# LEPROSY REVIEW

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THE BRITISH LEPROSY RELIEF ASSOCIATION

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## Principal Contents



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Edited by DR. J. ROSS INNES, Medical Secretary of the British Leprosy Relief Association, 8 Portman Street, London, W.1, to whom all communications should be sent. The Association does not accept any responsibility for views expressed by writers.

Contributors of original articles will receive 25 loose reprints free, but more formal bound reprints must be ordered at time of submitting the article, and the cost reimbursed later.

# EDITORIAL

## 1. Latest information on the 8th International Congress of Leprology

This important Congress will be held in Rio de Janeiro 12-20th September 1963. We are informed that Dr. Orestes Diniz whose address is Rua São Cristovão, 1298 Rio de Janeiro, Brasil, has issued No. 1 of a series of pamphlets of information, which contains lists of those who intend to be present at the Congress. We have received No. 1 in this office.

As indicated in previous lists of members of panels and Round Tables given in *Leprosy Review* (the Editorial, January 1963) some change in the names was expected because some members would not be able to attend and most unfortunately we have suffered the great loss of Dr. James Doull who has died. He was the Chairman of the Panel on Epidemiology and Control. The present list of the names of Chairmen and Secretaries, and Members of these panels and Round Tables is given below:

A. *Round Table on Pathology and Experimental Transmission*
*Chairman:* R. J. W. Rees (U.K.)
*Secretary:* Prof. H. M. Portugal (Brazil)
*Members:* M. Bergel (Argentina), C. H. Binford (U.S.A.), Y. T. Chang (U.S.A.), K. R. Chatterjee (India), J. Convit (Venezuela), W. H. Feldman (U.S.A.), W. A. Hadler (Brazil), S. Nishimura (Japan), J. M. Robson (U.K.), C. C. Shepard (U.S.A.), F. F. Wilkinson (Argentina).

B. *Round Table on Borderline and Indeterminate Leprosy*
*Chairman:* R. D. Azulay (Brazil)
*Secretary:* J. N. Rodriguez (Philippines)
*Members:* R. G. Cochrane (U.K.), F. Contreras (Spain), Dharmendra (India), T. Imaedo (Japan and Venezuela), W. H. Jopling (U.K.), V. R. Khanolkar (India), K. Kitamura (Japan), J. Gay Prieto (Spain), F. Sagher (Israel), H. W. Wade (President ILA—U.S.A.), J. R. Puchol (Spain), W. F. Kirchheimer (U.S.A.), A. M. Alonso (Brazil),

C. *Panel on Reactions*
*Chairman:* F. Latapí (Mexico)
*Secretary:* D. S. Ridley (U.K.)
*Members:* J. Gómez Orbaneja (Spain), C. K. Job (India), A. R. Mercau (Argentina), J. Mariano (Brazil), D. Periassu (Brazil), J. Ramos e Silva (Brazil), J. G. Tolentino (Philippines), I. Tajiri (Japan), J. H. Frenken (Dutch W. Indies).

D. *Panel on Therapy*
*Chairman:* S. G. Browne (Nigeria & U.K.)

*Secretary:* P. Laviron (France)

*Members:* A. Baccareda Boy (Italy), J. Barba Rubio (Mexico), M. B. Bhojwani (Malaya), T. F. Davey (U.K.), H. Floch (France), Latif K. Hanna (Egypt), Y. Hayashi (Japan), K. Ramanujam (India), K. F. Schaller (Ethiopia), S. Schujman (Argentina), M. F. R. Waters (U.K.).

E. *Panel on Epidemiology and Control*

*Chairman:* M. F. Lechat (Belgium and U.S.A.)

*Secretary:* A. Salazar Leite (Portugal)

*Members:* E. Agricola (Brazil), D. A. Akintonde (Nigeria), L. M. Bechelli (Brazil), W. M. Candidio (Brazil), O. Diniz (Brazil), C. Kettanurak (Thailand), C. M. Ross (U.K. & Uganda), Amado Saúl (Mexico), B. D. Molesworth (U.K. & Ghana), J. A. Madeira (Saõ Paulo), H. Sanssaricq (Mali).

F. *Panel on Bacteriology and Immunology*

*Chairman:* J. H. Hanks (U.S.A.)

*Secretary:* J. M. Fernández (Argentina)

*Members:* J. O. Almeida (Brazil), S. W. A. Kuper (U.K.), J. H. S. Pettit (Malaya and U.K.), E. Montestruc (France), A. Rotberg (Brazil), Candido Silva (Brazil), K. Yanagisawa (Japan), Y. Yoshie (Japan), G. P. Youmans (U.S.A.).

G. *Panel on Education and Social Aspects*

*Chairman:* T. N. Jagadisan (India)

*Secretary:* Luiza Keffer (Brazil)

*Members:* C. Costa Neves (Brazil), C. I. Crowther (U.S.A.), M. C. Estrada (Mexico), R. Follereau (France), N. D. Fraser (U.K.), K. Hamano (Japan), O. W. Hasselblad (U.S.A.), J. R. Trautman (U.S.A.), R. V. Wardekar (India), Mrs. E. Weaver (Brazil).

H. *Panel on Physical Medicine and Rehabilitation (including Surgery and Vocational Training)*

*Chairman:* P. W. Brand (India and U.K.)

*Secretary:* J. Arvelo (Venezuela)

*Members:* N. H. Antia (India), Mrs. Margaret Brand (India and U.K.), J. E. Faggin (Brazil), M. Itoh (U.S.A.), M. Nakita (Japan), D. E. Paterson (India and U.K.), E. W. Price (Ethiopia and U.K.), D. C. Riordan (U.S.A.), Linneau Silveira (Brazil), D. Ward (U.K.), E. Zamudio (Mexico).

**2. The Work of Dr. Weddell**

The work of Dr. Weddell was described in the last issue (April 1963). Since then Dr. S. G. SPICKETT of Cambridge, DR. R. J. W. REES, DR. G. WEDDELL and MISS ELISABETH PALMER and DR. J. WALTER have written 'Letters to the Editor'. All these appear in this

issue and raise many interesting points and call for serious thought from all of us. We think that the next need is a great deal of specialised epidemiology.

**3. Mast Cells**

Prof. P. C. SEN GUPTA and DR. S. GHOSH of the School of Tropical Medicine, Calcutta, have informed us that their contribution regarding Mast Cells in leprosy appears in *Nature* 197, 506, 1963. We direct attention to this paper in which the necessary technical details are given. They found tissue mast cells while examining the histology of lepromatous skin lesions and noted that there were many cells containing acid-fast granules in the cytoplasm. They point out that KHANOLKAR was the first to record such cells and called them fuchsinophil cells. He regarded these granules as partly digested *Myco. leprae* and the cells as adventitial cells or macrophages.

**4. 'Experimental leprosy'**

'Experimental leprosy' is an Editorial in *British Medical Journal* (20th April 1963, p. 1040) and is of such interest and importance that we have sought and obtained the kind permission of the Editor to reprint it and it is given here.

**' Experimental leprosy**

Although the human leprosy bacillus was the first bacterium to be recognised as causing disease in man, by Hansen in 1874, studies of the organism and even our knowledge and treatment of the disease have been hampered by failure to culture it or to transmit the experimental infection to animals. Now in view of recent reports of the successful transmission of leprosy to experimental animals progress in this field looks more promising.

K. R. Chatterjee, working in Calcutta, showed that when a particular hybrid strain of black mice was inoculated subcutaneously or intraperitoneally with freshly isolated human leprosy bacilli a fully established and progressive infection could be established eventually in some of the animals by repeatedly passaging the infected mouse tissues. These observations have been confirmed with seven out of seventeen samples of human leprosy bacilli by Chatterjee and R. J. W. Rees in work carried out at the National Institute for Medical Research, London. Once established the infection can be successfully passed to further animals, in which it produces a generalised infection of the reticulo-endothelial system involving particularly the liver, spleen, and lymph nodes and apparently also the nerves. The bacilli recovered from these animals failed to grow in bacteriological media. C. C. Shepard, working in the U.S. Public Health Service, Atlanta, has used the foot-pads of mice because of the apparent predilection of the leprosy bacillus for cooler sites in man, and he obtained limited multiplication of the bacilli. The infection was confined to the foot-pad and the bacilli

multiplied only under certain conditions. The infection could be maintained by serial passage in the foot-pads of mice, and it has been established for 50 out of 55 samples of leprosy bacilli obtained from different patients in the United States and Philippines. Again bacilli recovered from the mice failed to grow in bacteriological media. Rees has recently confirmed these observations at the National Institute for Medical Research with passaged material supplied by Shepard and also with nine freshly isolated strains of human leprosy bacilli from patients in Burma, East Africa and Malaya.

Although these studies are of the greatest importance there are major discrepancies between the two types of infections established in animals which must be further investigated. The obvious approach would be to compare characteristics of human leprosy bacilli derived from man with those of bacilli derived from the experimental infections. Unfortunately there are few such characteristics available for study in an organism that cannot be cultivated, though the antigenic structure is one. Until recently little progress had been made on the antigenic structure of mycobacteria. Now G. Castelnuovo and her colleagues have shown that immuno-electrophoretic methods can be used to define more precisely the antigenic structure of mycobacteria sufficiently to distinguish species differences, and these may be applicable to the human leprosy bacillus. While it is essential to clear up these fundamental points studies on the present experimental infections should be pursued. Because the foot-pad type of infection, unlike the infection established in hybrid black mice, can be initiated without subsequent serial passage, it is more directly applicable to studies on the human leprosy bacillus. Already it has been used successfully as a screening test for anti-leprosy drugs. So far the experimental infections have been established only with the bacilli from patients with lepromatous-type leprosy. Similar experiments should now be undertaken with bacilli obtained from patients with other types of leprosy. This might help to show whether different types of leprosy in man are determined by differences in the bacilli (perhaps with differences in virulence) or by different degrees of resistance in man. Occasionally patients relapse after several years of improvement on continuous treatment with diaminodiphenyl sulphone or other anti-leprosy drugs. The relapses may be due to the development of drug resistance by the bacillus, but it has not been possible to test this because the organisms cannot be cultivated. Now for the first time it should be possible to determine whether relapse is due to drug resistance of the bacilli by using the foot-pad infection in mice. Thus these advances in the transmission of leprosy to experimental animals are likely to be of practical value as well as putting leprosy research on a firmer experimental basis."

References:
Chatterjee, K. R., *Int. J. Leprsy*, 1959, **26,** 195.
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Rees, R. J. W. *The Pathogenesis, of Leprosy*, 1963. London, J. and A. Churchill.
Castelnuovo, G., Guadiano, A. Morellini, M. Penso, G., and Polizzi-Sciarrone, *Annal. Ist. Carlo Forlanini*, 1959, **19,** 40.
Shepard, C. C. and Chang, Y. T., *Proc. Soc. exp. Biol. (N. Y.)*, 1962, **109,** 636.

**Correction**

Club-forms of Mycobacterium Leprae by M. J. WISE (Vol.**34,** No. 2, 1963). On page 69, the first line of RESULTS should read "In all cases clubs were *most numerous*" instead of " . . . not numerous".

## GOVERNMENT OF WESTERN NIGERIA

Applications are invited for the post of
MEDICAL OFFICER (LEPROSY)
in the Western Nigeria Public Service:

**Qualifications:**

A medical degree registrable in Nigeria. Experience in the specialty is desirable, but not essential.

**Duties:**

The duties of the officer will be those of a Medical Officer (Leprosy) at the Leper Settlement, Ossiomo, near Agbor, Benin Province, Western Nigeria.

**Other Conditions of Service:**

On contract for one tour of 12–18 months in the first instance. Salary is between £1,734–£2,316 per annum for a male officer or £1,614–£2,196 per annum for a female officer. A gratuity of £37 10s. 0d. for every completed period of three months satisfactory service. £60 outfit allowance is payable for salaries below £1,750 per annum on first appointment. Free first class sea passages or Economy Class Air Passages for officer and family on first appointment and when proceeding on leave. Free medical treatment for officer and his family. Accommodation is provided at low rentals.

**Method of Application:**

Applications should be completed in quadruplicate on the prescribed form obtainable from the Official Secretary, (Recruitment Branch), Office of the Agent-General for Western Nigeria, 178/202 Great Portland Street, London, W.1, from whom further particulars may also be obtained.

Candidates living outside the United Kingdom and Western Europe should apply direct to the Secretary, Public Service Commission, Private Mail Bag No. 5005, Ibadan, Nigeria.

**Closing Date:**

31st July 1963.

## OBITUARIES

# THE LEONARD WOOD MEMORIAL

(American Leprosy Foundation)
Medical Department, 1832 M St., N.W.
Washington 6, D.C. has kindly supplied the following information.

### JAMES ANGUS DOULL, M.D.

James Angus Doull, M.D., Medical Director of the Leonard Wood Memorial for the Eradication of Leprosy and internationally known for his work in public health died 6th April 1963 at the age of 73 in Baltimore, where he had been a patient since early February.

He was born in New Glasgow, Nova Scotia, on 8th September 1889. His academic degrees were B.A. (1911) and M.D., C.M. (1914) from Dalhousie University, Halifax, N.S., D.P.H. (1919) from Cambridge University (England), and DR. P.H. (1921) from Johns Hopkins University.

Throughout World War I Dr. Doull served in the Royal Army Medical Corps, attaining the rank of major. Immediately after the war he was an intern at Brompton Hospital, London, and then at Willard Parker Hospital, New York City. He entered Johns Hopkins University School of Hygiene and Public Health as a Rockefeller Fellow in 1920, became associate in epidemiology in 1921, and subsequently served as associate professor from 1924 until 1930. For nearly a decade while in Baltimore, he conducted a comprehensive study of the epidemiology of diphtheria. Following this work he became director of the John J. Abel Fund for Research on the Common Cold at Johns Hopkins.

For fifteen years, beginning in 1930, Dr. Doull was the Elizabeth Severance Prentiss professor of Hygiene and Public Health at the School of Medicine, Western Reserve University, Cleveland. During this period, at the request of the then Surgeon General of the Public Health Service, Dr. Thomas Parran, Dr. Doull conducted surveys on public health in various parts of the world.

While serving Western Reserve University, Dr. Doull had three important governmental assignments related to World War II. The first was a special mission to the Pacific for the Lend-Lease Administration to help Australia and New Zealand obtain urgently needed medical supplies. The second was to England for the United Nations Relief and Rehabilitation Administration as a member of an international committee convened in London to draft new sanitary conventions for maritime and aerial commerce regulations for the medical control of displaced persons in Europe. The third was a trip to Europe to make preliminary arrangements for the proposed international health organization.

Dr. Doull resigned from Western Reserve University in 1946 to join the Regular Corps of the U.S. Public Health Service, from which he retired with rank of Medical Director in 1953.

Dr. Doull served with the U.S. Delegation to the United Nations Conference on International Organizations in San Francisco in 1945, which created the United Nations. He assisted in drawing up plans for the World Health Organization at the International Health Conference and was the representative of the United States, International Office of Public Health, in Paris 1946. He was deeply interested in the World Health Organization which he continued to serve as a consultant and member of the leprosy panel.

Other noteworthy services for the United States performed by Dr. Doull in the field of international health include his work with the Pan American Sanitary Organization in which he served as a delegate and as a member of the Directing Council. He contributed significantly to the International Leprosy Congresses in Cairo (1938), Havana (1948), Madrid (1953), and Tokyo (1958).

In 1948, Dr. Doull (on leave from the U.S. Public Health Service) assumed the position of Medical Director of the Leonard Wood Memorial for the Eradication of Leprosy. He was aware of the importance of establishing precise methods to evaluate the usefulness of new drugs in the treatment of leprosy. As a result of his guidance the first scientific method for determining the effectiveness of chemotherapy in leprosy was evolved. The procedure required that the patients treated be compared with a similar group that were not treated. This was carried out by what is known as the double-blind method, wherein neither patients nor doctors are aware of the specific agent used. Thus, personal prejudices are eliminated.

During the fifteen years of his medical directorship, numerous projects pertaining to the treatment, diagnosis, and epidemiology of leprosy have been carried out in the Philippines, Japan and South Africa, and the potential for basic research by the Leonard Wood Memorial established a unit for research in leprosy at the School of Hygiene and Public Health of Johns Hopkins University. The research facilities of the Memorial in Cebu, Philippines, have recently expanded. At the present time, due to Dr. Doull's leadership it is likely that more research in leprosy is being conducted by scientists employed by the Leonard Wood Memorial than by any similar group in the world.

Among his numerous duties as Medical Director of the Leonard Wood Memorial he served as consultant on leprosy for the Clinical Centre, National Institutes of Health, specifically assigned to the National Institute of Allergy and Infectious Diseases.

The Surgeon General of the U.S. Army in 1954 called upon Dr. Doull to make a comprehensive survey of leprosy in the Ryukyus Islands. Recommendations which resulted from the detailed study

have been of extreme importance in protecting American military and civilian personnel in Okinawa and improving the health of the native population.

Indicative of Dr. Doull's wide interest in public health and infectious diseases other than leprosy are his many publications on the epidemiologic aspects of diphtheria, poliomyelitis, typhoid fever and tuberculosis.

Dr. Doull was the recipient of many awards, including the Military Cross, Great Britain; Croix de Guerre, France; the medal of Chevalier, Ordre de Sante Publique, France; and Commander, Military and Sovereign Order of St. Lazarus of Jerusalem. He was elected an honorary member of the Belgian Society of Tropical Medicine, Antwerp; Honorary Fellow of the Royal Sanitary Institute, London; a Fellow of the Royal Society of Tropical Medicine and Hygiene, London, and an honorary Fellow of the Argentine Society of Leprology. He was a member of numerous medical and scientific organisations, including the American Epidemiological Society, which he served two terms as president; the American Public Health Association, of which he was a member of the governing council and the executive board; the Pasteur Club of Cleveland, Sigma Xi, Alpha Omega Alpha, and Delta Omega. Dr. Doull was the last of the original incorporaters of the Cleveland Health Museum founded in 1936. He was a member of the Cosmos Club of Washington.

Dr. Doull became a naturalized citizen of the United States in 1931. He is survived by his wife, Ethel Mary (MacQuarrie) Doull of the family home, 4202 25th St. North, Arlington, Virginia; a son, Dr. James A. Doull, Jr. of Cleveland; a daughter, Dorothy (Mrs. Richard M. Miller) of West Hartford, Conn. and six grandchildren. Also surviving are two brothers, the Rt. Hon. Justice Doull of Halifax, N.S., and G. Roy Doull of Moncton, N.B. and a sister, Mrs. Wm. B. MacDonald of Winnipeg, Canada.

Funeral services were held at Fort Myer Chapel, Wednesday, 10th April, with burial in Arlington National Cemetery.

(Dr. James Doull greatly respected and admired BELRA. When in London he never failed to call on the Medical Secretary, Dr. J. Ross Innes, and his generous and always valuable advice was always sought and freely given. His singleminded love and service to the cause of leprosy patients was ever evident. His loss is personally felt by all patients and all leprologists of the world. *Editor.*)

## PROF. DR. H. C. DE SOUZA ARAUJO

Professor Heraclydes Cesar de Souza Araujo was born in Paraná, at Sto Antônio de Imbituva and died in Rio, on the 10th August 1962 at the age of 76.

Professor of Leprology at the School of Medicine (*Faculdade de Ciências Médicas*) and Director of the Leprology Laboratory of the Institute 'Oswaldo Cruz', he dedicated 36 years of his professional life to the investigation and teaching of leprosy, in Rio de Janeiro.

With a brilliant intelligence and an extraordinary capacity of work, he wrote 300 medical essays, the majority on leprosy and the others on many subjects as the biographies of S. Lucas, Oswaldo Cruz, Janselme, Cardoso Fontes, Krauze, Baliña, etc.

He travelled around the world, teaching leprology courses, lecturing and participating of conferences or getting material for his books and researches.

His most important works on leprosy are: *Leprosy and Haematophages*, *Acid Fast Bacilli Cultures*, *Leprosy Survey made in Forty Countries*, *History of Leprosy in Brazil* in 3 volumes and 200 other publications. The trial of culture of the leprosy microbe attracted him very much. He has even isolated ten samples of bacilli from leprosy patients and studied them almost until his death.

The Brazilian Government, in recognition of his efforts, awarded the "Order of Medical Merit" in 1960.

Professor Souza Araujo was patron of the Centre for the Study of Leprosy of the University of Paraná to whom he donated his personal collection of leprosy books.

The death of this remarkable Professor is, for Brazil and for the world, an inestimable loss.

# A TRIAL OF BCG VACCINATION IN THE PROPHYLAXIS OF LEPROSY

by J. A. KINNEAR BROWN, B.SC., M.D., D.T.M.,
*Senior Specialist, Ministry of Health, Uganda*
and SISTER M. M. STONE, S.R.N., S.C.M.,
*Matron, Kumi-Ongino Leprosy Settlement, Uganda*

This is a preliminary account of the first phase of a field trial of BCG in the prophylaxis of leprosy. The second report of the World Health Organisation Expert Committee suggested that for such an investigation a number of children should be taken under 9 years of age who were in close contact with lepromatous or other open cases; that one third of those who were tuberculin negative should be vaccinated, one-third given sulphones at half the therapeutic dosage, and one-third observed as controls. The size of each group was to be 100. The number of cases of leprosy arising in each group and among those children regarded as initially positive would ultimately be compared. Provision was also to be made for allocating new born children in the various families to one or other of the groups. The number of children was based on the expectation that, because of the method of selection, there would normally be a very high incidence of leprosy among them.

One of us (J.A.K.B., 1955-59) has shown that the prevalence of leprosy in Uganda, and possibly elsewhere, cannot be dependent only upon the number of lepromatous cases and that the genetic inheritance of the individual in contact with infection plays a significant part in determining whether he will contract leprosy. During the last few years we have carried out extensive enquiries in the field about the families of patients. These confirm our views, and suggest that although both lepromatous and non-lepromatous patients share equally with the healthy in such social activities as communal harvesting and the celebrations that follow, the lepromatous patients marry less frequently and have fewer children. We concluded, therefore, that we might be following an unprofitable course if we tried to include only the children of lepromatous patients in household contact. We decided instead to concentrate on children related to patients whatever the type of leprosy, and to try to get a much larger number of children in each group.

The trial began in September 1960 in the Teso district of Uganda, which has an area of 4,649* square miles and a population of 453,474 including 154,466 children under 16. The density of population varies between 15 and 1,000 to the square mile, the average being 100. The district is divided into eight counties which are again subdivided into 186 eitelas or parishes. The population of an eitela is between 1,500 and 4,000, the majority being between 2,000 and 3,000.

* *Note:* Metric equivalents are sq. m. and density of population per sq. m.

The areas of the eitelas vary considerably. Some are compact which simplified the work; in others the people are scattered but in these units we frequently found more patients.

In a series of surveys held nine years ago the prevalence rate among all ages was consistently around 25 per 1,000; among children under 15, 9 per 1,000. In surveys held four years ago the general prevalence rate was the same except that half the 'patients' had been treated and showed no sign of active disease.

The first phase of the trial ended in September 1962, by which time we had worked in 147 eitelas and covered four-fifths of the district. Extensive and unprecedented floods interferred in 1961, but the one-fifth not included is mainly the area within close range of the Kumi-Ongino leprosarium on which this work was based, an area which has been under the influence of the leprosarium for 35 years, and which is not producing many cases. The number of children tuberculin tested was 18,848. Of these 1,267 were related contacts of lepromatous cases, but not necessarily their children.

In the early weeks of the work we excluded children with leprosy because we were anxious that the people should understand that we were undertaking not a new form of treatment but an experiment in prevention. When the health staff and the people understood better what we were doing, we recorded the children in the natural family groups who had leprosy. The leprosy prevalence rate varied around an average of 2.6%, almost three times that among the general population nine years ago, and nearly six times that of the active cases found four years ago. There were also almost as many children whom we labelled as 'doubtful', this word being applied where the lesions were very small or disfigured by caustics. It is possible that some of them may be self-healing. Nevertheless our method of selection produced a sample of children at much greater risk than the general child population. It is interesting that whereas the general prevalence rate was 2.6%, that among the contacts of lepromatous patients was only 2.2%, but it is a difference that is not significant, and for which there may be a number of explanations.

Each county has a leprosy assistant in charge of a treatment village, and a health inspector with auxiliary staff. Before we went into an eitela the health staff and chiefs completed a form for each child believed to be related to a patient, the latter being seen by the leprosy assistant to confirm the diagnosis. The leprosy assistant had a list of lepromatous patients in each of his eitelas who had been treated at the Kumi-Ongino leprosarium during the previous ten years, and his own list of patients of all types who had attended at his own treatment village. These lists enabled children to be traced who might otherwise have been missed.

The focus on children 'at risk' was a positive approach which the people understood, and should make the follow-up simpler in future

years. The patient-contact relationship of every child will not be completed until we revisit, although a considerable amount of re-checking has already been effected. Whether ultimately the history of the full sample correlated with the various shades of relationship will produce anything more than evidence of contact it is not possible to conjecture, but the attempts to define the relationships accurately have the advantage that they establish a bond of intimacy with the families concerned. The local concept of relationship is much wider than ours, and is complicated by polygamy and customs such as those whereby a widow becomes the wife or responsibility of her husband's brother; all the wives of one man are 'mother' to each of his children, and all a man's brothers are 'father' to every child.

The type of contact was recorded as 'house', 'compound' or 'neighbour'. It is difficult to be more precise than this. The lowest and smallest kinship unit is the family, which occupies a homestead (or compound), and includes the father with his wives, each with a separate hut, and his unmarried and, occasionally, married children, and any dependent relatives. The extended family means 'all those who come from one door', and includes all who spring from a common ancestor three or four generations back. The extended family usually lives in one particular area. Girls remain with their mothers until they are about 10 years old, when they go to live with their mother's mother. Thus all children have been in house contact with their own mother, to a lesser extent with their father, and in 'compound' contact with the other members of the kinship unit, but in many circumstances this may be as intimate as 'house' contact and, if the neighbour is a member of the extended family, the contact with him may be as close as that intended to be denoted by the word 'compound' and sometimes closer.

The routine at each tuberculin testing session was to examine the children in groups of twenty, give them serial numbers, and then photograph each child, if possible with a parent or near relative, with the corresponding serial number in a frame placed conspicuously at the side. Tuberculin testing followed the Heaf method. The tests were read one week later, as near as possible in the order of their serial numbers. Alternative 'negatives' were vaccinated. The alternation was 'as they came'.

In the tuberculosis survey in Uganda by the World Health Organisation (1959) two groups of reactions to the Mantoux test were reported; a group of large sized reactions distributed round a mode of 17 mm. and a group of zero and small sized reactions. The former group was considered to include the reactions of those infected with tubercle, the latter those of the uninfected. A clear separation of the two groups was obscured by a percentage of intermediate sized reactions in the size range 6-12 mm. These inter-

mediate reactions were interprete
antigenically related to the tubercle bacillus but not identical with *M. tuberculosis* of the human or bovine type. This feature is not peculiar to Uganda. In other work we had found that a Grade II Heaf corresponded with a Mantoux test (5 T.U.) of 7 mm. to 14 mm. with a mode of 11 mm. For these reasons we decided to consider all reactions less than Grade III Heaf as tuberculin 'negative'.

Making allowances for patients, doubtful cases, sick children and those who did not attend the BCG session, the following Table analyses 17,412 children according to age:

| *Age* | *Tuberculin Positive* | *Tuberculin Negative Controls* | *Tuberculin Negative Vaccinated* |
|---|---|---|---|
| 0+1 | 10 | 1,367 | 1,307 |
| 2+3 | 62 | 1,593 | 1,525 |
| 4+5 | 144 | 1,634 | 1,664 |
| 6+7 | 188 | 1,282 | 1,285 |
| 8+9 | 159 | 884 | 933 |
| 10+11 | 156 | 570 | 597 |
| 12+13 | 176 | 497 | 485 |
| 14+15 | 110 | 252 | 284 |
| 16+17 | 36 | 70 | 67 |
| 18+ | 55 | 8 | 12 |
| Total | 1,096 | 8,157 | 8,159 |

Children older than age 9 were included because we did not wish to strike a discordant note by sending them away, and because the peak incidence of leprosy occurs after the age of 10. A third group, having sulphones as a prophylactic, was not included as the primary object was to discover whether BCG vaccination had any effect. It is the intention to make return visits to every eitela periodically to examine those already in the trial and to vaccinate every alternate child born into the various families since the previous visit. The table above does not show any more than the numbers who were tuberculin positive or negative, but the actual Heaf response is known for every child. As this is a preliminary Report we have tried to keep the Table as simple as possible.

There were differences in the percentages of non-reactors among the patients and the normal children. In the 2-3 age group there were 28% less non-reactors among the patients (number of patients 6, Standard Error $\pm 14$). There were 12% less in the 4-5 group (number of patients 34, Standard Error $\pm 7$). In the 8-9 group there were 4.5% less non-reactors among the patients (number of patients 72, Standard Error + or —3.8). The patients in each age group

were too few to allow any conclusion, but if larger numbers confirmed the comparison it would suggest that *M. leprae* could stimulate a weak response to tuberculin.

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# EXPERIENCES WITH RECONSTRUCTIVE SURGERY AS A JOINT VENTURE BETWEEN A GENERAL HOSPITAL AND A LEPROSARIUM

by JOHS. G. ANDERSEN, CAND. MED. ET CHIR. (HAFN.)

*from Sevapur Hospital and Santipara Leprosy Colony (Assam)*

Although the technique of this speciality has been fairly well established, its placing is still under discussion. Of course one should realise that the loose term 'reconstructive surgery' is a composite work of physiotherapy, occupational therapy, crafts training, and social rehabilitation. The medical and public health aspects also come into the picture. In fact they are the very foundation on which we work.

It has been argued with considerable strength that as a surgical speciality reconstructive surgery in leprosy belongs in a general hospital, or—when available—in the orthopaedic or plastic surgical departments of a bigger hospital. On my return from Vellore in 1961 circumstances over which I had no control placed me in a situation where I have been able to gather some experiences with this approach. This paper is an attempt at evaluating these experiences.

For almost two years reconstructive surgery has now been undertaken as a joint venture between a leprosarium and a general hospital, where my permanent residence is. In order to understand the picture a brief description of the two institutions will be given.

The leprosarium, Santipara Leprosarium, is comparatively new and is at present able to accommodate about 250 patients, most of whom come from local communities. The leprosarium was originally of the 'home type', intended to be a home for the homeless and cast out. Even though a certain emphasis is now placed on the 'hospital idea' with short term admissions and continued treatment at the patients' own homes, a significant number of the patients are still of the permanent category. This means a large proportion of highly infectious lepromatous cases and a large proportion of cases with long-standing extremely difficult deformities. The medical staff consists of one medical officer, one lady physiotherapist, one senior nurse, some locally trained 'compounders', and otherwise patient staff. A physiotherapy room and a small, but adequate theatre has been provided. The leprosarium has a hospital side with 30 beds, mostly occupied by reaction cases, severely ill patients, and ulcer cases. The inmates are housed in cottages with fairly long distances to the central facilities. The climate is hot and wet, sometimes cold and dusty.

The hospital, Sevapur Hospital, is a 50 bed rural hospital. Two medical officers, one senior midwife-cum-nurse, one senior nurse, and a number of 'compounders' and 'nurses' of varying professional

standing are employed. This hospital runs an extensive surgical service and has a fairly good equipment.

The general plan of the joint venture is: The patients are admitted to the leprosarium or selected from the inmates. Preoperative physiotherapy is conducted there by the well qualified physiotherapist. When possible the surgeon will visit the leprosarium at monthly intervals, when he will join in preoperative assessments and selections, postoperative assessments, and if convenient will perform a few operations assisted by the resident medical officer. The main bulk of the surgery is undertaken at the general hospital, the patients being transported to and from the hospital by car or by public transport. Postoperative physiotherapy is conducted at the leprosarium. Lack of personnel and funds have so far prevented the establishment of a real craft training programme. The majority of the inmates are expected to partake in the agricultural programme of the leprosarium. No organized attempts at helping the discharged patients to a social rehabilitation are being made.

From April 1961 to December 1962, 90 surgical procedures were performed, of these 10 were done at the leprosarium. This is not the place for a full assessment of the results. However, the overall picture is of considerable interest. Most of the results have been satisfactory and only few have failed completely. But compared with the results that can be seen at training centres these results are not up to standard.

There are certain advantages with this programme: The surgeon maintains a close contact with general surgery, and he may be able to utilise his specialised knowledge to help other patients. I fully admit these advantages, but I think they are over-valued, particularly the last one. The important reason is that in order to let sufferers from other paralysing diseases benefit from his work, the surgeon must perforce have a fully qualified physiotherapist at his disposal.

The disadvantages are many:

The problem of surgically correctible and preventible disabilities in leprosy is immense. *A rough estimate shows that at this moment not less than* 2 *million operations are waiting to be done on leprosy patients in India alone.* If we are to have any impact on this problem, the amount of work a general or orthopaedic or plastic surgeon can interpose between his many other patients is far too little.

*Reconstructive surgery alone, with no real attempt at social and economic rehabilitation, is hardly worth the trouble.* A surprising number of people are able to work with a claw hand or a drop foot. The important emphasis is not so much on the technical reconstruction of a close to normal function as on the teaching of how to use this BETTER hand and BETTER foot to give BETTER service.

*The daily presence and active interest of the surgeon in the physiotherapy programme is extremely important.* One reason is the

help and advice he may be able to give. More important still is the fact that this is where he learns from his mistakes. Nothing keeps a surgeon on his toes as the critical co-operation of a competent physiotherapist.

Difficult travel conditions and the rarity of the surgeon's visits to the leprosarium tend to exclude a large number of cases from the benefits of surgery. These are mostly the tricky cases where the surgeon is unable to follow standard techniques, and where his personal presence is extremely important to the physiotherapy programme. It has been argued that a strict selection should be undertaken to exclude these cases. The reason is that in this way you will gain the confidence of the patients, who for a long time only see comparatively good results. In actual fact no such selection is possible. If you exclude the difficult cases from your list, the patients will loose faith and interest. And after all, one of the most important impacts of surgery on the leprosy patients is the amount of intense personal interest that is being taken in them.

The surgeon should participate in the work as a whole. The majority of the sufferers from leprosy are not found in the institutions. The physiotherapist-surgeon team must at least to some extent participate in case finding and education.

In this particular programme, the distance between leprosarium and hospital, 100 miles, is prohibitive. But even much shorter distances will hamper this work so much that it cannot be done as it should and can be done. The decisive factor is the full time occupation and constant presence, which alone will secure the best utilisation of the available personnel.

*An important part of the work should be training, both of the resident staff and of trainees, be they surgeons or paramedical workers.* When the work is split between two centres with a strictly limited programme, no training is possible. There will be probably a fairly competent theatre staff at the general hospital, but unless a steady amount of surgery is done at the leprosarium, the quality of assistance obtainable there will never reach a high standard. At the general hospital the staff will only see certain phases of the work and will have no chances of training. Under this set up the surgeon has no chances of sharing in the extremely important training of paramedical workers.

Although the demands for equipment are relatively modest, it is a moot question if we can afford to maintain it under conditions where it is not put to its full use. Transport of equipment between hospital and leprosarium is impractical.

Very few hospitals in this country are so well staffed, that they can afford to let a senior surgeon leave the hospital regularly. It is not so much the economic loss for the hospital. It is the more important question of a number of patients who have to be turned

away or asked to wait for the return of the surgeon. The comparatively large amount of time that has to be spent in the general hospital also tends to take away the surgeon from other patients.

Any medical man will be keenly aware of the need for maintaining and developing his skill and knowledge. This requires both a reasonable number of patients for him to work with, but it also requires conditions under which he can evaluate his own work in the light of other peoples' experiences. In a busy general hospital the demands on the surgeon will be so great and varied that this becomes very difficult, if not impossible.

Some of the less satisfactory results can undoubtedly be attributed to the travel up and down before and after surgery. The dust and dirt of the bumpy Indian road is not exactly the best treatment of a newly operated patient. So far we have had no real difficulty with public transport. But it is well known that people with recognized stigmata of leprosy are often not accepted on public transports. If this had been a simple problem of protecting the travelling public against infection it could have been tackled in a rational way. But it is rather a social ostracism that is very difficult to handle.

The conclusions are very straightforward:

*As far as possible every sufferer from preventible and correctible disabilities due to leprosy has a right to the benefit of this service. The best way of obtaining this goal is by placing the whole team, comprising physiotherapist, occupational worker, craft trainer, social worker, and surgeon in the leprosy hospital.* This will maintain the important connection with leprosy work in general and will give ample opportunities for teaching and learning. The field is in itself so large that there is very little danger of the surgeon losing contact with sister disciplines in surgery. It is far more dangerous if he loses his skill in this particular field.

Scarcity of workers and lack of funds make it impossible to open this service in all leprosaria. A better plan is to open centres on a regional basis and extend assistance to outlying leprosaria. How this should be done is outside the scope of this paper.

# INDICATIONS AND CONTRA-INDICATIONS IN RECONSTRUCTIVE SURGERY IN LEPROSY

by JOHS. G. ANDERSEN, CAND. MED. ET CHIR. (HAFN.)

(*Read at the Regional conference, Mission to Lepers, Purulia, January*, 1963)

Reconstructive surgery has been with us for several years. It has passed the initial, experimental stage, and has arrived at a reasonably definite pattern that enables us to undertake a standard teaching and application of recognized patterns. It is—or should be—a normal part of the service we offer to the sufferers from leprosy.

Scarcity of workers and lack of funds impose certain restrictions on the ideal conditions under which we would like to work.

What I have to say here, applies to a routine set up with competent workers that are not specifically engaged in teaching or research, that both have certain specific conditions outside the normal routine pattern of work.

The goal we should hold up for us is that every sufferer from leprosy with disabilities, amenable to surgery, should have the benefit of this work. This will not be possible for many years to come, maybe never. However, do not let us forget it.

There are certain general restrictions on the application of surgery that should be borne in mind. This will be particularly important where the selection of cases for surgery is not, or only partly, in the hands of a competent surgeon. The medical leprologist and the physiotherapist who may have to do the selection should keep these points in mind.

(1) *Surgical treatment is only part of the general treatment of the patients.* It must always be subordinate to the more important medical treatment, the aim of which is to enable the patient to return to society with an arrested or cured disease, offering no danger to his surroundings.

The general conditions are that the patient, chosen for surgery, should have been under regular, antileprosy treatment for not less than three months, and that he should not have presented any 'reaction' or signs of 'progressive disease' during that period, and that his therapy must be well stabilised before surgery.

(2) *Grossly infected patients with a high bacillary index are unfit for surgery.* The reason is the liability to reactions in these patients. I prefer to wait for the bacillary index to get below 1.0 before surgery. This does not mean that physiotherapy should be withheld from these patients. On the contrary, particularly in cases with violent reactions will certain types of preventive physiotherapy be of immense importance.

(3) *The pattern of paralysis should be stable.* The majority of cases of paralysis in leprosy tend to develop toward and remain at certain, well recognized patterns of paralysis. Certain muscles are paralysed, and they are then completely paralysed. No other muscles are affected. That recovery of damaged or lost nerve function can take place, spontaneously or consequent to therapy is a known fact. It is too early to pass any opinion on the effect of the various possible means of therapy. It does seem to be a fact that in case a paralysis has remained complete and stable for 8 weeks no possibility of recovery can be expected. No attempt at reconstructive surgery is indicated in this interval.

The surgeon or physiotherapist, trained in reconstructive surgery in leprosy is trained to detect and evaluate these patterns. It is necessary for the leprologist with no such training to consult either a physiotherapist or a surgeon in this matter. Disregard of this problem can be quite disastrous, since the results of surgery tend to become less impressive the more frequently operations are undertaken, and also because the technique may be quite different in a case with extensive paralysis from a case with limited paralysis. The less extensive surgery may make the more extensive surgery very difficult, certainly less satisfactory.

(4) *No patient in poor general health is a good surgical risk.* Proper care should be taken in this respect, so that we may offer the patient the best chances of a good result.

(5) *Since reconstructive surgery almost exclusively deals with tendons, bones, joints and valuable skin, postoperative infections have a most distressing result.* More than in any other branch of surgery we work under the maxim of 'once done, never redone'. The surgeon himself must be on his guard. He will naturally be mostly concerned with the influence of his technique on the risk of infection. But the condition of the skin in the involved area and generally should be of prime importance, also to the selecting medical officer. Skin rashes and particularly scabies can have horrible effects and are easily overlooked.

In the same category fall allergic conditions of the skin.

(6) *Concomitant diseases*, bowel diseases, upper respiratory infections, etc., are always troublesome and can be damaging to the final result.

(7) *A word about antibiotics.* Enough care cannot be executed in the use of these extremely valuable drugs. Some of us will recall the hopeful optimism about surgery under an 'antibiotic umbrella'. We know better now. Actually an antibiotic umbrella rather promotes infection with resistant and more dangerous strains. The highly unpleasant, not infrequently life-threatening side effects should make us extremely wary. Particularly in the treatment of plantar ulcers are many likely to shorten the period of treatment and

give 'just a few shots of penicillin' or whichever drug holds our fancy at present. It may conceivably have a good effect, occasionally, but it is a dangerous attitude. Good clean surgical procedures, as they have been laid down again and again over centuries are far better. And they are cheaper. Nobody has described or are likely to detect resistance to soap bath or mercurochrome. Nor can any antibiotic replace the physiological effect of immobilisation in a plaster of Paris cast or a Karigiri boot, properly applied.

We are, however, not only concerned with a medical aspect of our patients. Of equal importance is the fact that they should return to as closely as possible a normal life in a normal society—and as quickly as possible. It is an unpleasant, but unavoidable fact that certain persons are more likely to return to a normal society than others. We have a responsibility toward the individual man. But we also have a responsibility towards the society in which we live. That indicates certain preferences for our work.

*Under otherwise equal conditions I would suggest that we give preference to young people, to people who actually hold a job, and to people with a responsible attitude to life.*

Without going into details I would like to point out a few important considerations, relative to the selection of cases for particular kinds of reconstructive surgery.

(1) Intra-ocular surgery in leprosy is a most difficult and tricky discipline. I would strongly advise anybody who does not have considerable experience in opthalmology and leprosy not to undertake it. Precautions against reactions apply here with manifold force. A firmly negative bacillary index and a perfectly stationary morbid condition are obligatory.

(2) Temporalis transfer a.m. Gillies, the accepted method for correction of paralytic lagohthaloms, is an excellent prevention of the dreaded blindness. In experienced hands satisfactory results can be expected in close to 100% of the cases. Prevention of blindness is so urgent that nobody should be excluded, not even the confirmed beggar who defies all attempts at rehabilitation. The rules governing bacillary index may be slackened considerably. The only really valid contraindications are frank reaction and serious infection of the face. This is probably the only condition where it can be advisable to operate under the dangerous 'corticosteroid umbrella'.

(3) Surgery on bone in leprosy is concerned both with the effect of anaesthesia/infection and with direct leproma infiltration into bone. Together with surgery of the nerve this is the least explored and understood part of the discipline. The conditions relating to the morbid condition and to possibilities of secondary infection should be strictly observed.

(4) Ulcer surgery often deals with bone surgery, but is primarily a means to secure safe healing of the weightbearing surfaces. It

requires careful and expert evaluation of tissue, and even in competent hands the results are not very encouraging. The happy chopping away of diseased bone that was, and I believe still is, an important part of the ulcer regime in many places, should be discarded. Ulcer surgery is essentially a losing battle, where every millimetre of bone counts. Factors specific to leprosy make it extremely difficult, even for experienced radiologists and orthopaedic surgeons, to judge the viability of involved bone. So be careful and play it safe. Before actual surgery is resorted to the good old conservative methods of immobilization and drainage of frank infections should be given a very generous trial.

(5) The conditions grouped round the paralytic drop foot are probably the most rewarding for the surgeon. Given good skin conditions and a reasonably clear field as far as leprosy is concerned the only worry is really the presence of frank or obscured ulcers with deep seated smouldering infection of the foot. The freely mobile, but stable foot with no angular deviations or posterior contractures is naturally the choice for a perfect result, but even much worse feet can yield quite satisfactory results.

(6) In surgery of the hand conditions that are likely to yield poor results should be recognized. Extensive paralysis, particularly involving the radial nerve, always gives a comparatively poor result. The same is true of the long standing paralysis with stiff joints that do not respond to physiotherapy. The effects of anaesthesia/infection, particularly on the joints also tend to give less satisfactory results.

The problems concerned with the selection of cases for hand surgery throw light over a very important consideration. It may be possible to obtain a better result if you subject the patient to prolonged periods of physiotherapy. Are we justified in aiming at a near perfect result if this means so long absence of the patient from his normal surroundings that he comes home a social wreck with a near perfect surgical result? After all the social rehabilitation of the patient is the final test of our therapy.

(7) Surgery of the face, notably the nose and the eyebrows, is more than any other branch of the discipline a direct attempt at social rehabilitation. We who are accustomed to being with these deformed patients may not consider madarosis of the eyebrows or a collapsed nose a serious disability compared with a claw hand or a drop foot. To the person looking for a job in a normal society it may quite easily be the cornerstone of his surgical reconstruction. After all, what is the good of being able to do a job, if nobody wants to employ you?

The structures we deal with render a strict observation of the rules governing the morbid conditions extremely important.

I would like to add a few suggestions for the planning of this service. We should recognize that it calls for highly trained, dedicated

people. I do not want to be unduly pessimistic, but we are not likely to be flooded with trained physiotherapists or surgeons. And the job certainly is overwhelmingly big. This should compel us to think in rational lines about the way in which we can utilise available personnel and funds. I should imagine that the logical way would be to build up good centres at suitable places and then extend a real co-operation with outlying colonies and hospitals.

# TREATMENT IN LEPROSY WITH ETISUL PRELIMINARY INFORMATION

by Doctors V. K. LOGINOV, N. G. VANTANOVA and V. S. BRAGINA

(Reprinted from Ucheniye Zapiski No. 3/8, Astrakhan 1962, pp. 9-14, in English translation from the original Russian by the kindness of Dr. J. I. Mirilow of Medical Department, Imperial Chemical Industries Ltd., Macclesfield, Cheshire, England).

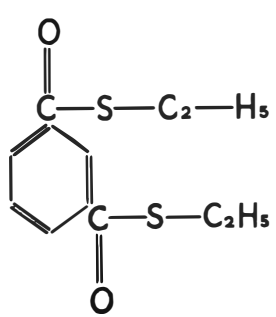
DEL PIANTO has established (1950) that a mixture of different thiols contains material capable of preventing development in experimental tuberculosis in guinea pigs. That information has attracted the attention of research workers towards a combination of thiols and towards the possibility of obtaining a remedy against tuberculosis. DAVIES *et al.* (1956) discovered that anti-tubercular action was inherent only in the ethyl homologous substances containing a mercaptan combination. Further research carried out by DAVIES and DRIVER (1958) has proved that Etisul has that anti-tubercular action which was comparable with the actions of isoniazide and streptomycin.

Mercaptan is a colourless, volatile liquid with an unpleasant odour. *Chemically it is very similar to alcohol, differing from them in their sensitivity to oxidate.* Etisul is an ester of isophthalic acid and ethyl mercaptan. This pale coloured oily liquid has an odour reminiscent of garlic and of decaying fruit.

The first thiol substance (sodium ethyl thiosulphate) for the medical treatment of leprosy patients was investigated by BERTACCINI in 1957. These observations were carried out on 31 patients with symptoms of leprosy (26 men patients with lesions were treated with sulpha drugs). Only 14 of these patients had active manifestations of the disease for the following 9 months. The authors found that the drug had a definite action in the treatment of leprosy, no less than certain other remedies.

DAVEY (1958) has observed that an application of Etisul on the skin by inunction (rubbing) brought about a quick and significant reduction of bacterioscopic index. Degenerative signs of *Mycobacterium leprae* have been noticed after 3 weeks of its application. DEL PIANTO himself came to the same conclusions in 1958.

Etisul:



DAVEY and HOGERZEIL in 1959 published their results after 19 months of clinical trials on 65 patients who had active manifestations of leprosy and were treated with Etisul. They came to the conclusion that Etisul displayed a visible chemotherapeutic action in the first two to three months of treatment. So the treatment continued. But on exceeding four months of treatment there were signs of *Mycobacterium leprae* resistance to the treatment observed in these patients. The authors noticed that if, after 8–12 weeks of treatment, they added to the Etisul DDS (Ciba 1906) or DDSO, the effect of treatment would be more noticeable. DAVEY and HOGERZEIL wrote that after one year of such treatment there were regressive changes for at least six months, surpassing such cases where only the treatment with the conventional preparations was administered internally They personally recommended the application of Etisul in combination with DDS.

Six months after publication of his first results DAVEY (1959) published his further observations and came to the conclusion that the best effects had been observed when Etisul was given in conjunction with DDS and DPT (Ciba 1906).

During the past two years a number of publications have appeared, the authors confirming the positive influence of Etisul on the course of a leprosy process. (LECHAT, 1959; ROSS, TELFER and HILTON 1960; ROSS INNES, 1960; BROWNE, 1960; MUKERJEE and GHOSAL, 1960; MOLESWORTH, 1961; JAMISON, 1961; DHARMENDRA and NORDEEN, 1961).

At that time (1961) DAVISON had applied Etisul in conjunction with DPT and DDS in 33 cases of leprosy during a period of 12 months and the results were identical with the results obtained in 33 patients treated only with DPT and DDS. He did not notice any real difference in therapeutic effect.

We had under our care 10 patients. They were suffering from the lepromatous type of leprosy and they were all treated at the Institute for the Study of Leprosy in 1961 (Dr. Subin's Institute at Astrakhan, U.S.S.R.) and until that time none of them had any treatment for the above mentioned complaint. In the age group between 17 to 20 years there were 3 patients, in the age group 21 to 30 years there were 4 patients, in the age group 41 to 50 years, 2 patients but in the age group over 50 there was only one patient. There were 4 male and 6 female patients. In all patients the leprosy process developed in an active form and was in a rather advanced stage. The manifestations of the skin were focal infiltrations, deep and diffused infiltrations and nodules. In four of those patients, because of the infiltrations which affected the mucosa of the upper respiratory tract and the muco-membranes of the nose, the respiration was impaired. One patient suffered from aphonia. Six patients were treated and cured where the process was affecting the peripheral nervous trunk.

They had a severe pain on palpation and a local temperature of the extremities. Six patients were treated simultaneously, the others according to the order of their admission to the Institute. Portions of skin were taken from the affected parts of the body for the purpose of histological examination. The lepromatous structure of the infiltrations was confirmed and contained a large number of *M. leprae* which were mainly homogeneous.

We applied the following method of treatment. Etisul was obtained in the form of a cream from I.C.I. Limited, at 5 g. and it was given to the patients twice a week by inuncting. The inunction was made both to the apparently unaffected parts of the body as well as those parts of the body which had nodules, but excluding the head, neck and hairy parts. At first the treatment of inunction was done by the nursing Sister, but as time went on the procedure was carried out by the patients themselves under Sister's supervision. The procedure of inunction lasted about 20 minutes. After that followed an hour's rest; at the time of rest the parts of affected and inuncted skin were left uncovered. Some time after the patients had a shower. The cream was rubbed into the skin, alternately the shoulders, chest, abdomen, along the spine, buttocks and hips. The disposition of the diseased lesions was not taken into account at this stage. Each of these patients received 'Avlosulfon' (DDS) by mouth; 100 gm. daily for the duration of 4 weeks. At the beginning of the fifth week the dose of 'Avlosulfon' was increased to 200 gm. daily, 100 g. morning and 100 g. evening. All these patients treated with Etisul were housed in a separate building. The unpleasant garlic odour due to Etisul did not worry the patients although its smell lingered persistently.

The course of treatment lasted six months. During that time the patients received 22 inunctions of Etisul and 28.2 g. of 'Avlosulfon' per month. On completion of the first course of treatment with Etisul and 'Avlosulfon' the six remaining patients received from 23 to 40 inunctions of Etisul and an adequate quantity of 'Avlosulfon'. As a result of treatment there was constant regression of the disease. It was noticed in all patients that there was a disappearance of infiltrations and nodules and reduction and complete disappearance of facial swellings and puffiness. Breathing through the nose became easier and freer and recovery of the voice set in. Worsening of the affected peripheral nervous system was not noticed in any patient.

Histological examination of the affected portions of the skin has been followed in six cases. In all these patients we were in a position to establish changes such as the appearance of regression in specific symptoms, infiltrations of the skin becoming much more limited, fibrous changes occurring and also a reduction in the number of *M. leprae* which became predominantly granular. In one case the infiltration of lepromatous structures was replaced by an infiltration

of the type of a simple inflammation with isolated granular *M. leprae.*

Marked improvement in general state of health was noticed, for the patients gained approximately 2 to 3 kg. in weight.

Symptoms of toxic dermatitis appeared in two cases in the course of treatment. Thus we had to stop the treatment temporarily, but after the symptoms of toxic dermatitis disappeared the treatment was resumed. In these two cases the dosage was reduced. One of these patients abandoned the double dose cycle. In two cases albumin was detected (0.099 mgm. per cent. and 0.165 mgm. per cent). The albumin disappeared during the course of treatment. In three cases sedimentation was slowed down. In three other cases on examination the bacterioscopic index was reduced to 0. At the same time, in five patients despite the dosage with vitamin B12, we noticed a depressing influence on the blood state. They had reduced haemoglobin by 1.4–1.7 g. per cent. and erythrocytes by 1–1.2 million. For illustration we shall give you short notes about the history of the disease on all those patients who are still under observation.

**Case 1**

**Patient Z**

(Female), 26 years old. Entered the Institute for the Study of Leprosy on 20th April 1961 with lepromatous type of leprosy showing an erythematous infiltration on her face, neck and upper and lower extremities. These infiltrations were diffused on both buttocks and rather superficial. In the region of the hips the infiltration was much more marked. At the elbow the cubital and ulnar nerves were moderately thickened on palpation. The lepromin test was negative. On histological examination a portion of the diseased skin showed an infiltration of lepromatous type which was observed together with a quantity of homogeneous leprosy bacilli. On the 8th May 1961 treatment started with 'Etisul' by inunction and 'Avlosulfon'. Regressive changes were observed after 5 inunctions with Etisul; loss of brightness in colour of the infiltrations, both on the patients face and on the extremities was noted. At the same time the patient had an abortion performed by a doctor which terminated her six weeks' pregnancy. As the treatment continued the regression of this patient's infiltrations progressed favourably. After 10–12 inunctions with Etisul there was a definite improvement for the infiltrations of the face became paler and on the extremities the infiltrations acquired rather a yellowish brownish colour. The infiltrations in other parts of the body began to decrease and gradually the facial infiltrations almost disappeared towards the end of the treatment. The infiltrations of the extremities disappeared as well; but on the skin around the hips pronounced infiltrations were noted at the beginning of treatment and patches of hyperchromia appeared. On repeating the histological examination

of the diseased skin (after the completion of treatment), regressive changes had taken place. There was a sort of replacement of infiltrations of the lepromatous type with homogeneous *M. leprae* by insignificant infiltrations with simple inflamed structure and an isolated granular mycobacterium. At the same time there was noticed a development of fibrous changes.

At the end of treatment the bacterioscopic index became equal to 0 (42.5% before the beginning of treatment). It was also noticed that previous to the course of treatment with Etisul and Avlosulfon albumin was present in approximately 0.165% but it disappeared at the end of treatment.

Erythrocytes which were at the beginning of treatment approximately 4,210,000 went down to 2,650,000 after the treatment was completed.

**Case 2**

**Patient G**

(Male), 20 years of age. Admitted to the Institute for the Study of Leprosy on 20th April 1961 with lepromatous type of leprosy. There were deep infiltrations present on his face, uneven infiltrations on the hands, and in places confluent lesions erythematous in colour and single nodules. On the skin of the chest, abdomen and along the spine marked infiltrations were present of a rosy red colour. The infiltrations were also present in the patient's lumbar region and they were slightly swollen. On palpation it was found that the elbow nerves were moderately thickened and diseased. The lepromin reaction was negative. On histological examination a portion of the skin was found to possess signs of lepromatous infiltration, together with a large quantity of homogeneous and granular bacilli. The treatment with Etisul and Avlosulfon began on 8th May 1961. After five inunctions with Etisul it was noticed that swollen infiltrations in the lumbar region became somewhat paler and less swollen. As the treatment went on it was observed that the infiltrations became gradually paler and resorption of the infiltrations took place on the face, lumbar region and extremities.

After 40 inunctions with Etisul it was observed that the fluid exudate regressed. There were noticeable reductions in infiltrations of the face and extremities. As far as the lumbar region is concerned, the infiltrations have almost disappeared. Once the course of treatment was completed there were only residual manifestations in the facial infiltrations. The original infiltrations which appeared in the lumbar region began to look macular. On histological examination which was repeated on a number of occasions it was found that changes had taken place in decreasing the infiltrations and there was an increase in granular forms of mycobacteria.

**Case 3**
**Patient D**

(Male), 17 years of age. Admitted to the Institute for the Study of Leprosy on 14th March 1961, with a rather large part of his body affected by the lepromatous type of leprosy. There were diffused infiltrations on the face, especially of external audiotory meatus and the ear lobe. Breathing through the nose was rather difficult and there was aphonia. Vast and deep infiltrations were situated on the chest and the abdomen. There were diffused infiltrations on the extremities. On both elbows the nerves were swollen. There was also disturbing pain of the polyneuritic type around the elbow and the knee joint.

The lepromin test was negative. On histological examination of the diseased portions of skin, structures of the lepromatous type were observed and also a large quantity of homogeneous and granular leprosy bacilli were seen. Thus the treatment began on the 8th May 1961 with inunction of Etisul, and Avlosulfon by mouth. After 5 inunctions of Etisul the patient's voice became clearer, more sonorous. Later the colour of the patient's face became paler, the infiltration regressed. Breathing through the nose became free. After 35 treatments with Etisul and 105 treatments with Avlosulfon the patient's voice became normal, the infiltrations on the face decreased, while the infiltrations on the back disappeared. At the end of treatment there was a noticeable decrease in the infiltrating process. The general condition of the patient as far as health goes during the treatment was good. His weight went up by 11 kg.

Aggravation in the process of the disease was not observed. By repeating histological examination regressive changes were noted which were expressed in reduction of infiltrations in the area and degeneration in the mycobacteria. Before treatment 0.099 mgm. per cent of albumin was found in the patient's urine and it disappeared altogether after 22 inunctions with Etisul.

We have carried out a comparative appraisal of the results of treatment by Etisul in combination with Avlosulfon (DDS) compared with the results obtained in treatment of the patients with DDS alone. Our preliminary observations allowed us to suppose that by application of Etisul in combination with Avlosulfon regressive changes in the cutaneous symptoms became more evident, and much earlier evident. So towards the end of the course of treatment the results were more permanent than in the patients where the treatment was carried out by Avlosulfon only.

In the groups of patients treated with Etisul and Avlosulfon there was evidence that one patient's treatment was aggravated by the combination of Etisul and Avlosulfon. In no case did we notice any reaction on the skin. In the patients who were treated with Avlosulfon only some reactions of nodular erythema were seen.

**Summary**

(*a*) Combined therapy of Etisul and Avlosulfon on patients with lepromatous type of leprosy who were not previously treated showed a rapid effect from the clinical point of view which was confirmed by histological examination.

(*b*) In some patients, in the process of treatment with Etisul and Avlosulfon it was possible to observe a depression in the function of the haempoietic system which is connected to some extent with the action of Avlosulfon.

(*c*) The foregoing observations on the action of Etisul and Avlosulfon on all types of leprosy ought to be continued and similarly the use of Etisul in combination with DPT should be tested.

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# THE USE OF TRIAMCINOLONE* IN THE TREATMENT OF SEVERE *LEPRA REACTIONS*

by DR. K. F. SCHALLER,

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## Introduction

The large variety of drugs and the great number used in the treatment of lepra reactions indicate that there does not exist a drug of choice for the treatment of a condition which has gained increased importance in leprosy since the introduction of efficacious chemical therapeutics.

Drugs which show anti-inflammatory and anti-allergic properties are usually tried out in lepra reactions. Optimistic reports are often published on drugs which later prove to be without value because of the fact that patients were not well selected and reactions were treated which would have disappeared in a short time by themselves.

The majority of leprologists nowadays agree with COCHRANE that cortisone is considered to be the drug of choice in the treatment of lepra reactions but there are also other opinions of authorities who find the use of cortisone in lepra reactions contra-indicated.

At the Princess Zenebework Memorial Hospital corticosteroids and the anterocorticotrophic hormones were used in complicated lepra reactions for more than 5 years with satisfactory results, but it must be admitted that the success depends on the right dosage which varies from individual to individual. In what follows, the results of the trials made with one of the recent corticosteroids, 'Triamcinolone' will be reported. A preliminary study was made on 12 cases with encouraging results and then used on 30 patients suffering from erythema nodosum leprosum.

## Chemistry

Triamcinolone is a new corticosteroid synthesised by BERNSTEIN which has an anti-allergic and anti-rheumatic activity. This compound is said to have considerably less sodium-retaining properties than earlier agents and at the same time is also said to possess good gluco-corticoid activity. Studies in human beings demonstrated a potency of 4 mg. of Triamcinolone as being equivalent to 5 mg. of Prednisolone.

Triamcinolone diacetate has the generic formula 9 alpha-fluoro, 16 alpha-hydroxy, $d^1$ -hydrocortisone or 9 alpha-fluoro, 16 alpha-hydroxy prednisolone.

*LEDERCORT—American Cyanamid Company.

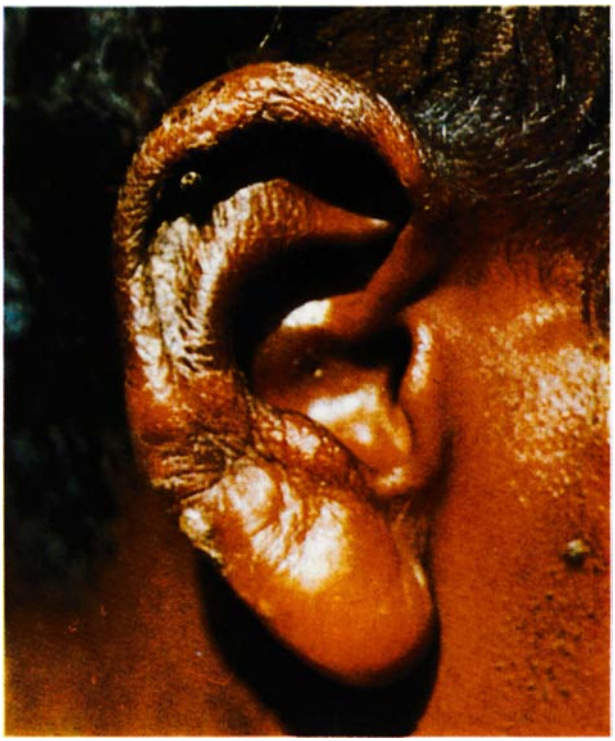


*Fig. I*

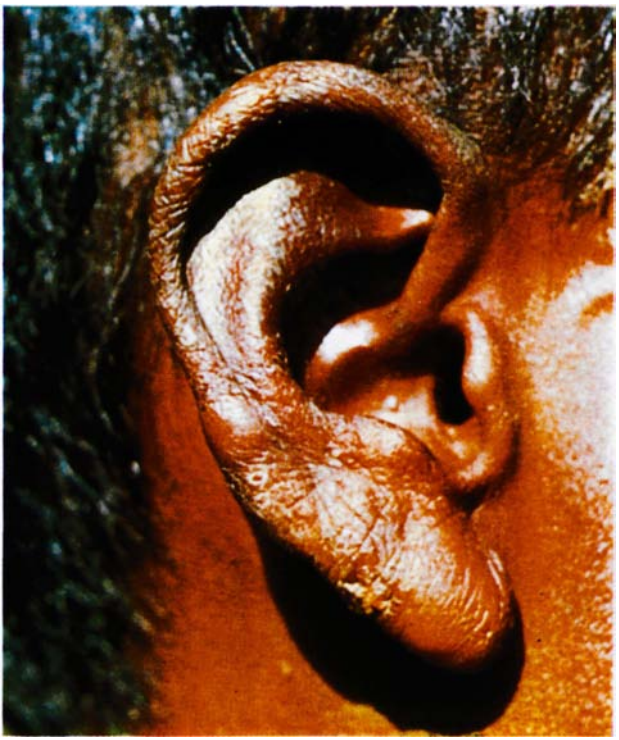


*Fig. II*

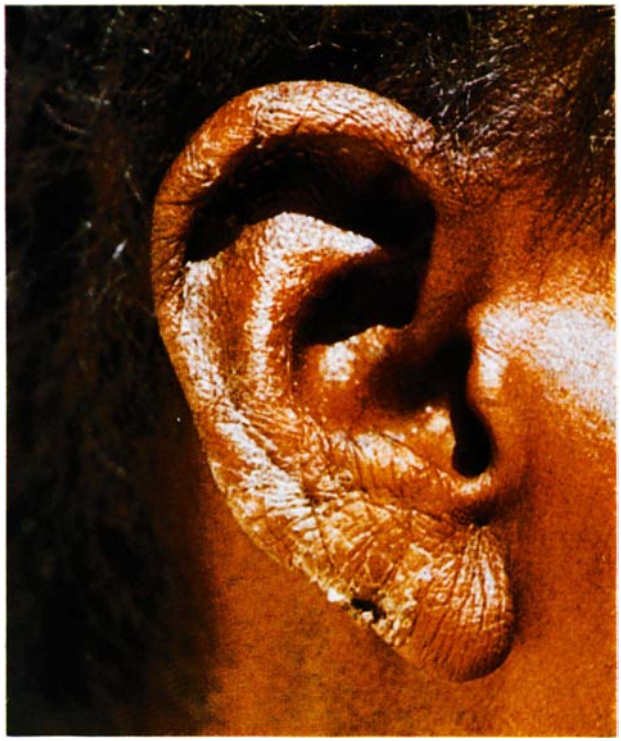
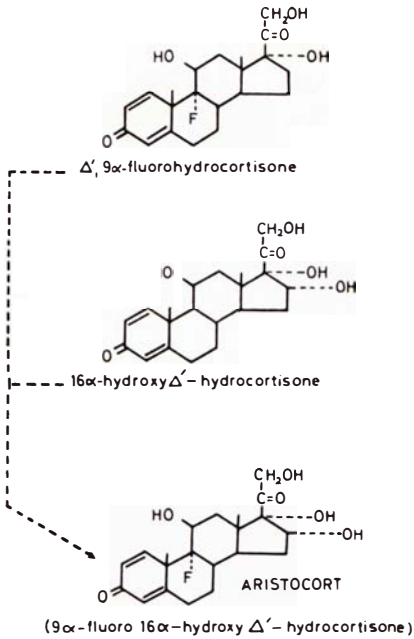


*Fig. III*

*I. Before treatmemt with Triamcinolone.*

*II. 24 hours after the inception of treatment.*

*III. 48 hours after the inception of treatment.*




**Choice of Patients**

Only patients suffering from recurrent and longstanding erythema nodosum leprosum were taken for this trial. Nearly all the patients showed severe impairment of their health and all of them had had previous treatment with DDS (diamino diphenylsulfone) ranging from six months to five years. Eighteen patients were males, between 18 and 45 years of age and with a leprosy history of one to eight years. The female patients ranged in age between 24 and 42 years, had been ill from two to nine years and had been under treatment for periods ranging from eight months to four years. The course of the reactions in all selected cases lasted longer than 15 days. This was easily demonstrated by stopping the drug, such a procedure being almost immediately followed by recurrence of the temperature, pains and other signs characteristic of continuing activity.

**Dosage**

Triamcinolone was used in tablets of 4 and 2 mg. starting with daily doses of 24 up to 32 mg., being given 4 hourly or in 3 divided doses. The reduction of the dose then was made by 6 or 4 mg. daily until the maintenance dose was reached. This could be easily assessed by observing the conditions of the patients carefully. In most of the cases (18), the maintenance dose was 4 mg., being reached in 6 to 7 days. In 4 cases 8 mg. was necessary for keeping suppressed the signs of reaction. Six cases required only 2 mg. daily

as a maintenance dose. In 3 cases the results were uncertain and higher doses had to be given for longer periods. The treatment on an average lasted for 12 days with a total dose of 92 up to 140 mg. of Triamcinolone. The 3 cases which had to be treated for 15 up to 22 weeks were not included in the statistics.

**Clinical Results**

Out of the 30 patients only 3 did not show marked improvement, which was usually observed within 12 to 24 hours after the treatment started. Often the response was dramatic; the patients were relieved from their pains; the temperature dropped to normal or below and part of the lesions disappeared within 12 hours. The earlobes which were oedematous and glossy appeared soft and wrinkled after one day.

Figure II shows the ears of a patient taken 24 hours and Fig. III 48 hours after the inception of the treatment.

Within 3 to 6 days in most instances, the erythema nodosum lesions became flat and appeared less indurated accompanied by an improvement of the patient's general health. The 3 patients who required prolonged treatment did not react favourably and exacerbations occurred during the long course of their condition. Also clinically no improvement was observed but the patients complained less of pains when Triamcinolone was given. The red blood sedimentation rate remained high and the temperature could not be influenced by the doses of Triamcinolone given to them. In the other cases, as mentioned before, the temperature dropped within a few hours and remained normal whilst taking the drug. The blood sedimentation rate decreased with the general improvement.

**Side Effects**

The patients under treatment up to 24 days did not show any significant side effects. One of the 3 patients who required longer treatment showed Cushingoid changes. In 6 patients the raised temperature suddenly dropped within a few hours to below normal and could not be measured by the thermometers used in the ward. This effect did not give rise for complaints from the patients' side.

**Summary and Conclusion**

Out of 30 patients suffering from severe *erythema nodosum leprosum*, 27 showed marked improvement of their symptoms when treated with Triamcinolone. The starting dose, ranging from 24 to 32 mg. daily, could be quickly reduced to the maintenance dose which varied between 2 and 8 mg. a day. The average length of treatment in 27 severe cases was 12 days by the end of which time the reaction had generally completely subsided.

The administration of Triamcinolone is indicated in severe *lepra reactions*, since it suppresses the constitutional symptoms and complications and makes the patient feel more comfortable.

Further studies employing long-acting corticosteroids, especially those of the repository type, should be of interest. Trials with triamcinolone diacetate, 40 mg. per cc., administered intramuscularly in once-weekly doses are being carried out at present and the results will be reported on in the near future.

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# A, B, O BLOOD GROUPS AND LEPROSY

by John Hsuen, m.b.b.s., Eapen Thomas, m.b.b.s.,
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Of late the role of genetic factors in the development of disease has become a subject of great interest. This study is an attempt to find out whether there is any association between ABO blood groups and the incidence of leprosy.

**Materials and Methods**

(1) *Study Series:* Blood group frequency distribution was determined for a series of 526 leprosy in and outpatients (male and female and all age groups are included) receiving regular treatment at Schieffelin Leprosy Research Sanatorium, Karigiri, South India, during a period of one and a half months (10th July 1962 to 24th August 1962). Almost all the above patients come from nearby villages within a radius of 25 miles from the hospital.

(2) *Control Series:* Blood group frequency distribution was determined for a series of 1,000 first time blood-donors at the blood bank, Christian Medical College Hospital, Vellore, S. India, situated 10 miles away from the Schieffelin Leprosy Research Sanatorium, Karigiri. These thousand donors consisted of two samples of 500. The first 500 was taken during the period 24th November 1959 to 1st June 1960 and the second 19th October 1960 to 30th June 1961 with an interval of about four months between the two samples.

These donors come from the same areas and belong to the same racial group as the leprosy patients and therefore they can be considered as representatives of the general population from which the leprosy patients come. However, it must be mentioned that though the donors composed of both male and female subjects, they are all adults and leprosy has been excluded only by gross examination.

*Method:* Blood was obtained from the leprosy patients by the finger-prick method (and whenever it was not possible that way, blood was drawn from the vein), and grouped within 48 hours by the slide technique. Great care was exercised by the investigators to avoid technical errors in grouping. No effort was spared in repeating the whole procedure when there was any doubt. Similar technique was employed by the blood bank in grouping the donors.

Leprosy was diagnosed and the type classified by experienced leprologists after a thorough physical examination of the patient. Bacterial Index was done on all the cases, and when there was any

doubt the diagnosis was confirmed by histopathology. International classification was followed in classifying the cases under study.

**Results**

Table 1 shows the frequency distribution of different types of leprosy among the 526 patients.

TABLE 1: Frequency distribution of different types of leprosy among the 526 patients:

| *Type of disease* | *No. of cases* |
|---|---|
| Lepromatous | 258 |
| Non-Lepromatous: | 268 |
| (1) Tuberculoid | 130 |
| (2) Borderline | 51 |
| (3) Indeterminate | 85 |
| (4) Neural | 2 |

Table 2 gives the frequency distribution of blood groups among the two series.

TABLE 2: Blood group distribution of 526 leprosy patients and 1,000 first time blood donors.

| *Blood Group* | *Control Series* *No. of cases* | % | *Study Series* *No. of cases* | % |
|---|---|---|---|---|
| A | 214 | (21.4%) | 130 | (24.7%) |
| B | 331 | (33.1%) | 123 | (23.4%) |
| O | 397 | (39.7%) | 257 | (48.9%) |
| AB | 58 | (5.8%) | 16 | (3.0%) |
| TOTAL | 1,000 | (100%) | 526 | (100%) |

From Table 2 it can be seen that the distribution of the blood groups in the two series differ ($X^2 = 24.776$ $P < 0.001$), suggesting an association between the blood groups and the incidence of leprosy. Compared to the control series, the incidence of leprosy is higher in the 'O' group and lower in the 'B' group in the study series. In the other two blood groups the difference between the two series are not significant.

In Table 3 the blood group distribution among the lepromatous and non-lepromatous patients are shown.

Table 3: Blood group distribution among 258 lepromatous and 268 non-lepromatous patients. The two distributions do not differ significantly: ($X^2 = 2.594$ $P > 0.05$).

| *Blood Group* | *No. of cases in lepromatous* | | *No. of cases in non-lepromatous* | |
|---|---|---|---|---|
| A | 62 | (24.03%) | 68 | (25.37%) |
| B | 68 | (26.36%) | 55 | (20.52%) |
| O | 121 | (46.90%) | 136 | (50.75%) |
| AB | 7 | (2.71%) | 9 | (3.36%) |
| Total | 258 | (100%) | 268 | (100%) |

Tables 4 and 5 show the distribution of blood group among lepromatous and non-lepromatous patients as compared to that found in the control series.

Table 4: Blood group distribution among 258 lepromatous patients and the 1,000 blood donors :

| *Blood group* | *No. of cases in control* | | *No. of cases in lepromatous* | |
|---|---|---|---|---|
| A | 214 | (21.4%) | 62 | (24.03%) |
| B | 331 | (33.1%) | 68 | (26.36%) |
| O | 397 | (39.7%) | 121 | (46.90%) |
| AB | 58 | (5.8%) | 7 | (2.71%) |
| Total | 1,000 | (100%) | 258 | (100%) |

Table 5: Blood group distribution among 268 non-lepromatous patients and the 1,000 blood donors:

| *Blood group* | *No. of cases in control* | | *No. of cases in non-lepromatous* | |
|---|---|---|---|---|
| A | 214 | (21.4%) | 68 | (25.37%) |
| B | 331 | (33.1%) | 55 | (20.52%) |
| O | 397 | (39.7%) | 136 | (50.75%) |
| AB | 58 | (5.8%) | 9 | (3.36%) |
| Total | 1,000 | (100%) | 268 | (100%) |

It is evident from the above tables that the blood group distribution among lepromatous and non-lepromatous patients differ

significantly from the control series ($X^2 = 9.923$ $P < 0.02$, $X^2 = 21.002$ $P < 0.001$ respectively). These results are comparable with the overall results given in Table 2.

In Table 6 the relative incidence of leprosy among 'O' group as compared to 'B' group leprosy patients are obtained by simple cross multiplication. Thus, for example, the results for the study series show 121 O's and 68 B's among the lepromatous leprosy patients as against 397 O's and 331 B's amongst the controls:

$$\frac{121}{68} \times \frac{331}{397} = 1.48$$

So we can say that this sample indicates an incidence of disease of 1.48 in persons of 'O' group as compared with 1.00 in persons of group 'B'.

TABLE 6: Relative incidence of Leprosy in 'O' group as compared to 'B' group in the study series:

| *Type of Leprosy* | *Relative incidence* O : B |
|---|---|
| Lepromatous | 1.48 : 1 |
| Non-Lepromatous | 2.06 : 1 |
| TOTAL: Lepromatous and Non-Lepromatous | 1.74 : 1 |

**Discussion**

In analysing the results of this study, two facts must be borne in mind.

(1) There is no uniformity between the control and study series in age and sex distribution.

(*a*) In the study series the ratio of male to female patients is approximately 5:1, while that in the control series is approximately 10:1.

(*b*) In the control series the subjects are all adults between the ages of about 20–50, while patients of all age groups are found in the study series.

(2) Leprosy was excluded in the control series only by a gross examination.

Apart from the above considerations, this study may be of significant value in pointing out the following facts:

(1). That the distribution of blood group in leprosy patients differ significantly from that of the general population, suggesting an

association between the incidence of leprosy and the ABO blood groups.

(2) Incidence of leprosy is high in 'O' group and low in 'B' group.

(3) Incidence of leprosy is nearly twice as high in 'O' group as compared to the 'B' group.

**Acknowledgement**

We wish to thank Dr. C. K. Job, M.D., Medical Superintendent, S.L.R. Sanatorium, Karigiri, S. India, who not only made available to us the facilities to carry out this study, but worked with us personally to make this study valuable.

We also wish to thank the staff of S.L.R. Sanatorium and the paramedical workers for their willing co-operation, Mr. Rose of the Blood Bank, Christian Medical College Hospital, Vellore, for providing us with the necessary data.

# TRAINING IN PHYSIOTHERAPY FOR LEPROSY WORKERS

by R. S. BUKER, M.D., D.P.H.

*Course conducted at the McKean Leprosy Colony, Chiengmai, Thailand, 8th January – 12th February*, 1963

One of the weakest links in the total therapeutic programme for leprosy patients has been physiotherapy. This applies in most places of the world except those few areas which have realized its value and have put in full time units to meet the needs. Even these full time units often need to be rejuvenated as it is easy to get 'routine' in a task which has to be done daily for years. Another weak point of our physiotherapy programme is that we fail to get the activity down to the root of the problem. The early case of deformity usually gets no instructions as to what he should do to prevent further deformity and the majority of cases have no instructions as to the value of prevention and how it can be accomplished.

**Preparation for the Physiotherapy Course in Thailand**

In all Thailand there are two trained physiotherapists. One is a young lady recently trained at Vellore. She is working in the Government Leprosy Programme. The other is a missionary of the Overseas Missionary Fellowship working in the Christian Hospital at Manorom where there is a splendid Leprosy Wing as a part of the general hospital. Physiotherapy of the hands and feet is being used at the McKean Leprosy Colony and in over 50 clinics being conducted by the various Missions in Thailand. No carefully planned courses for physiotherapy training, however, have been available for the many leprosy workers needing it.

Dr. Hasselblad, President of the American Leprosy Missions, feeling that here was a place that leadership was needed, arranged with Mrs. Ruth Thomas Thein (formerly in charge of the physiotherapy training at Vellore) to conduct such courses; one in Thailand, one in Vietnam, and one in Hongkong. Normally the length of a course of physiotherapy is twelve to eighteen months. As it is impossible to give this length of time by most of our workers, it was decided to attempt a course of 6 weeks' duration, emphasizing the basic needs.

**The Course**

Fourteen participants actually took the course. There were a few visitors for a day or more. The class was divided into groups, about equal in size, one group who knew English and one group which required interpretation into Thai. The lectures were translated into Thai by Acharn Prachim R.N. assistant supervisor of nurses at the

McCormic Hospital. She had studied in America and handled the medical terminology with great ease. The entire course was, therefore repeated during the six weeks. Mrs. Thein lectured on the basic anatomy to one group in the morning and repeated it in the afternoon to the second group. Mr. Thein, a Vellore trained physiotherapist, took the other group, giving a short lecture on methods, using the remainder of the half day having the class do actual physiotherapy on the patients. This practical work added 100% to value of the course. The course was conducted at Chiengmai, at the McKean Leprosy Colony. Here there are 500 patients with ample number of all kinds needing physiotherapy. Full facilities of wax baths and electricity were available. Pre- and post-operative physiotherapy was not emphasized due to the shortness of the course. Several post-operative cases, however, were dealt with showing marked improvement following the physiotherapy.

All who participated in the course observed crooked fingers become straight as they put on daily finger casts; dropped feet became markedly improved from special exercises in three weeks time; post-operative cases of feet and hands which had not been properly exercised changed from failure to success under this therapy. It was realized afresh that surgery of the hands and feet is useless without pre- and post-operative physiotherapy. People with facial paralysis actually took on new life and hope, though nothing was done for them except physiotherapy. One case, a young man of 22 years, who had suffered many things at the hands of many so-called doctors, was made new again. His dropped foot and early crippling were almost completely cured. All this happened during the course. None of those who took the course will ever belittle physiotherapy as a real tool in the therapeutics of leprosy cripples.

There was no attempt to use Faradic and Galvanic currents to locate muscle damage. Vibrators and Infra-red lights were utilized but are not essential to those having no electricity.

**Summary**

Six missionaries and eight paramedical workers (nationals of Thailand) took the course. One doctor, six nurses, one physiotherapist, and six paramedical workers made up the group. Four different missions, The Christian and Missionary Alliance Mission, The Southern Baptist Mission, The Overseas Missionary Fellowship of the China Inland Mission and the Presbyterian Mission were represented.

Out of this course it is expected several other teaching facilities will develop. The Overseas Missionary Fellowship will teach nurses and nurses aids, active work on pre- and post-operative physiotherapy will continue at the Manorom Christian Hospital.

The Christian and Missionary Alliance Mission will introduce a part time four year course in physiotherapy in its Maranatha Bible School for leprosy patients.

The Southern Baptist Mission will promote the use of physiotherapy in its outside clinics reaching the early cases as far as possible together with active physiotherapy teaching in its new hospital yet to be finished.

The Presbyterians will continue to give instruction to paramedical workers in physiotherapy at the Chiengmai McKean Leprosarium.

A continued effort is needed in all places doing clinic work to disseminate preventive and corrective physiotherapy methods for those suffering from leprosy. This course is making it increasingly possible to do this.

# OJI RIVER SETTLEMENT

## REPORT ON THE PATELLA-TENDON BELOW-KNEE PROSTHESES PROJECT

by W. F. ROSS,

*Area Superintendent, Ministry of Health, Rural Health Division, Oji River, via Enugu*

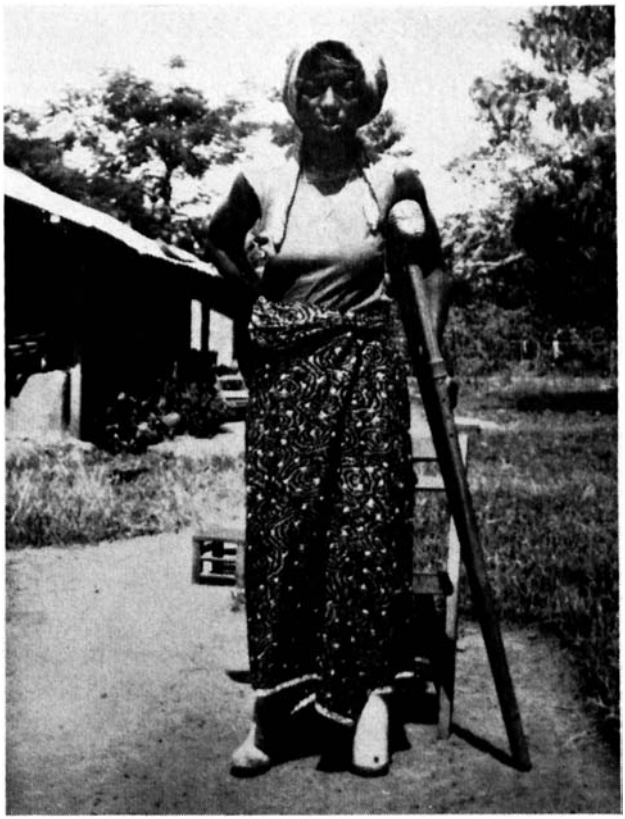
This project was undertaken during 1962 with the help of Mr. Thomas Forrest, a Voluntary Service Overseas volunteer, who was financed by a special grant from British Leprosy Relief Association. Materials and workshop for the project were provided by the Ministry of Health, Eastern Nigeria.

Prior to coming to Nigeria, Mr. Forrest spent three weeks at Queen Mary's Hospital Artificial Limbs Centre, Roehampton, where he worked in the experimental workshop under the guidance of Dr. Mackenzie.

A real start was not made with the limbs until April, by which time we had obtained all necessary materials and a copy of the manual published by the University of California. Since then, more than 30 limbs have been made for leprosy patients, including a pair of limbs for a patient with bilateral below-knee amputations. This particular patient had not walked for more than fifteen years. Her feet were completely destroyed, and her only means of locomotion was crawling with the aid of a stool.

A few of the limbs have had to be modified following fitting, as they caused friction blisters, but the majority of the patients have been able to wear the limb as made, and have been walking well within ten days of receiving it.

We have very much simplified the construction of the limb from the instructions laid down in the University of California manual, and have used cotton stockinet only as the filler in socket and shin. This has a disadvantage that when either part is machined, it leaves a slightly rough edge, but makes for a very much simpler supply situation. Cotton stockinet has been found easy to work with, and used in six or seven layers is of adequate strength, even for the biggest amputee. We have found that although it is possible to fit a prostheses to a below-knee stump as short as four inches, it is easier to fit the longer stumps and re-education of the patient is easiest also, when the stump is as long as possible. We have also used, in one instance, leather cloth instead of horsehide to line the socket. This appears to have many advantages in humid climates and we have been prevented from fitting all our patients with leather cloth only because of delay in obtaining suitable supplies of this material.



We have not yet been able to obtain an alignment device, and have had to align the socket and the shin by eye. This seems to be a perfectly satisfactory procedure. The earlier limbs were all fitted with a peg leg, but later, patients have had a modification of the 'Hanger' foot made at our own workshops. This is not strictly necessary, and we feel that the patients walk better with the peg leg than with the foot; but for aesthetic reasons, the patients very much prefer the foot.

Two Nigerians were trained by Mr. Forrest in making limbs and for the last three months of his visit, when he was engaged part of the time on other projects, they carried on with only general supervision.

We are satisfied:—

1. That the patebear limb is suitable for fitting to leprosy patients in tropical countries.
2. That very good limbs can be made with simple equipment by locally trained workers.
3. That the cost of the limbs compares extremely favourably with the cost of standard type below-knee prostheses.

The limbs are fully described in the manual called 'The Patella-Tendon-Bearing Below-Knee Prostheses'. Authors: C. W. Radcliffe and J. Fort, published by University of California Press, Berkley, California. No one should attempt to make these limbs without first obtaining the manual.

We shall be pleased to supply notes on the modification made on the limb at Oji River and also a list of essential materials and sources of supply to anyone who wishes.

# LETTERS TO THE EDITOR

30th April, 1963

(1) From DR. S. G. SPICKETT

(*Victoria Woodhull Fellow of the Royal Institution*)
*Department of Genetics, University of Cambridge.*

*on the 'Weddell Theory'.*

Dear Sir,

The recent paper of WEDDELL and PALMER[1] raises a number of important issues and although they have received some discussion elsewhere[2] I should like to comment on two problems relevant to my own work[3,4,5].

If the portal of entry of *Mycobacterium leprae* is not the skin, but rather the alimentary and respiratory tracts, then the site of the first cutaneous manifestation of leprosy can bear no relationship to the site that is most likely to come into contact with a lesion of an affected individual. The 'Weddell Theory' argues that the bacilli are distributed by way of the circulation to the sensory nerves and that the site of the first lesion is determined by neural turn-over and hence is very frequently induced by trauma. The problem as to whether the site of the initial lesion is random, associated with skin to skin contact or associated with areas of high neural turn-over might not be easy to solve unequivocally, but should be amenable to some degree of resolution by a careful analysis of the locations of intial lesions.

The widely held view, that the portal of entry is the skin and that the bacilli are acquired from skin to skin contact, is based on a great mass of observation to the effect that the initial lesion is very frequently at the site of skin to skin contact with an infected individual. Perhaps the clearest example of this is in the high frequency of forehead lesions in African infants as compared with Korean infants, where the mother is the infected contact. In the Africans the back of the mother is naked and in prolonged contact with the child's forehead whereas in the Korean mothers the back is clothed and there is no skin contact. Although these observations are not the result of carefully designed surveys they cannot be disregarded and the evidence they give is clearly in favour of the skin as the portal of entry.

WEDDELL and PALMER concede that the portal of entry may be the skin through cuts, abrasions, insect bites and the like, but it is implied that this is an exceptional circumstance. There have been many attempts to incriminate certain arthropod vectors. Transmission by arthropods is a persuasive hypothesis, and it may well be that many arthropods are capable of effecting transmission of the bacilli but here also there is the difficulty that some of them, e.g. the

mosquito, do not fit the observations consistent with skin to skin contact. One arthropod in particular (*Demodex folliculorum*) does satisfy all the criteria demanded of a transmitter and moreover there is the supporting evidence of bacilli having been seen in its gut at a time in its life cycle when it may penetrate to the dermis. Since this parasite is ubiquitous in man its role in the transmission of leprosy could be sufficient to explain the very large numbers of cases where the disease does appear to be acquired by skin to skin contact.

The evidence of WEDDELL and PALMER does appear to establish that *M. leprae* may be disseminated throughout the body by the circulation, and this being so one of the major problems connected with a respiratory or alimentary portal of entry is solved. However this does not in any sense provide evidence that such portals of entry are used and it is difficult to see how the type of evidence that WEDDELL and PALMER have produced can provide such evidence.

The second point I should like to raise relates to the problem of 'natural immunity'.

It is now apparent that resistance and susceptibility to leprosy are, in part, attributable to genetic variability in the human host[4,5]. It has been shown that a single irregularly dominant gene controls susceptibility to leprosy and that the penetrance of this gene varies between populations[6]. Although the main effect is due to a single gene, irregular dominance and variation in penetrance between populations implies a strong possibility of there being other genes influencing susceptibility. Furthermore, environmental variation may be of considerable importance in the determination of resistance and susceptibility. This then is one mechanism of 'natural immunity' but nothing is known as yet of the way in which the genes exert their effects. It may be that the gene controls the ability of the body to produce antibody to *M. leprae*; it may be that the control is over some aspect of the chemistry of the host cell that is essential to the pathogen. Moreover there is another genetic system influencing the course that the disease may take, e.g. whether it is lepromatous or non-lepromatous in expression, or whether there are severe reactions or not. The point at issue is that there are many genes in man affecting the relationship with *M. leprae*, and many of them affect what is loosely termed 'natural immunity'. It is therefore clear that natural immunity in man to *M. leprae* is a very heterogeneous phenomenon. Similar levels of 'natural immunity' may be gained through different mechanisms controlled by different genes and it will be difficult to make useful reference to natural immunity until it can be specified in pathological and genetic terms. The studies of WEDDELL and PALMER may well come to demonstrate the way in which some of the genes act, provided that some work is done on genetically specified material.

Most of the genetic variation between races and populations is quantitative rather than qualitative. The variation is in the frequency of particular genes rather than in the possession of genes unique to them. It is probable that the bulk of the inherited variation between races, with respect to leprosy, is due to variation in gene frequencies. Racial variation in leprosy is therefore a strong indication of individual variation. Distinction between 'racial immunity' and 'natural immunity' is therefore artificial when applied to the pathogenesis of leprosy since the same mechanisms are covered by both terms.

S. G. SPICKETT

**References**

[1]WEDDELL, G. and PALMER, ELIZABETH (1963). The pathogenesis of leprosy: an experimental approach. *Leprosy Review* **34** (2), 57–61.
[2]WOLSTENHOLME, G. E. W. (1963). Ed. Ciba Foundation Study Group. 15. The Pathogenicity of Leprosy, Churchill, London. (In press).
[3]SPICKETT, S. G. (1961). A preliminary note of *Demodex folliculorum* Simon (1842), as a possible vector of leprosy. *Leprosy Rev.* **32** (4), 263–268.
[4]SPICKETT, S. G. (1962). Genetics and the epidemiology of leprosy. I—The incidence of leprosy. *Leprosy Rev.* **33** (2), 76–93.
[5]SPICKETT, S. G. (1962). Genetics and the epidemiology of leprosy. II—The form of leprosy. *Leprosy Rev.* **33** (4), 173–181.
[6]SPICKETT, S. G. (1963). Genetic factors in leprosy. *Leprosy in Theory and Practice*, ed. R. G. Cochrane, 2nd edn., Wright, Bristol. (In press).

22nd May, 1963

(2) From WEDDELL, PALMER and REES commenting on SPICKETT

Dear Sir,

We accept Dr. SPICKETT's comments (in this issue) with respect to the portal of entry of *M. leprae* into the body and we welcome them.

Our observations have established that *M. leprae* can be disseminated by the blood stream. They also suggest that the organism does not enter the skin merely by contact or even by inunction.

We have no evidence to support or refute the suggestion that they enter the body via the respiratory or alimentary tracts but we felt that this was a problem which required investigation since it is well recognized that there are patients with leprosy in whom skin lesions cannot be found at all.

We may have given the impression that our observations indicate that the portal of entry is *not* via the skin. This was quite unintentional for an analysis of the cases we ourselves have examined, quite apart from the evidence in the literature, suggests that the skin is the commonest *known* portal of entry. The point which we wished to stress is that though we have examined over 2,000 slides of skin from patients exhibiting a wide range of clinical forms of leprosy including those who had been in close and continuous contact with patients having leprosy but themselves exhibiting no symptoms of leprosy, we have, so far, never seen any organism in the epidermis. Moreover,

we have been unable to find organisms in any centrifuged fractions of skin biopsy homogenates taken from close contacts.

This strongly suggests that the organisms must be inoculated *into* the skin. They would then be available for entry into macrophages, the Schwann cells associated with intact or degenerating cutaneous nerves, or blood vessels or lymphatic channels.

Clinical evidence, together with our experimental observations, suggest that once the organisms are *in* the skin, either: (1) they are destroyed and the subject does not develop leprosy, (2) they become related to the Schwann cells associated with cutaneous nerves at the site of inoculation and a single self-limiting lesion eventually develops (which always appears to involve both cutaneous nerves and the sensory nerve trunk serving the area involved), (3) they enter the blood stream and are conveyed to Schwann cells related to other sensory nerves and polyneuritic leprosy eventually develops, or (4) they enter the bloodstream and become widely disseminated and lepromatous leprosy eventually develops.

So far, nothing we have said is at variance with the clinical evidence available but the point we wished to stress to leprologists is that on the evidence available inoculation *into*, not passive contact with or inunction through, the skin is the route taken by the organism into the body via the skin.

In our view this is of the greatest importance in relation to the prevention of the spread of the disease, and there are two points which emerge and which we wished to emphasise: (1) it means that subjects in areas where leprosy is endemic should understand the importance of elementary hygiene in the prevention of leprosy, e.g. (*a*) that *M. leprae* from open cases should either not get smeared onto their skin at all or that they should not be allowed to remain there in large numbers. This means washing, the destruction of infected fomites, and the disinfection of the dwellings, particularly sleeping quarters and floors; (*b*) the importance of all available measures to reduce superficial skin injuries and insect bites. In some regions light clean clothing might possibly be advocated. (2) a continuation of the efforts to reduce the number of lepromatous cases by the setting up of networks of rural clinics for the distribution of therapeutic drugs which Dr. C. M. ROSS has demonstrated in Northern Nigeria to be highly successful.

Our reasons for going into print at this possible premature stage was to stimulate leprologists into renewed vigilance with respect to hygiene for, if as SPICKETT (1961) suggests *Demodex folliculorum* Simon is a possible vector, then it is *not* enought merely to *treat* patients suffering from leprosy.

SPICKETT'S suggestion would certainly account for the occurrence of the disease in patients who have never come into contact with

either an open or closed case of leprosy, a suggestion which it is hard to discount in view of the evidence of BADGER (1959).

We remain aware that we have too little evidence at our disposal to be categorical, but we feel strongly that the evidence so far available entitles us to the view that it would be wrong not to regard leprosy as potentially highly infectious and to point out to those living in areas where leprosy is endemic the protective value of elementary personal and public hygiene which has proved such an effective measure in protecting those trained in these subjects, who have emigrated to these areas. In other words, we think that measures modelled on the prevention of tuberculosis are likely to be highly effective. We realise how difficult this may be, but because there are still a few leprologists who do not believe that leprosy is potentially infectious like other mycobacterial diseases we felt impelled to speak.

We of course accept Dr. SPICKETT's views with regard to the importance of the genetic factors and are pleased to find that another academic research worker is as interested in leprosy as we are.

GRAHAM WEDDELL
ELISABETH PALMER
R. J. W. REES

**References**

BADGER, L. F. (1959), Chapter VI, *Epidemiology in Leprosy in Theory and Practice*, R. G. Cochrane, John Wright, Bristol.
SPICKETT, S. G. (1961), *Leprosy Rev.*, **32**, 263.

(3) From Dr. J. WALTER of Ghana.

P.O. BOX 26,
ELMINA/GHANA.

Dear Sir,

Comments on Dr. G. WEDDELL's *Pathogenesis of Leprosy* (*Lep. Rev.* 1963, **34,** 51.)

Dr. WEDDELL's research into the pathogenesis of leprosy must be studied with great interest.

Leprologists in the field will agree upon the unsatisfactory past and present concepts of transmission which, although generally accepted are more empiric than scientific. Numerous cases of leprosy either officially reported or personally observed just do not fit in with their history of short or unaccounted contact with contagious cases into the concept of prolonged or intimate contact (skin), and why is there a high tuberculoid incidence in areas with a low 'infections' (lepromatous) rate? There seems to be more proof in Dr. WEDDELL's new experimental approach and in his conclusions than in the present hypothesis about transmission.

The Editor of *Leprosy Review* (*idem*) rightly advocates that it would be premature at this stage to initiate changes of control measures, but in the light of Dr. WEDDELL's findings it should also be

desirable to start a re-orientation about immunological wide scale preventive measures (lepromin? B.C.G. ?) and to place such at least in the field of research much more prominently than this has been done hitherto.

J. WALTER.

(4) From Dr. RAO on the Indian Classification of leprosy

CHILAKALAPALLI (P.O.)
ANDHRA PRADESH, INDIA.

Dear Sir,

I read with interest Dr. R. CHAUSSINAND's article on 'The So-called "Maculo-anaesthetic form" of the Indian classification of Leprosy',[1] But I am amazed that he so strongly disagrees with it when he is in entire agreement with the first Expert Committee on Leprosy[2], which stated that the basic criteria of the primary classification of leprosy should be clinical and bacteriological. If, as he says, 'a scientific study of cases is made, immunological and histopathological criteria should be fully used to determine certain groups', the major classification of 'Lepromatous' and 'Tuberculoid' ought to be different, because they are essentially histopathological diagnoses even though the clinical picture in these types is definite.

It is not that the Indian leprologists alone who consider that a 'Supplemental form named maculo-anaesthetic should be introduced in the primary classification of leprosy'. Dr. WADE and Dr. COCHRANE who belong to two other different nations speak of it. There was much discussion about it (and much disagreement) at the Madrid Congress. Neither the Madrid Congress nor the Tokyo Congress could make up its mind about the 'Maculo-anaesthetic' and the 'Polyneuritic' types of the disease.[3],[4].

Again let it be noted that COCHRANE, BROWNE, RAMANUJAN, DAVEY and a lot of others have all agreed to the existence of the 'maculo-anaesthetic' group, as a distinct, well-defined clinical entity.

Dr. CHAUSSINAND has quoted DOULL as the only person who raised an objection. Actually his sentence is taken out of context. The first few lines spoken by Dr. DOULL at the same time are 'Dr. DHARMENDRA has given an exceedingly clear description of the maculo-anaesthetic group and I have no objection whatever to the terminology which is proposed'.

Dr. CHAUSSINAND can see only one difference between the maculo-anaesthetic macule and the Indeterminate macule (according to the paper of DHARMENDRA and CHATTERJEE)—one is dry and the other is not. But for me, the following things also strike as important differences.

(1) Anaesthesia is a prominent feature in the maculo-anaesthetic type, it is not so in the other.

(2) Thickening of the nerve is usually present in the maculo-anaesthetic type. It is uncommon in the other type.

(3) Bacteriological examination is usually negative.

(4) In evolution, the maculo-anaesthetic is far more stable and chronic than the unstable and fleeting indeterminate type.

(5) Histologically it is a pre-tuberculoid form whereas the changes in the indeterminate are non-specific.[5]

I am afraid that Dr. CHAUSSINAND gives another misleading argument when he says that the Indian classification consists of 'a mixture of pure indeterminate and pre-tuberculoid indeterminate cases . . . '. An indeterminate case is either pure or it is not 'indeterminate'.

Leprosy is a disease with two polar types and the spectrum in between shows definite entities whose shadows overlap this way or that way causing immense confusion unless one sticks to certain characteristic criteria. The stress should be on the different, clinically recognizable entities rather than the nomenclature according to some water-tight compartments such as immunological, histopathological etc. Let us not forget that these compartments are made by man for a better understanding of the subject. 'A rose smells as sweet by any other name'.

M. S. NEELAKANTA RAO.

**References**

[1]*Leprosy Review*, Vol. 34, No. 1, January 1963, 29–34.
[2]Comité Experts de la leprae 1953, 71.
[3]Leprosy in Theory and Practice, by R. G. COCHRANE (1959), 157.
[4]Second Report of Expert Committee on Leprosy, W. H. Q., 1960, 27.
[5]KHANOLKAR in "Leprosy in Theory and Practice".

(5) From Dr. WHEATE on leprosy in Bali.

CHAZI LEPROSARIUM,
PRIVATE BAG, TURIANI,
MOROGORO,
TANGANYIKA.
28th March 1963.

Dear Sir,

Dr. SPENCER REED'S account of the Bali Leprosy Campaign (*Leprosy Review*, **34,** 40, January 1963) is of great interest.

He makes one statement, however, which seems to be contrary to experience in Africa: 'The eradication of leprosy bacilli by DDS in a tuberculoid case is undoubtedly too slow, with consequent danger in nerve reactions and other clinical incidents which lead to ultimate deformity'.

Our experience is precisely the reverse, namely that in indeterminate and tuberculoid leprosy, even a single dose of 100 mgm. of DDS may be sufficient to trigger off an acute neuritis. We find that

tuberculoid cases seldom develop neuritis after stabilization on a routine dosage schedule of DDS (by contrast with lepromatous cases which often do, especially when the bacterial index is approaching negativity).

I shall be interested to learn of the evidence on which Dr. REED bases his conclusion.

H. W. WHEATE.

# ABSTRACTS

*Percutaneous Absorption and Routes of Excretion of Ditophal (Etisul).*

G. A. ELLARD* and J. M. B. GARROD, and B. SCALES and G. A. SNOW. Biochemical Pharmacology, 1963, Vol. 12, pp. 271–281.

Ditophal (diethyl dithiolisophthalate, Etisul†) is the most active member of a series of derivatives of ethyl mercaptan in protecting mice against acute experimental tuberculosis. It is used effectively in leprosy and *Lupus vulgaris*. Since the usual routes of administration are unsatisfactory ditophal is rubbed into the skin, and has both a local and a general effect. Leprous lesions remote from the site of inunction respond satisfactorily to the treatment. In *Lupus vulgaris* some patients with bilateral lesions were inuncted on one side only; lesions cleared on both sides, although the inuncted side healed more quickly.

The fate of ditophal and some other esters of ethyl mercaptan has been studied in the mouse, guinea pig and rabbit. The compounds were administered orally or by subcutaneous injection and were rapidly eliminated together with their metabolites. Most of the dose was accounted for, and the nature of the principal metabolites of ethyl mercaptan in these animals was elucidated.

Attempts to follow the metabolism of ditophal in man by chemical methods failed. The drug was therefore labelled with $^{35}S$ and radioactivity measurements were used to follow its excretion. $^{35}S$ is an isotope with a half-life short enough to limit the radiation received even if it were retained in the body.

When $^{35}S$-labelled ditophal is rubbed into the skin about 90% of the drug is absorbed in 1 hour. Excretion of $^{35}S$ occurs in urine, faeces and sweat and less so in breath. The greatest rate of excretion is at 6–24 hours after inunction, but excretion continues for several weeks. The principal forms of excretion are toluene-extractable material and sulphate.

*Leprosy and Mental Disorders.* L. P. VERMA. Indian Journal of Psychiatry, **5**, 1954.

The author studies the psychology of leprosy patients during the various stages of the disease. Leprosy is a great psychological stress and is likely to cause mental troubles, as it also makes the individual liable to various physical privations.

*Present address: Department of Biochemistry, University College, London.
†Etisul is a trade mark, the property of Imperial Chemical Industries Limited.

Leprosy occurs in mental patients but usually it does not make any alterations in the mental picture. The author describes a case of schizophrenia who developed leprosy during the course of his mental illness, and in this patient there was a definite change in his mental condition. He became quiet and docile while formerly he used to be excited and boisterous. This is difficult to explain. There was a group of patients where leprosy seemed to act as a precipitating factor and led directly to the onset of mental disorder. Such cases were usually schizophrenics or manic depressives. With the improvement in their lepromatous condition, such patients recover mentally as well.

# REPORTS

*Annual Report, Leprosy Research Unit, Uzuakoli*, 1961.

## Introduction

The Leprosy Research Unit at Uzuakoli is under the administrative control of the Ministry of Health, Eastern Nigeria. It is an integral part of the Regional Leprosy Service, being intimately associated with this Service in the Owerri Province and related to that in other Provinces through Settlements that co-operate in drug trials.

The financial support, which used to come from the Colonial Welfare and Development Fund, through the Federal Government, is now assured directly by the Federal Government.

The research projects of the Unit are made possible and greatly facilitated in all ways by the Settlement at which it is located. The advantages of the complete fusion of administrative, medical and laboratory activities, are everywhere apparent.

## A. Chemotherapy

Therapeutic trials have been completed on the following drugs:

(*a*) Diamino-diphenyl sulphoxide;
(*b*) An azulene derivative: AZ-8;
(*c*) A long-acting Prednisolone.

Trials are still in progress on the following drugs:

(*d*) Thiambutosine; Diphenyl thiourea; DPT or Compound SU 1906;
(*e*) Ditophal; Diethyl-dithiol-*iso*phthalate;
(*f*) A substituted Anilino-*apo*safranin;
(*g*) Methimazole; Tapazole (Lilly).

As opportunity offers, studies are proceeding on other drugs of possible use in the dyschromias of leprosy (especially persistent hypopigmentation in quiescent and resolved lesions) and other conditions;

(*h*) Mono-benzyl ether of hydroquinone (Boots Chemists, Limited);
(*i*) 8-methoxy-psoralen; 'Oxsoralen' (Paul B. Elder);
(*j*) Dihydroxyacetone (Boots Chemists, Limited).

(*a*) *Diamino-diphenyl sulphoxide.*—All patients who had received this drug were reviewed clinically and bacteriologically, both those still in the Settlement and those who had been discharged. Particular attention was paid to possible signs of residual nephrotoxicity. It was gratifying to note that there was little indication of permanent kidney damage among the patients who had during the course of treatment shown albuminuria and haematuria. Dr. Davey co-operated in the

publication of a paper which summarized the findings and contained a warning regarding the nephrotoxicity of the drug. Similar conclusions have been reached when the drug was employed in high doses for the treatment of dermatitis herpetiformis.

(*b*) *An azulene derivative:* 1.4 *dimethyl-7-isopropyl-azulene; AZ*-8 (*Beris Laboratories*).—The 23 patients who took part in this trial were reviewed. The initial improvement noted, though not maintained, is suggestive that the anti-inflammatory action of the drug may possibly potentiate anti-leprosy therapy if given in conjunction with standard treatment, e.g., dapsone. The patients have since responded to accepted treatment for lepra reaction, most of them having had severe and persistent episodes.

(*c*) *A long-acting Prednisolone* (*Pfizer*).—Despite the recognized limitations and side effects and disadvantages of prolonged corticosteroid therapy, there is an unfortunate class of patients with severe lepromatous leprosy who respond only to these drugs. They are subject to persistent lepra reaction that fails to respond when anti-leprosy therapy is stopped and other treatment instituted. When indicated, the long-acting prednisolone under trial, given by injection at weekly intervals, not only controls the distressing clinical manifestations of lepra reaction, but also in some cases permits of the resumption, in carefully graduated doses, of anti-leprosy therapy. A publication summarizes the results of our enquiry.

(*d*) *Thiambutosine; a Diphenyl thiourea, DPT, Compound SU* 1906 (*Ciba*).—Work has continued on this useful drug, and a trial of an injectable compound will shortly be instituted. The occurrence of a modified form of drug 'resistance', observed towards the end of the second year of treatment, is confirmed. It is therefore advisable to introduce another drug during the second year, with a view to postponing the onset of resistance and in order to assure that adequate anti-leprosy therapy may be continued.

(*e*) *Ditophal: Diethyl-dithiol-isophthalate;* '*Etisul*' (*I.C.I.*).—The patients who have taken part in previous trials have continued under observation; it is particularly important to discover if ditophal given alone has a beneficial effect on lepromatous leprosy, and if the addition of ditophal to standard therapy reduces the total time necessary for treatment and accelerates bacteriological negativity.

Five patients were given ditophal in addition to the Rimino-compound, B 663.

It would appear that ditophal in certain cases has a definite effect in lepromatous leprosy; and that it may reduce the period of treatment. Several aspects of this problem remain obscure.

(*f*) *Rimino-compound: a substituted Anilino-aposafranin B* 663 (*J. R. Geigy, S.A.*).—In view of the distinctly encouraging early results obtained in the small pilot trial of this compound (6 untreated lepromatous patients, of whom 3 received dapsone in addition), more

patients were added to the trial when further supplies of the drug were made available by the manufacturers. Twenty-two additional patients receive the drug, of whom 7 received dapsone in addition and 5 received ditophal ('Etisul' I.C.I.). Further investigation suggests that the beneficial effect of the drug may not be maintained and that a modified form of drug 'resistance' may develop. Unfortunately, in view of the expense and technical difficulties of manufacturing this promising compound, it is probable that no more will be available for trial or therapy, since it could never replace such an inexpensive and chemically simple drug as dapsone.

(*g*) *Methimazole:* 1-*methyl*-2-*mercaptoimidazole;* '*Tapazole*' (*Eli Lilly and Company Research Laboratories*).—In view of the fortuitous observation that a patient suffering from leprosy benefited from Tapazole (given for hyperthyroidism), a South American worker reported favourably on the use of the drug in leprosy. Notwithstanding the paucity of bacteriological supporting evidence, it was decided to proceed cautiously with a small pilot trial to ascertain if the drug was worthy of fuller investigation. Five patients willingly agreed to co-operate, though the tentative nature of the trial was explained to them, as also the necessity for frequent blood examinations. The clinical and bacteriological findings do not suggest the advisability of further trial, and the risk of disabling side-effects and even leucopenia and agranulo-cytosis would render the drug unsuitable for mass treatment even though it should have some value in leprosy therapy.

**B. Other Investigations**

Several studies in the diverse fields of immunology, classification and differential diagnosis have been pursued in the Unit during the year.

1. *Immunology.*—Investigations have continued on the tuberculoid response to the intradermal injection of particulate matter in patients suffering from polar forms of leprosy. In particular, and in continued collaboration with Dr. D. S. Ridley, Pathologist at the (London) Hospital for Tropical Diseases, the efforts of the inoculation of micronised Bentonite have been studied histologically.

2. *Classification.* Further studies have been undertaken with a view to shedding light on certain controversial matters: borderline leprosy (especially its unstable clinical and immunological features); the maculo-anaesthetic variety of tuberculoid leprosy (*vide* India leprologists); the macules of dimorphous leprosy.

3. *Differential* diagnosis necessarily occupies a prominent place in the daily Diagnostic Clinic in the Unit, where approximately half the patients thought to have leprosy are found in reality to be suffering from a wide variety of tropical and non-tropical cutaneous and neural conditions.

4. *Miscellaneous* investigations covering a wide field in tropical medicine continued to be pursued in the Unit for their possible help in the elucidation of some of the outstanding problems of leprosy, its epidemiology and its clinical manifestations.

**Laboratory Aspects**

The laboratory is an essential part of the work of the Unit, and its maintenance at a high level of efficiency is a primary concern. More good work could be done, and more varied investigations attempted, if staff and equipment could be augmented.

Within the limits imposed, however, the laboratory undertakes the routine procedures necessary for the cover of drug trials, immunology and diagnosis.

(*a*) Skin biopsy, the preparation of sections, clinical photography, tuberculin and lepromin reactions; these are undertaken for research patients, and as necessary for other patients on admission;

(*b*) Laboratory cover for drug trials proceeds according to a standardized schedule involving blood, urine and liver function;

(*c*) Bacteriological examination of multiple smears is carried out routinely on all patients in the Settlement, and on all patients presenting themselves at the Diagnostic Clinic. All patients under treatment with new drugs are smeared at regular intervals, and the detailed morphology of the *M. leprae* is recorded for each site examined. This information is of great value in indicating degenerative changes presumably due to therapy, even when the actual bacteriological index may show little change.

**Statistics**

| | 1960 | 1961 |
|---|---|---|
| Patients smeared for *M. leprae* | 3,042 | 3,049 |
| Lepromin test | 187 | 153 |
| Tuberculin test | 142 | 143 |
| *Examinations:* | | |
| Blood | 2,197 | 3,204 |
| Serology | — | 230 |
| Urine | 3,731 | 3,249 |
| Faeces | 763 | 1,599 |
| Sputum | 107 | 107 |
| Biochemical (various) | 719 | 677 |
| Histological: Blocks | 114 | 74 |
| Slides | 336 | 238 |
| Miscellaneous | 128 | 143 |
| Radiographic | 147 | 122 |
| Bentonite | — | 4 |

**Training**

The benefits accruing from the short courses of training given for laboratory workers from other Leprosy Settlements in Eastern Nigeria where drug trials are in progress, and elsewhere, have been apparent during the past year. More trainees have followed these courses during 1961.

The existence of these facilities should be more widely known.

**Personal**

Mr. O. U. Osoagbaka, F.I.M.L.T., has continued in charge of the Laboratory. During his leave (6th June to 4th September) Mr. E. A. Okpo assured this service.

Deep appreciation must be expressed for the continued valuable co-operation of Dr. L. M. Hogerzeil in assuring the administrative oversight of the Settlement. His sharing of the clinical work of the Unit, his lively interest in the various research projects undertaken, and his assumption of responsibility for these projects during the absence on leave of the Senior Specialist (from 11th November) are here gratefully acknowledged. He is joint author of a number of scientific papers prepared in the Unit during the year.

Help has also been forthcoming from Medical Officers attached for a time to the Settlement: Drs. J. C. Uzoma, F. O. C. Peters and E. Fern.

Dr. S. G. Browne was elected to the Fellowship of the Royal College of Physicians of London early in the year.

During the year, he gave a course of lectures and demonstrations on Leprosy to the clinical medical students and senior student-nurses at Ibadan University. He also gave lectures to the medical staff of University College Hospital, Ibadan, on 'Some Observations on Onchocerciasis' and to the Ibadan Medical Society on 'Medical Services in the Belgian Congo before Independence'. Dr. Browne gave courses of lectures and demonstrations in Leprosy to Leprosy Inspectors at Oji River and Ekpene Obom, and twice addressed Conferences of doctors from the southern half of Eastern Nigeria (at Ikot Okoro and Ekpene Obom) on 'The Differential Diagnosis of Leprosy', and 'Clinical Varieties of Leprosy'. While on leave, he addressed various scientific bodies, including the Edinburgh Branch of the Royal Society of Tropical Medicine and Hygiene ('Present Perspectives in Leprosy'), and the School of Pharmacy of the Glasgow College of Science and Technology ('Problems and Prospects of Chemotherapy in Leprosy').

*Annual Report of the Tanganyika Health Division*, 1961.

**Leprosy**

Significant although unspectacular progress continued during the year in control measures directed against this disease.

The Eastern Region has the advantage of having the Leprologist stationed within it and he reports, with particular reference to leprosy in the Morogoro district, as follows:—

'There are 19 out-patient centres including Chazi Leprosarium, the Government Hospital, Morogoro, and the Tawa Health Centre. The total of patients registered is of the order of 4,000 and the attendance rate, on average, is about 50%.

'The epidemiology of leprosy, particularly in the Uluguru Division of the District is of great interest. A publication by Dr. Peiper (1912) "Leprosy in German East Africa" has been consulted. Dr. Peiper reports that Mr. Robert Koch visited Morogoro during the early years of the century and gave it as his opinion that leprosy was of recent origin and rapidly spreading. All the evidence to date indicates that he was right. The German administration set up a number of leprosy villages, providing such treatment as was then available, but with the primary object of segregating as many cases as possible throughout the territory. Some of these survive to this day (e.g. Tabora near Mahenge).

'In the Ulugurus these villages were situated along the old road from Ngerengere to Kisaki. With the coming of the Great War, 1914–18 and the change in the administration, together with Hutchison's theory (that leprosy was due to eating bad fish) which was current in Britain at that time, these villages ceased to function. The natural movement of the population into the Uluguru area was through the leprosy village zone. In consequence a large number of susceptibles came into contact with an artificially concentrated focus of infection and the resulting "epidemic" is still with us.

'This series of events serves to illustrate that leprosy spreads in a community simply and solely because of opportunity for contact between infective cases and susceptible individuals. Climate, age, sex, and even standards of living have little if any effect on its epidemiology. (It is now not accepted that children are especially susceptible, but merely that in some rural societies they have ideal opportunities for infection.) It is as yet unknown to what extent or how quickly sulphones "sterilize" the infective case (sulphones are bacteriostatic not bacteriocidal) and our policy must be to retain such facilities as we have for partial, voluntary segregation, while concentrating our main attack on the disease through mass treatment in rural dispensaries.'

In the West Lake Region the Swedish and Norwegian Save the Children Organization agreed to establish an extensive anti-leprosy campaign. Plans were finalized towards the end of the year and two medical officers of the Organization arrived at Bukoba to gather preliminary information. The main administrative and treatment centre in this scheme is being built at Kitendaguro, three and a half

miles from Bukoba, and the scheme will include satellite dispensaries throughout the region.

In the Central Region considerable progress was made by the Church Missionary Society in establishing the new leprosy and control centre at Hombolo. Building operations were hampered very considerably by very heavy rains. In Singida District the activities of the Augustana Lutheran Mission at Iambi and those of the local authorities were well integrated and co-operation in this field is very good.

In the Western Region there are now out-patient treatment facilities at all hospitals, rural health centres and a large percentage of the rural dispensaries. The percentage of defaulting patients unfortunately remains high. By far the greater part of institutional treatment is carried out at the Moravian Mission leprosarium at Sekonge in the Tabora District. Unfortunately, owing to the great size of this region, a relatively small proportion of leprosy patients requiring in-patient treatment are actually admitted to Sekonge and consideration is being given to the establishment of another leprosarium in the western part of that region.

In the Northern Region, out-patient treatment is available at the major government hospitals and patients requiring in-patient treatment are admitted to the government leprosarium at Chazi in the Eastern Region. A new out-patient leprosy clinic was established at Mbugwe by the Medical Missionaries of Mary stationed at Ndareda.

In the remaining regions, leprosy control measures were substantially the same as in previous years.

*The Mission to Lepers.*

*Annual Report of the Work in Southern Asia*, 1961–62

This report consists of 39 pages, with many illustrations, and the general plan is followed of a page or less of description and messages on the local work, e.g. on Andhra, Assam, Bengal West, Bihar, Kerala, etc. Of particular interest is the page of medical statistics as follows:

**Medical Statistics for the Mission's Own and Aided Homes in Burma, India and Pakistan**

*Compared with the figures for the previous year*

| | 1960 | 1961 |
|---|---|---|
| **(a) In-Patients** | | |
| I. In residence on January 1st | 8,971 | 8,853 |
| II. Received treatment during the year | 14,416 | 14,521 |
| *Progress:* | | |
| I. Became free from active symptoms | 2,842 | 2,760 |
| II. Showed improvement | 8,107 | 8,431 |
| III. Remained stationary | 1,833 | 1,886 |
| IV. Became worse | 225 | 196 |
| V. Died or discontinued treatment | 1,409 | 1,248 |
| *Discharged:* | | |
| I. In the course of the year, total | 4,978 | 4,874 |
| II. With no active symptoms | 2,694 | 2,533 |
| III. Of those discharged with no active symptoms, | | |
| (*a*) With no disability | 1,516 | 1,673 |
| (*b*) With some degree of disability | 1,178 | 860 |
| **(b) Out-Patients** | | |
| I. Treated in the course of the year | 66,875 | 71,342 |
| II. Became symptom free | 4,431 | 9,677 |
| III. Improved | 24,575 | 26,108 |

(These returns are not complete in all respects. The figures represent, however, a substantially fair analysis of the results of treatment given during the year.)