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First recognized community outbreak of haemorrhagic colitis due to verotoxin-producing *Escherichia coli* O 157.H7 in the UK

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SUMMARY

The first recognized outbreak of haemorrhagic colitis due to *Escherichia coli* O 157.H7 in the United Kingdom affected at least 24 persons living in East Anglia over a 2-week period. The illnesses were characterized by severe abdominal pain and bloody diarrhoea of short duration. Eleven patients were admitted to hospital and there was one death. Patients were mainly adult women who had not eaten out of the home in the 2 weeks before onset. Unlike previously reported outbreaks hamburgers were not the vehicle of infection, and a case-control study suggested that handling vegetables, and particularly potatoes, was the important risk factor.

INTRODUCTION

Verotoxin-producing *Escherichia coli* O 157.H7 has been identified recently as the causal agent of outbreaks (Riley *et al.* 1983; Pudden *et al.* 1985; Ryan *et al.* 1986; Spika *et al.* 1986) and sporadic cases (Remis *et al.* 1984; Pai *et al.* 1984) of haemorrhagic colitis in North America, and as one of the causes of the haemolytic uraemic syndrome (HUS) (Karmali *et al.* 1985). In England and Wales this organism has been isolated from 39% of sporadic cases of haemorrhagic colitis (Smith *et al.* 1987) and 33% of sporadic cases of HUS (Scotland *et al.* 1988) and from cases in an outbreak of HUS in the West Midlands (Taylor *et al.* 1986). We describe the first community outbreak of *E. coli* O 157.H7 haemorrhagic colitis in the UK.

THE OUTBREAK AND INVESTIGATION

Between 1 and 7 July 1985 seven patients with bloody diarrhoea and severe abdominal pain were admitted to the Norfolk and Norwich Hospital. Faeces were negative for *Salmonella*, *Shigella* and *Campylobacter* sp. On 11 July, Addenbrooke's Hospital Cambridge, 50 miles away, reported a similar cluster of four cases admitted to hospital. Faeces examined by the Division of Enteric Pathogens of the Central Public Health Laboratory were positive for verotoxin-producing *E. coli* O 157.H7. A collaborative investigation was undertaken by local microbiology laboratories, community physicians, the PHLS Communicable Disease Surveillance Centre and the Division of Enteric Pathogens (DEP) of the Central Public Health Laboratory.

The following case definitions were used. A confirmed case was a patient with diarrhoea whose faeces were negative for *Salmonella*, *Shigella* and *Campylobacter* sp. and were positive for *E. coli* O 157.H7 either detected by (i) culture and serological identification, or, (ii) by the use of specific DNA probes for verotoxin genes with subsequent confirmation by serotyping and tissue culture test for verotoxin.

A case of unconfirmed haemorrhagic colitis was a patient with bloody diarrhoea (three or more stools in 24 h) and abdominal pain who was negative for *Salmonella*, *Shigella* and *Campylobacter* sp. but whose faeces were either not examined for verotoxin-producing *E. coli* or were negative on examination.

Case finding was undertaken as follows. Local general practitioners, hospital clinicians and all microbiology laboratories in East Anglia were informed of the outbreak and asked to report current or retrospective cases of bloody diarrhoea. Occupational health staff in Norwich were also informed and asked to notify possible staff cases. In Norwich a retrospective review of hospital admissions during the preceding 6 months was made by reference to the diagnosis and symptoms recorded in nursing records or ward registers. Where there was an indication that an individual had suffered from haemorrhagic diarrhoea full case notes were examined. Nationally, all Public Health Laboratories were informed of the outbreak by the Director of the Communicable Disease Surveillance Centre and, in addition, notice of the outbreak appeared in the Communicable Disease Report. Twenty-four confirmed cases and 25 unconfirmed cases were identified.

In a case control study of possible sources of infection three age (± 10 years) and sex-matched neighbourhood controls were systematically sampled from the list of the general practitioners who had referred the case. Where an age-sex register was available the next names on the register were approached. When an age-sex register was not available, every tenth record following the index case record was examined. The first six persons within 10 years of age of the case were identified and they were contacted in the order their names appeared, and at least two attempts were made to contact a control before proceeding to the next on the list. Cases and controls were questioned over the same period in July and August, using a standard questionnaire, about food consumed over a 2-week period prior to the onset of symptoms in the case, by one of two investigators. Statistical analysis was by means of a logistic regression model fitting technique which allowed for the matched design (Lubin, 1981) and which calculated odds ratios as an estimate of

relative risk. When the lower 95% confidence interval (L 95% CI) of the odds ratio was >1 this was equivalent to a P value of $<0{\cdot}05$.

Faecal samples from suspected cases were cultured for *Campylobacter*, *Salmonella* and *Shigella* sp. At the DEP, faeces were examined with radio-labelled DNA probes which were specific for the VT genes. This technique allowed the examination of several hundred colonies from each faecal specimen. The probe-positive colonies were identified biochemically, serotyped and tested for VT production in the Vero-cell tissue culture test (Smith *et al.* 1987).

RESULTS

Clinical features

Case history 1. A 50-year-old woman became ill on the morning of 4 July and passed three loose stools before going to work. She remained well throughout the day but the following day had watery stools about every hour and then every 20 min during the night. During the night she suffered very severe abdominal pain which was relieved by evacuation. She noted dark red blood mixed with the stool, until eventually she passed blood only. She was admitted to hospital but recovered by the 8 July. Her temperature did not rise above 37·5 °C.

Case history 2. A 28-year-old woman became ill on 5 July with feverishness and headache and developed mild abdominal pain with four loose stools that day. Diarrhoea persisted ($\times 5$) the following day but on the 8 July the pain became much more severe and bright red blood was passed in the stool. She was admitted to hospital and a laparotomy was performed but there were no specific findings.

Full clinical information was available on 21 of 24 confirmed cases and 17 of 25 unconfirmed cases (Table 1). Eleven confirmed and 8 unconfirmed cases were admitted to hospital as medical or surgical emergencies, 2 confirmed and 1 unconfirmed case underwent laparotomy and 1 19-year-old male required a blood transfusion. One confirmed patient case, a woman of 64, died and post-mortem examination was reported as 'acute fulminating idiopathic colitis'.

Faecal samples from confirmed cases had been taken a mean of 3·0 days (range 1–10, median 2 days) after onset of symptoms compared with a mean of 6·6 days (range 1–19, median 6 days) in 19 unconfirmed haemorrhagic colitis. In patients with haemorrhagic colitis in whom the date of onset was known, 19 of 21 faecal specimens obtained within 6 days of onset were VT probe positive compared with only 2 of 11 samples obtained later.

Epidemiological features

The clusters of cases identified by the two microbiology laboratories occurred concurrently (Fig. 1). Cases were spread throughout the north-east of East Anglia in both urban and rural areas, although there were small clusters in Norwich and Cambridge (Fig. 2). Eighteen of the 24 confirmed cases and 20 of 25 unconfirmed cases were women. The ages of confirmed cases ranged from 6 to 84 years (mean 43 years, median 42 years) and only three individuals were aged under 16 years. In unconfirmed cases the ages ranged from 17 to 82 (mean 46 years, median 41 years). No common factors including restaurant use and dairy and meat supplies

Table 1. *Clinical symptoms*

Symptom	Confirmed *E. coli* O 157.H7 (%) (n = 21)	Unconfirmed haemorrhagic diarrhoea (%) (n = 17)
Haemorrhagic diarrhoea	18 (85)	17 (100)
Profuse watery diarrhoea	9 (45)	13 (76)
Severe abdominal pain	19 (90)	12 (70)
Nausea	8 (40)	14 (82)
Vomiting	10 (50)	6 (35)
Headache	8 (40)	6 (35)
Chills	6 (30)	6 (35)
Fever	6 (30)	5 (29)
Muscle aches	4 (20)	6 (35)
Admitted to hospital	10 (50)	6 (35)

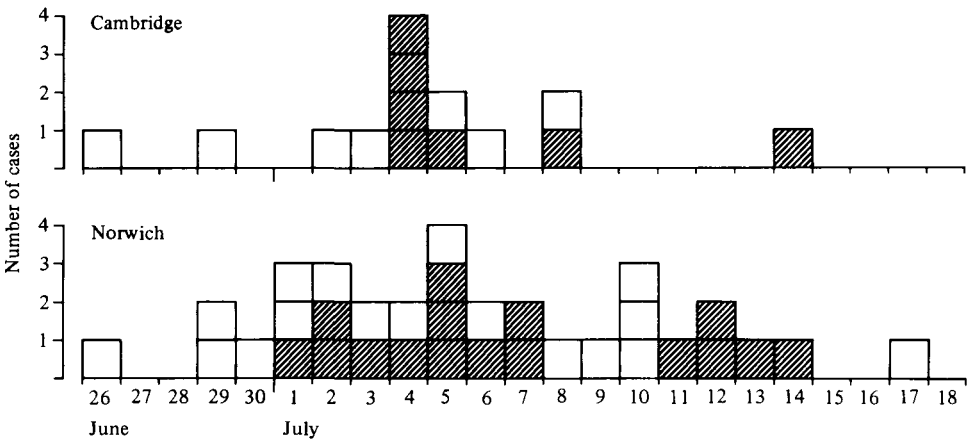

Fig. 1. Date of onset of confirmed ($n = 23$) and unconfirmed ($n = 24$) cases by laboratory. ▨, Confirmed; □, possible.

were identified despite extensive enquiry. There were no secondary family cases. Three confirmed cases were vegetarians and 3 were employed as food handlers, although one was not working because of a broken wrist. Of the 4 subsequently confirmed cases who developed symptoms whilst already in-patients, 1 elderly woman was an in-patient in a long-stay hospital, 1 man was admitted for a routine cholecystectomy and developed symptoms post-operatively. The remaining 2 women aged 47 and 70 years were admitted to one surgical ward on 1 July, for minor operative procedures. On 7 July both developed mild symptoms which in the 47-year-old woman mounted to only three loose, non-bloody stools. On 2 July two other symptomatic confirmed cases had been admitted to this ward and a nurse on the ward who was also a confirmed case developed symptoms on 3 July.

Case control study

Most confirmed cases had not eaten out of the home in the 2 weeks before onset of symptoms and food histories did not identify a common food consumed at

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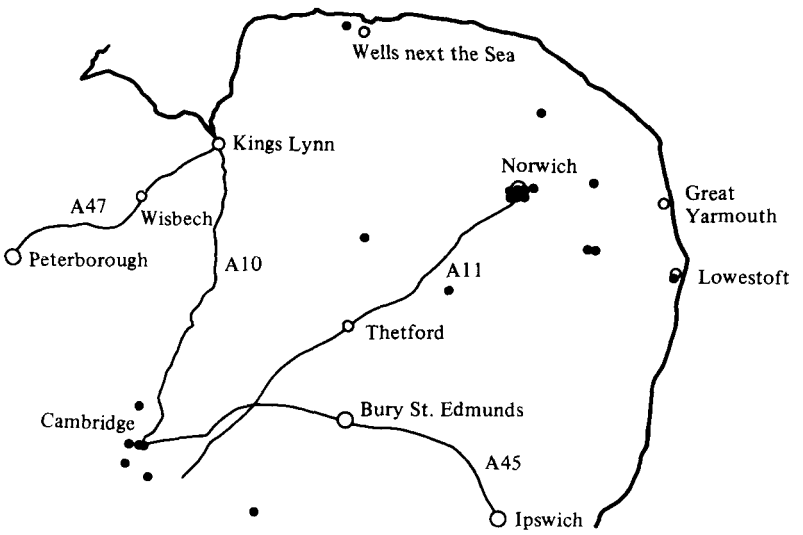

Fig. 2. Confirmed cases in East Anglia.

home. The cases were spread geographically throughout north-east East Anglia which suggested that the vehicle of infection would have been a food distributed widely in East Anglia alone, whilst the short duration of the outbreak suggested that the food was fresh rather than frozen and thus consumed over a relatively short time period. Contacts with retailers revealed that foods sold by large retail outlets were distributed nationally as were meat products which were also likely to be stored in freezers. The foodstuffs most likely to be vehicles of infection were considered to be fresh fruit and vegetables produced and distributed within East Anglia. Because of the preponderance of adult female cases a hypothesis was proposed that the handling of fresh contaminated foods, distributed throughout East Anglia from a common source was the cause of the outbreak. A case control study was set up to test this hypothesis.

Twenty confirmed cases were entered into the study. Of the 4 individuals excluded, 1 had died, 1 refused to co-operate, 1 was a long-stay patient in a psychiatric ward and 1 could not be contacted. Questionnaires were completed on 18 of the 20 cases and information on the remaining cases was available from food histories taken during the initial phase of the investigation. In total 56 of 60 possible controls were interviewed.

There was not a significant association with buying or eating fresh meat, beefburgers, salad vegetables, other vegetable or fruit (Table 2). A significant association ($P < 0{\cdot}05$) was found with preparing non-home produced vegetables (odds ratio (OR) = 14·6 L 95% CI = 1·8). In particular there was a strong association with preparing potatoes, carrots and lettuce (Table 3). When the correlation between preparing potatoes and carrots was examined, potatoes (OR = 5·8, L 95% CI = 1·1) but not carrots (OR = 2·3, L 95% CI = 0·6), remained significant. When the correlation between preparing potatoes and lettuce, and preparing lettuce and carrots was examined none were significant at

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Table 2. *Percentage of cases and controls eating food*

Type of food	Cases (n = 20)	Controls (n = 56)	Odds ratio (lower 95% confidence intervals)	
Fresh meat	65	82	0·4	(0·1)
Beefburgers	45	50	0·8	(0·3)
Salad vegetables	95	96	0·7	(0·1)
Lettuce	80	70	2·0	(0·5)
Other vegetables	95	89	2·1	(0·2)
Potatoes	89	68	2·2	(0·6)
Carrots	75	54	2·6	(0·8)
Fruit	95	98	0·3	(0·02)

Table 3. *Percentage of cases and controls preparing food*

Type of food	Cases (n = 20)	Controls (n = 56)	Odds ratio (lower 95% confidence intervals)	
Fresh meat	35	45	0·6	(0·2)
Beefburgers	35	30	1·4	(0·4)
Salad vegetables	80	59	4·9	(1·0)
Lettuce	70	41	6·8	(1·4)
Other vegetables	80	45	14·6	(1·8)
Potatoes	75	41	7·9	(1·6)
Carrots	55	25	4·1	(1·2)
Fruit	90	84	1·8	(0·4)

the 5% level, but potatoes (OR 4·5 L 90% CI = 1·0) in the first model, and lettuce in the second model (OR = 4·9 L 90% CI = 1·2), were significant at the 10% level.

The vegetables handled by confirmed cases were bought from a variety of retail outlets and market stalls. Information from the wholesale vegetable trade revealed that only potatoes were likely to have been locally produced but widely distributed throughout East Anglia. Attempts were made to trace the source farms of potatoes bought by cases, but the complexity of the wholesale trade and the lack of documentation by suppliers made this impossible.

DISCUSSION

Haemorrhagic colitis was first described when two outbreaks occurred in the USA in 1982 which were caused by eating contaminated hamburgers from one fast-food chain (Riley *et al.* 1983). The disease was characterized by severe abdominal pain, frank blood in the faeces, but little or no fever, and illness lasted about 1 week. Following the discovery that the causative agent was *E. coli* O 157 . H7-producing verotoxin a wider spectrum of illness has been revealed, which ranges from asymptomatic carriage through non-bloody diarrhoea to haemorrhagic colitis and haemolytic uraemic syndrome (Ryan *et al.* 1986; Spika *et al.* 1986). In the outbreak in East Anglia the spectrum of cases identified was limited

by the use of a strict case definition for haemorrhagic colitis, but two infected patients who did not have bloody diarrhoea were identified. Rigors and feverishness were reported by only a minority of cases.

Surveys in N. America (Ratnam & March, 1986) and in England and Wales (Smith *et al.* 1987) suggest that *E. coli* O 157.H7 is a relatively common cause of bloody diarrhoea and common source outbreaks have been described in the USA and Canada (Ratnam & March, 1986; Ryan *et al.* 1986; Spika *et al.* 1986). In N. America, undercooked hamburger meat (Riley *et al.* 1983; Ryan *et al.* 1986) and raw milk (Martin *et al.* 1986, Borczyk *et al.* 1987) have been identified as vehicles of infection. A reservoir of infection in cattle has recently been described (Martin *et al.* 1986; Borczyk *et al.* 1987) and infection with *E. coli* O 157.H7 is a newly recognized zoonosis. However, person-to-person spread has been convincingly documented in a day care centre outbreak (Spika *et al.* 1986). In the East Anglian outbreak, two patients and one nurse may have been infected in hospital by person-to-person spread, although, surprisingly no secondary household cases occurred.

The median incubation period reported to date in outbreaks is between 3 and 8 days with a maximum incubation period of 12 days. In the East Anglian outbreak the onset of symptoms in confirmed cases was spread over 10 days in Cambridge and 13 days in Norwich and so both possibly could be explained by a single simultaneous exposure. However most cases had not eaten out so infection probably occurred within their own homes. The sudden and simultaneous occurrence of cases suggests that the vehicle was rapidly disseminated throughout East Anglia. Unlike other outbreaks of haemorrhagic colitis, beefburgers were not the vehicle of infection in this outbreak, and three of the confirmed cases were vegetarians. The outbreak affected mainly adult females, and three confirmed female cases worked as food handlers, so that handling foods followed by hand-to-mouth transmission, rather than foodborne infection, was suspected. This was supported by the case-control study which showed a strong association of infection and preparing raw vegetables, especially potatoes. We found it impossible to trace the complete wholesale chain of supply of the vegetables but it is possible that a single load of potatoes could have become contaminated by cow manure and then distributed widely over East Anglia. We were told by wholesalers that other vegetables produced within East Anglia would be sold in the immediate locality of producing farms and therefore would not explain the widespread distribution of the outbreak.

The rapid identification of verotoxin-producing *E. coli* was possible through the use of DNA probes (Smith *et al.* 1987; Willshaw *et al.* 1987) and this tool can be of great help in outbreak investigation. However for routine laboratory use identification of sorbitol-negative isolates accompanied by serogrouping for *E. coli* O 157 may be useful for screening purposes (Gransden *et al.* 1986; Walker, Upson & Warren, 1988) although this technique is not as sensitive as the direct use of DNA probes (Smith *et al.* 1987). The recovery of organisms from faeces obtained 7 or more days after onset of symptoms is low (Wells *et al.* 1983) and the importance of obtaining early faecal samples has been emphasized (Riley *et al.* 1983; Remis *et al.* 1984; Walker *et al.* 1988). Of the 47 cases which met the case definition for haemorrhagic colitis faeces samples were available for examination

by DEP from 32, and 21 were positive. Negative faeces samples were obtained later in the course of illness than positive samples. They could have been from true cases as was suggested by the sudden increase of unconfirmed cases of bloody diarrhoea at the same time as the outbreak of confirmed haemorrhagic colitis, and their similar clinical and epidemiological features. Investigation of sporadic cases and clusters is essential if the reservoir of infection and modes of transmission of the infection in the UK are to be identified.

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