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# Investigating Gastroenteritis: The Merseyside Experience 1983–1987

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Outbreaks of gastroenteritis may lead to serious disruption when many persons are absent from work or school. The illness may be life-threatening, particularly in the very young and very old. Control of gastroenteritis associated with microbial infection is therefore an important aspect of preventive medicine. Laboratory investigations are necessary to establish the source of an outbreak, to determine whether chemotherapy is necessary as it is in, for example, Giardia lamblia infection and to identify long-term changes in the pattern of infections related to altered dietary habits and other social factors. In this survey we draw attention to the many infective agents which have to be considered in the investigation of cases and outbreaks of gastroenteritis. The examination of faecal samples in the microbiology laboratory is becoming increasingly complex requiring as it does the use of additional new techniques for previously unrecognised bacterial, viral and protozoal causes of gastroenteritis including, in the last two decades, Campylobacter, Clostridium difficile, rotavirus, Norwalk virus and Cryptosporidium. These investigations are however expensive and in the face of increasing pressure to economise, it is of paramount importance that the best use should be made of the resources available. To this end we make recommendations about the information that should accompany faecal and other samples submitted to the laboratory from outbreaks of gastroenteritis.

## Introduction

The control of gastroenteritis associated with bacterial, protozoal and viral infection of the alimentary tract is a major public health responsibility. Although vomiting and diarrhoea of short duration in individuals is common and not a serious problem, spread of infection by the faecal-oral route may lead to outbreaks with numerous cases in families, institutions including hospitals, day nurseries and schools and among persons attending large social functions. Gastroenteritis associated with rapid fluid loss may be life-threatening particularly in the very young and very old and prevention is very important in, for example, maternity and special care baby units and in geriatric wards. Laboratory investigations show that a wide range of micro-organisms may be responsible for outbreaks of gastroenteritis some of which have only recently been added to the list of those taken into account by microbiologists carrying out tests on faecal samples. Thus, to long-recognised

organisms such as Salmonella, Shigella, enteropathogenic Escherichia coli (EEC), Clostridium perfringens, Staphylococcus aureus and Giardia lamblia must now be added others including Campylobacter, Yersinia enterocolitica, Aeromonas hydrophila, enterotoxigenic (ETC), enteroinvasive (EIC) and verotoxin-producing strains of E. coli, Clostridium difficile, Bacillus cereus, Cryptosporidium and enteropathogenic viruses including, most commonly, rotavirus and Norwalk virus. Travellers from abroad may be infected with Vibrio cholerae, Vibrio parahaemolyticus or Entamoeba histolytica.

Laboratory investigations are thus expensive and time-consuming but are necessary to establish the source of an outbreak and to prevent further spread or recurrence of the problem. Identification of the causative organism will also enable a decision to be made about specific chemotherapy which is required in *G. lamblia* infection and may be indicated in other cases associated with severe systemic illness, for example, salmonella bacteraemia. Moreover monitoring of the prevalence of gastroenteritis and the causative agents reveals changes reflecting, for example, altered dietary habits and other social factors. These include the greatly increased consumption of mass-produced food of animal origin, notably poultry, and the much larger proportion of people who take holidays abroad during the summer. We have analysed the results of the laboratory investigation of gastroenteritis in the Merseyside conurbation consisting of 5 boroughs with a population of about  $1\frac{1}{2}$  million in the 5 years 1983–1987.

#### Methods

Faecal samples or, in some cases rectal swabs (for culture only), were received by Liverpool Public Health Laboratory (PHL) from general practitioners and environmental health departments in the 5 Merseyside boroughs, Knowsley, Liverpool, St. Helens, Sefton and Wirral, with a total population of about 1½ million, and from the Mersey Regional Infectious Diseases Unit and other departments of Fazakerley Hospital Liverpool (1,000 beds). Microbiology departments of most of the other hospitals in the area submitted cultures to PHL for identification. These were mainly salmonellas isolated from specimens submitted by general practitioners through open access to hospital laboratories. Faecal samples for electron microscopy were also referred by hospital microbiology departments to PHL from cases of suspected viral gastroenteritis, the majority from ward outbreaks.

All first faecal samples from patients with gastroenteritis were cultured for Salmonella, Shigella and Campylobacter and, if from infants up to 2 years old, enteropathogenic E. coli. Microscopy and culture for other bacteria were also undertaken when indicated by information accompanying the sample. In cases of Bacillus cereus, Cl. perfringens or Staph. aureus food poisoning, these organisms were only sought in faeces if incriminated food was also available for examination.

The total numbers of specimens each year from 1983 to 1987, including positive cultures referred by hospital laboratories were:

1983 1984	8,607 8,313
1985	6,334
1986	7,308
1987	4,696
Total	35,258

Up to August 1984, when the practice ceased, women admitted to the Maternity Unit, Fazakerley Hospital, were screened for salmonella excretion representing nearly 4,000 specimens per annum. This was discontinued because over a 9-year period only 60 (0.2%) of 30471 women screened were salmonella-positive and only 7 of the 60 babies excreted salmonellas. Reduced numbers in 1987 compared with 1985 and 1986 reflected the absence of major outbreaks in the later year. During the period under review however the workload per specimen increased with introduction of additional special techniques for the detection of Cl. difficile and its toxin, Cryptosporidium and, in 1987, Aeromonas and Yersinia.

Cultures of Salmonella were sent for serotyping and/or phage typing to Division of Enteric Pathogens (DEP), Central Public Health Laboratory, Colindale, London. Cultures of Shigella other than sonnei were also sent to DEP for serotyping.

Details of each patient's home address, age, sex and, in some cases, illness were available from the specimen request form or were obtained, if possible, by telephone. Questionnaires in respect of salmonella-positive patients were sent to the doctors concerned and also in the case of outbreaks of infection of any kind requesting information about number of patients with symptoms or found to be positive for the causative organism.

## Results

## Salmonella serotypes

Control of salmonella infections in man depends on identification of sources of infection usually foods of animal origin. Infection by person-to-person transmission is less common, except in, for example, clinical situations involving infants or elderly and incontinent persons or, in the household, close family contacts. By antigenic analysis about 2,000 Salmonella serotypes can be identified and the more common of these have been further divided in phage types (PT's). Thus there are 232 PT's of S. typhimurium and 32 PT's of S. enteritidis but in both cases a small minority of the PT's account for most of the infections in man. Accurate recognition of sources of infection depends on the use of these typing systems to 'finger-print' salmonellas which are widely distributed, often without causing disease, in animals that are sources of human food such as cattle, pigs or poultry and, as a result, frequently cause infection in man when there are lapses in standards of cooking or hygiene. Epidemiological typing is therefore an essential part of the laboratory investigation of salmonella infections.

The numbers of patients from whom salmonellas other than S. typhi and S. paratyphi were isolated annually from 1983 to 1987 are shown in Table I together with the numbers of the serotypes most frequently isolated. The main change in the distribution of Salmonella serotypes in the period under review was the emergence of S. enteritidis as a rival to S. typhimurium which has occupied first place for many years. Of the S. enteritidis isolates PT4 predominated accounting for 127 (71%) of 179 cases in 1986 (including a hospital outbreak of 37 cases) and 73 (78%) of 94 in 1987. This is the enteritidis PT most commonly isolated from chickens and eggs including some batches of liquid egg and these are probably the food sources mainly responsible for the rapid increase in human S. enteritidis infections. There was however an outbreak of 12 cases of S. enteritidis PT8 infection in 1985 at an old people's home and 35 cases of S. enteritidis PT6 in 1986 including many in travellers returning from Spain and Portugal.

The high proportion of the *enteritidis* serotype among salmonellas acquired by holdiday-makers in these two countries (Table II) reflects the predominance of *S. enteritidis* among human salmonella infectious in the Iberian peninsula. The Spanish National

Table I Distribution of Salmonella serotypes (other than S. typhi and S. paratyphi) 1983-1987 including in each year the 3

		mc	st frequ	most frequently isolated	ited					
		1983		1984		985	-	1986	198	12
Serotype	и	(%) u	и	(%)	и	(%) u	z	(%)	и	(%) u
S. typhimurium	219	(63)	109	(41)	112	(43)	101	(27)	87	(33)
S. enteritidis	19	(5)	27	(10)	20	(61)	179	(48)	94	(35)
S. virchow	22	9							18	(
S. panama			70	<u>(</u>			13	4		
S. stanley					19	()				
Others	68	(56)	111	(42)	78	(30)	77	(21)	99	(25)
Total	349		267		259		370		265	

Table II Salmonella serotypes associated with foreign travel 1983-1987

Reference Laboratory received 4,068 salmonellas in 1986 of which 2,742 (67%) were S. enteritidis and only 375 (9%) were S. typhimurium.<sup>2</sup> It is encouraging that there was an increase in proportion of returned questionnaires with information about foreign travel each year between 1983 and 1987. It is noteworthy (Table III) that the increase in proportion of S. enteritidis isolates appears not yet to have affected infants under one year who are less likely to be involved in the dietary hazards of foreign travel. There were however in this age group 6 cases of S. enteritidis PT8 infection in 1985 which were evidently not epidemiologically related.

The decline in numbers of *S. typhimurium* cases from 219 in 1983 to 87 in 1987 cannot be explained because of the variety of phage types involved indicating many different sources and routes of infection. In the earlier years however there were several large outbreaks of *S. typhimurium* infection. In 1983 there were outbreaks at 2 social functions of PT99 (9 persons) and PT135 (26 persons), in 1985 a hospital outbreak of PT12 (23 persons)<sup>3</sup> and in 1986 an outbreak of PT110 (14 identified cases) at a medical students ball.

## Campylobacter infections

Since Skirrow<sup>4</sup> reported the first cases of Campylobacter infection recognised in UK, laboratory investigations have shown that these outnumber Salmonella infections among cases of gastroenteritis not associated with large outbreaks. Special techniques are required in the laboratory to detect campylobacters and much of the rapid increase in cases reported to CDSC during the 1980's has been the result of the successful use of these techniques by an increasing number of laboratories. At Liverpool PHL an earlier increase reached a peak in 1984 and then 'levelled off' (Table IV). The total numbers of cases for each year from 1983 to 1987 is substantially less than those of Salmonella infections (Table I) but the impact of Campylobacter infections in the community is certainly underestimated in Table IV. This is because campylobacters isolated in hospital laboratories from specimens submitted by general practitioners were not from large outbreaks and were not usually referred to PHLS for biotyping and serotyping. This is in sharp contrast to the practice in most hospital laboratories of submitting all Salmonella cultures to PHL for further investigation including many from general practitioner patients. Where a direct comparison of the prevalence of the two infections is possible it is noteworthy that between 1983 and 1987, 253 cases of *Campylobacter* infection were admitted to Fazakerley Hospital, nearly all to the Regional Infectious Diseases Unit and the comparable figure for Salmonella cases was 209. In 1987 an outbreak of milk-associated gastroenteritis at a residential school affected 296 children and 17 adults. At Liverpool PHL Campylobacter jejuni was isolated from 16 of 17 patients investigated and positive cultures from 7 other patients were received from hospital laboratories.

## Shigella infections

Table V shows the total number of cases of *Shigella* infections diagnosed in each of the years 1983 to 1987. There was a low and unchanging level of *Sh. flexneri*, *Sh. boydii* and *Sh. dysenteriae* infections but a striking increase in *Sh. sonnei* infections starting in 1984, reaching a peak in 1985, falling in 1986 and reaching a low level in 1987 similar to that in 1983. The national trend was similar and the waxing and waning of this infection cannot be explained. The short-lived increased in Merseyside was associated with outbreaks in day nurseries mainly in Liverpool and Knowsley but not confined to them as spread to home contacts frequently led to family outbreaks.

Table III Salmonella serotypes in infants under 1 year 1983–1987

				N	lumber	of case	s			
		1983		1984	1	985		1986	19	987
Serotype	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
S. typhimurium	20	(65)	8	(22)	8	(33)	9	(32)	6	(32)
S. enteritidis	1	(3)	2	(6)	7*	(29)	3	(10)	2	(10)
S. virchow	0		3	(8)	1	(4)	1	(4)	6	(32)
Others	10	(32)	23	(64)	8	(34)	15	(54)	5	(26)
Total	31		36		24		28		19	

<sup>\* 6</sup> were PT8 but not epidemiologically related

Table IV Campylobacter infections 1983-1987

		Nun	nber of ca	ses diagn	osed	
Patient in:	1983	1984	1985	1986	1987	Total
Fazakerley Hospital	36	49	51	61	56	253
Community	60	98	91	115	111	475
Other hospitals (referred cultures)	11	11	1	6	7	36
Total	107	158	143	182	174*	764

<sup>\*</sup> Including 23 from a school outbreak

Table V Shigella infections 1983-1987

		Numbe	r of cases dia	agnosed	
Shigella species	1983	1984	1985	1986	1987
Sh. flexneri	7	3	4	2	3
Sh. boydii	2	1	0	0	1
Sh. dysenteriae	2	2	1	1	2
Sh. sonnei	11	69	214	82	20
Total	22	75	219	85	26

## Enteropathogenic Escherichia coli

Major outbreaks of EEC infection did not occur and are now rare in, for example, maternity units probably because of the recognition of the need to isolate mothers and babies with diarrhoea and the provision of appropriate facilities. The decline in the number

		Numbe	r of positive	patients	
Patient in:	1983	1984	1985	1986	1987
Fazakerley Hospital	<u> </u>				
Maternity Unit:	21		0		,
mothers: infants:	21	1	0	1	1
infants:	2	1	2	1	0
Community including day nurseries	20	18	16	12	9

Table VI Enteropathogenic Escherichia coli infection 1983–1987

of positive patients detected in this survey (Table VI) was accentuated by the ending in 1984 of the routine screening for intestinal pathogens of women admitted to Fazakerley Hospital Maternity Unit. There was no change between 1983 and 1987 in the very low level of isolations from new-born infants in the Unit. In the community there was a cluster of 3 cases of 0128 infection in a Liverpool day nursery in 1985 but none of the other isolates were from related cases.

Verotoxin-producing E. coli 0157:H7 the cause of haemorrhagic colitis was sought in selected cases in 1987 but none were positive.

## Protozoal infections

The protozoa most commonly associated with gastroenteritis in UK are Giardia lamblia detected by wet-film microscopy of faecal samples and Cryptosporidium newly recognised as a human pathogen<sup>5</sup> and also detected by microscopy of faecal samples after special staining. The number of positive cases of these two infections diagnosed at Liverpool PHL are shown in Table VII.

The peak age group for *G. lamblia* infections was the pre-school, including day nursery, group aged 1–4 years but many cases also occurred in adults, 16–59 years (Table VIII). Among the latter there were 7 instances identified of patients whose children were infected with *Giardia*. In 1985 there was an outbreak at a Liverpool day nursery involving 5 children aged 20 months to 3 years, 3 of whom were also excreting enteropathogenic *E. coli*. The distribution of positive cases in the 4 quarters of the year was respectively 44, 35, 74, 58, i.e. higher in July to September than in the rest of the year. Some cases were associated with foreign travel.

Number of cases diagnosed Protozoon 1983 1984 1985 1986 1987 Total Giardia lamblia 19 61 41 36 54 211 Cryptosporidium NT NT 26 30 46 102

Table VII Protozoal infections 1983–1987

NT = Not tested

Protozoon	less than 1 year	1–4 years	5–15 years	16–59 years	60 years and over	Not known	Total
Giardia lamblia	6	67	22	102	9	5	211
Cryptosporidium	7	48	10	25	5	7	102

Table VIII Protozoal infections 1983–1987. Distribution of positive cases by age groups

Compared with G. lamblia, there was a larger proportion of Cryptosporidium cases in the pre-school 1-4 years age group and a small proportion in adults aged 16-59 years (Table VIII). In the latter age group, 4 instances were identified of patients whose children were excreting Cryptosporidium including one Liverpool family in which 2 adults and 4 children were infected with this pathogen. The distribution in the 4 quarters of the year was respectively 37, 28, 12, 25 with thus a higher incidence in the spring than in the rest of the year. The relatively large numbers of cases of protozoal infection, particularly of Cryptosporidium in the 1-4 years age group may reflect the greater likelihood both of faecal samples from children with diarrhoea being submitted for examination and of the samples being selected for microscopy in the laboratory.

## Aeromonas

Three species are recognised among Aeromonas strains isolated from faecal samples, A. hydrophila, A. sobria and A. caviae, of which the first 2 are regarded as probably pathogenic. Faecal samples were screened routinely for Aeromonas spp. for the first time in 1987. During the year Aeromonas was isolated from 84 persons, 79 with diarrhoea of whom 17 were also positive for a recognised pathogen, for example, Salmonella, Shigella, Campylobacter or G. lamblia. Among these 79 patients, A. hydrophila was isolated from 17, 3 also positive for other pathogens, A. sobria from 7, 3 with other pathogens and A. caviae from 55, 11 also with recognised pathogens. The 5 patients without diarrhoea were positive for A. caviae. Further work is clearly required to establish whether Aeromonas can be regarded as a major cause of gastroenteritis.

## Other organisms associated with gastroenteritis

Yersinia enterocolitica is regarded as an important cause of gastroenteritis in some Western European countries. In 1987 faecal samples from patients with diarrhoea were tested for Yersinia in parallel with tests for Aeromonas but only 3 were positive for Yersinia spp.

Patients with gastrointestinal symptoms recently arrived from Asia or from other countries known to have cholera cases were tested for *Vibrio* spp. Between 1983 and 1987, none were positive for *V. cholerae* but *V. parahaemolyticus* was isolated from one patient with diarrhoea after arriving by air from Bangkok.

Diarrhoea is a common complication of antibiotic treatment and probably associated in many cases with overgrowth in the bowel of *Cl. difficile* with production of sufficient toxin to cause gastrointestinal symptoms. Tests for this organism and its toxins are however recommended only for the more severe cases including those presenting as pseudomembranous colitis. They are largely confined to hospital practice where outbreaks occasionally occur involving cross-infection in wards for elderly or immunocompromised

patients. During the period under review Liverpool PHL identified 61 positive patients in hospitals but only 4 from general practitioners.

Diagnosis of food-poisoning caused by *Bacillus cereus*, *Clostridium perfringens* or enterotoxigenic *Staphylococcus aureus* depends on demonstration of large numbers of the causative organism in food consumed by those affected. Between 1983 and 1987 there were 5 major episodes of food-poisoning in which one of these organisms was identified as responsible.

## Viral gastroenteritis

Most viruses associated with gastroenteritis cannot be isolated by tissue culture methods and their detection depends on the use of electron microscopy or, in the case of rotavirus, demonstration of specific antigen by, for example, enzyme immunoassay. These methods require, however, the presence in faecal samples of relatively large amounts of virus and specimens must be collected in the acute phase of the illness for there to be much chance of a positive result.

During 1986 and 1987, faecal samples from 2,529 patients were examined by electron microscopy at Liverpool PHL. The samples selected for this examination were mainly from those patients with gastroenteritis in whom no bacterial or protozoal agents had been demonstrated and which had been collected within a few days of the date of onset of illness. The numbers of patients positive for viruses recognised as causes of gastroenteritis were:

rotavirus	316
Norwalk virus	40
adenovirus	69
astrovirus	8
coronavirus	6
calicivirus	3
Total positive	442 (17%)

The patients investigated included those involved in 24 outbreaks of gastroenteritis in the community, 3 in childrens' units, 21 in homes for old people, and 27 outbreaks in hospitals, 2 in paediatric, 21 in geriatric and 4 in general wards. Rotavirus or Norwalk virus were detected in 9 (18%) of the 51 outbreaks investigated (Table IX).

Table IX Outbreaks investigated for viruses 1986–1987

		Viruses id	entified	
Location of outbreak:	Rotavirus	Norwalk virus	Negative	Total
Community units	1	2	21	24
Hospital wards	i	5	21	27
Total	2	7	42	51

#### Discussion

It is clear that control of gastroenteritis in the community is an important aspect of preventive medicine. In severe cases the symptoms are very distressing and the illness may be life-threatening particularly in the very young and very old. At all ages however there may be serious social disruption. Persons affected must take time off work or school and exclusion, for a time, of employees in high-risk occupations such as nursing or food-handling is necessary. Children have to be excluded from day nurseries and schools affecting attendance of parents at work. Gastrointestinal infection acquired at a social function is a disaster when large numbers of guests are affected. Gastroenteritis is often a disturbing accompaniment or aftermath of foreign travel. In this survey in an almost entirely urban area we draw attention to the many infective agents which have to be considered in the laboratory investigation of cases and outbreaks of gastroenteritis. The examination of faecal samples in the microbiology laboratory is becoming increasingly complex requiring as it does the use of additional new techniques for previously unrecognised bacterial, viral and protozoal causes of gastroenteritis including, in the last two decades, Campylobacter, Clostridium difficile, rotavirus, Norwalk virus and Cryptosporidium. To cover all, or most, possibilities it is now necessary to employ a wide range of techniques which may include as many as 12 different solid or liquid culture media incubated aerobically and anaerobically and at 3 different incubator temperatures, 30°C, 37°C and 43°C; light microscopy of stained and unstained preparations; electron microscopy and either tissue culture or latex agglutination for detection of bacterial toxin.

In addition to work in the laboratory that receives the specimens, it is necessary in some cases for specialised investigations to be undertaken by the Division of Enteric Pathogens, Central Public Health Laboratory, Colindale Avenue (DEP) including tests for enterotoxin and epidemiological typing, for example, phage typing which may be necessary to define the source and pattern of spread of an outbreak. An example of this was the nationwide outbreak early in 1988 of Salmonella typhimurium PT124 infections traced to imported salami and halted after investigation by Communicable Diseases Surveillance Centre (CDSC) based on case-control studies of patients from whom this STM phage type had been isolated. Plasmid profiles may also be used increasingly in future in this field.

It may be argued that laboratory investigation of gastroenteritis is often unnecessary because, for most cases, specific chemotherapy is not recommended and because in 'high-risk' situations persons with diarrhoea are excluded irrespective of the results of laboratory tests. It is important however to take into account that specific treatment is required for patients with *Giardia lamblia* infections including symptomless carriers often identified among contacts of clinical cases. Also the epidemiology of gastroenteritis caused by different organisms varies so much that it is necessary to identify the agent responsible for an outbreak before appropriate and effective measures can be taken to bring it under control and prevent a recurrence. Precise identification of the cause of cases of gastroenteritis can only be achieved by microbiological examination of faecal samples or, in the case of some types of food-poisoning, the food thought to be responsible for the illness. In some food-related outbreaks, the length of the incubation period may give an important clue to the diagnosis, for example, 2 to 4 hours for staphylococcal food-poisoning, but laboratory investigation is necessary to identify the source of infection with certainty.

Such investigations are expensive and in the face of increasing pressure to economise it is of paramount importance that the best use should be made of the resources available. To this end laboratory work should be based on as much information as possible about the illness under investigation. We advise medical staff, environmental health officers and

others who submit specimens to the laboratory that the information accompanying them should include:

- 1. Home address, age and sex of patient.
- 2. Nature of symptoms and date of onset.
- 3. Whether illness associated with a particular food or meal and if so the incubation period before onset of symptoms.
- 4. Whether patient has recently been in contact with similar cases.
- 5. Whether patient has recently been abroad and if so where.
- 6. Whether patient has been in hospital or been given antibiotic treatment recently.

If this information is lacking the causative organism may not be identified because the appropriate techniques have not been used. If, on the other hand, it is available it may be possible for staff from the laboratory to suggest further investigations including collection of additional specimens from likely sources of infection. The information provided may also reveal evidence of a link with other cases under investigation in the laboratory or, through CDSC, with cases in other parts of the country. Data derived from tests on large numbers of patients can also be used in the longer term to monitor changing trends in the incidence of different types of gastroenteritis in the area served by the laboratory and at national level through transmission of data to CDSC.<sup>6</sup>

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