Lepr. Rev. (1969) **40**, 186 190

Abstracts

Unsatisfactory results with thalidomide as a specific treatment for leprosy, by J. Sheskin, F. Sagher, M. Dorfman and H. W. von Schrader-Beielstein. *Israel J. Med. Sci.*, 1968, **4**, 901.

This report concerns 24 patients (20 male and 4 female) who received treatment with thalidomide at a dose of 400 mg daily (given in 4 divided doses) for periods of from 3 to 19 months. Five patients improved as regards leprosy, 11 became worse, and the remaining 8 showed no change. The treatment had no antibacterial effect. In all 13 patients who began treatment when in reaction, the acute condition was controlled. The main side-effects noted were constipation, drowsiness, dryness of oral and nasal mucosa, peripheral oedema and psychiatric disturbance.

S. G. Browne.

A talidomida no tratamento da lepro-reaccao (Experiencia efectuada no Hospital Rovisco Pais) (Thalidomide in the treatment of reaction in leprosy), by A. Barbosa and R. Almeida. *Rovisco Pais*, 1969, **8**, 23.

The English summary appended to the paper is as follows:

"The results of the treatment of lepra reaction with thalidomide in 10 male in-patients of Rovisco Pais are presented.

All the patients had lepromatous leprosy and suffered from long lasting severe reactions with cutaneous and nevritic symptoms and fever. Almost all had previously been treated with corticoid drugs.

The initial dose was 300 mg a day (3 tablets), lowering as the patients got better.

Results: (1) Fast recovery of the general condition, followed by the cutaneous and nevritic symptoms, leading to the cure of lepra-reaction in one week. (2) Several weeks after suspending treatment, there were relapses that responded promptly to a new treatment. (3) There were no side effects with the doses used.

For these results, which agree with others referred to in the literature, thalidomide is considered as the most efficient drug for the control of lepra-reactions. It acts faster and more safely than the corticoids. Relapses, if any, respond promptly to a new course of thalidomide."

Histopatologia dos vasos cutaneos na lepra (Histopathology of the cutaneous blood vessels in leprosy), by H. Seabra Santos and M. L. C. de Matos Beja. *Rovisco Pais*, 1969, **8**, 3.

The English summary appended to the paper is as follows:

"From 2000 skin biopsies from leprosy patients, 90 were selected which contained sections of blood vessels. Preparations were stained by different methods, for studying vascular changes.

In lepromatous progressing lesions, from the earliest to the most evolved, the following changes were seen: 1st—Cells loaded with acid-fast bacilli (lepra-cells) in the endothelium. 2nd—Lepromatous endarteritis. 3rd—Lepromatous obliterative pan-arteritis; fragmentation of elastic fibres, fine network of reticular fibres.

In lepromatous regressing lesions, there was progressive substitution of the granuloma by collagen fibres, reticulin thickening and rebuilding of the elastic. As a residual change, after complete absorption of dermal granuloma, acid-fast bacilli were frequently seen, alone or in globi, in the *tunica media* and/or *tunica intima* of otherwise normal-looking arterise.

In dimorphous and tuberculoid leprosy, no significant changes were found in cutaneous blood v sels."

4. **Nasal care in leprosy: a means by which to help prevent deformity,** by C. W. Emerick. *J. Rehab. Asia*, 1969, **10**, 36.

The author issues a timely reminder that regular adequate cleansing of the nose in leprosy patients will reduce the risk of infection of soft tissue, cartilage and bone by septic organisms. While recognizing the role of *Myco. leprae* in specific destruction of cartilage, he has found that mechanical removal of crusts, and daily irrigation of the nasal cavity with ordinary saline solution, will prevent the nasal deformity that foll ws pyogenic infections.

5. **Protecting the patient from himself.** *Wld Medicine*, 1969, **4** (18), 38.

This short unsigned article reports recent work conducted at the United States Public Health Service Hospital at Carville, Louisiana, under the direction of Dr. Paul W. Brand, Chief of Rehabilitation. With the co-operation of the Southwest Research Institute in San Antonio, a polyurethane foam has been developed which is impregnated with microcapsules containing various dyes. The capsules are so made that they rupture when subjected to certain well-defined pressures. It is possible to make capsules that will rupture at different pressures, releasing minute amounts of coloured liquid. When a sock, or glove or prosthetic stump sock, lined with the dye-impregnated foam, is worn by a patient with cutaneous anaesthesia, the colour that appears after use indicates the degree of pressure that has been exerted: green signifies safety, and blue means potential danger. Appropriate measures can then be taken to obviate actual tissue destruction.

At present, the dye-impregnated foam is being used experimentally at Carville, and as a means of educating patients in the use of their anaesthetic extremities. We understand that a group of leprosy patients at Carville are at present making slipper-socks and stump socks, and may soon embark on the making of gloves.

The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 2:

6. **Caractères épidémiologiques de la lèpra en Haute-Volta** (Epidemiology of leprosy in Upper Volta), by H. SANSARRICQ, H. HELIES and B. LAGARDERE. *Méd. Trop.*, 1968, **28**, 327.

This interesting paper is based on reasonably complete and reasonably accurate statistics concerning the 4 million inhabitants of a country stretching from the sparsely-populated thorn-scrub of the near-Sahara in the north to the more densely-peopled and greener savanna of the south. The medical facts are based on systematic and regular examination of the population by medical assistants, who have latterly supplemented their clinical findings by microscopical examination of the skin for *Mycobacterium leprae*. Ethnic and climatic studies complete the picture. The average density of the population is relatively high for rural Africa, being 14.6 per square kilometre (or 37.4 per square mile). In spite of an infant mortality rate of 174 per 1000, the population shows a natural increase of 2% per year, the expectation of life at birth being 31 years. The demographic situation is complicated by the temporary or permanent migration of about 8% of the young men to neighbouring countries, principally the Ivory Coast and Ghana.

Each of the 65 doctors in the Upper Volta has about 62,000 people under his care. The health of the people generally is poor; malnutrition is widespread, and there are deficiencies particularly of animal protein and animal fats, and even of calories.

The number of patients with leprosy is over 140,000, giving a gross prevalence rate of 35.01 per 1000, and ranging from 100 to 8.5 per 1000. The sex rate is unusual: females are affected more than males at all ages (39.20 against 30.85 per 1000), the difference being more marked in children than in adults. The authors attribute this preponderance of women to the greater opportunity the Upper Voltaic woman has of both intra- and extra-familial contacts with people suffering from open leprosy. Another unusual feature is the low child rate; for every 1000 adults with leprosy there are but 55 children. The lepromatous index (probably too low) is reported to be 1.51 per 1000 for males, and 1.27 for females. In both children and adults, males preponderate.

The prevalence of leprosy does not apparently depend on the density of the population, but it is correlated with rainfall—the greater the rainfall, the higher the prevalence. There is much variation between one ethnic group and another, but the reasons for the observed differences are by no means obvious.

S. G. Browne.

Troubles spastiques des membres inférieurs en milieu lépreux mélanésien. A propos de 12 cas observés en Nouvelle-Calédonie (Spastic disorders of the lower limbs among Melanesian leprosy patients. A report on 12 cases observed in New Caledonia), by G. DESMOULINS and G. ZELDINE. *Méd. Trop.*, 1967, **27**, 663.

The authors draw attention to a neurological condition of unknown aetiology appearing only among patients with leprosy in New Caledonia who have been treated within the past 20 years with sulphones. It is essentially an upper motor neurone type of spasticity of the lower limbs, with the usual symptoms (sensation of weight in the legs, difficulty in walking, progressive weakness and spasticity, muscular cramps), and signs (accentuation of the deep reflexes, Babinski response, marked ankle clonus and occasionally patella clonus). In the patients studied, the condition usually appeared a variable time after the cessation of sulphone treatment.

All enquiries into possible causes have so far proved abortive: trauma, infection (including syphilis), nutritional deficiencies, heredity, and anaemia appear to play no part. In the absence of post-mortem material—the disease is not fatal—further lines of investigation are suggested.

The authors reject the possibility that such a relatively common condition (12 cases in 879 leprosy patients) could be due to the extremely rare varieties of damage to the central nervous system reported in leprosy, in which leprosy bacilli are found only exceptionally. It is only since 1956 that the condition has been seen. No case has been reported among the 40,000 inhabitants not suffering from leprosy. They suggest tentatively the possibility that sulphone treatment of leprosy might, in the particular ethnic context of Melanesia, facilitate the emergence of some nerve disorder, recalling the "kuru" of New Guinea or the amyotrophic lateral sclerosis of the island of Guam. [Further investigation of this condition is called for, cluding the search for organic and inorganic toxins.)

S. G. Browne.

8. **BCG vaccination of children against leprosy in Uganda: results at end of second follow-up,** by J. A. K. BROWN, M. M. STONE and I. SUTHERLAND. *Br. med. J.*, 1968, *i*, 24.

This important controlled trial of BCG vaccine in the prevention of leprosy, begun in Uganda in 1960, is carried a stage further by this report.

The present total intake of child contacts of known leprosy patients now numbers 19,169, the majority of whom have been followed up for 3½ years. All the children were allocated randomly to a BCG vaccinated and an unvaccinated group, and at subsequent follow-up examinations precautions were taken to ensure that the observer was unaware of the vaccinal status of the individual children. The protection against leprosy apparently and solely attributable to BCG vaccination is of the order of 87% after 3½ years, as against about 80% after 2 years. Of the 162 cases of leprosy dis-

covered in children with initial tuberculin grades 0 to II, 143 were in the unvaccinated and 19 in the vaccinated group, giving attack rates of 15.8 and 2.1 per 1000 respectively. The efficacy of the protection afforded against the appearance of overt leprosy lesions in this context is thus not reduced after a further period of observation.

The percentage reduction of leprosy infection afforded by BCG vaccination was similar for children who initially had either weak degrees of tuberculin sensitivity or none. On the other hand, the incidence of leprosy in the unvaccinated children varied with the initial tuberculin sensitivity, those with the strongest tuberculin reaction having the lowest incidence of leprosy. Infection with other mycobacteria (apart from *Mycobacterium leprae*) apparently confers little or no protection against leprosy.

Further observation of this trial population is necessary to confirm that the substantial protection afforded by BCG vaccination will persist. If these findings can be shown to be applicable to other situations, particularly where the proportion of patients with lepromatous leprosy is higher, then a potent and practicable control measure will be available for large-scale application in countries where leprosy is still a formidable problem.

[For a preliminary account of this trial see *Trop. Dis. Bull.*, 1963, **60**, 1123; see also *ibid.*, 1960, **57**, 1181; 1965, **62**, 537; for the interim report, see *ibid.*, 1966, **63**, 413.]

S. G. Browne.

he following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 3:

9. **Intradermal tests with mycobacterial substances and normal tissue suspensions,** by D. L. Leiker. *Int. J. Lepr.*, 1968, **36**, 52:

The author sets out to illustrate the fact that in patients with leprosy there is a common pattern of reaction to various mycobacterial substances, and that those with the lepromatous type of the disease are less capable of reacting than are healthy subjects to intradermal injections of mycobacterial suspensions. He proposes the hypothesis that the size of the reactions could depend firstly on a genetically determined potential capability of reacting to a common component of mycobacteria; secondly, on the degree of sensitization to this component; and thirdly, on the quantity of the common component in the test material.

This hypothesis suggests that a substitute for lepromin might be found, that there is little hope of developing a vaccine to immunize against the lepromatous type of leprosy, and that the decline of leprosy in Europe may have been due to a marked reduction in the leprosy-susceptible stock of the population because of a killing mycobacterial disease—tuberculosis.

[See also *Trop. Dis. Bull.*, 1962, **59**, 160, 1068.]

W. H. Jopling.

0. **Streptomycin combined with sulfones in the treatment of relapsed lepromatous leprosy,** by R. C. Hastings and J. R. Trautman. *Int. J. Lepr.*, 1968, **36**, 45.

This paper purports to show that when patients with lepromatous leprosy relapse, in spite of continuous sulphone therapy, a satisfactory response can be obtained by the addition of streptomycin injections. Ten patients were selected for the trial, all having been on long-term sulphone therapy with an average duration of 14.7 years prior to relapse. 1 g of streptomycin was given intramuscularly 3 times a week and oral sulphone therapy was continued. Blood levels of sulphone were determined throughout the trial. Satisfactory clinical and bacteriological progress was recorded during the 21 months of treatment; 8 of the patients developed erythema nodosum leprosum; no toxic effects of streptomycin were encountered.

[The abstracter's criticism of this paper is that the authors omitted the important first step of observing the response to parenteral sulphone before instituting streptomycin therapy, for it is well known that the longer a patient has been free from signs and symptoms of leprosy the more likely he is to neglect treatment. It is significant that blood levels of sulphone were recorded after commencement of the trial, not before.]

W. H. Jopling.

1. **Leprosy control in Australia.** *Med. J. Aust.*, 1967, **2** (27), 1209.

This report, made by the members of the Tropical Medicine and Health Committee (with the collaboration of several locally knowledgeable experts) and endorsed by the National Health and Medical Research Council of Australia, is an authoritative document embodying both factual information and guidance for the medical practitioner and administrator. The definitions take cognizance of recent work on the non-viability of morphologically abnormal forms of *Mycobacterium leprae*, and, in general, reflect modern conceptions of leprosy control. Thus, it is stated that "every attempt should be made by the States and Territories to avoid unnecessary isolation of cases", and "isolation should be applied only to patients with whole or viable bacilli in their smears". [Exception might be taken to the inclusion of "nerve pain or tenderness" as indubitable indications of "activity", since it is recognized generally that this symptom may persist for years in the absence of clinical or bacteriological activity.] It is considered that the protective value of BCG vaccination in leprosy is now established, and that vaccination should be offered to all children born into households in which a parent has leprosy.

At the end of 1966, there were 1557 patients with leprosy in Australia: 792 in the Northern Territory, 549 in Western Australia, and 185 in Queensland. The great majority of the patients are aborigines, but in Queensland the disease is found in all racial groups. Since many patients when diagnosed and notified appear to be suffering from relatively advanced leprosy, a salutary warning is issued that there must be many with active disease who are unsuspected and un-

diagnosed, and that others are in the long incubation or latent period. The recommendation is made that the words "leper", "lazaret" and "leprosarium" should no longer be used. [The enlightened modern outlook shown in this document will commend itself to all.]

S. G. Browne.

following 4 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 4:

12. **L'endémie lépreuse en Republique Centrafricaine** (Leprosy in the Central African Republic), by J. Saugrain. *Med. Trop.*, 1968, **28**, 143.

This detailed report on the anti-leprosy campaign (1959-1965) in the Central African Republic (ex-Oubangui Chari) provides practical information concerning the well-known French methods of attacking leprosy in an area of high prevalence. These consist of repeated whole population surveys, and mass treatment by teams of supervised auxiliaries working either at fixed centres or cycling to visit patients regularly over a pre-determined route. The prevalence rates of leprosy increased from north to south, and from west to east, reaching 10%; the overall figure was as high as 55 per thousand.

In spite of a decline during the past 4 years both in the total number of persons examined and in the proportion of the population responding to the call to be medically examined, there has a gratifying reduction in the numbers of new patients. Interesting features of the report concern the low proportion of patients with lepromatous leprosy (less than 5%), and the relative increase of this form among recently diagnosed patients, the approximately equal male/female ratio and the low child rate (14% in 45% of the population).

Bacteriological examinations are apparently confined to the nasal "mucus" [is this a misprint for *muqueuse* = mucosa?] and to skin biopsies. The nasal "mucus" contains bacilli (whether viable or not is not indicated) in 1-2% of patients, but the skin biopsies are positive in 4-6%.

Treatment consists of weekly oral sulphone for the majority of patients, and bimonthly injectable sulphone for the rest. The average annual dose of oral dapsone works out at about 150 tablets each containing 100 mg of the drug, which is quite adequate, and suggests that an acceptable regularity of treatment (90% of the patients making over 75% of possible attendances) is being attained.

Costly Land Rover treatment runs have been abandoned, as have attempts at providing patients with stocks of tablets to take when weather conditions made regular visits impossible for long periods.

Patients are discharged from treatment 2 years after clinical arrest of the disease, as judged by itinerant teams capable of differentiating between the sequelae of leprosy and active progressive disease. There follows a period of 3 years of observation without treatment, but with regular bacteriological examinations before the patients are finally pronounced cured.

S. G. Browne.

13. **Comparison in man of lepromins prepared from leprosy infections in man and mice,** by P. Draper, R. J. W. Rees and M. F. R. Waters. *Clin. Exp. Immunol.*, 1968, **3**, 809.

"Two methods for preparing a suspension of *Mycobacterium leprae* from tissues of infected mice, using enzyme digestion, are described. The suspensions of mouse "lepromin" were compared with standard human lepromin as skin test antigens in 49 leprosy patients with various types of the disease. The reactions to mouse 'lepromin' were closely similar to those produced by standard lepromin, and patients with lepromatous leprosy failed to react to either antigen. This helped to confirm that the same organism produced human leprosy and the infection in mice and that *Myco. leprae* was the main cause of the lepromin eaction.'

14. **Tratamiento de la reaccion leprosa con talidomida. Primeras observaciones en la Republica Dominicana** (Treatment of the lepra reaction with thalidomide), by H. Bogaert Diaz, G. Herrera and M. Fernández Henriquez. *Revta Dominicana Derm.*, 1968, **2**, 36. English summary.

The authors, in the Dominican Republic, treated 35 patients suffering from lepra reaction with thalidomide [see also *Trop. Dis. Bull.*, 1968, No. 8, abstr. 2232]. Ten patients were treated in hospital; 2 groups (5 and 20) were ambulatory.

The first group included 7 men aged from 27 to 51 years and 3 women aged 40 to 48 years. They received 200 mg of the drug daily in 2 divided doses for 15 days, then a rest of 1 week; this was followed by combined therapy beginning with 25 mg of dapsone (DDS) and 100 mg of thalidomide daily, the doses being adjusted every 15 days so that at 60 days the daily doses of dapsone and thalidomide were respectively 100 and 25 mg; thereafter dapsone alone was used.

The second group, of 2 men each aged 35 years and 3 women aged between 40 and 54 years, were treated on similar lines, but the initial dose of thalidomide was given for 1 week only and the final dose of dapsone was 50 mg only.

The third group, 8 men aged 15 to 54 years and 12 women aged 40 to 51 years, received 100 mg thalidomide only, daily for 1 week, after which it was reduced weekly until a daily dose of 25 mg was attained.

Details of all 35 patients are given. In general, manifestations of reaction disappeared rapidly. Eighteen patients were able to renew treatment with dapsone without further treatment with thalidomide, 3 patients required a second course and 14 needed a maintenance dose of 25 mg thalidomide daily in conjunction with dapsone. Tolerance was good in all patients. The authors note that improvement was more complete and stable in patients having an initial daily dose of the drug of 200 mg than in those receiving only 100 mg.

[The authors refer very briefly to the danger of thalidomide to the products of conception, but it is

noted that while most of the women in this series were aged more than 45 years, a number of them were aged only 40 years. The warning against the inclusion of women in trials of this kind, given by Jopling (see abstract quoted above), needs to be underlined.]

H. J. O'D. Burke-Gaffney.

5. **Cell walls from** *Mycobacterium tuberculosis* **(BCG) as vaccine against** *Mycobacterium leprae* **infections in mice,** by C. C. Shepard and E. Ribi. *Proc. Soc. Exp. Biol. Med.*, 1968, **127**, 517.

The cell walls from BCG used in this study were prepared by the method described by Ribi *et al.* [*Bull. Hyg.*, 1966, **41**, 1146]. After lyophilization 100 mg of the preparation were mixed with 0.48 ml 7-*n*-hexyloctadecane and suspended in 40 ml saline containing 0.2% Tween 80; the mixture was then heated at 65°C for 30 minutes, and was referred to as the oil-treated vaccine. A similar vaccine was also prepared but without the treatment with oil.

Groups of CFW mice were vaccinated either intravenously or intradermally with the oil-treated vaccine, with the vaccine without oil-treatment, or with viable BCG, and after 34 days the mice were inoculated into the footpad with 5×10^3 *Mycobacterium leprae*. At 6 months, when the count in unvaccinated control mice had reached more than 10^6 bacilli, the number of bacilli in the vaccinated mice was determined and again 3 months later; these counts were made on pools of up to 8 mice.

The results showed that intradermal vaccination with the oil-treated cell wall preparation gave less protection, as judged by depression of multiplication of the leprosy bacilli, than did intravenous vaccination, and that at 6 months the degree of protection was similar to that produced by viable BCG, although at 9 months it was somewhat inferior. Cells walls without treatment with oil afforded no protection.

The amount of local induration produced by the intradermal vaccination was less with the oil-treated cell wall preparation than that produced by the viable BCG vaccine; the enlargement of the draining lymph glands was also less. Intravenous injection of the oil-treated vaccine and the viable BCG produced pulmonary nodules with a peripheral zone of macrophages.

S. R. M. Bushby.