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ADVISORY COMMITTEE ON MEDICAL RESEARCH

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THE MYCOSES AS A POTENTIAL PUBLIC HEALTH PROBLEM
IN THE TRANS-AMAZON HIGHWAY REGION

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I. INTRODUCTION

At the request of the Pan American Health Organization's Department of Research Development and Coordination, Drs. Libero Ajello, Chief of the Mycology Division of the Center for Disease Control, Atlanta, Georgia, and Hillel B. Levine, Chairman of the Medical Microbiology Department, Naval Biomedical Research Laboratory, Oakland, California, undertook to "determine the extent of the mycotic problem in the Brazilian Amazon area, evaluate the resources available to cope with it, and recommend steps for the development of a program of mycotic disease surveillance along the Trans-Amazon and Cuiabá-Santarém Highways." They departed for Belém, Pará, Brazil on 11 February 1974.

II. BACKGROUND

A. Trans-Amazon Highway and Amazonia Colonization Projects

In 1970 the Brazilian Government initiated a bold and grandiose plan to open up the hinterland of Amazonia for colonization and economic exploitation. Amazonia covers an area of 4,871,487 square kilometers, and encompasses 57 percent of Brazil's territory. This vast region has currently a population of approximately 7,199,529 (1970 census) for an average density of only 1.48 inhabitants per square kilometer. Amazonia takes in the states and territories of Acre, Amapá, Amazonas, Pará, Rondônia, and Roraima and parts of the states of Goiás (above parallel 13), Maranhão (west of the 44th meridian) and Mato Grosso (above parallel 13). See Figure 1 and Table 1.
Table 1. Population Distribution of Amazonia

<table>
<thead>
<tr>
<th>States and Territories</th>
<th>Area (Km²)</th>
<th>Population</th>
<th>Inhabitants per Km²</th>
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<tr>
<td>Acre</td>
<td>152,589</td>
<td>216,200</td>
<td>1.42</td>
</tr>
<tr>
<td>Amapá (territory)</td>
<td>139,068</td>
<td>114,687</td>
<td>0.82</td>
</tr>
<tr>
<td>Amazonas</td>
<td>1,558,987</td>
<td>955,394</td>
<td>0.61</td>
</tr>
<tr>
<td>Pará</td>
<td>1,227,530</td>
<td>2,161,316</td>
<td>1.76</td>
</tr>
<tr>
<td>Rondônia (territory)</td>
<td>234,044</td>
<td>113,659</td>
<td>0.47</td>
</tr>
<tr>
<td>Roraima (territory)</td>
<td>230,104</td>
<td>40,915</td>
<td>0.18</td>
</tr>
<tr>
<td>Goiás (above parallel 13)</td>
<td>285,793</td>
<td>597,494</td>
<td>2.09</td>
</tr>
<tr>
<td>Maranhão (west of 44th meridian)</td>
<td>257,451</td>
<td>2,493,815</td>
<td>9.69</td>
</tr>
<tr>
<td>Mato Grosso (above parallel 16)</td>
<td>776,921</td>
<td>506,049</td>
<td>0.65</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4,871,487</td>
<td>7,199,529</td>
<td>1.48</td>
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</table>
Construction of the principal east-west highway through Amazonia was initiated in September 1970 and completed in 1974. The Trans-Amazon Highway branches off the east side of the paved Belém-Brasília Highway at longitude 50° and extends 3,000 kilometers to the Peruvian border, close to the Brazilian city of Cruzeiro do Sul.

Other road projects under way are a northern perimeter road extending from Pôrto Grande in the territory of Amapá to Cruzeiro do Sul, and two north-south roads traversing Amazonia from the southern borders of Brazil to the frontiers of Guyana, Surinam, and Venezuela (Figure 2). One is a 1,600-kilometer route from Cuiabá, capital of Mato Grosso state, to Santarém, on the Amazon river. The other, when completed, will provide a paved 3,200-kilometer route from Brasilia to Pôrto Velho in Rondônia and then northward through Manáus to the Venezuelan border.

Figure 2. Map of the Amazon Region
The labor force involved in the construction of the Trans-Amazon Highway numbered 3,500 workers. They and their families, about 10,000 people, inhabited the area during the 3-year construction period of the unpaved road.

Now a well-planned 10-year colonization program has been initiated. The first wave of colonists has settled along a 1,000-kilometer stretch of the Trans-Amazon Highway between the cities of Marabá and Itaitúba (Figure 3). The organization of the colonies is based on a series of interdependent communities designated, in ascending order of size and resources, as agrovilas, agropoli, and ruropoli (Figure 4).

![Figure 3. Rural-urban integration](image)

![Figure 4. Plan for rural-urban colonization along the Trans-Amazon Highway](image)
An agrovila is made up of a community of 50 families. Each community has certain basic support services such as a primary school, a general store, and a small clinic. Each resident receives from the government a small cabin and 100 hectares of land, seeds, and agricultural advice, which he is bound to repay with the products of the land.

An agropolis, second in size among the communities, is the center for 20 agrovilas or 1,000 families and of families living in nonagricultural areas. The agropolis has administrative offices of the various support agencies, a cooperative store, a social and health center, a technical assistance office, a primary school and eventually a secondary school, agricultural industries, and other basic services.

Ruropoli are regional centers with jurisdiction over groups of agrovilas and agropoli and are urban in nature, situated approximately 140 kilometers from each other. At the moment Marabá, Altamira, and Itaituba are the only existing ruropolio.

At the time of our visit approximately 4,500 families had settled along the Marabá-Itaituba sector of the Trans-Amazon Highway.

B. Public Health Aspects

The clearing and development of a vast tropical rain forest area for colonization presented the possibility that the highway labor force and the colonists would encounter or create infectious disease problems. In anticipation of such problems, a surveillance and research program on infectious diseases along the Trans-Amazon Highway was initiated in 1971 by the Evandro Chagas Institute with the collaboration of the Pan American Health Organization. This program was deemed to be of great importance since the whole undertaking of road construction, colonization, and exploitation of Amazonia could be jeopardized by outbreaks of infectious diseases.

A team of workers, with headquarters at the Evandro Chagas Institute in Belém, has begun field and laboratory studies on the bacterial, parasitological, and virological diseases of Amazonia. Quarterly reports on
this long-term surveillance and on the research programs have already been published.

Since the mycoses were not included in these programs, the presently described site visit was undertaken.

III. OBSERVATIONS AND DISCUSSION

The survey of actual and potential medical mycologic problems in Amazonia was carried out during 11-24 February 1974. Visits were paid to medical and public health institutions and hospitals in Belém, Santarém, and Altamira. Our findings in each of these centers are summarized individually.

A. Belém

In Belém, the capital of the State of Pará and the principal shipping port for Amazonia, discussions were held with the directors and staff members of PAHO's Amazon Regional Office; the Evandro Chagas Institute; the PAHO/U.S. Army Medical Research Unit in the Trans-Amazon; the Federal University of Pará's Faculty of Medicine, Regional Pathology Center for the Amazon, and Biology Department; the Chest Disease Center; and the Santa Casa Hospital (Annex I).

The picture that emerged after these site visits and discussions was that all but one of the endemic mycoses of Latin America (coccidioidomycosis) occur in Amazonia. Skin diseases such as tinea versicolor, tinea capitis, and tinea corporis are prevalent among adults and children. The majority of scalp ringworm infections are caused by *Trichophyton tonsurans*.

Among the subcutaneous mycotic diseases, chromoblastomycosis is one of the most frequently encountered. In a survey, Silva recorded 41 cases in Pará. According to Londero, throughout Brazil, sporotrichosis is the most prevalent of the mycoses, next to the dermatomycoses.
Amazonia is the classic area for lobomycosis, a rare disease confined to the Americas. The overwhelming majority of the new world's cases of this disease, 70 of 102, have originated there.\textsuperscript{1}

Cases of paracoccidioidomycosis have been recorded in Pará.\textsuperscript{5,6} In the 12-year period of 1954-1966, 28 cases had been diagnosed. The hospitals in Belém currently receive 6 to 10 patients with this disease yearly. The state of Goiás and the territory of Rondônia have recorded 3 and 40 cases of paracoccidioidomycosis, respectively.\textsuperscript{5} A paracoccidioidin skin test survey in Goiás revealed that 72 of 550 (13 percent) individuals tested gave positive reactions.\textsuperscript{5}

Histoplasmosis is relatively rare: only two cases were on record in the Regional Pathology Center. Other systemic diseases diagnosed in this region are aspergillosis and cryptococcosis. Candidiasis is a common problem among women. Although there are few case records, there is reason to believe that the disease in many patients is not properly diagnosed or that patients do not reach the principal hospitals of the region. Little culture work and no serology for the diagnosis of the mycoses is done. Most cases are diagnosed by pathologists who encounter the tissue-form cells of the pathogenic fungi in their histologic sections.

Sporadic skin test surveys with histoplasmin indicate that histoplasmosis has a higher incidence and prevalence in Amazonia than the two case records would indicate. For example, in 1966 Tesh and Marques\textsuperscript{10} tested 258 individuals in Belém with histoplasmin. Positive reactions were obtained in 43 percent of the subjects tested. Drs. Mochi and Edwards\textsuperscript{6} reported in 1952 findings of an earlier histoplasmin survey conducted by Morehead and Macedo in Santarém, in which 187 of 623 school-children (30 percent) gave positive reactions. Lacaz, Padim, and Minami\textsuperscript{3} skin tested 91 inhabitants of the Conceição do Araguaia in the state of Pará. Twenty-five (27 percent) of these individuals gave positive reactions. Recently, investigators from the Amazonia Research Institute in Manaus and the Institute of Tropical Medicine in São Paulo gave histoplasmin skin tests to 294 inhabitants of the state of Amazonas. Positive reactions were elicited in 120 or 40.82 percent of those tested.\textsuperscript{2}
Definitive proof of the existence of *Histoplasma capsulatum* in Amazonia was uncovered by the survey teams of the Evandro Chagas Institute and the PAHO/U.S. Army Medical Research Unit in the Trans-Amazon. In the survey of wild rodents for parasites, Dr. Mario Moraes of the Evandro Chagas Institute isolated *H. capsulatum* from three spiny wood rats (*Proechimys guyannensis*). These rats had been collected along the Itaituba-Jacaréacanga sector of the Trans-Amazon Highway.

Other evidence supporting the high prevalence of histoplasmosis in Amazonia comes from the Yonomana Indians of the territory of Roraima. Sera collected by Dr. James V. Neel of the University of Michigan's Department of Human Genetics were tested by the Center for Disease Control's Mycology Division. Of 210 sera tested, 129 gave positive titers with the histoplasmosis complement fixation test.

Dr. Moraes has also surveyed rodents and soil specimens collected in Amazonia for keratinophilic fungi. Among the isolates, two species, *Microsporum gypseum* and *Trichophyton mentagrophytes*, are causes of ringworm infections in humans.

### Santarém

Santarém is a ruropolis on the Amazon River that serves the agrovilas and agropoli along the north-south highway that connects Santarém with the city of Cuiabá in the state of Mato Grosso. During our brief stay there we visited the hospital built in 1944 by the Serviço Especial de Saúde Publica (SESP).

This 35-bed hospital handles about 70 to 80 new patients a day. It has a small laboratory that does no culture or pathology work. The basic services provided include direct examinations of stools for parasites, staining of smears from clinical materials, hemoglobin determinations, and Venereal Disease Research Laboratories' (VDRL) syphilis serology.

Aside from tinea versicolor and ringworm infections, the only other mycotic disease encountered is candidiasis. A high percentage of the women who enter the maternity clinic suffer from vaginal infections.
caused by *Candida albicans*. Leishmaniasis, leprosy, and tuberculosis are the principal infectious diseases encountered in this area of Amazonia.

One other medical facility was visited in Santarém. It was the adjacent private maternity hospital run by Franciscan sisters. The Maternidade Sagrada Familia has a clinic that serves 50-100 patients. Here again the prevalence and incidence of vaginal candidiasis was high. Fifty to 70 percent of the patients are afflicted with this complicating disease. More than 95 percent of the women served by this hospital have heavy infestations of parasites.

C. Altamira and Vicinity

1. Altamira is a ruropolis of 18,000 inhabitants, virtually midway between Marabá and Itaituba on the Trans-Amazon Highway. In the past 4 years its population has grown from 4,000 to 18,000 inhabitants. Its SESP hospital serves a region with 48,000 inhabitants. The hospital primarily deals with maternity and surgical cases.

This hospital's laboratory, as the one in Santarém, does not carry out any culture work. Only direct examinations of clinical materials are performed for parasites and bacteria. Hemoglobin tests are carried out along with the VDRL test for syphilis. Aside from candidiasis among pregnant women, mycotic diseases have not been diagnosed.

2. Agrovila of Nova Fronteira and agropolis of Brasil Novo. During our stay in Altamira we visited the agrovila of Nova Fronteira, situated approximately 16 kilometers due west on the Trans-Amazon Highway, and the agropolis of Brasil Novo, located 45 kilometers west of Altamira. Both of these centers had first aid stations to serve the immediate needs of the colonists and the staffs of their support agencies.

IV. CONCLUSIONS

Our conversations and observations, combined with a thorough review of the literature, revealed that within the vast territory of Amazonia,
cutaneous, subcutaneous, and systemic mycoses occur with varying degrees of frequency. Because the mycoses are not reportable diseases and medical mycologic diagnostic laboratories staffed and equipped to isolate pathogenic fungi do not exist, adequate statistical data on the number of cases of mycotic diseases that have occurred in Amazonia are not available. Nevertheless, it is evident that the colonists of Amazonia are entering a vast region where a great variety of pathogenic fungi exist in the environment. As yet, aside from ringworm infections and candidiasis, there have been no reports of subcutaneous and systemic mycoses having developed among the settlers. It must be remembered, however, that the colonization program is just getting under way. None of the agrovilas are more than 2-years old in the Marabá-Itaitúba area of the Trans-Amazon Highway. Given the mycoses potential of the region, it is most reasonable to infer that cases of chromoblastomycosis, cryptococcosis, histoplasmosis, lobomycosis, and paracoccidioidomycosis will make their appearance among the colonists.

Now is the time to anticipate such problems and to take steps to ensure that diagnostic facilities manned with trained personnel are available in the clinics of the agropoli and ruropoli.

V. RECOMMENDATIONS

Because of the probability that mycotic diseases will be encountered in Amazonia, implementation of a mycosis diagnostic, research, and surveillance program is considered necessary. Logically, this program would be integrated with the already initiated surveillance and research programs for bacterial, parasitic, and viral diseases of the Trans-Amazon Highway region.

The recommendations made are as follows:

A. Establishing a Medical Mycologic Diagnostic Reference Center in Belém

Possible location for this much-needed regional service could be:
1. The Evandro Chagas Institute. Dr. Mario Moraes has there the nucleus for such a laboratory. One of his technicians, Miss Maria Roque, has just taken the PAHO-sponsored mycology course in São Paulo given by Dr. Carlos da Silva Lacaz in November 1972.

2. The Dermatology Department of the Faculty of Medicine of the State University of Pará. Dr. Domingos Silva of that department is well acquainted with the mycoses and, with adequate staffing, could develop the required service.

The proposed Reference Diagnostic Laboratory for the Mycoses should not only be prepared to detect, isolate, and identify fungus pathogens, but should have the competency to perform immunofluorescence and serodiagnostic tests for aspergillosis, candidiasis, cryptococcosis, histoplasmosis, sporotrichosis, and paracoccidioidomycosis.

Under the auspices of PAHO, such a laboratory could obtain guidance, training of staff members, and the necessary diagnostic reagents.

B. Upgrading of SESP Hospitals

The hospitals of the Serviço Especial de Saúde Pública in the several ruropolis should be encouraged and aided to isolate and identify infectious disease agents. At present none of the hospitals visited did any diagnostic culture work. Such a diagnostic service would be of invaluable aid to physicians and could be of life-saving benefit to patients.

C. Training

A training program consisting of lectures, demonstrations, and laboratory instruction should be developed to acquaint and train physicians and technicians with the clinical signs of the mycoses, their pathogenesis, therapy, and laboratory diagnosis. Such a program is clearly needed
since awareness and knowledge of fungus diseases is lacking among medical and paramedical personnel.

A program of this type could be set up in Belém and the trainees brought in from the various hospitals in Amazonia. To supplement this centralized training program, field workshops of short duration could be developed to bring knowledge to the far-flung health centers.

D. Surveillance and Research

The staffs of the Evandro Chagas Institute and of the PAHO/U.S. Army Medical Research Unit should be augmented and directed to develop a surveillance and research program for the mycoses.

This activity would entail regional skin test surveys of colonists and aborigines with histoplasmin and paracoccidioidin, screening of wild animals for superficial and systemic mycotic infections, ecologic and epidemiologic studies of the pathogenic fungi of Amazonia and of outbreaks of mycotic diseases whenever they occur.

To add such a study program to the ones already under way for bacterial, parasitic, and viral diseases, additional staff members would be required. But these would be few in number since members of the existing staff could collect field specimens and conduct surveys under the guidance of a medical mycologist.

The colonization and exploitation of Amazonia offers a unique opportunity to public health workers to develop a model program for the control and understanding of the infectious diseases of the tropics. The mycoses, along with the bacterial, parasitic, and viral diseases must be included in any such program to safeguard the health of the colonists and to ensure the success of this ambitious project.
ANNEX I

Directors and Staff Members of Institutions Visited in Belém

A. Pan American Health Organization's Amazon Regional Office
   Chief: Dr. Juan Ponce de Leon

B. Evandro Chagas Institute
   Director: Dr. Miguel Cordeiro de Azevedo
   Dr. Mario Moraes - Chief, Pathology Division
   Dr. Francisco Pinheiro - Chief, Virology Division
   Dr. Gilberta Bensabath - Chief, Epidemiology Division
   Dr. Zéa C. Lins - Chief, Bacteriology Division
   Dr. Amelia H. P. de Andrade - Chief, Serology Division
   Dr. H. Fraiha - Chief, Entomologist
   Miss Margarida M. A. Roque - Mycology Technician
   Dr. R. Lainson - Parasitologist (Wellcome Parasitology Unit)
   Dr. R. D. Ward - Entomologist (Wellcome Parasitology Unit)

C. PAHO/U.S. Army Medical Research Unit in the Trans-Amazon
   Team Leader: Dr. Craig H. Llewellyn
   Dr. N. Peterson - Wild Life Ecologist

D. Faculty of Medicine, Department of Dermatology, Federal University of Pará
   Dr. Domingos Barbosa da Silva, Professor of Dermatology
   Dr. Tarciso Carvalho, Dermatologist

E. Pathology Center (Nucleo de Patologia, Regional da Amazonia), Federal University of Pará
   Director: Dr. Amyntor Bastos
   Dr. José Monteiro Leite - Pathologist

F. Biology Department, Federal University of Pará
   Dr. Mario M. Sampaio
G. Chest Diseases Hospital (Hospital dos Servidores do Estado)
Director: Dr. Almyr Gabriel

H. Santa Casa Hospital (Santa Casa de Misericordia do Pará)
Director: Dr. Rainero Maroja
ANNEX II

Directors and Staff Members of Institutions Visited in Santarém

A. SESP Hospital (Serviço Especial de Saúde Publica)
   Director: Dr. José Abrantes
   Dr. Vicente Paiva - Surgeon
   Dr. Dias da Silva - Surgeon

B. Maternidade Sagrada Familia
   Director: Sister Dolores
   Sister Alicia
ANNEX III

Directors and Staff Members of Institutions Visited in Altamira

A. SESP Hospital

   Chief Surgeon: Dr. Walter W. Amoras

B. Agrovila Clinic

C. Agropolis Brasil Novo Clinic
REFERENCES


