Control of an Outbreak of Infection with the Hypervirulent *Clostridium difficile* BI Strain in a University Hospital Using a Comprehensive “Bundle” Approach

Carlene A. Muto,1,7 Mary Kathleen Blank,1 Jane W. Marsh,1 Emanuel N. Vergis,2 Mary M. O’Leary,1 Kathleen A. Shutt,7 Anthony W. Pasculle,1 Marian Pokrywka,1 Juliet G. Garcia,1 Kathy Posey,1 Terri L. Roberts,1 Brian A. Potoski,2,6,9 Gary E. Blank,4 Richard L. Simmons,5 Peter Veldkamp,2 Lee H. Harrison,7,8 and David L. Paterson2,6

Divisions of 1Hospital Epidemiology and Infection Control, 2Infectious Diseases, Department of Medicine, 3Microbiology and 4Pathology, Department of Pathology, and 5Department of Surgery, and 6Antibiotic Management Program, University of Pittsburgh Medical Center, Presbyterian Campus, University of Pittsburgh School of Medicine, 7Infectious Diseases Epidemiology Research Unit and 8Department of Epidemiology, University of Pittsburgh, Graduate School of Public Health, and 9Department of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania

(See the editorial commentary by McDonald on pages 1274–6)

**Background.** In June 2000, the hospital-acquired *Clostridium difficile* (CD) infection rate in our hospital (University of Pittsburgh Medical Center–Presbyterian, Pittsburgh, PA) increased to 10.4 infections per 1000 hospital discharges (HDs); the annual rate increased from 2.7 infections per 1000 HDs to 7.2 infections per 1000 HDs and was accompanied by an increase in the frequency of severe outcomes. Forty-seven (51%) of 92 HA CD isolates in 2001 were identified as the “epidemic BI strain.” A comprehensive CD infection control “bundle” was implemented to control the outbreak of CD infection.

**Methods.** The CD infection control bundle consisted of education, increased and early case finding, expanded infection-control measures, development of a CD infection management team, and antimicrobial management. Process measures, antimicrobial usage, and hospital-acquired CD infection rates were analyzed, and CD isolates were typed.

**Results.** The rates of compliance with hand hygiene and isolation were 75% and 68%, respectively. The CD management team evaluated a mean of 31 patients per month (11% were evaluated for moderate or severe disease). Use of antimicrobial therapy associated with increased CD infection risk decreased by 41% during the period 2003–2005 ($P$ < .001). The aggregate rate of CD infection during the period 2001–2006 decreased to 4.8 infections per 1000 HDs (odds ratio, 2.2; 95% confidence interval, 1.4–3.1; $P$ < .001) and by 2006, was 3.0 infections per 1000 HDs, a rate reduction of 71% (odds ratio, 3.5; 95% confidence interval, 2.3–5.4; $P$ < .001). During the period 2000–2001, the proportion of severe CD cases peaked at 9.4% (37 of 393 CD infections were severe); the rate decreased to 3.1% in 2002 and further decreased to 1.0% in 2006—a 78% overall reduction (odds ratio, 20.3; 95% confidence interval, 2.8–148.2; $P$ < .001). In 2005, 13% of CD isolates were type BI (20% were hospital acquired), which represented a significant reduction from 2001 ($P$ < .001).

**Conclusions.** The outbreak of CD infection with the BI strain in our hospital was controlled after implementing a CD infection control “bundle.” Early identification, coupled with appropriate control measures, reduces the rate of CD infection and the frequency of adverse events.

*Clostridium difficile* (CD)–associated disease (AD) remains the most common cause of hospital-acquired (HA) diarrhea and is responsible for >300,000 cases per year [1–3]. An increased number of cases of CDAD has been observed in North America in the past 5 years, [4–8] with rates reported in excess of 20 cases per 1000 hospital admissions [6]. Historically, severe disease (e.g., toxic megacolon, perforation, colectomy, and death) was reported to occur in ~3% of patients [9, 10]. CD has reemerged as a life-threatening pathogen,
and increased frequency of severe outcomes has been reported worldwide [5, 6, 11, 12]. Recent data suggest that a hypervirulent CD strain overproduces toxins A and B in vitro [13]. This strain has been typed as BI by restriction enzyme analysis (REA), as North American PFGE type 1 (NAP1), and as PCR ribotype 027 [8]. Since 1996, HA CD infection rates at our facility (University of Pittsburgh Medical Center–Presbyterian, Pittsburgh, PA) have ranged from 2.7 infections per 1000 hospital discharges (HDs) to 3.5 infections per 1000 HDs. In June 2000, the HA CD infection rate at our hospital increased to 10.4 infections per 1000 HDs, marking the beginning of the CD infection outbreak in our hospital; this outbreak was ultimately associated with a disproportionate increase in severe cases during the period 2000–2001, with a total of 26 colectomies and 18 deaths being attributable to CD infection (the rate of severe CDAD increased from 0.15 cases per 1000 HDs [5.6%] in 1999 to 0.60 cases per 1000 HDs [9.4%] in 2000–2001; \( P = .004 \)) [7]. REA typing identified 2 highly related clusters representing 51% of HA CD isolates. Subsequent testing classified the clusters as the BI strain, which was later reported in 6 other health care facilities [8]. Another study performed at our institution assessed the presence of binary toxin in 49 randomly selected CD isolates from the period 2001–2002 [14]. Binary toxin genes were identified in the majority of isolates regardless of outcome. More recently, we conducted a retrospective, matched case-control study that assessed risk factors for CDAD [7] and that molecularly subtyped (by REA) 135 consecutive isolates to determine if an outbreak had occurred. This same group of isolates served as the baseline for the present study.

Barrier precautions for CD infection control have been recommended by the Centers for Disease Control and Prevention (CDC) [15, 16]. In addition, various infection-control measures, including environmental cleaning, use of single-use rectal thermometers, endoscope disinfection, and limited use of select antibiotics, have been described in other guidelines [17–19]. Environmental cleaning with sodium hypochlorite (bleach) solutions decreases CD surface contamination [20] and has been associated with a significant reduction in the number of cases of CDAD [21]. Since 2000, an outbreak investigation has guided the sequential introduction of control measures and the development of a comprehensive CD infection control “bundle.” This article reports the successful control of a CD infection outbreak and a significant reduction in the rate of infection and proportion of the CD BI outbreak strain.

**METHODS**

The University of Pittsburgh Medical Center–Presbyterian is an 834-bed tertiary care teaching facility. Before the period when the epidemic occurred, there was no obvious change in patient population, infection-control policies, or diagnostic testing for CD infection. Alcohol sanitizer for hand hygiene was introduced in July 2000, 7 months after the CD infection outbreak began.

**HA CD Infection Rates**

HA CD infection rates were calculated monthly and annually (during the period 1996–2005) and were reported as the number of HA CD infections per 1000 HDs, unless otherwise stated. HA CD infections in patients who developed the infection \( \geq 72 \) h after hospital admission were classified using CDC National Nosocomial Infections Surveillance System criteria [22].

**Severe HA CDAD Rates**

Severe CDAD was defined by the presence of CD infection (positive results of a stool toxin assay or pseudomembranes visualized endoscopically), with resulting colectomy and/or death attributable to CD infection. All potential cases were reviewed by a trained team of health care professionals (4 physicians, 1 pharmacist, and 1 infection-control professional). Agreement of the majority of team members, including \( \geq 2 \) physicians, that outcomes were attributable to CD infection was necessary for the classification of severe CDAD. The severe HA CDAD rate was defined in 2 ways: as a percentage of all HA CD infections and as the number of cases of severe HA CDAD per 1000 HDs. The rates were calculated for the period 1999–2005.

**CD Infection Control Bundle: Interventions and Timeline**

Our CD infection control bundle consisted of education, increased and early case finding methodologies, expanded infection-control measures, development of a CD management team, and targeted antimicrobial management (figure 1).

**Education.** A standardized CD education module and printable materials for providers and patients were developed in July 2000 and made available electronically. The module was presented at a variety of quality, leadership, nursing liaison, and interdepartmental meetings. It included information on epidemiology, risk factors, clinical findings associated with severe disease, the epidemic strain, control measures, and HA CD infection rates.

**Increased and early case finding methodologies and rapid initiation of appropriate therapy.** In July 2000, primary care nurses were granted authority to order testing for CD infection, and methods were developed to identify patients at high risk of CD infection using electronic markers to encourage prompt testing and contact precautions. A CD infection email alert was sent from the Medical Director to the attending physician requesting CD infection testing consideration. High-risk patients were defined as follows: (1) patients with a length of hospital stay \( \geq 7 \) days and a WBC count >10,000 cells/μL or <2000 cells/
Figure 1. Hospital-acquired *Clostridium difficile* (HA CD) infection rates and intervention timeline. Monthly HA CD infection rates are reported for the period January 1999–January 2007 on the primary X and Y axes, and yearly HA CD infection rates (for the period 1999–2006) are shown on the secondary X and Y axes. The intervention timeline is shown, with each different period represented by an arrow. Specific interventions corresponding to the dates are explained in Methods.

μL or with >10% bands, (2) patients readmitted to the hospital within 14 days after hospital discharge with a WBC count >10,000 cells/μL, and (3) patients with previous CDAD. The monthly alert volume was monitored, and a 3-month subset analysis was performed to assess CD infection testing and CD positivity rates.

A CD management team, comprised of infectious diseases clinicians, was established in May 2001. All CD toxin–positive patients were reported and evaluated in near real time. The goal was to assess the severity of illness using a standardized clinical assessment process and to prescribe appropriate therapy. All patients meeting clinical criteria for potentially severe disease were surgically evaluated. Intravenous immunoglobulin therapy was considered when colectomy was imminent.

**Expanded infection-control measures.** Expanded infection-control measures included environmental cleaning, electronic flags and alerts, hand hygiene with soap and water, prolonged duration of isolation, and infection-control audits.

In July 2000, contact isolation requirements were expanded from the duration of illness [16] to the duration of hospitalization, unless approved by infection control. Informatics tools were developed to facilitate CD isolation. In November 2001, the registration system was used to electronically flag CD-positive patients during index hospitalization and to block placement of patients who were not CD coded to the same room. Monitoring of isolation compliance began in July 2001. Daily enhanced environmental bleach (concentration, 1:100) cleaning of CD-positive patients' rooms (high-touch flat surfaces for a contact time of 10 min) was initiated in May 2001; in July 2003, the concentration increased 10-fold.

In May 2003, hand hygiene with soap and water (not alcohol sanitizers) was recommended for care of CD-positive patients. Concurrently, a CD real-time notification alert was generated from the Laboratory Information System. The program uses incident CD testing results to prompt notification to the current point of patient care via email, fax, printer, and text pager, thus, eliminating isolation implementation delay. Alerts included patient name, location history, isolation requirement (contact precautions) instruction, and an electronic link to the CD education site.

**Infection-control audits.** Compliance with isolation and hand hygiene was monitored. Rooms where patients with CD infection stayed were audited for 1 month for proper signage and product availability (e.g., soap, gowns, and gloves). Thirty monthly hand hygiene opportunities per patient care area were audited from November 2002 thereafter. During hand hygiene audits, compliance with isolation was also monitored. Generally, 28% of the average daily census required contact precautions (11% because of CD contamination). Infection-control audits were initially conducted by unit-based observers (i.e., nurses or aides who received no special infection control or audit training). In April 2004, unit-based observers were replaced by dedicated independent observers (i.e., nursing students trained by infection-control professionals).

**Targeted antimicrobial restriction.** Clindamycin, ceftriaxone, and levofloxacin were associated with increased CD infection risk in our case-control analysis of CD infection [7]. A formal antimicrobial management program, which required prior approval by infectious diseases physicians and pharmacists for these and other broad-spectrum antimicrobials, was
HF CD infection and severe CD-associated disease.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of infections</th>
<th>No. of hospital discharges</th>
<th>Rate, no. of infections per 1000 hospital discharges</th>
<th>No. of patient-days</th>
<th>Rate, no. of infections per 1000 patient-days</th>
<th>No. (%) of cases</th>
<th>Rate, no. of cases per 1000 hospital discharges</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>89</td>
<td>28,453</td>
<td>3.1</td>
<td>192,243</td>
<td>0.46</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1997</td>
<td>97</td>
<td>27,622</td>
<td>3.5</td>
<td>163,329</td>
<td>0.59</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1998</td>
<td>76</td>
<td>28,552</td>
<td>2.7</td>
<td>164,120</td>
<td>0.46</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1999</td>
<td>72</td>
<td>27,029</td>
<td>2.7</td>
<td>157,099</td>
<td>0.46</td>
<td>4 (5.6)</td>
<td>0.15</td>
</tr>
<tr>
<td>2000</td>
<td>214</td>
<td>29,757</td>
<td>7.2</td>
<td>183,540</td>
<td>1.17</td>
<td>18 (8.4)</td>
<td>0.60</td>
</tr>
<tr>
<td>2001</td>
<td>179</td>
<td>31,864</td>
<td>5.6</td>
<td>191,874</td>
<td>0.93</td>
<td>19 (10.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>2002</td>
<td>161</td>
<td>31,930</td>
<td>5.0</td>
<td>198,770</td>
<td>0.81</td>
<td>5 (3.1)</td>
<td>0.16</td>
</tr>
<tr>
<td>2003</td>
<td>164</td>
<td>31,837</td>
<td>5.2</td>
<td>196,824</td>
<td>0.83</td>
<td>5 (3.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>2004</td>
<td>148</td>
<td>32,182</td>
<td>4.6</td>
<td>205,095</td>
<td>0.72</td>
<td>3 (2.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>2005</td>
<td>188</td>
<td>34,067</td>
<td>5.5</td>
<td>211,883</td>
<td>0.89</td>
<td>8 (4.3)</td>
<td>0.23</td>
</tr>
<tr>
<td>2006</td>
<td>102</td>
<td>33,844</td>
<td>3.0</td>
<td>221,107</td>
<td>0.46</td>
<td>1 (1.0)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

NOTE. NA, not available.

phased in beginning in October 2002 and was fully implemented by July 2003.

Antimicrobial use trends. Monthly antimicrobial use was formulated from a pharmacy patient charges dataset. Antimicrobial use was calculated as defined daily doses (DDDs; using the World Health Organization standards [23] from 1999–2005) and expressed as DDDs per 1000 patient-days.

Microbiologic Methods
The presence of CD toxin in a stool specimen was determined using a standard cell culture cytotoxicity assay with MRHF cells (Diagnostic Hybrids) and antitoxin (TechLab). Toxin testing was performed throughout the CD infection outbreak. Culturing for CD began in March 2001 and was accomplished using previously published methods [24]. Historically, only unformed stool specimens were acceptable for testing; however, because it became evident that CD was being identified in patients who did not have diarrhea, both formed and unformed stool samples were accepted.

Molecular Methods
Molecular subtyping was performed for available CD isolates collected from March through December 2001 and from a similar time period in 2005, using a modification of a published method [25]. REA typing was performed for the isolates collected in 2001. REA types were assigned on the basis of visual inspection findings. For REA type classification, the banding pattern had to be indistinguishable from the REA prototype isolate and was confirmed by testing the isolate and the prototype on the same gel.

Isolates collected in 2001 and 2005 were subtyped using multilocus variable number tandem repeat analysis (MLVA), as described elsewhere [26], because MLVA is faster, easier, and more objective for epidemiologic investigation. One hundred twenty-five (93%) of 135 of the isolates collected in 2001 were available for MLVA typing. Clonality of the isolates was defined as a summed tandem repeat difference ≤2. REA was performed on a subset of outbreak isolates collected in 2001 at Hines VA Hospital (Hines, IL), and the isolates underwent further testing at the CDC (Atlanta, GA). MLVA genotypes were extrapolated from known BI REA types isolated in 2001 to identify the BI strain in 2005.

Statistical Methods
HA CD infection and severe CDAD rates were compared using Epi Info, version 3.3 (CDC). The Cox-Stuart test for trend was performed to analyze antimicrobial use during the 12-month baseline period (1999); this result was compared with the annual use after implementation of the antimicrobial management program during the period 2003–2005.

RESULTS

HA CD Infection Rates
The HA CD infection rate peaked in June 2000 to 10.4 infections per 1000 HDs. The overall CD infection rate in 2000 was 7.2 infections per 1000 HDs, which was more than twice the rate in 1999 (2.7 infections per 1000 HDs) (table 1, figure 1). By 2001, the rate decreased to 5.6 infections per 1000 HDs and has since been maintained between 3.0 infections per 1000 HDs and 5.5 infections per 1000 HDs. Overall, the HA CD infection rate decreased significantly from 10.4 infections per 1000 HDs.
to an aggregate rate (for the period 2001–2006) of 4.8 infections per 1000 HDs (0.77 infections per 1000 patient-days; OR, 2.2; 95% CI, 1.4–3.1; P < .001) and, by 2006, was reduced by 71% to 3.0 infections per 1000 HDs (OR, 3.5; 95% CI, 2.3–5.4; P < .001).

During the period 2000–2001, the severe CDAD rate increased to 0.60 cases per 1000 HDs (37 [9.4%] of 393 HA CD infections were severe; P = .004). By 2002, after the implementation of infection-control measures, the severe CDAD rate decreased to 3.1% or 0.16 cases per 1000 HDs and has been maintained within a range of 1.0%–4.3%, with an aggregate rate (for the period 2002–2006) of 2.9%, or 0.13 cases per 1000 HDs. The severe CDAD rate decreased to 3.0 infections per 1000 HDs (OR, 3.5; 95% CI, 2.3–5.4; P < .001).

Interventions and Timeline

**Infection-control alerts.** Since 2001, >3000 alerts of high-risk patients were sent annually. A subset analysis of 728 alerts found that CD testing was prompted for 134 patients (18.4%), and 84 (62.7%) of these 134 patients tested positive for CD.

**Isolation and hand hygiene monitoring.** Of 321 rooms where CD-positive patients stayed, 316 (98.4%) had proper signage, 301 (93.8%) had available gloves, 307 (95.6%) had available gowns, and 321 (100%) had available soap. From November 2002 through December 2005, a total of 42,927 hand hygiene audits were conducted, and from June 2004 through December 2005, there were 3464 isolation interactions. Overall, hand hygiene and barrier compliance rates were 75% and 68%, respectively. Compliance differed significantly by health care worker type, with registered nurses being most compliant when unit-based observer methodology was used but lower when dedicated independent observers were used. Hand hygiene compliance among physicians never exceeded 70% (figure 1, table 2).

**CD management team.** From May 2001 through December 2005, the CD management team evaluated 1859 patients (mean, 31 patients per month). Of these patients, 211 (11%) met the clinical criteria for potentially severe disease using standardized assessment, and intravenous immunoglobulin therapy was prescribed for 45 (21%) of these patients.

**Antimicrobial management program.** Overall fluoroquinolone use (assessed as DDDs per 1000 patient-days) increased by 40% during the period 1998–1999 (figure 2). Levofoxacin was added to the formulary in 1999. That year, the use of levofloxacin was 106.2 DDDs per 1000 patient-days; the use increased by 37%, to 145.5 DDDs per 1000 patient-days, in 2000 (P < .001). The use of all CDAD-associated antimicrobials (i.e., clindamycin, ceftriaxone, and fluoroquinolones) peaked at 212.7 DDDs per 1000 patient-days in 2001. Following initiation of the antimicrobial management program, aggregate use of these agents decreased in 2003 by 54% (P < .001); clindamycin had the greatest reduction (69%), followed by fluoroquinolones (54%; P < .001). Ceftriaxone use also decreased but, by 2005, increased to baseline values—likely as a result of the adoption of Infectious Diseases Society of America guidelines for community-acquired pneumonia. In 2005, moxifloxacin replaced levofloxacin for respiratory infections and ciprofloxacin for gram-negative coverage, resulting in a decrease of levofloxacin use but an overall increase in quinolone use, from 70.1 DDDs per 1000 patient-days in 2004 to 88.4 DDDs per 1000 patient-days in 2005.

**REA.** Of 135 CD isolates analyzed in 2001, 92 were HA CD isolates. Of these 92 HA CD isolates, 47 (51%) were 2 highly related REA types and 5 (5.4%) represented another unrelated clonal population. REA typing performed at Hines VA Hospital identified the predominant clonal population as BI [8]. In addition, testing at the CDC identified the isolates in this population as toxinotype III, binary toxin positive, with a tcdC deletion—all characteristics of the hypervirulent BI strain [8]. The other clonal population was identified as J9.

**MLVA.** In 2001, of the 125 isolates analyzed, 102 MLVA types were identified, including 3 clonal complexes determined by minimum spanning tree analysis, with a summed tandem repeat difference = 2 (figure 3). The largest complex comprised 50 isolates (40%) (figure 3) and was consistent with the REA BI type. Two smaller complexes, consisting of 8 (6%) and 2

### Table 2. Hand hygiene compliance, by health care worker type, 2002–2005.

<table>
<thead>
<tr>
<th>Health care worker type</th>
<th>Compliance, no. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2002</td>
</tr>
<tr>
<td>Physician</td>
<td>269 (65.4)</td>
</tr>
<tr>
<td>Nurse</td>
<td>512 (88.1)</td>
</tr>
<tr>
<td>Nurse’s aid</td>
<td>255 (78.8)</td>
</tr>
<tr>
<td>Housekeeper</td>
<td>80 (70)</td>
</tr>
<tr>
<td>Other</td>
<td>123 (79.7)</td>
</tr>
<tr>
<td>All</td>
<td>1239 (79.3)</td>
</tr>
</tbody>
</table>

**NOTE.** It appears that hand hygiene compliance decreased, but this was likely related to the change in audit methodology that was implemented in 2004.
C. difficile Hypervirulent BI Strain

• CID 2007:45 (15 November) • 1271

Figure 2. Antimicrobial use (defined daily doses [DDDs] per 1000 patient-days) for selected antimicrobial agents (Abx). DDDs per 1000 patient-days are shown for Abx associated with the risk of Clostridium difficile infection during the period 1998–2005. Overall Abx use decreased in 2003, as did use of fluoroquinolones, clindamycin, and ceftriaxone. In 2005, ceftriaxone use increased to baseline, and a quinolone formulary change resulted in decreased levofloxacin use but overall increased quinolone use.

(2%) isolates, corresponded to the J and BK REA groups, respectively (figure 3).

In 2005, of the 74 isolates analyzed, 70 MLVA types were identified. Only 1 clonal complex of 10 isolates (13.5%) that were consistent with the BI strain was identified, which was significantly less than the BI strain incidence in 2001 (50 of 126 isolates; \( P < .001 \)). Three BI MLVA types (65, 97, and 100) from individual patients were detected during both periods (figure 3), demonstrating that the clonal complex determined in 2005 was genetically related to the BI group. In 2001, 36 (72%) of 50 BI isolates were defined as HA, and in 2005, 2 (20%) of 10 BI isolates were HA. REA J and BK types were not detected in 2005.

DISCUSSION

The outbreak of infection with the CD BI strain in our hospital began in 2000. Infection-control measures were initiated, and by 2001, a significant decrease in the HA CD infection rate occurred. A targeted rate of 5.0 infections per 1000 HDs was reached and sustained and was accompanied by a significant reduction in the rate of severe CDAD disease. This may have been because of the documented reduction in the incidence of infection with the BI strain. These data suggest that the CD infection control “bundle” successfully limited the spread of the hypervirulent BI strain in our facility and controlled the outbreak.

Appropriate control measures to curtail outbreaks of CD infection have been debated [27–29]. Alcohol-based hand sanitizers are thought to be ineffective in controlling CD infection transmission, because they have poor activity against CD spores [30]. This would not explain the spread of CD infection in our hospital, because use of alcohol-based hand sanitizers was not implemented at our facility until after the onset of the CD infection outbreak. Some postulate that increased toxin production and hypersporulation [13, 31] facilitate environmental contamination and contribute to outbreaks of infection and that infection-control measures alone can reduce infection incidence [28, 29]. Others have suggested that formulary modification alone may elicit control of CD infection outbreaks [32–34]. None of the CD infection outbreaks in these studies involved BI strains. Control measures for this strain may differ from those previously reported. BI strains are resistant to fluoroquinolones. Increased use of these antimicrobial agents is proposed to have contributed to the current CD infection epidemic. Some investigators speculate that gatifloxacin and moxifloxacin pose a greater risk than levofloxacin or ciprofloxacin [35] and that changing the quinolone formulary may be enough to control outbreaks of CD infection [27].
Figure 3. Minimum spanning tree analysis of multilocus variable number tandem repeat analysis (MLVA) data for 125 Clostridium difficile (CD) isolates in 2001 and 74 CD isolates in 2005. Circles represent unique MLVA types (numeric value). REA types (from the Hines VA Hospital) are designated α-numerically. MLVA types representing 1, 2, 3, or 6 isolates are white, light blue, dark blue, or violet, respectively. Numbers between the circles represent the summed tandem repeat difference between MLVA types. No number being depicted indicates a summed tandem repeat difference of 1. Pink, green, and light blue shading identifies clonal complexes corresponding to the REA BI, J, and BK groups, respectively.

The HA CD infection rate at our hospital significantly decreased in 2001, before the implementation of the antimicrobial management program. In 2005, a formulary switch from levofloxacin to moxifloxacin plus ciprofloxacin resulted in increased overall fluoroquinolone use, yet CD infection rates further decreased in 2006. Therefore, blaming antimicrobial agents alone may be too simplistic; however, reducing the use of antimicrobials agents may contribute to sustained low rates of infection. This study demonstrates that a comprehensive infection control “bundle” was associated with rapid and sustainable CD infection control. Although we are unable to determine the contributory effect of each intervention within the bundle, we believe that this management strategy will effectively control the spread of infection with the epidemic BI strain of CD in affected institutions. In addition, early identification, followed by appropriate therapeutic management, may reduce the frequency of adverse events associated with CDAD.


Acknowledgments

Potential conflicts of interest. C.A.M. is on the Robert Michael's Speakers' Bureau. E.N.V. has received a ViroPharm research grant to study Clostridium difficile infection. B.A.P. is on the speakers’ bureaus of Wyeth, Pfizer, and Merck and has received research support from Pfizer. D.L.P. has received lecture honoraria from Merck, AstraZeneca, and Cubist; has acted as a consultant for Acureon, KeyBay, protez, and Merck; and has received research support from AstraZeneca, Elan, and Pfizer. All other authors: no conflicts.

References