Lecture.

ENCEPHALITIS LETHARGICA.

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(*Concluded from p.* 77.)

(2) *Nervous Symptoms.*

These may roughly be classified as follows:—(i) Cerebral. (ii) Cerebellar. (iii) Mesencephalic, including basal ganglia, pons, and medulla. (iv) Spinal. (v) Vegetative.

There is bound to be some overlapping in such a system, as several, if not all, the segments, have some influence in each nerve action.

(1) *Cerebral.*—Symptoms pointing to *meningeal irritation* are common, and all the symptoms of meningitis may be simulated, except those due to persistent high intracranial pressure, e.g., choked disk. Stiffness of the neck and cutaneous hyperæsthesia are common, and Kernig's and Brudzinski's signs of meningitis are frequently positive in encephalitis lethargica.

Motor Cortex.—Jacksonian fits occur in a few cases, and may be followed by a cortical or subcortical paralysis. Epileptiform convulsions also occur.

Speech Centres.—Aphonia, monotony of speech with slowness or rapidity of word utterance are common. Stammering has been noted in a few cases. Aphasia also has been noted, but rarely.

Sensory Cortex.—Some of the pains and hyperæsthesias are probably cortical in origin, for the distribution does not follow the spinal root type; others, however, are distinctly of spinal type. Hallucinations dependent upon irritation of the spinal sensory cortex are not infrequent.

Higher Psychic Centres.—Mental irritability is frequent in the early stages. Delirium is usually present at some stage of the illness in all but the milder cases: Nocturnal delirium, a striking contrast to the frequent diurnal lethargy is very common, and is a point of great diagnostic significance. All stages of mental depression are met with. The converse—active maniacal states—are not infrequent. Mentality, on the whole, is slow in the vast majority of the cases, but it is not abolished; the degree of mentality present contrasts strikingly with the almost comatose appearance of the patient; this point was noted by Galen 2,000 years ago [24].

(2) *Cerebellar Symptoms.*—Most of the symptoms which might be regarded as indicative of a cerebellar lesion are more easily dealt with in the next section, i.e., spasticity, vertigo, and nystagmus. Cerebellar ataxy of a generalized nature has been described, in one case accompanied by vertigo and nystagmus.

(3) *Mesencephalic* (including basal ganglia, pons, and medulla).—These are the most frequent—so much so that at first it was thought that the pathological condition was confined to this area, and one of the proposed names for the condition was mesencephalitis. Indications of a lesion on this area will usually be found at some stage of the disease.

Somnolence.—The characteristic symptom of the disease is almost always present at some stage—in fact, one would hesitate in the diagnosis if some indication of its presence was not evident at some time. The centre for sleep, if such a name can be given, has been localized in the mid-brain near to the centre of the oculomotor nerve [25]. This fact explains the frequency with which somnolence and ocular palsies are met with in the disease. The mere presence of somnolence is by no means pathognomonic of the condition, however, for any similar lesion in this area will produce the same reaction, and somnolence has been noted in tubercular and syphilitic encephalitis, and also in true sleeping sickness or trypanosomiasis. The patient appears to be soundly asleep, but may respond to questions rapidly, may take a small part in a conversation, and take food without appearing to wake up. The somnolence is most marked in the day time as a general rule; at night delirium and insomnia are frequent.

Symptoms produced by Involvement of the Nuclei of the Cerebral Nerves.—For brevity only the more important of these will be noted:—

(*a*) *Optic Nerves.—Amaurosis* of a transient nature has been noted. Optic *neuritis* was observed by Symonds in four cases [26]; until this description appeared, the absence of optic neuritis was regarded as of importance in differential diagnosis: it is evident, however, that optic neuritis is very infrequent. Optic atrophy has not been noted.

Photophobia is frequently present, especially in the early stages.

(*b*) *Oculomotor Group, including Trochlear and Abducens.*—Paralysis of a more or less transient character, or more frequently paresis, constitute one of the most frequent and important of symptoms. *Ptosis* is almost always present—it is usually bilateral and incomplete, and is a factor of some importance in the production of the facies of the condition.

Strabismus is frequent, but may be of very brief duration. Of greater frequency, and of equal diagnostic value, is a symmetrical diminution of the vertical movement of the globes: the movement being good above the horizontal, but markedly deficient or even absent below the horizontal plane.

Aniscoria is frequent and may or may not depend upon paralysis of the ciliary muscle. Paralysis of accommodation is commonly met with and this paralysis is of a less transient nature than most of the other palsies.

(*c*) *The Facial Nerve.*—The presence of signs of involvement of the facial nucleus is almost constant—though the duration of these symptoms, like all the symptoms of encephalitis, may be very short. Symptoms vary from paralysis, which is infrequent to slight paresis which has been present in all the cases I have seen. The resultant facies is of great value in diagnosis, but is very much easier to recognize than to describe: the face is smooth, wrinkles and folds being largely obliterated; the complexion is usually pale, the eyelids droop or are closed, and the mouth is a little open. Any facial movement is executed slowly and the impression given by the face is one of advanced fatigue. Whether or not, however, this facies is purely dependent upon involvement of the facial nucleus remains to be proved—for a somewhat similar facies, the so-called Parkinsonian mask, is met with in paralysis agitans, in which lesions of the substantia nigra have been described—the substantia nigra is only separated from the oculomotor nucleus by the red nucleus. In myasthenia gravis a somewhat similar facies is encountered.

(*d*) *The Auditory and Vestibular Nerves.*—Transient deafness has been noted occasionally. Tinnitus aurium is fairly frequent. Vertigo is common and may be the presenting symptom, as in one of the local cases: usually the vertigo is of vestibular origin, but when strabismus is present may be dependent upon diplopia. Nystagmus is not infrequent, but more frequently nystagmoid jerks are met with and only when the eye muscles are in strained positions and are probably due to imperfect balance in the oculomotor muscles. In some cases the vertigo and nystagmus are of cerebellar type.

(*e*) *Glossopharyngeal, Vagus and Hypoglossal Symptoms.*—More or less intense paresis of these nerves is usually present in cases of any severity, and leads to the difficulty in swallowing which is so common. Diminution of the sensibility of the larynx and pharynx with resultant diminution or absence of the cough reflex, due to involvement of these nuclei, is probably one of the chief factors in the production of the pneumonia, which is frequently aspiration type. The aphonia and dysarthria noted above are to some extent dependent upon a paresis of the hypoglossal nerve.

Spasticity is frequently noted in the muscles of the limbs or trunk and is probably due to involvement of the red nucleus or interruption of the cerebellar-vestibular or rubro-spinal tracts at some other point, or to a lesion of the lenticular nucleus. The spasticity is frequently accompanied by clonus and may be general or localized to a single group of muscles, thus Massari [27] noted a stiffness of the abdominal muscles, which in the absence of other signs, simulated the reflex spasticity of an acute abdominal lesion.

Tremor is frequently noted and is another symptom attributable to a lesion of the red nucleus.

Convulsive laughter without a visible causation, attributable to involvement of the corpus striatum has been observed by Netter, Sicard and Paraf [28].

(4) *Spinal Symptoms.*—A lower neurone paralysis, similar to that of poliomyelitis but not so acute, and chiefly involving the upper cervical levels has been observed. The symptoms of irritation of the anterior cornua of the spinal cord have also been noted—these are the fibrillary twitching and tremor met with in progressive muscular atrophy. Motor spinal symptoms are unusual, however.

Numbness, formication paræsthesias and hyperæsthesias of spinal type are more frequently observed—and somewhat persistent neuralgic pains of spinal distribution are not uncommon. This is not to be wondered at when Bashford states that the most characteristic lesion of the disease is noted in the upper cervical ganglia.

(5) *Symptoms due to Involvement of the Vegetative System.*—Hiccough complicating encephalitis appears to be a much more frequent symptom in the later cases. The epidemic hiccough noted of late in France and England is regarded by Netter, Sicard, and Paraf [29] as a manifestation of mild encephalitis. The hiccough is not a pure hiccough, i.e., it is not limited to the muscles of the glottis and the diaphragm, and only one side of the latter muscle may be involved (*v.* Note D).

Involuntary movements of choreiform, athetoid or myoclonic type are becoming increasingly frequent. They are present chiefly during the stage of the declared disease. They may disappear during sleep, but owing to their presence sleep may be prevented. They vary considerably in frequency, kind and amplitude of

movement and when frequent are very exhausting to the patient. Their classification under the vegetative group of symptoms can be disputed—but, as will be seen under treatment, some observers have noted an intensification of the movements on the exhibition of adrenalin and a marked dimunition with atropine [30].

Sweating is not uncommon and may be localized or generalized.

Salivation more or less marked is not uncommon and further attention will be given to this symptom under the discussion of treatment.

Myalgies.—Some of the pains are possibly dependent upon vasomotor involvement with anæmic spasm.

Tropic Sores.—Bed sores develop with great rapidity in severe cases and after pneumonia they may be regarded as the most fatal complications.

Retention and incontinence of urine and fæces are frequently observed in cases of any severity. Retention of urine is as frequent as incontinence. Of late cases have been noted where incontinence of urine has been the outstanding symptom [31],

The Reflexes.—The condition of the reflexes is as variable as the symptomatology, and equally dependent upon the anatomical site of the lesion. The cutaneous reflexes are commonly preserved—but Babinski's reflex is commonly obtained. The tendon reflexes may be lost or exaggerated and early loss is of some prognostic importance. The variability of the reflexes from day to day in an individual case is a point of some importance.

Clinical Pathology.—The *blood*—no abnormality has been noted in the cytology of the blood: this is of importance, for in the early stages of poliomyelitis and frequently in tubercular meningitis a well marked leucocytosis has been found. The absence of leucocytosis is important. With the exception of one series of cases noted under ætiology, culture of the blood has been negative. A Wassermann reaction of the blood should always be made and is negative in uncomplicated cases.

Cerebrospinal Fluid.—As a rule the cerebrospinal fluid is under some pressure but is clear. A slight excess of protein is not unusual. The glucose is found to be increased: Netter has found as much as 0·97 gramme per litre [32] and regards this increase as a factor of diagnostic importance; he attributed the increase to stimulation of Claude Bernard's centre in the floor of the fourth ventricle. The cell content is of interest—at the onset of the disease and of remissions there may be an increase of the lymphoid cells; these diminish as the disease progresses and in a stationary or recurring case a normal count may be found. Not a sufficient number of cases have been observed to estimate the constancy of this finding, however. In poliomyelitis an initial occurrence of polymorph cell has been noted [33] with disappearance and appearance of lymphoid cells later. In tubercular meningitis a progressive increase of the lymphoid cells is the rule, and the amount of protein is proportional to the number of cells.

The urea content of the cerebrospinal fluid has shown no changes in encephalitis: in one doubtful case of this series a finding of 0·95 per cent of urea lead to a diagnosis of uræmia, which was confirmed by the lesions found at the autopsy. The Wassermann reaction should be negative.

Urine, as a rule, shows little or no changes. A trace of albumin has been

noted. Signs of cystitis or pyelitis are not infrequent in long standing cases where there has been much catheterization necessary. The urea is normal or reduced. The ammonia-urea nitrogen ratio in one case was reduced to below the acidosis level. In two cases I found acetone in the urine. (*v.* Note E.)

The *Duration* of the disease is very variable. In 88 cases recovery followed within one month in 23 cases; within two months in 22 cases; within three months in 10 cases, and exceeded this time in 33 cases [34]. The duration is proportional to the severity of the case, with the exceptions of the severe and rapidly fatal cases. No statement should be hazarded as to the probable period of invalidity. Remissions are not infrequent, and a case at present in hospital, who apparently recovered in a week, but was kept under observation for a month, returned to hospital with a remission very soon after joining his unit. At present mild or abortive types appear to be occurring with greater frequency than in the earlier epidemics, but this may be due to the more frequent recognition of the disease.

Sequelæ.—An alteration in the mental condition of the patient of a retrograde nature may persist for long, or may be permanent. Persistence of the various palsies has been noted, but is infrequent. The completeness of recovery is astonishing when the degree of prostration and the extent of the symptomatology are considered.

Prognosis.—The individual prognosis must be guarded; an apparently mild case may become severe, and an apparently severe case may recover. Of serious prognostic omen are: deepening of stupor, the onset of coma, abolition of the tendon reflexes and the occurrence of complications such as bed sores, pneumonia or signs of cardiac involvement. Death is most frequently due to pneumonia, septic absorption or pyæmia from bed sores, or involvement of the respiratory or cardiac centres. Netter gives the percentage mortality as about 40 per cent; Parsons gives a figure of 50 per cent for the English cases.

Diagnosis.—Many of the points of diagnosis have already been considered, and repetition is unnecessary. The common triad of symptoms is the presence of fever, lethargy, and localized paresis of some of the cerebral nerves. The variability of the symptomatology in each individual case is of importance. The facies is almost pathognomonic.

Differential Diagnosis may be briefly recapitulated.

Cerebrospinal Meningitis.—Investigation of the cerebrospinal fluid will show the presence of polymorph cells, the presence of specific micro-organisms and a diminution of the sugar content.

Tubercular Meningitis.—The dissociation of the pulse-temperature ratio is met with early in this condition, and only in the later stages of encephalitis. The cerebrospinal fluid shows an increase of protein, which is usually marked and a progressive increase of the lymphoid cells. The sugar content is usually diminished, but in one recent case of tubercular meningitis a normal reduction of Fehling's solution overbalanced the evidence in favour of encephalitis, which was disproved at the autopsy. The tubercle bacillus may be found in the deposit in tubercular meningitis.

Poliomyelitis.—The acute development of lower neurone paralysis after a few days of fever; the presence of an early leucocytosis in the blood and polymorph leucocytes in the cerebrospinal fluid are the chief points of difference; other differences have already been noted.

Syphilis of the mid-brain must be excluded by the Wassermann test on the blood and cerebrospinal fluid in all cases.

Trypanosomiasis, or African sleeping sickness, is not encountered in temperate climates; in an endemic area puncture of the swollen lymphatic glands, and examination of the blood and cerebrospinal fluid would be necessary to exclude the presence of the trypanosome. *Polio-encephalitis superior hæmorrhagica of Wernicke*, chiefly affects alcoholics, is not accompanied by pyrexia; delirium is more marked and more active and a greater mortality is present [35].

Botulism is not accompanied by fever, and, like other varieties of food poisoning occurs in greater or smaller epidemics with a familial or house distribution.

Treatment.—Efficient nursing is of the greatest importance—special attention must be given to the skin of the back—circular pads and frequent application of methylated spirits should be employed to prevent the formation of bed sores. The kind of diet must vary with the gravity of the case; a light, easily digested diet should be given containing much uncooked milk and raw or lightly cooked eggs; fruit or fruit juices should be given and fluids should be given freely.

Constipation may require special treatment. Retention of urine is common in the early stages and must be specially watched for; on its occurrence catheterization must be performed regularly. Where there is difficulty in swallowing, food should be given by the nasal or stomach tube.

Lumbar puncture, originally performed for diagnosis, has been frequently observed to lead to marked improvement, lasting a longer or shorter time; such an improvement was noted in all the cases of any severity I have seen.

Serum Treatment.—In 1918 Netter tried injection of the serum of convalescents, a treatment which had some success in poliomyelitis; in encephalitis the results were not fortunate, and he no longer advises its employment, for it is not yet known how long the serum remains ineffective [36]. Favourable results have been reported after the use of various non-specific sera, e.g., normal horse serum, polyvalent influenza serum, and anti-tetanic serum [37].

Urotropin is advisable, for urotropin is said to be rapidly excreted via the choroid into the cerebrospinal fluid, where it appears as formalin, and a local antiseptic action might thus occur: it is difficult to believe that a sufficient concentration of formalin could result from the small doses of the drug which can be given safely; large doses rapidly produce toxic effects, the chief being a hæmorrhagic nephritis. The urine must be examined daily for blood and albumin when urotropin is given. It is advisable that small doses be given and given frequently—for though formalin is said to appear within twenty-five minutes of oral administration it very shortly disappears. Urotropin has been given intravenously and a successful result followed in one case at least.

Sialogogues.—Netter noted that in encephalitis a swelling of the parotid glands and salivation were not infrequent symptoms of the disease, and he likens encephalitis to mumps, poliomyelitis, and rabies, in which diseases the saliva is known to be infective and the ætiology at all events somewhat similar. He therefore concluded that the elimination of the virus occurred via the saliva and attempted to increase this by the exhibition of jaborandi [38]. This conception is more interesting since de Fano has demonstrated a possible virus in the salivary glands in encephalitis—intracellular inclusions similar to those found in the nerve cells. Successful results have followed the administration of the drug, and it is

advised that adrenalin should be given as a corrective for the cardiac depression occasioned by pilocarpine.

Fixation Abscess.—The same authority has advised the injection of turpentine to produce a fixation abscess; the only known action of this procedure is to cause a marked leucocytosis. Good results are reported of this treatment. Netter quotes Hippocrates, who noted that recovery from somnolent conditions frequently followed the appearance of an abscess. According to Cheinisse this treatment was first suggested by Pic. In a series of eighty-three cases of encephalitis treated in this manner by Netter the following results are recorded: In sixteen cases the abscess did not take and there were fifteen deaths, the one recovery was a benign case. In sixty-seven cases an abscess followed injection of turpentine, and of these cases five only died. That is a mortality of 7·46 per cent of the successful and 93·6 per cent of the unsuccessful cases—and a mortality of the whole series of 24·1 per cent [39].

Atropine has been found of value in the control of the involuntary movements, in five out of six cases the action of this drug was marked [40], adrenalin had the opposite effect.

NOTE A.—For some of the facts here recorded acknowledgment must be made to the writings of Netter, *Presse Med.*, 1920-21, and Walshe, *Med. Science*, August, 1920.

NOTE B.—Marinesco, *loc. cit.*, noted the presence of similar bodies, but only in cells with no obvious nucleus; he concluded that the findings resulted from mitosis. De Fano notes the presence of the nucleus in the affected cells he describes.

NOTE C.—*Vide* "Contagiosité de l'encéphalite lethargique," Netter, *Bull. de l'Acad. de Med.*, No. 17, 1920. Also "Un Cas de Contagion d'encéphalite lethargique," Guillain et Leehelle, *ibid.*, p. 31.

NOTE D.—*Vide* a case of epidemic hiccough which after two days developed signs of encephalitis. At the autopsy typical lesions of encephalitis were found involving the upper cervical cord, and especially the third and fourth segments. Clerc et Foix, *Soc. Med. des Hopitaux*, March 18, 1921.

NOTE E.—Cf. Paulus Aegineta, Bk. III, *Syd. Soc. Trans.*, "Their urine is like that of cattle."

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[4] NEWSHOLME. Local Government Board Reports, No. 121.
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[7] *Brit. Med. Journ.*, May 17, 1919.
[8] *Med. Science*, July, 1920, p. 381.
[9] *Ibid.*, June, 1920, p. 285.
[10] *Ibid.*
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[12] *Med. Science*, August, 1920, p. 406.
[13] MARINESCO. Local Government Board Reports, No. 121.
[14] *Brit. Med. Journ.*, January 20, 1921.
[15] *Med. Science*, August, 1920.
[16] *Presse Med.*, April 7, 1920.
[17] *Vide Med. Science*, August, 1920.
[18] Following MARINESCO and DRAPER. Local Government Board Reports, No. 121.
[19] *Ibid.*
[20] *Loc. cit.*
[21] *Med. Science*, 1920, p. 365.

[22] *Brain*, November, 1920.
[23] *Med. Science*, 1920, p. 411.
[24] *Vide* NETTER, *Presse Med.*, April 7, 1921.
[25] NETTER. *Loc. cit.*
[26] *Lancet*, December 18, 1920.
[27] *Med. Science*, 1920, p. 409.
[28] *Soc. Med. des Hôpitaux*, February 18, 1921.
[29] *Ibid.*, December 3, 1921. (*Vide* also "L'Hermite," *Presse Med.*, December 18, 1920.)
[30] RADOVICI et NICOLESCO. *Presse Med.*, January 29, 1921.
[31] PFEIFFER, *Berl. klin. Wochenschr.*, February 7, 1921; and HERZOG, *ibid.*, March 7, 1921.
[32] *Presse Med.*, *loc. cit.*
[33] MCNALTY. Local Government Board Reports, No. 121, p. 28. N.B.—In one case of McNalty's series polymorph cells were found in the cerebrospinal fluid.
[34] MCNALTY. *Loc. cit.*
[35] STRÜMPELL. "Spezielle Pathologie und Therapie," 1919, vol. ii.
[36] *Presse Med.*, *loc. cit.*
[37] *Med. Science*, August, 1920.
[38] *Presse Med.*, *loc. cit.*
[39] CHEINISSE. *Presse Med.*, February 19, 1921.
[40] RADOVICI et NICOLESCO. *Presse Med.*, January 29, 1921.

Report.

REPORT ON "SADDLE PEAK"[1] (ANDAMANS).

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ON February 18, 1882, a party organized and headed by Major Protheroe, C.S.I., Officiating Chief Commissioner, Andaman and Nicobars, made the first known ascent of the high hill on the east coast of north Andaman Islands, shown in the chart under the name of "Saddle Peak."

The expedition was undertaken with the view of ascertaining the height of the peak, the nature and general character of the country surrounding it, and whether the configuration of its summit was such as would be likely to afford a suitable site for a sanatorium.

The ascent commenced at 8 o'clock a.m., on February 18, and was made from the sea beach, up the eastern slope of the north peak, the party gaining the top at 1 o'clock p.m., thus accomplishing the upward journey in five hours; a remarkably short space of time, when the steepness of the hill-side, together with the fact that a pathway had to be cut through the thick jungle undergrowth at almost every step, is taken into consideration. Also a sharp lookout had to be kept in case the wild or untamed Andamanese in these jungles made an attack on us.

The descent by means of the track already cleared was not difficult, and only

[1] Report made on March 10, 1882.