CURRENT LITERATURE

ABSTRACTS OF CONGRESS PAPERS

This department contains abstracts or notes of the papers actually presented in the sessions of Tokyo Congress. It includes no items "read by title." The compilation has been far easier in this instance than after the previous congresses because Dr. Ross Innes, acting as a recording secretary at all sessions (herein referred to as the Recorder), kept meticulous notes on who spoke, and when, and—in gist—what he said. Those notes have been drawn upon in many instances, with the reservation that they may not in every instance be precisely what the author would have chosen to write himself.

For the most part the abstracts are those which were supplied by the authors, as required, and were printed in three languages before the Congress convened. The English version is used except when the authors were French nationals. In general they have been edited to reduce space requirements. On the other hand, at times they have been supplemented from the Recorder's notes. In several (16) instances author's abstracts were not provided, and only the Recorder's notes provide information as to what was presented.

The abstracts are grouped according to the topics of the Congress, as was usually the case in the program, but a few papers which were misclassified there are grouped at the end under the heading of "Other Topics." The chairmen of four of the six symposia presented either summaries of the previous discussions of their panel groups, or the draft reports of the corresponding technical committees. For information about those presentations the reader is referred to the Technical Resolutions of the Congress.

1. CLASSIFICATION

KITAMURA, K. Classification system of leprosy, newly drafted in Japan. *(Symposium paper.)*

This is to present the classification system which was drafted in Japan in 1957, primarily for a standardized classification of leprosy patients submitted to the joint studies on the lepromin test made by Yanagisawa and associates. For this, the Madrid classification was converted into a more simplified and—for Japan—more practical usable form. There are two *types,* L (lepromatous) and T (tuberculoid); two *subtypes,* TM (tuberculoid macular) and TN (tuberculoid neural); and one *group,* A (atypical). For both type L and subtype TM three *stages* are set up and defined: p (progressive), r (retrogressive), and q (quiescent). These types, subtypes, stages and group are tabulated as follows:

Type L.....Stages p, r, q
Type T.....Stages p, r, q
  Subtype TM
  Subtype TN
Group A

(The Recorder's notes include the following further information.) TN, or tuberculoid neural, signifies polyneuritic. Group A is for atypical cases which do not clearly belong to one of the definite types, but which under observation may be moved into one of them.)

COCHRANE, R. G. A critical appraisal of the classification of leprosy. *(Symposium paper.)*

The main reason for confusion and controversy about classification is that the over-all picture of leprosy differs so much in different parts of the world that a

description of it as seen in one region may not agree with that which is seen in another. Classification must be approached along two lines. (1) A simple and practical classification for the field worker. (2) One which would meet the needs of the specialist leprologist. The simplest classification so far presented is the field classification of the Indian Association of Leprologists. It is entirely clinical, and the great majority of cases can be classified without reference to laboratory tests. Further, it avoids the controversy as to stability of types, and leaves that discussion to those who have facilities to investigate the evolution of leprosy. A more detailed classification is necessary for better international understanding of leprosy, and the author puts forward a modification of the Havana classification which holds that the earliest picture of leprosy is a nonspecific cellular response indicating little or no tissue defence (potentially lepromatous), and that as the disease develops a tissue response is built up and the case then passes through a dimorphous phase toward true tuberculoid leprosy. The nearer the dimorphous picture is to tuberculoid, the less likely is it to transform to lepromatous. The great majority of cases start as potentially lepromatous, but once they transform to true tuberculoid leprosy the immune response is fixed and it is not possible then to develop lepromatous leprosy. The actual terminology of classification is of little importance so long as it can be understood by all field workers, and is sufficiently flexible to be capable of such modifications as will make it of value to international leprologists.

DHARMENDRA. The classification of leprosy in India. *(Symposium paper.)*

The Indian Association of Leprologists has evolved a system which is presented for consideration and approval. There are no unsurmountable difficulties in reaching an agreed system of classification. The chief difficulty lies in choosing the original terms and in expressing the process of evolution of the disease. We believe that the basis of classification should be clinicobacteriologic; histology and immunology should be brought in next. The system should have a minimal number of classes. It should be simple enough for field workers, yet contain room for refinements by experts. In the Madrid classification we find two discrepancies, (1) the flat "tuberculoid" macule, and (2) "tuberculoid" polyneuritis in the absence of clinical tuberculoid manifestations. In that classification the polyneuritic cases are split up and put in either the lepromatous or the tuberculoid type. We would solve this problem by forming two more classes, the maculoanesthetic and the neuritic. Dr. Wade has helped in this synthesis. We have thus six forms. (From the Recorder's notes, lacking an author's abstract.)

2. BACTERIOLOGY AND PATHOLOGY

HANKS, J. H. Introductory review. *(Symposium paper.)*

(This introductory paper by the chairman of the symposium on pathology and bacteriology was in effect a preliminary draft of what became the report of the technical committee on this aspect of leprosy, which see.)

HANKS, J. H. Evaluation of the physiologic state of *M. leprae* by cytologic methods. *(Symposium paper.)*

After developing a test-tube method for measuring the metabolic capacity of mycobacterial suspensions, the yields of formazan were shown to be proportional to the plate counts of cultivable mycobacteria and also to predict the infectiousness of *M. leprae murium*. Many of the bacilli in these preparations exhibited brilliant internal granules of formazan. When similar principles were applied to mycobacteria affixed to coverslips suitable for direct microscopic examination, the proportions of saprophytic organisms exhibiting metabolic activity were correlated with viability. Similar results could not be obtained with pathogenic species. In samples possessing

high viability or infectiousness only low proportions of bacilli contained formazan deposits. Simultaneous use of tetrazole acceptors and dyes demonstrated that such compounds failed to penetrate into the internal sites of metabolic activity in high-quality, pathogenic bacilli. Direct studies of permeation by 0.001 M crystal violet at 37° revealed: (a) that in any species the least permeable individuals contained the greatest numbers of cytologically perfect structures, (b) that rates of permeation distinguish saprophytes (which stain in minutes) from pathogens (which may require 14 days). *M. leprae* from sulfone-treated patients differed from the typical pathogens (and from *M. leprae* from untreated patients) in two respects: staining within less than 60 minutes, and lack of the capsular structures with which impermeability is associated.

NAYLOR, R. F. Study of the action of sulfones on the metabolism of mycobacteria. *(Proffered paper.)* (See original in this issue, page 313.)

HANKS, J. H. Enumeration of *Mycobacterium leprae* for the standardization of lepromin. *(Proffered paper.)*

Standardization of lepromin in terms of its least significant component (human tissue) is an expedient necessitated by lack of convenient methods for determining its bacillary content. Studies on the centrifugal purification of *M. leprae* had defined conditions permitting maximal yields of single bacilli. Modification of these methods has recently been shown to permit convenient estimation of the numbers of bacilli in lepromin. Declumping and dispersion of bacillary masses without protein precipitation or destruction of bacilli is accomplished by flowing 0.02 cc. of chloroform beneath an 0.2 cc. aliquot of well-shaken lepromin in a 3 cc. glass-stoppered tube (Kimble No. 45152) and by shaking vigorously for 3 minutes. Serum 1% in water is added to rinse down the walls of the tubes and make the final tissue concentrations equivalent to 1%. A standardized 0.7 mm. platinum loop is used to transfer 0.000,2 cc. aliquots as a series of small droplets in vertical rows on clean glass slides. These are dried, formalinized, stained, counted and assayed by methods already published. A comparison of three lepromins revealed 195, 60 and 555 million bacilli per cc. of 3% tissue suspension. If these samples were adjusted to the bacillary concentration in the most reliable pool (Wade's = 195), the second sample would contain 9.7% tissue and the third 1.1% tissue. The need for large pools of lepromas and the probability that such differences in tissue content would modify the results of the lepromin test are discussed.

REES, R. J. W. The study of rat leprosy bacilli in tissue cells as a contribution to the problem of propagating human leprosy bacilli in tissue cultures. *(Symposium paper.)*

Rat leprosy is undoubtedly the one disease exhibiting a host-parasite relationship most closely resembling human leprosy, since both are chronic mycobacterial infections in which the bacilli exist as intracellular parasites of mononuclear cells. The use of tissue-culture systems for attempts to grow rat leprosy bacilli *(M. leprae murium)* is suggested by (1) the intracellular existence of the bacilli *in vivo*, (2) failure of the bacilli to derive energy from any extracellular substrates, and (3) inhibition of endogenous metabolism of the bacilli by serum. Using precise methods for counting the total number of bacilli per culture before and after cultivation, unequivocal though limited multiplication has recently been obtained in tissue culture. Unfortunately, the types of tissue used in these two studies cannot be maintained in a healthy state for the long-term studies required to obtain more continuous multiplication of the slow-growing leprosy bacillus. Recently, multiplication of *M. leprae murium* has been initiated in an established laboratory strain of rat fibroblast. The initial rate of multiplication in tissue culture corresponds closely to what which ob-

tains *in vivo*. No significant multiplication was obtained in comparable cultures containing high concentrations of streptomycin and isoniazid. The significance of these results in the problem of obtaining continuous multiplication of leprosy bacilli in tissue culture is discussed.

SHEPARD, C. C. Tissue culture studies of mycobacterial pathogens. *(Proffered paper.)*

The monolayer tissue culture systems conveniently and reproducibly provide healthy human and simian cells that are well suited for the growth of many human viruses. When the tissue-culture media used in virus work are modified by the inclusion of suitable sera (e.g., 10% horse serum) the cells actively take up mycobacteria, and the intracellular growth of these organisms can be followed. All of the cultivable mycobacterial pathogens have been studied, and kodachromes illustrate the distinctive patterns exhibited by these species. The intracellular growth rates bear a direct relationship to the growth rates of the species in bacteriological medium. Results with leprosy bacilli so far are inconclusive. The systems developed seem very helpful in the vexatious problems of classification of mycobacteria, since many of the known pathogenic species are easily identified by their growths in the cells. Strains of modified virulence, such as BCG, do not grow in the cells as rapidly as the pathogens from which they were derived, and the saprophytes *M. phlei* and *M. smegmatis* do not grow at all. Several cultures of acidfasts reputed to be *M. leprae* have also been studied in cells, but these have shown no signs of intracellular growth.

MACFADZEAN, J. A. and VALENTINE, R. C. An attempt to determine the morphology of living and dead mycobacteria by electron microscopy. (Preliminary communication.) *(Proffered paper.)*

This paper describes observations made on the morphology of *M. leprae murium* and *M. leprae* with the electron microscope. Specimens from rat lepromata and from biopsy specimens from leprosy patients were prepared in the same manner by grinding with sand and phosphate buffer pH 7.4 for two minutes and separating the bacilli from cellular debris by centrifugation. The specimens were fixed with formalin. In a freshly prepared suspension, 95% of *M. leprae murium* have an almost uniform electron density, apart from darker areas often at the poles and some electron-dense granules. If a fresh suspension is stored at 4°C. for one month without fixation the morphologic picture remains the same. The infectivity in rats of the fresh suspension and that stored at 4°C. is similar. In a suspension stored at 37°C. for one month the cytoplasm of the organisms is shrunken and the cell membranes are largely empty. A similar morphologic picture is presented by organisms heated in a water bath to 80°C. In both cases the organisms are no longer infectious to rats. It would appear that one can differentiate morphologically between viable and nonviable bacilli. The value of the application of such a technique of *M. leprae* is obvious. Similar clear-cut differences between what appear to be viable and nonviable forms have been observed in the human leprosy bacilli. Suspensions of *M. leprae* have been prepared from 20 biopsy specimens from untreated cases, and the percentages of apparently viable forms found ranged from 0-75% with a mean of 54%. It is too early as yet to say if the percentage of viable forms falls during sulfone treatment.

REES, R. J. W., VALENTINE, R. C. and WONG, P. C. The biological significance of different appearance of rat and human leprosy bacilli as shown by electron microscopy. *(Proffered paper.)*

The appearance of rat and human leprosy bacilli have been compared with other cultivable species of mycobacteria in this study, designed to confirm MacFadzean's observations. The leprosy bacilli obtained from lepromatous tissues were also com-

pared with tubercle bacilli from infected animal tissues. No differences could be found in the general morphology of the different species, nor did different methods of preparation or growth of tubercle bacilli *in vitro* alter the appearances. In suspensions of *M. leprae murium* three distinct morphologic types could, in general, be distinguished, "normal," "degenerate," and "segmented." The distinction is based on differences in the internal structure of the bacilli seen with the electron microscope, but not with the light microscope. When suspensions of "normal" murine bacilli are incubated in phosphate buffer at 37°C. a high proportion are transformed to the "degenerate" type. Whereas animals with untreated murine leprosy yield mainly "normal" bacilli, "degenerate" forms predominate in animals receiving effective chemotherapy. (From the Recorder's notes: In the lesions of untreated rats only 13% of the bacilli were degenerate, but 75%—rising later to 95%—in rats treated with INH.) It has been shown that "normal" bacilli are infective, whereas the "degenerate" and "segmented" forms are noninfective. Electron microscopy therefore affords a rapid method for following the survival of *M. leprae murium*, and has proved valuable in attempts to grow the organism in tissue culture. Similar morphologic differences have now been found in *M. leprae* from cases of lepromatous leprosy. Relatively high proportions of "degenerate" bacilli have been found in apparently untreated cases.

OKADA, S. Electron microscope studies of murine leprosy bacilli. *(Proffered paper.)* (See original in this issue page 352.)

YAMAMOTO, T., NISHIURA, M., HARADA, N. and IMAEDA, T. The difference between lepromatous and tuberculoid lesions of leprosy as observed with the electron microscope. *(Proffered paper.)*

By means of electron microscopy of ultra-thin sections of lepromatous and tuberculoid lesions, both of the skin and of peripheral nerve trunks, we have tried to elucidate the differences of the ultra-fine structures of lepromatous and tuberculoid lesions. The observations are summarized as follows: 1. In lepra cells, the leprosy bacilli are wrapped within moderately electron-dense opaque droplets. Foamy spaces appear in the opaque droplets, and thus there are finally formed intracellular foamy structures in the cytoplasm of lepra cells. 2. In the early stage of reactional tuberculoid lesions, there are small quantities of tiny opaque droplets in the phagocytes loaded with leprosy bacilli. The morphologic features of the bacilli in such lesions are not different from those of the bacilli in lepromatous lesions. The cell membrane of phagocytes in tuberculoid lesions is frequently broken, and in such cases mitochondria and microsomes together with phagocytosed bacilli are discharged from the broken cells into the extracellular body fluid. 3. In the peripheral nerve trunks, the tuberculoid lesions of endoneural spaces involve the Schwann cells of the cord of Büngner stage and destroy them, while the lepromatous lesions of endoneural spaces do not destroy the Schwann cells of the cord of Büngner stage. (From the Recorder's notes:) The electron-transparent zone around *M. leprae* is a kind of biostabilizer for the bacillus.

RIDLEY, D. S. Observations on the prognosis of different classes of leprosy in different races. *(Symposium paper.)*

Serial biopsies in cases of leprosy with bacilli demonstrate two independent forms of response to treatment, namely, diminution in the size of the lesion, and decrease in the bacterial density in the lesion; the two factors combined give an estimate of the rate of progress. Lepromas from different countries of Europe and Asia respond at very much the same rate: under sulfones the index is multiplied by three-fourths every 6 months. Lepromas from certain parts of Africa progress at about

twice this rate, and from this point of view correspond to a European or Asian borderline state. The rapid rate of progress of these cases is correlated with an excess of lymphocytes or fibrocytes in the lesions, and the bearing of this finding on classification is discussed. (The following is added from the Recorder's notes.) In different regions lepromata may even differ in parts of those regions, and the bacterial index varies in typical cases. But the new serial biopsy gives fall at a standard rate, i.e., 25% in Europeans in 6 months. The Anglo-Indian rate is the same. Not enough data are available for any statement about other races. Histologically the estimation of the figure for the picture is quite easy and practicable. Borderline and intermediate cases are harder to estimate. Lymphocytic reaction is less in East Africa than in West Africa. Fibrosis in a lesion represents rapid resolution. Lymphocytic infiltration is often followed by a fall in bacterial density. Borderline cases respond to treatment twice as fast as lepromatous, it is a matter of individual resistance.

BRAND, P. Association between damage from leprosy and temperature. *(Proffered paper.)*

Observation and biopsy in the course of reconstructive operations on leprosy patients have suggested that leprosy attacks all tissues [except perhaps muscle] including skin, collagen, fat, bone, cartilage, glands, tendons, synovial membranes, nerves, etc. The infected tissue is first infiltrated, and later partially replaced by granulomatous tissue. This infiltration and replacement do not occur in infected tissues which are maintained constantly at body temperature. It occurs maximally in tissues at the surface of the body in areas which are exposed to temperature change (unclothed). It also occurs in such deep areas of the body as are exposed to a stream of air which causes cooling by evaporation (e.g., nasopharynx and larynx). Certain very susceptible tissues, such as nerves, may be affected rather more deeply in the body than other tissues, but not at depths which never fall below body temperature. Paralysis occurs only in nerves which are (*a*) very superficial (within about one-quarter of an inch of the skin), or, (*b*) less superficial (one-half or three-quarters of an inch deep) but are so thick that nerve swelling causes ischemia. Damage in the reticuloendothelial system deeper in the body is probably associated with the destruction, not the local activity, of *M. leprae*. It is suggested that *M. leprae* either grows better at temperatures below body temperature or exercises its damaging effect on the body only at lower temperatures. This observation may have application in its cultivation; it may also suggest means for the prevention of the damaging and deforming effects of leprosy in certain important parts of the body.

CHATTERJEE, K. R. Experimental transmission of human leprosy to an inbred strain of black mice. *(Symposium paper.)*

(An author's abstract not being available, the Recorder's notes are used here. See also original article in THE JOURNAL, third issue of the present volume, p. 195.) In undertaking the experiments reported, two things were considered important: (1) to find a susceptible experimental animal, and (2) to avoid the introduction, along with the inoculated bacilli, of any human tissue element which might operate to inhibit their multiplication. The animal used was a laboratory cross-bred hybrid black mouse, inoculated when very young, 10-15 days old. Out of the variegated products of crossing a native gray male and a Swiss white female, the black ones were chosen, and, by selection, only black ones appeared after 13 generations. Of 100 such animals used and not lost, more than 50% of those which survived for 14 months showed heavy infection. The inoculation bacilli were separated by differential centrifugalization, and each inoculation (subcutaneous or by other routes) consisted of 20 million bacilli. Little evidence of multiplication was seen under 6 months. Microscopically, fuchsinophil cells in tissues were to be found early, before bacilli.

Later bacilli became numerous in various tissues; nerves were found invaded. Could this bacillus be a saprophyte? Cultures were made on various media, and all remained negative. An antigen prepared from lesions by the Dharmendra technique gave reactions in leprosy patients similar to those given by the Dharmendra antigen. Infection of these mice by *M. leprae* thus seems to have been successful.

BINFORD, C. H. Histiocytic granulomatous mycobacterial lesions produced in the golden hamster *(Cricetus auratus)* inoculated with human leprosy; negative results in ten experiments using other animals. *(Symposium paper.)* (See original in this issue, page 318.)

LAI, S. H. Experimental studies on transmission of human leprosy to monkey by frequent, long-term implantation. *(Proffered paper.)*

The author has previously reported on this work [THE JOURNAL **23** (1955) 48-52]. He now reports further observations regarding the symptomatology, the lepromin reaction, the demonstration of acid-fast bacilli, the objective tests for sensation, and the examination of the skeleton by x-ray. The findings are all quite similar to those in human leprosy.

3. IMMUNOLOGY

FERNANDEZ, J. M. M. Report on Immunology. *(Symposium.)*

(The Committee on Immunology having completed its report, the speaker presented that document in place of his report as panel chairman which was originally scheduled.)

YANAGISAWA, K. Basic observations for the settlement of criteria for reading the lepromin test. *(Symposium paper.)*

(1) The Mitsuda and Dharmendra antigens were employed in testing 3,137 leprosy patients, the injections being made intradermally on the flexor surface of the forearm, one in the right arm and the other in the left arm simultaneously. The correlation between the early reactions at 48 hours, and the late reactions after 15 days, concerning the size of redness with induration, proved to be high. The correlation coefficient was $\gamma = 0.7694$ with the Mitsuda reaction, and $\gamma = 0.8056$ with the Fernandez reaction elicited by the Dharmendra antigen. (2) Analyzing the frequency distribution curve of the sizes of the early reactions to the two antigens, the criteria for reading this reaction were recommended as follows: (*a*) With the Mitsuda antigen, 0-6 mm., negative; 7-10 mm., doubtful; larger than 11 mm., positive. (*b*) With the Dharmendra antigen, 0-9 mm., negative; 10-12 mm., doubtful; larger than 13 mm., positive. (3) The criteria for the late reaction at 15 days were found to be difficult to determine from the analysis of the frequency distribution curve of the reaction sizes. Therefore, considering the fact that a high correlation is observed between the early and late reactions, the following criteria were presented so that they may correspond to the classification in the early reaction. (*a*) With the Mitsuda antigen, 0-4 mm., negative; 5-6 mm., doubtful; larger than 7 mm., positive. (*b*) With the Dharmendra antigen, 0-3 mm., negative; 4-5 mm., doubtful; larger than 6 mm., positive. [Not without precedent, these schedules leave certain dimensions unassigned: 2a, 11 mm., 2b, 13 mm.; 3a, 7 mm.; 3b, 6 mm.—EDITOR.]

BECHELLI, L. M. The influence of repeated lepromin testing. *(Symposium paper.)*

Repeated injections of lepromin have been used to convert negative lepromin reactors among children to positive. The results were excellent, with more than 70% of conversions or intensifications. The results were similar to those obtained

with BCG vaccination. There were some variations in the different age groups; most positivizations were in the 5-14 years groups. The lepromin acts as a sensitizing agent, and it may perhaps increase the resistance although this is more uncertain. (From the Recorder's notes, lacking an author's abstract.)

GUINTO, R. S. and WADE, H. W. Results of tests with serial dilutions of lepromin in separate groups of normal young children, with a comparison of two lepromins and the Dharmendra antigen. *(Proffered paper.)* (See original in this issue, page 328.)

DOULL, J. A., GUINTO, R. S. and MABALAY, M. A note on the origin of natural reactivity to lepromin. The association between Mitsuda and tuberculin reactions for graded doses of tuberculin. *(Proffered paper.)*

The principal theories which have been offered to explain natural reactivity to lepromin are prior infection with *M. leprae*, or *M. tuberculosis*, or some other species of mycobacterium. The evidence for infection with *M. leprae* or *M. tuberculosis* is found inadequate, although either or both species may contribute some part to reactivity. The third theory is that the factor chiefly responsible is infection with some other mycobacterium possessing an antigen which is present also in *M. leprae*, and probably present, in greater or lesser quantity, in all members of the genus. If present in *M. tuberculosis*, tuberculin would be expected to elicit reactions in an increasing proportion of Mitsuda-positive persons as the dosage is increased. Data are presented showing that the positive correlation which exists between the Mitsuda reaction and reactions to a low dose of tuberculin is not improved by increasing the dose. It is concluded that the correct explanation of the greater part of Mitsuda reactivity is still unknown and that there is urgent need for further studies of the subject.

ALEIXO, J., MARIANO, J., STANCIOLI, J. and SALOMÃO, A. Results of the Mitsuda test carried out after mass calmetization without previous immunologic tests, in areas where leprosy is endemic. *(Proffered paper.)*

In view of the change in the Mitsuda reactivity following BCG vaccination observed in widely different regions, the authors decided to investigate the index of lepromin reactivity after calmetization in areas of severe endemic infection where no previous immunologic tests had been made. By comparing the rates of Mitsuda positivity (1) where there had been no BCG vaccination and (2) where there had been BCG vaccination (but no Mitsuda testing), they eliminated the possible but doubtful factor of change in the Mitsuda reaction due to previous lepromin testing. [Conclusions not available.—EDITOR.]

WADE, H. W. Nomenclature of skin-test antigens. *(Symposium paper.)*

There are several skin-test antigens which differ from the original Hayashi-Mitsuda preparation, and to call them all "lepromins" would be utterly confusing. The word "lepromin" (suffix -min) should be reserved for the original type of antigen prepared from the whole leproma. A similar preparation of murine-leprosy lesions would be properly be "Stefansky lepromin." Suspensions of bacillus-rich lesions such as have been recently induced in animals (provided they are proved to be lepromas) might be distinguished as "experimental mouse" (or rat, or hamster) "lepromins." On the other hand suspensions of bacilli extracted from the tissue elements, by whatever method which leaves them acid-fast, should not be called lepromins; they have been called "purified bacillus suspensions." (South American workers have used the term "bacillary lepromin," the Hayashi-Mitsuda antigen being called "integral lepromin.") The Dharmendra preparation, the bacilli made nonacid-fast ("defatted") by the chloroform-ether sequence, is a still different preparation and should be distinguished as

the "Dharmendra antigen." Extracts of leprosy bacilli or lepromas which contain only the soluble components, designed to elicit only the early (Fernandez) reaction, should be called "leprolins" (suffix -lin), in analogy with tuberculin. Regarding the reactions, the early one, which demonstrates pre-existent sensitization analogous to tuberculin reactivity, should—in parallel with the latter phenomenon—be called a "reaction of hypersensitivity." The late reaction, of very different nature, should be referred to as the "Mitsuda reactivity" or some similarly distinctive term.

BECHELLI, L. M., RATH DE SOUZA, P. and QUAGLIATO, R. Correlation between the clinical reading and the histopathology of the Mitsuda reaction. *(Proffered paper.)*

This study is based on material from 250 cases, leprosy patients and contacts. Histopathologic interpretation: (*a*) Positive, a granulomatous infiltrate, predominantly epithelioid, of tuberculoid structure; bacilli absent or very rare. (*b*) Negative, simple chronic inflammatory infiltrate (bacilli usually absent or few), or histiocytic granulomatous but not tuberculoid (many bacilli). (*c*) In favor of positive, chronic inflammatory infiltrate not totally granulomatous nor predominantly epithelioid, although such cells are grouped here and there; bacilli absent or rare. Results:

Mitsuda reading	Negative histology	Inclined positive	Positive histology	Total
Neg.	40 (89%)	5 (11%)	—	45
±	19 (58%)	12 (36%)	2 (6%)	33
1+	17 (21%)	26 (32%)	38 (47%)	81
2+	8 (12%)	19 (29%)	39 (59%)	66
3+	—	9 (36%)	16 (64%)	25
				250

Extremes are seen in the negative reactions, almost always histologically negative, and the 3+ positives, never negative histologically and usually frankly positive. The clinincally doubtful reaction may show histologic evidence of a certain degree of resistance in about one-half of the cases. The 1+ and 2+ reactions are very similar histologically. In none of the lepromatous cases that had become bacteriologically negative was the histology definitely positive, although in an occasional case the reaction was clinically positive. In indeterminate and tuberculoid cases, and also in contacts, the 1+ and 2+ reactions were usually positive histologically or in favor of positive. Cases with such clinical reactions but with negative histology sometimes followed an unfavorable course. Emphasis is laid on the similarity of the 1+ and 2+ reactions. Further study is required to decide if they should be placed together in the same group. If so, there will be only two grades of positive reactions, a 1+ corresponding to the 1+ and 2+ of the Madrid Congress, and 2+ corresponding to the actual 3+.

KUPER, S. W. A. Skin reactions to lepromin and tuberculin; effect of BCG vaccination on the histologic reaction. *(Proffered paper.)*

A large series of lepromin and tuberculin tests were done in South Africa on healthy subjects, patients with active tuberculosis, and patients with tuberculoid and lepromatous leprosy. Analysis of the results showed a definite positive correlation in tuberculosis patients, a less obvious correlation in healthy Mantoux-positive subjects, and no correlation whatever in leprosy patients. (There was no evidence that the correlation in tuberculosis patients was part of a generally heightened nonspecific protein sensitivity in this disease.) Four weeks after the lepromin injections biopsies were made of the sites of injection in about 150 leprosy patients. In lepromatous cases there is usually only histiocytic proliferation; tuberculoid subjects

characteristically show a lymphocytic infiltration often associated with giant cells and tubercles. Classification of the type of disease could be made with reasonable reliability from the histologic response to lepromin. An attempt was later made to ascertain whether BCG vaccination alters the histology of reactions to lepromin. No striking change was found in a small series of healthy subjects, and of tuberculoid leprosy patients. In lepromatous leprosy, however, 22 out of 30 patients tested showed an altered response. The change varied in degree but showed a distinct trend toward the lymphocytic type of reaction, suggesting that a systemic immunologic response had been evoked.

HAYASHI, Y. Phagocytosis of leprosy bacilli by the leucocytes originating in leprosy patients, with reference to the phagocytosis of other acid-fast bacilli. *(Proffered paper.)*

This investigation was designed to determine whether or not the leucocytes derived from leprosy patients possess specific phagocytic activity on leprosy bacilli. A fresh leprous nodule was made into a suspension with 0.85% saline containing 1.5% sodium citrate, and dispensed into small test tubes each in amounts of 0.1 to 0.2 cc. each. After mixing with the same amount of the patients' blood, the tubes were placed in the water bath at 37°C. for 20 minutes, after which smears were made and stained. A total of more than 300 neutrophiles and monocytes were counted for the calculation of the percentage of phagocytizing leucocytes. This procedure was applied to the sera of a total of 141 patients representing all types of the disease, as well as 20 normal controls. The phagocytic activity of the leucocytes of lepromatous patients was the strongest, averaging 70%; that of the neural patients was the weakest, averaging 43%; the tuberculoids were intermediate, 60%. The normal persons averaged only 25.8%. In all types of the disease there was a tendency for stronger phagocytosis with advance in morbidity. These findings are interesting from the immunologic point of view, and will serve as a supplementary measure in diagnosis, especially for discrimination of the disease types. The phagocytic activity of the leucocytes of leprosy patients was also investigated on a total of 18 strains of nonpathogenic acid-fast bacilli. As in the case of the leprosy bacillus, the activity of the leucocytes of lepromatous patients was the highest, of the tuberculoid patients intermediate, and of the neural patients least.

OGATA, TOMOSABURO. On the disease types of leprosy studied from the basis of experimental pathology. *(Proffered paper.)*

Comparing human and murine leprosy histologically, their cell structures and and reactional mechanisms are similar. Despite the difference in the nature of their causative organisms, we were able to produce the tuberculoid type in rats, besides the lepromatous type, and also the muri-lepromin reaction, by performing various experiments from the double standpoint of tissue immunity and resistance caused by mesenchymal-system cells, and humoral immunity. Thus by comparing the lepromatous and tuberculoid types of human and murine leprosy, we were able to obtain a basis for the explanation of the relation between immunity and the formation of leprosy types, and also of the genesis of the lepromin reaction as well as the scientific basis of therapy by activation of the mesenchymal system cells. Various experiments were performed with rats regarding the increase or decrease in the activity of the cells of the reticuloendothelial system. Also performed were various immunity experiments with subcutaneous injections of living and killed murine leprosy bacilli in mice. With living bacilli: In extreme RES hypofunction, lepromas were not formed and exudative inflammation was observed. In moderate RES hypofunction a typical lepromatous lesion was formed locally, more speedily and conspicuously than in the normal animal, and the bacilli were widely disseminated. On

the other hand, the group with RES hyperfunction showed transition from lepromatous to tuberculoid type as in human leprosy, with the tuberculoid formation in some small foci, and the localization of bacilli. In the immunity group a typical tuberculoid-type lesion appeared, and there was demonstrable production of antibodies. The disease type is determined and modified by the inherent resistance and the diverse factors imposed upon it by acquired immunity. Thus, weak resistance and lepromatous, strong resistance and tuberculoid. [Etc.] Both human and murine leprosy possess the same mechanism of immunity and allergy.

OGATA, TOMIO and ABE, M. Serologic agglutination of leprous sera using cardiolipin-lecithin antigen. *(Proffered paper.)*

Following the technique of syphiloagglutination (Ogata), leprosy sera were tested using cardiolipin-lecithin solutions with varying proportons and concentrations adsorbed to kaolin particles. It was found that the solution containing equal parts of cardiolipin and lecithin (both in 0.05%) gives the highest agglutinating end titer with leprosy sera, in strong contrast with syphilis sera, which give the highest end titer with 1 part of cardiolipin and 10 parts of lecithin (0.01% and 0.1% respectively), which will also frequently give positive reactions with leprosy sera. This new serologic reaction of leprosy sera using the 1:1 antigen is called leproagglutination (Ogata). The antibody in leprosy serum involved in this reaction is clearly distinguishable from syphilis antibody in several respects: affinity for cardiolipin-lecithin antigen, instability to heat, and distribution of antibody in serum fractions obtained by ammonium sulfate or by zonelectrophoresis fractionations. The leproagglutination test is well correlated with the clinical pictures in leprosy. Definitely higher agglutination end titers were encountered in lepromatous than in tuberculoid cases. In lepromatous cases the agglutination end titers were lower in light cases and higher in severe ones. Higher end titers were demonstrated in the retrogressive stage of leprosy than in the progressive or quiescent stages. (Added from the Recorder's notes:) The leprosy antibodies are mostly in the beta globulin of the serum, and to a less degree in the alpha globulin.

FUJINAMI, T. and HONDA, H. Antigenicity of BCG wax (D-IV) towards leprosy and tuberculosis sera. *(Proffered paper.)*

Recently the polysaccharide antigen of the Middlebrook reaction has been used by many investigators as a common antigen in leprosy, tuberculosis and murine leprosy. One of the authors (Honda) had since 1951 conducted studies on the early reaction in leprosy using a lipid of the ox brain, i.e., a cephalin fraction, purified by the Holch method, in conjunction with the hemolytic reaction using purified cardiolipin and cholesterin reported by Pangborn, and satisfactory results have been obtained. The biochemical characteristics of the lipid was examined with an attenuated strain of BCG. The D-I, D-II, D-III and D-IV fractions of wax-P have been isolated by Ono and Nojima, and the D-IV fraction and brain lipid were studied comparatively. With the organ lipid antigen (cephalin fraction 1, 3, 5), a positive reaction is obtained in leprosy but not in tuberculosis or in the healthy subject. However, a pseudo-positive reaction is obtained in syphilis and in pregnancy. Wax-IV obtained from BCG gives a positive reaction in tuberculosis but none in pregnancy and only a weak one in syphilis. These results appear to verify the theory of Ono and Nojima that organ lipid does not contain saccharides, but in the case of BCG mannose is attached to inositol and this coincides with the reaction. In other words, it is believed that this quantitative test proves that the reaction against the tuberculosis serum is based on the presence of mannose. It is suggested that the significance of the Middlebrook reaction using tuberculin, and the structure of the specific and nonspecific factors in leprosy, may gradually become clearer because of this finding.

AZULAY, R. D., NEVES, R. G. and AZULAY, J. D. Lepromin test in guinea-pigs after previous inoculation with BCG and *M. tuberculosis* killed by irradiation. *(Proffered paper.)*

Vaccination (oral) gives undoubted protection of guinea-pigs against rat leprosy. Effects vary with the dose of BCG; 30 mgm./kgm. of guinea-pig body weight was the best. We tried larger doses of BCG for lepromin conversion, and *M. tuberculosis* killed by irradiation. The positive results decreased with increase of the BCG dose, and there were no positive results (only some doubtfuls) with *M. tuberculosis*. With ordinary doses of BCG the results are good. The optimum dose is similar to that for children. (From the Recorder's notes, lacking an authors' abstract.)

4. THERAPY

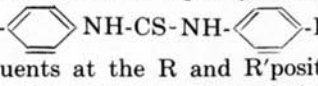
RODRIGUEZ, J. N. Relapses following DDS treatment. *(Chairman's symposium paper.)* (See original in this issue, page 305.)

TAKASHIMA, S. Present status of sulfone therapy at the Nagashima Aisei-en National Leprosarium. *(Symposium paper.)*

All of the regular drugs have been used, and comparative studies have been made. With DDS up to 1958, 72% of the patients are much improved. The Diasone group was much the same, somewhat less than in Doull's cases (1952). Comparing the cutaneous and nerve lesions, the former showed the better results. There has been no marked anemic effect. Lesions other than those of the skin also were much improved: keratitis, corneal leproma, lepromatous ulcers of the body (quickly improved); perforating ulcers improved to some extent. Bacillus findings, by an index worked out from Doull's criteria, were good: a five-fold improvement in 7 years. There have been a few complete negatives. Histologic findings showed steady regression of the tissue reaction in all types, but with tuberculoid some scarring, degenerated nerve branches and atrophy of sweat glands. The lepromin test used in 430 lepromatous cases for 2 years (Mitsuda and Dharmendra antigens) showed a high proportion of conversions to positive. There was an increase in negatives in 5 cases, so there must have occurred in them a weakening of resistance, in spite of arrest of the disease. Further observations are needed in this matter. Lepra reactions appeared in the early stages of sulfone therapy. We do not know if they are beneficial or harmful, but they interfere with the treatment.

DAVEY, T. F. Progress with new anti-leprosy drugs. *(Symposium paper.)* (See original in this issue, page 299.)

SCHMIDT, K. Ciba 1906 (DPT); experimental investigation of its absorption and excretion. *(Proffered paper.)*

1. Of the various compounds that have been tested for antituberculosis activity in the last few years, derivatives of diphenylthiourea have turned out to be the most active. Formula:  A number of thiourea derivatives with various substituents at the R and R′positions have been made and tested. It was established that the antituberculosis activity was markedly influenced by the type of substituent. Highest activity was attained when both substituents were in the para-position and consisted of alkyl or alkoxy groups of a definite length, 4 or 5 carbon atoms. Shortening or lengthening of this chain resulted in partial loss of activity. One of the substituents may, without influencing the activity, be replaced by a dialkylamino group. This is the case with Ciba 1906 [1-(*p*-N,N-dimethylaminophenyl)-3-(*p*-butoxyphenyl)-2-thiourea], at present the most active compound for the treatment of human leprosy.

II. In order to investigate the metabolism of this drug a colorimetric detection method was developed, and studies with a radioactive-labelled preparation were undertaken. The findings in rabbits were as follows: (1) Blood: After a single oral application (30 mgm./kgm.) the levels rise in 4-6 hours to a maximum of 4-8 μgm./cc., falling to zero in 12-24 hours. (2) Urine: With unlabelled Ciba 1906 only traces were detectable in the urine, whereas when the C^{14}-labelled substance was used it was found that considerable amounts are excreted in the urine. After either intravenous or oral administration, 40-60% of the radioactivity appeared in the urine within 24 hours. The product excreted appears to consist essentially of a metabolite of Ciba 1906. (3) Bile: In animals with a biliary fistula, 15-20% of the dose given intravenously could be detected in the bile within 12-24 hours. (4) Distribution in the organism: The usual dose (30 mgm./kgm.) was fed daily for 7 days, and 50-65% of the total dose was excreted in the urine and 10% in the feces. Detectable amounts were not found in any of the organs examined with the exception of the intestinal tract.

MAYER, R. L., EISMAN, P. C., GEFTIC, S. and KONOPKA, E. The antituberculosis and antileprosy activity of substituted thiocarbanilides, in particular Ciba 1906. *(Proffered paper.)*

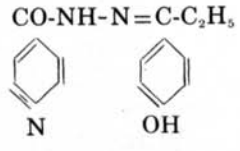
Numerous thioureas and thiocarbanilides were tested for antifungal and antimycobacterial activity. Many of them demonstrated excellent *in vitro* activity, and very good *in vivo* activity against *M. tuberculosis*. A number of them were also active in murine leprosy. Referring particularly to Ciba 1906, it was considerably more active than PAS in tuberculous animals. In murine leprosy its activity was more irregular. Since clinical reports on the action of Ciba 1906 in human leprosy show that activity is similar to that of DDS, these results confirm the general observation that the correlation between sensitivities of the tubercle and leprosy bacilli to various chemotherapeutic agents are qualitative rather than quantitative. (According to the Recorder's notes, Dr. Mayer remarked, in the discussion:) All sulphur-containing compounds found since the thioureas apparently have a similar mode of action. It appears that resistance is interchangeable between them. So if resistance develops, do not substitute one compound by another of this group, but look for compounds with complete difference in mode of action which do not have the CS group. Cross resistance does not apply to DDS.

DEL PIANTO, E. Thioethyl-compounds in the therapy of leprosy; clinical results in a pilot trial with sodium ethyl thiosulphate. *(Proffered paper.)*

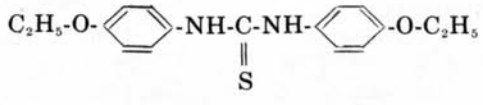
Chemical compounds having an ethylthio group which is easily breakable *in vivo* exhibit chemotherapeutic activity against acid-fast bacilli. A pilot trial of chemotherapy of leprosy with one of these compounds, sodium ethyl thiosulphate (ET), is reported. Three homogenous groups of 11 patients each were treated for 12 months: (*a*) one group received a daily dosage of 1.2 gm. of ET, (*b*) another received 0.2 gm. of DDS, and (*c*) the third group received a combination of the two drugs. All of the patients treated with ET alone or in combination showed a very good and rapid response, whereas only a few of those treated with DDS alone showed improvement. The tendency for leprosy bacilli to disappear from nasal smears was most marked in the ET groups. This drug was very well tolerated, and was free from toxic side effects, including lepra reactions. There was no complaint about the garlic smell (ethyl mercaptan is the active part of the molecule). Paper electrophoresis of sera of a number of patients indicated a favorable effect of the drug in a decrease of the gamma globulin fraction, which is generally increased in active lepromatous leprosy.

BUU-HOI, N. P., BANG, T. V. and XUONG, N. D. Sur l'emploi des isonicotinylhydrazones dans le chimiotherapie de la lèpre. [On the use of isonicotinyl hydrazones in chemotherapy of leprosy.] *(Proffered paper.)*

The biological properties of a number of isonicotinyl hydrazones resulting from the condensation of isonicotinyl hydrazide (INH) with various aldehydes and ketones have been investigated from the viewpoint of their possible application to chemotherapy of leprosy. The isonicotinyl hydrazones studied show better chemotherapeutic indexes than INH in tuberculosis tests, and have lower solubilities in water, which make them more convenient for chronic treatment. Limited clinical results in human leprosy are reported on one of these substances, *p*-hydroxypropiophenone isonicotinylhydrazone (Formula I); they indicate that the compound is well tolerated and possesses definite chemotherapeutic activity, although this activity is notably lower than that of 4:4′-diaminodiphenyl sulphoxide (DDSO) or of 4:4′-diethoxythiocarbanilide, or Dralide (Formula II). No bacterial negativity was achieved even after more than a year of treatment.



(I)



(II)

ROLLIER, R. and REBOUL, E. Traitement de la lèpre lépromateuse par la cycloserine en association avec la D.D.S. *(Proffered paper.)*

Des 12 malades lépromateux soumis à cette association médicamenteuse ont vu leurs lésions cutanéomuqueuses et leurs troubles de la sensibilité s'améliorer de façon spectaculaire en quelques semaines. Les modifications histologiques sont caracterisées dans les deux premiers mois par un aspect pseudo-epithélioïde et la transformation des cellules spumeuses en cellules macrophagiques type corps étranger. Cet aspect est plus ou moins net suivant les cas et s'accompagne toujours d'une vacuolisation cellulaire intense, avec formation de néocollagène "enserrant les cellules." Plus tardivement on ne retrouve que les modifications de vieilissement de l'infiltrat propres à la DDS. Au point de vue bacteriologique, très rapidement l'effet de la cycloserine s'éstompe, et les résultats ne sont pas supérieurs, après un an, à ceux de la DDS seule. La tolérance est bonne, pas d'accident neurologique, aucun trouble de la formule sanguine (stabilisation des globules blancs entre 4 et 6,000). La cycloserine ne parait pas représenter au point de vue bactériologique et prophylactique un net progrès sur les sulfones.

BACCAREDDA-BOY, A. and FARRIS, G. Traitement de la lèpre par la viomycine, la pyrazinamide et la cyclosérine. (Rapport préliminaire.) [Treatment of leprosy with viomycin, pyrazinamide and cycloserine. (Preliminary report.)] *(Proffered paper.)*

In consideration of the analogies between tuberculosis and leprosy, we experimented with the most recent antituberculosis drugs. The treatment was of 8 previously untreated lepromatous cases, all with nodular infiltrations and lepromas, bacilli

in the nasal mucus, and negative lepromin reactions. There was no improvement in the two patients who received only viomycin (1 gm. intramuscularly each day for 60 days and then 2 gm. every third day for 2 months), or in the two patients who received pyrazinamide alone (3 gm. in 4 doses a day by mouth for 75 days). Of two patients who took the combination of pyrazinamide (2 gm. daily) and isoniazid 0.25 gm. daily) for 90 days, one showed slight bacteriologic improvement. Two patients received cycloserine (0.75 gm. daily for 2 days followed by 1 day of rest) for periods of 7 and 8 months, resp., and they showed marked clinical and bacteriologic improvement, with disappearance of bacilli from the nasal mucus, although they showed slight lepra reactions.

FARRIS, G. Antigène marianum dans le traitement de la lèpre. [Marianum antigen in the treatment of leprosy.] *(Proffered paper.)*

Treatment with marianum antigen was tried in 41 lepromatous and 4 tuberculoid cases, most of whom had previously received sulfones and continued to do so during the period of treatment with the antigen. Intradermal injections of 0.1 cc. were given each month for 6 months. An ulcerative lesion always appeared at the point of inoculation, healing slowly with scarring. After the inoculation most of the patients had an increase of temperature and symptoms of lepra reaction. Because of these results 13 of the patients discontinued the treatment after the second or third inoculation; the others completed the cycle, and 6 of them were submitted to a new cycle 3 months after the end of the first. One result was that the Mitsuda test gave 2+ positive results in 7 cases, and 1+ in 11 cases; 27 cases did not change. As for the general state of health, the patients showed marked improvement, but with respect to clinical and bacteriologic criteria no difference was observed in comparison with the patients submitted only to sulfone therapy. (According to the Recorder's notes, the author expressed the opinion that the study with this antigen should be continued.)

TOLENTINO, J. G. Clinical evaluation studies of the Leonard Wood Memorial (American Leprosy Foundation); purposes, methods and potentials. *(Proffered paper.)*

In cooperation with the governments of Japan, the Republic of the Philippines, and the Union of South Africa, the Leonard Wood Memorial commenced in 1952 large-scale, controlled studies designed to evaluate the effectiveness of sulfones and other chemotherapeutic agents in leprosy. These studies have been restricted to cases of the lepromatous type, and the fourth series is now under way. This paper discusses the reasons for undertaking these studies and their objectives; and the methods by which patients are selected and assigned to treatment groups, by which changes in clinical and bacteriologic status are measured and recorded, and by which the data are analyzed. The actual findings are not presented except to illustrate these methods. Certain of the difficulties which have been encountered are discussed. It is emphasized that such studies are essential if progress in therapy is to continue, and that they should be extended to cases of the tuberculoid type.

VELLUT, C. Lepromatous reaction in a mass treatment center and its management. *(Proffered paper.)*

Leprosy patients react to the disease in very individual ways, hence the danger of small series. The large number of cases under investigation is the interest of this present study. The Center, in South India, takes care of about 15,000 patients, all under treatment with DDS tablets. Reactions occurred in about 40% of them; there were 60% who never had reactions. Reactions are often repeated. They are less frequent in children than adults. January to March, the driest and coolest period of the year, is the season when reactions are most frequent. Reactions come

early in treatment. Our treatment of reactions is by potassium antimony tartrate, cortisone and derivatives, and chlorpromazine, DDS being temporarily suspended. Temporary hospitalization is used very often. Three-quarters of the patients could soon be restored to the DDS treatment. Potassium antimony tartrate is quite effective. Cortisone is useful in small doses, even for a long time, but we prefer it for short-term therapy. Outpatient treatment is possible for lepra reactions.

BRAND, P. Treatment and prevention of deformities in leprosy. *(Symposium paper.)*

1. The treatment of deformities of the hand is in two stages, physiotherapy and reconstructive surgery. The latter requires special training and equipment; the former is simpler. The functions of the physiotherapist are threefold: (1) He should train all patients who have any paralysis or anesthesia of the hands in a daily routine which will keep their hands supple and mobile by moving them through their full range of movement regularly and by keeping the skin in good condition with oil massage, wax treatments, and avoidance of scars. (2) For hands that are paralyzed, anesthetic, and contracted, he should conduct regular massage and exercise sessions, which are very useful to the patient even if not to be followed by reconstructive surgery. (3) He should have a small workshop where splints and shoes may be prepared for patients with severe deformities. Severe contractions of the fingers will respond astonishingly well to the persistent gentle corrective action of well-fitting splints. A number of simple, standard techniques have been developed, which makes it easy for a previously unskilled person to do very useful work with splintage. Regarding reconstructive surgery, suffice it to say that, providing a hand has been mobilized by a physiotherapist, a skilled reconstructive surgeon can restore a simple, strong grasp and a useful pinch between fingers and thumb to any patient who still has his fingers remaining. The basis of facial surgery is the correction of the nose, of the eyebrows, of lagophthalmos, and of excessive wrinkling and sagging of the skin of the face. None of these things should be beyond the skill of an experienced plastic surgeon.

II. Most of the deformities of leprosy are preventable, but an intensive educational program is required to convince patients that they can preserve their hands from damage and destruction. The following points are important: (1) Prevention of open wounds and burns. Special attention should be paid occupations like cooking, and heavy, rough occupations like building. (2) Care of injured hands and feet. Every burn or wound however small must be splinted, because the normal "splinting" by pain is absent. (3) Regular inspection. Every patient with anesthetic hands and feet should inspect himself, or be inspected, daily for unnoticed thorns, splinters, etc. (4) The use of force. Pain sensation automatically limits the strength that a normal hand will use. Anesthetic hands habitually use many times the force needed, and frequently more force than is safe to use. (5) Swollen fingers may indicate lepra reaction within the fingers. These hands need special care, with rest in a functional position. With proper care, anesthetic fingers need never suffer absorption or become stiff.

IKEDA, K. Orthopedic treatment of the hand and foot in leprosy. *(Proffered paper.)*

Paralyses and deformities of the extremities are the most frequent complications in leprosy, seen 80% in the hand and 30% in the foot. Before applying the necessary reconstructive surgery for irreversible paralyses, each case must be studied with respect to the factors of mobility, the electric reaction, electromyography, angiography, and the x-ray picture. We have performed 233 operations (191 on the hand, 42 on the foot) by various methods based on our investigations. These have included experimental studies on the dog [details given], and observations of the mechanisms in the cadaver.

KIBBY, S. V. Physical therapy in Hansen's disease. *(Proffered paper.)*

This paper consists of a review of the literature, and notes on personal experiences in establishing and developing a physical therapy service at Kalaupapa, Molokai, Hawaii. Much can be accomplished with little in the way of equipment, although the latter is helpful. A great deal of patience is required by the staff and patients. Physical therapy should be linked closely with occupational therapy and other aids to rehabilitation. Hydrotherapy, massage and active and passive motions are the most effective methods used, and securing the cooperation of the patient is the most important factor, so assistants should be selected with care.

YANAGISAWA, K., NISHIMURA, S., TAKAHASHI, T., OSHIMA, S., UEMURA, M. and NOJIMA, T. Therapeutic effects of Kanamycin on murine leprosy in rats. *(Proffered paper.)*

Kanamycin is a new antibiotic isolated from *Streptomyces kanamyceticus* n.sp., discovered by Umezawa and his associates at the National Institute of Health in Tokyo. Yanagisawa and others confirmed that its therapeutic effects in experimental tuberculosis is similar to those of streptomycin and isoniazid. To determine whether or not it is effective on murine leprosy in rats, 30 rats were inoculated subcutaneously with *M. leprae murium* and, after palpable lepromas developed, they were divided into 3 groups. The rats of one group received subcutaneously 5 mgm. of Kanamycin each day, and those of another received streptomycin in the same dosage; the third group served as the untreated control. In the treated groups the lepromas decreased in size, some becoming imperceptible, while those of the controls enlarged gradually. After 93 days of treatment all animals were autopsied. It was concluded that Kanamycin is effective in the same degree as streptomycin.

5. EPIDEMIOLOGY AND CONTROL

DOULL, J. A. Report on Epidemiology and Control. *(Symposium.)*

(The Committee on Epidemiology and Control having completed its report, the speaker presented that document in place of his report as panel chairman which was originally scheduled.)

MONTESTRUC, E. Le B.C.G. constitue un des moyens les plus efficaces à notre disposition actuellement dans la prophylaxie de la lèpre et doit être étendu dans les pays à endémicité lépreuse à tous les nouveaux-nés. *(Symposium paper.)*

Dès 1934, avant même que des travaux sérologiques et immunologiques récents, aient démontré qu'il existait une certaine communauté antigénique entre le *M. leprae* et *M. tuberculosis*, nous basant sur les caractères de similitude morphologique de ces deux micro-organismes, nous avons utilisé le BCG à titre préventif, chez quelques nouveaux nés, issus de parents atteints de lèpre. Les résultats, que nous avons publiés en leur temps, ont été extrèmement encourageants et, aujourd'hui, avec un recul de plus de vingt ans, ils se sont confirmés. Depuis 1954, cette méthode prophylactique a été étendue aux grands enfants audessous de quinze ans dont les parents étaient reconnus lépreux ou qui vivaient en contact de lépreux. Notre expérimentation date donc de trop peu de temps pour pouvoir en retirer des conclusions définitives. Cependant, il ressort de toutes ces recherches et aussi d'autres concernant la lèpre du tout jeune enfant, dont la sensibilité au bacille de Hansen est extrême, que le BCG protège indiscutablement contre l'infection lépreuse, que son administration doit être le plus précoce possible et de préférence à la naissance, que les grands enfants en contact avec des lépreux de toutes formes du mal et non seulement avec des lépromateux, sont susceptibles de présenter une imprégnation lépreuse mise en évidence par une lépromine-réaction positive coïncident avec une

tuberculino-réaction négative et que, par conséquent, les deux tests doivent être pratiqués concurrement au cours des campagnes de prévention par le BCG. Il serait même raisonnable, dans le pays de forte endémicité lépreuse, d'étendre la vaccination au BCG à tous les nouveaux-nés sans exception; on réaliserait ainsi une double premunition; de la tuberculose et de la lèpre. (Date from the Recorder's notes:) There are only 300,000 inhabitants in Martinique, with a leprosy rate of 7-8 per thousand. None of the newborn children given BCG during the author's 22 years experience has developed leprosy, whereas 10 children living in leprosaria have done so. Also, in a large special group of children [numbers?], those given BCG have had only 2 cases and those not vaccinated have had 54 cases. The effect of BCG in prophylaxis is believed to be very clear.

YANAGISAWA, K. Prophylactic effects of BCG vaccination on the occurrence of leprosy in nursery children. *(Proffered paper.)* (See original in this issue, page.)

DINIZ, O. The new program of leprosy control in Brazil and its results. *(Symposium paper.)* (See original in this issue, page 350.)

AGRICOLA, E. The epidemiology and control of leprosy in Brazil. *(Proffered paper.)*

The control of leprosy in Brazil has proved to be a difficult task. In spite of a determined attack, we know we have not controlled the endemic. Now we propose to open up the campaign by integrating all doctors and health units, and by going to the patients as outpatients, using several mobile teams. We also retain the leprosaria and preventoria. The case-finding and registration of contacts should go together. (From the Recorder's notes, lacking an author's abstract.)

WARDEKAR, R. V. Importance of an annual case detection campaign in the success of sulfone therapy. *(Symposium paper.)*

This is a report of field work in one part of India during the last 7 years. Emphasis is placed on the important part played by "paramedical" workers, functioning under medical supervision, in securing growth of the clinics and of the care of the patients. Most patients take the treatment, and the results are excellent. The cases are detected in early stages of the disease, and this early detection has a marked effect in the prevention of deformities as well as a high arrest rate for the disease. The clinical clearing of lesions is surprisingly high. Over a period of 6 years only 23% of bacilliferous cases remained positive. Widespread case-detection campaigns are the only solution for poor countries, using specially trained paramedical workers. The cost of a patient in a leprosarium is $100 a year; the outpatient costs amount to $9 per annum. (From the notes of the Recorder, in the absence of an author's abstract.)

ARIF, M. The antileprosy campaign in Indonesia. *(Proffered paper.)*

The population of Indonesia is 80 million, among whom there are 100,000 leprosy cases. There are 182 outpatient clinics dealing with 20,000 patients, and 5 leprosaria; a main central leprosarium of 450 beds is being built. There is a laboratory and a research section, and courses of lectures are given for doctors and medical students, nurses, propaganda officers, health officers, and people in social services. Rehabilitation is not forgotten, nor research in therapy and epidemiology. Preventive and curative surgery are available, and psychic and social rehabilitation are attended to. Treatment is with DDS by tablets or injections, and with chaulmoogra. Home segregation is arranged, in a separate room or hut, or patients are admitted to the leprosaria or segregation villages. Social assistance is given. Children are removed at once after birth and cared for in other homes or orphanages or by social workers. Social rehabilitation is considered very important. (From the Recorder's notes, lacking an author's abstract.)

SOBUE, A. Epidemiologic studies of leprosy in Aichi Prefecture. *(Proffered paper.)*

A total of 1,546 cases of leprosy was recorded in Aichi Prefecture, Japan, in the period of about 50 years between 1906 and 1957. The annual incidence was 0.2-2.4 per 100,000 population. In the first half of this period the rate was about 1.1, but after 1931, owing to the confusion of the war and to the general economic stress, it became 1.4-2.0. Since the war, however, because of activities in the public health field, the rate has decreased, and since 1952 it has been less than 0.5. Analysis by type: lepromatous, 59%; macular (tuberculoid), 17%; and neural, 33%. The recent trend shows a decrease in the lepromatous and an increase in the macular types. The average age of onset was 25 in 1931-1935 and 40 in 1951-1955, there having been a gradual rise. The sex ratio has been 2.6:1.0. Seventy-seven per cent of the patients agreed to leprosarium confinement, and the average length of time between onset and hospitalization was about 7 years. But now there are twice as many leprosy patients unregistered as registered by our office, and (according to the Recorder's notes) there is no cause for satisfaction. The prefecture contains over 3,700,000 population, with a density of 774 per square kilometer, and is said to have the heaviest incidence in Japan (29 new cases every year). BCG vaccination was made compulsory by a law enacted in 1949. [Aichi Prefecture is in southern Honshu, Nagoya being the capital.—EDITOR.]

LEW, J. and CHUNG, M. The epidemiologic studies of leprosy in Korea. *(Proffered paper.)*

The necessary information for leprosy control in Korea has been gained since 1947. The historical background has three phases: (*a*) before the Japanese and western medicine were introduced, (*b*) the Japanese administration, and (*c*) since World War II. There is no agreement regarding the total number of cases in the country, but the number has been steadily increasing since 1924 and at present it is generally estimated at not less than 100,000. Approximately 90% are from the historically endemic four southern provinces, although the endemic area is gradually spreading northward. Lepromatous cases are about twice as frequent as tuberculoid, and male patients are about twice as many as females. About 40% of the patients give a history of contact; only about 15% admit family contact. The age of onset is under 20 in 63%. Onset is more frequent in the younger age groups in the highly endemic area than in other places. An average of 2 years 8 months is wasted between onset and diagnosis because of the social stigma, fear complex, and ignorance on the part of both the public and the medical personnel, particularly the herb doctors. After the diagnosis is made another 2 years 5 months go by before proper treatment is obtained. During these periods most of the patients squander their money for useless treatment. About 70% of the patients in institutions [there are 8 leprosaria with about 20,000 patients] are physically capable of participating in productive labor, which has greatly aided with respect to their economic welfare.

BONNIOL, P. Campagne antilépreuse à Madagascar. *(Proffered paper.)*

Le nombre des lépreux dans l'île de Madagascar n'est pas si important que dans quelques autres territoires, mais les cas connus en juillet 1958 sont 23,500, qui correspondent 5 pour 1,000 de la population. Les nouvelles téchniques pour découvrir et traiter les cas et la propagande dans toutes les différentes classes sociales ont amené la confiance spontanée psr les malades, qui viennent aujourd, hui volontairement sans cacher. Tous les membres médicaux dans l'île coopèrent à leurs recherces, travaillant soit dans le Centre de l'assistance médicale soit dans les équipes mobiles qui arrivent à toutes les régions de l'île. Le traitement est donné dans 9 léproseries gouvernementales, et 5 non-gouvernementales, la fondation missionnaire aidée par les fonds gouvernementaux; il y a 9 village spéciaux qui contiennent 3,196 malades,

ils sont les cas infectieux restés à l'hôpital pendant 6 mois à 2 ans ou les cas régistrés dans le stade tardif de la maladie et noninfectieux. Les autres lépreux recoivent le tratement dans 314 cliniques thérapeutiques; Le médicament utilisé est la disulone [DDS]. Les autres médicaments sont étudiés à léproserie de Tananarive. Aujourd'hui nous sommes en train d'étudier le DDSO (4-4′-diaminodiphenyl sulphoxide) qui nous montre les résultats cliniques et bactériologiques similaires à ceux de la DDS, et la tolérance bien meilleure. (From the Recorder's notes:) The estimated total number of cases is 95,000. Child contacts are subjected to BCG vaccination.

Nuñez Andrade, R. Leprosy in Mexico in 1958. *(Proffered paper.)*

Mexico is a big country, with 32 million inhabitants. In July 1955 an enlightened law on leprosy was promulgated. A preliminary survey showed 1,460 cases of leprosy. In 1934, 2,449 were found, and in 1958, 1,511, but the total of known cases is 13,000. The various provinces have been assessed for prevalence. The average is 41.3 per 100,000 population. The total estimated number of cases is over 60,000. The Pacific coast and the geographic center of the country have the heaviest incidence. The state of Yucatan was infected from the east, from the Antilles, the Pacific coast from the Far East. (From the Recorder's notes, lacking an author's abstract.)

Barba Rubio, J. The national campaign against leprosy in Mexico. *(Proffered paper.)*

In Mexico we have opened up and modernized the campaign. We use "ambulatory" and "dermatology" and other general terms. We reject coercion and respect individual human liberty; nor is special legislation needed. Leprosaria should be called "dermatologic centers" and the leprosy clinics "dermatologic clinics." Prevention should be based on early diagnosis and treatment in outpatient departments. Children separated from leprosy patients should be cared for in general institutions. (From the Recorder's notes, lacking an author's abstract.)

Salazar Leite, A. Orientation for the antileprosy campaign in Portuguese overseas territories in Africa. *(Proffered paper.)*

An essential basis for a campaign, especially in the territories of Africa, is an initial survey which includes a sufficiently large percentage of the population to be representative. This initial survey provides data for the orientation of the treatment campaign which is the next step: intensity of the endemic; the prevalent types of the disease; the distribution of the population; and the roads and their availability (all seasons or only part of the year). During the 1957 survey of Angola (Portuguese West Africa), 2,251 cases of leprosy were found, 1.5 to 3.6 per thousand. The disease was relatively benign, with 69% of the cases indeterminate and 18% tuberculoid, and only 12% lepromatous. To meet the existing conditions, two types of treatment campaigns were set up: (1) For areas with a good sanitary control (i.e., with many sanitary posts covering the area, the population uniformly distributed, and the roads available all the year round), an ambulatory method of treatment is used by means of mobile units describing a circuit and passing the same localities every 2 or 3 weeks. The drug has been the sulfones "retard" (100-150 μ crystals in a suspension of 0.2% agar-saline). (2) In less suitable areas (i.e., poorer sanitary coverage, a scattered or small population, and/or with roads interrupted during rainy season), the patients are settled in small, specially constructed villages. (From the Recorder's notes:) Ambulatory treatment is very popular, and the patients attend well. The mobile units are more effective than the static units.

PINTO, A. R. Practical application of modern methods to leprosy control. *(Proffered paper.)*

After a description of the endemic disease in Portuguese Guinea before the beginning of the antileprosy work, the methods used in the present campaign are described and the results obtained are pointed out. (From the Recorder's notes:) The incidence of leprosy was found to be 25 per thousand (2.5%). Surveys are made periodically. Treatment is given in outpatient clinics and is free. BCG is used. There are 9 physicians, and hospital space for 1,500 patients. Laboratory work is available at headquarters and in the field. Mobile teams are used, and during surveys for other diseases a search is made for leprosy cases. The mobile teams use small Citroen cars or even scooters. The people cooperate actively, and attendances are good. We bring the treatment to the home of the patient. DDS is used by injection or as oral tablets. The latter are given once a week in the presence of the physician or nurse. This simple, low-cost campaign has covered 80% of the total patients.

GABRIEL, M. H. A note proposing the abolition of strict segregation of white Hansen's disease sufferers. *(Proffered paper.)*

Segregation of all bacteriologically positive cases has been required by law in the state of Queensland since 1892. There are two groups of patients, white and colored, which differ greatly in social status and therefore present differing problems. The conditions under which white patients are held are largely the result of an attempt to maintain some uniformity between the two groups. Over the years this position has become increasingly difficult to maintain, and the Queensland health department has been seriously considering the relaxation of segregation as it affects white patients (and it has already effected some relaxation for them), but it is less certain of the wisdom of such relaxation for the colored population. The proposal is put forward that strict segregation should be abolished for white patients, and for those colored patients who live under the same conditions as whites.

FASAL, P. A dermatologist's report on leprosy in California. *(Proffered paper.)*

The 136 cases diagnosed in California during the last 10 years form the basis of this paper. The people affected were Mexicans, Filipinos, Koreans, Chinese, Japanese, Polynesians, Negroes, and Caucasians. All types of leprosy and various subform were represented. Clinical and histopathologic features are discussed with special emphasis on differential diagnosis. The problem of ruling out leprosy in patients who have resided in an endemic area and who present clinical or histological findings compatible with the disease is discussed.

FITE, G. L. Principles guiding the USPHS Hospital, Carville, Louisiana. *(Proffered paper.)*

Institutions grow old and get senile diseases, and become somewhat useless in their old age. They need to be revitalized. Even Carville should take a new look at itself. The hospital becomes a focus for study of the disease, a museum of specimens. There are many causes in leprosy besides the bacterial agents. We must study the reaction of host and parasite in all directions. A cured patient is not cured until reaccepted by his family and community. Carville has to take note of these other factors: it will study all these inter-related components. The medical officer will study to bring Carville into its new and conclusive role and bring in the changes without fear. (From the Recorder's notes, lacking an author's abstract.)

6. SOCIAL ASPECTS

JAGADISAN, T. N. Report on Social Aspects. *(Symposium.)*

(The Committee on Social Aspects having completed its report, the speaker presented that document in place of his report as panel chairman which was originally scheduled.)

HEMERIJCKS, E. The pattern of social assistance in countries of high endemicity. *(Symposium paper.)*

Highly endemic countries usually have little money. Priority should be given to the medical and preventive side, but social problems must not be forgotten. The general medical profession shows no interest in leprosy patients and avoids treating them. Medical workers in the leprosy teams, however, must take more interest in the condition of the patients. More workers must be trained, preferably in the medical colleges. Our own fault as leprologists is to keep leprosy too complex. Paramedical personnel are very important; we must train many, and train them carefully. Education should start in schools with the teachers; propaganda at the village level is essential. Propaganda must be repeated and found everywhere, and be very practical in answering the natural questions about leprosy. The real difficulty for the patient begins when we pull the patients out of their families: mass treatment has a great advantage in this respect. The patients themselves are very conscious of the advantages of treatment. They should get psychic and social understanding. (From the Recorder's notes, lacking an author's abstract.)

CONTRERAS, F. Protección social al enfermos de lepra en paises poco endemiados. [Social assistance to leprosy patients in countries with moderate endemicity.] *(Symposium paper.)*

I agree with Mrs. Weaver about the value of complete, organized social assistance. I also congratulate the Japanese workers. These leprosy congresses are of great value, but the amount of leprosy in the world is still huge. At the Rome Congress we saw the need of many teams and much cooperation. Social work must go hand in hand with the best possible treatment. We avoid special legislation for leprosy. Entry into sanatoria must be voluntary, also discharge from them. Leprosaria are still of great value in many ways, as are the preventoria. We also have dermatologic wards in general hospitals where leprosy patients are admitted. All patients in Spain receive social security payment. All members of the family are protected, especially the children. There are various ways of overcoming any possible psychologic damage to children put into preventoria or colleges: e.g., visits of relatives can be encouraged. (From the Recorder's notes, lacking an author's abstract.)

WEAVER, E. Social problems arising from the struggle against leprosy. *(Symposium paper.)*

It is essential to consider the social problems not only of the sick but of those in contact with them. To be practical, effective and humane, plans must take into account not only the economic, social and educational status of each country, but also the difficulties and possibilities of individual regions, especially in the case of large countries with undeveloped areas. Political and religious sectarianism must be avoided in the assistance program, nor should its norms be established by medical authorities alone, since social problems require the knowledge of social workers. In countries where leprosy is widely endemic and where economic, transport and educational difficulties are great, assistance programs should be progressive stages so as not to sacrifice those who are meant to be helped, and always bearing in mind special

regional problems. The problems of each country should be carefully considered before generalized recommendations are made. Among the most serious problems are the poverty of most of the families of leprosy patients, and the lack of proper facilities for their children. Those who leave leprosy colonies often find difficulty in adapting themselves to work and society and in being received by society, even by relatives. Those who leave preventoria have no difficulty in returning to society once they have been suitably prepared, and this is being done.

FOLLEREAU, R. Pourquoi j'ai crée la Journée Mondiale des Lépreux. *(Symposium paper.)*

Obtenir que les malades de la lèpre soient soignés, comme tous les autres malades, en respectant leur dignité et leur liberté d'homme, et guerir les bien portants de la peur absurde et parfois criminelle qu'ils ont de cette maladie et de ceux qui en sont atteints, tel est le double but de cette Journée des Lépreux que j'ai creee en 1954 et qui aura lieu, pour la sixième fois, le dimanche 25 janvier 1959. Chaque année son message va, plus loin, atteindre au fond des forêts et des brousses ceux qui n'avaient jamais connu l'espoir. Chaque année, son appel éveille un nombre plus grand de consciences et bouleverse les coeurs. Des millions de lépreux oubliés, abandonnés, jadis parias du monde, se voient aujourd'hui adoptés par une opinion publique mieux eclairée, et dont l'immense voix se fait chaque jour plus forte, plus pressante, pour exiger qu'on les soigne, qu'on les respecte et qu'on les aime. La Grèce, le Portugal, le Vietnam, les Antilles, le Congo Belge, l'Ethiopie, le Mexique, l'Ile Maurice, le Mozambique, sont parmi les premiers pays qui ont célébré la Journée Mondiale les lépreux dont l'appel est, chaque année, diffusé dans le monde entier. En 1958, sous la présidence du Haut-Commissaire, toutes les autorités civiles, religieuses et militaires de la Fédération d'A.O.F., se rendirent au centre de traitement de M'Balling, tandis que trente mille personnes allèrent à Bamako faire une "visite d'amité" à ceux qui, malades de la lèpre, ne doivent plus jamais être "des lépreux." Ainsi, se justifie la fière et noble déclaration inscrite en 1956 au fronton de l'ancienne léproseria de Santa-Barbara (Grèce), lors de la IIIème Journée Mondiale des lépreux: L'amour a vaincu, les murailes sont tombees.

OZAWA, R. Social activities at the leprosaria in Japan. *(Proffered paper.)*

It is estimated that there are 15,000 leprosy patients in Japan, and (1958) there are 10,854 in the leprosaria, with another 1,098 registered but not admitted. Isolation is employed as the only preventive measure. There are 14 leprosaria with 14,261 beds, of which 11 are national with 13,950 beds and the other 3 are private ones with 311 beds. The number of patients at present is about one-half of the figure, 30,393, that was reported in 1904. The average age is higher than before. The facts indicate that the summit of prevalence is past, but the patients not in leprosaria may serve as sources of infection and should be admitted as soon as possible. The following measures of social significance apply. (1) All the expenses of the admitted patients necessary for their living and recuperation are guaranteed by the government. (2) If the families have financial troubles because of the segregation of the patients, aid is provided them. (3) For uninfected children without provisions for their care, there are asylums accommodating 335 children attached to 8 of the national leprosaria. (4) For the elderly who are affected by the segregation of the patients, an old people's home accommodating 70 persons is run by the Tofu Kyokai in Kumamoto. There are also other asylums for children or the aged in each prefecture. Sulfone treatment of the patients in the leprosaria has resulted in increasing numbers of recovered cases who are to be discharged. Vocational training is being given to recovering patients, and a system of advancing rehabilitation funds has now been put in operation to promote their returning to society.

ESTRADA, M. C. Social aspects of leprosy; the experience of Mexico. *(Proffered paper.)*

The erroneous idea of former times that leprosy is a highly contagious disease gave occasion to the greatest injury that humanity attacked by this illness has suffered. It led to the idea of isolating this kind of patient and to the establishment of special laws and regulations. No account was taken of the human quality of the patients; on the contrary it was destroyed, with great repercussion on the family group, by damnation to a life of fear, despair and hopelessness without end. One is a person first, and afterward a patient. In Mexico, several years ago, thanks to Professor Latapí, obligatory segregation by force was abandoned. The old antileprosy dispensaries are now called dermatologic centers, the word "leper" is no more in use among us. The former regulations have been rescinded, and the present rules of leprosy prophylaxis contain basic concepts of the new ideas which have entirely changed the panorama. Our aim has always been to fight against the disease itself, never against the patients, in order that they may in all ways lead a normal life.

7. OTHER TOPICS

SKINSNES, O. K. The defense mechanism in leprosy as related to the internal lesion and malnutrition. *(Proffered paper.)*

In the preoccupation with classification and the external manifestations of leprosy, the concept of leprosy as a systemic disease and its relationship to the reticuloendothelial system as a whole are inadequately explored. The inadequacy of the defense mechanism in lepromatous leprosy often seems to overshadow its efficiency in the tuberculoid type and various stages of intermediate leprosy. Factors affecting the defense mechanism are of significance in determining the course of the infection and its manifestations. Malnutrition, particularly protein deficiency, has been shown to have a deleterious effect on the production of phagocytic cells and on their phagocytic abilities. In addition, the tendency toward edema in severe protein malnutrition alters the histopathologic pattern of inflammation. Studies of comparative survival periods of patients with leprosy in presulfonamide days, under conditions of both inadequate and adequate nutrition, together with necropsy studies of patients who were severely emaciated, suggest that adequate nutrition is of significance in enhancing the patient's resistance to infection, and that malnutrition depresses the defense against leprosy and may serve as a pathogenic factor in the development of lazarine leprosy.

GAY PRIETO, J. Classification of disabilities. *(Proffered paper.)*

The author, surprised by the lack of data on the proportions of patients with deformities, attempted a classification of 3,600 patients in Spain according to disabilities. This sort of information will be useful in evaluating the campaign. Of 1,877 patients, 41% were in hospital. Among them, 53% showed disabilities; the rate was much less in patients not hospitalized. In French West Africa there is a classification of deformities, such as perforating ulcer, loss of vision, etc. In our cases, in the first grade of our classification, mutilations were 25% in men, 15% in women. The significance of mutilations is obvious. The cost of dealing with them would be great anywhere. Even after eradication of the disease there would be plenty of mutilations to be dealt with. (From the Recorder's notes, lacking an author's abstract.)

MINATO, J. Clinical investigation of the peripheral nerve involvement at the upper extremity of leprosy. *(Proffered paper.)*

The involvement of the nerves of the upper extremity, viz., the ulnar, median, radial, musculocutaneous, axillary and other nerves, was investigated in 250 cases (150 lepromatous and 100 nonlepromatous) with Daniel's muscle testing and routine sensory testing. It was concluded that the sensory nerves were affected peripherally, and in each nerve the distal cutaneous branches were more liable to involvement except for the median nerve, the sensory branches of which are the least liable to be affected. On the other hand the majority of motor paralyses (of the ulnar, median and radial nerves) are due to proximal nerve trunk lesions at the "site of predilection." The sites of predilection are: Ulnar: (1) just proximal to the wrist joint, and (2) just proximal to the ulnar groove. Median: (1) just proximal to the retinaculum flexorum, and (2) between the branching of the flexor superficialis and the plamaris longus. Radial: (1) the superficial ramus (sensory branch) just as it winds around the lower end of the radius, and (2) just distal from the branching of the triceps. However, the individual paralyses of the hypothenar, m. ext. poll. longus, m. ext. poll. brevis, or m. abd. poll. longus, observed in the early stages of the nerve involvement, were due to the peripheral lesion. Based on these findings, the motor paralyses are divided into three forms in each of the three nerves, ulnar, median and radial. [Details.]

BANG, T. V. and TIEP, N. D. Artériographie des plaies perforantes chez les lépreux. *(Proffered paper.)*

Le rôle des lésions nerveuses dans la génèse des plaies perforantes chez les lépreux est certainement prépondérant, mais il n'est pas le seul. Nous nous sommes demandés s'il n'y avait pas dans cette génèse une participation des lésions vasculaires, en particulier artérielles. Pour vérifier cette théorie, nous avons pratiqué des artériographies des pieds chez plus d'une trentaine de lépreux porteurs de maux perforants. A côté de 26 images normales, nous avons constaté 8 cas d'imagess anormales appartenant à trois types: 1° Arrêt total ou partiel de la matière opaque, l'arrêt partiel se présentant sous l'aspect d'un noeux. 2° Modification du calibre des artères (soit dilatation, soit effilement). 3° Hypervascularisation des collatérales de suppléance, ce qui laisse supposer la présence d'une gêne de la circulation principale.

LECHAT, M. and CHARDOME, J. L'artériographie du pied chez les lépreux mutiles. *(Proffered paper.)* (See original in this issue, page 346.)

TAJIRI, I. On acute infiltration of the lepromatous type of leprosy. *(Proffered paper.)*

In the course of leprosy there develops an acute infiltrative condition. It occurs in the lepromatous type after long duration of the resorption stage, or in an early stage of transition from the tuberculoid type to the lepromatous. This condition in lepromatous cases I wish to call "acute infiltration." These exanthemas seem like erysipelas or macular tuberculoid, and they appear with fever up to 39°C. When this acute infiltration occurs the prognosis becomes good. The Mitsuda reaction, although negative before an appearance of the acute infiltration, turns positive at the time of its occurrence. With the acute infiltration as a turning point, the reaction becomes positive and remains so for a fairly long period (about two years at least). Histologically, in acute infiltration there are more bacilli in the eruptive lesions than in the macules of the tuberculoid type, or than in lepromatous infiltration, and the bacilli are usually degenerated. The structure of acute infiltration resembles the tuberculoid type—proliferation of leucocytes, epithelioid and giant cells, which sometimes have bacillary globi.