increases production of toxins A and B, which is thought to increase the severity of disease.

McDonald *et al.* retrospectively typed and examined 187 *C. difficile* isolates from eight health-care facilities in six US states. All had experienced outbreaks of *C. difficile*-related disease between 2000 and 2003. A database of more than 6,000 isolates collected from 1984–1990 was used for comparison. BI/NAP1 isolates accounted for 51% of all current isolates (those from 2000–2003). All current—but no historical—BI/NAP1 isolates were resistant to gatifloxacin and moxifloxacin. By contrast, only 42% of current non-B1/NAP1 isolates were resistant to these antibiotics ($P<0.001$).

In 12 Canadian hospitals within one province, Loo *et al.* prospectively evaluated the incidence and complications of *C. difficile*-associated diarrhea (CDAD), and conducted a case–control study to identify CDAD risk factors. CDAD was identified in 22.5 per 1,000 patients, with 6.9% of patients dying within 30 days from causes attributable to CDAD. Patients with CDAD were more likely than control patients treated in the same hospitals to have used fluoroquinolones (an antibiotic class that includes gatifloxacin and moxifloxacin) or cephalosporins. The BI/NAP1 strain was present in 84.1% of isolates; again, this strain was predominantly resistant to fluoroquinones.

CDAD is commonly treated with the antibiotic metronidazole, although not always successfully. Modena *et al*. have reported results from their single-center, prospective US study investigating the risk factors involved in failure of metronidazole therapy for treatment of post-antibiotic CDAD, among 27 patients who had received 14 days of metronidazole. CDAD resolved in all 10 patients who stopped using the CDAD-precipitating antibiotic during metronidazole treatment, but in only 10 of 17 patients who continued their original antibiotic treatment ($P=0.02$). The authors suggest that metronidazole treatment is most likely to succeed when other antibiotics are withdrawn, although they acknowledge that this is not always possible. Exploration of alternative treatment options is, therefore, warranted.

These studies highlight the importance of careful selection of antibiotics for the treatment of *C. difficile*-related disease, and illustrate the potential for new microbial strains to appear within short periods. New measures to prevent the spread of the BI/NAP1 strain, and to discourage the development of new strains, are sorely needed.

Rebecca Doherty

Original articles Loo VG *et al.* (2005) A predominantly clonal multi-institutional outbreak of *Clostridium difficile*-associated diarrhea with high morbidity and mortality. *N Engl J Med* **353:** 2442–2449
McDonald LC *et al.* (2005) An epidemic, toxin gene-variant strain of *Clostridium difficile*. *N Engl J Med* **353:** 2433–2441
Modena S *et al.* (2006) Continuation of antibiotics is associated with failure of metronidazole for *Clostridium difficile*-associated diarrhea. *Clin Gastroenterol* **40:** 49–54

New molecular links with hereditary colorectal cancer?

Early studies describing the cancer now known as hereditary nonpolyposis colorectal cancer suggested that this cancer type is genetically transmitted and could be molecularly defined. Further work showed, however, that a subgroup of patients who met the AMSTERDAM CRITERIA had neither the instability in their MICROSATELLITE SEQUENCES nor the germline mutations in particular DNA-repair genes to lead to that suggestion. To better define this subgroup, Mueller-Koch and co-workers compared the clinical features of patients whose tumors did or did not have DNA-repair gene mutations and high levels of microsatellite instability.

Of the 41 families studied, 25 (106 patients) had truncating mutations in DNA-repair genes ('positive'), and 16 (71 patients) had no mutations in these genes and no identified instability, but fulfilled the Amsterdam criteria ('negative'). The median age of cancer onset was earlier in positive families for both all tumors and colorectal tumors. The positive group had a higher incidence of extracolorectal tumors and a greater proportion of colorectal tumors that were near the splenic flexure. Adenomas were less common than carcinomas in the positive group, suggesting that progression to malignant tumors is faster in these patients.

These findings have implications for surveillance programs generally and for the frequency of monitoring. Cancer research should focus on defining the germline mutations that are associated with the development of this cancer type in the negative subset of patients.

Kate Matthews

Original article Mueller-Koch Y *et al.* (2005) Hereditary nonpolyposis colorectal cancer: clinical and molecular evidence for a new entity of hereditary colorectal cancer. *Gut* **54:** 1733–1740

GLOSSARY

AMSTERDAM CRITERIA
The criteria developed by the International Collaborative Group in Amsterdam in 1990, to define hereditary nonpolyposis colorectal cancer

MICROSATELLITE SEQUENCES
Short repetitive DNA sequences, usually of 1–4 nucleotides, which can be used as markers for genetic linkage studies