AN ADDITIONAL CONTRIBUTION TO THE SYMPTOMATOLOGY OF EPIDEMIC ENCEPHALITIS *

FOSTER KENNEDY, M.D.; THOMAS K. DAVIS, M.D.
AND GEORGE H. HYSLOP, M.D.

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At the request of the organization committee, we have reviewed our cases of epidemic encephalitis occurring during the past year, with a view to the discovery of novel symptomatology or disease incidence which might be of either diagnostic or pathologic interest. It has always, of course, been clear that an infection flung far and wide through the nervous system would inevitably produce in different persons extraordinarily diverse clinical pictures. In epidemic encephalitis the diversity observed becomes greater with increased experience, and we have been fortunate enough in the neurologic department of Bellevue Hospital to find many examples of disease incidence in the sensorimotor system both central and peripheral, and, we believe, in the vegetative nervous system as well.

We have grouped cases in this paper under the headings: spinal types, disturbances of metabolism, disorders of motility and symptoms evidencing impairment of the vagosympathetic mechanism. The cord syndromes which have been described heretofore are confined to cords having an affection of the ventral horns and those in which a transverse softening has taken place. It becomes certain, however, that more discrete destruction can occur in the cord giving rise to clear-cut pictures of transient syringomyelia.

One such case was that of a young woman with general constitutional symptoms of infection, who, after having violent shooting pains in the left arm, experienced paresis of the arm, together with pyramidal weakness of the left side of the body and loss of temperature and pain sensibilities over the right side of the trunk between the spinal segments—the fifth cervical and the ninth dorsal. The left hand became swollen and succulent in appearance, indicative of vasomotor stasis, due to the lesion having involved not only the ventral horns and crossed sensory paths but the intermediolateral tracts as well. This grave picture was removed in four months, when the patient's health had been entirely restored.

Our second example was the case of a young man who one of us at first thought had a case of conal tumor. After two weeks of acute insomnia, he developed weakness in dorsiflexion of both feet and abduction of the thighs and clear-cut loss of pain and temperature senses in the skin areas served by the

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* From the Neurological Department, Bellevue Hospital.

lumbar and first sacral segments. The ankle reflexes were abolished and the knee reflexes depressed. The right plantar reflex was of extensor type. There were myoclonic movements of one leg. Entire recovery took place within three months.

DISTURBED VEGETATIVE FUNCTION

We believe that the significance of disturbed vegetative function in encephalitis can hardly be overstated; not only are such cases difficult to diagnose, but some of them may furnish valuable data for a future comprehension of neurotic and psychotic phenomena on a physical rather than on a purely emotional or psychic basis.

H. G., aged 21, served as a private in the United States Marines during the war and was supposed to have disintegrated mentally after an alleged attack of influenza in London, during the month following the armistice. He was placed in a hospital for mental diseases for about eight months after his return home. The clinical picture seen in the spring of this year was sufficiently confusing; a young man of splendid physique, carried his height of 6 ft. 2 in. (1.87 meters) with a pronounced stoop, an acquisition of his illness. Despite the exclusion of the possibility of syphilitic infection, the pupils were distinctly sluggish to light, the right side of the face definitely flattened in its creases, and there was a fine jelly-like, but most definite, nystagmus on lateral conjugate deviation of the eyes to the right or left. There was pronounced tremor in the extended hands. He had lost over 30 pounds (13 kg.) since his illness; but except for the absence of the abdominal reflexes, great increase in the arm, knee and ankle reflexes and involuntary shivering movements of the pectoral muscles, nothing more of pathologic interest could be made out in the sensorimotor system. He suffered, however, from severe nocturnal insomnia, rarely sleeping more than two hours before dawn, after which he would grow drowsy and might sleep three or four hours before noon. Whether he slept or not, during the first part of the day he was utterly inert and exasperated by his inertia. He had the utmost difficulty in accomplishing simple acts, such as shaving, dressing or bathing. He agonized for hours in futile efforts to write a short note or keep an important engagement. In his mental attitude there was not a trace of negativism; he desired passionately to do those things which he could not do at that time, but which later in the day he often could do with relative ease. There seemed to be a distinct resemblance between his inability to perform acts to the completion of which he was urged by will only without the stronger adjuvant of emotion, and the palsy of purely voluntary movements in midbrain encephalitis of the parkinsonian type—palsies so often abolished by affective stimulation. He complained frequently of "numb attacks," during which he felt very cold and during which he shivered and his teeth would chatter like a man with a rigor. During these attacks, even in July weather, his rectal temperature was always subnormal, on several occasions being 97 F.; and on his skin were large patches of goose-flesh which covered a third of the body area at a time and which, under observation, changed their position like a breeze over still water.

In the same general period but not necessarily and indeed rarely at the same hours, he had attacks of disturbed breathing rhythm of from a quarter to half an hour's duration. During these attacks he felt as though he could not fill his lungs with air, and he breathed with all his accessory respiratory muscles

from fifty-six to sixty-four times a minute. At other times he experienced what seemed like a spasm of the laryngeal muscles and breathed more and more stertorously and ineffectively so that the lips were cyanosed and the eyes protruded. Phenomena such as these have appeared at times in hysteria, and various physicians had considered them hysterical in this case. This explanation, however, would not account for the patient's abnormal thirst for ice water. He consumed for a period of eighteen months, between thirty and forty quarts of water every twenty-four hours and had proportionate polyuria.

An analysis of the initial illness in December, 1918, which he had always considered influenza, revealed the only symptoms to have been severe headache and intense sleepiness by day and by night. Two negative features of value, however, were that he had had no feeling of fever and that he had never reported sick to a medical officer. It is highly unlikely that this would be true of any youthful patient with the influenza which was prevalent in London at the end of 1918. Furthermore, after three or four weeks sleepiness disappeared during the night time and was only present by day, a reversal of the sleep mechanism sufficiently familiar to all students of epidemic encephalitis.

This patient's symptoms during the last eight months have gradually improved so that now he is almost normal, with little or no morning inertia, no difficulty with respiration and no rigors, and diabetes insipidus has been reduced to an intake of only 3 quarts of water a day. It is possible that this happy result has been assisted by the constant administration of scopolamin during the last four months of his illness; on this subject more will be said later.

A case brought under our observation recently has afforded us a fortunate diagnostic corroboration in that this strange syndrome is to a large degree duplicated. In this second instance, the patient, a boy of 14 years, had a similar polydypsia and polyuria with tremors in the upper extremities, excessive salivation and similar distressing paroxysmal attacks in which breathing was exceedingly rapid, labored and difficult. At these times there was great emotional distress and suffering. In this boy, acute encephalitis occurred in January, 1920, with visual disturbance, diplopia, fever and excessive insomnia; this was followed for many months by apparent recovery and was then gradually succeeded by a rhythmic incessant cough and thereafter by the distressing symptoms mentioned.

Another example of seriously deranged metabolism was the case of J. D., a well-developed young man of 24, who in the late spring of 1920 had an acute illness accompanied by headache, diplopia, diarrhea and nervousness. Shortly afterward an increasing desire to sleep and difficulty in the use of the right arm, leg and right side of the face appeared. A month later excessive thirst and polyuria developed, and at this time sugar was found in the urine. A low carbohydrate diet for two months improved the glycosuria and entirely relieved his thirst and polyuria. As these symptoms waned a gradually increasing slowness of speech and movement began. In Bellevue Hospital in July of this year, he presented a typical unilateral pseudoparkinsonian syndrome without any evidence of diabetes mellitus.

Another patient, a woman, aged 28, developed severe hypertrichosis of the face and arms following encephalitis. Great increase in body weight has been a fairly common sequel of epidemic encephalitis. It happens that this disturbance of metabolism was seen in our series only in female patients. One patient within a year gained over 100 pounds (45 kg.). She eventually died, probably of myocarditis. Among five other patients, gains of from 40 to 70 pounds (18 to 31 kg.) were noticed. The blood sugar was found to be normal in two instances, but in a woman, aged 52, with an increase in weight of 60 pounds (27 kg.), sugar tolerance was below normal. The climacterium as a contributing factor in the increase in weight could be excluded in all but one of our cases.

DISORDERS OF MOTILITY

Certain disorders of motility, some of which may not be new to other observers, we feel to be worthy of report. In particular, we feel that stammering, rhythmic movements, breathing irregularities and eccentric stations may be attributed to disturbance of the toning mechanism of the muscles.

In five patients, all with a pseudoparkinsonian syndrome, stammering developed as a sequel to their illness. In one of these cases the disorder accompanied a severe relapse, precipitated by a fright occurring two months after the onset of encephalitis. In the other instances, stammering appeared from three months to two and a half years after the first symptoms and without any psychic trauma. Rhythmic movements were observed in three patients. A. B., aged 28, had from the onset of her illness bilateral tremor of the masseters, associated with rhythmic muscular action, which gave a champing movement of the jaws. This was constant during the waking hours, and, with the immobile facies and unwinking stare, resembled remarkably the breathing movements of a fish.

In H. B., aged 32, the left side of the face suddenly began to twitch three months after an alleged influenza in the winter of 1919. The movement involved only the mouth, and did not cease or spread, but gradually the contractions became stronger. E. P., aged 19, had a similar affection from the onset of her illness.

In all these cases the movements occurred about once a second, were not under control of the will or varied by attention or emotion and could not be inhibited by any voluntary use of the involved muscles. The absolute rhythm of these movements distinguishes them, to some extent, from habit spasms, in some of which, however, there may be a striatal origin; indeed, we think many cases of hysteria may be in essence a retreat from a cortical to a more primitive reflex level of motor expression.

Breathing spasms were seen twice. One patient, E. P., just mentioned, had had from the beginning very irregular breathing—both in depth and rate—accompanied by curious noises which occurred only during sleep. S. J., fifteen months after apparent total recovery from encephalitis, had a parkinsonian relapse, accompanied by attacks of rapid deep breathing. These increased in frequency and at length continued through the waking hours, causing much fatigue. Emotion would initiate them, but when started they could not be stopped until their course was run—usually in a minute or two. There was never any feeling of dyspnea, but a sensation that the lungs could not be filled, and he had a desire to expand them as much as possible.

A patient, during the course of encephalitis which began with headache and spinal root pains, soon followed by a hemiplegia and later by various cranial nerve involvement, developed recurrent vomiting which persisted for three weeks. Several times a day, with or without food in the stomach, expulsive movements occurred; we speak of the case at this point in the belief that the vomiting was probably in morbid process analogous to the rhythmic movements and breathing spasms just described, and also analogous to the hiccup seen in certain cases of encephalitis.

Anteropulsion of the trunk was seen in a boy of 12. Another boy, aged 15, maintained when sitting or standing, a deviation of the trunk to the left. Neither patient ever fell. At a certain point the pull would cease and the attitude would be maintained. No cerebellar symptoms were found in either case.

Two parkinsonian patients developed bulbar palsy with lingual and pharyngeal atrophy nine months after the initial illness. Of these, one improved, the other died.

Limitation of parkinsonian symptoms to the upper extremities and the face was observed twice. Another patient presented curious irregularities of posture, owing to acute spasm of particular muscle groups. These phenomena lead us to speculate on the possibility that individual centers in the corpora striata may govern individual spinal segments.

We have the following evidence of disturbance in the vagosympathetic mechanism: In nine of fifteen cases tested there was a strongly positive oculocardiac reflex. Ocular pressure stopped the pulse absolutely in four patients—in one for a period of twenty-eight seconds after pressure was relieved. The pulse rate dropped 15, 20, 35 and 40 beats a minute, respectively, in four other cases. The ninth patient showed a pulse rate increased by twenty beats a minute. The other six patients gave no reaction to ocular pressure. The degree of reaction in a given case could not be foretold on a basis of the general clinical picture and had no relation to the patient's ordinary pulse rate. The percentage

of strongly positive oculocardiac responses is much higher in epidemic encephalitis than in numerous control tests made on a variety of other cases.

EXOPHTHALMOS

In twelve patients we observed exophthalmos. This varied in degree, was most marked in the definite parkinsonian cases, and was accompanied by a diminution of the wink reflex. It is perhaps noteworthy that this exophthalmos, a sympathicotonic sign, was often present in patients who were vagotonic, as judged by a strongly positive oculocardiac reflex.

THERAPEUTIC RESULTS

A few words on the result of treatment of residual cases may be of interest. It has seemed to us that medication should be based on a drug or drugs acting chiefly on the vegetative nervous system. The problem is a broad one and is complicated by the fact that in any given case of encephalitis the symptoms are not characteristic of damage to either the autonomic or the sympathetic system alone. There is instead a confused picture evidencing functional impairment of both divisions of the vegetative nervous system. It is possible in this paper to give only a mere sketch of our therapeutic results, which will have to be corroborated by further observations before any definite conclusion can be reached.

Thyroid and pituitary substances have no effect on residual encephalitic symptoms. Epinephrin, given to three patients in 20 minim subcutaneous doses of 1:1,000 solution, increased the pulse rate 50 per cent. and increased the rigidity of extremities for a period of two hours. In three controls the maximum pulse increase was 15 per cent. Nicotin in doses of $\frac{1}{30}$ grain (0.002 gm.) subcutaneously, did not affect the pulse rate, but did decrease rigidity for a period of from ten to fifteen minutes. Atropin, when used in large doses, increased rigidity and made the patient subjectively worse. Scopolamin, doses of $\frac{1}{100}$ grain (0.006 gm.) by mouth three times a day over a period of several days, has produced in about half the cases in which it was used a lessening of rigidity; it has restored facial mobility and has made the patients generally more comfortable. Gelsemium—the fluid extract—in doses of 7 minims (0.42 c.c.) three times a day or gelseminin hydrochlorate $\frac{1}{30}$ grain by mouth three times a day, has an effect similar to that of scopolamin in the same proportion of cases. These favorable effects of gelsemium persist as long as it is used; in one case these effects lasted for a period of over three months.

In perhaps a quarter of the cases, cumulative drug effects have been observed. These consist of heaviness of the eyelids, diplopia and, at times, a feeling of languor and confusion. They disappear within

twenty-four hours of the withdrawal of the drug, and they were alarming only once. In this case fluid extract of gelsemium, 5 minims (0.3 c.c.) three times a day, had been used for six days, and then scopolamin $\frac{1}{100}$ grain (0.0006 gm.) given subcutaneously. Within five minutes after the injection of the latter, the patient became confused, weak to the degree that lying down was necessary and flushed of face, with rapid pulse and dilated pupils. Her severe parkinsonian tremor absolutely ceased. This state lasted four hours. Scopolamin alone by mouth or subcutaneously never had any such effect on this patient. The situation was reproduced, and the same cumulative phenomena recurred. These observations suggest a synergism between scopolamin and gelsemium. The action of gelsemium on true paralysis agitans cases was studied. It produced the same relief which scopolamin has long been known to give. Thus both in true paralysis agitans and in postencephalitic pseudoparkinsonian disease, gelsemium seems to be ameliorative in approximately half the cases. While both scopolamin and gelsemium, according to Cushny, act by depressing the central nervous system, gelsemium has a distinct advantage over scopolamin in that it can be used for an indefinite time and has none of the dangerous concomitant effects of the latter. Why scopolamin, "which produces a sensation of fatigue and drowsiness" and after a dose of which "the patient moves about less and speaks less,"¹ can relieve symptoms of the same sort in encephalitis, we cannot yet answer.

Our most striking therapeutic result, however, was obtained in January, 1921. A woman of middle age who had been unable to articulate, chew or move the arms or legs on volition—so intense was the parkinsonian spasm—after a suppository of belladonna, was able to talk fluently, move quickly and with grace, and express emotion easily by gesture and facial expression. Congealment of function gradually returned, but temporary dramatic amelioration has always been possible by the rectal use of belladonna in tolerance dosage.

1. Cushny: *Pharmacology and Therapeutics*, Philadelphia, Lea & Febiger, 1910, p. 295.