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Campylobacter bacteraemia in England and Wales, 1981–91

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SUMMARY

Routine surveillance of infection in England and Wales detected 394 cases of campylobacter bacteraemia in 11 years. This represented an average incidence of 1·5 per 1000 intestinal campylobacter infections, with a range of 0·3/1000 in children aged 1–4 years to 5·9/1000 in patients aged 65 years or more. Definitive identification of 257 isolates showed that 89% were *Campylobacter jejuni* or *C. coli*; other species were *C. fetus* (8·6%), *C. lari* (0·8%), *C. upsaliensis* (0·8%), *Helicobacter* (*Campylobacter*) *fennelliae* (0·8%), and *Helicobacter* (*Campylobacter*) *cinaedi* (0·4%). Most (71%) of the *C. jejuni*/*C. coli* bacteraemias were in patients with acute enteritis. Of the patients with *C. fetus* bacteraemia only 27% had diarrhoea; they were older than patients with *C. jejuni* or *C. coli* bacteraemia (54·1 *v.* 45·9 years) and proportionally more of them were male (M:F ratio 2·7:1 *v.* 1·9:1): 41% had endovascular pathology or cellulitis. There was a higher proportion of *C. jejuni* serogroup O 4 (Penner) and O 18 strains among blood than faecal isolates, which suggests that they were unusually serum resistant and/or invasive.

INTRODUCTION

The last major review of campylobacter bacteraemia was published in the USA in 1978 before it was widely known that campylobacter enteritis was a common infection [1]. In that review, reports of bacteraemia due to *Campylobacter fetus* outnumbered those due to *C. jejuni* (*C. fetus* subsp. *jejuni* in the review) by 50 to 10. In England and Wales, routine reporting of campylobacter infection began in the second half of 1977, and as laboratories became experienced in isolating these bacteria, reports of campylobacter bacteraemia began to increase. It soon became apparent that many more *C. jejuni* bacteraemias were being recorded than in the 1978 American report. The purpose of this survey was to define the species of campylobacter causing bacteraemia, the types of patient affected, and the clinical context of infection. We also wanted to find out whether any campylobacter strains are especially associated with bacteraemia.

MATERIALS AND METHODS

Patients

Patients with campylobacter bacteraemia were identified from laboratory reports sent to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) during the period 1981–91 inclusive. These reports formed part of a wider reporting scheme that included all bacteraemias as well as other infections of epidemiological interest. Participants of the scheme included all 52 PHLS regional and area laboratories and 200–300 National Health Service and other clinical laboratories. Bacteraemia reports normally give the patient's name, age, sex, main clinical features, and the name of the organism as identified by the reporting laboratory. In the present series, missing information was sought retrospectively from reporting laboratories. Statistics on intestinal campylobacter infections (faecal isolations) were obtained from the same source, but data on the age and sex of patients were available only for the 3 years 1989–91.

Bacteriology

The identity of campylobacter isolates came from two sources: (1) from the stated identity on report forms, usually '*Campylobacter* sp.' or '*C. jejuni*' (the latter probably included *C. coli*, as the name *C. jejuni* is sometimes used generically); (2) from the definitive identification of cultures obtained from reporting laboratories. This was carried out at the Worcester Royal Infirmary laboratory by conventional methods [2].

Serotyping of *C. jejuni* and *C. coli* isolates was done at the Public Health Laboratory, Manchester. All isolates were grouped according to O antigens of the Penner serogrouping scheme [3], using a panel of 43 antisera. In addition, more recent isolates were typed according to the heat-labile antigens of the Lior scheme [4], using a reduced panel of 12 antisera.

RESULTS

Incidence

During the 11 years of the study, 394 episodes of campylobacter bacteraemia were reported. Reports increased annually, but in proportion to faecal campylobacter isolations, which increased almost threefold over the study period. In the same period, 267565 faecal isolations were reported, giving a bacteraemia incidence of 1·5 per 1000 intestinal infections.

The distribution of bacteraemia reports by age is shown in Fig. 1. The highest number was in patients aged 65 years or more and the second highest in young adults (continuous line). However, by expressing incidence as a proportion of intestinal infections, the distribution became more even, with a more progressive rise from the lowest rate of 0·3/1000 intestinal affections in children aged 1–4 years to 5·9/1000 in patients aged 65 years or more (broken line).

Bacteriology

The *Campylobacter* species making up the 394 isolates are shown in Table 1. The three isolates of *Helicobacter fennelliae* and *H. cinaedi* are included, as they have

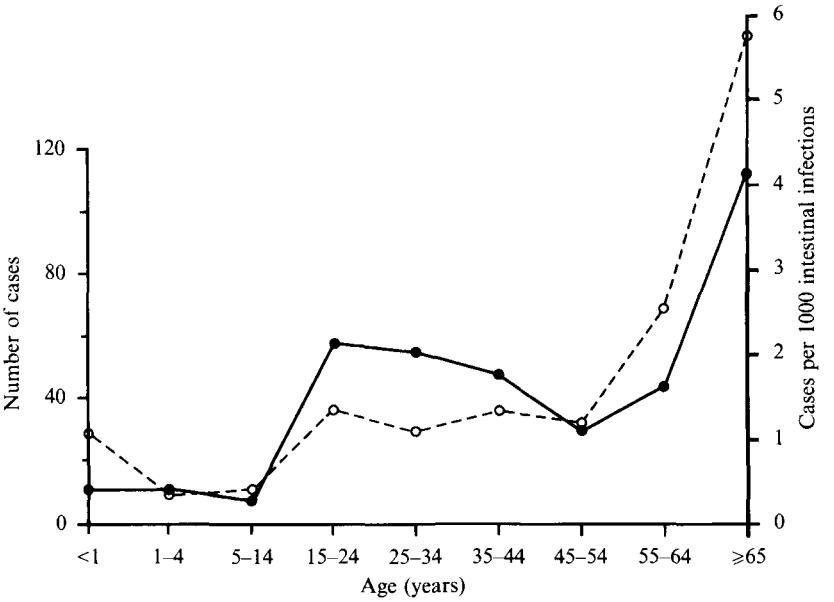

Fig. 1. Distribution of campylobacter bacteraemia cases by age, England and Wales, 1981–91. ●—● number of cases ($n = 374$); ○---○, cases per 1000 intestinal infections.

Table 1. *Campylobacter species isolated from blood in England and Wales 1981–91*

Species	No. isolated
'*Campylobacter* sp.'*	137
'*C. jejuni*'*	91
C. jejuni subsp. *jejuni* biotype 1†	103
C. jejuni subsp. *jejuni* biotype 2†	11
C. coli	23
C. fetus	22
C. lari	2
C. upsaliensis	2
Helicobacter (*Campylobacter*) *fennelliae*‡	2
Helicobacter (*Campylobacter*) *cinaedi*	1
Total	394

* As stated on report forms; cultures not available.

† Biotype of Skirrow and Benjamin [5].

‡ Both isolates atypical in that they were sensitive to rifampicin and resistant to cephalothin; possibly epidemiologically related.

only recently been transferred from *Campylobacter* and are phenotypically similar to campylobacters.

Clinical features

Patients are analysed in two groups according to their infecting organism: (1) *C. jejuni* or *C. coli*; (2) *C. fetus* (Table 2). Differences are apparent in average age, sex ratio, frequency of diarrhoea or other intestinal symptoms, and presence of a significant underlying illness. The underlying illnesses stated in the reports are

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Table 2. *Main features of patients with bacteraemia due to* C. jejuni/C. coli *and* C. fetus

	C. jejuni/C. coli (n = 228)	*C. fetus* (n = 22)
Mean age (range)	45·9 years (4 days–90 years)	54·1 years (27–81 years)
Male/female ratio	1·9:1	2·7:1
No. with diarrhoea or other gastro-intestinal symptom (%)	162 (71)	6 (27)
No. with underlying disease or immuno-deficiency (%)	65 (29)	9 (41)
No. with endovascular pathology and/or cellulitis (%)	1 (0·4)	9* (41)

* Thrombophlebitis 4; aortic aneurysm 1; endocarditis 1; post embolectomy 1; cellulitis 2.

Table 3. *Underlying diseases recorded in patients with campylobacter bacteraemia. England and Wales 1981–91*

Malignant neoplastic disease	30
Renal disease	16
Liver disease	15
Diabetes mellitus	11
HIV/AIDS	11
Inflammatory bowel disease	7
Hypogammaglobulinaemia	4
Miscellaneous	15
Total	109*

* 28% of all cases.

summarized in Table 3. Abdominal pain without mention of diarrhoea was recorded in 19 (8%) of the 228 patients with *C. jejuni* or *C. coli* bacteraemia.

Patients with bacteraemia due to other species had miscellaneous febrile illnesses. Both patients with *C. lari* had underlying diseases; one had diarrhoea. One of the patients with *C. upsaliensis* had a transient viral illness (unspecified) with meningism; the other was a 9-year-old Asian boy with diarrhoea complicating hepatitis A. Both patients with *H. fennelliae* were Asian males: an adult with plain fever, and another boy with hepatitis. *H. cinaedi* was isolated from a 39-year-old man with suspected endocarditis.

There were 10 (2·5%) deaths among the 394 patients. Three were stated to be unrelated to the campylobacter infection. In the remaining seven, the infection probably contributed to the cause of death. Most deaths were due to an underlying disease, such as malignancy or heart disease.

Frequency of serogroups among C. jejuni *and* C. coli *isolates*

Fig. 2 compares the distribution of serogroups among blood and faecal isolates of *C. jejuni* and *C. coli*. *C. jejuni* strains possessing antigens of the 4.13.16.50 complex (serogroup O 4) were more frequent among blood than faecal isolates (RR 1·49; 95% CI 1·13–1·97). Fourteen (74%) of the 19 serogroup O 4 strains that were grouped according to the Lior scheme possessed Lior antigen 1; Lior antigens

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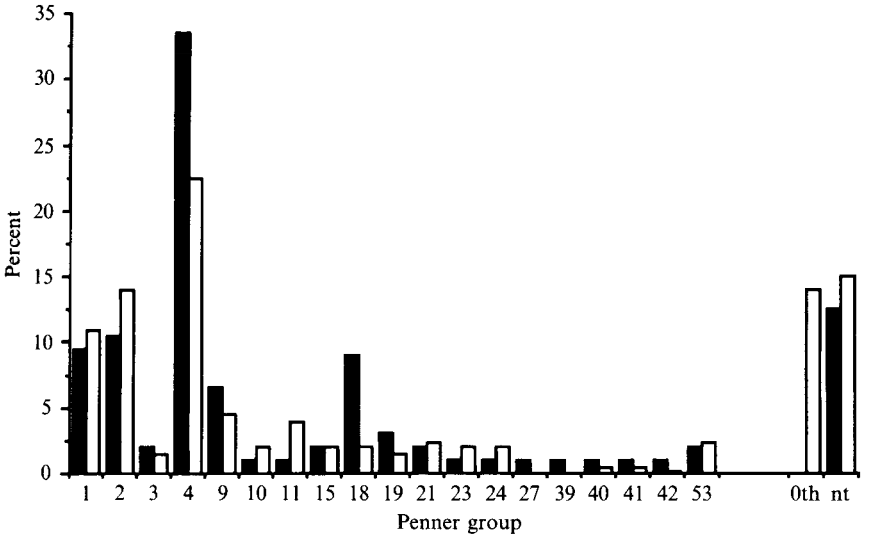

Fig. 2. Distribution of O (Penner) serogroups among blood and faecal isolates of *C. jejuni* and *C. coli*. ■, Blood isolates ($n = 105$); □, faecal isolates ($n = 3472$); oth, other serogroups; nt, not typable.

2 and 7 were represented among the remaining five isolates. Similarly, strains of serogroup O 18 were more frequent among blood than faecal isolates (RR 4·19; 95% CI 2·15–8·16).

DISCUSSION

This survey confirms that campylobacter bacteraemia is uncommon; only about 50 cases a year are reported in England and Wales (population 46 M). Salmonella bacteraemia is ten times as frequent [6]. *C. jejuni* and *C. coli* accounted for 89% of identified isolates, and the fact that 71% of these bacteraemias were in patients that had diarrhoea or other gastrointestinal symptoms indicates that most arise during an attack of campylobacter enteritis. The frequency of diarrhoea was probably under-reported, as the CDSC bacteraemia report forms do not ask specifically about the presence or absence of diarrhoea, but simply leave a space for free text on main clinical features. That *C. jejuni* or *C. coli* strains were isolated from the faeces as well as the blood of 40% of patients is further evidence of their intestinal origin.

This preponderance of *C. jejuni* and *C. coli* is in striking contrast to the 91 cases of campylobacter bacteraemia listed by Guerrant and colleagues in 1978, in which *C. jejuni* isolates were outnumbered by *C. fetus* isolates by five to one. It is likely that the difference is artefactual, reflecting improved laboratory performance in isolating *C. jejuni* and *C. coli* from blood after 1978. Later reports from South Africa [7] Australia [8], and the USA [9] are more in line with our findings. In the first two reports all 30 cases of bacteraemia were due to *C. jejuni* or *C. coli*, and in the American report 60% of the 172 cases were due to these species.

The absence of *C. jejuni* subsp. *doylei* and low frequency of *C. upsaliensis* in the present study reflects the scarcity of these organisms as a cause of diarrhoea in the UK. This contrasts with reports from other parts of the world. *C. jejuni* subsp.

doylei caused 13 of 25 campylobacter bacteraemias in aboriginal children in Australia [10] and *C. upsaliensis* caused 23 of 49 campylobacter bacteraemias in black children in South Africa [11].

The peak incidence of bacteraemia in patients aged 65 years or more (one in every 170 intestinal infections) was predictable (Fig. 1), but the low incidence in children aged 1–14 years (one in every 3000 intestinal infections) was not. although children of this age are generally less ill with campylobacter enteritis than are adults. A similar pattern has been reported in the USA [12]. This relatively low incidence of bacteraemia in children does not seem to be a feature of salmonellosis [13].

There were almost twice as many male as female patients with *C. jejuni/C. coli* bacteraemia, but only a slight excess in intestinal infection (1·16:1). This difference requires explanation. No such excess was reported in the American survey [12].

The 22 *C. fetus* bacteraemias represent most of the *C. fetus* isolations reported during the 11-year period of the study, which emphasizes the scarcity of this organism as a human pathogen. More of these patients were reported to have some underlying disease or immunodeficiency than patients with *C. jejuni/C. coli* bacteraemia (41 *v.* 26%), but both figures are lower than in previous reports, e.g. 75 *v.* 29% [14]. Again, unstructured reporting almost certainly failed to identify some of these patients. An excess of male patients in the *C. fetus* group (2·7:1) has been observed before; so has the association of *C. fetus* infection with vascular pathology and cellulitis [15, 16], which were recorded in 9 (41%) of the 22 reports in the present study. The fact that a high proportion of the few *C. fetus* infections are bacteraemic can be explained by the high degree of serum resistance shown by *C. fetus* strains relative to *C. jejuni* or *C. coli* strains. This is due to the possession of a 100000 MW protein capsule (S-layer), which is absent in *C. jejuni* or *C. coli* [17].

Although *C. jejuni* and *C. coli* are generally serum sensitive and unlikely to cause more than transient bacteraemia in immunocompetent hosts, we wanted to find out whether there were exceptions, such as there are among salmonella strains (e.g. *Salmonella dublin*). The distribution of *C. coli* and *C. jejuni* biotypes followed that of faecal isolates, but strains of *C. jejuni* serogroup O 4, particularly serotype O 4:Lior 1, were more frequent among blood than faecal isolates (Fig. 2). Likewise, O 18 strains, though less common, were also more frequent among blood than faecal isolates. It is possible that these strains are more than usually serum resistant, but whether this is due to the character of their LPS or to an associated factor is not known [18]. Many more strains causing bacteraemia need to be typed.

The main conclusion from this study is that campylobacter bacteraemia is usually a transient complication of campylobacter enteritis due to *C. jejuni* or *C. coli* in otherwise healthy people. Its incidence is low, but rises sharply in patients over 65 years of age. Certain strains of *C. jejuni* have an enhanced ability to cause bacteraemia.

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