The bacterium *Clostridium difficile* was initially named because it was difficult to culture in the laboratory. Today, the name is thought just as appropriate because of the increasing difficulties in treating this potentially life-threatening infection.

Over the past decade the incidence of *C. difficile* has increased dramatically and it is now a major threat to public health. Of particular concern is the frequent implication of hypervirulent strains, which cause more severe and relapsing illness, increasing the likelihood of life-threatening complications. In addition relapse rates are currently twice those of 20 to 30 years ago, indicating current treatments are becoming less successful.

Initial treatment of *C. difficile* should be with metronidazole or vancomycin, following discontinuation of potentially causative antibiotics whenever possible. This practice has not changed for 30 years and highlights the continuing limited treatment options available and the little progress that is being made in finding alternatives.

**Increasing resistance**

An increasing resistance of *C. difficile* to metronidazole is resulting in one in five patients suffering treatment failure and nearly one in three a relapse. As metronidazole resistance becomes more common oral vancomycin will increasingly be the first-line treatment. In severe disease, oral vancomycin remains the first-line choice since intravenous administration is not an option because effective concentrations cannot be reached in the colon. But there is a diminishing effect of vancomycin owing to escalating resistance. For patients whose treatment has failed surgery is increasingly required, and post-operative mortality is high. Vancomycin-resistant *C. difficile* will be a major challenge in the future unless alternative treatments are developed.

An ideal alternative would be one that is more effective than current options and restores the normal flora in order to limit relapses while not being associated with resistance. So what alternative treatment options do we currently have?

Alternative antibiotic treatments that have been suggested include teicoplanin, ramoplanin, fidaxomicin and nitazoxanide. However, all have limitations to their use, the most notable of these being that they are not more efficacious than metronidazole or vancomycin, and there remains the likelihood of resistance developing. Furthermore, these alternatives do not restore the normal flora and so the natural resistance to colonisation is impaired, potentially leading to recurrent infection.

Other alternative treatments have been based on non-antimicrobial mechanisms of action. These fall into two main groups: those that bind *C. difficile*’s toxins (such as tovelamer), and those that restore the normal commensal flora (such as probiotics). Unfortunately the efficacy of tovelamer is inferior to that of metronidazole and vancomycin, and a recent Cochrane review found insufficient evidence to recommend probiotics.

A further option could be to prevent infection. Again probiotics have been suggested for this but a Cochrane review is still awaited. Vaccination has also been proposed due to asymptomatic carriers having high levels of IgG antibodies to toxin A. But effective vaccinations are unlikely to be available in the near future owing to that fact that *C. difficile*’s complex outer S-layer has only recently been discovered.

Decreases in the number of *C. difficile* cases have been reported in the past year. This should not be seen as evidence of this highly evolving killer’s demise, since the *C. difficile* genome is an array of genes enabling resistance to many antibiotics. Assuming it is no longer a major threat to public health and not urgently addressing the shortage of new treatments could leave us poorly equipped to deal with its re-emergence.

The mandatory reporting system for all individuals aged two years or over infected with *C. difficile* is not well equipped to deal with its re-emergence.

**Extended patents**

The vast cost of developing new treatments means that for a mostly acute condition such as *C. difficile* infection it is unlikely that pharmaceutical companies will be able to make a profit on their investment. It is now the time for treatments developed specifically for diseases that are a major threat to public health to be given extended patents to encourage this so desperately needed research? With current *C. difficile* treatment options threatening to become more and more ineffective over the forthcoming years the need for new treatments is greater now than ever.