

## ABSTRACTS

*Progressive Experimental Infection with M. leprae in a Chimpanzee: Preliminary Report.* A. E. GUNDERS, Journ. of Trop. Med. & Hyg., **61**, 9, Sept. 1958, pp. 228-230

Human lepromatous material was inoculated into a female chimpanzee of six to seven months of age. The sites of the inoculation were sub-arachnoid, round the left ulnar nerve, and intravenously and intraperitoneally. At 11 months the chimpanzee developed signs of acute and progressive leprosy, with many nodules on the limbs and some depigmentation. Sections from skin biopsies showed a granulomatous process of epithelioid cells and smaller cells, and bacilli were found in all sections. Regression of nodules began at the 14th month after inoculation. Another chimpanzee aged 2½ years was similarly inoculated, but has shown no lesions to date.

*Haemagglutination and Haemolytic Reaction of Red Cells Sensitized with Extracts of Murine Leprosy Bacilli.* N. YAMADA, La Lepro, **27**, 2, March 1958, pp. 126-135.

The findings appeared to verify the idea that a common antigen between *M. tuberculosis*, *M. leprae*, and *M. lepraemurium* exists. Also the hæmolytic reaction occurring on addition of complement to the haemagglutination reaction system using murine leprosy bacilli was more specific and sensitive than haemagglutination similar to old tuberculin antigen. Leprous involvements of the internal organs in murine leprosy seemed closely to influence the reaction: this has also been reported by Kawaguchi. With the haemolytic reaction using old tuberculin about one half of the sera of leprosy patients showed prozone but it is thought that this is a pattern occurring in the optimal relation between antigen and antibody, and is not due to anti-complement action of the serum. The haemagglutination and haemolytic reaction of tuberculosis serum and murine leprosy antigen are closely interrelated and coincide with the results obtained with old tuberculin antigen.

*Studies on the Lepromin Test: Sensitization Experiments with Trypsin Isolated Bacilli.* K. YANAGISAWA and N. ASAMI. La Lepro, **27**, 2, Mar. 1958, pp. 107-113.

After 5.2 g. of lepromatous tissue had been homogenized, trypsin was added and it was left for three days at 30° C. then centrifuged for thirty minutes at 10,000 r.p.m., yielding a sediment of 180 mgm. of bacteria, almost free of tissue fragments. Using this sediment and also the purified wax of tubercle bacilli, sensitivity tests were carried out in guinea pigs, by inoculation of 3 mgm. and 15 mgm. of the leprosy bacilli. There was a third group in which 2 mgm. of the purified wax of tubercle bacilli was given in addition to 3 mgm. of leprosy bacilli. The fourth group had 2 mgm. of

purified wax of tubercle bacilli as the sole inoculum, and the fifth group was an untreated control. After the inoculations, spaced tests were given with Dharmendra lepromin and with tuberculin. Enhancement of allergy was noted in both the lepromin and tuberculin tests: in the first two groups where leprosy bacilli had been inoculated both the lepromin and tuberculin tests became positive three weeks after inoculation and the lepromin reaction was retained up to 24 weeks and was stronger than the tuberculin. Both reactions, especially the tuberculin, were stronger in group 3 where purified wax of tubercle bacilli had been given in addition to leprosy bacilli. The Dharmendra antigen does not enhance allergy whereas the bacilli collected by the trypsin method do so. It appears that the Dharmendra method removes the wax substance of the bacteria because of the use of chloroform.

*Sensitization of the Dog with Lepromin and BCG, and Evidence of Cross Sensitization: Persistence of the Sensitization and Cross-Sensitization.* (2 papers). N. O. CASTRO and P. A. ARCURI, Internat. J. of Leprosy, **25**, 3, July-Sept. 1957, pp. 231-242.

Their experiments show that whole lepromin can sensitize dogs, confirming the observations of Wade, similar to the effect of BCG in causing sensitization to BCG. There is further a cross-sensitization between BCG and lepromin. The cross-sensitization to lepromin induced in the dog by BCG appears to be a transitory phenomenon which may disappear within nine months. The non-specific sensitization to BCG induced by lepromin is more stable. The specific sensitization to either lepromin or BCG is equally stable.

*Studies on the Immunology of Murine Leprosy*, T. TANIMURA, S. NISHIMURA, Y. TANIMURA. Internat. J. of Leprosy, **25**, 3, July-Sept. 1957, pp. 247-256.

Young white rats of a mixed strain were used as the experimental animals, and the material was derived from lepromas of the Kumamoto strain of murine leprosy. Injection of a saline vaccine of heat-killed *M. lepraemurium* into such rats some time before inoculating them with live bacilli, caused inhibition of the onset of the infection to a high degree, though not completely. There is a lesser degree of inhibition with the simultaneous inoculation of dead and live bacilli. By adding liquid paraffin to the vaccine of dead bacilli there was also strong inhibition of the onset of an infection to live bacilli, more so than with the saline vaccine of dead bacilli. There was only a slight degree of inhibition when a vaccine was used of non-pathogenic acid-fast bacilli with liquid paraffin added. When a secondary infection was tried in rats already infected with murine leprosy there was seen to be a greater resistance than anything the paraffin murine leprosy vaccine could induce, and complete prevention was noted to a challenge inoculum of 0.5 cc. of  $10^4$  leproma suspension. There was no kind of Koch phenomenon as in tuberculosis, in

the shape of an acute reaction of the skin over the reinoculation site. The size of the primary lesion did not influence the results of the secondary inoculation, nor did the latter influence the progress of the primary lesion.

*Chemotherapy of Murine Leprosy. The Effect of Cycloserine (Sermoycin) on Mouse Leprosy.* Y. T. CHANG. *Inter at. J. of Leprosy*, **25**, 3, July-Sept. 1957. pp. 257-261.

Cycloserine was given against mouse leprosy induced by intraperitoneal infection. It was found to be moderately effective in suppressing the infection, similar to streptomycin but less than INH. Cycloserine was reported beneficial in human tuberculosis though without effect in experimental tuberculosis of mice and guinea pigs. As it has now been found that it is effective against murine leprosy, this and other forms of mycobacterial infections should be included in the screening tests for more active anti-tuberculous agents.

*Réaction de la Peau des Lépreux aux Injections Intradermiques d'Acides Gras Provenant du Bacille Tuberculeux (Reactions in the Skin of Leprosy Patients to Intradermal Injections of Fatty Acids from Tubercle Bacilli)* N. P. BUU-HOI and T. V. BANG. *Revue Française D'Etudes Cliniques et Biologiques*, **3**, 7: Sept. 1958, pp. 770-773.

The bacilli of tuberculosis and leprosy are very similar in their content of lipids. Fernández and Chaussinand have pointed out the phenomena of allergy and para-allergy between these bacilli, which suggest a similar chemical composition. Anderson has shown for the tubercle bacillus that the lipids are made up in great part by branch chain fatty acids of high molecular weight, one of the most interesting being pthienoic acid (C 27), which is especially abundant in the virulent strains. Buu-Hoi has tried the effect of fatty acids from tubercle bacillus in similar conditions to those of the Mitsuda. He obtained fractions with more than 20 atoms of carbon and by intradermal injection obtained skin reactions in lepromatous cases, both papules and nodules of varying intensity. These reactions are non-specific, as they also occur in non-leprosy subjects.

*Le Traitement de la Lèpre par Injections Mensuelles de DDS (Treatment of Leprosy by Monthly Injections of DDS).* P. LAVIRON, L. LAURET, P. KERBASTARD, and C. JARDIN. *Médecine Tropicale*, **17**, 6: Nov.-Dec. 1957, pp. 795-808.

The authors treated 107 patients for periods varying from 8 to 40 months by different suspensions of DDS, using one injection a month. The suspensions were (a) 2.50 g. DDS in hydnocarpus oil, (b) 2 g. in water containing gelose and saccharose, (c) 1.50 g. in saline containing gelose. The results are less rapid than from dosage at shorter intervals but are quite satisfactory and the method is useful for induction of treatment or as maintenance after the disappearance of the lesions.

*Le Traitement de la Réaction Léprouse (Treatment of the Lepra Reaction)*. M. F. LECHAT. Bulletin d'information sur la lèpre, No. 5, Foreami, Brussels. 1958, pp. 1-56: also Maroc Médical, **36**, 390: Nov. 1957, pp. 1039-1062.

This paper is a comprehensive review of the subject, with 159 references, and deals with the classic lepra reactions (lepra fever and the erythema nodosum type) and excludes the transitional phases, namely the tuberculoid reaction, the pseudo-tuberculoid exacerbation, and borderline cases. The author describes the many treatments that have been tried and mentions the contradictory results from chlorpromazine and the excellent results from ACTH and cortisone. He thinks zinc-ACTH is worth trying in borderline cases and tuberculoid reactions. He advocates more small hospital wards being made available everywhere for the bed treatment of reaction cases.

*Consideraciones sobre Quimioterapia de la Lepra (Thoughts on the Chemotherapy of Leprosy)*. M. BERGEL *Leprológia*, Buenos Aires, **2**, 2: 1957, pp. 107-110.

Drugs of which the therapeutic activity has already been demonstrated should serve to help us in further search. We do not know the mechanism of action of hydnocarpus oil. We only know it is an oil and that in patients who have had intense treatment with it there is a deposit of it in the fatty tissues. All the sulphones seem to act by the liberation of DDS in the tissues. DDS has a primary direct anti-oxidant action, e.g., it prolongs the induction period of the oxidation of methyl oleate (Lips). The sulphones can act as metallic inactivators: they form insoluble and inabsorbable complexes in the digestive tract, especially with iron (Brownlee). The thiosemicarbazones inactivate heavy metals such as iron, copper, and cobalt (Liebermeister). *In vivo* they diminish the level of copper in the body (Carl). They stabilize organic substances by means of their inactivation of metallic pro-oxygens (Clarkson). INH inactivates heavy metals, such as copper and iron (Albert), and has a primary direct anti-oxidant activity. In certain concentrations INH is up to ten times more active as an anti-oxidant than alpha-tocopherol (Hasselstron).

Because of its bacteriological, immunological, and histo-pathological connexions with tuberculosis, every drug active in tuberculosis is worth trying in leprosy. Similarly, because of the bacteriological connections every drug active in murine leprosy is worth trying in human leprosy, but there is a certain lack of parallelism between them and hence Domagk does not think that the chemotherapy of murine leprosy is a good index for the human. Because of the relations between actinomycetes and mycobacteria, fungostatic drugs might be worth while trying in human leprosy. Buu-Hoi thinks we should try any anti-tuberculous or fungostatic drug, especially if there is also a certain degree of liposolubility.

The lepromatous-like picture provoked in animals by the lack of anti-oxidants, when they are on a pro-oxidant diet, suggests that we should try in leprosy every drug which *in vivo* prevents the deposition of acid-resistant pigment. Methylene blue and nor-dihydroguayaretic acid can do this. Acid resistance is connected with a good bacillary oxygenation and the loss of acid resistance is thought to depend on an insufficient supply of oxygen (Gran Triana). The failure of inoculation and culture of *M. leprae* is related to its dependence on oxygen. Hanks in his study of the oxidative metabolism of the mycobacteria throughout their range from the saprophytic to the pathogenic noted less and less capacity *in vitro*: the oxidative capacity was lowest in *M. lepraemurium* and *M. leprae* which could not increase their respiration in the presence of many different substrates. Hanks thinks that conditions which favour a more rapid and continuous oxidation of lipids tends to preserve the infectivity of these mycobacteria and that in our studies of pathogenesis and chemotherapy we should not miss the chance of creating an oxygen deficiency in certain stages of leprosy or the chance of augmenting it if it exists. In connexion with this, it may be recalled that the lepromatous state does not progress in patients at high altitudes, where there is an environmental deficiency of oxygen. Referring to the conditions necessary to create this deficiency of oxygen, Hanks pointed out that the reducers as well as the toxins of the process of oxido-reduction and the anti-oxidants act in the same way, limiting the oxidations and creating what might be called "a system of negative oxygen" which we should seek to use to oppose *M. leprae*. The bacillus is favoured in its development by "a system of positive oxygen" (Bergel). In order to obtain the pro-oxidant action of diet in leprosy, there should be intake of crude fats and green vegetables as supply of tocopherols, and even of supplementary tocopherols by mouth.

The lipo-solubility of hydnocarpus oil seems to indicate that this may be a favourable condition in chemotherapy of leprosy. Buu-Hoi points out that of all the anti-tuberculous drugs, only those which also have lipo-solubility have activity against leprosy. The fact that hydnocarpus oil is deposited in the fatty tissues of the patients seems to indicate an active compound against leprosy should have this property: this is closely bound up with lipo-solubility. Hopeful compounds would also be those which are able to decrease oxidation at the tissue level, to inhibit respiratory enzymes, to form catalytically-inactive stable complexes with the pro-oxidant metals and to prevent the auto-oxidation of the lipids. So it would be worth while trying in leprosy every metallic and anti-oxidant inactivator which has low toxicity and can be absorbed by mouth and which has good conditions of distribution in the tissues and of elimination: if possible, it should be lipo-soluble and able to be deposited in the fatty tissues,

and better still have a degree of anti-tuberculous and anti-mycotic activity. Among the vast group of organic compounds patented for industrial use as preservers of organic substances, as anti-oxidants, and as metallic inactivators there should be some with a strong action against leprosy. We could benefit also from the industrial knowledge of the solubility and synergism and other practical details of these compounds.

*Familial Leprosy.* N. MUKERJEE and S. GHOSH. Journ. of the Indian Med. Assoc. **31**, 3: Aug. 1958, pp. 129-131.

A Hindu female aet. eight years, belonging to a family in which the mother and three sisters were cases of leprosy, developed flat hypopigmented macules over the face, and later on the limbs and back. There was no disturbance of sensation and no thickening of nerves, and the smears were negative. After three months of observation there was slight increase in size and a biopsy was taken from a lesion. This showed a moderate infiltration of round cells with a few epithelioid cells and the subepidermal zone was invaded in places. A few bacilli were seen in the infiltration and inside a nerve. Hence the diagnosis of leprosy was made. Of the family, the father was dead, the mother was lepromatous, the three sisters tuberculoid, and the brother was found free of leprosy.

*Acupuncture and Galvanic Current in the Treatment of Lepra Reaction.*

KAO HUAI-AN and colleagues; Chinese Journal of Dermatology, **6**, 4; 1958, p. 298 (reported in Chinese Medical Journal, **77**, 3, Sept. 1958, p. 287).

Nerve and joint pains and erythema nodosum in leprosy patients were treated by the typical techniques of Chinese acupuncture. Apparently the needle is inserted into the nerve trunk considered to govern the area, and galvanic current from a 1.5 volt storage cell is allowed to run for 30 to 50 minutes. This treatment is given every alternate day until 15 treatments have been given, and then a rest of one to two weeks is given. In 72 cases of severe arthralgia and neuralgia and in 21 cases with erythema nodosum the results were very good. Thus in 18 cases of erythema nodosum the lesions subsided rapidly in 15 and improved greatly in 3.

*O Emprego da D-Cycloserina no Tratamento da Lepra: Resultados Preliminares.* (The Use of D-Cycloserine in the Treatment of Leprosy: Preliminary Results) E. DE ALMEIDA NETO and J. P. REVELLES. Revista Brasileira de Leprologia. **26**, 2, Apr.-June 1958, pp. 63-91.

A full report, with details of bacterioscopy and haematology, and 28 clinical photographs, is given of a trial of D-cycloserine in 20 leprosy cases. This drug is a new antibiotic obtained from *Streptomyces orquidaceus*, and is given by mouth six-hourly in tablets of 250 mg. daily for the first seven days, increasing by one tablet per week up to four tablets daily. In one case only they tried six tablets

daily but on perceiving signs of intolerance, returned to four tablets daily. Treatment has lasted six months in most of the 20 cases. In four cases the drug was combined with DDS and in one with thiosemicarbazone.

There has not been time for full clinical cure, but the influence of the drug on clinical signs was early and considerable. There have been no cases of exacerbation, nor of drug resistance. Bacteriological results have been good and the histology shows a favourable modification. Tolerance has been good: central nervous system intolerance has been of the slightest and was easily avoidable. There were focal reactions of good prognosis noted at the beginning of treatment. Leprosy reactions were moderate. The drug seems to act directly on *M. leprae*. The combination with the sulphones seemed particularly advantageous, and the drug seemed very useful in cases which had reactivated after being resistant to the sulphones. The trial will continue.

*Nossas Observacoes Sobre a Difenil-Tiourea no Tratamento da Leprosy* (Our Observations on Diphenyl-Thiourea in the Treatment of Leprosy). A. M. ALONSO. Boletim do Servico Nacional da Leprosy, Rio de Janeiro, 17, 1: March 1958, pp. 5-11.

This is a report on 16 months of trial of DPT (Ciba 1906) on seven patients, of whom six were lepromatous and one tuberculoid. Clinical improvement was marked, and the new drug seemed superior to DDS in this regard. There was one case who had had a gastrectomy and was intolerant to thiosemicarbazone and DDS. This case tolerated DPT very well and had excellent clinical improvement. There was another case which had an abnormal resistance to the action of all anti-leprosy drugs: this case showed partial improvement in bacterial indices and histology but it is too early to expect much change in these.

*An Experimental Study on the Action Exerted by Certain Synthetic Anti-malarial Drugs upon the Endocrine System*. C. I. PARHON, V. SAHLEANU, and L. IANCU. Rumanian Medical Review, Bucarest: April-June 1958, 2, pp. 56-61.

The authors gave a daily oral dosage, with controls, of quinine sulphate, atabrine, chloroquine sulphate, and paludrine in different groups of rats, and studied the effect on the endocrine glands and liver. They found that these drugs in non-toxic doses caused no depression of the endocrine system. Chloroquine and paludrine stimulated the adrenals, as shown histologically, histochemically, and in the weight of the organs. They think that this action is similar to ACTH, probably due to a stimulation of the release of this hormone. The general cortisone-like action of these drugs is not, they think, exclusively due to the stimulation of the adrenals. It is possible that there is a peripheral action upon the fundamental substance of the connective tissue and upon inflammatory phenomena, as well as

a central adrenal stimulation. The adrenal hypertrophy they obtained in their experiments was more insignificant with the most toxic substances (quinine, atebine), so they do not think that it was merely part of the general adaptation syndrome of Selye. Liver histology showed the probable stimulation of the reticulo-histocytic system. It is well known that the adrenal hormones stimulate this system. The authors advance the hypothesis that the synthetic anti-malarials may influence the causal factors of a disease and stimulate the non-specific defence reactions of the body. They point out that their experimental results showed that paludrine can be introduced into dermatological therapy for the same purposes as those for which chloroquine is now being used.

*Tratamiento Local de las Ulceras Neurovasculares de los Miembros Inferiores.* (Local Treatment of Neurovascular Ulcers of the Lower Limbs). O. RAMIREZ. Boletín de la Sociedad Cubana de Dermatología y Sifilografía. **15**, 2, 1958, pp. 59-64.

In four cases of neurovascular ulcers of the lower limbs, which had failed to heal after long periods of treatment, the author applied *dehydrated coffee powder* of the "instant coffee" type, in a simple dressing covered by gauze, and changed at intervals of eight days for a similar dressing. There was healing of the ulcer in three or four weeks in three cases and in two weeks in one case. There have been no relapses, and this treatment was tolerated perfectly.

*Outstanding Achievements in Health Work in 1958.* Chinese Medical Journal, Dec. 1958, **77**, pp. 582-586.

In an enthusiastic article describing the stimulating influence of the political approach on the health campaign, rats, sparrows, flies and mosquitoes are said to have been slaughtered in huge quantities and 960 counties of China to have been made pest-free. One impressive item was that 62.7 million public latrines were built. Traditional Chinese medicine has been revived, including acupuncture, and is used alongside modern medicine. "Traditional medicine has given remarkable results in the treatment of hypertension, apoplexia, arthritis, joint sprains, pulmonary tuberculosis, *leprosy*, syphilis, *Taenia solium*, infantile paralysis, Japanese B encephalitis, chronic nephritis, liver cirrhosis, tetanus, whooping cough, scarlet fever, and diphtheria. Its successes in treating silicosis, malignant tumours, aplastic anaemia, and leukaemia are unprecedented in world medicine."

There is a further reference to leprosy on p. 583. "In leprosy prevention, Shantung has completed a thorough survey of this disease and has isolated all sufferers for care and treatment. In Kwangtung province, during the past six months, over one half the cases of leprosy of the lepromatous type have been concentrated in leper villages, and 1,104 patients have already been cured and discharged".