# ABSTRACTS

*A Survey of Leprosy amongst the Lovale Tribe in the Upper Zambesi Basin, Northern Rhodesia,* **J. T. Worsfield,** Central African J. of Med., III, Nos. 9 and 10, Sept. and Oct. 1957, pp. 359-365 and 401-406 resp.

This paper is in two parts, with 4 illustrations in the first and 7 in the second. The Lovale tribal area comprises about 8,000 sq. miles (20,720 sq. kilom.) with a population density of 2 per sq. mile (0.8 per sq. kilom.). It is largely a sandy dry country inundated for 3 months of the year by the Zambesi. Nearly all the villages lie along the banks of this river, and contain 20 to 50 people living a primitive life. A child sleeps with its mother until weaned, then is taken over by other female relatives. There is no fear of leprosy. The diet is scanty, deficient in protein, and based on cassava. In a survey of 5 months duration Worsfold visited every village and examined each individual, to a total of 20,148 people. The general leprosy prevalance was 11.85 per thousand, and 65% of all cases admitted to having a near relative with leprosy. The lepromatous rate was 23.75%. There was a low childhood rate, and a steadily increasing prevalence with the advancing age groups. The author supports the view that transmission is mainly through the skin, either intact skin or skin abrasion. He gives a clear account of the clinical features of leprosy in this region, and emphasizes the symmetry of lesions in lepromatous cases. The generally excellent result of oral DDS treatment are described, which has been in use in the area since 1950.

*The Significance of Experimental Murine Leprosy and Screening Test in Studies of Chemotherapeutic Agents for Leprosy,* **S. Nishimura,** Med. J. of Osaka Univ. VII No. 4, March 1957, pp. 735-776, 9 figs., 5 Tables.

He has studied the chemotherapeutics of murine leprosy since 1942. In the beginning it was thought that agents effective against murine leprosy would also act against human leprosy. Recently it has become clear that this is not necessarily so, and biological studies of the 2 diseases have revealed many points of difference. To draw analogies for human leprosy from experiments with murine leprosy is mistaken. The first step in a true advance would be to find an agent which would be effective both in murine and human leprosy, first collecting as many agents as possible which have an effect in murine leprosy. New agents with the double action have not yet been found and this may be only a mirage. However there may be some common point in the metabolic processes of the human and murine leprosy bacilli, and another hopeful line is to carry on with the screening test that he has devised. The results of chemotherapeutic tests in murine leprosy are given by the author,

both for his own department and for other workers, on hydnocarpus oil, cepharanthin, promin, DDS, etc., and Table 2 gives a comparative study of the therapeutic action in tuberculosis, leprosy, and murine leprosy.

Nuevos Aspectos y Problemas Actuales de la Lucha Contra la Lepra: *(New features and present-day problems of the leprosy campaign).* **Félix Contreras,** Revista de Leprología, Fontilles IV, No. 3, June 1957, pp. 103-122.

Great advances in leprosy control have been made in the last 15 years, not least in Spain, but Dr. Contreras notes a certain inquietude, in that our highest hopes have not been fulfilled. In Spain they share this inquietude, and intend to revise and rethink their work, and press on to attain perfection. He describes the origin and foundation of the Fontilles work by Padre Ferrís, and the collaboration of Guillén and La Portilla. The results have been highly satisfactory. Though it is too soon to proclaim the decline of prevalence, lepromatous cases grow less in proportion to the non-lepromatous, more and more child cases are found and less and less adults, patients attend at an earlier stage of their disease, and the advanced deformities are less common. The number of cases in Spain was estimated in 1943-47 as between 4,000 and 5,000, and they think this about correct for the present time. Improvement in clinical condition of the majority of patients has been very striking, such as in eye and throat complications, and secondary ulcers of the extremities, and deformities, and the psychic state of the patient is much calmer and co-operative. The humane and friendly attitude of the doctors and attendants has played a great part in the psychic change, as well as the expectation of cure by the sulphone drugs.

The Review ' Fontilles ' was' founded in 1944 and full contact has been kept with the world of leprosy. New leprosaria were founded in Trillo in 1942, and in other places. Sainz de Aja in 1943 enunciated the principles of leprosy control in Spain, and was hopeful of winning the battle against the leprosy endemia in 2 or 3 generations. Contreras in later works amplified these and introduced points for emphasis. In 1947 promin was first used in Fontilles: it and the later sulphones had a good effect. In 1953 the VI International Congress of Leprosy was held in Madrid, when many visitors studied the Spanish leprosy campaign and commented favourably on it.

*New features.* The medical, public health, and social aspects of leprosy have changed completely. The early curable forms of the disease are more readily diagnosed, and classification of all forms is better understood. Early and even later cases respond to the sulphones and the disease is arrested. Today we know that

leprosy is less contagious than tuberculosis and contagion requires a long period of living contact, and is less marked towards adults. The lepromatous cases are the most infectious, but even in them the infection can be terminated in time. In effect, leprosy today is a disease which is one of the most easily avoidable infections. Social conditions have also improved greatly, both for the patients and their dependants, and rehabilitation of former patients into civic life now receives a great deal of attention. Children of leprosy patients and child contacts are also cared for.

*Presend-day problems.* The solution of ancient problems and the new orientation have led to new problems. It has become clearer that *dispensaries* form the chief element in the leprosy campaign. These may be exclusively for leprosy in countries of high leprosy incidence, or polyvalent in countries of least incidence. In countries like Spain, with median incidence, use can be made of the Skin Dispensaries. For all dispensaries, however, one must not count on the patients to come; they must be sought out in their homes. Each dispensary must have transport, and in areas of heavier incidence must have a *mobile team*. The salaries for workers in the Skin and Venereal Diseases dispensaries which now undertake leprosy work should be augmented. *Sanatoria or leprosaria* of the ancient pattern, in which segregation was the only good obtained, are not necessarily to be condemned, for some countries did seem to attain a decrease in the endemic when they had them. Nowadays prophylaxis by means of treatment and by mass campaigns threatens to extinguish the leprosaria. If we understand leprosaria as dumps of patients segregated by force, Contreras thinks we should certainly close them. If we understand them as sanatoria, we should certainly continue these, because they are most valuable for the proper study of the disease and for skilled treatment and the prevention of complications. Admission should be voluntary, and open to all lepromatous cases, and all other bacilliferous cases, such as indeterminate and borderline and reactive cases. The home conditions of many patients are poor, and sanatoria offer definite advantages to such cases, as well as a sure way of removing infection from the family. All restrictive legislation should be abolished. In Spain legislation makes no difference between leprosy and other diseases. The less infectious types of leprosy can be treated at home, but they should not be barred from the sanatoria if other reasons exist, such as bad treatment by the neighbours, or membership of a family where other cases exist. Separate sanatoria for males and females are not advisable just now, when treatment takes a long time, but when in future the duration of treatment is shortened, it would be worth while. Discharge of patients from sanatoria on reaching arrest from their disease should

not be too hasty; a period of " consolidation " should intervene, and later when they go, a long period of supervision should be arranged. Propaganda is necessary to ensure a happy return to civic life. A talk between the leprologist and the employer is very useful, and also a talk to the work-mates. Previous plastic and reconstructive surgery is a great help in securing rehabilitation. It is most important in cases where the nose has been destroyed. *Preventoria* still remain of great value, for leprosy is a familial infection very largely, and child contacts must be cared for and given all the protection against the disease that can be given. Some of these children can be cared for by relatives or foster-parents, but preventoria still remain necessary for many. There has been a swing of opinion against preventoria, but it all depends on the national conditions. In Spain they still need them because there prejudice has not decayed enough to allow of all children being cared for by relatives or ordinary colleges. Those like Chapinería have saved many hundreds of children from becoming victims ot leprosy, and at the same time have fitted them for civic life. Children with early lesions and children with low resistance to leprosy have been rendered safe. Some children free from the disease from the beginning are later transferred to ordinary colleges or relatives outside the focus of disease. By the time of puberty all types are ready to resume normal life. *Treatment of leprosy* in Spain is based on the use of DDS, both orally, and by I.M. injection in oily suspension. As the latter is given weekly the author thinks it would be suitable for mass campaigns in countries of high endemia. The search for other treatments still goes on. *Work* is important to all patients according to their clinical state; it is beneficial both psychically and in helping towards cure; this importance of work should not be forgotten for out-patients. *Social assistance* to patients and relatives is also important, and is available in Spain. The climate of opinion towards discharged patients still hinders rehabilitation for some; in difficult cases where patients cannot make headway at home, they make place for them in the sanatoria again, perhaps in a separate section. *Marriage of patients* is a subject for much thought. The general trend is not to interfere with the marriage bond or contraction of it, though delay may be advised because of the probability of the arrest of the disease in a fairly limited time, but all cases are to be considered on their merits. All cases should have explained to them the full implications of the disease, as far as our present knowledge goes. *Propaganda* to explain the nature of leprosy to the people must continue, and a special campaign to the cultured classes is of value, so that they also can act as propagandists. Writers in particular need a special approach to persuade them not to use the word

leprosy in its horror context.

*The Chemotherapeutic Activity of Triton WR 1339 and Macrocyclon in Murine Leprosy.* **R. J. W. Rees,** Amer. Review of Tuberc. and Pulmonary Diseases. **76** No. 5, Nov. 1957, 915-916. (Letter to Editor).

Rees refers to the report of Kátó and Gözsy (Am. Rev. Tuberc. 1957, **75,** 684) confirming the powerful antituberculous activity of Triton A-20, which is a 25% aqueous solution of the solute Triton WR 1339, in the mouse and guineapig. This had been reported earlier by Rees and others (Cornforth, J. W. *et al.* Nature, London, 1951, **168**, 150; Rees, R. J. W. Proc. Roy, Soc. Med. 1953, **46,** 581: Solotorovsky, M. and Gregory, F. J., Am. Rev. Tuberc., 1952, **65,** 718). Favourable results agains murine leprosy in the rat or mouse on the part of the Triton type of surface-active agents can now be reported by Rees.

A partially purified suspension of *M. lepraemurium* obtained from homogenized rat lepromata was used by intravenous injection to infect mice. This method produces a fairly standard type of systemic infection bearing most on the liver, spleen, skin, and heart. To assess the progress of the infection macro- and microscopic examination of the various tissues was carried out, also bacillary counts of stainable acid-fast bacilli on homogenates from the liver and spleen. From the day after infection, twice weekly subcutaneous injections were given of Triton WR 1339 and Macrocyclon; the latter is less toxic though chemically similar. They showed high therapeutic activity in doses of 5 mg. for 20 to 27 weeks.

Rees mentions that Kátó and Gözsy failed to show any activity against murine leprosy infection in the rat or mouse. They used larger doses but assessed the result after only 6 to 8 weeks of treatment by the subcutaneous route in rats and intraperitoneal route in mice. The apparently contradictory results may be due possibly to the different routes of infection, but Rees thinks it much more likely that the favourable results in his work are due to the longer course of treatment.

Hence it seems that other mycobacteria than *M. tuberculosis* can share in the therapeutic activity of surface-active agents of the Triton type. Present study also suggests that the monocyte is the site of action of these agents *in vivo,* since murine leprosy is caused by an obligate intracellular organism infecting cells of the reticuloendothelial system.

*The Antituberculous Activiity of Ethyl Thiolesters,* by **G. E. Davies** and **G. W. Driver,** Brit. J. of Pharm. and Chemotherapy, **12,** No. 4, Dec. 1957, p. 434-437.

The authors refer particularly to diethyl dithiol*iso*phthalate

among the thiol esters. The thiol esters have been the most promising of the antituberculous derivatives of ethyl mercaptan, as reported by Davies, Driver *et al.* in 1956, and Solotorovsky *et al.* later in 1956.

They selected diethyl dithiol*iso*phthalate (ETIP) for study in mice because it seemed the most suitable of the series for later clinical trial in man. In the experiments now reported they found that ETIP in mice by *subcutaneous injection* of 500 mg/kg. was as active against tuberculosis as the best of the previously tried derivatives of ethyl mercaptan (diethyl dithiolcarbonate), and it had the advantage of being almost odourless (unlike diethyl dithiolcarbonate). Further, as it was noted that the application of ETIP to the intact human skin resulted in an odour of ethyl mercaptan in the breath, clearly indicating *percutaneous absorption,* experiments on infected mice were by this method carried out, and showed a high effectiveness of ETIP. The compound was also found highly effective against intracorneal tuberculous infection in mice, as shown also by Naguib and Robson (1956) for murine leprosy intracorneal infection.

ETIP action against an established infection was studied and found to be high. *Weekly doses* of ETIP were also studied; a marked antituberculous effect was obtained with a single subcutaneous dose given on the day of infection and still larger effects were obtained by giving one or more further doses at weekly intervals.

*Combined treatment* with INH proved much better than ETIP or INH alone, and a single dose of ETIP markedly prolonged the life of infected mice that had relapsed and were about to die after treatment with INH. There is no cross-resistance between INH and ETIP. When in the experiments ETIP-resistant strains were produced and used for infections, INH was found to be fully effective against them. The effect of ETIP on a streptomycin resistant strain was not tested, since earlier it had been found that other ethyl mercaptan derivatives were effective against infections caused by such strains.

A possible *mode of action* of ethyl mercaptan is that it interferes with a biological methylating or thiomethylating system. Some support was found for this hypothesis. The development of drug-resistance suggests that at least part of the action is exerted directly on the bacteria and not solely through the defence mechanisms of the host. It may be that a hitherto unknown biological system is involved.

*Limited Multiplication of M. lepraemurium in Tissue Culture.* **R. J. W. Rees** and **P. C. Wong.** Nature, **181,** No. 4605, 1st Feb. 1958, pp. 359-360.

Rees had previously shown that the generation time *in vivo* of the organism of rat leprosy was 13 days, and the authors devised a method for counting the total number of bacilli per culture before and after cultivation. The first attempt at culture they made on macrophages, but found no multiplication after 80 days, though bacilli recovered from some of these cultures were still infective. Experiments were now directed to tissue cultures on spleen explants obtained from previously infected animals. A mouse was infected intravenously with *M. lepraemurium* and 8 weeks later the spleen was removed and cut into uniform explants of 1 mm. The explants were put out, 6 per culture tube lined with plasma clot to which was added 1 ml. of medium containing 20% horse serum, 5% chick embryo extract, and 75% Hanks' balanced salt solution. Random groups of culture tubes were formed in two categories, those with no added antileprosy drugs and those to which streptomycin and INH were added, and the tubes were incubated at 37°C in roller drums and the medium changed twice weekly. By a modified Breed technique a count was made of equivalent standard samples of homogenates from each culture at 24 hours and at 15 and 29 days, after dispersal of the bacilli by ultrasonic vibration in each case. The results showed a highly significant increase in the number of bacilli in cultures free of streptomycin or INH, by the 15th day of incubation; after a further 14 days there was no increase. There was no increase in cultures which contained high concentrations of the drugs.

In 5 experiments by these methods limited multiplication *in vitro* of *M. lepraemurium* has been demonstrated. The rate of multiplication *in vitro* corresponds closely to that *in vivo* in the mouse. Hanks and colleagues have recently obtained much the same results. The confining of the multiplication to the initial period of cultivation seems to be due to release of the bacilli in increasing numbers from the infected cells as they degenerate, thus exposing the bacilli to relatively high concentrations of serum; (it has been shown by Hanks and Gray that this inhibits their endogenous metabolism). It looks as if success in continued culture will require a regular supply of healthy cells in a medium with low concentrations of serum. The authors continue work on methods to provide these culture conditions.

*Prophylaxie et Thérapeutique de la Lèpre* by **R. Chaussinand,** 1958, is a booklet of 98 pages published by Bibliotheque de Thérapeutique Médicale, Paris (G. Doin et Cie., 8 Place de l'Odéon, Paris VI).

This is a clear and concise work of great practical value, with useful bibliography and index. Chaussinand writes in beautiful, limpid, and unequivocal French, which brings an added pleasure

to the reading of this booklet. He gives a balanced account of all the modern aspects of prevention and treatment of leprosy, and there is a section on bacteriological methods and the lepromin test. Every section will be read with interest and profit. Because there is a special interest nowadays in BCG, the section dealing with *BCG vaccination in the prevention of leprosy* (Section D, pp. 25-27) may be summarized as follows:—

Because BCG vaccination produces a sensitivity to lepromin, it is tempting to assign to it a considerable influence in the prevention of leprosy, but many years of trial of BCG are needed before proof is available. Chaussinand thinks, however, that it should be widely used in tropical and subtropical countries; even if it turns out to be of little value in the prevention of leprosy, it will not have failed to be valuable against tuberculosis. The Brazilian method of BCG vaccination by the oral route (a single dose of 200 mgm. or 3 doses of 200 mgm. at intervals of a week) has the advantage that a tuberculin test is not necessary; but in a mass campaign large amounts will be required and the giving of 3 doses at weekly intervals might cause difficulty. The intradermal route is more precise and economical; however a preliminary tuberculin test is necessary, and a small chronic ulceration may develop in the site of the injection of BCG. The method of vaccination by skin scarification through 2 to 4 drops of the vaccine containing 75 mgm. of BCG per cc. is less precise than the intradermal method and also requires a preliminary tuberculin test. The simplest control experiment on the value of BCG would be to give it to 50% of the newborn of each sex, leaving the others unvaccinated. Also one could vaccinate 50% of the whole population, or 50% of the children, in an area of high prevalence of leprosy, leaving the rest as controls. One would have to remember for the two groups that leprosy might appear more than 3 years after the vaccination, and take care to eliminate those who were already incubating leprosy at the time of vaccination; annual examinations would need to be made of all subjects in both groups. The amount of protection against leprosy given by BCG cannot be other than relative. On the other hand it is highly probable that subjects of infection by the leprosy bacillus or virulent tuberculosis bacillus better resist the leprosy infection than those merely vaccinated by BCG. The attenuated bovine type bacillus of BCG can only maintain itself a relatively short time in the vaccinated subject. It would not be wise to believe that a subject of BCG vaccination is incapable of contracting leprosy, but at least it is reasonable to believe that there is an increase in resistance.