DIARRHOEA AND ENTERITIS AMONGST INFANTS IN THE LONDON AREA, 1930–8

By G. PAYLING WRIGHT
AND HELEN PAYLING WRIGHT

From the Department of Pathology, Guy's Hospital Medical School

There are reasons for believing that the category 'Diarrhoea and Enteritis'* in the Registrar-General's *Reports* includes a variety of diseases resembling one another in certain major clinical features, but which arise from quite different causes. Until some years after the 1914–18 war, the infant mortality records for this category were dominated by an epidemic variety, commonly known as 'Summer Diarrhoea', whose peaks generally reached their maximum in the late summer or early autumn. Such seasonal epidemics, even on a small scale when compared with their former devastating severity, have not taken place in the London area for nearly 20 years, and, as can be seen from Table 1, they have almost disappeared also in other large English cities. Although the formerly preponderating summer diarrhoea component of enteritis is no longer distinguishable in the *Weekly Returns of Infectious Diseases* published by the Registrar-General, there still remains a large number of deaths in this category. In the Administrative County of London, in the quinquennium 1934–8, they averaged more than 700 annually, but since they are distributed much more uniformly than before, both as regards time of year and borough of occurrence, they now tend to attract less attention than they deserve. Many of these deaths—in London and some of the large cities, an actually increasing proportion of them—take place in the winter and early spring months, and the view is now held by certain pediatricians that in these infants the intestinal disorder, which dominates the clinical picture, is often the consequence of a generalized intoxication which originates in some focus of infection elsewhere, very commonly in the respiratory tract and the sinuses connected with it. This clinical conception has been termed the parenteral form of enteritis. A further form has recently attracted much attention on account of its rapid spread and high case-fatality rate amongst recently delivered infants in maternity homes; since it rarely occurs in infants more than 1 month old, it has been distinguished under the

Table 1. *Average quarterly mean mortalities (per* 100,000 *live births in the preceding* 12 *months) of infants under* 2 *years from enteritis in London and eight large English cities for* 1911–14, 1923–6 *and* 1935–8

	1911–14				1923–6				1935–8			
Place	1st	2nd	3rd	4th	1st	2nd	3rd	4th	1st	2nd	3rd	4th
London	2·20	2·05	18·58	5·61	1·65	1·57	3·72	3·17	3·55	3·10	2·81	3·10
Birmingham	2·75†	2·17	18·76	6·88	2·11	1·72	3·64	3·58	2·26	2·06	4·30	2·85
Bristol	1·37	1·67	15·37	2·93	0·95	1·19	2·47	1·72	1·13	0·82	0·81	0·78
Hull	1·13	1·54	29·01	6·74	1·19	1·51	8·14	4·21	2·90	2·36	3·83	3·41
Leeds	1·26	1·83	23·09	3·92	1·44	1·49	7·23	3·13	2·27	1·71	2·70	2·84
Liverpool	2·44	3·71	27·59	7·28	2·66	3·13	8·54	5·44	1·92	2·14	3·48	2·87
Manchester	2·96	2·40	21·63	6·00	2·65	2·84	3·73	4·27	1·69	1·59	1·83	1·50
Newcastle	1·02	1·19	14·80	4·38	1·53	1·21	5·37	3·34	3·30	3·74	3·76	5·17
Sheffield	1·50	1·90	20·07	5·33	1·49	1·84	3·76	3·00	0·87	0·73	0·96	1·34
C.B. mean	1·80	2·05	21·29	5·43	1·75	1·87	5·36	3·59	2·04	1·89	2·71	2·60

† For Birmingham, the years 1913 and 1914 only could be used for these means, owing to the extensive boundary changes which the borough underwent about this time.

* Since the present study has covered the period 1930–8, the deaths included under 'Diarrhoea and Enteritis' are those assigned to categories 119 and 120 of the *International List* (Fourth Revision, 1929). Subsequently, for the sake of brevity, the term 'enteritis' only will be used for these categories.

name of epidemic neonatal diarrhoea. In some instances of enteritis, however, no infective factor can be inferred from the circumstances that surrounded the infant's illness. Such cases, in which the case-fatality rate is much lower, are possibly attributable to nutritional disorders, and the condition is known amongst pediatricians as dietetic enteritis. Lastly, cases of enteritis in infancy can arise from specific infections with members of the dysentery group of bacteria, but since their number is relatively small, and their case-fatality rate low, this variety of enteritis contributes little to the mortality records.

The main purpose of the present investigation is to make some estimate of the relative frequency of some of the varieties of enteritis in London shortly before the recent war. Since much of the material relevant to such a study is unobtainable from published sources, we have supplemented such data as are available by a more detailed study of the deaths of infants from enteritis in the large Greater London Borough of Willesden.

DEATHS FROM ENTERITIS IN THE BOROUGH OF WILLESDEN, 1930–8

Willesden is a middle-class and upper working-class district lying in north-west Greater London; in 1935 it had an estimated population of 198,433 persons and an area of 4385 acres. Its average crude birth-rate for the period 1930–8 was 15·7, and its infant mortality was 56. Several of its wards, especially those in the south-eastern part, are old-established residential districts dating from the middle of the last century; many of their houses have been sub-divided into tenements, and consequently have a relatively high density of housing (see p. 482). The more peripheral wards have developed, chiefly within the present century (the population of the borough trebled between 1891 and 1931), as mixed residential and light industrial suburbs. In most of these wards the housing density is lower, and there are large areas of public parks and undeveloped land. Railways and light metal work provide the main industries for men, and laundry and domestic work form the main employments for women, though a large proportion of residents of both sexes travel daily for work in the more central districts of London. In the New Survey of London Life and Labour, for which surveys were made between 1929 and 1931, the inhabitants of Willesden were placed in the following social categories: poverty, 6%; unskilled, 20·3%; skilled, 49·2%; middle class, 24·5%.

The data used in the following analysis of enteritis in Willesden were very kindly made available to us by Dr G. F. Buchan, the Medical Officer of Health for the Borough. They consisted of the card-index records of the deaths of 285 infants under 2 years, which were registered as 'Gastro-Enteritis', 'Diarrhoea and Vomiting', 'Enteritis', 'Infective Enteritis', etc., all diagnoses which were ultimately included by the Registrar-General in the category 'Diarrhoea and Enteritis' (119 and 120). The present data were compared with the records of deaths from 'Diarrhoea and Enteritis' in Willesden which have been published in the Registrar-General's *Weekly Returns of Infectious Diseases*. In these returns, 286 deaths were recorded as having taken place in the borough during that period, but, for the present study, the data obtained from the cards have been preferred to those in the *Weekly Returns*, largely because the actual date of death is given in the former. In 86% of instances, death took place in some recognized hospital; in the remainder, it occurred in some unrecognized institution, or a private domicile. The standard of certification is, therefore, probably good.

Table 2

	Age in months				
	0–	1–	3–	6–	9–12
Males	5	53	57	25	12
Females	12	31	45	22	10
Persons	17	84	102	47	22
Percentages:					
Willesden, 1930–8	6·3	30·9	37·3	17·4	8·1
Greater London, 1930–8	4·7	23·5	37·8	22·1	11·9

Deaths from enteritis amongst infants under 2 years in various divisions of the population

In the following paragraphs, the primary data obtained from the index cards for the years 1930–8 have been analysed by distribution of the 285 recorded deaths into various subgroups according to sex, age, legitimacy, locality and season of year.

(i) *Sex.* The numbers of deaths amongst male and female infants were 161 and 124 respectively. The sex ratio was thus 1·30 to 1, which does not differ widely from those found for England and Wales (1·45 to 1) and for Greater London (1·46 to 1) for the same period.

(ii) *Age.* The number of deaths by sex and age, together with their percentage distribution in Willesden and Greater London, are set out in Table 2. From this table, it can be seen that the percentage distribution of deaths by age in Willesden is not very different from that in Greater London as a whole. On the assumption that all deaths take place in the middle of the age month specified, e.g. that all infants recorded as 4 months old at death were aged 4½ months, the mean age at death of all the Willesden infants under 2 years which died from this syndrome was 4·83 months.

(iii) *Legitimacy.* In Willesden, for the greater part of the period studied, two non-municipal institutions took care of the infants of unmarried mothers, many of whom resided in other boroughs. The deaths of illegitimate infants maintained in these institutions is, therefore, given separately from the deaths of similar infants from private domiciles (Table 3). In Table 4 the deaths of illegitimate infants have been analysed by age and by private or institutional addresses. From this table it can be seen that the mortality of infants aged 1–3 months in Willesden is much higher amongst illegitimate than amongst legitimate ones, irrespective of whether they come from private houses or institutions specially for such children.

Table 3

	No.	Mortalities (per 1000 live births) of infants under 12 months (1930–8)	
		Willesden	Greater London
Legitimate	218	8·70	7·63
Illegitimate:			
Private houses	31	21·98	24·61
Institutions	36	—	—

Table 4

	Age in months					
	0–	1–	3–	6–	9–12	Total
Private houses	2	15	9	3	2	31
Institutions	1	19	12	2	2	36
Totals	3	34	21	5	4	67
Percentages:						
Illegitimate	4·4	50·8	31·4	7·4	6·0	100
Legitimate	6·8	24·4	39·5	20·5	8·8	100

(iv) *Locality.* In Table 5 are set out the populations (in thousands), the degree of overcrowding (estimated both by number of persons per room and persons per acre) and the deaths of infants under 2 years (institutional illegitimate infants excluded) from enteritis in the various wards of the borough. In 1936 the wards were rearranged and increased from 11 to 13; in order to maintain comparability, therefore, the deaths in the years 1936–8 inclusive have been reallocated to the eleven wards as they existed prior to 1936. From the corrected number of births and the number of deaths from enteritis in each of the wards before their rearrangement, it is possible to calculate the ward mortalities per 1000 births for the period 1930–5 inclusive. The coefficient of correlation between these mortalities and the number of persons per room had the significant value of 0·63.

Table 5

Ward no. ...	1	2	3	4	5	6	7	8	9	10	11
Population*	13·9	14·0	12·9	9·8	13·3	16·6	20·5	15·5	15·8	16·3	35·9
Persons per room*	1·40	1·09	0·81	0·75	0·94	0·88	1·17	0·98	1·02	0·91	0·72
Persons per acre*	199	100	47	33	97	74	32	62	24	50	26
Deaths from enteritis	32	26	14	4	17	22	27	31	24	24	28

* Data from 1931 census.

(v) *Season of year.* The numbers of all infants dying from enteritis in Willesden, together with their mean ages at death, for the four quarters of the year during the period 1930–8, are shown in Table 6. Since contributory pathological conditions of the upper respiratory tract (bronchitis, bronchopneumonia, otitis media) were sometimes recorded on the cards in addition to enteritis, the numbers of such infants have been shown separately. The distribution of deaths from enteritis in Willesden thus presents much the same seasonal uniformity, with a tendency to a rather lower incidence in the summer months, as has been recorded for the Greater London area since about 1930. It is also of interest, from the possibly heterogeneous etiology of enteritis, that those dying with an associated respiratory tract complication were relatively no more numerous in the colder than in the warmer seasons.

Table 6

	Jan.–	Apr.–	July–	Oct.–
No. of deaths	80	62	65	78
No. with accompanying respiratory tract disease	12	11	10	10
Mean age at death (months)	4·94	4·32	5·79	4·41
Percentages per quarter:				
Willesden	28	22	23	27
Greater London	28	25	22	25

From this brief examination of the Willesden data it can be seen that the proportionate distributions of deaths from enteritis for sex, age, legitimacy and season, are closely the same as those for the Greater London area. To this extent at least, therefore, this borough can be regarded as a representative sample of the metropolitan population as a whole.

The extent to which the deaths from enteritis in Willesden show evidence of epidemic association

(i) *Association in time.* If the deaths from enteritis were quite independent of one another, and took place at random intervals (as, for example,

might happen if the essential etiological factor were one of the less common dietary deficiencies, associated, perhaps, with unphysiological feeding), the distribution of the numerical values of the weekly deaths over a long period should conform fairly closely to a Poisson's series.* On the other hand, should the deaths be associated with one another etiologically (as by the transference of an infectious agent from one patient to another, or by the operation of some common fluctuating environmental factor), the recorded data should depart significantly from this type of frequency distribution. The results of comparisons of such observed and calculated series can thus be used to help to distinguish between independent and connected events (for a discussion of the application of Poisson's series to uncomplicated chance distributions, see Greenwood & Yule, 1920).

When the time unit of the data is roughly the same length as the clinical course of a fatal case of the disease, however, such a simple comparison no longer suffices for testing independence, because it takes into account only the numerical values of the deaths in each unit period, and is quite unaffected by the manner in which the deaths are distributed over the whole period covered. The need for some further test to distinguish randomness of positional distribution of particular numbers within the period, as well as for randomness of distribution of individual numerical values, can readily be appreciated from a comparison of the following two short number sequences, both of which contain the same digits in the same proportions, but which are indistinguishable from one another by the aid of a simple test with a calculated Poisson's series which has a mean of the same value, viz. 1:

0	1	1	0	2	1	0	3	1	1	0	2	0	0	2	0	1	4	0	1
0	0	0	0	1	1	1	1	2	3	4	2	2	1	1	1	0	0	0	0

Various tests have been proposed for the purpose of ascertaining the degree of random structure in a sequence of numbers, but most of them are not applicable to the present data.† We have, therefore, devised the following test to help to distinguish whether or not those weeks in which deaths are more than usually numerous are also aggregated, as in the second of the two number sequences set out above. To carry out this test, short runs of weekly figures are summated, each 'clutch' being of the same length and of several weeks' duration, and the new numbers thus obtained are compared with a second Poisson's series having an appropriately larger mean. If the deaths which occurred in the 468 weeks of the present 9-year survey are combined into clutches of four to form 117 monthly figures, the existence of occasionally persistent elevations in mortality, which constitute epidemics, will cause the disagreement between the observed and the calculated figures for this series of clutches to exceed that found formerly for the weekly data. The result of the creation of clutches in a collective which is fully random, and in one which is only random numerically but not positionally as well, can be seen by coupling the numbers in the above two sequences; the new clutches of two figures are as follows:

1	1	3	3	2	2	0	2	5	1
0	0	2	2	5	6	3	2	0	0

Whereas the upper of these two new sequences still approximates as closely as before to a Poisson's series, with a mean of 2 instead of 1, the lower sequence departs widely from it. In practice, the effect of the creation of short clutches is often striking for pertussis, diphtheria and other infectious diseases.

The 468 recorded figures for the weekly deaths from enteritis amongst legitimate and non-institutional illegitimate infants in Willesden have been analysed in this way, singly and in clutches of 4 weeks, and the observed and calculated frequencies are set out in Table 7. The probabilities of agreement between the two series, as judged by the χ^2 test for goodness of fit, are also given. The probabilities found are so low that Greenwood & Yule's caveat for tests of goodness of fit made *a posteriori* does not affect the interpretation of the results. For the recorded weekly series it is evident, both from the small value of P and from the fairly symmetrical distribution of the signs of the differences between the observed and the calculated figures, that the deaths from enteritis did not take place in an entirely random manner. There are too many weeks in which either no death occurred, or in which three or more took place, for their happening to be accepted as entirely unassociated. It also appears, from the fact that the values of P for the weekly and monthly series are almost the same, that there is little or no tendency for the deaths to be associated in small-scale epidemics of several weeks' duration, such as were heretofore common.

* Agreement with a Poisson's exponential series having the same mean depends on the conjunction of a low and uniformly operating probability for an event, and a large population at risk. Von Bortkiewicz (1898), the first to apply this mathematical series to social problems, regarded the 'Law of small numbers' as applicable when the events in each unit of time do not exceed 20, and the population at risk consists of 'at least several thousand'. It has since been shown that the smallness of the numbers is relative; the necessary condition for Poisson's series is that σ^2 = the mean.

† For discussion, see von Mises (1939), Kendal (1941–2) and Davis (1941).

(ii) *Association in place.* If any large proportion of cases of enteritis nowadays results from the transfer of some specific infective agent, it seems unlikely that the domiciles of fatal cases, of which alone we have records, will be distributed randomly throughout the borough. On the contrary, it seems more likely that specific deaths will tend to be associated in some focal manner both in time and place. Since the home addresses of all the fatal cases are recorded on the cards, the data for Willesden make it possible to throw some light upon the relative frequency with which deaths are closely associated in place in an urban community of this kind, and Table 8 has been set out to show that instances in which more than one infant (apart from twins) died in the same house or in nearby houses, often within a short time of one another, are by no means rare. Since the deaths from enteritis here tabulated were the only ones that took place in these roads in this 9-year period, their clustering in time and place would seem to be closer than could be fully accounted for by chance.

Some further evidence, relevant to this aspect of the problem, comes from the study of the distribution of deaths in twenty-eight short streets, which may be defined as all those streets in Willesden which are less than a quarter of a mile long, and in each of which more than one infant died from enteritis during the 9-year period. The greatest number of such deaths in any single short street was five. Had all the seventy-one deaths which took place in these streets been distributed randomly, two deaths would probably have occurred in the same street in the same year in seven instances; actually, such pairs of deaths (including three cases in which both of twins died) happened in sixteen instances. Further, had the pairs of deaths in any single year been unassociated, the average interval separating them would have been 26 weeks; actually it was 15 weeks with twins excluded, or 12½ weeks with twins included.

An interesting feature of the analysis of the Willesden data was the frequency with which twins died from enteritis within a short time of one

Table 7

Weekly figures ...	0	1	2	3 and over
Observed	302	115	34	17
Calculated	276·0	145·7	38·5	7·8
Differences	+26·0	−30·7	−4·5	+9·2

$\chi^2 = 20{\cdot}27$; $P = 0{\cdot}00004$.

Monthly clutches ...	0	1	2	3	4	5 and over
Observed	27	31	21	14	10	14
Calculated	14·2	29·9	31·6	22·2	11·7	7·4
Differences	+12·8	+1·1	−10·6	−8·2	−1·7	+6·6

$\chi^2 = 24{\cdot}57$; $P = 0{\cdot}00005$.

Table 8

91 A Villas	11. iv. 38	74 G Road	16. xii. 32
92 A Villas	6. viii. 38	79 G Road Same surname	24. iv. 33
31 B Avenue	19. iii. 35	79 G Road surname	10. iv. 35
37 B Avenue	13. iv. 35	79 G Road	16. ii. 37
37 B Avenue	1. ii. 37	79 H Road	18. ix. 32
35 B Avenue	29. iii. 37	87 H Road	24. ix. 32
165 C Road	4. v. 34	102 J Road	15. xi. 34
144 C Road	15. viii. 34	89 J Road	3. xii. 34
111 C Road	24. viii. 34	139 J Road	10. iv. 35
307 D Road	3. ii. 37	39 J Road	20. ix. 35
307 D Road	4. vii. 37	48 K Road	9. vii. 38
184 D Road	25. xii. 37	30 K Road	15. ix. 38
154 D Road	10. ii. 38	14 L Way	10. xi. 31
8 E Road Same surname	23. xii. 31	14 L Way	19. ii. 35
8 E Road surname	7. iv. 35	9 M Crescent	4. ix. 37
145 F Lane	3. x. 30	6 M Crescent	4. x. 37
145 F Lane	23. xii. 36	17 M Crescent	3. ii. 38
		83 M Crescent	15. vii. 38

another. Amongst 249 infants (legitimate and non-institutional illegitimate) which died with this syndrome, fourteen were twins and two more were cousins living in the same house and dying within 8 weeks of one another. Assuming the usual proportions for multiple births, about six of the 249 infants might be expected to be a twin. How many twins were actually included in the 249 infants it is not possible to state, for with some pairs one may have died and the other recovered, so that the fate of one only would be recorded upon the cards. For seven pairs of twins all to have died from the same disease in this borough during this period indicates an increased specific mortality amongst such infants. While it would be tempting to assume that their deaths had resulted from some common infection, and the brief interval* that elapsed between them would accord better with this etiological hypothesis than with that of some nutritional deficiency or congenital defect, it should not be forgotten that the likelihood of premature birth, less careful hygiene, and the difficulties attending breast feeding, are all greater for twins than for single infants. Such possible reservations, however, are clearly less valid for the case of two young cousins who lived in the same house, and died from enteritis within a few weeks of one another.

One privately organized institution for the care of fifteen (later reduced to twelve) illegitimate infants was opened in Willesden in 1932. In its first year of operation, twelve infants under care there died from enteritis; in its second year a further eight, and in the next 5 years, 1934–8, nine more died from the same cause. It is important to note that only one of these twenty-nine infants was under 1 month old at the time of death, so that the outbreaks cannot be attributed to the neonatal form of enteritis (see below). The deaths occurred at various times of the year,† and usually in groups of two and three.

From the distribution of the deaths of both single infants and twins from enteritis in Willesden—remembering that there were probably three to four times as many concomitant, but anonymous, cases which recovered—it seems difficult to regard them all as the product of uncomplicated chance. It seems more reasonable to believe that some common local factor, of which the most likely seems to be some specific infective agent, was responsible for such frequent associations.

* One pair of twins died on the same day, four pairs with an interval of 2 days, and one pair each with an interval of 14 and 18 days.

† These small groups of deaths took place on the following dates: 1932, 8, 21 and 27 Feb.; 21, 28 and 30 May; 19 and 23 Sept.; 1933, 24 Mar. (two); 14 and 21 June; 2 and 3 Oct.

DEATHS FROM ENTERITIS IN THE GREATER LONDON AREA, 1930–8

The more uniform seasonal incidence of infantile enteritis in the Administrative County of London since 1930 has resulted from a great decrease in the relative importance of epidemic forms in the summer, and a slight increase in those forms, supposedly parenteral in origin, which are prevalent in the winter. It would be unjustifiable, however, to assume from this more stable seasonal incidence that the infectious forms have disappeared with the cessation of the summer epidemics, for this uniformity may merely cloak the occurrence of large numbers of very minor outbreaks which are irregularly distributed in both place and season over the whole area of the county. It might, in fact, be an instance of a large statistical mass becoming stabilized by its heterogeneity.

The foregoing analysis of the Willesden records has been made in the hope of throwing some light upon the circumstances surrounding cases of enteritis in the Greater London area, by examining the mortality returns of a representative borough in greater detail than is possible for the area as a whole. For other boroughs, however, the distribution of such deaths in time though not in place can be obtained from the *Weekly Reports* published by the Registrar-General, and in the following paragraphs we have attempted to find out how far the inferences drawn from the Willesden data are applicable elsewhere in the London region. Unfortunately, no weekly returns are now published for deaths from enteritis amongst infants in the separate Metropolitan Boroughs; we have turned, therefore, for suitable material to the records of four other large satellite boroughs in the Greater London area, viz. Croydon, East Ham, Tottenham and West Ham. These boroughs, which vary widely in their social character, have been chosen chiefly because of their suitable sizes and populations, the steady numbers of their annual births during the period studied, and their close proximity to the Administrative County itself. For the purpose of such a comparison, it is worthy of note that the infantile enteritis mortalities in these boroughs have shown no summer rise during the period 1930–8. Through the kindness of Dr C. H. C. Toussaint, Deputy Medical Officer of Health, we have also obtained weekly mortality data for infantile enteritis in the more centrally situated Metropolitan Borough of Bermondsey. The annual and total deaths of infants under 2 years from enteritis in these six boroughs are shown in Table 9. Even though the deaths from enteritis in these boroughs varied considerably from

year to year,* the weekly returns themselves showed little evidence of any epidemic having taken place; indeed, on ordinary inspection, the deaths seemed to be distributed more or less indiscriminately over the whole 468 weeks of the period.

In order to determine whether these data, which at first sight seemed to be random numerically and positionally, were really so, the 468 recorded weekly totals of deaths from enteritis have been examined for the degree of their agreement with a Poisson's series, in the same way as was done formerly for the Willesden data. The probabilities, as judged by the χ^2 test, of agreement between the observed and calculated series, both of single weeks and of monthly clutches, are given in Table 10. From the probabilities obtained with the weekly data, it can be seen that the agreement between the observed and the calculated values is good for the smaller boroughs of Bermondsey and East Ham, hardly significant (especially in view of Greenwood & Yule's caution) for Tottenham and West Ham, and quite insignificant for Croydon and Willesden. In these two large boroughs at least, the deaths from enteritis do not seem to have occurred in an entirely random manner. At the same time it is clear, from the changes in probability which have resulted from the creation of monthly clutches, that any epidemic associations in all six boroughs must have been of very short duration. Thus, so far as distribution in time is concerned, the present findings on these further boroughs seem to support the main conclusion arrived at previously from the more detailed Willesden records.

Table 9

Year	Bermondsey	Croydon	East Ham	Tottenham	West Ham	Willesden	Totals
1930	17	21	13	11	46	19	127
1931	9	20	12	12	45	14	112
1932	11	17	14	5	60	32	139
1933	11	23	10	17	51	26	138
1934	23	11	12	5	33	21	105
1935	31	20	8	17	16	56	148
1936	15	17	20	12	57	25	146
1937	23	45	16	27	41	59	211
1938	12	28	8	15	38	33	134
Totals	152	202	113	121	387	285	1260

Table 10

	Bermondsey	Croydon	East Ham	Tottenham	West Ham	Willesden
Weekly	0·51	0·00003	0·83	0·12	0·07	0·00004
Monthly	0·09	0·00011	0·58	0·30	0·08	0·00005

* Lest the degree of variability of the yearly totals for these boroughs be thought to be too great for the proper comparison of their weekly or monthly components with a Poisson's series, it may be pointed out that it is not greater than that present in the yearly totals recorded by von Bortkiewicz in his famous example of the 'Law of small numbers'—the numbers of cavalry men in fourteen corps who were killed each year by the kick of a horse. For data for this example, see Keynes (1921).

DISCUSSION

As a preface to the discussion proper, it may be well to consider briefly in what respects a statistical approach along the present lines can help to clarify some of the problems in the etiology of enteritis amongst infants—problems which are all the more difficult to solve because their investigators have hitherto been restricted to exclusively observational methods of analysis.

Descriptive statistics, such as mortality data, although valuable for suggesting lines for inquiry, must always play a subordinate role in the initial development of theories of etiology; on the other hand, such statistics can play a much more important part in the deductive evaluation of the validity of such theories once they have been formulated. Inferences of an inductive nature are necessarily based originally upon a limited range of observations, often made under circumstances which are complicated by the concurrent operation of irrelevant factors whose causal connexion it is not possible at the time to exclude. The accumulated records which form the statistics of large populations, however, frequently provide material that can be used to test such preliminary hypotheses under the severer stresses imposed by conditions of a more diversified kind than those under which they were originally conceived. Moreover, it is legitimate to assume that the more varied the extraneous conditions, or negative analogy, which are implicit in the data while an hypothesis is under-

going development, the greater the likelihood that a misleading induction will ultimately be avoided, though how far the pruning away of irrelevant factors by increasing negative analogy will enable such generalizations to be extended to other times and places than those for which they were originally formulated, can, of course, only be ascertained by that cautious extrapolation through which scientific knowledge is usually advanced. The present study has been undertaken largely in the belief that it is by the deductive appraisement of hypotheses, most of which took their origin in the rather specialized field of clinical experience in infants' hospitals and institutions, that the analysis of the relevant descriptive statistics upon infantile enteritis can help to solve some of the major problems in the etiology of that disease as it is found nowadays in an urban population.

To what extent the distribution of deaths of infants from enteritis in the London area in the decade before the war, conforms to what might have been expected from the several current views on its etiology, will be examined in the following paragraphs.

(i) *Epidemic neonatal diarrhoea.* An apparently distinctive form of enteritis of great severity, which affects infants under 1 month old almost exclusively, was first clearly recognized by Rice, Best, Frant & Abramson (1937) in New York. Since these authors' review of their own and several similar epidemics, a number of outbreaks in maternity hospitals have been recorded both in the United States and in this country. In some instances, careful bacteriological studies have been made during the epidemic, but the nature of the infective agent still remains obscure (see Crowley, Downie, Fulton & Wilson, 1941).

In New York, Frant & Abramson (1944) have found from the city records that while the mortality of infants under 1 year from enteritis has been falling steadily in the previous decade, that of infants under 1 month has been increasing. In London no such reciprocal trends have been apparent. In the decade 1930–9, about one-twentieth of the deaths of infants under 1 year from enteritis took place in the first 4 weeks of life, a substantially smaller fraction than that in New York. In 1940, however, in the most recently published *Annual Report of the Registrar-General*, this fraction rose sharply to one-sixth, the change being due partly to a fall in the specific mortality of infants under 1 year, but chiefly to a rise in that of infants under 4 weeks, which rose to more than twice the average for the previous 10 years. Conditions in London were very abnormal in 1940, but the occurrence of this rise is worthy of notice, especially from its possible connexion with the large increase in the number and proportion of births which have taken place in maternity hospitals in London in recent years (see Menzies, 1942). Except for this single observation, nothing in the London data supports the belief that epidemic neonatal diarrhoea is increasing, or that it contributes seriously to the mortality of infants under 2 years in the metropolitan area.

Several of the recorded outbreaks of epidemic neonatal diarrhoea in the United States coincided with local epidemics of influenza, and the suggestion has several times been made that there may be some etiological connexion between them. In London, influenza epidemics occurred in the early months of 1932, 1933 and 1937; in those 3 years the mortality of infants under 2 years from enteritis in the first quarter was substantially below the average for that quarter for the whole decade. It seems unlikely, therefore, that the simultaneous appearance of the epidemics of the two diseases can have been other than fortuitous—the London data at least give no support to the belief that they share any common specific etiology.

(ii) *Parenteral enteritis.* The frequent discovery of foci of infection outside the alimentary tract at autopsies on infants dying from enteritis has led many pediatricians to believe that the pathological manifestations in the intestines are the result of a toxaemia arising in the parenteral focus. The parenteral lesions most commonly incriminated have been present in the upper respiratory tract, its associated sinuses and the middle ear. In Smellie's (1939) series of 500 cases of enteritis in Birmingham in the years shortly before the war, 125 infants had otitis media or mastoiditis, and seventy-four had bronchitis or broncho-pneumonia at the time of their admission to hospital. In Campbell & Cunningham's (1941) series of 574 cases of enteritis in a south-east London hospital during the period 1937–9, the incidence of otitis media was much lower, only twenty-three cases being found, while tonsillitis, laryngitis, bronchitis and broncho-pneumonia, with 104 cases, were roughly the same.

One of the principal reasons for the renewed interest in the possible causal association between parenteral infections and enteritis is the rise that has been recorded recently in the mortality of infants from the latter condition in the first quarter of the year—the season when both specific and non-specific respiratory infections also tend to be at their maximum. In the 4-year period 1923–6, the enteritis mortality amongst infants under 2 years in the Administrative County of London for the first 13 weeks of the year was 1·65 per 1000 live births in the preceding year; 12 years later, in the period 1935–8, it had more than doubled—the comparable mortality being 3·55.

The trends of vital statistics in this country have been so generally favourable during the present century that any retrogression at once arouses

a doubt as to whether it is real, or has merely resulted from modification in the classification employed, either in the reports of the central authority or in the certificates issued by individual physicians. The latter source of error, which alone needs consideration here, usually develops insidiously, and is often difficult to detect. While there is no certainty that changes in fashion in the certification of cases of enteritis have not taken place during this period, it seems unlikely, from the following evidence, that much alteration has taken place:

(*a*) The interval between the above 4-year periods is a short one, and one during which no striking advance has been made either in the pathology or therapeutics of enteritis.

(*b*) Although the mortality for the first quarter has risen by 116%, that for the remainder of the year has risen by less than 7%; any alteration in fashion of certification must thus apply only to one season.

(*c*) The increase has occurred in all the Metropolitan Boroughs except Hampstead.

Even were the increase in mortality a genuine one, however, it is worth while to consider a possible explanation for its occurrence which is not immediately obvious. Since the population of infants under 2 years in the Administrative County has diminished considerably in the past 20 years,* it is possible that the recorded rise in mortality may be partly attributable to some differential emigration from the county, in consequence of which the more vulnerable families have been left behind. Had such a selection of the population taken place, the recorded mortality might have risen without there having been any real worsening of the position. The fact that the mortality from enteritis has risen most between 1923–6 and 1935–8 in those Metropolitan Boroughs whose infant populations have fallen most (the coefficient of correlation between the two is $-0{\cdot}366 \pm 0{\cdot}189$) is compatible with this explanation. Differential emigration alone, however, could not account for the changes in mortality found, for the average number of deaths in this category in the first quarter have actually risen from 149 (151, 144, 131 and 169) in the earlier 4-year period to 198 (184, 218, 160 and 232) in the later one. The fall in the infant population of the county has thus been accompanied not only by a rise in the death-rate, but also by an increase in the actual number of deaths from enteritis during this season. There thus seems to be no reason to doubt that in this winter rise in mortality of infants from enteritis, we are confronted with a genuine problem in infant hygiene, though one which has so far escaped explanation.

* In 1922–5 the average annual total of live births in the twenty-eight Metropolitan Boroughs was 88,387; in 1934–7 it was 55,915.

In spite of the fact that the mortality of infants from enteritis has risen in the season when respiratory infections are at their height, there are several reasons for doubting whether parenteral infections of the respiratory system can have been responsible, as a primary etiological factor, for any large proportion of the deaths, even at their present level.

(*a*) In the investigation made by Campbell & Cunningham shortly before the war, the patients were examined on admission and at intervals subsequently for signs of parenteral infections. In a group of 283 dehydrated infants, such infections were present in seventy-four at the time of entry, but a further fifty-eight developed otitis media and broncho-pneumonia only after the symptoms and signs of diarrhoea and enteritis were well established. Wishart (1930) and Smellie have also drawn attention to the frequency with which infants suffering from enteritis develop otitis media while under care in hospital. Such observations clearly lessen the force of the evidence—much of it derived from post-mortem studies—upon which the idea of parenteral enteritis was originally based.

(*b*) A post-mortem study upon the incidence of 'latent mastoiditis' in a group of 120 infants, almost all under 2 years old, nearly half of whom had died from enteritis, has recently been published by Patterson & Smith (1944). Infection of the mastoid and middle ear was found in more than half the infants, but the frequency in the subgroup of infants dying from enteritis was hardly greater than that in the subgroup dying from respiratory conditions (broncho-pneumonia, bronchiectasis and atelectasis). Further, the bacteriological findings in the pus present in the middle ears scarcely differed in the two subgroups.

(*c*) In the records of deaths from enteritis in Willesden, supplementary information upon concurrent pathological conditions was frequently available. Of the 285 deaths from enteritis, only forty-three had records of accompanying infections of their respiratory tracts, and these cases were distributed almost uniformly in all quarters of the year.

(*d*) In the decade 1929–38, there has been little tendency for the mortality of infants under 2 years in the Administrative County of London to be unduly high in the years of raised mortality from broncho-pneumonia, measles or pertussis, nor was there any rise in those years in which influenza was prevalent amongst adults. The numbers of deaths of infants from enteritis, broncho-pneumonia, measles and pertussis, together with those of adults aged 25–44 from influenza, in the first 13 weeks of each year, are shown in Table 11. Two points stand out from this table: (i) the much greater yearly variations in the numbers of deaths from these respiratory infections; and (ii) the absence of any tendency for

unusually large numbers of deaths from the respiratory diseases, with the possible exception of measles, to be associated with correspondingly large numbers of deaths from enteritis. Secondary enteritis is known as a common complication of measles (see Mitman, 1936), so that a small but probably very small fraction of the deaths here recorded as due to enteritis should probably have been more correctly ascribed to that disease.

Table 11

Year	Enteritis	Broncho-pneumonia	Measles	Pertussis	Influenza
1929	138	1112	6	512	283
1930	195	428	354	38	20
1931	185	576	9	86	101
1932	156	346	211	80	111
1933	129	361	3	123	309
1934	177	573	280	92	28
1935	184	320	1	28	18
1936	218	452	128	77	19
1937	160	312	2	74	132
1938	232	343	82	33	9

(iii) *Infectious enteritis.* Hitherto much of the emphasis upon the infectious nature of enteritis has come from clinical experience in institutions for the care of young children, amongst whom epidemics of this complaint, some of them caused by members of the dysentery group of bacteria, have provided a large proportion of all nosocomial diseases. It must be emphasized, however, that the present study is primarily concerned with a different aspect of the problem, that of trying to make some estimate of the relative importance of the infective element in the etiology of those forms of enteritis which are contracted nowadays by infants which are living dispersed in ordinary houses and in contact with persons of all ages.

The records for Willesden, which may be regarded as a representative London suburban borough, both socially and epidemiologically, show that the deaths of infants from enteritis in the decade before the war were not distributed wholly randomly either in time or place, and the less complete records from several other London boroughs support this conclusion. At the same time, little evidence was found of any outbreak in private houses in Willesden which could properly be termed an epidemic. The outbreak that most nearly resembled one took place in the neighbouring Wards 6 and 7 in the summer of 1935, when eight fatal cases occurred in a little more than 3 months within an area of less than a quarter of a square mile. Since the case-fatality rate for enteritis in infants is about 20 %, as judged by the experience of the L.C.C. Infectious Diseases Hospitals in 1936, such a local outbreak probably gave rise to clinical attacks in at least forty of the roughly 250 infants under 1 year old who resided in the area affected. Nevertheless, although frank epidemics on their former scale no longer occur in London, and even small-sized outbreaks are probably infrequent, there seems to be some evidence in favour of the view that an infective factor is often in operation in those forms of enteritis that still occur from time to time in small suburban communities: the instances of multiple fatal cases, such as were found in short roads and in nearby houses, as well as the raised incidence amongst twins, acquire a certain cumulative force when taken together. It seems unlikely that so many deaths occurring in close proximity to one another, both in time and place, were entirely unconnected, either directly, or through the intermediary of some unrecorded surviving cases.

Any discussion upon the ecology of the organism or organisms which might be responsible for such an infectious form of enteritis, can at present be little more than speculative. The wide area in Willesden over which more or less contemporaneous fatal cases of enteritis were distributed, would suggest that any causative organisms must at the same time be widely diffused, yet unobtrusive in their behaviour, in the general population.

In comparison with what is known of the spread of non-pathogenic naso-pharyngeal bacterial species and their variants in a community, little is known of the rapidity with which intestinal organisms of species, which are harmless for adults and older children, ordinarily circulate from person to person, though from the field observations of Chapin (1916) and of Buice, Sehested & Dienst (1927) and many others, there may well be little to choose between them. Wallick & Stuart (1943) have made some observations on the persistence of particular serological strains of *Bact. coli* in the intestines of a subject by frequent sampling of his faeces. They found that any particular strain tended to remain as the predominant variant for several weeks or months at a time, and was then succeeded by some further temporary resident of the same species. If these observations are correct, and they are supported by a study, made by Parr (1936), upon the succession of *coli-aerogenes* organisms in the faecal flora of healthy adults, it appears likely that the coliform flora of the human intestine is undergoing frequent changes in its serological variants. It seems not improbable, therefore, that a coliform organism of a variety which is potentially pathogenic for certain infants may be disseminated freely in a restricted section of an urban community, which shares many possible vector objects in common, without evoking any symptomatic reactions in the older population.

That *Bact. coli* can be highly pathogenic for newly born infants is clearly shown by the occasional occurrence of a specific suppurative meningitis. So far as is known at present, the strain of *Bact. coli* which is responsible for this particular clinical manifestation is in no way distinctive, though the fuller serological investigation of the organisms recovered from such cases might lead to the identification of some particular variant analogous to that found with *Haem. influenzae*. It seems *a priori* probable, from our knowledge of those bacterial species that have so far been examined from this point of view, that potential pathogenicity is distributed in a more or less statistically normal manner amongst the variants of *Bact. coli*. The premature exposure of an infant, through the cessation of breast feeding, and the resulting disappearance of the typical aciduric flora from its intestines, to any of the more pathogenic strains prevalent at the time in the locality, may overtax any immunity that the infant might possess, and lead to the onset of enteritis. Such a conception of the etiology of this disease, involving the conjunction of such multiple contingencies, seems to be more in accord with the findings in the present study, than the conception of some single bacterial malefactor capable of causing the disease in all the infants infected, which has tended to dominate bacteriological investigations upon diarrhoea and enteritis in the past.

SUMMARY

The present inquiry was undertaken to obtain some indication of the relative frequencies of deaths amongst infants from the various forms of diarrhoea and enteritis—'neonatal', 'parenteral' and 'infectious'—in the Greater London area in the decade before the war. Since much of the material needed for such an analysis was not available in the published records, a sampling inquiry, making use of the more elaborate records maintained by the Medical Officer of Health, was undertaken for the Borough of Willesden. A comparison of the relevant epidemiological and social conditions in this borough with those in the Greater London area as a whole showed, that for such a purpose, it might properly be regarded as a representative sample.

There was little evidence for the occurrence of the neonatal form in Willesden during the period studied, nor did the seasonal distribution of the deaths suggest that many took place in consequence of preceding parenteral infections. On the other hand, there did seem to be some evidence that a significant proportion of these deaths were in some degree associated with one another, in time or place or both, and it is suggested that this distribution might have resulted from the widespread dissemination in the community of one or more strains of some common micro-organism of relatively low virulence for all but the infant population.

A less detailed study of data for other London boroughs, viz., Bermondsey, Croydon, East Ham, Tottenham and West Ham, supported the main conclusion reached from the Willesden records.

We wish to thank Dr G. F. Buchan, Medical Officer of Health for the Borough of Willesden, for his kindness in allowing us to make use of his records.

REFERENCES

VON BORTKIEWICZ, L. (1898). *Das Gesetz der kleinen Zahlen*. Leipzig.

BUICE, W. A., SEHESTED, H. C. & DIENST, R. B. (1927). *J. Infect. Dis.* **40**, 348.

CAMPBELL, R. A. & CUNNINGHAM, A. A. (1941). *Arch. Dis. Childh.* **16**, 211.

CHAPIN, C. V. (1916). *Sources and Modes of Infection*, 2nd ed. New York.

CROWLEY, N., DOWNIE, A. W., FULTON, F. & WILSON, G. S. (1941). *Lancet*, **2**, 590.

DAVIS, H. T. (1941). *The Analysis of Economic Time Series*. Bloomington, Illinois.

FRANT, S. & ABRAMSON, H. (1944). *Brennemann's Practice of Pediatrics*, **1**. Hagerstown, Maryland.

GREENWOOD, M. & YULE, G. U. (1920). *J. Roy. Statist. Soc.* **83**, 255.

KENDALL, M. G. (1941–2). *Biometrika*, **32**, 1.

KEYNES, J. M. (1921). *A Treatise on Probability*. London.

MENZIES, M. F. (1942). *Lancet*, **2**, 35.

VON MISES, R. (1939). *Probability, Statistics and Truth*. London.

MITMAN, M. (1936). *Ann. Rep. L.C.C.* **4**, pt. III, p. 76.

PARR, L. W. (1936). *Science*, **83**, 189.

PATTERSON, W. H. & SMITH, G. S. (1944). *Brit. Med. J.* **2**, 659.

RICE, J. L., BEST, W. H., FRANT, S. & ABRAMSON, H. (1937). *J. Amer. Med. Ass.* **109**, 475.

SMELLIE, J. M. (1939). *Lancet*, **1**, 969.

WALLICK, H. & STUART, C. A. (1943). *J. Bact.* **45**, 121.

WISHART, D. E. S. (1930). *J. Amer. Med. Ass.* **95**, 1084.

(*MS. received for publication* 27. VIII. 45.—Ed.)