ENCEPHALITIS LETHARGICA

AND ITS AFTER-EFFECTS

 theoretician

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ENCEPHALITIS LETHARGICA AND ITS AFTER-EFFECTS.

INTRODUCTION.

Encephalitis Lethargica or epidemic encephalitis belongs to the group of general infectious diseases, it is characterised by certain symptoms arising in the central nervous system. The progressive lethargy and stupor which are so often present, have given rise to the term "lethargica" being applied to the disease. The disease is popularly known as "sleepy sickness" but this may be misleading as it has no connection with the sleeping sickness of Africa.

HISTORICAL.

Soon after encephalitis became known as a distinct and separate disease, Netter who investigated several of the French cases, drew attention to the fact that this 'new disease' was almost identical with an epidemic that appeared in Northern Italy, Germany and France in 1890-92 to which the name Nona had been given. Nona or La Nonna was then considered to be a nervous form of influenza. Mauthner made investigations in 1890 and declared that the condition was a haemorrhagic poliomyelitis superior but now these are thought to have been cases of encephalitis. The accounts of past epidemics contain many references to outbreaks presenting clinical features which may easily be interpreted as epidemic encephalitis; many of these were thought to be influenza, and in others some form of food poisoning was discussed. Amongst the epidemics that may have been encephalitis are the following: - An epidemic of soporific nature in Copenhagen in 1657 (Bartholin); a fever affecting the spinal cord and brain in England in 1658 and 1660 (Willis);
and the comatose fever of Sydenham in 1673-75. In 1712 Elias Kammermeister recorded in Tubingen an epidemic disease - the "Schlafsucht". In the early 19th century there were several epidemics in Europe - the "electric chorea of Dubini" in Italy, that recorded by Lombard of Geneva and Gintron of Bordeaux; isolated cases have also been recorded in the literature of the past century.

SINCE 1917.

Early in 1917 an epidemic disease was described by Von Economo in Vienna - it was characterized by drowsiness or disorders of sleep, ophthalmoplegias and general toxoemia. He described a series of 13 cases and gave the name encephalitis lethargica to the malady. In March and April 1918 there were several cases of an obscure disease in England, these were first thought to be Botulism and later a cerebral form of influenza or acute superior poliomyelites, but the investigations of the Medical Research Council have proved that those cases were identical with those already described by Von Economo in Vienna. Subsequently, the disease has become scattered world-wide, and there have been epidemics in most countries of varying severity. The great increase in the number of cases notified during the early part of last year as compared with those of 1919, viz., - in four months of 1924, 2468 cases, as compared with 538 cases in 1919 - make it a condition of interest and importance from a public health point of view. Especially, when the sequelae of encephalitis are considered.
The disease was made notifiable in January 1919. The following are the notified cases in England and Wales during successive years:

<table>
<thead>
<tr>
<th>Year</th>
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<tr>
<td>1919</td>
<td>538.</td>
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<td>1920</td>
<td>914.</td>
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<td>1921</td>
<td>1470.</td>
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<td>1922</td>
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<td>1923</td>
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<td>1924</td>
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(Twenty weeks only)

The greatest number of cases occur during the winter and early spring months - not only in this country but in Europe and America. It affects both sexes equally (Ministry of Health Report 1922 No. 11) but Mlle. Levy finds a greater number of women than men affected.

Harris recorded in the Lancet a case in a new-born infant, and also in a woman of 70 and the cases seen at Cheltenham General Hospital, included a case of a man aged 74 and a baby one year and eighteen months.

RACE. In Poland, Sterling found that the case-incidence amongst the Jews was made greater than amongst Christians. The degree of infectivity is of a low order - it is rarely that association can be traced between cases which are notified, and there is rarely more than one case in a house; outbreaks in schools or institutions have been recorded both in this country and in Europe, e.g., an epidemic occurred in a Girl's School in Derby in 1919 - also one occurred at a Village School in Warwickshire in October, 1922. The incubation period is stated to be anything from one to two weeks or even more.

PATHOLOGY.

The disease has no relation with Botulism, as it has no known relation to food, and the Bacillus Botulinus has never been
present, neither is it a type of poliomyelitis, for its seasonal prevalence, age-incidence and symptomatology are quite distinctive. The naked eye appearances of the brain shows a characteristic change in colour, it may be a faint pink to a deep salmon colour, it has been called the rose-coloured brain. On section the grey matter on the cortex, in the basal ganglia and in the cord show the same change in colour. The severity of the case does not seem to affect the depth of colour found post mortem. Sub-mental haemorrhages may be found of varying size - also deeply seated haemorrhages in the region of the basal ganglia and brain stens - Bramwell called attention to the presence of surface haemorrhages over the cerebellum.

The microscopic appearance is that of vascular congestion and consists of a perivascular cellular infiltration with lymphocytes. The nerve cells show different stages of toxic degeneration - they may become swollen, chromatolysis occurs and the nucleus is eccentric; there is proliferation of the neuroglia. The degeneration of the cells may be local - the distribution of the lesions varies greatly, any part of the central nervous system may be affected, but the grey matter is chiefly affected, and the sites of election are the basal ganglia, and the nuclei of certain of the cranial nerves. Peri vascular and diffuse infiltration with round cells with small haemorrhages may sometimes be found around the cranial or spinal nerve roots, this corresponds to the paralyses affecting single peripheral nerve trunks clinically.

In cases that have run a chronic course, lesions at all stages of
development may be found - the recent acute one to the healed lesion.

Various observers, by innoculating a virus detained from cases, have obtained brain lesions in rabbits and monkeys that are indistinguishable from encephalitis. De Fano found that a virus obtained from cases of herpes febrilis produced the same lesions in the central nervous system; this has been confirmed by other observers. Levañite claims that encephalitis is an extension of the virus of herpes from the naso-pharynx to the central nervous system, following an increased virulence, due to unknown causes, in time of epidemic. But a virus from the cerebro-spinal fluid identical with herpes has been reported by Flexner in an affection of the central nervous system in which no signs of encephalitis lethargica had appeared so that at present no conclusion can be drawn (Mem of Ministry of Health 1924). and much more experimental work will have to be done.

CEREBRO-SPINAL FLUID.

Frequently blood-stained, due to the surface haemorrhage. The cell count may be normal but usually there is an increase in the number of cells, the increase being due to lymphocytes. There may be a slight increase in the protein content of the fluid and there is a change in Langley's colloidal gold reaction--the curve is of the luetic or paralytic type. The sugar content of the cerebro-spinal fluid is often increased, in 1917 Von Economo observed that the reducing substance was increased in most if not in all cases. The average figure for healthy fluid is about .07% whereas in a list of cases reported by Cookson the average was .42%. If an
estimation cannot be made an absence of a decrease in reducing sugar is valuable in diagnosing this condition from Meningeal diseases, especially tuberculous meningitis.

**SYMPTOMS.**

Considering the pathology of the disease is one of widely disseminated patches of infection in the brain and spinal cord, the clinical features must be expected to show great variation in their type and degree of severity. There are three types that may be distinguished. Clinically:

1). General disturbance of the central nervous system without localisation.
2). Various localising symptoms in the central nervous system.
3). Mild or abortive cases.

The onset may be sudden or gradual, taking two to three weeks before it is fully established. After a varying incubation period there may be general malaise, headache, fever, constipation or diarrhoea and vomiting and diplopia is common with lethargy of varying depth, usually increasing. Edward Bramwell called attention to the onset with severe neuralgic pains in head and limbs and in one of my cases (case 3) the patient had sharp neuralgic pains and in head and legs for a fortnight. When the pains occur in abdomen the case may simulate an acute abdomen, and it may be difficult to distinguish it at first. The onset may come on with acute mental symptoms - Mania, Confusional states or Delusional Insanity.

The general symptoms are those of a general toxic infection - fever is usually present at the beginning, but is not usually very high
100° F. to 102° F; hyperpyrexia occasionally occurs - Arthur Hall records a case 107.5° F at death and Gelpe records a case which reached 111° F and recovered. Headache is usually present and may be severe and persistent; also gastro-intestinal upset is common, obstinate constipation and vomiting - occasionally diarrhoea foul breath and furred tongue. Skin eruptions are sometimes seen, but none are characteristic. Unfortunately no diagnostic rash appears in this disease" (Arthur Hall) they are transient fading in twenty-four hours, they may be erythematous, petechial, purpuric or scarlatiniform. Lethargy is usually present - it varies in depth from mere drowsiness to deep coma - the severe cases lie in bed like a log, with absolute immobility and entire lack of expression; in others the patient can be roused to answer questions, he may answer quickly and there may be long delay, and when left alone will at once relapse into stupor, unrousable coma is a sign of impending death. The stupor lasts for a varying time, from a few days to several weeks. Subsequent memory of events during the early days of the lethargy may be remarkably retained (Case 2). Amongst the localising symptoms, ocular disorders are very common, diplopia occurs early, with or without strabismus, bilateral ptosis is common, there may be paralysis of accommodation or failure to react to light, or both, the pupils may be unequal on one eye only may fail to react. Nystagmus may occur. Ophthalmoplegias are most often nuclear in type but peripheral trunks or branches of the third or other cranial nerves may be affected; the degree of ophthalmoplegia varies greatly, it may be transient, coming and going
or it may persist for some weeks. The diplopia and loss of accommodation affect the vision, but in certain cases, the patients complain of a loss of vision in both eyes (Case 5). Optic neuritis occurs in a few case, and rarely, optic atrophy. Other cranial nerves may be affected giving rise to uni- or bilateral facial paralysis, weakness of the masticatory muscles is common, paralysis and atrophy of the tongue, dysphagia due to spasms pharyngeal muscles. Paresis of the limbs may occur giving rise to monoplegia, hemi or para-plegias. There may be other indications of involvement of the cerebral hemispheres, such as spasticity, increased jerks loss of abdominal reflexes, and positive Babinski - Meningeal symptoms such as Kernig's sign, head retraction, vomiting, etc., may be marked - but in these cases, which are difficult to distinguish from meningitis, the examination of the cerebro spinal fluid is a help.

In certain cases chorea-like movements occur, or the spontaneous involuntary movements may be rhythmic tremulous nature as in paralysis agitans, or slow athetoid, or myoclonic, in type. These movements may be met with at any stage of the disease, but are most common shortly after the acute stage has passed. In the myoclonic type of case, jerkings of extreme violence occur and may affect the muscles of the diaphragm, the abdominal wall, neck, shoulders or limbs. These cases are very distressing to watch, the patient can have no rest or sleep, the frequently recurring painful spasms of the muscles utterly exhaust them. Cases developing fits of an epileptiform nature have been recorded both at the onset and later
in the illness-showing the cortex of the brain to be affected. The cases in the 1924 epidemic were less severe on the whole than earlier ones, the lethargy was less profound and the illness was more like influenza at the beginning, it was later, when localising symptoms developed that encephalitis was suspected. The following cases seen in hospital or private illustrate many of the points mentioned:

**Case 1.** In a girl aged 21 years. In April 1924 patient had an attack of what appeared to be a mild influenza with slight temperature 100° F, furred tongue, and marked constipation. After five days of illness diplopia suddenly developed, she complained of headaches and abdominal pains and on sitting up was giddy and faint and she swayed about. In the day time she was drowsy and slept most of the time but was roused without much difficulty, but once roused, she could answer questions sensibly. Towards evening she became excitable, and had irrelevant fits of laughing and crying and sudden outbursts of temper. She developed choreiform movements of arms and legs, and during the night these irregular jerks kept her from sleeping. They were much milder or rarely occurred in the daytime. On rousing her from sleep she talked in a whining voice and giggled at every question even though she could answer it sensibly. She had slight temperature for about 10 days, it varied between 99.8 and 100.8 pulse about 90. Patient was very constipated and there was great difficulty in getting bowels to act, with aperients and enemata. Patient continued in the above state about a fortnight then began to improve. She gradually became quieter in the evening and then slept better at night, but it was at least another 10 days
before the drowsiness improved. After she had apparently quite recovered for some weeks she was very emotional, and cried and laughed for no reason, and she seemed rather childish in manner. Pupils reacted normally throughout, ophthalmoscopy showed nothing abnormal, diplopia transitory/strabismus; no mystagmus, Patellar reflexes normal, no ankle clonus, flexor response, Urine - sp. gr.1020 no alb. or sugar. Lumber puncture - fluid not under pressure, clear, lymphocytosis, reduced Fehling’s. I saw this patient a few weeks ago February, 1925, for a mild attack of enteritis, otherwise she had been in good health and so far has escaped any after effects of her previous illness. She appears normal in every way and she has no mental or physical impairment.

Case 2. in a girl aged 15 years. Admitted to Cheltenham General Hospital in March 1923 suffering from an acute attack of encephalitis; on the sixth day of illness. Her mother stated that the illness started suddenly, she was at school in the morning and when she came home she was very sick and vomited several times. She complained of headache and said she was very sleepy, she said she could see double; the following morning she was drowsy she could not be roused and they then sent for the doctor. On admission patient was in a deep stupor which lasted for about 12 to 15 days after. She could only be roused with difficulty to answer questions, and there was a long interval before she attempted to do so, and if left undisturbed she quickly lapsed into stupor again. If she was being fed, she had to be roused between each bite and she would fall asleep with food unswallowed in her mouth. Her face was entirely devoid of expression and she lay
in bed like a log. For three or four days after coming in to hospital there was paralysis of the sphincters in continence of urine and faces and her mother said she had had that almost from the beginning of her illness. She had a slight temperature varying from $99^\circ$ to $100^\circ$ pulse 70-82. The ocular symptoms were transitory there was ptosis and slight internal strabismus. Nothing to be noted in fundi . . . . After about the tenth day she began to improve, she was more easily roused, and she awoke at times on her own. She at first opened her eyes as if she could not bear the light and if she was spoken to she giggled. In a day or so, she said she was hungry and her appetite gradually improved. She appeared a particularly intelligent girl but she was slow to reply to questions. One curious incident occurred that indicated a certain receptive state just after her admission, while she was in a deep stupor, the chief remarked when visiting her, that she was like the doormouse in Alice in Wonderland. She was not apparently awake on any of his visits and later when she was improving, on questioning her I mentioned the chief's name and asked if she knew him. "Yes," she said, "He is the man who said I was like the doormouse." As she improved, she complained frequently of headaches and she could not bear the light. She was inclined to be emotional. For some days her pupils did not react at all either to light or accommodation, but that cleared up, knee jerks not exaggerated, flexor response, ankle clonus for a few days.

Lumbar puncture - blood stained fluid - not under pressure, reduces Fehlings. Few lymphocytes, no polymorphous. Leucocyte count 12,000 per c.m.m.
At the end of a month she was able to get up, at first she used to fall about - she said something took her in her head and she could not stand, she always fell backwards. There was no paralysis. On leaving hospital she seemed quite well and on hearing of her in December, 1924 (1 year and eight months) later, she was in good health, and no after effects have developed. (By permission of Dr. J. Rupert Collins).

Case 3 in a man aged 34 years. In April 1924 the patient suffered from malaise and drowsiness in the day time for a fortnight, but he managed to carry on his work. He also complained of severe neuralgic pains in his head and the front of his legs. At night he slept badly, was restless and tossed about, and felt he could not close his eyes. At the end of this period he had severe headaches, and he was too sleepy to keep about. He complained on two or three occasions of seeing double, but this did not last. He had no vomiting or diarrhoea but obstinate constipation. He slept most of the time for two weeks but was not in a deep stupor, he could be easily roused and could answer questions. He was disturbed frequently by sudden jerking at the lower limbs, worse on the left side, and the muscular spasm caused sharp pain. He complained of what he called muscular rheumatism, it was severe cramp-like pains, they came in one leg and thigh for a few hours, the following day they were in the opposite arm and shoulder and so on, moving to a different area after a few hours interval, the pain was very severe causing perspiration to pour off him. The pupils reacted normally, no ptosis or paralysis of recti, knee jerks somewhat exaggerated, no clonus or Babinski. Temperature normal throughout.
At the end of the third week, the spasms of the legs gradually stopped and the attacks of cramp passed off and he improved generally. At present he is able to work full time - builder's assistant - but his wife says since his illness his memory for everyday things is very bad he can remember past events, but cannot take in new impressions or remember people met recently. He rarely reads the newspaper now, or takes interest in Sport or Politics as he did formerly, he used to be anxious for the latest Cricket or Football results, now he does not care.

Case 4. in a woman aged 40 years. In April 1924 the patient had what she thought was a bad bilious attack - she had headache and vomiting for 3 to 4 days before she was seen and she was very constipated. On examining her on the fifth day of illness she looked toxic, was a bad colour with thickly coated tongue, she was nervous and apprehensive. She had slight ptosis both eyelids and marked internal strabismus of left eye which she said had come on suddenly the previous day while she was out. She complained of seeing double, dryness of the mouth and throat and very severe headache over a circumscribed patch at left side of head. She was tired and aching all over, but she could not sleep. The headache was so severe and persistent that with the urgent vomiting it suggested the possibility of a cerebral tumour. Her temperature varied from 102 to 99 for a few days. There was an erythematous rash on the abdomen, arms and chest the first she was seen but this had faded almost entirely the following day. The patient was very nervous and anxious about herself and talked incessantly, but there was a curious immobility of the face and entire lack of expression. Her tongue could be protruded normally and muscles of
deglutition acted quite well. Sphincters unaffected. The headaches were not relieved by ordinary means - safriglates, etc., but the vomiting stopped in a day or so. Lumbar puncture. - C.S.F was under pressure and the patient got some relief from drawing off 15 c.s. fluid was blood stained few lymphocytes present. Pupils did not react to accommodation but they reacted to light, ophthalmoscope showed nothing abnormal in fundi or discs. Patellar reflexes exaggerated, abdominal reflex absent; no Babinski or Clonus.

The patient gradually improved after 4 to 5 days and after a week the ptosis and strabismus passed off.

The patient did not regain her normal health or manner, she was anxious and worried about her state of health all the time and every-time she was seen, she had several complaints. She took no interest in her home, husband or children, and she would listen to nothing that was told her - her whole attention was fixed on herself and her troubles. She talked incessantly in a monotonous tone of voice. She complained more or less all the time of headaches. She gradually got worse and after 6 to 8 weeks developed delusions - she thought she had a hole in the top of her head through which part of herself got out, then she thought her throat was closing up and some days she had difficulty in swallowing and she had cancer in all parts of her body, insects in her head, etc.,

All this time, there was the peculiar lack of expression and immobility of the face. She walked slowly and stiffly and she turned her body as a whole if she wanted to look round, yet she could really turn her head if told to do so. There was no tremor.
Four months latter she got much worse, she was depressed and took to her bed and she would not eat or wash herself, she would not get up to use the commode, but would void urine or evacuate her bowels in bed - as she declared, she would die if she sat up, and she would not use the bed-pan. She was removed at the end of August to Cheltenham Union, and from there she was transferred to Gloucester County Mental Hospital at Barnwood.

The next case is interesting from the point of view of pathology - there was fairly rapid loss of vision in both eyes equally, before the optic atrophy set in - in such a case the trouble could not have been unclean in origin, and the discs were well marked and clear the progressive equal loss suggests the possibility of some toxic change in the retina.

Case 5. in a woman aged 34 - widow.

First attended Cheltenham Eye Hospital 28th April 1924.

History - Has three children - all good health. Had influenza three months ago with severe headache, also severe headache three weeks ago, sight being sick for two days. After this the eye began to fail, had had headaches for past three weeks.


Refracted under H and C = \[+ 2.5 \text{ R} \text{fr.} \text{ + 2.5 L} \text{fr.}\]

The retinal veins were full, discs well marked in outline, other parts of the retina normal, media clear.

1 May 1924. - Patient stated she was not sleeping well; was very constipated: and complained of severe pain over left eye. Both
pupils were dilated, with no contraction to light. Vision - can't count fingers at 1 ft. nor could she detect large red object, had to be led about. Ethmoidal region and maxillary sinus examined - negative - was admitted to hospital - ordered mercury inunctions and Mist. pot. *o.d. 1/2 tds.

2nd May - 9th. Eight septic teeth extracted. Wasserman negative. Was examined by Dr. S. M. Hebblethwaite (Consulting Physician, Cheltenham General Hospital) who reported 'Apart from the eyes I find nothing. The history is suggestive of encephalitis lethargica, e.g. initial vomiting, headache. I take it the eye symptoms are consistent with this view, but I find no collateral evidence. Personally I regard it as a case of encephalitis lethargica''

Progress - 6th May - Able to count fingers.

10th May - Pupils slightly active to light, and less dilated Distinct fullness of retinal veins.

20th May - Pupils small and contract moderately to light; reads large print with difficulty. Discs are paler and slightly filled in, edges clear cut.

18th June. Rt. vision 2/60. Lt. 2/60

24th Nov: Rt. vision 6/60. Lt. 6/60 decided atrophy of the discs.

(By permission of Mr. N. H. Pike, F.R.C.S).

Case 6. in a boy aged 19, occupation - Gardener.

Onset sudden; patient vomited one night, had pain in the back, severe headache, trembling and then became unconscious in a few hours. On admission to hospital the whole body was agitated by coarse tremors patient was in a deep stupor and could not be roused for two or three
days then for a fortnight was still in fairly deep stupor but could be roused with difficulty to answer questions - he could not answer clearly he appeared confused. The knee jerks were exaggerated, plantar reflex normal, no Kernig, some stiffness of the limb muscles.

Leucocyte count 7,800 per c.m.m.

Temperature normal throughout - pulse 60.

On admission there was incontinence - but after a fortnight obstinate constipation.

Eye symptoms - pupils equal and active, no strabismus fundi normal.

Discharged at the end of six weeks - quite well.

Case 7. In a man aged 74. Complained of headaches for a month; day before admission right eye was blurred, next morning on waking up, he found he was unable to see at all, failed to perceive light. On admission arteries very sclerosed - right pupil larger than left, neither reacted to light, outline of optic discs clear - no atrophy.

Partial paresis of right arm no paralysis of legs. Both knee jerks present, Babinski present right foot. Patient very lethargic difficult to rouse.

Vomited during night - retention or urine.

Cerebro-spinal fluid - clear, not under pressure no deposit, small amount of albumen, does not reduce Fehling's - few lymphocytes, no polymorphous. Patient died fifth day in hospital. - P.M. nothing abnormal found in brain - no tumour.

Case 8. In a girl of 15 years. March 1924. Five days before admission severe headaches and vomiting. Mental condition became unbalanced patient was laughing and crying for nothing. Two days later abdominal pain and she said she saw double. On admission to hospital she had
difficulty in passing water - it had to be drawn off by catheter for several days. She was very constipated. Unable to sleep for first week; complained of seeing various colours.

Temperature - 100° p. 90. Tongue furred; had a frightened look and started to weep and sometimes burst into hysterical laughter.

No paresis of facial muscles, no ptosis; kept her legs drawn up, legs spastic, no grip in hands, knee jerks exaggerated, abdominal reflexes+++ No Kernig of stiffness of neck.

Eyes - mystagmus laterally - no strabismus, pupils equal and active, still complains of seeing various colours and at times of diplopia.

Leucocyte count 10,000 per c.m.m.

Cerebro-spinal fluid - clear, no deposit, increase in lymphocytes, no polymorphes - reduces Fehling's.

Discharged much improved one month after admission.

Case 9. in a woman aged 38 - Single.

In the beginning of February 1923 patient had severe headache and attack of giddiness - that passed off - but two days later both legs became very weak and she was unable to walk; she was then admitted to Cheltenham General Hospital and two days later right arm felt weak, and she had vomiting for two days. Slight paresis of right side of face developed and she complained of diplopia which lasted for several days:

She was drowsy for about a week.

Temperature - normal, pulse 76, complained of headache, vomiting frequently. Mental condition - slightly dull. Pupils equal and active, slight mystagmus, fundi normal; weakness of right external rectus, at rest right eye wanders in.
Paresis of both legs and arms, right more affected than left. Loss of knee jerks, no clonus no Babinski.
Cerebro-spinal fluid clear, under pressure, no albumen, no globulin, does not reduce Fehling. No growth on culture - Lymphocytes increased.
Discharged four months later - face normal, good use use of right arm, legs still weak, unable to walk, mental condition has improved, but patient inclined to be emotional - some impairment of memory, cannot remember names.
The following is a very mild type of case :

Case 10. in a boy of 14 years - March 1924. One week before admission, suffered from headache - three days ago diplopia; the following day weakness of legs followed by weakness of arms - did not vomit - Twitching of muscles of right side of neck, Temperature 100 p.100 - Tongue furred.
Pupils equal and active - diplopia varies, no strabismus, slight mystagma on lateral movement, bi-lateral ptosis, knee jerks exaggerated no Babinski, no Clonus - Kernig's sign +
Slight hypotonus of muscles, co-ordination of muscles fair, grip in hands fair, sensation normal - Lethargic.
Discharged in two and a half weeks, condition normal.

Case 11. in a baby aged 1-8/12 years - in February 1924. - Mother stated it had a convulsion one night, and it was very sick, vomited every few minutes during the night. On admission it was drowsy, and difficult to rouse, it took no notice of being handled, or when it was bathed in the ward it did not cry at all, it would not take a feed, either, from a bottle or spoon - it vomited occasionally and was constipated. There was slight stiffness of the muscles of the limbs.
No head retraction, no Kernig's sign—there was slight strabismus of left eye, on admission, but that passed off the following day, became gradually more impossible to rouse the child and it died the third day. Not allowed to do P.M.

Case 12. in a woman aged 42 years. Admitted to Cheltenham General Hospital 14. 4. 24. One week ago patient had pain in abdomen and vomited occasionally, the pain gradually settled in the right side. She has had continuous hiccough for past five days, with no response to treatment; patient on admission in a state of extreme misery and no control over spasms. Temperature 99. 8° F. p. 80. tongue furred. There is a series of violent myoclonic spasms of abdominal muscles, these coincide with inspiration. The recti and oblique muscles are in spasm, also apparently diaphragm.

Patient complains of severe pain and tenderness in left upper abdomen impossible to examine owing to spasm. Morphia has very slight effect on spasms—it only eases the pain. Knee jerks + + no Babinski, No Kernig, no weakness in arms or legs. Lumbar puncture done each day with slight relief until she had to be anaesthetised to procure any rest at all. Leucocyte count—7,500 per c.m.m.

No lethargy—can't sleep for spasms.

21. 4. 24. Lumbar puncture done, 10.c.c. fluid withdrawn and injected intravenously.

22. 4. 24. Marked relief—patient was able to sleep as the spasms were so much quieter. Hiccup at times.

26. 4. 24. The process was repeated and patient improved again.

1. 5. 24. Still very miserable and complaining of pain continually.
Process again repeated - with similar improvement; it was done every other day for three weeks as the improvement only lasted a little over 24 hours.

25. 5. 24. Discharged - Still complaining of pain and hiccoughs at times but able to sleep in the interval of the attacks. (By permission of Dr. S. M. Hebblethwaite).

Residua or Sequelae.

After the outbreaks of epidemic encephalitis, it was noticed that following the acute phase of the disease, various sequelae, nervous, psychotic or otherwise developed. In chronic cases that acute febrile phase with its characteristic symptoms - fever, lethargy and eye symptoms, sometimes is absent, the history being vague, perhaps, of an attack of influenza - it may be one of the so-called abortive attacks. Thus it may be only diagnosed after the event.

The virus may cause an inflammatory affection of the central nervous system that may be progressive in nature or it may be a recurrent or intermittent process "Le virus de l'encephalite reste done vivant dans les centres nerveux, comme celui de la syphilis." Netter. The sequelae may appear in the course of the acute illness or after the original attack has apparently terminated, or they may appear after a variable period, a few weeks up to a year or so.

Prof. Arthur Hall divides the late manifestations into two groups - (1). Other residua. (2). Parkinsonism. Taking the "other residua" first, the more important of the after affects are: -

(1) Mental Symptoms. These symptoms may be of all degrees of severity - there may be purely psychotic symptoms, or they may be associated with nervous lesions. These may be confusion, delirium,
agitation or mania - in adults there is sometimes emotional disturbances, depression, hypochondriacal ideas (Case 4) sometimes connected with obsession or hallucinations of sight or hearing. The depression may lead to attempts at suicide or even suicide itself. In children and young adults, changes of morals and character take place; the patient is restless, meddlesome, talkative, inquisitive, wide-awake yet with erratic attention, they are irritable and liable to outbursts of temper, scolding and the use of abusive language, propensity to destructiveness, biting of nail and auto-mutilations; dirty in habits, and teasing and cruel to children. These children show precocious erotism, leading to masturbation, exhibitionism, obscene language and conduct, and offences towards small girls. Thus chronic encephalitis, becomes a question of medico-legal importance, as many of these children will reach the police courts as Juvenile offenders: in case 12 the girl was under police supervision for some months before she was certified. These children are backward at school, partly from their lack of interest and partly from inability to keep their attention. These psychotic disturbances in children may be of the "nocturnal type" - during the day the patient may be more or less normal, but at a certain fixed hour each night, the child becomes restless, excitable and unmanageable, singing, shouting with sometimes hallucinations, it may run about most of the night and then falls into a heavy sleep which may last till mid-day. There may be impairment of memory in a chronic encephalitis case - the memory for the past may be unaffected, just inability to remember new impressions or recent events (Case 3) or there may be a general loss.
Case 13. in a girl aged 15 years. Admitted to Cheltenham General Hospital in March 1923 for observation. Twelve months before patient had a typical attack of encephalitis lethargica, with somnolence ophthalmoplegia, diplopia, etc., she was previously a healthy normal girl, the second of a family of ten, not subject to nervous attacks and could help with younger children. The mother brought her to hospital as her disposition had so changed since her illness. She was quarrelsome and spiteful, interfering, she easily flew into violent tempers and she bullied the children. She could not get on at school, she could not take in what she was told or read and she showed no interest whatever, and she was so troublesome, finally they refused to have her back at school. She had been in one or two places as a domestic, but no one kept her more than a few days. She stopped children in the street and took their hair ribbons or the boy's caps away and destroyed them — and she pinched and generally ill-treated the smaller ones — that her parents were constantly in trouble in the neighbourhood. Just before admittance she had threatened the baby with a carving knife.

She was in hospital for a fortnight and during that time she was quiet and well-behaved on the whole, but when the Sister was off duty and she was attended by one of the younger nurses she became difficult to manage. She upset things within reach, spit on the floor and passed water in bed. Temperature — normal, during her stay she slept well, appetite good; very constipated. Pupils equal and active; knee jerks normal, no Babinski, no clonus.

In July 1924 patient was seen outside. Her condition was more or less as before, only worse. She bit and pinched children and she
and she would rush out into the street and molest children passing. People complained about her to the police, and for several months she was under police supervision - she threatened to strangle her mother. She also tried to knock her about with a poker or any other instrument. One of the smaller boys had a lump the size of an egg on his forehead, where she had thrown the clothes prop at him.

She could not sleep at night, she kept her parents up by singing and shouting, then in the morning she would not get up. She would not wash or dress herself till afternoon. She often went to the door when anyone came in her nightdress or with very little on and she would lift her clothes to passers by in the street. Masturbation not observed.

Patient was admitted to Children's Home of the Union - but after two days, she attacked the Sister-in-charge and ran away. She climbed the wall and ran home in her knickers. For an hour or two she was maniacal, shouting and screaming, utterly uncontrollable. She again was rushing about with a carving knife, which her father managed to remove. She was given a dose of hyoscine, which quietened her for the night and the following morning she was removed to Gloucester County Asylum at Barnwood where she is still remaining.

Excito-Motor Sequalee. Mlle. Lévy has published a monograph dealing with this group. They may take the form of myoclonic, choreatic or shaking movements - or what Mlle. Lévy calls bradyynesia, that is slow rhythmical movements, involving the limbs, head or trunk. These movements are involuntary and uncontrollable and they are essentially rhythmical. (Case 12. the acute attach passed into this group without an interval).
Amongst the other residua, paralysis may result but these are rare (Arthur Hall). Respiratory symptoms due to nervous origin, polypnea periods of apnoea in which the patient may become cyanosed. There may be dyspnoea, Cheyne-Stokes breathing and spasmodic cough - the latter may be very persistent and extremely violent - it may be worse at night.

There may be an upset in general nutrition following encephalitis - certain cases of Parkinsonism, suffer from cachexia and wasting may accompany certain cases with excito-motor phenomena.

Many cases have been recorded of patients putting on excessive weight - the adiposity is general, rarely segmental; associated with the obesity there may be polyuria, and increased tolerance for sugar, or glycosuria: Fröhich's Syndrome thus suggests some affection, transitory or permanent of the pituitary body.

In women with adiposity, menstrual disturbances are common or there may be amenorrhea, Sexual disturbances may occur - either eroticism or in males, feminism and frigidity. Mile. Lévy states that these cases of obesity have been observed following the epidemic of 1920.

Case 14. in a girl aged 14 years.

In April 1920 patient had typical encephalitis lethargica - fever, ptosis, diplopia, etc., and somnolence - she was said to have slept some weeks. Soon after she recovered her mother noticed changes in her disposition. Before her illness she had been a sweet-tempered and easily managed child, mental powers normal, but she became noisy irritable and talkative, liable to fits of temper - she tears her clothes and destroys things. She sleeps badly and then sings and shouts without of other people. She often walks in her sleep. She
shows no affection for anyone, or gratitude for anything done for her. She is never still, she cannot sit quietly in a chair for one minute she wriggles about and jumps up in constant restless activity. She will not follow any occupation for more than a few minutes, but keeps changing to start something else.

She is talkative and cheeky, and she is not emotional, never shows pleasure: no hallucinations; she is childish and her remarks are simple for her age, she says whatever comes into her head at the moment, one cannot keep her attention on any subject for more than a minute.

From the time of her illness, she steadily put on weight and now although she is short for her age, she weighs 14 stone 8 lbs. The fat is general all over the body no local deposits; abdomen somewhat prominent, breasts small, not well developed, hair over pubis and in axilla scanty. Thyroid not palpable. No polydipsia, no polyuria - urine - sp. gr. 1.010, acid, no sugar no ablumen.

Pupils equal and active, no mystagmus, no paresis of eye muscles or of face. No paresis of limbs, no tremor or abnormal muscular movements, no rigidity, knee jerks exaggerated both sides, no Babinski or clonus. She suffers frequently from severe frontal headaches. Occasionally vomiting at the same time, the attacks last 1 - 2 days. She suffers from menorrhagia, period lasts 10 - 12 days. She has to stay in bed first three days as there is a regular flooding - Periods irregular.

Her mother states that her irritability and restlessness is wearing her parents out, with also the bad nights.

There was a marked improvement at first when she was on Elixir
Polyglandin (A & H) but that did not last.

Parkinsonism. The Parkinsonian Syndrome, so called from its resemblance to paralysis agitans, consists of three main symptoms, rigidity, tremor, and slowness of movements - with certain secondary symptoms. It may be said to be one of the most important of the residua of encephalitis as it is completely disabling and it is the most frequent. Mlle. Lévy out of 129 cases, records 70 cases of Parkinsonian, and it is estimated that 25% of cases suffer from this residuum. This syndrome may develop early, a few days to a week or so after the onset of the acute phase, or there may be a delay of months or years or it may be present with more or less pronounced symptoms from the onset of the initial illness. The onset may be quite sudden or it may take some time to develop, with remissions and exacerbations of symptoms.

Its main characteristic is an increasing muscular hypertonia and rigidity, this rigidity may be localised, facial mono- or hemiplegia or more commonly it is generalised from the start, extending all over the muscular system of the body and these patients may assume at an early stage the characteristic facial expression and attitude of paralysis agitans.

The progressive stiffening of the body is accompanied by slowness of movement, and limitation of spontaneous movements, the patient has a fixed stare with no change in facial expression. The sluggishness of motion is shown in the gait of patients and it may be accompanied by retro-pulsion or autero-pulsion a tendency to run either backwards or forwards. The patient may be bent in different positions sideways or doubled up in foetus-like attitude and this may prevent
resting at night and sleeping. Catalepsy may occur either voluntary or passive movements stiffen with cata\textit{tonic} attitudes.\footnote{Wissler reports three cases of catalepsy.} There is frequently absence of tremor or if it occurs, it sets in much later. The full-rolling tremor at rest, so characteristic of paralysis agitans is of less frequent occurrence and if tremor is present, it is of a coarse, rhythmic or shaking movement, which only occurs with voluntary movements, increasing as the object\text\textit{}/approached - intention tremor - whereas in paralysis agitans, the tremor is lessened by active movements.

There are certain paradoxes met with in the motor functions - certain automatic movements are inhibited or impossible, the patient is unable to walk or swing arms while walking or eat, and yet suddenly with some outside stimulus he may be able to run, jump or do other complicated muscular actions. Mlle. Lévy records a case of a small girl with encephalitis parkinsonism, who could not eat or dress herself, yet could skip or play ball quite well.

These patients tire very easily. They cannot perform any movements or make any effort without bringing out this tireability of the muscles; it may be that this helps to cause the inertia of the encephalitis parkinsonian; disorders of speech occur frequently, the patient may talk in a monotonous drawling tone, very slowly and they will use as few words or sentences as possible.\footnote{They may repeat persistently a single word or phrase and after repeating it several times, the lips may continue to form the words without any sound being heard.} This may develop into \textit{mutism}. The voluntary Speech is first involved, while the more automatic reading, recitations,
exclamations in excitement are quite unaffected. Frequently other residua or nervous symptoms are present, associated with Parkinsonism, though that may be the predominant feature of the case.

Diagnosis:

In a typical case the diagnosis is not difficult - the lethargy, headache, fever and diplopia and ocular-palsies are pathognomonic together with the finding of the cerebro-spinal fluid, often blood stained, the presence of a reducing agent commonly an increase in the lymphocytes. The abortive or mild forms, with gradual onset and mild symptoms are those cases which present difficulties; the diagnosis must be based on the clinical signs and symptoms and can only be arrived at by method of exclusion - there is no specific laboratory test for the disease.

When meningeal symptoms predominate - it has to be distinguished from other meningeal diseases, especially, tuberculous meningitis - for this cerebro-spinal fluid may be of great help. Other diseases that may be simulated are: - acute poliomyelitis, cerebral syphilis, botulism, cerebral influenza, uroemia, cerebral tumour, cerebral haemorrhage, acute dementia, hysteria and occasionally acute abdominal disease. Later, when the sequelae develops these are easily recognised if they follow the acute lethargic stage or when the chronic nervous symptoms set in at a fluid not too far removed from the initial febrile phase. The chronic form of the malady has to be diagnosed from disseminated sclerosis - the persistent mystagmus intention tremor scanning speech, spastic paresis and positive Babinski - point to disseminated sclerosis, while rigidity tremor at rest, bradyesthesia
- 30-
disturbances of pupillary reactions, point to chronic encephalitis. Cerebro-spinal syphilis must be considered - hear the history, Wasserman and changes in the cerebro-spinal fluid help. Cerebral tumour will not be mistaken if the case is watched for any length of time. The symptoms in the latter condition develop and progress whereas in chronic encephalitis they are remittent with exacerbations. Encephalitis parkinsonism has to be distinguished from true paralysis agitans but there is only difficulty in patients over 40 or 50. The following points may help: - age - mostly under 40, past history whether there has be an acute or lethargic phase; absence of typical tremor, disturbances of pupillary-reactions and ocular-palsies, together with other nervous or psychotic symptoms - these indicate encephalitis parkinsonism. If there are any pathological findings in the cerebro-spinal fluid this may be a help. Certain cases may suggest neurasthenia or hysteria, with symptoms of a functional nature, such as disturbance of sleep, diurnal somnolence, asthenia, vertigo headaches, anxiety and failure of memory, emotional disturbances and tachycardia, etc., special care should be taken before diagnosing hysteria, mode of onset, development of symptoms should be noted and search made for organic nerve symptoms and by considering the clinical picture as a whole, a correct diagnosis should be possible.

Prognosis.
This includes the immediate prognosis as to life and also the prognosis as to how much permanent damage to the central nervous system may be felt.
The case - mortality is high - taking it on the whole since 1917,
it may be given as somewhere between 20 and 50%. Between the years 1919 and 1920, 48.3% of cases were fatal - while in the early part of 1924, 12 - 21% of notified cases were fatal. Rapid onset and quick development of severe symptoms, high fever, delirium, and maniacal excitement are bad, prognostic signs. Lethargy which steadily gets deeper day by day with rising temperature and in continence are serious signs.

Epidemic encephalitis is characterised by its numerous manifestations or residua; many of these are so late in appearing that the percentage of them is an increasing one. But no reliable forecast can be given - the prognosis doing mostly guess-work. The disease may have a course ending in perfect recovery, it may become stationery, it may be progressive either gradually with or without new nervous symptoms, or the course may be remittent - exacerbating or intermitting. It may end in death, either through protracted cachetic state or by a sudden aggravation or relapse.

Treatment.

There is no specific treatment. The patient should be confined to bed and isolated from the other members of the household; careful nursing is essential. Economy recommends urotropin as having a favourable influence during the acute stage, it may be given by the mouth or in larger doses intravenously. Lumbar puncture and withdrawal of cerebro-spinal fluid in some cases gives relief - it improves the headache and lethargy, this may be repeated at intervals as indicated by the condition of the patient, if improvement results.

Piticariu of Roumania treated cases of myoclonic form by intravenous
injections of the patient's own cerebro-spinal fluid, the injections being given in doses of 10 c.c. every five to seven days. He had good results in his cases - but Leagues of Mourgain treated ten cases by this method without any improvement - (Case 12) at the Cheltenham General Hospital improved and the spasms were lessened but she relapsed fairly quickly.

For the general nervous disturbances, emotional hyper-excitability, tachycardia, tics, etc., bromides may be tried. For the myclonic and choreatic types phenacetin combined with luminal is sometimes useful. For the rigidity and tremor of parkinsonism hyoscine is sometimes effective, also courses of baths, massage and mild exercises. For the asthenic or cachectic type sodium cacodylate intramuscularly has given good results, dose 6 - 7 daily for a week.

Psychotherapy, may be tried for the psychic disturbances of children and young people and a process or re-education should be carried out, these children will often be better if removed from their own home, either to a hospital or home for backward children, where they can receive care and discipline.

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