Abstracts

Paul Brand and his Mission. Healing and the Pursuit of Pain at a Hospital in India. N. COUSINS, *Saturday Review*, New York, Oct. 3, 1964, pp. 21–24 and 51.

The author gives a particularly appealing and informative article on Dr Paul Brand and his wife.

Paul Brand is Director of Orthopaedic Surgery at Christian Medical College, Vellore, S. India, and Mrs Brand is an ophthalmologist. Dr Paul Brand went to Vellore as a young man in 1947 and his wife joined him there a year later. Together they make up one of the most remarkable husband-and-wife teams in the world today. Dr Paul Brand has restored the use of their extremities to thousands of leprosy patients. Dr Margaret Brand has saved thousands of leprosy patients from blindness. Both of them teach at the medical college, undertake important research, and work at the hospital and in field clinics.

Dr Paul Brand's main purpose in coming to the Christian Medical College and Hospital in Vellore in 1947 was to explore how he might apply his highly developed skills in the reconstructive surgery of the hands to the special problems of leprosy patients. He began on the problem of 'claw hands' and was soon highly successful, but soon he moved on to the total problem of leprosy. He soon found from his reasearch that 'leprous tissue' as a cause of deformity was unimportant compared to a loss of pain sense and defective sensation generally. The bacillus of leprosy killed nerve endings, but the flesh itself was indistinguishable from normal tissue. The importance lay in the lack of the warning and protective influence of pain, as Prof. Brand found in an encounter with a boy leprosy patient who forced open a door at the expense of a wound, when Prof. Brand himself had abandoned the same task as dangerous. Dr Brand reasoned that leprosy patients lost fingers and toes as an ultimate result of damage to the part from injury and consequent sepsis. He observed leprosy patients as they went about their daily tasks and soon obtained convincing evidence that this idea was correct. He soon found that classes in preventive care were highly productive of undamaged hands and feet. One mystery, the continuing disappearance of digits, was now traced to the intervention of *the rat*, who destroyed insensitive hands, and devices were developed to protect patients from rats, with remarkable success. He next investigated the collapse of noses and found that the basis of this was the effect of the leprosy bacilli on the delicate membranes inside the nose. This resulted in severe contraction of the membranes and the nose was drawn in towards the head. Brand therefore reconstructed many noses successfully from the inside. The noses could be pushed back into place. In noses with loss of cartilege, insert cartilege grafts or acrylic resins might be needed. Blindness, the most serious affliction of leprosy patients, was long thought to be a specific manifestation. But here intense study at Vellore caused this idea to be questioned and blindness was found to be a bye-product of vitamin A deficiency, and destruction by paralysis of the protecting mechanisms of the eye. Dr Margaret Brand was very active in preventive and reconstructive surgery of the eye and in removing cataracts, and her operation list was of considerable volume, both in the hospital and in the clinics in the villages. Eye ulcerations were also traced to lack of protection of the eye by natural washing, and various reconstructive and plastic operations get the eyelids working protectively once more in a restored 'blink' and washing of the eye surface. The actions of certain muscles of the jaw were transfered to the eyelids.

Hand in hand with these practical measures the fact that leprosy is eradicable was taught, and demonstrated, and for the medical and functionally cured psychological rehabilitation was studied and taught. By job-training, self-respect as a citizen is given back to the patient.

The core of the whole surgical revolution is giving back the invaluable sense of pain and giving back function as far as possible, and in rehabilitating the patient by practical measures, but above all by research into the facts, and understanding of the patient as an individual.

Notes Concerning Dermatoses in our Countries: Leprosy. M. EL ZAWAHRY, *Journ. of the Egyptian Med. Assoc.*, 1964, **47,** Nos. 11 and 12, p. 1157.

The author deals with common dermatoses of Egypt, and includes a brief description of leprosy.

He states the endemic nature of leprosy in his country, and mentions that he met 111 patients in one year, and that child leprosy is common, which is serious for the survival of the endemic. Tracing leprosy patients to the source of infection is the only way to eradicate leprosy in a community. He finds lepra reactions more common than in the past, perhaps due to the wide use of the sulphones. He recommends more advanced therapy, and mentions Ciba-1906 because of its safety and efficiency and absence of side effects, and Thiosemicarbazone because with it reactions are minimal. Isoniazid and streptomycin he found disappointing in therapy. Anti-tuberculous treatment can be given without danger in presence of leprosy. In an endemic area BCG is helpful in immunization of contacts against leprosy. Corticosteroids are of value and may be life-saving in reactions of leprosy, but the reactive state is difficult to extinguish entirely.

Fixed Eruption in Deeply Pigmented Subjects: Clinical Observations on 350 Patients. S. G. BROWNE, *Brit. Med. Journal*, Oct. 1964, **2,** pp. 1041–1044.

The author, who is director of the Research Unit of the Leprosy Service, Uzuakoli, Nigeria, found primary sensitization mainly by dapsone and phenolphthalein to fixed eruptions in deeply pigmented African subjects. The fixed eruption, with typical discrete lesions undergoing recurrent exacerbation, merges imperceptibly into a diffuse type of post-inflammatory hypermelanosis after a widespread itching papular eruption. The more diffuse the hypermelanosis, the less marked is periodicity in the signs of exacerbation of the papular lesion.

Drugs incriminated in the sensitivity to the fixed eruption; 254 cases of dapsone, 13 cases of polysensitivity set going by dapsone, three cases of DDSO, two cases of Ciba-1906. There were 78 cases associated with drugs other than anti-leprosy drugs. These were 46 of phenolphthalein, nine of unidentified injections and indigenous purges, five of acriflavine, four each of emetine hydrochloride, acetylarsan, neoarsphenamine, sulphonamides, and amodiaquine, one case of polysensitivity following primary sensitization with chloroquine, and one each of iodide, penicillin, and mepacrine. Antileprosy drugs as well as phenolphthalein enter into wide use in Nigeria. Figures from Yakusu in the former Belgian Congo from 5,349 patients under treatment for leprosy, 160 or 3 per cent of them had fixed eruptions caused by dapsone and solapsone. In 300 patients at Ibadan, Nigeria, Harman found 3 per cent with fixed eruptions. In South Africa, Marshall in 1963 found fixed eruptions induced chiefly by phenolphthalein and the sulphonamides.

The polar types of leprosy, tuberculoid and lepromatous, are parallel in a certain way to the two polar types of fixed eruption.

Transmisión de la infeccion leprosa a animales de laboratorio bajo condiciones dietéticas especiales (*Transmission of the leprosy infection to laboratory animals under special diet*). M. BERGEL, *Acta Leprologica*, April–Sept. 1964, No. 17 and 18, pp. 33–38, 4 figs.

Dr Meny Bergel, of the Leprosy Research Laboratories, Rosario, Argentina, relates his experience with the inoculation of *M. leprae* into rats and mice during the past few years. He used males of rats and white mice of the age of 20 days. The inoculum was obtained directly from untreated lepromatous or borderline patients, and the inoculum was used immediately after being obtained or at the most after 24 hours of refrigeration. The site of inoculation and dosage were in the rat 0.10 ml. intratesticular and 0.03 ml. in the mouse. In the plantar cushion of the rat the dose was 0.05 ml. and in the mouse 0.025 ml. In addition grafts of lepromata of an approximate size of 1 to 2 mm. were introduced surgically under the skin in the right flank of the mouse.

The special dietetic regime was added to standard diet (pieces of compressed vegetables dehydrated and natural water *ad lib.*) and consisted of five slightly varied diets, namely (1) a semi-synthetic diet with a low content of Vitamin E, that is industrial casein 23.8, powdered brewers yeast 8.9, mineral salts 3.0, maize starch 48.9; crude linseed oil was added, 15 to 20 per cent; (2) a semi-synthetic diet similar to the first but with the addition of 15 per cent of cod liver oil; (3) this diet was also like the first with the addition of 15 per cent of an oil made up of pure ethyl esters of linoleic 2/3 and linolenic 1/3 acids, in a very marked state of rancidity with a large content of peroxides and an iodine index of about 13; (4) the semi-synthetic diet above mentioned with addition of 20 per cent of crude linseed oil containing chemotherapeutic compounds such as DDS to the amount of 0.5 to 1 per thousand and thioureas in the same proportion; (5) the drinking water of some of the animals contained silver nitrate (0.5 to 1 per thousand) ferrous gluconate (2.5 to 5 per thousand) and potassium iodide (0.5 per thousand). The water to which silver nitrate was added was distilled water so as to avoid the precipitation of the silver by the chorides.

All the animals were inoculated between 20 and 30 days of age. During the experiment (*a*) Some of the inocula, and organs in which *M. leprae* developed were sown in the Lowenstein-Jensen medium. (*b*) An integral lepromin was prepared in cases where transmission in series of *M. leprae* was attempted and also in some other cases. This lepromin was tested against lepromin of human origin on lepromatous and tuberculoid leprosy patients, as well as in apparently healthy patients. (*c*) Using the methods of Hilson, Elek and Hanks bacillary counts were made. (*d*) Baciloscopic studies were made of the inoculated area, regional glands, spleen, liver, etc. (*e*) Histological studies were made. There were control groups for each group of inoculated under special dietetic conditions.

RESULTS

The testicular inoculation of *M. leprae* in rats fed on a pro-oxidant diet (added linseed oil 20 per cent and 1/1000 silver nitrate in the water) produced a marked development of the germ which was not evident in the control animals on standard diet. The growth of *M. leprae* gave rise to an infiltrate of varying density in the inter-tubular spaces of the testis, and sometimes to the formation of rounded or ovoid granulomata containing bacilli. Inoculation of this material into other rats kept on the same dietetic conditions obtained successful passage. Integral lepromin obtained from the testes behaved like a lepromin of human origin.

When the diet was more pro-oxidant, namely containing 15 per cent of cod liver oil and 0.5/1000 of silver nitrate in the drinking water, a very marked growth of *M. leprae* was produced.

The addition of DDS (0.5 per thousand) and thioureas (0.5 to 1 per thousand) to pro-oxidant diets, inhibited the growth of *M. leprae* inoculated into the testes of the rat. This fact became evident on the third month after inoculation, compared with control animals.

It was found that *M. leprae* kept for 2.4 hours in refrigeration prior to inoculation kept viable on being inoculated into the testes of the rat nourished on a pro-oxidant diet (with 20 per cent linseed oil and 1/1000 silver nitrate). *In the mouse* the testicular inoculation of *M. leprae* using the pro-oxidant diet (20 per cent linseed oil added and 1/1000 silver nitrate) had a clear development of the bacillus in comparison with control animals. Intravenous, subcutaneous, and intra-peritoneal inoculation in mice on pro-oxidant diets obtained inconstant development of globi in the spleen, between the fourth and tenth month after inoculation. The surgical grafting of a piece of leproma under the skin of the flank into mice on the above-mentioned pro-oxidant diet resulted in the formation of a small foreign body granuloma, in which the original graft lay in a necrobiotic state. In this necrobiotic zone as in the surrounding connective tissue acidfast bacilli were found, mostly homogeneous and sometimes forming enormous bacillary masses. Part of the fatty tissue adjacent to this granuloma showed a cellular infiltrate with a great number of bacilli, and some of the adjacent nerves were invaded by the bacilli.

On the inoculation of *M. leprae* in the plantar cushion of the mouse according to the technique of Shepard the author noted that when a high count of bacilli was inoculated practically the development of the bacilli was not obtained and they slowly diminished up to six to eight months after inoculation. This occurred in mice on

standard diet as well as pro-oxidant diet. When the inoculation was small (about one million bacilli or less), a development occurred at the end of six to nine months. In the pro-oxidant animals this produced a well-delimited granuloma abundant in bacilli. In a certain number of animals inoculated when on a standard diet a diffuse infiltration resulted and a regular growth of *M. leprae*. This is much more marked in the pro-oxidant mice, and the granuloma is very marked and well-delimited, but this also only occurs in a certain number of the inoculated mice. When the pro-oxidant diet has added 2.5 per 1000 of ferrous gluconate, a much greater development of *M. leprae* is obtained. When the diet includes 0.5 per thousand there is an exuberant development which surpasses all other diets. The result obtained from 15 per cent cod liver oil surpasses that obtained from 20 per cent linseed oil, perhaps because there is less tolerance to the latter.

The diet with the ethyl esters and high rancidity and iodide index completely inhibits the development of *M. leprae*, as when DDS is added. In fact the mice of this type develop a syndrome of fatty acid deficiency with testicular atrophy, alopecia round the facial orifices, and marked segmentation of the tail. It seems that essential fatty acids are necessary to the development of *M. leprae*, which is supported by the fact that the diets with a high content of unsaturated fatty acids favoured the development of the bacilli.

The author states that he never noted macroscopic changes nor increase of size in inoculated organs in the rats and mice in the dietetic conditions of the experiment.

The author appends a graph which shows the marked effect in inoculation when on pro-oxidant diet, compared with standard diet and with control groups, all at nine months after inoculation.

Effect of Environmental Temperatures on Infection with Mycobacterium marinum (balnei) of Mice and a Number of Poikilothermic Species. Clark, H. F. and Shepard, C. C. Nov. 1963, *J. of Bacteriology*, **86,** 5, pp. 1057–1069.

Mycobacterium leprae (Shepard 1960) and two cultivable mycobacterial species, namely *M. marinum* (*M. balnei*) and *M. ulcerans* (Fenner 1956) grow preferably in the foot-pad of mice, this presumably due to its low temperature. The two cultivable species grow on artificial media at 31° to 35 °C, which is less than the deep body temperature of mice. The slow growth of *M. leprae* in the mouse foot-pad and the low yields of bacilli have limited the range of experiments. It seemed possible that the rate of growth and yield of bacilli in the mouse might be improved by altering the temperature of the mouse environment, and other animals with imperfect or absent temperature-regulating mechanisms might yield a more favourable result when placed at proper temperatures. The authors therefore inoculated *M. marinum* peripherally and systemically into mice and a variety of mammals and cold-blooded vertebrates held at different environmental temperatures. Tables 3 and 4 give a great deal of information about the poikilothermic animals used in this experiment, and Table 2 gives details of inoculation of *M. marinum* in mice maintained at different temperatures. For inoculations in the foot-pad of mice, the optimal temperature was 20 °C. In intravenously inoculated mice there was gross peripheral spread of the bacilli and lesions. The generation time of the bacilli was about 15 hours, which is roughly thrice that of *M. marinum* in bacteriological medium. Susceptiblity to *M. marinum* is very widespread among poikilothermic animals (alligator, turtles, salamander, chameleon, snakes, frogs, etc.). Bacillary multiplication could be obtained very consistently in small species and in the young of larger species. Natural conditions of transmission of infection by *M. marinum* were detected, e.g. tadpoles to tadpoles in water, minnows to tadpoles in water. The use of poikilothermic animals in the study of the effects of temperature on infections has definite advantages, since the temperature of the tissues is as easily adjustable as it is for *in vitro* systems. Making of cell cultures is easily done, and can be maintained for long periods. Of the poikilothermic animals many are too difficult to obtain, or do not live long under laboratory conditions. For growth in the mouse foot-pad, about five months of observation are usually needed.

The author concludes by mentioning sound evidence for assuming the identity of *M. marinum* and *M. balnei*, with priority to the former name.

Localização epithelial do Mycobacterium Leprae (Localization of *M. leprae* in the epithelium). H. Seabra Santos, *Rovisco Pais*, April-June 1964, **3,** 9, pp. 25-28, 5 figs – 2 of which in colour.

The author describes the occurrence of the bacilli of leprosy in the outer sheath of a hair, and not in the neighbouring epidermis of a patient 19 years of age. She had otherwise violaceous infiltration of the forehead, face, and pavilions of the ears, a diffuse discrete infiltration of the hands and forearms, and thickening in both cubital nerves. There were also rounded violaceous macules with ill-defined outlines in both buttocks, lateral aspect of the left hip, and medial aspect of the right hip.

The author thinks that the leprosy bacilli in the hair sheaths could be in part responsible for the hair atrophy and hair loss which occur in leprosy.