

ABSTRACTS

Inoculación de Mycobacterium Leprae a Ratas en Carencia de Vitamina E: Estudio Experimental: Nota Previa. (Inoculation of M. leprae into rats deficient in Vitamin E: experimental study: preliminary note). F. F. WILKINSON, R. A. CHERI, and E. FOLLMANN. *Leprológia*, **4**, 1: Jan.-Apr., 1959, pp. 35-44: 5 microphotographs, 14 figs.

The conclusions put forward by Meny Bergel from his work on the inoculation and reproduction of *M. leprae* in rats deprived of Vitamin E caused these authors to repeat the experiments. Bergel sought to favour the mechanisms of tissue oxidation in the rat by his special diets. These authors also used such a diet deficient in Vitamin E. They soon found the great drawback of a high mortality in the rats, due to the polyvalent vitamin deficiency, but think the method is promising and should be pursued with a modified diet, and more rats in the experiment (these authors had few).

Hipersensibilidad de Vacunación y de Infección por el Mycobacterium Leprae. (Hypersensitization from Vaccination and Infection by M. leprae). N. OLMOS CASTRO, P. B. ARCURI, R. L. USANDIVARAS, and colleagues. *Leprológia*, **4**, 1: Jan.-Apr., 1959, pp. 3-11.

The authors made a comparative study of the reactions caused by lepromin injections in healthy human subjects and in dogs, with reactions in the same conditions in subjects of tuberculoid leprosy. By this it was hoped to compare inoculation hypersensitization with hypersensitivity belonging to the disease. They found that the mechanism of the development of the hypersensitization seemed to be the same in all cases, and that the early reaction at 48 hours was conspicuous, and accelerated development of the small tubercle or nodule at the end of the first week. They think that this early Fernández reaction in these cases certainly means a state of hypersensitivity to *M. leprae* and should have the value of the Mantoux reaction in tuberculosis. They interpret the Mitsuda or late reaction as the terminal stage of the increase of tuberculin-type hypersensitization which began a few weeks before. Thus the early Fernández and the late Mitsuda reactions are different stages of the one process and it is not right to give them different meanings. They insist that in the immunology of leprosy the phenomena of hypersensitization should be studied independently from those of resistance or immunity and that there are many arguments which favour their being distinct states which obey different pathogenic mechanisms.

Persistencia de la Hipersensibilidad a Leprolina Proteica Total (L.P.T.) Inducida por BCG en el Hombre. (Persistence of Hypersensitization to Total Proteic Leprolin Induced by BCG in Man.) N. OLMOS CASTRO, P. B. ARCURI, L. B. TORNANZOS and colleagues. *Leprológia*, **4**, 1: Jan.-Apr., 1959, pp. 12-17.

They made a statistical study of the hypersensitization to total proteic leprolin and Koch's crude tuberculin 1/1000 at 6 weeks and at 7 months after BCG inoculation of healthy persons. They found that BCG is able to change a negative Fernández to positive at 6 weeks after inoculation in a high proportion of cases; but at 7 months there is a loss of hypersensitivity to total proteic leprolin, while that to 1/1000 crude tuberculin remains. It seems that this co-sensitization phenomenon (a specific group-hypersensitization) is maintained during the development of the immune process resulting from inoculation, but is lost in a short time; however the monovalent specific sensitivity to the causal germ remains.

Sensibilización de Cachorros por Mycobacterium Leprae (Sensitization of Pups by M. leprae.) N. OLMOS CASTRO, P. B. ARCURI, R. L. USANDIVARAS, and colleagues. *Leprológia*, **4**, 1: Jan.-Apr., 1959, pp. 18-20.

Ten dogs (pups) were sensitized to *M. leprae* by previous injection of an aqueous suspension of heated lepromatous tissue (whole lepromin) and unheated suspension. They were then injected intravenously with Mitsuda-Hayashi whole lepromin and showed no symptom of anaphylactic shock. The lack of this shock causes the authors to think that the hypersensitization produced in the Wade phenomenon is of tuberculinic type, a bacterial hypersensitization, and they affirm the specific nature of the Wade phenomenon.

Hipersensibilidad y Reacción Peritoneal en el Cobayo Inyectado con el M. leprae (Hypersensitization and Peritoneal Reaction in the Guinea Pig Injected with M. leprae.) N. OLMOS CASTRO, M. CONEJOS, P. B. ARCURI, and colleagues. *Leprológia*, **4**, 1: Jan.-Apr., 1959, pp. 24-30.

They studied histologically and bacteriologically the peritoneal reaction provoked in healthy guinea pigs by the injection of a suspension of lepromatous tissue rich in *M. leprae*. This suspension was heated or unheated. They found many signs of an active and effective mechanism of resistance, and point out the peculiarity of guinea pigs in that they do not react to lepromin by intradermal injection, even when repeated, but have an effective defence mechanism, as shown by these peritoneal reactions.

Naturaleza de la Reacción Nodular Tardía en el Fenómeno de Wade
(*Nature of the Late Nodular Reaction in the Wade Phenomenon.*)

N. OLMOS CASTRO, P. B. ARCURI, R. L. USANDIVARAS, and colleagues. *Leprológia*, 4, 1: Jan.-Apr., 1959, pp. 31-34.

Seven dogs were sensitized to *M. leprae* and its proteic derivative by a previous injection of an aqueous suspension of lepromatous tissue rich in *M. leprae* which was heated or unheated, and were then given injections of total proteic lepromin, an aqueous suspension of normal human skin, and total proteic lepromin plus an aqueous suspension of normal skin. The latter two groups gave hypersensitization reactions at 48 hours, decreasing in intensity on the following days: at 14 and 21 days there was no inflammatory reaction nor late nodular reaction. The suspension of normal skin provoked neither early nor late reactions. The authors think that the late nodular reaction observed in the second part of Wade's phenomenon is specific and only attributable to *M. leprae*.

Recent Advances in Leprosy Research. R. J. W. REES, *West Afr. Med. J.*, 8, 6: Dec., 1959, pp. 325-329.

The causative organism of human leprosy, described by Hansen in 1874, was one of the first bacteria to be identified, but progress has been slow and awaits its successful cultivation and/or transmission of the disease to an experimental animal. Any success in the treatment of leprosy in recent years has been obtained with drugs known to be active against tuberculosis, the causative organism of which is related to *M. leprae*. While direct attempts to culture and transmit *M. leprae* must go on, much of value may be learned from studies on other closely related and particularly non-cultivated strains of mycobacteria. In recent years there have been a number of studies based on rat leprosy. This was first described by Stefansky and Dean in 1903, and is a natural disease of wild rats throughout the world. Like human leprosy, it is a chronic infection in which the mycobacteria exist as intracellular parasites of cells of mononuclear type, nor, until recently, was there any convincing evidence that they will grow *in vitro*. The disease can be transmitted experimentally to rats and mice. Rees, and Hilton and Elek in 1957 reported quantitative techniques, adapted from those in tuberculosis work, and were able to determine the generation time *in vivo* of *M. lepraemurium*. They found that the bacteria divided every 10 to 12 days in the mouse and every 7 to 8 days in the rat. These generation times are the longest recorded for any micro-organism (c.f. every 20 to 24 hours for *M. tuberculosis*) and calculations based on transferring them to *M. leprae* would give an incubation period for human leprosy of 2 years or more, which fits in with clinical observations.

The use of tissue culture systems for attempts to grow human and rat leprosy mycobacteria follows from (a) the intracellular

position of the bacillus *in vivo*; (b) the failure of the murine leprosy bacillus to derive energy from a wide range of extracellular substrates (Gray, 1952); and (c) inhibition by serum of the endogenous metabolism of *M. lepraemurium*. In these respects the leprosy bacilli tend to resemble viruses. Rees and Wong (1958) first tried monocytes. Though they did not obtain multiplication, some of the bacilli from these cell cultures were viable at 40 days. They next obtained limited multiplication in cultures of spleen tissue, and similar results were reported by Wallace, Elek and Hanks (1958). Methods were also developed for precise enumeration of bacilli in cultures, and hence the definite detection of multiplication.

Primary cultures of explanted tissue from previously infected animals offer the greatest chance of success, but such cultures cannot be maintained in a healthy state for long-term studies. Garbutt, Rees, and Barr (1958) have succeeded with initiating multiplication in a strain of mouse fibroblasts.

The electronmicroscope is also proving of value in distinguishing live and dead bacilli of *M. lepraemurium*, (McFadzean and Valentine; and Rees, Valentine, and Wong, 1958). The degenerate forms predominate in animals receiving effective chemotherapy. This technique provides a new approach.

(McFadzean and Valentine have recently reported on this technique as applied to *M. leprae*. See *Leprosy Review* **31**, 1: Jan., 1960, pp. 6-11. They found normal and degenerate forms. The percentage of the latter increased after 6 months of sulphone therapy. The fragmented and granular bacilli found after treatment when stained by Z.N. and examined with the light microscope correspond with the degenerate bacilli with disordered protoplasm as seen by the electronmicroscope. EDITOR.)

Electronmicroscopic Studies of Tubercle Bacilli. Studies on Fixation in Ultrathin Sectioning. K. FUKUSHI. Reports of the Research Institute for Tuberculosis and Leprosy: **9**, 1: Dec. 1959, pp. 1-17. Tohoku University, Sendai, Japan.

With 18 figures on plates and full descriptions of material and methods and results Fukushima has reported on his studies in fixation for ultrathin sectioning by osmium tetroxide. Thin sections of *M. tuberculosis* var. *hominis* and *M. avium* and BCG were fixed under varying conditions of time and temperature. It was found that *M. tuberculosis* was fixed by 5 days at room temperature with the best results. For BCG, fixation at room or higher temperatures for 4 to 9 days gave the best results. For *M. avium*, fixation at room temperature for 2 days was best. Structures revealed were those resembling mitochondria, cell walls, cytoplasmic membranes, electron-dense granules, nuclei, vacuoles, and cytoplasmic granules, as the basal ultrastructures of mycobacteria.

Mutual Influence between Tuberculous and Leprous Infections in the Organs of Rats and Mice. Histopathological Study. T. HORIUCHI. Reports of the Research Institute for Tuberculosis and Leprosy, Tohoku Univ., Sendai, Japan, **9**, 1; Dec., 1959, pp. 34-53: 16 figures on plates.

Observing the double infection of murine leprosy bacilli and tubercle bacilli in rats and mice over several months, the author noted that in the early stage it is very difficult to differentiate the lesions. The only sure way is the finding of typical lepra cells with many bacilli. The evolution of murine leprosy is prevented by tuberculous infection. The occasional appearance of lepra cells is noted very early in tuberculous foci when both tubercle and murine leprosy bacilli are inoculated simultaneously into animals. It has been shown that early development of lepra cells follows rapid destruction of tubercle bacilli in the viscera. This finding suggests that cells infiltrated by tuberculous infection are temporarily liable to be invaded by leprosy bacilli in the early stage in which tuberculostatic activity has not developed. The process of tuberculosis is prevented by the infection by murine leprosy bacilli. When animals with mild leprosy are infected with tubercle bacilli of low virulence, tuberculous nodules in the viscera are delayed two weeks in formation, compared with the control animals. When the challenge is by tubercle bacilli of high virulence there is not much difference in the severity or extension of murine leprosy and of tuberculosis. But when rats with serious leprosy are inoculated intravenously with tubercle bacilli of low virulence, nodule formation is considerably prevented. Both tuberculous and leprotic lesions develop under mutual influence in lung, liver, spleen of rats and mice. The tuberculous lesions are suppressed and replaced by leprous lesions, because the former develop rapidly but do not progress and the latter slowly but always progressively and decisively. Murine leprosy finally produces generalized lesions in rats and mice. Polymorph leucocytes, foreign body giant cells, and eosinophils often appear in parts invaded simultaneously by leprotic and tuberculous infections.

Histopathological Study on the Inoculation of Human Leprous Tissue into Guinea Pigs. T. KAWAWAKI. La Lepro, **28**, 6: Nov., 1959, pp. 285-301. 10 plates.

The author investigated histologically the tissue reactions arising from the insertion of human lepromatous tissue into guinea pigs. He found the first reaction is a nonspecific inflammation in the subcutaneous tissue of the guinea pig into which the human lepromatous nodule had been inoculated. Later a specific granulation tissue appears, composed of an infiltration of round cells with leprosy bacilli, and some epithelioid cells, proliferation of reticulum

cells and leprosy bacilli appear in the adjacent lymph glands. The initial exudative tissue reaction around the inserted lepromatous nodule is greater in young than in adult animals. Necrosis is greater in adult animals, often with abscess formation. The reactive exudate is more myxomatous in young animals than in adults. Giant cell formation begins on the 6th day after inoculation. Firstly come cells of foreign body type, then Langhans type, lastly giant cells with very large nuclei.

Studies on the Infection Mechanisms of Murine Leprosy. M. SUZUKI.

La Lepro, **28**, 6: Nov., 1959, pp. 301-309 and pp. 311-317, 319-340.

Colloidal suspension of carbon black was used to block the cells of the reticulo-endothelial system in 104 mice and observed for 5 months. A marked inhibition of development of murine leprosy was noted in the group injected with carbon black before the inoculation of murine leprosy bacilli, and the group with before and after inoculations. Another group in which the blocking was done by the 15th day after inoculation also showed a marked inhibition. Blocking done after the 20th day of inoculation showed only slight inhibition. A marked acceleration was noted in the group of mice injected with a mixture of carbon black and murine leprosy bacilli.

In another experiment percutaneous blocking of the reticulo-endothelial system with carbon black was done in 35 rats. This caused a marked degeneration of the murine leprosy bacilli in the subcutaneous leproma and the inhibition of the development of fresh leproma and the dissemination of bacilli into whole organs. A group of rats injected with the mixture of bacilli and carbon black was not different from the control group in regard to the development of subcutaneous leproma but the dissemination of bacilli into whole organs was remarkably accentuated.

In another experiment murine leprosy was inoculated intraperitoneally and an intravenous injection given of carbon black. The dissemination of bacilli was not different from the control group. Next, intraperitoneal injections of carbon black were frequently repeated in animals who had been given subcutaneous inoculations of murine leprosy. Marked development of leproma was noted early, but the dissemination of bacilli into whole organs was inhibited as compared with the control group.

In the last experiment a reversed allergic reaction was induced in 126 rats by using the anti-monocyte serum obtained from rabbits who had been sensitized by the intraperitoneal monocyte of rats. It was found that in intraperitoneally inoculated murine leprosy there was marked inhibition of the multiplication of murine leprosy bacilli in the intraperitoneal monocyte. Leproma development was also markedly inhibited, as shown in autopsies at 40 days. After 5

months autopsy showed inhibition of dissemination of bacilli. In one group, which had been injected with liquid paraffin prior to the injection of anti-monocyte serum, multiplication of murine leprosy bacilli was inhibited as compared with the untreated group.

Detection of Acid-Fast Organisms in Tissue Sections by Fluorescence Microscopy. S. W. A. KUPER and J. ROBERT MAY, *J. of Path. and Bact.*, **79**, 1; 1960, pp. 59-68, 6 figs. on plates, 5 in colour.

The authors describe their method, with practical details, of staining mycobacteria by auramine-rhodamine and examination by optical apparatus delivering light of about 4320 to 5660 A.U. from a mercury-vapour lamp to the microscope using a dark-ground condenser and filters. The objects fluoresce reddish-gold in colour with great distinctness. Details are fully given in the paper with illustrations of the apparatus as set up and of the bacteria as they appear, and the work is well worth consulting in the original by all laboratory workers in leprosy. In the preparation of tissue sections an interesting addendum is that the authors have found that tissue sections are best treated with a mixture of 2 parts xylol and 1 part ground-nut oil. The authors think that this procedure is very good for the detection of tubercle bacilli and is indispensable for leprosy bacilli.

Studies on in vitro Reaction between Guinea Pig Peritoneal Cells and Leprolin or Tuberculin Antigens. K. OKAMURA. *La Lepro*, **28**, 6: Nov., 1959, pp. 331-360.

His previous work showed that guinea pig peritoneal cells which had been sensitized either with tubercle bacilli or BCG have a common factor reacting against leprolin and tuberculin. There was no passive transfer of this reactivity from rabbit to guinea pig. It has been found that both sensitized and non-sensitized peritoneal cells of the guinea pig combine leprolin antigen *in vitro*. This is only with the peritoneal cells of the guinea pig and cells heated previously at 48° C. for 15 minutes failed to show this combination. When leprolin antigen combines it seems to be freed easily by heating at 48° C. for 15 minutes. When peritoneal cells of a guinea pig sensitized by BCG combine leprolin, the common reaction factor of the sensitized cells was inactivated and the cells failed to transfer the passive reactivity against leprolin and tuberculin.

Classification of Experimental Mouse Leprosy. Y. KAWAGUCHI. *La Lepro*, **28**, 6: Nov., 1959, pp. 378-390. 2 plates.

Stefansky in 1903 in the first report of murine leprosy described two forms, glandular and muco-cutaneous. Now most workers think that these are merely early and late stages of the same disease. The present author has found remarkable differences between the various inbred strains of mice, and thinks that mouse leprosy should

be classified into benign and malignant. In the benign type the skin lesions appear early, and are small, hard, and sharply defined. Those of the malignant type appear later, and are soft and much larger, with a diffuse thickened appearance. These two clinical types are an expression of varying degrees of resistance. The malignant type progresses steadily, usually with fatal termination in about 30 weeks. In the benign type there may be gradual regression and sometimes spontaneous healing in the late stage.

It is of interest that giving BCG can sometimes convert the malignant to the benign type.

Mechanism of Blister Formation in Leprosy Patients. S. N. CHATTERJEE. *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 305-320, 7 figs.

Blisters are more commonly found on anaesthetic hands than on any other part of the body. Heat which is not enough to cause burns of normal parts can still produce blisters in anaesthetic parts. The author describes illustrative cases. He used a thermocouple and light-trace galvanometer to investigate this matter in 22 patients, recording the temperatures of the anaesthetic and corresponding non-anaesthetic parts before the application of heat at 52° C. for 5 minutes, and also immediately afterwards. There was usually a lower temperature in the anaesthetic parts before the application of heat. He thinks this is due to a contraction of blood vessels and a less active blood circulation, compared to the normal parts. When heat was applied the anaesthetic parts always rose to a higher temperature than the normal parts, because heat was less well dissipated, based on insufficient dilatation of blood vessels. Blisters arise in anaesthetic parts because of these 2 factors of lower initial temperature before being heated and more accumulation of heat after heating. A temperature not enough to produce blisters in a normal part may be just enough to do so in an anaesthetic part. This study confirms the author's previous observation that the neural signs in leprosy are closely associated with capillary contraction and consequent diminution of blood supply in the skin of anaesthetic parts, and that the temperature of anaesthetic is lower than in normal parts. A new and fruitful line of study is opened up.

A Study of Myositis Interstitialis Leprosa. S. ISHIHARA. *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 341-346. 6 figs. on plates.

Dr. Ishihara of Suruga Leprosarium, Japan, reports on a study of interstitial leprotic myositis. It is a rare but genuine part of lepromatous leprosy. He took specimens of muscle tissue from the calf of the leg in 4 cases, and found atrophic changes and lepromatous infiltrates and acidfast bacilli. In a case which had improved greatly under treatment there were swellings in the calves of both legs which were found to consist of an inflammatory exudate containing giant

cells and eosinophilic leucocytes; and few bacilli apart from globi. In the other 3 cases there was muscle atrophy and inflammatory infiltrates of histiocytes or macrophages and lymphocytes, with more or less abundant bacilli in various areas.

Reticulo-Endothelial Response in Murine Leprosy. L. KATO and B. GOZSY, *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 347-354.

In murine leprosy in rats the authors studied the capillary-endothelial and reticulo-endothelial responses, compared with those in uninfected controls (80 rats in each group). The inoculation of 0.5 ml. of a freshly prepared suspension obtained from a leproma of a rat 3 months old was given subcutaneously to 80 rats. The controls received saline inoculation. At 20, 70, and 120 days, the capillary and reticulo-endothelial responses were investigated on normal and serotonin-depleted rats: (the serotonin-depletion was achieved by an intraperitoneal injection of 0.3 mgm./100 gm. of Reserpine 18 hours before the experiment). Capillary reactions were provoked with dextran and with histamine, then made visible with India ink. As the disease progressed there was a definite fluctuation in capillary response. There is a stimulated systemic capillary response in the early stages of the infection, but this lapses in the late stage. There is a similar stimulation of endothelial response in the early lesions of inoculation, and none in the late necrotic stage of the granuloma. The phagocytic function of the reticulo-endothelial system is unchanged, as evidenced by the India ink test made 20 and 70 days after inoculation.

Results of Inoculation of White Rats with Human Leprosy Bacilli by the Intraneural Route: Preliminary Report. N. MUKERJEE and S. KUNDU, *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 355-359.

On the basis of the affinity for nerve tissues on the part of *M. leprae* the authors attempted to transmit it to white rats by exposing the sciatic nerve and injecting it with a suspension of leprotic tissue rich in bacilli, mixed with an equal amount of sterile egg albumen. One out of 5 rats so inoculated showed at 3½ months evidence of massive infection with an acidfast organism. Passages of this acidfast organism have been attempted in other rats and in guinea pigs. Lesions developed in one of the first-passage rats, and a second passage has been attempted in rats and mice. The guinea pig inoculations were negative, and cultures were negative. The bacillus therefore was probably not the tubercle bacillus nor any other mycobacterium readily cultivable; it may be the Stefansky bacillus as a rat of the first-passage group was infected by it. This brings out the importance of excluding the Stefansky bacillus as a chance infection in experiments where human leprosy material is inoculated into rodents.

The Bacteriologic Diagnosis of Early Leprosy by the Trypsin Digestion Method. J. LEW and M. CHUNG. *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 360-363.

As a practical method of obtaining bacilli free of tissue debris the authors chose and tried out the trypsin digestion method in 175 cases. The tissue specimen, freshly obtained or formalinized, about 0.5 g. in weight, was autoclaved for 15 minutes at 15 pounds pressure. It was then ground in a mortar in 7 to 8 ml. of Sorensen's buffered solution (pH 7.8) containing 0.5% trypsin (Difco 1/250). The preparation was then inoculated with frequent shaking for 3 hours at 39° C., and then centrifuged for 30 minutes at 3000 to 4000 r.p.m., and the supernatant fluid decanted. In the case of formalinized tissue the stage of autoclaving was preceded by washing in running water for 6 hours. This method was found very useful in the important early diagnosis of leprosy. It revealed acidfast bacilli in 26% of suspected cases which otherwise would have eluded certain diagnosis, and it was successful in almost 100% of clinically diagnosed leprosy lesions as yet untreated. The technique and instruments needed are simple and the method avails for specimens preserved by formalin and sent from a distance.

Acetate and Fumarate Permeases of Mycobacterium smegmatis. G. A. ELLARD and PATRICIA H. CLARKE. *J. of Gen. Microbiol.*, **21**, 2: Oct., 1959, pp. 338-343.

The impermeability of mycobacteria to many compounds which are normal cell metabolites has long been thought to be related to the high lipid content of the cell wall. The authors wished to test the hypothesis that it might be due to the absence of specific permeases. They grew *M. smegmatis* on Lemco agar in the presence and absence of acetate and fumarate. Organisms grown with fumarate oxidized fumarate rapidly, and Lemco-grown and acetate-grown organisms oxidized fumarate after a lag period at an increasing rate; this was inhibited by chloramphenicol. Disrupted bacterial preparations oxidized fumarate rapidly, irrespective of the growth medium. Acetate-grown organisms oxidized acetate at more than twice the rate of fumarate-grown and Lemco-grown. There was slight adaptation to acetate oxidation by acetate-grown and greater adaptation by Lemco-grown and fumarate-grown organisms. Acetate was oxidized by disrupted bacterial preparations. The evidence seems to suggest the existence of fumarate and acetate permeases, though less clear-cut in the case of the adaptive acetate permease.

The impermeability of mycobacteria cannot be ascribed solely to the high lipid content of the outer layers of the cell and specific permeability factors should be considered.

Reacción Leprosa: Su Tratamiento con Cloroquinas. (Lepra Reaction: its Treatment with the Chloroquines.) E. MACOTELA. Rev. Mexicana Dermatología, 3, 3: Sept., 1959, pp. 238-242.

The author discusses the types of lepra reaction and the treatment, which is the commonest accessory therapy for leprosy. A drug which is effective in all cases and without disadvantages for the patient has still not been found. The *antimonials* have been used for some time and continue to be used, and the results in general are good. There is little danger in their use but there are cases which fail to respond. *Transfusion* of small quantities of whole blood may give rapid improvement especially when the reaction is chronic or with grave deterioration of the general condition. The *corticosteroids* are powerful, but their use demands constant medical supervision because of the dangers of ulcers, diabetes, etc., and on stopping the treatment there may be a rebound reaction as intense or more than the original reaction. The *chloroquines* were reported on by Gonzalez Prendes and co-workers in 1955, who gave 25 reacting cases a daily dose for 7 days of 300 mgm. of Atebrin, with favourable result especially on fever and cutaneous lesions after the failure of other treatments. Merklen and Riou used Nivaquin in 14 cases in 1957. This also had a good effect, in doses of 600 mgm. orally daily for 5 to 14 days, with progressive decrease to 200 mgm. daily for several weeks. Germain and other workers have had similar good results. Merklen, Germain, and Riou think that the chloroquines not only have an action on the acute reactional episodes but are an adjuvant to the sulphones in the sense of increasing the tolerance of the patient to the sulphones and finally reinforcing their action. The chloroquines are worth trial in grave reactional states. At the beginning of treatment the intramuscular route may be better tolerated in many patients.

Terapeutica Actual de la Lepra. (Present Treatment of Leprosy.) M. MALACARA. Rev. Mexicana Dermatología, 3, 3: Sept., 1959, pp. 247-250.

The author quotes Chaussinand as saying that the number of leprosy patients in the world is about 10 millions, and about 600,000 of them receive adequate treatment. Because this disease is ancient the list of medicaments used for it is long, and many of them have no action or even make the patient worse. There is a sharp division between the two epochs, before the sulphones, and after the sulphones. In March, 1941 the first sulphone was used by Faget in Carville, U.S.A. DDS was first made synthetically in Germany in 1908, and in 1937 it was used with good results in streptococcal infections in animals. A little later the first sulphone derivative (Promin) was used in tuberculosis of guinea pigs, and a little later Cowdry and Ruangsiri used it in murine leprosy. This caused Faget

and his colleagues to think it could be useful in human leprosy, and they gave it to 10 patients, first by mouth and then intravenously, as the oral route seemed too toxic. By October, 1945 they found that 71.4% had improved after 6 months. By 1948 Cochrane and Lowe had shown that DDS itself could be used orally in moderate dosage. In Mexico, Latapí and colleagues first used Promin and in 1950 the use of DDS was established. The good results of the sulphones are slow, so new drugs have also been studied in the hope of getting more effect in less time. These newer drugs have either been those with an anti-tuberculous effect or successful in murine leprosy. Streptomycin and Dihydrostreptomycin were used on a dosage of 1 g. daily and found to have effect, but the danger of toxicity has inhibited their general use. TB-1 or thiosemicarbazone in a dose of 100 to 150 mgm. has good results which fade out and some authors advise against it. INH at 4 to 7 mgm./kg. daily is useful in some acute manifestations but is not recommended in general as a routine treatment. PAS has been found to have no action against leprosy. DDSO or diamino-diphenyl sulphoxide has a similar action to DDS, but in later stages of treatment is apt to be toxic. Antigen Marianum in intradermal injections of 0.1 ml. once a month for 6 months causes severe local and general reactions on account of which it should not be used. Diethyldithiolisophthalate (Etisul or ETIP) is applied by inunction. It has a marked antibacterial action from 3 weeks onwards, and has a disagreeable odour, and resistance is reported at 3 months. Cycloserine has been given at 500 to 700 mgm. daily and most report a good result, sometimes better than the sulphones. It deserves wider investigation. The author thinks that the diphenylthiourea Ciba 1906 has given the best results of the newer drugs. The dose is 3 g. daily in the adult and 1.5 g. in children. Davey has reported that it is perfectly tolerated, there is a marked improvement with its use which is as good as the sulphones and better and it is especially useful in severe neuritis. Kanamycin and Griseofulvin are worth trying in leprosy. Kanamycin is given by injection and has been shown to be effective in murine leprosy. Griseofulvin is given orally for fungal skin infections and might possibly be useful in leprosy. At the moment the sulphones continue to be the basic treatment for leprosy.

Cultural Determinants in Placebo Reaction. WM. A. SODEMAN, Jr.
Texas Reports on Biology and Medicine, **18**, 1: 1960, pp. 18-24.

The placebo effect of a drug may provide a major portion of its action, and may vary with the different cultural heritages of the people on whom it is used. It may also modify the drug's action, or have little or no effect on this. Placebo effect of a therapy may so alter subjective and objective symptoms without changing the basic disease state that both patient and doctor are lulled into a sense of

false security. The placebo effect can well apply to the inert substance given as a 'placebo' in drug trials, for toxic reactions have been reported by Wolf (1954) to occur from such an inert substance. Placebo effect is as old as therapy and in peoples of varying cultural heritage presents different patterns which act through neural and humoral systems, and there are groups in any culture who are placebo reactors or placebo non-reactors. There are both individual and cultural determinants of placebo action. The technique of the administration of the drug, rather than the drug itself, may elicit the effect in some peoples. In any case the drug concerned must fit into the group concept of disease or be reconcilable with it in order to have a placebo effect, and any individual recipient of the treatment must believe that it has a part to play in the alleviation of his disease state. It is worth while studying the disease concepts of every primitive and civilized group, so as to understand the working of placebo effects, which penetrate into therapeutic practices everywhere. Hillis (1952) tested several drugs with these points in mind, and found that by removing the placebo reactor group he obtained a truer assessment of the pharmacological effect of aspirin as an oral analgesic, compared with morphine and codeine. A drug with little or no pharmacological potency, if applied with a logic of treatment based on the patient's concept of disease, may prove successful. Treatment, both physical and pharmacological, as we know it, ever contains an unknown quantity of placebo action in its effect. The pharmacological effect may be denied, permitted, potentiated or added to. Dramatic therapeutic successes or failures should always be interpreted with regard to the placebo effect in individuals and cultural groups all round the world.

A Concurrent Comparison of Home and Sanatorium Treatment of Pulmonary Tuberculosis in South India. WALLACE FOX and colleagues, Tuberculosis Chemotherapy Centre, Madras. Bulletin of the World Health Organization, **21**, 1959, pp. 51-144.

This report is of great interest to leprosy workers, as it gives experience of a year's study of sanatorium and domiciliary therapy on balanced groups of about 96 patients in each category. It was found that the results of domiciliary chemotherapy approach closely enough to the results of sanatorium treatment, namely rest, diet, nursing, and supervised administration of the medicines, but there are also disadvantages, such as the disruption to family life. The standard of medical care during this study was very favourable, but it is thought that similar good results would be obtained from a domiciliary service if it is operated from a tuberculosis clinic, and if there is a satisfactory supply of anti-tuberculosis drugs, and if there is enough staff (including a public health nurse and a social worker). Adequate transport should be provided, including an

ambulance, and a small number of beds for special cases, an efficient appointment system, a system of surprise checks on the co-operation of the patients in taking their medicines, reliable smear examinations for tubercle bacilli in sputum, and a welfare fund for especially needy patients.

Griseofulvina en Micosis Cutaneas Profundas. (Griseofulvin in Deep Cutaneous Mycoses.) F. LATAPI, P. LAVALLE, J. NOVALES, and Y. ORTIZ. *Rev. Mexicana Dermatología*, 3, 1: Jan.-Mar., 1959, pp. 34-41, 8 figs. on plates.

The new antibiotic Griseofulvin has been shown by many authors, and also in Mexico, to have good activity as an oral treatment of superficial dermatomycoses. The authors now give a preliminary report on a trial in 2 cases of deep mycoses, one of mycetoma due to *Nocardia brasiliensis* and the other of Sporotrichosis due to *S. schenckii*. There was rapid and marked clinical response in both cases, and further observation is needed before a final assessment.

La Dexametasona en la Lepra Reaccional. (Dexametasone in Reactional Leprosy.) A. J. MELAMED, I. SIMONOVICH, J. GANOPOL, E. FUHRER, and M. MELAMED. *Rev. Asoc. Med. Argentina*, 73, 11: Nov., 1959, pp. 1-9.

The authors describe 13 cases of leprosy in reaction who were given the corticosteroid Dexametasone, and studies were made of their proteinograms by paper electrophoresis and the Landis test for capillary permeability. It was found that there were great changes in the capillary permeability for the serum and proteins of the blood, and intense dysproteinaemias. All these changes modified favourably or unfavourably according to the stage of the evolution of the reaction. Although these tests are valuable in the study of each individual, the study suggests that the greatest value lies in the appreciation of the successive variations in repeated tests in different clinical and therapeutic conditions. From this point of view it is possible to classify the patients studied in this investigation into (1) Toxic or co-ordinated, with a good prognosis. (2) Atoxic or unco-ordinated, with a bad prognosis. The functional capacity of the vessels (arterioles, capillaries, and venules) in leprosy and in the leprosy reaction may explain the different evolutive types of the disease and the varying results of the corticosteroid medication. Dexametasone showed an action on lepra reaction similar to drugs of the same nature used previously, but with much more activity and less of secondary effects.

Results of Investigation for the Physically Handicapped in Leprosy.

J. MIZUOKA and I. OYAMA. *La Lepro*, **28**, 5: Sept., 1959, pp. 183-191.

A study was made of 1209 leprosy patients (755 lepromatous and 454 tuberculoid). Crippled in some degree were 940 cases (77.7%). Of these 591 or 48.8% were mutilated in the upper and lower extremities, 295 or 24.4% in the upper extremity only, 54 or 4.4% in the lower only. Claw hand, wrist-drop, and lack of opposition in the thumb were common. Visual disturbance was frequent in lepromatous cases. Total amount of handicapping was 68.8% of those examined.

The Value of Thiacetazone (TB-1) in Leprosy. A. M. ALONSO. *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 321-327.

The author thinks that Thiacetazone has not been properly appreciated for its value in the treatment of leprosy. Since 1951 he has used it on 220 patients and assesses it as a drug of the first rank. He gives by mouth 100 to 150 mgm. daily, in tablets of 25 or 50 mgm. two or three times a day. In lack of toxicity it is superior to the sulphones. There have been no toxic or side effects in 220 patients. Any form of the disease responds well to it, and for neural disturbances it seems better than the sulphones. The effect on the bacillary index is similar to that of the sulphones, and there were a few cases where negativization was attained in shorter periods than usual, e.g., 12 months, 20 months, 24 months.

Treatment of Lepromatous Leprosy by a Combination of DDS and Sarsaparilla. (Smilax Ornata.) R. ROLLIER. *Internat. J. of Lep.*, **27**, 4: Oct.-Dec., 1959, pp. 328-340, 11 figs. on plates.

Sarsaparilla has been traditionally used by Moroccans in the treatment of leprosy. Two of the varieties used, *Smilax ornata* and *S. japicanga* were examined by Vaillant and Bernard and Cottet and the saponisides studied, and Rollier and colleagues in 1950 to 1957 studied the action in leprosy. Weak aqueous extracts were first used, and later tablets containing 240 mgm. of the extract of *S. ornata*. Rollier now reports on two groups of lepromatous patients observed over 3 years. The first group of 111 cases were given DDS in progressive doses from 25 mgm. to 150 mgm. and the sarsaparilla 4 to 10 tablets daily in the first week and remaining at 10 tablets for a minimum of 6 months and a maximum of 1 year, thereafter on DDS alone at 150 mgm. daily. In the second group of controls DDS was given in doses similar to the first group. With both groups the treatment was given 6 days a week. Activity on the part of sarsaparilla was indicated by significantly greater bacterial negativization after 12 months, compared with DDS alone. The author thinks that the

treatment of leprosy by a combination of red sarsaparilla (*Smilax ornata*) and DDS represents the best therapy at the present time, and is a therapeutic association such as will avoid drug resistance.

Health Services in the U.S.S.R. Public Health Papers No. 3, WHO, Geneva.

This is an interesting report on the health organization and medical care in the U.S.S.R., arising from a visit in October 1958 of an international team of 23 medical specialists and health administrators. There is a reference to leprosy on page 23 as follows: "The following diseases occur only sporadically or as isolated outbreaks: trachoma, typhoid fever, leprosy (6,000 cases only in the whole of the U.S.S.R.), malaria (5,000 cases only during 1957 in the whole U.S.S.R.)".

Control of Leprosy in the U.S.S.R.: Participation of Local Medical and Prophylactic Institutions. N. A. TORSUEV and P. S. GREBENNIKOV. *Indian J. of Dermatology*, **4**, 4: July, 1959, pp. 95-99.

These workers of the Rostov-on-Don Experimental and Clinical Leprosarium describe the process of integration of the anti-leprosy work in the U.S.S.R. into the broad medical and public health network of the country. Skin and V.D. clinics, health and epidemiological stations, and rural medical services all play their part, and the leprosaria existing (number and location not given) are to be fitted into the plan. (The number of known cases of leprosy in the U.S.S.R. is not stated. From other sources, particularly the WHO visit, the number is given as 6,000. EDITOR.) Care is being taken to include the instruction and training of health workers, rural medical aids (feldshers), doctors and students, and the search for and registration of contacts is not forgotten. In short, in Russia they are in the stage of modernising and improving their anti-leprosy work, and making it widespread.