LETHARGIC ENCEPHALITIS: THE GLASGOW EPIDEMIC OF 1923.

ITS INCIDENCE AND CONSEQUENCES, FROM THE POINT OF VIEW OF PUBLIC HEALTH.

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INTRODUCTION.

Epidemic encephalitis made its appearance in Glasgow in 1918, although it was only in 1919 that its prevalence was such as to lead to its recognition. It recurred annually till 1924, and, during this period, the change in the clinical features from year to year suggested that it had passed through an evolutionary phase. While ocular symptoms were probably the features most common to all epidemics, prolonged lethargy and somnolence characterised the earlier cases; choreiform and myoclonic movements were more prevalent in 1920 and in 1921, while in 1924 there appeared for the first time a considerable proportion of cases with spinal signs and symptoms, which simulated acute attacks of insular sclerosis.

When the epidemic of 1923 began the medical profession in Glasgow was well prepared for its diagnosis. Doctors were supplied by the Medical Officer of Health with a memorandum in which were set forth the manifestations of the disease, which had been noted in the previous epidemics. Provision was made for notification and for hospital treatment, and, in this way, it was possible to form a fairly accurate estimate of the extent and character of the outbreak.

The following study is concerned with the cases of the 1923 epidemic, and with these only in a general and limited sense. An attempt is made to present a general view of the course of the disease, according as it terminated in early recovery in some cases, in apparent convalescence in others, or as, in the majority, it followed a protracted course along diverging lines in the form of characteristic sequelae. To obtain the purpose of the review, it has been necessary to confine the description of the sequelae to outlines of the main neurological and psychological features. So varied were the phenomena as a whole, and so fleeting many of the most prominent pathological signs, that it is expedient, in describing the general course of the disease as an epidemic, to confine attention to the hall-marks in which its identity is disclosed.

The data employed in the analysis have been obtained from several sources.

The original list of all the cases notified to the Medical Officer of Health, and accepted after observation as possible cases of acute encephalitis, was used as a basis. Along with this list, I have had the notes from hospital

records, as well as the private notes belonging to Dr I. Mackenzie, referring to the initial illness (Table I).

A year after the epidemic Dr Mackenzie examined all the cases, and I have used the results of his observations as a basis of the review of the condition of the cases in the spring of 1924. In the construction of this review I have gone over all the earlier hospital records, and have supplemented the information in Dr Mackenzie's records by further data, elicited from the patients and their friends (Table II).

This reconstructive review of the position, as it was in 1924, has been taken as a basis for the estimate of the later effects, as observed four years later, that is in the spring of 1928 (Table III).

In the course of the investigation of spring 1928, all the patients, reported and accepted as suffering from epidemic encephalitis in the spring of 1923, have been accounted for. All those surviving, with the exception of two, whose relatives were interviewed, have been examined. I am obliged to the superintendents of the various hospitals and asylums, in which the patients have been resident, for access to the records, to Prof. Leonard Findlay for notes on children, the course of whose subsequent history has been followed, and to Dr I. Mackenzie for the use of his records, and for his assistance and suggestions in my own examination of the patients and in the interpretation of the varied courses which their diseases have followed. In this way it has been sought to delineate the course of a phase of the epidemic, and so, by observing the character of the scar, which its imprint on the populace has produced, to provide a standard of reference by which this form of encephalitis may be compared with polio-encephalitis on the one hand, and, on the other, with the type which follows in the wake of influenza.

It is necessary to make a reservation in claiming for the description a representative character; for, as suggested already, the phase of 1923, while typical for the disease as a whole, differed in some respects from the other annual visitations; it did not bring the profound and prolonged somnolence, as in victims of the earlier phase, and there was an absence, from the series, of cases simulating disseminated sclerosis, such as characterised the phase of 1924. It has, however, the advantage that practically all the cases, which occurred in that period, must be included, and that it has been possible to follow their fate for a period of 5 years.

Table I comprises all the cases (70) of the original list, which were notified to the Medical Officer of Health in 1923 as possible cases of encephalitis lethargica, and includes a summary of the symptoms present during the initial phase of the illness.

MANIFESTATIONS OF LETHARGIC ENCEPHALITIS.

With the appearance of this unusual disease the physician had no conception of the gravity of the malady before him; he had not the slightest notion of the varied forms of clinical manifestations that were to present themselves,

Table I.

Case no.	Age at onset	Lethargy	Insomnia	Eye phenomena	Fever	C.S.F.	Tremors and twitchings	Paresis	Reflexes	Neuralgias	Giddiness	Speech defect	Respiratory disturbance	Vomiting	Salivation	Classification according to condition in Spring 1928
1	8	–	+	–	+	+	+	–	+	–	–	–	–	–	–	Perversion of conduct
2	11	–	+	+	+	–	+	–	–	+	–	–	–	–	–	Died
3	11	+	–	–	+	+	–	+	+	–	+	–	–	–	–	Died
4	28	+	+	+	–	+	+	+	–	+	+	–	–	–	–	Parkinsonian (A)
5	24	...	...	...	...	...	...	...	...	...	...	...	...	...	...	Eliminated
6	33	–	+	–	+	–	+	–	–	+	–	–	–	–	–	Died
7	47	+	–	+	–	+	+	–	+	–	+	–	–	–	–	Recovery complete
8	10	–	+	+	+	+	+	+	–	+	–	–	–	–	–	Parkinsonian (A)
9	7	–	+	+	–	–	+	–	–	+	–	+	–	–	–	Recovery incomplete (B)
10	19	–	+	+	+	–	–	+	–	+	–	–	–	+	–	Recovery incomplete (C)
11	24	–	+	+	+	–	+	–	–	+	–	–	–	–	–	Parkinsonian (A)
12	12	+	–	–	+	+	–	–	–	–	–	–	–	–	–	Recovery incomplete (E)
13	26	+	–	+	–	+	–	–	+	+	+	–	–	–	–	Recovery incomplete (C)
14	27	+	–	–	+	–	+	–	–	+	–	–	–	–	–	Recovery incomplete (C)
15	11	–	+	+	+	+	+	–	–	+	–	+	+	–	–	Recovery incomplete (E)
16	7	–	+	–	+	–	+	–	+	–	–	+	–	–	–	Parkinsonian (B)
17	7	+	–	+	+	–	+	–	–	–	–	–	–	–	–	Parkinsonian (B)
18	19	+	–	+	–	–	+	–	–	+	–	–	–	–	–	Recovery incomplete (C)
19	9	–	+	–	–	–	+	–	–	+	–	–	–	+	–	Perversion of conduct
20	13	+	–	–	–	+	–	+	+	+	–	+	–	–	–	Parkinsonian (B)
21	56	–	+	+	+	–	+	–	–	+	–	–	–	–	–	Died
22	16	+	–	+	–	–	–	+	–	+	+	–	–	–	–	Recovery incomplete (C)
23	23	+	–	+	–	–	+	–	+	+	+	–	–	–	–	Recovery incomplete (C)
24	23	+	+	+	+	–	+	+	+	–	–	–	–	–	–	Parkinsonian (A)
25	11	+	–	+	–	+	+	–	+	+	–	+	–	+	–	Parkinsonian (A)
26	1½	–	+	+	–	–	–	–	–	–	–	–	–	–	–	Recovery incomplete (A)
27	8	+	+	–	+	+	+	+	–	–	–	–	–	–	–	Died
28	12	+	–	+	+	–	+	–	+	+	+	–	–	+	–	Recovery complete
29	12	+	–	+	+	+	+	+	+	+	–	+	–	+	–	Recovery incomplete (C)
30	15	+	–	+	+	–	–	+	+	+	+	–	–	–	–	Recovery incomplete (C)
31	40	+	+	+	–	–	+	+	–	+	–	–	+	–	–	Parkinsonian (A)
32	19	+	–	–	–	+	–	–	+	+	–	–	–	–	–	Recovery complete
33	14	+	–	+	–	–	+	–	–	+	–	–	–	–	–	Recovery incomplete (C)
34	27	–	+	+	+	+	–	–	–	–	–	–	–	+	–	Died
35	81	...	...	...	...	...	...	...	...	...	...	...	...	...	...	Eliminated
36	8	+	–	–	+	–	+	–	–	+	–	–	–	–	–	Recovery incomplete (A)
37	13	+	+	+	+	–	+	+	–	+	–	+	–	–	–	Parkinsonian (A)
38	12	–	+	+	–	–	+	–	–	+	–	–	–	–	–	Parkinsonian (A)
39	53	+	–	+	+	+	+	+	+	+	–	+	–	–	–	Died
40	13	–	+	+	+	+	+	–	–	+	–	–	–	+	–	Died
41	15	+	–	–	–	+	–	–	–	+	+	–	–	–	–	Recovery complete
42	2	+	–	–	+	+	+	+	–	–	–	–	–	+	–	Recovery complete
43	50	+	–	+	+	+	+	–	–	+	+	–	–	–	–	Parkinsonian (A)
44	22	+	–	–	+	–	–	+	–	+	+	+	–	+	–	Parkinsonian (A)
45	20	+	–	+	+	+	+	–	+	–	–	–	–	–	–	Died
46	9	–	+	+	–	–	+	+	–	+	–	–	–	–	–	Recovery incomplete (C)
47	4	+	–	+	+	–	+	–	+	–	–	–	–	–	–	Died
48	37	...	...	...	...	...	...	...	...	...	...	...	...	...	...	Eliminated
49	26	–	+	+	+	–	+	+	+	+	–	+	–	–	–	Recovery incomplete (C)
50	43	+	–	+	+	–	+	+	–	+	–	–	–	–	–	Died
51	7	+	–	+	–	+	+	–	+	–	–	+	–	–	–	Died
52	13	+	+	+	+	+	+	–	+	+	+	–	–	+	–	Parkinsonian (B)
53	5	+	–	+	+	–	+	+	+	+	–	–	–	–	–	Died
54	10	+	–	+	–	+	–	+	–	+	–	+	+	–	–	Parkinsonian (B)
55	19	–	+	+	+	–	+	–	–	–	–	–	–	–	–	Died
56	30	+	–	+	–	–	–	+	–	+	+	–	–	+	–	Recovery complete
57	19	–	+	+	+	–	+	–	–	–	+	–	–	–	–	Died
58	26	...	...	...	...	...	...	...	...	...	...	...	...	...	...	Eliminated
59	11	–	+	+	+	–	–	–	–	+	+	–	–	+	–	Parkinsonian (B)
60	5	–	+	–	+	+	+	+	–	–	–	–	–	–	–	Recovery incomplete (B)
61	48	+	–	+	+	–	+	+	–	+	+	–	–	+	–	Recovery incomplete (C)
62	23	+	–	+	+	–	+	–	–	+	+	–	–	–	–	Recovery complete
63	48	+	–	+	+	–	+	+	–	+	–	–	–	–	–	Died
64	5	–	+	–	+	–	+	–	–	–	–	+	–	–	–	Parkinsonian (B)
65	43	...	...	...	...	...	...	...	...	...	...	...	...	...	...	Eliminated
66	19	+	–	+	–	+	+	–	+	+	–	–	–	–	–	Parkinsonian (B)
67	5	+	–	+	+	–	+	–	–	+	+	–	–	+	–	Recovery incomplete (D)
68	20	+	–	+	+	–	+	–	–	+	–	–	–	–	–	Died
69	9	+	–	+	–	–	+	–	+	+	–	+	–	–	–	Recovery incomplete (C)
70	37	+	+	+	+	+	+	+	–	+	–	–	–	–	–	Died

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no idea of how perplexing the diagnosis would in many instances prove to be, and, above all, he had no glimpse, whatever, of the appalling sequelae that were in a multitude of cases to follow in its train. Of all diseases it is most protean in its phenomena, greatly excelling hysteria in its power of simulation, and in its milder phases frequently being mistaken for it. So atypical has it become in symptomatology that no longer can the cardinal signs of fever, headache, diplopia and lethargy be depended upon in reaching an authentic diagnosis. Amongst the expressions of its many-sidedness in the primary attack, the most pronounced are fever, insomnia, delirium, maniacal symptoms, lethargy, abnormal muscular movements, myoclonus, choreiform movements, convulsions, vertigo, headache, neuralgic pains, ocular and facial palsies, diplopia, ptosis, nystagmus, disorders of respiratory mechanism, apoplectiform attacks, skin eruptions, early Parkinsonism or katatonia. As to the later manifestations, the syndromes are legion, and all kinds can be established, depending on localisation of the process in the central nervous system. Among the many complications, which appear at varying times after the initial attack, are disorders of sleep, Parkinsonism, perversion of conduct, pyschotic and nervous disturbances, respiratory and circulatory derangements, ocular disorders, and endocrinal symptoms.

RE-GROUPING OF CASES.

The enquiry was begun with a provisional acceptance of the diagnosis of encephalitis lethargica in the whole series, as reported to the Medical Officer of Health. The observations have suggested a revision of diagnosis in some instances, and the conclusions have reference only to such cases as may now reasonably be regarded as belonging to this particular category of disease.

The course of the illness, as exemplified in the various sequelae, is epitomised in the following tables, where the series is grouped according to the more prominent manifestation of disorder. In Table II the grouping represents the state of the patients in March 1924; this is one year after the initial attack. In Table III the grouping represents their state in March 1928; this is five years later.

An attempt is made to describe the course of the disease, by transferring the cases from one group to another, according as the state has been found to have undergone change. Thus the groups represent (I) Recovery complete; (II) Recovery incomplete; (III) Perversion of conduct; (IV) Parkinsonians; (V) Died.

The method of re-grouping may be indicated by reference to the cases under the heading of "Recovery complete." In 1924 there were eight such cases in this group. In 1928 it was found necessary to transfer three of these to other groups, whereas examination of the rest of the series suggest the transfer of the other cases, who had not recovered at 1924, into the recovered group of 1928.

The results at the end of the first and fifth years' observations have been

Table II. *A constructive review of the condition of the patients in the spring of* 1924.

Italic numeral = Case number. Numbers in parentheses = Age at 1924.

Group I	Group II	Group III	Group IV	Group V
Recovery complete	Recovery incomplete	Perversion of conduct	Parkinsonians	Died
4. (29)	*Class A. Mental retardation*	*1.* (9)	*Class A.*	*2.* (11)
7. (48)	*36.* (9)	*17.* (8)	*Normal mentality*	*3.* (11)
14. (28)		*52.* (14)	*8.* (11)	*6.* (33)
28. (13)	*Class B. Mental instability*		*20.* (14)	*21.* (56)
32. (20)	*9.* (8) *59.* (12)		*24.* (24)	*27.* (8)
42. (3)	*16.* (8) *64.* (6)		*25.* (12)	*34.* (27)
43. (51)	*19.* (10)		*37.* (14)	*39.* (53)
62. (24)			*44.* (23)	*40.* (13)
	Class C. Nervous instability		*66.* (20)	*45.* (20)
	10. (20) *33.* (15)		*Class B.*	*47.* (4)
	11. (25) *38.* (13½)		*Abnormal mentality*	*50.* (43)
	13. (27) *41.* (16)		*15.* (12)	*51.* (7)
	18. (20) *46.* (10)		*54.* (11)	*53.* (5)
	22. (17) *49.* (27)			*55.* (19)
	23. (24) *56.* (31)			*57.* (19)
	26. (2½) *60.* (6)			*63.* (48)
	29. (13) *61.* (49)			*68.* (20)
	30. (16) *69.* (10)			*70.* (37)
	31. (41)			
	Class D. Physical defect (Not Parkinsonism)			
	12. (13) *67.* (6)			
	Class E. Physical defect + Mental instability			
	Nil			

Table III. *A reconstructive review of the condition of the patients in the spring of* 1928.

Italic numeral = Case number. Numbers in parenthesis = Age at 1928.

Group I	Group II	Group III	Group IV	Group V
Recovery complete	Recovery incomplete	Perversion of conduct	Parkinsonians	Died
7. (52)	*Class A. Mental retardation*	*1.* (13)	*Class A. Normal mentality*	*17.* (12)
28. (17)	*26.* (6½) *36.* (13)	*19.* (14)	*4.* (33) *31.* (45)	*37.* (17)
32. (24)	*Class B. Mental instability*		*8.* (15) **37.* (17)	*64.* (9)
41. (20)	*9.* (12) *60.* (10)		*11.* (29) *38.* (17)	
42. (7)	*Class C. Nervous instability*		*24.* (28) *43.* (55)	
56. (35)	*10.* (24) *30.* (20)		*25.* (16) *44.* (27)	
62. (28)	*13.* (31) *33.* (19)		*Class B. Abnormal mentality*	
	14. (32) *46.* (14)		*16.* (12) *54.* (15)	
	18. (24) *49.* (31)		**17.* (12) *59.* (16)	
	22. (21) *61.* (53)		*20.* (18) **64.* (9)	
	23. (28) *69.* (14)		*52.* (18) *66.* (24)	
	29. (17)			
	Class D. Physical Defect (Not Parkinsonism)			
	67. (10)			
	Class E. Physical defect + Mental instability			
	12. (17) *15.* (16)			

* Died

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divided, as above mentioned, into five groups, and in each review the grouping corresponds.

Group I. Recovery complete. The patients in this group are those, who have apparently regained their normal health and have resumed their occupation, showing so far no residual signs of their previous illness.

Group II. Recovery incomplete. In this group are those, who have been left with some defect, but where the complication does not take the form of the more pronounced and characteristic states of Perversion of conduct and Parkinsonism following the disease.

Group III. Perversion of conduct. This group is composed of children, who have become abnormal in conduct and have undergone a complete change of character, showing signs of moral imbecility.

Group IV. Parkinsonians. In this group are those, who have, as a complication, developed Parkinsonism during or after the initial attack.

Group V. Died. This group comprises the cases which have proved fatal up to 1928.

GROUP I. RECOVERY COMPLETE.

It is impossible to state a definite period of time, when freedom from the danger of epidemic encephalitis can be regarded as permanent. Recovery, or apparent recovery, from the acute attack does not ensure that the patient will be wholly free from further trouble, and in this series it is found that one patient, after an apparent recovery of $4\frac{1}{2}$ years, developed Parkinsonian symptoms. There is, however, no evidence of a relapse, nor recrudescence, nor extension of an infective process in the nervous system; but, rather, there is evidence of the appearance of new phenomena, which may present themselves months, or even years, after the acute symptoms of the initial attack have disappeared, and which would seem to be due to a breakdown of a mechanism, damaged in the acute stage of the disease. The presumption is that a complicated nervous system, although injured by disease, may survive the effects of impairment for a considerable time without showing disorder of function, and subsequently break down under strain. Such an assumption is in perfect accord with what is known to occur in heart disease.

In considering the recovered groups of 1924 and 1928 jointly, three types of cases are included:

(*a*) Those in which an uninterrupted and complete recovery has been made.

(*b*) Those of patients who have now recovered from complications, which were still present a year after the initial attack.

(*c*) Those of patients who, after an initial recovery, have developed complications after a year.

In the re-examination of the patients in 1928, it was found that, of the original eight recovered in the first review, there are only five who now remain

recovered (Nos. 7, 28, 32, 42, 62). Owing to the development of further symptoms after an initial recovery, it has been found necessary to transfer three patients, presumed to have been recovered in 1924, to other groups, two of these having developed Parkinsonism (Nos. 4, 43), and the third (No. 14) having become neurasthenic after pregnancy. There have been added to the recovered list, from the first review, two cases (Nos. 41, 56), both patients having recovered from complications which were still present a year after the initial illness, so that there are now altogether seven cases in this group.

Of those five patients, who have now made a complete and uninterrupted recovery, the first case (No. 7) is of a man of middle age, who showed symptoms at the onset of fever, drowsiness, diplopia, twitchings, and giddiness. His illness lasted for 6 weeks, during which time he was very nervous, although, while in hospital, he was suspected of exaggerating his symptoms. He is at present quite well, and has resumed his occupation of fireman on board an Atlantic liner.

The second case (No. 28) is that of a girl whose illness lasted for three weeks, and was characterised by drowsiness, pains all over the body, giddiness, vomiting, and diplopia, symptoms as of influenza. The girl made a rapid recovery, and was able to return to school shortly after leaving hospital.

The next case (No. 32) is that of a woman, whose illness was of 4 weeks' duration, with symptoms of drowsiness, lymphocytosis, increased pressure, and no diplopia. The patient was sufficiently recovered to return to service 2 months after her discharge from hospital. She married 6 months later, and has had one child. Owing to a contracted pelvis Caesarean section was performed at the birth. The child is healthy, and the mother made a good recovery. She remains well and fit for her household duties.

In the fourth case (No. 42) the initial illness was acute and subsided after eight weeks. The primary symptoms were lethargy, twitchings, lymphocytosis, increased pressure, marked Kernig's sign. Temp. 103° F. P. 130. R. 48. The lungs were clear to percussion, R. M. more harsh over left apex than right. The child made a gradual recovery, and was dismissed well from hospital. She has been at school since the age of 5, and is at present quite strong. Meningismus might be suspected in this case.

The fifth patient (No. 62) had mild symptoms in the initial stage, and altogether the illness lasted for 2 weeks. A few days before his admission to hospital, the patient had a fall from his cycle, and the illness commenced with drowsiness, diplopia, slight nystagmus, giddiness, and twitchings. In the initial stage he took a succession of fainting turns, after which he wept readily, and was confused in his ideas. After a few days of drowsiness he rapidly recovered, and later was dismissed from hospital well.

Of those two patients, who have now made a complete recovery from symptoms which were still present a year after the acute attack, the first (No. 41) had in the initial stage an illness lasting for 4 weeks, with symptoms of lethargy, headache, giddiness, lymphocytosis, but no diplopia. After his

discharge from hospital he had some weakness of the lower limbs and, for more than a year, salivation was excessive. This condition has now cleared up, and he is at present quite fit.

The other patient who recovered is a married woman (No. 56), in whom the onset was gradual, with drowsiness, headache, squint, giddiness, and vomiting. There was no fever and no diplopia, and the illness lasted for 6 weeks. She complained of giddiness and nystagmus for more than a year after leaving hospital, but later these symptoms disappeared and she is now well.

Of the three patients, who, after an apparent recovery, developed complications since the time of the first review, two have become Parkinsonians.

The first (No. 4), a police constable, developed Parkinsonism about 4½ years after the primary attack. His illness lasted for 4 months in the initial stage, and was characterised by pain in the right side of the neck, diplopia, nausea, giddiness, and lethargy, with intervals of delirium. He was able to resume his duties 6 weeks after leaving hospital, although for a few months he complained of pain in the right arm. He made a good recovery, and married 2 years after his illness; he has two children, both of whom are healthy. Some months ago tremors of the left arm were felt, and since then Parkinsonian symptoms have gradually developed. He has become stolid in appearance, speaks hurriedly in a thick monotonous voice, and there is excessive salivation. When walking he has a forward bend, and when sitting there is a tendency to droop from the waist. There is also a suspicion of stiffness in the left arm, and the eyesight is weak. His condition is such that it is doubtful if he will be able to continue his duties for any length of time.

The other patient (No. 43), who developed Parkinsonism, made an apparent recovery from her initial illness. She sustained a shock 3½ years after the onset, and, from that time forward, Parkinsonism has steadily progressed.

In the remaining case (No. 14) pregnancy was responsible for the development of nervous symptoms after an apparent recovery from the primary illness. This patient, a married woman, had an illness of 3 months' duration, with symptoms of delirium, restlessness, twitchings, and pyrexia. She made an apparent recovery, and at the end of the first year was seemingly well. A few months after the birth of a child she became emotional, irritable, and quick-tempered. She now suffers from violent headaches, accompanied by tremors and her eyesight has become weak.

After following out and investigating these cases of recovery it seems very doubtful, from the course of the illness and the subsequent recoveries, if all of the seven cases were of true encephalitis. Owing to the occurrence of these cases during an epidemic, and to the difficulty of diagnosis in the early stages of the disease, and also to the fact that, in the 1923 epidemic, medical practitioners were circularised regarding encephalitis, and were consequently on the *qui vive* for this "new disease," many may have been overhasty in the diagnosing and notifying of cases.

GROUP II. RECOVERY INCOMPLETE.

This is the largest of the five groups, and has been sub-divided into five classes.

Class A. Mental retardation.
Class B. Mental instability.
Class C. Nervous instability.
Class D. Physical defect. (Not Parkinsonism.)
Class E. Physical defect + Mental instability.

Class A. Mental retardation.

This class is comprised of those cases showing signs of mental backwardness. In only two of the cases in this series is there mental retardation, and both of these are of children, this process having become evident in one child at the age of 9 years and in the other at the age of 6 years.

On re-examining this class in 1928 it is found that the original one case (No. 36) still remains from the first review; another case (No. 26) has now been added, having been transferred from the Nervous instability class, as it is evident, on interrogation, that the patient's mental processes are much slower than those of the average child of her years.

In the first case (No. 36) the child was acutely ill at the onset, being fevered, restless, delirious, and later lethargic. From the time of her illness a complete change of disposition was noted. From being bright and lively she became dull and apathetic, and, on her return to school 6 months later, she made little headway, and found great difficulty with her lessons. She lacked concentration and her memory was not good. There has been no improvement in the child's condition within the last 4 years. At present she is backward and dull, and shows signs of irritability and temper. Excessive salivation and respiratory disturbance (snoring) have been in evidence for about $3\frac{1}{2}$ years.

The other case (No. 26) which has now been added was of a young child of 18 months at the time of her illness. She had initial symptoms of irritability, restlessness, wakefulness by night, and drowsiness by day. Nervous symptoms persisted for more than a year, but gradually wore off. She went to school at the age of 5, but made very slow progress. She still finds great difficulty in coping with her school work, and lately was held back a class.

Class B. Mental instability.

This class is composed of those cases, showing signs of abnormal mental excitability, without perversion of conduct or mental retardation. This milder and less distinct upset of conduct, involving a change in disposition, may be the only sign of incomplete recovery.

At present only one case (No. 9) out of the original five remains in this class. It has been necessary to transfer four cases to other groups, and to add one case from another class. Of the four cases which have been transferred,

three (Nos. 16, 64, 59) have become abnormal Parkinsonians, one patient died (No. 64), and the fourth (No. 19) has become perverted in conduct. The case (No. 60) which has been added showed nervous symptoms at the time of the first review, and was then in the Nervous instability class.

In investigating the series, it is found that this class comprises children, who are boys with one exception. In the first review the children varied in age from 6 to 12 years, and all uniformly showed, from the time of their illness, symptoms of marked restlessness with excitability, especially at night-time. In two cases (Nos. 16, 19), since transferred, the behaviour disorder assumed a more severe form, and, from the time of the acute attack, they showed extreme emotionalism, turning night into day, whistling and singing, tossing and burrowing in bed, tearing the bed-clothes, until they were utterly spent and became drowsy by day.

The following two cases illustrate the present condition of this class, showing the effect of encephalitis upon the development of the disposition of the child. Here the intelligence is good, there is no lack of moral ideas, but mental instability is evident.

In the first case (No. 9) the child had an illness of 3 months' duration with, in the initial stage, symptoms of insomnia, restlessness, twitchings, delirium, and strabismus. At the time of leaving hospital he suffered from fleeting apprehensions of emotional instability with great restlessness. Two months later he returned to school, but was nervous and fearful. He refused to leave the class-room at play-time, and informed his teacher he was afraid of someone going to do him harm. One day, when out walking with his mother, he suddenly ran ahead, always glancing backwards with a look of terror on his face; when at last she managed to get hold of him, he said, "There is someone chasing me, trying to do something to me." This abnormal condition lasted for over a year. Since his illness he has become extremely restless and emotional, showing marked eccentricities of conduct, and his disposition has changed completely. Prior to his illness he was shy and reticent, but now he will talk to anyone he meets; when in school he addresses his teacher in the middle of a lesson, and occasionally rises and walks round the class-room. In acquiring abstract knowledge he has made average progress. He is neither malicious nor vicious, but is affectionate and thoughtful in the home.

The second patient (No. 60) also shows peculiarities of conduct. His initial illness was characterised by delirium, restlessness, twitchings, and drowsiness, and lasted for 6 weeks. Following the illness a definite change of conduct was observed; from being shy and aloof, he became bold and obtrusive, and would brook no interference. He was quick-tempered, restless, and slept badly, and was unable to attend school for 8 months. Since his return to school his progress has been quite good, but the teacher complains he is difficult and quarrelsome, and at times forgets himself and where he is. On one occasion, during a lesson, he suddenly left his seat, walked to the window and exclaimed, "This is a fine day, Miss Smith." Under any emotional stress, such as a fit of

temper, salivation becomes excessive. His habits are good, and he is quite intelligent.

The following patient (No. 59), a boy, at present 16 years of age, now transferred to the Parkinsonian group—Abnormal mentality—is interesting on account of his having frequent lapses of memory. The boy showed a decided change of disposition from the time of his illness, becoming emotional, childish, and shunning his contemporaries. He repeatedly went for long walks, and afterwards had no recollection of his wanderings. On one occasion he took a walk without his boots.

Class C. Nervous instability.

This class embraces all those cases showing in a varying degree a residuum of nervous disturbances, including insomnia, drowsiness, irritability, tremor, headache, and weak eyesight.

Of the initial nineteen cases of the first review, twelve cases remain in this class (Nos. 10, 13, 18, 22, 23, 29, 30, 33, 46, 49, 61, 69). Seven cases have been transferred to other groups, and one case has now been added to the list, so that at the present time the class numbers thirteen. Of the seven cases transferred, in three cases the patients have become Parkinsonians (Nos. 11, 31, 38), two cases have made a complete recovery (Nos. 41, 56), one (No. 60) is now mentally unstable while another (No. 26) is mentally retarded. The case (No. 14), which has been added, is from the Recovered group, nervous symptoms having developed after pregnancy.

The majority in this class are adults, and it can be seen that complete recovery is the exception rather than the rule. Of those patients who have sufficiently recovered to allow them to return to work, all show residual signs of their previous illness, and complain of various forms of psychic and physical disturbances. After the acute attack of encephalitis has passed, it is common in this class to find a persisting insomnia, which in some cases lasted for months, and in a few cases for years, although, as a rule, the insomnia gradually disappeared within or shortly after the first year. Twelve patients in this class suffered from nocturnal insomnia after the acute stage, and, in all cases but two, this troublesome condition cleared up at times varying from 6 months to 2 years. In these two cases (Nos. 23, 31) insomnia still persists as a residuum.

Drowsiness is also found to occur as a late effect, but it is not a common sequel as is insomnia, having appeared only in four cases in this class, in two of which it is still evident (Nos. 18, 22), in the other two the patients have got rid of it within the first few months (Nos. 13, 30).

Of the nineteen cases in this class at the time of the first review, irritability occurred in twelve cases, weak eyesight in four cases, headache in three cases, and tremors were absent. In ten cases there was excessive salivation, and in one there was in addition respiratory disturbance (hyperpnoea). Of the thirteen cases at present in this class, irritability occurs in ten, weak eyesight occurs in eight, headache in five, and tremors in three. Eight patients have excessive

salivation, and two have also respiratory disturbance (clearing of throat and yawning).

From the above findings it can be seen that nervous symptoms, with the exception of insomnia, have increased during the five years.

In one case of this class (No. 61) it is interesting to note a sequela, simulating the acute attack 4 years after the initial illness. The patient was suddenly stricken down with severe headache, vomiting, and loss of power of the lower limbs, symptoms similar to those in the initial attack. For 10 days she remained in a lethargic condition, after which these symptoms gradually disappeared. At present she suffers from irritability, headache, and weak eyesight.

Class D. Physical defect.

This class is made up of those patients suffering from physical disabilities without signs of Parkinsonism.

There were originally two cases in this class, and of these two cases, one now remains (No. 67), while the other has been transferred to the Physical defect + Mental instability class. The latter case (No. 12), who, after her illness, became abnormally fat, has, since the first review, become mentally unstable in addition to this physical defect. She is extremely emotional, violent tempered, and shows unaccountable aversions to people, especially to men.

The remaining case (No. 67) is unique and of unusual interest, being the only case in the series with severe physical disability without Parkinsonism or mental disturbance. This case, of a girl aged 5, showed initial symptoms of fever, vomiting, headache, delirium, restlessness, drowsiness, twitching of the facial muscles, and strabismus. The child was very drowsy during the first few weeks of her illness, but was dismissed well from hospital 6 weeks after the primary attack. She remained at home for the next few months, and then resumed school. At that time, she complained of pain in the right leg, which gradually increased. Two years ago she was sent to a special school owing to her physical condition. The child tired very easily, and the mother then noticed a slight wasting of the right leg. This wasting became more pronounced, later the foot dropped and, consequently, walking became difficult.

At present the right leg is about half an inch shorter than the left, the muscles are atrophied, and the foot is dropped and turns inward. She flings her foot when walking. She complains a good deal of pain in the leg and stiffness and numbness on awakening in the morning; during the winter she suffers from chilblains on the soles of both feet. She is troubled with frontal headaches, and, when in bed, the head perspires freely. She sighs and yawns frequently; her eyesight is weak, and for the last 3 months she has worn spectacles. There is no excessive salivation, although this was slightly present after leaving hospital. She is quite intelligent, is well up to the average at school, and is equable in temper. On examination the knee jerks were elicited on both sides, the right somewhat brisk, and the temperature of the right foot was lower than that of the left; otherwise physical examination was negative.

Class E. Physical defect + Mental instability.

This class is composed of those suffering from physical disability, with in addition mental instability, but without signs of Parkinsonism.

At the time of the first review there were no cases in this class, but, at present, there are two, the first case (No. 12) having been transferred from the Physical defective class and the second case (No. 15) having been transferred from the Abnormal Parkinsonian class. The latter case is of considerable interest owing to its simulation of other conditions.

This patient, a girl, was 11 years of age at the time of the initial illness. The onset commenced with severe pain in the right arm and the right side of the back. The following day she complained of severe abdominal pain, which persisted for 7 days, and, during that time, the child was extremely constipated. She became fevered, restless, delirious, and drowsy, and was admitted to the surgical ward, diagnosed as a case of appendicitis. Fortunately, owing to the presence of myoclonic movements of the abdominal wall, she was saved from an unnecessary operation. The child remained in hospital for 6 months and, at the time of her dismissal, her speech was slurred, and there was ptosis of both eyelids present. A year later she suffered from nocturnal insomnia, and, owing to severe pain in the left leg, was unable to attend school. At this time Parkinsonism seemed to develop. There was a tendency, when sitting, to adopt a markedly crouching attitude and, when standing or walking, there was a decided stoop. The arms were held stiffly, and the eyes had a staring expression, winking seldom, with slight bilateral ptosis of the eyelids. The face was somewhat masked, and increased salivation was present. There was continuous twitching of both arms, the right arm especially being affected. Hyperpnoea was also evident, and had been present since the onset. Abdominal pain still persisted, and, regularly after meals, there was vomiting without nausea. After her illness, her teeth dropped out, one by one.

Within the last 3 years improvement has been gradual; abdominal pain and vomiting have disappeared, salivation has become normal, and twitchings of the arms have ceased, and, at the present time, there is no sign of Parkinsonism. In appearance she is ruddy and healthy, but is of stunted growth. The head and entire trunk are bent toward the left, with spasm of the spinal and occipital muscles. There is considerable lordosis and scoliosis, with a convexity to the right; the chest wall shows marked deformity (pigeon chest). Pain in the back of the legs has lately worn off. She becomes easily exhausted, and has not yet menstruated. A complete change of character has taken place; since her illness she has become mentally unstable, and is precocious, sly, impulsive, and quarrelsome. As in this case Parkinsonian symptoms, which appeared a year after the onset, subsequently disappeared, on retrospection it seems doubtful if this was a true Parkinsonian state.

GROUP III. PERVERSION OF CONDUCT.

This group, though small, is not without interest, and is composed of children, in age ranging from 8 to 14 years, who show as sequelae personality changes and moral delinquency.

In the review of 1924 there were three cases in this group, but, at the time of the present review, only one of that number remains. Two patients (Nos. 17, 52) have developed Parkinsonism in addition to conduct perversion, and have been transferred to the Abnormal Parkinsonian class. One case (No. 19) has been added to this group, that of a boy who, previously being mentally unstable, has since become perverted in conduct.

The behaviour syndrome, as found in the post-encephalitic child free from severe neurologic symptoms, has some special features. In this group of children, encephalitis is followed by more or less severe conduct changes, although no such transformation has been observed in the adults of the series, in whom are mostly found physical conditions and psychotic changes. This change of personality and character in the child is due to the fact that the nervous system has been attacked during the formative period of development. The personality of the child is transformed by the virus of the disease, so that the ill-effects following such an infection are disastrous and far-reaching. In some cases, disorders of conduct have been such that these young people have been brought into conflict with the law, and ultimately consigned to mental institutions. These children are impulsive, destructive, and violent; they lie, steal, beg, swear, and show erotic and sexual tendencies. They are not feeble-minded in the technical sense, although mentally defective in respect of morals. Their intelligence is good, and this troublesome and dangerous behaviour would seem to be caused by an involvement of the emotional, rather than of the intellectual, tendencies; thus, after the commission of an impulsive act, regret is often immediately expressed (Nos. 17, 19).

Unless there are steps taken to provide proper supervision and training of these children, there is the danger that in the future crime may be rife amongst this community. On the other hand these young people, under right conditions, might be so trained that there would be a surprising reduction in undesirable behaviour.

The following case well illustrates the characteristics of this group. The patient (No. 19), a boy, 9 years of age at the time of his illness, had severe chorea of 7 days' duration in the initial attack. For over a year there was extreme restlessness and an inversion of the sleep rhythm with nocturnal excitement and drowsiness during the day. His character, from the time of his illness, changed completely, and, after the first year, he became unmanageable, and was expelled from school owing to bad behaviour. He is now completely beyond control, and it is most difficult to keep him indoors; if deterred in any way, he threatens to jump out of a three-storey window. He leaves home every day about 7 a.m., returning at a late hour, and spends his time

associating with men at the docks. He lies and steals, and, about 5 months ago, he was taken up by the police for stealing newspapers out of a shop and selling them in the street. After this he got a job with a milkman, but speedily was dismissed for appropriating the customers' money. He has violent bouts of temper, and cannot be thwarted in any way. He is constantly hitching up his stockings to the extent of tearing the tops off them. The boy is highly intelligent, his memory is excellent, and, in spite of his being absent from school for a considerable length of time, he is able to recall all he ever learned. He is bright and attractive in appearance; occasionally he becomes penitent, and seems sorry for his bad behaviour.

Group IV. Parkinsonians.

Parkinsonism is the most common and malignant form of residua, and can manifest itself at any time and at any age; once this state has been established, there is little hope of abatement, and remissions, if any, are fleeting. Most of the patients with this form of sequela realise the gravity of their malady, and feel themselves progressively growing worse. The young show no more recuperative power than those more advanced in age.

Parkinsonism has developed in eighteen cases of this series, and in eight of this number conduct changes are also present. Fifteen of these cases are below 30 years of age and three are above that age.

The Parkinsonian group is divided into two classes. Class A, Normal mentality; Class B, Abnormal mentality. The first class is composed mostly of adults, and the second class mostly of children, the latter having developed Parkinsonism in addition to Perversion of conduct.

Class A. Parkinsonism: Normal mentality.

The patients in this class show slight deviation from the normal, but they are not such as would, by common consent, be included amongst the mentally afflicted.

Of the seven patients originally in this class there are four still remaining (Nos. 8, 24, 25, 44). Three have now been transferred from this class, two of these having becoming Abnormal Parkinsonians (Nos. 20, 66), and the third (No. 37) having died. Five have been added, two (Nos. 4, 43), coming from the Recovered group, having lately developed Parkinsonism after an apparent recovery, and three (Nos. 11, 31, 38) having now been transferred from the Nervous instability class.

In many of these cases, the early phase of Parkinsonism was first recognised by a tendency to easy fatigue and a reduction of energy, with perhaps a slightly fixed facial expression. Further symptoms gradually developed with stiffness in the neck or in one or more limbs, drooping of the body, tremors of the arms or legs, difficulty and slowness in walking, rising, and sitting, monotony of speech, excessive salivation, and progressive fixity of the facial expression, until the typical Parkinsonian picture was presented. The con-

dition at this stage is sometimes stationary, but later steadily progresses; the rigidity increases, tremor becomes more marked, or is completely suppressed by the rigidity, saliva increases, and eventually the patient can no longer feed himself. At the end, emaciation is extreme, and, bed-ridden and helpless, he lies in a fixed position, staring into space.

All the patients display some disturbance in the psychic sphere, although the intellect is usually spared. To their physical disabilities is added a marked emotionalism, causing them to become a burden to themselves and to those around them. Some are hysterical, being readily exhilarated or depressed, alternately laughing and crying—from tears to laughter and from laughter to tears. Some are neurasthenic, being timorous, fearful, and tired, unable to create new thoughts or new ideas; they linger in bed most part of the day, and arise only to sit about listless and unoccupied. Others are worried, anxious, and harassed, showing an anxiety as to the ultimate issue of their trouble.

Among the group of Parkinsonians with normal mentality, only two (Nos. 4, 43) are at present able to carry on their usual occupation, although, probably before very long, these patients will require to discontinue owing to their increasing incapacity.

The following case of Parkinsonism, accompanied by neuralgias, is of special interest, being of rare occurrence. This patient (No. 44), a young woman, 22 years of age, had, in the initial phase, symptoms of drowsiness, delirium, vomiting, severe pain in the back of the head and neck, also pain in the feet and legs. She remained in hospital for 3 months, and during that time signs of Parkinsonism became evident; the face was mask-like and katatonia was present. After leaving hospital Parkinsonism gradually developed, although the neuralgic pains greatly lessened. She carried on a part-time job for about 2½ years, but was forced to discontinue owing to her physical condition. About a year ago there was a recurrence of severe pain in the back of the head and neck, shoulder blades, soles of feet, also in the joints of the large toes. This painful condition still persists, while Parkinsonism is now firmly established. In this case there is no past history of neuritis or rheumatism.

In another case (No. 11), that of a woman, 24 years of age, Parkinsonism manifested itself 4½ years after the initial attack, and, 6 months after the appearance of this syndrome, there was a sudden outburst of a maniacal nature. Immediately before the primary illness, the patient had a great deal of trouble, owing to the death of her fiancé, and to worry in business. At the beginning the illness was characterised by insomnia, delirium, headache, and diplopia. She gradually improved, and, after convalescing for a few months, was able to return to business. During the next few years she felt fairly well, except for a feeling of irritability and depression with occasional headache, until June 1927, when she complained of weakness and shakiness of the right arm and leg. Symptoms increased, and 3 months later Parkinsonism was pronounced and she was forced to give up work. In December 1927 there was a sudden attack of acute maniacal delirium, and she was confined to bed for

4 weeks. This acute condition passed off, but Parkinsonism increased, and at present she presents the typical picture of that syndrome.

Class B. Parkinsonism: Abnormal mentality.

The criterion of abnormal mentality in these patients is their mode of behaviour, including such aberration as suicidal impulse, necessitating treatment and supervision.

It is observed that all the cases in this class are of children with one exception, and, at the time of the first review, two patients (Nos. 15, 54) were in this class, one of whom still remains. It has been found necessary to transfer the other (No. 15) to the Physical defect + Mental instability class, as in this case symptoms of Parkinsonism have disappeared, while other physical disabilities have become very evident. Seven cases have now been added to the list, two cases (Nos. 20, 66) from the Normal Parkinsonian class, three (Nos. 16, 59, 64) from the Mental instability class, and two (Nos. 17, 52) from the Perversion of conduct group, so that altogether there is a total of eight cases in the class.

Although in the majority of the children showing Parkinsonism the same physical symptoms characterise the disease as in the adults with this form of sequela, there is, however, a difference in the mental attitude. Mental deterioration is found to take place prior to the development of the Parkinsonian syndrome, and, with the advancement of Parkinsonism, the psycho-motor excitement grows less, until, eventually, there is a cessation of impulsive acts. In all the children of this class, changes occur both in character and behaviour, even to the extent in some cases of utter perversion. Four of the children coming under this class (Nos. 16, 17, 52, 54) exhibit misbehaviour of the lowest order, with a history of explosive conduct, such as outbreaks of violent temper, cruelty, lying, thieving, profanity, destructiveness, and sexual abnormalities. Not all of these symptoms occur in one child, but this enumeration suggests the condition.

The following case (No. 17) is a typical example of Parkinsonism in a child, with mental deterioration. The illness commenced with fever, drowsiness, hallucinations, tremors, and strabismus. At the time of leaving hospital, 6 months after the onset, the child was still drowsy and very emotional and querulous. On returning to school, 2 months later, she was found to be uncontrollable and unresponsive to discipline, so much so that, after 3 months, it was necessary to have her removed. She was constantly in trouble, and her habits were of the lowest; she lied, stole, used obscene language, played about with faeces and urine, was violent and showed sexual abnormalities. At times, she seemed conscious of her sad behaviour, and on one occasion after striking a child, prayed, "Oh God, make me better." She was ravenous for food, and, although well fed at home, would enter neighbours' houses and seize anything in the way of food, to the extent of snatching it from people's mouths; at times her thirst was abnormal. She was certified for Woodilee Asylum 16 months

after the initial illness, and on two occasions she managed to escape. About this time Parkinsonism began to develop, and physical deterioration gradually progressed, whilst malbehaviour lessened, until finally there was a cessation of impulsive acts. Since December 1927 she has been confined to bed, a helpless wreck, in the grip of Parkinsonism and lethargy is pronounced. In this case the family history is not good, the child's father being alcoholic and the mother neuropathic.

The second case (No. 52) is that of a boy, whose misbehaviour includes a long list of misdemeanours and crimes. His illness commenced with headache, sleeplessness, later drowsiness, vomiting, diplopia, fever, twitchings and vertigo. After an illness of 5 weeks he was discharged well from hospital. He then returned to school, but his behaviour was so bad that he was expelled 2 months later. After the age of 14 he was employed by different tradespeople and was dismissed, time and again, owing to thieving, lying and violent temper. His appetite was ravenous, and he could rarely be satisfied. He was continually in trouble with the police on account of his interfering with young girls; on one occasion he almost strangled a shop-girl, but was deterred through timely intervention. Two years after his illness, he applied and was appointed to a Naval Training Ship at Devonport. He remained there for 5 months, but, as he was found to be homosexual and generally degraded in conduct, he was certified as mentally unsound. At this time a tendency to Parkinsonism was observed. When visited in Hartwood Asylum in the spring of 1928, he was going about and performing his quota of work daily. There was then evidence of the advancement of the Parkinsonian syndrome; the face was expressionless, the gaze fixed, speech difficult, but there was no loss of co-ordinated movements. He was reported to be emotional, irritable, childish and facile, with an underlying astuteness. He requires careful watching on account of homosexual practices. This patient is an illegitimate child, and his parentage is not good. He showed signs of abnormal conduct prior to his illness.

In considering the relation of the onset of Parkinsonism to mental degeneration, it is found that, in all the children of this class, mental degeneration preceded Parkinsonism, and in only one case, that of an adult, mental degeneration followed Parkinsonism. All seven children exhibited deterioration within the first few months after the initial illness, and, in the case of the adult, mental deterioration became evident about 7 months ago. This patient, a young woman (No. 66), has become very depressed owing to her physical condition and to her inability to use her hands. She is constantly wailing, "Oh my hands, my hands," with which she has become obsessed. In August 1927 she attempted to commit suicide, taking a razor to her throat, and at that time was confined for a short period in a mental institution.

From the study of the asylum cases, the family history has been found to be unfavourable to the patient. In one case (No. 20) the mother is a confirmed drunkard and shows maniacal tendencies; in another case (No. 17) the mother is neuropathic, having frequent periods of depression, and the father is

alcoholic, and was so before he married; in a third case (No. 52) there is also a family taint, the boy being illegitimate, and the father belonging to a low and degraded class. In still another case (No. 66) the family history shows a neuropathic strain in many members, one uncle being confined to Gartnavel Asylum for the past 3 years, while other relatives show signs of mental instability. Thus, it would seem that the underlying personality and the hereditary factors play an important part in this expression of the disease, and deterioration in children, traced to heredity, is greatly aggravated by the infection, although it is also produced to a considerable extent in cases with no bad history. Children below the age of 16 are more prone to severe conduct changes, becoming less vulnerable after that age.

An attempt has been made to establish the length of time between the initial attack and the onset of the Parkinsonian syndrome. Although it is often assumed that a Parkinsonian condition is a late manifestation of epidemic encephalitis, it is found, in the cases under review, that it can also occur immediately after the initial attack, or even during that time as a complication. In some cases, after the recession of the acute phase, it was observed that a definite normal interval intervened, which varied from a few months up to 5 years, while, in a few cases, the development of symptoms was so gradual and so insidious that it is difficult to fix an exact time of onset.

There are altogether eighteen cases showing Parkinsonism in the series, and the following observations give approximately the time of onset of the syndrome in relation to the acute attack.

Four patients developed Parkinsonism during or immediately after the initial attack (Nos. 8, 20, 37, 44).

Four patients developed Parkinsonism within the first year of the initial attack (Nos. 24, 25, 54, 66).

Two patients developed Parkinsonism within the second year (Nos. 17, 64).

One patient developed Parkinsonism within the third year (No. 52).

One patient developed Parkinsonism within the fourth year (No. 43).

Five patients developed Parkinsonism within the fifth year (Nos. 4, 11, 16, 38, 59).

One patient developed Parkinsonism within the sixth year (No. 31).

It is, therefore, evident that Parkinsonism is liable to occur at any time and at any age, this phenomenon having appeared in patients varying in age from 6 years (No. 64) to 53 years (No. 43).

Group V. Died.

This group comprises the cases which have proved fatal up to 1928.

Apart from the eighteen cases, which ended fatally during the first few months of the illness, there are only three cases in which death has been delayed for much longer periods. Within the first year the earliest death occurred 6 days after the onset and the latest at 5 months. Of the eighteen deaths occurring within 5 months of the onset, in one case (No. 70) pneumonia

was contracted 7 days before the end. Eleven of the patients were over the age of 16 years, and seven were under that age. Of the three deaths, which occurred after the first year, Parkinsonism was found to be the terminating factor. Two of the patients were under the age of 14, and the other was 18 years of age.

Parkinsonism in the first case (No. 37) developed during the initial attack, and lasted for 4 years and 3 months; in the second case (No. 64) this sequela developed shortly after the first year, and lasted for 2 years and 9 months; and in the third case (No. 17) the sequela developed shortly after the first year and lasted for 4 years.

ELIMINATED CASES.

In reviewing the whole series, it has been considered necessary to eliminate five cases, as, after these cases have been traced and followed out, there does not appear sufficient ground for including them in the series.

The first case (No. 35) is that of a man, aged 81, whose initial illness was characterised by drowsiness and hallucinations, the patient imagining he was very poor, and that he had no money for food. He was full of fears, and believed he was being pursued by enemies. There was no defect of speech, nor any signs of paralysis. Towards the end he was in a state of coma, and died 3 months after the onset. In considering the course of the disease and the age of this patient, it would seem that this was a case of arterial brain disease, and a post-mortem examination would have been required before a diagnosis of lethargic encephalitis could be regarded as final.

The second case (No. 65) is that of a single man, aged 43. This patient had held a position in West Africa for 24 years previous to his illness. In 1918 he had an apoplectiform seizure, and was invalided home; since then he has done no work. His illness, in 1923, commenced suddenly with symptoms of headache, vomiting, coma, and right hemiplegia; later there was mental confusion with some difficulty of speech and convergent strabismus. After 5 weeks in hospital he made gradual improvement. At present he leads a fairly active life, reading, walking, and golfing. His memory is very poor, and he is unsocial, eschewing company; this he states is due to the fact that, while in conversation, he frequently forgets what he wishes to say. On examination it is found that the pupils are equal, and react well to light and on accommodation. Bilateral nystagmus is present, but more pronounced on the right side. The knee jerks are elicited on both sides, right somewhat exaggerated. There is no Babinski sign nor ankle clonus. There is slight tongue tremor, and also tremor of the right hand on extension. It seems very doubtful whether this is a case of encephalitis lethargica, but it would require careful observation of the development and course of the illness to determine a positive diagnosis.

The third case (No. 5) is of a man, 24 years of age. Restlessness, confusion of mind, and incoherence of speech characterised the onset. The patient was 5 weeks in hospital, and later was transferred to the asylum. He had served in the war, and had suffered from shell-shock. After the initial phase of the

illness, he became childish, incoherent, and completely disorientated. His habits were dirty and there was a marked degree of dementia. He had seizures of the general paretic character, showed a considerable amount of paresis, and exhibited many of the physical signs of general paralysis of the insane. Wassermann reaction of the blood and C.S.F. were positive. The patient died a year after the initial attack, having been confined to the asylum for 11 months. This is evidently not a case of encephalitis lethargica, and, from the symptoms expressed, a diagnosis of general paralysis would seem justifiable.

The fourth case (No. 58) is of a man, aged 26, whose illness, in the initial stage, showed symptoms of headache, dimness of vision, general pains, and weakness. After leaving hospital, the patient was at home for several weeks; during that time he developed convergent strabismus, and complained of weakness of the left arm and leg. He returned to hospital for nine months, and, according to the statement of his wife, he was treated at that time by "injections into the arm." From the beginning of his illness there was a gradual loss of power, both arms and legs ultimately becoming paralysed. Towards the end he lost the power of speech and became totally blind. He died 18 months after the onset of his illness. In following the general trend of this case with its ultimate blindness, syphilis would seem a more likely diagnosis than that of encephalitis.

The last case (No. 48) is that of a man, 37 years of age. The initial symptoms were fever, giddiness, drowsiness, and strabismus of the left eye; the speech was slow and slightly slurred, and the facial expression mask-like. The patient was in hospital for a month, during which time he became steadily worse. Twitching of the arms was present, and katalepsy was easily produced. On examination, the chest was clear to percussion, R.M. vesicular, and no increased V.R. or V.F. Reflexes were equal on both sides, but slightly exaggerated. A fortnight before the end, the patient suddenly had a fit. He died 5 weeks after the onset. A post-mortem examination was held, and the findings showed a tumour of the lung with metastases in the brain and in the right suprarenal.

POLIOMYELITIS—INFLUENZAL ENCEPHALITIS—LETHARGIC ENCEPHALITIS.

A COMPARISON AND A CONTRAST.

Fever, headache, vomiting, squint, convulsions, and delirium may constitute, individually or severally, the signal of acute infection, not only of the brain or its membranes, but of such diverse organs as bone, lungs, or kidneys; they may also herald the onset of the more general toxaemias of measles, scarlet fever, or typhus. Acute cerebral signs and symptoms do not, by any means, justify a diagnosis of cerebral disease. It is, as a rule, in the course of the disease, when the confusion of the incipient attack has abated, that the phenomena, which point to the nature of the infection, begin to reveal themselves.

It is no wonder, then, that, when lethargic encephalitis appeared, the equivocal character of its initial expression should have suggested a relationship with poliomyelitis and cerebral influenza. Poliomyelitis was an endemic form of acute nervous disease, which sometimes became epidemic; it was a disease with which the public and physicians were familiar; moreover, when it occurred epidemically, the cerebral variety was by no means rare. On the other hand, cerebral influenza was a well-recognised expression of that infection, and its incidence at a time when the disease had become pandemic was not unexpected.

In these circumstances it is not surprising that attempts should have been made to correlate the clinical phenomena of the "new disease" with those of other infections with which doctors were already acquainted, and to recognise in it an aberrant variety of the more familiar infections.

It soon became apparent, however, that the new disease had a way of its own. Despite its resemblance to other cerebral disorders, it followed a course which, however varied, presented features of distinction, which rendered its recognition a matter of comparative certainty. These features were not necessarily the lethargy or torpor, not in themselves peculiar to the disease; nor yet the chorea and myoclonus, which, in their atypical characters and epidemic incidence, constituted a strange and novel phenomenon; it was rather in the aftermath or relic of convalescence that the derangement revealed its truly original character. The records of medicine contain no reference to acute cerebral disease, followed by such characteristic sequelae, as have been noted and described in the "perversion of conduct" in children and in the "Parkinsonian syndrome" in children and in adults.

There is no difficulty at this time of day, despite the fragmentary and inadequate character of our knowledge of the relation of function to the structure of the nervous system, in recognising the broad outlines which differentiate lethargic encephalitis, poliomyelitis and influenzal encephalitis from each other; for although, in fulminating forms of each infection, the anatomical degeneration may be diffuse, in average cases the pathological changes are localised more or less to regions characteristic for each infection. Thus, in acute poliomyelitis, inflammation is mostly confined to the anterior cornual cells and involves, as a consequence, the disappearance of the somatic motor fibres to voluntary muscle. In the encephalitis of influenza, the mischief predominates in the superficial grey matter of the cerebral cortex, while, in lethargic encephalitis, the foci of primary reaction lie, as a rule, in the midbrain, in the hypothalamus, and in the basal nuclei of the cerebrum.

Elementary though such an anatomical conception may appear to be, it provides a key to the characteristic course pursued by each disease, as it emerges from the confusion of the initial derangement. Once the inflammatory and destructive phase has ceased, the organism tends to rehabilitate itself in response to the activity of those nervous structures that have not been destroyed.

In the case of acute poliomyelitis, the pathological conditions are simple, and are easily correlated with the clinical effects. The loss of anterior motor cells and fibres involves a very simple organic defect. These cells and these fibres are peripheral, and their disappearance does not prejudice the efficiency of any of the complicated internal mechanisms of neural integration. The defects, which follow the disease, are due exclusively to the paralysis and atrophy of voluntary muscle, and, as the extent of the physiological defect is proportionate to the amount of anterior cornual lesion destroyed, it is not difficult to formulate a prognosis, shortly after the acute illness has passed off.

With the involvement of the cerebral cortex in influenzal encephalitis, it is not surprising to find a clinical picture in which are portrayed defects and instability of psychic functions. The prolonged convalescence, characterised by loss of memory, asthenia and emotional depression, extending over weeks, months and even years, is the hall-mark of a disease, which, more than any other, carries in its train those signs and symptoms which commonly come under the designation of toxic neurasthenia. Whereas, in poliomyelitis, recovery consists in the restitution of somatic movements that have been paralysed through muscular wasting, convalescence from influenzal encephalitis is a process less defined, and consists in the gradual rehabilitation of mental and constitutional strength. While, in the former, the defect is essentially motor and to be met by mechanical therapy, in the latter, the anomalies are mainly visceral and psychic, and subject to therapeutic measures of a more general character. In each case, however, there is a tendency from the commencement, if not to recovery, at least to gradual improvement.

In striking contrast with these is the encephalitis of the lethargic type; for, however closely it may resemble them in the initial stages, and this is not always so, its later course and the relics of its primary damage claim for it a special place in the taxonomy of disease. The kaleidoscopic character of the clinical picture, as revealed in the foregoing review of the 1923 epidemic, finds no parallel in any other disease, not even in the protean expression of syphilis. The nature of the onset is no index as to what may follow. What appears to be a satisfactory convalescence, may only be a quiescent phase preceding the onset of one of the several sequelae, which terminate in permanent disability. Physical disability, change of character and disorders of nutrition, emerge in a manner which is bewildering in our present knowledge of the structure and function of the nervous system.

There are, however, biological considerations which suggest an organic basis for the peculiar features that distinguish the disease and its sequelae. Poliomyelitis, it has been noted, affects the peripheral motor nerves to voluntary muscle, and involves a comparatively simple interference with organic unity. The virus of influenza, when it selects the central nervous system, attacks the cerebral cortex and is responsible for psycho-neurotic disorders, related to derangement of the "higher centres" of neural integration. Lethargic encephalitis, while it may be diffuse like the other two forms, has a decided

preference for the mid-brain, the hypothalamus and the basal nuclei of the cerebrum. Although the anatomical and physiological relations of the constituent elements of these regions are still obscure, it is well known to biologists that they are the oldest and most fundamental parts of the nervous system. They contain the main centres of integration for the nervous regulation of both the visceral and somatic functions of the organism. The hypothalamus is the site of closely allied connections of the nervous mechanisms that control the organic systems of digestion, circulation, and respiration. Subsidiary centres of respiration and of vasomotor activity have been localised in the medulla, but there is experimental evidence to suggest that, in the hypothalamus, all the systems, which have to do with nutrition, are connected in a complicated integration. On the other hand, somatic movements, as contrasted with visceral reactions, are regulated and co-ordinated in their automatic activity by a compendium of reflexes, whose nuclear centres lie in the mid-brain and in the base of the cerebrum. These reflexes comprise the controlling and executive mechanism, which mediates between the higher associational centres of the cerebrum and the lower effector mechanisms of the brain-stem and spinal cord, to which the anterior cornual cells are related. On their afferent side they are related to the eyes and to the vestibular apparatus, and are thus concerned in the adjustment of conjugate deviations of vision, in the maintenance of equilibrium and in the automatic control of posture and of rotatory movements of the head and limbs in co-ordinate relation to movements of the axial skeleton.

When it is remembered that the main lesions of lethargic encephalitis are situated in the mid-brain, basal nuclei and hypothalamus, just in those centres concerned in the preservation of organic harmony as a whole, it is not difficult to appreciate, in a general way, the variety and extent of complications, which this devastating malady carries in its train. It selects just that part of the nervous system whose functional derangement might seek an expression in the greatest possible varieties of directions, and it is just this conception of a functional derangement which affords a clue to a rational understanding of what must otherwise appear to be a chaotic series of sequelae.

This conception of a functional nervous derangement, associated with organic destruction of tissue, is well established in British neurology, and dates back to Hughlings Jackson. It implies, in the present context, that the various sequelae, so far from being related each to the destruction of a particular locus, are the individual expressions of the disorder of a complicated central mechanism, injured and partially destroyed in the initial inflammatory process, and dislocated subsequently by the exhaustion of stress or strain or shock.

In this way, alone, would it appear to be possible to reduce to a common biological basis such heterogenous disorders as excessive salivation, profuse sweatings and respiratory tics on the one hand, and tremors, somatic tics, giddiness and all the phenomena of Parkinsonism on the other. In this way,

also, it is possible to understand that a disease, which commences with diplopia, squint, chorea, spasm, and myoclonus, may develop into a disability, characterised by defective posture and disorders of automatic movement.

Bearing these considerations in mind, it is not surprising that emotional instability should be a feature of the disease. Those reactions, known to the psychologist as emotional, and associated with abnormal excursions of excitement and depression, are supposed by some to be the expression of exaggerated or diminished activity of the central regulating mechanisms at the base of the brain. It is, in any case, a well-recognised fact that abnormality of movement, somatic and visceral, is the fundamental and palpable evidence of emotional disorder for which, indeed, the term "emotion" is literally a verbal symbol.

Retardation, impulse and automatism are characteristics of emotional disorder, affected, as it may be, by varying states of abnormal feeling. The retardation of the victim of Parkinsonism, whose intellect is usually unimpaired, is a perfect example of psycho-motor impediment. The impulse of the naughty child exhibits the licence of excitement, in which the will no longer represents the control of rational intelligence or of disciplinary habit. Criminal offences suggest the automatism of epilepsy and of hysteria, while salivatory exaggeration and respiratory tics represent corresponding excesses in the vegetative system.

It is highly probable that uncontrollable perversion of conduct, confined as it is almost exclusively to children, is to be related to disorder of basal centres. Attacked during the formative period of development, there is an interference with those constructive processes, whereby the instinctive or phylogenetic reactions of the most fundamental parts of the brain come gradually under the influence of the higher cortical centres, concerned with the evolution of rational intelligence. It is a matter of great significance that, whatever may have been the case in epidemics elsewhere or in other epidemics in Glasgow, mental defect, in the abstract sense of intellectual deterioration, was practically non-existent in the epidemic under review. It is feasible to suggest that the difference between children and adults, in respect of aberrant behaviour, is to be construed in the light of the difference in the stage of nervous and mental development at which the disease has occurred. In the case of children, dissolution of neural integration of basal centres has been produced before the higher faculties have assumed control; in adults, behaviour has already become regulated by precept and habit, so that the licence of instinctive reaction remains under the control of social custom.

The relatively greater frequency in young people of sequelae, involving the endocrine system, is also to be correlated with the incidence of the initial disease in the formative period of life; and these sequelae have been observed in eight of the cases under review, all of whom were children at the time of the onset. Of the varied forms of endocrine disturbances, obesity, menstrual irregularities, amenorrhoea, abnormal appetite, polydipsia, and polyuria are all found to occur.

Obesity, as a residual, is present only in one case (No. 12), that of a girl, aged 12. The initial illness was characterised by lethargy, and this condition still persists. A year after the illness it was noted that there was a gradual increase in subcutaneous fat, although, previous to the illness, the patient was inclined to be thin. In 1924, at the age of 13, her weight was 44·9 kg. and her height was 135 cm. An operation for appendicitis was performed 4 years later, and at that time several layers of fat were removed from the abdomen. In 1928, at the age of 17, her weight was 73·6 kg. and her height was 150·4 cm. Her appetite has been normal throughout.

Menstrual disturbances, it has also been noted, have occurred in girls when they reach the critical age at which normal menstruation should take place, and this abnormality is present in three cases of the series. An example of Parkinsonism in association with this disorder is illustrated by the following case (No. 8), that of a girl, at present 15½ years of age, whose illness commenced 5 years ago with sleeplessness, excitability, and twitchings. Parkinsonism developed immediately after the acute phase, and has steadily progressed, until now, when a state of helplessness has been reached. At the age of 14, menstruation took place on two occasions, but since then has not occurred. In the case (No. 12), previously described, that of a girl at present aged 17, there have been only two periods of menstruation, which happened at the age of 16. The third case (No. 15) is that of a girl, who is now 16 years of age, and has failed to menstruate.

In the case of five children (Nos. 1, 17, 52, 54, 59), diabetes insipidus is very marked and all of these children have voracious appetites, rarely being satisfied; two patients (Nos. 1, 17) have in addition abnormal thirst, accompanied by frequency of micturition. One of the most pronounced cases, showing this sequela, is that of a boy (No. 1), now aged 13, who, after his illness, developed an abnormal craving for food after having full meals at home. He goes begging round doors and, during the night, arises and devours all he can lay hands on; he drinks an excessive amount of water and has frequency of micturition.

The assumption that functional instability of the complicated basal mechanism, induced by partial dissolution of neural integration, explains in a superficial way the sequelae of encephalitis, finds support in the occurrence of such sequelae after knocks, shocks, and blows. This is clearly demonstrated in one case of this series (No. 43), a married woman of middle age, who, having made an apparent recovery from the initial illness, was able to resume household duties for 3½ years, when, suddenly, she sustained a shock, news being broken to her during the night of the serious illness of her daughter. Immediately after this happening symptoms of Parkinsonism appeared, and since have steadily developed.

[There is satisfactory evidence to show that in six cases of the series (Nos. 1, 9, 11, 17, 66, 69) a knock, shock, or blow has also acted as a precipitating factor in bringing about the onset of encephalitis, as in all six cases the

initial symptoms appeared almost immediately after the occurrence of some form of trauma. A history of a fall has been given in four other cases (Nos. 24, 43, 54, 62) and it would seem that here the fall was the direct outcome of a flaring up of the infection, as, shortly after the accident, acute symptoms manifested themselves.]

In the foregoing review an attempt has been made to portray in broad outline the main features of the Glasgow epidemic of encephalitis of 1923. The review is in no sense an intimate neurological study. It is sought, rather, to furnish a general impression of the clinical phenomena, as they first presented themselves, and to follow the picture, as it unfolded itself in the succeeding phases, one year and five years later. In this way there has been thrown into relief the characteristics which distinguish it from poliomyelitis and the encephalitis of influenza.

A critical summary of the sequelae reveals and illustrates the hypothesis that they are to be explained, not on the assumption of a progressive lesion of the nervous system such as general paralysis, but on the assumption of an initial and permanent damage to the complicated neural mechanism of the mid-brain, hypothalamus and basal nuclei. The consequent instability of the mechanism renders it prone to give expression to various forms of disability, depending on ill-defined proclivities, one of which is associated with the age of the patient at the time of the initial attack. However inscrutable its origin, however incalculable its course or obscure the conglomeration of its individual manifestations, there is no difficulty in recognising the scar it leaves on the health of the community.

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