An Address ON TUBERCULOSIS AND THE NERVOUS SYSTEM.*

BY
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THE title of my address gives me a wide choice of subjects for discussion, a choice which must be limited by the time at my disposal and influenced by the wish to touch upon matters of interest and importance. Before considering the direct results of the invasion of the nervous system by the tubercle bacillus let me call your attention to such changes as may occur in the personality of patients who suffer from tuberculosis of other organs. It would be surprising if changes did not occur, and equally surprising if they did not vary with, and to some extent depend upon, the inherent and acquired characters of the individual. What other factors may be concerned in their production? The psychogenic factor must be admitted, and this, at its outset anyway, can hardly fail to be a depressant in its action. In these days it is scarcely possible for a victim of pulmonary tuberculosis to be ignorant of the nature of his trouble or to be blind to the inferences to be drawn from the diagnosis of consumption or phthisis. The initial phase of depression, born of this knowledge, is not, however, necessarily of long duration; reassurance, the beneficial results of treatment, and possibly the absence of pain, combine to bring about a brighter outlook. But the "spes phthisica" denotes something more remarkable—that is to say, the inability of the patient to realize the gravity of his condition in spite of increasing distress, increasing disability, and all the signs which, to the onlooker, point to only one end. That "hope springs eternal in the human breast" is not a scientific explanation of this phenomenon and is not supported by another quotation from Pope: "Heaven from all creatures hides the book of Fate, All but the page prescribed, their present state." I would submit that in this instance it is the poisonous products of disintegrating bacilli, exerting their influence on the highest nerve centres, which hinder realization of the present state.

This suggestion does not seem so far-fetched if we recall the picture of Korsakow's psychosis, a clinical syndrome which in its earliest stages is characterized by a defect of retention for recent events, a lack of insight and some degree of euphoria, accompanied by the ability to converse with clearness, intelligence, and plausibility. In the majority of cases Korsakow's psychosis is etiologically concerned with the abuse of alcohol, but it has been observed in connexion with malaria, typhoid fever, and tuberculosis. In support of the toxic origin of phthisical optimism is the fact that it is more often observed in severe and chronic cases than in patients whose favourable progress would give it justification. In other words, its presence, although merciful, does not warrant a cheerful prognosis.

DISTURBANCES OF NERVOUS FUNCTION.

Most patients suffering from chronic tuberculosis undergo changes in disposition, changes which are common to many forms of invalidism and for which their relations and friends, on the one hand, and their general nervous exhaustion on the other, are mainly responsible. Irritability, lack of consideration, indecision, vacillation, and failure of concentration are all familiar features of any sick-room and cannot be considered pathognomonic.

Psychoses, generally speaking, have no special incidence on tuberculous patients, but the susceptibility of psychotic patients to pulmonary tuberculosis is, of course, well recognized, and the association of mental disorders with

tuberculosis in family histories is met with more frequently than can be explained by coincidence.

The evidence for a specific peripheral neuritis of tuberculous origin is not convincing, and I cannot recall a case which gives it support. Multiple neuritis may develop in bedridden patients suffering from septic absorption, and it is difficult to disregard that factor in a case of tuberculosis complicated by secondary infections.

The regulation of the autonomic nervous system is often unstable; pyrexia, sweats, localized vasomotor disorders such as those seen on the cheeks, are significant in this connexion, and a syndrome indicating hyperthyroidism may attract attention. In addition, the cervical sympathetic nerve supply may be involved in the local morbid process and oculo-pupillary phenomena develop on one side.

No physician whose practice is largely concerned with thoracic disease can afford to neglect the study of pains, nor to overlook the significance of painful and tender areas on the surface of the body remote from their site of origin. The pain referred to the shoulder region, accompanied by cutaneous hyperalgesia, when the diaphragm is the seat of disease, is a case in point, and the various locations of headache associated with pathological disturbances in different parts of the lung are more than haphazard in their determination.

So much for some of the casual disturbances of nervous function resulting from the presence of a tuberculous lesion in any part of the body. Such a lesion, however, once established, must be regarded as a potential menace to the nervous system itself, with the possibility of attack either by direct extension through the tissues which form its natural, but not always efficient, protection, or through the medium of metastasis. Of all infections of the nervous system, with the exception of syphilis, the tuberculous is the most frequent, especially during the periods of infancy, childhood, and adolescence.

TUBERCULOMA.

This age incidence is applicable to the occurrence of tuberculomata, which are probably the commonest tumours of the brain in the young. The majority of them are more of academic interest than of practical importance, as they are often small, multiple, and discovered in patients who have succumbed to phthisis or to a secondary meningitis. They are generally located in that part of the brain and brain stem which fills the posterior fossa.

A more important, though less common, problem is presented by a large tuberculoma developing in one cerebral or cerebellar lobe, and giving rise to the characteristic signs and symptoms of an intracranial neoplasm. Such an event may occur in a patient who has an apparently quiescent tuberculous lesion in the thorax and whose general health is more or less unimpaired. A typical example of such a problem is afforded by a case with which I had to deal a few years ago.

A young married woman, about 24 years of age, was under my care in hospital on account of headache, vomiting, and early optic neuritis. She presented physical signs which pointed to a tumour of the right frontal lobe, and others which were unmistakably those of a small tuberculous lesion at the apex of one lung. The probabilities were in favour of a cerebral tuberculoma, but it was quite possible that a growth of some other nature might be responsible for the patient's trouble, and my colleague Sir Percy Sargent agreed to explore the site of disease. He found and removed a spherical hard mass, about the size of a large marble, embedded just beneath the surface of the brain and easily detachable from the surrounding soft tissue. Its consistence and attachment to the pia-arachnoid were more suggestive of some form of meningioma than of a granuloma, but, on section, it proved to be an encapsulated tuberculous abscess or broken-down tuberculoma. Its liquid content included no living pyogenic organisms, and its fibrous wall was nearly an eighth of an inch in thickness.

The operation was one demanding great care and skill in avoiding any escape of fluid from the abscess, or injury to the adjacent structures, but was completely successful in its object. So successful, indeed, that after a long stay in hospital and a convalescent home, the patient was able to return to her family fully restored to health. Unfortunately domestic conditions were unfavourable, the lung disease flared up, and brought about her death a year or two later.

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The risk of setting up an acute tuberculous meningitis in the process of removing tuberculomata must be constantly present to the mind of a surgeon undertaking the task, and considerable judgement is required in deciding on the propitious moment for operation. In some instances it is wise to give the patient a prolonged course of rest and open-air treatment before any attempt is made to eradicate the disease, so long as it is possible to keep him under strict observation and watch the progress of papilloedema and other physical disturbances. Adopting these principles, I have seen at least one large tuberculoma, with a firm capsule and caseous centre, removed from a cerebellar lobe with excellent and lasting results.

Under the microscope tuberculomata of the brain and spinal cord may be recognized by their caseous centres, surrounding which will be found a zone either of giant-celled nodules or of infiltrating epithelioid cells, along with disintegrated nervous elements. Further afield there is evidence of toxic degeneration of nerve cells and often an abundance of granular corpuscles. Neighbouring blood vessels are congested and, where they penetrate the outer layers of the tuberculoma, are found to be thrombosed. The amount of fibrous wall depends on the local reaction of the tissues, the virulence of the bacilli, and the age of the growth.

CHRONIC TUBERCULOUS MENINGITIS.

A subject which is of interest, and perhaps of more far-reaching importance than appears at first sight, is that of local chronic tuberculous meningitis or meningo-myelitis. The following story will illustrate its clinical and pathological bearings and emphasize their significance.

A girl, 14 years of age, with a history of having suffered from frequent epileptic attacks during the previous two years, came under my care in St. Thomas's Hospital. Her attacks were of the Jacksonian type, beginning with spasm in one upper limb and following a definite line of march before consciousness was lost. In the intervals the girl was quite well and free from headaches. Examination revealed no physical signs of disease, and there was no story of illness or injury which could be regarded as of etiological importance. A routine x-ray examination of the head, however, revealed an unusual picture. There were seen scattered over the precentral convolution of one hemisphere a number of small very dark shadows suggestive of osseous or calcareous bodies, some of which were in a position to account for the epileptic symptoms. Finding that the attacks could not be controlled by bromides, and encouraged by the radiographical findings, I asked Sir Percy Sargent to explore. He discovered an area of chronic leptomeningitis in which a number of calcareous nodules were embedded, and proceeded to dissect the latter away from that part of the motor area which is responsible for movements of the upper limb. The osteoplastic flap was replaced and bromide treatment was resumed with very much more successful results. Many months passed without any attacks, and the child was able to resume her normal life.

Although positive proof was lacking, there could be no doubt that we had to deal with the scars of an old tuberculous meningitis limited to a small surface area of one hemisphere. The calcareous deposits alone enabled the lesion to be detected by the radiologist, and so provided a clue to the pathology of the condition. In the absence of calcareous deposits that clue would have been wanting, and the question naturally arises as to the frequency of localized tuberculous meningitis and its possible bearing on the origin of many obscure cases of epilepsy. In exploratory operations on patients suffering from Jacksonian attacks focal thickenings of the leptomeninges, sometimes associated with small loculated collections of fluid, are not infrequently met with, and it seems quite likely that some of these may be the cicatrices of old tuberculous lesions. Certain it is that calcareous nodules in this situation are very rarely come across, in spite of the general use of radiography in cases such as the one I have described. On the other hand, small tuberculomata may be found in relation to the soft meninges in patients dying from generalized tuberculous infection.

JACKSONIAN EPILEPSY.

Having been led circuitously into the field of Jacksonian epilepsy, I am disinclined to leave it without uttering a protest against the common but fallacious belief that the

removal of anything from the cerebral cortex or its meninges is an adequate measure in itself to arrest the disease. It cannot be too strongly emphasized that such a source of irritation is only one factor in the evolution of epilepsy, and that the habit or inclination to "fit" is not only as important, but a great deal more difficult to eradicate. An operation, therefore, should be followed by a prolonged course of bromide therapy if it is to be given any chance of achieving the object for which it has been undertaken. Surgical measures for the relief of epilepsy have often failed in the past on account of ignorance or neglect of this principle, and too much has been asked and expected of them.

ACUTE TUBERCULOUS MENINGITIS.

Acute tuberculous meningitis is so common, and so minutely described in all textbooks of medicine, that I shall make no attempt to retail to you its protean symptomatology. Since Robert Whytt of Edinburgh, in the eighteenth century, published his *Observations on the Dropsy in the Brain* its pathological features have been well recognized, and since 1833, when Gerhard of Philadelphia produced his monograph on *Tuberculous Meningitis in Children*, little of clinical interest has been added to our knowledge. But during the last ten years the advent of epidemic encephalitis has made the problem of diagnosis a more difficult one, in that both diseases can display identical symptoms and run very similar courses. When that diagnostic difficulty arises we are often obliged to rely on an investigation of the cerebro-spinal fluid in order to overcome it, and a short space of time will not be wasted in considering the information which can be derived from a lumbar puncture.

The fluid in tuberculous meningitis is usually clear, although in the later stages of the disease it may display a faintly yellowish turbidity. It always comes away under increased pressure, and, if allowed to stand, develops a fibrinous coagulum in the meshes of which a few tubercle bacilli can usually be detected. The cytology of the fluid is characterized by an increase of cells, chiefly, but not all, of the small lymphocytic variety, which may vary in number from 25 to several hundreds per cubic millimetre. Other cells, such as macrophage, large mononuclear, and plasma, are found in much smaller numbers in most cases. The amount of protein, always increased, varies from 30 to 200 or 300 mg. in 100 c.cm. of the fluid, and tends to rise in the course of the disease. Globulin reactions are usually positive. Glucose and the chlorides are progressively reduced in quantity, and the chlorides in particular may reach a lower level than is met with under any other pathological condition.

In encephalitis, on the other hand, the fluid is always clear except for the occasional presence of blood, and no coagulum ever forms unless haemorrhage has taken place. Its pressure is only moderately raised, and if cells are present in excess they are almost entirely of the small lymphocytic variety, and rarely number more than 80 or 100 per c.mm. Protein and globulin are generally within normal limits. The same remark applies to the chlorides, but glucose is often slightly increased in amount.

These are the essential features of the fluid obtained by lumbar puncture in the two diseases, and they afford a most competent guide to diagnosis when we are faced with an acute febrile condition in which there is evidence of diffuse and scattered lesions disturbing various functions of the central nervous system. A differential diagnosis based on the clinical picture alone is often difficult, sometimes impossible.

Another fairly common disease in children which may, in its early stages, give rise to a suspicion of tuberculous meningitis is that due to the virus of poliomyelitis and poliomyelitis. Symptoms and signs of meningeal irritation, in the form of headache, head retraction, and diplopia, with stabismus, are very frequent, and are often associated with vomiting and fever. The cerebro-spinal fluid in the pre-paralytic stage may afford help in arriving at a correct diagnosis. Its important features are a considerable increase of cells, from 30 to 1,500 per c.mm., of which the large majority are polymorphonuclear. Protein may or may not be slightly increased, while glucose and the chlorides remain normal. Changes in the cytological

picture rapidly appear, and in the course of a few days the cell count may reveal a large percentage of lymphocytes and a comparatively few polymorphs. But in spite of this lymphocytosis the glucose and chloride content is not diminished. In fact, the maintenance of the normal quantity of the chlorides must be regarded as strong evidence against the presence of increasing meningeal inflammation. The importance of this is further emphasised by the fact that in cases of poliomyelitis, as in cases of tuberculous meningitis, there may be seen a fibrinous coagulum which develops when the fluid is kept standing, and which is never met with in cases of epidemic or lethargic encephalitis.¹

The value attaching to examinations of the spinal fluid in the diagnosis of tuberculous meningitis is much increased when this disease occurs in older subjects. In adults the clinical picture often differs from that seen in infants, and sometimes presents great difficulties. I refer particularly to its insidious onset, long-drawn-out course, the slight or absent fever, and the prominence of mental as opposed to physical disturbances of function. It must be within the recollection of most of us to have met with cases of this kind in which the diagnosis has only been arrived at after much delay.

The prognosis in acute tuberculous meningitis when it is only a part of a general miliary tuberculosis is as bad as it can be. But the same cannot be said when the spread of infection is limited to the nervous system, and the diagnosis of tuberculous meningitis, even when acute, does not always justify a hopeless outlook. I have seen more than one patient recover, and careful review of this subject some years ago led A. E. Martin to these conclusions:

1. That undoubtedly long remissions and even recoveries do occur in tuberculous meningitis.
2. That recoveries are possibly more frequent than has been believed, since no fewer than twenty established cases have been recorded since 1894, together with a number of others in which the same definite proof has not been afforded.
3. That in these cases either the resistance of the individual is so much greater than usual that the disease is checked early in its course, or the virulence of the bacilli is so much less than usual that the lesion in the meninges becomes localized and undergoes a fibrous change.

On the other hand, he goes on to say "that the lesion in the meninges may at a later period form the focus of a fresh infection which usually terminates fatally, and that consequently the prognosis in these cases must be guarded."

Martin, as was natural, regarded the discovery of tubercle bacilli in the cerebro-spinal fluid as the fundamental evidence requisite for establishing a correct diagnosis. Later writers have shown that bacilli are discoverable in almost 100 per cent. of cases if care and skill are employed in the search for them.

Tubercles in the choroid were of more importance in the diagnosis of tuberculous meningitis before lumbar puncture became part of a physician's equipment. They were first seen with the ophthalmoscope by Jäger in 1855, but their presence cannot be regarded as sufficiently frequent to afford much help, and their absence cannot be advanced as an argument against the diagnosis of tuberculous meningitis. Moreover, it must be remembered that they have been observed in tuberculous subjects without other evidence of involvement of the nervous system. Although of little practical importance, therefore, they nevertheless provide us with the only opportunities for seeing isolated tubercles during life, and the white, yellowish, or reddish-yellow, rounded spots with pale centres are very characteristic when they come under observation. As a rule they cause no symptoms, although transient disturbances of sight have been recorded.

SPINAL CARIES.

No consideration of tuberculosis in relation to the nervous system would be complete without reference to Pott's disease of the spine, or spinal caries. That cases of

this disabling disease have become less numerous and less disastrous during the last quarter of a century can hardly be denied, and the credit for that blessing may be frankly given to those who are concerned principally with the preventive side of medicine.

Percival Pott was a surgeon on the staff of St. Bartholomew's Hospital whose name might not have been known to posterity except for two reasons. In the first place, he was fortunate enough to fall in the street and sustain a fracture of the fibula which thereafter bore his name. As the result of the enforced leisure consequent on this accident he took to writing, and some years later, in 1779, produced his epoch-making pamphlet on palsy from spinal deformity. In the second place, he earned our gratitude for being the man from whom John Hunter derived not only much of his medical knowledge, but his inspiration for pathological research.

Pott, however, did not really describe the tuberculous nature of his disease, which had been surmised by Hippocrates and Galen, but drew attention to the characters of spinal deformities and their sequelae. The tuberculous origin of spinal caries was finally established by a less fortunate Frenchman, Delpech of Toulouse, the pioneer of orthopaedic surgery in that country. He met a violent death at the hands of a patient on whom he had operated for varicocele and who thought he had thereby been rendered unfit for marriage.

So much for the romance of Pott's disease. It has another aspect worthy of our notice in the question of its treatment, the guiding principles of which demand some acquaintance with the pathology of the disease and with the mechanism of compression paraplegia.

Spinal caries is an osteomyelitis of the vertebrae commencing either in the cancellous tissue of the body close to an intervertebral disc or at the root of the laminae. Much erosion of the body may take place, with or without resulting deformity and without disturbance of the spinal cord. In the same way an abscess, arising from a small focus of bony disease, may track in various directions and attain a great size without the development of a kyphosis or paraplegia. On the other hand, paraplegia may be the first symptom of the disease without obvious abscess formation or angular curvature.

Speaking generally, it is not often that bony deformity alone produces paraplegia, nor is the presence of a psoas or lumbar or retro-pharyngeal abscess necessarily associated with nervous symptoms. Compression usually results either from an abscess bursting through the posterior common ligament or from tuberculous granulations filling up the epidural space and forming a cuff of dense tissue around the dura mater. As a consequence of this strangulation the subarachnoid space may be completely obliterated and the vascular supply of the cord seriously interfered with. Only rarely does the displacement of a sequestrum backwards from a diseased vertebral body cause direct pressure on the cord, or a sharp kyphosis bring about a kinking of that organ.

In deciding on the appropriate line of treatment for any particular case, all these pathological processes must be passed in review and the attempt made to assign the paraplegia to one or more of them. It is of paramount importance to remember that the injury done by compression largely depends on interference with vascular supply, which leads to ischaemia, softening, and finally sclerosis. Unless the circulation can be restored and maintained, return of function is impossible, and the longer circulation is inadequate, the less chance is there of an ultimate success for treatment. Therefore, before deciding on rest and extension as the measure to be adopted, every effort should be made to exclude the presence of such compression as will not be relieved by that form of treatment. An abscess inside the vertebral canal may need evacuation, or a simple decompression may suffice when the epidural space is filled with granular tissue.

On the whole, it is true to say that caries in children is more often cured by simple rest and extension than it is in adults, but every case must be considered on its own merits and in the light provided by the known pathology of the disease.

¹ Vide *Cerebro-spinal Fluid in Clinical Diagnosis*, Greenfield and Carmichael.