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Clostridium difficile in general practice and community health

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SUMMARY

The isolation rate for *Clostridium difficile* in diarrhoeal stools was investigated in patients from general practice and community health centres over a 14-month period. *C. difficile* or its cytotoxin was detected in specimens from 89 (4·7 %) of 1882 patients studied and accounted for 30·3 % of all enteropathogenic micro-organisms isolated. Overall *C. difficile* was second only to *Giandia lamblia* in frequency. Recovery rates in the different groups of patients surveyed varied from 3·6 to 27·5 %. The relationship between stool culture results and stool cytotoxin assay also varied considerably between groups of patients studied. Coincident infections with a variety of enteropathogenic bacteria and intestinal parasites were diagnosed in 14 of the 89 patients. It was concluded that laboratories servicing this type of practice should be aware that *C. difficile* may be a cause of diarrhoea. An adequate clinical history should facilitate proper processing of the specimen.

INTRODUCTION

The role of *Clostridium difficile* in antibiotic-associated diarrhoea and pseudomembranous colitis is well established (Bartlett *et al.* 1978; Larson *et al.* 1978). Both these conditions have been related to the use of antimicrobial agents (Bartlett *et al.* 1979), however this is not always the case (Wald, Mendelow & Bartlett, 1980; Howard, Sullivan & Troster, 1980) and the significance of *C. difficile* in other forms of diarrhoea is still being debated (Falsen *et al.* 1980; Bolton, Sheriff & Read, 1980; Brettle *et al.* 1982).

Previous studies on the frequency of isolation of *C. difficile* in relation to diarrhoeal disease have shown isolation rates of 11·9 % in the United States (Gilligan, McCarthy & Genta, 1981), 3 % in Sweden (Falsen *et al.* 1980), 12·3 % in Great Britain (Brettle *et al.* 1982) and 14·5 % in Australia (Riley, Bowman & Carroll, 1983). These studies have tended to concentrate on specimens obtained from patients attending large teaching hospitals and may have given the impression that *C. difficile*-associated diarrhoea was only a problem within large hospitals. The aim of our investigation was to determine the isolation rate for *C. difficile* in patients with diarrhoea presenting to their general practitioner or community

health centre and not necessarily requiring hospitalization, or patients in small rural hospitals under the care of their general practitioners.

MATERIAL AND METHODS

Patients and specimens

All patients were seen by their general practitioners or at community health centres in either rural centres throughout Western Australia, an area of one million square miles, or the metropolitan area of the capital city, Perth, between May 1983 and July 1984. Stool samples were submitted to the Public Health and Enteric Diseases Unit of the State Health Laboratory Services, in sterile plastic containers, having been transported in a refrigerated state. Specimens were usually cultured within 24 h of collection. However, due to the isolation of some rural centres (up to 1500 miles away) some longer delays were unavoidable. In the majority of cases specimens were accompanied with a request for 'routine' microbiological investigation. Unfortunately, in most instances a minimal amount of clinical information was provided, precluding the use of criteria which we had previously found satisfactory for the study of hospital patients (Riley, Bowman & Carroll, 1983; Bowman & Riley, 1984). Therefore, stool samples were cultured if they met only one of those criteria, that being that the stools were loose or watery. On the basis of information on the request form patients were divided into the following four groups: (1) those patients in whom a specific request for culture for *C. difficile* was made; (2) those patients who were known to have a history of antibiotic therapy; (3) those patients known to be in-patients at small rural hospitals; and (4) those patients remaining.

Because of the difficulty in interpreting the isolation of *C. difficile* in the very young, children under the age of 1 year were excluded from the study.

Demonstration of C. difficile *and other enteric pathogens*

The methods employed for the isolation of *C. difficile* and other enteric pathogens and for the demonstration of *C. difficile* cytotoxin have been described previously (Riley, Bowman & Carroll, 1983). They include the use of a selective broth for *C. difficile* containing gentamicin 5 mg/l, cycloserine 250 mg/l and cefoxitin 8 mg/l (GCC broth) (Carroll, Bowman & Riley, 1983). Final identification of *C. difficile* was made according to the criteria of Holdeman, Cato & Moore (1977). Enteric pathogens other than *C. difficile* were identified by means of appropriate microscopic, biochemical and serological techniques.

RESULTS

During the period of the study, stool samples from 14877 patients were received by the Public Health and Enteric Diseases Unit of the State Health Laboratory Service. Of these, specimens from 1882 patients (12·6%) were examined for *C. difficile*. From the 1882 patients, recognized enteric pathogens were recovered in 444 (23·4%). Two hundred and ninety-four patients (15·6%) yielded enteropathogenic bacteria; intestinal parasites were found in 217 (11·5%). Table 1 shows the incidence and types of enteric pathogens found in the study population. *C. difficile*

Table 1. *Incidence of enteric pathogens in 1882 patients from either general practice or community health centres*

Organism	No. positive	(%)
Giardia lamblia	131	(7·0)
Clostridium difficile	89	(4·7)
Shigella spp.	60	(3·2)
Campylobacter jejuni	60	(3·2)
Salmonella spp.	54	(2·9)
Hymenolepis nana	47	(2·5)
Aeromonas hydrophila	30	(1·6)
Ancylostoma duodenale	20	(1·1)
Strongyloides stercoralis	14	(0·7)
Enterobius vermicularis	3	(0·2)
Vibrio spp.	1	(< 0·1)
Entamoeba histolytica	1	(< 0·1)
Trichuris trichiura	1	(< 0·1)

Table 2. *Results of stool cultures for* C. difficile *and stool cytotoxin assays*

Patient group	No. of patients studied	Stool culture no. positive (%)	Cytotoxin assay no. positive (%)
(1) Requests for *C. difficile*	40	11 (27·5)	9 (22·5)
(2) History of antibiotic therapy	88	14 (15·9)	10 (11·4)
(3) Small hospital in-patient	446	16 (3·6)	6 (1·3)
(4) Loose or watery stools	1308	48 (3·7)	11 (0·8)
Total	1882	89 (4·7)	36 (1·9)

or its cytotoxin was found in 89 patients, and accounted for 30·3% of all enteropathogenic bacteria isolated.

Recovery rates for *C. difficile* in the different groups of patients surveyed are summarized in Table 2. There was no difference in isolation rate between in-patients in small rural hospitals and the remaining patients with loose or watery stools. However, there were significant differences between these two groups of patients and those with either a history of antibiotic therapy or a request for *C. difficile* culture.

An interesting trend is apparent in the relationship between stool culture results and stool cytotoxin assay. Only 23% of the 48 patients in group 4 had demonstrable cytotoxin in their stools, compared to 37% of the 16 in group 3, 71% of the 14 in group 2 and 82% of the 11 in group 1.

Of the 89 patients from whom *C. difficile* was isolated 14 had coincident infections with other enteric pathogens. There were 11 coincident infections in group 4 patients. These comprised seven different infecting agents; *Campylobacter jejuni* (5), *Salmonella* sp. (1), *Shigella* sp. (1), *Aeromonas hydrophila* (1), *Giardia lamblia* (1), *Ancylostoma duodenale* (1) and *Strongyloides stercoralis* (1). There were three coincident infections in those patients from small rural hospitals comprising

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A. hydrophila (1), *G. lamblia* (1) and *A. duodenale* (1). There were no coincident infections recorded in either of the other two groups of patients.

DISCUSSION

We have previously reported the isolation rate for *C. difficile* from patients with diarrhoeal disease to be 14·5 % (Riley, Bowman & Carroll, 1983). Since these results were derived from a study of patients attending a large general hospital we decided to conduct a further survey of patients from general practice and community health. The present study has demonstrated that the isolation of *C. difficile* from diarrhoeal stools does not occur only in large hospitals. *C. difficile* was the most common microbial isolate in association with diarrhoeal stools in 1882 patients from general practice and community health centres. The isolation rate was 4·7 % and *C. difficile* was second only to *G. lamblia* in frequency of detection.

While the overall isolation of 4·7 % was considerably lower than our previous report (14·5 %), it is of interest to compare isolation rates from the different groups of patients studied. The isolation rates of 3·6 and 3·7 % in groups 3 and 4 respectively were only slightly higher than the figure of 3 % quoted as the carriage rate in normal population studies (George, Sutter & Finegold, 1978). However, in a previous study we found a much lower isolation rate of 0·8 % in patients with an appropriate history, which suggested that the carriage rate of *C. difficile* may have been less than 3 % (Bowman & Riley, 1984). The isolation rates from patients in groups 1 and 2 of 27·5 and 15·9 % respectively are more in keeping with our previous findings (Riley, Bowman & Carroll, 1983; Bowman & Riley, 1984). Prior exposure to antibiotic agents (group 2) is the major predisposing factor for *C. difficile*-associated diarrhoea, and it may be assumed that specific requests to look for *C. difficile* probably originated when diarrhoea occurred after antibiotics. It is difficult to gauge antibiotic usage in general practice, however some inappropriate use of antibiotics must occur. In particular, clindamycin is apparently commonly used for the treatment of infections with *Staphylococcus aureus*. This is one of the main antibiotics incriminated in *C. difficile*-associated diarrhoea (Bartlett *et al.* 1979).

The relationship between stool culture results and stool cytotoxin assay for the different groups of patients was interesting. Bartlett *et al.* (1979) have reported a relationship between the concentration of *C. difficile* cytotoxin and the number of organisms present in the stool specimen. Although the clinical histories obtained in many cases were less than ideal, the apparent trend in this study indicates a relationship between the presence of cytotoxin and severity of disease. However, there appears to be no relationship between cytotoxin titre and severity of disease (Burdon *et al.* 1981).

Falsen *et al.* (1980) studied *C. difficile* in relation to other enteric bacterial pathogens and found shigella, campylobacter and yersinia in 36 % of their 56 patients from whom *C. difficile* was isolated, while Gilligan, McCarthy & Genta (1981) found no co-infections in 161 patients studied. We found other enteric pathogens in 16 % of our 89 patients. To our knowledge this is the first report of *C. difficile* being isolated from patients in whom various intestinal parasites had been detected such as *G. lamblia*, *A. duodenale* and *S. stercoralis*. In addition *C. difficile* was isolated coincidentally with *A. hydrophila*, a significant cause of

gastrointestinal disease in local studies (Gracey *et al.* 1982). These findings are in keeping with the suggestion made by Falsen *et al.* (1980) that any change in normal bacterial faecal flora due to other enteric infections increases the possibility of isolating *C. difficile.*

The most difficult aspect of this investigation involved trying to obtain an adequate clinical history from the requesting physician. In a previous study, carried out in hospital environment, to determine whether routine culturing for *C. difficile* was warranted, compliance of clinical staff enabled several criteria to be defined (Bowman & Riley, 1984). Unfortunately when dealing with general practitioners and community health workers up to 1500 miles away, obtaining an adequate history was sometimes impossible, precluding the use of our previously tested criteria.

In conclusion, this study has demonstrated that the isolation of *C. difficile* and detection of its cytotoxin is common in general and rural practice. Accordingly, microbiology laboratories servicing this type of practice should be aware of this fact and be able to provide the relevant diagnostic procedures.

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