

REVIEWS.

Leprosy in India. Vol. XXI. October 1949. No. 4.

The articles of association of the Hind Kusht Nivaran Sangh (the body appointed to take over the function of the Indian Council of BELRA) are given, together with a list of those forming the Governing Body, and the rules and regulations of the new Association.

Diseases Simulating Leprosy, by L. M. Ghosh. A short resume of the various diseases which may be mistaken for leprosy and information appropriate to their differential diagnosis.

Prevention of Deformities in Leprosy, by G. O. Teichmann. A discussion of various orthopaedic measures used in the combatting of deformity due to leprosy.

Report of the Study Tour on Leprosy, by Dharmendra. A detailed report of the world tour made by Dharmendra in 1948. The conclusions drawn by him were that whilst the research work in India compares favourably with that in other countries yet in the sphere of control and prophylaxis there is much to be learnt from other countries, notably Brazil.

Report of the Leprosy Research Department, School of Tropical Medicine, Calcutta for 1948. Investigations have continued into the use of the sulphones, the two studied being diasone and sulphetrone. Of 12 patients on diasone treated for a maximum period of 32 months, only one became negative bacteriologically though marked clinical improvement was seen. Of the 28 cases on sulphetrone, treated for a maximum period of two years, only one has become negative, although clinically the cases have shown marked improvement.

There were no serious toxic effects from either drug. Both drugs were administered orally and the regimen found most satisfactory was to give a two months' course of treatment followed by one month's rest.

The limitations of sulphone treatment are those of cost, lack of relief of nerve pains, lack of improvement in neural symptoms such as loss of sensation and deformity.

A study of nose and throat lesions in lepromatous leprosy has been commenced. Clinical and bacteriological evidence of infiltration are very common in the nasal mucosa but much less so in the naso-pharyngeal, pharyngeal and laryngeal mucosa. Biopsy

material removed from the epiglottis showed lepromatous granuloma.

Histological studies made in the Department tend to support the view that histological findings cannot be made the primary basis of classification. The report states that because the histological picture is not confined to a particular type, and also shows variations in the same macule with clinical activity, histological terms cannot be used as synonyms to indicate the clinical varieties of leprosy. It is also stated that the long term study of atypical histological features (e.g. marked vacuolation of epithelioid cells, non-infiltration of nerves in an otherwise tuberculoid histology) has shown that no special significance need be attached to these features. Such atypical features are caused by variations in type.

International Journal of Leprosy, Vol. 17, No. 4 (Oct.-Dec. 1949).

Traitement de la Lèpre par la "Sulfone-Mère" (Diaminodiphénylsulfone), by Floch, H. and Destombes, P. The authors, in the light of their experience with diasone and promin, discuss the drawbacks of sulphone therapy. Their chief objections, inter alia, are that the price of the complex sulphones is high, and that in the case of promin, daily intravenous injections have to be given. They refer to the work of Rist in treating tuberculous ulcers with D.D.S., and to his suggestion that the complex sulphones owe their activity to the D.D.S. liberated from their molecules. After discussing *in vitro* and *in vivo* activity, the authors refer to "il est remarquable, par exemple, que la promin est bien moins toxique par la voie veineuse que par la voie buccale qui libère beaucoup plus de sulfone-mère." The reviewer would point out that the reason why promin is not toxic when given intravenously is that (1) it is very rapidly excreted by the kidney; (2) it is excreted largely as promin, i.e. that little breakdown to D.D.S. occurs in the human body.

The authors used D.D.S. (in tablets of 10 and 20 mgm.) for oral administration, and used a suspension in water for intramuscular injection. The daily oral dosage commenced at 40 mgm. and increased by 20 mgm. weekly. Treatment was given for six days every week. The urinary excretion on a dose of D.D.S. equal to 200 mgm. per day was 161 mgm. (80%). Following the cessation of therapy, traces of D.D.S. were still in the urine for 7 days. The maximum oral dose aimed at was 200 mgm per day. This does not represent the maximum dose capable of being administered, the authors say. A suitable parenteral treatment has not yet

been worked out, but some cases receive 600 mg. twice a week. Toxic effects were not severe. The anaemia produced responded well to iron treatment. Clinical and histopathological results were similar to those obtained with the proprietary sulphones.

Estudio Comparativo entre la Lepromina Bacilar (Fernandez) y la Lepromina Cadavérica (Campos), by Bosombrio, G. and Gatti, J. C. The authors consider the effect of sulphone treatment upon the supply of lepromin. They confirm the work of Campos, who has used lepromin obtained from the viscera of corpses. The lepromin prepared (especially from liver and spleen) was stated to be better than that obtained from the usual sources, i.e. cutaneous nodules.

Comparative Studies of the Cardiolipin Antigens with the Regular Antigens in the Kolmer Complement Fixation and the Kahn Precipitation Tests in Leprosy, by Ross, H. and Gemar, F. The use of cardiolipin antigen in the Kahn Test for syphilis is suggested for use in leprosy. The cardiolipin antigen has a greater specificity, less false positives being encountered. It does not however remove the anomaly of positive Kolmer and Kahn reactions being obtained from non-syphilitic but leprous sera.

A Propos du Diagnostic Différentiel Histologique de la Lèpre Lépromateuse et de la Lèpre Tuberculoïde, by Noel, R. and Marie-Suzanne, Soeur. The purpose of this article is to indicate and emphasise the fundamental morphological differences, from the histological point of view, between the lepromatous and tuberculoid case. The authors suggest that these differences are—(1) Giant cells only form very slowly in the lepromatous case, and always contain leprosy bacilli. The nuclei are distributed throughout the protoplasm as in the macrophage. Epithelioid cells are not seen, only a collection of various lymphocytes and histiocytes; (2) tuberculoid leprosy giant cells are seen from the beginning. They are present in large numbers and they never contain bacilli. The nuclei are peripheral in distribution and the cells at first present a typical tuberculoid picture of inclusion in a mass of characteristic epithelioid cells; (3) Polymorphonuclear eosinophiles are a constant characteristic feature of tuberculoid leprosy—they are not found in lepromatous histology. Ten microphotographs illustrate the article.

Leprosy in Fiji and the South Seas, by Austin, C. J. A historical and geneological survey of leprosy in the South Seas with special reference to Makogai, for which settlement statistics of types and distribution, etc. are given.

Leprosy in Niue Island. A Note on the History of the Disease, by Dempster, G. O. L. A genealogical study of the growth of leprosy in a small island.

The International Leprosy Association. An article dealing with the constitution and by bye-laws of this Association.

The Pharmacologic and Chemotherapeutic Action of some new Sulphones and Streptomycin in Experimental Tuberculosis, by Smith, M.I. et al. The authors examine the pharmacological characteristics of promin, sulphetrone and a new half-sulphone, 4-amino-4' hydroxyethylaminodiphenylsulphone. From complex degradation studies the authors produce evidence to show that whilst promin and sulphetrone are metabolised to D.D.S. in the body, HES (hydroxyethyl sulphone) is not so degraded. Further, this compound has a good chemotherapeutic activity in experimental infections in animals. HES is preferentially distributed in the liver, kidney, lungs and spleen, and thus blood levels following oral administration are low. The authors demonstrate the point that the intravenous toxicities of promin and sulphetrone can be considered to be equal when computed on their D.D.S. equivalents.

The Silvering of Lepra Bacilli in Tissues, by Blanco, L. F. and Fite, G. L. The authors give details of a method for staining (silvering) bacilli in histological sections. This method they claim yields tissue with a minimum of distortion, and thereby presents some new aspects of the pathology of leprosy. The method is, however, time consuming (a minimum of 32 days being required) and would not therefore appear to be practicable for routine histological studies. However, due to the negligible distortion position relative to the surrounding tissue elements. By study of what occurs in this process, the bacilli may be studied in their true section of leproma stained by their technique, the authors suggest that some considerable revision is necessary in our concepts of the morphology and histology of the leprotic process, this in particular applying to the globus. The article is illustrated by eight microphotographs. It is to be hoped that further work will be presented on this subject.

Leprosy in India. Vol. XXI. October 1949. No. 4.

From 'Cities of Refuge' to 'Villages of Hope,' by W. Bailey. A thoughtful article upon the development of the leprosarium in India.

Massage in Leprosy, by W. F. Joseph. A short note giving details of massage movements useful in leprosy.

Diet and Susceptibility to Leprosy, by Dharmendra. A comprehensive survey of the role of diet in connection with susceptibility to leprosy. The scope of this article, which has 76 references, is wide and as such unsuitable for abstracting. The author concludes that there is evidence that malnutrition plays a role in predisposing to leprosy but that this evidence is not conclusive.

Leprosy in India. Vol. XXII. January 1950. No. 1.

Two Cases of Leprosy treated with Para-aminosalicylic Acid, by Dharmendra. A report of the treatment of two cases of lepromatous leprosy treated with P.A.S. (sodium salt). Treatment was commenced at 20 gramme daily but at this dosage gastric intolerance was manifest and the dose was reduced to 15 grammes daily. This was generally well tolerated and continued for 30 weeks. The total dose of P.A.S. administered was 3,500 g. in one case and 2,500 g. in the other.

Bacteriological improvement was not seen and clinical improvement was not equal to that produced by the sulphones.

Intradermal Reaction with Lepromin Inside and Outside the Leprous Macules, by Dharmendra and N. Mukherjee. Owing to contradictory reports of the variations in the lepromin test outside and inside and on the edge of macules, the authors undertook a detailed study of this subject. Using the refined lepromin of Dharmendra they injected 0.1 cc intradermally both inside and outside macules of both the lepromatous and tuberculoid type. Only the early reaction was read, the 24 hour period being used. One hundred and six macules of different varieties were used—50 lepromatous, 50 neural, 6 tuberculoids. The neural macules were further subdivided into simple, Tb minor, Tb major, Tb reacting.

The results indicate that in the lepromatous macule no marked difference is seen in the reaction *in* the macule compared to that *outside* in normal skin. Where a difference is seen it is more frequently stronger outside the macule than in. In general the reaction is usually negative.

In the majority of neural macules the reaction is generally stronger inside the patch than outside. In the neural macules the thickness of the macules appreciably influences the degree of reaction to lepromin, the reaction being more marked with the thicker patch.

Marked variation in response to lepromin injected in different parts of the body was not generally the experience of these workers.

International Journal of Leprosy, Vol. 18, 1, Jan.-Mar. 1950.

Sulphone Therapy in Leprosy: A Three Year Study. Sloan, N. R. et al. A report of the treatment of 346 patients with promin, diasone and promizole. The maximum daily doses were: promin 5 gm.; diasone 1.2 gm. and promizole 6 gm. A week's rest was given after every two weeks' treatment with promin, and after every three weeks' treatment with diasone and promizole.

Haemolytic anaemia was said to be common (though no evidence to suggest that anaemia was haemolytic was given) necessitating blood transfusions in a large number of patients. This anaemia was more prone to develop in females than males. Lepra reaction occurred in 99 per cent. during treatment. Twelve patients developed cutaneous eruptions, 9 patients developed polyneuritis, often severe and crippling. Nausea was reported as common. The clinical results were those now usually accepted. Fifty cases were granted a temporary release (presumably bacteriology negative), and definite improvement occurred in 83 per cent. of all cases treated. The authors feel that tuberculoid cases respond well to treatment, that early treatment is desirable, that pregnancy is no bar to treatment, and that the death rate is greatly reduced by treatment. No evidence as to the best sulphone for treatment is available.

Transformation of a Case of Tuberculoid Leprosy in reaction to the Lepromatous Form by Schujman, S. The author first reviews the literature upon the question of the transformation of tuberculoid leprosy to the lepromatous form. He concludes this review with the observation that transformation of a known reactional tuberculoid to lepromatous has never been reported, nor has he himself observed it. With regard to reactional tuberculoid cases, the only well documented cases are those of Velasco. He then goes on to give in detail a report of the transformation of a reactional tuberculoid into a frank lepromatous form. This article should be consulted in the original by those interested in the subject. The detail presented does not permit of abstraction. Photographs and photomicrographs are included.

Tar and Kerosene Paint for Tinea complicating Leprosy. by Muir, E. and Roy, A. T. The authors advocate the use of a tar and kerosene solution for the treatment of tinea. Those workers in tropical climates will appreciate how difficult it usually is to clear up tinea infections in cases of leprosy. This remedy, the effectiveness of which is shown by photographs, should prove

invaluable. Tar should be shaken with about five times its volume of kerosene, and the solution painted on to the affected parts once daily. The application should continue for a month or longer.

Leprosy and its Control in South Africa, by Winter, P. D. An article giving details of the legislative measures in force in S Africa, the policy of the Health Department, the organisation of the various leprosaria, and the incidence and type of leprosy within the Union of S. Africa.

Three Factors which may Influence the Experimental Transmission of Leprosy, by Hanks, J. H. A highly technical laboratory study of the transmission of the leprosy bacillus in rats and mice. It was found that bacilli from either a rat or mouse source were handicapped when transmitted to the heterologous species. When bacilli, plus blood cells, were inoculated, the lesions failed to develop or were delayed. Such lesions as were produced were equalled or surpassed by lesions produced from bacilli, free from tissue material, representing 100th of the amount of those injected with cellular material. Rats were shown to acquire a considerable degree of resistance by multiple cutaneous inoculations.

Rat Leprosy: Susceptibility of the Black Mouse (American race) to the Stefansky Bacillus, by de Souza Araujo, H. C. The author reports that the strain of mice (*mus musculus*) black race, C.57 ex Rockland Farm, U.S.A. is very susceptible to inoculation with Stefansky's bacillus. The bacillus also appears to cause a far more virulent infection in this mouse than in the rat. It is also reported that from the lesions induced in these mice, acid-fast bacilli have been cultivated (on Loewenstein's medium). Other reports on this subject will be eagerly awaited.

Diffuse Lepra: The Lucio Form of Lepromatous Leprosy. Report of a Case by Obermayer, M. E., et al. (Reprinted from the *Journal of Inv. Dermatology*, 12, (1949). 243.) An interesting report accompanied by photomicrographs of the unusual variety of lepromatous leprosy first described by Lucio in 1852. This case, occurring in a resident of S. California, is of particular interest, in that the case history is completely presented to confirm the diagnosis of the Lucio form in a patient not resident in any of the areas previously associated with this type of leprosy.

Positive Bacillary Findings in the Skin of Contacts of Leprosy Patients, by Figueredo, N. and Desai, S. D. (Reprinted from the *Indian Journal of Medical Sciences*.) A remarkable article, the

findings of which, if substantiated, will fundamentally affect many aspects of leprosy. Briefly the authors, with a new technique for making smears, were able to demonstrate bacilli in 10 per cent of 254 contacts of leprosy, who had no clinical evidence of the disease. The number of bacilli found varied from 4 to 25 per 100 fields—most workers would describe this as a 1+ smear. Their technique differs from the usual (Wade), resembling that earlier advocated by Muir, in that an actual piece of skin is excised and smeared on the microscope slide. Whereas Muir's method was to snip a piece of skin with scissors curved on the flat, the method used by the authors was to remove a wedge-shaped piece of skin with a scalpel—in fact a small biopsy. At least half an hour was spent in the microscopic examination of each slide. Four of the contacts in whom bacilli were demonstrated later (7-18 months) developed hypopigmented macules. The significance of the above article will be appreciated by all leprosy workers, and the confirmation of this report most eagerly awaited.

Studies of Murine Leprosy, by Hadler, W, A. and Mauri, A. C. (Abstracted from the Revista Brasileira de Leprologia, 16 (1948) 139. A comprehensive study of the pathogenesis and evolution of murine leprosy. The article is extremely well documented, and includes 91 references. The authors studied the evolution of *M. leprae muris* injected intraperitoneally, and came to the conclusion that this route possesses many advantages, especially when chemotherapeutic studies are contemplated. Peritoneal inoculation gives rise to a generalised infection which presents constant and regular lesions, showing no tendency to spontaneous retrogression. Twenty-four photomicrographs illustrate the article. The only comment the reviewer has to make is that in the preparation of the bacillary suspension for inoculation, use is made of a triturated mass of internal organs and nodules rich in bacilli. It would surely not be a difficult task to centrifuge off the coarse cellular matter and use for the inoculation the supernatant fluid containing only bacilli?

Leprosy in India. Vol. XXII. April 1950. No. 2.

Bacterioscopic Assessment of Progress in Leprosy, by E. Muir. The author discusses the technique of bacteriological examination in leprosy from the standpoint of having a criterion by which progress can be estimated. From his experience he gives advice on the selection of sites, the number of smears to be taken, the method of making smears, their staining and the microscopic

examination of slides. It is the author's practice to make five smears on one slide, assess the positivity on a scale of from plus $\frac{3}{4}$ to plus 4 and then to calculate the mean of the five smears, designating this as the "bacillary index." The author emphasises that this calculation is only an approximation and that the results thereof must be interpreted in the light of the grossness of the general examination.

This article should be of great value to the technicians, laboratory workers and those engaged in the recording or interpreting of bacteriological results.

The Results of Sulphetrone Treatment of Leprosy in the Gobra Hospital, Calcutta, by Dhannendra. A report of sulphetrone therapy in 87 patients treated, either orally or parenterally, for periods from 6 months to 3 years.

Orally the dose administered has been stabilised at 4-5 g. per day. Intramuscularly the dose has varied from 1.8 g. to 6 g. per week.

Clinical improvement follows the same course as that seen with the use of other sulphones: the bacteriological improvement is slow but definite, during 3 years of treatment only 4 cases have become bacteriologically negative. Of the 93% of cases included in the 3+ and 4+ category (bacteriological) at the commencement of treatment, 59% still remain in this category after from 9 months to 3 years' treatment.

Toxic effects were slight, and the anaemia produced was not severe, necessitating a temporary cessation of treatment in only a small percentage of cases. The author then goes on to discuss the relative merits of the oral and parenteral route. Although no valid comparison of results is possible, clinical improvement appears to be more rapid when intramuscular sulphetrone is used. Economically the saving in sulphetrone is tremendous—a dose of 4 grammes per week intramuscularly being approximately equal to a dose of 36 grammes by mouth.

After investigating various pharmaceutical preparations for injection, the author concludes that the preparation of choice is that of the aqueous solution rather than the oily emulsion, although there would seem to be some slight advantage (from the point of view of clinical improvement) in using a hydnocarpus oil/sulphetrone emulsion. However, because of abscess formation, frequency of reaction and instability of the emulsion, the author suggests injecting hydnocarpus and sulphetrone separately if the combined treatment is ultimately found to be advantageous.

A 50% aqueous solution is suggested as suitable, the total weekly dose being given in two injections of 4 cc each. In anaemic patients, or those suffering from intercurrent debilitating diseases, smaller doses may be given. Good progress is reported upon 0.5 cc daily.

Sixteen photographs illustrate the article and there are over 30 pages of tables giving details of each patient's progress.

Leprosy in India. Vol. XXII. July 1950. No. 3.

Treatment of Leprosy with Sulphetrone Injections in Out-Patients, by Dharmendra, N. Sen and S. N. Chatterji. The authors have studied the applicability of intramuscular sulphetrone treatment to out-patients with a view to establishing its effectiveness and suitability in this particular sphere.

Fifty-six cases of leprosy, out-patients, 23 of whom had not benefited from oil treatment for 1-16 years previously, and 25 of whom had repeated attacks of lepra reaction were placed on treatment. Sulphetrone was given intramuscularly as an aqueous solution.

Two dosage groups were used (1) 0.25 gm twice a week, (2) 1.5 gm twice a week. Cases were placed alternately on the two regimens; some degree of selection occurred, however, since patients with lepra reaction were placed in the lower dosage group. Treatment has been continued to approximately one year in most cases.

Results have been remarkable considering that in one group the dosage of sulphetrone has been only 0.5 grammes per week *at a maximum*. In this lower dosage group significant clinical improvement occurred, whilst twelve patients in this group previously experiencing repeated lepra reaction had the reactions controlled.

Unfortunately the authors have placed all the lower dosage group of patients upon the highest dosage group, and we shall not therefore be able to evaluate the long term value of low dosage therapy. The reason for discontinuing the low dosage experiment was given as that "a perusal of the table would indicate that the big dose is decidedly superior to the small dose." The reviewer gives this table below and cannot agree with the figures considering (1) the selection of cases that occurred and (2) the small number of cases available for comparison.

Types of cases.	Dosage.	Number of cases.	DEGREE OF IMPROVEMENT.			
			Marked.	Much.	Moderate.	Slight.
Lepromatous.	Small	28	—	2	13	13
	Big	13	—	6	5	2
Tuberculoid.	Small	8	—	6	2	—
	Big	7	1	6	—	—

It would seem that the very promising results obtained with low doses of sulphetrone were worthy of a separate assessment and experiment in view of the controversy regarding the positive activity of this compound. It is to be hoped that the authors will recommence another similar experiment with a low dosage group.

The conclusions drawn are that aqueous sulphetrone is quite suitable for outpatient treatment provided that the initial dose is small. Sulphetrone is considered to be of value in the treatment of the tuberculoid form of leprosy.

Lepromin Test in Cases of Lepromatous Leprosy Treated with Sulphones, by Dharmendra and N. Mukerjee. The authors tested the lepromin reaction in 78 cases of lepromatous leprosy treated for from 1 to 4 years with sulphones. All cases had shown clinical improvement. One case had become bacteriologically negative. Fifteen were almost negative and the others were positive. The lepromin used was the refined (Dharmendra) type. On early (24 hr.) readings were taken, and the criterion of positivity was an area of erythema of at least 10 mm. accompanied by definite thickening and oedema of the erythematous area.

The result in all cases was either no reaction or only slight reaction, only one case being classified as a weak positive.

The reports of other workers (that a change from negative to positive is seen under sulphone therapy) was, therefore, not confirmed.

Annual Report Leprosy Research Department—Indian Council of Belra. The main work during the year has been the therapeutic study connected with the parenteral administration of sulphetrone.

Studies of the blood concentration of sulphetrone show that the drug is rapidly disturbed in the blood stream when injected in aqueous solution. The drug also appears to be rapidly excreted from the blood stream. Apparently very little difference is recorded between absorption and excretion rates when either an oily suspension or a watery solution are used.

Blood concentrations were studied following oral and parenteral administration; the conclusions were that to maintain the same blood concentration the dose required by an intramuscular injection is about 1/5th of that required by oral administration.

Following an intramuscular injection of 2 grammes 50% of the drug is excreted in 24 hours and a total recovery of 70-80% in 6 days was found.

No concentration of sulphetrone has been found in the skin. Values for skin sulphetrone are parallel to those of the blood.

The interval recommended between injections is 24 hours (1.0 g. per injection).

Few marked or serious toxic effects were encountered, although two cases of mild exfoliative dermatitis were seen (apparently not sensitive to further treatment as is the case in Nigeria). Patients were given iron and yeast as a routine, although even with this a slight anaemia was encountered. No case has, so far, become bacteriologically negative under sulphetrone therapy.

Lesions Simulating Leprosy Caused by a Stab Wound in the Thigh, by Dharmendra and S. N. Chatterji. A report of a differential diagnosis made on a patient attending the leprosy clinic having anaesthesia, muscular wasting, drop foot and a trophic ulcer

The absence of any thickened nerves or patch made the diagnosis of leprosy questionable, and after detailed examination of the patient a history of a deep stab wound on the thigh was elicited.

Evidence is presented to support the diagnosis of damage to the sciatic nerve—effecting incomplete diversion of this nerve—thus causing the symptoms which had (presumably) been diagnosed as due to leprosy by another practitioner.

Leprosy in India. Vol. XXII. October 1950. No. 4.

Diaminodiphenylsulphone in the treatment of leprosy—pharmacological aspects, by Dharmendra, K. R. Chatterjee and R. Bose. The authors studied various pharmacological aspects of D.D.S. therapy in an attempt to assess the value of the oral as opposed to the parenteral route and to establish a satisfactory dosage regimen for treatment.

D.D.S. appears to be rapidly absorbed following both intramuscular and oral administration appearing in the blood within 5 minutes.

Blood concentrations were studied following single, 8 day and continuously administered doses. Following a single dose blood tests were higher with orally administered D.D.S. than with intramuscular but the drug is retained for longer periods by the latter route. After 8 days, these differences tend to disappear and, naturally, the levels found were higher than following a single dose.

When D.D.S. was continuously administered the blood levels were only slightly higher than after 8 days' administration and the differences between the two routes had practically disappeared.

D.D.S. is retained in the blood stream for very long periods after treatment has been suspended, 35 days in the case of oral treatment and appreciably longer following intramuscular treatment. Studies were made of the blood levels following biweekly administration, alternating daily treatment and twice daily treatment. The most constant blood level was found with twice daily oral administration.

The intramuscular route was shown to possess no advantages, a twice weekly oral dose being as good as an intramuscular injection at that interval. As with injections of the material used, a good deal of induration and abscess formation was encountered. (The use of D.D.S. in a plain coconut oil base overcomes this difficulty—the D.D.S. oil beeswax is now known to be too irritant.)

The total urinary excretion of D.D.S. was found to be 60%-75% of the dose administered, with considerable daily variations in output.

No evidence that the sulphones concentrate in the skin has been found; it is present there, and also in tears, sweat and saliva, but not in concentrations exceeding that of the blood.

Studies of toxicity show that D.D.S. tends to be a more haemolytic drug than other sulphones when the daily dosage exceeds 50 mg per day. At a 100 mg. daily dosage, however, the anaemia produced is not severe (drop of 2 gm. of Hb). No febrile and eye reactions were seen if the daily dose did not exceed 100 mg.

The authors conclude that oral administration of D.D.S. is the method of choice and that twice daily treatment is best. The maximum dose should not exceed 200 mg. per day.

The Lancet. (1951) January 6th. Page 21.

Haemolytic Anaemia during treatment of leprosy with Diaminodiphenylsulphone by mouth, by K. Ramanujam and Michael Smith. A case of acute haemolytic anaemia occurring during the initial stages of D.D.S. therapy is described. An adult male (Indian), in good physical condition, suffering from tuberculoid leprosy was treated with D.D.S. Prior to treatment extensive laboratory tests had revealed no abnormalities of liver function. Treatment consisted of 0.1 gramme of D.D.S. daily for 13 days, 0.2 gramme daily for 10 days, 0.3 gramme daily for 13 days—the interval

between the increase of dose was approximately, therefore, a fortnight.

At the end of the third fortnight a strongly positive Schlesinger test for urobilin was obtained, and the patient complained of nausea and weakness. The blood sulphone level was 1.3 mg%. Treatment was, by an oversight, continued and 36 hours later the patient was admitted to hospital in an acute toxic state.

The subsequent history was one of an acute haemolytic process—the detailed laboratory reports should be consulted in the original by those interested in this aspect—with enlargement of spleen and liver and a fall in haemoglobin of 4 gramme% within seven days. Fever of 103°-104° was present and vomiting and extreme asthenia were marked symptoms of the haemolysis.

No evidence of permanent damage to the liver was recorded. The patient re-acted to an attempt to recommence treatment with 25mg D.D.S. with headache and backache and the urine (having become free from urobilin) again contained large amounts.

The diagnosis of infective hepatitis was considered by the authors and ruled out for reasons which appear to be sound. This paper would repay study by those who are using D.D.S. for the treatment of leprosy—it must be pointed out, however, that the exhibition of D.D.S. was (as is now known) too rapid and the final dose attained, i.e. 0.3 grammes, too high. (Authorities now place the absolute maximum dose at 200mg daily and the increase from a commencing dose of 50 mg daily should be at not less than 14 days, preferably monthly intervals.)