A STUDY OF EPIDEMIC ENCEPHALITIS IN CHILDHOOD.

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Thesis Submitted for the Degree of M.D.

by

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INTRODUCTION.

The history of the disease known as epidemic or lethargic encephalitis is now well known. Described by Von Economo (1) in Vienna in 1917 under its present title, it was seen also in France in the same year and described there by Cruchet, Moutier and Calmette (2) by whom it was entitled sub acute encephalomyelitis.

In the Spring of 1918 the disease reached Britain and the first cases in Glasgow occurred early in that year. In March a case was brought to the Royal Hospital for Sick Children in Glasgow and was shortly followed by others. The first three were reported by Professor Findlay (3) in 1918 and in 1920. 23 cases were described by Findlay and Shiskine (4) with special reference to the cerebro spinal fluid. At that time nocturnal excitement had been observed but the other late manifestations had not become so prominent as has since been the case. In 1923, Dr Grace Anderson (5) described the sequelae in 38 cases seen up to 1921. Since that time these later manifestations have become more and more striking and the consequent difficulties more pressing. After eight years it is apparent that no limit to the possible developments is yet known.

Seventy-nine cases were seen in the Royal Hospital for Sick Children from 1918 to the end of 1925.

In the following pages the course of the disease, as it has been seen in these cases, has been traced and analysed. Sixty-one have been examined personally by the present writer, in the great majority of cases on several occasions. Those

from/

from 1923 have been observed constantly by her from their admission to hospital until the present time. It has been possible to complete the history of 71 cases up to 1926.

The following table gives general details showing the distribution and fate of the 79 cases.

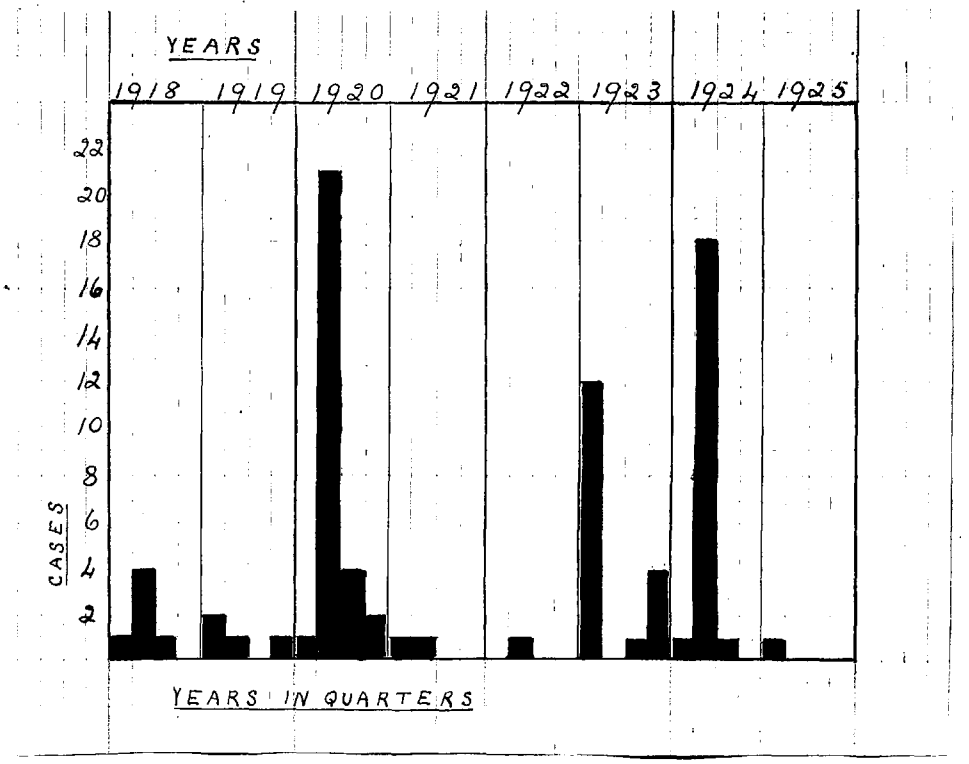
Table 1.

Year of onset.	Cases.	Died in acute stage.	Died in later stage.	Known now.	Not traced.
1918	6	1	1	3	1
1919	4	-	-	4	-
1920	28	-	5	20	3
1921	2	-	-	-	2
1922	1	-	-	1	-
1923	17	1	-	14	2
1924	20	2	-	18	-
1925	1	-	-	1	-
Total:	79	4	6	61	8

EPIDEMIOLOGY.

The following table gives the incidence of the cases in years and quarters, with reference to the date of onset.

Table 2.



Incidence in years.

The years 1920, 1923 and 1924 which show the highest numbers were those in which the disease assumed epidemic proportions. In 1922 no new case was seen in the hospital, nor was any patient brought with a history of onset in that year, until early in 1926. A child, who showed the Parkinsonian syndrome most definitely was then sent for examination with a typical history of the acute illness in 1922. 1925 was also almost free, only one case being seen during the acute stage.

Incidence in quarters.

The disease was originally considered to be one of the winter months. The Ministry of Health Report (6) of 1922 emphasized this seasonal incidence with regard to England and Wales. Charts given by Hall (7) for Colombia, New York, Switzerland, Warsaw, Turin and Helsingfors for 1919, 1920 and 1921 show the same rise early in the year. In 1920, however, the highest figures in England were reached in May, June and July. The incidence in our series emphasizes the second quarter of the year as being the usual period of onset though in 1923 the first quarter was decidedly the heaviest.

Sex.

Out of the 79 cases, 23 were girls, 56 boys. Males therefore form 70.8% of the total number.

The following table gives the sex incidence at the various ages:-

Table 3.

Age.	Under 1 year.		From 1 up to 5 yrs.		From 5 up to 10 yrs.		From 10 up to 15 years.	
Sex.	M.	F.	M.	F.	M.	F.	M.	F.
Number.	1	3	12	4	27	9	16	7

This preponderance of males is not so strongly marked in other and larger series. The Ministry of Health Report (8) shows an almost equal number of cases in the two sexes. The equality appears to be roughly maintained at the various ages.

Kennedy (9) had in his series 29 boys and 22 girls. In the Glasgow cases from 1919 to 1924 60% were males.

Age.

The following table gives the distribution according to age during the acute illness.

Table 4.

Age.	Cases.
From birth to end of 1st year.	4
" 1st yr. " " 2nd "	5
" 2nd " " " 3rd "	1
" 3rd " " " 4th "	5
" 4th " " " 5th "	5
" 5th " " " 6th "	6
" 6th " " " 7th "	11
" 7th " " " 8th "	8
" 8th " " " 9th "	4
" 9th " " " 10th "	7
" 10th " " " 11th "	12
" 11th " " " 12th "	7
" 12th " " " 13th "	3
" 13th " " " 15th "	1

The numbers increase slightly as the age rises. The drop in the last two years is explained by the fact that children over/

over 12 years of age are seldom admitted to the Children's Hospital. The youngest of our patients was aged 2/12ths of a year.

Association with other Diseases.

In none of the cases was there any history or appearance of an associated disease such as influenza or epidemic hiccough. In one or two the original illness had been diagnosed as influenza or pneumonia, but a careful scrutiny of the early symptoms made the real diagnosis evident.

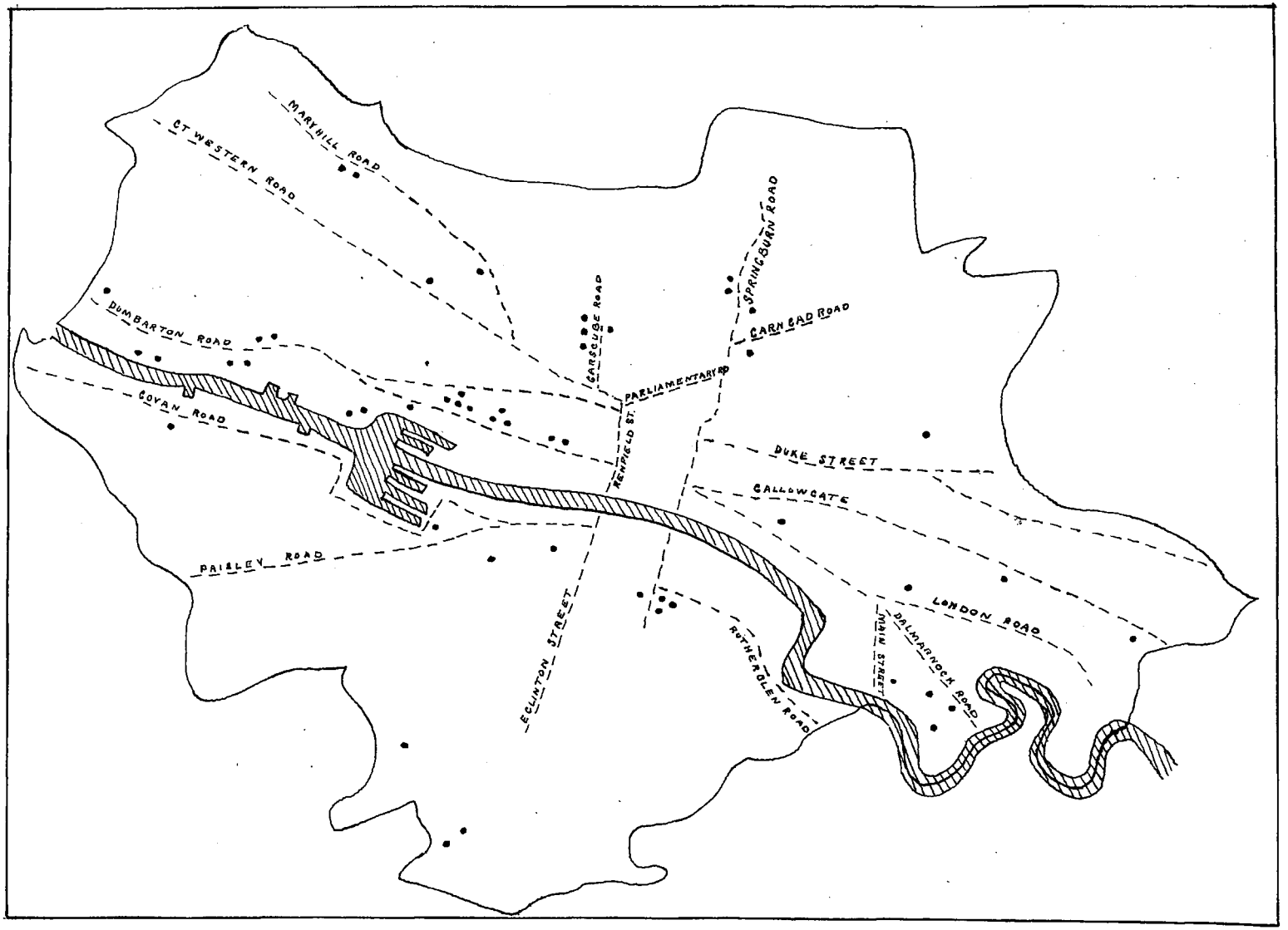
Infectivity.

Apart from the exceptions mentioned below there is no evidence of infection in this series. No two children came from one house, although more than 90% of the hospital patients came from houses of one or two rooms, where the inmates are brought into the closest contact.

The possible exceptions occurred in 1924, when 4 cases were admitted during one month from one school, and 3 during the same month from another school. Those 7 cases formed 63% of all the acute cases admitted during that epidemic. The following tables give details of these cases:-

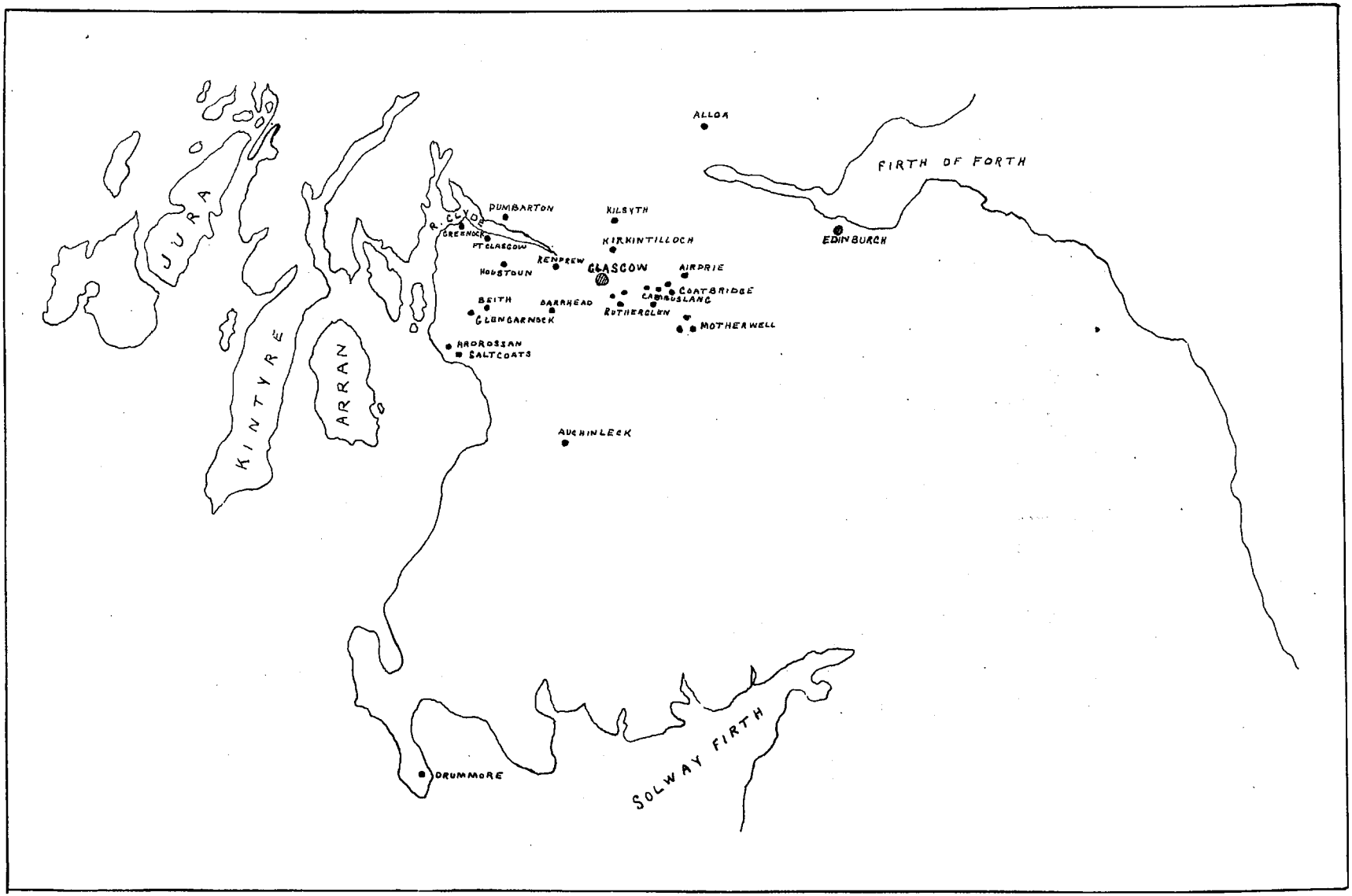
Partick. Table 5.

Case.	Sex.	Age.	Month of onset.
77	F.	9 years.	April.
66	M.	6^{9}/12th yrs.	April.
74	M.	12 years.	April.
70	M.	7 "	April.



CITY OF GLASGOW

DISTRIBUTION OF CASES IN THIS SERIES



MAP SHOWING DISTRIBUTION OF CASES FROM DISTRICTS OUT OF GLASGOW

Table 5. (Contd.)

Anderston.

Case.	Sex.	Age.	Month of onset.
71	M.	11½ years.	April.
72	M.	12 9/12th yrs.	April.
69	M.	6 years.	April.

Distribution.

Fifty of the cases occurred in the city, and 29 came from outside. Of the 50 who came from the city, Anderston and Partick supplied more than other districts but the fact that they are very near the hospital may explain this. No two cases came from any one of the various outlying districtions in the same year. The accompanying maps seem, however, to show a certain grouping of cases.

Mortality.

Ten deaths have occurred, 4 during the acute stage and 6 at varying intervals afterwards.

From the 39 cases treated in the hospital during the acute stage, 4 or 10.2% died. During the same years the mortality in the cases of the city of Glasgow as given in Dr Chalmer's (10) report was 20%.

Table 6.

Deaths during the acute stage in R.H.S.C.

Case.	Year of illness.	Sex.	Age at onset.	Period at which death occurred.
2	1918	M.	10 years.	11th day.
78	1924	M.	11 "	12th "
77	1924	F.	9 "	14th "
48	1923	M.	11 "	16th "

Eliminating the 8 cases not traced, the history of 67 children who survived the acute attack is complete to this time. Four of these died from the late results of the disease and two from intercurrent disease, viz., Cases 34 and 15 died of pneumonia and pulmonary tuberculosis respectively.

Table 7.

Case.	Yr. of acute illness.	Sex.	Age at acute illness.	Period at which death occurred.
22	1920	M.	10 years.	3rd month.
30	1920	F.	7/12th year.	8th month.
1	1918	F.	10/12th year.	9th month.
34	1920	M.	2/12th year.	14th month.
38	1920	M.	1 1/12th yr.	20th month.
15	1920	M.	7 years.	24th month.

Pathology.

Permission to have a post-mortem examination was obtained in four cases, two of whom died in the acute stage, and two at intervals afterwards.

Acute Stage.

The two cases who died in the acute stage of the illness did so on the 15th and 16th days from the onset.

Macroscopical examination of the brain in both cases showed congestion of the veins. In Case 78 this was specially marked/

marked in the great venous sinuses, in the pia arachnoid and in the small vessels in the basal ganglia and pons. In Case 48, there was congestion of the dura mater and the veins of the cortex. In both there were petechial haemorrhages in the basal ganglia and pons and in Case 48 these were also seen in the internal capsule, the cerebellum and medulla.

The histological examination of the brain in Case 78 showed in the pons well-marked perivascular infiltration with round cells and a few plasmic cells. In this area there was marked congestion of the vessels with degeneration of some nerve cells and an apparent increase of neuroglial cells. The vessels in the basal ganglia were congested and there was some degeneration of nerve cells here also.

In both of these cases an emulsion of the brain was inoculated into rabbits, in case 48. by Dr Strachan, in the other, 78, by Dr Blacklock. The results were negative in both cases.

The two children - Cases 1 and 38 - who died in the later stages, did so after 9 and 21 months. Case 1 was aged 1 month at the onset of illness. Case 38, aged 13 months.

Both, when death occurred, were definitely imbecile, unable to sit up or to show more than the faintest signs of intelligence, Case 1 being both blind and deaf. The examination of Case 1 showed a generalised congestion of the meninges and of the brain substance, most marked on the white matter of the hemispheres. The ventricles were normal in size and the choroid plexus/

plexus on both sides was markedly congested.

In Case 38 there was marked atrophy of the convolutions of the brain and of the brain generally, the consistency being definitely increased. No haemorrhages were found. The grey and white matter were very sharply demarcated.

Unfortunately a histological examination was not made in either of these cases.

GENERAL DESCRIPTION OF DISEASE.

The disease, as seen in our series of children, was definitely divided, in the great majority of cases, into an acute attack and a later stage. The particular point of interest in a series consisting entirely of children is the severity and duration of these later changes, since the acute attack seems to be very similar to that found in adults. I shall endeavour to give a general picture of the disease as it has been seen in the majority of our cases and shall follow this by a more detailed account of the outstanding signs and symptoms.

The limits of the acute stage are taken as from the onset of the illness to the time at which there was apparent recovery and the child was well enough to be sent home. This stage varied in length from about a fortnight to three months.

Owing to the protean character of the disease, which varies in character with each case, it is difficult to present any one picture. Economo's (1) description written after seeing eleven cases, still covers very much of the ground, although/

although, since that date, it has become necessary to lay more stress on choreiform restlessness. In the present series, however, one or more of the various signs - lethargy, respiratory disturbance and fever - were seen in every case which was brought during the acute stage, and were reported in the great majority of these seen later.

A typical story is that of a child, apparently in perfect health, who suddenly becomes violently restless and may complain of double vision. He does not sleep but moves about the room doing household work, getting ready for school or dressing and undressing himself. He is garrulous. Occupational delirium is usually present. The next morning he may appear slightly better but restlessness continues in various degrees of severity and at night insomnia recurs. This condition may continue for some days, when the child gradually becomes lethargic. The restlessness and delirium may last for some nights after he has become lethargic by day. Lethargy, however, then becomes continuous. It is of a peculiar type. In all but the very worst, the child if roused will respond in a most surprising way although the appearance is of deepest sleep. The face becomes expressionless but in the present series there was never a Parkinsonian condition dating from this stage, such as Gullan (11) and others describe.

The mask-like face, which may give a deceptive appearance of double ptosis is usually part of a general weakness. It

is accompanied by extreme emaciation. This is the period at which incontinence of urine and faeces appears, if at all.

Fever is present during the first week or two of illness, not generally rising above 103° except in fatal cases. At the end of this time the temperature falls by lysis and remains normal.

Ocular symptoms, squint, and loss of accommodation with preservation of the reaction to light are very frequently present. Fundal changes, e.g., general hyperaemia and definite optic neuritis are also observed.

Less common than these signs are paralyses of the limbs. These are usually transient and flitting in character.

Disturbances of the reflexes in most cases consist in exaggeration of the knee jerks, but an extensor response may be present either on one or both sides.

Apart from the loss of accommodation and occasionally the extensor response, the signs and symptoms mentioned so far are characteristic of the acute stage only. In this stage there may, however, appear signs which continue for years unchanged. Myoclonus, that is, a regular twitch of a muscle or group of muscles, is extremely characteristic of this disease, as also are disturbances of respiration, such as loud panting breathing coming on in sudden and frequent attacks, or a steady rise in the respiration rate interrupted by such attacks. Either myoclonus or hyperpnoea may appear during the first few days of the illness.

Less usual forms of the acute period are those in which lethargy or choreiform restlessness form the whole acute stage, usually accompanied by one or more of the other signs already mentioned. Occasionally this stage may be represented only by some days' fever and malaise. The acute stage lasts from 10 days to 2 or 3 months, and is followed in the majority of cases by a period of apparent restoration to health. This is, however, temporary and is in some cases extremely short. Disturbances now begin which may last for years. Frequently in this series it happened that the child was dismissed from hospital well, only to develop, a few days later, night restlessness. On the other hand, a month or two might elapse before any further signs appeared. Compared with figures given by others, this time would seem to be very short. McAlpine (12) reports a case in whom there was an acute attack with insomnia, paresis of accommodation and one-sided facial paralysis, in 1918. In 3 months the woman was again working, apparently well. She remained so till August 1922, when there was insomnia and blurring of vision and 2/12th year later onset of the Parkinsonian Syndrome.

Symonds (13) and McNalty (14) found that the latent period may extend to 2 years or over. Nonne (15) in examining 162 cases, saw normal periods lasting for 3 and 4 years and in Wimmer's (16) experience patients have been seen wholly or partially free from nervous symptoms for four years.

Later Stages.

Judging from this series, the period of convalescence and apparent recovery is in children invariably followed by further signs and symptoms of the disease.

In 87% of the cases the first sign that the child's health was not normal, was the onset of nocturnal excitement with inversion of the sleep rhythm. This nocturnal restlessness, as seen in the early cases of the series, was described in detail by Dr Anderson (5). Her description has remained correct in the succeeding cases. No other disease seems to produce in children the extraordinary excitement during the normal sleeping hours with heavy sleep during the early morning and greater part of the day. The child may merely be awake chattering to himself or may be extremely noisy, destructive, and even violent. Other sequelae such as hyperpnoea, sniffing and restlessness become more marked during the wakeful hours and the child is frequently brighter and more intelligent as night approaches.

Night wakefulness may persist for long periods but eventually disappears gradually, for no apparent cause, and the child once more resumes the normal routine of sleep. In three of our cases there has been an apparent recovery from the disease at this stage, which has now lasted for periods of more than 18 months. In the great majority of cases, however, this inversion of the sleep rhythm is either accompanied or followed very shortly by other sequelae. These do not occur in any known combination, or according to any apparent sequence, though some are more frequent/

frequent than others. Thus the order of frequency in this series has been

Mental Change.
Nocturnal restlessness.
Changes in conduct.
Respiratory changes.
Parkinsonian syndrome.
Loss of accommodation.
Choreiform restlessness.
Myoclonus.
Obesity.

The appearance and condition of the child naturally varies according to the sequela which is most prominent, but any one or still more, any combination of these sequelae, produces a typical picture which, along with the history, often makes diagnosis very much more simple than at any previous period.

The various sequelae, once established, tend to be persistent over years but on the whole tend towards disappearance. As, however, they are seldom present singly, improvement in one does not, in the great majority of cases, mean definite improvement in the child's condition. Also from the eight years under observation it is not yet possible to recognise a point at which another one of the sequelae may not appear. The exceptions to the general trend of improvement are mental deterioration and the Parkinsonian Syndrome. With only one or two exceptions, these are in this series progressive and either may eventually dominate the picture.

The outlook for a child suffering from this disease is therefore very grave.

SIGNS AND SYMPTOMS IN DETAIL.

Onset.

The onset was very frequently absolutely sudden. This was referred to by Findlay and Shiskine (4) in 1920. In cases since then, the fact has been equally striking. Out of our series of 79 cases, 69 gave a clear history, naming the day and even in many cases the hour of onset. This was so remarkable as to be of the greatest use in differentiating the disease from others such as rheumatic chorea, cerebral tumour, etc. The following are typical histories of the onset:-

Case 15.

"Patient was quite well and perfectly normal in his behaviour. Suddenly one night he wakened up as if he had had nightmare. He got out of bed and wandered about the room pulling out drawers, knocking over the chairs and chattering excitedly to himself."

Case 77.

"The child was perfectly well till six days ago when she suddenly became exceedingly restless. She could not sit or stand still for a moment. That night she did not sleep at all, talked continually, wanted to get up to light the fire."

In most cases the history of the suddenness of the onset was volunteered by the parents.

In Hall's cases (17) also, the day and even the hour of onset was usually stated but Bramwell (18) found the onset "insidious/

"insidious, may be a few days or even a week or two before the symptoms become prominent." In this prodromal period he includes abnormal drowsiness, diplopia, defective vision due to loss of accommodation, etc., but in the present series these were so pronounced that they could by no means be referred to as prodromal.

In 10 cases no clear history of onset was obtained. Two children were about one year old and apparently the parents had not noticed the beginning of the illness carefully. In another the child was away from home at the onset, another had had measles before and the drowsiness was put down to lack of strength, and so on. In no case is there any definite history of a prodromal period. In every case in which a clear history was obtained, the suddenness of onset was a marked feature.

The following table shows the initial symptoms in their order of frequency.

Table 8.

Symptoms.	1918	1919	1920	1921	1922	1923	1924	1925	Total.
Insomnia	-	2	9	1	-	12	15	-	39, 50%.
Choreiform restlessness.	-	1	7	-	-	4	11	-	23, 29%.
Lethargy	3	1	9	1	1	3	3	-	21, 26%.
Diplopia	1	-	4	-	-	1	10	-	16, 20.5%.
Headache	1	-	1	-	-	5	5	-	12, 15.3%.
Pain	-	-	3	-	-	4	4	-	11, 14.1%.
Delirium	-	-	4	-	-	-	7	-	11, 14.1%.
Fever	-	-	9	-	-	1	-	-	10, 12.8%.
Vomiting	1	-	2	-	-	1	3	-	7, 9%.
Twitchings	-	-	2	-	-	3	1	-	6, 7.6%.
Squint	1	-	-	-	-	-	3	1	5, 6.4%
Nocturnal excitement.	-	-	-	-	-	4	-	-	4, 5.2%.
Malaise	1	-	2	-	-	-	-	-	3
Convulsions	1	-	1	-	-	-	-	-	2
Loss of speech	-	-	-	-	-	1	-	-	1
Rhinitis	-	-	-	-	-	1	-	-	1
Vertigo	-	-	1	-	-	-	-	-	1

Insomnia, the most frequent sign of onset in this table, is always of a very complete kind. The child may not sleep at all for several nights and days so that parents frequently say that they "do not know how the child is alive." The behaviour during the night may be extremely violent or there may only be a continual chattering and restlessness. This insomnia is of quite a different character to that appearing as a sequel where the child sleeps heavily from about 4 or 5 a.m. till mid-day or later. Diplopia was certainly present in 13 cases as a primary symptom. These cases being often young children, who cannot state their sensations, it is very probable that it was missed in other cases.

Table 9.

Duration of diplopia where it occurred on first day of illness.

Number of cases.	Duration.
7	1 day or less
3	2 days " "
2	4 " " "
1	14 " " "

It is interesting to note that in all cases where diplopia occurred it was followed by a period characterised by irritative symptoms.

Squint/

Squint was an early sign in 5 cases but like diplopia it was transient, lasting only for a few days.

Pain at onset was common. Headache was frequently complained of but there was little unanimity in its location. In eleven cases pain in the limbs or the trunk was severe enough to make the children cry out. It was apparently of a lancinating character and usually situated in the limbs, though often it was of a wandering variety. In some cases it accompanied twitching of the affected muscles. Thus in four cases there was abdominal pain with twitchings of the muscles. These will be dealt with later as in one or two cases the diagnosis from an acute abdominal condition came into consideration. In each of the 11 cases other excito-motor signs were present, either localised or generalised.

The 3 cases in whom nocturnal excitement was said to be the first symptom gave no history of any febrile attack. In these it was definitely the nocturnal excitement with sleep by day which is characteristic of the later stages. Wimmer (19) frequently found these later phenomena appearing in his cases with apparently no acute attack previously, but considering the frequent carelessness of the class which composes this series, it seems likely that these three children suffered from slight febrile attacks which passed unnoticed or at least un-remembered.

Fever.

Fever was usually present in the early weeks of the acute stage. Of the 37 cases who were brought to hospital early in the illness, the temperature was raised in 30. The remaining 7 were admitted about 9 days to 2 weeks after the onset and were afebrile. Whether these had already passed through a febrile period or not one cannot be certain but judging from the others, it would seem not improbable.

Table 10.

Maximum temperature reached in acute cases.

Temperature.	Cases.
99-100° Fah.	2
100-101° "	3
101-102° "	4
102-103° "	10
103-104° "	7
104-105° "	2
105-106° "	1
108° "	1

Thus, in 19 cases out of 30, fever did not exceed 103°. The Ministry of Health (20) report that in 410 out of 600 cases, the temperature did not rise above 103°.

The temperature before death in the four fatal cases during the/

the acute stage, was respectively 101°, 102.6°, 104° and 108°. All of these were feverish during the entire illness, with a rise of temperature in the last few days.

The Ministry of Health Report (21) mentions three cases where the temperature at death reached 107°, 107.6° and 110° respectively.

Only one case in this series reached 105° without a fatal result. This child had a series of convulsions on the 9th day of illness during which the fever reached this height.

Table 11.

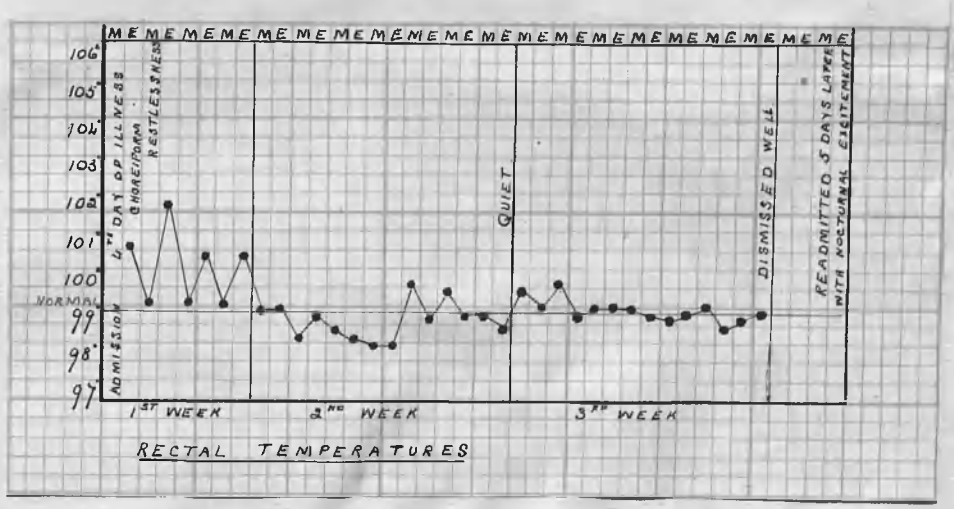
Duration of fever in those who survived.

Duration.	Cases.
1 week or less.	8
2 weeks or less	11
3 weeks or less	5
6 weeks or less	2

It would therefore seem exceptional for fever to last more than three weeks, although the other signs and symptoms of the acute illness, in the majority of cases, remain much longer. Thus, in Case 72, fever was present for two weeks, profound lethargy for seven weeks. In Case 33 fever and chorea lasted for one week, but were followed by lethargy which persisted for five weeks with a normal temperature.

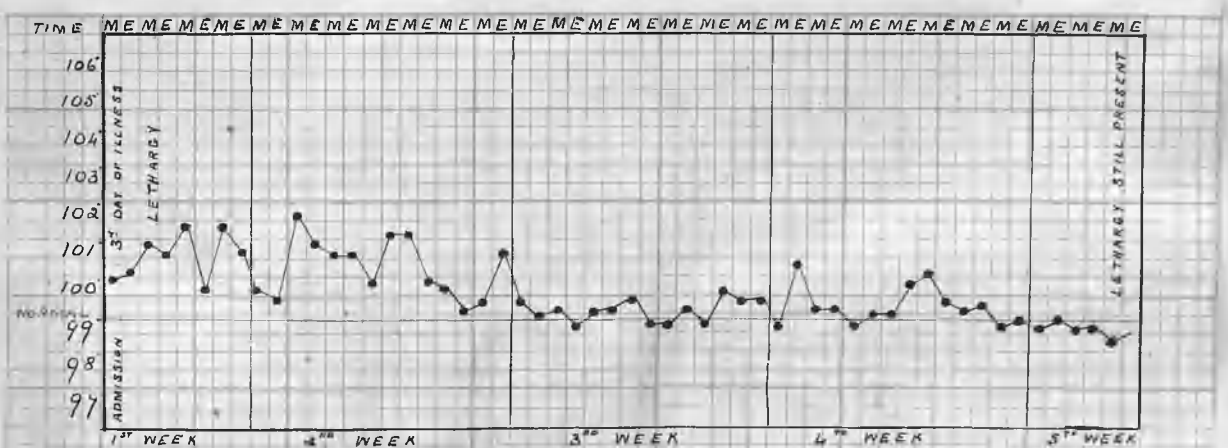
Course of fever in cases which survived.

CASE 73



RECTAL TEMPERATURES

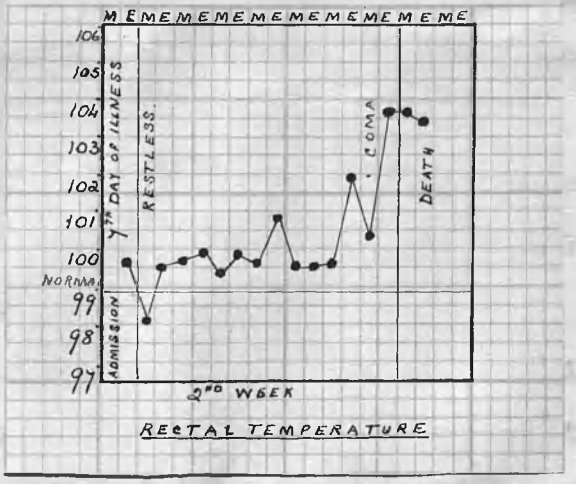
CASE 70



RECTAL TEMPERATURES MORNING AND EVENING

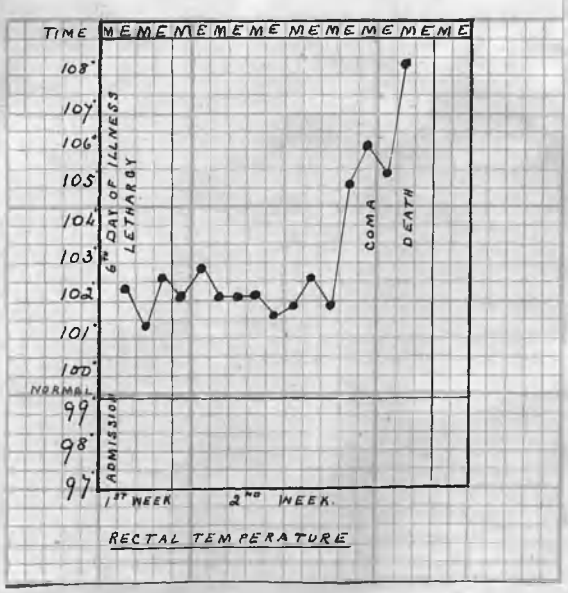
Course of fever in fatal cases.

CASE 48



RECTAL TEMPERATURE

CASE 77



RECTAL TEMPERATURE

Lethargy.

Lethargy was present in 47 of the 79 cases during the acute stage. In 21, it was the first symptom of the malady. In many of these the relatives attempted to counteract the child's proclivity to sleep, by dragging him about from place to place but always to no avail.

In 19 of the cases, the lethargy followed upon a period of choreiform restlessness and insomnia, which varied in length from 2 to 10 days. This type appeared first in 1920 and was even more frequent in 1924. This variation of type in different epidemics is very characteristic and is worthy of note.

The duration of lethargy was widely variable but, in far the greater number of cases, was from 10 to 23 days. The most outstanding exceptions were, on the one hand, two cases in whom lethargy lasted for 12 and 24 hours respectively and, on the other, 4 in whom it persisted for 9, 10, 14 and 16 weeks. These variations did not appear to influence the later course.

Character of lethargy.

Lethargy varied in depth in different cases and at different times in the same case. In some, the child merely slept when left alone. In most he lay showing no spontaneous action, the face entirely devoid of all expression. To all appearances the child was unconscious at this stage, but, if roused, the intelligent response to questions was most surprising even while the face remained impassive. There was often an appearance of paresis/

paresis, especially of the facial muscles which was, however, generally part of a severe general weakness. On occasions a real, though transient, paralysis was detected in this series.

In a few cases, lethargy deepened into unconsciousness accompanied by incontinence. Where this took place without a rise of temperature, recovery followed, but in each case where the temperature rose at the same time, the result was fatal.

Recurrence of lethargy.

In a few cases, there have been intervals, usually towards the latter part of the period of lethargy, during which the child would sit up, play with toys, feed himself and take an interest in the other children. This would be followed by another period of lethargy. In Case 49, for example, there was a distinct improvement for a day or two at the end of 10 weeks. This was followed by six weeks' drowsiness, not so deep as before, but still definite.

Later Stages.

There has been no recurrence of this type of lethargy, beginning with fever, during the later stages. The drowsiness by day with wakefulness at night which occurred in the majority is of quite a different nature. In two cases, however, there have been long periods of lethargy accompanied by obesity. In Case 23, both obesity and lethargy disappeared after about 18 months. In Case 45, they are persisting beyond that period.

Motor Disturbances.

Disturbances of the motor system which occurred in the series were as follows:-

1. Convulsions.
2. General choreiform restlessness.
3. Myoclonus.
4. Parkinsonian Syndrome.

Of these, convulsions have only occurred in the acute stage. Choreiform restlessness has appeared both in the acute and later stages, though in different forms. Myoclonus has been present in some cases both in the acute and later stages, in others it has been purely late. The Parkinsonian syndrome has always occurred in the later stages.

Convulsions.

In two cases the onset was marked by convulsions. In only one case have there occurred convulsions when the disease was fully developed. This child, Case 69, was admitted to the Royal Hospital for Sick Children on 22nd April, 1924. On 20th April there had been sudden onset of pain in the fingers sufficient to make him cry out, with twitching of the arms and thorax. Insomnia and delirium were present that night and during the next forty-eight hours. On admission, myoclonic jerkings of the extraordinary muscles of respiration were very marked with rapid respiration. On the 24th respiration rose to 80 per minute and on the 26th the child became very restless, later quite unconscious/

unconscious and the temperature rose to 103.4°. For about 2 hours he had a continuous series of generalised convulsions, with temperature at 105°. For the next 2 days the child was restless but no further convulsions occurred and no paralysis appeared. Temperature was high for three days and did not return to normal till 4 days later. The child made a good recovery except for the persistence of myoclonus and hyperpnoea. He is now very backward mentally, the mental ratio being 73.

Choreiform Restlessness.

In the acute stage, general choreiform restlessness was a very marked feature in 39 cases and was divided over the years as follows:-

Table 12.

General Choreiform Restlessness.

	1918	1919	1920	1921	1922	1923	1924	1925
Total Cases.	6	4	28	2	1	17	20	1
Choreiform restlessness.	-	1	14	1	-	7	15	1

The appearance of choreiform restlessness as a prominent symptom in 1920 was noted by Findlay and Shiskine (4), and was found elsewhere at the same time. In 1923 it was again seen but in 1924 it was one of the most characteristic features of that epidemic. The child suffering from this symptom is in a constant state of movement/

movement, varying from slight but constant restlessness, to an almost maniacal condition. The movements resemble those of chorea although they appear more purposeful than those occurring in that disease. They cease neither by night nor day. Indeed, the tendency is towards an increase in the violence of the movements during the night. The condition is usually accompanied by insomnia and frequently by delirium or some degree of mental confusion, though usually the child will answer fairly intelligently and respond to requests even when much excited. The movements may, however, be controlled voluntarily, but only for a moment. The violence of the movements is, at times, so extreme that the child may bruise his limbs severely and he can only be kept in bed with the greatest difficulty. Hypnotics, in ordinary doses, we have found quite useless.

Onset and Duration.

In all but three cases when it occurred on the seventh day, this restlessness appeared at the onset of the disease. It lasted in most cases from four to fourteen days and in 50% was followed by lethargy.

In three atypical cases, the chorea continued for one to two months and in two others, where it was of a very violent description, it persisted for eighteen months and two years respectively, being accompanied by very wild behaviour. In the first of these, Case 29, the child now suffers from the Parkinsonian syndrome but is still restless. In the other, Case 10, the child is now quieter but still requires to be kept in an institution.

Cases/

Cases showing choreiform restlessness were frequently admitted to hospital as examples of rheumatic chorea and at times it was very difficult to differentiate between the two until some days had elapsed. Wimmer (22) considers that there is no semiological distinction between the choreiform restlessness of epidemic encephalitis and that of Sydenham's chorea. Some signs were, however, helpful in our cases. The suddenness of onset of epidemic encephalitis is quite unlike the gradually increasing twitching of rheumatic chorea. The fact that the violence often increases at night and is accompanied by insomnia and that even in sleep the movements usually continue, is specially significant, and the presence of fever in the absence of any possible rheumatic complication, or of ocular symptoms, is of importance.

Later stages.

The choreiform movements of the later stages of the disease are not of the violent character of those of the early days. These movements resemble those of a mild attack of chorea. The child may twitch some muscles of his face, shrug his shoulders, run round the room, touch everything within reach in the course of a minute or two, but there is none of the wild excitement of the early stage.

In Case 21, the choreiform movements began faintly in the right arm and hand a year after the acute illness and while remaining most marked there, general restlessness has increased rapidly. Now, after five years, the boy is apparently quite unable/

unable to keep still, although always anxious to do so.

In some cases these children acquire habits such as stopping every few steps to rub one foot on the ground. One boy (Case 13) walks about 10 steps, then turns a complete circle balancing on the right toe. He gives no reason for this but prefers to hold some one's arm in walking to prevent it.

This late choreiform restlessness is very persistent. Two children (Cases 10 and 29) show improvement after 7 and 6 years. The condition of the others is unchanged.

Myoclonus.

Myoclonus has occurred in only 6 of the 71 cases in this series whose complete history is known, but has been, nevertheless, one of the most striking signs when present.

It was not till 1923 that a case showing these muscular contractions was seen in the Royal Hospital for Sick Children, although in 1920 Walshe (23) reported cases in which rhythmical clonic contractions were present. In that year also, Sicard (24) defined them as "secousses musculaires, breves, rapides, explosives, a type rhythme electrique, qui siegent sur la musculature des membres, de la face et du diaphragme, frappant un muscle ou un groupe des muscles."

This description covers very accurately the contractions which have been and are present in six cases of this series.

The following table gives the details of these cases.

Table 13.

Myoclonic Cases.

Case.	Year of acute illness.	Onset of Myo-clonus.	Site.	Rate per minute.	Pain.	Hyperpnoea.	Present state of myoclonus.	General condition.
52	1923	2nd week.	Respiratory muscles.	44	Abdominal. General at onset.	Coincid-ing in rate.	Lessening.	Parkinsonism improving.
69	1924	1st week.	Extraordin. muscles of respiration and arms.	48	At onset in arms.	Coincid-ing in rate.	Lessening.	Hyperpnoea. Mentality very poor.
79	1925	1st week.	Respiratory muscles and diaphragm.	60	None.	Coincid-ing in rate.	Lessening. Still strongly present in sleep.	Nocturnal excitement. Conduct very bad.
70	1924	4th week.	Right side of mouth & platysma.	60) 80)	None.	-	Unchanged.	Parkinson-ism.
49	1923	2 years after.	Left side of nose.	50	None.	Present. Not coin-ciding.	Gone.	Conduct bad. Mentality very poor.
71	1924	19 months.	Right side of mouth.	44	None.	-	Marked. In series of 3 or 4 then slight pause.	Mentality poor.

Time of appearance.

In 4 of the 6 cases, myoclonus appeared as an early sign. In 2 of these it was one of the first signs of the disease.

Case 70 was very interesting as regards the onset of the myoclonus. This boy was admitted on the second day of illness. A right sided facial paresis was then noted. This paresis was steadily present until the fourth week of illness when a regular myoclonic twitch affecting the same area was observed. In none of the other cases was there any previous paresis nor does such a sequence appear to have been seen by other observers.

In all four it has persisted and has been as marked in the later as in the earlier stages. The remaining two cases (49 and 71) showed no indication of any myoclonic movements till the later stages.

Site.

The sites have shown a striking similarity, three being in the facial muscles and three including the diaphragm and extraordinary muscles of respiration. The facial twitch in each case is unilateral, in two, one side of the mouth being affected and in one the muscles at one side of the nose. In the three cases where the jerk affected the respiratory muscles, it was and is strong enough to move the arms. It is remarkable that the myoclonic twitch has remained confined to the original muscles affected. This was also noted by Wimmer (25).

Rate.

The rate is individual to each case and has always remained fairly constant.

Thus, in Case 70, the contractions of the right side of the mouth have been at the rate of 60 to 80 per minute for the last two years and have been constant. Renault and Benicty (26) report a case exceedingly like this one in both site and rate. In Case 49 the contractions were occasionally absent but when present were about 50 per minute. In this case the twitch has now disappeared. In Case 71, though constantly present, the contractions are in series of 3 or 4 and at about 40 per minute. Cases 49 and 71 were of late onset.

Where the contractions involve the respiratory muscles, they have from the beginning been synchronous with a continuous hyperpnoea, ranging from 40 per minute in one case to 60 in another. Buzzard (27) reports a case in which myoclonus coincided with the pulse rate but this has not been found in the present series.

The contractions are in all six cases as strongly present during sleep as in the waking hours. In Case 79, indeed, the contraction is now much less by day but is still very definite during sleep. Walshe (28) reports a case in which an additional contraction is present during sleep.

The twitch is not influenced by will in any of the six children. They, indeed, appear now to be unconscious of its presence/

presence although in two it was originally accompanied by pain.

This association with pain is extremely interesting. Sicard and Kudelsky (28) and Marie and Levy (29) mention cases in whom lancinating pain and fever at onset were succeeded by the appearance of short rapid explosive muscular contractions. In Case 69 of this series the child complained first of pain in the hands which made him cry out. This was followed in a few hours by contractions of the thorax and arms. On admission to hospital next day fever was present with myoclonic contractions of the thorax and arms which still persist after 2 years.

Where the contractions affect the abdominal muscles, the presence of pain at onset may confuse diagnosis. Hinds Howell (30) reports one case of this kind which was at first diagnosed as appendicitis and Stevenson (31) reports 3 sent to the Glasgow Royal Infirmary as acute abdominal cases.

In the present series there has been one very striking example of this possibility. This child (Case 52) complained suddenly, on 23.2.23 of severe pain in the wrist, arm and back and next day in the abdomen. She was treated for a week as a case of acute rheumatism. Fever then rose and pain in the abdomen became more severe. She was, therefore, sent to a surgical ward in the Royal Hospital for Sick Children as a case of appendicitis. Two days later she was transferred to a medical ward. There were twitching movements of the whole body with much complaint of pain, but a few days later the abdominal contractions were noted to be myoclonic in character. Hyperpnoea appeared about 10 days later. The condition improved gradually but eight months later she/

she was again admitted as suffering from abdominal pain and diagnosed as "appendicitis," and again transferred to a medical ward. Myoclonic contractions now coincided with respiration. Fever was again present and there was much complaint of pain. The condition again improved but in April 1924 she was for the third time sent to hospital supposed to be suffering from appendicitis.

This child has been observed very frequently since 1923. The condition has improved very much, the myoclonus being now much less severe.

In no case does myoclonus appear as the only sign in the later stages. Other sequelae have invariably accompanied it in this series.

Prognosis as regards Myoclonus.

Myoclonus is in this series one of the long standing sequelae. In four cases it appeared in the acute stage and is still present after 1, 2, and 3 years. In three of the cases it is now definitely less marked, in the fourth it is unchanged after 2 years. As regards the two cases where it appeared as a late manifestation, it is still present in Case 71 but has disappeared in Case 49 after remaining for only a few months. The tendency does therefore appear to be towards improvement.

Parkinsonian Syndrome.

Of the 68 cases seen in the later stages of the illness, 21, or 30.8%, have shown some degree of this syndrome. As 5 of these were brought to hospital on account of the syndrome itself it is perhaps more accurate to give also the incidence among those cases who have been seen from the earliest stages.*

Fifty-four cases were seen in the first 4 months of illness. Of these 14 cases are now Parkinsonian, i.e., 25.9%.

Kennedy (9) found that 21 out of 59 children seen by him on account of the sequelae of the disease had developed the Parkinsonian syndrome. Riddoch (32), from the London Hospital, found over one quarter developed these signs. Ebaugh (33), on the other hand, in a series of 17 children saw only one case of the Parkinsonian Syndrome.

Sex. 16 of the 21 children showing this syndrome are boys. The incidence of the disease itself in boys, in this series, is 70.5%.

Age. The ages at the time of acute illness are seen in the following table:-

Table 14.

3 yrs.	4-6 yrs.	6-8 yrs.	8-10 yrs.	10-12 yrs.	12-14 yrs.	Over 14 yrs.
1	3	5	5	3	3	1

* i.e., 14 of the children were under 10 years.

7 " " " " over 10 years.

The age of the child does not therefore seem to affect the incidence of the syndrome in this series since 66.6% were under 10 years when acutely ill.

Table 15.

Incidence in relation to the year of the acute illness.

Year of acute illness.	Total Cases.	Number of Parkinsonian Cases.
1918	6	1
1919	4	-
1920	28	8
1921	2	not traced.
1922	1	1
1923	17	2
1924	20	9
1925	1	-

Onset of Parkinsonian Syndrome.

Cases have been recorded by Hinds Howell, (30) Buzzard (34) and others in which the syndrome appeared first during the acute illness. This was never so in the present series. The period between recovery from the acute illness and the onset of Parkinsonism was, however, in two cases (Nos. 68 & 72) very short. In neither of these children was the normal animation fully recovered before the characteristic immobility became apparent. In Case 73, also, the first signs were early, appearing three

weeks/

weeks after recovery from the acute illness. The child had been re-admitted to hospital on account of nocturnal restlessness. Shortly afterwards the mask-like face and general immobility were noted.

In six cases the period was between 2 and 3 years, the longest occurring in Case 33, where the Parkinsonian syndrome developed at least after 3 years. This child, after a typical attack, was dismissed from hospital well. Three nights later nocturnal restlessness appeared, with hyperpnoea some months later. Three years after the onset, apart from hyperpnoea and mental deterioration, examination was absolutely negative. He was not seen again for two years. Examination at the end of that period then showed marked Parkinsonian syndrome with mask-like face, general immobility more marked on the right side, festination and retropulsion, profuse salivation and typical speech. Hyperpnoea had persisted.

In all, the interval was invariably bridged by other sequelae. It is evidently possible, nevertheless, that there may be long periods altogether free of symptoms since in McAlpine's (12) case, already quoted, there was a normal period of 3 years and 9 months between the acute illness and the first signs, and Nonne (15) has found normal intervals of 3 and 4 years.

PARKINSONIAN SYNDROME.

Case 70. Right sided facial myoclonus is also present.

Case 74. The syndrome is progressing rapidly in this case.

Symptoms and Signs of the Parkinsonian Syndrome.

The earliest signs have in the majority of cases been a localised immobility either of the face alone, or of one or two limbs, usually on the same side. A disappearance of facial expression apparently did not strike the relatives frequently, therefore this may have been missed in some cases. In those cases closely under observation from the beginning, facial immobility was frequently the first sign, and has been present to some extent in all our 21 cases. The immobility of the facial muscles and lack of expression are very striking when fully developed and closely resemble the facial appearance of paralysis agitans. In several of the most advanced cases, however, the expression is even more like that seen in progressive lenticular degeneration. The lower jaw is dropped and slow, wide smiles or expressions of deep depression cross the face frequently, with little or no obvious cause. McAlpine (35) considers that this type occurs seldom and always in patients under 20 years of age. In this series it is more frequent.

The Attitude has a fixed and wooden appearance. In most cases there is a slight bend of the trunk forwards with flexion of the elbows. In one, Case 72, the angle is rather backwards. This child began to hold his back extremely erect and to walk stiffly a few weeks after the apparent recovery. This rigidity increased fairly rapidly until the whole body was held in a very wooden manner, the arms slightly flexed and the back sloping slightly backwards. His gat and manner of sitting down became extraordinarily rigid.

Two/

Two children keep the head constantly bent to one side with the trunk slightly sloping in the same direction. In both the head can be held in the normal position at will for a moment or two but then returns to the first position. In these the rigidity only affects the upper part of the body.

The position varies to some extent with each patient but the general appearance is very typical.

The gait is little affected in some cases, as in those where the rigidity mainly affects the upper part of the body. Where the legs are affected, the steps are short and the feet hardly lifted from the ground. Well developed festination and retropulsion were present in only 5 cases, but in all these were quite definite. As the syndrome becomes more marked talipes equinovarus develops, being occasionally one sided, but most often bilateral. It is very markedly present in all 5 of our worst examples, being bilateral in 4, unilateral in 1.

Slowness of movement. Deliberation is present in all to some degree. The most remarkable are 3 of the older boys. One of these (Case 72), if left to feed himself, would take hours. The hand holding the spoon moves with extraordinary slowness towards his mouth, which is open long before the spoon is near. Frequently there are long pauses in the act. Another patient takes about half an hour to put on his boots. On the other hand, in those where the rigidity is localised, deliberation is not one of the striking signs; e.g., one child (Case 41) exhibits/

exhibits choreiform restlessness and rapidity of movement along with an unmistakably mask-like face and drooping head.

Combined with immobility, there is present in three of the series the phenomenon named by Souques (36) 'kinesia paradoxa.' Souques in describing this refers to patients of his own who are unable to walk or perform the simplest everyday movements but who may, momentarily, by certain external or internal impulses be induced to run or jump. Wimmer (37) regards its presence as an important diagnostic point, and Cruchet (38) mentions several patients who, with an extremely immobile appearance, may show great activity.

The first child (Case 36) in whom it was noted in our series, is a boy who was acutely ill in 1920. Since then he has suffered from nocturnal excitement, hyperpnoea and change of behaviour. He is now a very definite example of the Parkinsonian syndrome with mask-like face and slurring, high speech. The attitude is very characteristic, with flexion of trunk and arms. Salivation is profuse. The general immobility is very striking and the movements are extremely deliberate. This boy during the last examination in his home appeared incapable of any but the slowest action. On a sudden noise, however, he ran quickly to the door. The action was extremely surprising and in absolute contrast to his appearance. This had been noticed by his parents on other occasions.

In another (Case 12) the child is confined to bed constantly on account of her rigidity and deliberation. The attitude in bed/

bed is typical; there is slight flexion of trunk, arms and legs, with a bilateral extensor response and talipes equinovarus. She is apparently incapable of looking after herself. If lifted out of bed and placed on her feet there is festination and retropulsion. On occasions, this child is said to get out of bed herself and go rapidly across the room. This has not been seen on any occasion by the writer, but was reported by the mother, who is a fairly accurate observer.

Tremor has been present in 7 of the 21 cases. In Cruchet's series it occurred in less than 10%. In no case in this series does it at all resemble the pill rolling form of the true paralysis agitans. The most frequent form, found in 4, is unilateral, affecting at first only one limb. This tremor is produced apparently on excitement and is very much increased on the effort to bring the limb into action, becoming irregular in rate and of wide amplitude. As it increases it spreads to the other limbs. All the children who show this are very marked examples of the Parkinsonian syndrome, 2 being now permanently in bed and unable to do anything for themselves. One is a severe case who, though still able to go about, is becoming rapidly worse, and one shows the syndrome very definitely in head, arms and trunk. The condition of this last has been stationary for more than a year except for the appearance of tremor a few months ago. This type is described by both Wimmer and Hinds Howell as the most frequently seen in their series.

The/

The second variety was a coarse bilateral tremor which appeared in one case (Case 73), a boy who developed the Parkinsonian syndrome very early. It also increased, to some extent, on intention. This child during the 6 months when he was most closely under my observation in hospital was suffering from inversion of the sleep rhythm with marked nocturnal excitement. The tremor came on as evening approached and during the night became much exaggerated along with all the other signs. Thus when trying to take hold of any object his hands and arms showed a very coarse tremor, increasing as they neared the object but almost ceasing when he had succeeded. This is the only one of our series who now shows a very marked regression of the Parkinsonian syndrome. The third form seen in this series is that of fine tremor affecting all the limbs and constantly present. This is present in the case of two children who are severe examples of the syndrome but are as yet able to go about. Marie and Levy (29) refer to both this and the first form.

Voice.

In the most pronounced cases the voice has become high in pitch and monotonous in tone. Emotion is frequently expressed by a long sustained note of this kind which is very reminiscent of that uttered by a child suffering from progressive lenticular degeneration.

Articulation becomes very slurring and indistinct. This may, of course, be due to the facial immobility although it certainly/

certainly varies from time to time, apparently usually becoming more pronounced during the evening and through the night. This increase of the Parkinsonian signs in the evening, or after fatigue, is frequently present. Sainton and Schulmann (39) lay much emphasis on the Parkinsonism of fatigue which they found more frequently than is the case in this series.

Excessive salivation was present to an excessive degree in all but two of the Parkinsonian cases. The front of the child's clothes is soaked several times a day, and in the worst cases the child is seldom to be seen without saliva flowing from his mouth. The lower jaw is usually to be seen hanging open, with saliva pouring down. Although it forms a most striking part of the Parkinsonian Syndrome it exists also in about 6 cases who have shown no other signs of the Parkinsonian syndrome. In these, it is not quite so marked and is usually associated with the act of spitting. One child has now for years been known to the neighbours as "Spitting Jean." Marie and Levy (29) refer to an "abnormally abundant flow of saliva apart from the Parkinsonian syndrome"and Symonds speaks of "true sialorrhea apart from the drooling in cases of the Parkinsonian type" and refers to two cases in his own experience, both children, who developed in consequence the constant habit of spitting. These persisted for months. The child known as "Spitting Jean" in this series who was referred to by Dr Anderson (5) is still, after 5 years, addicted to it.

The following table gives details of the 21 cases.

Table 16.
Parkinsonian Cases.

Case	Attitude	Face	Gait	Speech	Salivation	Tremor	Previous Sequelae.	Seq. at present.	General Condition
23	typical	mask-like.	Festination & retropulsion. Double equino-varus.	High Slurring.	excessive	coarse	Nocturnal restless-ness. Obesity.	None.	Very weak.
12	typical	mask-like.	Double equino-varus.	High Slurring.	excessive	coarse	Nocturnal restless. Conduct.	Double	Very weak.
28	typical	mask-like.	Festination & retropulsion.	High Slurring.	excessive	coarse	Noct.rest-lessness. Hyperpnoea Conduct.	None	Very weak.
68	typical	mask-like.	Slow Unilat. equinovarus.	High Slurring.	excessive	coarse	None.	None.	Very weak.
72	typical	mask-like.	Very rigid.	Slow.	excessive.	None.	Chorea conduct.	None.	Very weak.
18	typical	mask-like.	Rigid. Unila-teral equino-varus.	Slow.	excessive.	None	Noct.rest-lessness. Chorea.	None.	Can walk fairly well.
17	typical	mask-like.	Festination & retropulsion.	High Slurring.	excessive.	Coarse	Nocturnal restless-ness.	None	Can walk fairly well.
62	typical	mask-like.	Festination.	Slow.	normal.	None.	Noct.rest-lessness & sniffing.	None.	Can walk fairly well.
33	typical	mask-like.	Festination & retropulsion.	Slurring.	normal.	None	Noct.rest-lessness. Hyperpnoea	Hyperp-noea.	Can walk fairly well.

Table 16 (Contd). Parkinsonian Cases.

Case	Attitude	Face	Gait	Speech	Salivation	Tremor	Previous Sequelae.	Seq. at present.	General Condition
76	Typical	Mask-like.	Immobile. Drags one foot.	Slurring	Normal.	None.	Nocturnal restlessness.	None.	Can walk fairly well.
36	Typical	Mask-like.	Immobile. Drags one foot.	High Slurring	Normal	Fine.	Noct.restlessness. Hyperpnoea	None.	Can walk fairly well.
75	Typical	Mask-like.	Immobile. Drags one foot.	Good.	Normal.	None.	Noct.restlessness.	None.	Can walk fairly well.
41	Typical	Mask-like.	Unaffected.	Slurring	Excessive	None	Choreiform restlessness. Hyperpnoea.	Choreiform restlessness. Hyperpnoea	Can walk well.
74	Typical	Mask-like.	Rigid.	Good-high varies greatly.	Normal	Fine	Nocturnal restlessness.	None.	Deteriorating.
70	Head to one side	Mask-like.	Rigid.	Slurring.	Excessive	Coarse.	Noct.restlessness. Myoclonus Conduct.	Myoclonus. Conduct.	Deteriorating.
65	Immobile	Mask-like.	Unaffected.	Unaffected.	Excessive.	None.	Noct.restlessness.	Noct.restlessness. Cruel Conduct.	Deteriorating.

Table 16 (Contd). Parkinsonian Cases.

Case	Attitude	Face	Gait	Speech	Salivation	Tremor	Previous Sequelae.	Seq. at present.	General Condition.
52	Typical	Mask-like.	Little affected.	Slurring. quick.	Normal.	None.	Myoclonus Hyperpnoea Conduct.	Hyperpnoea. Myoclonus.	Improving.
11	Typical	Mask-like.	Immobile.	Indistinct.	Excessive.	None.	Bad Conduct.	Cruel. Violent.	Deteriorating.
73	Typical	Mask-like.	Almost unaffected.	Very indistinct slurring.	Very excessive.	Coarse at night.	Noct.restlessness Conduct.	Bad Conduct.	Very much better.
51	Slightly immobile.	Mask-like.	Almost unaffected.	Very indistinct slurring.	Excessive.	None.	Noct-restlessness.	Bad Conduct.	Improving.
4	Slightly immobile.	Mask-like.	Almost unaffected.	Very indistinct slurring.	Excessive.	None.	Mentally Deficient.	Poor Mentality.	Improving.

Table 17.

Shows the frequency of other sequelae with the Parkinsonian Syndrome.

9	cases	are	completely	dominated	by the Parkinsonian picture.
1	case -	Parkinsonism	is	accompanied	by myoclonus and dirty habits.
1	"	"	"	"	" myoclonus neuritic pain and hyperpnoea.
2	"	"	"	"	" nocturnal excitement.
2	"	"	"	"	" nocturnal excitement and bad conduct.
2	"	"	"	"	" bad conduct.
1	"	"	"	"	" hyperpnoea.
1	"	"	"	"	" extensor reflex.
1	"	"	"	"	" mental defect.
1	"	"	"	"	" choreiform restlessness.

It is probable that Parkinsonism will eventually dominate the picture in many of these mixed cases. The greater number of those showing the most severe results have already passed through periods of bad behaviour, cruelty, filthy habits, etc., which were engulfed in the tide of immobility.

Likeness to Progressive Lenticular Degeneration. The close resemblance between the picture of progressive lenticular degeneration and that of some of these cases is very striking. In Cases 12, 17, 23, and 28 the general picture reminds one even more strongly of this disease than/

than of paralysis agitans. The vacant rather than mask-like facial expression, the open mouth, the facile smiles and depression which cross the face, the attitude in bed, the talipes equino-varus and the high monotonous voice with the peculiar cry are all extremely similar to what is met with in Wilson's Disease. The history of the acute illness in all, however, is typical of epidemic encephalitis and unlike lenticular degeneration, and none presented any enlargement of the spleen.

Roger (40), Piltz (41), Ramsay Hunt (42) have all remarked on the similarity of the two conditions and reported illustrative cases.

Prognosis in the Parkinsonian Syndrome.

There have been no deaths among the 21 children who developed this syndrome. Nevertheless the prognosis for the child seems to be worse in this than in the other sequelae.

At the present date the condition of these children is as follows:-

Great improvement.	One case.
Slight "	Two cases.
Stationary	Two cases for 2 & 3 years respectively.
Deteriorating after stationary period	Two cases.
Steadily progressive	Fourteen cases.

Only three, or 14%, show any signs of disappearance of the syndrome.

It appears impossible to find a relation between the early history/

history of the case and the development. Case 73, for example, a boy, who is now almost free of any Parkinsonian signs, had a short acute illness in May, 1924, consisting of choreiform restlessness, insomnia and delirium with some pain in the legs. After three weeks he appeared perfectly well and was sent home. He was re-admitted a few days later suffering from nocturnal restlessness with heavy sleep by day. Very shortly afterwards the face, attitude and gait assumed a very immobile aspect. The condition progressed rapidly with coarse tremor, salivation and inarticulate speech, all most marked at night. A year later improvement began and the boy is now practically free of the syndrome. He is, however, violent and extremely restless with persistent nocturnal excitement.

In all the other cases in which the syndrome appeared with so much severity, the condition has been progressive. Cruchet (38) concludes that improvement, when it occurs, does so where the syndrome has been of early onset. In these cases he finds it pretty often curable. Case 73, just quoted, appears to support this theory. On the other hand, of the two who show slight improvement, one, Case 52, presented none of the signs till ten months after the acute illness. In the other, the onset of the syndrome cannot be accurately timed. Two of the worst cases, Cases 68 and 72, showed the first signs very early and have been rapidly progressive. Of the six, who are now bedridden, the period between the acute illness and the onset of the syndrome varied between 5 months and 2 years.

The type of acute illness shows no regularity in these cases. In Case 17 the acute illness was very slight. In Case 73, it was severe but short, in others it lasted for 2 and 3 months. Nine cases suffered at no time from lethargy. Three after a few days of excitement were lethargic for 5, 7 and 9 weeks. Fourteen of the twenty-one were violently restless for the whole or part of the acute illness so that if anything the syndrome seems more likely to follow this type. This is quite contrary to Rey's (43) experience. In 76% of his cases the syndrome followed on the lethargic type.

Ocular Signs and Symptoms.

Since the first report of this disease, by Economo (1), in 1917, ocular signs and symptoms have been features of all clinical records. Netter includes them in his triad of cardinal symptoms. Bielschowsky (44) considers that no disease presents such a variety of ocular symptoms, and Foster Moore (45) found ocular paralyses in 75% of a series of 97 cases.

In this series, out of 39 acute cases, 29 or 74.3% showed some paralysis of the eye. For the greater part these paralyses appeared in the acute stage and were characterised, like the other paralyses met with in the disease, by their transient nature. The striking exception to this has been in paralysis of accommodation, which once being present has tended to remain and has often been a valuable aid in the diagnosis of a case coming under observation for the first time during the later stages of the disease.

Diplopia.

Diplopia was definitely present in 18 or 23% of the series. The patients being children, and many of them very young children, it is probable that this may be a low estimate of the cases in which it actually existed, although it is above the 18% of the Ministry of Health Report (46).

Table 18.

Diplopia.

Number of Cases.	Day of illness.	Duration.
13	1st	(7 lasted some hours. (3 " about 2 days. (2 " " 4 " (1 " " 14 "
2	2nd	(1 lasted about 1 day (1 " " 6 days.
1	3rd	A few hours.
1	5th	About 2 days.
1	5th month	About 2 days.

In Case 23 diplopia recurred after some days following on 15 hours of amaurosis and persisted for several days.

Except for one case in which it appeared in the 5th month none of the children has ever complained of it in the later stages. It is interesting to note that in all cases where diplopia occurred it was followed by a period of excitement of varying duration.

Strabismus was present in 11 cases during the acute stage, usually in very transient form. In one case, however, it was still slightly present a year after the acute illness. In this case it had been the first sign of illness and was followed immediately by complaint of double vision and extreme choreiform restlessness.

Ptosis was only found in 7 cases and in two of these it was double. This figure is low as compared to the Ministry of Health Report where about half of the cases are said to have been affected. In many more cases during the lethargic period there was an appearance suggesting ptosis but only really in proportion to the general immobility and asthenia of the patient. It has not occurred in the later stages.

Nystagmus occurred in 6 cases during the acute stage and has been present occasionally in the later stages also.

Internal muscles of the eye.

Loss of the reaction of the pupils on accommodation while the reaction to light is retained appears to be of great importance from a diagnostic point of view. Seventeen of the 79 cases have shown this sign while in one other the accommodation reflex has been sluggish from the beginning. Once present, the paralysis of accommodation has persisted over long periods. The following table gives the history of this paralysis in the cases in which it occurred.

Table 19.

Reaction on Accommodation.

Case	Year of acute illness.	Accommodation during the acute stage.	Accommodation after				
			1 year	2 yrs.	3 yrs.	4yrs.	5 yrs
9	1918	lost 3rd week.	present	-	-	-	present
11	1920	child not seen	lost	lost	-	-	not traced.
12	"	"	-	lost	-	-	lost
17	"	present	sluggish	lost	-	-	?
32	"	present	lost	-	-	-	-
35	"	present	lost	-	-	-	not traced.
37	"	present	-	-	lost	-	lost
36	"	lost	-	-	-	-	lost
21	"	lost	lost	lost	-	lost	lost
41	1922	child not seen	-	-	lost	-	-
42	1923	sluggish	-	lost	-	-	-
44	"	child not seen	lost	lost	-	-	-
49	"	lost 2nd week	lost	-	lost	-	-
52	"	lost	present	present	present	-	-
62	1924	child not seen	lost	-	-	-	-
65	"	"	"	-	-	-	-
75	"	"	"	-	-	-	-
79	1925	sluggish	sluggish	-	-	-	-

It will be noticed that the reflex has returned in two cases. In both of these it was absent only for a short period during the acute stage. All the others are unchanged.

Boveri (47) lays much stress on loss of accommodation with retention of the light reflex in this disease and considers it one of the last manifestations to disappear. Genet (48) and Wimmer (49) also regard it as important in diagnosing cases in after years.

The reactions on accommodation and to light were both lost in one case but only in one pupil and for a very short period. This was observed on the 4th day of illness and remained not more than 10 days. Both reflexes then became normal. In a case of Fawcett's mentioned by Symonds (50) the pupils reacted neither to light nor on accommodation but 10 days later reacted to light.

The Argyll Robertson pupil was never met with in our cases although Symonds (50), Hinds Howell,(30), and Hume, Nattrass and Shaw (51) have all encountered it.

Inequality of the pupils was present in 4 cases during the acute stage. All, after 1, 2 and 5 years, are now normal. Seven cases first seen in later stages had then unequal pupils. Of these, 4 are now normal, 5 years after their acute illness, 3 are still unequal, 5 years, 16 months and 1 year after.

Fundi.

Early in the history of the disease, it was agreed by many observers that the fundi were unaffected. Wimmer (52) refers to this as having been accepted almost as dogma in the early days, and Hume, Nattrass and Shaw (51) regarded optic/

optic neuritis as evidence definitely against the diagnosis. Findlay (3), however, as early as 1918, found in one case "slight redress and swelling of both discs," and in 1921 Findlay and Shiskine (4) reported "swelling of the discs with tortuosity of veins and obscuration of the vessels in places." This last case is now an extreme example of the Parkinsonian syndrome.

Since then Buzzard (27), Foster Kennedy and Wimmer (52) all report cases (the last two in the later stages) and in the Ministry of Health Report in 1922, 20% of the cases are reported to show changes in fundi with definite optic neuritis in 5.5%. The table below gives our results. All of these have been undoubted examples of epidemic encephalitis.

Table 20.

Fundi in Acute Stage.

33 of our 39 acute cases were examined ophthalmoscopically. 21 were normal. The findings in the other cases were as follows:-

Case	3	"Discs slightly red and swollen - vessels engorged and tortuous."
"	2	"Fulness of both discs with obscuration of the margins."
"	23	"Both fundi red and swollen with vessels obscured in places."
"	47	"Right disc distinctly pink."
"	56	"Both discs congested - vessels full - margins obscured but slight cupping in centre - left disc greyish in colour."
"	49	1st week "nil." 2nd week, "pink discs - congested veins, all fundus very red."
"	51	"Pink discs and congested retinal veins. No sign of exudate in or around disc."
"	54	"Both optic discs pink in colour but well defined. Veins turgid with greatly increased calibre as compared with the arteries."
"	53	"Both discs slightly swollen." Week later - "nil."
"	74	"General appearance of right fundus is considerably more congested than that of the left. The appearance of the right is that associated with encephalitis."
"	71	"Increased tortuosity of retinal veins in left eye as compared with the right. Otherwise the fundi are normal."
"	67	"Discs red and slightly full. Margins obscured."
"	78	"General hyperaemia."

Table 21.

Fundi in late stage.

Late, i.e., after 2/12th year. 29 cases examined.

21 were normal. The findings in the remainder are given below.

Case 16.	After 6/12th yr.	"Fundus in both eyes is abnormally red in colour. The optic discs are congested and the red colour of the disc merges with the general red of the fundus so that its outline is obscured. The retinal veins are swollen and the light reflex is absent."
" 12.	After 9/12th yr.	"Discs well defined. Fundi unduly red."
" 15.	After 3/12th yr.	"Congestion of fundi of both eyes but nothing abnormal in the disc."
" 23.	After 3/12th yr.	"Veins enlarged. Slight swelling of discs."
" 19.	After 2 8/12th yrs.	"General hyperaemia of whole fundus more marked on left side than on the right. Veins congested."
" 38.	After 1 year.	"Discs very pale - vessels small - optic atrophy." Died 6 days later.
" 45.	After 1 year.	"Discs are congested but both congenital cup and margins are well defined. Veins are greatly congested and the calibre of the arteries is increased."
" 63.	After 8/12th yr.	"Right disc slightly swollen on temporal side, otherwise nil."

The greater number of these were examined also by Dr Maitland Ramsay who confirmed the findings given above.

Paralyses.

After the ocular paralyses, the most frequent paralysis was of the VII cranial nerve. This was found in 7 of the 39 acute cases and like the majority of the paralyses in epidemic encephalitis was transient in character, sometimes changing in the course of a few days from one side to the other.

Among the children who are now in the chronic stage, and with whom I am in touch, only one has a facial paralysis. This appeared about one year after the onset in 1920 and affects the lower right half of the face. The child is definitely feeble-minded but shows no other sequelae at present.

In six cases transient pareses of the limbs were present during the acute stage.

In only one, Case 22, was there evidence of a definite hemiplegia. This boy was not seen till the 11th week of illness. There was a history of sudden onset of lethargy which had lasted for 3 weeks. A day or two after its disappearance the child complained of pain in left arm and hand.

On admission there was generalised rigidity, most marked in the left arm and leg, both flexed, with hand in position of "main-en-griffe." Reflexes active. The plantar response on left side was extensor. No anaesthesia. Pupils normal. Cerebro-spinal fluid showed a few lymphocytes. The child was almost unconscious and died a few days after admission. No post mortem examination was obtained.

Reflexes.

In the majority of cases the knee jerks were increased during the acute stage of the disease though in 10.2% they were diminished. In the later stages they are usually exaggerated also. Ankle clonus was present in 4 cases during the acute stage and in one during the later stages.

An extensor response of the toes was present in 4 cases during the acute stage. In 3 it was transient. In Case 22, quoted above, it remained till death. In two cases the extensor response appeared first in the later stages. One of these, Case 12, was admitted to hospital in the 8th month of illness, while suffering from nocturnal excitement. The reflexes were normal. One year and nine months later she was re-admitted as she had begun to be quarrelsome, disobedient and unmanageable, though the hours of sleep were improving. Accommodation was found to be absent, light reflex being normal. No other paralysis was present. Knee jerks active. Babinski's sign was present on both sides. A month or two after this, immobility of the left arm and leg was noticed and since then the Parkinsonian syndrome has gradually and steadily developed. She is now a typical example of the generalised type. An unusual point in her condition is the continued presence of Babinski's sign, very definitely on the left, doubtfully on the right side. The left leg is more spastic. There is double ankle clonus and double talipes equinovarus. The pupils still do not react on accommodation. This is one of the children who presents such a close resemblance to the picture in Wilson's Disease. Wimmer (55) also reports a case/

case of Parkinsonism in which there was a double extensor reflex.

McAlpine (12) describes a very similar case which showed "Parkinsonian facies, smile and speech; slight right hemiplegia with definite extensor response on the right side; on left side doubtful extensor reflex. Power quite good in all four limbs.

Pain of severe neuralgic character was present during the early stages of the disease in 23 cases.

Table 22.

Cases.	Site.
10	Headache varying in site.
9	Pain in limbs.
6	Pain in abdomen.
1	Pain in nose.

In most cases, the site of the pain varied from day to day or even from hour to hour yet physical examination revealed nothing abnormal. The pain, however, is severe and the diagnosis of rheumatic fever or some acute abdominal condition may be made, as we ourselves have seen and as has been reported by Hinds Howell (30), Spence (56), Stevenson (31), and many others. In Case 52, in our own series quoted when discussing myoclonus, the child was for a week treated as acute rheumatic fever and was then sent in to hospital as an example of acute appendicitis. In her case pain has recurred frequently and on two subsequent occasions she has been/

been sent to hospital as a case of appendicitis. On each occasion on which pain recurred while she was under observation in hospital there was fever, the temperature rising to 103°. During these attacks the child sat looking extremely miserable and calling out "the pain, the pain." Examination was always negative.

In most cases, however, pain was an early symptom. In three, it consisted of headache alone and was in each followed by lethargy. In the others, where there was pain in the limbs or abdomen, some form of hyperkinesis invariably followed. The hyperkinesis usually appeared as a severe choreiform excitement, with insomnia and delirium, but in two cases it took the form of myoclonus. Hyperaesthesia has also been present occasionally for short periods, but always in the hyperkinetic cases.

Later Stages.

In four cases there was pain during later stages. Case 52 has already been quoted. In Case 22 pain occurred in the left arm after the acute illness was over and was followed rapidly by a hemiplegia of the left side, death ensuing shortly afterwards. A post mortem examination was not obtained.

In Case 24, pain in one arm was followed by slight atrophy of the muscles affected, but no paralysis. This child described the pain as being of a "tingling" nature.

Case 68, a girl who is now a very severe example of the Parkinsonian syndrome, complained frequently of tingling pain in one arm about a year after the acute illness. Examination so far has been negative.

Cerebro-spinal fluid.

In 63 cases the cerebro-spinal fluid was examined. In 1920, Professor Findlay and Dr Shiskine (4) gave a full report of 24 of these. Since then the examination has been continued in the same way, and the following figures include the total number. The examination of these later cases has produced very much the same results as were found in the earlier cases.

The fluid has been in the majority of cases under increased pressure and has been clear except in one or two cases where it was blood-stained. The results from these are not included. Pandy's test was invariably negative.

Cytological examination showed that there was usually a slight increase in the number of cells, when done during the acute stage. In this estimate five cells are taken as the maximum normal figure. During the first three months the figures 30, 20, 10 were common although in one case during the 10th week only two cells were found. In the later stages the cells have been normal with the exception of two cases in whom at the end of one year the cells numbered 7 per c.mm. Unfortunately in many cases the cells were not counted. The notes made on the films of these, however, correspond with the figures.

The increase in cells was found in every case to be due to lymphocytes.

Boveri (57), Netter (58) and Symonds (59) all found an increase of cells in early stages, Symonds finding that the

cells/

cells in the acute stage varied on average from 0 to 50 per c.mm. and very occasionally to 100.

Since 1920, the Colloidal gold test of Lange has been done as a routine on these fluids. The early results in these were included in the paper by Professor Findlay and Dr Shiskine. Since then the test has been done by Drs Scott and McClusky and for the past eighteen months by myself. Professor Findlay and Dr Shiskine obtained a positive result, i.e., a precipitation in the tubes of low dilution, in 17 out of 21 cases. At that time Bassoe (60), who had obtained a positive result in 5 out of 6 cases, was apparently the only other worker using the test. Since then Symonds (59), and Heagey (61), Davis and Kraus (62), and others have also obtained positive results in a fair number of cases. Regan, Litvak and Regan (63) obtained reduction in the syphilitic zone invariably in poliomyelitis, but do not find that the test is always positive in epidemic encephalitis In this series the test has now been done 70 times, on 56 children. The results are as follows:-

Table 23.

Colloidal Gold Tests.

38 cases tested in acute stage.	(Positive in	20	52.6%
	(Faintly " in	8	21%
	(Negative in	10	26.3%
24 cases between 2 months and 1 yr. after onset.	(Positive in	10	41.8%
	(Faintly " in	7	29.1%
	(Negative in	7	29.1%
8 cases between 1 and 3 years after onset.	(Positive in	1	
	(Faintly " in	2	
	(Negative in	5	

As time goes on, the test therefore becomes less frequently positive.

The cases in whom we had the opportunity to repeat the test gave the following results:-

Table 24.

Colloidal Gold Tests repeated at intervals.

Case	Period of illness.	Colloidal gold test.	Present state.
38	(1st week (3rd week	00000000000 55555432000	Dead in 13th month.
32	(2nd week (4th week (3rd month	11232200000 01221000000 12331000000	Parkinsonian.
37	(2nd week (3 years	01211000000 negative	Mentally defective.
31	(3rd week (9th week	01121100000 1221100000	Mentally defective.
52	(2nd week (4th week (8th month	negative 23444310000 negative	Parkinsonian.
51	(1st week (13th week	01232100000 12223210000	Mentally very poor.
68	(1st week (13th week (1 year	negative 22341000000 00121000000	Parkinsonian.
72	(2nd week (17th week	01355420000 01232210000	Parkinsonian.
30	(1st week (4th week (7th week (11th week	01132100000 34443200000 55555200000 55540000000	Lethargy in this case continued for 9 months when death occurred.

It will be noticed that the test is sometimes negative very early, becoming positive after a week or two. After the acute stage is past it again gradually becomes negative. Of 3 cases who died during their acute illness, two gave a positive reaction, one a negative.

It is always necessary, of course, in using this test, to have the Wasserman reaction done at the same time since the reaction occurs in the same zone. In all the cases cited this was negative.

This test is undoubtedly valuable when positive, especially in the earlier months of the disease. It is, however, not invariably positive even when the clinical signs are very striking. In the later stages it is usually negative.

Wimmer (64) finds that the fluid is normal after 8 months and that the pleocytosis vanishes first. In the present series the fluid had become normal in the great majority of cases after one year, the increase in cells having invariably vanished by that time, and the colloidal gold test being usually negative.

The fluid was cultured in about one third of the cases. No growth was obtained except in one, where contamination was suspected.

Nocturnal Excitement.

In a series of cases composed entirely of children, nocturnal restlessness assumes an importance which is quite lacking in one of more varied ages. Findlay and Shiskine and later Anderson in writing of the early cases have described it in detail and since then/

then it has been mentioned by almost all observers dealing with children.

Kennedy (9) found this sequel occurring in 19 of his 51 cases, Shrubsall (65) in 40 out of 119. The proportion of children showing it in this series is very much larger.

In 60 out of 68 cases of the series seen in the later stages nocturnal insomnia and restlessness have been present in varying degree. The course of events is now well known. These children as evening comes on become brighter, more talkative and more excited. In the mildest cases, the child will lie awake till 4 or 5 a.m. talking quietly to himself. At the other extreme, the child will climb out of bed in an almost maniacal condition, be most destructive, shriek for hours so that a whole ward is kept awake. He may become extremely dirty in his habits at night. Respiratory disturbances when present are often also more marked. Attacks of hyperpnoea are more frequent than by day, and habits such as sniffing and blowing the nose, as in Case 59, become extremely marked during the night. A pitiful aspect of the case is the frequent anxiety of the child to rest. Some children will assure one again and again of their desire to sleep. One child in this series spent the night in the search for what he described as a "good position."

At about 5 or 6 a.m. these children fall asleep and sleep heavily till the next afternoon. No sedatives at night nor efforts to keep the child awake by day seem sufficient to disturb this sequence.

Onset.

Most commonly, nocturnal excitement follows rapidly upon the brief recovery from the acute illness. In some cases where the acute stage lasted about 10 days, the sleep disturbance appeared in the 3rd week of illness. In one case on the other hand it did not appear till $3^{3}/12$th years afterwards, being preceded in this case by other sequelae. The average time after the onset of the acute illness is about 10 weeks.

In 4 cases, however, nocturnal excitement with sleep by day was the first sign of illness noticed; no history of any previous febrile disturbance or malaise could be obtained. All these cases have otherwise followed a typical course. The following table gives details of these cases.

Table 25.
Cases in which inversion of the sleep rhythm was the first sign.

Case	Duration of N.R.	Present Condition.
14	$2\frac{1}{2}$ years.	Very backward. Mental ratio 57.
44	$2\frac{1}{2}$ years.	Hyperpnoea, loss of accommodation, mentally backward. Mental ratio 67.
47	$2\frac{1}{2}$ years.	Nocturnal restlessness still present. Bad tempered, quarrelsome. Mental ratio 89.
43	$1\frac{1}{2}$ years.	Choreiform restlessness, mentally backward. Mental ratio 80.

In these cases there is no history of the acute attack. In one or two others, inversion of sleep rhythm was the first sign complained of, but careful investigation of the history disclosed suggestive facts. Thus in Case 60, the child developed nocturnal excitement in August 1924. The only illness from which he had suffered for years was appendicitis two months earlier. He had then been operated upon. On further inquiry it was discovered that shortly after his operation and while still in hospital, he had been noticed to be exceedingly quiet and lacking in interest in his surroundings. The parents had been questioned at that time concerning his usual behaviour. This condition had improved after a week or two. On inquiry it appeared that on operation the appendix was found to be only slightly inflamed, not at all in proportion to the previous pain. It is extremely probable that this was one of the type in which abdominal pain is the striking symptom at onset. In Case 11, the history again gave nocturnal excitement as the first sign, but later it was discovered that the child had been feverish and drowsy for a fortnight, 3 months earlier. This illness had been diagnosed as pneumonia, but in view of the after events was obviously the acute stage of epidemic encephalitis.

Judging from the difficulty in obtaining the early facts in such cases as these, it would appear very probable that in cases 14, 43, 44, and 47 the acute attack was present in some slight form and did not impress the parents. In such cases, and where children are concerned especially, Rolleston (66) believes the

acute attack may often escape detection.

There seems to be no relationship between the type of acute attack and the incidence of nocturnal excitement. In many cases a very short acute attack was followed by severe nocturnal restlessness as in Case 83. This child after an illness of about 10 days in May 1924 was dismissed apparently well. He returned 4 weeks after the onset suffering from severe nocturnal restlessness which has persisted until the present (1926).

The age of the child is also apparently of no importance in determining the nocturnal excitement, as children of 11 and 12 years suffered exactly in the same way as younger children.

Psychic factor in the production of night restlessness.

This is noticeable in many cases. Change of surroundings, e.g., from home to hospital, or even from one ward to another, has frequently caused the children to sleep for a few nights. Within the last few months, one boy,who had been lying awake for months and whose favourite occupation during these wakeful hours was tearing the bed-clothes into strips, was sent to a home for a month. While there he behaved and slept well. On his first night at home insomnia and destruction returned as badly as before. Since then, however, it has gradually improved.

Dr Anderson (5) was successful in producing sleep by injections of sterile water for some time but found that relapse followed if the patient realised the innocuous nature of the injections.

The onset of fever certainly produces normal sleep while it lasts, such as an intercurrent febrile attack or even artificially produced fever. In two cases to whom I injected vaccine

intravenously, normal sleep followed with the resulting fever. This, however, was only temporary in its effect and disappeared with the fever.

So far as experience of this series goes, there is nothing to guide one as to the cause of the final disappearance. Morley Fletcher (67) and Reh (68) have noted improvement following upon hot baths or intercurrent fever from measles. These, I think, must be looked upon as coincidences. In one case of this series, Case 73, hot baths or a change to a warmer room produced sleep temporarily, but after almost 2 years nocturnal restlessness is still present. In the cases where intercurrent disease produced sleep the improvement was also only temporary. The permanent improvement has always occurred gradually and for no apparent reason.

Duration.

The duration of this nocturnal excitement and sleep by day is very variable. In the shortest, it remained for one month, in the longest, for 5 years, the average duration being about 18 months. It is still present in 8 out of the 61 cases traced. Four of these were acutely ill in 1923 and 4 in 1924, so that they are among the later cases.

Compared with other sequelae, this is not the most persistent but is certainly one of the most difficult with which to deal, either at home or in hospital. This difficulty is complicated by the fact that frequently nocturnal excitement runs synchronously with a period of extremely bad behaviour which disappears slowly/

slowly along with the gradual return to normal sleep.

In all cases but three, these children are now suffering from other sequelae or from mental deficiency. That these are not the direct effect of the nocturnal excitement is proved by the fact that the only three children, Cases 47, 59 and 61, who are normal at present, have suffered from nocturnal excitement for periods of 2 years, 6 months, and 9 months respectively.

Disturbances of Respiration.

Disturbances of respiration form one of the sequelae found by practically all observers of this disease. Goodheart and Cothrell (69), Levy (70), and others refer definitely to a respiratory type of the disease. Kennedy (9) found such disturbances in 20 out of 51 cases, Levy (70) in 10 out of 129, Hinds Howell (71) in 3 out of 28. In the present series these changes have been present in 29 of the 68 cases seen in the later stages. Details of these are given in the following table.

Table 26.

Case.	Original Respiratory Abnormality.	Period at which disturbance appeared.	Duration since onset of disturbance to present.	State of respiratory abnormalities at present.
8	Panting attacks	2nd year.	5 years.	Present occasionally.
10	" "	4th week	6 "	Present less frequently.
11	" "	3rd year.	3½ "	Present occasionallly.
13	" "	7th month.	(2 years. 5 years.	Improving. Gone.

Case.	Original Respiratory Abnormality.	Period at which disturbance appeared.	Duration since onset of disturbance to present.	State of respiratory abnormalities at present.
14	Panting attacks.	3rd year.	(3 years (4 years	Improving. Gone.
16	Sighing and smacking lips.	2nd year	4 years	Gone.
19	Panting attacks	6th week	5 years	Less frequent.
20	" "	2nd year	(3 years (4 years	Improving. Gone.
21	(Panting attacks (Clearing throat	3rd year "	4½ years "	Present. "
24	Grunting noises	2nd year	Not traced	-
25	(Panting attacks (Blowing down nose	2nd year "	4½ years. "	Gone. "
28	Panting attacks	14th mnth.	4½ years.	Gone.
29	" "	2nd year	4 years	Less frequent.
32	" "	3rd year.	Not traced	-
33	" "	2nd year	4 years	Present. Unchanged.
36	" "	3rd year	3 years	Improving.
40	" "	3rd mnth.	Not traced	-
41	(Panting attacks (Apnoea	1st year "	2 years "	Present. Apnoeic attacks still present.
44	Panting attacks	2nd year	1 year	Occasional.
46	" "	1st year	2 years	Unchanged.
49	(Continuous, rapid (respiration. (Panting attacks.	Acute attack	2½ years "	Present, 44 p.min. "
52	(Contin. rapid (respiration. (Panting attacks	2nd week "	2½ years "	Present: Improving Gone. (Myoclonus of resp.muscles).

Table 26 (Contd).

Case	Original Respiratory Abnormality.	Period at which disturbance appeared.	Duration since onset of disturbance to present.	State of respiratory abnormalities at present.
57	Panting attacks	1st year	2 years	Occasional.
59	(Blowing nose & (sniffing.	3rd month	1½ years.	Present.
60	Panting attacks	2nd month	1½ years	Present. Apnoea now present. (Violent conduct during attacks).
62	(Sniffing & blowing nose	1st month	1½ years	Present.
67	Panting attacks	1st year	1 year	"
69	(Contin. rapid respiration, (40 per min. (Panting attacks	2nd week "	1½ years "	Present. (Myoclonus of resp. muscles). Present.
79	Panting attacks	1st month		Present.

In considering these cases, the classification used by Marie, Binet and Levy (72) has been used. These observers divided the disturbances into three classes:-

(a) Respiratory troubles properly speaking.

(b) Phenomena of spasmodic cough.

(c) Manifestations of the nature of respiratory tics.

In the present series, there have been no cases suffering from spasmodic cough but of the 29 cases, 23 belong wholly to the first class, 2 to the third and 3 have shown manifestations of both.

(a) Those derangements which come under the first heading as purely respiratory in this series can be arranged as follows:-

1. Attacks of rapid and noisy breathing.
2. Continuous rapid breathing with occasional attacks of noisy respiration.
3. Apnoea.

To these, Marie, Binet and Levy add bradypnoea, which they found in one case. Wimmer found that it occurred seldom and in this series it has never been observed.

Attacks of rapid and noisy breathing form the most common respiratory disturbance. They begin without warning and with no apparent cause. Parents have described the child as "panting like a dog" or "as if he had run a race." If the child is suffering from night restlessness, the attacks are much more frequent and severe by night. If sleep is normal, excitement of any kind appears to encourage an attack. In some children the attacks are very frequent, coming on almost every half hour.

In all cases but one, the child shows little disturbance during the attack though one or two seem restless while it lasts. The exception is formed by a boy of 10 years of age (Case 60) who is between attacks a quiet and pleasant-looking child with a happy expression. About every 20 minutes or half hour, rapid noisy respiration begins, without any warning. It is accompanied by very violent behaviour in which he may break windows, tear clothing or rush wildly out of any place or vehicle he may be in. His expression becomes sullen and distant and he pays little attention/

attention to remonstrances. After some minutes there is a period of apnoea which lasts for about a minute and in which his face becomes blue. He then resumes his former normal appearance and behaviour. He is very intelligent, and has a mental ratio of 102 but owing to the violence of his behaviour cannot be kept at school. This coincidence of violence or hyperkinesis with the disturbance of respiration was present in the majority of Kennedy's (4) series and is to him very characteristic. In our series, the boy mentioned is the only example and he has only developed it within the last year.

Only four cases (49, 52, 69, 79) have shown a permanent increase in the respiration rate. In these it maintains a rate of 40 to 60 a minute and has done so over periods of 1, 1½, and 2½ years. It appears to cause little or no inconvenience to the children though in Case 49 it causes speech to be staccato and indistinct. In the other three it might easily pass unobserved. In one, Case 52, this rate was originally broken by attacks of noisy breathing. These have now disappeared after 2½ years, though the increased respiration rate remains unchanged.

In three cases (52, 69 and 79) respiration corresponds with a myoclonic twitch of the diaphragm and extraordinary muscles of respiration.

Apnoea. Periods of apnoea occurred in two cases, always at the end of an attack of noisy breathing. Case 60 has been quoted in discussing these attacks. The other child (Case 41) is a marked example of the Parkinsonian Syndrome. The hyperpnoeic attacks/

attacks occur almost every half hour and are very frequent during examination. At the end of each there is a period of about half a minute during which she does not breathe and the face becomes extremely cyanosed. She responds faintly to requests during this period. It is ended by a cough and return to her usual appearance and behaviour.

Respiratory tics, such as a constant clearing of the throat, nose-blowing, sniffing, are present in several cases and like many of the other signs in the disease are most marked by night. One boy aged 10 years (Case 59) was in hospital for months suffering from nocturnal restlessness which followed immediately upon the acute illness. During the whole of his stay, he blew his nose and sniffed loudly almost without cessation from about 5 p.m. till 4 or 5 a.m. His recovery appears at present to be exceedingly good, but after two years he still sniffs very frequently.

The Onset of the respiratory disturbance occurred in eight cases during the first two months of illness. In 21 it appeared after intervals of from three months to three years. In the majority of cases it has therefore been purely a late manifestation.

The duration was always long in this series, the shortest period being two and a half years. In one case the disturbance still remains after six years.

Prognosis. The tendency of these respiratory abnormalities appears to be towards disappearance. Three of the 29 cases can not be traced but of the remaining twenty-six, respiration is now normal in six, improved in nine and unchanged in eleven. Of the eleven unchanged, six were included in the years 1924-25

so that they are still recent. In some of the cases in which the disturbance has disappeared it existed in the most marked degree for long periods.

Mental Changes in Later Stages.

Shrubsall (65) found, in examining London school children who had suffered from this disease, that the attention to school work and the value of the response steadily improved in most cases, though in some he found a diminished capacity for education. This is very much more hopeful than the results in the present series of cases.

At the present time, our cases might be roughly classified as follows:-

(1) Intelligent and without other sequelae.

(2) Fairly intelligent and showing other sequelae. These are frequently Parkinsonian in type.

(3) Definitely backward.

(4) Feeble-minded.

The first class consists of three children, Cases 47, 59 and 61. These children appear now to be quite bright and able to lead a normal life.

The second group consists mainly of children suffering from the Parkinsonian syndrome or from behaviour defects. Most of these have a rather abnormal emotional reaction and some display a lack of concentration, but the intelligence is found to be on a fairly high level.

The third class is by far the largest. These suffer very markedly from the lack of concentration and of perseverance which is spoken/

spoken of so much in adult cases. In these children the defect is very obvious. Most display a lack of normal reserve which leads one at first to estimate their intelligence too highly. At school, however, they are unable to learn and even in play they show little sustained interest. In the majority of cases this is accompanied by other sequelae but in a few long-standing cases it is the only sequel left.

The definitely feeble-minded are not very numerous. One of these children was "backward" before his attack of encephalitis.

In the effort to attain some systematic idea of the mental capacity, we were fortunate in having the assistance in the early cases of the late Dr Watt and in the more recent years of Mr Conn, from the Psychological Department of the University of Glasgow. The mental age and ratio were estimated by them while the children were in hospital. Mr Conn has repeated the test in many of the children whom it has been possible for me to trace. The full results of these tests with further investigations are about to be published by Dr Dawson and Mr Conn (73), who have kindly allowed me to use the following figures.

The value of these tests has been doubted by some authorities on account of the difficulty of fixing the attention of these children and of the motor incapacity of those suffering from the Parkinsonian syndrome, but in comparing the capacity of these children for their response to ordinary life with that of normal children, they are surely useful.

In Dawson and Conn's paper the method of calculating the results has/

has been revised, hence the figures given there vary slightly from those which follow here.

The mental ratio of the average patient in the Royal Hospital for Sick Children is 90.27.

Forty-four children of the series have been tested. In 23 of these the test has been repeated.

Table 27.

Showing Mental Ratios.

Case.	Time after acute illness.	Actual Age.	Mental Age.	Mental Ratio.	Remarks.
4	7 years.	$11^{10}/12$ yrs.	$9^{1}/3$ yrs.	78.	Parkinsonian syndrome.
7	(3 " (6 "	12 years. 16 "	10 yrs. $11^{2}/3$ yrs.	83) 71)	Changes in conduct.
8	(3 " (6 "	10 " 13 "	7 " $7^{4}/12$ "	Betw.66 & 73) 53.)	Change in conduct wh. has improved
12	$2^{5}/12$ "	11 "	$7^{1}/12$ "	65.	Parkinsonian Syndrome. Change in conduct.
13	5 "	8 "	$5^{8}/12$ "	74.	Change in conduct.
14	$4^{10}/12$ "	$9^{6}/12$ "	$5^{5}/12$ "	57.	Change in conduct.
19	$2^{8}/12$ " $4^{9}/12$ "	$8^{7}/12$ " $10^{9}/12$	$7^{8}/12$ " $7^{8}/12$ "	89) 71)	
20	($\frac{4}{12}$ " ($4^{8}/12$ "	10 $14\frac{1}{2}$ "	$9^{10}/12$ " $10^{9}/12$ "	99) 75)	Change in conduct.
21	$5^{3}/12$ "	$11^{4}/12$ "	$7^{2}/12$ "	63.	Change in conduct.

Table 27 (Contd).

Case.	Time after acute illness.	Actual Age.	Mental Age.	Mental Ratio.	Remarks.
26	(2 5/12 yrs. (5 5/12 "	8 8/12 yrs. 11 8/12 "	6 5/12 yrs. 5 10/12 "	74) 54)	Change in conduct.
31	5 years.	16 years.	9 years.	56.	Change in conduct.
32	2 "	6 "	4 4/12 "	71.	Change in conduct.
37	(2 10/12 " (4 10/12 "	4 6/12 " 6 6/12 "	3 " 4 "	67) 61)	Change in conduct.
42	4/12 "	10 "	11 1/12 "	119.	
43	11/12 "	7 "	5 10/12 "	80.	Change in conduct.
44	(6/12 " (2 10/12 "	3 2/12 " 6 "	2 3/12 " 4 "	71) 67)	Change in conduct.
45	1 yr.	12 "	9 8/12 "	81.	Change in conduct.
47	(2 8/12 " (3 9/12 "	4½ " 5 7/12 "	4 3/12 " 5 2/12 "	89) 93)	
49	(5/12 " (2 6/12 "	5 " 7 7/12 "	4 10/12 " 5 10/12 "	97) 77)	Change in conduct.
50	3rd week 1 10/12 yrs.	3 1/12 " 5 "	2 10/12 " 4 "	92) 77)	
51	(3/12 " (2 8/12 "	5 5/12 " 8 1/12 "	4 4/12 " 5 10/12 "	80) 73)	Parkinsonian Syndrome. Change in conduct.
52	(8/12 " (2 4/12 "	11 8/12 " 14 "	11 yrs. 11 2/3 "	94) 87.5)	Parkinsonian Syndrome. Change in conduct.
53	2/12 yr.	5½ "	5 8/12 "	100.	Change in conduct
55	3/12 "	10 "	5 11/12 "	59.	
56	(2/12 " (2 9/12 yrs.	9 9/12 " 12 "	10 " 9 8/12 "	108-10) 81)	

Table 27 (Contd.)

Case.	Time after acute illness.	Actual Age.	Mental Age.	Mental Ratio.	Remarks.
57	3rd week	9 8/12 yrs.	9 4/12 yrs.	97) 83)	Change in conduct.
58	2 years.	7 years.	5 9/12 "	81.	
60	1 5/12 "	9 11/12 "	10 2/12 "	102.	Change in conduct.
61	(5/12 yr. (1 1/12 "	3 6/12 " 4 2/12 "	3 5/12 " 3 10/12 "	97) 89)	
62	1 5/12 yrs.	13½ "	10 2/12 "	76.	Parkinsonian Syndrome.
65	(7/12 yr. (1 5/12 yrs.	8 10/12 " 9 8/12 "	9 8/12 " 8 9/12 "	109) 91)	Parkinsonian Syndrome.
66	(2/12 yr. (1 year.	6 9/12 " 7 10/12 "	5 9/12 " 6 6/12 "	85) 62)	Change in conduct.
67	3/52 yr.	11 "	11 "	95.	
68	(13/52 " (1 year.	7 7/12 " 8 7/12 "	5 7/12 " 5 8/12 "	74) 69)	Parkinsonian Syndrome.
69	(6/52 yr. (10/12 "	6 " 7 "	4 9/12 " 5 1/12 "	74) 73)	
70	(8/12 " (1 2/12 yrs.	7 " 7½ "	6 9/12 " 7 8/12 "	87) 87.6)	Change in conduct. Parkinsonian Syndrome.
71	(6/52 yr. (1 yr.	11 10/12 " 12 10/12 "	10 5/12 " 10 "	87) 78)	
72.	(8/52 yr. (6/12 "	13 " 13 4/12 "	7 6/12 " 10 "	58) 75)	Parkinsonian Syndrome Change in conduct.
74	(18/365 yr. (1 7/12 "	12 1/12 " 12 7/12 "	10 7/12 " 11 "	87.5) 81)	Parkinsonian Syndrome.
75	15/12 "	9 3/12 "	7 10/12 "	84.	Change in conduct. Parkinsonian Syndrome.
76	1 8/12 "	9 2/12 "	8 7/12 "	84.	Parkinsonian Syndrome.
79	3/52 "	7 6/12 "	7 "	90.	Change in conduct.

As time progresses from the onset of the illness, there appears in the majority of cases a greater disproportion between the actual and mental age. This takes place in spite of the fact that there may be some actual increase in the mental age.

Thus, the table just given shows that of the 22 cases tested on two occasions, only two, Cases 47 and 61, have risen to a normal mental standard, 15 have progressed in mental age though by no means in proportion to the increase in their physical age, one has remained stationary in mental age though $2\frac{1}{2}$ years elapsed between the two tests and six have lost in mental age to a varying extent up to eleven months. This mental deterioration is brought out by the average mental ratios obtained in the first and second tests. The average ratio on the first occasion was 86.6 and on the second 75.2. (In the revised figures these become 87.73 and 76.13 respectively).

The following table is of much less value as evidence of deterioration owing to the varying number of cases at the different periods.

Nevertheless the fall in proportion to the duration of illness is suggestive.

Table 28.

Period since acute illness.	Number of cases tested.	Average Percentage.
Under 1 year.	26	88.1
Between 1 & 2 years.	14	83.1
" 2 & 3 "	11	76.4
" 3 & 4 "	3	78.3
" 4 & 5 "	4	66.
" 5 & 6 "	4	61.7
" 6 & 7 "	3	67.3

Age as a factor in the production of mental sequelae.

The age of the child when acutely ill apparently has a bearing on the later mental state.

Comparing the most recently performed tests with the age at the acute illness the following results are obtained:

Table 29.

Ratios at present.	Average age during acute illness.
Below 70.	$6^{3}/12$th years.
Between 70 and 80.	$6^{11}/12$th years.
Between 80 and 90.	8 years.
Over 90.	$8^{11}/12$th years.

The influence of age during the acute illness, though slight, appears quite definite. This is in accordance with the findings of Hallowell (74), Hall (75), Paterson and Spence (76), Ebaugh (33) and others who believe that the younger the child at the time of the acute illness the greater is the degree of mental deficiency. Paterson and Spence, for example, found that 7 out of 17 children who were under 5 years when ill became idiots.

Of this series 20 were under 5 years when acutely ill. Of these, 5 cannot be traced. Of the remaining 15, 2 are now intelligent and normal children, 6 are of very poor intelligence, 3 are examples of the Parkinsonian syndrome, with fair intelligence, 4 died, at intervals from 8 to 20 months after the original onset of illness, all being imbecile.

Of the eleven surviving children, it has been possible to test nine. The results are given in the following table.

Table 30.

Case.	Age at acute illness.	Mental Ratio.
47	1½ years.	89.
37	1 8/12th yrs.	61.
13	2½ years.	74.
44	3 2/12th yrs.	67.
61	3½ years.	89.
41	3½ "	83.
50	3½ "	77.
32	4 "	71.
14	4½ "	57.

Average: 74.1%.

This average is low as compared with the average of the series as a whole.

Table 31 gives details of the four who died.

Table 31.

Case	Age at acute illness.	Duration of illness.	Condition before death.
1	10 months	9 months	Blind, deaf, imbecile.
30	7 "	8 "	Lethargic, imbecile.
34	2 "	14 "	Lethargic, imbecile.
38	13 "	20 "	Imbecile, unable to sit up.

The low mental average of the children who survived and the condition of those who died certainly appear to support the opinion that the disease bears more hardly on the young child than on those of more advanced years. It must nevertheless be remembered that the disease affected these children before the mentality was of a very developed order. The mental condition is therefore necessarily of a lower standard than those who were more advanced before the illness.

Kennedy (9) in his series of 23 cases of the Parkinsonian type in children formed the impression that the mind in these was little affected. The general appearance and facial expression of these children certainly would lead one to expect a very low level of intelligence. In dealing with them carefully, however, this appearance is in the majority of cases found to be misleading since their mental standard is much higher than one at first expects. This experience led the present writer to form the same impression in this series as Kennedy had done in his.

This impression, however, is not confirmed by the results of the Binet Simon tests. When the ratios of the Parkinsonian cases are compared with those of children suffering from other encephalitic sequelae, they are found to be very similar; and there would seem to be a definite deterioration of the mental capacity of the Parkinsonian cases just as in the others.

With regard to those children who have exhibited marked change of conduct, Kennedy thinks that "there is no evidence that a considerable proportion of these are mentally retarded or deficient." In this series, however, the result of ordinary observation certainly points to mental deterioration. Children who have passed through periods of extremely violent behaviour and/

and who have now become docile, such as Cases 5, 8, 10 and 29 show a very obvious feeble mindedness. Lack of normal shyness frequently gives at first a false impression of intelligence which is soon found to be incorrect.

This opinion is substantiated by the actual figures obtained in the mental tests. The average mental ratio of children showing conduct changes is 75% of the normal, a level which is on the border of feeble-mindedness.

One or two exceptions are present in the series. One boy, for example. - Case 60 - exhibits most violent and destructive behaviour during attacks of hyperpnoea. He has, however, a mental ratio of 102 and is well able to maintain a good place in a class with boys of his own age.

Change in Conduct.

Much attention has recently been directed to the change in disposition or in conduct in post-encephalitic cases, especially with regard to those children whose behaviour places them in the criminal ranks. There are, however, many gradations in this change of behaviour, ranging from children who, after their illness, are disobedient and wilful to those of most violent tendencies. The most common remark of the parents in these cases, is that the child has "completely changed."

In dealing with this change the bad conduct which in many cases accompanied the hours of nocturnal excitement is not included. Under these circumstances the child during his waking hours in the afternoon is fairly well behaved but as evening comes on he becomes/

becomes more and more excited, noisy and destructive.

In this series 44 out of the 68 cases seen in later stages showed a definite deterioration in conduct, shown as follows:

Irritability, bad temper, violence.

Destructiveness.

Cruelty to children and animals.

Untruthfulness.

Dirty habits.

Thieving.

Sexual precocity.

The first four have been by far the most frequent.

In many of the children, sudden bursts of temper are common. They throw dishes, knives, in fact anything that is within reach, so that the greatest care has to be taken for others. One child suddenly breaks windows, another rushes into the houses of neighbours and upsets their dishes and pans. Parents frequently describe their behaviour as "very treacherous."

Thieving has been common in only four cases. In these, the thefts have been continual and never with intent to retain the stolen property. One child habitually gives the objects to any friend who may be near and none makes any attempt to conceal the theft. There appears to be no realisation of the situation. All have been repeatedly punished by their parents with no effect. One, however, has now ceased the habit after a long time.

Many of the children become cruel. One boy, Case 73, can not be left alone with his younger brothers for a moment on this account.

Children suffering from these changes of conduct often show no other stigma of the disease and if the history of the case is unknown, their exploits may lead to police intervention, as has happened in some of our cases. Details of these cases are given in the following table.

Table 32.

Change of Conduct.

Case.	Year of acute illness.	Change in Behaviour.	Conduct. Present Condition.	Mental Ratio.	General Condition.
5	1918	Destructive, dirty, unmanageable.	Very good.	-	Mentally very backward.
7	1919	Violent temper, cruel.	Unchanged.	71	Mentally very backward.
8	"	Scratching, biting, vicious in temper.	Docile.	53	Mentally very backward.
9	"	Destructive, unmanageable.	Obedient, quiet.	-	Mentally very backward.
10	"	Vicious, destructive, violent.	Improved.	-	Mentally very backward.
11	1920	Treacherous, cruel.	Unchanged.	-	Parkinsonism.
12	"	Unmanageable, violent temper.	Much improved.	-	Parkinsonism.
13	"	Destructive.	Improved.	74	Mentally very backward.
14	"	Destructive, violent temper.	Docile.	57	Mentally very backward.
15	"	Deceptive, violent, cruel, destructive.	Died of pulmon. tubercle.	-	-
18	"	Disobedient, unmanageable.	Improved.	-	Parkinsonism.

Table 32 (Contd).

Case.	Year of acute illness.	Change in Behaviour.	Conduct. Present Condition.	Mental Ratio.	General Condition.
20	1920	Emotional, dirty, morose, resentful.	Unchanged.	75	Very backward.
21	"	Restless, bad temper, uncontrolled.	Unchanged.	63	Very backward.
23	"	Irritable, emotional.	Much improved.	-	Parkinsonism.
24	"	Violent, sexually precocious.	Worse.	-	Very backward.
25	"	Bad tempered, uncontrolled.	Quite good.	-	Backward.
26	"	Thieving, bad temper.	Improved.	-	Backward.
27	"	Bad temper, unmanageable.	Not known.	-	-
28	"	Quarrelsome, cruel, dirty.	Improved.	-	Parkinsonism.
29	"	Destructive, vicious, dirty.	Improved.	-	Very backward Hyperpnoea.
31	"	Rude, cruel.	Improved.	56	Very backward.
32	"	Cruel, destructive, thieving.	Not traced.	-	-
33	"	Destructive.	Good.	-	Parkinsonism.
35	"	Bad tempered. Irritable. Quarrelsome.	Not traced.	-	-
37	"	Irritable, destructive.	Improved.	61	Very backward.
41	1922	Bad tempered.	Unchanged.	82	Parkinsonism. Hyperpnoea.
43	1923	Quarrelsome. Bad-tempered.	Improved.	80	Backward.
44	"	Curel, destructive.	Improved.	67	Very backward.

Table 32 (Contd).

Case.	Year of acute illness.	Change in Behaviour.	Conduct. Present Condition.	Mental Ratio.	General Condition.
45	1923	Irritable.	Improved.	-	Obese. Lethargic.
46	"	Irritable, forgetful.	Unchanged.	-	Backward.
47	"	Bad tempered, cruel.	Good.	93	Normal.
49	"	Quarrelsome, unmanageable.	Unchanged.	77	Very backward. Myoclonus. Hyperpnoea. Accom. lost.
51	"	Wild, violent, throws weapons.	Worse.	73	Parkinsonism.
52	"	Bad tempered, quarrelsome.	Improving.	87.5	Parkinsonism.
53	"	Wild, rude, restless.	Unchanged.	-	Very backward.
57	"	Untruthful, unmanageable, destructive.	Unchanged.	83	Restless and backward.
60	1924	Bad tempered, violent.	Worse.	102	Hyperpnoea.
61	"	Irritable, bad tempered.	Good.	89	Good.
66	"	Stealing, unmanageable.	Unchanged.	62	Chor. restlessness.
70	"	Bad tempered, violent.	Worse.	87.6	Parkinsonism. Myoclonus.
72	"	Bad tempered, cruel, quarrelsome.	Improved.	75	Parkinsonism.
73	"	Bad tempered, flings knives, spits.	Unchanged.	-	Parkinsonism. Improving.
75	"	Bad tempered, cruel.	Unchanged.	84	Parkinsonism.
79	1925	Stealing, disobedient.	Worse.	-	Myoclonus. Hyperpnoea.

Apart from definite deteriorations of character, few of our series of cases have been free of some less marked change. Almost all show an emotional reaction which was not present before. Laughter, tears, anger, expressions of affection, appear in rapid succession from slight cause. Few show a normal shyness or reserve. They are garrulous, curious and demonstrative. In coming to hospital to report, they will shout out to members of the staff and greet them uproariously. One boy who was before his illness shy and retiring now attends every entertainment possible and is always anxious to perform.

In adult cases there appears to be most frequently a continuously depressed attitude, leading sometimes to suicidal tendencies. In children, this appears to be unusual. There is an almost uniform friendliness and cheerfulness in these children. They express regret for their misdeeds and desire to behave well, but this does not prevent early and continual repetition. There appears to be a compulsion in their acts.

Only one child, Case 20, is morose and resentful in her attitude. She is said to be unwilling to enter into the life of the family at home and has never shown any sign of friendliness when brought to hospital. If questioned, she sometimes bursts into tears. Mentally she is very backward, the mental ratio having fallen from 99 to 75. No other sequel is found at present.

Prognosis as regards conduct changes.

Auden (77) found a gradual improvement in the behaviour and self-control of the larger number of his series of children even where the conduct had been very bad.

In/

In the present series the prognosis as regards defects in behaviour is, on the whole, equally favourable.

The children whose acute illness occurred in the years 1918 to 1923 are, in the main, greatly improved in conduct though there are still eight whose behaviour is unchanged, one dating back to 1919. In seven cases improvement in behaviour coincided with improvement in the time of sleep and children who had been quite unmanageable became docile. In the majority, however, this had no effect. Where the acute illness was more recent improvement is not so marked.

Children who are suffering from a progressive Parkinsonian syndrome are sometimes reported to be improving in behaviour. In these, motor incapacity rather than real improvement may be producing the change.

Obesity has only been seen in two children, both girls. In both cases, it was of late onset. One girl, Case 23, had suffered from an acute choreiform attack in 1920 followed by typical night restlessness. A year later an increase in weight was noticed at the same time as the mask-like face and general immobility became apparent. After two years the girl was very stout and lethargic with pronounced Parkinsonism. She was not seen again till 1925 but was then thin, almost to emaciation. She is now (1926) almost constantly in bed owing to extreme immobility, tremor and the festination and retropulsion which render walking impossible.

This girl resembles a case reported by Wimmer (78) in which the patient developed Parkinsonism with transitory obesity. The other/

other child, Case 45, was lethargic during the acute illness. A year later she was found to weigh 28 lbs more than the normal for her age. She was lethargic both by day and night. The blood sugar curve was normal. She remains in this condition after two years.

Apart from these two, no other case has suffered from lethargy in the late stages.

Circulatory System.

Cyanosis was marked in 2 cases out of the 39 who were in hospital during the acute period. In 2 cases the pulse rate fell for a time. In one, Case 16, the bradycardia persisted for 4 days when the child was most deeply lethargic, the pulse running between 56 and 64 per minute. In the other child (Case 72) there was a sudden drop in pulse rate to 48 accompanied by rise in temperature to 102° during the 6th week. The temperature returned to normal after a few hours but the pulse remained about 60 during the remainder of the illness. In both of these cases the fall occurred during the time of very deep lethargy.

Gastro-intestinal system.

The Ministry of Health Report (79) and Hall (80) mention cases in which the parotid glands were swollen during the acute illness. This was not seen in any case in this series. Abdominal pain was present in six cases at onset. In two it accompanied myoclonus and in three there was severe constipation. Constipation was a prominent symptom in about 50% of the cases at onset and was always very severe.

Urinary System. Nothing abnormal has been noted in our series of cases.

Skin. No characteristic rash appeared.

Labial herpes was very marked in the febrile stage in two, Cases 67 and 77. In both it was as severe as that seen in lobar pneumonia. Piltz (41) saw it frequently at this stage but other observers regard it as uncommon.

In Case 10, there was a definite bilateral herpes zoster which occurred in the 3rd month of illness. A similar one was seen by Souques (81) in the 8th month but was regarded by him as a coincidence.

PROGNOSIS IN EPIDEMIC ENCEPHALITIS.

The prognosis as regards the life of children affected by this disease appears from this series to be fairly good. Only four or 10% died in the acute stage. Six or 8.9% of the children traced died at varying periods after the acute illness, two of these deaths being due to intercurrent disease.

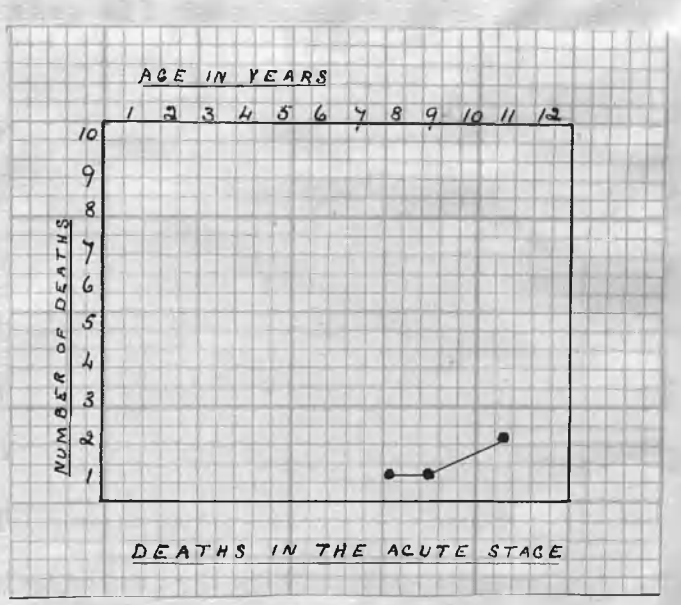
No one type of acute illness points in this series to a fatal result. The four cases of death during the acute stage included two of the violently choreic type, one which included both chorea and lethargy and one purely lethargic. The "algo myoclonic" type which was found to be fatal in France and to be very severe by Hall did not produce any deaths. There were, however, only two of this type, Cases 52 and 69, the first being severe, the second mild.

Fever rising above 104° rectally was certainly of bad omen.

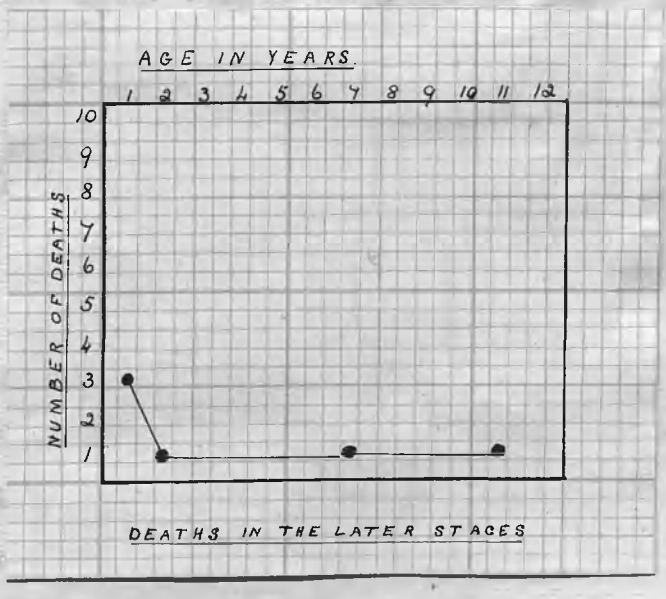
Only/

Mortality in Relation to Age.

Acute Stage.



Later Stages.



Only in one case did the temperature rise above this without fatal result.

The age of the child did not appear to influence the deaths in the acute stage, all four occurring in children of from 9 to 11 years, ages at which the disease was commonest. Four out of the six, however, who died later were under 13 months when acutely ill. As the other two died respectively of pulmonary tuberculosis and pneumonia this means that all deaths which have occurred during the later stages from the disease itself have occurred in infants.

Period of Mortality. Parsons (82) found that 51.2% of the fatal cases occurred within the first fortnight of illness and 82.8% within the first month.

In this series all deaths in the acute stage occurred within the first sixteen days, the average being the 13th day.

Deaths in the later stages occurred in the 3rd, 8th, 9th, 14th, 20th, and 24th months after the onset of the disease.

Sex does not appear to have influenced the mortality. Three out of the four children who died in the acute stage and four of the six who died in later stages were males, but the fact that males form 70% of the series probably accounts for this.

Prognosis as regards survivors.

Shrubsall (65) in a series of 191 children found that 26 or 13.6% made complete recoveries, Robb (83) 5%. Nonne (35) found few definite cures out of 161 cases. Grossman (84) gives figures which are most significant. In examining a series of 89 cases at intervals ranging from 6 to 24 months after the acute illness, he/

he concluded that 70% had made a good recovery. He re-examined these cases, with a few added, bringing the number up to 92, this time at periods of from 1 to 3 years after the acute illness and found that only ten could now be regarded as complete recoveries. Of the remainder 14 were at work but showed some nervous signs, and 62 showed a progressive involvement of the nervous system.

In the present series 61 cases are now alive and have been examined recently. Of these only three have made good recoveries, both physically and mentally. Of the others one boy is able to do regular daily work and earn a fair wage though his powers of concentration appear to be deteriorating. The other 57 children are all incapacitated for ordinary life either by one of the nervous sequelae of the disease, or by mental defect.

It is interesting to note that in not one of the 61 cases did the recovery from the acute stage become permanent. Practically all these children had a short period of improvement, frequently resembling complete recovery after the acute illness. This was invariably brought to an end by one or more of the sequelae. The three children, who have now been normal for periods of 1 year, 18 months, and 2 years, all suffered from periods of nocturnal excitement and irritability of temper between the acute illness and the present improvement. The length of these periods, which is much greater than has occurred in any other case in this series, makes one hopeful that these may eventually be regarded as complete recoveries. The fact also that two of these have now regained the normal level of mental ratio is of good omen. Of the 58 children/

children who are more or less incapacitated for normal life, 20 are now over school age.

The following table gives details of these 20 cases.

Table 33. Condition of children now over 14 years of age.

Case	Age during acute illness.	Present Age.	Present Condition.
7	9 years	16 years	Backward mentally, violent temper, M.R.71
8	7 "	14 "	Very backward mentally.
9	6 "	14 "	Backward mentally.
10	8 "	15 "	Still some choreiform restlessness. Backward mentally. (In mental hospital).
11	9 "	15 "	Parkinsonian in type, behaviour very violent. (In mental hospital).
12	10 "	16 "	Parkinsonian in type.
16	10 "	16 "	Very backward mentally.
17	10 "	16 "	Parkinsonian in type.
20	10 "	16 "	Mental and moral deterioration.
23	14 "	20 "	Parkinsonian in type.
24	10 "	16 "	Mental and moral deterioration. (Waiting for admission to mental hospital).
25	10½ "	16 "	Backward. (Not seen but quite apparent from information).
31	11 "	16 "	Very backward mentally.
36	9 "	14 "	Parkinsonian in type.
42	10 "	15 "	Mentally slow.
45	11 9/12 "	14½ "	Lethargic, obese.
52	11 "	14 "	Parkinsonian in type, improving, hyperpnoea.
62	12 "	14 "	Parkinsonian in type.
72	12 9/12 "	14½ "	Parkinsonian in type.
74	12 "	14 "	Parkinsonian in type.

As mentioned above, only one of these, Case 7, is able to earn any money. He unfortunately is becoming less fit to do so. Four are in institutions, being beyond home control and four are almost constantly in bed at home..

The position with regard to the younger children is equally bad. Five are in institutions and the others are, with only one or two exceptions, either in special schools or reported as ineducable.

No order or sequence can be discerned in the late manifestations of the disease. The most serious and most frequently progressive and crippling is the Parkinsonian syndrome, but mental deterioration is almost equally progressive. The other sequelae tend, on the whole, towards improvement after a considerable time.

SUMMARY.

Introduction.

Epidemiology.

Seventy-nine cases of epidemic encephalitis have been seen in the Royal Hospital for Sick Children, whose illness occurred between the years 1918 and 1925.

Thirty-nine were seen in the acute stage. Forty were brought for the first time in the late stages. Sixty-eight were seen in both stages or in the late stage alone. Sixty-one have been traced at the present time.

Incidence. The onset of the disease has been most frequent in the first six months of the year.

Sex. 70.8% were males.

Age. The ages at onset range from 2 months to 15 years. The highest numbers occurred in the 7th and 11th years.

Infectivity. With possible exceptions in 1924, where two schools were affected, there is no evidence of infection.

Locality. Fifty cases came from the city, 29 from surrounding districts.

Mortality. Four out of 39 acute cases died.

Six out of 68 chronic cases died.

Pathology. Four post-mortem examinations were held. Two of these deaths had occurred in the acute stage, two at intervals after.

General Description of Disease as it occurred in this series.

(a) The acute stage varied from 2 weeks to 3 months and was characterised by lethargy, choreiform restlessness, fever, ocular symptoms and less often by respiratory disturbances and myoclonus.

(b) Latent period. Duration from 2 days to 1 month, during which there were no symptoms.

(c) Later stages were marked by the following signs, in order of their frequency:- mental changes, nocturnal restlessness, conduct changes, respiratory changes, Parkinsonian syndrome, ocular changes, choreiform restlessness, myoclonus, obesity.

Signs and Symptoms in Detail.

Onset was sudden in 69 cases. No clear history of onset could be obtained in 10 cases.

The symptoms at onset were most frequently insomnia, choreiform restlessness, lethargy or diplopia.

Fever was present in 30 out of 37 cases seen very early. In 26 cases the temperature did not rise beyond 104°.

In 19 cases fever lasted less than 2 weeks, in 24 less than 3 weeks.

Lethargy was present in 47 out of 79 cases.

In 21 cases lethargy was the first sign; in 19 it followed upon a period of choreiform restlessness of 2 to 12 days. The second type appeared first in 1920 and was prominent again in 1924.

The duration of lethargy was from 12 hours to 16 weeks, the usual duration being from 10 to 23 days.

Lethargy occasionally deepened into unconsciousness. When

unconsciousness/

unconsciousness was associated with a rise in temperature death always resulted.

In the later stages lethargy was present in two cases. In both it was accompanied by obesity.

Motor Disturbances.

(1) Convulsions - always early in their appearance.

(2) Choreiform restlessness - (a) early.
(b) late.

(3) Myoclonus - (a) both as early and late signs.
(b) as late sign only.

(4) Parkinsonian syndrome.

(1) Convulsions occurred in two cases at onset, and in one on the 6th day of illness.

(2) Choreiform restlessness

(a) in the acute stage was most frequent in 1920 and 1924 and occurred in 39 out of 79 cases.

Duration was in most cases from 4 to 14 days and was followed in 50% by lethargy. In 3 cases it persisted up to 2 months and in 2 for 18 months and 2 years respectively.

(b) In very much less violent form it has appeared in 10 cases in the later stages and has been very persistent.

Myoclonus has occurred in 6 out of 67 cases. In 4 it appeared during the acute stage and has remained until the present. In 2 it appeared in the late stages.

The contraction was situated in 3 cases in facial muscles, in 3 in the diaphragm and respiratory muscles.

The/

The rate has remained fairly constant in each individual, though varying in different cases. The two cases of late onset vary from the others, one in rhythm, the other by its occasional absence. The second of these has now disappeared. Myoclonus is uninfluenced by will.

Pain has accompanied myoclonus in 2 cases.

Myoclonus is of long standing when once established but is now definitely less marked in four of the six cases.

Parkinsonian Syndrome.

21 or 30.8% of the 68 cases seen in the late stages have suffered from this syndrome. 14 or 25.9% of the 54 seen in the first four months of their illness have also been of this type.

Age.

14 of the 21 cases were under 10 years of age when acutely ill.

Onset. The onset of the syndrome varied from about two weeks after recovery from the acute stage to one case in which there was an interval of at least 3 years.

The most characteristic signs have been immobility of limbs and face, the attitude, deliberation, tremor, excessive salivation, changes in the voice, festination and retropulsion.

In nine cases the syndrome dominates the picture, in 12 others sequelae are also present.

Kinesia paradoxa is present in two cases.

There is a strong resemblance between the severe examples of this syndrome and cases of progressive lenticular degeneration.

Prognosis. One marked case has now improved very greatly; two have improved slightly; two are stationary at present, but 16 are deteriorating steadily. The outlook is therefore very bad.

Ocular signs and symptoms. Ocular paralyses occurred in 29 out of 39 cases in the acute stage.

Diplopia was present at onset in 18 or 23% and in 15 lasted 2 days or less. In each case it has been followed by a period of excitement.

Strabismus was present in 11 cases in acute stage, being transient in all but one.

Ptosis was present in 7 cases, in acute stage, in two being bilateral

Nystagmus was present in 6 cases, in acute stage, and occasionally in later stage.

Paralysis of Accommodation has been present in 17 out of 79 cases seen at varying periods and once present has been persistent in all but two.

The reactions on accommodation and to light were in one case lost in one pupil but became normal in 10 days.

The Argyll-Robertson pupil was never present.

Ophthalmoscopic examination of the fundi:-

Acute stage - 33 cases were examined - the fundi were abnormal in 12.
Later stage - 29 " " " " " " " 8.

Paralyses. The facial nerve was temporarily paralysed in 7 out of the 39 acute cases, in only one during the later stages.

Six cases showed temporary pareses of limbs.

In one case there was a definite hemiplegia followed by death.

Reflexes. The knee jerks have been in the majority of cases exaggerated both in the early and late stages.

An extensor reflex was found in four cases during the acute stage and in two during the later stages.

Pain was present as an early symptom in 23 cases, and was always, except in the case of headache, followed by some form of hyperkinesis. In four cases there has been pain in the late stages.

Cerebro-spinal fluid was examined in 63 cases. It was always found to be under increased pressure but clear. Pandy's test was always negative.

In the acute stages the cellular content was usually increased, the highest figure being 30 cells per c.mm. This increase consisted of lymphocytes, and had always disappeared after the third month of illness. The colloidal gold test was performed on 70 occasions, 38 in the first two months of illness, 24 between the third and twelfth month and 8 between the first and third years. The test was usually positive in the acute stage but became less frequently so as time progressed.

Nocturnal Excitement has occurred in 60 out of 68 cases. The average time of onset has been about 10 weeks after the onset of illness. The duration has varied from one month to five years, but in all cases it disappears eventually.

In four cases this inversion of sleep rhythm was the first sign of illness noticed by the parents.

A psychic element is noticeable in this condition.

Disturbances of Respiration occurred in 29 out of 68 cases seen in the late stages.

Attacks of noisy respiration in 18 cases.

Attacks of noisy respiration with continuously increased respiration rate in 3 cases.

Attacks of noisy respiration followed by an apnoeic period in 1 case.

Attacks of noisy respiration followed by an apnoeic period and accompanied by violent behaviour in 1 case.

Attacks of noisy respiration with respiratory tics in 2 cases.

Respiratory tics alone in 4 cases.

The onset occurred in the first two months of illness in 8 cases; in 21 at a later date.

The duration varied from one of two and a half years to one of six years, which still persists.

In 15 cases the disturbances are either gone or lessened. Among those which are unchanged 6 are of recent date. The tendency is therefore towards improvement.

Mental condition in the later stages.

Three children have apparently been little harmed mentally by their illness. These are normal also in behaviour and health.

All the others show varying degrees of damage.

Forty-four children have been tested by a modification of the Binet Simon method, 23 of these more than once.

90% is the average ratio of patients in the hospital.

The three children who have recovered are of normal mental ratio, thus confirming the impression of improvement.

In/

In the others tested twice or more there has been an average fall from 86.6% to 75.2%.

Age is of some importance at the time of acute illness. Four infants under 1 1/12th year died imbeciles at intervals of from 9 to 20 months after the onset. The other children who were under 5 years when acutely ill now show an average mental ratio of 74.1%. Children who are of the Parkinsonian type give an impression that the mentality is little damaged. This impression is not borne out by the mental tests.

Moral changes are accompanied by mental degeneration in all cases but one. Mental change remains after improvement in behaviour has appeared.

Changes in Conduct.

Forty-four cases have shown definite conduct changes. These have been difficult to manage, cruel and pettily dishonest, but none so far has been really criminal in type.

Emotional changes have been present in the majority of the cases seen in the late stages.

Bad conduct has certainly a tendency to disappear. Of those ill between 1918 and 1923, all but eight are now perfectly manageable. Those whose acute illness occurred later are in most cases improving gradually.

Endocrine Disturbance. In two cases obesity accompanied by lethargy has been a late manifestation. In one case this was transient. In the other it is still present after 3 years.

Other Systems.

Circulatory System. Cyanosis and bradycardia were occasionally present in the acute stage.

Gastro-intestinal System. Abdominal pain was present in six cases at onset. In two it was accompanied by myoclonus.

Constipation was marked in 50% of the cases at onset.

Urinary System. Nothing abnormal was found.

Skin. Labial herpes was very marked in two cases at onset. A bilateral herpes zoster occurred in one case in the third month of illness.

Prognosis in epidemic encephalitis.

The prognosis as regards life is fairly good. 10% of this series died in the acute stage. 8-9% in later stages.

No one type of acute illness was fatal but high fever was of bad omen.

Age did not influence deaths in the acute stage, but four of the six deaths in the later stages occurred in infants.

All deaths in the acute stage occurred before the 16th day; these in the later stages occurred at intervals between the 3rd and 24th months.

Sex did not influence the mortality.

Prognosis as to survivors.

No child among those traced has made a complete recovery after the acute stage.

Three children after suffering from night restlessness and some irritability of temper have been apparently normal for periods of 1 year, 18 months, and 2 years. Two of these have improved in mental capacity between the last two examinations and have normal mental ratios. The third has not been retested but/

but appears exceedingly bright.

In all other cases, sequelae are still present.

Thirty of the sixty-one children traced are now over 14. Only one is able to earn money and he is becoming less able to do so. The others are quite incapable of normal existence.

The children under 14, apart from the three mentioned above, are all suffering from various sequelae.

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