Correspondence

Importance of Culture for Detection of Clostridium difficile Toxin from Stool Samples to Report True Incidence and Mortality Related to C. difficile in Hospitals

To the Editor—In their excellent article, Gravel et al [1] reexamined the incidence of health care–associated Clostridium difficile infection (CDI) in Canadian hospitals. They found an overall incidence of 65 cases per 100,000 patient-days, which was similar to the findings of their previous study [2]. The mortality rate associated with CDI, however, increased almost 4-fold. Their clinical criteria were well stated and have been endorsed in the accompanying Editorial Commentary [3]. Unfortunately, the same clarity and uniformity was not explicit for the laboratory diagnosis, and there may be a bias in their evaluation. More information was provided in the previous study [2], which reported that 11 of 19 participating sites used cytotoxin B neutralization assay on cell culture. Enzyme immunoassays (EIA) for toxin A or toxins A and B were used at 9 sites. Culture of C. difficile was performed in addition to toxin assay at 2 sites. The toxin assay results were positive for 264 patients, and 4 additional patients had a culture positive for toxin-producing C. difficile. These latter 4 cases may represent an additional 14% of cases for the 2 hospitals that used this method, considering that 264 cases have been found at 19 sites, which results in a mean of 14 cases per site [2].

Culture has been reported to detect an additional 15% of cases of CDI [3]. Culture has also been reported to detect additional cases of CDI missed by direct cytotoxinity neutralization assay (DCNA), in a comparison between culture and a 2-step algorithm method. In this approach, tests for enzyme glutamate dehydrogenase (GDH), a specific antigen of C. difficile, are performed in a first step, and DCNA is performed in a second step [4]. The 2-step algorithm and broth culture of stool samples (instead of culture on agar plates) have been evaluated in our hospital. Detection of GDH was performed in a first step, and if positive results were obtained, the DCNA was performed. All stool samples with positive GDH results were also inoculated in chopped meat broth and tested, after incubation, with the cytotoxin neutralization assay for detection of C. difficile toxin. An additional 12% of cases of CDI were obtained with this method, compared with DCNA [5]. This broth method is easier to perform and results are obtained more quickly than with bacterial colonies.

EIA tests for toxins A and B are only 70%–80% as sensitive as the cell cytotoxicity assay [6]. Because of the low sensitivity of immunoassays, toxigenic culture is recommended to optimize the diagnosis of CDI if EIAs are used [7–9].

Gravel et al [1] have identified their eligible patients by reviewing the results of toxin assays for the detection of C. difficile in stool samples. Without the use of culture, they probably underestimated the true incidence of CDI. To arrive at a valid estimate of CDI incidence, an additional 12%–15% of cases should probably be added. The national surveillance allows an interhospital collaboration. It is a good opportunity for the authors to highlight the importance of culture of toxin-producing C. difficile in the participating hospitals. This will allow a better standardization of their surveillance methodology. This approach may also facilitate better prevention and control of CDI.

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References

Reply to Bayardelle

The Canadian Nosocomial Infection Surveillance Program (CNISP) is a collaborative effort of the Canadian Hospital Epidemiology Committee (CHEC), a subcommittee of the Association of Medical Microbiologists and Infectious Disease–Canada and the Public Health Agency of Canada. CHEC members participate in CNISP by working on subcommittees that direct the development, implementation, and analysis of surveillance projects. CHEC members and their corresponding health care institution(s) participate voluntarily in CNISP projects by collecting standardized, case-by-case, nonnominal data on hospitalized patients at risk of health care–associated infections. Although data collection is conducted by experienced and trained infection control professionals who use standardized definitions, the data collection remains unmonitored. Because the diagnosis of a health care–associated infection, including *Clostridium difficile* infection (CDI), is frequently made on the basis of laboratory findings, we recognize that there may be some variability in the microbiological laboratory testing between the CNISP hospitals.

The testing methods in our hospitals during this surveillance period have been described elsewhere [1]. Six different laboratory methods were used to detect *C. difficile* toxin in patient’s stool. Sixteen hospitals (48%) used only enzyme immunoassays (EIAs) that detected toxins A and B. The remaining 17 hospitals (52%) used 1 or more other tests, including cytotoxin testing using tissue culture (12 hospitals; 36%), EIA detecting only toxin A (6; 18%), or Triage (Biosite Diagnostics) panel for toxin A and glutamate dehydrogenase (3; 9%). No hospital performed cultures for *C. difficile* or used latex agglutination.

Appropriate management of CDI, including infection control management, requires timely access to sensitive diagnostic testing. Fewer than one-half of the responding hospitals had access to same-day testing, and in 2 instances, only twice weekly testing was available. Some of the hospital-to-hospital variation in CDI rates in Canada may be attributable to differences in the sensitivity of diagnostic assays used in these hospitals. We also recognize that culture testing has a better sensitivity than either EIA or tissue culture cytotoxin assay [2]. However, culturing is both slower and more costly than toxin assays. EIA testing method may have an added infection control advantage because of the rapid testing results, especially in outbreak management.

Members of the CNISP have collaborated successfully on a number of other surveillance projects, including surveillance for methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and hemodialysis-associated blood stream infections, to name only a few. The success of our program relies solely on the collaborative nature of our members. As such, we do not impose stringent requirements for participation and do not ask hospitals to change their microbiology laboratory protocols. Despite the limitations, the data obtained from our surveillance projects provide an important contribution to understanding the impact of CDI in patients admitted to Canadian hospitals. We believe the results are sufficiently robust to be used as baseline indicators for future comparisons.

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References


Consequences of Early Treatment for Individuals at Risk of Human Immunodeficiency Virus Infection

Crum-Cianflone et al [1] provide convincing evidence that there has been a steady decrease in CD4+ cell counts among individuals with human immunodeficiency virus (HIV) who recently underwent seroconversion and some evidence that this decrease may now be slowing down. They argue that the most likely explanation is that the virus has evolved over time. They mention a number of factors that may have led to increased viral virulence and suggest that this may have been countered more recently by the availability of treatment. Recently, a suggestion has been made that transmission of HIV infection could be greatly reduced and that the epidemic eventually eliminated by testing once a year, on average, all those at risk of HIV infection and by starting them on treatment immediately [2]. This could substantially change the selection pressure on the virus, and it will be important to consider this in relation to the use of treatment as prevention.

As the set-point viral load increases, there is an increase in rate of transmission of HIV infection [3], CD4+ cell count loss [1], and mortality [4]. In epidemics of sexually transmitted HIV infection, the number of cases of HIV infection resulting from a particular case of HIV infection...