Mysteries of a hospital infection – How to fight the superbug *Clostridium difficile*?

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Hospitals are not only inhabited by pleasant organisms such as doctors and nurses, but also by vicious creatures seeking to make you ill. The best known of these bugs is perhaps MRSA, the methicillin-resistant *Staphylococcus aureus*, but there is one bacterium that puts its colleague's well-deserved reputation to shame. The name of this superbug is *Clostridium difficile,* which is the major underlying cause of antibiotic-associated diarrhoea and responsible for more than ten times as many deaths as MRSA.

The vehicle for transmission of *C. difficile* infections is the spore, a metabolically inactive particle manufactured by the process of sporulation. Essentially, the spore is the hibernating state of the bacterium, which due to its characteristic structure protects it against a wealth of cleaning products widely used in hospitals while also carrying all the necessary information to rebuild a functional bacterial cell.

Even the vigorous use of alcohol hand gels will not prevent the spread of *C. difficile* spores in hospitals. So, if you come in contact with spores, will the consequences be severe? The answer to this is yes and no. Yes, you might be carrying around a superbug and risk to infect yourself and others, but ingestion of the spores will not necessarily lead to development of disease. Certain patients, especially the elderly that have been treated with antibiotics are at increased risk of developing disease. The applied antibiotic might disrupt the natural bacterial defence line in the gut, allowing spores of *C. difficile* to return to cell growth in a process called germination. Growing cells produce toxins that act on the cells lining the gut causing diarrhoea that in its most severe form can be fatal.

The recent emergence of more infectious strains of *C. difficile* demonstrates the need to conduct research into this organism. Researchers are especially interested in the question of how *C. difficile* spores sense optimal conditions for bacterial growth and how this then starts the germination process. Unfortunately, most of the processes involved in germination are still a mystery. You might ask: if *C. difficile* causes that many deaths, why do we know so little about this crucial pathway? As it name implies, research into *Clostridium difficile* is *difficult*. Special methods need to be applied to gain insights into its functionality, further complicating the search for potent countermeasures.

However, the development of suitable genetic tools at the University of Nottingham allows for exciting new research into *C. difficile*'s functions. The question is, how will this have an impact on the hospital environment?

Discovery of germination mechanisms could eventually lead to the development of novel disinfectants or novel drugs. A potential disinfectant could be applied to contaminated surfaces to force residing spores to return to cell growth. Cells of *C. difficile* are sensitive to alcohol and industrial cleaning products and could be cleared off easily.

A potential drug on the other hand could stop spores developing into growing, toxin-producing cells once ingested by the patient. This could prevent progression into more severe disease and lower the risk for spread of infection, subsequently lowering the incidence of *C. difficile* infection in the healthcare environment. Eventually, the development of novel countermeasures could equip us with potent ammunition to fight the superbug *C. difficile.*