YEAR BOOK®

YEAR BOOK OF MEDICINE® 1993

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1993

The Year Book of MEDICINE®

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1993 YEAR BOOK OF MEDICINE®

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The YEAR BOOK series was devised in 1901 by practicing health professionals who observed that the literature of medicine and related disciplines had become so voluminous that no one individual could read and place in perspective every potential advance in a major specialty. In the final decade of the 20th century, this recognition is more acutely true than it was in 1901.

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- to provide *abstracts* of those articles that are readable, convenient summaries of their key points
- to provide *commentary* about those articles to place them in perspective

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addition, the editor indicates when to include figures and tables from the article to help the YEAR BOOK reader better understand the information.

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The published YEAR BOOK contains enhanced bibliographic citations for each selected article, including extended listings of multiple authors and identification of author affiliations. Each YEAR BOOK contains a Table of Contents specific to that year's volume. From year to year, the Table of Contents for a given YEAR BOOK will vary depending on developments within the field.

Every YEAR BOOK contains a list of the journals from which papers have been selected. This list represents a subset of the nearly 1,000 journals surveyed by the publisher, and occasionally reflects a particularly pertinent article from a journal that is not surveyed on a routine basis.

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American Heart Journal
American Journal of Hematology
American Journal of Hypertension
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European Heart Journal
European Journal of Cancer
European Journal of Surgery
European Respiratory Journal
Fertility and Sterility
Gastroenterology
Gut
Hepatology
Human Pathology
Intensive Care Medicine
Journal of Clinical Endocrinology and Metabolism
Journal of Clinical Investigation
Journal of Clinical Microbiology
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Journal of Family Practice
Journal of General Internal Medicine
Journal of Gerontology
Journal of Rheumatology
Journal of Surgical Research

Journal of Urology
Journal of the American College of Cardiology
Journal of the American Medical Association
Journal of the American Society of Nephrology
Kidney International
Lancet
Leukemia
Maturitas
Mayo Clinic Proceedings
Medicine
Nephrology, Dialysis, Transplantation
Nephron
New England Journal of Medicine
Pediatric Nephrology
Proceedings of the National Academy of Sciences
Reviews of Infectious Diseases
Science
Stroke
Thorax
Transplantation
Yale Journal of Biology and Medicine

Standard Abbreviations

The following terms are abbreviated in this edition: acquired immunodeficiency syndrome (AIDS), the central nervous system (CNS), cerebrospinal fluid (CSF), computed tomography (CT), electrocardiography (ECG), human immunodeficiency virus (HIV), and magnetic resonance (MR) imaging (MRI).

Publisher's Preface

The 1993 edition of the YEAR BOOK OF MEDICINE represents the twenty-eighth and final edition in which the Infectious Diseases section bears the stamp of David E. Rogers, M.D. During his term as Editor, Dr. Rogers has provided readers with discerning and informative literature selections, and editorial commentary of the highest caliber. Readers of this series no doubt have recognized David Rogers' intellectual curiosity, enthusiasm, and clinical acumen throughout these many years of publishing.

The urge among those of us who have worked with Dr. Rogers these past years is to fill the next few pages with emotional appreciation of his warmth and kindness, and with sincere admiration for his dedication to the publication. As publishers, it has been a joy to work with him, and for this we are grateful. We wish Dr. Rogers nothing but satisfaction in all his future endeavors.

With this 1993 edition of the YEAR BOOK, Robert A. O'Rourke, M.D., Professor of Medicine and Director of Cardiology at the University of Texas Health Science Center at San Antonio, joins our distinguished team of Editors as Editor of the Cardiology section. Dr. O'Rourke, a former Editor of the YEAR BOOK OF CARDIOLOGY, brings his many years of YEAR BOOK experience and knowledge to this publication, and we look forward to his continued participation.

Tuberculosis and AIDS: A Review

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Introduction

Since 1985, the incidence of tuberculosis in this country has demonstrated a slight but significant increase that has largely been attributed to the ongoing epidemic of AIDS. More recently, several outbreaks caused by multidrug-resistant (MDR) strains of *Mycobacterium tuberculosis* have occurred in patients with AIDS. These developments, particularly the latter, have attracted wide attention among both the medical and lay communities. This article addresses some of the recent developments concerning the unique relationship between tuberculosis and HIV infection.

The Changing Epidemiology of Tuberculosis

The steady decrease in tuberculosis morbidity that has been observed ever since accurate statistics became available at the turn of the century reached a nadir in 1984, with 9.4 cases reported per 100,000 population in the United States. However, in 1985, the incidence leveled off and then increased, with 28,000 "excess" cases reported between 1985 and 1990 (i.e., cases in excess of what would have occurred had the previous rate of decline continued) (1). Two epidemiologic observations link this resurgence to the AIDS epidemic. First, most of this increase has been observed in blacks and Hispanics between the ages of 20 and 45 years, who also bear much of the burden of HIV infection (2). Second, the incidence of extrapulmonary tuberculosis, which connotes less effective immunity, increased to a much greater extent than pulmonary tuberculosis—to such a degree that, at present, at least 20% of extrapulmonary tuberculosis in the United States is said to be HIV associated (3–5). The potential for interactions between HIV and *M. tuberculosis* on a global scale are immense. An estimated 1 million individuals in this country and 10 million worldwide are infected with HIV (6), whereas one third of the world's population is infected with *M. tuberculosis* (7). The frequency of co-infection with HIV and *M. tuberculosis* in a given population is, of course, determined by the incidence of infection caused by each pathogen. In some developing countries in which most persons are infected with *M. tuberculosis* before adulthood, the prevalence of HIV infection becomes the only determinant of co-infection (3).

Early Observations of Tuberculosis Complicating AIDS

The first observations of tuberculosis in patients with AIDS were reported in Haitians. In 1983, Vieira et al. at Kings County Hospital in

New York City described 10 Haitian men with AIDS, 6 (60%) of whom also had active tuberculosis (8). Pitchenik *et al.* subsequently reported that 27 (60%) of 45 Haitian immigrants with AIDS in Miami had active tuberculosis (9). Because most Haitians are infected with *M. tuberculosis* in childhood, tuberculosis in these patients was thought to reflect reactivation of remote and previously latent infection as a consequence of waning cellular immunity.

Tuberculosis in a Methadone Clinic Population

In 1989, in a landmark study, Selwyn *et al.* documented the incidence of active tuberculosis developing in 49 *asymptomatic* intravenous drug users attending a methadone clinic who were positive for both HIV and tuberculin (10). During 22 months of follow-up, 7, or approximately 8% per year, had active tuberculosis develop. The other very important observation in this study was that active tuberculosis did not develop in any of 13 drug users who were treated prophylactically with isoniazid. The known high rates of tuberculin reactivity in urban ghetto populations indicated to Selwyn et al. that "tuberculosis in HIV-infected persons most commonly indicates the reactivation of latent tuberculous infection in the context of HIV-induced immunosuppression." Indeed, AIDS appears to be the strongest predictor of progression from infection to active tuberculosis identified to date.

Epidemic Nosocomial Tuberculosis in Patients With AIDS

The first indication that tuberculosis in HIV-positive patients might also be caused-by new (exogenous) infection was provided by a report of an outbreak on an HIV ward in Italy (11). The index patient had fever, cough, a normal chest radiograph, and negative acid-fast smears but a positive sputum culture for *M. tuberculosis*. Seven (39%) of 18 other patients with AIDS on the ward had active tuberculosis develop within 60 days. The similar antibiotic susceptibility patterns of the isolates strongly suggested that nosocomial spread had occurred. A number of subsequent studies have documented the spread of tuberculosis among patients with AIDS. In an important study of 1 such epidemic, Daley et al. used molecular biology techniques to describe the epidemiology of an outbreak of tuberculosis in a residence for HIV-positive individuals in San Francisco (12). Ten (34%) of 29 residents exposed to the index patient had very rapidly progressive tuberculosis develop. Restriction fragment length polymorphism (RFLP) analysis confirmed that a single strain of *M. tuberculosis* caused all cases. In addition, at least 6 (21%) of 28 previously tuberculin-negative staff members converted to positive status, with 1 having active tuberculosis develop. These and other studies have now established that AIDS may favor acquisition of new tuberculous infection, that tuberculosis in such patients usually progresses rapidly, and that transmission of tuberculosis from HIV-positive patients to HIV-negative individuals may also occur (13).

TABLE 1.—Prevalence of HIV Seropositivity Among Patients Attending Tuberculosis Clinics in Selected Cities of the United States

	Patients	Percent HIV-seropositivity		
	N	U.S. Born	Foreign Born	Total
New York City	82	57.4	31.4	46.0
Boston	188	30.9	24.6	26.6
Miami	358	28.5	19.5	23.5
Dallas	301	11.2	4.6	8.6
Chicago	50-132	1.3	1.8	1.1-3.6
Cleveland	121	2.3	0.0	1.7
Los Angeles *	58-158	13.0	3.3	0-12.3
Honolulu	325	0	0.0	0.3
All Cities †	3077	11.2	2.9	3.4

* Range from numerous participating clinics.
† Includes 6 clinics represented in the original study but not presented in this table.
(Courtesy of Onorato IM, McCray E, Field Services Branch: *J Infect Dis* 165:87–92, 1992.)

Prevalence of HIV Seropositivity in Tuberculosis Clinic Patients

A recent study from the Centers for Disease Control reported the prevalence of HIV seropositivity in 3,077 patients attending tuberculosis clinics in 14 metropolitan areas across the United States (14). Although the percentages varied widely, ranging from 46.3% in New York to .3% in Honolulu, 3.4% overall were HIV positive (Table 1). In general, HIV infection was more prevalent among native-born clinic patients, perhaps in part because of a U.S. Public Health Service policy of serologic testing and exclusion of HIV-seropositive individuals applying for admission to this country.

Clinical Features of Tuberculosis Complicating HIV Infection

In Advanced HIV Infection

The earliest clinical reports, from New York City and Miami, emphasized the atypical clinical picture of tuberculosis in patients with AIDS. Specifically, noncavitary lower lung field pulmonary disease, extrapulmonary tuberculosis (often without pulmonary disease), lymph node involvement, and disseminated disease were frequent, and the tuberculin test was usually negative (9, 15–17). The clinical picture described in the more recent reports of nosocomial epidemics in patients with advanced HIV infection was most often characterized by diffuse pulmonary infiltration without cavitation (11).

TABLE 2.—Clinical Manifestations of Tuberculosis in 60 Patients at a San Francisco Tuberculosis Clinic

	HIV-seropositive N = 17 (%)	HIV-seronegative N = 43 (%)
Location		
Pulmonary only	76	72
Pulmonary and Extrapulmonary	24	14
Extrapulmonary only	0	14
Radiographic Findings		
Focal Infiltrate	46	54
Cavitary Disease	31	35
Miliary Infiltrate	8	0
Sputum Smear Positive	47	51
Tuberculin Positive (≥10mm)	80	93

(Courtesy of Theuer P, Hopewell PC, Elias D, et al: *J Infect Dis* 162:8–12, 1990.)

In Early HIV Infection

In 1990, a study from a San Francisco tuberculosis clinic reported that the clinical features of tuberculosis in HIV-positive patients who had come to medical attention because of tuberculosis rather than AIDS were quite similar to those seen in HIV-negative patients in the same clinic (Table 2) (18). The median $CD4^+$ cell count among these HIV-positive patients with tuberculosis (326 cells/mm^3) indicated that many were early in the course of their HIV infection, with relatively intact cellular immunity. Even in this population, HIV-positive patients with extrapulmonary tuberculosis had lower mean $CD4^+$ cell counts (153 cells/mm^3) than those with isolated pulmonary disease (367 cells/mm^3). These and other studies indicate that the clinical manifestations of tuberculosis in HIV-infected individuals are determined in large part by the degree of HIV-associated immunosuppression. Table 3, adapted from a review by Dr. John Murray, compares and contrasts tuberculosis in early and late HIV infection (3).

Extrapulmonary and Disseminated Tuberculosis

Clinical features of extrapulmonary and disseminated tuberculosis, both of which have long been regarded as indicators of relatively compromised immunity, are also modified by co-infection with HIV. Shafer et al. recently compared extrapulmonary tuberculosis in a large number