Dr. Binford. I should have mentioned before, a very unique feature of this conference held in Washington, D. C. Travel to it was *not supported* by a grant from the U. S. Government.

Some years ago, as a member of the Public Health Service Subcommittee on Leprosy Research, I participated in planning conferences on Progress and Potentials in Leprosy Investigations, held at Carville, in 1956 and 1958. Our PHS Committee was greatly impressed by the enthusiasm shown by scientists in participating in these Carville conferences. Although each scientist invited had to provide his own travel, the conferences were highly successful and did much to stimulate leprosy research in the United States.

With very few exceptions, all of the participants in this Washington meeting have been able to provide their own travel or obtain travel through their organizations or governments. I would like, however, at this time, to note that Dr. Oliver W. Hasselblad, President, American Leprosy Missions, has provided travel for one of the participants from India, and Mr. O. Gheeraert, Executive Secretary of the Foundation Pere Damien pour la Lutte Contre La Lepre (FOPERDA), provided support for two other scientists from India. The Leonard Wood Memorial provided travel support to bring two scientists from the Philippines who were not on its full-time staff. Although the Federal Government is not supporting this meeting by a special grant, I am sure that some of the participants in the meeting have been able to travel as government employees or through grants provided to their organizations by the Federal Government.

Dr. Long, who will edit the *Proceedings* of this meeting, will now say a few words about manuscripts.

Dr. Long. All I want to say has been indicated several times. We hope to publish the *Proceedings* of this conference between a single pair of covers. Our hope is to raise the necessary funds, in ways that Dr. Binford has indicated, so that we can make the *Proceedings* a supplementary number of the INTERNATIONAL JOURNAL OF LEPROSY. Such supplementary numbers are truly dividends. They do not cost the members of the International Leprosy Association anything over their usual subscription, for we include them as part of THE JOURNAL year. According to present plans we shall publish what is presented here including both the formal papers and the discussions. So we ask you to speak as clearly as possible so that our tape recording will be accurate.

Dr. Binford. The next speaker will be introduced by Dr. E. B. Johnwick,[1] a U. S. Public Health Service officer who has had a notable career in various areas of the Service, including one period in which he was intensely interested in studying a disease now receiving less attention, syphilis. Dr. Johnwick went to Carville in 1956 as Medical Officer in Charge, where for nine years he has directed an active program of research and education in leprosy. On several occasions Dr. Johnwick has invited Dr. Paul Fasal to come to his institution to teach leprosy to physicians assembled there. Therefore I have asked him to introduce Dr. Fasal.

Dr. Johnwick. I note in the program that we are going to hear a paper by Dr. Møller-Christensen on new knowledge through paleopathology. I would like to keep in step with this trend in the program and go back to the beginnings of time. When the world's first medicine man brewed his wooden glass of fluorescent tea and put out a few bloody chicken feathers in a forest clearing to hold his first clinic, undertaking the responsibility of making his neighbors well, I am sure a patient with leprosy soon appeared to baffle him and test his diagnos-

[1]Deceased 14 October 1965.

tic skill. The recognition of leprosy is now in the province of the dermatologist, who sees this illness imitating almost every skin disease.

It is significant that the next speaker will be one closely identified with Vienna, the charming city that was the birthplace of dermatology. Dr. Hugo Fasal was a dermatologist and his son Paul Fasal was trained in Vienna in internal medicine, pathology and dermatology. His interest in leprosy was aroused during a stay in Kuala Lumpur in British Malaya between 1938 and 1941. In 1941 he came to the United States but he has remained mobile and has continued to travel with no apparent fatigue, and no ill effects. The people of the world are very fortunate to have among them this outstanding citizen and dermatologist, who has an almost limitless capacity of affection for people and a pair of observant eyes that see beautiful or ugly things with an inquisitive, understanding, and extremely orderly mind. In 1947 Dr. Fasal was certified by the American Board of Dermatology and Syphilology, and since 1949 he has been consultant in dermatopathology at the Letterman General Hospital in San Francisco. Since 1950 he has been consultant in leprosy to the California State Department of Public Health, and for the last 10 years has been on the panel of Dermatopathology of the American Academy of Dermatology. Since 1960 he has been director of a leprosy clinic at the USPHS Hospital in San Francisco and consultant to the hospital at Carville. He is also associate clinical professor of dermatology at the University of California Medical School. Dr. Fasal will now address you on the "Differential diagnosis of leprosy."

Differential Diagnosis of Leprosy

Paul Fasal, M.D.[1]

More than one hundred years ago Ferdinand von Hebra, Professor at the University of Vienna Medical School, intensely interested in the diagnosis and treatment of skin diseases, delineated dermatology, making it a specialty of its own. In his teaching he emphasized the importance of correlating clinical picture and histopathologic findings in order to arrive at the correct diagnosis.

I feel strongly that the teaching of this man is of special importance for everybody concerned with the diagnosis of leprosy. In our country many cases of leprosy are missed, being mistakenly diagnosed as other diseases, especially those accompanied by skin manifestations. Conversely, in countries where leprosy is encountered frequently, many persons are diagnosed as suffering from leprosy who do not have this disease. This is done not only on clinical, but also on histopathologic examination.

The reason for these mistaken diagnoses is that leprosy can imitate many diseases. Therefore, knowledge of dermatology and dermatopathology is essential to diagnose or rule out leprosy.

On the basis of actual cases, I shall now attempt to illustrate the points just made. A Caucasian, born in Japan, who had lived most of his life in the Philippine Islands, came to the San Francisco Bay Area 10 years ago. While in California, he was treated for arthritis, gout, a hip fracture, and stomach ulcers. All through this time he had an erosion on his nose, a small papule on his upper lip and a macular eruption on his trunk. No doubt because of all his other pathologic conditions, no physician paid attention to his skin lesions. Finally, his nose became obstructed, and in the mass that was removed numerous acid-fast bacilli were found. Histopatho-

[1]Chief, Leprosy Service, U. S. Public Health Service Hospital, San Francisco, California. Mailing address: 706 D St., San Rafael, Calif. 94901.

Editor's note: In presenting this paper, Dr. Fasal illustrated his descriptions with color transparencies. Unfortunately, because of the expense involved, only a limited number of illustrations could be reproduced, and these in black and white.

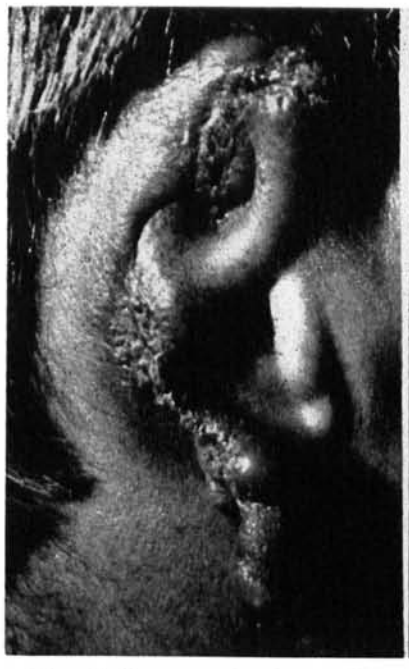

FIG. 1. Lupus vulgaris mutilans

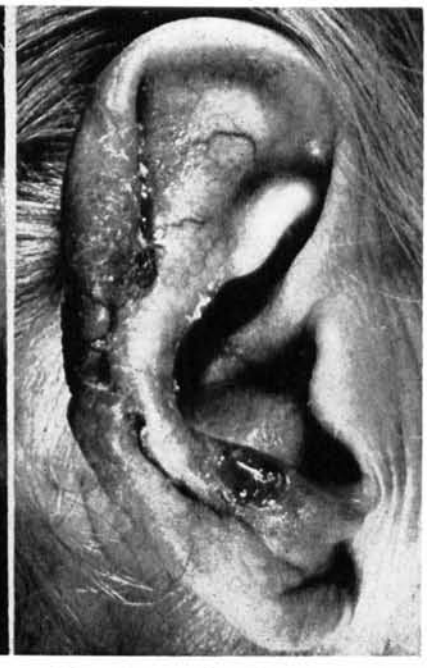

FIG. 2. Basal cell carcinoma

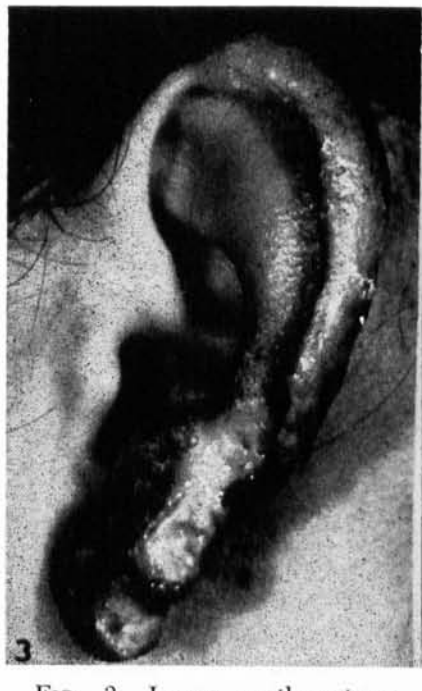

FIG. 3. Lupus erythematosus hypertropicus profundus Brocq-Becket.

FIG. 4. Lupus vulgaris

logic examination of a biopsy specimen obtained from the papule on his upper lip showed in the H & E stain a granuloma in the corium, separated from the epidermis by a zone of normal connective tissue. The acid-fast stain revealed innumerable acid-fast bacilli in a pattern so colorful and distinct that I call it the "wallpaper pattern." Another section from the same patient demonstrated classically the affinity of the lepra bacillus for nerve tissue.

The history of the next patient illustrates the long delay in arriving at the diagnosis of leprosy so often encountered in this country. This man was born in the state of Minnesota and had never left the continental United States. Because of areas of anesthesia on his body and deformities of his hands, he sought aid at a renowned teaching institution; there his disease was diagnosed as syringomyelia. When he developed eye lesions, the diagnosis remained syringomyelia plus iritis, cause unknown. And when nodules on his nose appeared, these were thought to be due to excessive alcohol consumption. At the time I saw him first, he presented the typical picture of lepromatous leprosy. That the correct diagnosis had been overlooked for 15 years is not surprising when one recalls that this man had lived all his life in the continental United States; the index of suspicion for leprosy was low. Actually, in this case the origin could be traced easily. The patient is a descendant of one of the 140 persons afflicted with leprosy who had migrated from Scandinavia to Minnesota about 100 years ago. He belongs to the second generation born in this country and is apparently one of the few cases of leprosy left from this once existing endemic focus.

The other diagnostic mistake, viz., diagnosing leprosy when it is not present, is illustrated by the following case I saw in a leprosarium in the South Pacific. This woman had a severe deformity of her right upper extremity and mutilating changes of her nose, the typical picture of the "leper" shown in movies like "Ben Hur." Examination revealed that this patient did not have leprosy. She suffered from yaws and elephantiasis.

Even if leprosy is considered in the differential diagnosis, the clinical picture can be misleading. Consider the following examples: The only lesions a young woman had were several reddish plaques on the face; the typical picture of seborrheic dermatitis. Another woman presented hypopigmented areas on her back, suggesting a diagnosis of superficial fungus infection. A man showed a plaque with an elevated border on his right wrist which had been treated for years as granuloma annulare. All these lesions were found to be manifestations of tuberculoid leprosy. No bacilli were detected on histopathologic examination, as was to be expected. But the histopathologic picture was diagnostic for tuberculoid leprosy. While the granuloma observed in the upper corium could have been tuberculosis, a tuberculid, sarcoid, or leprosy, the selective involvement of nerves removed from the granuloma established tuberculoid leprosy as the correct diagnosis.

One of the organs often affected in leprosy is the external ear. The degree of ulceration, deformity or infiltration is of no help in diagnosing leprosy. Of ten external ears shown, the first five exhibit the most spectacular changes. The diagnoses are: tuberculosis (Fig. 1), basal cell carcinoma (Fig. 2), deep lupus erythematosus (Fig. 3), tuberculosis (Fig. 4), and Kaposi sarcoma (Fig. 5). The next five ears (Figs. 6-10) prove that the clinical manifestations of leprosy can be much less dramatic than those caused by other diseases.

Let me at this time digress a little and talk about the merits of skin scrapings in the diagnosis of leprosy. A patient who had had lepromatous leprosy for many years, showed a cartilage-like nodule in his ear. His disease had been declared inactive elsewhere after twelve consecutive monthly scrapings for lepra bacilli had been negative. In our clinic the results of skin scrapings are not accepted as proof of activity or inactivity. Therefore a biopsy was performed. Histopathologic examination showed a granuloma separated from the epidermis by such a wide zone of normal connective tissue that no skin scraping would have been able to penetrate it. Large Virchow cells were present in the

FIG. 5. Kaposi's sarcoma

FIG. 6. Tuberculoid leprosy

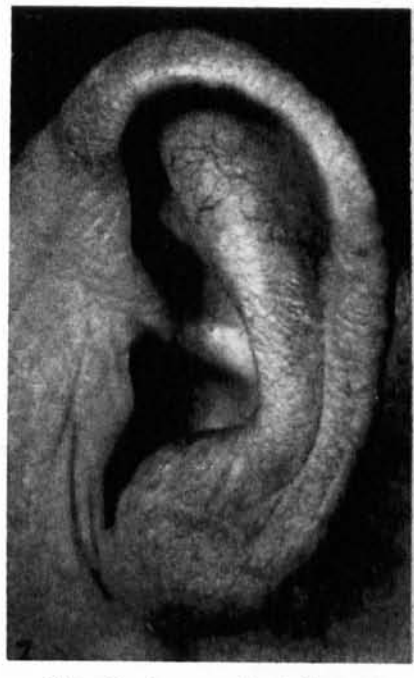

FIG. 7. Lepromatous leprosy

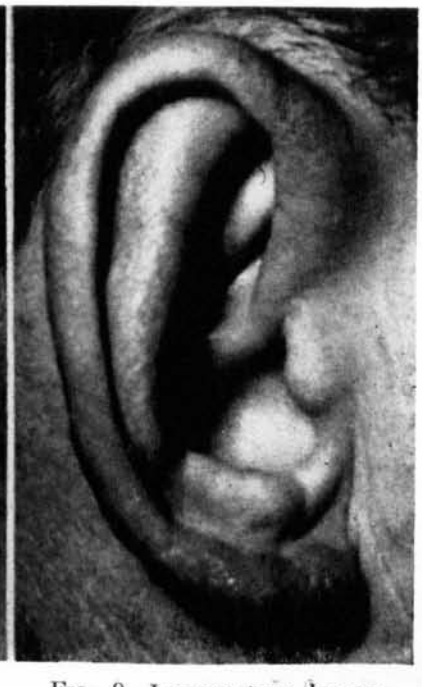

FIG. 8. Lepromatous leprosy

depth and acid-fast bacilli could be demonstrated. While the presence of acid-fast bacilli in skin scrapings will often be indicative of leprosy, their absence does not rule out leprosy and does not give any clues to the etiology. When you are called upon to diagnose or rule out leprosy, I urge you to perform biopsies. This will enable you not only to establish that the patient has leprosy or does not have leprosy, but will also put you in a position to make the diagnosis in those cases where leprosy is not present.

Another point I would like to make is that clinically normal-appearing skin can show the histopathologic picture of leprosy. A woman whose only subjective symptom was numbness of her extremities, had no skin lesions, but her eyebrows and eyelashes were missing. Histopathologic examination of a biopsy specimen obtained from normal-appearing skin showed minute foam-cell granulomata containing acid-fast bacilli. This form of leprosy is called diffuse lepromatosis and was first described in patients from the state of Sinaloa in Mexico. However, it has since been found also in other countries. There is diffuse involvement of the skin, affecting also nerves and blood vessels. If such a patient suffers a lepra reaction, he will develop the so-called erythema necroticans or Lucio's phenomenon, which leaves bizarre scars frequently resembling artefacts (Fig. 11a).

The scars seen in the next illustration (Fig. 11b), very similiar to those just shown, were caused by a deep fungus infection *(Actinomyces mexicanus)*. The next ten pictures are other paired comparisons, the first always a manifestation of leprosy, the second a similar lesion caused by another disease. The latter were mycosis fungoides (Fig. 12b); scleroma (Fig. 13b); syphilis (Fig. 14b); reticulum cell lymphoma (Fig. 15b); and tinea corporis (Fig. 16b). These are to be compared respectively with Figure 12a, tuberculoid leprosy; Figure 13a, lepromatous leprosy; Figure 14a, erythema necroticans in diffuse lepromatosis; Figure 15a, lepromatous leprosy; and Figure 16a, tuberculoid leprosy.

These pictures all show leprosy to be a great imitator, as far as the clinical manifestations are concerned. I would like to

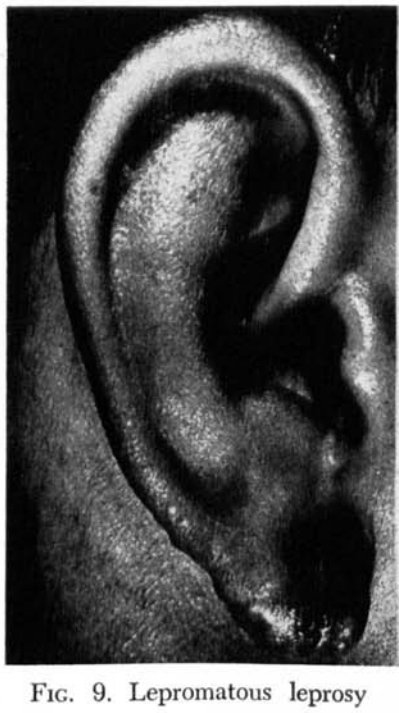

FIG. 9. Lepromatous leprosy

FIG. 10. Lepromatous leprosy

FIG. 11a. Scars after erythema necroticans (Lucio's phenomenon) in diffuse lepromatosis

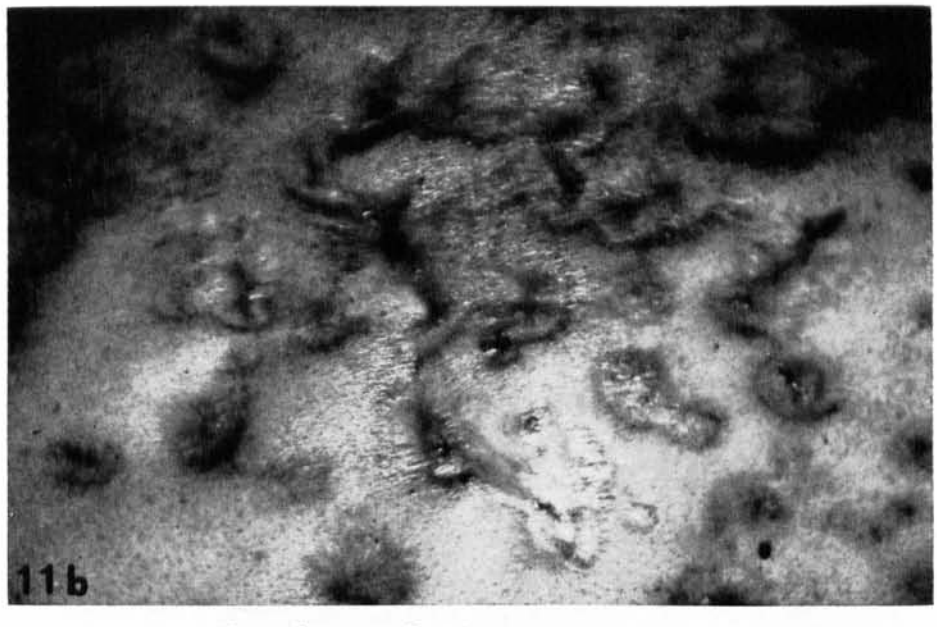

FIG. 11b. Scars after *Actinomyces mexicanus*

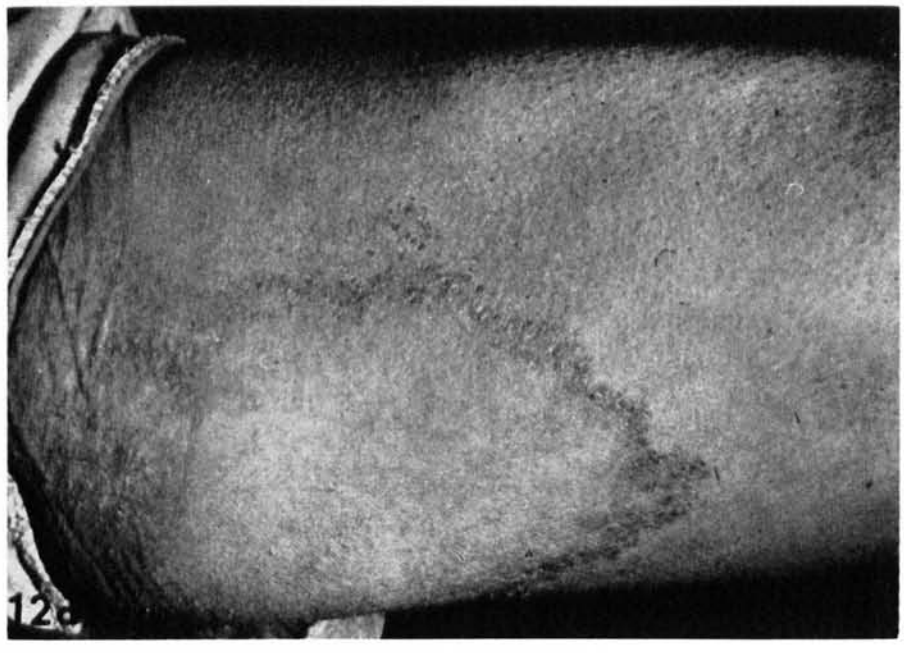

FIG. 12a. Tuberculoid leprosy

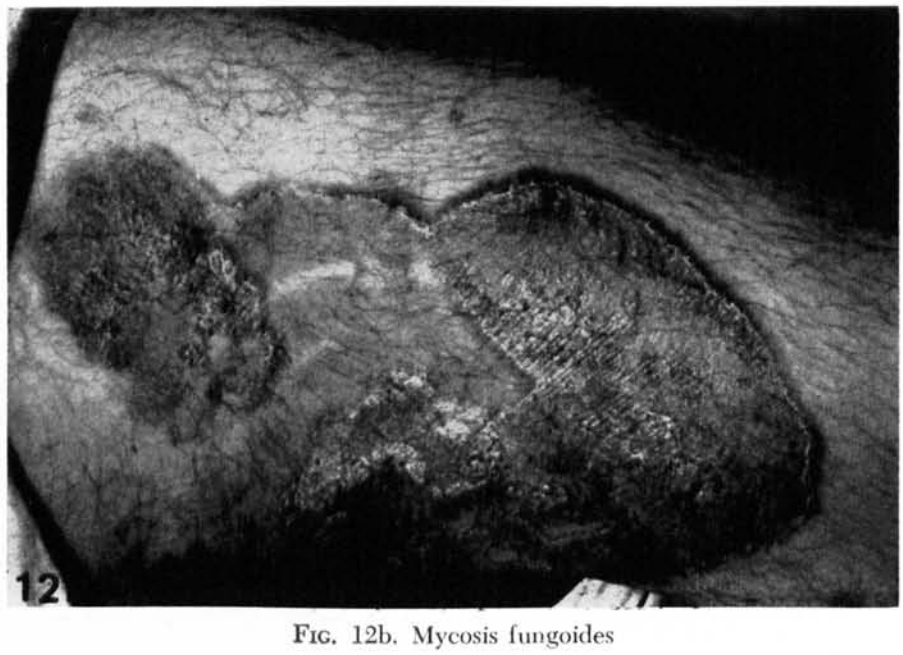

FIG. 12b. Mycosis fungoides

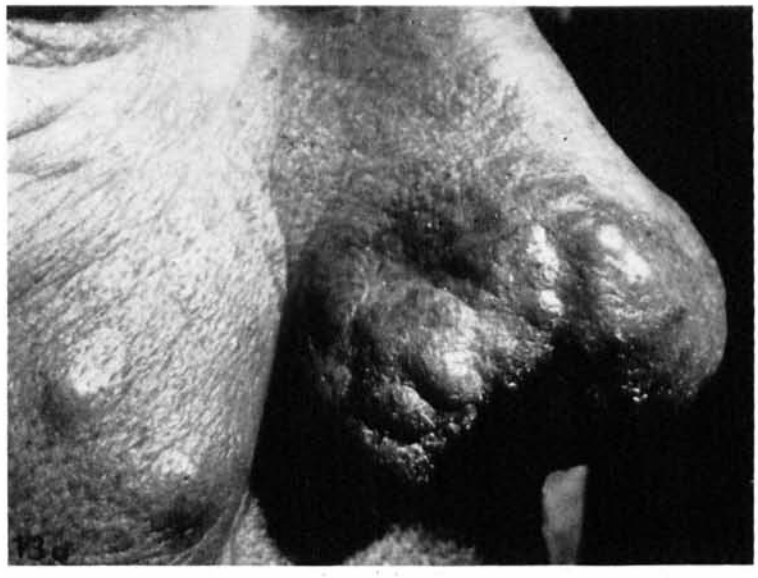

FIG. 13a. Lepromatous leprosy

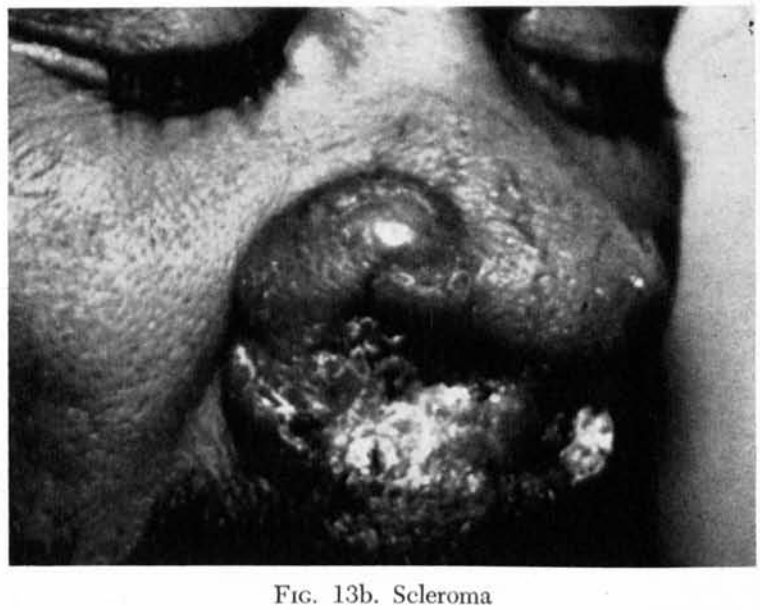

FIG. 13b. Scleroma

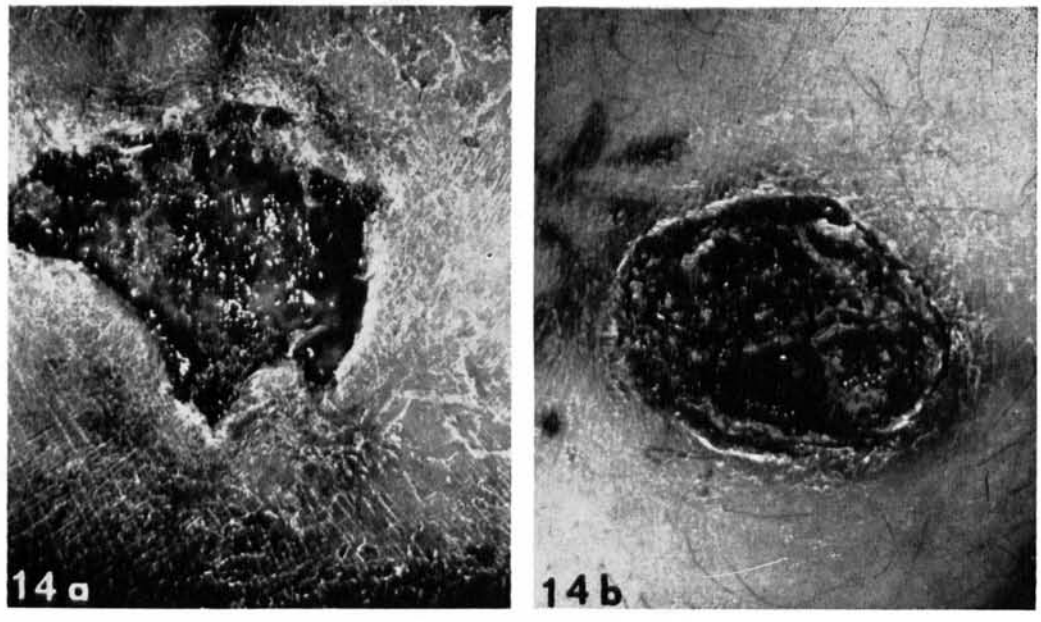

FIG. 14a. Erythema necroticans (Lucio's phenomenon) in diffuse lepromatosis
FIG. 14b. Gumma

emphasize, however, that it is not only the clinical picture which can be misleading. Differential diagnostic difficulties are encountered also at the histopathologic examination. In lepromatous leprosy an important finding is the zone of normal connective tissue between epidermis and the granuloma. This same picture, a granuloma separated from the epidermis by a zone of normal tissue, can be present also in eosinophilic granuloma of the skin. Another condition shows an inflammatory infiltrate separated from the epidermis by a zone of normal tissue; this is idiopathic atrophy of the skin. One patient referred to our clinic with a clinical and histologic diagnosis of leprosy, actually suffered from a granuloma annulare; another, from sarcoidosis.

Although most cases of leprosy have lesions on the skin, occasionally the only visible manifestations will be an enlarged nerve lying close to the surface of the skin. Thickening of one great auricular nerve is a characteristic sign of leprosy. Several years ago an "epidemic of leprosy" was reported to have been found to exist in American Samoa. Many of the cases were diagnosed on the basis of a markedly enlarged great auricular nerve. When I examined these patients; all healthy and very muscular men, there was no evidence of leprosy. Histopathologic examination of nerve biopsies showed the nerves to be hyperplastic but otherwise normal. It was found that all the men exhibiting this hypertrophied nerve manned so-called longboats, row boats which bring passengers and supplies from ocean liners, unable to land because of the coral reefs, to the shore. They also carry these heavy boats on their shoulders. It was felt that the hypertrophy of the nerve was a physiologic variant in these men probably connected with the specific work they performed.

Finally, I want to tell you more about a patient sent to me by a colleague with the tentative diagnosis of leprosy. The clinical picture shown earlier (Fig. 15b) was such that leprosy definitely had to be considered in the differential diagnosis. The histopathologic examination of a biopsy specimen showed the typical picture of a reticulum cell lymphoma. He was dead within six months. A few weeks later, a patient appeared at the Leprosy Clinic exhibiting a clinical picture (Fig. 15a) practically identical with that of the patient

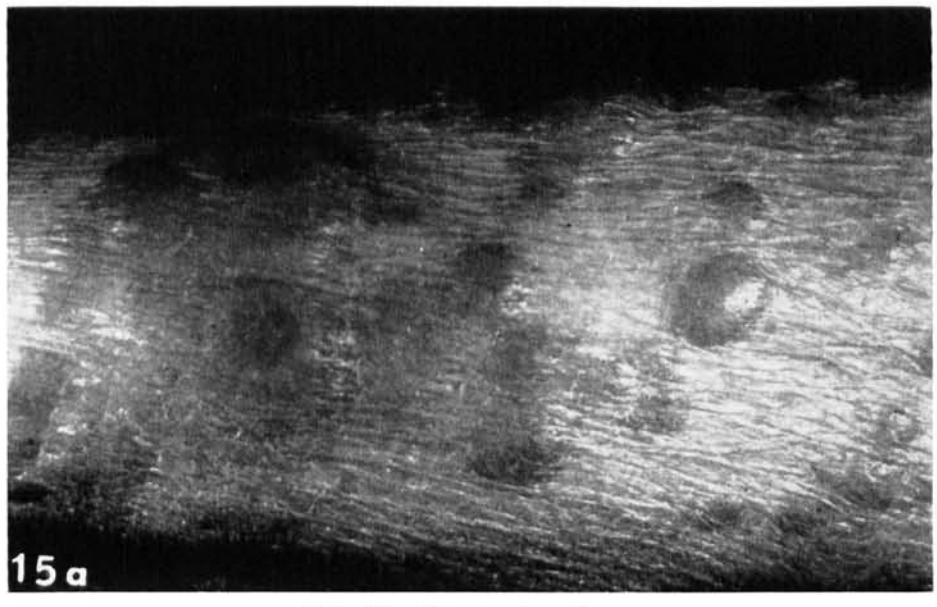

FIG. 15a. Lepromatous leprosy

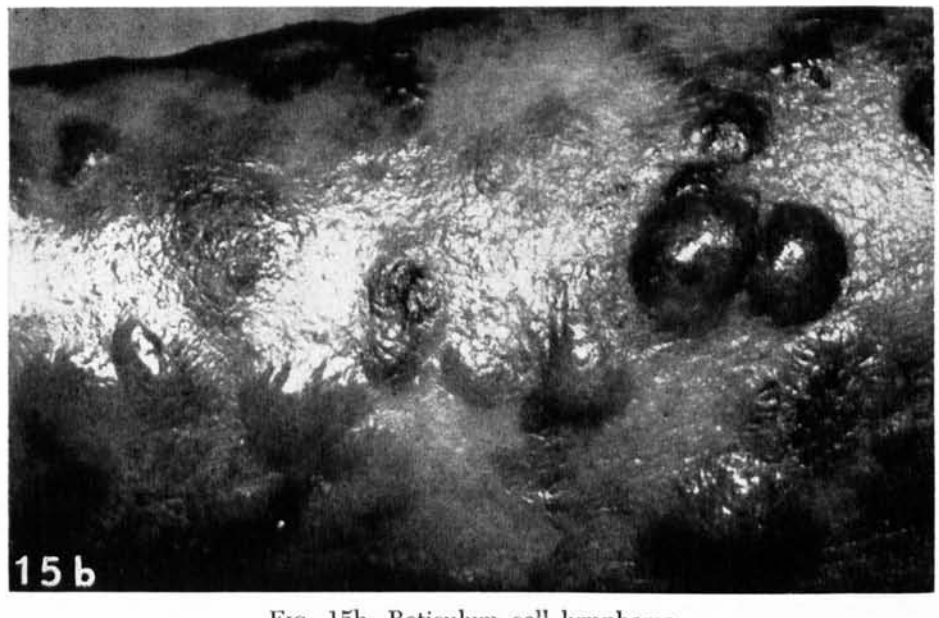

FIG. 15b. Reticulum cell lymphoma

FIG. 16a. Tuberculoid leprosy

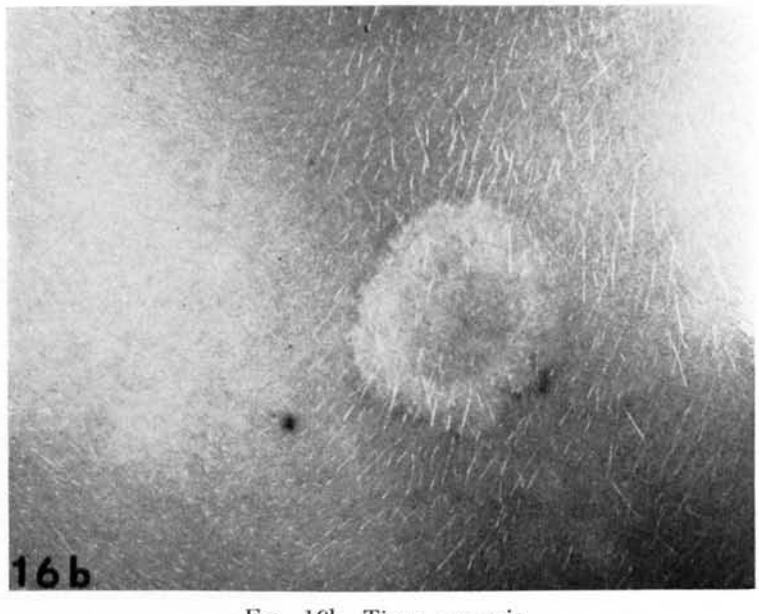

FIG. 16b. Tinea corporis

just mentioned. In this case, however, histopathologic examination showed the typical picture of lepromatous leprosy with numerous bacilli in the acid-fast stain. This man is very much alive today.

As has been pointed out earlier, the reason why the diagnosis of leprosy is missed so frequently in this country is that physicians seldom consider leprosy in the differential diagnosis. The average time between appearance of symptoms and correct diagnosis in patients admitted to the U. S. Public Health Service Hospital in Carville, according to Dr. Edgar B. Johnwick, as well as at our clinic, is over three years. The range is six months to 20 years. It is high time that we improve this score.

I am fully aware that I did not tell you anything really new, but I am also aware that repetition is an important factor in successful teaching. Actually, there is very little that has not been said or done before. I started this presentation by paying homage to Hebra, and I want to close it by quoting from a letter Emperor Franz Josef wrote to Ferdinand von Hebra in 1849. It informed Hebra of his appointment as Professor of Dermatology. The next sentence, literally translated, reads, "However, this new title will not be accompanied by an increase in salary." Tempora mutantur?

Dr. Binford. Those of you who felt from the lectures this morning that you could go out and diagnose leprosy probably now have a different opinion. Dr. Fasal, I want to thank you for this very instructive and excellently illustrated presentation, made in your usual interesting fashion.