INFANTILE DIARRHOEA

AN ANALYSIS OF 216 CASES WITH SPECIAL REFERENCE TO INSTITUTIONAL OUTBREAKS

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During a period of thirteen and a half months, from March, 1942, to April, 1943, 216 cases of diarrhoea in children under fifteen months of age were admitted to the children's isolation ward of the West Middlesex County Hospital, Isleworth. Of these cases 109 died. As this represents a case mortality which is unusually high, even for this lethal disease, an analysis of the cases was made in an attempt to assess the importance of various etiological factors and to find the actual cause of death in fatal cases. Although the main problems—the cause of the disease, and the cause of death—remain unsolved, some interesting points arose in the course of the investigation, and these are set out below. Special attention has been paid to institutional outbreaks which accounted for a high percentage of the total number of cases.

Seasonal incidence

There was no preponderance of admissions during the late summer months. Both the institutional and non-institutional admission rate tended to fluctuate, as may be seen from the graph below (fig. 1). March and February were the worst months for district cases; transfers from the maternity wards (representing the bulk of the institutional cases) were most numerous in December and April.

Although it is well recognized that the one-time heavy incidence during the late summer months no longer occurs, most workers have found some excess of admissions during the summer. Thus Campbell and Cunningham (1941) in a series of 574

cases found 52.3 per cent. were admitted between June and October; Smellie (1939) reported that in Birmingham the incidence was highest from July to October, though not markedly so, while McConkey and Couper (1938) found August to October the worst months.

The cases were all nursed in a ward consisting of thirty cubicles, with one cot to a cubicle, observing strict 'barrier' technique. The ward admitted children aged 0–12 years suffering from various infectious diseases, but cases of infantile diarrhoea usually predominated during the period in question.

Source of case

Cases were admitted throughout the year from all parts of the hospital district—a mixed urban and suburban area extending from Staines to Chiswick with a pre-war population of over 660,000. A large number, however, were transferred from other wards or other institutions, and a further series was admitted having developed symptoms within a week of discharge. Henderson (1943a) gives the incubation period of neonatal diarrhoea as two to twenty-one days; had the latter figure been adopted in classifying these cases an insignificant number would have been transferred from group 3 to group 2.

Group 1. Cases transferred from institutions, 69 (30.8 per cent.).

Group 2. Cases recently discharged from institutions, 25 (11.7 per cent.).

Group 3. No institutional history, 122 (57.5 per cent.).

FIG. 1.—Seasonal incidence.

TABLE 1
SOURCE OF INSTITUTIONAL CASES

	Trans- ferred	Died	Recently discharged	Died
Maternity wards ..	47	31	14	6
Infants' medical ward ..	12	5	3	2
Childrens' isolation ward ..	1	1	3	1
Other wards ..	4	1	2	0
Nursing home ..	1	1	0	0
Cottage hospital ..	0	0	1	1
Orphanages ..	2	1	0	0
Wartime day nur- series ..	2	0	2	1
	69	40	25	11

Some of these groups warrant further description.

Maternity cases. Explosive outbreaks of neonatal diarrhoea have recently been described by Ormiston (1941) and Sakula (1943) and the disease is often considered to be distinct from that affecting older infants. The forty-seven cases in this series which were transferred direct from the maternity wards occurred sporadically and in small groups. Following a small outbreak in December, 1942, the main maternity block, where the majority of the cases had occurred, was closed. After the block was re-opened on January 28 no further cases occurred until March 3, after which cases occurred sporadically, not only there but in an annexe in Chiswick, four miles away. The case incidence over the whole period was in the region of 3.5 per cent. [Compare Henderson (1943a and b), who found an incidence of 1.5 per cent. over a period of three years at the Simpson Maternity Pavilion, Edinburgh, and Rice et al. (1937), who, in a survey of eleven maternity homes in New York over a period of three years found an average case incidence of 14 per cent.] There was never a time when practically every infant at risk was affected, as in Sakula's series.

There was nothing to distinguish these cases from others in the same age group. There were altogether seventy-one cases aged under one month with forty-eight deaths (67.6 per cent.); of the forty-seven maternity cases thirty-one died (66 per cent.). The history, course and complications were as varied in all these tiny infants as they were in the older patients, and post-mortem findings were similar. For instance, in twenty-six out of forty-seven post-mortem examinations on infants of all ages there were signs of middle ear suppuration (55 per cent.), and in eight out of fifteen 'neonatal' cases (53 per cent.).

FEEDING HISTORY. Among the sixty-one cases transferred or re-admitted after discharge from the maternity wards not one had been wholly breast fed. One very mild case, who made a rapid recovery, was breast fed on admission to the children's ward, but had had complementary feeds before transfer. Three premature infants were having expressed breast milk intranasally or from a bottle; seven

infants were partially breast fed at the onset of the disease; the remaining fifty were wholly artificially fed.

MATURITY. Ten infants were premature (weighing 3 lb. 2 oz. to 5 lb. 4 oz. at birth) and of these eight died.

Cases from the infants' medical ward. This ward supplied an occasional case of diarrhoea. After a long period of freedom from diarrhoeal conditions five cases occurred within forty-eight hours; two died and the rest were very ill for a long time. This was the only outbreak affecting several cases at once in this ward during the period in question; it followed, and may have been attributable to, the arrival of a new nurse on the ward with a severe cold.

Cases from the isolation ward itself. One case of diarrhoea occurred in an infant admitted for a non-diarrhoeal infection—in a boy aged fourteen months who developed fatal diarrhoea ten days after having been admitted with whooping cough. Three cases were re-admitted shortly after discharge from the ward, their former admissions having been for some other infection, and one of these cases died.

Relapses and re-infections. In a disease where no specific pathogen has been isolated it is often impossible to distinguish between relapses and re-infections. In forty-six cases a sudden relapse occurred; twenty-nine died. In fourteen of these cases, of whom ten died, the relapse occurred when the infant seemed to be improving; four were definitely convalescent; the remaining cases were already very ill when the relapse occurred.

Mortality

As in other series the death rate falls with increasing age, and is highest in the dehydrated cases.

TABLE 2
MORTALITY BY AGE AND DEHYDRATION

Age in months	Cases	Died	Per- centage died	Dehy- drated on admission	Dehy- drated per cent.
0-1	71	48	67	40	56
1-3	50	26	52	23	46
3-6	52	21	40	23	44
6-9	18	6	33	8	44
9-12	11	5	45	5	45
12-15	10	3	30	3	30
	215	109	51	102	45

Dehydrated on admission, died 71 (70 per cent.)
Not dehydrated on admission, died 38 114 (33 per cent.)

Although it is difficult to compare mortality rates in a disease in which objective standards of severity are lacking, it is clear that the death rates quoted above are unusually high. The total mortality in this series (51 per cent.) approximates to that among Campbell and Cunningham's dehydrated cases. Indeed, the difference in mortality between dehydrated and non-dehydrated cases and between different age groups is much less than in their series

—their non-dehydrated cases had a mortality of only 2.7 per cent. Other series quoted by Cohen, Miller and Kramer (1933) vary from 14 to 88 per cent. mortality. Field, MacCarthy and Wyllie (1943) among a hundred cases, of whom seventy-eight were dehydrated, had only twenty-three deaths, but they do not state whether the series included any very young infants. It may be noted that, of the thirty-eight fatal cases in this series not dehydrated on admission, nineteen were under one month of age. Of one hundred and fourteen cases not dehydrated at the onset forty-four later became so, and twenty-two died. Sixteen died without showing dehydration at any time.

Etiology

This subject will be considered under four headings—history, clinical findings, pathology and results of treatment, each of which throws some light on the question.

History

(i) FEEDS. The outstanding feature in the feeding history of these infants is the frequency of early weaning.

TABLE 3
FEEDING HISTORY

	Cases	Per- cent- age of Cases	Died	Per- cent- age died
1. Breast fed for six months or more or at onset of disease	15	7	5	33
2. Artificially fed	201	93	104	52
i. Breast fed for less than one month	131	60.7	80	61
(a) cases aged under one month	71	32.8	47	66.2
(b) cases aged over one month	60	27.7	33	55
ii. Breast fed for over one month	39	24.3	11	28
iii. Date of weaning not recorded	33	15	13	40

The fact that 60.7 per cent. were weaned before reaching the age of one month is noteworthy. Even a few weeks breast feeding appears to offer some protection against this disease. Thus the mortality among those weaned under one month was 61 per cent. as compared with 28 per cent. among those breast fed for a month or longer. Similar figures (76.6 per cent. and 25.9 per cent.) are given by Smellie, derived from a series of five hundred cases of whom 59 per cent. had been breast fed for less than a month.

REASONS FOR WEANING. In three cases this was due to maternal illness, in four to medical advice, in two to having to go out to work, and in a few to local conditions of the breast. The overwhelming majority, however, gave up because lactation failed. By far the commonest story was 'When I got up, the milk went.'

TYPE OF BOTTLE FEED. Twenty-one out of two hundred and one bottle-fed patients were receiving cow's milk mixtures. All the others were fed on dried or condensed milk, which is evidence against an ordinary milk-borne infection. All the popular brands of infants' foods were well represented, there being little to choose between them in this respect.

The overwhelming preponderance of bottle-fed infants in all published series of cases of infantile diarrhoea is perhaps the most notable feature of this disease, but its exact etiological significance is less clear. It can be argued that either the milk or the bottle is the vehicle of a pathogenic organism or virus, or that artificial feeding irritates the bowel and makes it less resistant to bacterial invasion (enteral infection) or toxins (parenteral infection): antibodies in human milk have also been postulated. However, in this last case, one would expect an equal protection to be offered to the breast-fed infant against other infections, and although there is a considerable amount of evidence that breast-fed babies are less liable than are bottle-fed infants to such diseases (e.g. Ebbs and Mulligan, 1942; Deeney and Murdock, 1944), it is not found that they are practically confined to the bottle fed as in infantile diarrhoea.

(ii) PRESENTING SYMPTOMS. In eighteen cases this was stated to be a 'cold,' and in seventeen cases loss of weight was first noticed. In the remaining cases the earliest symptoms were diarrhoea, vomiting or loss of appetite. The seventeen cases showing early loss of weight were mostly institutional cases; were babies normally weighed daily this presenting symptom might prove to be much commoner, and suggests some disturbance outside the alimentary tract.

Clinical findings

Seventy-five cases (34.7 per cent.) showed clinical signs of parenteral infection on admission.

TABLE 4
PARENTERAL INFECTIONS ON ADMISSION

	Cases	Died
Otitis media	21	8
Bronchitis or pneumonia	25	17
Septic skin lesions	21	11
Upper respiratory tract	5	1
Thrush	3	3
	75	40 (53.3 per cent.)

Too much weight must not be attached to such findings in the absence of a control series of infants admitted with other diseases. Furthermore, the high percentage of extremely small infants made accurate diagnosis exceptionally difficult, and in nineteen cases post-mortem evidence was found of an infection undiagnosed during life. It is interesting that the mortality among these cases is almost identical with that of the whole series (51 per cent.).

Bacteriology and pathology. In the few cases where the stools were fully examined no pathogenic organisms were found—even in three infants whose

stools contained blood or mucus, and notwithstanding the fact that several cases of Sonne dysentery were nursed in the ward during this period.

TABLE 5
POST-MORTEM FINDINGS

Otitis media	12	} 34 (70 per cent.)
Mastoiditis	4	
Bronchopneumonia ..	8	
Otitis and pneumonia ..	10	
Cranial sinus thrombosis (without ear disease) ..	3	
Intestinal haemorrhage ..	1	
Intestinal exudate	2	
Various	7	
	47	

Whatever may be the etiological significance of the various parenteral infections noted above, the absence of any signs of inflammation of the gut in all but three cases is noteworthy and is typical of this disease. The part played by infections such as otitis media in the causation of infantile diarrhoea has been the subject of much controversy.

Thus Marriott and Hartman (1933) stated that one hundred and sixty-six out of two hundred cases had signs of disease in the ear or throat on admission, and even more after the initial dehydration has been treated. Maizels and Smith (1934) found post-mortem evidence of otitis media in forty-one out of sixty-eight fatal cases of 'D and V,' in only ten out of thirty-three other cases. On the other hand, Findlay (1932) points to the differing seasonal incidence of otitis media and diarrhoea (though that would not apply to the present series) and the different breast-feeding rate in cases of diarrhoea and pneumococcal otitis with meningitis (9 per cent. and 44 per cent. respectively). He did routine myringotomies on all cases of diarrhoea in one ward and none in another without affecting the results, and finally reports seven deaths in nine cases on whom bilateral mastoidectomy was performed—in five cases on not very ill babies. Wishart (1930) reports an exhaustively investigated series of one hundred and sixty-eight cases of infantile diarrhoea. He found the bacterial flora of the upper respiratory tract and ears the same in his cases and in the controls; fifty-seven had infections on admission, and one hundred and five developed such infections in hospital. Twelve out of thirteen patients subjected to mastoidectomy died. He points out that in a series of one hundred and thirty-three patients under two years of age on whom mastoidectomies were performed, diarrhoea, vomiting or loss of weight were present in only eighteen cases, constipation being frequently present in the remainder. Smellie (1939), who found evidence of parenteral infection in 46.2 per cent. of admissions for infantile diarrhoea, also points to the differing seasonal evidence in the two conditions. Others (Cooper, 1937; Campbell and Cunningham, 1941) report various parenteral infection rates (40.7 per cent. and 30.5 per cent. respectively), but do not state categorically whether or not they regard these infections as the cause of diarrhoea. It seems unlikely, taking other factors into consideration, that otitis media or any other parenteral infection can be considered *the* cause of the diarrhoea, even when present, though it may be a contributory or precipitating factor.

In the voluminous literature, however, adequately controlled series which enable a comparison of the incidence of otitis media in diarrhoeal and in non-diarrhoeal diseases of infancy are seldom found. Finally, the comparative infrequency of diarrhoea as a dangerous complication of severe cases of frank parenteral infection must be noted (e.g. Wishart, 1930; Stirk Adams, 1937). In the present series only two infants would have been dangerously ill without their diarrhoea—a case of lung abscess in which the diarrhoea was a terminal condition, and a severe case of septic burns in whom it responded as rapidly as did the burns to treatment with propamidine jelly.

Results of treatment. If infantile diarrhoea were solely attributable to parenteral infection treatment of the latter should be an effective way of treating the diarrhoea. In this series cases of otitis, bronchitis and pneumonia, and many cases with unexplained pyrexia were treated with full doses of sulphapyridine or sulphadiazine, by mouth or intravenously. Fifty-six cases were so treated and twenty-eight died (50 per cent.)—again no improvement on the general mortality (51 per cent.). Myringotomy was performed when required, but did not appear to affect the result as far as the diarrhoea was concerned.

In March, 1943, sulphasuxidine, a non-absorbed sulphonamide the action of which is to sterilize the gut, first became available. Sixteen cases were treated with courses of 1.5 to 3 grammes per day for one week, and three died. Of seven dehydrated cases so treated none died. Eight treated cases were passing the dreaded orange stools, and of these two died, compared with thirty out of thirty-six untreated cases with this symptom. Two of the treated cases who recovered were so desperately ill as to be described as 'moribund on admission' in the case records.

The success of sulphasuxidine in this very small group is interesting, and it is to be hoped that the results of treatment in larger series will be published. Similar results are reported by Twyman and Horton (1943) in a series of twenty-two cases of neonatal diarrhoea. Henderson (1943) obtained striking improvement in the results of treatment of neonatal diarrhoea following the introduction of sulphaguanidine. Should the non-absorbed sulphonamides be definitely proved superior to those of the sulphapyridine series in the treatment of infantile diarrhoea the fact would be of definite etiological significance, and should help to determine the relative importance of enteral and parenteral infections in this disease.

Course and complications

No attempt will here be made to describe the all too familiar course of the typical fulminating 'D and V,' showing on admission the depressed fontanelle, inelastic skin, greyish pallor, unnaturally red lips and sunken, rapidly glazing eyes. There were fourteen such infants who died within a few hours of admission, and many others whose death was merely postponed a few days by intravenous

'drips' which corrected the dehydration but could not cure the disease. Instead, some account will be given of the still larger group (in this series), in which the infant, who was either not dehydrated on admission, or in which water balance had already been successfully corrected, had a relapse, generally became dehydrated, and all too frequently died.

There is a large, well-marked group of cases who on admission are pale and hollow-eyed, but not dehydrated, and have from the start severe and intractable diarrhoea. Frequent, offensive, watery green or orange stools are passed, but vomiting is either absent or responds to twenty-four to forty-eight hours' starvation. Some slight progress may be made, but such notes as 'not dehydrated—but still pale and hollow-eyed' or 'still ghastly diarrhoea' reappear with surprising frequency in the case records. Then after a period which may be as long as two or three weeks, a relapse occurs. The temperature rises, diarrhoea becomes, if possible, worse; the infant refuses his feeds and may even vomit and become slightly dehydrated. Mouth feeds are discontinued, an intravenous drip is set up, and within a few hours the dehydration is relieved. Nevertheless watery, offensive stools continue to pour from the child, and soon the dreaded 'coffee ground' vomitus appears, an almost infallible herald of death.

Perhaps an even more distressing type of case is seen in the infant who, not desperately ill on admission, or at any rate apparently on the road to recovery, suffers such a relapse and dies. It is this type of case which gives rise to the suspicion of reinfection in the ward, leading to a constant overhauling of the barrier-nursing technique, a repeated scrutiny of the therapeutic measures adopted. As long as the etiological agent is unknown, it can never be proved whether or not such cases represent reinfections or relapses. Suspecting reinfection led to the discharge of infants at the first possible moment, yet even so the average stay in the ward of recovered cases was 43.1 days, and in twenty-two cases was over two months—a measure of the severity of this illness in young infants.

There are four symptoms of grave if not fatal import—orange stools, blood-stained or 'coffee grounds' vomitus, jaundice and hyperpyrexia.

ORANGE STOOLS occurred in forty-four cases with twelve recoveries.

'COFFEE GROUND' VOMITUS was noted in twenty-six cases, with but one recovery. Such vomiting is usually an agonal symptom, but in a few cases it was the first sign that the illness was likely to be fatal.

JAUNDICE is especially common in young and premature infants, in whom it was frequently seen unaccompanied by dehydration. Of twenty-three jaundiced cases, one was taken home against advice and could not be traced—all the others died.

HYPERPYREXIA is a common terminal event. As noted above, a rise of temperature frequently heralds a relapse, especially if it is accompanied by marked lassitude and irritability. Just before death a temperature of 106° to 107° F. is not uncommon. A

curious case was that of a tiny infant of twenty-six days whose temperature swung between 95° and 107° F. for ten days, without any signs beyond the usual dehydration and orange stools, but who made a complete recovery after a course of sulphapyridine.

Parenteral infections occurring during the course of the disease

Twenty-six such cases occurred—otitis media (11), bronchitis and pneumonia (4), skin lesions (2). Nine of these cases died. Two case histories serve to illustrate some of these points.

Case 131. Male infant aged nine days. Transferred from maternity ward where diarrhoea had been noted for one day. Never breast fed. On dried milk.

ON ADMISSION. Pale, not dehydrated, no abnormal signs, severe diarrhoea, occasional vomiting. Slight improvement but stools frequent and offensive till the fifteenth day, when vomiting and slight dehydration were noted. All feeds by mouth were stopped and an intravenous drip set up and continued for three days, during which there was marked improvement. Next day copious vomiting and frequent watery stools occurred. Fluids were administered by means of a gastric drip for two days, when another intravenous drip was set up and continued for two days. Two cyanotic attacks followed and the child was put in an oxygen tent. Some improvement was noted until the twenty-fifth day, when once more dehydration reappeared. A third intravenous drip was set up and continued until the child's death on the twenty-ninth day.

POST MORTEM. R. mastoiditis, bronchiolitis.

Case 206. Male infant aged three months. Breast fed three weeks: on dried milk. Cough and running eyes three days.

ON ADMISSION. Cyanosed but not dehydrated. Signs of right basal pneumonia. Offensive stools. He was given a course of sulphapyridine (6.5 gm. in 5 days). By the fourth day the temperature was normal and the chest clear. The general condition was very poor and the diarrhoea became worse. Fifth day, temperature 100° F., offensive stools. Tenth day, slight improvement. Sixteenth day, temperature 100° F., reluctant with feeds. Pale, not dehydrated. Left drum injected. Eighteenth day, pale, hollow-eyed, offensive stools. Ears and chest clear. Twenty-fourth day, diarrhoea slightly better. Thirtieth day, severe diarrhoea, very slight dehydration, no vomiting. Took saline well by mouth. 3.30 a.m. Vomited. Intravenous drip set up. Thirty-second day, not dehydrated, no vomiting, took 2 oz. saline hourly, drip discontinued. Thirty-third day, died.

Treatment

The routine treatment of these infants consisted of early starvation, graduated feeds, correction of water balance according to a schedule (based on that of Arnott and Young, 1942), and blood transfusion once the acute stage was over. In all but the mildest cases of dehydration fluid was administered by means of an intravenous drip. This could be relied upon to correct dehydration, but only too frequently failed to save life. Drug treatment has been described above.

Discussion

The results of the analysis of this series of cases throws little new light on the etiology of infantile diarrhoea or on the actual cause of death in fatal cases. The high incidence of post-mortem evidence of parenteral infection is suggestive, but the association cannot be proved to be causal. The high incidence during the winter months, the cases in which illness appeared to start as a 'cold' and the small ward outbreak following exposure to adult coryza lead to the suspicion of the upper respiratory tract as the portal of entry of the infection. The absence of pathological or bacteriological evidence of intestinal infection and the frequency of loss of weight as a presenting symptom make it at least seem likely that the cause of the illness lies outside the bowel. On the other hand the uniquely high incidence of artificial feeding in this disease, and the success (should this be confirmed) of the non-absorbed sulphonamides in treatment lead to opposite conclusions. It seems unlikely that infantile diarrhoea is a disease that can be attributed to a single cause. Many factors appear to be involved, and when several act together on an infant of the susceptible age group the result seems to be diarrhoea of a severity that treatment is only too often powerless to mitigate, whether that treatment be aimed at curing parenteral infection or correcting water balance.

When epidemiology is considered, this series emphasizes the danger inherent in infant communities, whether in maternity homes, hospitals or nurseries. Forty infants died of diarrhoea contracted in an institution, or fifty-one if 'recently discharged' cases are included.

The remaining one hundred and twelve cases, of whom fifty-eight died, were admitted from the hospital district over a period of just over a year. This points to a high incidence of a highly fatal type of diarrhoea in an area which is largely 'residential' in character and by no means poverty stricken. Elsewhere (Gairdner, 1944) it has been shown that Greater London, including the residential suburbs, has a diarrhoeal mortality out of all proportion to its total infant mortality, and that, whereas the diarrhoeal mortality of the aggregate of county boroughs has shown a more or less steady decline since 1921 that of London has tended to rise since 1928 and, since 1930, has been consistently above the county borough rate (fig. 2).

Why the mortality from infantile diarrhoea should be stationary or increasing in an area where other causes of infant death are not ill controlled (the infant mortality in the outer ring of Greater London is among the lowest in the country) it is difficult to see. Two incontrovertible facts stand out from the confusion concerning the etiology of this disease—its high incidence among bottle-fed and among institutional infants. There does not appear to be any evidence that breast feeding has declined more rapidly in London than in the country as a whole (Gordon, 1942; Robinson, 1942). Are London infants sent into hospital and other institutions more

FIG. 2.

frequently than elsewhere? If this is so, and if this is the cause of the deplorably high incidence of one of the most fatal diseases of infancy in our capital, it should cause even greater reluctance than already exists in many quarters to sending infants into institutions, unless the latter are fully equipped with sufficient isolation accommodation to prevent such outbreaks.

Thanks are due to Dr. J. B. Cook, Medical Director of the West Middlesex County Hospital, for permission to publish these cases, and to Professor J. Ryle, Dr. J. O. F. Davies and Dr. P. Holman for their helpful advice and suggestions.

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