ACUTE NODULAR LEPROSY ORIGINATING IN THIS COUNTRY AND CURED BY VACCINE TREATMENT.

BY

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(With Special Plate.)

MR. X., a Chinese student, aged 36, who had been six months in this country, was brought to me on May 14th by Dr. Sherwill Dawe, with the following remarkable history:

The patient had been under his care for some weeks, suffering from severe pain in the left arm from the axilla to the wrist. Local applications, but no medicine, were given until three weeks later, when an eruption of nodules came out quite suddenly upon the face, and later upon the body. These gave rise to no subjective symptoms; there was no itching or pain. Under the impression that the eruption was an urticaria, calcium lactate was given by the mouth, and no other medicine had been taken by the patient. The eruption spread rapidly over the trunk and hands, and a patch of infiltrated skin, approximately four inches by two inches, appeared near the wrist, and a similar patch of induration upon the back a little later. He was brought to see me ten days after the first onset of the rash. The photograph (Fig. 1) gives a very fair impression of the state of the face when I saw him on May 14th. The skin over the forehead and cheeks was studded with granulomatous nodules; the face was generally swollen, especially over the forehead and nose. A large number of granulomatous nodules and plaques of indurated reddened skin were also found upon the back and front of the trunk. Upon the left forearm there was a very prominent induration of the skin, with a typical dusky flush; the ulnar nerve upon this side was greatly swollen and tender. The patient was obviously acutely ill, but no rise of temperature had been noted. The glands were generally enlarged.

I told Dr. Sherwill Dawe that I regarded the eruption as a lepride, and I obtained his permission to show the patient at the meeting of the Dermatological Section of the Royal Society of Medicine on May 20th. My diagnosis was confirmed by the unanimous opinion of the members present.

In the discussion which followed, Dr. Sequeira mentioned a case with an acute outbreak—the only one in his experience—in a woman who came from South Africa. Dr. Macleod gave an instance under his care of a boy in whom an acute outbreak of nodules, practically covering the body within forty-eight hours, had occurred, but the patient had had a previous attack of leprosy two years before. Dr. Whitfield mentioned a case under Dr. Pringle in whom an acute leprosy swelling of the face had come on within a few hours of an attack of malaria. Dr. Adamson pointed out the analogy between these cases and post-exanthematous lupus, which occurred after measles or other fevers in children who suffered from tuberculous glands. The rarity of such acute cases may be gauged from the fact that four medical men, with vast experience of skin disease, could each cite only one instance within their individual observation.

Further discussion ensued upon the measures to be taken, and it was again the unanimous opinion of the meeting that the prognosis was so desperate that the patient should be urged to take immediate steps to return to his home in China, if arrangements could be made for his transit.

Leprosy is not a notifiable disease in this country, and there is no adequate provision for the reception of such cases. Some years ago one of the members of the Section was confronted with an extremely difficult position, in which he sought the advice and assistance of his colleagues. A man suffering from leprosy had been living in lodgings in London. A lawsuit for damages, brought by the landlord, appeared probable, and this lesson of the very serious plight of a patient suffering from leprosy in England added to the urgency of the advice which I gave to Dr. Dawe, that the patient should leave England as speedily as possible, before his condition would prevent him from doing so.

Now comes the remarkable sequel. Mr. X. had the good fortune to come under the observation and treatment of Dr. James Hasson, whose very extensive experience of leprosy in Egypt enabled him to give a much more promising prognosis. The treatment adopted by Dr. Hasson is appended in a communication for which he is solely responsible.

The opportunities for seeing leprosy in this country are necessarily very limited, but I have had some exceptional opportunities of observing the disease in South Africa, the West Indies, and the Canary Islands. Some fifteen years ago I had the privilege of watching a case of leprosy under treatment by my colleague Sir Almroth Wright, who was giving small intramuscular doses of an emulsion of leprosy tissue obtained from a tumour excised from the patient. Some improvement at first resulted from this treatment, but it was never very encouraging, and was abandoned. Several other attempts have been made with the same means, notably by Dr. Winkelried Williams, but the improvement has not been such as to recommend a wide adoption of the method. It is the general experience that the products of chaulmoogra oil have not fulfilled the hopes expressed by Sir Leonard Rogers in his Croonian lectures of 1924.

The astonishing results obtained in the case now under consideration can best be apprehended by comparing Fig. 2, after treatment, with Figs. 1 and 3, before treatment. I examined Mr. X. in October, and am happy to report that the nodules and the tumefaction of the skin of the face have completely disappeared, the nodules leaving no trace of their presence other than a slight deepening of pigmentation. The indurated plaques upon the back and forearm have also vanished, leaving only a deepening of pigmentation in the flaccid skin covering the site of the induration. The general health of the patient has improved beyond all recognition, and it would really seem that we have at last obtained an effective method of treatment of this dreadful disease.

COMMUNICATION BY DR. JAMES HASSON.

The patient mentioned by my colleague Dr. Graham Little was sent to me by Dr. Manson-Bahr last June. I have nothing to add to the above account of the patient, except that there was a specific rhinitis which made breathing difficult. His temperature was one degree below normal, and the large lepride of the forearm was in certain parts anaesthetic, and in other parts hypo-aesthetic.

I commenced vaccine treatment immediately, and after a series of injections of 23 ampoules, a majority of which were given into the veins, the lepromata described above, as well as the large infiltrated lepride, melted away.

I showed the patient to Dr. Manson-Bahr after this series of injections, and we agreed to let the patient have a rest of one month, during which time I gave him one or two injections a week of 2 per cent. solution of lecithin in olive oil, inasmuch as his urine contained an appreciable quantity of phosphates. He lost a stone in weight.

The vaccine injections were resumed about July 20th—four a week, then three a week, and finally two a week—in very small doses so as to avoid the strong reaction from higher doses.

The patient has had fifty-three injections in all of vaccine in small doses, after a special formula containing three milliards of Hansen's bacilli instead of five, and five milliards of *Bacillus pyocyaneus* instead of fifteen, in each ampoule—an alteration, as explained above, determined by the general health of the patient.

The present situation is as follows: All the lepromata of the face and the body have completely disappeared; the large lepride of the forearm has gone. The rhinitis is cured to such a degree that the patient breathes normally. The nasal septum is intact and there is no indication of destruction of the bones of the nose. The anaesthesia of the lepromata and of the lepride gave place during the first week of treatment to hypo-aesthesia. Both these symptoms have disappeared now and the hair is growing normally. Blistering of an old nodule shows in the blisters complete absence of Hansen's bacillus. The

method of preparing vaccine has been described in the *Transactions* of the Royal Society of Tropical Medicine and Hygiene, No. 7, vol. xix.

By means of a stick of carbonic acid snow applied for from a half to one minute upon the lepromata or upon the anaesthetic macules a blister results, which if emptied twenty-four hours later contains a large number of the bacilli of Hansen. This method may also be used to confirm or to contradict the diagnosis of leprosy when it is doubtful.

The preparation of the leprosy vaccine is a very delicate process, and necessitates a long practice. When the blisters are formed on the patients with the CO₂ snow they must not be emptied until after a lapse of twenty-four hours. Thirty-six hours are necessary if it is desired to obtain a fair number of Hansen's bacilli. The serum taken from one patient with one special form of Hansen's

disease is then mixed with the serum taken from other patients suffering from different forms of leprosy, and the whole mixture is kept in the incubator from fifty days to three months at 36°C. Then a mixed culture of *Bacillus pyocyaneus* is added to the serum containing the Hansen's bacilli (previously rendered incoagulable by the addition of a sterile solution of 2½ per cent. sodium citrate). The whole is transferred to the centrifuge for twenty minutes, the requisite quantity of distilled water is added to the solution, the bacilli are counted, then washed with petrol-ether, and the vaccine put up in 2 c.cm. ampoules. An ampoule of 2 c.cm. contains five milliards of Hansen's bacilli and fifteen milliards of *Bacillus pyocyaneus*.

The conditions vary for each case according to the general state of the patient; but the average dose is two ampoules, to be injected into the veins weekly.

British Medical Association.

PROCEEDINGS OF SECTIONS AT THE ANNUAL MEETING, NOTTINGHAM, 1926.

SECTION OF NEUROLOGY AND PSYCHOLOGY.

E. FARQUHAR BUZZARD, M.D., F.R.C.P., President.

DISCUSSION ON PITUITARY DISORDERS.

OPENING PAPERS.

I.—GORDON HOLMES, C.M.G., C.B.E., M.D., F.R.C.P.,
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My aim in opening this discussion will be to give a general survey of pituitary disorders and leave it to those who follow me to fill in details. I am fully conscious of the difficulty of the task, for the hypophysis, or pituitary body, is a complex structure composed of several distinct parts of different origin and different function, and disease may involve all of these parts together, or any one or more of them at a time; again, it may produce either loss or excess of function. Further, recent investigations have thrown doubt on hypotheses which we have accepted as physiological facts; it may, indeed, be said that the physiology of the pituitary body is still in the melting-pot. Another difficulty in the subject is that whatever may be the normal functions of the hypophysis they are so closely related to the activities of other glands, and especially to those of the sex organs, that a distinction of the clinical symptoms produced by their disease is often not easy, or their interpretation is uncertain.

It will, however, be my aim to deal with the clinical manifestations only of pituitary disease, and to place before you mainly the practical applications of my own experience. I shall have to refer from time to time to recent experimental work, but I shall do so only when this is necessary for the recognition and treatment of pituitary disorders.

It is now generally admitted that the pituitary body has important influences on growth, on sexual development and activity, and on the general metabolism of the body, and that these separate functions depend on different parts of it. A secretion or hormone of cells of the anterior lobe stimulates the growth of bones and influences the development of the skin and of some visceral organs; the pars intermedia and the posterior lobe control the development of the sex organs, while carbohydrate metabolism is also influenced by the posterior lobe. The infundibulum, or rather the pars tuberalis that lies on it, is probably concerned with the secretion of urine.

The functions of the pituitary may be disturbed by many different types of disease. Tumours arising from its cells are probably the most common lesion in clinical practice, but it may be invaded by metastatic growths too. Then

it may be injured by disease originating outside the sella turcica, as by tumours growing from the meninges or from Rathke's pouch; by the distended floor of the third ventricle in the case of hydrocephalus; or by syphilis or encephalitis in the region of the infundibulum. These extrasellar lesions may compress the gland, or produce effects by blocking the secretions from the posterior lobe that normally enter the cerebro-spinal circulation through the third ventricle, or interrupt the nervous connexions between the pituitary and the hypothalamus. In other cases there is an aplasia or defective development of the pituitary, owing to either congenital or mechanical causes, or the organ may undergo regressive changes. Finally, alterations in the size and functions of the pituitary may be associated with disease or functional disturbances of other endocrine organs, as in pregnancy, in castration or atrophy of the sex glands, and with disease of the thyroid.

The clinical symptoms of pituitary disease are generally divided into those due to overactivity of a part of the gland, producing the condition of hyperpituitarism, and those that result from loss or deficiency of some of its secretions, or hypopituitarism. This classification is probably the most useful that can be proposed in the present state of our knowledge. It is, however, as yet an unproved assumption that the secretions of the cells of an adenoma are identical with those of normal cells, and the gross pathological lesions that most commonly cause symptoms can scarcely have selective actions on one part of the gland only. Adenomata of the anterior lobe, for instance, necessarily compress other parts in addition to altering the functional state of the anterior lobe cells. Many clinical symptoms must therefore be regarded as those of a dyspituitarism or altered cellular function, or as the combined result of the abolition or defective activity of some cells or parts, and the overactivity of other cells or parts. For clinical purposes, however, it is still advisable to retain the terms "hyperpituitarism" and "hypopituitarism."

The best method of presenting the subject for discussion will probably be to describe to you some of the more important clinical features of pituitary disease, and the more common modes in which they are grouped together.

DISTURBANCES OF GROWTH.

The best known and most common form of pathological overgrowth is acromegaly, which, since Marie described it in 1886, has been known to be associated with an enlargement or a tumour of the anterior lobe of the pituitary. It is true that in a few of the recorded cases no tumour or other lesion of the hypophysis was found, but in these there may have been a similar growth or an overfunction of an accessory pituitary, the common presence of which in the neighbourhood of the main gland or along the course of the pharyngo-cranial canal has been pointed out by Erdheim and others.

Benda originally showed that the characteristic lesion in acromegaly is an adenoma of the eosinophil cells of the anterior lobe, which usually deviates so little from the structure of the normal elements that we may assume the tumour produces a similar secretion; in other words, there is a physiological excess as well as an anatomical increase

FIG. 1.—Pituitary adenoma. Typical x-ray appearance of sella turcica. Note the characteristic even "ballooning." Film by Dr. Hope Fowler. J. W., female, aged 40; Deaconess Hospital, 1925; transphenoidal operation with marked improvement to vision.

FIG. 3.—Hydrocephalus due to pericerebellar adhesions. Ventriculography. Air outlines enormously distended anterior horns. The third ventricle is seen to dip into the flattened sella turcica. The dorsum sellae is eroded. Note marked atrophy at vault and gaping of coronal suture. J. S., male, aged 15; Deaconess Hospital, 1926; cerebellar decompression; adhesions freed. (Film taken with head in inverted position.)

FIG. 2.—Suprasellar cyst. Typical calcification in solid base of tumour. Slight erosion of posterior clinoid processes. (Film by Dr. Hope Fowler.) Female, aged 11. Private series, 1923. No operation possible.

FIG. 4.—Large right parietal glioma. Typical pressure atrophy with obliteration of dorsum sellae, thinning of floor and anterior clinoid processes and orbital plates; stippling of inner table over vault. (Film by Dr. Hope Fowler.) Male, aged 42. Private series, 1925. Wide decompression over growth.

E. GRAHAM LITTLE: ACUTE NODULAR LEPROSY.

FIG. 1.—Face, before treatment.

FIG. 2.—Face, after treatment.

FIG. 3.—Back of trunk, before treatment.