

## Some Highlights of the Week's Work

**Stanley G. Browne, Secretary-Treasurer**

I undertake with some trepidation the task of summarily reviewing the scientific proceedings of the Congress, since I was not able to sit through a single session. But I have read the abstracts many times—and not only in English—and have also read many of the complete papers. It is particularly appropriate at this stage to remind ourselves of the factually true words uttered by Sir Max Rosenheim at our banquet, that the matters reported at this Congress, especially the microbiologic investigations, are of more significance for more people in the world than heart transplantation.

In this review, I will select from the Chairman's reports of each of the scientific sessions some of the features that they themselves would wish to emphasize.

### Session II. Epidemiology, Including Genetics

**Chairman: Dr. Carl E. Taylor**

The dominant features of the epidemiology of leprosy are a general dissatisfaction with traditional approaches and a hunt for new methods. The search for genetic markers that have an association with specific types of leprosy has so far furnished only suggestive leads, and no clear indication of their significance. Other methods of genetic study that are now available give as yet no indication of their potential value.

The epidemiologic significance of the lepromin test continues to be minimal and the evidence that large proportions of positive conversions are unrelated to leprosy infection, but possibly associated with non-pathologic mycobacterial infections has been increasingly demonstrated. The Kari-mui research project team has proved the value of intensive and continuing observations on population groups sufficiently small and, sufficiently isolated, to give consistent data; incidentally, more evidence of spontaneously healing, self-regressing lep-

rosy lesions has come to light. More such clinical and field studies are needed.

We have been reminded of the value of anthropologic research in leprosy. It may be that such factors as marriage patterns will provide suggestive leads concerning infection, and emphasize the importance of repeated close or skin-to-skin contacts, with index cases disseminating viable mycobacteria from skin and nasal mucosa.

A timely reminder came from Bengal, that many healthy people not in contact with open leprosy patients may harbor mycobacteria in skin and deeper tissues. So far, there is no laboratory confirmation that these organisms are indeed *Mycobacterium leprae*. This work underlines our lack of appropriate cultural media, perhaps including some specific adjuvants as postulated by Hanks, that will permit the cultivation and identification of *M. leprae* among all the mycobacterial contaminants of the skin surface and the deeper tissues. Japanese workers have demonstrated that acid-fast bacilli are found in normal human skin in subjects having no possible contact with leprosy. More intensive investigation and carefully planned surveys, with well-documented records and adequate statistical control, must be organized in an attempt to answer the simple, but extremely profound, questions: How is leprosy spread? Is there an extra-human reservoir? Where does *M. leprae* live? And how does this fastidious organism, with its extremely particularized growth requirements, manage to survive and multiply? These are questions that still await elucidation. The simple questions, the most profound, are frequently the most difficult to answer.

### Session IV. Experimental Leprosy—Bacteriology

**Chairman: Dr. Charles C. Shepard**

Dr. Shepard's session was one of the most

important of the Congress. More new work, and more new significant work was reported here than elsewhere. Details of accurate technical estimations of limited multiplication of *M. leprae* in the mouse foot pad, were supplemented by Rees' work on the production of widespread bacilliferous granulomata in the thymectomized and irradiated mouse. The observation that muscle as well as nerve tissue provides a suitable nidus for mycobacterial multiplication has been further investigated by several workers.

The fundamental immunologic differences in the human host, differences that are clinically exteriorized in the polar types of leprosy, may be associated with physiologic disparity in certain tissue and blood cells. Antilymphocytic globulin is reported to enhance the susceptibility of mice to mycobacterial challenge.

The well-known parasitization of human reticuloendothelial cells in patients suffering from lepromatous leprosy, has stimulated further work in cell culture and attempts to induce cells from patients already exhibiting failure to lyse and clear mycobacteria, to harbor *M. leprae*. Human skin fibroblasts appear to possess the requisite biochemical and immunologic properties to permit such multiplication. Various adjuvant factors are being investigated in the hope that the ideal substance may one day be found.

"All is not gold that glitters," and mycobacterial strains labelled *M. leprae* in the past are now found to have been incorrectly identified; they mostly belong to the fast-growing mycobacteria differentiable from *M. leprae* by recently developed and more sophisticated laboratory techniques. Filterable forms of mycobacteria may exist. We need to know more about this possibility.

Morphology and viability, pleomorphism of mycobacteria, L forms, phenoloxidases and other adjuvant or inhibitory enzymes—all were discussed and notable contributions came from laboratory workers from many countries.

## Session VI. Experimental Leprosy—Pathology, with Special Reference to Neurologic Aspects

**Chairman: Dr. A. G. M. Weddell**

Dr. Weddell's session considered the pathology of leprosy with special reference to its neurologic aspects. The most important findings reported were ultrastructural changes in nerves as revealed by electron microscopy. There is a growing awareness that immunologically significant changes occur as a response in tissue hypersensitized in some way by mycobacteria or by certain biochemical moieties of their breakdown products. It is not yet possible to distinguish the basis for the extremely varied response at the cellular and at the ultramicroscopic level in leprosy. Is it pressure? Is it edema? Is it cellular infiltration? Is it something else? And, whatever it is, what is the fundamental, the ultimate pathology? This may seem to some to be an academic question, but it is of extreme significance to the patient who has leprosy and who is liable to rapid and progressive and irreversible damage to his peripheral nerves with the orthopedic consequences, paralyses, pareses, anesthesiae, etc.

## Session VIII. Immunology, with Special Reference to Hypersensitivity in Leprosy

**Chairman: Dr. John H. Hanks**

In Dr. Hank's session clear evidence was presented that the anergy of lepromatous leprosy is due in part to a subnormal response of leucocytes to physiologic stimuli, and to antigens that may be totally unrelated to *M. leprae*. These responses are suppressed by factors occurring in lepromatous serum. The investigations by Dr. Bechelli and others on the Mitsuda reactivity in a noncontact population demonstrated the usefulness of a lepromin containing only 20 million organisms per milliliter, not

the 600 million that has hitherto been regarded as the optimum for field work. These results suggested that the lepromin reaction might become positive after the 28th or even the 35th day. This work has been anticipated in São Paulo and elsewhere.

Laboratory investigations disclose further refinements of method for analyzing the serologic alterations in leprosy and the cross reactions between *M. leprae* and other nearly or distantly related mycobacteria.

### Session X. BCG and Prophylaxis

**Chairman: Dr. P. D'Arcy Hart**

Dr. D'Arcy Hart's session provided extremely useful data for the continuing debate on the value of BCG vaccination in leprosy. If BCG does really enhance innate potential resistance to challenge by *M. leprae*, or induce such resistance where it was nonexistent, and if it will do this in children exposed intrafamilially to such challenge, then this would be the most important single advance in leprosy prophylaxis. If it is true, everybody should know, and voluntary organizations and governments should be devoting a high proportion of their resources to controlling leprosy by these means. But wherein lies the truth? (Uganda, 80%; Papua and New Guinea, 56%; Burma, 0%)

Many millions of people are exposed to *M. leprae*, and many will develop leprosy this year, next year and the year after. It is quite impossible to treat adequately and to render noncontagious all patients with lepromatous leprosy in the world within the foreseeable future. If BCG should show the way to prevent leprosy, we beg the epidemiologists to tell us; meanwhile we encourage them to pursue their investigations. In some ways, therefore, this was a disappointing session, not because of the quality of the papers, but because of the complexity and the contradictions of the conclusions. It remains for WHO to stimulate further trials, with impeccable statistical control, and severe and critical evaluation; field work, standards and methods must be sys-

tematized and correlated, for weighty edifices cannot be built on a collected mass of unreliable primary data. The kingpin in these large-scale investigations is the man working in the field, and not those who, by means of sophisticated instruments, summarize his observations.

It now appears to be established that dapsone (DDS), regularly administered to children exposed to leprosy, will protect a high proportion of them against the development of overt lesions.

### Session XII. Reactions—Immunologic Aspects

**Chairman: Dr. D. S. Ridley**

Dr. Ridley's session on the immunologic aspects of reaction provided much light and no little heat. Four types of reaction can be identified, which differ in their immunologic and prognostic significance, although they have a number of important points in common. Research on their pathogenesis is still in the stage of collecting data. Some promising approaches have produced negative or even inconsistent and contradictory results.

The concept of leprosy as an infection in which immunity is essentially cell-mediated by lymphocytes, and in which anergy is associated with suppression of lymphocyte production, sheds light on several problems. Reactions associated with an increase of immunity and a movement toward the borderline form of leprosy, may be precipitated in experimental infections in thymectomized mice by injection of normal lymphoid cells. These results represent a distinct advance and, coupled with the work of Rees and Gaugas at Mill Hill, give us some extremely useful pointers to future research in this aspect of leprosy. It is a well-known fact that erythema nodosum is associated with an increase of complement; immuno-globulins are also increased, and a number of auto-antibodies are sometimes present. But these are no greater in amount—and sometimes are actually less—than in patients with nonreacting lepromatous leprosy. Here again a problem is presented, and questions are asked that may seem

facile to pose but are extremely difficult in practice to answer. The fluorescent antibody technics (on which many of us pinned a certain amount of faith), are giving inconstant results. Erythema nodosum leprosum has a number of parallels with serum sickness, which is due to circulating antigen-antibody complexes.

### Session XIV. Reactions— Clinical Aspects and Therapy

**Chairman: Dr. R. D. Azulay**

Dr. Azulay's session was concerned with the clinical and practical aspects of leprosy reaction and the therapy of such reaction. The two main points brought out in this session were the remarkable progress in the therapy of leprosy reaction, the first being thalidomide, and the second, the riminophenazine derivative, the *aposafranin*, B.663. With recent memory of its teratogenic and neurotoxic properties, and the knowledge that legal process against its German manufacturers is now taking place, some practitioners are chary of thalidomide. The drug seems to have a specific anti-inflammatory effect in leprosy reaction, and, as Professor Sagher's working party suggests, it is indicated precisely in acutely reacting lepromatous leprosy. The dose recommended is between 100 and 400 mgm. per day; after remission of the acute phase, it may be decreased. The drug has no effect on the disease itself; in fact, its use may be followed by some increase in the leprosy lesions. Some side-effects have been noted, mainly edema of the extremities and some dizziness and pruritis, but in the main these are not serious. Homologs and derivatives and breakdown products of this drug are being investigated for their possible activity in lepra reaction. We await with interest further researches along these lines.

B.663 is reported to have a definite anti-inflammatory action in the acute exacerbation of lepromatous leprosy. It is active both in the acute exacerbation and also in leprosy itself; in the future it may find its main sphere of usefulness in patients with established reaction. It must be given in

adequate doses, just as the dose of corticosteroids, given for their inflammatory-suppressive activity, must vary. It may also be given to patients with severe lepromatous leprosy, especially to those who appear prone to develop acute exacerbation. This may prove to be a wide field for this drug, since it may usefully be presented in those situations where it is economically feasible and advisable to give such a drug, e.g., because of the consequences of persistent and prolonged acute exacerbation in lepromatous leprosy in a wage-earner, or head of a family, who has lepromatous leprosy but wants to be allowed to continue working.

### Session XVI. Chemotherapy of Leprosy—Experimental Aspects

**Chairman: Dr. S. R. M. Bushby**

In Dr. Bushby's session it was noted that the most valuable advance in the field of experimental chemotherapy since the last Congress is the exploitation of the observation by Shepard that *M. leprae* multiplies locally when injected into the foot pads of mice. This discovery has produced an experimental model that will permit determination of the sensitivity of *M. leprae* to drugs suspected of having an antileprotic activity. Using this model, Dr. Rees and his colleagues have confirmed that the bacilli from patients who relapse during dapsone (DDS) therapy are less sensitive to the drug than are those from untreated patients. Truly resistant bacilli, in certain cases, may show cross-resistance with the sulfonamides, but rarely with other antileprotic drugs of unrelated chemical constitution. Although fully sensitive strains are inhibited by serum levels as low as 0.02 microgram of DDS per milliliter (which corresponds to a daily dose of 0.1 milligram for an adult weighing 50 kgm.), the need for maintaining in the human subject relatively high concentrations is apparent, when it is realized that mycobacteria develop resistance to sulfones by a stepwise process (as reported from Baltimore) and that the degree of resistance to the strains

from relapsing patients varies within wide limits. By this method, DDS has been shown to be bactericidal, and there is a distinct difference between bacteriostatic and bactericidal activity. We are grateful to Shepard for developing the kinetic method of demonstrating this difference. It may be that the minimal inhibitory dose should be increased many times in the human patient if the emergence of resistant strains is to be forestalled.

## **Session XVII—Chemotherapy of Leprosy—Clinical Aspects and Therapy**

**Chairman: Dr. M. F. R. Waters**

Dr. Waters' session concentrated particularly on B.663, low-dose dapsone, and long-acting sulfonamides, drugs that together seem to provide some prospect of hope for patients with lepromatous leprosy in rural campaigns who are able to receive a visit from a physician but infrequently.

The long-acting sulfone, DADDS, when given as a single intramuscular injection once every three months, may produce and maintain a therapeutic blood level of active drug.

The pharmacology and toxicology of B.663 were considered at some length; the antileprosy activity of the drug is apparently of the same order as that of dapsone. It has been found invaluable in cases of proven dapsone resistance. The main disadvantage from its use is a ruddy pigmentation of the skin, following by darkening. These changes of color tend to disappear slowly when the drug is discontinued.

Dapsone is reported to be active in extremely low doses, such as 5 or 10 mgm. a week, which, however, are theoretically still well above the minimal inhibitory dose. With these low doses, a vigilant watch must be kept for the emergence of drug-resistant strains.

In Argentina it is found that patients with lepromatous leprosy respond more rapidly to sulfonamides than to dapsone, while in Africa some workers have found the long-acting sulfonamides to be particularly valuable in tuberculoid leprosy.

Numerous long-acting sulfonamides are now being synthesized, and it is not outside the bounds of possibility that one day a new compound will be developed that is very much better than the existing long-acting and depot sulfonamides, and can be used in mass treatment campaigns without grave risk of complications and toxic effects. Meanwhile it is well to remember that these drugs have certain inconveniences and disadvantages, and that they are expensive.

A plea for regular treatment of patients with lepromatous leprosy was reinforced by the report that bacterial negativity could be achieved more rapidly by regular treatment. However, even when approved dose-schedules were followed, the relapse rate in a rural leprosy control scheme concerned mainly with patients with nonlepromatous leprosy, was found to be nearly 5 per cent.

Some work was reported on newer drugs. Ethambutol is effective for a short time, and Rifamycin was used in a small uncontrolled series with apparently good results. These two drugs may open the door to new advances in leprosy therapy, particularly the derivatives and related antibiotics of the latter, some of which show definite and high mycobactericidal activity.

Several speakers at this session emphasized the need for carefully controlled trials of drugs with suspected antileprosy activity, and for comparison with standard dapsone therapy.

In the concurrent sessions, extremely important and useful papers were read, and fruitful discussions followed, as noted in the next section summaries.

## CONCURRENT SESSIONS

### Session III. Ophthalmologic Aspects

**Chairman: Mr. H. E. Hobbs**

In Mr. Hobb's session the ophthalmologic aspects of leprosy provoked lively debate. It was reported that many clinicians and many laboratory workers were quite unaware of the dimensions of eye complications. The proportion of patients with lepromatous leprosy who have ocular complications at some time or other in the course of their disease is extremely high. Rarely, ophthalmologic manifestations may be the presenting sign of leprosy, heralding very serious lepromatous disease, before there are any apparent skin changes. All clinicians should familiarize themselves with the slit lamp, a small portable instrument that possibly can be used by the amateur in tropical jungles. Every leprologist may not be an ophthalmologic specialist, but all clinicians should know how to use a slit lamp. Physicians were urged to spread knowledge of the ophthalmologic complications of leprosy not only to fellow physicians but especially to paramedical workers and nurses. The latter, in fact, are treating over nine-tenths of the patients under leprosy control today, and they should be aware of the early signs of ocular involvement. Early recognition of signs of ocular disorder, very often in the presymptomatic stage, is perfectly practicable. For the more highly sophisticated, the budding ophthalmic surgeons, one speaker emphasized that cataract-extraction or keratoplasty, in the past considered unsafe and not worth the risk, can be quite feasible and is effective in expert hands.

### Session V. Physiotherapy and Prostheses

**Chairman: Professor T. N. Jagadisan**

In Professor Jagadisan's session emphasis was placed on physiotherapy and its role in the prevention of deformity. Many countries cannot afford a physiotherapy service,

but they can afford perhaps one physiotherapist, who can train others. I would beg of you to cooperate with the Leprosy Mission and LEPRO and with certain governments that can afford physiotherapists; invite them, and give them the opportunity of teaching others, not to produce a highly sophisticated (and admittedly rather expensive) reconstructive surgery unit, but to encourage them to disseminate knowledge of prevention—prevention of deformity, prevention of ulceration of anesthetic feet. Prevention is better, and cheaper, than cure. Conservative measures will prevent ulceration of anesthetic extremities, and permanent dropping of the feet. Prevention will ensure that very acutely inflamed nerves will be rested until the phase of edema is over.

When secondary deformity is established, recourse must be had wherever possible to the surgeons; they provide reconstructive surgery that helps the patient who caught leprosy too long ago, and who has suffered since.

It is not only the orthopedic and reconstructive surgeons who must be enlisted in this task—as they do their Cockett's operation on the nose, and postnasal inlays, and the rest—but also the "jobbing surgeon," who is confronted by row upon row of people with ulcerated and dropped feet, with sagging faces, and with paralyzed ulnar nerves. Jobbing surgeons can do much, provided they do not spend time and energy attempting to perfect sophisticated surgery while allowing thousands of patients in the villages to develop deformities. When secondary deformity has occurred, however, there is real need for the cooperation of the prosthetist, the footwear maker, and the occupational therapist.

As far as physiotherapy is concerned, the selection and preparation of patients for tendon-transfer surgery is all-important. In order to obtain maximal postoperative functional capacity, with good appearance, active cooperation of the patient with the physiotherapist, the surgeon, and the prosthetist is essential. These skills must be

shared with the ordinary poly-competent paramedical worker, who is responsible for most of the leprosy treatment in the world today. It is he who mediates our skills and educates the patient in the protection of anesthetic extremities, and it is he who helps the patient back to life and health again.

## Session VII. Leprosy Control

*Chairman: Dr. B. D. Molesworth*

Dr. Molesworth's session had to confess that successful leprosy control is achieved but rarely. This failure is in part a reflection on us, and on governments for not making more money and more people available; but, in any case, much more should be done. The integration of leprosy services with existing services and the training of paramedical workers were repeatedly stressed.

The speakers took note particularly of the time consumed and the proportion of finance involved in institutional care. Some countries can afford it; most cannot. And where intensive campaigns are in progress, a great increase in the number of registered cases occurs. Leprosy is always far more prevalent than is realized on initial surveys.

## Session IX. Reconstructive Surgery

*Chairman: Dr. P. W. Brand*

## Session XI. Clinical and Surgical Aspects of Nerve Damage in Human Leprosy

*Chairman: Dr. N. H. Antia*

Through sessions IX and XI the surgeons had most stimulating meetings. Drs. Brand and Antia contributed magnificently to the application of reconstructive surgery to patients who caught leprosy too long ago, or who were inadequately treated. They emphasized the value of visits from one country to another, from one surgical group to another; they considered various technical matters, such as the excision of metatarsal

heads for persistent ulceration of the fore-foot.

At the close of Session IX, the place of surgery in leprosy control programs was considered. It was demonstrated in New Guinea how a single surgeon, working out from a base hospital, can organize "surgical camps" in a large number of small general hospitals. In each center, there is a trained auxiliary who carries on before and after the visit of the surgeon. Therefore, post-operative and preoperative treatment can be given, and the evidential value of these expert visits has to be seen to be believed. This system has resulted in general hospitals becoming willing to cooperate, first in the rehabilitation program and later in leprosy control. This is, in other words, a practical demonstration, through the surgeons, of what can and should be done. The surgeon has thus built a bridge between the highly specialized orthopedic and reconstructive surgery units and the leprosy team and the ordinary patient in the villages scattered in the remote mountain valleys of Papua and New Guinea.

In Dr. Antia's session, there was some excellent discussion on certain surgical aspects of nerve-pain and the prevention of paralysis, but the greatest interest was evoked by reports on the pathology of nerve damage in leprosy—nothing new, but all very stimulating. Not only nerves, but smooth muscle cells are now seen to be microscopic sites of predilection for *M. leprae*.

## Session XIII. Psychologic Aspects of Leprosy

*Chairman: Dr. O. W. Hasselblad*

The psychologic aspects of leprosy provided a varied program. The main conclusion was that there is much ignorance—ignorance among physicians and paramedical workers, among administrators, among leprosy patients themselves, and in the community. Much more must be done to investigate psychologic attitudes of the individual patient and of the community in which he lives, so that, eventually, the stigma of leprosy will disappear and leprosy will be treated in the patient's inner

mind, as well as in the community, as a disease, like other diseases. Results from Bombay, as well as from the United States of America, stressed these findings. Confidentiality should be preserved at all points and secrecy must be maintained, but a tremendous amount needs to be done to prevent the leprosy patient from becoming dependent on the community and isolated from that community.

## Session XV. The Rehabilitation of the Leprosy Patient

**Chairman: Mrs. E. Weaver**

In this session several interesting papers were presented that covered familiar ground and emphasized old truths in new ways. While some countries are able to report certain progress in leprosy sociology and acceptance by society of the fact that leprosy exists, and the associated and often equally unpalatable fact that those who suffer from leprosy are indeed human beings and should be treated as such, elsewhere the stigma dies hard and the unwarranted aura of superstition and folklore shows little sign of dispersing.

The urge of social rehabilitation often depends on the informed enthusiasm of the individual, in government service or in a voluntary organization. Planning is essential, but impersonal planning may defeat its own end; much depends on the drive and personal sympathy of those in charge.

The knowledge that social services are available, that discrimination is officially frowned upon, that employment for the patient and support for his family are assured, may do much to augment and strengthen any antileprosy campaign. It is in the relatively wealthy countries, and in urban and sophisticated communities, that these welfare and social services are not only working but are seen to be effective. Nevertheless, in the developing countries, with their larger and less tractable leprosy problem, rural rather than urban, such schemes for the rehabilitation of the leprosy patient are no less essential.

Much discussion was aroused over the proposal to abolish the word "leprosy," and

to replace it by an eponymous or neutral scientific descriptive term, but some contributors were of opinion that the *disease* rather than the *name of the disease* needed rehabilitation, and that all efforts should be bent toward education of the public, the medical profession (including medical students) and politicians on the true nature, importance, and curability of this widespread and crippling disease.

## Session XVIII. Discussion—Co-operation and Priorities

**Chairman: Dr. T. F. Davey**

Dr. Davey's session attempted to translate into the humdrum world of practical politics the scientific advances now available, and to relate the leprosy problem to the human and material resources at our disposal. The essential intractability of leprosy as a disease of the physical nature of man, with its nonmaterial overtones, renders any piecemeal attack abortive and ineffective. We are dealing with persons, living in a social environment and conditioned by many and diverse factors. If existing knowledge could be applied on a world scale, even though many of the answers to the problems leprosy poses still elude us, then the slow spread of leprosy could be halted. More emphasis should be placed on well-planned leprosy control schemes, integrated wherever possible with general health measures. Unless and until the huge reservoir of patients with "open" leprosy is tackled realistically and cooperatively, the endemic will continue to smoulder.

The session ended with a plea for cooperation—between governments and voluntary agencies, between national and international agencies, between the more affluent and the poorer countries of the world, and between the research scientist and the field worker. Cooperation is also necessary among those engaged in all aspects of leprosy, and those coming into leprosy from other branches of science. Given these priorities, and this degree of cooperation, leprosy could be "controlled in our generation and eradicated in the next."