Leading articles

Clostridium difficile and inflammatory bowel disease

Ever since discovery of the 'difficult' clostridium in patients with pseudomembranous colitis (Bartlett et al., 1978; George et al., 1978) the pathogenic role of this organism has been questioned (Editorial, 1980). Undoubtedly, the organism, or rather its enterotoxin, is implicated in antibiotic-associated Clostridium difficile colitis, since elimination of the measurable cytotoxin by vancomycin (Keighley et al., 1978; Pashby, Bolton & Sherriff, 1980) or metronidazole has been associated with rapid clinical and sigmoidoscopic improvement. The role of Cl. difficile in antibiotic-associated diarrhoea is more enigmatic, since toxin is not always present (Lishman, Al Jumaili & Record, 1981) and diarrhoea is a common complication of antibiotics in the absence of Cl. difficile. Is the emergence of Cl. difficile merely the result in an altered colonic microflora? Or, is the organism normally present in the gastrointestinal tract, but unrecognisable on the agar plate, even with selective media, because of the other bacteria that constitute the normal faecal flora?

With this background of scepticism regarding the role of Cl. difficile in the pathogenesis of diarrhoea, reports have emerged suggesting that the organism might be implicated as a cause of relapse in inflammatory bowel disease. Six cases of relapse associated with Cl. difficile were reported from Boston (La Mont & Trnka, 1980) and cytotoxin was identified in five cases. The underlying disease was ulcerative colitis in five and Crohn’s disease in the sixth. Four of the patients rapidly improved with vancomycin therapy. Disappearance of the organism was associated with clinical remission. However, we are told that three of these patients were receiving antibiotics during their relapse. The medical gastrointestinal unit in Bristol reported results of screening 56 patients with diarrhoea for Cl. difficile toxin (Bolton, Sherriff & Read, 1980). Nine patients were found to have Cl. difficile toxin and five had underlying inflammatory bowel disease in relapse (four ulcerative colitis and one with Crohn’s disease). Two of the cases were receiving salazopyrine. Improvement in symptoms coincided with elimination of toxin. We have also investigated the incidence of Cl. difficile in our own gastrointestinal unit (Keighley, Young & Johnson, 1982) from 69 consecutive patients during relapse of established inflammatory bowel disease. Cl. difficile, but not cytotoxin, was identified in ten patients. Only three patients had Cl. difficile toxin: all had Crohn’s disease and had had a recent operation during which they had received systemic antibiotics. Of the ten patients with Cl. difficile alone, six had Crohn’s disease and four ulcerative colitis. Seven of these patients had recently received antibiotics or were on maintenance salazopyrine therapy. We concluded that isolation of Cl. difficile alone was of doubtful pathological significance since it disappeared spontaneously without therapy. In a separate study, 35 patients with Crohn’s disease in relapse were screened before entry to a trial of antimicrobial therapy, and none had Cl. difficile or toxin.

So much for the evidence. How should these findings be interpreted? Many patients with inflammatory bowel disease receive maintenance therapy with salazopyrine, a drug which we know has an appreciable influence of faecal flora (Krock, 1980). Emergence of Cl. difficile is quite frequent among patients receiving antimicrobials. Even a single intravenous dose of a variety of cephalosporins in 36 subjects was associated with detection of Cl. difficile in nine, two of whom had evidence of toxin (Ambrose et al., 1982). In each case, emergence of Cl. difficile was accompanied by marked changes in faecal flora. We are fully aware that the faecal flora of patients with Crohn’s disease is abnormal (Keighley et al., 1978) and such a disturbance in the ecology of the large bowel either predisposes to colonisation by Cl. difficile or facilitates the detection of the organism. Where the faecal flora has not become established, Cl. difficile may be detected in 40% of neonates (George, Sutter
It is likely, therefore, that either exposure to antimicrobial agents or the changes in the intestinal flora consequent to disease is responsible for the occasional appearance of *Clostridium difficile* in such patients. However, we should not forget that these subjects, like anyone else, can develop *Clostridium difficile* antibiotic-associated colitis, particularly if they are given broad-spectrum antimicrobials, as, for instance during a surgical operation or for severe systemic infection.

To treat or not to treat? If *Clostridium difficile* is detected in a patient attending outpatients with a mild relapse of inflammatory bowel disease, treatment may not be necessary, since the organism in our experience spontaneously disappears in most subjects. If the patient is in hospital, treatment is probably indicated, particularly if toxin is present, because of the risk of cross infection in the hospital environment. If the patient has clinical or endoscopic evidence of antibiotic-associated colitis, particularly if confirmed by biopsy, treatment to eliminate *Clostridium difficile* toxin is definitely advised. I suspect that in ten years' time *Clostridium difficile* will be recognised as a member of the normal intestinal flora which microbiologists find easier to identify in patients with inflammatory bowel disease and that it has nothing to do with relapse of their underlying disease, but I may be wrong. Surgeons sometimes make mistakes.

M. R. B. KEIGHLEY
Consultant Surgeon/Reader in Surgery,
Gastrointestinal Unit,
The General Hospital,
Birmingham B4 6NH, England

References


Chemotherapy of hydatid disease

Hydatid disease is relatively uncommon in the U.K. but can be associated with considerable morbidity (Morris, 1981). Almost all cases seen in this country are likely to be due to *Echinococcus granulosus*, which is a common parasite of dogs and sheep (as primary and secondary hosts respectively). In man 70% of primary cysts are hepatic, followed by lung (15%), but cysts of kidney, spleen, bone, brain, heart and virtually every anatomical site have been described. The more aggressive form *Ech. multilocularis* is unlikely to be seen in the indigenous population of the U.K., but central Europe and Alaska are affected by this variant. The surgical removal of hydatid cysts sometimes entails relatively major surgery, and post operative problems such as subphrenic abscess and biliary fistula are not uncommon (Pissiotis, Wander & Condon, 1972). Surgery for hydatid cyst must involve removal of the inner two layers, that is, the germinal and laminated membranes, but the ectocyst formed from compressed host tissue is normally left in situ. The simplest method