THE TREATMENT OF MYCOTIC AND PARASITIC DISEASES OF THE CHEST

The Treatment of Mycotic and Parasitic Diseases of the Chest

Edited by

JOHN D. STEELE, M.D.

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Contributors

DUANE CARR, M.D., *Memphis, Tennessee*

Professor in Surgery, University of Tennessee College of Medicine
Consultant, Thoracic Surgery, West Tennessee Tuberculosis Hospital
Thoracic Surgical Service, University of Michigan, 1931-1934

EDGAR W. DAVIS, M.D., *Washington, D.C.*

Clinical Professor of Thoracic Surgery, Georgetown University School of Medicine
Past Chairman, Medical Board, and Past President, Medical Staff, Washington Hospital Center
Chief of Thoracic Surgery, Georgetown University Hospital and Georgetown University unit, District of Columbia General Hospital
Thoracic Surgical Service, University of Michigan, 1934-1936

BYRON H. EVANS, M.D., *Fresno, California*

Chief of Chest Services, Fresno County General Hospital
Consultant Thoracic Surgeon, Veterans Administration Hospital
Attending Thoracic Surgeon, Valley Childrens Hospital, Community Hospital, and St. Agnes Hospital
Thoracic Surgical Service, University of Michigan, 1946-1948

MILTON HUPPERT, PH.D., *San Fernando, California*

Assistant Professor of Microbiology, California College of Medicine
Chief, Mycology Research Laboratory, Veterans Administration Hospital

SOL KATZ, M.D., *Washington, D.C.*

Associate Professor of Medicine, Georgetown University School of Medicine and Professorial Lecturer in Medicine, George Washington University School of Medicine
Chief, Medical Service, Veterans Administration Hospital
Consultant in Chest Diseases, Georgetown University Hospital, the National Institutes of Health, the Children's Hospital, and the District of Columbia General Hospital

WILLIAM S. LYONS, M.D., *Washington, D.C.*
Clinical Instructor in Thoracic Surgery, Georgetown University School of Medicine
Consultant in Thoracic Surgery, District of Columbia General Hospital
Attending in Thoracic and Cardiovascular Surgery, Washington Hospital Center
Junior Associate in Thoracic Surgery, Children's Hospital of the District of Columbia

JULIAN A. MOORE, M.D., *Asheville, North Carolina*
Late Surgical Consultant to the Veterans Administration Hospital, Oteen, and the Western North Carolina State Sanatorium, Black Mountain
Late Attending Surgeon, Memorial Mission Hospital and St. Joseph's Hospital
First Resident, Thoracic Surgical Service, University of Michigan, 1928-1929

JOSEPH W. PEABODY, JR., M.D., *Washington, D.C.*
Assistant Clinical Professor of Thoracic Surgery, Georgetown University School of Medicine
Senior Attending Thoracic Surgeon, Washington Hospital Center and Suburban Hospital
Junior Associate in Thoracic and Cardiovascular Surgery, Children's Hospital
Lecturer in Thoracic Surgery, National Naval Medical Center

CARLOS A. PESCHIERA, M.D., *Lima, Peru*
Principal Associate Professor of Surgery, Universidad Peruana de Ciencias Médicas y Biológicas
Chief of Thoracic Surgery, Hospital Obrero
Chief of Department of Thorax, Instituto Nacional de Enfermedades Neoplásicas
Head of Medical Staff and Thoracic Surgeon, British American Hospital
Thoracic Surgical Service, University of Michigan, 1943-1945

CÉSAR RODRÍGUEZ, M.D., *Caracas, Venezuela*
Chief of Service, Sanatorio Antituberculoso Simón Bolívar
Chief of Surgical Service, Sanatorio Antituberculoso Infante Luisa Cáceres de Arismendi
Chief of Thoracic Service, Instituto Oncológico Luis Razetti
Chief of Surgical Personnel Department, Division of Tuberculosis and Chest Diseases, Ministry of Sanitation and Social Assistance
Thoracic Surgical Service, University of Michigan, 1944-1946

DAVID SALKIN, M.D., *San Fernando, California*
Clinical Professor of Thoracic Diseases, Loma Linda University School of Medicine
Clinical Professor of Medicine, California College of Medicine
Chief of Staff, Veterans Administration Hospital
Chairman, Veterans Administration-Armed Forces Cooperative Study on Coccidioidomycosis

JOHN D. STEELE, M.D., *San Fernando, California*

Clinical Professor of Surgery, University of California, Los Angeles
Chief, Surgical Service, Veterans Administration Hospital
Thoracic Surgical Service, University of Michigan, 1935-1937

WHEELAN D. SUTLIFF, M.D., *Memphis, Tennessee*

Associate Professor in Medicine, University of Tennessee College of Medicine
Chief, Infectious Disease Section, Veterans Administration Medical Teaching Group Hospital
Chairman, Veterans Administration-Armed Forces Cooperative Study on Histoplasmosis

HARRY E. WALKUP, M.D., *New York, New York*

Director, Research and Statistics, National Tuberculosis Association
Former Chief, Surgical Service, Veterans Administration Hospital, Oteen, North Carolina
Former Chairman, Veterans Administration-Armed Forces Cooperative Study on Blastomycosis

TO
EMMA WOOLFOLK ALEXANDER
and
HELEN ALEXANDER CAMPBELL

Preface

WHEN the publication of this book first was planned, it was intended that the surgical aspects of mycotic and parasitic diseases of the chest would be emphasized and that other aspects of these various diseases would be brought in as background material. The title was to have been *The Surgical Treatment of Mycotic and Parasitic Diseases of the Chest.* However, as the various contributors developed their chapters it became quite evident that the medical treatment of the diseases covered (with the exception of hydatid disease) was so intimately interlaced with the surgical treatment that they could not be separated. The present title was adopted accordingly.

Only the 2 most important parasitic diseases of the chest have been included. It is recognized that there are a number of others which do involve thoracic organs. In order to be sure that we were not omitting the treatment, particularly the surgical treatment, of other important parasitic diseases, a tabulation was made by the Armed Forces Institute of Pathology through the courtesy of Samuel H. Rosen, M.D., of their surgical specimens of flat and round worm involvement of the lungs. In their vast collection, there were only 2 surgical specimens of trematode and 6 of nematode involvement.

As in the previous books in this Series, thoracic surgeons who were trained by Dr. John Alexander formed a nucleus for contributions to this book although it will be noted that in a number of chapters close associates of the men in the nucleus were major contributors.

No attempt was made to standardize the style and structure of the various chapters although an attempt was made to hold repetition to a minimum.

It is a privilege to dedicate this book to Dr. Alexander's wife and to his sister both of whom have taken a keen interest in the John Alexander Monograph Series.

JOHN D. STEELE, M.D.

San Fernando, California

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Valuable data from Veterans Administration-Armed Forces cooperative studies on coccidioidomycosis and histoplasmosis are included in the chapters on these diseases; co-authors of these chapters have been chairmen for these cooperative studies.

Assistance with proofreading by Ralph B. Dilley, M.D., and Betsy Owen Steele, M.D., is gratefully acknowledged.

J.D.S.

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Diseases of the Chest

CHAPTER 1

North American Blastomycosis

By HARRY E. WALKUP *and* JULIAN A. MOORE*

INTRODUCTION

IN 1894, Thomas C. Gilchrist was examining a slide that had been referred to him by a Dr. Duhring of Philadelphia with a tentative diagnosis of scrofulodermia. Dr. Gilchrist could not find acid-fast bacilli in the section, but he did observe bodies that he described as being more typical of plant life than of microorganisms. Unfortunately, this was a section from an excised cutaneous lesion and culture material was not available. This case was presented as "protozoan dermatitis" before the American Dermatological Association on June 1, 1894 in Washington, D. C. (43). In 1896, Gilchrist (44) published a more complete description of his original case, naming the disease *blastomycetic dermatitis* after the morphologically similar fungus that had been described by Busse (15, 17) and Buschke (13,14), in Germany, also in 1894. By 1896, Gilchrist, working with Stokes (45, 46), encountered an additional case of blastomycetic dermatitis from which they were able to obtain a culture. These authors recognized the fungus to be quite different from Busse's yeast organism. They called the fungus *Blastomyces dermatitidis* and classified it as one of the nonfermenting, mycelia-producing "wild yeasts." Busse's case, which unfortunately had the more rare cutaneous manifestations, actually represented the first reported case of cryptococcosis. This fact was not to be proven until 1934 (8, 75). Gilchrist and Stokes had pointed out certain histologic and clinical differences between their case and that of Busse, but this latter author had placed the name "blastomycosis" on his disease and, through interpretation of the ability of this fungus to produce endospores, it was destined to be reported as a case of blastomycosis for the next 40 years.

By the year 1901, it was becoming apparent that Gilchrist's disease was endemic to certain localities and 15 cases had been observed at the Rush Medical College in Chicago, Illinois (93). Ricketts (93) had made a thorough study of the mycelial phase of *B. dermatitidis* in that same year, but it remained for Hamburger (54) in 1907, to demonstrate the biphasic characteristic of this fungus. Stoddard and Cutler (116) subsequently reported their extensive evaluations of this fungus which, with the exception of Busse's case, clarified all existing confusion between *B. dermatitidis*, *C. neoformans*, and other pathogenic fungi.

The designation "blastomycosis" for Gilchrist's disease is rather unfortunate, for it implies that causative agent to be a yeast (18, 19, 26, 77, 82). However, all authorities agree that, unsuitable as the term blastomycosis may be, it has come to stand for a definite clinical entity in medical literature and one would hesitate to recommend changing it.

*Dr. Moore died on November 7, 1959.

The basic clinical concepts of blastomycosis, as we know them today, were worked out by the Chicago group at the Rush Medical College and Cook County Hospital (56, 82, 83, 93, 115, 121). The prevalence of blastomycosis in this area after the turn of the century led to the name "Chicago disease" for this condition. Our knowledge on this disease was completed, in the late 1930's, through the efforts of investigators at Duke University (3, 4, 5, 26, 27, 77, 78, 107, 108, 109, 110, 111). With the exception of the introduction of specific drugs and antibiotics for the treatment of this disease, and a minor disagreement as to the exact portal of entry of the organisms into the body (102), we have been able to add little information to the fundamental concepts of blastomycosis, established by the Chicago and Durham groups, during the past 20 years.

EPIDEMIOLOGY

Prior to 1961, it had been demonstrated the *B. dermatitidis* could be grown in sterilized soil (31, 35) but the organism had never been isolated from nature. During that year, Denton *et al.* (32) reported the isolation of *B. dermatitidis* from the soil floor of a barn that had housed a dog known to have had blastomycosis 2 years previously. This represented the first isolation of this fungus organism from nature and tended to support the heretofore assumed exogenous source of the infection. Numerous reports demonstrated the fact that domestic animals contract the disease (7, 41, 85, 91, 96, 97, 98) but no authentic case of animal-to-man transmission has ever been recorded. Baker (3) has demonstrated that both the yeast-like phase and the mycelial phase can cause the disease when injected into experimental animals.

In the epidemiologic surveys of Martin and Smith (77) and Schwarz and Goldman (103), a large proportion of the cases were occupationally exposed to nature's elements. Stober (115) had, as early as 1910, associated the disease with the poorer classes, especially those living in damp, crowded, unhygienic environments. The sex incidence, male: female (8:1), can be accounted for by the fact that male occupations are more frequently in contact with nature's elements, where contact with the saprophytic form of the fungus is probably initiated (65).

The portal of entry of *B. dermatitidis* has been a subject of debate for a number of years. The Duke University group is of the opinion that 2 primary forms of blastomycosis exist, a cutaneous form, in which the fungus gains entry directly into the skin; and a systemic form, which has the respiratory tract as its portal of entry (77, 107, 108, 110). Schwarz and Baum (102), on the other hand, believe the lung to be the primary focus in all cases of blastomycosis. These investigators demonstrated healed pulmonary lesions in untreated cases and attributed the presence of cutaneous blastomycosis, in the absence of roentgenographically demonstrable pulmonary lesions, to be the result of "a strong healing tendency in the lung." Each of these authoritative schools of thought has strong clinical support for its contentions, but we favor the existence of a chronic primary cutaneous form of the disease. Our support to the Duke group is based on the divergent clinical course of cutaneous blastomycosis, the location of lesions, and the character of the lesions at the time of onset—epidermis vs. the subepithelial location of hematogenous lesions seen in the systemic form.

As to geographic distribution, blastomycosis can still be listed as a disease almost exclusively limited to the United States. Cases from foreign countries have been reported but only presumptive diag-

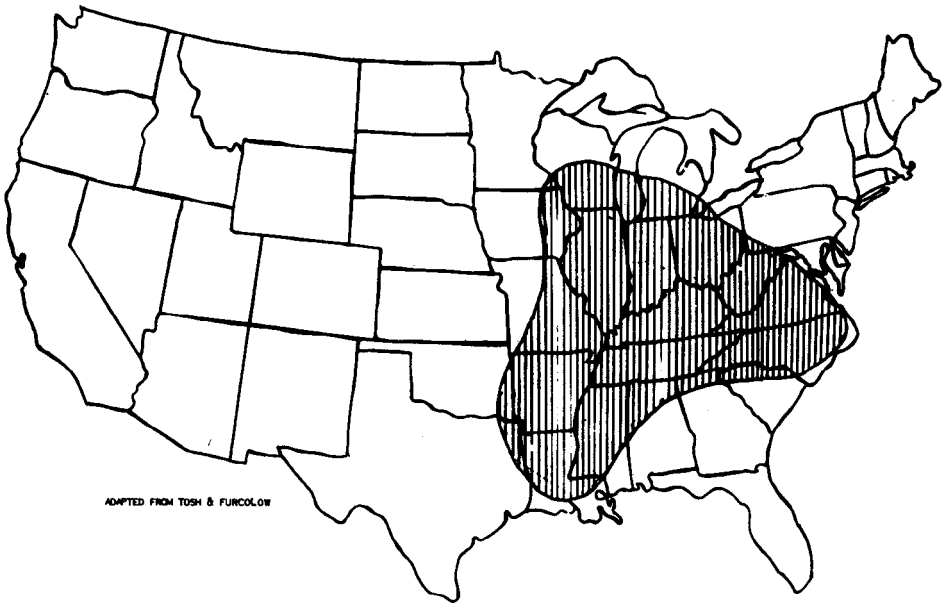

Fig. 1. Geographic distribution of blastomycosis.

nostic evidence is available in the majority of them. Various surveys (77, 103) have demonstrated endemic areas in the North Central States, the Mississippi River Valley, the Great Lakes Region and the Southeastern States (Fig. 1). The states of Wisconsin, North Carolina and Tennessee report the largest number of cases (103). One epidemic of blastomycosis has been reported (111) from North Carolina, in which 10 cases were diagnosed within a period of 5 months.

CLINICAL MANIFESTATIONS

In this discussion of the clinical features of North American blastomycosis the existence of a chronic primary cutaneous form will be assumed. The following classification is presented to emphasize the existence of an accidental inoculation form of the disease and to point out the fact that the primary pulmonary form can exist, for a variable time period, without dissemination.

Accidental Inoculation Cutaneous Form

This form of blastomycosis occurs through the accidental inoculation of *B. dermatitidis* directly into the skin of a previously uninfected person (36, 102, 124). These accidents usually occur in pathologists and laboratory workers during the handling of cultures or the performance of necropsy examinations. The resulting lesions have been described as "indolent blastomycotic furuncles" (102) and "chancriform" (74). They are characteristically accompanied by a lymphangitis with involvement of the regional lymph nodes. Of the 4 instances of accidental inoculation lesions reported in the literature, 3 had the primary site excised and the other had the regional lymph nodes removed. Despite this fact, these lesions were reported as exhibiting a tendency toward spontaneous regression. In 2 of these cases (124), weak or absent complement fixation antibody titers were reported. These findings support the con-