hematologic Manifestations of HIV Infection

HARRY HOLLANDER, M.D.

Associate Professor of Clinical Medicine,
University of California, San Francisco;
Director and Attending Physician, AIDS Clinic,
San Francisco General Hospital,
San Francisco, California

Care of the Individual with Early HIV Infection: Unanswered Questions, Including the Syphilis Dilemma

PHILIP C. HOPEWELL, M.D.

Professor of Medicine,
University of California, San Francisco;
Chief, Chest Service,
San Francisco General Hospital,
San Francisco, California
Pneumocystis carinii Pneumonia

ALLISON IMRIE, B.Sc.

Senior Scientific Officer,
Centre for Immunology, St. Vincent's Hospital,
Sydney, Australia

Primary HIV Infection: Clinical, Immunologic and Serologic Aspects

DENNIS M. ISRAELSKI, M.D.

Assistant Clinical Professor,
Infectious Diseases in Medicine,
Department of Medicine, Stanford University School of Medicine,
Stanford, California;
Medical Director, Palo Alto Veterans Administration Hospital,
AIDS Program, Palo Alto, California;
Medical AIDS Position, San Mateo County General Hospital,
San Mateo, California

Toxoplasmosis in Patients with AIDS

MARK A. JACOBSON, M.D.

Assistant Professor of Medicine in Residence,
University of California, San Francisco;
Attending Physician,
San Francisco General Hospital,
San Francisco, California

Mycobacterial Diseases: Tuberculosis and Mycobacterium avium Complex

PAULA JESSON, J.D.

Deputy City Attorney for the City and County of San Francisco,
San Francisco, California

Legal Ramifications of AIDS

LAWRENCE D. KAPLAN, M.D.

Assistant Clinical Professor of Medicine,
University of California, San Francisco;
AIDS/Oncology Program,
San Francisco General Hospital,
San Francisco, California

The Malignancies Associated with AIDS

JAY A. LEVY, M.D.

Professor of Medicine and
Research Associate,
Cancer Research Institute,
University of California, San Francisco, School of Medicine,
San Francisco, California

Features of HIV and the Host Response That Influence Progression to Disease

GRACE MINAMOTO, M.D.

Instructor in Clinical Medicine,
Columbia University, College of Physicians and Surgeons;
Junior Assistant Attending Physician,
St. Luke's-Roosevelt Hospital Center,
New York, New York

Fungal Infections in AIDS: Histoplasmosis and Coccidioidomycosis

LORI A. PANTHER, M.D.

Chief Medical Resident,
San Francisco General Hospital,
San Francisco, California

Cryptococcal Meningitis in AIDS

RONALD PENNY, M.D., D.Sc., F.R.A.C.P., F.R.C.P.A.

Professor of Clinical Immunology,
University of New South Wales;
Director, Centre for Immunology,
St. Vincent's Hospital,
Sydney, Australia

Primary HIV Infection: Clinical, Immunologic and Serologic Aspects

JOHN P. PHAIR, M.D.

Professor of Medicine,
Northwestern University Medical School,
Chicago, Illinois

Natural History of HIV Infection

RICHARD W. PRICE, M.D.

Professor and Head and Clinical Chief,
Department of Neurology,
University of Minnesota Hospital and Clinic,
Minneapolis, Minnesota

Management of the Neurologic Complications of HIV-1 Infection and AIDS

THOMAS C. QUINN, M.D., M.S.

Senior Investigator,
National Institute of Allergy and Infectious Diseases;
Associate Professor of Medicine,
Johns Hopkins University,
Baltimore, Maryland
Global Epidemiology of HIV Infections

JACK S. REMINGTON, M.D.

Professor of Medicine, Division of Infectious Diseases,
Stanford University School of Medicine,
Stanford, California;
Marcus A. Krupp Research Chair and Chairman,
Department of Immunology and Infectious Diseases,
Research Institute,
Palo Alto Medical Foundation,
Palo Alto, California
Toxoplasmosis in Patients with AIDS

MERLE A. SANDE, M.D.

Professor and Vice Chairman,
Department of Medicine,
University of California, San Francisco;
Chief, Medical Service,
San Francisco General Hospital,
San Francisco, California
Cryptococcal Meningitis in AIDS

JOHN D. STANSELL, M.D.

Clinical Instructor of Medicine,
University of California, San Francisco;
Attending Physician, AIDS Consult Service,
San Francisco General Hospital,
San Francisco, California
Cardiac, Endocrine, and Renal Complications of HIV Infection

BRETT TINDALL, B.App.Sc., M.Sc.

Senior Project Scientist,
National Centre in HIV Epidemiology and Clinical Research,
University of New South Wales;
Scientific Officer, Centre for Immunology,
St. Vincent's Hospital,
Sydney, Australia
Primary HIV Infection: Clinical, Immunologic and Serologic Aspects

PAUL A. VOLBERDING, M.D.

Associate Professor of Medicine,
University of California, San Francisco;
Director, AIDS Program,
San Francisco General Hospital,
San Francisco, California
Clinical Care of Patients with AIDS: Developing a System

JAMES R. WINKLER, D.M.D.

Assistant Professor, Periodontology,
University of California, San Francisco,
San Francisco, California

Diagnosis and Management of the Oral Manifestations of HIV Infection and AIDS

CONSTANCE B. WOFSY, M.D.

Professor of Clinical Medicine,
University of California, San Francisco;
Co-Director, AIDS Activities Program,
Assistant Chief, Infectious Diseases Division, and Director,
AIDS Provider Education Experience,
San Francisco General Hospital,
San Francisco, California

Prevention of HIV Transmission

PREFACE

No disease in modern times has had quite the impact on the civilized world as has the acquired immunodeficiency syndrome (AIDS). The disease has rapidly afflicted over 100,000 persons in the United States, and between 1 and 2 million more are believed to be infected with the causative agent, the human immunodeficiency virus (HIV). The scope of the epidemic is even more dramatic in equatorial Africa, where millions of people are already infected. Although the outlook in the near future for curative treatment or effective vaccine is grim, some measure of success in responding to this tragedy has been achieved. The medical and scientific communities have effectively cooperated to quickly accumulate epidemiologic, clinical, and basic science knowledge about this pandemic infection. We have rapidly expanded our knowledge of retrovirology and have turned many of our most creative minds toward unraveling the biology of HIV. Also, we have developed highly efficient mechanisms for treating HIV-infected individuals.

Amid the social and political upheaval precipitated by the AIDS epidemic, a critical problem has silently but steadily emerged: Who is to provide care for the increasing numbers of afflicted individuals? There is a desperate need for physicians, nurses, and other health care workers to provide skilled care for these patients. Although few practitioners have denied their responsibility to provide care, there is a reluctance on the part of some to actively assume a role in caring for these stricken individuals. In some, the reluctance is undoubtedly due to fears of acquiring the infection through patient care activities. For others, inadequate reimbursement schedules for HIV-related problems reduce the economic incentive to devote the large amounts of time and resources required to treat HIV-infected patients. Perhaps most importantly, the newness of AIDS and the rapid evolution of knowledge about the complications of HIV infection have made it difficult for practitioners not directly involved in AIDS research to keep abreast of new developments in the field. It is common for individual physicians, especially those who have limited opportunities for immediate consultation, to feel poorly equipped to handle AIDS patients.

For these reasons, we believe that an important contribution to the medical literature can be made by publishing an up-to-date text that addresses the clinical issues commonly encountered by practitioners who accept the challenges that AIDS provides. In our second edition, we have again com-

piled contributions from many of the world's leading authorities on AIDS. The biology and epidemiology of HIV infection and approaches to reduce sexual and nosocomial transmission of the virus are reviewed. The initial diagnostic evaluation of HIV-infected patients is outlined, and a summary of the multidisciplinary approach to treating these patients within the community is provided. We have also addressed the controversies related to HIV testing and have discussed some of the legal ramifications that the physician must face when caring for this patient population. Probably the most important and rapidly changing section deals with zidovudine—how and when to use it.

The infectious complications of HIV infection, including diagnosis and treatment of *Pneumocystis carinii* pneumonia and other protozoal, mycobacterial, fungal, and bacterial and viral infections, have been reviewed from a clinical perspective, as have the AIDS-related malignancies, including Kaposi's sarcoma and lymphomas. In this edition we have also included a review of the hematologic, endocrine, renal, and cardiac complications of AIDS. In each chapter an attempt has been made to present information in a practical format that should allow the primary care physician dealing with the disease for the first time to attack the problem in a logical and up-to-date fashion. Discussions on the approach to antiviral treatment for HIV infection and the special problems faced by HIV-infected children have also been included.

We hope that this will provide a useful update and review of contemporary clinical issues relevant to caring for individuals with HIV-related illnesses. We also hope that it will help alleviate some of the apprehensions elicited when patients with HIV infection and its myriad complications are encountered for the first time, so that patients can be approached with confidence and compassion.

We would like to thank The Burroughs Wellcome Company for providing the educational grant that made this publication, and the associated conference, possible. Also, special thanks are extended to Jan Rogerson and her staff for their valued assistance and to our publisher, the W. B. Saunders Company, who again with the second edition has set a record in completing publication 6 months from the time the chapters were completed. This rapid turnaround has allowed us to provide the most up-to-date review possible of the clinical aspects of caring for patients with AIDS.

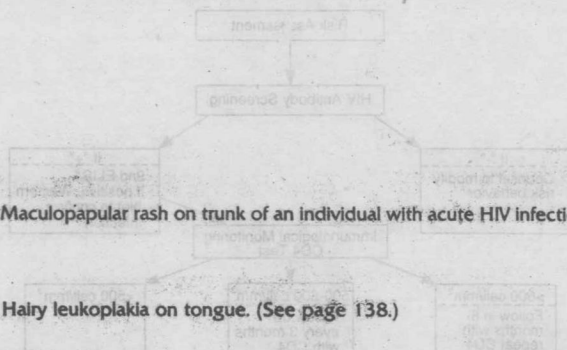
MERLE A. SANDE, MD

```

graph TD
    A[Immunological Monitoring CD4 Test] --> B[">600 cell/mm³  
Follow in 6 months with repeat CD4"]
    A --> C["500-600 cell/mm³  
Follow up every 3 months with CD4"]
    A --> D["<500 cell/mm³"]
    B --> E["If CD4 approaches 500"]
    E --> C
    C --> F["If CD4 goes below 500"]
    F --> D
    D --> G["Repeat CD4 <500 one week apart"]
    G --> H["Recommended ZDV Therapy"]
    H --> I["Initiate Zidovudine  
(Following 2 CD4 counts <500, 1 week apart)"]
    I --> J["Follow up in 2 weeks"]
    J --> K["Follow up Monthly for 3 months  
-----  
• CBC each month  
• then *  
Follow up every 3 months  
-----  
• CBC every visit (every 3 months)  
• CD4 every other visit (every 6 months)"]
    K --> L["If new symptoms or toxicity  
-----  
Follow up as clinically indicated."]
    K --> M["* or *  
If CD4 <300 and no new symptoms or toxicity  
Repeat CD4 every 3 months"]
    M --> N["If CD4 <200  
-----  
• Initiate PCP prophylaxis  
• Further CD4 testing not medically indicated"]
  
```

The flowchart outlines the management of HIV infection based on CD4 counts and clinical status. It begins with an immunological monitoring CD4 test, which leads to three different follow-up schedules depending on the CD4 count: >600 cell/mm³ (6 months), 500-600 cell/mm³ (3 months), and <500 cell/mm³ (1 week). If the CD4 count approaches 500, the follow-up schedule changes to 3 months. If the CD4 count goes below 500, the follow-up schedule changes to 1 week. If the CD4 count is <500 , repeat CD4 testing is recommended every 1 week. If the CD4 count is <500 and the patient is recommended for ZDV therapy, Zidovudine should be initiated following 2 CD4 counts <500 1 week apart. The patient should then be followed up in 2 weeks. After 2 weeks, the patient should be followed up monthly for 3 months. During this period, a CBC should be performed each month, and then every 3 months. After 3 months, the patient should be followed up every 3 months. During this period, a CBC should be performed every visit (every 3 months), and a CD4 count should be performed every other visit (every 6 months). If the patient has new symptoms or toxicity, they should be followed up as clinically indicated. If the patient has no new symptoms or toxicity and the CD4 count is <300 , the CD4 count should be repeated every 3 months. If the CD4 count is <200 , PCP prophylaxis should be initiated, and further CD4 testing is not medically indicated.

An expert panel convened by the National Institute of Allergy and Infectious Diseases participated in a March 3-4, 1990, State-of-the Art Conference on AZT Therapy for Early HIV Infection. The panel recommended use of low doses (500 mg) of zidovudine for HIV-infected individuals with CD4 cell counts of less than 500/mm³ and published a series of recommendations derived from its deliberations. Because of the importance of these recommendations, we have adapted the following composite algorithm from the panel's algorithms for management of HIV-infected patients.



COLOR PLATE IA. Maculopapular rash on trunk of an individual with acute HIV infection (See page 68.)

COLOR PLATE IB. Hairy leukoplakia on tongue. (See page 138.)

COLOR PLATE IC. Giemsa stain of induced sputum demonstrating cysts and trophozoites of *Pneumocystis carinii*. There is no uptake of stain by cyst wall; therefore, walls appear as clear-to-white circles. Trophozoites appear as dark dots. ($\times 960$) (See page 218.)

COLOR PLATE ID. Acid-fast stain of lymph node tissue demonstrating large numbers of red-staining *Mycobacterium avium-intracellulare*. (See page 298.)

COLOR PLATE IE. Severe edema complicating advanced lower extremity cutaneous Kaposi's sarcoma. (See page 342.)

COLOR PLATE IF. Cytomegalovirus-associated retinitis. Note characteristic hemorrhages and exudates. (See page 317.)

COLOR PLATE IG. Widespread cutaneous Kaposi's sarcoma in a Caucasian individual: typical violaceous appearance of skin lesions. (See page 342.)

COLOR PLATE IH. Typical appearance of early Kaposi's sarcoma involving the palate. (See page 342.)

CONTENTS

I THE VIRUS: ITS TRANSMISSION AND INFECTION	
1	
GLOBAL EPIDEMIOLOGY OF HIV INFECTIONS.....	3
<i>Thomas C. Quinn</i>	
2	
FEATURES OF HIV AND THE HOST RESPONSE THAT INFLUENCE PROGRESSION TO DISEASE.....	23
<i>Jay A. Levy</i>	
3	
PREVENTION OF HIV TRANSMISSION.....	38
<i>Constance B. Wofsy</i>	
4	
OCCUPATIONAL HIV TRANSMISSION: Issues for Health Care Providers	57
<i>Julie Louise Gerberding</i>	
5	
PRIMARY HIV INFECTION: Clinical, Immunologic and Serologic Aspects.....	68
<i>Brett Tindall, Allison Imrie, Basil Donovan, Ronald Penny, and David A. Cooper</i>	
6	
NATURAL HISTORY OF HIV INFECTION.....	85
<i>John P. Phair</i>	

II MANAGEMENT OF HIV INFECTIONS AND ITS COMPLICATIONS

7

CARE OF THE INDIVIDUAL WITH EARLY HIV-INFECTION:

Unanswered Questions, Including the Syphilis Dilemma.....93

Harry Hollander

8

TREATMENT OF HIV INFECTION..... 103

Margaret A. Fischl

9

DERMATOLOGIC CARE IN THE AIDS PATIENT:

A 1990 Update 114

Timothy G. Berger

10

DIAGNOSIS AND MANAGEMENT OF THE ORAL
MANIFESTATIONS OF HIV INFECTION AND AIDS..... 131

John S. Greenspan, Deborah Greenspan, and James R. Winkler

11

AIDS-ASSOCIATED GASTROINTESTINAL DISEASE..... 145

John P. Cello

12

MANAGEMENT OF THE NEUROLOGIC COMPLICATIONS
OF HIV-1 INFECTION AND AIDS 161

Richard W. Price and Bruce Brew

13

HEMATOLOGIC MANIFESTATIONS OF HIV INFECTION..... 182

Julie Hambleton and Donald I. Abrams

14

CARDIAC, ENDOCRINE, AND RENAL COMPLICATIONS
OF HIV INFECTION..... 195

John D. Stansell

III SPECIFIC INFECTIONS AND MALIGNANT CONDITIONS

15

PNEUMOCYSTIS CARINII PNEUMONIA..... 209

Philip C. Hopewell

16

TOXOPLASMOSIS IN PATIENTS WITH AIDS..... 241

Dennis M. Israelski, Brian R. Dannemann, and Jack S. Remington

17

CRYPTOCOCCAL MENINGITIS IN AIDS..... 265

Lori A. Panther and Merle A. Sande

18

FUNGAL INFECTIONS IN AIDS: Histoplasmosis and
Coccidioidomycosis..... 280

Grace Minamoto and Donald Armstrong

19

MYCOBACTERIAL DISEASES: Tuberculosis and
Mycobacterium avium Complex..... 291

Mark A. Jacobson

20

INFECTIONS DUE TO ENCAPSULATED BACTERIA,
SALMONELLA, SHIGELLA, AND CAMPYLOBACTER..... 304

Richard E. Chaisson

21

MANAGEMENT OF HERPES VIRUS INFECTIONS
(CMV, HSV, VZV)..... 316

W. Lawrence Drew, William Buhles, Ronald J. Dworkin, and Kim S. Erlich

22

THE MALIGNANCIES ASSOCIATED WITH AIDS..... 339

Lawrence D. Kaplan