

MANUAL OF
**CLINICAL
MYCOLOGY**

THIRD EDITION

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North American Blastomycosis

James H. Baker, Professor of Dermatology,
The University School of Medicine

NORMAN F. CONANT, Ph.D.

James B. Duke Professor of Microbiology,
Duke University School of Medicine

DAVID TILLERSON SMITH, M.D.

James B. Duke Professor Microbiology, Emeritus,
Duke University School of Medicine

ROGER DENIO BAKER, M.D.

Professor of Pathology, Rutgers Medical School

JASPER LAMAR CALLAWAY, M.D.

James B. Duke Professor of Dermatology,
Duke University School of Medicine

PREFACE TO THE THIRD EDITION

In the sixteen years since the publication of the Second Edition of this *Manual*, our knowledge of the fungi that are pathogenic to man has been widened and deepened. This has necessitated a complete revision of the *Manual*, with special emphasis on immunology and therapy. Now chapters have been added on African Histoplasmosis, Lobomycosis, Cladosporiosis and Mycotic Keratitis. The previous chapter on Nocardiosis has been divided to give equal emphasis to systemic Nocardiosis and Actinomycotic Mycetoma.

Blastomycosis can no longer be considered a disease confined to the North American continent (i.e., the United States and Canada). Autochthonous cases have been reported from Mexico, South America and Africa. This has demanded a serious revision of the epidemiology of this disease. Furthermore, *Blastomyces dermatitidis* has been isolated from soil and its perfect state has been described.

One of the surprises concerning the mycology of the pathogenic fungi has been the discovery of the perfect state of some of the dermatophytes. This discovery came about as a sequel to the "hair baiting" technique for culturing fungi from soil. It is hoped that knowledge of the perfect state will have some influence on the taxonomy of the dermatophytes.

A great increase in fungus disease has been caused by the widespread use of antibacterial antibiotics, corticoid hormones

and the chemotherapeutic drugs for leukemia and neoplasms. These agents lower the resistance of the patient's tissues and result in an increased number of infections with the known fungal pathogens. In addition to these infections, practically all the so-called "saprophytic" fungi can, and do at times, invade the tissues of patients whose resistance has been lowered by a debilitating disease, a chemotherapeutic agent or both. This has been especially dramatic in patients with organ transplants.

Antifungal antibiotics have been discovered and used successfully in human infections since the last edition of the *Manual*. Nystatin, amphotericin B and griseofulvin have been used successfully for candidiasis, systemic fungus infection and dermatomycosis, respectively.

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NORMAN F. CONANT, PH.D.

DAVID T. SMITH, M.D.

ROGER D. BAKER, M.D.

JASPER L. CALLAWAY, M.D.

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ACTINOMYCOSIS

(Lumpy Jaw, Streptothricosis,
Leptothricosis, etc.)

This infection is caused by microaerophilic to anaerobic obligate parasites of the genus *Actinomyces*, which are more closely related to the bacteria than to the higher fungi.

Definition. Actinomycosis 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 israelii* is a normal inhabitant of the oral cavity 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. Thompson and Lovestedt, Garrod, and Howell et al. have demonstrated the presence of the pathogenic *A. israelii* as well as the non-pathogenic facultative anaerobic *A. naeshundii* in the so-called normal mouth and saliva; this indicates that the source of infection in most cases of actinomyco-

sis is endogenous. A third species, *A. propionicus*, has been isolated from human lacrimal canaliculitis by Buchanan and Pine; and a fourth species, *A. eriksonii*, from pleural fluid and lung abscesses, has been described by Georg et al.

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. The disease is not transmitted naturally from man to man. Infection in cattle, caused by *A. bovis*, 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 israelii* 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 cervico-facial, 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



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

rarefying osteomyelitis expanding the cortex into a pseudocyst.

Thoracic Actinomycosis. Primary infection of the lung results from aspiration of *A. israelii* from the mouth or by the blood stream by means of an embolus from a vessel associated with a focus of infection in the cervicofacial area. 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 retracted and limited in motion. The heart may be displaced. The presence of subcutaneous abscesses or open, draining sinuses should suggest the diagnosis.

X-RAYS. Films of the chest show smooth, massive areas of consolidation, often containing several small, ill-defined areas of rarefaction. The lesions are usually bilateral and occur most often in the lower half of the lungs (Fig. 3). Areas of massive consolidation may project from the hilum, suggesting neoplasm. The pleura is involved in most of the advanced cases, either as massive pleural adhesions or as accumulations of fluid which may or may not be encapsulated. The ribs are invaded frequently and show both destructive and prolifera-

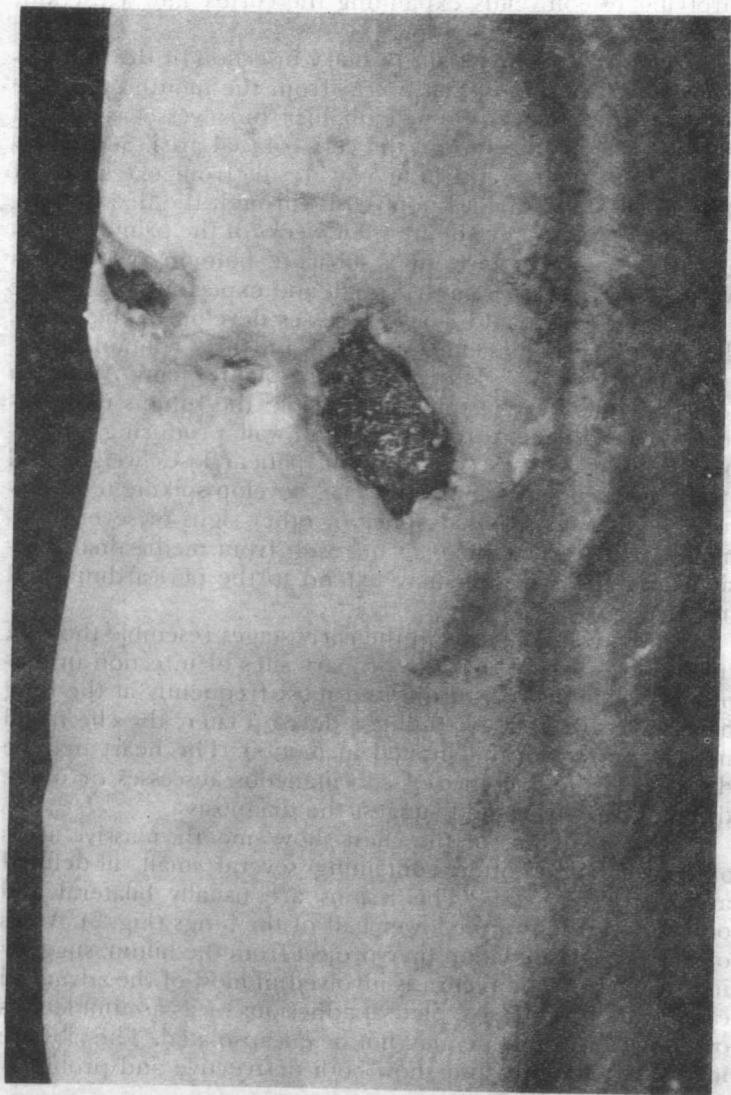


Figure 2. Actinomycosis of the thorax with multiple sinuses in the skin.

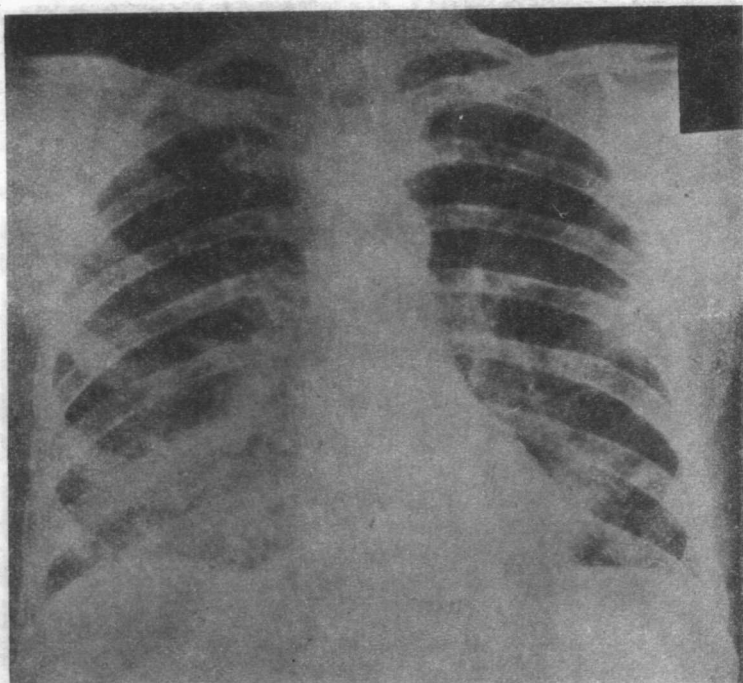


Figure 3. Actinomycosis involving both bases.

tive changes. Occasionally chronic lesions in an upper lobe will stimulate tuberculosis (Fig. 4).

Abdominal Actinomycosis. The organisms, which enter through the mucosa of the intestinal tract, probably represent oral strains of *Actinomyces* which have been swallowed with the saliva. The infection may reach the abdomen by metastasis or by direct extension from the thorax, but more often the reverse process is observed, the infection extending from the abdomen to the chest.

The first SYMPTOMS are found usually in the ileocecal region, presenting a picture suggesting acute or subacute appendicitis. These symptoms are often minimal, the first indi-