Editorial Commentary

Clostridium difficile: (Re)emergence of Zoonotic Potential

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(See the article by Gould and Limbago, on pages 577–582.)

Transmission routes of pathogenic bacteria can be very complex and can include direct transmission from human to human, contact with environment, contact with animals, aerosol transmission, vectors, and food and water intake. Clostridium difficile was historically regarded as a typically nosocomial pathogen, and hospitalization was one of the main risk factors for development of C. difficile infection. Within this environment, hand contamination with spores was the most important transmission mode.

If hospital environment is the main reservoir for C. difficile, one would expect a very limited number of genotypes to prevail in a single hospital for a prolonged time. However, in nonoutbreak situations with good hospital hygiene, the number of genotypes found in a single hospital is rather high. A low number of genotypes (1 or 2) is constantly present, but many others are changing during time. This indicates that external sources play an important role in overall epidemiology and are constantly imported to the hospitals from the community. Outside hospitals, C. difficile can be found in symptomatic and asymptomatic humans as well as soil, water, food, and animals.

The article by Gould and Limbago [1] reviews the recent findings on C. difficile in animals and food and discusses all major issues associated with this topic. These issues include (1) the overlap of types present in humans and animals, (2) qualitative and quantitative aspects of C. difficile in food, and (3) what type of data we still need to confirm the zoonotic and food transmission of C. difficile.

It is clear by now that C. difficile is often present in symptomatic as well as asymptomatic animals; therefore, its role as a major animal intestinal pathogen is somewhat disputed [2, 3]. Also, and in contrast to the situation in humans, results of commercial toxin tests in animal fecal samples often poorly correlate with culture results. Are different animals, such as poultry, more adapted to C. difficile than the others and serve only as multiplying hosts? This is possible, because a single pig farm is usually associated with 1 or 2 polymerase chain reaction (PCR) ribotypes, whereas we found 12 PCR ribotypes on a single poultry farm [4].

The overlap between human, animal, and food strains is another issue, and Gould and Limbago [1] first discuss difficulties regarding the comparability of typing techniques. Indeed, poor comparability of the results obtained with different typing methods (eg, pulsed field gel electrophoresis vs PCR ribotyping) and even poor comparability of the results of a single method among various studies (PCR ribotyping) significantly affect our understanding of C. difficile ecology. Even if we keep in mind the possible misinterpretation of the results and low comparability between studies, the evidence is growing that overlap between animal and human reservoirs was modest in the past but has increased in the past few years. Interestingly, in the past genotypes producing binary toxin in addition to toxin A and B were more often isolated from animals (30%–100% of all isolates, depending on species), whereas they were rare in humans (usually up to 10%).

Currently, almost 300 PCR ribotypes are known in humans, but only ~30 PCR ribotypes have been detected in animals. As studies on different animals continue, the number of strains and, therefore, the number of animal-associated genotypes will increase, and we will learn that the overlap of C. difficile types between humans and animals is much larger than currently thought. Much attention has been devoted recently to PCR ribotype 078, and there is some speculation that this is a new emerging type associated with increased virulence for humans and an example of transmission of C. difficile from animals to humans. Indeed, genotype 078 used to be the most prevalent type isolated in many animals (calves, pigs, and horses) in several countries (Canada, United States, and the Netherlands), whereas it was extremely rare in human isolates. However,
it is important to understand that, as in humans, the prevailing genotype in animals differs from country to country. For instance, our data from Slovenia demonstrate that PCR ribotype 078 is absent in different farm animals, but some other closely related (066) and unrelated PCR ribotypes (029, SI011) are present.

With regard to food being one of the possible vectors between animals and humans (or vice versa), many questions still remain. As discussed by Gould and Limbago [1], a limited number of studies can be summarized in 2 observations. First, isolation of *C. difficile* from food requires enrichment steps, indicating that bacterial numbers are low. Second, the percentage of positive samples varies greatly from country to country. Whereas 6%–50% of samples are reported to be positive in North America, data for European countries indicate that the rate of positive samples is <3%. The most obvious possible reason for this disparity is the difference in slaughter techniques between North America and Europe, but the extent to which slaughtering contributes to food contamination is unclear. A single study on *C. difficile* in animals prior to slaughter (in Austria) found *C. difficile* in feces of cows (4.5%), pigs (3.3%), and broilers (5%) [5].

It is possible that *C. difficile* was always (and still is) normally present in the gut microbiota of young animals and young humans. From this primary reservoir, it can be distributed via contact, shedding, or food consumption. Since the introduction of antibiotics with broad-spectrum and anti-anaerobe activity (eg, clindamycin), *C. difficile* has established itself in hospitals. However, it has also remained present in other reservoirs, which are perhaps less studied, and at subdetectable levels. Although published data are missing, one could speculate that with changed selective pressure, such as changed antibiotic policies in animal production, the presence of *C. difficile* in animals has increased in such way that the overlap between humans and animals is now much more likely. Therefore, it seems that we have a unique opportunity to witness the evolution of the (re)emergence of certain reservoirs of *Clostridium difficile*.

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**References**