MISCELLANEOUS PUBLICATION 28

LABORATORY-ACQUIRED MYCOSES

Everett Hanel, Jr.
Richard H. Kruse

DECEMBER 1967

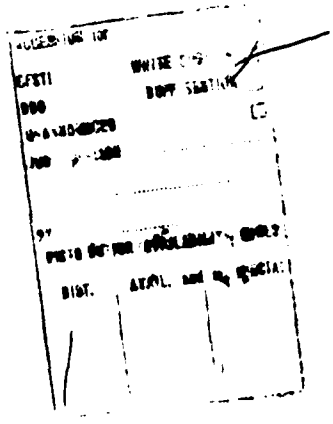
DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

DDC AVAILABILITY NOTICES

Distribution of this publication is unlimited; it has been cleared for release to the general public. Non-DOD agencies may purchase this publication from Clearinghouse, ATTN: Storage and Dissemination Section, Springfield, Virginia, 22151.

DISPOSITION INSTRUCTIONS

Destroy this publication when it is no longer needed. Do not return it to the originator.



DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland 21701

MISCELLANEOUS PUBLICATION 28

LABORATORY-ACQUIRED MYCOSES

Everett Hanel, Jr.

Richard H. Kruse

Research and Radiological Division
INDUSTRIAL HEALTH AND SAFETY OFFICE

Project 1B622401A072

December 1967

ACKNOWLEDGMENTS

The authors thank Norman F. Conant, Duke University Medical Center; Lucille K. Georg, National Communicable Disease Center; Howard W. Larsh, University of Oklahoma; Edwin P. Lowe, Fort Detrick; and Charles E. Smith, University of California, for review of the manuscript and many excellent suggestions.

ABSTRACT

The most widely quoted of studies that summarize cases of laboratory-acquired infections are by Sulkin and Pike, who included laboratory-acquired infections in the U.S. from 1930 to 1950 and worldwide infections from 1950 to 1963. Because these studies do not give specific details on modes of exposure and other summaries are similarly meager, a comprehensive search of the literature was undertaken to establish a more complete summary of laboratory-acquired mycoses. Insofar as possible, the etiological fungus, type of laboratory, classification of personnel, type of work conducted, and other pertinent data have been listed in this study.

More than 288 laboratory-acquired mycoses are described here, including 108 cases of coccidioidomycosis, 81 of histoplasmosis, 8 of blastomycosis, 7 of sporotrichosis, and 84 of dermatophytoses. Known accidents or incidents accounted for only 13% of the infections. Analysis of the type of laboratory work performed shows that most of the infections resulted from exposure to accidentally created mycotic aerosols.

CONTENTS

TABLES

I. INTRODUCTION

Every microbiologist realizes that laboratory-acquired infections do occur. A survey of 1,342 laboratory-acquired infections from 1930 to 1950, principally in the U.S., included 63 caused by fungi.[138] An additional 58 fungal infections were reported 14 years later.[109] Details were not given. The present review brings the total number of reported laboratory-acquired mycoses to 288.

Inhalation of accidentally created microbial aerosols is the principal means of infection.[108,148] The sequence of events following the inhalation of an airborne fungus depends on the (i) invasive ability and virulence of the inhaled fungus; (ii) susceptibility of the individual determined by race, age, health, and specific resistance; (iii) total intake; (iv) rate of intake; and (v) amount of inoculum retained. These factors determine whether an individual remains unaffected, becomes infected, or becomes sensitized.

Animals have long been known to transmit dermatomycoses. Dr. Sabouraud in 1908 stated, "It is one of the most interesting questions for man to know what are the diseases he can contract from animals which surround him." Farmers, animal breeders, veterinarians, miners, etc. have incurred mycotic occupational infections. Georg[56,57] thoroughly reviewed the history of dermatophytic infections and cited numerous animals that serve as reservoirs of these fungi. Rowsell[120] reviewed not only the dermatophytes but discussed other animal mycotic infections. Wedum[148] emphasized hazards that animal handlers encounter and the aerosols that are formed by microbial particles shed from the fur or in excretions. In a recent review,[84] Coccidioides immitis and Histoplasma capsulatum were added to the listed fungi excreted in urine and feces of laboratory animals.

Occupational illness may result from typical mycologic laboratory techniques. Huppert[73] designed a new container for culturing C. immitis. Kruse[83] quantitatively analyzed laboratory procedures and equipment for mycotic studies and demonstrated that almost every one of these procedures created aerosols. Mycotic laboratory infections have provided valuable information on the pattern of disease. For example, a laboratory infection showed that the respiratory tract was the portal of entry for C. immitis and that there was a benign form of the disease.[34-38] The incubation period for some fungal diseases has been established by accidental inoculation. Nevertheless, occupational illness may (i) result in monetary loss, (ii) interrupt laboratory functions, and (iii) result in temporary or permanent incapacitation or even in death.

Available data on laboratory-acquired mycoses probably represent only a fraction of the actual cases because many infections either are not reported in the literature or are not recognized. We have reviewed the literature and discussed the problem with mycologists. This study summarizes the laboratory accidents and the procedures that may have led to the infections.

II. COCCIDIOIDOMYCOSIS

A. BACKGROUND

The recorded history of coccidioidomycosis began in Buenos Aires, Argentina, in 1891, when a soldier with verrucous patches on his body entered the University Hospital.[111,112,149] In California a second case was investigated[118] and the causative organism was isolated and named Coccidioides immitis.[119] A comprehensive history of the disease and etiologic agent has been presented by Fiese.[47]

This diphasic fungus is found as a saprophyte in soil[136] and has been isolated from air.[3,72] On solid media C. immitis grows rapidly to form, within a few days, a white mycelial mat that gradually darkens. Arthrospores, characteristically 2 to 4μ in diameter, may approach 10μ[7] and are produced in large numbers by septation of the hyphae. The arthrospores survive well under normal atmospheric conditions. However, a combination of persistent low humidity and elevated temperature reduces survival.[50]

The parasitic form or spherule is 10 to 80μ in diameter. Endospores form inside the spherule, are characteristically 2 to 5μ in diameter, and are liberated to repeat the cycle. The parasitic phase is less resistant than the saprophytic phase.[133]

The contagion of coccidioidomycosis in animals has been the subject of controversy for almost 20 years. A recent paper[85] reviewed this controversy and reported that there was no contagion except for one case reported involving the intimate contact of an infant monkey with its infected mother.[17]

No direct man-to-man transmission of coccidioidomycosis has been reported. Critical studies were conducted among personal family contacts[9,128,155] and hospital staff personnel,[48] but no evidence of interhuman transmission was found.

B. CASE REPORTS OF LABORATORY-ACQUIRED COCCIDIOIDOMYCOSIS

The first report of coccidioidal laboratory infection found in the literature was that of Morris.[98] However, this is a conflicting study because Morris called the disease blastomycosis. A physician engaged in postgraduate medical work developed a cold. He complained of pain in various joints and had a slight fever. A small pustule developed on the left index finger that eventually became indurated and crusty. During a trip to England in January 1913, he developed sharp pains in the chest. He was admitted to a London hospital for chest surgery; part of the ninth rib was necrotic and was removed. He arrived in New York February 28 and was admitted to the hospital by Dr. Morris because of severe pain. In March, pain developed in the right lower chest and X rays revealed consolidation at the base of both lungs. Dr. Morris thought the patient had a subphrenic abscess of the right lobe of the liver; on the basis of X-ray films, other physicians thought the patient had bronchopneumonia with lung abscess. Three operations were performed and, in April, superficial abscesses appeared on the chest and legs. Thin yellow to brown pus was recovered from these abscesses. In May, Dr. Hjelm evacuated an abscess on the neck and recovered a fungus he labeled Blastomyces dermatitidis. The patient stated that he had pricked himself on the left index finger in November 1912, when he was performing an autopsy. Potassium iodide was administered but later discontinued. Two intravenous injections of Neosalvarsan were administered with no response. On May 11, 1913, the patient died and permission for postmortem was denied.

Examination of pus from the patient caused MacNeal and Hjelm[94] to contradict the diagnosis of blastomycosis. They reported that microscopic examination revealed numerous doubly contoured spheres with a diameter of 4 to 25μ. The large spheres were granular and filled with globular bodies 1 to 5μ in diameter. They further reported that some of the larger spheres had ruptured, with small spheres "ready to escape from their interior." They found no budding cells and termed the organism "identical with that described by Posadas and Wernicke," C. immitis. We believe this to be the first report of laboratory-acquired coccidioidomycosis because, according to MacNeal and Hjelm's description, the large spheres with globular bodies seem to have been spherules. No further information on this case could be found.

Tomlinson and Bancroft[141] reported that a medical student spent September 1926 at the University of Pennsylvania engaged in research with C. immitis. He returned to the University of Nebraska, where he continued his research on fungi, including C. immitis. In April 1927, he developed an acute respiratory illness. Two weeks later his left foot swelled and he was admitted to the hospital. A longitudinal incision in the midplantar area of the left foot revealed pus from which spherules of C. immitis were demonstrated. The patient responded to treatment, but 4 years later the lesion recurred. Treatment at that time appeared to be effective.[142]

Whether this infection was a result of a known laboratory accident or "just working the usual way" with the fungus was not stated. Work with C. immitis was stopped at the University of Pennsylvania until proper room ventilation and the installation of a chemical hood could be arranged.

The next recorded case also involved a medical student.[34-36] In August 1929, a student at Stanford University began a research problem involving the life cycle of C. immitis. When he opened a petri dish containing an old, dried culture of C. immitis, he noticed a light brown cloud drift out of the plate. This was his only known exposure. He developed a respiratory infection and, later, erythema nodosum. His symptoms, including pulmonary involvement, gradually subsided and he returned to work after recuperating for 5 months in Arizona. The course of the disease was observed intensively and provided a unique opportunity to study coccidioidomycosis from the moment of exposure to the etiologic agent through treatment to recuperation. This case also proved that not only was there a granulomatous form of the disease, but also a benign form, and that the portal of entry was the respiratory tract.

Bush[15] reported that, in April 1942, in the Department of Pathology and Bacteriology, University of Alabama School of Medicine, a medical technician wearing a surgical mask prepared several cultural mounts of pathogenic fungi. The cotton plug from a test tube containing an old culture of C. immitis dropped, creating a cloud of "dust" as it struck the table top. Fifteen days later the technician became ill. Two days later he was admitted to the hospital, where respiratory coccidioidomycosis with erythema nodosum eventually was diagnosed.

Willett and Weiss[151] mention a laboratory technician who converted from a negative to a positive coccidioidin skin test after he cultured sputa and inoculated animals with clinical specimens from acute pulmonary cases. He had no clinical symptoms of coccidioidomycosis.

Smith and Harrell[131] described seven cases of coccidioidomycosis that occurred in the Department of Medicine and Bacteriology, Duke University School of Medicine. In June 1946, the outsides of several flasks containing liquid cultures of C. immitis were accidentally contaminated and, presumably, some of the infectious arthrospores dried on the flasks and contaminated the air. Four individuals working in the room with the flasks reacted to a 1:1000 dilution of coccidioidin; three dishwashers reacted to a 1:100 dilution. The cases were subclinical, except for one individual who developed primary pulmonary coccidioidomycosis that progressed to coccidioidal meningitis from which he succumbed within 6 months. Smith and Harrell stated that students and laboratory personnel can study C. immitis without danger of infection if the cultures are maintained on slants in test tubes, not in petri dishes, and bacteriologic loops are moistened before handling the powdery aerial hyphae.

The 13th infection, related by Nabarro,[101] involved a research chemist working at the University College Hospital, London, in December 1946. She prepared extracts for skin testing by grinding dried cultures of C. immitis in saline; she wore a gauze mask because so much "dust" was produced in the process. Within 7 days a respiratory infection ensued. Erythema nodosum appeared 2 weeks after the first symptoms. C. immitis was isolated from sputum and gastric contents.

Gonzalez-Ochoa[62] reported two laboratory-acquired coccidioidal infections at the Laboratory of Mycology of the Institute of Health and Tropical Diseases in Mexico. No details were given on how infection occurred. One patient developed progressive bronchial fever. The second had a febrile condition with severe prostration and erythema nodosum.

Looney and Stein[90] investigated one disseminated and three subclinical coccidioidal infections of technicians in the Clinical Laboratories, Veterans Administration Hospital, West Roxbury, Massachusetts. A laboratory technician, 2 or 3 weeks before his illness, studied some old cultures of C. immitis by removing the top of the petri dish and then examining the cultures with a magnifying glass. He also made smears for microscopic examination. The diagnosis was confirmed by recovery of C. immitis from sputum, positive complement fixation, and a positive skin test. This patient was discharged from the hospital but later was readmitted with involvement of the right metatarsals and left metacarpals. After 14 months he was discharged, but he was not able to return to work for several months. As a result of this case and the three subclinical cases, a prohibition was placed on opening any culture that looked as if it might be C. immitis.

Smith[129] reported 79 cases, 16 of which had been described previously in the literature and are listed above. Sixty-three new laboratory-acquired infections were revealed by replies to his questionnaire sent to various hospitals and by collecting experiences at Stanford University. These are described as follows.

At LaGarde General Hospital, Louisiana, during the fall and winter of 1943, there were many patients with disseminating coccidioidal infection. In December 1943, a laboratory worker stated that the cotton plug fell out of one culture tube while he was examining cultures of C. immitis. Later he developed an acute respiratory infection and was ill for 2 weeks. In March his coccidioidin test was positive. Although a laboratory infection was probable, it could not be proved because there had been no preceding negative skin test. However, another laboratory worker converted from a negative to a positive coccidioidin skin test.

At Letterman General Hospital, California, in January 1944, two laboratory infections occurred when technicians cultured material from a patient's excised "pimple." The cultures were examined in the laboratory without realizing that the fungus was C. immitis.

At Hammond General Hospital, California, a laboratory technician contracted coccidioidomycosis. He did not work with C. immitis, but was often in the room when C. immitis cultures were examined.

In July 1944, at DeWitt General Hospital, California, a laboratory officer received a culture of C. immitis from the Army Medical School. Although warned of the extreme risk of laboratory infection and advised to destroy the culture, the officer made five slide preparations at night, alone in the laboratory, and with extreme precautions. Three weeks later, the officer had a respiratory infection; coccidioidal infection was diagnosed by elevated precipitins and a positive coccidioidin skin test.

At the 42nd Station Hospital, Alaska, culturing unrecognized C. immitis resulted in a laboratory-acquired coccidioidal infection. The laboratory officer made transplants every 2nd to 4th day of an isolated "yeast." He later developed a progressive respiratory infection with erythema nodosum and a possible metastatic lesion on the right index finger.

At Rhodes General Hospital, New York, a laboratory officer used great caution in culturing C. immitis. When the test tubes were opened, the open end of the tube was held close to a Bunsen flame. Nevertheless, after a respiratory illness he converted from a negative to a positive coccidioidin skin test.

After making a subculture of C. immitis, a dermatologist at Percy Jones General Hospital, Michigan, developed a respiratory illness and, later, erythema nodosum. Coccidioidomycosis was confirmed by a positive coccidioidin skin test and the presence of complement-fixing antibodies.

At a Veterans Administration Hospital in California, a bacteriologist who had recently isolated C. immitis from a veteran converted from a negative to a positive coccidioidin skin test. He had no symptoms of infection, but precipitins and complement-fixing antibodies were found in his serum.

The London School of Tropical Medicine received a culture of C. immitis. Although strict precautions were used during transfer by the physician, a laboratory infection was identified by conversion to a positive coccidioidin skin test.

At a private hospital in Ohio, a laboratory technician recovered C. immitis from postmortem material of a patient who died of miliary coccidioidomycosis. Three weeks after transferring cultures, she developed a respiratory infection. Her skin test had converted to positive, and C. immitis was recovered from her sputum.

Stanford University cases were reviewed in chronological order by Dr. Smith.[139] All cases occurred in the building occupied in part by The Department of Health and Preventive Medicine of which Dr. Smith was the Chairman. In 1937, skin tests were initiated with coccidioidin. Four technicians, a medium maker, a dishwasher, five physicians, and a secretary reacted strongly to the coccidioidin skin tests. Only one had been in known coccidioidal endemic areas. In addition to these, there were the following additional cases.

An assistant resident was tested with coccidioidin in July 1938, with negative results. He did not work with C. immitis but was in the same room where work with this fungus was performed. In September he converted to a positive skin test.

A medical student who worked part-time developed fever with malaise in August 1938. X rays showed haziness in his right lower lobe. Diagnosis of coccidioidomycosis was confirmed by a conversion from a negative to a positive coccidioidin skin test, and recovery of C. immitis from his sputum was proved by culture and animal inoculation.

A graduate student mycologist worked in a room where cultures and soil from the San Joaquin Valley had been handled. He used a small inoculating chamber when he transferred cultures. In April 1939, he developed malaise, fever, headache, and backache. Diagnosis was confirmed by conversion of the coccidioidin skin test and isolation of C. immitis from sputum.

A medical student worked in the Stanford Mycological Laboratory. In September 1938, his coccidioidin test was negative, but in the spring of 1939 his coccidioidin skin test was strongly positive.

A laboratory technician prepared tissues. In September 1938, her coccidioidin skin test was negative, but 1 year later it was positive. She recalled having a severe respiratory infection several months before her coccidioidin conversion.

In September 1939, the Department of Health and Preventive Medicine moved from the hospital laboratory to a new building. The offices and research area were located on the first floor, and other departments occupied the second and third floors. In November, a technician who did not work with C. immitis in the Department, but who was in the room where cultures were studied, thought she had influenza because she had headaches, chest pain, and fever. X rays revealed a large lesion above the left leaf of the diaphragm. She converted to a positive coccidioidin skin test, and C. immitis was isolated from sputum.

A secretary frequently assisted in laboratory work, but never with cultures of C. immitis. In April 1940, she developed a cough, anorexia, malaise, and fever. Coccidioidomycosis was confirmed by isolating C. immitis from sputum and by conversion from a negative to a positive coccidioidin (1:100) skin test.

A medical student worked as a part-time dishwasher on the second floor. He visited the research laboratory only once, but at a time when they were unloading dirt collected from the San Joaquin Valley. In September 1940, he had slight fever and malaise and was admitted to the hospital. Coccidioidomycosis was confirmed by a conversion of skin test and by precipitins. He remained in the hospital for 7 weeks.

A physiologist visited Dr. Smith in January 1942. He had visited an endemic area shortly before his visit at Stanford. On January 16, he developed bronchitis that continued until January 27, when he became acutely ill with atelectasis of the right lung. Dr. Smith stated that, if the bronchitis was the onset of his infection, the infection was incurred elsewhere, but if onset was January 27, it was a laboratory infection. In February a subcutaneous lesion developed. Coccidioidomycosis was confirmed by a 4+ coccidioidin skin test, isolation of C. immitis from sputum and the subcutaneous abscess, and presence of precipitins and complement-fixing antibodies in sera. Dr. Smith believed it was a laboratory infection because of the patient's recollection of "sniffing a culture."

A boy, age 5, visited the laboratory with his father and older brother, who previously had coccidioidal infections. While the father examined animals and specimens, the brothers weighed guinea pigs. Ten days later the boy developed fever and, 2 days later, a rash. Coccidioidomycosis was confirmed by the conversion of the coccidioidin skin test.

In November 1945, a research assistant developed malaise, headache, and fever. She had worked in the Department 11 days, and then converted from a negative to a positive coccidioidin skin test. As a result of this and other cases, additional control measures were instituted. Coccidioidin testing and retesting were systemized to detect infection as early as possible. Culturing was done in a separate locked room, which only those people with a positive coccidioidin skin test could enter.

A physician, whose office was on the third floor of the building, became ill in March 1946 while en route to Massachusetts. He was admitted to the hospital with fever, malaise, and cough. X ray showed many "cotton-ball" shadows through both lungs. He remained in the hospital for a month. In December, a coccidioidin skin test was strongly positive and complement-fixing antibodies were present in his serum. These findings were compatible with a severe coccidioidal infection several months before.

A medical student visited the Stanford laboratory in March 1946. Two weeks later he developed chest pain, headache, and slight malaise. One week later erythema nodosum developed on his legs. A coccidioidin skin test was strongly positive, and precipitins were found in his serum.

A secretary worked on the third floor of the building from January to May 1946. In March she had malaise. In June and August, she had severe "colds." X ray in August revealed a parenchymal lesion in the left lung. In October, the lesion had cavitated. C. immitis was isolated from her sputum in November.

Five workers in the building exhibited positive coccidioidin skin reactions in the summer of 1946. These positive recordings were found as a result of skin testing all personnel in the building including those not in the Department of Health and Preventive Medicine. This survey was made because four monkeys used in poliomyelitis research were found to have coccidioidomycosis. Of the five coccidioidin skin test reactors, three worked on the second floor and two worked on the third floor. One worker on the second floor had been in an endemic area, but the other four had not. All four recalled having a severe respiratory infection the preceding spring.

A technician reported to work in April 1946. Coccidioidin skin tests each month were negative, but in August she converted to a positive test. She recalled that she had dropped a petri dish containing C. immitis in July.

Eleven days after visiting Dr. Smith in July 1947, a physician developed malaise and chest pain. X ray showed a lesion in his right lower lobe. In August he developed erythema multiforme on his hands. Diagnosis of coccidioidomycosis was confirmed by conversion of his coccidioidin skin test, the presence of precipitins and complement-fixing antibodies in his sera, and isolation of C. immitis from his sputum.

A physician moved to an office on the third floor of the building. In November 1947, he developed a cough, headache, malaise, and fever. His coccidioidin skin test converted and precipitins were elevated.

A technician on the second floor had a sudden onset of pain in his right lower chest in February 1948. He developed a cough and was admitted to the hospital. X ray showed two small parenchymal lesions in his left lung. Serological tests showed precipitins but no complement-fixing antibodies. His coccidioidin skin test converted. Two days after discharge, he developed erythema nodosum that persisted for several months.

Another technician, on the third floor, had chills, malaise, and fever in March 1947. Her coccidioidin skin test converted, and her serum had elevated precipitins.

A Filipino animal caretaker on the second floor was not permitted to visit the laboratory on the first floor. However, in March 1948, he had a sudden pain in his chest. X ray showed a small amount of fluid in his right lung. Coccidioidomycosis was diagnosed by conversion of his coccidioidin skin test and precipitins in his serum. Review of the laboratory procedures revealed that cultures had been transferred only once since January 1948. However, in February the motor of the exhaust ventilating system was not functioning. During February, the prevailing winds were from the north and the ventilating system outlet faced north. Propylene glycol was vaporized throughout the ventilating system and into each room. Until the protective cabinet[97] was completed in June, cultures were not transferred.

An assistant and a secretary became infected while the cabinet was being constructed. The assistant on the second floor converted from a negative to a positive coccidioidin skin test. The secretary on the first floor cleaned one of the offices and a considerable amount of dust was raised. Two weeks later she had a slight cough and malaise. Her coccidioidin skin test converted from a negative to a positive test.

When the cabinet was completed it was believed that the problem of laboratory-acquired infection was solved. The cabinet was closed and all work was performed in arm-length gloves. Vaporized propylene glycol disinfected the interior. Cultures were transferred frequently and on six occasions dry cultures of C. immitis were scraped. All the cultures were transferred from February 22 to 24, 1949.

Fourteen medical students attended a seminar on February 25, 1949, on the third floor of the building and on the next day attended another seminar with a different physician. Seven students contracted coccidioidomycosis diagnosed by X ray, conversion of skin test, serological studies, and isolation of C. immitis from sputum. All the patients had respiratory symptoms and two had erythema nodosum.

The physician who held the second seminar developed pain, anorexia, fever, malaise, and a slight cough in March. X ray revealed multiple lesions. His coccidioidin skin test converted and precipitins were present in his serum.

A professor, whose room adjoined the conference room where the seminars were held, had an influenza-like illness in March. His coccidioidin skin test converted from a negative to a positive test.

A technician prepared tissues for histological study in another room adjoining the conference room. In March he had chills. A later X ray showed infiltration in the right mid-lung. Diagnosis was confirmed by a conversion of coccidioidin skin test and by isolating C. immitis from sputum.

A physician who worked in the room with the technician converted from a negative to a positive skin test the latter part of March 1949.

A secretary working on the side of the building opposite the conference room stopped work in mid-March to assist her husband, a roentgenologist, who was setting up his own office. He took a routine X ray of her and found three parenchymal lesions. Three days later an X ray showed that the three lesions had doubled in size. One week later her coccidioidin skin test had converted, and precipitins were present in her serum.

An assistant in the Department of Radiology, located across the hall from the mycology laboratory, met two people from the third floor for coffee in the main laboratory room. On February 25, 1949, she took some tissues to the histology laboratory on the third floor. The latter part of March she developed a cough and a slight fever. Coccidioidomycosis was confirmed by X ray, a coccidioidin skin test conversion, and precipitins in her serum. Fifteen physicians who were in the building at that time developed positive coccidioidin skin tests. Three had respiratory symptoms in March 1949. However, all had negative X rays and serologic tests, and are listed as probable.

Izzo, Bonfiglioli, and Martinez[75] report a laboratory-acquired coccidioidal infection. A laboratory technician who cultured C. immitis developed a respiratory infection that was diagnosed as coccidioidal infection from X rays and conversion of coccidioidin skin test.

Conant[20] reported there were four laboratory-acquired coccidioidal infections at Duke University. A laboratory technician who handled animals infected with C. immitis converted from a negative to a positive coccidioidin skin test. A student transferred a culture of C. immitis in December 1954; 4 days later he had a respiratory illness. Approximately 1 month later a small lesion developed on his abdomen and a pimple on his nose from which C. immitis was isolated. A physician working in the laboratory where research on C. immitis was performed developed a cold in February 1955. In March, C. immitis was isolated from his sputum. No overt accident was known.

A student sprayed a saline suspension of C. immitis over her face and hands in August 1954. She washed thoroughly with soap and water and decontaminated the work area with phenol. Eight days after this accident a small lump appeared on the third finger of her left hand; it became larger and C. immitis was isolated from it. Trimble and Doucette[144] gave more details of this accident. While the student was filling the syringe with the contents of a small rubber-stoppered bottle, the stopper blew off, apparently from pressure created when she attempted to clear a clogged needle.

Wilson, Smith, and Plunkett[153] described a primary cutaneous infection in a mortician who severely abraded the dorsal surface of his right middle finger on a casket. Shortly after this injury he embalmed the body of a person who had died of disseminated coccidioidomycosis; this entailed handling coccidioidal-infected visceral organs. A lesion, from which C. immitis was isolated, developed at the injured site.

J.W. Millar and C.E. Meyers* reported that in 1957 two laboratory-acquired coccidioidal infections occurred in California. A laboratory worker transferred dry arthrospores from agar plates into screw-capped bottles containing saline and glass beads. He removed the bottle from the cabinet before sealing the top with tape. As he taped the bottle, the tape unscrewed the cap and jerked the cap off. Contents of the bottle splashed close to the investigator's face; he was not wearing a face mask. C. immitis was demonstrated in oropharyngeal washings 12 days after the accident, and 3 weeks later pulmonary infection resulted. A laboratory technician checked the oropharyngeal washing culture plates of this patient. He worked outside a cabinet and did not wear a face mask. Six days after examining the cultures he developed a respiratory illness. His X ray was positive and he converted from a negative to a positive coccidioidin skin test.

Levine[89] mentioned that at the Naval Biological Laboratory from 1953 to 1959 there were six infections, one clinical and five asymptomatic, in a group of nine people who worked with C. immitis. These coccidioidal infections occurred even though precautionary methods and equipment were utilized.

Wright, Newcomer, and Nelson[158] investigated the infection of a laboratory technician who began working with C. immitis in October 1957. At that time his coccidioidin skin test was negative. In December 1957, he injured the tip of his left index finger with a hypodermic needle that contained C. immitis. However, no symptoms of disease followed. On January 13, 1958, the same finger was inoculated accidentally with a hypodermic syringe that contained C. immitis. Nine days later he was admitted to the hospital with fever and malaise; his finger was tender and sore. A small lesion developed on the inoculated finger from which C. immitis was cultured repeatedly, and the patient converted to a positive coccidioidin skin test. Spherules with endospores were seen on histopathological examination. Complement-fixing antibody titer was negative, but in February 1958 the precipitin test was 4+ in 1:10 titer. Amphotericin B was not administered and recovery was slow. The patient returned to work with no further complications.[158]

* Personal communication.

Sorensen and Cheu[134] reported a laboratory-acquired cutaneous coccidioidal infection. In September 1962, a technician accidentally injected his left index finger while injecting mice with C. immitis. Sixteen days after the accident a small pustule had formed from which C. immitis was isolated. Urticaria developed in the palms of both hands and spread to all parts of his body. A small granuloma was biopsied, from which C. immitis was cultured and identified in stained sections.

Overholt and Hornick[105] described three laboratory-acquired primary cutaneous coccidioidal infections at Fort Detrick. A laboratory technician who harvested C. immitis had a "thorn puncture in the right fifth finger." Later he had a lesion at the site of the thorn puncture, from which C. immitis was isolated.

Another laboratory technician accidentally inoculated himself with a needle containing viable arthrospores while working in a ventilated cabinet breaking clumps of arthrospores for animal inoculation. Three days later the puncture site was red, nodes developed eventually, and C. immitis was isolated from the lesion. The infection became worse and invaded a metacarpal. Before recovery, surgery with bone graft was required because of bone fusion.

The third technician contracted dermatitis after exposure to poison ivy. Although he did not work with C. immitis, he worked in gloves attached to a ventilated cabinet in which C. immitis had been used. A small lesion developed over the dorsum of the left wrist, from which C. immitis was isolated. There was no overt accident; however, C. immitis was recovered by surface sampling the work area.

Johnson and co-workers[78] reported six laboratory infections at Fort Detrick, including the three previously described.[105] In one of the others, a laboratory technician was infected "when another worker was carelessly handling dry spores of C. immitis." C. immitis was isolated from sputum. The second infection occurred when a laboratory technician was accidentally exposed to dried arthrospores while working in a ventilated cabinet. Coccidioidal infection was diagnosed by X ray and conversion of coccidioidin skin test from negative to positive. The third laboratory technician worked for several months culturing and inoculating animals with C. immitis. He was admitted to the hospital with respiratory infection; coccidioidomycosis was diagnosed by isolating the fungus from sputum and by skin test conversion. There was no overt accident.

Review and analysis of the first two laboratory infections revealed the following: In case 1, the technician's supervisor had turned off the blower of the ventilated cabinet in direct violation of safety regulations. In case 2, the patient stated that the glove attached to the ventilated cabinet ruptured while he was weighing powdered arthrospores.

Three hitherto unpublished subclinical cases occurred at Fort Detrick in addition to the six cases described above. These were diagnosed by conversion from a negative to a positive coccidioidin skin test. There were no overt accidents to cause two of the infections. However, the third infected person worked with C. immitis in a cabinet with open glove ports. Once, before shaking and reconstituting a culture contained in a prescription bottle, he had difficulty connecting rubber tubing to a gas cock. He raised the window of the cabinet and made the necessary connection. In addition, the infection may have resulted from another unsafe procedure. After the fungus was grown in flasks on a reciprocal shaker in a walk-in incubator, the flasks were placed in the cabinet, where 10-ml samples were transferred with a safety pipettor to prescription bottles. All items removed from the cabinet were wiped with a towel wet with a quaternary ammonium compound; although this was considered a safe procedure at the time, the efficacy of quaternary ammonium as a disinfectant has since been questioned.[86]

Johnson and co-workers[78] reported that 204 individuals converted from a negative to a positive coccidioidin skin test. We believe that these conversions may not represent occupational infections because the syringes and needles used in skin testing had been used to administer skin tests with other biologicals. Smith and associates[130] emphasized the necessity of using the same syringes and needles for coccidioidin skin tests or soaking the equipment overnight in dichromate cleaning solution. Other biologicals (like tuberculin) may be adsorbed on equipment and give false positives. As evidence of this, skin tests of a typical microbiologist with 1:100 dilution of coccidioidin were: 1951, negative; 1952, 1+; 1956, 2+; 1958, negative; 1959, negative; 1960, 2+. Disposable needles and syringes eliminate this possibility.[127] Many of those whose skin test converted had never been in a building where C. immitis was present.

Klutsch and co-workers[81] reported two laboratory-acquired infections in Germany. The first occurred in a mycologist who cultured material from a coccidioidal patient. Four weeks later he had difficulty in breathing, with pains in his head and legs. Assuming it was a viral infection, he took penicillin and tetracycline. On his admission to the hospital, X rays revealed confluent pneumonic infiltration and hilus node enlargement. Coccidioidomycosis was confirmed by recovery of C. immitis from sputum, a positive coccidioidin skin test, and a complement-fixing antibody titer of 1:32.

The second case occurred in a "scientific collaborator" who helped the mycologist. He was admitted to the hospital with fever, cough, and urticarial exanthema. X rays revealed infiltration and enlarged hilus. One month later he developed erythema nodosum. An X ray revealed a thin walled cavity in the right middle field. C. immitis was recovered from sputum, his coccidioidin skin test was positive, and his complement-fixing antibody titer was 1:8.

C. OTHER OCCUPATIONALLY ACQUIRED CASES

Eckmann, Schaefer, and Huppert[39] described an unusual fomite transmission of C. immitis in a hospital. Six cases of primary coccidioidomycosis developed almost simultaneously among hospital personnel. Infection varied from frank clinical disease with recovery of the organism to conversion of the coccidioidin skin test with X ray and serologic findings consistent with a diagnosis of coccidioidomycosis. The method of transmission in these cases was apparently a plaster cast in proximity to a draining coccidioidal sinus of the ankle. Arthrospores were readily recovered from the cast.

Transmission of C. immitis by fomites to nonendemic areas is fairly common. Workers have been infected by fruit, grain, wool, soil, and many other fomites. There is no need to report the numerous fomite-transmitted infections here because Albert and Sellers[4] published a thorough and comprehensive report.

D. ACCIDENTAL LABORATORY INFECTION OF MONKEYS

Although this report concerns human mycoses, monkey infections at Stanford University[129] showed that the building ventilating system could carry spores from the first floor to the other floors. In June 1946, four monkeys used in poliomyelitis studies on the second floor developed coccidioidal lesions that were confirmed at autopsy by isolating C. immitis from lung tissue. Work with C. immitis was done on the first floor. The air from the building was exhausted on the roof, but when this exhaust fan was not functioning a negative pressure back-siphoned dirt from the louvers into the room.

III. HISTOPLASMOSIS

A. BACKGROUND

Histoplasmosis was first identified in 1905 at the Ancon Hospital in the Panama Canal Zone. While studying lesions resembling those of tuberculosis under a microscope, Samuel T. Darling saw intracellular organisms that he named Histoplasma capsulatum.[24] Like C. immitis, H. capsulatum was thought to be protozoan. Darling[25] later observed two more fatal cases of histoplasmosis. The first case recognized in the United States occurred in Minnesota.[117]

Schwarz and Baum[125] should be known as "histo historians." Their report ties together isolating, culturing, and describing the fungus,[29,66] how histoplasmin skin tests originated,[18,106] isolating the fungus from soil[40] and air,[74] epidemiology,[51,82] and morphologic stains.[114,137] Among other standard works on histoplasmosis are those of Sweany[129] and Negroni.[102]

H. capsulatum is a diphasic fungus present in soil around the world in temperate and tropical zones. The parasitic phase of H. capsulatum in tissue and in culture at 37 C is a typical oval yeast characteristically 1.5 to 3.5μ in diameter that reproduces by budding.[110] The more resistant saprophytic phase grows in soil and on solid media at room temperature, forming a white to brown mycelium that reproduces by two types of spores: microconidia, 2 to 6μ in diameter, and tuberculated macroconidia, 8 to 14μ in diameter. Cozad and Furcolow[33] and Helmbright and Larsh[71] measured the spores of H. capsulatum and reported considerable variation in size among strains. These studies showed that approximately 95% of the spores are less than 5μ in diameter. The size of these spores is certainly compatible with the particle size needed to produce airborne infection.[71]

In 1945 histoplasmosis was generally considered a rare and fatal mycotic disease of universal distribution.[1] However, 6 years earlier DeMonbreun[30] had stated, "It is probable, then, that the disease is more common than is generally supposed, possibly because the disease may occur in a relatively mild and nonfatal form and not be recognized." Histoplasmin skin testing and isolation of the fungus from the soil around the world subsequently confirmed this early judgment. Many laboratories have undertaken intensive studies with H. capsulatum.

B. CASE REPORTS OF LABORATORY-ACQUIRED HISTOPLASMOSIS

Sulkin and Pike[136] did not list any cases of histoplasmosis in their survey of 1,342 laboratory-acquired infections occurring in over 2,500 laboratories.

Furcolow, Guntheroth, and Willis[56] first reported laboratory-acquired histoplasmosis. A study of 56 employees at the U.S. Public Health Field Station, Kansas City, Kansas, where H. capsulatum had been studied for more than 6 years revealed that 17 individuals had converted from a negative to a positive histoplasmin skin test. Of these 17, seven had had an influenza-like illness about the time of their skin test conversion. Seven of the 17, including two asymptomatic individuals, had X-ray findings compatible with acute pulmonary histoplasmosis. The infection rate among laboratory personnel was 26 times greater than that for school children of Kansas City, which is an endemic area for histoplasmosis. Furcolow, Guntheroth, and Willis concluded that the laboratory appeared to be the ideal environment for human infection with H. capsulatum if adequate precautions were not afforded.

Nilzen and Paldrok[103] reported seven laboratory-acquired histoplasmosis infections at the Karolinska Institute, Stockholm, Sweden, where the histaminase activity of H. capsulatum had been studied for approximately a year. A physician developed excessive malaise with fever, and X rays disclosed lesions in the second and third intercostal spaces characteristic of bronchopneumonia. About 14 days before the onset of disease he had transferred H. capsulatum from test tubes to petri dishes.

Three days after the physician became ill, a laboratory technician developed a "running cold" and fever. X rays suggested bronchopneumonia. Investigation disclosed that she had scraped a culture from the petri dishes 4 days after the physician had inoculated them. A second physician and another laboratory technician developed chills and fever a month later with "bronchopneumonia." They had handled cultures of H. capsulatum approximately 14 days before their illnesses. Three other individuals on the laboratory staff had respiratory illness suggestive of bronchopneumonia. However, they were not admitted to the hospital.

All seven individuals converted from a negative to a positive histoplasmin skin test, but H. capsulatum was not isolated. Because the positive histoplasmin skin test incidence in eastern Sweden is 6%, and other laboratory personnel did not have positive skin tests, the authors concluded that these seven respiratory illnesses were histoplasmosis from laboratory exposure to the etiologic agent.

Raphael and Schwarz,[116] in their article on occupational hazards from fungi, mentioned that one of the authors contracted histoplasmosis in the laboratory at Cincinnati General Hospital. No details were given.

Salvin and Furcolow[123] reported three laboratory-acquired infections and one probable laboratory-acquired infection at the U.S. Public Health Field Station, Kansas City. A laboratory worker developed an influenza-like illness, and histoplasmosis was diagnosed from X rays and conversion from a negative to a positive histoplasmin skin test. A secretary working

in the Field Station laboratory developed a respiratory infection. Three weeks after the onset of illness her histoplasmin skin test converted from negative to positive. X rays revealed a pneumonic patch in the right third and fourth interspaces. Healing was slow, and the pneumonic patch disappeared a year after onset of illness. A janitor working in this Field Station laboratory developed an influenza-like illness. One month after onset of illness his histoplasmin skin test converted from negative to positive.

Before he reported for work in the U.S. Public Health Field Station, Kansas City, a physician had visited a cave in Arkansas where H. capsulatum was present. After working 34 days, he went to Colorado, where he was ill for a week. X rays showed a minimal pneumonic-type lesion in the right second interspace. His histoplasmin skin test was positive. There was no record of a previous skin test.

Dickie and Murphy[33] investigated 1. cases of laboratory-acquired histoplasmosis in the Department of Preventive Medicine, University of Wisconsin. Seventeen female students in medical technology transferred 4-week-old cultures of H. capsulatum and prepared microscopic mounts. The laboratory exercises were performed without an obvious break in technique. Approximately 2 weeks later, one of the students became ill. She reported to the Student Health Department with fever and malaise. Approximately 2 months later, tender, reddened areas characteristic of erythema nodosum appeared on both shins. A histoplasmin skin test was positive and a complement-fixing antibody titer was 1:2048. The remaining 16 students were skin-tested and found to be strongly positive. Four students had complement-fixing antibody titers of 1:256, 1:32, 1:16, and 1:8.

The 18th student was an Australian doing graduate work in agricultural bacteriology. Two months before the onset of illness, he transferred both Blastomyces dermatitidis and H. capsulatum cultures three or four times. X rays showed five nodular infiltrates characteristic of histoplasmosis. Diagnosis was established from a positive histoplasmin skin test and a rise in complement-fixing antibody titer to 1:512.

Loosli[91] recounted ten laboratory-acquired infections of histoplasmosis in the laboratory at the University of Chicago. Four of the infected individuals were hospitalized for 4 to 8 weeks. Although there was no evidence of pulmonary involvement in one case, H. capsulatum was isolated from the patient's blood during the 3rd week of illness. All ten infected individuals converted from a negative to a positive histoplasmin skin test. Loosli concluded that the experience in the laboratory at the University of Chicago emphasized the hazard of working in a routine way with the saprophytic phase of H. capsulatum.

Spicknall, Ryan, and Cain[135] collected data on three cases of laboratory-acquired histoplasmosis. The first infection occurred in a laboratory technician who worked with cultures of H. capsulatum. X rays revealed a

nodule in the right lung, which was removed by surgery. The pathologist observed small spherical bodies in the sections that he thought were H. capsulatum. A pathologist at another laboratory stated that the spherical bodies were not H. capsulatum, but he did not rule out histoplasmosis because the nodule was granulomatous. The patient converted from a negative to a strongly positive skin test with histoplasmin diluted 1:1000.

The second case was a physician who injected the heart valves of a dog with a yeast-phase culture of H. capsulatum and accidentally sprayed culture on his forehead. One week later, while performing the same operation on another dog, he sprayed culture into his right conjunctival sac. Six days after the second accident a soreness developed in his cervical region. Four days later edema of the palpebral conjunctiva and upper lid developed. The patient was treated with 5% sodium propionate ophthalmic drops six times daily. On admission to the hospital a histoplasmin skin test was negative, but a similar test 10 days later was positive.

The third case occurred in an engineer at the Environmental Health Center, U.S. Public Health Service, Cincinnati, Ohio. He did not work with H. capsulatum, but his office was on the floor below a laboratory where H. capsulatum was studied. Several times he had visited a classroom that had a common ventilation system with this laboratory. X-ray findings were negative on his admission to the hospital but later showed infiltration, possibly with cavitation, in the right upper lobe. The patient's upper right lobe was resected and the lung tissue was injected intraperitoneally into guinea pigs. Twenty days later H. capsulatum was recovered from the guinea pigs.

Vanselow, Davey, and Bocobo[146] reported two cases of laboratory-acquired histoplasmosis that occurred at the University of Michigan. A medical student who was engaged in a research project involving soil prepared soil suspensions and injected mice intraperitoneally. While caring for and observing the injected mice he transferred them periodically to new cages. Eight days later the student developed chills and fever and was admitted to the University Hospital. The histoplasmin skin test was positive on admission. X rays revealed scattered nodular densities compatible with histoplasmosis. Three weeks after admission to the hospital, another histoplasmin skin test was strongly positive and the complement-fixing antibody titer was 1:32. His titer continued to rise, and 2 months after discharge from the hospital his complement-fixing antibody titer was 1:256.

The other case was that of a physician who supervised the medical student but did not work with the soil suspensions. He "looked over the shoulder" of the student while this work was done. The physician had frequently been in the laboratory where the mice were inoculated and the animal room where they were maintained. He developed an influenza-like illness but did not enter the hospital. His histoplasmin skin test, which 2 years before had been negative, now was strongly positive. Histoplasmosis was confirmed by a 1:128 complement-fixing antibody titer.

Hartung and Salfelder[89] studied the circumstances surrounding a death from laboratory-acquired histoplasmosis. A mycologist, in preparing suspensions of soil from the Venezuelan Andes for intraperitoneal inoculation of mice made microscope mounts of H. capsulatum without protective measures. Twelve days before onset of illness, he and four other persons visited a cave and chicken coops. Eight days after onset of symptoms he converted from a negative to a positive histoplasmin skin test. X rays revealed no one primary center, but multiple infiltrates and bilateral hilus swelling were present. Blood taken on the 33rd day of illness had a complement-fixing antibody titer of 1:64. H. capsulatum was isolated from sputum. Fifty-one days after onset of illness the patient died. Microscopic examination of lung sections showed "caseous foci and granulomes in which numerous conidia, round or oval and clearly delineated, were seen." Exactly how this infection occurred is not clear, but this mycologist carried out many laboratory procedures with large amounts of H. capsulatum without protective measures. At first it was thought that the visit to the cave and chicken coops was the underlying cause; however, none of the individuals accompanying the mycologist became ill, and their histoplasmin skin tests were negative.

Hartung and Salfelder believed the patient was infected by inhaling elements of fungus cultures. They reasoned that finding multiple primary foci with localization in the vicinity of the bronchi and vessels and observing conidia in postmortem sections coincided with experiments on intratracheally injected animals.[113]

Murray and Howard[99,100] investigated laboratory-acquired histoplasmosis among students at the University of California Medical Center. One student was hospitalized with chest pains and fever. X rays revealed infiltrations in the right lower lobe and pericardial effusion. The histoplasmin skin test was positive. Precipitins were positive and the complement-fixing antibody titer was 1:256+. Five months after onset of illness a subcutaneous nodule developed over his right lower lateral chest. Although biopsies showed a caseating granulomatous lesion, H. capsulatum was not demonstrated.

Epidemiologic investigation showed that H. capsulatum had been used in a microbiology course 2 months before onset of symptoms. Sixty-six students prepared slides from infected mice and culture plates that were distributed throughout the laboratory. No overt accidents occurred. Data collected on 62 of the 66 students showed: (i) 26 had positive histoplasmin skin tests; (ii) 19 of the 26 students with positive skin tests had complement-fixing antibodies; (iii) nine of the 19 with complement-fixing antibodies had lesions revealed by chest X rays; and (iv) several of the class had reported to the Student Health Service with malaise, aches, chest pain, and cough. Of the 26 students with positive skin tests, X rays revealed multiple areas of calcification; these antedated the laboratory exposure in ten students; these ten also lived in known endemic areas.

The next two classes in microbiology worked with heat-killed H. capsulatum cultures. Histoplasmin skin testing demonstrated a significant difference. Where histoplasmin sensitivity in the class of 1963 was 41.9%, in the classes of 1964 and 1965 it was 10.1 and 11.1%, respectively.

Two years later a mycologist who worked in a different laboratory developed lesions characteristic of erythema nodosum on both legs. She worked with H. capsulatum and C. immitis cultures. Histoplasmosis was diagnosed by a positive skin test, pulmonary infiltration, and a complement-fixing antibody titer of 1:256+.

Tosh and co-workers[143] reported a laboratory-acquired histoplasmosis infection. During the autopsy of a patient who died of pulmonary histoplasmosis, an assistant punctured the dorsum of his gloved left hand with a scalpel. Ten days later an indolent ulcer developed. Microscopic examination of the exudate revealed yeast bodies. H. capsulatum was not isolated by culture, probably because medication had already been started. One month after the accident the histoplasmin skin test was positive. No preceding skin test was reported, but Tosh and co-workers stressed that the patient had recently moved into the area where histoplasmosis is endemic. Histoplasmosis was confirmed by a rise in complement-fixing antibodies of 1:32; 1 month later it was 1:16. Topical application of nystatin and amphotericin B ointments were used and the ulcer healed within several months.

Furcolow[54] reported three infections in personnel transporting air samples to the laboratory. No details of exposure were given, but two individuals wore industrial-type respirators.

Tesh and Schneidau[140] reported cutaneous histoplasmosis caused by self-inoculation. A laboratory worker accidentally inoculated his left thumb with a needle that contained blood from an infected bat. Thirteen days after the accident the thumb was tender; 6 days later an erythematous nodule developed at the inoculation site. The nodule was indurated and lymphangitis extended up the forearm. Histoplasmosis was confirmed by a conversion from negative to positive histoplasmin skin test, presence of complement-fixing antibodies, and demonstration of H. capsulatum on culture and histopathologic examination of the nodule.

C. OTHER OCCUPATIONALLY ACQUIRED CASES

Lehan and Furcolow[88] reviewed 41 epidemics of histoplasmosis. Raising chickens, cleaning cellars, exploring caves, working in soil—these were the origin of many infections. Two physicians and one nurse were infected while collection soil samples. It has been estimated that probably 30 million people in central United States have been infected with H. capsulatum.[91]

IV. BLASTOMYCOSIS

A. BACKGROUND

T.C. Gilchrist[58] published details of the first infection. After he had received the tissues of a patient from Philadelphia, he and Stokes[59] reported a second infection and described the diphasic forms of the fungus that they named Blastomyces dermatitidis.[60]

B. dermatitidis is a diphasic fungus found in the soil of North America.[38] The fungus grows slowly on solid media at room temperature. The colonies at first resemble a yeast but develop a white aerial mycelial mat that becomes tan to brown. Coremia may develop, giving the culture a prickly appearance. Microscopic examination reveals many spherical to oval conidia, 3 to 4μ in diameter, borne on short conidiophores, or spherical to pyriform conidia, 4 to 5μ in diameter, borne terminally.

At 37 C, growth is slow; yeast-like colonies develop that become waxy and wrinkled. Microscopic examination shows large spherical cells, 8 to 15μ in diameter, with refractile walls 0.5 to 0.75μ thick. B. dermatitidis reproduces by budding, suggesting a "double-contoured" appearance.[21]

B. CASE REPORTS OF LABORATORY-ACQUIRED BLASTOMYCOSIS

The first mention of a laboratory infection with B. dermatitidis was made by Evans.[43] A physician accidentally pricked the palmar surface of his left index finger with a needle while performing an autopsy on a patient who had died of systemic blastomycosis. One week later a small pustule appeared at the injury site. Pus was removed by incising the pustule, but the pustule reappeared several days later. About a month after the accident, the puncture site was red, swollen, and painful. The lesion was incised and 1 week later it was curetted. Microscopic examination revealed double-contoured, budding microorganisms identical to those recovered from the autopsied patient. One month later the saprophytic phase of B. dermatitidis was cultured from pus. Prognosis of the patient was not known until Wilson and co-workers[154] reported that the patient was Dr. Evans himself, and that after the infection had subsided, the finger was amputated at the metacarp phalangeal joint because of deformity.

Schwarz and Baum[124] reported two cases of primary cutaneous blastomycosis resulting from laboratory accidents. Very little information was given, and again Wilson and co-workers[154] supplemented the basic report with additional details and reported an additional laboratory infection. A pathologist who worked with fungi in 1927 noted an indolent abscess on his left wrist that persisted after evacuation.

Two weeks later he had enlarged lymph nodes. At the end of 1 month the primary lesion was a soft papule with central ulceration. B. dermatitidis was demonstrated by microscopic examination of the pus and by culture. Pus was injected into a mouse, and B. dermatitidis was demonstrated 5 weeks later. Treatment consisted of X-ray therapy and potassium iodide; the patient recovered in 4 months.

In 1950, a physician scratched his gloved left index finger with a scalpel while conducting an autopsy on a patient who died of systemic blastomycosis. The finger was cleansed with soap and water and treated with tincture of iodine. One month after the accident, a solitary, tender node developed in the left axilla. One week later, a papule appeared at the scratched area, from which B. dermatitidis was demonstrated in tissue and recovered by culture. The blastomycin skin test had converted from negative to positive. Treatment consisted of iodides, with recovery in 3 months.

In December 1952, an autopsy room attendant accidentally inoculated his left fifth finger with a needle while assisting at an autopsy of a case of disseminated blastomycosis. One week later a papule appeared at the inoculated site. A week after that the papule was incised. Swelling occurred in the next 2 weeks in the left epitrochlear region, which also was excised. Excision removed a swollen lymph node in the left axilla. B. dermatitidis was demonstrated in these tissues but could not be isolated on culture. Skin tests to a 1:100 dilution of blastomycin were 2+, and later 4+. No medication was given. Recovery was complete.

E.A. Benbrook[11] reported that a veterinarian engaged in diagnostic laboratory work died from blastomycosis. No details were given.

Harrell and Curtis[67,68] stated that in 1953 a graduate student cut his index finger picking up pieces of glass from a dropped culture of B. dermatitidis. About 14 days later a slight erythematous, nontender area of induration developed at the healed laceration site. This enlarged and eventually was excised. From the excised specimen, B. dermatitidis was isolated in culture and seen in histopathological examination.

Schwarz and Baum[124] skin-tested 58 nurses, attendants, and maids who were in direct contact with patients who had discharging sinuses, ulcerated skin lesions, and pulmonary blastomycosis. B. dermatitidis was isolated from dressings and bed clothes; nevertheless, skin tests were negative, and there was no evidence of transmission. This is consistent with the absence of evidence for man-to-man transmission.

J.E. Niederhuber* reported that a mycologist was injecting hamsters in a ventilated cabinet when he accidentally stuck the median side of his left middle finger on the needle. He applied pressure to the finger,

* Personal communication.

expressing blood, and then applied tincture of merthiolate and powdered amphotericin B. Two weeks later, a 3-mm slightly raised papule formed. Six days later, purulent material was oozing from a 15- by 15-mm lesion from which B. dermatitidis was identified in a potassium hydroxide preparation and later was isolated by culture.

Denton, DiSalvo, and Hirsch[31] reported that a laboratory assistant, who sterilized discarded B. dermatitidis cultures and washed glassware, complained on February 10, 1964, of pain just below her right knee. After 9 days the pain increased and she went to an orthopedic surgeon. X ray revealed no abnormalities. Ten days later she had chills and fever and her family physician prescribed antibiotics and bed rest. She returned to work for 8 days. On March 23, she was admitted to the hospital with a tumorous mass below her right knee. This was incised and B. dermatitidis was cultured and identified in stained sections from the purulent material. She was released from the hospital after 10 weeks of therapy with amphotericin B. Blastomycin skin tests converted from a negative to a positive. However, complement-fixation tests were negative. The authors believed that she inhaled microconidia, probably on 20 December 1963, when she removed cellophane tape from petri dishes that contained cultures of the saprophytic phase of B. dermatitidis.

V. SPOROTRICHOSIS

A. BACKGROUND

B.R. Schenck[123] reported isolating a previously unreported organism in pus from abscesses of a patient. Hektoen and Perkins[70] reported the second infection and named the causative fungus Sporothrix schenckii. DeBeurmann and Ramond[28] reported sporotrichosis in France. DeBeurmann and Gougerot[27] described five varieties. The terminology of pathogenic species was debated for years. However, only one pathogenic species is now recognized, Sporotrichum schenckii.[42]

S. schenckii is a diphasic fungus found in all parts of the world. The parasitic phase is found in tissue as yeast-like, spherical budding cells, 2 to 3μ in diameter, or fusiform budding cells, 1 to 2μ in diameter and 4 to 5μ in length. Asteroid bodies, round, single budding cells 5 to 10μ in diameter, may be found.[21,42] At 37 C on enriched blood media, similar fusiform, round, and budding cells are formed within the soft yeast-like growth.

The saprophytic phase grows in soil,[41] on timber,[14,38] and on plants,[12,63] and has been isolated from air.[38] On Sabouraud's agar at room temperature, growth is slow, with small, white colonies developing. Later the colony becomes moist, wrinkled, leathery, and folded; pigmentation varies from cream through brown to black. The branching, septate hyphae are 1 to 2μ in diameter. Conidia are formed on the lateral surface or in groups at the tip of the conidiophore. The conidia are pyriform, 2 to 4μ by 2 to 6μ.

B. CASE REPORTS OF LABORATORY-ACQUIRED SPOROTRICHOSIS

The first reported case of a laboratory infection with S. schenckii occurred in France.[45] On 4 March, while he was injecting rabbits with needle and syringe, part of the fungal suspension sprayed into Fava's eyes. Thirty minutes later he rinsed his eyes with 1:4000 solution of mercuric oxycyanide. On 15 March he had slight pain in the lower eyelid of his right eye. The next day the pain increased and a small pimple appeared. Eventually ulcerated nodules appeared from which S. schenckii was cultured. Both eyes were infected; the right at 11 days and the left at 15 days after the accident. Recovery was complete after 75 days of potassium iodide treatment.

Carougeau[18] reported that a veterinarian deeply scratched his left index finger while lancing a sporotrichotic subcutaneous abscess on a mule. The veterinarian cleansed the area with creosote. About 25 days later the injured area became inflamed, swollen, and painful. An ascendant lymphangitis developed and one axillary ganglion became swollen. Incising

the injured site produced blood-streaked pus. Lymphatic gummata developed. Carbolic solution baths and wet compresses applied to the area attenuated the lymphangitis in 2 weeks. The sore on the index finger was very slow in healing. Small purulent pustules that formed along the edges of the original injury healed after 3 months of treatment with phenol antiseptic bandages and tincture of iodine. Shortened forms of S. schenckii were demonstrated from pus of the man and the mule by microscopic examination.

Fielitz[48] reported his own laboratory infection, which resulted either from inoculating or dissecting animals or from agglutination experiments. In December, Dr. Fielitz abraded an area on the flexor side of his right forearm for experimental work with mollusk material. This area healed within 2 weeks. In March, a painful abscess approximately 0.5-cm wide developed on the flexor and radius side of the right forearm. The lymph glands were swollen. The diagnosis of sporotrichosis was confirmed by the isolation of S. schenckii from serous secretion and tissue scraped from the ulcer. Iodide treatment resulted in complete recovery 6 months later.

Jeanselme and Chevallier[76,77] reported that a laboratory attendant was bitten on the thumb by a rat that had been inoculated with S. schenckii. She cleansed the site with alcohol and a tincture of iodine. Several days after the bite an inflammatory reaction took place and a lesion appeared. The lesion was excised 18 days after the bite and pus, from which S. schenckii was isolated, was cultured. Potassium iodide treatment was started and 8 weeks after the accident the ulcerations diminished. However, 1 month later nodules appeared and 2 months later had migrated up both arms. A small amount of thick pus seeped from these nodules. Seven months after the accident the nodules disappeared, but iodide treatment was continued for several weeks.

Wilder and McCullough[150] wrote that one of the authors (McCullough) broke capillary pipettes containing S. schenckii approximately 8 to 10 inches from his face. In July 1913, both eyes became sore. The next day the eyelids were swollen and there were elevated areas resembling small ulcers. A smear made of exudate from an elevated area revealed only pus cells. The following day scrapings from the ulcers were cultured and 5 days later S. schenckii was isolated. Treatment consisted of potassium iodide, irrigation of the eye with oxycyanide of mercury, and tincture of iodine. Two weeks after the onset of symptoms, the ulcers had healed and the pain disappeared. However, the eyes remained swollen and red for 2 months before returning to normal.

Meyer[96] reported his own laboratory-acquired infection that occurred when he handled flasks of an equine strain of S. schenckii. In April 1913, he noticed a small ulcerated area on the third finger of his left hand. He treated the ulcer with mercuric chloride and iodine. Nevertheless, 5 days later his left arm was swollen with a tumor on the internal surface

of the humerus. A nodule developed on the carpal joint, and numerous nodules developed along the lymph vessels. Ten days later the ulcer on the hand was incised and S. schenckii was isolated from the pus on culture. Agglutinating and complement-fixing antibodies were present in sera. A skin test with killed spores of S. schenckii was positive. Iodine treatment was intensified and recovery was complete by the middle of July.

Norden[104] was infected in his own laboratory. In July 1949, he noticed a pimple on his left ring finger that became ulcerous in 8 to 10 days. Dr. Norden had injected rabbits with S. schenckii and, although the ulcer developed under a finger ring, he could recall no accident. Pus was streaked on media from which S. schenckii was isolated. A skin test with heat-killed S. schenckii was positive 18 days after the pimple was first noticed. Twenty-one days later, a subcutaneous nodule was found above the wrist, and 2 days after that a nodule was found near the elbow. Treatment consisted of potassium iodide, but the primary lesion reappeared when treatment stopped. Complete recovery occurred approximately 1 year after the onset of the disease.

VI. DERMATOPHYTOSES

A. BACKGROUND

The dermatophytoses are among the oldest infectious diseases of animals and man. Ajello,[2] in his excellent review of the dermatophytes, reported that evidence of human mycosis dates from 1837. Georg[56] reported the world-wide distribution of Microsporum gypseum in soil. Using the technique of Vanbreuseghem,[145] Trichophyton mentagrophytes has been isolated from soil in Europe and South America.[10] M. audouinii, M. gypseum, and T. tonsurans have been isolated from the air of mycology laboratories with opened petri dishes.[44,49] Gip[61] sampled the air with slit samplers in a mycological laboratory and did not recover fungi before work had started. After work was under way, the air was again sampled and 92 representative colonies of dermatophytes that had been handled that day in the laboratory were isolated. He took surface samples from an animal room that housed infected guinea pigs and recovered T. mentagrophytes from the floor.

B. CASE REPORTS OF LABORATORY-ACQUIRED DERMATOPHYTOSES

Parish and Craddock[107] described a T. gypseum epizootic infection in mice. The entire colony (2,500 mice) was sacrificed because more than 1,000 mice were infected. Three laboratory attendants who were in daily contact with the infected mice developed dermatophytosis. One attendant had a lesion on his finger, one had a lesion on his wrist, and one had lesions on his hands, wrists, and forehead. A boy who was a contact of the laboratory attendants developed a lesion on the back of his neck. Recovery was complete approximately 2 months after infection.

Scully and Kligman[126] reported that a pet shop owner developed erythematous plaques with pruritus on her neck and forearms. A monkey in the pet shop had scratched constantly at his coat, which was sparse and mangy. After recurrent episodes of dermatophytosis, the owner gave the monkey to a mycologist for study. The mycologist developed lesions on exposed portions of his body, as did his wife. M. audouinii was isolated from the monkey and the pet shop owner.

Booth[13] described the case of a laboratory technician who developed dermatophytic lesions on both hands. She handled white mice in her work and stated that many of the mice had "hair loss" areas. T. mentagrophytes was cultured from the vesicles on the technician's hands and from the mice.

Rowsell and Kennedy[121] reported a disease of the fur and skin of chinchillas in the colony at Ontario Veterinary College. Hair and skin from infected animals inoculated on Sabouraud's agar at 25 C yielded T. mentagrophytes. A similar dermatophyte was cultured from a laboratory technician 1 month after exposure to the infected animals.

LaTouche,[87] at the University of Leeds Medical Laboratory, recorded that 11 attendants were infected with T. mentagrophytes over a period of 5 years and 4 months. The cause of these infections was unknown. Later, a female laboratory attendant developed folliculitis on her right forearm that was diagnosed as T. mentagrophytes infection. Mycotic investigation revealed that the laboratory mice were infected with T. mentagrophytes.

Meyer[95] found that two technical assistants who handled guinea pigs were infected with T. mentagrophytes and had developed lesions on their fingers, thumbs, and forearms. Whether gloves were worn was not stated.

Dolan and co-workers[37] reported three dermatophytic infections with T. mentagrophytes. The first infection developed in an individual who injected 100 to 150 mice per day. A dense group of vesicles developed on the thumb, which later became scaly and eczematous. The second person injected mice intraperitoneally and orally and developed a similar lesion on the left forearm. The third person handled 80 to 100 rats each day. A vesicular lesion developed on the right forearm. In these three infections the organism was isolated from the lesions over a period of 6 weeks to 6 months. When animals were handled, personnel used a 2% cresol hand dip, but no gloves were worn. The wearing of sterile rubber gloves was initiated. No human infections occurred in the 8 months that followed.

Balabanoff[8] tabulated T. mentagrophytes infections occurring in scientific personnel. Although most infections were in breeders of experimental animals, there were three dermatophytic infections in laboratory technicians. No details were given about the type of work these technicians performed or how they were infected.

Kaffka and Rieth[79] described a laboratory infection with T. mentagrophytes that occurred at the School of Medicine and Hygiene, Hamburg, Germany. A technical assistant, in the course of his work in serology and clinical chemistry, handled rabbits that were infected with T. mentagrophytes. Dermatophytic lesions from which T. mentagrophytes was isolated developed on his face, neck, jaw, and hands.

Koch and Rieth[82] reported laboratory-acquired infections in seven institutes where 22 to 750 guinea pigs were housed. They proved that people who worked in the laboratory or took care of guinea pigs became infected with the same fungus as that infecting the guinea pig. Laboratory-acquired infections with either T. mentagrophytes or T. rubrum occurred in six of seven institutes, but the number of infected personnel or means by which they became infected were not reported.

Rieth and associates[116] noted two laboratory-acquired infections of T. mentagrophytes. A technical assistant injected mice with T. mentagrophytes. A dermatophytic lesion appeared on his thumb 1 week later. A mycological worker who assisted the first patient developed a dermatophytic lesion on the underside of the forearm.

Mackenzie[93] described T. mentagrophytes infections in mice. He suspected that the infection of two laboratory workers was caused by handling mice. He recovered a single colony of T. mentagrophytes with two agar settling plates. From nonsymtomatic mice, T. mentagrophytes was recovered both by swabbing and by allowing the animals to walk on culture media.

Sonck[132] had three human infections in his laboratory in Finland. T. mentagrophytes was isolated from patches on the ears of the rats and from the mice. A laboratory technician had similar infected patches on the back of her left index finger. These patches were treated with antibiotics but they continued to enlarge. She was admitted to the hospital, where T. mentagrophytes was isolated. Two animal caretakers also developed lesions on the arms. In these two infections T. mentagrophytes also was isolated.

Lyman and Rogers[92] treated six children who developed dermatophytic lesions 5 days after purchase of a kitten from a local kennel. M. canis was isolated from these lesions. A health department investigator was scratched by this kitten. Two lesions developed at the site of the cat scratch 2 weeks later. M. canis also was isolated from the lesions. Another kitten purchased from the same kennel was responsible for dermatophytosis in eight children of another family. An investigator also developed the infection. M. canis was isolated from the kittens. The kennel was closed because it was unlicensed, and a humane society worker who removed the kittens became infected with M. canis.

Davies and Shewell[28] reported that six of 13 laboratory workers who handled mice infected with T. mentagrophytes developed dermatophytosis. Although less than 1% of the mice showed overt dermatophytosis, random sampling of 50 mice revealed that more than 90% of the mice were carriers of T. mentagrophytes. T. mentagrophytes was isolated from the air with slit-type air samplers.

Alteras[6] reported 40 dermatophytoses acquired from laboratory animals. During a 10-year period in Romania, 20 laboratory workers, 18 animal attendants, and two physicians were infected. The responsible fungi were T. mentagrophytes, T. rubrum, M. audouinii, and M. canis from hamsters, guinea pigs, rats, mice, rabbits, dogs, and a cat. How the infections were incurred is not explained.

Cetin, Tahsinoglu, and Volkan[18] reported that a bacteriologist who examined mice infected with T. mentagrophytes developed a draining lesion on his elbow. Diagnosis was made by recovery of T. mentagrophytes from the lesion. Treatment consisted of topical applications of iodine-alcohol and nystatin, with recovery in 7 days.

VII. DISCUSSION AND CONCLUSIONS

This literature survey reveals more than 288 laboratory-acquired mycoses. Definite figures cannot be given because various authors report in their tables only that infections did occur. Among the 288 cases, only 30 known accidents occurred that resulted in 36 known and four probable laboratory-acquired mycoses (Table 1).

TABLE 1. KNOWN ACCIDENTS OR INCIDENTS CAUSING LABORATORY-ACQUIRED MYCOSES

Accident or Incident	Number	People Infected
Aerosol created while grinding	1	1
Aerosol from needle and syringe	3	3
Animal bite or scratch	2	2
Auto-inoculation with needle and syringe	7	7
Blower of safety cabinet turned off	1	1
Broken pipettes	1	1
Cotton plug dropped from culture	2	2(1)[a]
Dropped culture	1	1
Improper autoclaving	1	7
Laceration from broken glassware	1	1
Laceration incurred during autopsy	1	1
Opened petri dish	2	2(3)
Opened safety cabinet	1	1
Ruptured glove on safety cabinet	1	1
Sniffed culture	1	1
Splash of culture (not needle and syringe)	1	1
Totals	30	36(4)

a. Probable infections in parentheses.

Most laboratory infections occur through respiratory exposure. Furcolow[53] stated that, of all pathogens, the fungi are perhaps the most ideally suited to cause airborne infection. Fungi produce an enormous number of spores that are extremely hardy and easily airborne, and their size enables them to reach the alveolar spaces when inhaled. In a number of mycoses reported here, the workers were wearing gauze masks. The usual

hospital gauze mask has been evaluated as being 16 to 20% efficient in removing airborne particles 1 to 5μ in diameter.[65] Respirators are available that have a filtering efficiency of 99+%. However, when the aerosol is so concentrated that it is visible, as stated by some infected workers, then confinement of the work in a ventilated hood or cabinet appears to be the solution to the problem. Keeney[80] designed a protective cabinet to handle C. immitis. Many other ventilated cabinets have been described.[22,64]

Well designed laboratories with proper ventilation, good equipment, and the use of safety devices are certainly essential to reduce laboratory infections. Laboratory personnel have been alerted and they know how hazardous certain microorganisms or procedures might be, but as Albrecht[5] stated, "Protective devices are often regarded as exaggerated and superfluous and it is interpreted as fear, timidity, or even cowardice to utilize them." The martyr-to-science attitude—"Have the disease and get it over with"[147]—has become less common because of the cost of occupational illnesses, the legal complications involved, and the moral obligations of an employer to his employees.

It might be helpful to know the type of personnel who were infected and what type of work was performed (Tables 2 and 3). Apparently all personnel entering an infectious disease laboratory are subject to some risk of infection, and several types of work produce conditions that may lead to infections. Obviously, those surveys and studies of laboratory-acquired infections reported in the literature account for only a fraction of the actual number of infections. There is no standard reporting system available. Some laboratory directors do not wish to publicize their laboratory infections. Clinically unapparent or slight infections do not result in lost time and consequently are not diagnosed or recorded.

A second factor increasing the difficulty of evaluating infectious disease laboratory hazards is the fact that most laboratory-acquired infections fall into the "cause-unknown" category. Surveys generally show that only 16 to 30% of the infections can be attributed to a known accident or to a definite technique, procedure, or piece of equipment. Many standard procedures used in the mycologic laboratory produce aerosols. The manipulation of pathogenic fungal cells or spores in the open air of the laboratory constitutes a risk for the worker, his colleagues, and personnel in the surrounding areas.

Because many systemic mycotic infections may be subclinical and many laboratories do not maintain a periodic skin testing program, it is probable that many laboratory-acquired infections are not discovered. The systemic mycoses must be treated as high-risk microorganisms. All laboratory personnel should be skin-tested before their initial exposure, and a program of periodically repeated skin tests in negative personnel should be established. An acute febrile influenza-like illness in a person working with these fungi should be investigated to rule out the possibility of mycotic infection.

TABLE 2. OCCUPATION OF INFECTED PERSONNEL

Occupation	Fungus					Total
	C. immitis	*H. capsulatum*	*B. dermatitidis*	*S. schenckii*	Dermatophytes	
Animal caretaker	1				20	21
Autopsy room assistant		1	1			2
Dishwasher	4		1			5
Engineer		1				1
Janitor		1				1
Laboratory staff		6				6
Laboratory worker	11	29		1	51	92
Medical technician	33	3			6	42
Microbiologist	3	3	1		2	9
Military laboratory officer	4(1)					4(1)[a]
Mortician	1					1
Nurse		1				1
Physician	14(4)	8	3	5	2	32(4)
Professor	1					1
Public health investigator					3	3
Research assistant	3					3
Research chemist	1					1
Secretary	5	1				6
Student	16	27	1			44
Veterinarian			1	1		2
Unknown	11					11
Total	108(5)	81	8	7	84	288(5)

a. Probable infections in parentheses.

TABLE 3. WORK PERFORMED BY INFECTED INDIVIDUALS

Procedure or Circumstance	Fungus					Total
	C. immitis	H. capsulatum	B. dermatitidis	S. schenckii	Dermatophytes	
Autopsying	1	1	3	1		6
Collecting soil samples		3				3
Culturing	39(1)	7	1	1		48(1)[a]
Culturing and handling animals	1			1	36	38
Culturing and inoculating animals	2					2
Did not work with fungus, but in same room	6	1				7
Diluting with needle and syringe	1					1
Dishwashing	9		1			10
Embalming	1					1
Grinding cultures	2					2
Inoculating animals with needle and syringe	3	2	1	2	4	12
Inoculating and dissecting animals				1		1
Janitor		1				1
Making media	1					1
Preparing slides from culture	1	27				28
Preparing soil suspensions and inoculating animals		2				2
Preparing tissues	1					1
Personnel working 2nd floor above mycology laboratory	5	1				6
Personnel working 3rd floor above mycology laboratory	18					18
Picking up broken glass of culture			1			1
Pipetting				1		1
Scraping culture		1				1
Secretarial work in mycology department	3	1				4
Visitor	4					4
Weighing dried spores	2					2
Unknown	8(4)	34	1		44	87(4)
Total	108(5)	81	8	7	84	288(5)

a. Probable infections in parentheses.

Safety in the laboratory can be established by "people" and by "things." Well trained workers who have a conscientious attitude toward safety and who accept their safety responsibilities in the same way that they accept and carry out their other responsibilities will go a long way toward making the infectious disease laboratory a safe place to work. However, this alone is not always enough, as has been thoroughly proved by the experience with Coccidioides immitis at Stanford University. Good building design, good equipment, and the proper safety devices are the "things" needed to create a safe laboratory. Of all the safety equipment, the ventilated cabinet, properly designed, operated, and used, will provide the most effective biological safety.

LITERATURE CITED

1. Ajello, L. 1956. Histoplasma capsulatum: A review of its background. U.S. Public Health Monograph 39:57-60.

2. Ajello, L. 1962. Present day concepts of the dermatophytes. Mycopathol. Mycol. Appl. 17:315-324.

3. Ajello, L.; Maddy, K.; Crecelius, G.; Hugenholtz, P.G.; Hall, L.B. 1965. Recovery of Coccidioides immitis from the air. Sabouraudia 4:92-95.

4. Albert, B.L.; Sellers, T.F. 1963. Coccidioidomycosis from fomites: Report of a case and review of the literature. Arch. Intern. Med. 112:253-261.

5. Albrecht, J. 1965. Laboratoriumsinfektionen. Deut. Med. Wochensch. 37:1637-1642.

6. Alteras, I. 1965. Human dermatophyte infections from laboratory animals. Sabouraudia 4:143-145.

7. Baker, E.E.; Mrak, E.M.; Smith, C.E. 1943. The morphology, taxonomy, and distribution of Coccidioides immitis Rixford and Gilchrist 1896. Farlowia 1:199-244.

8. Balabanoff, V.A. 1958. Der professionell Charakter mancher Dermatomykosen. Berufsdermatosen 6:8-31.

9. Bass, H.E.; Schomer, A.; Berke, R. 1949. Question of contagion in coccidioidomycosis: Study of contacts. Amer. Rev. Tuberc. 59:632-635.

10. Baxter, M. 1966. Isolation of Trichophyton mentagrophytes from British soil. Sabouraudia 4:207-209.

11. Benbrook, E.A. 1952. Cited by Ramsey, F.K.; Carter, G.R. 1952. Canine blastomycosis in the United States. J. Amer. Vet. Med. Ass. 120:93-98.

12. Benham, R.W.; Kesten, B. 1932. Sporotrichosis: Its transmission to plants and animals. J. Infect. Dis. 50:437-458.

13. Booth, B.H. 1952. Mouse ringworm. Arch. Dermatol. Syphilol. 66:65-69.

14. Brown, R.; Weintroub, D.; Simpson, M.W. 1947. Timber as a source of sporotrichosis infection, p. 5-13. In Sporotrichosis infection on mines of the Witwatersrand: A symposium. Proc. Transvaal Mine Med. Officers' Ass., Transvaal Chamber of Mines, Johannesburg.

15. Bush, J.D. 1943. Coccidioidomycosis. J. Med. Ass. Alabama 13: 159-166.

16. Carougeau, M. 1909. Premier cas Africain de sporotrichose de deBeurmann: Transmission de la sporotrichose du mulet a l'homme. Bull. Mem. Soc. Med. Hop. (Paris) 28:507-510.

17. Castleberry, M.W.; Converse, J.L.; Del Favero, J.E. 1963. Coccidioidomycosis transmission to infant monkey from its mother. Arch. Pathol. 75:459-461.

18. Cetin, E.T.; Tahsinoglu, M.; Volkan, S. 1965. Epizootic of Trichophyton mentagrophytes (interdigitale) in white mice. Pathol. Microbiol. 28:839-846.

19. Christie, A.; Peterson, J.C. 1945. Pulmonary calcification in negative reactors to tuberculin. Amer. J. Publ. Health 35:1131-1147.

20. Conant, N.F. 1955. Development of a method for immunizing man against coccidioidomycosis, Third Quarterly Progress Report. Contract DA-18-064-CML-2563, Duke University, Durham, N.C. Available from DDC, AD 121 600.

21. Conant, N.F.; Smith, D.T.; Baker, R.D.; Callaway, J.L.; Martin, D.S. 1954. Manual of clinical mycology. 2nd ed. W.B. Saunders Co., Philadelphia, Pennsylvania. 456 p.

22. Couling, C.W.; Rees, R.J.W. 1959. A protective cabinet for the postmortem examination of infected animals. J. Hyg. 57:407-409.

23. Dozad, G.; Furcolow, M.L. 1953. Laboratory studies of Histoplasma capsulatum: II. Size of spores. J. Infect. Dis. 92:77-84.

24. Darling, S.T. 1906. A protozoon general infection producing pseudotubercles in the lungs and focal necrosis in the liver, spleen, and lymph nodes. J. Amer. Med. Ass. 46:1283-1285.

25. Darling, S.T. 1908. Histoplasmosis: A fatal infectious disease resembling kala-azar found among natives of tropical America. Arch. Intern. Med. 2:107-123.

26. Davies, R.R.; Shewell, J. 1964. Control of mouse ringworm. Nature 202:406-407

27. DeBeurmann, L.; Gougerot, H. 1912. Les sporotrichoses. Librairie Felix Alcan, Paris. 852 p.

28. DeBeurmann, L.; Ramond, L. 1903. Abces sous-cutanes multiples d'origine mycosique. Ann. Dermatol. Syphilol. (Paris) 4:678-685.

29. DeMonbreun, W.A. 1934. The cultivation and cultural characteristics of Darling's Histoplasma capsulatum. Amer. J. Trop. Med. 14:93-125.

30. DeMonbreun, W.A. 1939. The dog as a natural host for Histoplasma capsulatum: Report of a case of histoplasmosis in the animal. Amer. J. Trop. Med. 19:565-588.

31. Denton, J.F.; DiSalvo, A.F.; Hirsch, M.L. 1967. Laboratory-acquired North American blastomycosis. J. Amer. Med. Ass. 119:935-936.

32. Denton, J.F.; McDonough, E.S.; Ajello, L.; Ausherman, R.J. 1961. Isolation of Blastomyces dermatitidis from soil. Science 133:1126-1127.

33. Dickie, H.A.; Murphy, M.E. 1955. Laboratory infection with Histoplasma capsulatum. Amer. Rev. Tuberc. 72:690-692.

34. Dickson, E.C. 1937. Coccidioides infection: Part I. Arch. Intern. Med. 59:1029-1044.

35. Dickson, E.C. 1937. "Valley fever" of the San Joaquin Valley and fungus coccidioides. Calif. Western Med. 47:151-155.

36. Dickson, E.C.; Gifford, M.A. 1938. Coccidioides infection (coccidioidomycosis): II. The primary type of infection. Arch. Intern. Med. 62:853-871.

37. Dolan, M.M.; Kligman, A.M.; Kobylinski, P.G.; Motsavage, M.A. 1958. Ringworm epizootics in laboratory mice and rats: Experimental and accidental transmission of infection. J. Invest. Dermatol. 30:23-25.

38. DuToit, C.J. 1942. Sporotrichosis on the Witwatersrand. Proc. Transvaal Mine Med. Officers' Ass. 22:111-127.

39. Eckmann, B.H.; Schaefer, G.L.; Huppert, M. 1964. Bedside inter-human transmission of coccidioidomycosis via growth on fomites. Amer. Rev. Resp. Dis. 89:175-185.

40. Emmons, C.W. 1949. Isolation of Histoplasma capsulatum from soil. Public Health Rep. 64:892-896.

41. Emmons, C.W. 1950. The natural occurrence in animals and soil of fungi which cause disease in man. Presented at the 7th International Botanical Congress, Stockholm, Sweden.

42. Emmons, C.W.; Binford, C.H.; Utz, J.P. 1963. Medical mycology. Lea & Febiger, Philadelphia, Pennsylvania. 380 p.

43. Evans, N. 1903. A clinical report of a case of blastomycosis of the skin from accidental inoculation. J. Amer. Med. Ass. 40:1172-1175.

44. Evolceanu, R.; Donciu, G. 1963. Prezenta sporilor de dermatofiti in atmosfera laboratoarelor. Dermato-Venereol. 8:49-54.

45. Fava, A. 1909. Un cas de sporotrichose conjonctivale et palpebrale primitiv es. Ann. Ocul. (Paris) 141:338-343.

46. Fielitz, H. 1910. Ueber eine Laboratoriumsinfektion mit dem Sporotrichum de Beurmanni. Centralbl. Bakteriol. Parasitenk. Abt. I Orig. 55:361-370.

47. Fiese, M.J. 1958. Coccidioidomycosis. Charles C. Thomas, Springfield, Illinois. 253 p.

48. Fiese, M.J.; Cheu, S.; Sorensen, R.H. 1955. Mycelial forms of Coccidioides immitis in sputum and tissues of the human host. Ann. Intern. Med. 43:255-270.

49. Friedman, L.; Derbes, V.J.; Hodges, E.P.; Sinski, J.T. 1960. The isolation of dermatophytes from the air. J. Invest. Dermatol. 35:3-5.

50. Friedman, L.; Smith, C.E.; Pappagianis, D.; Berman, R.J. 1956. Survival of Coccidioides immitis under controlled conditions of temperature and humidity. Amer. J. Public Health 46:1317-1324.

51. Furcolow, M.L. 1949. Development of calcification in pulmonary lesions associated with sensitivity to histoplasmin. Public Health Rep. 64:1363-1393.

52. Furcolow, M.L. 1950. Further observations on histoplasmosis: Mycology and bacteriology. Public Health Rep. 65:965-994.

53. Furcolow, M.L. 1961. Airborne histoplasmosis. Bacteriol. Rev. 25:301-309.

54. Furcolow, M.L. 1965. Environmental aspects of histoplasmosis. Arch. Environ. Health 10:4-10.

55. Furcolow, M.L.; Guntheroth, W.G.; Willis, M.J. 1952. The frequency of laboratory infections with Histoplasma capsulatum: Their clinical and X-ray characteristics. J. Lab. Clin. Med. 40:182-185.

56. Georg, L.K. 1960. Animal ringworm in public health: Diagnosis and nature. Public Health Serv. Publ. 727, U.S. Government Printing Office, Washington, D.C. 61 p.

57. Georg, L.K. 1960. Epidemiology of the dermatophytoses, sources of infection, modes of transmission, and epidemicity. Ann. N.Y. Acad. Sci. 89:69-77.

58. Gilchrist, T.C. 1896. A case of blastomycetic dermatitis in man. Johns Hopkins Hosp. Rep. 1:269-291.

59. Gilchrist, T.C.; Stokes, W.R. 1896. The presence of an Oidium in the tissues of a case of pseudo-lupus vulgaris: Preliminary report. Bull. Johns Hopkins Hosp. 7:129-133.

60. Gilchrist, T.C.; Stokes, W.R. 1898. A case of pseudo-lupus vulgaris caused by a Blastomyces. J. Exp. Med. 3:53-78.

61. Gip, L. 1966. Investigation of the occurrence of dermatophytes on the floor and in the air of indoor environments. Acta Dermato-Venereol. 46:Suppl. 58:1-54.

62. Gonzalez-Ochoa, A. 1949. Coccidioidomycosis: Algunos conceptos actuales del padecimiento con especial mencion del problema Mexicano. Prensa Med. Mex. 14:246-252.

63. Gougerot, H.; DeBeurmann, L. 1908. Decouverte du Sporotrichum beurmanni dans la nature. Bull. Mem. Soc. Med. Hop. (Paris) 26:733-738.

64. Gremillion, G.G. 1960. The use of bacteria-tight cabinets in the infectious disease laboratory, p. 171-182. In Proc. 2nd Symp. Gnotobiotic Technol., 1959. Univ. Notre Dame Press, Notre Dame, Indiana.

65. Guyton, H.G.; Buchanan, L.M.; Lense, F.T. 1956. Evaluation of respiratory protection of contagion masks. Appl. Microbiol. 4:141-143.

66. Hansmann, G.H.; Schenken, J.R. 1934. A unique infection in man caused by a new yeast-like organism, a pathogenic member of the genus Sepedonium. Amer. J. Pathol. 10:731-738.

67. Harrell, E.R. 1964. The known and the unknown of the occupational mycoses, p. 176-178. In Occupational diseases acquired from animals. Continued Education Series No. 124, Univ. Mich. School Public Health, Ann Arbor, Michigan.

68. Harrell, E.R.; Curtis, A.C. 1959. North American blastomycosis. Amer. J. Med. 27:750-766.

69. Hartung, M.; Salfelder, K. 1962. Histoplasmose mit todlichem Ausgang als Berufserkrankung bei einem Mykologen. Arch. Gewerbepathol. Gewerbehyg. 19:270-289.

70. Hektoen, L.; Perkins, C.F. 1900. Refractory subcutaneous abscesses caused by Sporothrix schenckii: A new pathogenic fungus. J. Exp. Med. 5:77-89.

71. Helmbright, A.L.; Larsh, H.W. 1952. Size of spores of Histoplasma capsulatum. Proc. Soc. Exp. Biol. Med. 81:550-551.

72. Hoggan, M.D.; Ransom, J.P.; Pappagianis, D.; Danald, G.E.; Bell, A.D. 1956. Isolation of Coccidioides immitis from the air. Stanford Med. Bull. 14:190.

73. Huppert, M. 1957. A technique for the safe handling of Coccidioides immitis cultures. J. Lab. Clin. Med. 50:158-164.

74. Ibach, M.J.; Larsh, H.W.; Furcolow, M.L. 1954. Isolation of H. capsulatum from the air. Science 119:71.

75. Izzo, R.A.; Bonfiglioli, H.; Martinez, H. 1951. Primoinfeccion pulmonar de laboratorio producida por Coccidioides immitis. Publ. Centro Invest. Tisiol. (Buenos Aires) 15:79-91.

76. Jeanselme, E.; Chevallier, P. 1910. Chancres sporotrichosiques des doigts produits par la morsure d'un rat inocule de sporotrichose. Bull. Mem. Soc. Med. Hop. (Paris) 30:176-178.

77. Jeanselme, E.; Chevallier, P. 1911. Transmission de la sporotrichose a l'homme par les morsures d'un rat blanc inocule avec une nouvelle variete de Sporotrichum: Lymphangite gommeuse ascendante. Bull. Mem. Soc. Med. Hop. (Paris) 31:287-301.

78. Johnson, J.E.; Perry, J.E.; Fekety, F.R.; Kadull, P.J.; Cluff, L.E. 1964. Laboratory-acquired coccidioidomycosis: A report of 210 cases. Ann. Intern. Med. 60:941-956.

79. Kaffka, A.; Rieth, H. 1958. Laboratoriumstiere als Ursache einer Berufsdermatomykose und Massnahmen zur Verhutung weiterer Pilzinfektionen. Zentralbl. Bakteriol. Parasitenk. Abt. I Orig. 171:319-321.

80. Keeney, E.L. 1946. A protective cabinet for investigators studying Coccidioides immitis and other infectious fungi. Bull. Johns Hopkins Hosp. 78:113-118.

81. Klutsch, K.; Hummer, N.; Braun, H.; Heidland, A. 1965. Zur Klinik der Coccidioidomykose. Deut. Med. Wochensch. 90:1498-1501.

82. Koch, H.; Rieth, H. 1958. Endemische Trichophytie bei Meerschweinchen. Arch. Klin. Exp. Dermatol. 205:577-585.

83. Kruse, R.H. 1962. Potential aerogenic laboratory hazards of Coccidioides immitis. Amer. J. Clin. Pathol. 37:150-158.

84. Kruse, R.H.; Wedum, A.G. 1965. Recovery of specific microorganisms from urine and feces of infected animals, (Miscellaneous Publication 12). Industrial Health and Safety Division, Fort Detrick, Frederick, Maryland. 53 p.

85. Kruse, R.H.; Green, T.D.; Leeder, W.D. 1967. Infection of control monkeys with Coccidioides immitis by caging with inoculated monkeys, p. 387-395. In L. Ajello (ed.) Coccidioidomycosis. (Proceedings of Second Coccidioidomycosis Symposium, Phoenix, Arizona, December 8-10, 1965.) University of Arizona Press, Tucson, Arizona.

86. Kruse, R.H.; Green, T.D.; Chambers, R.C.; Jones, M.W. 1964. Disinfection of aerosolized pathogenic fungi on laboratory surfaces: II. Culture phase. Appl. Microbiol. 12:155-160.

87. LaTouche, C.J. 1957. Ringworm in laboratory mice, p. 279-282. In A.N. Worden and W. Lane-Peter (ed.) The UFAW handbook on the care and management of laboratory animals. 2nd ed. Universities Federation for Animal Welfare, London.

88. Lehan, P.H.; Furcolow, M.L. 1957. Epidemic histoplasmosis. J. Chron. Dis. 5:489-503.

89. Levine, H.B. 1960. Cited by Chatigny, M.A. 1961. Protection against infection in the microbiological laboratory: Devices and procedures, p. 131-192. In W.W. Umbreit (ed.) Advances in applied microbiology. Vol. 3. Academic Press, New York.

90. Looney, J.M.; Stein, T. 1950. Coccidioidomycosis. New Engl. J. Med. 242:77-82.

91. Loosli, C.G. 1955. Histoplasmosis: Some clinical, epidemiological, and laboratory aspects. Med. Clin. N. Amer. 39:171-200.

92. Lyman, E.D.; Rogers, E.A. 1963. Microsporum canis - Nebraska. Morbidity and Mortality 12:378-379.

93. Mackenzie, D.W.R. 1961. Trichophyton mentagrophytes in mice: Infections of humans and incidence amongst laboratory animals. Sabouraudia 1:178-182.

94. MacNeal, W.J.; Hjelm, C.E. 1913. Note on a mold Coccidioides immitis, found in a case of generalized infection in man. J. Amer. Med. Ass. 61:2044.

95. Meyer, G. 1957. Uber zwei Laborinfektionen mit Trichophyton mentagrophytes, ausgehend von spontan erkrankten Meerschweinchen. Mykosen (Berlin) 1:70-73.

96. Meyer, K.F. 1915. The relationship of animal to human sporotrichosis: Studies on American sporotrichosis III. J. Amer. Med. Ass. 65:579-585.

97. Meyer, K.F.; Quan, S.F.; Larson, A. 1948. Prophylactic immunization and specific therapy of experimental plague. Amer. Rev. Tuberc. 57: 312-321.

98. Morris, R.T. 1913. A case of systemic blastomycosis. J. Amer. Med. Ass. 61:2043-2044.

99. Murray, J.F.; Howard, D.H. 1963. Observations on a laboratory epidemic of histoplasmosis. Amer. Rev. Resp. Dis. 88:106.

100. Murray, J.F.; Howard, D.H. 1964. Laboratory-acquired histoplasmosis. Amer. Rev. Resp. Dis. 89:631-640.

101. Nabarro, J.D.N. 1948. Primary pulmonary coccidioidomycosis: Case of laboratory infection in England. Lancet 1:982-984.

102. Negroni, P. 1965. Histoplasmosis: Diagnosis and treatment. Charles C. Thomas, Springfield, Illinois, 190 p.

103. Nilzen, A.; Paldrok, H. 1953. A laboratory infection caused by Histoplasma capsulatum. Acta Dermato-Venerol. 33:329-341.

104. Norden, A. 1951. Sporotrichosis: Clinical and laboratory features and a serologic study in experimental animals and humans. Acta Pathol. Microbiol. Scand. Suppl. 89:3-119.

105. Overholt, E.L.; Hornick, R.B. 1964. Primary cutaneous coccidioidomycosis. Arch. Intern. Med. 114:149-153.

106. Palmer, C.E. 1945. Nontuberculous pulmonary calcification and sensitivity to histoplasmin. Public Health Rep. 60:513-520.

107. Parish, H.J.; Craddock, S. 1931. A ringworm epizootic in mice. Brit. J. Exp. Pathol. 12:209-212.

108. Phillips, G.B. 1965. Causal factors in microbiological laboratory accidents and infections, (Miscellaneous Publication 2). Industrial Health and Safety Division, Fort Detrick, Frederick, Maryland. 251 p.

109. Pike, R.M.; Sulkin, S.E.; Schulze, M.L. 1965. Continuing importance of laboratory-acquired infections. Amer. J. Public Health 55:190-199.

110. Pine, L. 1960. Morphological and physiological characteristics of Histoplasma capsulatum, p. 40-75. In H.C. Sweany (ed.) Histoplasmosis. Charles C. Thomas, Springfield, Illinois.

111. Posadas, A. 1892. Ensayo anatomo-pathologico sobre una neoplasia considerada coma micosis fungoidea. Ann. Circ. Med. Argent. 15:481-497.

112. Posadas, A. 1892. Un nuevo caso de micosis fungoidea con psorospermias. Ann. Circ. Med. Argent. 15:585-597.

113. Procknow, J.J.; Page, M.I.; Loosli, C.G. 1960. Early pathogenesis of experimental histoplasmosis. Arch. Pathol. 69:413-426.

114. Puckett, T.F. 1953. Pulmonary histoplasmosis: Study of 21 cases with identification of H. capsulatum in resected lesions. Amer. Rev. Tuberc. 67:453-476.

115. Raphael, S.S.; Schwarz, J. 1953. Occupational hazards from fungi causing deep mycoses. Amer. Med. Ass. Arch. Ind. Hyg. Occup. Med. 8:154-165.

116. Rieth, H.; Schirren, C.; Al-Fiki, A.Y.; Ito, K. 1960. Beziehungen zwischen humanen und animalen Dermatomykosen: III. Direkte und Indirekte Ubertragung von Mause-Trichophytie auf Menschen. Bull. Pharm. Res. Inst. Osaka-Takatsuki 25:15-18.

117. Riley, W.A.; Watson, C.J. 1926. Histoplasmosis of Darling with report of a case originating in Minnesota. Amer. J. Trop. Med. 6:271-282.

118. Rixford, E. 1894. A case of protozoic dermatitis. Occidental Med. Times 8:704-707.

119. Rixford, E.; Gilchrist, T.C. 1896. Two cases of protozoan (coccidioidal) infection of the skin and other organs. Johns Hopkins Hosp. Rep. 1:209-268.

120. Rowsell, H.C. 1963. Mycotic infections of animals transmissible to man. Amer. J. Med. Sci. 245:117-128.

121. Rowsell, H.C.; Kennedy, A.H. 1954. A dermatophyte infection in chinchillas transmitted to man. Can. J. Public Health 45:31.

122. Salvin, S.B.; Furcolow, M.L. 1954. Precipitins in human histoplasmosis. J. Lab. Clin. Med. 43:259-274.

123. Schenck, B.R. 1898. On refractory subcutaneous abscesses caused by a fungus possibly related to the sporotricha. Bull. Johns Hopkins Hosp. 9:286-290.

124. Schwarz, J.; Baum, G.L. 1951. Blastomycosis. Amer. J. Clin. Pathol. 21:999-1029.

125. Schwarz, J.; Baum, G.L. 1957. The history of histoplasmosis, 1906 to 1956. New Engl. J. Med. 256:253-258.

126. Scully, J.P.; Kligman, A.M. 1951. Coincident infection of a human and an anthropoid with Microsporum audouini: Report of a case. AMA Arch. Dermatol. Syphilol. 64:495-498.

127. Sinski, J.T.; Kadull, P.J. 1965. Coccidioidin retest reaction: Observations of tests on a coccidioidin-sensitive person. Calif. Med. 103:424-426.

128. Smith, C.E. 1940. Epidemiology of acute coccidioidomycosis with erythema nodosum ("San Joaquin" or "Valley Fever"). Amer. J. Public Health 30:600-611.

129. Smith, C.E. 1950. The hazard of acquiring mycotic infections in the laboratory. Presented at 78th Ann. Meeting Public Health Ass., St. Louis, Missouri.

130. Smith, C.E.; Whiting, E.G.; Baker, E.E.; Rosenberger, H.G.; Beard, R.R.; Saito, M.T. 1948. The use of coccidioidin. Amer. Rev. Tuberc. 57:330-360.

131. Smith, D.T.; Harrell, E.R., Jr. 1948. Fatal coccidioidomycosis: A case of laboratory infection. Amer. Rev. Tuberc. 57:368-374.

132. Sonck, C.E. 1961. Laboratoriumsinfektion durch hautpathogene Pilze in Finnland. Z. Haut. Geschlechtskrankh. 31:117-122.

133. Sorensen, R.H. 1964. Survival characteristics of mycelia and spherules of Coccidioides immitis in a simulated natural environment. Amer. J. Hyg. 80:275-285.

134. Sorensen, R.H.; Cheu, S. 1964. Accidental cutaneous coccidioidal infection in an immune individual: A case of an exogenous reinfection. Calif. Med. 100:44-47.

135. Spicknall, C.G.; Ryan, R.W.; Cain, A. 1956. Laboratory-acquired histoplasmosis. New Engl. J. Med. 254:210-214.

136. Stewart, R.A.; Meyer, K.F. 1932. Isolation of Coccidioides immitis (Stiles) from the soil. Proc. Soc. Exp. Biol. Med. 29:937-938.

137. Straub, M.; Schwarz, J. 1955. Healed primary complex in histoplasmosis. Amer. J. Clin. Pathol. 25:727-741.

138. Sulkin, S.E.; Pike, R.M. 1951. Survey of laboratory-acquired infections. Amer. J. Public Health 41:1-13.

139. Sweany, H.C. 1960. Histoplasmosis. Charles C. Thomas, Springfield, Illinois. 538 p.

140. Tesh, R.B.; Schneidau, J.D., Jr. 1966. Primary cutaneous histoplasmosis. New Engl. J. Med. 275:597-599.

141. Tomlinson, C.C.; Bancroft, P. 1928. Granuloma coccidioides: Report of a case responding favorably to antimony and potassium tartrate. J. Amer. Med. Ass. 91:947-951.

142. Tomlinson, C.C.; Bancroft, P. 1934. Granuloma coccidioides: Further observations on the use of antimony and potassium tartrate and the roentgen rays in treatment; report of an additional case. J. Amer. Med. Ass. 102:36-38.

143. Tosh, F.E.; Balhuizen, J.; Yates, J.L.; Brasher, C.A. 1964. Primary cutaneous histoplasmosis: Report of a case. Arch. Int. Med. 114:118-119.

144. Trimble, J.R.; Doucette, J. 1956. Primary cutaneous coccidioidomycosis: Report of a case of laboratory infection. AMA Arch. Dermatol. 74: 405-410.

145. Vanbreuseghem, R. 1952. Technique biologique pour l'isolement des dermatophytes du sol. Ann. Soc. Belg. Med. Trop. 32:173-178.

146. Vanselow, N.A.; Davey, W.N.; Bocobo, F.C. 1962. Acute pulmonary histoplasmosis in laboratory workers: Report of two cases. J. Lab. Clin. Med. 59:236-243.

147. Wedum, A.G. 1961. Control of laboratory airborne infection. Bacteriol. Rev. 25:210-216.

148. Wedum, A.G. 1964. Laboratory safety in research with infectious aerosols. Public Health Rep. 79:619-633.

149. Wernicke, R. 1892. Ueber einen Protozoenbefund bei Mycosis fungoides(?) Centralbl. Bakteriol. 12:859-861.

150. Wilder, W.H.; McCullough, C.P. 1914. Sporotrichosis of the eye. J. Amer. Med. Ass. 62:1156-1160.

151. Willett, F.M.; Weiss, A. 1945. Coccidioidomycosis in Southern California: Report of a new endemic area with a review of 100 cases. Ann. Intern. Med. 23:349-375.

152. Wilson, J.W.; Wright, E.T. 1960. Cured primary cutaneous coccidioidomycosis. Arch. Dermatol. 81:300-302.

153. Wilson, J.W.; Smith, C.E.; Plunkett, O.A. 1953. Primary cutaneous coccidioidomycosis; the criteria for diagnosis and a report of a case. Calif. Med. 79:233-239.

154. Wilson, J.W.; Cawley, E.P.; Weidman, F.D.; Gilmer, W.S. 1955. Primary cutaneous North American blastomycosis. Arch. Dermatol. 71:39-45.

155. Winn, W.A. 1951. Pulmonary mycosis-coccidioidomycosis and pulmonary cavitation: A study of 92 cases. Arch. Intern. Med. 87:541-550.

156. Wright, E.T.; Newcomer, V.D.; Nelson, N.H. 1959. Primary inoculation coccidioidomycosis. Arch. Dermatol. 79:118-120.

Unclassified
Security Classification

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY (Corporate author)
Department of the Army
Fort Detrick, Frederick, Maryland 21701

2a. REPORT SECURITY CLASSIFICATION
Unclassified

2b. GROUP

3. REPORT TITLE
LABORATORY-ACQUIRED MYCOSES

4. DESCRIPTIVE NOTES (Type of report and inclusive dates)

5. AUTHOR(S) (First name, middle initial, last name)
Everett Baretz, Jr.
Richard D. Kruse

6. REPORT DATE
December 1967

7a. TOTAL NO. OF PAGES
52

7b. NO. OF REFS
14

8a. CONTRACT OR GRANT NO.

b. PROJECT NO. 1B622401A072

c.

d.

9a. ORIGINATOR'S REPORT NUMBER(S)
Miscellaneous Publication 28

9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)

10. DISTRIBUTION STATEMENT
Distribution of this publication is unlimited, it has been cleared for release to the general public. Non-DOD agencies may purchase this publication from Clearinghouse, ATTN: Storage and Dissemination Section, Springfield, Virginia, 22151.

11. SUPPLEMENTARY NOTES

12. SPONSORING MILITARY ACTIVITY
Department of the Army
Fort Detrick, Frederick, Maryland, 21701

13. ABSTRACT

The most widely quoted of studies that summarize cases of laboratory-acquired infections are by Sulkin and Pike, who included laboratory-acquired infections in the U.S. from 1930 to 1950 and worldwide infections from 1950 to 1963. Because these studies do not give specific details on modes of exposure and other summaries are similarly meager, a comprehensive search of the literature was undertaken to establish a more complete summary of laboratory-acquired mycoses. Insofar as possible, the etiological fungus, type of laboratory, classification of personnel, type of work conducted, and other pertinent data have been listed in this study.

More than 288 laboratory-acquired mycoses are described here, including 108 cases of coccidioidomycosis, 81 of histoplasmosis, 8 of blastomycosis, 7 of sporotrichosis, and 84 of dermatophytoses. Known accidents or incidents accounted for only 13% of the infections. Analysis of the type of laboratory work performed shows that most of the infections resulted from exposure to accidentally created mycotic aerosols.

14. Key words

*Coccidioidomycosis
*Histoplasmosis
*Blastomyces
*Infections

DD FORM 1 NOV 65 1473 REPLACES DD FORM 1473, 1 JAN 64, WHICH IS OBSOLETE FOR ARMY USE.

Unclassified
Security Classification