ABSTRACTS

DE ALMEIDA, J. O., DE FREITAS, J. L. P., BRANDAO, H.

"Electrophoretic Studies on the Protein Distribution in the Serum of Leprosy Patient", The Reports of the Research Inst. for Tuberculosis and Leprosy, Vol. 56, No. 3, Jan., 1954. (Japan.)

A quantitative complement fixation test using a triple antigen, made up of cardiolipin No. 72 for syphilis, T. cruzi extract for Chagas' disease, and a tubercle bacillus extract for tuberculosis and leprosy, is presented. Experimental work has been done to establish the basic principles governing the reaction by demonstrating that the specific systems react independently of the presence of other antigens.

Sera from 786 blood donors were tested against the triple antigen and against each one of the specific antigens, in complement fixation tests. The 599 sera that did not react with the triple antigen did not show any reactivity with the antigens for syphilis, tuberculosis, leprosy or Chagas' disease; no false negatives occurred with the triple antigen. The 103 sera which reacted with any one of the specific antigens, reacted also with the triple antigen. Four sera were anti-complementary, simulating "reaction" with the triple antigen; 76 sera gave "reaction" with the triple antigen but did not show any specific reaction in the tests for syphilis, Chagas' disease, tuberculosis or leprosy. These results could be due to the cumulative anticomplementary effect of these sera plus that of the antigens composing the triple antigen.

The preceding results indicate that a screen test employing the triple antigen should be used instead of the regular test for syphilis, in areas where syphilis, tuberculosis, leprosy, and Chagas' disease are endemic. *(Authors' Summary)*

MAYAMA, A.

1953, "Electrophoretic Studies on the Protein Distribution in the Serum of Leprosy Patient", The Reports of the Research Inst. for Tuberculosis and Leprosy, Vol. 56, No. 3, Jan., 1954.

(1) Electrophoretic studies on serum protein were performed in 63 leprosy patients.

(2) Almost no differences were demonstrated in electrophoretic findings between the healthy persons and neuro-macular patients except for far advanced cases.

(3) In lepromatous patients, elevation of total serum protein, a decrease in albumin and an increase in gamma-globulin were demonstrated. Consequently, albumin-globulin ratio were less than 1.0. But any relationship could not be found between electrophoretic findings and clinical conditions.

(4) In lepromatous cases with complication of " erythema nodosum leprosum ", however, more characteristic findings were obtained, viz., remarkable decrease in albumin and significant elevation in gamma-globulin with a rise in total serum proteins.
(5) No parallelism between gamma-globulin component and tuberculostatic activity of the blood was confirmed so far in leprosy patients. *(Author's Summary).*

" INTERNATIONAL MEDICAL ABSTRACTS AND REVIEWS "—Vol. 15, No. 5, May, 1954, is a special leprosy number dealing particularly with the social aspects of leprosy. A symposium on social aspects of leprosy prevention was apparently held recently in Calcutta and the papers published in this issue were contributed to that symposium.

The papers were by: Dr. M. Bose, Mr. S. Roy, Dr. G. Panga, Mr. M. Diwan, Dr. D. N. Bose, Dr. P. Sen.

" LEPROSY IN INDIA." Vol. XXVI, No. 2, April, 1954.

This issue contains editorial notes surveying the activities of the World Health Organisation in relation to leprosy. An article by Dharmendra and K. R. Chatterji reports the study of isoniazid in the treatment of leprosy in 31 patients. The report covers absorption, excretion and dosage. The experiment continued for periods up to 57 weeks. No toxic effects were observed. Early therapeutic results were favourable but the later results were less favourable. The conclusions reached are as follows:—

> " It may be concluded that INH has been found of definite value in the first 8 to 12 weeks, specially in reducing the bacteriological concentration, but that on the whole it is not very effective in the treatment of leprosy, since there is usually a set back in the initial improvement. Neither has it been found of value in the treatment of acute or subacute lepra reaction. It is possible that in combination with some other anti-leprotic drugs, INH may be of some value in the treatment of leprosy. If our assumption regarding the development of resistant strains of leprosy bacilli to INH early in the course of treatment be correct, it would indicate the need for combining INH with some other anti-leprotic drugs (sulphones or thiosemicarbazones) either from the start, or for changing over from INH to one of these drugs after about 2 months of treatment with INH during which initial improvement will be noted in most cases."

Two articles deal with a new sulphone (2:2' Dihydroxy 4:4' Diaminodiphenylsulphone). Dr. Biswas writes a note on preparation and Drs. Dharmendra, Chatterjee and Bose a note on preliminary tests against acid-fast bacilli in vitro. A small test on human beings is planned.

This issue also contains the first report on the World Health Organisation Expert Committee on leprosy and also a report by Mr. W. Bailey of the International Leprosy Conference of the Mission to Lepers and American Leprosy Missions.

DUARTE, I. G. & DE MELLO, P. H.

" Dapsone in the Treatment of Lepromatous Leprosy ", Rev. Brasileira Leprologia. S. Paulo. 1153, Sept., Vol. 21, No. 3, 207-20. (40 refs.)

First the literature of sulphones is reviewed. Then an account is given of 90 cases of leprosy treated with dapsone (DDS). The daily dose given orally was 100 to 200 mgm., the latter being tolerated when 42 days of treatment was followed by 15 days' rest. Having formerly used promin, diasone and other DDS derivatives, the author considers that because of its efficiency, ease of administration and moderate price, DDS is the treatment of choice for leprosy.

ERNEST MUIR.

LAVIRON, P., LAURET, L. & JARDIN, C.

" Contribution to the Study of Delayed-Action Chemotherapy in the Anti-leprosy Campaign in French West Africa. Bull. Soc. Path. Exot. 1954, Vol. 47, No. 1, 127-39, 6 figs. and 6 graphs.

Because of the long distances that have to be covered in Africa a twice-monthly injection of DDS is given. Two suspension media have been used, groundnut oil and chaulmoogra ethyl esters. The latter is preferred as the curve of blood concentration remains more level during the time between the injections. The rate of absorption can also be regulated by the size of crystals used in the suspension. The dose of 1.25 gm. twice a month appears to be sufficient and is not toxic for the African. Details are given of 10 patients treated and an addendum sets out the technique used for estimation of DDS in the blood and in the urine. ERNEST MUIR.

FLOCH, H. & GELARD, A.

" The Use of Delayed-Action DDS in Relation to the Size of Crystals in the Suspension ". Bull. Soc. Path. Exot. 1954, Vol. 47, No. 1, 35-40.

The authors aim at giving patients 1.5 gm. every 3 weeks in suspension in 0.2 per cent. agar saline. They find that the larger the DDS crystals in the suspension the more slowly is the drug absorbed. The dosage given amounts to 0.5 gm. intramuscularly per week; the amount recommended at the Madrid Congress was between 0.3 and 1.2 gm. per week. The authors give 50 mgm. a week for the first month, 1.0 gm. per fortnight for the second 2 months, and then 1.5 gm. every 3 weeks. They find that on the day after the injection there is a blood concentration of 0.460 mgm. per 100 cc. which gradually diminishes but is 0.100 mgm. per 100 c.c. on the 21st day. The rate of absorption can be regulated by increasing or diminishing the size of the crystals in the suspension.

ERNEST MUIR.

LIPPELT, A.

" BCG and Erythema Nodosum in Leprosy ". Rev. Brasileira Leprologia. S. Paulo. 1953, Sept., Vol. 21, No. 3, 221-4.

Two hundred adult lepromatous patients who had been on

sulphone treatment and had improved to a greater or less degree were given 3 gm. of BCG in weekly doses of 200 mgm. by mouth. Some improved and were able to go back to work, but in many there were exacerbations and attacks of erythema nodosum. On the whole the results were not very encouraging. ERNEST MUIR.

JOPLING, W. H. & RIDLEY, D. S.

" Isoniazid in Lepromatous Leprosy. Trans. Roy. Soc. Trop. Med. & Hyg. 1954, Mar., Vol. 48, No. 2, 138-8 (10 refs.).

Eight lepromatous patients were treated for a period of 6 months with isoniazid. Some of them had already been treated with sulphones with poor results. Clinical notes of the 8 patients and laboratory findings are given. The usual daily dose was 1 to 2 mgm./kgm. increasing gradually to 5 mgm./kgm., but there was variation in the amounts tolerated. In all cases there was a certain amount of lepra reaction, so severe in 2 cases that treatment had to be temporarily suspended. There was no evidence of clinical improvement in any of the patients, and though there seemed to be bacteriological improvement in some, it was not maintained. The conclusion confirms the view of Lowe and others that under the conditions of trial isoniazid is not an effective treatment for lepromatous leprosy. ERNEST MUIR.

SHARP, L. E. S.

" A Trial of Iso-Nicotinic Acid Hydrazide in Leprosy ". East African Med. J. 1954, Feb., Vol. 31, No. 2, 59-62.

During 5 months 18 lepromatous and 5 tuberculoid cases of leprosy were treated with isoniazid, 200 mgm. being given daily. The results were that 87 per cent. were much improved or improved, and 13 per cent. were stationary. This computation is based on clinical results, and no mention of bacteriological examination is made. At the same time, and acting as controls, the following number of cases were treated with other drugs, the percentage improvement being shown in brackets: 121 with DDS (84), 128 with DDS and intradermal chaulmoogra oil (95), 27 with thiosemicarbazone (89), 45 with thiosemicarbazone and chaulmoogra (89) and 38 with sulphetrone (87). The conclusion reached is that " although these observations on isoniazid in the treatment of leprosy cover only twenty-three cases, yet the marked improvement observed in a good proportion of the cases, particularly the highly infected ones, given some solid ground for concluding that this drug has a definite therapeutic value in such cases. It will further be noted that the results obtained with isoniazid have been approximately as favourable as with other forms of treatment. It deserves a more extensive and prolonged trial, by itself and also in combination with chaulmoogra oil intradermally ". ERNEST MUIR.

MARKIANOS, J.

" The Action of Isoniazid in the Treatment of Leprosy ". Bull. Soc. Path. Exot. 1954, Vol. 47, No. 1, 32-4.

The author treated with isoniazid 2 patients having combined leprosy and tuberculosis with no amelioration of the tuberculosis but with slight improvement of the leprous lesions. In 13 patients with leprosy alone, of the macular type, there was some improvement, especially in recent cases. In 25 more advanced lepromatous cases there was slight improvement, and the author considers that this drug may be used when there is intolerance of the sulphones. In all, 45 patients were treated. Three of these were attacked by jaundice which lasted 2 to 3 months, and there were various other reactionary complications requiring withdrawal of the drug. These were observed most commonly when the daily dose was increased from 150 mgm. to 300 mgm. and maintained at that level. (The author does not use the modern form of classification.)

ERNEST MUIR.

CARTER, F. S.

" Primary Tuberculosis in African Children and the Value of Isoniazid in Treatment ". East African Med. J., 1954, June, Vol. 31, No. 6, p. 265.

In this paper the author considers that tuberculosis has been introduced into Kenya comparatively recently and that the native population has had little time to develop any natural resistance. The disease, therefore, is often not localised and the primary infection does not lead to a healing focus but to dissemination and death. Mantoux tests in over a thousand children under 10 years in the medical wards of the King George VI Hospital, Nairobi, gave only 11.5% positives and, in addition, 31 children with rapidly progressive tuberculosis had a negative Mantoux test. In the present study 41 children with positive Mantoux tests, and showing evidence of an active primary tuberculosis infection, were studied. The majority were obviously sick, with marked constitutional disturbance, and local signs are described. Thirty-eight children were specially studied, some treated with Isoniazid and some without. The effect of the treatment on the temperature, on the weight, the sedimentation rate and radiological findings and also on the general clinic condition, are recorded.

The following conclusions were drawn:—

1. Thirty-eight African children with active primary tuberculosis were observed for periods varying from four to fourteen months.

2. It was found that the severity of the disease is greater than that usually seen among children in the United Kingdom, and the

outlook much less favourable. Fever and mental apathy were prominent features. All the deaths occurred within three months of the first symptoms of the primary infection.

3. Radiologically, there was enlargement of the hilar glands in 40 out of 41 children (97.5%), and it was to a considerable degree in 24 of them (58%).

Absorption collapse or collapse-consolidation was observed in 28 children (68%). Clinical progress outstripped radiological evidence of improvement almost invariably.

4. The value of isoniazid therapy was investigated.

5. Twenty-two children were treated with isoniazid (Rimifon) and sixteen acted as controls. Those receiving isoniazid gained weight more quickly than the controls, and their temperature fell to normal more rapidly.

6. When the disease ran a benign course, those receiving isoniazid appeared to be restored to health more quickly than the controls, but the drug was not able to prevent dissemination of the disease. Two children developed suppurative tuberculosis cervical adenitis, one phlyctenular conjunctivitis, one tuberculous meningitis, one miliary tuberculosis, and two died from tuberculous bronchopneumonia. Three cases of tuberculous bronchopneumonia occurred among the controls.

It is probably unjustifiable to use isoniazid in the treatment of primary tuberculosis as the drug does not prevent the development of fatal complications, and a drug resistant organism is produced in a large percentage of patients when used by itself. It is suggested that isoniazid therapy should be reserved for use in conjunction with streptomycin when such complications occur.

7. The ultimate prognosis appears to be favourable if the child survives the first three months of the infection.

(Author's Summary)

CHAUSSINAND, R., VIETTE, M. & KRUG, O.

Action de l'Hydrazide de l'Acide Isonicotinique sur le rat infecté par le bacille de Stefansky. Annales de l'Institut Pasteur, **84**, p. 431, February, 1953.

The authors' conclusions are as follows:—

Thirty rats subcutaneously inoculated between 6½ and 7 months ago with suspensions of Stefansky's bacilli were treated for 16 days after the inoculation with isonicotinyl hydrazide, 0.76-1 mgm daily. The treated animals showed no clinical lesions. Histological examination showed slight lesions at the point of inoculation, and in the local lymph node, these lesions showing a few altered bacilli. Fifteen controls inoculated at the same time with the same dose,

but not treated, showed a classical picture of marked lesions at the point of inoculation and a massive lymphatic spread.

The interest of these results lies in the fact that previously no antibiotic or chemotherapeutic agent had been able to control the formation of the local lesion and the spread of this infection.

CHAUSSINAND, R., VIETTE, M. & KRUG, O.

Evolution de l'infection a Bacille de Stefansky chez le rat traité par l'Hydrazide de l'Acide Isonicotinique. Annales de l'Institut Pasteur, **85**, p. 398, Sept. 1953.

The authors' conclusions are as follows:—

Isonicotinic hydrazide given by mouth in doses of 0.75-1 mgm during a period of 10 months has not eliminated the disease produced by the subcutaneous inoculation of Stefansky bacillus. Nevertheless, the appearance of the local lesions and the lymphatic spread and visceral involvement when they occurred were seen to be much retarded, and the pathological lesions are less extensive and less marked than in the controls. On the other hand, the treatment with I.N.H. appears more effective if it is not started until the seventeenth day after inoculation.

CHAUSSINAND, R., GABBAI, A., DORENLOT, H. & VIETTE, M.

Action de l'Hydrazide de l'Acide Isonicotinique sur la maladie de Hansen. Bulletin de la Société de Pathologie exotique, **46**, p. 905, Nov.-Dec., 1953.

The authors' conclusions are as follows:—

Forty-four patients (31 lepromatous, 12 tuberculoid and 1 indeterminate) have been treated for between 3 to 12 months, some with INH alone, or with INH and DDS. The dose of INH varied and the highest was 8 to 12 mg per kilo body weight. INH is better tolerated, but less active than sulphones in leprosy. Its use alone cannot be recommended. In low doses the results are mediocre, and high doses are sometimes not tolerated, but results are better.

The interest of this product appears to be in its use together with sulphones in patients either in poor general condition or tolerating sulphones badly. A longer study of this combined treatment is desirable.

CHAUSSINAND, R.

" Therapeutique de la Lepre ". Extract from *La Revue du Practicien*, No. 21, of 21st July, 1954.

In this article Chaussinand reviews the development of modern treatment of leprosy and assesses the present position. The ground covered is familiar to most of our readers and does not lend itself to abstraction. The opinion is expressed that DDS constitutes without doubt a most powerful weapon against leprosy. The author

mentions and discusses briefly treatment with thiosemicarbazone, chaulmoogra oil, INH, streptomycin, PAS etc.

CHAUSSINAND, R. & TOUMANOFF, C.

"Cellular Reactions and Phagocytosis in Guineapigs Inoculated Intraperitoneally with Living and Dead Leprosy Bacilli". *Ann. Inst. Pasteur.* **85**, p. 713-23, Dec., 1953.

Inoculation of suspension of leproma was followed by an exudate containing first polymorphonuclears and then monocytes, the latter being either macrophages or lymphocytes. The reaction was the same in nature whether the bacilli were alive or had been killed by heat, but was sometimes more intense if the bacilli were alive. This less intensity in the case of the dead bacilli may follow some chemical change in the lepromatous tissue injected and may be due to the heating of the suspension. The polymorphonuclear reaction lasts only some 24 to 48 hours, but bacilli can often be found inside macrophages as long as 3 months later. Thus the natural immunity of guineapigs to human leprosy is due to their power to phagocytose the bacteria. ERNEST MUIR.

NEYRA-RAMIREZ, J.

"Study of the Action of BCG on the Leucocyte Formula and on Phagocytosis in the Peritoneal Exudate when Guineapigs are Inoculated with Living and Dead Rat Leprosy Bacilli". *Ann. Inst. Pasteur.* **86**, Jan. 1954.

Five guineapigs were vaccinated intradermally with BCG, and after 6 weeks all had become Mantoux-positive; 3 of these and 3 unvaccinated controls of the same weight were inoculated intraperitoneally with living rat leprosy bacilli. Likewise, the other 2 vaccinated animals and 2 unvaccinated controls were inoculated similarly with a suspension of rat leprosy bacilli which had been autoclaved for an hour. The peritoneal exudate was aspirated and studied for a period of 100 days.

First polymorphonuclears phagocytosed the bacilli, followed by monocytes which ingested and destroyed bacilli, and also destroyed both polymorphonuclears and monocytes containing bacilli. The rate at which this "autophagie" took place varied in the different groups. In the vaccinated animals it took 4 to 8 days with the living bacilli, and 4 to 6 days with the dead ones. In the unvaccinated controls it took 12 to 16 days with the living bacilli, and 12 to 14 with the dead. There was pyknosis of the nuclei of the polymorphonuclears in the animals inoculated with living, but not dead, bacilli, which may have been due to toxins either from the living bacilli or from the rat tissue. The more rapid autophagie in the vaccinated animals is taken as an indication of increase in the defence mechanism in animals which are naturally resistant to rat leprosy bacilli. ERNEST MUIR.