AN OUTBREAK OF INFANTILE GASTRO-ENTERITIS IN ABERDEEN

THE ASSOCIATION OF A SPECIAL TYPE OF *BACT. COLI* WITH THE INFECTION

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During the first 5 months of 1947 there occurred in the city of Aberdeen an outbreak of gastro-enteritis affecting children in the first year of life. The disease was of a severe nature and was associated with a high mortality rate.

Infantile gastro-enteritis of unknown aetiology has been recognized for a long time. The old name of 'summer diarrhoea' still figures in some of the text-books, indicating its former seasonal prevalence. During the last three decades, however, summer epidemics have diminished and minor outbreaks are apt to occur throughout the whole year (Payling Wright, 1946); Bloch (1941) even reports a peak incidence during the winter months. Most authors are agreed on the clinical course of the disease, the high death-rate—varying from 16 to 83 % in different outbreaks—the inadequacy of any form of treatment and the paucity of definite pathological lesions found at autopsy.

The first full reports, in recent years, of gastro-enteritis epidemics—mainly among new-born babies—come from America (Barénberg, Levy & Grand, 1936; Rice, Best, Frant & Abramson, 1937; Best, 1938; Frant & Abramson, 1938; Greenberg & Wronker, 1938; Lembcke, Quinlivan & Orchard, 1943). In this country Ormiston (1941) described three separate hospital outbreaks in England, and Bloch (1941) a similar epidemic in Glasgow. Sakula (1943) reviewed the clinical picture and the pathological changes found at autopsy. Gairdner (1945) analysed 216 cases in great detail and Gunn (personal communication, 1947) summarized the whole subject of gastro-enteritis, which is, according to Henderson (1943), the most lethal among all infections of the young infant.

Most workers agree that infantile diarrhoea should be classified on the following lines (Ormiston, 1941; Gairdner, 1945; Laurent, 1944; Payling Wright, 1946):

(1) *Non-infective*, where symptoms are due to faulty feeding, dentition, etc.

(2) *Secondary or symptomatic*, where the diarrhoea accompanies parenteral infection, e.g. otitis media, skin disease, measles, etc. In such cases toxaemia is held to be the usual cause.

(3) *Primary or infective.* (*a*) *Specific*, where a known and established causative agent is found, viz. *Bact. dysenteriae* and organisms of the enteric and salmonella groups. Cases due to infestation with parasites, such as helminths and flagellates, may also be included in this group. (*b*) *Non-specific*, a group in which the aetiology is unknown or uncertain. The existence of more than one infective agent in this group has not been proved, but some workers tend to separate the neonatal type of gastro-enteritis from varieties affecting older infants, although no causative organism has as yet been identified.

In this investigation we have dealt altogether with 159 hospital cases of infantile diarrhoea and have attempted, from the available clinical, pathological and bacteriological data, to divide these into non-infective, secondary and primary infective diarrhoea. In sixty-six patients the diarrhoea was deemed to be dietetic in origin or presented as a secondary feature of parenteral disease. Ninety-three cases appeared to belong to the primary infective group, in one of which *Bact. dysenteriae* Sonne was isolated. The remaining ninety-two showed no known pathogens but represented a clinical entity and were very frequently associated with a particular type of *Bact. coli*. We have therefore classed these cases as primary infective gastro-enteritis and append the following description of the disease.

EPIDEMIOLOGY

The majority of cases admitted to hospital were unrelated and no common source of infection could be established. On the other hand, the disease affected four sets of twins, and in one group of four cases direct contact infection appeared probable, before they were admitted to hospital. The majority of these cases came from parts of the town in which environmental conditions were not good. Two ward outbreaks were observed wherein it was possible to

trace the infection from case to case. In general, the distribution, the likely modes of infection and the infectivity of the disease were not unlike those of bacillary dysentery.

The distribution of the cases over the first 5 months is given in Table 1. The highest incidence occurred in March and the highest mortality in February. There were altogether fifty-two deaths among the ninety-two cases of primary gastro-enteritis, giving a case mortality of 56·5 %. The age incidence of the disease is given in Table 2. The age limits were 1 week to 1 year with a maximum incidence in the first 5 months. Both sexes appeared to be equally affected.

Table 1. *Distribution of cases over the first 5 months of* 1947

Month	No. of cases	No. of deaths	Mortality (%)
January	8	5	62·5
February	12	11	91·6
March	27	20	74
April	22	9	40·9
May	23	7	30·4
Total	92	52	56·5

Table 2. *Age incidence of cases of non-specific gastro-enteritis*

Age in months	No. of cases	No. of deaths	Mortality (%)
0–1	14	9	64·2
1–2	19	12	63·1
2–3	14	9	64·2
3–4	13	8	61·5
4–5	14	8	57·1
5–6	7	2	28·5
6–7	3	2	66·6
7–8	2	0	0
8–9	2	1	50
9–10	1	0	0
10–11	1	0	0
11–12	2	1	50
Total	92	52	56·5

Certain factors predispose the individual to the disease. First, in the present series, all affected infants, with one exception, were artificially fed, either by bottle or spoon. Secondly, although no parallel sociological investigation was carried out, it is highly probable that bad environmental conditions play an important part in the transmission of the disease. Thirdly, prematurity and general debility are obvious predisposing factors. Fourthly, other diseases, such as respiratory infection, may be contributory in that they render the infant more susceptible to infection.

CLINICAL MANIFESTATIONS

From a study of hospital infections, the incubation period would appear to be from 3 to 10 days, the majority of cases occurring before the fifth day.

The onset was usually sudden, although in a small number of cases less well defined. Vomiting was frequently the first sign and occurred in most cases. At first feeds were returned, but if vomiting persisted the vomit was usually bilious and later often brown, owing to the presence of altered blood.

Diarrhoea was the predominant feature and was present in some degree throughout the disease. Stools were usually numerous—up to eight or ten per day—loose and offensive; their appearance varied from time to time, but the predominant colour was green of varying shades. Orange-coloured and also brown-black stools were seen in some cases, indicating a severe attack. Mucus was usually present and occasionally frank blood.

The resulting picture was one of dehydration, disordered metabolism and toxaemia similar to that occurring in other conditions with diarrhoea and vomiting. In some cases these effects appeared early, in others late, depending chiefly on the severity of the diarrhoea and/or the effect of treatment. Peripheral circulatory failure was frequently encountered, especially in severe cases and those of sudden onset. Insomnia and restlessness were common signs, but abdominal pain did not appear to be severe. Appetite varied considerably and in mild cases was often little affected. Pyrexia and tachycardia were present in all cases. An initial rise in temperature characterized all cases which were seen early in the course of the disease and an irregular pyrexia followed, with a tendency to elevations of 103° F. or higher, whenever the child's condition deteriorated and immediately prior to death. Pyrexia at the onset of the disease, in the absence of obvious septic lesions, was probably due to toxaemia, since gross dehydration did not, as a rule, develop until later.

Examination of urine, blood and cerebro-spinal fluid failed to reveal any significant changes, apart from those directly due to dehydration and toxaemia.

The course of the disease was very variable. As a rule, symptoms would abate after the first few days, in response to general treatment, and in mild cases an uneventful recovery followed. Quite frequently, however, the patient deteriorated suddenly after an apparent improvement and death ensued within a few days. Sometimes the course was more prolonged, extending over several weeks. The outcome could never be predicted with any certainty, being independent of age and previous general health. Relapses were not infrequent in infants who appeared to have made a complete recovery; this occurred even in cases who had already been discharged from hospital.

SEQUELAE AND COMPLICATIONS

Dehydration with its side-effects, anaemia and atrophy naturally ensued, particularly in prolonged cases. The only true complication of this disease appeared to be an acute hepatic necrosis, manifested by icterus and increasing hardness of the liver on palpation. This was observed in seven cases, all of which proved fatal; in nearly all these cases the jaundice appeared within 11–12 days of the onset of the disease. Respiratory infection was occasionally encountered, at any stage of the disease. However, in view of the severe winter conditions and the presence of a 'catarrhal diathesis' in some cases, no definite assessment of its importance could be made, except when it occurred as a terminal event. Clinical middle ear disease was seen in only five cases. Since it was always associated with respiratory catarrh, this figure does not appear to be significant. Dentition, being common in the age group principally affected, appeared to prolong convalescence, as it may do in the case of other illnesses. Abdominal, particularly gastric, distension, following the prolonged use of a gastric drip, was seen in several cases.

PROGNOSIS

Prematurity, congenital debility and the presence of other diseases naturally tended to render the outlook more serious. Grave prognostic signs were the presence of altered blood in faeces or vomit, abdominal distension and persistent circulatory failure. In all cases which developed icterus death ensued within 48 hr. of its appearance. The main criteria of recovery were improvement in the general condition, tolerance of normal feeds and a continued gain in weight.

TREATMENT

In the absence of a specific remedy, treatment was on general lines, aimed at restoring metabolism to normal, as far as possible—by the replacement of water, electrolytes, proteins and essential metabolites—and at giving comparative rest to the alimentary tract.

In very ill cases with moderate to severe degrees of dehydration the oral route was used to a minimum. Fluids, such as 5% glucose saline, Lactate-Ringer solution (Hartmann's), amino-acids ('Casydrol') and plasma were given by continuous intravenous drip infusion, according to estimated requirements. After 48 hr. or so it was often possible to commence oral feeding by pipette or bottle, using dilute milk fluids often alternated with half strength 5% glucose saline or Hartmann's solution. If these were tolerated well, they were gradually increased in strength until normal feeds were taken without difficulty.

Intra-tibial drip infusion of glucose saline or plasma was employed in a few cases, but this method was considered unsuitable for routine use, in view of the danger from local sepsis. Intra-peritoneal injections of normal saline or Hartmann's solution were sometimes used as an initial treatment, preparatory to intravenous infusion, in very small babies.

When dehydration was less marked continuous subcutaneous drip infusion proved effective in supplementing oral feeding on several occasions. Normal saline or Hartmann's solution were given by this method, which could be maintained for 3 or 4 days, if necessary, without risk of infection. Likewise, in the less severe cases, a gastric drip was found to be useful, but if this was continued for more than 72 hr., gastric distension was liable to occur. However, relatively large amounts of fluid were administered in this way; to avoid undue strain on stomach and intestine an hour's rest was allowed in every three.

If a low diet had to be given over a long period, vitamins A, B, C, D and E were administered either orally or by injection. Neither penicillin nor any of the sulphonamides (including Sulphaphthalidine) had any apparent effect on the course of primary gastro-enteritis, although they proved helpful in controlling complications such as respiratory conditions.

Varying dosages of penicillin buffered with aluminium hydroxide ('Aludrox') were given orally to a few cases, without any encouraging results. Parenteral penicillin was frequently administered prophylactically in conjunction with intravenous and subcutaneous infusions. Further investigations on the therapy of these cases are in progress.

PROPHYLAXIS

Infants should be breast-fed whenever possible. One of the reasons for the prevalence of the disease in recent years may well be the growing tendency to wean babies during the first few weeks of life. In our own experience of hospital infections, primary gastro-enteritis appears to be a highly infectious disease, and, therefore, strict individual isolation is essential, if ward outbreaks are to be prevented. No infant who develops diarrhoea and vomiting should be kept in an institution or nursed in an open hospital ward. Since cubicle isolation of all cases of infantile diarrhoea was introduced at the City (Fever) Hospital in Aberdeen, hospital infections there have virtually disappeared. General prophylaxis resolves itself into an improvement of social and hygienic conditions.

POST-MORTEM FINDINGS

Autopsies were carried out on twenty-four of the fifty-two fatal cases in our series. In each instance microscopic sections were prepared of the brain, stomach, intestine, liver, spleen and kidneys and of any organ which exhibited any naked-eye changes.

An infant who has suffered for days or weeks from a profound gastro-intestinal disturbance might be expected to show well-marked changes in the stomach and the intestine. It is, however, remarkable that only the minority of cases who die from this type of gastro-enteritis show any definite lesions in the gastro-intestinal tract (Ormiston, 1941; Gairdner, 1945; Bray, 1945). In our series only five cases exhibited a haemorrhagic gastro-enteritis; the remainder showed merely a mild hyperaemia of the mucous membranes, while in several instances the alimentary tract appeared quite normal. In fifteen cases, however, altered blood was present in the stomach.

The liver was the only organ which consistently showed some evidence of damage. This varied from a mild degree of fatty degeneration to complete necrosis. Six cases, in all of which the course of the disease had been exceptionally rapid, presented merely a mild hepatic congestion. Where fatty changes were relatively slight a peripheral lobular distribution could be clearly recognized; in the more severely damaged organs the whole lobule was involved. Liver damage in itself serves little to elucidate the aetiology of the disease, for it is frequently found in infants who have died from other causes. Starvation and toxaemia are probably in themselves sufficient to produce these changes.

The brain and meninges were nearly always intensely congested and small extravasations of blood were quite often visible to the naked eye. Christen & Biering-Soerensen (1946) claim to have found evidence of meningo-encephalitis in twenty-one out of thirty-two autopsies performed on cases of infantile gastro-enteritis in Copenhagen. No such changes were observed in our present series. In three instances there was a mild degree of cerebral oedema; on one occasion the cerebrospinal fluid, before death, contained 21 lymphocytes and 120 mg. % of protein, but the post-mortem findings in this case were in no way remarkable. Slight increases of the cell count and protein content of the cerebrospinal fluid were not uncommon, but could be explained by the degree of dehydration.

Both spleen and kidneys were deeply congested in most cases, but in only two instances was a definite nephritis observed. The suprarenals were normal in all but one case, which exhibited bilateral adrenal haemorrhages. Broncho-pneumonia, quite possibly terminal, was present in eight of the twenty-four autopsies.

Evidence of middle ear disease was found in only one instance, although many authorities (e.g. Maizels & Smith, 1934; Gairdner, 1945; Marriott, Hartmann & Senn, 1933) stress the frequent association of gastro-enteritis and otitis media. Blacklock, Guthrie & Macpherson (1937) and Leathart (1943) attribute aural infection to the aspiration of vomit by way of the Eustachian tubes and do not regard the association as aetiologically significant.

Neither the thymus nor the lymph glands exhibited any pathological changes worthy of note.

BACTERIOLOGICAL FINDINGS

(1) *Previous literature*

A study of publications on the subject of gastro-enteritis in infants reveals a bewildering array of different hypotheses, which try to explain the aetiology of this condition (Crowley, Downie, Fulton & Wilson, 1941; Topley & Wilson, 1946). Clostridia, proteus, paracolon bacilli, staphylococci (Draper & Brown, 1946), *Bact. lactis aerogenes* (Cass, 1941), faecal streptococci (Gale, 1944) have all been blamed as the causative agents. Most widely held at the present moment is the hypothesis that an as yet unidentified virus is responsible for the disease. Light & Hodes (1943) claimed to have isolated from the faeces of affected infants a filterable agent, which gave rise to diarrhoea in young calves. Pappenheimer & Enders (1947) recently described viral inclusion bodies in the intestinal epithelium of mice suffering from enteritis, thereby supporting the view that *prima facie* enterotropic viruses exist. Christen and Biering-Soerensen's claim to have found a meningo-encephalitis in the brains of fatal cases lends colour to the virus theory.

More and more authorities, however, tend to the view that *Bact. coli* as such or specially virulent strains of this organism are pathogenic to the infant, whereas they represent mere commensals in the adult and the older child (Payling Wright, 1946). As early as 1913 Jensen identified certain strains of *Bact. coli* with the diarrhoea in young calves, known as 'White Scours'; this has since been confirmed by Lovell (1937) and a commercial polyvalent *Bact. coli* anti-serum is already in general veterinary use. Hamburger (1920) claimed to have had similar success in the treatment of gastro-enteritis in infants with anti-sera prepared against *Bact. coli*, but this has never been confirmed. In 1923 Adam, in Germany, appears to have isolated a special strain of *Bact. coli* from the faeces of infants suffering from diarrhoea. This 'dyspepsia-strain', as he styled it, was again described by Cziglány in Budapest (1941). In this country Bray (1945) recovered serologically homogeneous strains of *Bact. coli neapolitanum* in a very large proportion of infants suffering from gastro-enteritis.

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(2) *Preliminary investigations*

At the outset of this study twenty-two specimens of faeces from cases of gastro-enteritis and twenty-eight from normal infants and adults were examined for any bacterial organism common to the first but not to the second group. Our findings can be briefly summarized as follows: *Staph. aureus* was isolated in five cases, three of them controls; the streptococci most commonly seen in both cases and controls belonged to Lancefield's group D, but showed no uniformity in their biochemical behaviour. Members of the paracolon group, *P. vulgaris* and *P. morgani* were isolated with equal frequency from cases of gastro-enteritis and from controls. Clostridia were found in only two instances, whereas Sonne dysentery was responsible for one case of infantile diarrhoea (vide supra). On microscopic examination of the faeces, a true bacillary exudate was found in only three instances. Intestinal parasites could not be detected in any of the specimens.

With regard to *Bact. coli*, however, it was soon established that a serologically homogeneous type, closely resembling Bray's *neapolitanum* strains, was present in a large majority of severe and fatal cases of gastro-enteritis and in relatively few controls. It was, therefore, decided to abandon, for the time being, other bacteriological investigations in favour of a study of the coliform flora.

(3) Bact. coli *in gastro-enteritis*

The variability and inconstancy of fermentation reactions of the coliform organisms—even within serologically related groups of strains (Kauffmann, 1943; Wallick & Stuart, 1943)—greatly complicate their recognition. Sera, were, therefore, prepared against strains isolated from the first three fatal cases of gastro-enteritis in our series. These sera were found to have identical properties and also agglutinated to the full titre strains of *Bact. coli* recovered from the majority of fatal or seriously ill cases of gastro-enteritis. As a control, five sera were made against strains isolated from three normal controls and from two infants suffering from diarrhoea judged to be secondary to parenteral infection; all these five sera were distinct from one another and from the three sera prepared against gastro-enteritis strains. Moreover, they tended to agglutinate few other strains besides their own. In order to demonstrate that the organism was not merely an incidental contaminant, which happened to be prevalent in this hospital, all initial specimens—consisting of faeces or rectal swabs—were collected immediately on admission, and yet this particular type of *Bact. coli* continued to be isolated.

It thus became very probable that we were dealing with a type of *Bact. coli* characteristic of that variety of gastro-enteritis which we were investigating. A preliminary slide agglutination test on colonies picked off the primary culture was performed in over eight hundred specimens, both from infants with diarrhoea and from healthy controls. In nearly every positive specimen the organism in question was found to be the predominant strain of *Bact. coli* present; sometimes it was grown in practically pure culture. Whenever a strain was agglutinated on the slide by sera prepared against the original gastro-enteritis strains, to confirm its identity, tube agglutination and agglutinin-absorption tests were carried out.

(*a*) *Cultural characteristics.* The organism is non-motile; its colonial appearance shows little to distinguish it from other faecal strains of the coli group. A characteristic seminal odour, which was first described by Bray (1945) in connexion with his work on *Bact. coli* in gastro-enteritis, is given off when the organism is grown on a non-inhibitory medium. Growth is slow at 22° C., but it grows readily at 44° C. On blood agar it produces haemolysis after 24 hr.; extra-cellular haemolysins to horse, sheep and human blood cells could not be demonstrated, however, in the filtrate of an 18 hr. broth culture.

(*b*) *Biochemical properties.* The strain belongs to the indole- and methyl-red-positive and Vosges-Proskauer- and citrate-utilization-negative group. Lactose, glucose, mannitol, maltose and trehalose are fermented after 24 hr. with the production of acid and gas. In saccharose, after 24 hr., only a faint pink colour appears; a small gas bubble is usually present after 3 days. Salicin and dulcitol are fermented with acid and gas production after 2 or 3 days' incubation. Four out of 128 strains of the organism did not ferment salicin at all.

(*c*) *Antigenic properties.* Between 1942 and 1944 Kauffmann (1943, 1944 *a*, *b*) made a detailed study of the serological properties of the coli group and discovered that, in addition to the thermolabile flagellar (H) and the heat-stable somatic (O) antigens, certain strains of *Bact. coli* also possess a thermolabile antigen associated with the body and not the flagellae of the organism. This he labelled the L-antigen, and over a series of several hundred strains found it predominantly in organisms isolated from urinary infections, peritonitis and appendicitis, whereas the vast majority of faecal strains are devoid of an L-antigen.

Adopting Kauffmann's method of classification, we found that our own agglutinable strain possesses both an O- and an L-antigen. Furthermore we proved it to be biochemically and serologically identical with two strains of *Bact. coli* isolated by Bray from his series of infantile gastro-enteritis. Dr R. D. Stuart of Glasgow kindly gave us subcultures of these strains and their respective antisera. We also sent our strain to Dr Kauffmann in Copenhagen who found it to be antigenically quite distinct from any of his own coliform types.

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In addition to agglutination tests, a series of fifty strains—twenty serologically identical with the agglutinable coliform and thirty sero-negative strains—were tested for the presence of a precipitin, using Lovell's method of preparing bacterial extracts. The results obtained ran parallel with those of the agglutination tests—i.e. gastro-enteritis-sera possessed a precipitin specific for the agglutinable strains and not shared by non-agglutinable types of *Bact. coli*. The five sera prepared against normal controls gave a positive precipitin-test only with their own strains and not against 'agglutinable' forms isolated from gastro-enteritis patients.

(*d*) *Pathogenicity.* The organism was administered *per os* and *per rectum* to eight new-born mice and six new-born kittens but failed to produce any signs of disease in the animals, although it could usually be recovered from the faeces after 48 hr. of controls. In addition, a number of specimens from infants with mild diarrhoea, who were treated at home by their own doctors, are included in this bacteriological review.

(i) Cases of primary gastro-enteritis (§§ 1 and 2 of Table 3) were selected on clinical criteria discussed at the beginning of this paper. The organism was recovered in over 90 % of cases. In twenty-two out of the twenty-four autopsies on fatal cases (§ 1 of Table 3) the organism was likewise isolated from the alimentary tract. In a few instances it was also grown from the liver, spleen and the middle ears, but these results were of doubtful significance, since intestinal coliforms tend to migrate into the blood-stream soon after death. During a routine examination of ward contacts the agglutinable *Bact. coli* was isolated in four infants who were incubating the disease and developed the first symptoms 24 hr.

Table 3. *The incidence of agglutinable strains of* Bact. coli *in cases of infantile diarrhoea*

Sections	No. of cases positive for agglutinable *Bact. coli*	No. of cases negative for agglutinable *Bact. coli*	Total no. of cases	% of positive cases
1. Fatal cases of primary gastro-enteritis	48	4	52	92
2. Cases of primary gastro-enteritis who recovered	38	2	40	95
3. Doubtful cases of gastro-enteritis	8	15	23	34
4. Cases of infantile diarrhoea, attributable to other causes (parenteral infection, teething, dietetic disturbances, etc.)	2	42	44	5
5. Infantile diarrhoea from all causes (§§ 1–4) who were admitted to hospital	96	63	159	60
6. Infants with diarrhoea (unclassified) who did not require hospital admission	3	69	72	4

Unlike Vincent (1925), who found a thermolabile toxin in urinary strains of *Bact. coli*, an exotoxin could not be demonstrated, though 1 ml. of a boiled broth culture proved fatal to a rabbit on intravenous injection and to a mouse on intraperitoneal inoculation. Unfortunately, scarcity of animals did not permit of a large-scale experiment. It might be interesting to observe the effect of the organism on newly born calves. Since the disease is most prevalent among artificially fed infants, it would be desirable to work entirely with bottle-fed young animals, but the technical difficulties involved are obviously very great. Animal work on this subject is, however, still in progress.

(*e*) *Bacteriophage.* Repeated attempts to find a specific phage were unsuccessful.

(*f*) *Incidence.* In order to assess the true incidence of the organism, not only were specimens from cases in our own series examined but also a large number later. Twenty-seven out of the thirty-eight cases who recovered (§ 2 of Table 3) were followed up with several clearance specimens and became negative about the same time as they had clinically improved. In one further case the baby was discharged still carrying the organism, but he also became negative 2 weeks later.

(ii) Doubtful cases and secondary diarrhoea. § 3 of the table includes twenty-three cases, in which symptoms were mild, but which clinically might have been primary gastro-enteritis. In this category the percentage of positives is 35. § 4 comprises all cases of diarrhoea in infants, in which it was probably secondary to parenteral infection—e.g. skin and middle ear disease, measles, etc.—and never presented as the main symptom. Also cases of mild diarrhoea due to dietetic disturbances and dentition are included in this section, where the percentage of positives has dropped to 5.

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Taking the overall percentage of positives for all cases of diarrhoea in infants, who were admitted to hospital (§ 5 of Table 3), the agglutinable strain of *Bact. coli* was recovered from 60 % of cases. Such a high incidence is likely to be found only in hospital patients. Very many babies suffer from diarrhoea at some stage or another of their development but are not, as a rule, sufficiently ill to warrant admission to hospital. For that reason seventy-two specimens from cases of infantile diarrhoea, treated at home, were examined for the presence of the agglutinable *Bact. coli* (§ 6 of Table 3). In this group the percentage of positives resembles that in § 4 and in the controls (Table 4); the organism was found in only three cases, two of which were subsequently admitted to hospital and turned out to be primary gastro-enteritis. Although no clinical details of these cases are available, it may be assumed that the majority of them were relatively mild, since hospital admission was not necessary.

from, the organism under discussion. Possibly we were dealing in that instance with a mixed infection of Sonne dysentery and 'non-specific' gastro-enteritis of the kind recently described by Martin & Wilson (1947).

(v) The organism was found to be both biochemically and serologically distinct from eleven strains of *Bact. coli* isolated from calves with neonatal diarrhoea—White Scours. (Cultures and sera by courtesy of the Burroughs Wellcome Research Laboratories and the Aberdeen Veterinary Research Station.)

(vi) Equally, sixty-five strains of *Bact. coli* isolated from urinary infections, forty-one strains recovered from milk and thirteen strains from vaginal swabs were examined and found to be serologically unrelated to the gastro-enteritis strain.

(*g*) *Antibody production.* Agglutinins for the organism in question could not be demonstrated in the blood of six infants convalescent from primary gastro-enteritis, nor in six specimens of blood taken

Table 4. *The incidence of the agglutinable strain of* Bact. coli *in a group of controls*

Section	No. of cases positive for agglutinable *Bact. coli*	No. of cases negative for agglutinable *Bact. coli*	Total no. of cases	% of positive cases
1. Infants (10 days to 18 months) not suffering from diarrhoea	7	162	169	4·2
2. Adults and older children (includes both normal controls and cases suffering from diarrhoea)	5	266	271	1·8

(iii) Controls: Table 4 illustrates the incidence of the agglutinable strain of *Bact. coli* in babies not suffering from diarrhoea and in adults and older children. Just under 5 % of infants, who showed no evidence of diarrhoea, appeared to be carriers of this particular organism (§ 1 of Table 4). Six out of the seven positive controls were ward contacts of cases of gastro-enteritis.

A small number of adults and older children showed the presence of the agglutinable strain in question. One of these was a nurse in one of the wards where an outbreak of the disease had occurred, but she was found to be negative on re-examination a fortnight later. Another positive result was obtained from an out-patient suffering from mucous colitis; the remaining positive cases were all ward contacts of infantile gastro-enteritis.

(iv) In addition to the cases reviewed in Tables 3 and 4, it might be interesting to record a small outbreak of Sonne dysentery in a nursery in the County of Aberdeen—not included in our present series—in which about twelve infants were affected. In five of these a strain of *Bact. coli* was recovered—serologically identical with, though biochemically different

at autopsy from fatal cases. One of the adult carriers was likewise tested and found to be negative.

(*h*) *Bacteriostatics.* Neither penicillin nor any of the soluble sulphonamides had any bacteriostatic effect on the growth of the organism *in vitro*. Of the sparingly soluble intestinal sulphonamides Phthalyl Sulphathiazole (Sulphaphthalidine) inhibited its growth, but only in saturated solution. Studies on the effect of other bacteriostatics are still in progress.

(4) *Search for the presence of a possible virus*

In view of our failure to demonstrate the pathogenicity of the agglutinable coliform, the possibility remains that the organism is merely a constant concomitant of a hitherto undiscovered virus, comparable with the presence of *Bact. suipestifer* in the virus disease of hog cholera. All efforts to demonstrate such a virus have as yet been unsuccessful.

Faecal filtrates from cases of primary gastro-enteritis and filtered post-mortem material were administered to young mice and kittens but produced no symptoms whatever. Like Reimann, Price & Hodges (1944), we inoculated with faecal filtrates and autopsy material the chorioallantoic membrane

and the amniotic cavity in a number of developing chick embryos, using the methods described by Beveridge & Burnet (1946). Up to date no evidence of any virus has been found, but the work in this direction is only just beginning.

DISCUSSION

From clinical and bacteriological observations of 159 cases of infantile diarrhoea it would appear that ninety-two belonged to one and the same type of 'non-specific' primary infective gastro-enteritis. The salient feature of this disease is an acute gastro-intestinal disturbance. Although parenteral infections may either co-exist as complications or precede the gastro-enteritis, thereby rendering the patient more susceptible to it, the patient's general condition is not determined by such extraneous diseases but by the toxaemia and dehydration resulting from the gastro-intestinal upheaval. Secondary diarrhoea, on the other hand, which may in turn complicate a variety of parenteral infections, does not usually influence the patient's general condition to any marked extent. Quite frequently, however, a differential diagnosis, on clinical grounds alone, between primary and secondary diarrhoea can be very difficult. Although there were a few very young infants in this series, no opportunity arose of studying a true epidemic among newly born babies. Therefore, the question as to whether the above-mentioned variety of gastro-enteritis is identical with neonatal gastro-enteritis—such as occurred recently in maternity hospitals at Derby and elsewhere—must remain unanswered for the time being.

Recovery of the previously described type of *Bact. coli* in the faeces of an infant suffering from diarrhoea affords, in our opinion, strong presumptive evidence of at least one variety of primary gastro-enteritis, but whether its presence in over 90 % of cases is of true aetiological significance remains to be seen. Certainly all attempts to demonstrate its pathogenicity have failed, and the notable absence of agglutinins in the sera of convalescents and patients would also point to its being merely a concomitant. On the other hand, it is often difficult to demonstrate antibodies in the sera of young infants. The possibility of a symbiosis between this particular coliform and a hitherto unidentified virus must be borne in mind. Alternatively, the organism might conceivably appear as a result of some biochemical change in the intestinal contents, which favours its growth.

Artificial feeding, a poor standard of personal hygiene and of infant care were observed in a large number of cases of gastro-enteritis, and these factors almost certainly play an important part in the epidemiology of the disease. Hospital infections were relatively numerous in our series. The reasons for the liability to ward outbreaks are probably first of all the high infectivity of the disease, which is not always sufficiently appreciated, secondly the difficulty in early diagnosis, and thirdly the fact that in many hospitals accommodation for nursing all infants in individual cubicles is not available. Prophylactic measures should, therefore, be self-evident.

SUMMARY

1. Ninety-three cases of primary infective gastro-enteritis are reviewed. In only one instance was a known pathogen isolated.

2. The clinical features, epidemiology and post-mortem findings are discussed.

3. A serologically homogeneous strain of *Bact. coli* is described which was isolated in over 90 % of cases.

4. A discussion follows on the significance of these findings.

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