Campylobacter enteritis: a "new" disease

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Summary

By selective culture campylobacters (C jejuni and C coli) were isolated from the faeces of 57 (7·1%) out of 803 unselected patients with diarrhoea; none were isolated from 194 people who had not got diarrhoea. Specific agglutinins were found in the sera of 31 out of 38 patients with campylobacter enteritis and 10 of them had a rising titre. Half the patients were aged 15 to 44 years, but the incidence was highest in young children. All the patients with campylobacters had a distinctive clinical illness with severe abdominal pain. Campylobacters are a relatively unrecognised cause of acute enteritis, but these findings suggest that they may be a common cause.

Spread of infection was observed within 12 out of 29 households, and in these cases children were usually implicated. Several patients were apparently infected from chickens, both live and dressed, and poultry may be the primary source of the organism. In two cases dogs with diarrhoea were found to be infected with strains indistinguishable from their human contacts. Ten patients acquired their infections while travelling abroad.

Introduction

The term campylobacter (Greek, a curved rod) may be unfamiliar to many. It was proposed by Sebald and Véron[1] in 1963 as a generic name for the microaerophilic vibrios on the grounds that these organisms differed from the classical cholera and halophilic groups in certain fundamental respects. The type species, *Campylobacter fetus* (*Vibrio fetus*), has been known to veterinarians for many years as a cause of infectious abortion of cattle and ewes, and other members of the genus are associated with several diseases of domestic animals including enteritis of calves and pigs.

King[2,3] was the first to study human strains in depth. She recognised that while some conformed to the classic type, others formed a similar but distinct group characterised by an unusually high optimum growth temperature. She provisionally called these "related vibrios" (now considered by Véron and Chatelain[4] to be represented by the two species *C jejuni* and *C coli*, but listed by Smibert[5] as *C fetus*, subspecies *jejuni*) and pointed out that the most prominent symptom in patients infected with this type was diarrhoea; such an association had also been recorded by others.[6,7] Although the organisms in these cases were cultured from the blood, it was logical to suppose that they might also have been present in the gut, but attempts to culture them from faeces failed owing to overgrowth by coliforms.

Close on 10 years were to pass before Butzler *et al*[8] in Brussels hit on a successful selective coproculture technique. This was based on the fact that campylobacters are small enough to pass through a filter that holds back other organisms. By this means they isolated campylobacters from the faeces of 5·1% of children with diarrhoea and 1·3% of children without diarrhoea. Clearly this was an important discovery that needed to be confirmed and extended, and it was with this aim that the present study was undertaken.

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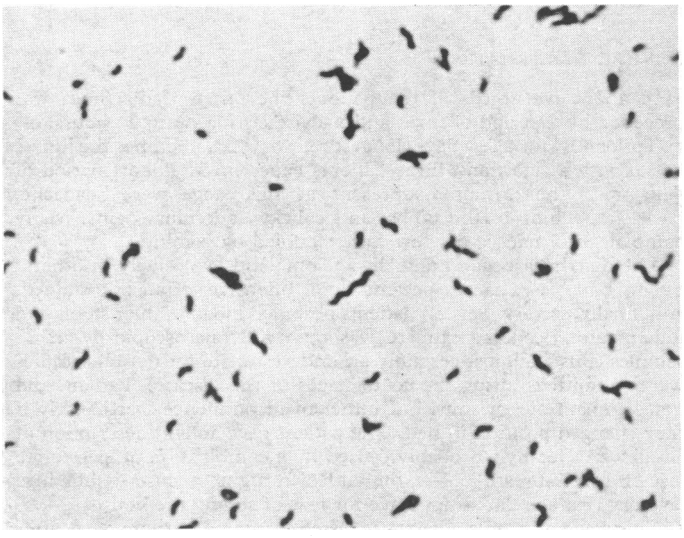
Methods

Selective techniques for culturing campylobacters were used for examining routine faecal samples received in this laboratory over 18 months. These were performed in addition to the methods used for detecting known pathogens—salmonellae, shigellae, enteropathogenic *Escherichia coli* (in children less than two years old), and, when relevant, protozoa and food poisoning organisms. Viruses were not looked for routinely.

Initially filtrates of faecal suspensions, passed through Millipore filters (mean pore size 0·65 μ) in the manner described by Butzler,[8] were cultured on plain blood agar. Later the filtration process was abandoned in favour of a culture medium made selective by the addition of vancomycin (10 mg/l), polymyxin B (2·5 IU/ml), and trimethoprim (5 mg/l). Plates were incubated at 43°C in an atmosphere of 5% oxygen, 10% carbon dioxide, and 85% hydrogen. Campylobacters, which are very small highly motile spiral or S-shaped Gram-negative bacteria, were easily recognisable after overnight incubation (see figure). All isolates conformed to the *C jejuni-C coli* group of Véron and Chatelain.

Formolinised suspensions of bacteria were used for detecting agglutinins in patients' sera.



Smear of campylobacter colony from 18-hour primary culture on selective medium. (Carbol fuchsin stain ×1700.)

Results

FAECAL CULTURES

The results of the faecal cultures are shown in table I. The proportion of diarrhoeal samples positive for campylobacters was higher than that for all other pathogens. This difference was enhanced when the analysis was limited to those samples that were fluid or semi-fluid (about one third of the total), for the proportion positive for campylobacters then became 15%, whereas that for other pathogens remained virtually unaltered. All but five of the samples from patients with campylobacter enteritis were submitted by general practitioners.

TABLE I—*Results of faecal cultures*

	No tested	No positive for *Campylobacter*	No with *Campylobacter* as sole pathogen	No positive for other pathogens
Patients with diarrhoea (unselected)	803	57 (7·1%)	54 (6·7%)	50 (6·2%)
Controls*	194	0	0	
Contacts of patients with campylobacter enteritis	113 (29 households)	19 (12 households)		

*Normal people and patients without gastrointestinal symptoms.

Table II shows the age distribution of all patients with campylobacter enteritis. Although half of the patients were aged 15 to 44 years, the incidence was highest in the very young.

TABLE II—*Age distribution of patients with campylobacter enteritis*

Age (years):	<1	1–4	5–14	15–44	45–64	≥65	Total (all ages)
No of patients	5	11	9	37	8	1	71
Incidence per 10 000 of the population*	13·0	9·5	2·5	4·3	1·6	0·32	3·2

*Worcester district.

SEROLOGY

Sera were obtained from 38 patients. Thirty-one contained specific agglutinins to a titre of 1/80 or more (highest 1/10 240) to their own strains, and 10 showed a fourfold or greater rise of titre between acute and convalescent samples. It was difficult to get samples sufficiently early to show a rise in titre, because antibody was often already present by the fifth day of illness.

CLINICAL MANIFESTATIONS

In about two-thirds of the patients the onset of diarrhoea was preceded by a period of fever and malaise lasting up to 24 hours, or, exceptionally, for a few days (longest four days). Sometimes the illness began with a rigor, and three patients experienced a short period of delirium. Other symptoms present at this stage were headache, backache, aching of the limbs, and colicky abdominal pains. Many complained of nausea but few were troubled by vomiting.

The diarrhoea began gradually in some and explosively in others; but in both cases faeces became fluid, offensive, often bile-stained, and, finally, watery. Several patients observed blood in their stools and inflammatory cellular exudate was observed microscopically in 18 samples (this is almost certainly an underestimate for not all samples were submitted during the acute stages of the disease). Patients did not complain of tenesmus but rather of incontinence, particularly if they changed position in bed. One patient gave a vivid description of an attack of tetany—probably caused by a combination of electrolyte loss and over-breathing—at the end of a night of misery shut in a lavatory that she dared not leave for fear of soiling the house.

This stage of profuse diarrhoea lasted from one to three days, after which the bowel actions became less frequent and the faeces semi-formed. Despite the easing of the diarrhoea, however, many patients continued to feel ill and were troubled for several more days by the persistence of intermittent central or upper abdominal pain. Indeed throughout the illness many patients were more distressed by the pain than the diarrhoea. In some patients the illness followed a biphasic course with one or two days of relative calm in the middle. Recovery was often protracted, especially in adults; children tended to get better more quickly. Many found that a premature return to solid foods precipitated a recurrence of symptoms, and several patients stated that they lost over 6·5 kg. The illness lasted from a few days to three weeks and on average patients were away from work for 10-14 days. The incubation period, as judged by circumstantial evidence, ranged from two to 11 days.

The most severely affected patient, a 33-year-old housewife with profuse watery diarrhoea, underwent an emergency laparotomy for suspected bowel perforation on account of the intensity of her abdominal pain. No perforation was found, but most of her ileum was inflamed and oedematous, there was some free fluid in the peritoneal cavity, and many large fleshy mesenteric lymph nodes were seen. A blood culture was negative but a profuse growth of campylobacters was subsequently obtained from the diarrhoeal fluid.

EPIDEMIOLOGY

A total of 113 contacts of patients with campylobacter enteritis were tested and among them 14 new cases and five symptomless excreters were discovered (table I). In each case organisms were isolated that were indistinguishable both culturally and serologically from those isolated from the index cases. Spread took place mainly between children or from an infected child to its mother; in only three cases did spread occur from an adult to another person.

Animal sources of infection were also found. Three patients—two young farmers and a child—were apparently infected from chickens. In each case the faeces of the birds with which they were in contact contained organisms that were indistinguishable from their own. Similarly three more patients—two butchers' assistants and a housewife—were presumed to have been infected from handling dressed chickens found to be contaminated with campylobacters that matched their own strains.

Dogs with diarrhoea were thought to have been the source of infection in three cases. This assumption was based on bacteriological evidence in two cases, but in the third there was only circumstantial evidence.

Ten patients became ill while travelling abroad or within a few hours of arriving home.

Discussion

The close association between the presence of campylobacters in faeces and the occurrence of a distinctive clinical enteritis alone suggests that these organisms are pathogens. The appearance of specific antibody in the sera of infected patients provides additional evidence of pathogenicity. So also do reports of the isolation of such organisms from the blood of patients with diarrhoea[2 3 6–15]; these few reports probably do not reflect the true incidence of infection, for campylobacters may not immediately be recognised for what they are and they die out easily in the laboratory unless maintained under the right conditions.

The site of the infection seems to be the ileum and jejunum. Certainly the ileum was affected in the patient who had a laparotomy, and there are clinical features of the illness that suggest that the small rather than the large intestine is affected. Cadranel[16] isolated campylobacters from ileal, jejunal, and gastric aspirates from affected children. King[3] quotes the case of a chicken farmer who died from acute enteritis and in whom acute haemorrhagic necrosis of the jejunum and first part of the ileum was observed at necropsy. Similar appearances were described by Evans and Dadswell in a baby girl.[11] Invasion of the bowel has yet to be shown in man, but this has been shown in chickens fed with human isolates.[17]

The concept that chickens might be the primary source of human infection was suggested by King,[3] who drew attention to the fact that organisms of this type are alleged to cause vibrionic hepatitis in poultry.[18] Whether they do or not, these preliminary results suggest that infection might be widespread among poultry flocks in Britain. The risk of contracting the infection from contaminated dressed poultry is probably small provided raw and cooked foods are kept separate and hands are washed after handling the raw product. Organisms would be likely to survive only in undercooked meats. Nevertheless, the possibility that food might be a vehicle of infection is suggested by the fact that 10 patients were infected abroad and that some of these infections occurred simultaneously in more than one member of a party.

As yet we have no proof that the strains obtained from dogs originated in birds, but dogs could easily pick up infection by eating poultry products. A dog with diarrhoea was thought to

have been the source of infection in a case reported by Wheeler and Borchers.[7]

In conclusion, it seems that campylobacters (*C jejuni* and *C coli*) are an important addition to the growing list of known enteric pathogens. Indeed, if the samples received in this laboratory are typical of those in the rest of the country they are the commonest identifiable cause of infectious diarrhoea. Moreover, the fact that these organisms are highly sensitive in vitro to the aminoglycoside and macrolide antibiotics (less so to the penicillins) means that chemotherapy is likely to be effective. Erythromycin has the advantage of a narrow spectrum of activity, and the stearate is a logical choice on account of its acid-resistance and incomplete absorption, which should provide therapeutic concentrations of the antibiotic in the gut as well as in the blood.

The development of a selective culture medium has now made the isolation of campylobacters from faeces a simple matter requiring only a vacuum jar and an incubator set at about 43°C. Although it may seem burdensome to laboratory staff to add yet another medium to those already in regular use for detecting enteric pathogens, the returns are likely to be great.

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Prognosis of Henoch-Schönlein nephritis in children

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Summary

All the survivors of a series of 88 patients with Henoch-Schönlein nephritis were examined after a follow-up of six and a half to 21 years (mean 9·9). Sixty-one patients had no demonstrable abnormality; six had minor urinary abnormalities; five had hypertension without urinary abnormality or renal dysfunction; four had heavy proteinuria; eight were in chronic renal failure, three of whom were on regular dialysis; and four patients had died within 25 months of onset. Neither corticosteroids nor immunosuppressive drugs alone or in combination appeared to influence the outcome. A clinical presentation with a combination of acute nephritis and a nephrotic syndrome and a high proportion of crescents in renal biopsy specimens was associated with a poor outcome. Neither the clinical presentation nor the renal morphology were, however, precise determinants of outcome. Outcome was not related to age, associated streptococcal infection, or recurrences of the rash. The clinical state two years after presentation was compared with the state six and a half years or more after presentation in 76 patients. The clinical state had changed in 32 patients, in 17 of whom it had deteriorated. It was not possible to identify with any certainty the patients who would deteriorate (or improve). Patients who have had Henoch-Schönlein nephritis should be followed up for at least five years.

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Introduction

The clinical course and outcome in 88 children with Henoch-Schönlein nephritis were reported by Meadow *et al*[1] in 1972. Follow-up information was then available for 62 patients, who had been followed for two or more years. Since that study we have traced all the survivors and reassessed their outcome six and a half to 21 years after presentation. Our purpose was to re-evaluate clinicopathological correlations after this longer follow-up. We have also introduced a new renal histological grading system.

Patients and methods

With the permission of the general practitioner each of the 84 survivors was examined by one of us or, in a few patients who pre-