INFANTILE DIARRHOEA AND VOMITING

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A study of the literature shows that a clinical entity under the more familiar names of gastro-enteritis or alimentary toxicosis has been recognized for many centuries as an important cause of death in the first two years of life. Certain well-defined causes of infantile diarrhoea have been determined, but there still remains a large group of cases containing a medley of types not yet clinically demarcated. According to Reuss (1936) there is among these cases no sharp division between the purely alimentary and the purely infectious types, but a continuous transition and it is therefore necessary to consider a combined alimentary-infectious aetiological complex. In the present state of knowledge the following classification of infantile diarrhoea has been adopted :—

1. SPECIFIC {
 - (a) Infective, e.g. b. dysenteriae Sonne, b. dysenteriae Flexner, the typhoid-salmonella group.
 - (b) Toxic, e.g. staphylococci.
2. DUE TO LOCAL INFECTION, e.g. pelvic peritonitis.
OR SYMPTOMATIC OF GENERAL DISEASES.
3. DIETETIC.
4. ALIMENTARY-INFECTIOUS COMPLEX {
 - (a) Associated with parenteral infection.
 - (b) Without evidence of parenteral infection.
 GROUP (A.I.C. GROUP).

The A.I.C. group. The exact role of parenteral infection in any given case is difficult to assess. There is no doubt that in certain infants, infections such as cerebrospinal fever, pneumococcal pneumonia, otitis media with mastoiditis or pyelonephritis, may produce diarrhoea and vomiting and when the primary cause is effectively treated, either medically or surgically, the signs and symptoms of intestinal upset may disappear in a striking manner. On the other hand, when the demonstrable parenteral infection is a late development and presumably a complication, treatment, although advantageous, has usually little effect in comparison and the alimentary symptoms are unaffected.

Many investigators (Bessau and Bossert, 1919; Moro, 1929; Deák, 1933; Blacklock et al., 1937), have shown that in this disease, with or without clinically demonstrable parenteral infection, the upper small intestine which is normally sterile or contains only a few enterococci may harbour large numbers of coliform

organisms which have made their way upwards from the small intestine. Blacklock et al. (1937) found that in older children with parenteral infections there was also an increase in the coliform organisms in the upper small intestine, but the change was not so marked as in infants with gastro-enteritis. This seems to suggest a close relationship between parenteral infection and disturbance of alimentary function. In infants digestive processes are very unstable and physical environment as well as infection may be responsible for the disturbance of the intestine which predisposes to the altered bacteriology. The coliform organisms which gain the upper small intestine take on a pathogenic rôle in their new environment and, according to their varied fermentative and cultural characteristics, have been named dyspeptic coli by Adam (1927) or paracolon bacilli by Hassmann and Hertzmann (1934) and Reuss (1936) and Hassmann (1936). These bacilli have been shown by Goldschmidt (1931) to produce on culture outside the body a toxic substance which in small doses irritates the intestine and in larger doses actually paralyzes it (Reuss, 1936; Hassmann, 1936; Deák, 1933; Hassmann and Scharfetter, 1934). These variant forms have been known to continue in the stools into convalescence when the infants have been regarded as possible carriers. Immunological investigations by Reuss (1936) and Hassmann (1936) appear to confirm the importance of these 'paracolon' organisms in infantile diarrhoea. An exogenous genesis has been postulated by Catel (1937) in which the variant *b. coli* by their growth on a suitable medium outside the body produce toxic substances which after ingestion cause diarrhoea and vomiting. The intensely fatty liver which is frequently found at autopsy bears testimony to the absorption of toxins in the portal system, but the exact nature of the toxic products is open to speculation. Products of protein decomposition have been blamed, such as histamine by Boyd (1923), Finkelstein (1931) and Keller (1932), and cholin by Paffrath (1930); and others have been mentioned. Catel (1937) thinks that the irritant effects may be due to the presence of certain lower fatty acids in the upper small intestine. Although variant *b. coli* have been held responsible for outbreaks of gastro-enteritis, there is another aspect of the situation to be considered. As the altered intestinal bacteriology has been shown to follow parenteral infections it is, therefore, possible that some as yet unknown infection may cause outbreaks in infants in institutions. There is a form which occurs from time to time and may spread very rapidly through an open ward attacking all the susceptible infant population under two years of age. The infants affected may simply show diarrhoea with vomiting until death occurs, and the only other symptom demonstrable may be a short cough. Specimens of sputum are negative for pneumococci and streptococci and, although no current evidence can be offered, it is a clinical opinion that this is a serious and deadly form which spreads like a respiratory infection caused by a filter-passing virus.

Bessau (1935) thinks that the picture of alimentary toxicosis, with its heavy and continued loss of water and mineral salts, can only be explained on the basis of an abnormal increased permeability of the cellular membranes consequent on toxic absorption. The cells are no longer able to retain their specific contents of colloids and mineral salts and a certain interchange takes place. Thus Na and Cl ions enter the cells and substances of the K group (K, P, Mg) escape into the blood stream. Water and salt metabolism will be discussed in detail in another paper.

Present series

The five hundred and seventy-four infants in this series of cases of gastro-enteritis were admitted to the Park Hospital between January, 1937 and August, 1939. During these years two or, at times, three wards have been assigned to

infants who were certified before admission as suffering from 'zymotic enteritis,' 'gastro-enteritis,' 'diarrhoea and vomiting' and the like. A small number was placed in individual cells, but in view of the large number treated, it was necessary to use open wards, in which these infants can be successfully nursed by adhering strictly to the details of the technique of bed isolation and liberal standards of bed spacing. The patients with diarrhoea came from their homes and from institutions such as nurseries and hospitals. The diagnosis given on admission was revised in many instances, for it was based on the clinical features only; and the cases were classified into the groups specified at the beginning of this paper. The faeces of each infant were examined on two occasions for pathogenic organisms, and when the clinical features suggested dysentery, enteric fever or a specific gastro-enteritis, the agglutination reaction of the serum was tested against organisms of the dysentery, enteric and salmonella groups. A history of any recent error in feeding leading to symptoms such as vomiting, diarrhoea, alteration in the character of the stools and loss of weight was sought, and an attempt was made to assess its bearing on the current illness. By careful examination on the day of admission and on the following day an attempt was made to detect infections or other causes of diarrhoea.

It will be clear that this series is of a mixed character since the term 'gastro-enteritis' (or A.I.C. group) has been used for the cases of diarrhoea which remain after excluding the specific gastro-intestinal infections, local causes of diarrhoea, digestive disorders, and the parenteral infections or infectious diseases in which diarrhoea was an insignificant symptom. To give more uniformity the cases have been divided into dehydrated and non-dehydrated groups as shown in table 1, for the signs of dehydration are obvious and its presence influences adversely the severity and outcome of the illness. There were two hundred and eighty-three dehydrated infants in the series, and it is these cases which will mainly be used in a discussion of the etiology and mortality of gastro-enteritis.

TABLE 1

MORTALITY IN DEHYDRATED AND NON-DEHYDRATED CASES OF NON-SPECIFIC INFANTILE DIARRHOEA

INFANTILE DIARRHOEA (NON-SPECIFIC)	NO. OF CASES	NO. OF DEATHS	PERCENTAGE MORTALITY
All cases	574	159	27.7
Dehydrated cases	283	152	53.7
Non-dehydrated cases	291	7	2.4

Etiology

Age. No patient aged over two years has been seen with gastro-enteritis of the infantile type. When infants with severe gastro-enteritis were admitted from a nursery during the course of a local outbreak, children between two and five years of age came into hospital from the same institution suffering from a

mild diarrhoea which resolved on a light and mainly carbohydrate diet with gradual increase to normal feeding. Whilst these illnesses were not due to specific organisms or known dietary error, a connexion between the cases could not be proved and the value of this observation in the epidemiology of the disease must remain conjectural. Typical gastro-enteritis did not occur in children over two years of age and was less common and milder in the second year of life.

In table 2 the cases are arranged in five groups, comprising the first four trimesters and the second year for dehydrated and non-dehydrated infants. In the series 69.7 per cent. of all cases were under nine months old. The figures for dehydrated and non-dehydrated cases were 80.9 per cent. and 58.8 per cent. respectively. Infants in the second year formed 17.1 per cent. of all cases, 7.4 per cent. of dehydrated cases, and 26.5 per cent. of non-dehydrated cases. The incidence was highest between three and nine months, and above this age for the final three-monthly period of the first year there was a rapid fall to one-half the numbers in the second trimester.

TABLE 2
ANALYSIS BY AGE GROUPS

AGE IN MONTHS	ALL CASES			DEHYDRATED CASES			NON-DEHYDRATED CASES		
	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY
0-3	109	32	29.3	61	32	52.5	48	0	—
3-6	158	56	35.4	93	54	58.1	65	2	3.1
6-9	133	47	35.3	75	47	62.7	58	0	—
9-12	76	15	19.7	33	13	39.4	43	2	4.7
12-24	98	9	9.2	21	6	28.6	77	3	3.9

Published reports show a similar picture of a disease which affects chiefly the infant under one year, but observers in Britain commonly describe the highest incidence at an earlier age. In Parsons' (1924) series most of the infants were less than three months old. Cooper (1937) found that cases were most common between three and six months, and afterwards the number affected fell rapidly. A peak in incidence between one and two months and a regular decline in frequency from the third month is described by Smellie (1939). In the present series no significant reduction in the number of cases occurred before the later age of nine months.

The percentage of the cases with dehydration in any age-group showed a parallel course which is presented in table 3 and was highest between three and six months (58.9 per cent.); it fell to lower levels between nine and twelve months (43.4 per cent.) and in the second year (21.4 per cent.). A real decrease in the severity of the illness accompanied the lessening prevalence after the eighth month of life.

TABLE 3
INCIDENCE OF DEHYDRATION IN AGE GROUPS

AGE IN MONTHS	NO. OF CASES	NO. OF DEHYDRATED CASES	PERCENTAGE OF CASES DEHYDRATED
0-3	109	61	56.0
3-6	158	93	58.9
6-9	133	75	56.4
9-12	76	33	43.4
12-24	98	21	21.4
0-24	574	283	49.3

Feeding. In this series eighteen infants or 4.5 per cent. of the infants under nine months were breast-fed at the onset of the illness, and only three of them died. The infrequency of the disease in breast-fed infants has been recognized for many years, and is further supported in recent reports on gastro-enteritis.

Findlay (1932) found 9 per cent. of the infants breast-fed in a series of three hundred cases, Cooper (1937) 3 per cent. among three hundred cases, and Smellie (1939) 2½ per cent. in five hundred patients. Breast-fed infants according to Spence (1938) enjoy a greater freedom and enhanced recovery from disease than artificially-fed infants; and in infantile diarrhoea figures given by Smellie (1939) show that the death-rate in infants who have been breast-fed in the early months of life is as little as one-third of that in infants fed artificially from birth. The breast-fed infant is not frequently affected by the disease and is unlikely to die of uncomplicated gastro-enteritis.

Residence. The risk of infections spreading among infants living in a community such as a nursery, institution or hospital ward is well known to paediatricians; but to say that gastro-enteritis is a disease of such communities is an exaggeration, which is not supported by the present figures. One hundred and twenty-seven (22.1 per cent.) of all the cases had developed the illness in an institution, and of the two hundred and eighty-three dehydrated cases sixty-eight (24.0 per cent.) were of similar origin. No information of the populations at risk is available in order to compare the frequency of the disease in the home and institution, but it can be said that however great the likelihood of transmission of gastro-enteritis may be in communities of infants, the problem of the control and treatment of the disease in the home is the wider one. Cooper (1937) found a great increase in incidence in families of five or more, and stressed the influence of overcrowding.

Seasonal incidence. For the first quarter of this century and even longer the summer diarrhoea of infants was known as an annually recurring disease which rose to epidemic proportions in hot dry summers.

Findlay (1932) reports that in the epidemic year of 1921, 64 per cent. of the cases occurred between July and September, and in Nabarro's (1923) series of the same year the highest numbers were affected in the last two weeks of July and the first week of September. In America Marriott and others (1933) found that non-dysenteric diarrhoea in children was most frequent in the early autumn months. More recent reports show a change in the seasonal

prevalence, while they do not support the view that gastro-enteritis is now more common in winter. Almost half of Cooper's (1937) series of cases seen in Glasgow between 1931 and 1934 occurred in August, September and October, and 68.8 per cent. from June to October. Smellie (1939) regarded the slight increase in incidence from July to October in his series as insignificant, and considered that the summer diarrhoea of text-books has been replaced by a disease of mixed etiology which is present throughout the year.

The figures for the years 1937 and 1938, which are the completed years in the present series, are shown in the tables. Cases seen in 1939 have been excluded because the period until August only has been analysed; later in the year the rate of admission of patients was altered by a reduction in the available beds and by evacuation of infants as well as by a decline in the incidence of enteritis, which is suggested by the fall in the weekly number of deaths from this cause in the later months of 1939. The cases are grouped in the month of onset of the illness, and table 4 presents the results for all cases seen in the two years. Table 5 deals with dehydrated cases and those without parenteral infections on admission have been analysed in table 6.

TABLE 4
INCIDENCE OF CASES AND DEATHS IN YEARS 1937 AND 1938
GROUPED BY MONTH OF ONSET OF SYMPTOMS

MONTH	NO. OF CASES	PER-CENTAGE OF TOTAL	NO. OF DEATHS	PER-CENTAGE DEATH RATE	MONTH	NO. OF CASES	PER-CENTAGE OF TOTAL	NO. OF DEATHS	PER-CENTAGE DEATH RATE
January	17	3.8	4	23.5	July ..	53	11.9	17	32.1
February	39	8.8	4	10.3	August ..	43	9.7	10	23.3
March ..	20	4.5	7	35.0	September	53	11.9	17	32.1
April ..	31	7.0	11	35.5	October ..	43	9.7	5	11.5
May ..	35	7.9	10	28.6	November	29	6.5	7	24.1
June ..	40	9.1	14	35.0	December	41	9.2	14	34.1

444 cases; 120 deaths.

TABLE 5
MONTHLY INCIDENCE AND DEATH RATE IN 211 DEHYDRATED CASES
(YEARS 1937 AND 1938)

MONTH	NO. OF CASES	PER-CENTAGE OF TOTAL	NO. OF DEATHS	PER-CENTAGE DEATH RATE	MONTH	NO. OF CASES	PER-CENTAGE OF TOTAL	NO. OF DEATHS	PER-CENTAGE DEATH RATE
January	5	2.6	4	80.0	July ..	24	11.4	17	70.8
February	7	3.3	3	42.9	August ..	23	10.9	10	43.5
March ..	10	4.7	7	70.0	September	33	15.6	17	51.5
April ..	19	9.0	11	57.9	October ..	21	10.0	5	23.8
May ..	13	6.2	10	76.9	November	15	7.1	7	46.7
June ..	17	8.1	13	76.5	December	24	11.4	13	54.2

211 cases; 117 deaths.

TABLE 6
MONTHLY INCIDENCE IN 1937 AND 1938 IN CASES WITHOUT
INFECTIONS ON ADMISSION

MONTH	ALL CASES	DEHYDRATED CASES	MONTH	ALL CASES	DEHYDRATED CASES
January ..	9	3	July ..	43	21
February ..	23	3	August ..	30	17
March ..	17	10	September ..	40	25
April ..	25	16	October ..	37	20
May ..	25	11	November ..	17	8
June ..	33	16	December ..	18	12

317 cases; 162 dehydrated.

Of the four hundred and forty-four cases more than half (52·3 per cent.) occurred in the five months from June to October. The highest number of cases was in July and September and the lowest in January and March, whilst in the other months the variation in the figures was small. The analysis of the two hundred and eleven dehydrated cases gives similar results; 56 per cent. occurred in the same five months, and the highest incidence was in September and the lowest in January and February. It is noteworthy that July and December had the same number of cases, which was exceeded only in September.

Since gastro-enteritis may be a disease of mixed causation, it might be thought that the seasonal incidence of any series of cases would be the result of the interplay of a variety of infections of different epidemic constitution. Cases without parenteral infections early in the illness have been analysed in order to see if they have a different seasonal incidence from the whole group; since respiratory infections such as bronchitis, bronchopneumonia and otitis media are more common in winter, it was thought that a more marked seasonal increase in the summer months might be seen when the patients in whom gastro-enteritis and a parenteral infection were associated early in the illness were excluded from the series. Table 6 does not show any wide divergence from the incidence in the previous tables. In the five months from June to October a slight increase in the percentage of cases occurred especially among the dehydrated infants; the figures were 57·7 per cent. for all cases and 66·0 per cent. for dehydrated cases. An alteration of some note is that the incidence in December was lowered, being less than half that in July. In gastro-enteritis unassociated with parenteral infections there was a greater tendency to assume epidemic increase in summer and autumn and to maintain a lower incidence without peaks in the other seasons of the year.

Parenteral infections. Infections in systems other than the gastro-intestinal tract are frequently found in infants with gastro-enteritis, but only the parenteral infections which appear in the early days of the illness can be regarded as playing a part in causing the disease. An attempt has been made to detect all of these conditions by a full examination of the infant, including inspection of the ear-

drums, on the day of admission and the following day. A catheter specimen of urine was examined when symptoms such as fever, vomiting and meningism indicated the probable presence of an infection of the urinary tract.

One hundred and seventy-five (30.5 per cent.) of the five hundred and seventy-four infants had one or more parenteral infections on admission to hospital, and of the two hundred and eighty-three dehydrated cases seventy-four (28.1 per cent.) can be placed in the same group. Even if these parenteral infections acted as causal agents in every instance, less than one-third of the cases could be attributed to this source. Smellie (1939) found that 46.2 per cent. of his patients had unequivocal signs of parenteral infection on admission to hospital. Over half of these infections in Smellie's series were otitis media and mastoiditis, while among the present cases there was a much lower frequency of otitis and mastoiditis, which formed only 13.2 per cent. of the infections in all patients and 19.0 per cent. in the dehydrated cases. The great difference in the incidence of disease of the middle ear accounts for the significant variation in the percentage of cases with parenteral infections early in the illness in these series seen in different parts of Britain during approximately the same years.

The nature of these conditions is shown in tables 7 and 8. The figures for all cases and dehydrated cases were similar. Infections of the respiratory tract such as otitis media, mastoiditis, stomatitis, pharyngitis, laryngitis, bronchitis and bronchopneumonia formed 78.9 per cent. of the accompanying diseases in all cases and 81.4 per cent. in the dehydrated cases. Other infections were present only in a small number of cases. Four-fifths of the infections which occurred early in the course of gastro-enteritis in this series involved the respiratory tract, including the middle ear and mastoid.

TABLE 7

NATURE OF PARENTERAL INFECTIONS PRESENT ON ADMISSION

PARENTERAL INFECTIONS	NO. OF CASES	PERCENTAGE OF TOTAL	NO. OF DEATHS	PERCENTAGE MORTALITY
Otitis media and mastoiditis	14	8.0	1	7.1
Tonsillitis, laryngitis, bronchitis and broncho-pneumonia	96	54.9	21	21.9
Urinary infections	7	4.0	2	28.6
Stomatitis	10	5.7	3	30.0
Eczema or dermatitis	17	9.7	2	11.8
Congenital syphilis	1	0.6	1	100.0
Vaccinia	4	2.3	1	25.0
Measles	1	0.6	1	100.0
Whooping cough	7	4.0	1	14.3
Bronchitis and otitis media	7	4.0	3	42.9
Bronchitis and urinary infections	3	1.7	1	33.3
Bronchitis and stomatitis	3	1.7	1	33.3
Bronchitis and dermatitis	2	1.1	2	100.0
Urinary infection and stomatitis	1	0.6	1	100.0
Otitis media and dermatitis	1	0.6	0	0
Bronchitis, otitis media and stomatitis	1	0.6	0	0
Total	175	—	41	23.4

TABLE 8
NATURE OF PARENTERAL INFECTIONS PRESENT ON ADMISSION
IN 74 DEHYDRATED CASES

PARENTERAL INFECTIONS	NO. OF CASES	PERCENTAGE OF TOTAL	NO. OF DEATHS	PERCENTAGE MORTALITY
Otitis media or mastoiditis	7	9.5	1	14.3
Laryngitis, bronchitis and pneumonia ..	33	44.6	18	54.6
Urinary infections	5	6.8	2	40.0
Stomatitis	5	6.8	3	60.0
Eczema and dermatitis	4	5.4	1	25.0
Congenital syphilis	1	1.4	1	100.0
Vaccinia	1	1.4	1	100.0
Measles	1	1.4	1	100.0
Whooping cough	2	2.7	1	50.0
Bronchitis and otitis media	6	8.1	3	50.0
Bronchitis and urinary infections	3	4.1	1	33.3
Bronchitis and stomatitis	2	2.7	1	50.0
Bronchitis and dermatitis	2	2.7	2	100.0
Urinary infection and stomatitis	1	1.4	1	100.0
Otitis media, bronchitis and stomatitis ..	1	1.4	0	—
Total	74	—	37	50.0

Otitis media and mastoiditis were less common in the present series than in others of which reports have been published and around which controversy has developed on the rôle of middle-ear disease in the causation of gastro-enteritis.

For example, the percentage of the cases showing otitis or mastoiditis was as high as 25 per cent. in Smellie's (1939) series and 26 per cent. in Cooper's (1937) cases, whereas only 5 per cent. of the cases now reported suffered from these conditions. Findlay (1932) expressed doubts about there being a causal relationship between otitis media and gastro-enteritis, but observations indicating an etiological connexion between these diseases have been recorded by several observers (Floyd, 1925; Marriott, 1928; Ebbs, 1937; and McConkey and Couper, 1938) on a wide range of clinical and post-mortem material. Smellie (1939) thinks that parenteral infection (especially disease of the middle ear) is sometimes the cause and sometimes the consequence of infantile diarrhoea.

This opinion must be accepted, but the proportion of cases due to parenteral infections must be regarded as variable. Whilst infections of the middle ear, bronchial tree and lungs form the greater part of these conditions, there are local and seasonal differences in their relative importance. Otitis media was found much less often than chest infections in the present series. These divergences in the frequency of the different infections may depend on the interplay of such factors as climate, season and variation in the prevalence and virulence of the haemolytic streptococcus. Many of the parenteral infections were mild and would not in themselves be a cause of severe illness; and even if it is accepted that such minor infections play a causal rôle in gastro-enteritis, they can act only as trigger mechanisms on the basis of a constitutional abnormality or gastro-intestinal imbalance of infancy.

Mortality

The average death rate in this series was 27·7 per cent. A striking difference is seen in table 1 between the death rate in the two hundred and eighty-three dehydrated infants (53·7 per cent.) and in the two hundred and ninety-one non-dehydrated infants (2·4 per cent.), and this remarkable disparity indicates how important it is to assess correctly the state of the water balance in these sick infants. Many of the non-dehydrated patients may have suffered from diarrhoea due to a digestive upset, for dietetic errors are difficult to detect, but this error is less probable in the dehydrated cases. If the term gastro-enteritis is confined to the severer cases of diarrhoea which show dehydration, cyanosis or toxicity, the clinical syndrome is more sharply defined, although the individual element in detecting dehydration will influence the mortality rates in the series of different observers.

Cooper (1937) had a death rate of 47·2 per cent. in a series of three hundred patients, of whom 66·8 per cent. were dehydrated. A death rate of 48 per cent. was recorded by Smellie (1939). These figures are of the same order as the mortality rate of 53·7 per cent. among the dehydrated infants in this series. Lower death rates which have been described by other observers such as Cohen (1933) may be due to inclusion of milder cases of gastro-enteritis in the series.

In comparing the effect of certain factors on mortality rates attention will be paid mainly to the dehydrated cases.

Age. The figures in table 2 show that the disease was most fatal under nine months of age. In the three monthly periods under nine months the death rates were 52·5 per cent., 58·1 per cent. and 62·7 per cent. respectively for the dehydrated cases. There was a sharp fall to 39·4 per cent. between nine and twelve months and in the second year this decline in the mortality continued to 28·6 per cent., which was less than half the highest percentage between three and nine months. Too few infants under one month were seen to give figures for the neonatal period, in which Cooper (1937) found a high mortality of 73·6 per cent. It may be concluded that under nine months over half of the affected infants will die and even above this age death is a probable issue in one-third of the patients.

Duration of symptoms. The results in one hundred and sixty-eight cases which were treated by constant subcutaneous fluid have been analysed according to the day of illness on admission in table 9. There is little difference in mortality between the infants who had been ill for not more than three days and others whose symptoms were of four to six days' duration; when the symptoms had been present for seven days or longer there was a definite decrease in the death rate. Under the age of nine months the duration of symptoms had no definite influence on the death rate. In infants over nine months old the proportion with symptoms of seven or more days' duration was increased because of the lessening severity of the disease. The period of the illness at which treatment was begun did not affect the outcome in this analysis, but an examination by individual days over a large series would be required to decide whether early treatment improves the prognosis.

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TABLE 9

EFFECT OF DURATION OF ILLNESS BEFORE ADMISSION ON DEATH RATE IN 168 CASES TREATED MAINLY BY CONSTANT SUBCUTANEOUS DRIP

AGE IN MONTHS	1 TO 3 DAYS		4 TO 6 DAYS		7 DAYS OR MORE	
	NO. OF CASES	NO. OF DEATHS	NO. OF CASES	NO. OF DEATHS	NO. OF CASES	NO. OF DEATHS
0-3	24	11	8	4	10	6
3-6	21	12	22	14	9	3
6-9	14	7	18	9	10	5
9-12	6	2	4	2	12	3
12-24	4	2	2	1	4	0
0-24	69	34	54	30	45	17
		(49.3)		(55.6)		(37.8)
0-9	59	30	48	27	29	14
		(50.8)		(56.3)		(48.3)
9-24	10	4	6	3	16	3
		(40)		(50)		(18.8)

Six of the 174 cases in table were excluded because of an inadequate history of symptoms. Figures in brackets represent percentages.

Season. Among the dehydrated cases shown in table 5 the death rate was high throughout the year except in the month of October, and the highest percentages in January and March of the winter months and May, June and July of the summer months differed little.

Parenteral infections. Table 10 presents a comparison of the death rates in the two hundred and eighty-three dehydrated cases with and without parenteral infections on admission. Fifty per cent. of infants with parenteral infections died, while death occurred in 55 per cent. of the cases showing no infections. Under six months of age, however, the mortality rate was higher among the infants with parenteral infections, but at later ages a lower fatality rate was uniformly present in this group. Thus the cases of gastro-enteritis

TABLE 10

ANALYSIS OF THE 283 DEHYDRATED CASES IN AGE GROUPS ACCORDING TO THE PRESENCE OR ABSENCE OF PARENTERAL INFECTION ON ADMISSION

AGE IN MONTHS	ALL CASES			PARENTERAL			NON-PARENTERAL		
	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PER-CENTAGE MORTALITY
0-3	61	32	52.5	10	6	60.0	51	26	51.0
3-6	93	54	58.1	20	15	75.0	73	39	53.4
6-9	75	47	62.7	25	12	48.0	50	35	70.0
9-12	33	13	39.4	11	2	18.2	22	11	50.0
12-24	21	6	28.6	8	2	25.0	13	4	30.8
0-24	283	152	53.7	74	37	50.0	209	115	55.0

which may have been caused by infections outside the gastro-intestinal tract had a death rate which was higher than the mortality in cases of other origin only among infants less than six months old; and, indeed, at the later ages the prognosis in the parenteral cases was slightly more favourable than in the whole dehydrated group. Cooper (1937) reported that in his cases the results of the illness were not strikingly affected by parenteral infections, and that otitis media had not adversely influenced the outlook. In table 8 it is evident that the infections associated with a high mortality were bronchitis and broncho-pneumonia, urinary infections and stomatitis. The death rate in infants with otitis media and mastoiditis was much below the average level and, even when instances of otitis media in patients with more than one parenteral infection were included, it amounted to only 28.6 per cent. in the dehydrated cases.

Only the infections already present on admission have so far been considered. Gastro-enteritis was in seventy-four of the two hundred and eighty-three dehydrated infants complicated by parenteral infections at this time and another fifty-eight patients developed a complication of this kind after admission to hospital. The nature of the infections and the death rate in the fifty-eight cases are set forth in table 11. Twenty-six of them (48.8 per cent.) died. One hundred and thirty-two (46.6 per cent.) of the dehydrated infants with gastro-enteritis had a parenteral infection at some stage of the illness and death occurred in sixty-three of the number (47.7 per cent.), a percentage which is lower than the average mortality rate of 53.7 per cent. Infections of the respiratory tract remained the most fatal of the complications, and diseases of the middle ear and mastoid were more prominent and were associated with a higher death rate in the smaller group, in which it complicated the gastro-enteritis, than in the infants in whom otitis media and mastoiditis were a presenting feature.

TABLE 11
PARENTERAL INFECTIONS AFTER ADMISSION TO HOSPITAL

PARENTERAL INFECTIONS	DEHYDRATED CASES		ALL CASES	
	NO. OF CASES	NO. OF DEATHS	NO. OF CASES	NO. OF DEATHS
Otitis media	11	5	14	5
Rhinitis, bronchitis and broncho-pneumonia	31	14	45	14
Urinary infections	0	0	3	1
Stomatitis	2	1	2	1
Eczema, boils and dermatitis	2	0	4	0
Pertussis	5	2	6	2
Submaxillary adenitis	1	1	1	1
Staphylococcal pyaemia	1	1	1	1
Otitis media and bronchitis	3	2	5	2
Otitis media and pertussis	1	0	1	0
Stomatitis and eczema	1	0	1	0
Total	58	26	83	27

Whether the parenteral infections were present as a causal factor or developed during the course of the illness, they had no adverse influence on the mortality rate. Bronchitis and bronchopneumonia were the most common of the infections and occurred in the majority of the fatal illnesses. The importance assigned to otitis media and mastoiditis by several observers cannot be confirmed; in the series only twenty-five out of the one hundred and thirty-two cases with parenteral infections had these conditions and the nine deaths among these patients imply a death rate of 36 per cent., which is lower than the average level for the dehydrated infants whether with or without parenteral infections.

Treatment

Prophylaxis. Breast-feeding from birth is almost a sure guarantee that the infant will not succumb to infantile diarrhoea and vomiting and when diarrhoea supervenes it generally signifies digestive upset, parenteral infection or specific infection. When this occurs, it is imperative that breast milk be continued and it is, therefore, a mistake of judgment to deprive the child of the mother's milk. Treatment is best carried out at home if the mother is unable to feed her child in hospital. In spite of the undoubted safeguard provided by breast-feeding, it has been estimated that only 30 per cent. of mothers at the present time completely feed their infants for the first six months of life, and it is certain this percentage will drop still lower as the rigours of war upset the conditions of home life.

Parenteral infection. A complete clinical examination must be carried out as soon as possible after admission, but this must be done in a warm atmosphere, preferably in front of a fire. With the good results from chemotherapy in several infections the importance of early treatment cannot be too strongly stressed. Details of treatment follow modern accepted teaching.

Feeding. A starvation period of 24 to 48 hours is a good routine, but severely dehydrated and toxic infants will benefit from an even longer period. During this time water should be given by mouth in small amounts at frequent intervals and if parenteral fluid is not being given concurrently, half-normal saline should also be given by mouth. Lelong (1938) and other French authors prefer to give vegetable soups and cereal concoctions, but the value of the latter is mainly due to their salt content in some palatable form. This regime leads to such a marked improvement in toxic cases that it would appear desirable to prolong the starvation period for a much longer period if a more satisfactory method of parenteral feeding could be evolved. Some attempts in this direction will be described later. Glucose is next added to alternate feeds. At this stage many authors favour a milk-free transition diet. Thus Czerny and Keller (1928) recommend the use of whey with, later, the addition of a 10 per cent. rice gruel, but it has generally been possible by careful and gradual change to pass from glucose and water to a separated dried milk using small feeds at regular intervals with modifications as dictated by progress. If vomiting has ceased, the character of the stools has improved, and the weight is more or less constant, the next step is the gradual replacement measure by measure of the

separated by half-cream dried milk. In general, all infants with gastro-enteritis tolerate fats badly and too sudden increase of fat in the feeds will invariably precipitate a relapse of the diarrhoea. When the infant is taking adequate amounts of half-cream dried milk, it is advisable in convalescence to give extra iron in the form of the ferrous sulphate syrup advised by Mackay (1937). When the acute symptoms have subsided and the stools returned to normal, daily amounts of the concentrated vitamin preparations should also be given and continued for some time afterwards.

The most difficult and the most disappointing patients are those with persistent vomiting without any causative parenteral infection. When there is marked acidosis and large amounts of fluids have been given parenterally without abatement of vomiting, it is usually found that other measures, such as the giving of sodium bicarbonate, are only temporary expedients and if the vomit contains coffee ground material the prognosis is almost invariably fatal. The giving of milk in any form to these patients results in an exacerbation of symptoms. It is almost impossible to get nourishment by the mouth absorbed, and the slow but continuous wasting is soon fatal. The use of acid milk feedings goes back to antiquity to the days when Herodotus recommended sour milk in the treatment of diarrhoea. Buttermilk has also been used in various countries for several centuries and good results have been reported following the use of commercial preparations by Langstein (1927), Engel (1930), Feer (1934), Glanzmann (1934) and Studer (1935). The power of precipitation of casein curds in finely divided form and the low fat, high calcium content of these foods are therapeutic advantages, but it is almost generally agreed that as stated by Marriott (1927) and Feer (1934) the value is chiefly in the lactic acid content and is not due to any specific action of the lactic acid bacilli.

Marriott (1935) and Freudenberg (1929) think that the acidification of the milk causes neutralization of a portion of buffer substances so that the acidity attained in the stomach approximates to that when human milk is fed. This acidity is sufficient to inhibit the growth of paracolon bacilli as demonstrated by Hassmann (1936) whose experimental work appears to justify the use of acid milks as prophylactic agents to prevent exogenous paracolon bacilli infection.

The results, however, from acid milk feeding in treatment, have not been better than those with ordinary dried milk.

The apple diet was first introduced by Moro (1929) and Heisler (1929) and since then various authors have reported such widely divergent results that this form of treatment has been relegated to the background only to be revived by enthusiasts from time to time. Finely divided apple and a commercial preparation have been used in the present series, but no improvement following their use in young infants has been noticed. In older infants, however, over nine months of age, with a sub-acute form of illness and capricious appetite, the commercial preparation is a useful diet when ringing the changes, and from time to time an infant is met with who prefers it to dried milk. It is interesting to note that Voss (1937) has demonstrated by x-ray examination that the reaction of the intestine to apple diet in infants in the first six months of life is strikingly different

from that in older infants and children. Pectin and cellulose are the elements reputed to be of specific value, and recently Howard and Tompkins (1940) have reported excellent results using a standard pectin agar milk mixture. Their chief success was in the treatment of a rather unusual epidemic of diarrhoea with mucus and blood in the stools in a group of twenty-three newly born infants, from the faeces of whom no known pathogenic organisms were isolated. This latter treatment was also successfully applied in a group of older infants and children.

Parenteral fluid therapy. This will be discussed in a later communication when the question of water and salt metabolism is reviewed in detail. Suffice it to say that at present the continuous subcutaneous route for dehydrated cases is favoured, ringing the changes between normal saline, Ringer's solution and 3 per cent. glucose in 0.25 per cent. saline, and in severely ill patients this should be supplemented in the first twenty-four hours by intraperitoneal or intravenous therapy.

Blood transfusion. Marriott (1927) believed that beneficial effects of parenteral fluid therapy were more lasting if combined with blood transfusion. Blood was found only of value in the present series in patients with a definite anaemia and in those with a long-standing infection, such as otitis media. Plasma transfusions as recommended by Aldridge (1938) are valuable in the later stages of the illness when there is hypoproteinaemia, either with or without oedema. When the serum protein is maintained at a normal level parenteral fluid therapy by the continuous subcutaneous route can be maintained. Blood transfusions are, therefore, chiefly of value in the rather older infants, approximately nine months of age and over, as they appear to tide the child over the danger period till it reaches an age when the body powers of recovery appear to be better developed.

Drugs. Apart from the chemotherapy of certain parenteral infections, drugs are of little value in treatment. Aperients are of value in a limited number of cases in which food poisoning is suspected, but are of little value in any case after the first twenty-four hours of the illness. Alcohol has its advocates but Keller (1932), and others think it is contra-indicated. In the present series brandy in 20 to 30-minim doses has been used several times a day, as it has been found of value as a stomach sedative in certain cases in which there was difficulty in feeding and recurrent vomiting. It is of no value when vomiting is persistent and intractable and associated with gross metabolic disturbance. Nephenthe, also, has been used when there was persistent restlessness and resultant loss of sleep, but these symptoms are of evil import and usually signify a fatal issue.

Parenteral alimentation. Present methods of treatment are designed to combat dehydration by the use of various salt solutions and water, but the greatest proportion of the caloric food intake is still given by mouth to be absorbed from the alimentary tract under adverse conditions. Broadly speaking, to sustain life six elements must be supplied—water, salts, carbohydrate, protein, fat and vitamins. The first three have been used extensively in treatment and certain vitamins (B₁, B₂, C and nicotinic acid) can also be given, but so far suitable solutions of protein and fat have still to be found. Human

plasma transfusions are the best means available of replacing depleted serum protein and their value is undoubted when hypoproteinaemia with or without oedema is present, but plasma protein has the drawback that it must first be hydrolysed in the body into its constituent amino-acids before it can be of any value as a source of tissue protein, and it is very doubtful if this process can occur in a severely ill child. Of the twenty odd amino-acids which make up protein foods, only nine, and possibly ten, are essential.

Rose (1937) has calculated the ideal formula of essential amino-acids for growth, but it is a practical impossibility to prepare each of these essential amino-acids separately and mix them in the right proportions. A much more economical method is to select a relatively pure protein like casein which when hydrolysed produces all the essential amino-acids except tryptophane, which is almost completely destroyed in the process. This mixture also contains relatively little cystine. In animals it has been found that a 10 per cent. hydrolysate of casein to which has been added 2 per cent. tryptophane and 2 per cent. cystine can be used parenterally to maintain the nitrogen balance. This solution has been well tolerated also by man when given intravenously, by Elman and Weiner (1939) with either Ringer's solution or dextrose solution. Experimental and clinical studies by Elman and Weiner (1939) have shown that the injected amino-acids are rapidly utilized leading to the regeneration of serum protein and the reduction of nutritional oedema.

In the present series a dilute isotonic solution has been used and found to be satisfactorily absorbed by the subcutaneous route without any apparent ill effects. Unfortunately, however, as the treatment is necessarily prolonged and the cost of preparation of tryptophane is still high, the cost of undertaking an extensive investigation was found to be prohibitive. Amino-acid therapy must therefore wait until a more economical method of preparation has been discovered. From the viewpoint of caloric intake the advantage of giving fat is obvious and actually a fine emulsion for intravenous injection has already been prepared by Holt et al. (1935); it is doubtful, however, if it is really necessary for maintenance. It has also been found that, even for growth, fat is dispensable if one unsaturated fatty acid—linoleic acid—is provided, as the other necessary lipoids can be manufactured from protein and carbohydrate. By developing a natural balanced and economic form of parenteral alimentation, the beneficial effects of starvation treatment can be prolonged to give rest to the alimentary tract. The best results from present methods of treatment mean recovery in only half the dehydrated infants, but in a proportion of the others there develops after several weeks a characteristic picture of starvation combined with toxæmia leading to an 'old man' appearance; it is therefore hoped that new methods of treatment along the lines suggested will lead to a reduction in infant mortality from the disease.

Other measures. Stomach lavage is always worth a trial in cases of persistent vomiting, but the benefit is usually only temporary and once the vomit has reached the coffee ground stage, lavage produces little if any clinical improvement.

Colonic lavage with warm saline solution has a definite place in treatment when the stools are frequent, watery and so acid in character that excoriation of the buttocks is liable to occur.

Ward management

The only guides in dealing with the management of isolation are based on empirical knowledge of gastro-enteritis and inexact analogy with other infections of which experience is securely founded. Measures designed to control the spread of infection should aim at eliminating the transmission of pathogenic organisms of intestinal origin and bacteria or viruses from the respiratory tract in droplets; in open wards the conditions should be such as to prevent aerial carriage of pathogenic bacteria and viruses, which has been established as a factor in the spread of infection by the work of Wells and Wells (1936) and Cruickshank (1939). Individual cells or chambers in association with an open ward or the Hiorns ward (described by Brincker, 1938) provide the necessary isolation with reasonable economy of staff and beds. For various reasons this may not be practicable; and an open ward can be used with little risk of spread of enteritis or relapses but with a high rate of complications. Relapses or fresh attacks of severe enteritis were seen on three occasions when there were too many acute cases in the ward; complications developed after admission in about one-fifth of the dehydrated cases. Bed isolation should prevent indirect transmission and much can be done to reduce droplet infection or aerial carriage by free ventilation, damp or vacuum cleaning, and careful disposal of soiled linen.

The ratio of nurses to infants was four to seven in the ward described by Smellie (1939). In the present series eight nurses were available in a sixteen-bedded ward and the number increased by one or two when occasion arose. The infant with enteritis requires frequent attention throughout the day and night and hours of duty by day and night have to meet this need; in practice one nurse can attend to four to six infants according to the severity of the illness. Dilution of the ward with older infants suffering from gastro-enteritis and convalescent cases lessens the work of nursing and diminishes the risk of cross-infection; four or five acute cases in a sixteen-bedded ward is a safe limit, ensuring against relapses and overworking of the staff. A system of 'feeders' and 'changers' is preferable, and essential if the nurses are not experienced in isolation methods. It is estimated that separation of 'feeding' and 'changing' increases the requirement of nurses by one-third. When this system cannot be adopted, one nurse should attend to the preparation of the feeds whether they are done daily or by single feeds and should not engage in 'changing.'

The ward temperature requires to be maintained and free ventilation across the ward secured. The standard of twelve feet between the bed centres is necessary for spacing. Attendants or visitors with acute infections should be excluded from the ward. Masks were adopted at seasons when acute illnesses were prevalent among the nurses; the envelope type can be worn at work for long periods. Daily weighing of the infants in the acute phase and accurate records of the fluid intake, stools and vomits give valuable information.

Destructible squares are convenient and should be used in the acute period of the diarrhoea. Later a small square of lint or gamgee inside the napkin is convenient. Bins on movable stands should be used to receive and dispose of

destructible squares or any dressings to the buttocks, and separate bags should be used for ordinary squares and linen. Clean squares and linen should be kept covered and handled only by a 'clean' nurse. Sluicing is the duty of 'changers,' but it is better that the ward staff should not do sluicing, and dispose of the bags to a central sluice-room or 'foul washer' for separate treatment. Bathing is confined to convalescents, but as convalescent carriers of paracolon bacilli have been described the possibility of conveying infection by bath water should be foreseen by providing individual baths. A refrigerator is required for the feeds. Detailed rules are necessary to establish a technique of bed isolation. As far as possible the acute cases can be put in the isolation rooms attached to an open ward.

Summary

The etiology of infantile diarrhoea and vomiting is discussed and a simple classification given.

In the series of five hundred and seventy-four cases of gastro-enteritis (A.I.C. group) there was a death rate of 27.7 per cent. The greater proportion of the patients contracted the disease at home and only about 20 per cent. of the total number were admitted from institutions. Although cases were admitted throughout the year, the demand for beds was greater in summer and autumn. On admission there was evidence of parenteral infection in less than one-third of the total number and approximately four-fifths of these showed involvement of the respiratory tract. Infections of the middle ear and mastoid accounted for a relatively smaller proportion of the total respiratory infections than has been noted by other observers. Taking the series as a whole, parenteral infection had no apparent effect on the general death rate. Age seems the most important feature in prognosis as the great majority of the deaths occur in infants less than nine months of age.

Whilst the general nursing management must be of a high order to ensure success with consistently good results, the most important single factor in treatment is the relief of dehydration. The value of constant subcutaneous infusions, supplemented in severe cases by fluid given either by the intraperitoneal or intravenous route is important. The death rate in two hundred and eighty-three dehydrated cases—53 per cent.—is in marked contrast to that in two hundred and ninety-one non-dehydrated cases—2.4 per cent.—and serves to emphasize the great importance of a careful assessment of the water balance in these infants.

Some notes on intravenous alimentation are recorded.

Management in open wards is possible only if there is adequate bed spacing, proper dilution of cases and if a strict nursing technique on the 'barrier' or 'bed' isolation method is rigorously enforced. Individual isolation accommodation is the ideal method.

The great prophylactic value of breast-feeding is again demonstrated and it can confidently be asserted that if a properly breast-fed infant is protected from parenteral infection, the danger to life from infantile diarrhoea and vomiting is negligible.

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