Manual of Clinical Mycology

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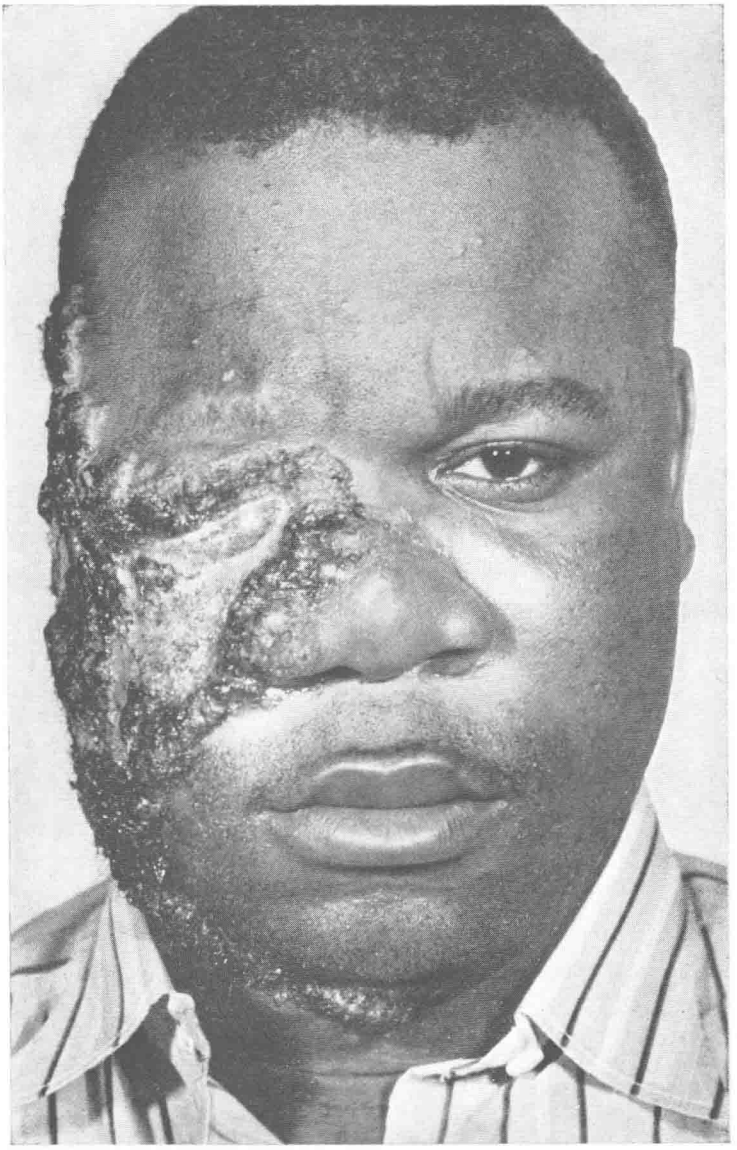

North American Blastomycosis

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THIS MANUAL IS DEDICATED TO THE MEMORY OF

ARCHIE S. WOODS

Late Vice-President and Treasurer

of the John and Mary R. Markle Foundation

FOR HIS CONSTANT PERSONAL INTEREST

IN RESEARCH IN FUNGUS DISEASES

Preface to the Second Edition

Fungus infections are relatively, if not actually, more frequent in occurrence since the introduction of penicillin and other potent antibiotics for the control of the acute bacterial diseases.

Since the first edition of this Manual, many new facts concerning the epidemiology and immunology of the mycoses have been discovered. Coccidioidomycosis has been found to be endemic in a much wider area of the Southwest, and primary infections in residents and visitors in these areas are increasing in occurrence. Primary benign histoplasmosis infections occur in 50 to 75 per cent of the residents in the central part of the United States as well as in other localized areas. Explosive epidemics of histoplasmosis have occurred when groups of individuals have been exposed to dust from pigeon, chicken and bat manure. These epidemics have occurred both in and outside of recognized endemic areas. A reinfection type of histoplasmosis has been discovered which closely simulates reinfection tuberculosis in symptoms, signs and x-ray shadows. Standardized skin testing material is now available commercially for detecting sensitivity to coccidioidin, histoplasmin and blastomycin. Antigens also have been prepared for the detection of antibodies in the sera of patients having coccidioidomycosis, histoplasmosis and blastomycosis. Penicillin, sulfonamides, Aureomycin and some of the other antibiotics are effective in the treatment of actinomycosis; sulfonamides remain the treatment of choice for South American blastomycosis and nocardiosis; while stilbamidine and 2-hydroxystilbamidine are proving curative even in advanced cases of North American blastomycosis.

Perhaps one of the most important contributions to the study of pathology of the mycotic infections has been the application of the periodic acid-Schiff stain for the demonstration of fungi in tissue. This technical advance should allow better diagnosis by examination of tissues obtained from patients who present difficult differential diagnoses.

The terminology adhered to in the first edition of the Manual

has been changed very little. For the most part, the synonymy as previously presented has been acceptable, and the few changes made in this edition have been based on new investigations, particularly physiological and nutritional, which have shown many fungi to be variants of well known species. We have tried to follow closely these studies and have used them as a basis for the changes in nomenclature.

To facilitate the laboratory diagnosis of mycotic infections a chapter has been included on the fundamentals of mycology, in which the descriptive terms used by mycologists are defined and illustrated, and another chapter on the contaminants which may be confused with pathogenic species.

The literature on mycotic infections is so voluminous that a complete bibliography would have equaled the size of this Manual. Bibliographies containing a few of the more recent publications, particularly those with full reference lists, have been selected and appear at the end of each chapter.

This edition contains 88 new illustrations and a total of 202.

We are indebted to Elon Clark, H. E. Pickett, Nealy Webster, Weaver Tripp, Mrs. Ilse Ebert and Miss Rennie Ross-Duggan for making many photographs and illustrations; and to Carl M. Bishop for making many of the photomicrographs for this edition. We are most grateful for the help given by Miss Dorcas Sumrell in the preparation of materials and for the assistance of Dr. Isabel Christison in checking the bibliography, reading proof and performing many other chores concerned with the manuscript. We wish to thank Miss Shirley Owens and Mrs. Patricia Thames for their excellent typing of the manuscript through its many revisions. Last, but not least, we wish to thank our many friends and associates for their suggestions, criticisms and their generous offer of needed illustrative materials.

THE AUTHORS

Preface to the First Edition

Fungus infections are of such common occurrence that we have found it necessary to consider mycotic disease in the differential diagnosis of practically every obscure infection. During the past ten years at Duke Hospital we have had the opportunity of studying all types of mycoses described in this Manual. One of the greatest deterrents to the clinical study of fungus infections is the confusion concerning the mycologic nomenclature of the fungi pathogenic for man. Such confusion exists largely because the mycologic laboratory usually is too far separated from the clinic, and the personnel of most hospital laboratories is unacquainted with the methods of study used for identification of the pathogenic fungi.

It is obvious that knowledge concerning the clinical aspects of the mycoses can be obtained only when more cases are recognized and reported and that the diagnosis must be made by the clinical laboratory. For this reason, we have experimented with blood agar and incubated cultures at 37° C. in order to obtain characteristics which can be interpreted by the bacteriologist using media and technics to which he is accustomed.

A chapter has been included on the contaminants to which pathogenicity sometimes is erroneously attributed. There is another chapter on the fundamentals of mycology in which the descriptive terms used by mycologists are defined and illustrated. The classification of the pathogenic fungi has been simplified, in accord with the other investigators who are studying the mycoses. In some instances, the synonymies of the fungi have been abbreviated to conserve space. For example, only 11 of the 172 names for *Candida albicans* have been listed. To some, the classification presented in this Manual may seem to be oversimplified; but, in our opinion, information concerning the mycoses is possible only if such a classification is employed—one which is sufficiently simplified to be used by the bacteriologist in a hospital laboratory.

In preparing this Manual, each of the authors contributed a sec-

tion for each chapter. The sections on symptomatology, differential diagnosis, prognosis and treatment of the systemic mycoses were prepared by David T. Smith, the mycologic sections by Norman F. Conant, the sections on pathology by Roger D. Baker, and those on geographic distribution and immunology by Donald S. Martin. The chapter on the clinical aspects of the dermatomycoses was written by Jasper L. Callaway, as were the clinical descriptions of the other superficial mycoses. In order to coordinate the various sections and to make the style more uniform, the manuscript was rewritten by Donald S. Martin.

We are indebted to Dr. Frederic M. Hanes who read the entire manuscript and made many valuable suggestions.

We are indebted to Robert E. Little, Carl M. Bishop, Elon H. Clark and Carlin P. Graham for the making of many of the photographs and illustrations. We would like to express appreciation to Mrs. Doris Coltrane Grimes and Mrs. Helen Shipp Johns for their valuable technical assistance and to acknowledge the extremely valuable assistance of Mrs. Eugenia Speed Pulliam who cheerfully has typed and retyped the manuscript many times.

Particularly, we wish to thank the John and Mary R. Markle Foundation, whose grants made possible many of the fundamental studies out of which this Manual was developed.

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CHAPTER 1

Actinomycosis

(LUMPY JAW, STREPTOTHRICOSIS, LEPTOTHRICOSIS, ETC.)

THIS INFECTION, the commonest of the systemic mycoses, is caused by the anaerobic, obligate parasite *Actinomyces bovis,* an organism more closely related to the bacteria than to any of the higher fungi.

Definition. Actinomycosis, caused by *Actinomyces bovis,* is a chronic suppurative and granulomatous disease. The abscesses discharge through multiple draining sinuses. In the lesions, sinus walls or discharges are found either the characteristic "sulfur granules" or small, tangled masses of gram-positive branching filaments.

Geographic Distribution. The world-wide occurrence of actinomycosis is illustrated best by Cope's statement that ". . . wherever there is a microscope and a laboratory, the fungus has been found to be the cause of disease."

Source of Infection. The anaerobic *Actinomyces bovis* is a normal inhabitant of the mucous membranes of the mouth and may be found around carious teeth and in tonsillar crypts. It has not been isolated from natural substrates such as vegetable matter or other debris in the soil. Emmons, Slack, Rosebury, and others have demonstrated the presence of pathogenic *A. bovis* in the so-called normal mouth, indicating that the source of infection in most cases of actinomycosis probably is endogenous.

From the mouth, the *Actinomyces* enters injured mucous membranes and by contiguity infects the face and neck to cause "lumpy jaw"; it may be aspirated into the lungs and cause pulmonary or thoracic actinomycosis; or it may be swallowed and, with invasion of the intestinal mucosa, cause abdominal actinomycosis. Although Robinson has recorded a case of actinomycosis of the subcutaneous tissues of the forearm following a human bite, the disease is not transmitted naturally from man to man. Infection in cattle likewise is not transmitted from animal to animal or from animal to man.

Age, Sex, Race and Occupational Incidence. Actinomycosis has been observed in a 28-day-old infant and in a patient 75 years of age. The disease is rare in children under 10 years of age, the majority of the cases occurring between the ages of 15 and 35. Infection occurs in approximately twice as many males as females. All races seem to be equally susceptible to infection. It is stated frequently that agricultural workers are infected more often than those engaged in other occupations, which suggests that the infection is acquired from some exogenous source; however, in view of our present knowledge concerning the presence of *Actinomyces bovis* in the mouth, the higher incidence in this class of workers may be due to poor oral hygiene.

SYMPTOMATOLOGY

The clinical picture varies with the location of the disease, as does the prognosis. Cope's series of 1330 cases, collected from the literature, revealed that 56.8 per cent began in the neck, 22.3 per cent in the abdomen, 15 per cent in the thorax and 5.9 per cent in other parts of the body. The tongue was infected in 3 per cent. In rare instances, isolated lesions have been described in the skin, kidneys, genital tract, liver, ovaries, bones, joints and central nervous system; these structures frequently are involved when a primary lesion in the neck, thorax or abdomen develops into a generalized infection.

It is customary to classify the disease clinically into cervicofacial, thoracic and abdominal actinomycosis, depending upon the site of the initial infection.

Cervicofacial Actinomycosis. Cervicofacial actinomycosis is the commonest form of the disease and, fortunately, has the best prognosis. The organisms enter presumably through the mucous membranes of the mouth and pharynx, by way of the gums about carious teeth or through the tonsils. Occasionally, the salivary and lacrimal glands are invaded by direct extension through their ducts. The orbit may be involved by extension of the infection from the sinuses. More rarely, the infection begins lower in the pharynx, producing a perichondritis and laryngeal edema, or the first symptoms may arise from infection deep in the neck or mediastinum. Infections originating in the maxilla may extend upward to infect the cranial bones and precipitate a meningitis or brain abscess.

Most frequently, the infection is noted first in the lower jaw, particularly in the region of an infected tooth or in the socket left by a recent extraction. A history of previous toothache or other dental affection frequently is obtained. The swelling usually is most marked over the angle of the mandible, but may be posterior to it if the fungus gained entrance through the tonsils.

The swelling in the soft tissues of the face is not characteristic at first; but the overlying skin soon assumes a dark red or purplish color, the tumor develops a "wooden" type of hardness and the surface appears uneven or "lumpy." As the disease progresses, abscesses develop and multiple sinuses appear (Fig. 1). Trismus is a frequent symptom when the muscles of mastication are affected. Pain is minimal unless there is a marked secondary infection, and the general health of the patient remains good if the disease is localized in the face and neck.

X-RAYS. Roentgenograms show no involvement of bone in the early stages of the disease, but later there may develop periostitis, true osteomyelitis with bone destruction or central rarefying osteomyelitis expanding the cortex into a pseudocyst.

Thoracic Actinomycosis. Primary infection of the lung results from aspiration of *A. bovis* from the mouth. Secondary infection of pleura and lung may result from extension of abdominal or hepatic actinomycosis through the diaphragm.

The SYMPTOMS in the first few weeks of the primary form of the disease are those of a subacute pulmonary infection with a mild, irregular fever, cough and expectoration. As the disease progresses and small abscesses develop in the lungs, the sputum becomes mucopurulent and may contain blood. Involvement of the pleura may cause pleural pain. Although some patients develop pleural effusion, the fungus more often invades directly through the chest wall, producing numerous draining sinuses (Fig. 2). The patient loses weight and strength, becomes anemic, and may develop spiking temperature, night sweats and dyspnea or other signs of severe pulmonary disease. Dysphagia can result from mediastinal invasion, and the infection may extend to the pericardium and heart.

The PHYSICAL SIGNS in the early stages resemble those of tuberculosis except that the primary sites of infection in pulmonary actinomycosis are found most frequently at the lung bases. Massive areas of dullness develop later; the chest wall may be re-

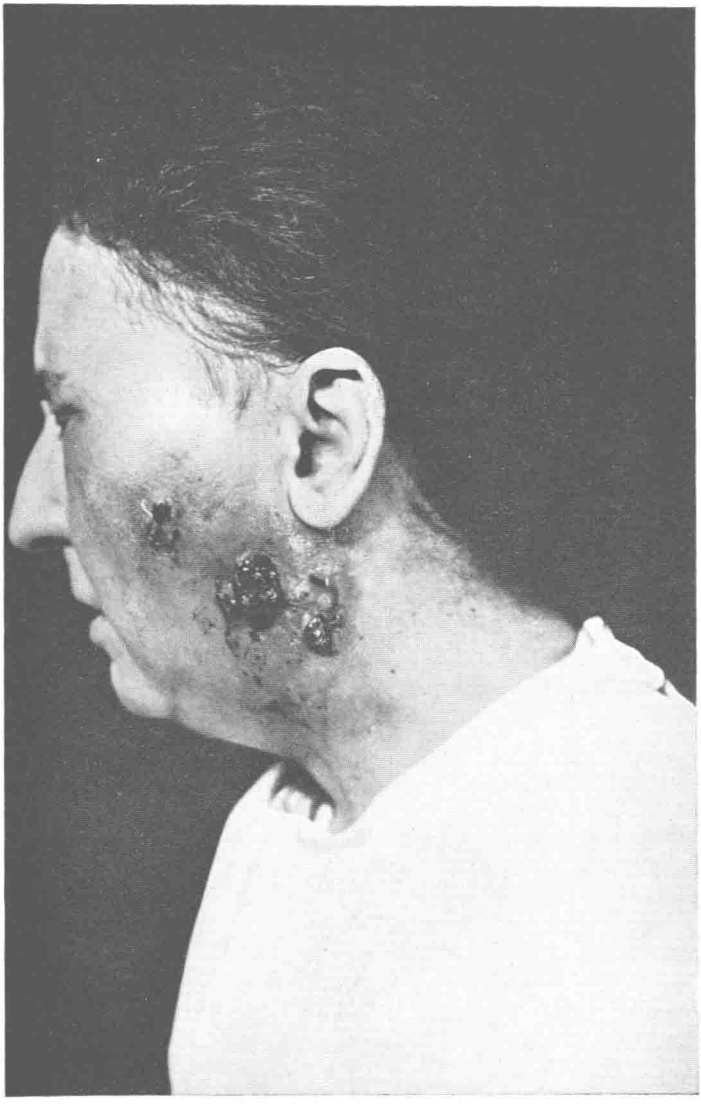

FIG. 1. Actinomycosis of the face. Note swelling of subcutaneous tissues and multiple sinus formation.

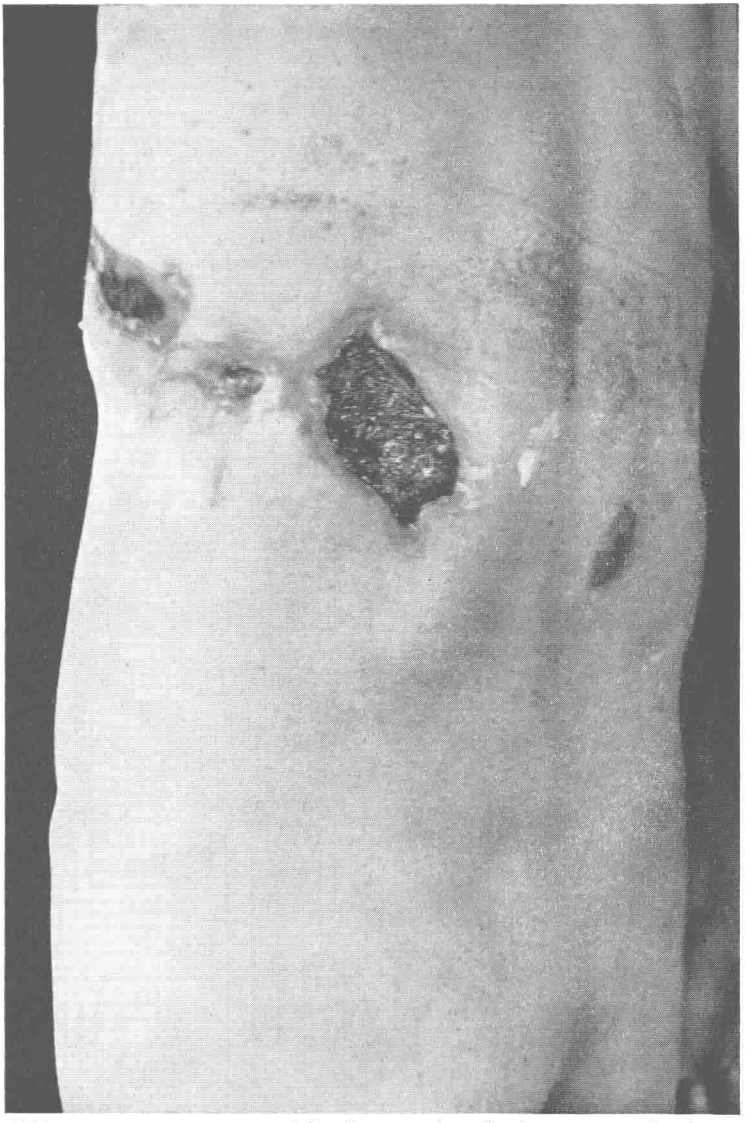

FIG. 2. Actinomycosis of the thorax with multiple sinuses in the skin.