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# INTERNATIONAL SYMPOSIUM ON MYCOSES

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# INTERNATIONAL SYMPOSIUM ON MYCOSES

## REPORT TO THE DIRECTOR

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PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION

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INTERNATIONAL SYMPOSIUM ON MYCOSES

24-26 February 1970

Report to the Director

The Symposium was formally opened by Dr. Charles Williams, Deputy Director of the Pan American Health Organization, who pointed out the increased public health importance of mycotic infections in the wake of medical advances that have permitted greater control of bacterial, parasitic, and viral diseases. He called specific attention to problems created by the superficial fungi, which affect tens of millions of people throughout the world, and by the crippling and life-threatening deep-seated mycoses, which are now believed to be far more prevalent in their mild, subclinical forms than had been suspected in the past. In view of the potential effects of population growth, shifts in age composition, migration, urban development, forest penetration, and colonization of arid lands on the spread of the mycoses in the Western Hemisphere--where their frequency is already highest in the world--PAHO is taking a special interest in the field, he stated. Following his introductory remarks, the Symposium began its sessions under the guidance of the several chairmen and rapporteurs.

## 1. The Mycoses as a Public Health Problem

A broad review of existing knowledge on the prevalence and incidence of the cutaneous, subcutaneous, and systemic mycoses throughout the Americas stressed the likelihood that most of these diseases are far more widespread than has heretofore been supposed. There is good reason to believe that the reports currently in hand reflect only a small fraction of the whole situation. Since the mycoses are not universally notifiable, hard data on this subject are either fragmentary or nonexistent. The true

dimensions of the medical mycological problem therefore remain unknown; however, a careful investigation--carried out for the purposes of this Symposium--of available case studies, reviews, and surveys has made it possible to draw certain assumptions.

## 1.1 Cutaneous mycoses

Some of the cutaneous mycoses approach dental caries and the common cold in frequency. Throughout the world untold numbers of people are afflicted by fungi that invade and destroy the skin, hair, and nails. In Latin America, the dermatophytoses are among the most common of human diseases, accounting for 17 per cent of all skin conditions in Mexico and from 15 to 22 per cent in Brazil. The tineas, although they are not usually disabling, constitute an important public health problem. With ringworm of the scalp, the most prevalent of the various tineas in all the Latin American countries, levels of infection range from 39 to 77 per cent in some areas. In many countries, children with this infection are barred from school and forced to wear distinctive headwear that can be a source of deep embarrassment. Over all, the toll of the cutaneous mycoses in terms of suffering, disability, man-hour losses, psychological trauma, and monetary expenditure is significant indeed, and probably much greater than is generally realized.

## 1.2 Subcutaneous mycoses

Chromoblastomycosis, mycetomas, and sporotrichosis are the most prevalent of the subcutaneous mycoses in Latin America. They occur or have been reported from nearly all the countries in this area. The victims of chromoblastomycosis and mycetomas lead lives of resigned desperation, since in the absence of competent medical services and effective chemotherapy they face irreparable disfigurement and even loss of limbs. These infections are a challenge to public health workers to develop preventive programs and to establish centers for early diagnosis and prompt surgical intervention. Chromoblastomycosis has been reported to occur in Costa Rica at a rate of one case per 24,000 inhabitants, and it is also prevalent in Brazil, Cuba,

and Venezuela. Mycetomas are especially frequent in Mexico, where 206 cases have been recorded, Venezuela (68 cases), and Argentina (23 cases). Sporotrichosis, well known as an occupational hazard for florists, pottery packers, and others who come in contact with Sporothrix schenckii, is especially common in Brazil and Mexico. So many cases go unreported that its true incidence remains unknown. However, a sporotrichin skin test has been developed, and its use has begun to reveal the occurrence of widespread subclinical infections in the general population. A survey in one part of Brazil elicited a 24 per cent level of reactions in the group tested.

1.3 Systemic mycoses

The deep fungus infections are responsible for high levels of morbidity and death throughout the Americas.

Coccidioidomycosis is a disease of restricted geographic distribution. It is only known to occur in North, Central, and South America, specifically in a zone extending from northern California to southern Argentina. Its etiologic agent, Coccidioides immitis, flourishes in semiarid regions. In its endemic areas in the United States, it is a major disease. Some 35,000 new infections are said to occur yearly in California alone, and for the entire endemic area that includes Arizona, California, New Mexico, Nevada, Texas, and Utah the annual total is believed to be in the neighborhood of 100,000. In Mexico, skin test surveys have hinted at prevalence rates ranging from 5 to over 50 per cent in many states. In Central America, small endemic areas are seen in Guatemala and Honduras. In South America, the most extensive endemic areas are found in Argentina and in Venezuela, where coccidioidin sensitivity levels reached 46 per cent in the state of Lara and 24 per cent in Falcón. Paraguayan studies revealed a 44 per cent level of reactivity among a group of Indians. Considerable investigation still needs to be done before the full extent of coccidioidomycosis in Latin America is known.

Cryptococcosis is one of the most serious and dreaded of the systemic mycoses. It may be regarded as the "sleeping giant" among the deep infections. When reporting and surveillance programs are established, the

number of cases will prove to be very high. Even now, cases have been recorded in virtually all parts of the world. It is a serious disease, frequently involving the central nervous system, and the clinical picture can resemble tuberculosis, neoplasms, brain tumors, and insanity. Failure to recognize this mimicry leads to delays in accurate diagnosis and prompt administration of specific therapy, and has even resulted in commitment to mental institutions. In the United States, 734 deaths were attributed to this disease over the 10-year period from 1958 through 1967. Statistics are not available for other countries.

Information on histoplasmosis, compared to the other deep mycoses, is relatively extensive. Cases have been diagnosed in virtually all regions of the world, although histoplasmin skin test surveys have shown that the incidence and prevalence of the disease varies greatly from place to place. In the Americas, fourteen countries had sensitivity levels of 10 per cent or higher in one or more of their regions: Argentina, Brazil, Canada, Colombia, Cuba, Ecuador, French Guiana, Honduras, Mexico, Nicaragua, Panama, Paraguay, the United States, and Venezuela. In the United States, estimated infections number in the millions. In the 48 contiguous states, histoplasmin sensitivity averages 20 per cent; at this rate, it can be assumed that in the entire country 40,000,000 people have been infected. Approximately 200,000 acute cases occur yearly, and 736 deaths were attributed to this disease during the period 1958-1967.

Paracoccidioidomycosis, or South American blastomycosis, has the most restricted geographical distribution of all the mycoses. It is only known to occur in Latin America. Brazil, Colombia, and Venezuela report the greatest number of cases, with 1,724, 373, and 300, respectively. In all of Latin America, 3,037 cases have been recorded. A newly developed skin test antigen for paracoccidioidomycosis promises to be of great aid in determining the prevalence of infections and in locating endemic areas.

### 1.4 Opportunistic mycoses

In recent years it has been found that certain fungi previously thought to be saprophytic possess latent pathogenic potentialities that can be

activated by therapeutic agents such as corticosteroids, broad-spectrum antibiotics, immunosuppressive drugs, and radiation. The victims of these iatrogenic infections are patients suffering from chronic diseases such as tuberculosis, diabetes, and leukemia and other malignancies. In addition, the opportunistic fungi complicate the management of organ transplant recipients, heart surgery patients, drug addicts, and individuals on corticosteroids and broad-spectrum antibiotics.

## 2. Recent Advances in Diagnostic Procedures

In the second session, some of the latest procedures for diagnosis were considered.

A new selective medium with an indicator has recently been developed and evaluated by field use. It does not identify the individual dermatophyte species, but it does distinguish between saprophytic fungi and the agents of ringworm infections. The medium incorporates glucose and peptone for growth, and three antibiotics--cycloheximide to inhibit saprophytic molds, and gentamicin and chlortetracycline to inhibit bacteria. In addition, it contains phenol red. Since all the dermatophytes produce alkaline metabolites, the change of the indicator from yellow to red denotes that the fungus present is in all likelihood a dermatophyte.

For success in the isolation and identification of systemic pathogenic fungi, much depends on the proper collection and preliminary treatment of clinical specimens before inoculation. Sabouraud's dextrose agar still has value in the isolation of many pathogenic fungi. But the use of antibiotics to discourage the growth of bacteria and saprophytic fungi significantly improves the chances of successful isolation of pathogens. Selective isolation media should not be used indiscriminately, for they have their limitations. Judicious use of both types, selective and nonselective, ensures the greatest success. Once a pathogen has been isolated, differential media are required for further species identification. These are used for such varied purposes as conversion of a mycelial to a yeast form, sporulation, and biochemical reactions. Tissue culture procedures and animals have to be employed at times to complete and verify identification.

The yeasts present a special diagnostic problem. Physiological and biochemical procedures are needed to distinguish saprophytes from pathogens and to identify the various genera and species encountered. Morphology is of little diagnostic value with this group of fungi. Advances in surgical and chemotherapeutic procedures during the past 20 years have been accompanied by an increased incidence of infections caused by yeasts. To further complicate matters, taxonomic research has led to the discovery and recognition of hundreds of new yeast species. Simplified schemes for yeast identification are very much needed. The germ tube test is an accurate and rapid means for the identification of C. albicans, one of the principal organisms in question. Assimilation tests that employ various carbohydrates and potassium nitrate help with the identification of other species.

The most important advances in the application of fluorescent antibody techniques to the diagnosis of mycotic diseases were reviewed. Specific conjugates for the detection and identification of the tissue forms of Blastomyces dermatitidis, Coccidioides immitis, Cryptococcus neoformans, Paracoccidiodes brasiliensis, and Sporothrix schenckii have been developed and put to use. Progress was reported on the development of useful fluorescent antibody reagents for the identification of the Candida species and Histoplasma capsulatum as well.

Encouraging results have been achieved in the application of immunofluorescence for the detection of antibodies to Coccidioides immitis, cryptococcus neoformans, and Histoplasma capsulatum in blood serum and spinal fluid.

The value of serologic procedures for the diagnosis of coccidioidomycosis, cryptococcosis, and histoplasmosis was emphasized. Procedures for complement fixation, immunodiffusion, latex agglutination, tube agglutination, and tube precipitin tests have been shown, when used either alone or in combination, to be invaluable for diagnostic and prognostic purposes. The most significant advance in recent years has been the development of serological tests for cryptococcosis. The concurrent use of the latex agglutination, the indirect fluorescent antibody, and tube agglutination tests has given effective serologic results for this disease for the first time.

The successful development of serological procedures for paracoccidioidomycosis was also reported. Two techniques, complement fixation and agar gel immunodiffusion are currently in use. The antigen employed in both tests is prepared from the yeast form of Paracoccidioides brasiliensis. Only a limited amount of cross-reactions have been encountered with sera from patients with histoplasmosis. The two tests are of proven value in diagnosis, prognosis, and case-finding.

## 3. Therapy

With few exceptions, treatment of the mycotic diseases is prolonged and difficult, and much work still remains to be done in the field of mycotherapeutic research. The current status of procedures being used in the management of the various types of mycoses was reviewed in the third session.

### 3.1 Cutaneous mycoses

The diffuse superficial mycoses caused by members of the genera Trichophyton, Microsporum, and Epidermophyton have been treated systemically with griseofulvin, the first oral antifungal drug that has proven effective against these agents. "Glabrous skin" dermatophytosis can be cured with microcrystalline griseofulvin given in amounts of no less than one gram daily for a minimum of 30 days. Tinea capitis requires a daily dosage of 25 mg per kg of body weight for four to six weeks. Onychomycosis of the fingers responds after four or six months' treatment with the drug, and onychomycosis of the toes, after eight to twelve months' therapy. However, as yet there is no topical antifungal agent effective against widespread dermatophytosis, tinea capitis, or onychomycosis. Future research should focus on the development of a topical antimycotic preparation for the treatment of these diseases.

The ultimate prevention and control of ringworm of the scalp is felt to lie in epidemiological rather than clinical approaches to the disease (see Section 4).

Cutaneous candidiasis responds well to topically applied polyene antibiotics such as amphotericin B, nystatin, and pimaricin.

3.2 Subcutaneous mycoses

No measures for the prevention of sporotrichosis, mycetomas, or chromoblastomycosis are known at present.

Potassium iodide continues to be the only specific treatment for the fixed and lymphangitic forms of tegumentary sporotrichosis, although it is not as effective in the hematogenous type. When the disease is located in bone or viscera, the drug is inadequate unless it is combined with griseofulvin, or, in severe cases, with amphotericin B. Other drugs and regimens have been tried with little success.

Mycetomas are extremely hard to cure. For the actinomycetic kind--especially the form caused by N. brasiliensis, which is the most common--the drug that has been used in Mexico since 1947 is diaminodiphenylsulfone. Long-acting sulfamides have been used as well. Improvement has been noted in many cases after treatments lasting two to four years, but cure rates are still not very high. The variability of the results depends on the extension and age of the lesions, and, more important still, on the degree, if any, of bone or visceral involvement. More recently, trimethoprim, a bactericide with antifolic action, has been used with some success in combination with sulfamethoxazole. For maduromycotic mycetomas the only treatment is surgical removal.

No efficient treatment is known for chromoblastomycosis. Isolated cures have been reported with a number of drugs, but the results are so haphazard that therapy which is successful in one patient may fail in another. Recently, two cases were cured with a new agent, 5-fluorocytosine, which is an antimetabolite of the cytosine of certain fungi.

3.3 Systemic mycoses

Coccidioidomycosis, cryptococcosis, and histoplasmosis are all treated with amphotericin B, a major antifungal medicament introduced in 1958. Although

5-fluorocytosine shows promise in the treatment of cryptococcosis, and saramycetin in the management of histoplasmosis, neither of these latter two agents is available for general evaluation.

Experience has shown that amphotericin B can be expected to be successful in the treatment of about 80 per cent of patients with cryptococcosis or histoplasmosis, if failures during the first two weeks are eliminated. Coccidioidomycosis does not yield so readily. Matters of single and total dosage, interval between doses, and primary case selection for treatment are not settled. Usually, the length of treatment is tailored to the particular disease in question, its duration, localization, and whether or not surgery is performed. So far, in cryptococcosis and histoplasmosis, the progressive reduction of individual and total dosage has not been related to an increase in therapeutic failure. Side effects and acute toxicity from amphotericin B are frequent and annoying, but they rarely prevent successful therapy, and recent experience with the drug has not shown it to produce the serious toxicity of which it is commonly accused. It has some drawbacks, however, from the standpoint of management; namely, it is costly to administer, and it requires long periods of hospital care. Although amphotericin B is not obligatory for all cases of fungal meningitis, the uncertainty of case selection suggests that its early administration by the intrathecal, intracisternal, and/or intraventricular routes is advisable and should be continued if clinical and laboratory studies indicate persistent infection.

The use of resectional surgery in the management of pulmonary coccidioidomycosis is accepted. However, in pulmonary histoplasmosis and cryptococcosis, the natural history of these infections is still too little known to justify dogmatism about surgery.

Paracoccidioidomycosis is the most common deep mycosis in Colombia and in a number of other Latin American countries. It is caused by Paracoccidioides brasiliensis, a dimorphic fungus whose habitat and portal of entry are not known. Since its pathogenesis has not been established, preventive measures are yet to be developed. No effective therapy was known until 1940, when various types of sulfas began to be tried, in general with good therapeutic response and even cure. Doses vary with the type of sulfa. Treatment

should be continued for months, years, and, in some cases, life. Sulfa resistance has occasionally been noted. Amphotericin B has also been used for paracoccidioidomycosis since 1958, and the results appear to have been good, although relapses are common. Sulfanilamides still have their place in the treatment of this disease, since amphotericin B is expensive and cannot be administered to ambulatory patients.

The promising development of an immunological defense against Coccidioides immitis infections was reported. C. immitis infections in mice offer distinct advantages as a model system for the study of immune responses in the deep mycoses. The fungus is strongly immunogenic and induces delayed hypersensitivity reactions. In additon, the parasite occurs in vivo both as a small organism (endospore) and as a large one (spherule). Inoculation with killed spherule confers protection that appears to be mediated largely by an augmented and accelerated cellular response in the immunized subjects. Vaccination regimens and procedures have been developed that afford very strong immunity to experimentally produced pulmonary coccidioidomycosis in mice and monkeys.

## 4. Ecology and Epidemiology

Control of the mycoses depends in large measure on a full understanding of their ecology and epidemiology. Accordingly, the current status of this knowledge was reviewed for several of the diseases.

### 4.1 Cutaneous mycoses

Ringworm of the scalp caused by anthropophilic dermatophytes is widely distributed throughout the world, and endemic foci of tinea capitis are mainly found in poor areas where standards of living are low. The infection is acquired in childhood, with 96 per cent of the cases occurring before the tenth year of age. In endemic areas, a considerable sector of the adult population, particularly women, is also found to be infected with T. violaceum, T. schoenleinii, and T. tonsurans. Frequently the mother, bearing a subclinical infection from childhood, may be the source of infection for her children, and, in turn, for the community. Thus, tinea capitis should be regarded in endemic areas as a familial disease.

The anthropophilic ringworm infections of the scalp follow their natural course in unrestricted transmission to susceptible individuals independently from infections in animals, which have their own epidemiological pattern with limited dynamics of transmission among human beings.

4.2 Subcutaneous mycoses

Chromoblastomycosis occurs most frequently among males, and the lesions are principally localized in the lower extremities. Although all races are equally susceptible, most of the cases have been described in Caucasian individuals between 25 and 50 years of age. Occupational incidence is an important factor, since most cases occur in agricultural workers exposed to traumatic accidents in which wood fragments and thorns are involved. The endemic areas are located in tropical moist and wet forest and in lower montane wet and rain forest environments. The fungus in its saprophytic phase does not require special soil conditions.

Mycetomas are found most often in middle-aged males. Race does not appear to be a factor in the frequency of the disease. The incidence is definitely higher among rural populations and among persons whose activities tend to result in frequent and neglected skin abrasions. Inoculation of the agent by direct trauma has been established to be the mechanism of infection, although some authors have cited epidemiological and experimental evidence suggesting the existence of a previous sensitivity to homologous organisms. In experimental mycetomas in hamsters and mice there has been no proof as yet that a previous sensitization state is necessary in order for these lesions to develop.

Actinomycotic and maduromycotic mycetomas are produced by more than 14 different organisms, some of which have been isolated from the soil, which is their natural habitat. Each of the responsible species has a special geographic distribution. The agent most commonly isolated in the Americas is Nocardia brasiliensis.

Sporotrichosis is most frequently contracted in places where high humidity values coincide with temperatures between 16° and 20° C. As mentioned before, it is considered an occupational hazard for gardeners, florists, and

other persons who are frequently in contact with soil and plant debris inhabited by Sporothrix schenckii. The fungus is introduced through injuries to the subepithelial layers of the skin. The possibility of infection through the pulmonary route has been suggested in recent clinical records and in experiments showing that the mouse may be infected by inhalation of the xerospores or fuliginous conidia of S. schenckii. The pulmonary portal of entry would explain both the existence of positive reactors to sporotrichin among persons without preceding overt disease and the pathogenesis of disseminated sporotrichosis. Many patients have been cured after local application of heat and rubefacients. The remarkable immunological response elicited by S. schenckii suggests that the thermotolerance of the fungus in the tissues might be lower than that recorded in the cultures (38° to 39° C).

### 4.3 Systemic mycoses

As stated before, coccidioidomycosis is a Western Hemisphere disease. Skin test surveys have contributed to the delineation of endemic zones, but care has to be taken in places where histoplasmosis may contribute cross-reactivity. Disseminated coccidioidomycosis may occur with greater frequency in children than was formerly thought. The precise extent of racially determined dissemination in "dark skinned" individuals other than Negroes and Filipinos requires clarification. Thus, the picture is not clear with respect to the Indians in North and South America, whose forebears must have had the earliest encounters with the agent Coccidioides immitis. Although most coccidioidomycosis occurs as sporadic, isolated infections, several small-scale epidemics have provided pinpoint information on the whereabouts of C. immitis in nature. Sentinel animals, natural or intentionally placed, may serve as biological detectors of the presence of C. immitis.

The statistics available on human cryptococcosis probably do not reflect the true incidence, or even the frequency of diagnosis, of this world-wide disease. Reporting is most likely to indicate the presence of interested mycologists and physicians and diagnostic capability in medical schools and hospitals. During the 1960's, serologic and skin-testing methods similar to those used for coccidioidomycosis and histoplasmosis were developed. Application of these new techniques to small groups of subjects in the United

States suggests that the pattern of human cryptococcal infections is similar to that of other soil-associated fungal diseases. Although infection appears to be relatively frequent, manifestations of the symptomatic disease are quite rare.

Cryptococcus neoformans, first recovered from the soil in 1951, has been found in all parts of the world. It is more frequent in soils contaminated with bird droppings, particularly from the pigeon. This fungus has been recovered from the immediate environment of many patients, which suggests that the infection is acquired by breathing air containing dust particles from the soil or other materials in which the fungus has grown. The organism survives best in cool, shaded places and under dry, rather than moist or humid, conditions.

The occurrence of cryptococcosis in animals provides another key to the world distribution of this fungus. The disease has been noted in a large variety of mammals. Interestingly, it does not occur in birds, despite the wide association with bird droppings.

Disseminated histoplasmosis--the originally diagnosed form of the disease--occurs frequently among all age groups; nevertheless, it is not the most commonly observed manifestation. Although male and female children appear to be equally susceptible, studies among adult patients in sanatoria show that men are more frequently infected than women and that the white race is more susceptible than the dark races. Published distribution maps often imply erroneously that endemicity of the disease is limited to the central and eastern United States. Investigations since World War II have established that Histoplasma capsulatum is endemic throughout the world. Skin testing with histoplasmin continues to be an important procedure for epidemiological study, and recent reports estimate that over 40 million persons in the United States show hypersensitivity. At least 800 deaths due to histoplasmosis occur annually in that country.

Distribution of the fungus in nature has been shown to be significantly associated with soils contaminated with bird and bat excrement, and epidemic histoplasmosis has occurred in individuals after exposure in caves, abandoned

chicken houses, and storm cellars. Isolations of the fungus have been made from specific foci with contiguous negative areas, and recently the organism has been found in several species of bats.

## 5. Training in Medical Mycology

Increasing awareness of the mycoses problem is accompanied, unfortunately, by an also increasing shortage of medical mycologists. At a time when they are acutely needed, many of the pioneers in this field are reaching the age of retirement, and a whole new generation needs to be trained. The Symposium recognized the critical proportions of the problem, and a full session was given over to consideration of the question of medical mycological training.

In view of the high prevalence of mycotic infections and the need to distinguish the mycoses from the bacterial and viral diseases that they closely mimic, the incorporation of medical mycological training in the curricula of the medical schools is an absolute necessity. Teaching programs should vary in scope and intensity according to the medical specialties of the students. Short-term courses are generally sufficient to meet the needs of most medical groups. However, longer programs should be available for physicians who care to specialize in this field. To provide the needed variety of teaching, service, and research programs at such a level, a well-staffed and well-equipped mycology center is required.

Training in medical mycology at the graduate level is offered either as an intensive course lasting several weeks or else as part of the courses being taught in other related specialties--for instance, microbiology. The general purpose of the intensive course is to provide the necessary expertise to permit laboratory identification of fungi recovered from patients or from the environment. The students are usually medical doctors; they are seldom biologists, plant physiologists, or geneticists, although all these disciplines offer insights into the problems of medical mycology. It is important to try to interest such other persons in working in this field. Since medical institutions are currently the only places where there is strong

interest in medical mycology, they should provide opportunities for the training of nonphysician researchers as well.

There is also an obvious need for better laboratory training of medical technologists in the diagnostic aspects of medical mycology. Examination of the curricula in a number of schools where such personnel are trained has revealed significant deficiencies in the time students actually spend in the mycology laboratory. There are several reasons why their education and training in medical mycology is so inadequate. Perhaps the most important one is that many schools of medical technology and microbiology staffs in clinical laboratories do not have the faculty or the technologists with adequate training in this specialty. Consequently, the subject is sometimes omitted, presented very briefly, or taught by someone who does not have the proper preparation or experience.

The laboratories themselves are badly in need of upgrading, too. Results from proficiency tests in mycology sent out by the U.S. National Communicable Diseases Center, Atlanta, have indicated that a number of laboratories engaged in diagnostic medical mycology in the United States are unable to correctly identify some of the most common pathogenic fungi seen in that country.

## 6. Future Directions

The last session of the symposium was devoted to a discussion of future needs in medical mycology.

One of the obvious requirements is the standardization of antigen reagents and test procedures. An ideal standard would contain a single molecular species eliciting the specific biological (immunological) activity to be studied. Such an antigen could be assayed reproducibly by a dose-response curve. No preparation of this kind is currently available, however. Workers are obliged to rely on reference antigen solutions that have been carefully characterized for a specified biological activity, and to which new antigen preparations can be compared. The principal criteria to be considered in diagnostic reagents are potency, specificity, sensitivity, and the procedural conditions for performing the tests and reading the results. For skin-testing

materials, potency and specificity can be assayed initially in experimental animals, but the final determination must be made in humans. While potency and specificity can be determined in known reactors, sensitivity can be evaluated only in population studies. Similarly, for serological antigens, potency and specificity can be assayed with selected antisera of known reactivity, but sensitivity must be determined against multiple specimens.

Surveillance programs for mycotic infections are necessary if preventive and control measures are to be effectively instituted. For some infectious diseases, physicians are required to report the cases they see to official health agencies on a regular basis, and for most illnesses baselines have been established that are useful in detecting unusual increases in morbidity and evaluating the extent of the problem. The need to take steps in this direction for the mycoses is evident. In addition to the reporting of cases, there are other means of maintaining surveillance of a given disease. Routine tests performed in public health laboratories can be used to provide data on its prevalence and to detect new cases. Under special circumstances, periodic skin test surveys of selected populations may be used to measure the prevalence of infection of some mycotic diseases, but they will not provide data on new clinical cases. If official health agencies are to establish surveillance programs for the mycoses, there must be sufficient evidence to show that the benefits will justify the shifting of resources from other programs.

Survey programs are generally the most effective and most economical means of obtaining extensive information on diseases of public health importance. Much of the existing knowledge on the epidemiology and distribution of the mycotic diseases has been gathered by this means. With the improved test materials and methods now being developed in laboratory studies, additional gains may be expected in the not-too-distant future.

In summing up, it was the consensus of the Symposium that continuing dialogue and support of studies pertaining to the mycoses should be of concern and interest to the Pan American Health Organization. Accordingly, to establish a productive liaison between PAHO and professional personnel working in this

field, it was proposed to establish a Coordinating Committee for the Mycoses, which would serve as an advisory board to PAHO on all matters related to medical mycology. The Committee would meet periodically to assist PAHO's Department of Research Development and Coordination in implementing the following recommended steps:

1. Creation of a Subcommittee on Training for the Mycoses to plan and develop regional programs for the training of physicians, scientists, and technicians in the field of medical mycology;

2. Formation of a Subcommittee on Regional Diagnostic Centers for the selection and strengthening of such units throughout the Americas;

3. Appointment of a Subcommittee on Diagnostic Procedures for the Mycoses, which would report to the Coordinating Committee on immunological procedures and reagents in current use for the diagnosis of mycotic infections, and, on the basis of this information, make recommendations for the adoption of reference reagents and standardized techniques;

4. Facilitation of the production and distribution of the fungus antigens recommended by the Subcommittee above;

5. Encouragement of compulsory reporting of the mycoses in the Member Countries as soon as they are technically prepared to take this step, while in the interim various investigators would be asked to gather statistics on mortality and morbidity caused by the mycoses and transmit this information to the Coordinating Committee;

6. Development, in coordination with the PAHO Regional Library of Medicine, of specialized bibliographic centers on medical mycology;

7. Encouragement of medical mycological teaching within the curricula of medical schools throughout Latin America;

8. Fostering of cooperative efforts between institutions in the United States and Latin America for the exchange of staff members and graduate students, and development of joint medical mycological projects for research and research training; and

Continuation of the scientific dialogue on medical mycology at intervals of not less than three years, and at a level as high as that of the present Symposium; and, furthermore,

Provision of assistance in the form of an Ad Hoc Planning Committee for the forthcoming Symposium on Paracoccidioidomycosis to be held in Medellín, Colombia, in October 1970.