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AN OUTBREAK OF ENCEPHALOMYELITIS IN THE ROYAL FREE HOSPITAL GROUP, LONDON, IN 1955

BY

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On July 13, 1955, a resident doctor and a ward sister on the staff of the Royal Free Hospital were admitted to the wards with an obscure illness. By July 25 more than 70 members of the staff were similarly affected, and it was plain that there was in the hospital an epidemic of a highly infectious character, producing amongst other things manifestations in the central nervous system. Because of the threat to the health of patients, and because of the large number of nurses involved, the hospital was closed on that date and remained closed until October 5. By this time the epidemic was almost over, although sporadic cases appeared up to November 24.

Between July 13 and November 24 292 members of the medical, nursing, auxiliary medical, ancillary, and administrative staff were affected by the illness, and of these 255 were admitted to hospital; 37 were nursed at home or admitted to other hospitals from their homes. It is remarkable that, although the hospital was full at the onset of the epidemic, only 12 of the patients who were already there developed the disease.

The course of the outbreak by admissions is shown in Fig. 1, and the location of the different establishments involved is shown in the Map (Fig. 2). When the epidemic began there was free intercommunication between various communities in the group, and in particular between the Royal Free parent hospital in Gray's Inn Road and its branch hospitals at Lawn Road and Liverpool Road. There were numerous opportunities for cross-infection. Both before, during, and after the epidemic in the group, the medical staff saw a number of similar cases occurring sporadically in North-west London. Eight such cases have been described (Ramsay and O'Sullivan, 1956).

Establishments shown in the accompanying Map are: Royal Free Hospital, Gray's Inn Road; North-western Branch, Lawn Road, Hampstead; Liverpool Road Annexe; Royal Free Hospital Medical School; Nurses' Preliminary Training School; Hampstead General Hospital; Elizabeth Garrett Anderson Hospital; Elizabeth Garrett Anderson Maternity Home; Eastman Dental Hospital.

Clinical Manifestations

The clinical picture has been drawn from observations on 200 of the cases admitted to hospital, in which the diagnosis seemed certain and the records complete.

Few instances of single isolated exposure were found among the cases which occurred in the hospital staff, but there were a number of cases among the relatives and friends of staff who had paid single visits to one of the hospitals. There were also several instances of either husbands or wives of staff who contracted the disease in their homes. The sum of their evidence suggests that the incubation period was seven days or less and five to six days for the majority.

The disease when fully developed showed features of a generalized infection with involvement of the lymphoreticular system and widespread involvement of the central nervous system. It varied from case to case, both in its content of symptoms and signs and the speed with which it evolved. Inevitably, in the course of a severe epidemic where the slightest departure from health is viewed with suspicion, mistakes in early diagnosis were made. However, experience was gained rapidly, and certain symptoms occurring early in the illness were soon realized to be characteristic.

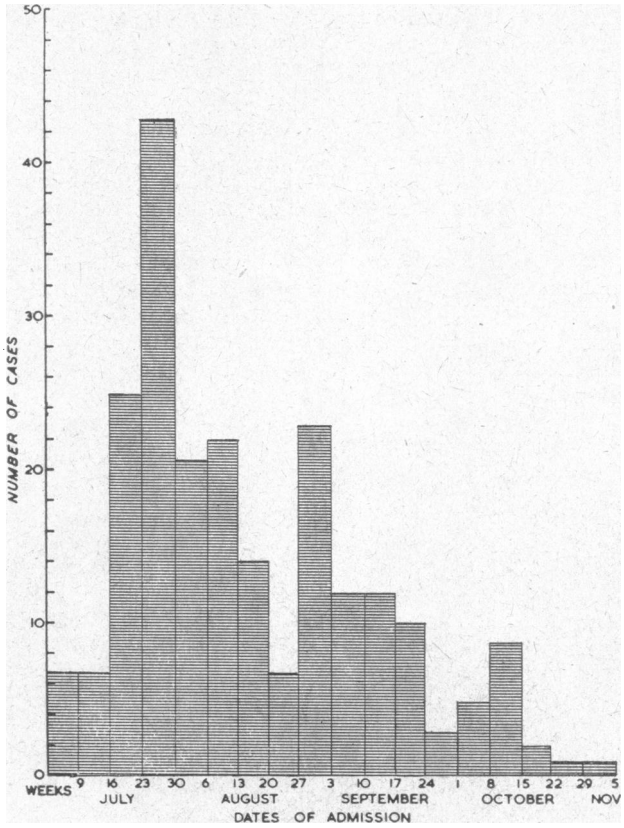

FIG. 1.—Graph showing dates of admission.

The initial manifestations in the 200 cases are recorded in Table I. The earliest symptoms were usually malaise and headache, frequently associated with disproportionate depression and emotional lability. Early

symptoms fluctuated markedly, often disappearing for a day or two, only to recur more severely. A mild sore throat was also usual. Headache, frontal or occipital, though often transient, was sometimes persistent and

TABLE I.—*Initial Manifestations in 200 Cases*

Symptoms	No.	%	Symptoms	No.	%
Headache ..	154	77	Stiff neck ..	65	32·5
Sore throat ..	127	63·5	Pain in back ..	64	32
Malaise ..	124	62	Depression ..	38	19
Lassitude ..	102	51	Abdominal pain ..	29	14·5
Vertigo ..	94	47	Vomiting ..	24	12
Pain in limbs ..	93	46·5	Diplopia ..	18	9
Nausea ..	81	40·5	Tinnitus ..	8	4
Dizziness ..	67	33·5	Diarrhoea ..	8	4

occasionally severe. Nausea, with anorexia, was frequent. Transient abdominal pain, vomiting, and diarrhoea were far less common.

The symptoms so far described are common to the prodromal phase of most infections, but the intensity of the malaise, particularly when related to the slight pyrexia in this disorder, requires emphasis.

Within the first week of the disease usually all the characteristic symptoms had appeared. Occasionally all the symptoms were present from the very beginning. In a few, however, the fully developed picture did not develop until the second or third week. This consisted of pain in the neck, back, or limbs, and of "dizziness." The pain was out of all proportion to the general constitutional disturbance and was sometimes present when fever was absent. It was usually confined to one limb, one side of the body, or to both legs, and, as with other symptoms, pain exhibited marked changes in intensity from day to day. Pain below both subcostal margins was common. At times the severity of these pains was such as to require the strongest analgesics for their control.

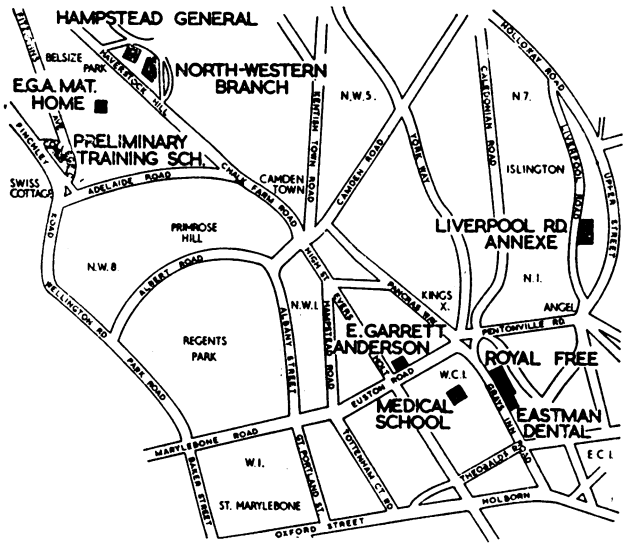

FIG. 2.—Map showing location of the different establishments.

Dizziness, usually meaning a transient feeling of imbalance on sudden movement but in about an eighth of the cases a true vertigo, characterized the disease early in its course. Sometimes this vertigo was very marked, being readily induced by slight movement of head or eyes.

A clear division of symptoms into those appearing early and late is not possible; in some cases objective neurological manifestations, usually more characteristic of the second and subsequent weeks of the disease, were seen in the first week of the illness.

In those in which no neurological manifestions were present, physical abnormalities in other systems were few. Abnormal signs other than those in the central nervous system are shown in Table II.

TABLE II.—*Abnormal Signs Other Than Those in the Central Nervous System*

Signs	No.	%
Severe injection of pharynx	6	3
Vesicles on pharynx	6	3
Enlarged cervical glands, ant. ..	104	52
,, ,, ,, post. ..	158	79
,, axillary ,, ...	73	36·5
,, epitrochlear glands	20	10
,, inguinal glands	65	32·5
Neck rigidity	22	11
Subcostal tenderness (left)	65	32·5
,, ,, (right)	64	32
Palpable liver	17	8·5
Temperature Range		
Up to 98 4° F. (36·9° C.)	22	11
98·6–100° F. (37–37·8° C.)	169	84·5
100·2–101° F. (37·9–38·3° C.) ..	2	1
101·2° F. + (38·4° C.)	7	3·5
Pulse Range		
60–80	91	45·5
80–100	92	46
100+	17	8·5

Pyrexia rarely exceeded 100° F. (37.4° C.), and there was only a slight tachycardia. The pharynx was usually mildly injected, but in a few cases there was more marked involvement with vesiculation. In almost all cases superficial lymph nodes were enlarged and tender, and the tenderness was often extreme. The commonest group to be involved was the posterior cervical. The liver was enlarged in just under a tenth of the cases, but no instance of unequivocal splenic enlargement was encountered.

During the second and third weeks many of the patients became more severely ill. In addition to the intensification of the earlier symptoms, particularly of the pain, vertigo, and prostration, other neurological symptoms and signs developed. Of the cases, 148 (74%) showed objective evidence of affection of the central nervous system, and the neurological manifestations formed a characteristic picture that distinguishes this disease from other infections of the nervous system.

Frequently the patients complained of hypersomnia, of nightmares, and of panic states, and sometimes of uncontrollable weeping. In addition to neck rigidity, photophobia was also sometimes seen. Frequently an amnesia developed for these symptoms. Even when the clinical picture seemed fully established there was the same fluctuation in the day-to-day intensity of the symptoms, as in the earlier stages.

Table III indicates the incidence of involvement of the cranial nerves.

The fundi and visual fields were not affected, but transient blurring of near vision, probably due to ciliary weakness, was encountered. Pupils were sometimes unequal, and might be defective in reactions to light and accommodation. External ophthalmoplegia was common, usually affecting one or both sixth nerves and occasionally the third nerve. Total external ophthalmoplegia with ptosis occurred in one patient.

Paraesthesiae or pain with sensory impairment in a trigeminal distribution was present in 6 patients. Facial palsy occurred in just under a fifth of the cases, and was occasionally bilateral, when it was associated with other

TABLE III.—*Incidence of Cranial-nerve Lesions* (148 *Cases*)

	Cases	%
Cranial nerves	69	46
Ocular	63	43
Trigeminal	6	4
Facial	28	19
Eighth	63	42
Bulbar	11	7
Optic	1	0·7
Olfactory	1	0·7

brain-stem manifestations. Vertigo, already mentioned as an early symptom, sometimes persisted and occasionally became very severe. It might be associated with tinnitus or perceptive nerve deafness, and fine nystagmus was frequently present. Bulbar palsy occurred in 11 patients; two of these required tube-feeding. Respiration was never impaired to such a degree as to require assistance.

The limbs and trunk were involved in almost all the cases in which there was invasion of the nervous system (Table IV).

TABLE IV.—*Incidence of Motor and Sensory Signs in Limbs and Trunk* (148 *Cases*)

	Cases	%
Limbs and trunk	144	97
Abnormal tendon reflexes	112	76
Motor weakness	102	69
Sensory disturbances	82	55
Muscle spasm	18	12
Myoclonus	5	3·4
Micturition disturbances	39	26

Motor weakness was more common than sensory disturbances. Initially paresis was accompanied by slight hypotonia, and might be associated with severe and prolonged painful muscle spasms. These spasms often occurred in limbs in which objective sensory disturbance was marked. The slightest attempt at active or passive movement often invoked extreme pain. The usual initial distribution of weakness was hemiplegic, or less commonly monoplegic or paraplegic, but later the remaining limbs were often affected to some degree. Loss of power in the affected limbs was more marked distally than proximally, and in some the paralysis might be complete. Weakness occasionally showed a segmental distribution, predominantly in the upper limbs. The tendon jerks were preserved; early on they tended to be sluggish, but in established cases they were slightly exaggerated. In only two cases were frank extensor plantar responses encountered; an absent or equivocal response was common in the disease. Wasting of muscle was exceptional, but was well marked in the tongue and thenar eminence of one severely affected nurse, and in the muscles below the knee in another.

Sometimes early on, but more commonly during recovery from weakness, a peculiar jerking could be observed in a limb on voluntary movement. This is considered to be a distinctive and characteristic feature of the nervous involvement in this form of encephalomyelitis.

Irritative phenomena observed in addition to spasm were fasciculation of muscle and myoclonic movements, which all became more prominent when the patient was disturbed by physical examination or nursing treatment. Bladder dysfunction occurred in about a quarter of the patients. This consisted of difficulty in initiation of micturition, and sometimes resulted in retention, requiring tidal drainage for a few days.

Spontaneous pain was the commonest sensory manifestation, and has already been mentioned, but its part in the clinical picture cannot be overemphasized. It was usually felt diffusely throughout a weak limb, and was associated with marked muscle tenderness. The pain was sometimes of segmental distribution in the upper limb, or frequently involved the lower thoracic and upper abdominal segments as in Bornholm disease. In such cases there was extreme tenderness in the subcostal regions, and attempts at palpation might evoke resentment due to pain. It was sometimes difficult to decide whether such pain was of visceral or muscular origin. Numbness and coarse tinglings were other sensory symptoms which occurred chiefly in the limbs. Objective sensory loss was usually maximal peripherally, and its distribution frequently coincided with the motor weakness. Cutaneous sensory loss was more prominent than loss of joint sense and vibration sense, but hemianaesthesia for all forms of sensation occurred in a number of patients with a hemiplegia, though the face usually escaped. Radicular sensory loss was sometimes found in the upper limbs. Cutaneous hyperaesthesia or hyperpathia was common and severe, and might be associated with sensory loss to the same limb. In no case was an ataxia of cerebellar type seen.

The clinical impression was that this disease produced a diffuse disorder of the nervous system with a combination of irritative and paralytic signs, which were frequently transient. Weakness of a hemiplegic distribution suggested an upper motor neurone dysfunction, but, as is not uncommon in encephalomyelitis considered to be of virus origin, the reflex changes were slight and prone to fluctuation. Even in patients with paralyses of several months' duration the evolution of the spastic picture, reminiscent of vascular lesions, did not take place. In two patients with paraplegia reduction of reflexes has persisted.

It was thought that the disturbance of function of the lower motor neurone was irritative rather than destructive; peripheral nerve reflex conduction measurements were normal.

Course of the Disease

The course of the disease has been most variable. The mildest cases which showed no evidence of invasion of the nervous system became symptom-free within a month and the patients were able to return to work. On the other hand, in others the illness was more protracted, its duration depending largely on the severity and extent of the nervous manifestations.

Table V indicates the duration of hospital in-patient treatment.

TABLE V.—*Duration of Hospital In-patient Treatment*

	No.	%
Less than 1 month	114	57
1–2 months	57	28·5
2–3 ,,	15	7·5
3+ ,,	14	7

Throughout the foregoing account of the clinical manifestations of the disease emphasis has been placed upon the tendency for day-to-day variation in the intensity of symptoms and signs. Long-term observation of cases showed a similar variation. There might be periods of two weeks in which the symptoms were mild and fever had disappeared. Such periods were often followed by marked recrudescence of old symptoms and sometimes the appearance of fresh neurological manifestations. In such relapses further fever and tender enlargement of glands occurred. Relapses occurred in some cases after patients had been fit enough

to return to their homes or had been transferred to convalescent homes. The protracted illness, with a large element of doubt in the mind of the victim as to the ultimate prognosis, naturally engendered considerable anxiety and depression. Functional manifestations in a few cases overlaid the organic picture, particularly in those cases longest in hospital.

In the large majority of cases recovery of neurological function has been complete, but it has been a slow process. Extreme fatigue and general 'aches and pains have made the rehabilitation period extremely tedious and long. Even after a six-weeks period of convalescence, which was soon found to be necessary in those who were in bed for more than a month, these patients, with the best will in the world, were often able to work for only four hours a day, and minor residual symptoms are still very common. In four cases marked disability is still present at the time of this report. One nurse, whose right hand was paralysed from the onset, has now developed cogwheel rigidity with choreo-athetoid movement in the same arm when voluntary movement is attempted in that arm. Two nurses need leg callipers to aid their weakened lower limbs in walking, and the fourth, who showed some wasting of both lower limbs, still needs crutches.

Complications

One patient developed jaundice: clinically and biochemically the findings were similar to those in infective hepatitis. Three other patients who had slight enlargement of the liver, but not jaundice, also showed some biochemical evidence of hepatitis.

Other complications were few and were not considered to be directly related to the disease. A small outbreak of streptococcal sore throat affected a group of nurses. Two patients developed the clinical picture of inhalation pneumonia. Urinary infection developed in certain of the patients with retention of urine. This infection responded to treatment.

Psychiatric Aspects

Many of the patients suffered from various psychological symptoms, most of which were of a depressive nature with sometimes a hysterical overlay. All of them cleared up fairly quickly without any special psychological treatment.

Six cases were of a more serious nature. They comprise three severe depressive reactions, one anxiety state, one schizophrenic, and one paraphrenic. There was an additional patient with severe depression who subsequently committed suicide by taking an overdose of "carbrital." The three other cases of depression responded quite well to electric convulsion therapy (E.C.T.) and were treated as in-patients.

The anxiety case was the only patient who was not a member of the hospital group staff, and she was treated as an out-patient, her chief symptoms being vertigo, emotional upset, and anorexia. She responded quite well to treatment and supportive psychotherapy, and was discharged after two months; she had a mild relapse, however, in November, 1956.

The two more serious cases of psychotic manifestation, the schizophrenic and the paraphrenic, had to be certified and committed to a mental hospital. They have now been discharged; one is back at full-time work and is very well, and the other is improved and doing part-time work. In both these cases E.C.T. was given in the mental hospitals.

It is of interest, therefore, that the common denominator in these mental illnesses seems to be one of depression which has reacted quite well to E.C.T.

Another factor which is fairly consistent is the time-lag between the onset of the disease and the onset of these more serious psychological manifestations. This was from two to three months. We do not think it should be said that the disease is in any way a causal agent, but it does appear that with certain individuals the disease has been responsible for precipitating an underlying latent psychosis or psychoneurosis. So far as we are aware, there is no evidence of any delinquent behaviour as was seen as a sequel to the cases of encephalitis lethargica after the first world war.

Case Histories

As has already been pointed out, a large number of the cases were extremely mild, and in 52 (26%) no neurological manifestations developed. Such a mild case is the following:

A nurse aged 25 was admitted on July 27, 1955, with seven days' history of headache, sore throat, nausea, and pain in the legs. She also had lassitude, and on the morning of reporting sick felt giddy, and she complained of pain in both subcostal regions, which were tender on palpation. She was apyrexial. The throat was slightly inflamed; the tonsillar glands and those in the left posterior triangle, axillary, and inguinal regions were enlarged. Aching pains in the limbs continued. On the fourth day after admission she had a severe headache with pain in the back. By the ninth day she was feeling better and was able to get up. She returned to work five weeks after the onset.

Sixty-six cases showed severe and widespread involvement of the nervous system. Such cases needed a long period in hospital, considerable nursing care, and much encouragement. Such an example was that of a nurse aged 21, among the earliest of our admissions.

This patient was admitted on July 18. She complained of depression for eight days, a slight sore throat for four days, and pain in the neck and feet for two days. On the day of admission she also complained of pains in the back and over the chest. She developed double vision and severe vertigo, and this vertigo was accompanied by nausea. Yet she showed no fever, and, apart from some pharyngitis and slight enlargement of the cervical glands, there was no other abnormality whatsoever. On the following day, however, she began to experience difficulty in micturition. On the fifth day she noticed tingling in all limbs and the temperature rose to 99° F. (37.2° C.), with a pulse of 100. This mild pyrexia continued throughout her illness. She also showed some neck rigidity, but Kernig's sign was negative. There was marked tenderness in the subcostal regions, but the liver was not at that time palable. The inguinal and axillary glands were tender. There was diplopia on lateral deviation of the eyes to the right and on elevation. The tendon reflexes were increased in the right upper limb only. The abdominal reflexes were absent. There was some weakness of the right leg, and the right knee-jerk was increased, but both ankle-jerks were diminished. At that time the left plantar response was extensor. There was some sensory loss below the right knee. The micturition difficulties increased and tidal drainage had to be instituted for four days. On the tenth day the liver became palpable and tender. The vertigo persisted and the nausea was most distressing. During the second week she complained of aching pain in the left arm, and this was accompanied by fasciculation in the muscles of the forearm. At that time a patchy erythema was noticed. In the third week, although there had been some general improvement, a weakness of the left arm and left leg was noticed, with sensory impairment over the whole of the left arm. A period of gradual improvement followed, but five and a half weeks after admission there was a recrudescence of the right-sided weakness.

She was discharged to convalescence at the end of the second month, but a month later she complained of palpitations on exertion and that her left leg remained weak. The tendon jerks were diminished in the left arm, and there was now some weakness of both lower limbs with an increase of the left tendon jerks. She began to do part-time work a few weeks later, and it was six months from the onset of her illness before she was able to engage in full-time work. The increase of tendon jerks in the left lower limbs persisted, and the left plantar response was unobtainable.

Fifteen of the patients showed a hemiplegic distribution, and the following case is an example of the severer group.

A nurse aged 26 was admitted at the height of the epidemic with seven days' history of malaise and frontal headache, with pain in the left lumbar region. The day before admission she experienced attacks of vertigo, bilateral tinnitus, and nausea, with some blurring of vision. There was no fever, but the patient looked ill, complained of photophobia, and showed slight mental inaccessibility. The cervical and inguinal lymph nodes were enlarged, and there was bilateral subcostal tenderness. The day after her admission she became drowsy and complained of double vision; this was due to left external rectus paresis. There was transient hypalgesia of a bilateral trigeminal distribution, and there was also hypalgesia along the distribution of the right fifth

and sixth cervical segments. This was accompanied by tenderness of the muscles of the right arm, and the jerks in that arm were diminished. On the following day the left arm was found to be hypotonic. On the next day, four days after admission, she developed a complete flaccid right-sided hemiplegia, also affecting the lower face on that side. The tendon reflexes became exaggerated and the plantar response was a weak extensor. There was hemi-analgesia, and hemi-anaesthesia for all forms of sensation, but the face was spared. This sensory loss included joint sense as well. Seven days after admission she complained of

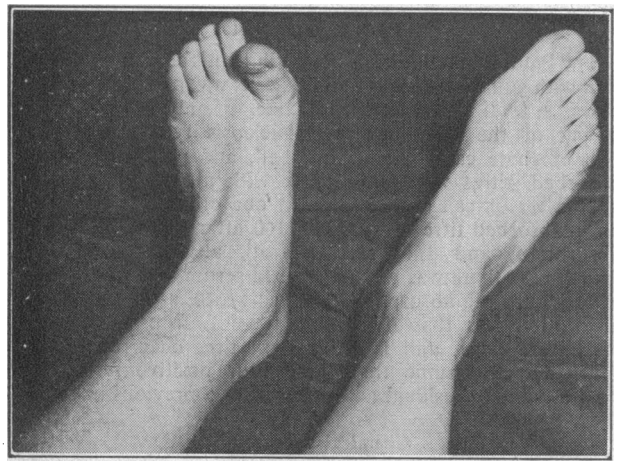

FIG. 3.—Photograph of foot in spasm.

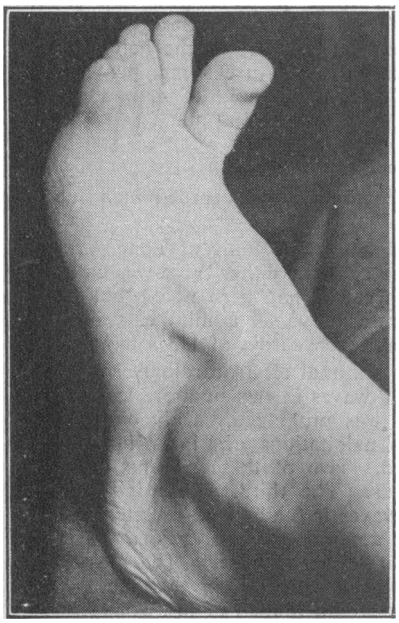

FIG. 4.—Photograph of foot in spasm.

headache and showed slight meningism. At that time her temperature was over 100° F. (37.8° C.), and a low pyrexia persisted throughout the illness. Her condition fluctuated with minor changes in the neurological abnormalities, but the right arm and leg remained flaccid and weak and the arm was intensely painful.

By the fifth week there was some improvement in power and she was able to sit out of bed, although the sensory loss was still severe. During the sixth week of her illness intense spasm developed in the left leg, resulting in a posture of extension of the knee with acute dorsiflexion of the foot and digits. The spasm persisted for five weeks but ceased to be painful, so that the patient was able to walk on the affected limb. During the ninth week there was an episode of behaviour disorder with screaming, followed by stupor for 45 minutes. She then improved steadily, and was discharged home five months after the onset, with a right hemiparesis, maximal in the arm, and residual relative hemianalgesia with sensory loss of cortical type in the hand. The tendon jerks in the left leg were slightly increased; the left plantar response was a doubtful extensor. She has since returned to full duty, but a slight right hemiparesis with impairment of all forms of sensation in the upper limb, without reflex abnormalities, persists 18 months after her illness.

Sixty-two of the cases showed signs with a predominance within the spinal cord. The following case is such an example:

A nurse, aged 21, was admitted on August 9, complaining of diffuse aches and pains, frontal headache, and a slightly stiff neck. She had had a sore throat on the previous day. She showed a temperature of 99.2° F. (37.3° C.), pulse 72, and respiration rate 18. She did not look ill. Enlarged tender glands were found in the anterior and posterior triangles of the neck and in the inguinal regions; there was also tenderness in the left subcostal region. Physical examination revealed no other abnormality. Three days later the frontal headache was more severe, and was accompanied by vertigo. On the fifth day she was allowed up to toilet, for she had lost all her symptoms. Next day her headache and vertigo returned, but there were still no abnormal signs in the nervous system. On the seventh day she had severe backache and neck stiffness, and Kernig's sign was positive. There was also tenderness below the right and left subcostal margins, and she experienced difficulty in initiating micturition. The low-grade pyrexia persisted.

Two weeks after admission she developed very severe pain in the arms and complained that they felt heavy. On examination, power in the left arm was much diminished, and the muscles were tender. The left supinator jerk was absent. The legs were slightly hypertonic and the muscles tender. The tendon reflexes were increased, but the plantar responses were flexor. Sensation, except for some transient loss of sensation in the left forearm, was normal. Once more the condition improved, and in the third week she felt reasonably well, although still complaining of slight headache and pains in the lower limbs. Power was still diminished in the left upper limb, and tone in both lower limbs was increased, but the plantar responses were flexor. Fasciculation was noticed in the legs, and myoclonic jerks developed. From day to day there was considerable fluctuation both in power and in reflexes in arms and legs.

In the fourth week difficulty in micturition was more pronounced, but it did respond to carbachol. At this time there was a diminution of sensation to cotton wool from the waist downwards, and postural sense was also impaired. She still complained of muscle pains, although power began to improve. In the fifth week, although her general condition appeared to be fairly good, complete paralysis of the left leg occurred, and tendon reflexes were absent. The weakness of the left arm was still present, and a patchy sensory loss was noted in both arms. From this time there was a general improvement, in spite of minor relapses, until after three months she was fit to be discharged to a convalescent home.

After a month away she was readmitted. She had severe backache and complained that she suffered "cramps" during her stay at the convalescent home. On examination at this time there was again photophobia, the neck muscles were weak, power in the upper limbs was reduced, but the reflexes were brisk and equal. There was patchy anaesthesia over the shoulders and sensory ataxia in both arms. The left leg was held in flexion. There was gross impairment of power on the left; on the right side the movements were a little stronger, but the reflexes were brisk and equal. There was also patchy anaesthesia over the lower limbs. During the second admission there was irregular pyrexia up to 100° F. (37.8° C.) for periods up to five days. Her general condition improved more rapidly than previously, and by the sixth month from the original admission she was able to be mobilized. Lumbar backache continued to be troublesome, but it was possible to discharge her two weeks later.

Management

Rest proved the sheet-anchor in the management of the acute stage. Rest, as absolute as was practicable, was prolonged beyond the febrile period and beyond the stage when the neurological complications had already improved. Attempts to reduce this rest period were always followed by a relapse. The evil effects of premature exertion, even a prolonged neurological examination, became apparent to all.

A confident and, above all, a reassuring attitude on the part of the medical and nursing staff proved of increasing value. This is not surprising when the patients in the main were nurses knowing we were dealing with an unknown disorder.

In the convalescent recovery stages occupational and diversional therapy proved most helpful.

Drug Treatment

The clinical picture did not suggest that antibiotics would be of any value. In a proportion of cases suffering such complications as urinary infections, streptococcal sore

throat, or chest infections, antibiotics were used. No influence on the course of the basic disease could be demonstrated.

Faced with the problem of a seemingly new disease entity caused by an unknown agent, treatment resolved itself into general management, drugs being used solely for the relief of symptoms. All symptoms proved remarkably drug-resistant. Trunk and limb pain, headache, muscle spasm, and vertigo failed to yield to orthodox preparations.

For pain, aspirin and its compounds proved as serviceable as the more potent preparations. Ergotamine tartrate was found to be more helpful when the headache was severe than the customary analgesic drugs. For the vertigo, promethazine and related compounds were also tried, but relief was not constant. Antispasmodic drugs were also used for muscle spasm, but the relief was inconstant.

In a few cases where dysphagia was a complication, tube feeding was instituted, and in a few intravenous therapy had to be resorted to for a short period.

For the commonest urinary problem—that is, difficulty in initiation of micturition with a tendency to retention—carbachol was effective in the big majority, though catheterization with prophylactic chemotherapy was required in some. In two severely affected cases tidal drainage had to be used.

Convalescence

Convalescence was slow. The policy was soon adopted to allow as many weeks convalescent leave as had been spent in the ward. Any attempt to shorten this time was met by a relapse. Nearly all patients confessed that, on leaving hospital, to their surprise they felt very unwell for some time. Some suffered recurrences of limb pain, headache, and physical weakness. On their return all were placed on half duty, but in many the half-duty time had to be extended on account of their persistent ill-health. Even now, many still complain, in addition to weakness and readily induced fatigue, of vertigo, recurrent headache, depression, double vision, and pain in an arm or a leg. This persistence of symptoms long after the infection is over is a notable feature.

Physiotherapy

Physiotherapy was instituted in the acute stages of the disease. This consisted of passive movements to all the joints of the affected limbs, aimed at maintaining full joint range and preventing contractures. Passive movements also had the effect of relieving muscle spasm. Muscle spasm also responded to heat, the most effective form being electric pads or radiant-heat lamps.

After the acute stage had passed, graduated active exercises were begun, but these had to be kept to a minimum to avoid invoking painful muscle spasm and cramps. Excessive activity rapidly produced fatigue. Some patients exhibiting marked neurological signs and persistent muscle spasm were placed in warm baths for their exercises. This proved a most effective measure, as it produced relief of the muscle spasm and thereby facilitated active movements. In the re-education of the weak limbs in some patients orthopaedic appliances were utilized, including long leg and below-knee braces.

Special Investigations

Haematology

A total of 750 blood counts were examined from over 400 confirmed or suspected cases. Analysis of the counts from a selected group of 138 nurses was reviewed by three independent observers; these results are considered to be representative of the patients as a whole.

Haematological changes were not specific. There was a tendency for a low-normal neutrophil count, with a high-normal lymphocyte count, during the first week of the disease. This change was seen in about half the cases. Abnormal lymphocytes of the type described on numerous occasions in a variety of virus diseases (Leibowitz, 1953) were seen, such as vacuolation of cytoplasm of adult lymphocytes, and the presence of Türk or plasma-cell-like forms with coarsely reticulated nuclei and deeply basophilic cytoplasm. But the changes characteristic of infectious mononucleosis were not found, nor did the white count as a whole correspond with the picture seen in that condition.

In most cases the E.S.R. was normal. In three cases only did it exceed 20 mm. in the hour (Westergren). There was no anaemia.

Paul–Bunnell Test

The Paul–Bunnell test for heterophil antibodies with absorption with guinea-pig kidney and ox cells was performed on 121 cases. A total of 250 tests were done. In only four were antibodies of the infectious mononucleosis type present. In two of these cases the unabsorbed, and guinea-pig-kidney absorbed, titres were only 1/40, with a titre of less than 1/20 after ox-cell absorption. In one other case there was an unabsorbed titre of 1/320, 1/160 after guinea-pig-kidney absorption, and 1/40 after ox-cell, absorption. In the fourth case there was an unabsorbed serum titre of 1/1,280; after guinea-pig absorption this was 1/640, and after ox-cell absorption less than 1/20. In these four cases repeated tests were done, and no change in titre occurred. It is justifiable to assume that these four positive results are possibly due to residual antibodies after a previous infection.

Chemical Pathology

Flocculation Reactions.—No abnormality in the thymol and colloidal-gold reactions was found in the sera of 119 patients. The sera of three patients who had slightly enlarged and tender livers gave weak positive reactions. One patient who developed jaundice at the height of this condition had a serum bilirubin of 9.5 mg. per 100 ml., thymol turbidity of 24, colloidal gold of 4, and alkaline phosphatase of 10 K.-A. units per 100 ml.

The Electrocardiogram

Routine electrocardiograms were recorded in a random sample of 42 patients.

Thirty-nine patients had no significant abnormality in their records. In seven of them, either there was complaint of palpitations or tachycardia had been noted, but in only one record was the rate above 84 a minute, and in this patient there was a sinus tachycardia of 115 a minute.

Three patients had abnormal electrocardiograms. In two there were abnormal T waves in two or more leads and in one the Q–T interval was prolonged. Only one of these patients complained of palpitations, and in no instance was a tachycardia recorded. Two of these patients now have entirely normal records. The third, whose initial record showed isoelectric T waves in lead I and inverted T waves in lead V_3, still had an abnormal electrocardiogram eighteen months after the onset of her disease. The most recent record shows improvement, however, in that the T waves in leads I and V_3 are upright, though of low voltage. This patient still has extensive neurological abnormalities.

Prolongation of the Q–T interval and T wave abnormalities may be evidence of biochemical as well as histological changes in cardiac muscle. Only one of the three patients with abnormal records was among the more seriously ill nurses.

Electrodiagnostic Investigations

Electrodiagnostic investigations were carried out on 28 cases (Richardson, 1956). All the 28 cases referred for these investigations showed marked motor involvement. A few were examined in the early stages. The majority were examined on a single occasion between one and two months after the onset of the disease. Five with severe and prolonged motor involvement were examined at intervals for 12 months.

Nerve-muscle Excitability Measurements.—These were determined by the plotting of strength-duration (I/T) curves

of the involved muscles. With the exception of isolated muscles in one case, which showed incomplete denervation, none of the muscles tested showed any evidence of lower motor neurone degeneration. Nerve-conduction measurements were all within normal limits.

Electromyography.—Electromyography in the early stages of the disease occasionally showed some irregularly occurring fasciculation potentials of normal motor-unit-potential form. The myoclonic spasms were recorded as bursts of asynchronous motor-unit potentials. With the onset of paralysis the most important sign was abnormality in the recruitment of the motor units. Thus, in normal willed muscle contraction, the motor units begin activity one by one, each joining the discharge at rates of up to 20–30 a second, separately and asynchronously, but building up into an interference pattern. Further, small motor-unit potentials initiate the contraction, and only with an intense effort or on fatigue are large motor-unit potentials normally recorded. In contrast, the affected muscles in this disease showed a severe reduction in the number of motor-unit potentials on volition, and some were of long duration and polyphasic (Fig. 5). Further, in the less severely involved, and particularly during recovery, the motor-unit potentials were grouped (Fig. 6). The result of this grouping was a tremulous contraction with a frequency of 5–10 a second which rapidly fatigued. The combination of a severe volitional disturbance with retention of nerve conduction, without signs of lower motor neurone degeneration but with a reduction in the number of motor units on volition and its occasional initiation by large polyphasic potentials, is suggestive of a so-called myelopathic lesion (Bauwens, 1955). This term is used to describe involvement of the motor unit at the level of the cord, a finding common to vascular lesions of the cord, anterior poliomyelitis, and other conditions. However, prolonged paralysis from these lesions is usually accompanied by signs of lower motor neurone degeneration. The peculiar grouping of motor-unit potentials has not been described in them or any other myelopathic lesions. Its origin remains obscure.

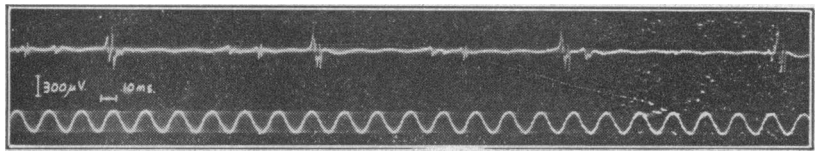

FIG. 5.—Recording from severely involved tibialis anterior muscle on maximal sustained volition.

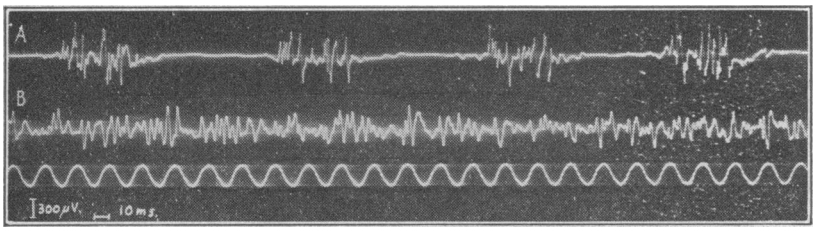

FIG. 6.—Recordings with concentric needle electrode and maximal sustained volition. A, From weak tibialis anterior muscle. B, From normal contralateral tibialis anterior muscle. Calibration 50 cycles. 300 microvolts.

Histopathological Material

No specific changes were observed in the very limited material available for histological examination. This consisted of a small lymph node, excised two weeks after the onset of the disease, which showed well-marked reactive hyperplasia of non-specific type; and post-mortem tissue from a further two patients, both of whom had died from other causes several months after attacks of the epidemic disease.

In one of these fatal cases post-mortem examination showed an ovarian carcinoma with multiple metastases and a terminal clostridial peritonitis and septicaemia. Microscopical examination of the brain, spinal cord, and peripheral nerves showed no abnormality except for that attributable to either the septicaemia or carcinomatosis.

The second fatality, due to acute "carbrital" poisoning, occurred in a woman, aged 32, who had the epidemic disease seven months before death, and who had had definite clinical evidence of organic disease of the central nervous system for the last seven months of her life. In her case it was considered on clinical grounds that she had disseminated sclerosis as well as the epidemic disease. Post-mortem examination revealed small circumscribed grey or yellowish plaques in the white matter of the cerebral hemispheres, mainly paraventricular in distribution, in the brain stem and in the spinal cord, particularly in the cervical segment.

Microscopical examination showed multiple small well or fairly well demarcated areas of demyelination with associated microglial and astrocytic proliferation and a variable degree of gliosis. There was no evidence of primary neuronal damage, and no viral cell-inclusions were seen. Occasional cellular foci composed of lymphocytes and cerebral histiocytes, mainly perivascular in distribution, were present in the leptomeninges overlying the brain, but this was not a marked feature except in one section taken from the hypothalamus which showed intense perivascular cuffing.

The distribution and character of the lesions in the central nervous system, with the exception of the changes in the hypothalamus, were typical of disseminated sclerosis, and a histological diagnosis of disseminated sclerosis in a fairly early phase was made. The lesion in the hypothalamus in this case may represent the effects of a superadded viral encephalitis, but such an explanation is conjectural, and it is more probable that the intense perivascular cuffing represents an unusual but not unknown reaction associated with disseminated sclerosis.

Other Investigations

In 16 patients radiographic examination of the chest showed no hilar-lymph-node enlargement. The cerebrospinal fluid was examined in 18 cases, and no abnormalities were discovered.

Estimations of the serum cholinesterase in seven cases were normal. The electrophoretic patterns also showed no abnormality in any of these sera. Cholinesterase was 1.0 μl./ml./min. (normal) in a cerebrospinal fluid examined during a severe relapse.

Epidemiology

Sex, Age, and Occupation.—The case incidence in relation to sex, age, residence, and occupation is shown in Table VI. Residence in hospital and occupational risk (nursing) are factors which contributed to a high case incidence. A comparison of the number of times that nurses were in personal contact with other nurses, as opposed to other members of the staff, showed that the chances of exposure were at least 4:1. Since nurses form about half of the average hospital population the high case incidence did not necessarily indicate that nurses as a group of young women were peculiarly susceptible to the infection.

Mode of Spread.—The explosive character of the outbreak suggested the possibility that the infective agent was disseminated through a common vehicle, but investigations relating to water, milk, food, food handlers, and launderers were negative. There is at present no evidence that the infection was spread either by arthropods or by animals. In this connexion the possibility of toxic trace chemicals in paints, insecticides, and detergents was also considered.

At present the aetiology of the disease remains unknown, and the mode of transmission has not been elucidated.

Evidence of case-to-case infection accumulated during the epidemic, though individuals were often exposed to infection on two or more occasions.

A detailed report of the epidemiological aspects has been published (Crowley *et al.*, 1957).

TABLE VI.—*Attack Rate Among Hospital Workers in Various Categories*

Hospital Staff	Population at Risk	No. of Cases	Attack Rate per 100 People
Royal Free Hospital group ..	3,500	292	8·3
Men	950	27	2·8
Women	2,550	265	10·4
Domicile:			
Non-resident	2,740	128	4·7
Resident	860	164	19·0
,, men	20	4	20·0
,, women	840	160	19·0
Occupation:			
Nurses	800	149	18·6
Medical and ancillary medical staff in contact with nurses ..	400	54	13·5
Resident domestic workers ..	240	33	13·7
Others	2,060	46	2·2
Age*: 18 to 35	—	247	—
,, over 35	—	45	—

* About one-third of the population is probably 35 or over, and two-thirds are over 18 and under 35.

Studies on the Aetiology

Sera from a number of patients were tested for antibodies to the viruses of influenza A, B, C, psittacosis, A.P.C., herpes simplex, mumps, and louping-ill, and to *Rickettsia burneti*; and sera from six typical cases with neurological signs were tested against encephalomyocarditis virus, all with negative results. Tests for toxoplasmosis and leptospirosis were also negative.

All attempts at the Virus Reference Laboratory to isolate an agent from specimens of blood, throat washings, and stools collected in the acute stage of the disease have been negative in fertile hen eggs, suckling mice and rats with or without cortisone treatment, adult mice, suckling hamsters and ferrets, guinea-pigs and monkeys with or without cortisone treatment, following intracerebral, intranasal, and intraperitoneal inoculation. Two monkeys also received intraspinal and intrasciatic inoculations. Negative results have also been obtained with the same materials in tissue cultures of HeLa cells (nine experiments), monkey kidney (10 experiments), human embryo brain (2), liver (1), spleen (1), kidney (6), and human infant kidney (3). Experiments are continuing in additional animal species and tissue cultures.

Experiments conducted at the London School of Hygiene with throat washings from cases of the disease suggested that the washings might contain an agent capable of infecting suckling mice and of causing a cytopathic effect in cultures of human amniotic epithelium. The response in neither system was clear-cut, and the results could not be used at the time to discover the nature of the agent or to decide whether it was causally related to the disease in man.

Discussion

A number of outbreaks in recent years of obscure forms of encephalomyelitis have been reported (*Lancet*, 1956). Those outbreaks which had most features in common with this disease were the epidemics in Iceland in 1948–9 (Sigurdsson *et al.*, 1950), Adelaide in 1949–51 (Pellew, 1951), New York State in 1950 (White and Burtch, 1954), the Middlesex Hospital, London, in 1952 (Acheson, 1954), Coventry in 1953 (Macrae and Galpine, 1954), and Durban, South Africa, in 1955 (Alexander, 1956). A small epidemic recently reported in Berlin in 1954 (Sumner, 1956) does not seem so closely related as those outbreaks already mentioned.

These forms of encephalomyelitis may show a high infectivity in closed populations, particularly among nursing staff in hospitals; or in schools, as in the Iceland outbreak. Institutional epidemics have usually been associated with a number of cases in the general population, with the exception of the Middlesex Hospital epidemic, during which no similar illness was present in adjacent boroughs. In all the epidemics in which the sex incidence has been reported there has been a female preponderance. The peak incidence of cases has occurred in the summer, with the exception of Icelandic disease. The clinical features described in these outbreaks resemble each other in many aspects of the clinical course, and, although no contact has been traced between these widely separated epidemics, a common infective agent would seem to be the cause.

A prodromal stage of malaise, sore throat, headache, nuchal pain, lassitude, sometimes with gastro-intestinal symptoms, has occurred in every epidemic except in the Icelandic disease, in which headache and malaise occurred but visceral disturbances were absent.

Relapses also have been a common feature, and the course has lasted up to several months except in the Middlesex and Coventry outbreaks, in which the duration of the disease was usually a month and did not exceed two months. Pyrexia has been absent or slight, and when slight has lasted a few days or even several weeks. Paralyses usually appear a few days after the onset of the illness, but may occur simultaneously or be delayed as long as a few weeks. Loss of voluntary power may be severe although disturbances of tone and reflex changes tend to be slight. Muscle tenderness, spasm, and fasciculation are common signs, and sometimes myoclonic jerks may be observed. Wasting of muscle, particularly of the proximal muscles of the upper limbs in Icelandic disease, has been exceptional in other epidemics.

Sensory symptoms consist of pain, which is often severe, and paraesthesiae with objective findings of cutaneous hyperaesthesia or sensory loss and sometimes impairment of postural and vibration sense. Micturition difficulties are not infrequent except in the Iceland outbreak, when they occurred in two patients only. The frequency of involvement of the cranial nerves varies in different epidemics, but ocular pareses, symptoms referable to the eighth nerve, and facial weakness predominate, though bulbar pareses may occur.

In all the United Kingdom epidemics the cerebrospinal fluid has been normal, but a slight pleocytosis was observed in four cases in the Adelaide outbreak and in two cases in the New York State epidemic, and an increase of globulin in the later stages in some of the Durban cases. The Icelandic epidemic differed in that the cerebrospinal fluid which was examined in eight cases showed an increase of cells in five cases and an increase of protein in four. Two of these four had normal cell counts.

The clinical identity of the epidemic of the Royal Free Hospital Group with the Coventry and Durban outbreaks was confirmed by visits from the Medical Superintendent from the Whitley Hospital, Coventry, and by the Neurologist from the Addington Hospital, Durban, who examined our cases and considered that the disorder was the same as they had encountered in their respective outbreaks. Neurologists from the Middlesex Hospital were also impressed by the clinical resemblance of our patients to their series, but were of the opinion that the manifestations of the disorder in the Royal Free Hospital Group outbreak were more severe and prolonged.

The major point of difference between the Royal Free Hospital Group epidemic and other outbreaks has been the prominence of lympho-reticular involvement, although in retrospect enlargement of the cervical glands was found in some of the Durban cases (R. W. S. Cheetham, personal communication, 1955) and also had been observed in two cases at the Middlesex Hospital, and four cases in the New York State epidemic.

One of the most important problems in diagnosis has been the differentiation of this condition from poliomyelitis. The resemblance has been commented on by Macrae and

Galpine (1954) and more recently by Ramsay and O'Sullivan (1956). Initially the Middlesex Hospital outbreak also was thought to be a manifestation of poliomyelitis. Patients exhibiting paralysis after a short prodromal illness in the summer months might well be diagnosed as cases of poliomyelitis, but if the clinical features of this form of encephalomyelitis are familiar the resemblance is superficial. In the early stages vertigo and painful stiff neck are common, and although the posterior cervical muscles are tender, there is usually no true neck rigidity and Kernig's sign is negative. Malaise is disproportionate to the slight or absent fever, which is another distinguishing feature.

At the stage when neurological manifestations have appeared, distinction between this disease and poliomyelitis is not difficult. Sensory manifestations, migrating myalgia, and often fleeting paralyses, more often of an upper motor neurone distribution, distinguish this form of encephalomyelitis from poliomyelitis, in which the sensory manifestations are exceptional and myalgia and motor weakness do not tend to migrate. Motor weakness of a lower motor neurone distribution in poliomyelitis is associated with progressive loss of tendon reflexes, whereas in the present illness, even if paralysis persists and progresses, the reflexes can usually be elicited and may be exaggerated. Poliomyelitis, except in the early stages of infection, shows none of the tendencies of partial remission and subsequent exacerbation which characterize many of the cases described above. The relapsing lympho-reticular manifestations referred to again tend to distinguish the diseases even if the neurological picture proves confusing. The normal cerebrospinal fluid would also differentiate the condition, as in poliomyelitis abnormalities are present in the cerebrospinal fluid in at least 90% of cases.

The presence of a vesicular stomatitis in some patients, combined with painful spasm of the muscles of the trunk, was suggestive of a Coxsackie infection, but the absence of a meningeal reaction in the cerebrospinal fluid, and the failure to identify the causal virus, excluded this diagnosis. The normal cerebrospinal fluid was also evidence against a parenchymatous invasion by other organisms causing a lymphocytic meningitis such as Armstrong and Lillie's virus.

The complaint of sore throat with generalized lymph-node enlargement, leucopenia, and the presence of abnormal lymphocytes led to a diagnosis of infectious mononucleosis being suspected in the early stages of the epidemic. However, the typical blood count did not develop, and the Paul–Bunnell test remained negative in the great majority of cases.

The arthropod-borne encephalitides have not yet caused an epidemic of encephalomyelitis in the United Kingdom. A few sporadic cases of louping-ill due to tick-bites have occurred as an occupational disorder in veterinary surgeons, shepherds, and abattoir workers. Louping-ill as a possible cause of the epidemic of encephalomyelitis under consideration was excluded by serological tests.

A mild form of tick-borne meningo-encephalitis has been endemic in Slovenia for some years, causing epidemics in 1947 and 1953 without deaths, and has been described by Kmet and his colleagues (1955). The disease affected rural workers and caused an acute diphasic illness of short duration with marked meningeal signs and changes in the cerebrospinal fluid. Serological tests by Pond and Russ (1955) have identified the viruses of these epidemics, and of a similar virus meningo-encephalitis in Austria, as members of the tick-borne group. Mosquito-borne forms of virus encephalomyelitis such as Western equine encephalomyelitis produce epidemics in the United States and Canada in districts with surface water due to flooding. There is a case mortality of 8–15%, and the cerebrospinal fluid shows abnormalities. On epidemiological grounds it seems most improbable that any of the arthropod-borne infections have been the cause of this London epidemic.

The question naturally arose whether the Royal Free Hospital Group outbreak was a reappearance of encephalitis lethargica in an epidemic form. Epidemiological features, cerebrospinal fluid findings, and case mortality are points which distinguish the epidemics. Von Economo (1931) regarded encephalitis lethargica as a disease with maximal incidence in the first quarter of the year, of low infectivity and without any sex predominance. Changes in the cerebrospinal fluid were not uncommon, the case mortality was 40% in the acute stage with 30% resultant invalidism in survivors. The symptom-complexes of encephalitis lethargica described by Walshe (1920) have considerable interest because of their polymorphism, which he attributed to the irritative and paralytic action of the infective agent. Although of a much less severe character, this double action was observed in the neurological manifestations of the Royal Free Hospital Group infection. There has been no mortality attributable to the latter disease, and encephalitic Parkinsonism has not been a feature of it nor of any of the other similar outbreaks mentioned in this review.

A distinctive feature of the cases under consideration has been the peculiar nature of the motor weakness. It has only occasionally resembled a lower motor neurone type. Although often of an upper motor neurone distribution the positive elements of hypertonia classically associated with lesions of the pyramidal tract, though present in a mild degree initially, have not persisted even in the presence of a severe residual hemiplegia or paraplegic weakness. An extensor plantar response has been present as a transient phenomenon indicating disturbance of function of the pyramidal tract, but has not persisted as a frank abnormality of the cutaneous reflexes, and the abdominal reflexes have only been minimally disturbed. Another characteristic feature has been the peculiar jerking quality of volitional movement which was present in the milder cases throughout and was particularly noticeable during recovery from severe weakness. The associated electromyographic changes suggested that the peculiar grouping of motor-unit potentials with a hemiplegic weakness is a manifestation of long motor tract involvement.

The occurrence of hemiplegia without spasticity due to cortical or deep subcortical lesions has long been recognized, and the evidence for another descending pathway for the control of hypertonus has been discussed by Walshe (1919, 1942), who concludes that this problem cannot as yet be answered in man. The presence of hemiplegia, spontaneous pain, and disorder of all modalities of sensation on the same side, as occurred in one case, would suggest that structural damage was situated in the deep subcortical region. Another distribution of signs which not uncommonly occurred was a crural monoplegia or paraplegia combined with hyperpathia and diminution of posterior column sensibility. Muscle irritability, spasm, and sometimes myoclonic jerks made it difficult to assess the reflexes in this type of case. The posterior region of the cord which receives the sensory inflow and also probably the termination of the lateral corticospinal tract (Nathan and Smith, 1955), might be postulated as the site for the causal lesions to produce this combination of signs. Campbell and Garland (1956) have described three fatal cases attributed to virus infection under the title of "subacute myoclonic spinal neuronitis" with myoclonic jerks and painful spasms in the legs but without reflex changes. The histological findings were those of an inflammatory lesion of the grey matter of the cord, maximal in the dorsal horns in the thoracic and lumbar regions. Bradshaw (1954) has suggested that the internuncial neurones might be primarily involved in myoclonus, and that the anterior horn cells were only secondarily affected by afferent stimuli.

In the absence of pathological evidence any view regarding the nature of the lesion in the Royal Free Hospital epidemic must remain hypothetical.

Encephalomyelitis of virus origin in any event shows a discrepancy between the widespread impairment of nervous function and histological changes, which even in a fatal case may consist only of round-cell infiltration of the perivascular spaces.

There does not seem much doubt that the outbreaks reviewed in this discussion and the outbreak at the Royal Free Hospital constitute a clinical entity in which encephalomyelitis is the most serious feature. The name recently suggested for the entity is benign myalgic encephalomyelitis (*Lancet*, 1956). This title has certain merits and certain disadvantages; the use of the adjective "benign," although it correctly implies that there is no loss of life, gives a misleading impression of the severity and possible permanency of the neurological manifestations of the disease. The use of the adjective "myalgic" is a valuable reminder of this important and common feature of the illness. The title as a whole, however, fails to indicate that there is involvement of lympho-reticular structures.

Summary

An epidemic illness which affected nearly 300 members of the staff of the Royal Free Hospital Group between July 13 and November 24, 1955, is reported.

The clinical picture is studied in 200 in-patients. There is evidence of involvement of lympho-reticular structures in almost every case and of involvement of the central nervous system in about three-quarters of the 200.

The illness tends to run a fluctuating course. Treatment was symptomatic, but in 20 cases antibiotics were tried without effect. No patient died of the disease.

In the majority of cases recovery is the rule. Severe disability, however, may persist for many months and has persisted in at least four patients who are still disabled at the time of this report.

Laboratory investigations give no aid to diagnosis; haematological changes are non-specific and the cerebrospinal fluid is normal.

Electrodiagnostic investigations failed to show any evidence of lower motor neurone degeneration except in one case. The motor paralysis was accompanied by a reduction in the number of motor-unit potentials recruited on attempted volition, the residual potentials often being polyphasic. Occasionally, particularly during recovery, volition was accompanied by grouping of the motor-unit potentials.

Epidemiological studies suggest that the disease is spread by case-to-case contact and that the incubation period is five to six days.

Extensive investigations with the help of outside laboratories have failed, so far, to reveal either an infective agent or a causative factor.

The relationship of the outbreak in the Royal Free Hospital Group to similar epidemics reported in recent years from almost every quarter of the globe is discussed.

We received help from many sources, and we would like to record our gratitude to the staffs of the Public Health Departments of the Boroughs of St. Pancras and of Islington, the Virus Reference Laboratory, the London School of Hygiene, the M.R.C. Group for Research on Virus Diseases the Ministry of Health, the National Hospitals for Nervous Diseases, the Middlesex Hospital, the Hospital for Sick Children, the Radcliffe Infirmary, Oxford, the Whitley Hospital, Coventry, the Addington Hospital, Durban, the Eastman Dental Hospital, to the late Sir Lionel Whitby, C.V.O., *M.C.*, and to the nursing, auxiliary administrative, and ancillary staff of the R.F.H. Group. The Royal Free Hospital medical staff would also like to put on record the constant service of our Senior Medical Registrar, Dr. P. E. Jackson, in co-ordinating this report.

Figs. 1 and 2 are included by courtesy of the Editor of the *Journal of Hygiene*.

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AN OUTBREAK OF ACUTE INFECTIVE ENCEPHALOMYELITIS IN A RESIDENTIAL HOME FOR NURSES IN 1956

BY

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The outbreak of encephalomyelitis in the Royal Free Hospital Group began on July 13 and ended on November 24, 1955. During this time approximately 300 persons contracted the disease. This included 8 out of the 40 nurses and staff of the Royal Free Hospital Nurses' Preliminary Training School, N.W.8. The cases here all occurred from the end of July to the beginning of August, 1955.

In order that the report of the epidemic may be complete we record a further small outbreak associated with the Preliminary Training School which started in May, 1956. At this time there were resident 27 students, 3 teaching staff, one warden, and 7 domestic staff, a total population at risk of 38.

The number of notifications from the Preliminary Training School was seven, divided as follows: Student nurses, 5; sister, 1; member of domestic staff, 1. The dates of onset were: May 16, one student nurse; May 20, one student nurse; May 27, one student nurse; May 30, one student nurse; May 31, one sister; June 1, one student nurse; June 6, one maid.

The following is a summary of the illness in these seven patients, including the dates when they were admitted to the Sick Bay of the Royal Free Hospital and transferred or admitted direct to the Lawn Road Fever Hospital.

Case 1

Student nurse aged 18. Onset of illness, May 16; admitted to sick bay May 17; admitted to Lawn Road Hospital on June 1.

Symptoms.—Right earache, general malaise, severe headache, retrosternal pain, dizziness, nausea, and occasional