

---

# YEAR BOOK<sup>®</sup>

---

## YEAR BOOK OF FAMILY PRACTICE<sup>®</sup> 1990

RAKEL  
AVANT  
DRISCOLL  
PRICHARD  
SMITH

**NOT FOR RESALE**

1990

# The Year Book of FAMILY PRACTICE®

Editor

**Robert E. Rakel, M.D.**

*Professor and Chairman, Department of Family Medicine, and Associate  
Dean for Academic and Clinical Affairs, Baylor College of Medicine*

Associate Editors

**Robert F. Avant, M.D.**

*Professor and Chairman, Department of Family Medicine, Mayo Clinic*

**Charles E. Driscoll, M.D.**

*Professor and Head, Department of Family Practice, University of Iowa  
College of Medicine*

**John G. Prichard, M.D., M. HS**

*Associate Clinical Professor of Family Medicine, University of California, Los  
Angeles, School of Medicine; Chief, Medical Service, Ventura County Medical  
Center, Ventura, California*

**Charles W. Smith, Jr., M.D.**

*Executive Associate Dean for Clinical Affairs, Medical Director; Professor of  
Family and Community Medicine, University of Arkansas for Medical Sciences,  
Little Rock*



**Year Book Medical Publishers, Inc.**

**Chicago • London • Boca Raton • Littleton, Mass.**

NOT FOR REUSE

Copyright © June 1990 by YEAR BOOK MEDICAL PUBLISHERS, INC.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher.

Permission to photocopy or reproduce solely for internal or personal use is permitted for libraries or other users registered with the Copyright Clearance Center, provided that the base fee of \$4.00 per chapter plus \$.10 per page is paid directly to the Copyright Clearance Center, 21 Congress Street, Salem, MA 01970. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collected works, or for resale.

Printed in U.S.A.

International Standard Book Number: 0-8151-7227-3

International Standard Serial Number: 0147-1996

Editor-In-Chief, Year Book Publishing: Nancy Gorham  
Sponsoring Editor: Rebecca A. Ede  
Senior Medical Information Specialist: Terri Strorigl  
Assistant Director, Manuscript Services: Frances M. Perveiler  
Associate Managing Editor, Year Book Editing Services: Elizabeth Fitch  
Production Coordinator: Max F. Perez  
Proofroom Supervisor: Barbara M. Kelly

---

## Journals Represented

Year Book Medical Publishers subscribes to and surveys nearly 700 U.S. and foreign medical and allied health journals. From these journals, the Editors select the articles to be abstracted. Journals represented in this YEAR BOOK are listed below.

Acta Paediatrica Scandinavica  
Acta Psychiatrica Scandinavica  
Adolescent and Pediatric Gynecology  
American Heart Journal  
American Journal of Cardiology  
American Journal of Diseases of Children  
American Journal of Emergency Medicine  
American Journal of Epidemiology  
American Journal of Medicine  
American Journal of Obstetrics and Gynecology  
American Journal of Otolaryngology  
American Journal of Perinatology  
American Journal of Psychiatry  
American Journal of Public Health  
American Journal of Sports Medicine  
American Review of Respiratory Disease  
American Surgeon  
Angiology  
Annals of Allergy  
Annals of Emergency Medicine  
Annals of Internal Medicine  
Annals of Surgery  
Archives of Disease in Childhood  
Archives of General Psychiatry  
Archives of Internal Medicine  
Archives of Neurology  
Archives of Otolaryngology—Head and Neck Surgery  
Archives of Pathology and Laboratory Medicine  
Archives of Surgery  
Australian Family Physician  
British Heart Journal  
British Journal of Medical Psychology  
British Journal of Psychiatry  
British Journal of Surgery  
British Journal of Urology  
British Medical Journal  
Canadian Family Physician  
Canadian Journal of Surgery  
Canadian Medical Association Journal  
Cancer  
Chest  
Circulation  
Clinical Chemistry  
Clinical Pediatrics  
Clinical Pharmacology and Therapeutics  
Clinical Radiology  
Clinical Care Medicine  
Danish Medical Bulletin

Deutsche Medizinische Wochenschrift  
Digestive Diseases and Sciences  
Diseases of the Colon and Rectum  
Ear, Nose, and Throat Journal  
European Respiratory Journal  
Family Medicine  
Family Practice Research Journal  
Family Process  
Family Systems Medicine  
Gastroenterology  
Geriatrics  
Gynecologic Oncology  
Hepatology  
Hypertension  
Injury  
International Journal of Eating Disorders  
Israel Journal of Medical Sciences  
Journal De Chirurgie  
Journal of Acquired Immune Deficiency Syndromes  
Journal of Adolescent Health Care  
Journal of Allergy and Clinical Immunology  
Journal of Bone and Joint Surgery (American volume)  
Journal of Bone and Joint Surgery (British volume)  
Journal of Child Neurology  
Journal of Clinical Endocrinology and Metabolism  
Journal of Clinical Microbiology  
Journal of Clinical Psychiatry  
Journal of Clinical Psychopharmacology  
Journal of Consulting and Clinical Psychology  
Journal of Dermatologic Surgery and Oncology  
Journal of Epidemiology and Community Health  
Journal of Family Practice  
Journal of Marital and Family Therapy  
Journal of Marriage and the Family  
Journal of Obstetrics and Gynaecology  
Journal of Pediatric Gastroenterology and Nutrition  
Journal of Pediatric Orthopedics  
Journal of Pediatric Surgery  
Journal of Pediatrics  
Journal of Perinatology  
Journal of Psychosomatic Research  
Journal of Rheumatology  
Journal of the American Academy of Dermatology  
Journal of the American College of Cardiology  
Journal of the American Medical Association  
Journal of the Royal College of General Practitioners  
Journal of Trauma  
Journal of Urology  
Lancet  
Laryngoscope  
Mayo Clinic Proceedings  
Medical Aspects of Human Sexuality

Medical Journal of Australia  
Metabolism  
Neurology  
New England Journal of Medicine  
New York State Journal of Medicine  
Obstetrics and Gynecology  
Ophthalmology  
Oral Surgery, Oral Medicine, Oral Pathology  
Pain  
Pediatric Infectious Disease Journal  
Pediatric Neurology  
Pediatric Pulmonology  
Pediatric Research  
Pediatrics  
Pharmacotherapy  
Physician and Sportsmedicine  
Postgraduate Medical Journal  
Postgraduate Medicine  
Psychiatry Research  
Psychosomatic Medicine  
Radiology  
Respiratory Medicine  
Scandinavian Journal of Clinical Laboratory Investigation  
Scandinavian Journal of Primary Health Care  
Southern Medical Journal  
Stroke  
Surgery, Gynecology and Obstetrics  
Thorax  
Urologic Radiology  
Western Journal of Medicine

---

## Publisher's Preface

Publication of the 1990 YEAR BOOK OF FAMILY PRACTICE marks the end of an outstanding era of YEAR BOOK editorship by Robert E. Rakel, M.D., and his team of colleagues. During Dr. Rakel's 14 years of editorship, dating back to the inception of this YEAR BOOK in 1977, the volume's readers have been treated to perceptive selections and commentary of the highest caliber. Dr. Rakel's leadership and vision set the tone for this volume and made it the success it is today. We extend to him and to his associates, Drs. Robert F. Avant, Charles E. Driscoll, John G. Prichard, and Charles W. Smith, Jr., our deepest appreciation for the services they have provided and for their unending support and enthusiasm for the YEAR BOOK.

Beginning with the 1991 edition, editorship of the YEAR BOOK OF FAMILY PRACTICE will be placed in the hands of Alfred O. Berg, M.D., M. P.H., Associate Professor and Director of Research in the Department of Family Medicine at the University of Washington, who will carry on the tradition of distinguished editorial direction of this YEAR BOOK. We welcome Dr. Berg and the team of associates that he is establishing as we extend our heartfelt thanks and appreciation to Dr. Rakel and his associates for their years of excellent contribution.

---

## Introduction

The primary objective of this book has always been to assist the family physician in remaining current with recent advances in medicine. It has been my privilege to be the editor since the YEAR BOOK OF FAMILY PRACTICE began in 1977. For 14 years the feeling of keeping up to date with the medical literature has been a source of comfort. It has been a time-consuming task for the associate editors and me to collectively review more than 20,000 articles annually, select those most appropriate for the family physician, and comment on the usefulness or appropriateness of each study. I regret, however, that multiple demands have constricted the time available to continue with this responsibility. For that reason, this is the last edition with which I will be associated. After 14 years a transition is appropriate, and I am confident that the quality of the book will be maintained with a fresh approach under the leadership of Al Berg.

I have been blessed these 14 years with outstanding and selfless help from top-notch associate editors. We have divided the work evenly, each year reviewing the material with which each individual was most familiar. I am particularly appreciative of the excellent contributions made by Charlie Driscoll who has worked with me as an editor since the 1980 edition. From 1977 to 1985 the editors were all faculty at the University of Iowa in an effort to maximize communication and maintain consistency during the early years. My thanks to those who helped: Phil Couchman did yeoman's work for six editions (1982–1987); Jim Wilson (1977–1980); Larry Lawhorne (1977–1979); Rex Coble (1977–1978); Harold Moessner (1977–1978); Forrest Dean (1979–1981); Les Weber (1982–1984); Jim Maroc (1981); and Charlie Smith (1980).

In 1985 the appearance of the book was considerably improved with a new design. At that time the editorial group was restructured and faculty from other schools were added. The first was Bob Avant from the Mayo Medical School, who has remained a faithful contributor for the past 6 years (1985–1990). John Prichard, then at Baylor, joined us in 1987 (1987–1990), and Charlie Smith, then dean at the University of Alabama in Huntsville, rejoined us in 1988 (1980, 1988–1990). A great deal of time, thoughtfulness, and insight went into the selections and comments provided by my colleagues.

Over the years I have also been blessed with superb secretaries who helped with the organization, typing, and distribution of materials. My special thanks to Barbara Owens who has performed this task so well for the past 4 years, and to Caroline Mast before her.

The staff at Year Book Medical Publishers are professionals who insist on quality and maintain high standards. My special thanks to Nancy Gorham, Editor-in-Chief, and Dan Doody, Executive Vice-President. All of the people I have been associated with at Year Book Medical Publishers have been a pleasure to work with.

Last but far from least, my appreciation to the many family physicians who not only support this publication but who have contributed ideas



for its improvement. My wife Peggy has tolerated me throughout the years, doing the driving while I reviewed articles and helping me in so many ways while I stole time from my family to meet deadlines. Now it is time to slow down and stick to the speed limit.

**Robert E. Rakel, M.D.**

---

# Table of Contents

The material in this volume represents literature reviewed through June 1989.

JOURNALS REPRESENTED . . . . .	ix
PUBLISHER'S PREFACE . . . . .	xiii
INTRODUCTION . . . . .	xv
1. Infectious Disease . . . . .	1
2. Neoplasms. . . . .	47
Cancer Risks and General Therapy . . . . .	47
Breast Cancer . . . . .	53
Gastrointestinal . . . . .	60
Genitourinary . . . . .	69
Skin . . . . .	70
3. Endocrinology . . . . .	75
Diabetes. . . . .	75
Thyroid . . . . .	84
Miscellaneous Topics . . . . .	89
4. Hematology . . . . .	99
5. Psychiatry . . . . .	109
Depression . . . . .	109
Anxiety and Related Disorders . . . . .	119
Drug Abuse. . . . .	121
Miscellaneous. . . . .	124
6. Neurology . . . . .	133
7. Eye, Ear, Nose, and Throat Disease . . . . .	149
8. Diseases of the Circulatory System. . . . .	161
Arrhythmias . . . . .	161
Risk Factors . . . . .	162
Cholesterol . . . . .	177
Coronary Artery Disease . . . . .	183
Myocardial Infarction . . . . .	192
Hypertension . . . . .	209
Congestive Heart Failure . . . . .	222
Cerebrovascular Disease . . . . .	224
Peripheral Vascular Disorders . . . . .	225
Miscellaneous. . . . .	230

9. Respiratory Diseases . . . . .	237
Asthma . . . . .	237
Effects of Smoking. . . . .	245
Chronic Obstructive Pulmonary Disease . . . . .	248
Infectious Diseases. . . . .	254
Miscellaneous Topics . . . . .	260
10. Gastroenterology . . . . .	271
Stomach and Duodenum . . . . .	271
Biliary Tract . . . . .	282
Colon . . . . .	289
Miscellaneous. . . . .	296
11. The Genitourinary System . . . . .	303
12. Gynecology. . . . .	321
Infections. . . . .	321
Endocrinology . . . . .	330
General . . . . .	337
13. Obstetrics . . . . .	341
Prenatal . . . . .	341
Intrapartum . . . . .	354
Postpartum . . . . .	357
14. Neonatology and Pediatrics. . . . .	361
Apgar Score . . . . .	361
Circumcision . . . . .	363
Immunization. . . . .	364
SIDS. . . . .	366
Cardiology . . . . .	368
Congenital Hip Disease . . . . .	370
Infant Feeding . . . . .	372
15. Dermatology . . . . .	385
16. Musculoskeletal. . . . .	395
17. Accidents, Poisoning, and Violence . . . . .	409
18. Family Problems . . . . .	429
CUMULATIVE SUBJECT INDEX . . . . .	439
AUTHOR INDEX . . . . .	507

# 1 Infectious Disease



---

## Measurement of the False Positive Rate in a Screening Program for Human Immunodeficiency Virus Infections

Burke DS, Brundage JF, Redfield RR, Damato JJ, Schable CA, Putman P, Vintine R, Kim HI (Walter Reed Army Inst of Research, Washington, DC; Centers for Disease Control, Atlanta; Biotech Research Labs, Rockville, Md; US Military Entrance Processing Command, North Chicago, Ill; Damon Labs, Newberry Park, Calif)

*N Engl J Med* 319:961-964, Oct 13, 1988

1-1

Concern has been expressed over the value of routine testing for human immunodeficiency virus (HIV) among lower risk groups, such as persons applying for marriage licenses. A major concern has been that the predictive value of positive test results for HIV would be very low among populations with low prevalence rates of HIV. Rational decision making about appropriate public health policies has been hindered by lack of concrete data on the rate of false positive diagnoses in HIV screening programs. The frequency of false positive diagnoses was studied among applicants in the United States for military service.

The seropositive individuals studied comprised a subpopulation having a very low prevalence of infection. The subpopulation consisted of all applicants tested in a specified period who were 17 or 18 years old and resided in a rural county in a state with a low incidence of reported acquired immunodeficiency syndrome. There were 135,187 persons in this group. Serum specimens from 15 applicants positive for HIV were retrieved from a serum bank and retested by 2 Western blot methods, radioimmunoprecipitation and an immunoassay constructed from a molecularly cloned and expressed viral enveloped polypeptide. Fourteen samples were unequivocally positive on all retest assays and 1 was negative. Thus the measured rate of false positive diagnoses in this screening program was 1 in 135,187.

Factors important in achieving a low false positive rate were a redundant, multistep testing algorithm, conservative criteria for interpreting Western blot assays, the requirement that a second, newly drawn serum specimen can be tested for verification before a diagnosis of HIV is established, and tight quality control of testing procedures. A screening program for HIV infection in a low-prevalence population can have an acceptably low false positive rate.

► The false positive rate of 1 in 135,187 tests in this study is an important and significant demonstration of the limitations of statistical predictions of test results, because it is *far* lower than expected from a population with a low "pre-test" likelihood of HIV infection. This should help to clarify the place of the test

for physicians who find themselves in a quandary about testing for the presence of HIV infection. In general, if these data are confirmed by other studies, we should assume that a positive screening test indicates HIV infection rather than a *falsely* positive test. Conversely, negative test results are excellent evidence that HIV infection does not exist.—C.W. Smith, Jr., M.D.

### Characterization of the Acute Clinical Illness Associated With Human Immunodeficiency Virus Infection

Tindall B, Barker S, Donovan B, Barnes T, Roberts J, Kronenberg C, Gold J, Penny R, Cooper D, the Sydney AIDS Study Group (St. Vincent's Hosp; Univ of New South Wales; Sydney Hosp, Sydney, Australia)

*Arch Intern Med* 148:945–949, April 1988

1–2

The primary infection with human immunodeficiency virus (HIV) occurs both symptomatically and asymptotically. To determine the fre-

Symptoms Reported by Seroconverted Patients and Controls

Symptom	No. (%)		P
	Seroconversion Subjects (N = 39)	Controls (N = 25)	
Fever	30 (76.9)	6 (24)	<.005
Lethargy	26 (66.7)	6 (24)	<.005
Malaise	26 (66.7)	5 (20)	<.005
Sore throat	22 (56.4)	7 (28)	<.005
Anorexia	22 (56.4)	3 (12)	<.005
Myalgias	22 (56.4)	4 (16)	<.005
Headache	19 (48.7)	6 (24)	<.05
Arthralgias	19 (48.7)	5 (20)	<.025
Weight loss	18 (46.2)	2 (8)	<.005
Swollen lymph nodes	17 (43.5)	0 (0)	<.005
Retro-orbital pain	15 (38.5)	1 (4)	<.005
Dehydration	12 (30.8)	1 (4)	<.01
Nausea	12 (30.8)	2 (8)	<.05
Depression	11 (28.2)	0 (0)	<.005
Diarrhea	11 (28.2)	3 (12)	NS*
Irritability	11 (28.2)	0 (0)	<.005
Truncal rash	9 (23.1)	0 (0)	<.01
Dry cough	9 (23.1)	5 (20)	NS
Abdominal pain	6 (15.4)	2 (8)	NS
Rhinorrhea	6 (15.4)	6 (24)	NS
Dark urine	6 (15.4)	0 (0)	<.05

\*NS, Not significant

(Courtesy of Tindall B, Barker S, Donovan B, et al: *Arch Intern Med* 148:945–949, April 1988.)

quency and nature of symptomatic seroconversion, the clinical and serologic features and immune status of 39 homosexual men who had seroconversion to HIV positivity were compared with these findings in 26 homosexual men who remained seronegative during a 6-month period.

An acute clinical illness developed in 92.3% of the patients who seroconverted and in 40% of the control group. The seroconverted patients reported 17 of the 42 symptoms significantly more frequently than did controls. These symptoms were fever, lethargy, malaise, sore throat, anorexia, myalgias, headaches, arthralgias, weight loss, swollen glands, retro-orbital pain, dehydration, nausea, depression, irritability, truncal rash, and dark urine (table). Of these, swollen lymph nodes, truncal rash, depression, irritability, anorexia, weight loss, and retro-orbital pain most clearly differentiated patients with seroconversion from controls. The duration of illness was significantly longer in patients with seroconversion. Because of the illness, 87.2% of them sought medical attention as compared with only 20% of the control group. Also, 12.8% of those with seroconversion required hospitalization. Changes in T cell subsets were not found in the controls, but the number of T4+ cells and the T4+:T8+ ratio decreased significantly in the patients who seroconverted.

A clinical response to acute infection with HIV does exist. It is characteristically similar to mononucleosis and is present in most persons with evidence of seroconversion to HIV. Recognition of this illness should lead to earlier identification of infected persons and development of specific therapeutic strategies.

► The clinical picture of HIV infection continues to evolve from its original conceptualization as a "silent" process that slowly destroys the immune system. As this article notes, it is associated with acute symptoms similar to many other viral illnesses. Also, HIV infection may cause symptoms secondary to direct infection of the central nervous system and lungs. Patients who experience the above-noted symptoms should be further evaluated for the presence of HIV infection.—C.W. Smith, Jr., M.D.

---

### **Heterosexual Human Immunodeficiency Virus Transmission Among the Middle Class**

Glaser JB, Strange TJ, Rosati D (The Staten Island Hosp, NY)  
*Arch Intern Med* 149:645–649, March 1989

1–3

Heterosexual acquired immunodeficiency syndrome (AIDS) has occurred mainly in persons who acquired the human immunodeficiency virus (HIV) after sexual relations with intravenous drug abusers (IVDAs). Most AIDS infections related to heterosexual acquisition from IVDAs have occurred in nonwhites among the urban poor. The patterns of heterosexual HIV spread among the middle class have not been reported previously. The clinical experience of a private physician who specializes in infectious diseases and practices in a predominantly white middle-class borough of New York City was evaluated.

The physician's office records from July 1984 through October 1987 were reviewed retrospectively to identify patients who were heterosexual contacts of HIV-infected individuals. The contacts were administered a questionnaire to collect information on risk factors for HIV infection among source cases and contacts, demographic characteristics, medical histories, numbers of sexual partners, frequency of sexual relations, and the dates of initiation and cessation of these relations.

Identified as heterosexual contacts of HIV-infected persons were 35 women and 4 men. Of the 39 contacts, 35 were white. Of the contacts, 3 women and 1 man had been referred with documented HIV infection, 2 women had been referred with hepatitis B infection, and 30 women and 3 men were evaluated after being identified as heterosexual contacts of HIV antibody-positive individuals. Of the 4 patients referred with documented HIV infection 3 were symptomatic. The mean household income of the 39 heterosexual contacts was \$41,200.

Of the 39 source cases, 32 (82%) were IVDAs, and 34 were white. After excluding the 6 contacts referred because of HIV or hepatitis B virus infection, 27 women and 3 men agreed to be tested for HIV. Of these, 6 women and 1 man were seropositive for HIV. All were heterosexual contacts of a patient with AIDS or AIDS-related complex, whereas none of the 10 heterosexual contacts of asymptomatic HIV-infected individuals was seropositive. Condoms were rarely used in relationships that involved IVDAs.

The findings confirm that heterosexually acquired AIDS from contact with IVDAs is not confined to urban poor minorities.

► Clearly, AIDS can no longer be considered the exclusive disease of homosexual patients. Recent evidence also suggests that the disease can be transmitted via saliva, but much more work will need to be done to clarify the risk involved in oral transmission. Patients at risk for acquiring AIDS, however, should be advised that initial reports that the virus cannot be transmitted by the oral route may need to be retracted as more data become available. As noted by Fischl et al. (see the 1988 YEAR BOOK OF FAMILY PRACTICE, pp 30–31), barrier protection resulted in 1 of 10 seroconversions compared with 12 of 14 in persons who reported sexual contact with an infected person without use of a condom.—C.W. Smith, Jr., M.D.

---

### **Mother-To-Child Transmission of HIV Infection**

European Collaborative Study (Inst of Child Health, London)

*Lancet* 2:1039–1043, Nov 5, 1988

1–4

---

The prognosis for children with acquired immunodeficiency syndrome (AIDS) is poor, but little is known about the outcome for the many more human immunodeficiency virus (HIV)-infected children who have less severe or no symptoms. Data were reviewed concerning the first 271 children enrolled in a multicenter European study.

The children were born to HIV-infected mothers in 8 hospitals. By

1988, 45% had been followed for more than 1 year. Ten children had contracted AIDS or AIDS-related complex, all by the age of 9 months. Five of these children had died. Twenty-two other children had symptoms or signs suggestive of HIV infection. Of these, 12 had immunologic abnormalities, 9 of whom were infected. Five children had problems unrelated to HIV, 3 of whom died. The remaining 234 children were immunologically normal and clinically well. The median age of antibody loss was 10.3 months; 1 did not lose antibody until after 18 months. None lost antibody, then became and remained seropositive.

Of 1,000 children followed for more than 15 months, 19 had persistent antibody and 5 were antibody negative but presumed infected because of virus isolation or antigen detection. These 5 children were immunologically and clinically normal. The vertical transmission rate was estimated to be 24%.

In this series most of the children born to HIV-infected mothers remain clinically well. However, the outcome was poor for the 24 children older than 15 months presumed infected: 8 had AIDS or AIDS-related complex, 5 died, and only 8, or 33%, were asymptomatic.

► That only 10 of 271 children born to mothers with AIDS were infected is encouraging. However, the data give the clinician no reason to believe that children with the condition have a better prognosis than adults. Careful efforts should be made to prevent women of child-bearing age with AIDS from becoming pregnant.—C.W. Smith, Jr., M.D.

---

### **Human Immunodeficiency Virus Type I Infection in Homosexual Men Who Remain Seronegative for Prolonged Periods**

Imagawa DT, Lee MH, Wolinsky SM, Sano K, Morales F, Kwok S, Sninsky JJ, Nishanian PG, Giorgi J, Fahey JL, Dudley J, Visscher BR, Detels R (Univ of California, Los Angeles, Northwestern Univ; Cetus Corp, Emeryville, Calif)

*N Engl J Med* 320:1458–1462, June 1, 1989

1–5

Some persons appear to be infected with the human immunodeficiency virus type 1 (HIV-1) before antibodies to HIV-1 can be detected. In 1 study enzymatic amplification of HIV-1 DNA with use of a polymerase chain reaction showed HIV infection in seronegative persons involved in high-risk sexual activities.

Isolation of HIV-1 and DNA amplification were carried out in 133 infected, but seronegative, homosexual men. In all, 225 samples of peripheral blood lymphocytes were cultured, with mitogen stimulation used to activate the integrated HIV-1 genome. These cultures yielded HIV-1 in samples from 31 of 133 men (23%). Four of these patients seroconverted after being negative for 11–17 months; the other 27 remained seronegative at 28–36 months. Virus isolation was not always successful with each culture. One man had detectable HIV-1 on his second visit, although seroconversion was not detected for another 30 months. In the 4 men who seroconverted during the study, the level of CD8 cells declined



during the 2 visits preceding seroconversion, then rebounded. The number of CD4 cells fell only at the time of seroconversion, suggesting that viral replication and the release of viral antigens are needed for seroconversion.

Apparently, a significant latent period can occur in homosexual men with HIV infection; the expression of HIV-1 may not be activated by stimuli for a long time. Seroconversion may occur far sooner—within 1–2 months—after direct bloodstream infection, such as that occurring in a transfusion. It is not known whether infected persons who have not seroconverted can transmit the infection, or whether some persons may harbor the virus but never seroconvert.

► This important study demonstrates that in some individuals antibody to HIV may not be produced for more than a year after infection. The difficulty is that most seroepidemiologic studies are based on an enzyme-linked immunosorbent assay. The latter test has been used to determine the usual time of seroconversion following infection (usually within 60 days) and the incidence of infection within various populations. Using sensitive methods of detecting viral DNA, the authors were able to demonstrate that HIV infection occurred as long as 35 months before seroconversion. Hence, despite an HIV infection, tests based on detecting antibody would give falsely negative results.

Given the biology of retroviruses it is perhaps not surprising that infection can occur without serologic evidence thereof. The frequency with which infection is not followed by antibody production has not been determined. Whether such “silent infections” ultimately result in immunodeficiency and AIDS-defining illnesses, or if such individuals are capable of transmitting the infection to others, is also unknown.—J.G. Prichard, M.D., M.H.S

---

#### **Incidence of Symptoms and AIDS in 146 Swedish Haemophiliacs and Blood Transfusion Recipients Infected With Human Immunodeficiency Virus**

Giesecke J, Scalia-Tomba G, Berglund O, Berntorp E, Schulman S, Stigendal L (Karolinska Hosp, Stockholm; Roslagstull Hosp, Stockholm; Univ of Lund, Malmö, Sweden; Univ of Gothenburg)

*Br Med J* 297:99–102, July 9, 1988

1–6

The development of acquired immunodeficiency syndrome (AIDS) was investigated in a prospective series of 98 hemophiliacs and 48 blood recipients infected with human immunodeficiency virus (HIV). The median follow-up after infection was 61 months, or 70 months for the hemophiliacs. Symptoms developed in 39 hemophiliacs, 7 of whom progressed to AIDS. Of 16 transfusion recipients with symptoms, 10 had AIDS. The rate of progression to AIDS was greater in the transfusion recipients (Figs 1–1 and 1–2), and the difference in time to initial symptoms was less marked.

These findings suggest that about half of HIV-positive persons will ex-