ON THE INCIDENCE OF ENCEPHALITIS LETHARGICA AND ACUTE ANTERIOR POLIOMYELITIS IN LANCASHIRE AND ELSEWHERE.

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(With 2 Figures in the Text.)

Introduction.

Difficulties in cultivation outside the body have rendered the exact study of the immunity reactions of the filtrable viruses less easy than in the case of many of the bacteria, and the extension of our knowledge of immunity in these infections is at the present time largely dependent upon observation of the behaviour of human beings when exposed to infection through natural channels. For this reason it is important that the utmost use should be made of such reliable statistics as are available for the study of the epidemiology of such diseases as Encephalitis Lethargica and Acute Anterior Poliomyelitis, with a view to understanding their mode of spread and obtaining some clue as to how they may in the future be controlled.

The chief diseases of man believed to be due to the agency of filtrable viruses are (1) small-pox and vaccinia, chicken-pox, zoster, herpes simplex, measles, mumps, acute anterior poliomyelitis, encephalitis lethargica, acute disseminated encephalomyelitis, and perhaps molluscum contagiosum, trachoma, rubella and the common cold, all of which are believed to be transmitted directly from man to man; (2) yellow fever, dengue, trench fever, typhus, Japanese river fever, Pappataci fever and Rocky Mountain fever, which are transmitted by a specific insect mite, or tick vector; (3) rabies and foot-and-mouth disease, which are transmitted from animals to man.

In the second group of diseases immunity after attack is known to be strong in all cases of yellow fever, whose serum can be shown experimentally to be protective for about 7 years; in dengue it may last several years, though second attacks have been known to occur as early as 7 months; in typhus it is not thought to be very lasting, but second attacks are usually mild; in trench fever, and Japanese river fever also, it lasts only a short time, re-infection having been observed after 3 months, whilst in Pappataci fever second attacks have been observed after a few weeks. To most of this group of diseases children living in endemic areas are relatively insusceptible, but they exhibit what appear to be mild, abortive attacks, often repeated, and since the indigenous popula-

tions of such areas are throughout life much less subject to severe attack than are immigrants, it is reasonable to conclude that an immunity is built up by these repeated attacks.

In the case of yellow fever it has indeed been demonstrated in West Africa that the serum of villagers may be protective to monkeys, although no frank cases of the disease are known to have occurred in the village. The Formosan aborigines are likewise almost immune to Japanese river fever. In areas where typhus epidemics recur from time to time, children are undoubtedly subject to mild and scarcely recognised attacks, and they are believed to provide the reservoir of infection from which these epidemics arise. Dengue epidemics are observed in some areas to occur at intervals of 3 to 10 years, and if the interval is long the same people may be attacked, though the second attack is not as a rule so severe.

The diseases of the first group do not present any unique epidemological features which are not exhibited by some bacterial diseases. Their infectiousness varies from a high degree, as in measles and variola major, to a very low degree as in encephalitis lethargica. Infection via the naso-pharyngeal route seems to be common to most of this group, except vaccinia and molluscum contagiosum. Carriers play a large part in the spread of acute anterior poliomyelitis, for only a small proportion of persons who have been exposed to infection and whose serum has become protective to monkeys exhibit any symptoms of involvement of the central nervous system. I shall show that there is some justification on statistical grounds for believing that the same is true, to an even more striking degree, of encephalitis lethargica.

Most of the first group of diseases mentioned above are endemic in England, and it is possible to utilise such notification records as exist for statistical studies of the behaviour of populations exposed to them. This has been done in the present contribution in regard to encephalitis lethargica and acute poliomyelitis in the county of Lancashire and some of the large towns of England and Wales.

Encephalitis lethargica.

Encephalitis lethargica provides us with an almost unique opportunity to study the widespread reaction of an unprotected population to a new epidemic disease. It was described first as a distinct entity in May, 1919, by von Economo, and in that and the following year it spread through Europe. Whether it is in fact a new disease or not cannot of course be stated with certainty, but at least cases had not occurred prior to 1917 with sufficient frequency as to be described by medical writers, and it may safely be assumed that when it reached England in 1918 it found a population unaffected by any immunity produced in the past. The first cases in Britain were reported in London and in Sheffield early in 1918. During the first 6 months of that year it was chiefly apparent round the large population centres of the midlands and eastern counties, but towards the end of the year it spread to the west of

England[1]. It was made a notifiable disease from the beginning of 1919, and 541 cases were notified in England and Wales during 1919, a rate of about 14 per million living. In the course of that year the disease, to all appearances in a somewhat random fashion, spread itself over most of England. The successive totals of annual notifications from 1920 to 1923 were 890, 1470, 454, 1025, and in the next year, 1924, the total suddenly rose to 5039, afterwards gradually declining to 1036 by 1929. The histogram in Fig. 1 represents the annual notified cases in England and Wales over the 11 years 1919–29, and in Table I are given the annual numbers of cases notified, the notification rates per million of the population in 1925, and the annual deaths registered in England and Wales during 1919–29. For comparison of the trend of incidence during that period, the numbers of cases and of deaths in Sweden, Denmark and Holland, according to an international survey of the disease made by the Health Section of the League of Nations[2], are also given.

Table I.

	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929
England and Wales:											
Cases notified	541	890	1470	454	1025	5039	2635	2267	1615	1308	1036
Deaths registered	290	471	729	339	531	1407	1372	1325	1155	1072	1037
No. of cases per million population	14	23	38	12	26	130	68	58	41	34	27
Sweden:											
Cases notified	—	352	1512	192	530	301	198	153	129	144	136
Deaths registered	5	134	370	79	181	119	114	107	91	80	?
Denmark:											
Cases notified	—	223	138	42	87	107	150	72	116	105	139
Deaths registered	—	?	57	39	30	57	76	65	?	?	?
Holland:											
Cases notified	—	—	—	—	—	35	120	85	101	67	85
Deaths registered	—	—	85	47	41	53	59	59	64	47	39

The mean annual rate per million living during the decade 1920–29 was 45·6 in England and Wales and 43·5 in London. The county most heavily affected was Lancashire, the mean annual rate being about 68 per million. Through the courteous co-operation of the County Medical Officer of Health, Dr Butterworth, it has been possible to analyse the records of all patients who during the decade 1920–29 were either notified as suffering from encephalitis lethargica or registered as dying from it in the whole Administrative County of Lancashire, with the exception of a few small districts[3].

The notifications and deaths in each separate area during 1920–29 are shown in Table II. These figures are corrected for duplication and transfer, and their total may differ slightly from previously published totals. In the districts

[1] The early history of encephalitis lethargica in England and Wales has been studied in a Ministry of Health Report, published in 1922. *Reports on Public Health and Medical Subjects*, No. 11.

[2] League of Nations, Health Section. *Monthly Epidemiological Report*, **9**, No. 8, August 15, 1930, pp. 329–333.

[3] Urban districts of Great Harwood, Huyton, Leyland, Little Crosby, Little Lever, Poulton-le-Fylde, Urmston, Wardle, Widnes and the rural district of Sefton.

Table II. *Total incidence of encephalitis lethargica and acute poliomyelitis in Administrative County of Lancashire*, 1920–29.

No. of area	Registration area	Encephalitis lethargica: Cases notified	Encephalitis lethargica: Deaths of cases notified	Encephalitis lethargica: Deaths of cases not notified	Acute poliomyelitis: Cases notified	Acute poliomyelitis: Deaths of cases notified	Acute poliomyelitis: Deaths of cases not notified
	Urban Districts and Municipal Boroughs.						
1	Abram	4	.	.	.	.	.
2	Accrington	19	11	6	5	.	1
3	Adlington	.	.	.	.	.	.
4	Ashton-in-Makerfield	4	.	.	11	4	.
5	Ashton-under-Lyne	32	13	13	1	.	.
6	Aspull	3	2	.	.	.	.
7	Atherton	32	9	2	2	.	1
8	Audenshaw	4	1	1	2	.	.
9	Bacup	6	4	3	2	.	.
10	Barrowford	.	.	1	.	.	.
11	Billinge and Winstanley	3	.	1	.	.	.
12	Blackrod	2	1	.	1	.	.
13	Brierfield	10	5	.	.	.	.
14	Carnforth	.	.	.	.	.	.
15	Chadderton	17	9	6	3	1	.
16	Chorley	12	8	2	5	2	.
17	Church	1	1	.	.	.	.
18	Clayton-le-Moors	3	.	1	.	.	.
19	Clitheroe	8	3	2	2	1	.
20	Colne	15	3	2	1	.	.
21	Crompton	10	4	.	3	.	.
22	Croston	.	.	1	.	.	.
23	Dalton-in-Furness	4	4	.	.	.	.
24	Darwen	30	20	1	3	.	.
25	Denton	9	5	1	1	.	.
26	Droylsden	5	.	1	1	.	.
27	Eccles	27	8	6	5	.	.
28	Failsworth	31	14	.	.	.	.
29	Farnworth	26	7	.	2	.	1
30	Fleetwood	16	12	.	3	.	1
31	Formby	2	.	.	.	.	.
32	Fulwood	2	1	1	.	.	.
33	Golborne	4	2	.	.	.	.
34	Grange-over-Sands	3	3	.	1	1	.
35	Great Crosby	8	4	2	1	.	.
36	Great Harwood*	.	.	.	.	.	.
37	Haslingden	23	7	2	.	.	.
38	Haydock	2	2	1	2	.	.
39	Heywood	22	9	3	1	.	.
40	Hindley	14	8	.	2	.	.
41	Horwich	8	4	1	1	.	.
42	Huyton-with-Roby*	.	.	.	.	.	.
43	Ince-in-Makerfield	14	.	.	.	.	.
44	Irlam	7	4	.	2	1	.
45	Kearsley	.	.	1	1	1	.
46	Kirkham	1	.	.	.	.	.
47	Lancaster	18	9	3	5	.	.
48	Lathom and Burscough	10	4	2	1	.	.
49	Lees	1	1	.	.	.	.
50	Leigh	27	12	8	.	.	.
51	Leyland*	.	.	.	.	.	.
52	Litherland	7	2	1	.	.	1
53	Littleborough	6	5	1	1	.	.
54	Little Crosby*	.	.	.	.	.	.
55	Little Hulton	4	1	4	.	.	.
56	Little Lever*	.	.	.	.	.	.
57	Longridge	1	1	.	.	.	.
58	Lytham St Annes	9	2	.	1	.	.
59	Middleton	24	18	1	2	.	.
60	Milnrow	2	1	.	2	.	.
61	Morecambe and Heysham	9	7	.	2	.	.
62	Mossley	1	.	.	2	.	.
63	Nelson	15	12	3	.	.	.
64	Newton-in-Makerfield	15	10	1	4	2	.
65	Norden	2	1	.	.	.	.
66	Ormskirk	8	.	.	.	.	.
67	Orrell	1	.	.	3	1	.
68	Oswaldtwistle	8	6	.	.	.	.
69	Padiham	2	.	.	2	1	.
70	Poulton-le-Fylde*	.	.	.	.	.	.
71	Preesall	3	2	.	.	.	.
72	Prescot	2	.	.	.	.	.
73	Prestwich	8	4	2	3	.	.
74	Radcliffe	25	6	.	5	1	.
75	Rainford	.	.	.	.	.	.
76	Ramsbottom	7	2	3	4	.	.
77	Rawtenstall	21	4	3	5	.	1
78	Rishton	3	.	2	.	.	.
79	Royton	12	9	7	.	.	.
80	Skelmersdale	5	.	.	.	.	.
81	Standish and Langtree	9	1	.	1	.	.
82	Stretford	59	27	10	3	1	2
83	Swinton and Pendlebury	41	13	.	2	.	.
84	Thornton Cleveleys	2	2	.	4	.	.
85	Tottington	5	1	1	1	.	.
86	Trawden	1	1	.	.	.	.
87	Turton	8	1	.	2	.	.
88	Tyldesley and Shakerley	11	4	.	4	.	.
89	Ulverston	7	5	.	.	.	.
90	Upholland	2	2	.	.	.	.
91	Urmston*	.	.	.	.	.	.
92	Walton-le-Dale	4	2	1	2	.	.
93	Wardle*	.	.	.	.	.	.
94	Waterloo and Seaforth	20	5	2	7	.	.
95	Westhoughton	21	7	4	1	.	.
96	Whitefield	8	1	.	1	.	.
97	Whitworth	2	2	.	1	.	.
98	Widnes*	.	.	.	.	.	.
99	Withnell	1	1	.	.	.	.
100	Worsley	10	3	1	1	.	.
	Rural Districts.						
101	Barton-on-Irwell†	12	6	.	2	.	1
102	Blackburn	1	.	.	1	.	.
103	Burnley	8	.	2	1	.	.
104	Bury	9	2	.	2	.	.
105	Chorley	5	4	.	1	1	.
106	Clitheroe	8	.	.	.	.	.
107	Fylde	1	.	.	1	.	.
108	Garstang	2	2	1	1	.	.
109	Lancaster	5	2	.	1	.	1
110	Leigh	6	3	.	2	.	.
111	Limehurst	4	4	1	.	.	.
112	Lunesdale	1	.	.	.	.	.
113	Preston	8	3	.	4	.	1
114	Sefton*	.	.	.	.	.	.
115	Ulverston	7	6	1	2	.	.
116	Warrington	14	3	.	3	2	.
117	West Lancashire	24	9	1	5	.	.
118	Whiston	7	.	1	.	.	.
119	Wigan	3	.	.	1	.	.

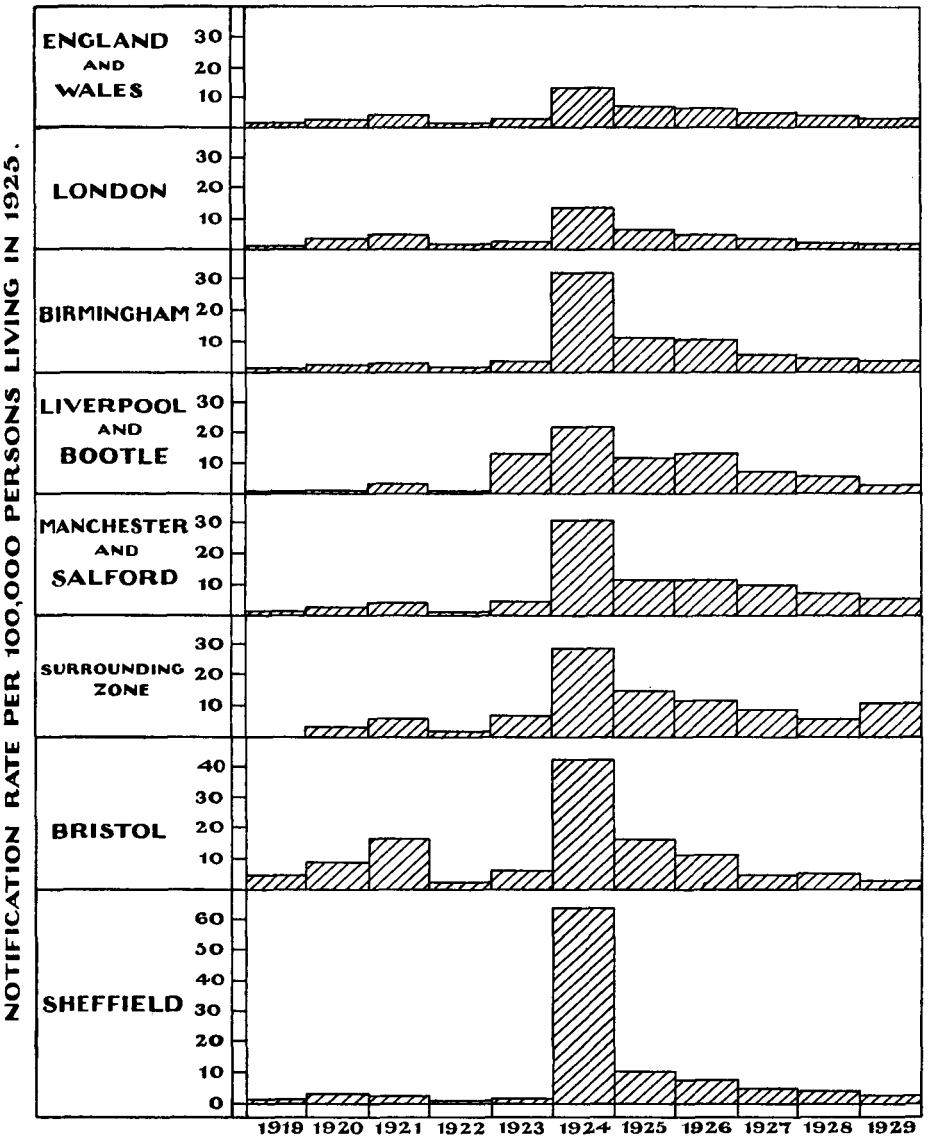
* Records not available.

† Records obtained too late for inclusion in Table V.

for which the original records were not available there were 36 cases notified and 22 deaths according to the Annual Reports of the Medical Officers con-

FIG. I

INCIDENCE OF ENCEPHALITIS LETHARGICA 1919–29



cerned. The total notified cases in the areas studied were 1022, of whom 423 died, and in addition 129 deaths were registered of cases not previously notified. It is known that notification of this disease is not quite complete, and if death occurs quickly the notification is sometimes omitted, as the above figures

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	Urban Districts and Municipal Boroughs.						
1	Abram	4	.	.	.	.	.
2	Accrington	19	11	6	5	.	1
3	Adlington	.	.	.	.	.	.
4	Ashton-in-Makerfield ...	4	.	.	11	4	.
5	Ashton-under-Lyne ...	32	13	13	1	.	.
6	Aspull	3	2	.	.	.	.
7	Atherton	32	9	2	2	.	1
8	Audenshaw	4	1	1	2	.	.
9	Bacup	6	4	3	2	.	.
10	Barrowford	.	.	1	.	.	.
11	Billinge and Winstanley	3	.	1	.	.	.
12	Blackrod	2	1	.	1	.	.
13	Brierfield	10	5	.	.	.	.
14	Carnforth	.	.	.	.	.	.
15	Chadderton	17	9	6	3	1	.
16	Chorley...	12	8	2	5	2	.
17	Church	1	1	.	.	.	.
18	Clayton-le-Moors ...	3	.	1	.	.	.
19	Clitheroe	8	3	2	2	1	.
20	Colne	15	3	2	1	.	.
21	Crompton	10	4	.	3	.	.
22	Croston...	.	.	1	.	.	.
23	Dalton-in-Furness ...	4	4	.	.	.	.
24	Darwen...	30	20	1	3	.	.
25	Denton...	9	5	1	1	.	.
26	Droylsden	5	.	1	1	.	.
27	Eccles	27	8	6	5	.	.
28	Failsworth	31	14	.	.	.	.
29	Farnworth	26	7	.	2	.	1
30	Fleetwood	16	12	.	3	.	1
31	Formby	2	.	.	.	.	.
32	Fulwood	2	1	1	.	.	.
33	Golborne	4	2	.	.	.	.
34	Grange-over-Sands ...	3	3	.	1	1	.
35	Great Crosby	8	4	2	1	.	.
36	Great Harwood* ...	.	.	.	.	.	.
37	Haslingden	23	7	2	.	.	.
38	Haydock	2	2	1	2	.	.
39	Heywood	22	9	3	1	.	.
40	Hindley	14	8	.	2	.	.
41	Horwich	8	4	1	1	.	.
42	Huyton-with-Roby* ...	.	.	.	.	.	.
43	Ince-in-Makerfield ...	14	.	.	.	.	.
44	Irlam	7	4	.	2	1	.
45	Kearsley	.	.	1	1	1	.
46	Kirkham	1	.	.	.	.	.
47	Lancaster	18	9	3	5	.	.
48	Lathom and Burscough	10	4	2	1	.	.
49	Lees	1	1	.	.	.	.
50	Leigh	27	12	8	.	.	.
51	Leyland*	.	.	.	.	.	.
52	Litherland	7	2	1	.	.	1
53	Littleborough	6	5	1	1	.	.
54	Little Crosby*	.	.	.	.	.	.
55	Little Hulton	4	1	4	.	.	.
56	Little Lever*	.	.	.	.	.	.
57	Longridge	1	1	.	.	.	.
58	Lytham St Annes ...	9	2	.	1	.	.
59	Middleton	24	18	1	2	.	.
60	Milnrow	2	1	.	2	.	.
61	Morecambe and Heysham	9	7	.	2	.	.
62	Mossley	1	.	.	2	.	.
63	Nelson	15	12	3	.	.	.
64	Newton-in-Makerfield ...	15	10	1	4	2	.
65	Norden	2	1	.	.	.	.
66	Ormskirk	8	.	.	.	.	.
67	Orrell	1	.	.	3	1	.
68	Oswaldtwistle	8	6	.	.	.	.
69	Padiham...	2	.	.	2	1	.
70	Poulton-le-Fylde* ...	.	.	.	.	.	.
71	Preesall	3	2	.	.	.	.
72	Prescot	2	.	.	.	.	.
73	Prestwich	8	4	2	3	.	.
74	Radcliffe...	25	6	.	5	1	.
75	Rainford...	.	.	.	.	.	.
76	Ramsbottom	7	2	3	4	.	.
77	Rawtenstall	21	4	3	5	.	1
78	Rishton	3	.	2	.	.	.
79	Royton	12	9	7	.	.	.
80	Skelmersdale	5	.	.	.	.	.
81	Standish and Langtree...	9	1	.	1	.	.
82	Stretford...	59	27	10	3	1	2
83	Swinton and Pendlebury	41	13	.	2	.	.
84	Thornton Cleveleys ...	2	2	.	4	.	.
85	Tottington	5	1	1	1	.	.
86	Trawden	1	1	.	.	.	.
87	Turton	8	1	.	2	.	.
88	Tyldesley and Shakerley	11	4	.	4	.	.
89	Ulverston	7	5	.	.	.	.
90	Upholland	2	2	.	.	.	.
91	Urmston*	.	.	.	.	.	.
92	Walton-le-Dale	4	2	1	2	.	.
93	Wardle*	.	.	.	.	.	.
94	Waterloo and Seaforth...	20	5	2	7	.	.
95	Westhoughton	21	7	4	1	.	.
96	Whitefield	8	1	.	1	.	.
97	Whitworth	2	2	.	1	.	.
98	Widnes*	.	.	.	.	.	.
99	Withnell	1	1	.	.	.	.
100	Worsley	10	3	1	1	.	.
	Rural Districts.						
101	Barton-on-Irwell† ...	12	6	.	2	.	1
102	Blackburn	1	.	.	1	.	.
103	Burnley	8	.	2	1	.	.
104	Bury	9	2	.	2	.	.
105	Chorley...	5	4	.	1	1	.
106	Clitheroe	8	.	.	.	.	.
107	Fylde	1	.	.	1	.	.
108	Garstang	2	2	1	1	.	.
109	Lancaster	5	2	.	1	.	1
110	Leigh	6	3	.	2	.	.
111	Limehurst	4	4	1	.	.	.
112	Lunesdale	1	.	.	.	.	.
113	Preston	8	3	.	4	.	1
114	Sefton*	.	.	.	.	.	.
115	Ulverston	7	6	1	2	.	.
116	Warrington	14	3	.	3	2	.
117	West Lancashire ...	24	9	1	5	.	.
118	Whiston	7	.	1	.	.	.
119	Wigan	3	.	.	1	.	.

* Records not available.

† Records obtained too late for inclusion in Table V.

indicate. A fatal termination may not be reached for several years, a fact which partly explains the lag in the fall of annual mortality behind the fall in annual notifications since the peak year of 1924 in England and Wales, as shown in Table I.

In addition to this special study of the distribution of the disease in the small towns and rural districts of Lancashire, the Annual Statistical Reviews of the Registrar-General provide information of the total notifications in each County Borough, so it has been possible to study the behaviour of the disease in the county as a whole, and also in some of the large towns in other parts of England. It is only possible here to give a brief account of the first results of this analysis.

In Table III are set out the numbers of notified cases in the large towns of more than 100,000 population outside Lancashire, a few neighbouring towns being combined.

In Table IV a similar analysis of the incidence in the County Boroughs of Lancashire is given, and in Table V a comparative analysis of the whole county. For this purpose seven groups of large towns have been taken and the intervening rural and urban areas have been mapped out into zones surrounding each of these densely populated centres. The total notifications of encephalitis lethargica during the decade 1920–29 in the seven groups of large towns numbered 2513 amongst a population estimated at the middle of 1925 to be 3,714,400, giving a mean annual rate of 67·6 per million; in the total surrounding zones of less densely populated country there were 913 cases amongst a population of 1,324,517, leading to a mean rate of 68·9 per million. The zonal figures include deaths of cases which were not notified and are therefore more complete as an estimate of the real incidence than the figures for the large towns, which should be increased by about 10 per cent. in order to make them strictly comparable with the others. Even so there is no appreciable difference between the gross incidence of the disease upon the densely populated towns in Lancashire and upon the intervening areas as a whole. When the rise and fall of incidence in successive years is studied, there is again no pronounced difference between the large population centres and the zones around them; the maximum was reached in 1924 in all the seven centres of population, and simultaneously in all the intervening areas of south Lancashire, but in the two northern areas (Preston and Blackburn) the incidence in the zonal districts reached its maximum a year later. The close correspondence between the annual distribution of incidence in town and country is illustrated in Fig. 2 for the whole of Lancashire, and in Fig. 1 for the Manchester area alone.

In Fig. 1 are shown also the rise and fall of incidence in London, Birmingham, Bristol and Sheffield. These epidemic histograms, if they may be so termed, show a remarkable similarity for all the large towns; the modal year was 1924 in all except Cardiff, Huddersfield, Leicester and Stoke, where it was delayed one or two years. In most of the towns a preliminary maximum was reached in 1921 followed by a sudden fall in the following year and a rise to a

Table III. *Notified cases of encephalitis lethargica in towns of more than* 100,000 *population, excepting Lancashire*, 1919–29.

Town	Population in 1925 (thousands)	Total cases 1920–1929	Mean rate per million	No. of notified cases											Immunisation factor *c*
				1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	
Birkenhead	155·5	90	58	4	2	3	3	14	13	13	7	10	13	12	869
Birmingham	945·9	725	77	11	20	27	13	30	301	105	100	55	42	32	1109
Bradford	290·2	157	54	2	7	20	6	12	35	26	17	15	12	7	1619
Brighton	138·3	55	40	2	6	5	—	1	7	4	17	6	7	2	2431
Bristol	386·0	440	114	18	34	62	8	23	162	62	43	17	19	10	823
Cardiff	227·3	65	29	5	6	3	1	7	10	5	13	7	6	7	3077
Coventry	129·1	133	103	10	8	5	—	7	47	19	19	14	8	6	829
Croydon	199·3	85	43	12	4	4	5	9	21	13	11	11	3	4	1929
Derby	134·7	51	38	11	4	5	—	4	18	9	3	2	3	3	2242
East Ham and West Ham ...	465·7	127	27	14	18	17	3	2	34	20	14	6	5	8	3265
Gateshead	129·0	41	32	—	1	—	—	2	13	8	5	3	1	8	3123
Huddersfield	112·1	34	30	—	1	5	1	4	3	2	9	2	3	4	3158
Kingston on Hull	297·3	143	48	2	11	6	2	1	35	23	20	13	12	20	1656
Leeds	472·9	137	29	5	9	16	5	10	42	21	9	8	10	7	3462
Leicester	242·1	113	47	—	8	9	4	11	20	26	16	9	6	4	1936
Middlesbrough	136·2	32	23	—	2	2	—	1	7	4	5	3	5	3	1034
Newcastle and South Shields...	411·7	319	77	8	10	26	6	7	102	48	47	26	29	18	919
Norwich	124·2	50	40	3	7	3	5	2	10	5	2	10	4	2	2446
Nottingham	270·6	86	32	—	6	1	4	4	29	11	18	8	3	2	2653
Plymouth	205·4	78	38	9	3	12	3	1	21	12	11	9	4	2	2257
Portsmouth and Southampton	418·7	156	37	7	17	16	3	14	33	20	15	13	16	9	2504
Sheffield	527·1	529	100	6	16	14	5	9	336	54	40	24	18	13	952
Stockport	125·9	86	68	—	1	2	—	2	37	20	6	7	9	2	1436
Stoke	278·9	80	29	3	2	8	4	5	9	18	10	5	11	8	2145
Sunderland	166·0	116	70	1	4	3	3	4	37	28	7	11	10	9	1347
Walsall and Wolverhampton...	211·1	74	35	4	3	4	2	3	34	11	7	3	6	1	2855
LONDON	4,612·0	2009	43	44	148	224	62	101	614	297	225	143	102	93	1747

Table IV. *Notified cases of encephalitis lethargica in the County Boroughs of Lancashire*, 1919–29.

County Borough	Population in 1925 (thousands)	Total cases 1920–29	Mean rate per million	No. of notified cases										
				1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929
Barrow	73·5	17	23·1	—	1	1	—	—	6	4	1	1	2	1
Blackburn	126·9	82	64·6	4	3	2	1	11	31	5	9	8	7	5
Blackpool	80·7	49	60·7	—	1	3	—	—	29	4	4	4	2	2
Bolton	180·4	108	59·9	—	—	7	1	3	40	23	8	13	12	1
Bootle	83·3	38	45·6	1	1	2	—	9	11	4	6	3	2	—
Burnley	102·3	46	45·0	1	4	1	3	6	5	2	3	13	4	5
Bury	56·9	26	45·7	—	1	2	—	3	11	3	1	2	—	3
Liverpool	856·0	720	84·1	3	17	28	5	111	190	107	115	65	54	28
Manchester	755·8	714	94·5	11	19	34	12	37	245	87	97	82	58	43
Oldham	146·2	95	65·0	4	—	4	1	17	30	7	7	14	7	8
Preston	122·9	34	27·7	2	1	2	—	1	5	5	4	8	3	5
Rochdale	92·9	49	52·7	1	2	2	—	—	13	8	14	5	2	3
St Helens	109·6	27	24·7	2	2	1	—	9	4	2	3	2	3	1
Salford	244·7	156	63·8	4	6	6	—	7	59	25	15	17	12	9
Southport	74·3	27	36·3	2	—	2	1	4	11	3	1	2	2	1
Warrington	78·3	72	91·9	2	4	4	—	—	14	8	20	11	5	6
Wigan	91·0	28	30·8	2	1	3	—	1	7	4	5	4	1	2

Table V. *Encephalitis lethargica in Lancashire, divided into seven densely populated centres and the zones surrounding them.*

Area	Population in 1925	Total cases 1920–1929	Mean rate per million	No. of notified cases* 1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	Immunisation factor *c*
Barrow, Lancaster, Blackpool, Southport, Preston	391,740	148	37·8	4	3	8	1	5	58	19	14	19	10	11	2240
Surrounding zone (*a*)	244,402	136	55·6	?	10	13	3	7	23	26	17	13	7	17	
Blackburn, Darwen, Colne, Nelson, Burnley, Accrington, Haslingden, Rawtenstall	423,070	268	63·3	5	8	6	6	24	81	28	29	32	27	27	1023
Surrounding zone (*b*)	166,668	83	49·8	?	1	6	2	3	14	18	11	12	6	10	
Rochdale, Heywood, Bury, Oldham	321,980	195	60·6	5	5	10	1	20	54	21	29	25	14	16	868
Surrounding zone (*c*)	132,475	95	71·7	?	1	7	—	4	33	10	10	10	8	12	
Manchester, Salford	1,000,500	870	87·0	15	25	40	12	44	304	112	112	99	70	52	865
Surrounding zone (*d*)	320,719	309	96·3	?	10	18	6	21	92	47	37	27	17	34	
Bolton	180,400	108	59·9	—	—	7	1	3	40	23	8	13	12	1	1493
Surrounding zone (*e*)	166,653	141	84·6	?	1	9	3	3	43	29	21	17	5	10	
Liverpool, Bootle	939,260	758	80·7	4	8	30	5	120	201	111	121	68	56	28	1002
Surrounding zone (*f*)	82,870	47	56·7	?	4	2	1	12	11	4	8	—	3	2	
St Helens, Warrington, Wigan, Chorley, Leigh	457,450	176	38·5	6	8	12	—	14	33	19	33	24	13	20	1283
Surrounding zone (*g*)	210,730	102	48·4	?	2	10	1	4	31	15	15	11	10	3	
Total large towns ...	3,714,400	2513	67·6	39	57	113	26	230	771	333	346	280	202	155	
Total surrounding zones...	1,324,517	913	68·9	?	29	65	16	54	247	149	119	90	56	88	1039

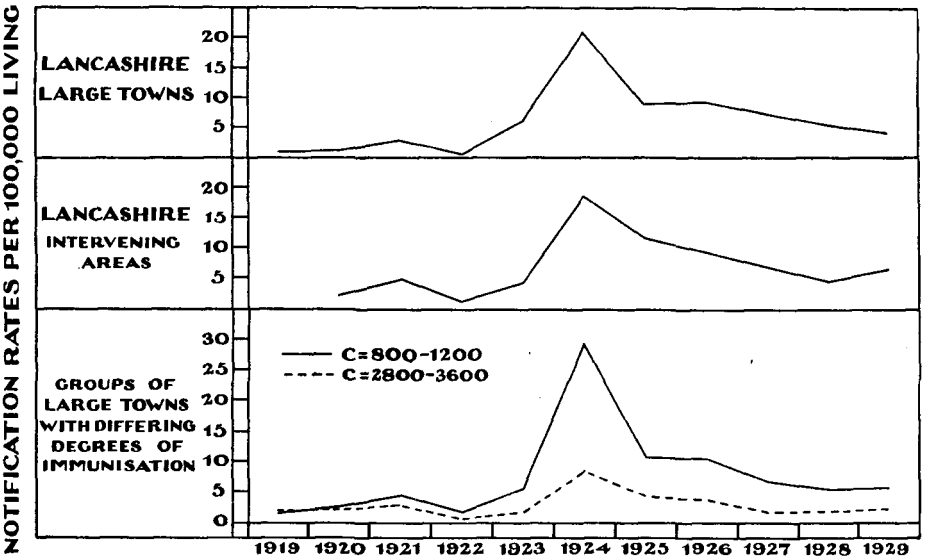
* The figures in this table include deaths of cases which had not been notified in all the surrounding zones, but this correction could not be made for the County Boroughs. See text for effect of this correction.

(*a*) to (*g*). The areas included in these zones are as follows, the numbering being that in Table II:
(*a*) 14, 22, 23, 30, 31, 32, 34, 46, 48, 57, 58, 61, 66, 71, 84, 89, 107, 108, 109, 112, 113, 115, 117.
(*b*) 9, 10, 13, 17, 18, 19, 68, 69, 76, 78, 86, 99, 102, 103, 106.
(*c*) 21, 49, 53, 60, 62, 65, 74, 79, 85, 96, 104, 111.
(*d*) 5, 8, 15, 25, 26, 27, 28, 59, 73, 82, 83, 100.
(*e*) 6, 7, 12, 29, 40, 41, 45, 55, 87, 88, 95.
(*f*) 35, 52, 94, 118.
(*g*) 1, 3, 4, 11, 33, 38, 43, 44, 64, 67, 72, 75, 80, 81, 90, 105, 110, 116, 119.

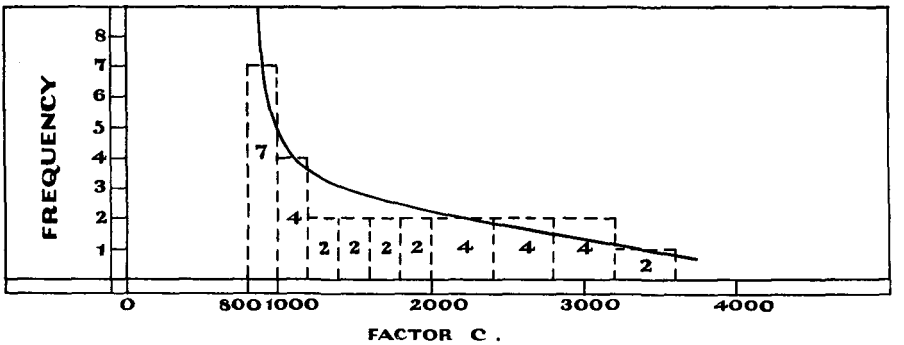
much higher level in 1924; in Sheffield, however, the epidemic reached its height in more explosive fashion. Since 1924 there has been a continuous decline to 1928, with a slight rise in some towns in 1929. Of the 34 large urban

FIG. II

ENCEPHALITIS LETHARGICA IN RELATION TO POPULATION DENSITY AND IMMUNISATION.



DISTRIBUTION OF 33 LARGE TOWNS OF OVER 100,000 POPULATION ACCORDING TO THE IMMUNISATION FACTOR C.



centres given in Tables III and V, 30 had mean annual rates during the decade between the limits 2 and 8 per 100,000; those with higher rates were Bristol 11·4, Coventry 10·3, Sheffield 10·0, and Manchester with Salford 8·7. In none of the large towns had more than 60 people out of 100,000 been notified as suffering from encephalitis lethargica up to the middle of 1924, when the epi-

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demic began rapidly to decline. Since it may be assumed that there was no previous active immunity present in the population, we may ask why this rapid fall set in. Either it was due (1) entirely to a sudden decline in the activity of the virus throughout the country; or (2) to a reduction in the proportion of susceptible persons in the population by a parallel "invisible epidemic" immunising hundreds of people to each recognised case until a level was reached at which the disease could no longer make headway; or (3) to a combination of these causes. If the first explanation is correct, we should expect to find the same average rate of fall from 1924, the peak year, to 1925 in those towns where the total incidence up to the middle of 1924 per thousand of the population had been high as in those towns where it had been low. In this case, since the depletion of the population at risk by deduction of the cases notified is a negligible factor, the new cases arising in 1925 would depend only upon R, the reservoir of infection present in the town, and A, the activity of the virus, and of these R would presumably be proportional to the number of carriers of infection left from 1924, and A would be independent of the previous incidence. Hence on this assumption the notification rates of 1925 should be highly correlated with those of 1924 in the same towns. If the second or third explanations are correct, however, the fall would be expected to be most rapid in those towns where the total incidence per thousand population up to the middle of 1924 had been greatest, owing to the greater depletion of people left at risk in those towns.

This can be readily put to the test from the data of Tables III and V, by dividing the towns into two groups according to whether the incidence up to the middle of 1924 was greater or less than 25 per 100,000, and finding the ratio of 1925 cases to 1924 cases in the groups. The first group consists of Birmingham (27), Bristol (59), Coventry (41), Leicester (26), Newcastle and South Shields (26), Sheffield (32), Manchester and Salford (29), Liverpool and Bootle (29), with a total population of 4½ millions and mean incidence to mid-1924 of 32 per 100,000; in 1924 there were 1464 cases, and in 1925 there were 536, the ratio being 0·366. London, with 4½ millions population and incidence to mid-1924 of 19 per 100,000, had 614 cases in 1924 and 297 in 1925, the ratio being 0·484. All the remaining towns, with incidence less than 25 per 100,000 up to 1924, having a total population of 6½ millions and mean incidence to mid-1924 of 16 per 100,000, had 679 cases in 1924 and 367 in 1925, the ratio being 0·540. The rate of fall from the epidemic peak therefore increases with the total incidence up to the peak, as would be expected if the fall is mainly brought about by diminishing ease of propagation of the virus owing to widespread immunisation of the population.

It seemed, therefore, worth while to examine the epidemic curves of the towns more closely with a view to discovering what is the extent of the invisible epidemic producing latent immunisation, whose presence is suggested by these results. It has been shown in Liverpool and elsewhere that cases of an atypical character do occur alongside the clinically recognisable cases of

encephalitis, and that subsequently a few of these abortive cases have developed post-encephalitic symptoms which were unmistakable. Such instances are not very frequent, but feverish catarrhal attacks attributed to mild influenza have been very rife in England since the pandemic of influenza in 1918, and it is by no means impossible that great numbers of these attacks might be abortive attacks of encephalitis lethargica in which active immunisation is produced without the virus reaching the central nervous system.

Moreover it has been demonstrated that in diphtheria latent immunisation can be brought about in the presence of carriers of the bacillus without even a sore throat being developed in the process. By indirect evidence the same thing has been shown to occur in acute poliomyelitis, cerebro-spinal fever, scarlet fever, tuberculosis, and probably in leprosy, enteric fever, typhus, cholera, and yellow fever. It is quite reasonable to suppose that the same phenomenon occurs in encephalitis lethargica, and that each notified case is only an indicator of the existence of a large body of active infection hidden beneath the surface. Let us suppose that only one out of every s infected persons develops sufficiently pronounced symptoms to be notified, but that all the s persons acquire a lasting immunity. Suppose that there is no inherent immunity to the disease, other than the power to acquire it when in contact with the virus, and that the population of England had acquired no immunity prior to 1918.

In a given town, neglecting the effects of death and migration, let

p = population, assumed constant and equal to that of 1925.

mp = effective population, meaning the total number in the population who are at risk of coming into contact with sources of infection.

n_x = number of notified cases in year x.

N_x = cumulative total of cases since beginning of epidemic to middle of year x.

Then sn_x = number during year x, of persons previously susceptible becoming immune.

sN_x = number of persons immune by middle of year x.

If the reservoir of infection remains constant in amount when the disease has become thoroughly diffused, then after the epidemic has reached its height the number of fresh people infected should, if the virus maintains a constant activity, be proportional to the effective number susceptible, *i.e.*

$$sn_x = k\,(mp - sN_x),$$

where k is a constant for all values of x, depending upon density of population and amount of circulation in the particular town. Then writing $c = s/m$ and using the suffix 0 to indicate the peak year of greatest incidence

$$c = kp/(n_0 + kN_0) = kp/(n_1 + kN_1) = kp/(n_2 + kN_2), \text{ etc.},$$

$$\therefore \quad k = \frac{n_0 - n_1}{N_1 - N_0} = \frac{2\,(n_0 - n_1)}{n_0 + n_1} = \frac{2\,(n_0 - n_2)}{n_0 + 2n_1 + n_2} = \frac{2\,(n_0 - n_3)}{n_0 + 2n_1 + 2n_2 + n_3}, \text{ etc.}$$

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The constancy of k in successive years 1, 2, 3 ... after the peak year can thus be tested, and if found to be fairly constant the equation

$$c = \bar{k}p/(n_0 + \bar{k}N_0)$$

can be used to evaluate c, where $\bar{k}$ is the mean value of k obtained by the successive equations above. By applying this method to the data in Tables III and V it is found that in some towns (Birkenhead, Bradford, Croydon, Derby, Gateshead, Leeds, Leicester, Plymouth, Stockport, Sunderland, West Ham and East Ham, and Bolton) the successive values of k do not show variations greater than might be expected from the smallness of the numbers, and c has therefore been calculated from the mean value $\bar{k}$. In London and other large towns, and in all the Lancashire areas except Bolton, the successive values of k evaluated for 1925, 1926, etc., which we may call k_1, k_2, k_3 ... decrease in fairly regular fashion, and this may be due to either the reservoir of infection or the activity of the virus, or both, diminishing or changing, and infection pressure changing in consequence. Let this be unity in the peak year and π_1, π_2, π_3 ... in successive years after, then

$$sn_0 = k'(mp - sN_0), \quad sn_1 = k'\pi_1(mp - sN_1)$$

and so on, where k' is a constant for the town. This leads to

$$c = \frac{s}{m} = \frac{k'p}{n_0 + k'N_0} = \frac{k'\pi_1 p}{n_1 + k'\pi_1 N_1}, \text{ etc.,}$$

whence

$$k' = \frac{2(n_0 - n_1/\pi_1)}{n_0 + n_1} = \frac{2(n_0 - n_2/\pi_2)}{n_0 + 2n_1 + n_2} = \frac{2(n_0 - n_3/\pi_3)}{n_0 + 2n_1 + 2n_2 + n_3}, \text{ etc.}$$

Since we do not know π_1, π_2, etc., it is not possible to calculate k' exactly, but it can be estimated by tabulating its successive values when π is given values 0·1, 0·2, 0·3, up to unity, and choosing the highest value of k' which leads to reasonably smooth values of π in successive years, for all the epidemiological evidence is against the occurrence of rapid local fluctuations in infectiousness. Thus for Manchester and Salford, $k_1 = 0{\cdot}923$, $k_2 = 0{\cdot}600$, $k_3 = 0{\cdot}482$, $k_4 = 0{\cdot}459$, $k_5 = 0{\cdot}441$, indicating a falling off in infection pressure on our assumptions. Hence trying a few values of k' in the above formulae it is found that k' cannot exceed 0·44 without assuming a higher infection pressure in 1929 than in 1924, which is unlikely, and the value which is associated with the smallest range of fluctuation in π (viz. $\pi_1 = 0{\cdot}5$, $\pi_2 = 0{\cdot}6$, $\pi_3 = 0{\cdot}65$, $\pi_4 = 0{\cdot}55$, $\pi_5 = 0{\cdot}5$) is $k' = 0{\cdot}35$, from which $c = 865$. (The mean value $\bar{k}$, that is assuming π equal to unity, leads to $c = 1255$.)

Applying the same method to other large cities, London also gives $k' = 0{\cdot}35$, $\pi_1 = 0{\cdot}65$, $\pi_2 = 0{\cdot}6$, $\pi_3 = 0{\cdot}5$, $\pi_4 = 0{\cdot}4$, $\pi_5 = 0{\cdot}4$, leading to $c = 1747$; Liverpool gives $k' = 0{\cdot}3$, $c = 1002$, and Birmingham $k' = 0{\cdot}5$, $c = 1109$. The values of c for the whole series of towns are given in Tables III and V. All the Lancashire population centres except those north of the Ribble give a c between 850 and 1500; the total intervening areas give $c = 1039$.

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The distribution of c in the 33 large towns, excluding London, is shown in Fig. 2, and seems to indicate that there is a limiting value of c in the region of 800. Now $c = s/m$, where s is the number of people undergoing latent immunisation to every case notified, and m is the fraction of the entire population of the town for whom contact with the virus is a possibility at any time. Moreover s is a function of the efficiency of the internal defensive mechanisms of man to the virus and is presumably approximately the same in each town, and m has a limiting value of unity when the whole population is being effectively exposed to the virus. It was shown in Bristol in 1920–21 that some parts of the city remained free from notified cases[1], and in some towns the virus may not have become sufficiently diffused even in 1924 to place the entire population at risk. This is the probable explanation of the distribution of c, in which there is a tailing off of higher values of c, none, however, exceeding 3500. If m is approximating to its limit of unity in those towns where c appears to approach its limit of about 800 (Bristol, Coventry, Birkenhead, Manchester, Newcastle, Rochdale and Oldham, Sheffield) it means that in these towns almost the entire population have been in danger of contact with the virus, and about three-quarters of them have become immunised by such contact. It also leads to the conclusion that upwards of 800 people can deal effectively with the virus, developing immunity in the process, to every one who develops serious symptoms of invasion of the central nervous system. If this is a true interpretation of the facts, and if the latent immunity so developed is very lasting, which of course may not be the case, it may be expected that the towns just mentioned will not be liable to further epidemics of the disease for some years, whereas towns giving large values of c may have large portions of their populations unprotected against such epidemics. It would also appear that the virus must have become fairly well diffused over the whole of south Lancashire, town and country alike, on this theory, since the intervening areas as a whole give a value $s/m = 1039$.

The total incidence of notified cases in two aggregates of large towns, (1) those giving $c = 800$–1200, namely Birkenhead, Bristol, Birmingham, Middlesbrough, Sheffield, Coventry, Newcastle and four groups of Lancashire towns, and (2) those giving $c = 3000$–3600, namely Cardiff, Gateshead, Leeds, Huddersfield, Walsall and Wolverhampton, West Ham and East Ham, is represented in Fig. 2, where the difference in the steepness of fall from 1924 to 1925 is clearly seen.

Another approximate method of estimating the value of the latency factor s is from the number of instances where more than one case was notified from the same house. In 1921 the average number of persons per dwelling in Lancashire as a whole, according to the census definition, was 4·5, so the average number of home contacts would be 3·5, and the chance of a second case being notified from any one house where a case had already occurred would be $3{\cdot}5/s$. Actually about 1100 notified or registered cases occurring in

[1] Ministry of Health. *Reports on Public Health and Medical Subjects*, No. 11, 1922.

private dwellings were followed by four second cases in the same houses. Details of these are as follows. In Leigh Municipal Borough a girl aged 15 was notified in March, 1924, and 2 months later a man aged 43 was notified from the same address. In Failsworth Urban District a girl aged 13 was notified in January, 1925, and a woman aged 51 was notified in May, 1929, from the same family and house. In Golborne Urban District a boy aged 9 was notified on March 1, 1926, and a week later a girl aged 6 from the same house. In Latham and Burscough Urban District a man aged 35 and a woman aged 55 were both notified from the same address in April, 1925. The interval of 4 years in one of these instances may have been due to the initial attack being mistaken for influenza or entirely missed, and the diagnosis being made long after from delayed appearance of post-encephalitic symptoms. In addition to these 4 cases there were several instances of 2 or more cases occurring in a large college or in county mental hospitals, but these need not be taken into account, since attention is being confined to the conditions of contact in private dwellings. Hence, equating 4 in 1100 to the expected chance, which is $3{\cdot}5/s$, this gives $s = 962$, which has a probable error of several hundreds and is therefore in reasonable agreement with the previous estimate.

Although these observations do not constitute a complete proof, they suggest that encephalitis lethargica will eventually be found to present a more striking example of latent epidemisation than any disease whose epidemiology has been investigated. The age and sex distribution of the cases notified or registered in the Administrative County of Lancashire during three successive periods, 1920–24, 1925–26 and 1927–29 are analysed in Table VI. It is noteworthy that the mean age increased as the disease became more established; thus the percentages of all cases under 10 years of age in the three periods were respectively $38{\cdot}4 \pm 1{\cdot}5$, $31{\cdot}3 \pm 1{\cdot}7$, $24{\cdot}6 \pm 1{\cdot}6$, and the percentages over 40 were $33{\cdot}4 \pm 1{\cdot}4$, $36{\cdot}1 \pm 1{\cdot}8$ and $42{\cdot}3 \pm 1{\cdot}9$. There was a curious excess of male children in the first period, but in the later periods the incidence on the sexes became the same.

ACUTE ANTERIOR POLIOMYELITIS.

This disease has been endemic in England for many years, and immunity to it has undoubtedly become widespread. The studies of Wickman and Wernstedt on the distribution of cases in Sweden during the two epidemics of 1905 and 1911–13 proved almost beyond question that invisible epidemics on a large scale accompany the recognised cases when the disease attacks communities which have not been visited by it for a long period of years. Thus it was found that villages in which only two or three cases were notified during the 1905 epidemic almost invariably escaped the second epidemic, which picked out those districts and localities which had been missed by the first one. The only reasonable explanation was that an immunising wave of infections by the virus, in which immunity was established without the central nervous system being involved, had passed over those districts where scattered cases had been

Table VI. *Distribution by age and sex of notified cases* of encephalitis lethargica and acute poliomyelitis in the Administrative County of Lancashire,* 1920–29.

	Encephalitis lethargica													Acute poliomyelitis			
	1920–24				1925–26				1927–29				1920–29		1920–29			
Ages	M.	F.	Total	%	M.	F.	Total	%	M.	F.	Total	%	Total	%	M.	F.	Total	%
0–	19	13	32	6·4	16	12	28	8·5	6	8	14	4·4	74	6·4	54	50	104	60·5
5–	15	12	27	5·4	11	6	17	5·2	9	8	17	5·4	61	5·3	19	15	34	19·8
10–	44	30	74	14·8	12	7	19	5·8	6	8	14	4·4	107	9·3	5	9	14	8·1
15–	34	25	59	11·8	17	22	39	11·8	21	12	33	10·4	131	11·4	7	2	9	5·2
20–	32	20	52	10·4	19	16	35	10·6	21	13	34	10·8	121	10·5	4	2	6	3·5
25–	18	9	27	5·4	11	12	23	7·0	17	14	31	9·8	81	7·0	2	—	2	1·2
30–	22	12	34	6·8	11	15	26	7·9	8	7	15	4·7	75	6·5	2	1	3	1·7
35–	16	15	31	6·2	14	10	24	7·3	7	17	24	7·6	79	6·9	—	—	—	—
40–	22	18	40	8·0	11	15	26	7·9	10	8	18	5·7	84	7·3	—	—	—	—
45–	25	13	38	7·6	7	7	14	4·2	12	15	27	8·5	79	6·9	—	—	—	—
50–	14	15	29	5·8	9	9	18	5·5	14	14	28	8·9	75	6·5	—	—	—	—
55–	12	13	25	5·0	14	11	25	7·6	11	10	21	6·6	71	6·2	—	—	—	—
60–	9	12	21	4·2	10	11	21	6·4	6	11	17	5·4	59	5·1	—	—	—	—
65–	5	5	10	2·0	3	4	7	2·1	8	7	15	4·7	32	2·8	—	—	—	—
70 and over	1	3	4	0·8	2	6	8	2·4	2	6	8	2·5	20	1·7	—	—	—	—
All ages	288	215	503	100·6	167	163	330	100·2	158	158	316	99·8	1149	99·8	93	79	172	100·0

* Includes registered deaths of cases not notified.

notified. The obvious cases were merely sign-posts of the passage of this wave and were accompanied by numerous febrile illnesses of indefinite character, which in some Swedish villages affected half the population. This has been confirmed by investigations elsewhere.

A survey of the epidemiology of acute poliomyelitis during recent years has been made by the Health Section of the League of Nations[1], and it is only intended in this paper to make a few observations arising out of the Lancashire data. In regard to the incidence of the disease in town and country, Kling showed that in Sweden and Roumania rural areas were more severely affected than towns, and Aycock has shown that in America there is a higher rate of incidence upon children under 10 in towns, and a corresponding excess at later ages in country districts.

Through the kindness of the County Medical Officer of Health, Dr Butterworth, I have been able to make an analysis of the distribution of notified cases during the decade 1920–29 in most of the urban and rural districts of Lancashire. Table II shows the total cases notified, the deaths of notified cases, and deaths registered of cases not notified in each separate area. In Table VII is given the distribution in the large population centres of notified cases in each separate year, as shown by the Registrar-General's Reports, and in the areas of the Administrative County surrounding them, the analysis being similar to that used in Table V, but rather more detailed. In the County Boroughs it has not been possible to add to the notifications the deaths registered of cases not notified, and a small correction amounting to about 6 per cent. is therefore necessary in making comparisons with the zonal areas.

Although most of the adult population has no doubt acquired an immunity in the towns, children may grow up without coming in contact with infection for a period of years and thus form a susceptible soil for a local epidemic. Thus Barrow-in-Furness, a town of over 70,000 persons, had no notified case in the 10 years, though 5 cases were notified in the neighbouring urban and rural districts. In all the large towns of Lancashire, using the same classification as in Table V, the mean annual rate was 1·01 per 100,000, and in all the intervening zones 1·10 per 100,000. It is remarkable that these figures are, as for encephalitis lethargica, almost identical after correcting the first figure by addition of deaths of cases not previously notified, which are included in the second rate (a 6 per cent. addition). It is evident that under present conditions of immunity in Lancashire, density of population does not affect the rate of incidence of new cases.

A study of Table VII shows that there was little if any correspondence between the occurrence of local epidemics in the large towns, and in the zones surrounding them. Thus in Liverpool and Bootle, with an expected incidence of 9 or 10 cases annually, there occurred 40 cases in 1923, but in the surrounding zone only a single case was notified in the two years 1923–24, the expected number in a random distribution being 2 cases. The only instances

[1] *Monthly Epidemiological Report*, **9**, Nos. 2, 3, pp. 47–70, 97–113, 1930.

Table VII. *Distribution of acute poliomyelitis cases in Lancashire.*

	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929
North:										
Barrow	.	.	.	.	.	.	.	.	.	.
Surrounding zone	2	.	.	1	.	.	.	.	.	.
Lancaster	.	.	.	.	.	1	3	1	.	.
Surrounding zone	.	2	.	.	.	1	.	1	.	.
Blackpool	1	2	.	.	1	1	1	2	1	.
Surrounding zone	1	.	.	3	.	.	.	2	1	3
Preston	.	.	1	.	1	1	2	.	1	1
Surrounding zone	.	.	.	1	2	.	2	2	.	1
Middle:										
Southport	.	1	1	1	.	.	2	1	1	4
Surrounding zone	.	.	.	.	.	2	2	.	.	2
Blackburn and Darwen ...	1	3	.	1	1	.	.	.	.	2
Surrounding zone	.	1	.	.	.	.	2	.	.	.
Burnley, Colne, Nelson ...	1	1	1	.	3	3	.	2	.	1
Surrounding zone	.	.	.	.	2	1	.	.	.	.
Accrington, Haslingden, Rawtenstall	.	.	.	1	1	1	3	4	2	.
Surrounding zone	1	1	.	1	1	.	.	2	1	.
Rochdale, Bury, Heywood ...	1	1	.	2	1	.	.	5	3	.
Oldham	1	.	1	1	3	.	.	.	1	1
Surrounding zone	4	1	2	4	.	.	1	1	2	2
South:										
Manchester and Salford ...	8	8	6	4	8	11	16	16	9	6
Surrounding zone	3	2	4	5	2	.	7	2	2	2
Bolton	1	1	.	1	1	.	6	3	1	1
Surrounding zone	2	.	3	1	3	1	4	1	2	1
Wigan and Chorley	1	.	.	.	1	2	4	.	2	1
Surrounding zone	.	.	1	.	.	1	.	2	1	1
Warrington and Leigh ...	2	1	.	1	.	1	1	1	1	5
Surrounding zone	.	2	1	.	1	.	2	.	1	.
St Helens	1	2	.	1	1	1	.	.	.	9
Surrounding zone	3	.	1	1	7	.	1	.	1	3
Liverpool	6	3	10	40	15	4	19	14	7	23
Surrounding zone	3	.	1	1	.	1	.	2	.	1

where a local epidemic seems to have spread into the surrounding districts to any considerable extent are Manchester, and perhaps Bolton, in 1926, neither of them at all striking. Larger epidemics covering wider areas do sometimes occur in England; an example is that of Leicester and the surrounding county in 1926, the notifications during 9 years, 1921 to 1929, being as follows:

Leicester City	2,	1,	1,	11,	0,	80,	6,	7,	3
Rest of County	5,	0,	1,	6,	1,	69,	9,	7,	4

It would appear that only when conditions are exceptionally favourable does the infection pressure become sufficient to overcome the immunity barriers to such an extent as to cause an epidemic wave to travel any considerable distance. In regions hitherto scarcely touched by the virus, however, as in Sweden in 1905, the epidemic wave may traverse long distances. The sporadic occurrence of the cases notified in the administrative county of Lancashire can be shown by analysing the grouping of cases in the 68 districts where at least 1 case occurred during the decade. In 18 districts there were 2 cases in the decade, and in 6 of these the 2 cases occurred in the same year; the chance of this happening from random causes was about 1 in 10, whereas it actually

occurred 6 in 18 times. One of these pairs of cases was that of two brothers, the only instance of a pair of cases being notified from the same house. In 9 districts having 3 cases each in the decade, all 3 occurred in the same year in one (Chadderton, May, July, August, from different streets), and 2 occurred in the same year in two instances; the chance of at least 2 cases occurring in the same year was slightly less than 3 in 10, the actual occurrence being 3 in 9. In 5 districts having 4 cases each in the decade, a pair of these occurred in the same year in three instances only; the chance of at least 2 occurring in the same year was slightly less than 4 in 10, the actual occurrence being 3 in 5. In 7 districts having 5 cases, 2 districts having 6 cases, and one district having 7 cases in the decade, coincidences of 3 cases in a year occurred twice, and of at least 2 in a year 9 times, which is not much in excess of expectation. The mean intervals between cases occurring in the same district were not appreciably different from expectation on the basis of a chance distribution, namely 2·7 years in the districts having only 2 cases as compared with an expectation of about 3 years.

In the Administrative County therefore the indications are that outbreaks during the decade were small and scattered, and it is reasonable to assume that a more or less steady level of immunity was being maintained. According to Aycock's observations, after exposure to infection about 1 per cent. of persons contract the disease. If n be the average number of persons per house, this would mean, supposing them all to be exposed to infection when a case occurs in the family, that a second case would be expected approximately in a fraction $(n - 1)/100$ of all houses where a case has occurred[1]. Greenley in 1916 found more than one case to occur in 348 families out of 8635 he investigated, or about 4 per cent., and if the average persons per family, n, may be taken as about 5, this is the proportion to be expected from Aycock's estimate. Longhin and Aurian, however, found that in the Roumanian epidemic of 1927 more than one case occurred per family in about 12 per cent. of all families attacked, a result which may be due to one or more of the following causes: (1) a larger value of n in this area, (2) a greater virulence in the epidemic, or (3) a lower proportion of the population already immunised. In the Lancashire data a second case occurred only once in 162 houses affected, and since from Census data $n = 4{\cdot}5$, the number exposed to infection in those houses may be taken as $162\ (n - 1) = 567$, of whom only 1 developed the disease in notifiable form. This low ratio may be due to the fact that the data relate to an area where the disease has been endemic for a long time, and to a steady period of incidence when there was no severe epidemic. If we approach the problem in another way, and take into account the proportion, ϕ, of the population who had not previously become immunised, and let s be the ratio of the number

[1] It has been shown that when pairs of cases occur in the same family these usually develop within 2 or 3 days of each other, suggesting a common source of infection rather than that the first infects the second. This does not, I think, really invalidate the reasoning, though it needs to be borne in mind.

becoming immunised to the number of cases being notified, there are to begin with ϕn persons at risk in the average house, and when a case occurs $\phi n - 1$ are exposed to risk of also developing it. Hence, ignoring any selective family immunity, in a fraction approximating to $(\phi n - 1)/s$ of all houses where a case occurs, a second case may be expected to follow. If this fraction is 4 per cent. as shown by Greenley's data, and if $n = 5$, this leads to $s = 25\,(5\phi - 1)$. If the population was entirely unprotected, $\phi = 1$ and $s = 100$, but if 40 per cent. were protected by previous immunity $\phi = 0{\cdot}6$ and $s = 50$.

In a recent experimental investigation[1] Aycock and Kramer tested the sera of 75 persons, from urban and rural districts in America, who had never had poliomyelitis. The serum was tested *in vitro* against a 5 per cent. virus suspension, the mixture incubated and injected into monkeys; neutralisation was regarded as indicating that the person from whom the serum was taken had acquired an immunity from exposure to previous infection, without clinical symptoms being recognised. Out of 46 living in urban districts where cases of the disease had occurred in recent memory, 32 gave the reaction for such immunity, and out of 29 living in rural districts only 6 gave the reaction. That this immunity was not inherent but acquired was shown by the fact that the percentage of immunes in the urban group increased from 42 per cent. at ages 0–4 to 87 per cent. in adults, and in the rural group from zero in children under 10 to 40 per cent. in adults. It seems probable therefore that in areas where acute poliomyelitis is endemic more than 50 per cent. of the population as a whole have acquired an immunity to it, and in a densely populated county such as Lancashire we may reasonably expect that 60 to 70 per cent. are immune. Returning to the equation above, and putting $n = 4{\cdot}5$, $\phi = 0{\cdot}35$, this gives from

$$(n\phi - 1)/s = 1/162,$$

the value $s = 93$, which serves to show in conjunction with the previous result that s, the ratio of persons being immunised to cases being notified is probably of the order 100.

The available evidence therefore points to the conclusion that, where the disease is endemic, upwards of a hundred persons acquire an immunity to the virus of acute anterior poliomyelitis, by mild unrecognised infections, to every person who develops paralytic symptoms, and that by the time adult life is reached the majority of people living in areas where the disease has become endemic have become immune by such processes of latent epidemisation. This is also indicated by the incidence of the disease on the population of different ages, as shown in Table VI. It will doubtless become more fully recognised that the obscure febrile attacks and naso-pharyngeal catarrhs of childhood are the reactions of the child to viruses of this and other diseases, and are of the greatest importance in establishing lasting future immunity to them.

[1] *Journal of Preventive Medicine*, **4**, May, 1930, pp. 189–200.

Under epidemic conditions, where the infection pressure is unusually high, or when the virus is unusually active, it is of course possible for a higher proportion of persons exposed to infection to develop serious symptoms of acute poliomyelitis, but it is very rare for an epidemic, however intense, to attack in this way more than 5 per cent. of any local population. Immunity requires time for its development, and it seems likely that what Dudley, in connection with bacterial diseases, calls the "velocity of infection," may be of importance here in determining whether the virus gains access to the central nervous system or not, and hence in producing variations in s, the latency factor.

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