Gastroenteritis in London and Jamaica: a clinical and bacteriological study

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SUMMARY

The flora of both faeces and small bowel lumen was studied in children with gastroenteritis from London, England, and Kingston, Jamaica.

Clinical and laboratory differences between these two groups are described.

All bacterial groups in the faeces were greatly altered during gastroenteritis and this particularly affected anaerobic organisms. These changes generally reverted rapidly to normal after the illness.

The small bowel flora was also altered during gastroenteritis; there was a tendency for a wider range of organisms including anaerobes to be isolated from the children in Jamaica than from those in England.

INTRODUCTION

Gastroenteritis remains a common disease in children in both industrialized and developing countries. Its impact is, however, much greater under poor socio-economic conditions and where malnutrition is common. We have made a clinical and bacteriological study of gastroenteritis in two different environments. Recent advances in anaerobic bacteriological techniques (Drasar, 1967; Holdeman & Moore, 1973) have permitted further studies of the changes in the anaerobic as well as the aerobic flora during such episodes, and we include a detailed analysis of the jejunal and faecal flora of these children.

METHODS

Controls

Aerobic and anaerobic flora in the stools of 17 normal children from South London (median age four months: range 1–15 months) was quantified (Ellis-Pegler, Crabtree & Lambert, 1975).

Acute gastroenteritis

Children were selected for this group if they had a history of acute diarrhoea of less than 10 days duration. Children with any other diagnosis made were excluded but a few children had minor respiratory tract symptoms, e.g. cough without

physical signs, or 'runny nose'. Children who had received antibiotics within one month of admission were also excluded.

Twenty-five patients were studied in South London and 13 in Kingston, Jamaica. Stool cultures were obtained from 22 of the U.K. children in the acute stage and from 12 of them during convalescence. Ten of the U.K. children (and two others who did not have stool cultures) had jejunal cultures (i.e. 12 U.K. children), as did all 13 Jamaican children, 10 of whom also had stool cultures. Three of these Jamaican children had convalescent jejunal cultures. Convalescent jejunal cultures were analysed from three U.K. children not studied in the acute phase.

The U.K. children were studied after admission to the Communicable Diseases Unit of St George's Hospital, London, S.W.17. The Jamaican children were studied after admission either to the Paediatric Department of the University of the West Indies Hospital, University of the West Indies, Kingston, Jamaica, or to the Tropical Metabolism Research Unit attached to that hospital.

Clinical and laboratory data

Duration of diarrhoea

The duration of diarrhoea before admission was estimated to the nearest half-day.

Two methods of assessing the end-point of the illness were used.

All stools passed were recorded and the frequency of stooling was recorded in six hourly periods. Diarrhoea generally stops relatively suddenly. The end of the six hourly period during which stooling rate decreased suddenly was noted. The time at which a decision was taken to introduce feeds, other than oral electrolyte mixtures, was also noted. The interval from admission to these end-points was calculated and recorded as 'duration of diarrhoea'.

Haematological and electrolyte measurements were estimated on either capillary or venous blood in the routine laboratory service of St George's Hospital, or the T.M.R.U. Laboratory. Dehydration was assessed by comparing the weight of the child after initial fluid repletion with its admission weight, and expressing the difference as a percentage of the rehydrated weight. Intubation time is the interval in hours between admission and aspiration of the small bowel lumen sample. Malnutrition is not uncommon in Kingston, Jamaica. The child's weight was expressed as a percentage of the 50th percentile weight of a normal North American child of the same height (Nelson, 1964). If the weight for height is less than 90% of that expected, the child is described as malnourished.

Collection of specimens

Stool collection during gastroenteritis

On admission the infants were seated in an 'Ekco baby-sitter' adapted for stool collection, and stools (separate from urine collected in a urine bag) passed directly into a sterile aluminium foil bowl. A stool passed within 4 h of admission was collected and cultured, or frozen, within 5 min of being passed.

Jejunal intubation

The nature of this procedure was explained to parents, including the fact that any findings would usually not be of therapeutic benefit to the child concerned. Food and fluid were withheld for at least 3 h before the procedure, which was performed after initial rehydration. They were premedicated with oral trimetopazine (Vallergan) 1 h, and oral metoclopramide 30 min before intubation. Intubation was carried out with a clean PVC tube (internal diameter 1.0 mm), weighted with a hollow stainless-steel weight (external measurements approximately those of a paediatric Watson biopsy capsule) and with three aspiration ports cut in the distal 30 mm. This was supported externally by an outer radio-opaque PVC tube (external diameter 5 mm) and advanced through the mouth to the fourth part of the duodenum or first part of the jejunum. The final position was checked either by plain abdominal X-ray or fluoroscopy. This procedure generally took about 1 h: if the tube would not leave the stomach, attempts were not continued beyond 2 h. A volume of fluid greater than the volume of the tube was aspirated and discarded before the definitive specimen was taken. This was cultured, or frozen, within 5 min of aspiration.

Bacteriology

Organisms were cultured and identified as described elsewhere (Ellis-Pegler *et al.* 1975). Organisms were grouped as enterobacteria, staphylococci, streptococci, bacilli, lactobacilli, yeasts, diphtheroids, neisseria, bacteroides, bifidobacteria, clostridia and veillonella. Specimens were frozen as described by Crowther (1971). A 10% dilution of the sample was made in 10% glycerol broth and frozen in an alcohol acetone solid CO₂ mixture. The Jamaican specimens were held at -20 °C and transported at that temperature to the U.K. before thawing and culture. Ten coliform colonies from McConkey medium were selected and slide agglutinations carried out, using Wellcome *E. coli* polyvalent sera 2, 3 and 4 and Difco Bacto-*E. coli* sera O20:B7, O20:84(B) and O28:B18. If positive, biochemical identification and monovalent serum titrations were added. From the patients intubated, strains of *E. coli* isolated from small bowel or stool were subjected to more detailed analysis (Ellis-Pegler *et al.* 1978), and fully serotyped at the Central Public Health Laboratory, Colindale.

Trophozoites of *Giardia intestinalis* were sought in all jejunal specimens from the Jamaican children and in 11 of the 12 London children.

RESULTS

Clinical features

Clinical and pathological features of the two groups are summarized in Table 1. Both groups were moderately or severely ill and required admission to hospital by the medical criteria prevailing in the two centres. They differed most strikingly in the background of malnutrition common in Jamaica and absent in London. Five of the 13 Jamaican children were malnourished and the median expected

Table 1. *Clinical and biochemical features of children with gastroenteritis*

	Diarrhoea duration						Hb (g/dl)	Urea (mmol/l)	Na ⁺	K ⁺	HCO ₃	In- tubated hours after ad- mission	Percentage dehydration
	Age mission (months)	Before ad- mission (days)	After admission (h)		Method	2							
			Method	1									
U.K. children (group with bacteriological studies of faeces only)													
No. of observations	22	22	22	22	22	22	21	11	12	12	11	—	22
Mean	4	2	26	34	34	34	12.3	7.2	135	4.1	13	—	Nil
Range	1-15	1-7	13-60	8-82	8-82	8-82	9.3-13.8	3.8-17.5	124-158	3.3-5.2	8-19	—	7.5% (Nil-11%)
U.K. children (group with bacteriological studies of faeces and jejunal aspirate)													
No. of observations	12	12	12	12	12	12	10	6	5	5	5	12	12
Mean	8	2	25	36	36	36	12	14.7	135	4	12	21	6
Range	2-24	1-7	13-50	14-82	14-82	14-82	10.5-17.3	5.0-17.5	124-158	3.5-5.2	8-19	6-54	7.5% (Nil-11%)
Jamaican children (bacteriological studies of faeces and jejunal aspirate)													
No. of observations	13	13	12	8	8	8	13	13	13	13	13	13	13
Mean	9	3	39	29	29	29	11	3.2	133	3.9	16	21	Nil
Range	5-17	1-9	20-70	25-42	25-42	25-42	8.4-14.9	1.3-10.7	128-149	2.6-5.2	10-23	6-40	1.5% (Nil-6%)

weight/height ratio of the whole group was 90 %. On the other hand, the patients studied in London were in general more severely dehydrated than those in Jamaica (5/13 more than 5 % depleted in London, 1/13 in Jamaica). In other respects the groups were clinically similar. The duration of diarrhoea before admission and the speed with which it remitted was similar, although early introduction of high caloric feeds in Jamaica often made the second method of estimating duration of diarrhoea inapplicable. Haemoglobin and electrolyte values were similar in the two groups, but plasma urea concentration was significantly higher in the London children (median 14.7 mmol/l in London, median 3.2 mmol/l in Jamaica).

Bacteriological features

Stools in acute gastroenteritis and convalescence in London

Stool flora from 22 London children with acute gastroenteritis, 12 of these children during convalescence, and 17 normal controls are analysed in Fig. 1. Enteropathogenic *E. coli* were isolated from the stools of 6 of the 22 patients with gastroenteritis. The faecal flora of these six patients did not differ from the rest of the group in any other respect and are included in the analysis. Children with *Shigella* or *Salmonella* infections were excluded from this study.

All anaerobic groups were significantly reduced in number in the stools in acute gastroenteritis. Bifidobacteria were not isolated in 11 of 22 patients with gastroenteritis compared with one in 17 controls. By contrast, the aerobic flora did not change significantly in gastroenteritis, although a wider range of concentrations was found than in the control and convalescent groups. The less numerous members of the flora tended to be isolated even less frequently than in the controls. The stool flora rapidly resumed its normal pattern after recovery from gastroenteritis. By a median of 5 days after admission, the numbers of bifidobacteria, alone among the main groups, was still significantly different from the controls. The ranges of concentrations of all groups had now narrowed towards the normal pattern.

Stools in acute gastroenteritis in London and Jamaica

The concentrations of faecal organisms in the two groups are shown in Fig. 2. They show similar trends to those in the previous study (Ellis-Pegler *et al.* 1978), and reveal no striking differences between the two geographical groups.

Jejunal flora in acute gastroenteritis in London and Jamaica

For both groups, staphylococci and streptococci were the organisms most commonly isolated from the small bowel lumen (Fig. 3). Only one child in the series (from Jamaica) had a small bowel aspirate from which no organisms were isolated. Anaerobic organisms were often not isolated, five times in each group, but of those that were, veillonellas were most common in both groups. Bacteroides were isolated on four occasions from the Jamaican group but never from the U.K. group, and the highest concentration of anaerobes was noted in the Jamaican group. Enterobacteria were isolated from 5/13 Jamaican children and 5/12 U.K.

Fig. 1 (part 1). Aerobic stool flora in acute gastroenteritis (a), convalescents (b) and normal controls (c)

children and are further investigated and discussed elsewhere (Ellis-Pegler *et al.* 1978).

Three Jamaican children were intubated again during convalescence (6, 6 and 7 days respectively after admission) when their diarrhoea had stopped. Two were malnourished on admission but their percentage expected weight/height was

Fig. 1 (part 2). Anaerobic stool flora in acute gastroenteritis (a), convalescents (b) and normal controls (c).

unaltered at reintubation. The total concentrations of aerobic and anaerobic organisms fell in all three (Table 2). Within these concentrations, however, staphylococci in two patients increased at least tenfold and streptococci in another rose similarly.

Three U.K. patients were intubated during convalescence (5, 5 and 6 days respectively after admission) although these children had not been intubated in the acute stage (Table 2). Staphylococci and neisseria were present in the highest numbers: the concentrations of all organisms lay within the range recorded in those intubated in the acute stage.

Trophozoites of *Giardia intestinalis* were not seen in any jejunal specimen.

Fig. 2. Stool flora in acute gastroenteritis in London and Jamaica. U = United Kingdom; J = Jamaica.

Fig. 3. Jejunal flora in acute gastroenteritis in London and Jamaica. U = United Kingdom; J = Jamaica.

DISCUSSION

Acute diarrhoeal diseases are widely prevalent throughout the world, but their impact is much greater in developing than in wealthy countries. In conditions of poverty, poor hygiene and malnutrition, gastroenteritis ranks as a major cause of ill-health at all ages and of death in childhood. The variation between the severity of gastroenteritis in different countries cannot be generally ascribed to differences in the type or prevalence of particular causal pathogens. On the contrary, except during an epidemic, only a minority of illnesses can be assigned to a specific bacterial pathogen, and this low incidence of causal diagnosis is as evident in tropical as in temperate countries. Viral causes of gastroenteritis are being increasingly recognized but epidemiological evidence of their relative importance in different communities is as yet incomplete.

It is not surprising with such difficulties of definition and description that detailed comparisons between the features of gastroenteritis in a tropical and a temperate setting are hard to make, yet such a comparison may provide evidence about some of the vexed questions of aetiology and pathogenesis in gastroenteritis. We have compared two groups of patients, one in London and the other in Jamaica, employing uniform clinical criteria and bacteriological methods. Both groups were ill enough to need admission to hospital but well enough, in the immediate aftermath of fluid repletion, to justify jejunal intubation. None the less, the clinical features noted in the two groups cannot be used to make a direct comparison between gastroenteritis in the two communities, since criteria for admission to hospital differ in different countries. A number of clinical and biochemical features were similar in the two groups (Table 1) but the London children selected for study were on average more fluid-depleted than those in Jamaica, five of 12 being moderately or severely dehydrated in London compared with one of 13 in Jamaica. The lower plasma urea concentration of the Jamaican children may reflect this difference, and also perhaps their state of relative protein deficiency. Clinical assessment of their degree of illness and their need for admission is evidently based both on features of fluid depletion as well as those of malnutrition.

Faecal flora in gastroenteritis

During the acute illness the faecal flora is greatly disturbed, the alteration being most marked among the anaerobic groups. Similar changes have been noted in many diarrhoeal states (Gorbach *et al.* 1970*a*; Gorbach *et al.* 1971; Mata, Mejicanos & Juinenez, 1972) and have been ascribed to non-specific causes, such as alterations in bowel transit times. Continuous flow culture techniques do show relatively simple relations between flow rates and the concentration of bacteria, but *in vivo* the situation in the large bowel is more complex (O'Grady & Vince, 1971) and experimental bowel perfusion studies have not always shown reduction of counts in faeces (Levison & Kaye, 1969; Gorbach *et al.* 1970*b*) or in the fluid effluent from the perfused isolated colon (Vince *et al.* 1973). The tendency to a sharp reduction in anaerobic flora during diarrhoea may reflect the greater sensitivity of these

Table 2. *Small bowel luminal organisms concentrations during acute gastroenteritis and in convalescence*

		Total aerobes		Total anaerobes	
		Acute	Convalescent	Acute	Convalescent
Jamaica	1.	6.4	→ 4.0	7.9	→ 3.3
	2.	6.4	→ 3.7	4.7	→ 2.5
	3.	6.8	→ 4.9	6.1	→ < 2
U.K.	1.		6.7		< 2
	2.		4.2		3.9
	3.		4.8		3.2

(U.K. children not studied in the acute phase: concentrations expressed as in Fig. 1.)

groups to local changes in pO_2 and Eh (Gorbach *et al.* 1971). Of the anerobic groups, bifidobacteria showed the greatest reduction during gastroenteritis and were slowest to return towards their normal stool concentration. Haenel (1970) also comments on the disappearance of bifidobacteria from babies' stools even under such minor influences as bowel infections, vaccination or sudden changes in nutrition. In contrast, Mata *et al.* (1972*b*) found no changes in the faecal flora of breast-fed infants with respiratory tract infections, measles and whooping cough.

The generally rapid return to normal concentrations of the majority of faecal organisms after apparently severe local disruption, is notable evidence of the intrinsic stability of this micro-environment.

Flora of the small bowel lumen

The small bowel flora of well adults in tropical countries is more diverse and luxuriant than that of adults in temperate climates. Little information is available about well children in developed countries but Challacombe, Richardson & Anderson (1974) demonstrated low counts of less than 100 bacteria per ml in the small bowel in nearly half the children they studied in Britain. In contrast, the jejunal flora of apparently normal Guatemalan children is more profuse and varied (Mata *et al.* 1972*a*). Our findings show no major differences between the London and the Jamaican children but we isolated bacteroides on four occasions and bifidobacteria on one occasion from the small bowel of Jamaican children. The tendency for higher counts in the small bowel during acute diarrhoea was shown by the re-intubations during convalescence, indicating a general decrease in both aerobic and anaerobic flora. Nevertheless, the numbers of some genera did not decrease within these totals and the higher counts during the acute illness might well be attributable to a non-specific effect of diarrhoea itself (Gorbach *et al.* 1970*b*).

Another factor, bowel motility, may also be related to the differences between the small bowel flora in gastroenteritis in the two populations. We found that the carmine transit time was always greatly reduced during gastroenteritis in England (Higgs, Ellis-Pegler & Lambert, 1975) whereas Heyworth & Brown (1975) showed very variable and sometimes remarkably prolonged carmine transit times in the malnourished Gambian children they studied.

The effects of malnutrition on the small bowel flora is uncertain. James, Drasar & Miller (1972) found no bacteriological differences before and after the treatment of childhood malnutrition in a metabolic ward, although the recovered group they studied were different children from the group with malnutrition. Mata *et al.* (1972*b*) studying the same malnourished children (without diarrhoea) before, during and after recovery from malnutrition noted significant reductions in the bacterial populations of the jejunum but not of stomach or duodenum. They implied that the admission findings in the malnourished were 'abnormal' but, as previously discussed, found similar concentrations in four 'normal' children from the same environment.

Gracey & Stone (1972) and Gracey *et al.* (1973) showed that the small intestinal flora in malnourished Aboriginal children and malnourished Indonesian children, all with chronic diarrhoea, is generally more luxuriant and diverse than that of normally nourished Caucasian Australian children with chronic diarrhoea. They comment specifically on the ethical and practical problem of obtaining truly appropriate controls for this sort of study.

It is clear that in a complex situation the spot sampling of luminal fluid gives at best a very crude indication of the total small bowel flora, and deductions from information obtained in this way must obviously be made with this reservation. Multiple sampling sites give more satisfactory results but the effect of prolonged intubation itself on the flora has been emphasized (Challacombe *et al.* 1974).

It is evident that diarrhoea itself may result in an abnormal small bowel lumen flora: it seems that those who live in the tropics have more bacteria in their small bowel lumina than those who live in temperate climates. It is less certain however that malnutrition alone is accompanied by a small bowel flora abnormal for their background environment. The possibility that 'normal' bacteria in a malnourished bowel might however have special effects is still not excluded, and the relative significance of organisms attached to bowel mucosa is now under active study both in tropical sprue (Tomkins, Drasar & James, 1975) and in gastro-enteritis (McNeish *et al.* 1975; Leading Article, 1977). Klipstein *et al.* (1976) have found enterotoxin-producing strains of *Klebsiella* and *E. coli* in the small bowel of patients with tropical sprue in Haiti.

Whereas changes associated with chronic colonization of the small bowel have been extensively studied, those during and after acute infections are less clear and more difficult to evaluate. Widespread colonization of the bowel is found in cholera and many other organisms, in particular certain strains of *E. coli* and other bacteria have been shown to produce enterotoxins which act in experimental systems in a manner generally similar to that of cholera toxin (Leading Article, 1975). If production of enterotoxin is an important mechanism in the pathogenesis of acute diarrhoea, abnormal jejunal colonization should be found commonly in diarrhoeal disease, although such a finding must be interpreted cautiously in view of the non-specific influences of diarrhoea previously discussed (Gorbach *et al.* 1970*b*). Nevertheless it would be valuable to know how general a phenomenon is jejunal colonization with particular organisms in gastro-enteritis. If the mere

presence of raised bacterial counts in the small bowel cannot be ascribed a pathogenic role, the significance of individual bacterial genera must be assessed. We have studied especially the serotype and toxin production of the strains of *E. coli* found in stool and jejunum in Jamaica and England and these, reported elsewhere (Ellis-Pegler *et al.* 1978) do not support the notion that small bowel invasion by toxigenic *E. coli* is a common cause of gastro-enteritis, although widespread colonization of the bowel with a particular strain of *E. coli* is well described (Thomson, 1955) and was found in two of our patients. The possible significance of other components of the small bowel flora in causing diarrhoea can only be determined by further work on the metabolic activities of these organisms of the type now being undertaken by several workers.

If small bowel colonization is of potential importance in diarrhoea, by exposing mucosa to the action of bacterial toxins or by other mechanisms, can the notable differences between gastroenteritis in poor and rich communities be explained by differences in the intensity of colonization? We have been unable to support this hypothesis since the modest differences in the small bowel flora established between children in Jamaica and in England seem to reflect the background pattern found also in adults and children without diarrhoea. Again, more definite ideas about this must wait first upon more detailed knowledge of the pharmacological actions of bacterial products involved, and second, on more information on the viruses of gastroenteritis in different settings, their sites of colonization in the bowel and the relations of these viruses to the bacterial flora.

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