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The infection control audit: The standardized audit as a tool for change
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Of viruses, gloves, and crêpes
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READER SERVICES

Information for authors
Information for readers
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American Journal of Infection Control (AJIC) is the official scientific publication of the Association for Professionals in Infection Control and Epidemiology, Inc (APIC), a multidisciplinary international organization of health care professionals. The mission of AJIC is to improve health care by reducing risks of infection and related adverse outcomes by critical review, selection, and dissemination of new and relevant information in the fields of infection prevention and control and health care epidemiology in all health care settings and the community.
Survey of isolation practices at a tertiary care pediatric hospital

Joseph V. Vayalumkal, BSc, MD,a Laurie Streitenberger, RN, BSc, CIC,a,b Rick Wray, RN, BHS, CIC,a,b Carol Goldman, RN, BScN, CIC,a,b Renee Freeman, RN, BScN, CIC,a,b Steven Drews, PhD,b and Anne Matlow, MD, FRCPCa,b,c,d
Toronto, Ontario, Canada

Background: Although isolation precautions are an important aspect of hospital infection control, current rates of isolation in a pediatric hospital and rates of compliance with established precautions are unknown. We therefore initiated hospital-wide point prevalence studies to determine unit-specific rates of patient isolation and compliance with proper isolation requirements focusing on communication of isolation status and availability of personal protective equipment. In this report, we present data from the first 14 months of the study.

Methods: This was a prospective observational study. Twice monthly, between January 2004 and February 2005, infection control professionals reviewed the types and appropriateness of isolation of all hospitalized patients, except for those on the psychiatry unit.

Results: Seventeen percent of patients in the hospital during the study period were isolated, most frequently for community-acquired infections. Droplet isolation precautions were the most common form of isolation. Overall, only 74.6% of patients were isolated appropriately. The solid organ transplantation, hematology/oncology, and bone marrow transplantation units were those with the highest rates of inappropriate isolation.

Conclusion: At our hospital, community-acquired infections, in particular respiratory infections, were the most common reasons for patient isolation. Monitoring of the appropriateness of isolation precautions offers the opportunity to reduce health care-related transmission of infection and identify specific target areas for improvement. (Am J Infect Control 2007;35:207-11.)

Isolation precautions are an important aspect of hospital infection control programs and are particularly important in pediatric settings given the high admission rates for viral respiratory (VRI) and gastrointestinal (VGI) infections. Factors such as diapering of patients and inability of young patients to adhere to proper respiratory etiquette help facilitate transmission of infectious pathogens. The high prevalence of health care-associated VRI and VGI reported in pediatric institutions underscores the importance of compliance with isolation protocols. Education and periodic evaluation of adherence to precautions are recommended administrative controls to optimize isolation practices in hospitals.1

As the first step of a performance improvement initiative to improve isolation practices, we examined the epidemiology of patient isolation in the hospital and initiated regular evaluation of the appropriateness of isolation practices at our hospital. In this paper, we report our first 14 months of data.

METHODS

Setting

The Hospital for Sick Children is a 300-bed, university-affiliated tertiary care pediatric hospital in Toronto, Canada. All inpatient units in the hospital except for the psychiatry unit were included in this study.

Data collection

The study took place from January 2004 to February 2005 in the form of repeated point prevalence evaluations. Twice monthly, for a total of 28 observations, a certified infection control professional visited a unit to review the types (as per the Hospital Infection Control Practices Advisory Committee [HICPAC] guidelines1) and appropriateness of isolation precautions in place at the time of the visit, focusing on communication of isolation status (signage, computer entry) and availability of personal protective equipment. Times for the audit were based on convenience for the
practitioner and were approximately 2 weeks apart. The practitioner initially reviewed all patient diagnoses and any symptoms that would necessitate isolation (eg, cough, diarrhea). Patients were discussed with the clinical leader/charge nurse of the unit and walk-around rounds on the unit were conducted to review each patient’s isolation status. Appropriate isolation was defined as (1) type of isolation consistent with HICPAC recommendations, (2) isolation duration consistent with the Centers for Disease Control and Prevention (CDC) guidelines, (3) proper isolation sign on door, (4) proper personal protective equipment available outside patient room, and (5) proper documentation of isolation requirements in the computerized patient record system (KIDCOM), excluding the pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU), which do not have access to KIDCOM. Inappropriate isolation was defined as (1) type of isolation not consistent with HICPAC recommendations (eg, droplet instead of airborne precautions), (2) isolation duration not consistent with CDC guidelines (ie, too long or too short), (3) proper isolation sign not on door, (4) proper personal protective equipment not available outside patient room (this depended on type of precautions required, ie, gloves and gowns available for contact isolation), and (5) proper documentation of isolation requirements not entered in the computerized patient record system (KIDCOM). The computerized record alerts other health care workers about the isolation status of the patient in case the patient is transported to another part of the hospital for diagnostic tests, procedures, or treatments.

### Data management

All information was entered and stored in an electronic database (Microsoft Excel; Microsoft Corp, Redmond, WA).

### Statistical analysis

Testing was performed using the $\chi^2$ test on GraphPad Prism 4 for Windows (Hearne Scientific Software, New Zealand).

### RESULTS

Seventeen percent (623/3636) of all patients hospitalized during the study period were isolated, primarily for community-associated rather than health care-associated infection or multidrug-resistant organism.

#### Table 1. Isolation rates stratified by source of infection

<table>
<thead>
<tr>
<th>Unit</th>
<th>Isolation rate (total isolated/total census × 100)</th>
<th>Isolation rate for HAIC (total isolated for HAIC/total isolated × 100)</th>
<th>Isolation rate for CAIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU</td>
<td>21.9% (77/351)</td>
<td>31.2% (24/77)</td>
<td>68.8% (53/77)</td>
</tr>
<tr>
<td>NICU</td>
<td>5.7% (25/436)</td>
<td>80% (20/25)</td>
<td>20% (5/25)</td>
</tr>
<tr>
<td>Cardiology and cardiac surgery</td>
<td>7.9% (21/265)</td>
<td>38.1% (8/21)</td>
<td>61.9% (13/21)</td>
</tr>
<tr>
<td>Surgical wards</td>
<td>6.9% (62/901)</td>
<td>25.8% (16/62)</td>
<td>74.2% (46/62)</td>
</tr>
<tr>
<td>SOT, gastroenterology, and rheumatology</td>
<td>18.8% (55/293)</td>
<td>18.2% (10/55)</td>
<td>81.8% (45/55)</td>
</tr>
<tr>
<td>Neurology</td>
<td>6.7% (8/120)</td>
<td>0 (0/8)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>General pediatrics and respirology</td>
<td>39.2% (320/816)</td>
<td>2.5% (8/320)</td>
<td>97.5% (312/320)</td>
</tr>
<tr>
<td>Hematology/oncology/HSCT</td>
<td>12.1% (55/454)</td>
<td>43.6% (24/55)</td>
<td>56.4% (31/55)</td>
</tr>
<tr>
<td>Total</td>
<td>17.1% (622/3636)</td>
<td>17.7% (110/622)</td>
<td>82.3% (512/622)</td>
</tr>
</tbody>
</table>

HAIC, Hospital-associated infection/colonization; HSCT, hematopoetic stem cell transplant; PICU, pediatric intensive care unit; NICU, neonatal intensive care unit; CAIC, community-associated infection/colonization; SOT, solid organ transplant.

#### Table 2. Distribution of isolation precautions by category

<table>
<thead>
<tr>
<th>Unit</th>
<th>Contact (total No. in contact isolation/total No. isolated) (%)</th>
<th>Droplet/contact (total No. in droplet/contact isolated/total No. isolated) (%)</th>
<th>Airborne (total No. in airborne isolation/total No. isolated) (%)</th>
<th>MDRO (total No. in MDRO isolation/total No. isolated) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU</td>
<td>8/77 (10.4)</td>
<td>48/77 (62.3)</td>
<td>2/77 (2.5)</td>
<td>19/77 (24.7)</td>
</tr>
<tr>
<td>NICU</td>
<td>1/25 (4)</td>
<td>1/25 (4)</td>
<td>0/21 (0)</td>
<td>1/25 (4)</td>
</tr>
<tr>
<td>Cardiology and cardiac surgery</td>
<td>9/21 (42.9)</td>
<td>10/21 (47.6)</td>
<td>0/62 (0)</td>
<td>2/21 (9.5)</td>
</tr>
<tr>
<td>Surgical wards</td>
<td>35/62 (56.5)</td>
<td>22/62 (35.5)</td>
<td>0/62 (0)</td>
<td>5/62 (8.1)</td>
</tr>
<tr>
<td>SOT, gastroenterology, and rheumatology</td>
<td>26/55 (47.3)</td>
<td>21/55 (38.2)</td>
<td>0/55 (0)</td>
<td>8/55 (14.5)</td>
</tr>
<tr>
<td>Neurology</td>
<td>3/8 (37.5)</td>
<td>5/8 (62.5)</td>
<td>0/8 (0)</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td>General pediatrics and respirology</td>
<td>82/320 (25.6)</td>
<td>180/320 (56.3)</td>
<td>35/320 (10.9)</td>
<td>23/320 (7.2)</td>
</tr>
<tr>
<td>Hematology/oncology/HSCT</td>
<td>30/55 (54.5)</td>
<td>25/55 (45.5)</td>
<td>0/55 (0)</td>
<td>5/55 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>194/623 (31.1)</td>
<td>312/623 (50.1)</td>
<td>39/623 (6.3)</td>
<td>77/623 (12.5)</td>
</tr>
</tbody>
</table>

MDRO, Multidrug-resistant organisms; PICU, pediatric intensive care unit; NICU, neonatal intensive care unit; SOT, solid organ transplant; HSCT, hematopoetic stem cell transplant.
higher rates of isolation than the other units combined. The solid organ transplantation ward having a high rate of patients isolated for health care-associated infections/MDRO colonization, in this case, associated infections/MDRO colonization, in this case, was noted, with the solid organ transplantation unit together with the hematology/oncology/human stem cell transplantation ward having the highest percentage of patients under isolation precautions for health care-associated infection/MDRO colonizations. The distribution of isolation requirements is shown in Table 2. Overall, droplet precautions were the most common category of isolation precautions (50.2%), followed by contact precautions (31.2%). Isolation for MDROs accounted for 12.3% of patients in isolation.

One hundred sixty-seven of the 623 isolated patients (26.4%) were isolated inappropriately. The majority of those deemed inappropriately isolated lacked either documentation in the computerized medical record or had no or inappropriate signage. Patients were 4 times more likely to be under isolated than over isolated (Table 5). A complete breakdown of the appropriateness of isolation is provided in Table 4. A significant association between inappropriate isolation and clinical unit was noted, with the solid organ transplantation unit together with the hematology/oncology/hematopoietic stem cell transplantation wards having higher rates of isolation than the other units combined ($P < .001$) (Table 4).

**DISCUSSION**

A report from our institution close to 2 decades ago quantified hospital isolation in terms of extent of usage, seasonal variation, isolation category, and type of infection (nosocomial vs community acquired). The authors reported that 15% of the beds were occupied by patients requiring isolation and that the number of patients requiring isolation exceeded the number of isolation rooms on 32% of the days of the year. Twenty years later, the percentage of patients requiring isolation is similar at 17.1%. In another report from our hospital, multibed rooms were more likely to be associated with nosocomial transmission of VGI than single-bed rooms. An increased need for single-bed rooms in hospitals for isolation purposes has previously been identified; we are fortunate that 85% of the beds in our current hospital are in single-bed rooms.

In the current study, droplet precautions and contact precautions were the most common types of isolation precautions used, primarily for VRI and VGI, respectively (data not shown). The high rate of isolation on the general pediatrics ward for community-associated infections/MDRO colonization is consistent with the predominance of precautions for VRI and VGI at our center and at others. Although the NICU had the lowest rate of isolation overall, it had the highest rate of isolation for health care-associated infections/MDRO colonization, with colonizations with MDROs accounting for the majority of isolations. The hematology/oncology/hematopoetic stem cell transplantation ward followed, with a high rate of patients isolated for health care-associated infections/MDRO colonization, in this case, primarily contact isolation for gastrointestinal infection including VGI and *Clostridium difficile* infection. Isolation for MDROs accounted for 12.3% of patients in isolation.

Few studies have reported on actual compliance with isolation precautions. Compliance with infection control procedures for tuberculosis was evaluated in 2 pediatric hospitals, and significant breeches in infection control precautions were noted. In another study, widespread noncompliance in an isolation bay of a surgical intensive care unit was reported. In a study conducted at a children’s hospital in Nebraska, there was significant improvement in a number of infection control practices including adherence to isolation precautions as a result of surveillance rounds combined with ongoing education. In our study, in which the focus of the audit was the appropriateness of communication of isolation status (ie, signage, computer entry) and availability of personal protective equipment (as opposed to compliance with hand hygiene before and

### Table 3. Distribution of inappropriate events by category

<table>
<thead>
<tr>
<th>Criterion for inappropriateness</th>
<th>Number of inappropriate over-isolation events (%)</th>
<th>Number of inappropriate under-isolation events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect sign</td>
<td>12/167 (7.2)</td>
<td>13/167 (7.8)</td>
</tr>
<tr>
<td>No sign</td>
<td>0/167 (0)</td>
<td>32/167 (19.2)</td>
</tr>
<tr>
<td>No KIDCOM change</td>
<td>0/167 (0)</td>
<td>81/167 (48.5)</td>
</tr>
<tr>
<td>Isolated too long</td>
<td>22/167 (13.2)</td>
<td>0/167 (0)</td>
</tr>
<tr>
<td>No observed PPE</td>
<td>0/167 (0)</td>
<td>7/167 (4.1)</td>
</tr>
<tr>
<td>Total</td>
<td>34/167 (20)</td>
<td>133/167 (80)</td>
</tr>
</tbody>
</table>

PPE, Personal protective equipment.

### Table 4. Distribution of inappropriate isolation by clinical unit

<table>
<thead>
<tr>
<th>Clinical unit</th>
<th>Number inappropriately isolated/total number isolated</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU</td>
<td>10/77</td>
<td>13.1</td>
</tr>
<tr>
<td>NICU</td>
<td>0/25</td>
<td>0</td>
</tr>
<tr>
<td>Cardiology and cardiac surgery</td>
<td>1/21</td>
<td>4.8</td>
</tr>
<tr>
<td>Surgical wards</td>
<td>14/62</td>
<td>22.6</td>
</tr>
<tr>
<td>SOT, gastroenterology, and rheumatology</td>
<td>25/55</td>
<td>45.5</td>
</tr>
<tr>
<td>Neurology</td>
<td>2/8</td>
<td>25.0</td>
</tr>
<tr>
<td>General pediatrics and respiriology</td>
<td>96/320</td>
<td>30.0</td>
</tr>
<tr>
<td>Hematology/oncology and HSCT</td>
<td>19/55</td>
<td>34.5</td>
</tr>
</tbody>
</table>

PICU, pediatric intensive care unit; NICU, neonatal intensive care unit; SOT, solid organ transplant; HSCT, hematopoietic stem cell transplant.
after patient contact, or proper use of barriers/personal protective equipment), we found that approximately 25% of patients were inappropriately and usually under isolated, suggesting that here too there is great opportunity for improvement.

Although appropriate patient isolation is considered a standard of care, the numerous reports of health care-acquired infections and transmission of MDROs imply that it is often inadequately performed. There are negative consequences to both over isolation and under isolation. For example, a nationwide hospital survey investigating infection control practices in Thailand demonstrated that staff in a high percentage of hospitals performed unnecessary infection control procedures, including wearing protective gowns in intensive care units and overusing sterile gloves. Such practices consume valuable resources unnecessarily. Furthermore, evidence is emerging that some patients in isolation may receive fewer visits by health care workers, leading to suboptimal care and decreased patient satisfaction.

Donning precautions required for the care of an intensive care unit patient with MDROs has been reported to consume 2 hours of time, which may be considered a deterrent to patient care.

Conversely, under isolation of patients facilitates cross transmission of infection, as well as acquisition of infection by health care personnel. A recent study using pulsed-field gel electrophoresis to type bacteria isolated from clinical infections estimated that at least 37.5% of all nosocomial infections identified in a surgical intensive care unit were due to cross transmission. Reports of staff acquisition of infections such as tuberculosis and pertussis further attests to the importance of appropriate isolation practices.

In this study, we found the 2 main reasons for inappropriate isolation to be wrong or lack of signage and failure to update the computerized medical record (KIDCOM). The wrong signage was usually an airborne isolation sign instead of one for droplet precautions or inappropriate use of an MDRO sign. Thirty-two patients who should have been isolated had no sign outside their room.

The computerized medical record is of particular importance in relaying isolation information at transitions in care (eg, transfer to the operating room). Hand-offs are known to be vulnerable times for patient safety. In a multicenter, pediatric performance improvement collaborative study of patient transfers from the emergency department to an inpatient unit, isolation requirements were relayed only 60% of the time. Use of a checklist increased isolation information transfer to 98%. Although the current study did not assess the modes of information transfer between health care workers, it is generally accepted that built-in redundancies are important features of highly reliable organizations. As such, we feel justified to have included failure-to-enter isolation requirements on our computerized record as inappropriate isolation.

In summary, in this study, we have revisited isolation patterns and practices at our hospital. During the study period, close to one fifth of all patients required isolation, approximating data reported from our institution close to 2 decades ago. Consistent with other reports, the bulk of the burden of communicable disease was due to community-acquired VRI and VGI. Such information may be useful to other institutions planning new or renovating existing pediatric facilities. The study has identified units in our hospital that would benefit from focused interventions to improve isolation practices. Frequent surveillance by infection control professionals with real-time feedback to front-line workers is one way to improve compliance with isolation precautions. The resultant effect should be a decrease in infection transmission and saving of resources.

References

15. Weist K, Pollege K, Schulz I, Ruden H, Gastmeier P. How many nosocomial infections are associated with cross-transmission?


Emergence of resistant Acinetobacter baumannii in critically ill patients within an acute care teaching hospital and a long-term acute care hospital

Claudester Stephens, MT, MPH, CIC, Stephen J. Francis, MD, Virginia Abell, RN, BA, CIC, Joseph R. DiPersio, PhD, Diplomate, ABMM, and Patricia Wells, RN, CIC
Akron, Ohio

Background: Acinetobacter baumannii is a gram-negative, coccobacillus found in water and is a significant nosocomial pathogen in hospitals. This report chronicles the appearance in June 2003 of a multidrug-resistant A baumannii (MDR-AB) strain, its dissemination, and interventions used to control it in an acute care hospital (ACH) and long-term acute care facility (LTAC).

Methods: Molecular typing using pulsed-field gel electrophoresis (PFGE) showed that 88 of 99 strains (89%) gave an identical banding designated as clone A. Eight additional isolates were variants of clone A, and 3 isolates were unrelated.

Results: A baumannii was isolated from 229 patients between January 2003 and December 2004. Of these patients, 151 (66%) were colonized/infected with MDR-AB. Most isolates were resistant to antibiotics except for imipenem and ampicillin/sulbactam. Isolates included 108 (72%) in the respiratory tract, 32 (21%) in wounds, 6 (4%) in blood, and 5 (3%) in urine. Most isolates were found in the LTAC (70 isolates), ICU step-down (27 isolates), and ICU (26 isolates).

Conclusion: This epidemiologic history illustrates (1) epidemic clonal spread, (2) target populations, (3) variable monthly prevalence, and (4) intervention outcomes. With intervention, the number of new isolates in the ACH decreased by dedicating an infection control professional to critical care, daily surveillance, isolation of positive MDR-AB patients, universal gloving, and routinely reporting results. (Am J Infect Control 2007;35:212-5.)

Acinetobacter baumannii (AB) is a nonlactose-fermenting, gram-negative coccobacillus that is widespread in the environment and is increasingly found in medical facilities. AB has been implicated in skin and soft tissue infections, pneumonia, bacteremia, and urinary tract infections. Studies have shown that the increase in nosocomial infections caused by gram-negative multidrug-resistant organisms is related to the escalated use of broad-spectrum antibiotics. AB is an organism that can colonize or cause infection and has the ability to survive for long periods of time in the hospital environment, which increases the risk of horizontal transmission via a health care worker or an environmental source.

This study examined AB isolates from patients within a large, acute care (teaching) hospital (ACH) and a long-term acute care (LTAC) facility contained within the same building complex located in northeast central Ohio. The ACH facility has 4 intensive care units (ICUs) including a surgical/trauma ICU, a surgical cardiovascular ICU, a coronary care unit (CCU), and a medical ICU. The LTAC is an independent 40-bed hospital based within the physical building of the ACH. The LTAC admits critically ill long-term patients from the ACH facility and outlying hospitals.

In May 2003, the microbiology laboratory detected an increase in the number of multidrug-resistant Acinetobacter baumannii (MDR-AB) isolates. The patient with the initial resistant isolate (a sacral wound ulcer) on March 28, 2003, was admitted to the LTAC on January 28, 2006, from the ACH and may have been exposed to several other patients with a relatively more sensitive Acinetobacter baumannii on the LTAC. The first 3 isolates from April to June of 2003 were identified in the LTAC. Initial review of the room transfers of patients with MDR-AB indicates spread to the ACH units via readmissions to the ACH and LTAC. The majority of isolates were from respiratory specimens from patients located in the ACH ICUs and the LTAC. The largest numbers of MDR-AB isolates were seen in June 2003 (n = 15). Initial DNA fingerprinting studies indicated that the majority of resistant isolates belonged to 1 DNA fingerprint pattern. A search of computer...
records indicted that the resistant phenotype first appeared in late March 2003 in the LTAC unit. The organism next appeared in the ACH ICU. Of 229 patients identified as having at least 1 culture positive for AB, 151 had MDR-AB. This report outlines the epidemiologic study that was undertaken, the results of molecular testing, and the interventions taken to reduce transmission and prevalence of MDR-AB.

MATERIALS AND METHODS
Organism identification

Using standard commercial identification systems, 229 AB isolates were identified in the clinical microbiology laboratory between March 2003 and December 2004. Of the 229 isolates, 151 (66%) were MDR-AB.

Susceptibility testing

Initial susceptibility testing was performed by either disk diffusion or broth microdilution using a commercially prepared panel (DADE Microscan, West Sacramento, CA). Isolates were considered to be MDR-AB if they were sensitive to 3 or less antibiotics. A notable characteristic was that all MDR-AB isolates were sensitive to imipenem. The index case isolate was resistant to all antibiotics tested except ampicillin/sulbactam and imipenem. Resistance was noted with penicillins, aminoglycosides, and fluoroquinolones.

Molecular epidemiology

Pulsed-field gel electrophoresis (PFGE) of SpeI digests of bacterial chromosomal DNA was performed in house on 103 AB isolates (99 MDR-AB and 4 non-MDR-AB) using the GenePath system (Bio-Rad Laboratories, Hercules, CA). Analysis of fingerprint patterns was performed by visual inspection. MDR-AB isolates showing identical DNA banding patterns were considered to be clonal. Isolates that differed by 1 to 3 bands were considered possibly related, whereas isolates showing greater than 3 band differences were thought to be unrelated.

Data analysis

Statistical data was collected by review of patient medical charts, discharge summaries, pharmacy records, and microbiology laboratory reports.

RESULTS

Age and sex demographics show a total of 86 men ranging in age from 22 to 85 years and 65 women ranging in age from 34 to 84 years. Sources of isolates were respiratory tract, 108 (72%); wounds, 32 (21%); blood, 6 (4%); and urine, 5 (3%). An epidemiologic review of MDR-AB isolates revealed that 20% of the ventilator-associated pneumonias (VAPs) reported in 2003 and 22% of the VAPs in 2004 were associated with MDR-AB. A low percentage of bloodstream infections (BSIs) and surgical site infections (SSIs) were associated with MDR-AB. The infection rates were 0% for BSIs and 1% for SSIs with MDR-AB in 2003 and 2004.

The index case appeared in March 2003. The number of isolates from the LTAC peaked in May of 2003, and the number of isolates from ACH peaked in June of 2003. The highest monthly occurrence of MDR-AB occurred June 2003 (see Fig 1). The LTAC had the highest rate of MDR-AB, and the ACH had the highest number of isolates. There were 70 (46.4%) isolates on the LTAC, 27 (17.9%) isolates on the medical ICU, and 26 (17.2%) isolates on the surgical/trauma ICU. Of the 28 (18.5%) remaining isolates, none were concentrated on any one particular unit (including the surgical cardiovascular ICU and the CCU). Figure 2 shows the incidence rate of MDR-AB per 1000 patient-days.

Molecular typing of chromosomal DNA digest using PFGE showed that 88 of 99 MDR-AB strains tested (89%) gave an identical banding pattern, which was designated as clone A (see Fig 3). Eight additional isolates were variants of clone A, and 3 isolates were unrelated to clone A. These 3 isolates gave similar susceptibility patterns to the index MDR-AB isolate. The 4 non-MDR-AB isolates tested gave DNA fingerprint patterns distinct from all MDR-AB isolates tested.

DISCUSSION

To control the spread of this organism in the ACH, a 3-fold team approach was initiated. This approach included (1) the Microbiology Department’s rapid preliminary identification and notification to the Infection Control Department, (2) the placement of all new
patients with positive isolates into contact precaution, and (3) the notification of attending physicians of the increased occurrence of MDR-AB.

The original infection control precautions— isolation of patients into private rooms, contact precautions, and STOP signs at the door—failed to control completely the spread of this organism. Additional measures were taken beginning the first week of January 2004. Education of staff was provided on a case-by-case basis.

Timely notification of readmissions and transfers of affected patients were improved so that isolation precautions could be instituted immediately. The infection control staff instituted extended contact precautions. These precautions included universal gloving for the entire nursing unit in which these patients were admitted. Universal gloving is the use of disposable gloves for any patient contact regardless of the patient’s microbiologic status. The Infection Control Department increased the investigation to include room transfers of affected patients and comparisons of the sensitivities of the organisms to assess for horizontal transmission.

The infection control staff at the ACH worked collaboratively with the infection control nurse at the LTAC. Equivalent procedural revisions, as discussed above, were initiated at the LTAC. Several conditions made compliance more difficult for the LTAC: nurse/patient ratio, high-risk observation rooms, and turnover in the infection control position. There are more patients per nurse in the LTAC. The LTAC high-risk observation rooms are multibed. This demanded prioritization between close observation of respiratory status and the need for isolation. The change in the infection control nurse left the LTAC without adequate infection control expertise for several weeks. The newly hired nurse was without infection control experience. These factors created an environment less conducive to full compliance of the newest procedures. As time progressed, LTAC infection control compliance improved, including appropriate use of extended contact precautions and universal gloving.

CONCLUSION

MDR-AB, in agreement with the experience of others, is primarily a respiratory organism, with the majority of the isolates found to be colonizers rather than causing disease. The organism is very resistant to most antibiotics, but we do not believe it to be highly pathogenic. The incidence of new cases was as high as 15 isolates in June of 2003 and as low as 3 isolates in each of the months of March, April, and June of 2004. The LTAC appears to have been an ongoing reservoir for multidrug-resistant organisms.

Continuing surveillance of MDR-AB indicates that this organism has become entrenched in both the ACH and the LTAC facilities. Regardless of our stringent infection control measures, we have been unable to totally eradicate the organism. Surveillance of new admissions from local nursing homes are now showing various diagnostic isolates colonized with MDR-AB, indicating the presence of this organism in other facilities. The number of isolates has remained low in the ACH (1 or 2 per month) since the end of this study.
but the number of isolates in the LTAC continues to remain elevated (2 or 3 per month) with a high of 8 in June 2005 and a low of 0 in July 2005).

The infection control professional dedicated to the critical care units in the ACH maintains daily surveillance of AB occurrence in the LTAC and ACH, evaluates sensitivity patterns for increased resistance, and reviews antibiotic usage. The use of extended contact precautions, continuing education of medical staff in affected units, monitoring for readmissions and transfers of affected patients, and reporting results to the individual nursing units on a routine basis has kept transmission of MDR-AB controlled in the ACH. The Infection Control Department from the ACH continues to monitor for all emerging multi-drug-resistant organisms and works with the infection control professional at the LTAC. Additional actions could include aggressive environmental procedures and practice revisions including respiratory precautions.6,8

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References
Validation of surgical site infection surveillance in orthopedic procedures

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Background: Valid data are essential for a national surveillance system of nosocomial infections. Methods: In 8 hospitals conducting surgical site infection (SSI) surveillance for orthopedic procedures, a validation team performed a blinded retrospective chart review (10 operations with reported infections, 40 without) and interviewed infection control nurses.

Results: In total, 397 patient charts were reviewed. Positive and negative predictive values for routine surveillance were 94% (95% CI: 89%-99%) and 99% (95% CI: 99%-100%), respectively. When these results were applied to the aggregated surveillance data (403 infections, 10,068 noninfections), sensitivity was 75% (95% CI: 56%-93%) and specificity 100% (95% CI: 97%-100%). The following case finding methods were used: ward visits (in 7/8 hospitals), microbiology reports (5/8), ward notifications by link nurses (8/8), and other nursing (7/8) and medical (5/8) staff. The wound culture rate ranged from 9 to 67 per 1000 patient-days. All hospitals carried out postdischarge surveillance on readmission and all but 1 at follow-up visits and by an additional questionnaire.

Conclusion: Most SSIs reported by the hospitals were true infections, showing that, when an SSI was reported, the definitions were correctly implemented. Some SSIs were missed, which might be due to weaknesses in case finding. Variation in diagnostic practices may also affect SSI rates. (Am J Infect Control 2007;35:216-21.)

Since the Study on the Efficacy of Nosocomial Infection Control (SENIC) showed that hospitals with intensive infection surveillance and control activities were effective in reducing their nosocomial infection rates, surveillance has been an essential part of well-designed infection control programs. Efficacy of surveillance with feedback to practising surgeons in preventing surgical site infections (SSIs) has also been demonstrated in several other studies. To facilitate the prevention of SSI, national or regional surveillance networks for nosocomial infections have been widely introduced in the United States and Europe.

There are demands for interhospital comparison of SSI rates as a measure of the quality of patient care. Data should therefore be collected on accuracy and consistency. In surveillance networks, validation studies are essential to ensure credibility and validity of data.

SSIs in orthopedic prosthetic surgery are among the most serious health care-associated infections: prosthetic joint infections may prolong length of hospital stay, lead to reoperations, and increase health care costs. Orthopedic operations were the first procedures under surveillance in the Finnish Hospital Infection Program (SIRO), which has been operating since 1999, and more hospitals perform SSI surveillance for these operations than any other procedure. Our SSI rates for hip and knee prosthetic procedures have been relatively high compared with rates reported by other surveillance systems in Europe and the United States. Our previous study showed a wide variation in these rates between participating hospitals. The variation was due not only to differences in postdischarge surveillance but also to differences in in-hospital surveillance. We therefore focused our first validation study on surveillance data in orthopedic surgery.

METHODS

Surveillance system

Nine hospitals (3 tertiary care, 3 secondary care, and 3 other hospitals) conducted prospective surveillance for SSIs in orthopedic surgery on a continuous basis during 1999-2003. Procedures under surveillance were hip and knee joint replacements and open resections of femur fracture.

In-hospital surveillance was conducted by using the Centers for Disease Control and Prevention (CDC) definitions and the National Nosocomial Infection Surveillance System (NNIS) methodology. A written protocol with CDC definitions translated into Finnish
was provided. For case finding, the infection control nurses (ICNs) responsible for surveillance are recommended to visit wards once a week and obtain additional information from microbiology laboratory reports, patient charts, and medical/nursing staff. After discharge, all hospitals conducted surveillance on readmission and at follow-up visits and, in 7 hospitals, also by an additional postdischarge questionnaire, which was given to each patient at discharge. The standardized questionnaire included the following variables: purulent drainage, other signs or symptoms of infection (pain, tenderness, swelling, redness, or heat), incision opened by a surgeon, wound culture taken, and antimicrobial treatment given to SSI. If a patient had clinical signs or symptoms in the wound area and contacted the health care system, the questionnaire was filled out by a health care professional (nurse or physician). The training on surveillance methodology organized by the SIRO for local ICNs included a site visit at the beginning of the surveillance, meetings at least once a year, and an opportunity to consult the SIRO team by phone whenever needed.

For each infection, local ICNs collected and recorded manually the following data on a form: the patient's national identity code (includes age and sex), date of surgery, procedure code, date and type of SSI, microorganism if identified, and location of detection. When the SSI was detected after discharge, the location of detection was recorded, ie, on readmission to the hospital, at follow-up visit, or in outpatient setting by the postdischarge questionnaire. For each patient under surveillance, the following data were uploaded from hospital databases and sent in electronic form to the national center: the patient's national identity code, date of surgery, procedure code, American Society of Anesthesiologists (ASA) score, wound contamination class, duration and urgency of operation, date of admission and discharge, and discharge status. In the national surveillance database, the infection reports were linked to the uploaded data by using the patient's national identity code and the date and code of the procedure. At regular intervals, the infection reports not combined in the automatic process were examined. These reports were first checked for possible errors in data entering, and, second, the local ICNs were contacted, if needed. The errors found were manually corrected.

Feedback was given through the project Web site, which was only accessible by use of a password given to authorized persons from the participating hospitals. Each hospital had access to its own data, and all hospitals had access to the aggregated data. Feedback included several report tables generated on-line from the database according to the users' search criteria (hospital, time period, and procedure group).

Validation study

All 9 hospitals were invited to participate in the voluntary validation study. During 1-day visits, a retrospective chart review and a structured interview with the ICN were carried out.

At each hospital, a validation team retrospectively reviewed a sample of patient charts, including all clinical data and laboratory and radiology reports. The sample of charts contained 10 orthopedic operations with and 40 without infection. The surveys were blinded to the patient's infection status as recorded by the hospital ICN. The validation team, which was considered the gold standard for validation, consisted of 2 SIRO team members: an experienced ICN (N.A.) and an infectious disease specialist-in-training (K.H.), supported by the SIRO project leader (O.L.). If an SSI was assessed to be present, the CDC criteria that the SSI fulfilled and the type and date of the SSI were recorded. After the review, discrepant files were discussed with the ICN to determine sources of discordance.

Exhaustiveness (completeness) of the denominator was examined by checking the proportion of infection reports not combined in the automatic process (as a result of, eg, an error in the patient's national identity code or missing denominator data). The proportions of missing values in certain important fields (ASA score, wound contamination class, and duration of operation) were also evaluated.

In every hospital, the ICN responsible for quality of surveillance data was interviewed. The structured interview included questions about the process of data collection, interpretation of the case definition, and methods of postdischarge surveillance.

To calculate the rate of wound cultures per 1000 patient-days in orthopedic wards of each hospital, the number of wound cultures, both surgical and other wounds, taken by orthopedic wards in 2003 was obtained from local microbiology laboratories and the patient-days from hospital administration.
1999-2003 by the positive predictive value to obtain an approximation of the number of true infections. The same procedure was performed for negative cases with the negative predictive value. This allowed sensitivity and specificity for the aggregated surveillance data to be determined. Confidence intervals were calculated by the asymptotic normal theory with the delta method.

RESULTS

Eight of the 9 invited hospitals participated in the study. In total, the validation team reviewed 397 patient charts. Results of the chart review are presented in Table 1 Routine surveillance had identified 83 SSIs, 78 of which were identified as SSIs also by the validation team (ie, true positive infections). Thus, the positive predictive value was 94.0%, with a 95% CI of 88.9% to 99.1%. Among the charts reviewed, no infections during routine surveillance had been reported after 314 operations, and the validation team confirmed 310 of these negative reports (ie, true negative cases), yielding a negative predictive value of 98.7%, with a 95% CI of 97.5% to 100%.

When the results of the validation study were applied to the aggregated surveillance data (during 1999-2003: 592 infections and 14,551 noninfections), a sensitivity of 75.0%, with a 95% CI of 56.7% to 93.4%, and a specificity of 99.8%, with a 95% CI of 99.5% to 100%, were yielded (Table 2). One hospital was responsible for most of the infections missed (3/4) and for 1 false-positive infection (1/5). When the results of this hospital were excluded, the positive predictive value for the remaining 7 hospitals was 94.6%, with a 95% CI of 89.6% to 99.8%, and the negative predictive value 99.6%, with a 95% CI of 98.9% to 100%. When these predictive values were applied to the aggregated surveillance data, without the excluded hospital, the sensitivity for routine surveillance increased to 91.5% (95% CI: 76.4%-100%) and the specificity to 99.8% (95% CI: 99.6%-100%).

The reasons for missing 4 (2 superficial and 2 deep incisional) SSIs during routine surveillance were that an ICN had not received information about the SSIs from an outpatient department (2) or from a ward (2). Explanations for overreporting SSIs were related to interpretation of the case definition (5). Most (3/5) false-positive SSIs were superficial incisional without appropriate clinical signs or symptoms. One organ/space SSI with clinical onset 2 years after the operation was reported.

Of the 78 SSIs classified as true infections by the validation team, 49 (63%) were superficial incisional, 8 (10%) deep incisional, and 21 (27%) organ/space infections. The types of SSIs reported by routine surveillance differed from these (Table 3). Problems with classification most commonly occurred in the organ/space SSI: half of which were misclassified as deep. If the types of SSIs are given in 2 categories, superficial and severe (ie, deep incisional and organ/space), less misclassifications were found. Only 2 (4%) superficial SSIs were reported as severe and 4 (14%) severe SSIs as superficial in routine surveillance.

In the routine surveillance data for 1999-2003, the proportion of infection reports that was not combined in the automatic process of all infection reports was 4.4% (18/403): 8 with a typing error in the patient’s national identity code and 10 with denominator data missing. The typing errors were corrected, and infection and procedure data were then successfully combined. The proportions of missing values in the ASA score, wound contamination class, and duration of operation were 3.7%, 1.4%, and 1.1%, respectively.

According to the structured interviews, the most common case finding methods for prospective SSI surveillance were ICN ward visits (mostly once a week to once a month, in 1 hospital only when needed), ward notifications by link nurses and by other nursing staff, and postdischarge questionnaires, but microbiology laboratory reports were also used (Table 4). If a case of an SSI was found by ward notification, an ICN reviewed patient charts of every suspected SSI in 3 hospitals and selectively in 5 hospitals. Some incompleteness in medical records was reported by ICNs (7/8); most ICNs (6/8) particularly described a need for more

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**Table 1.** Results of the chart review*

<table>
<thead>
<tr>
<th>Infection</th>
<th>Total</th>
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<tbody>
<tr>
<td>+</td>
<td>Routine surveillance</td>
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<tr>
<td></td>
<td>Routine surveillance</td>
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<tr>
<td>-</td>
<td>Total</td>
</tr>
</tbody>
</table>

*Positive predictive value (PPV) = 78 / 83 = 94.0%. Negative predictive value (NPV) = 310 / 314 = 98.7%.

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**Table 2.** Chart review results applied to total SIRO surveillance data*

<table>
<thead>
<tr>
<th>Infection</th>
<th>Total</th>
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<tr>
<td>+</td>
<td>Surveillance</td>
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<tr>
<td></td>
<td>Surveillance</td>
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<tr>
<td>-</td>
<td>Total</td>
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</tbody>
</table>

*Sensitivity = 556/741 = 75.0%. Specificity = 14,366/14,402 = 99.8%.

PPV = 556 / 592 = 0.934.

NPV = 14,351 / 14,402 = 0.998.

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81% (36/45) and for 1 false-positive infection (1/5). When the results of this hospital were excluded, the positive predictive value for the remaining 7 hospitals was 94.6%, with a 95% CI of 89.6% to 99.8%, and the negative predictive value 99.6%, with a 95% CI of 98.9% to 100%. When these predictive values were applied to the aggregated surveillance data, without the excluded hospital, the sensitivity for routine surveillance increased to 91.5% (95% CI: 76.4%-100%) and the specificity to 99.8% (95% CI: 99.6%-100%). The reasons for missing 4 (2 superficial and 2 deep incisional) SSIs during routine surveillance were that an ICN had not received information about the SSIs from an outpatient department (2) or from a ward (2). Explanations for overreporting SSIs were related to interpretation of the case definition (5). Most (3/5) false-positive SSIs were superficial incisional without appropriate clinical signs or symptoms. One organ/space SSI with clinical onset 2 years after the operation was reported.

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accurate documenting of wound status. One ICN reported that antimicrobial agents used were not always documented (mostly prescribed at discharge).

Most of the hospitals conducted postdischarge surveillance at follow-up visits (7/8), on readmission (8/8), and in outpatient settings by an additional questionnaire (7/8). The postdischarge questionnaire was given to each patient under surveillance at discharge. Five hospitals used the standard questionnaire provided by the SIRO, which included all criteria of the CDC definition. Two hospitals used their own postdischarge questionnaires: one with no criteria and the other with the most important criteria. All questionnaires were requested to be returned by 4 hospitals: the response rate in these hospitals varied between 45% and 70%. In 3 hospitals, the questionnaires were requested to be returned only if an SSI was identified. Three ICNs noted that, also, local/regional settings taking care of follow-up treatment and rehabilitation were trained in postdischarge surveillance.

The ICNs experienced difficulties in the interpretation of SSI case definition and date of SSI (onset of signs and symptoms vs date of wound culture). Five ICNs had problems with distinguishing deep incisional infections from organ/space infections after orthopedic procedures. Two ICNs were uncertain of how to interpret prolonged serosal drainage with positive microbial culture. Six ICNs responded that they had also reported SSIs found after the time limit imposed by the CDC definition (30 days for superficial incisional infections and 1 year for deep and organ/space infections).

The rate of wound cultures was calculable for 7 hospitals (1 hospital did not have a separate orthopedic ward). The rate in the orthopedic wards of participating hospitals varied between 9 and 67 per 1000 patient-days, but did not correlate with SSI rates by hospitals ($P = .38$).

**DISCUSSION**

Our findings suggest that most SSIs reported to the national surveillance system by participating hospitals were true infections. Thus, when an SSI case was reported, the criteria of the case definition were correctly interpreted. Some SSIs were missed, which might be due to weaknesses in case finding. Variation in diagnostic practices may also have an effect on SSI rates.

When the sensitivity, specificity, and predictive values of different validation studies are compared, it is important to take into account the study design and the calculation method used. The results are straight applicable to the aggregated surveillance data when the study sample includes all operations during a certain time period.9-16 but, if not, as in our study, they need further calculations. The positive predictive value (94.0%), sensitivity (74.8%), and specificity (99.8%) calculated for routine SIRO surveillance were favorable compared with those reported in the few validation studies of national surveillance systems for SSI available.16 Our indicators were higher than in the first validation study of the NNIS system, in which positive predictive value, sensitivity, and specificity for SSI were 72%, 67%, and 97.7%, respectively.17 In this study, the gold standard was also the experts’ retrospective chart review. In the Dutch national surveillance system, a validation study of SSI surveillance confirmed high accuracy for routine surveillance: positive and negative predictive values were as high as 100% and 99%, respectively.4 Sensitivity and specificity for the aggregated data were not, however, published. When our results are compared with single-hospital validation studies, they are again quite similar or a little poorer. For example, in a validation study carried out in a single tertiary care hospital with experts’ prospective daily wound examination and chart reviews, accuracy for standard SSI surveillance was slightly higher than ours.16 During the first study period, sensitivity and specificity for routine surveillance were 83.8% and 99.8%, respectively, and, during the second period, sensitivity was 92.3%. However, in our study, the sensitivity and specificity increased markedly (to 91.4%
and 99.8%, respectively) when the surveillance data of the hospital with the most missed infections were excluded.

In our validation sample, some underreporting by hospitals was detected. Patients with missed SSIs had passed through the SIRO hospitals, either through an outpatient clinic or a ward, so that an ICN did not obtain information about them. Thus, as in the NNIS validation study, inadequate case finding explained the underreporting of SSIs. In the NNIS system, review of both the microbiology reports and the patient charts is mandatory, although case finding is not outlined in detail because the most suitable sources of information can vary locally. In our written protocol, all methods available for case finding are recommended to be used.

Overreporting of infections was not a significant problem. When it did occur, it was related to slight variations in interpretation of the case definition; most false-positive infections were superficial incisional SSIs without adequate clinical signs or symptoms—at least what was documented in charts. In addition, 1 organ/space SSI was reported 2 years after an operation; the patient had been completely symptom free at the 1-year follow-up visit. Even when the CDC definition is correctly interpreted, it is not fully objective because of 2 criteria: the surgeon’s diagnosis and wound culture. Variability in the clinician’s diagnosis and 7-fold variability in wound culturing activity is likely to affect SSI rates, as well as having an impact on the decisions made by the validation team. Although validation studies enable the accuracy of case finding and the surveillance process to be evaluated, SSI rates even after validation may be affected by differences in diagnostic practices between hospitals and surgeons. Although the positive culture is only one of the CDC criteria, SSIs without positive culture are more difficult to find.

The interpretation of the CDC definition was also examined by comparing the types of SSIs detected during routine surveillance and by the validation team. Discrepancies were less common when the infection types were analyzed in 2 categories instead of 3. This might be related to the difficulty of distinguishing between infection types after orthopedic surgery. Most severe SSIs misclassified as superficial had begun as skin infections that had progressed. The SSI was reported at the beginning of the infection, but no further report had been given, even when indicated. Thus, the importance of reporting these possible prosthetic joint infections should be emphasized.

According to the ICN interviews, an important case finding method in routine surveillance is information technology-based reporting of SSIs by link nurses in surgical wards. Most of the link nurses were trained in case finding and definitions, and the CDC criteria for SSIs were available in all wards. ICNs confirmed the reported SSIs by reviewing patient charts either always or when needed. Most ICNs visited surgical wards with a frequency from once a week to once a month, which is very likely to cause variation in sensitivity of case finding. ICNs carried out further case finding by reviewing microbiology reports, cooperating with infectious disease specialists, and following up the results of a postdischarge questionnaire.

A limitation of this study was the small number of charts reviewed. An optimal sample size would have been 2 to 3 times larger. The retrospective study design may also be considered a limitation, although this is often the only method available for validation of a national surveillance system with several hospitals. Despite these methodologic limitations, the results can be used to plan future training for ICNs and to improve the reliability of the surveillance system and the usage of surveillance data in preventing SSIs.

The authors thank infection control nurses in participating hospitals: Irma Merio-Hietaniemi, Erja Tenhunen (Helsinki University Central Hospital), Lisa Elin (Horvi Hospital), Merja Fellman (Kanta-Hame Central Hospital), Anne-Mar Kimmo (Peijas Hospital), Anne Reiman (Paijais-Hame Central Hospital), Sipra Harle (Orion Hospital), Irma Teirila (Oulu University Hospital), and Nina Elomaa (Vaasa Central Hospital). We also thank Petri Ruutu for valuable comments of the manuscript and Jukka Ollgren and Teemu Mottonen for data management and statistical advice.

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Surveillance of multidrug-resistant gram-negative bacilli in a neonatal intensive care unit: prominent role of cross transmission

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Background: Multidrug-resistant gram-negative bacilli (MDRGN) are an important cause of nosocomial infections in neonatal intensive care units (NICUs). We conducted a 1-year prospective surveillance study in an NICU to assess the epidemiology of MDRGN among newborns and the relative importance of acquisition routes.

Methods: Neonates admitted at the NICU of the Dipartimento Materno-Infantile, University Hospital, Palermo, Italy, from January 7, 2003, to January 6, 2004, were included in the study. Colonization of patients with MDRGN was assessed by cultures of rectal swabs sampled twice a week. Pulsed-field gel electrophoresis was used to determine relatedness among MDRGN isolates. Extended-spectrum β-lactamases (ESBL) and metallo-β-lactamases (MBL) production was investigated. The association between risk factors at admission and during the NICU stay was analyzed by multivariate logistic regression analysis.

Results: During the 12-month period January 7, 2003, through January 6, 2004, 1021 rectal swabs were cultured from 210 infants. One hundred sixteen infants (55.2%) were colonized by MDRGN. The monthly incidence of acquisition of MDRGN ranged between 12 and 53 cases per 1000 patient-days. Eighty-four (72.4%) of the 116 patients were cross colonized. Exclusive feeding by formula was significantly associated with cross transmission (RR = 1.8, P = .02). Fifty-seven (49.1%) of the 116 infants were colonized by ESBL-producing Enterobacteriaceae. Feeding by formula was significantly associated with colonization by ESBL-producing Enterobacteriaceae (RR = 1.6, P = .007), whereas breastfeeding proved to be protective (RR = 0.5, P = .001). Ninety-two (43.8%) of the 210 infants received antibiotics during the NICU stay, but exposure to those most frequently administered, ampicillin-sulbactam and gentamicin, was not significantly associated with MDRGN colonization.

Conclusion: The emerging picture of this study is that spread of MDRGN in an NICU may be the result of diffuse cross transmission and, consequently, of poor infection control procedures. (Am J Infect Control 2007;35:222-30.)

Nosocomial infections are an important problem in neonatal intensive care units (NICUs), in which environmental and host factors often contribute to higher rates of infection than pediatric and adult ICUs. Since the 1980s, NICUs more and more frequently provide care for high-risk infants, including very-low-birth-weight (VLBW) and chronically ill infants, and the need of prolonged stay along with large use of invasive life support measures increases the opportunity for acquisition of late-onset nosocomial infections.

Infections with gram-negative bacilli that are resistant to many commonly used antibacterial drugs are increasingly reported in NICUs. The major endogenous reservoir of multidrug-resistant gram-negative bacilli (MDRGN) is the intestinal tract of hospitalized infants. The large use of antimicrobial drugs and cross transmission via the hands of caregivers, contaminated equipment, or inanimate objects play a prominent role in selection and dissemination of MDRGN, and failures in infection control practices can be responsible for diffuse horizontal spread. The incidence of infections caused by organisms resistant to the β-lactam agents has also sharply increased in recent years and has often been associated to clonal outbreaks.

There have been several attempts to characterize the epidemiology of nosocomial MDRGN by identifying risk factors for their acquisition and using molecular typing to trace horizontal transmission between newborns. However, in “endemic” contexts, dynamics of transmission of MDRGN are expected to be widely variable, depending on interaction between human and environmental ecology of NICUs. Indeed,
surveillance studies have yielded quite different findings: drug-resistant bacilli clonally related on the basis of molecular analysis accounted for proportions varying between 12% and more than 50% of isolates from colonized patients.\textsuperscript{4,7-10}

A prospective study was performed in the NICU of the Dipartimento Materno-Infantile, University Hospital, Palermo, Italy, to address the epidemiology of MDRGN among newborns and determine by using pulsed-field gel electrophoresis (PFGE) the frequency of cross transmission. Risk factors for acquiring MDRGN in the NICU were also identified.

METHODS

Setting

We conducted a 1-year prospective surveillance study in the NICU of the University Hospital of Palermo, Italy. The unit is part of the Dipartimento Materno-Infantile, which is a reference center for congenital malformation in Sicily. The department includes also units of infertility and assisted reproduction and materno-fetal medicine. In the NICU under study, approximately 200 patients are usually admitted annually, including approximately 15% of VLBW newborns (birthweight $<1500$ g). The NICU is divided into 2 rooms connected by sliding doors. Sinks are available in each room. Gloves are used routinely in aseptic procedures. The average patient-to-nurse ratio is 3:1 and 2:1 in the intermediate care and intensive care section, respectively.

Prematurity is the most common reason for admission to the NICU (approximately 70%). Other diagnoses for admission include respiratory distress, congenital malformation, surgical conditions, and infections. First-line therapy for suspected early-onset sepsis is a combination of ampicillin-sulbactam plus gentamicin.

Patients

All patients admitted from January 7, 2003, to January 6, 2004, who remained hospitalized for at least 48 hours in the NICU and from whom at least 1 rectal swab culture could be obtained were enrolled in our study. Demographic, clinical, and microbiologic data were prospectively collected and entered into an Access Database (Microsoft Corp, Redmond, WA). The following parameters were recorded for all patients: demographic characteristics, gestational age, birth weight, inborn or outborn condition, delivery type, APGAR score, length of stay, comorbidity conditions. During the NICU stay, data regarding use and duration of the following devices and procedures that could be considered as possible risk factors were also collected: antimicrobial therapy, central venous and peripheral catheterization, nasogastric and endotracheal tube insertion, and type of feeding (ie, parenteral, breast milk, formula or mixed, breast milk plus formula).

A rectal swab culture yielding gram-negative bacilli in absence of clinical symptoms and signs was considered evidence of colonization. Nosocomial infection was identified according to the recommendations of the Centers for Disease Control and Prevention, Atlanta, GA.\textsuperscript{12} Diagnosis of infection was based on the presence of clinical symptoms and signs, laboratory findings (blood C-reactive protein level, white cell formula), and culture results. Congenital anomalies were defined as conditions listed under the International Classification of Disease (ICD-9) codes 740 to 759.

Microbiologic surveillance

Rectal swabs were collected twice a week every Tuesday and Friday from all infants throughout their NICU stay. These were inoculated onto 1 MacConkey agar plate per swab to obtain a continuous lawn after overnight incubation in ambient air at 37°C. Four antibiotic disks, containing gentamicin (10 µg), amoxicillin-clavulanic acid (20-10 µg), imipenem (50 µg), ceftazidime (30 µg), were placed on each plate before incubation, as previously described.\textsuperscript{13} Selective media were not used so that colonization by gram-negative bacteria susceptible to antimicrobial drugs could be detected. After incubation, plates were examined and, colonies growing into each antibiotic inhibition halo were Gram’s stained and subcultured for purity. Next, after biochemical identification by API20E or API20NE (BioMerieux, Marcy-l’Etoile, France), susceptibility to a panel of 10 antimicrobial substances was assessed by disk diffusion on Mueller-Hinton agar plates, according to the National Committee for Clinical Laboratory Standards guidelines.\textsuperscript{14} The following antimicrobials were tested: ampicillin (30 µg), amoxicillin-clavulanic acid (30 µg), carbenicillin (10 µg), cefotaxime (30 µg), ceftazidime (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), imipenem (30 µg), aztreonam (30 µg), and gentamicin (10 µg).

For the purpose of our study, a gram-negative organism resistant to at least 3 different groups of antimicrobial agents (penicillins, cephalosporins, aminoglycosides, carbapenems) was defined as MDRGN, and a gram-negative organism resistant to 2 or less groups of antimicrobial agents was defined as susceptible. Extended-spectrum β-lactamase (ESBL) production was detected by decreased susceptibility or resistance to third-generation cephalosporins and the synergy between disks containing cefotaxime, ceftazidime, cefepime, and aztreonam and a disk containing amoxicillin-clavulanic acid.\textsuperscript{15} Metallo-β-lactamases (MBL) production by imipenem-resistant strains of Pseudomonas

aeruginosa was detected by the EDTA-imipenem disk synergy test.16

Molecular methods

To evaluate the frequency of cross transmission, PFGE was performed on all available isolates associated with colonization, except for multiple isolates of the same species obtained from the same infant that did not exhibit differences in ≥1 biochemical reaction and/or in susceptibility to ≥1 antimicrobial agent.

Chromosomal DNA was digested using XbaI endonuclease and resolved by PFGE in a CHEF-Mapper apparatus (Bio-Rad). Restriction fragment bands were compared and analyzed using the Diversity Database software (Bio-Rad). Strains were interpreted as undistinguishable, closely related, possibly related, or unrelated strains according to the criteria of Tenover et al.17 Polymerase chain reaction (PCR) amplification of CTX-M and SHV-5 type ESBLs and VIM type MBL sequences were performed as previously described.18,19

Statistical analysis

The association between potential risk factors and MDRGN colonization was analyzed for variables present at admission and during the NICU stay. Time-dependent variables, ie, length of stay, nutrition, invasive procedures, and antimicrobial use, were also measured as days between admission and discharge or cumulative days of exposure because patients were assumed to be at risk of further colonization by a different species or strain of MDRGN after the first isolation of a similar organism.

The association was tested by the Pearson χ² test and the Fisher exact test for frequency analysis. The relative risk (RR) and the 95% confidence intervals (CI) for the risk factors were also calculated. One-way analysis of variance (ANOVA) and the Mann-Whitney U statistic test were used for parametric and nonparametric analysis, respectively, to evaluate differences between the variables considered. A multivariate model was analyzed by stepwise logistic regression. All P values were 2-sided, and P values less than .05 were considered statistically significant. Data were analyzed by the Epi Info software (version 6.0, Centers for Disease Control and Prevention) and the Systat Software 8.0 version (SPSS, Inc., Chicago, IL).

RESULTS

General

During the 12-month period January 7, 2003, through January 6, 2004, a total of 221 neonates were admitted to the NICU for at least 48 hours. Among these, only 11 missed rectal swab cultures and were excluded from further analysis.

A total of 1021 rectal swab cultures were sequentially obtained from 210 infants. The characteristics of the study population are summarized in Table 1. The average length of stay was 22.3 days (median, 15 days; range, 3-140). Ninety-two (45.8%) infants received antibiotics during the NICU stay. Criteria for infection were met by 25 (11.9%) patients, of whom 2 died. Association between infection and potential risk factors at admission and during the NICU stay were evaluated. No significant differences were noted between infected and noninfected patients, except for a higher frequency of malformation within the infection cases (20.8% vs 8.1%, P = .04), for the following variables: gestational age, gender, outborn/inborn condition, birth weight, twin birth, type of delivery, and APGAR score.

Culture results

On average, patients were monitored for a mean of 14.5 days (median, 7 days; range, 1-87). One hundred sixteen (55.2%) of 210 subjects were colonized with MDRGN at some point over the study period. Thirty-nine (18.6%) subjects were colonized by susceptible bacteria, whereas 55 (26.2%) had no positive culture for gram-negative bacilli (GN). Twenty-eight subjects were colonized with MDRGN at the time of entry into the study (ie, when their first rectal swab was taken at the start of the study). Patients colonized by MDRGN were monitored for a mean of 20.5 days (median, 11 days; range, 1-87), whereas patients colonized by drug susceptible GN were monitored for a mean of 8.4 days (median, 7 days; range 1-28) and those not colonized at any point over the study period for a mean of 4.8 days (median, 1 days; range, 1-85, P < .0005; MDRGN vs not colonized, P < .0005; MDRGN vs susceptible GN, P = .001; not colonized vs susceptible GN, P = .61)

The time interval between admission and first rectal swab for the patients colonized by MDRGN (mean, 5.7 days; median, 3 days, range, 1-107) was higher but not significantly (P = .12) than that of the infants colonized by susceptible GN (mean, 2.9 days; median, 2 days; range, 1-18) and not colonized at all (mean, 2.3 days; median, 2 days, range, 1-6). The interval between admission and first rectal swab for the 28 patients colonized with MDRGN at the time of entry into the study was significantly higher (mean, 10.7 days; median, 4 days; range, 1-107) than that of the infants whose first rectal samples were culture negative (mean, 4.1 days; median, 2 days; range, 1-81; P = .032).

Eighty-two (70.7%) colonized patients were still positive when their last rectal swab was taken before the discharge. Of the 116 colonized patients, 56 (48.3%) had 1 culture-positive rectal swab, 15 (12.9%) had 2,
Table 1. Characteristics of patients at the time of admission to the neonatal intensive care unit

<table>
<thead>
<tr>
<th>Population</th>
<th>No. infants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>106 (50.5)</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td></td>
</tr>
<tr>
<td>≤500</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>501-1000</td>
<td>11 (5.2)</td>
</tr>
<tr>
<td>1001-1500</td>
<td>17 (8.1)</td>
</tr>
<tr>
<td>1501-2000</td>
<td>45 (21.4)</td>
</tr>
<tr>
<td>2001-2500</td>
<td>36 (17.1)</td>
</tr>
<tr>
<td>&gt;2500</td>
<td>99 (47.3)</td>
</tr>
<tr>
<td>Gestational age, wk</td>
<td></td>
</tr>
<tr>
<td>24-29</td>
<td>13 (6.2)</td>
</tr>
<tr>
<td>30-36</td>
<td>99 (47.1)</td>
</tr>
<tr>
<td>&gt;36</td>
<td>98 (46.7)</td>
</tr>
<tr>
<td>Inborn</td>
<td>109 (51.9)</td>
</tr>
<tr>
<td>Age at admission &gt;24 h</td>
<td>16 (7.6)</td>
</tr>
<tr>
<td>Twin birth</td>
<td>25 (11.9)</td>
</tr>
<tr>
<td>Cesarean delivery*</td>
<td>153 (75.4)</td>
</tr>
<tr>
<td>APGAR score at 5 min ≤5¹</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Malformation</td>
<td>20 (9.5)</td>
</tr>
</tbody>
</table>

⁴Information about delivery type was available for 203 of the 210 infants.

¹Information about APGAR score was available for 189 of the 210 infants.

13 (11.2%) had 3, 11 (9.5%) had 4, and 20 (17.2%) had 5 or more. Thirty-nine patients (33.6%) were colonized simultaneously or subsequently with >1 MDRGN during follow-up. For patients not found to be colonized at the first rectal sampling, colonization was first detected on average 15.7 days after admission (median, 12 days; range 4-84). Fourteen (12.1%), 3 (7.7%), and 8 (14.5%) infection cases were included among the patients colonized by MDRGN, colonized by susceptible GN, and culture negative, respectively (P = .35).

The monthly incidence of acquisition of MDRGN varied over the 12-month period, with a minimum of 12 cases per 1000 patient-days and 3 clusters in March, May, and September (Fig 1). This last month was associated with an overcrowding of the NICU because of the contemporary admission of 5 groups of preterm multiple-birth neonates.

Risk factors for colonization with MDRGN

Selected clinical parameters at admission and during the NICU stay were tested by univariate analysis for their association with no growth of GN, with colonization with drug susceptible GN, and with at least 1 strain of MDRGN (Tables 2 and 3). Statistical analysis indicated that the characteristics at admission most strongly associated with resistant colonization were inborn status, twin birth, early gestational age, and low birth weight (Table 2).

Ampicillin-sulbactam and gentamicin were the most frequently used antimicrobials, being administered to more than 10% of patients. The mean time of use after admission was 9.2 days (median, 7.5 days; range, 1-35) for ampicillin-sulbactam and 6.8 days (median, 6.0 days; range 1-23) for gentamicin. However, when their use was assessed as a risk factor, no significant association with MDRGN acquisition was found (Table 3).

On the other hand, prolonged length of NICU stay and total exposure to antimicrobial drugs were strongly associated with MDRGN colonization (Table 3). In the 21 infants who were treated with third-generation cephalosporins, colonization by MDRGN (81.0%) was significantly (P = .04) more frequent than colonization by GN (4.8%) or negative culture for GN (14.5%).

Within the procedures used during the NICU stay, insertion of endotracheal tubes and nasogastric tubes proved to be significantly associated with MDRGN colonization by frequency analysis, although no significant differences were detected in terms of days of the device use (Table 3). On the contrary, insertion of central venous catheters was significantly associated with colonization by susceptible GN (4.8%) or negative culture for GN (14.5%).

Colonization by multiple MDRGN species or genetically discordant strains, simultaneously or in subsequent rectal swabs, was significantly associated (P < .001) with the length of stay; for the multicolonized patients, the average length was 47.0 days (median, 35.0 days; range 18-158) in comparison with that of the monocolonized patients, 21.8 days (median, 14.0 days; range 3-74). The use of central venous catheters (RR = 1.6;
95% CI: 1.2-2.3; P < .001) and nasogastric tubes (RR = 1.8; 95% CI: 1.2-2.7; P < .001) was also significantly associated with multiple colonization. By contrast, the use of endotracheal tubes (RR = 1.3; 95% CI: 0.9-1.8; P = .40), peripheral catheters (RR = 1.0; 95% CI: 0.8-1.4; P = .36), parenteral nutrition (RR = 1.1; 95% CI: 0.8-1.4; P = .26), feeding by formula only (RR = 1.2; 95% CI: 0.9-1.6; P = .07), and administration of ampicillin-sulbactam (RR = 1.2; 95% CI: 0.9-1.6; P = .07) or gentamicin (RR = 1.1; 95% CI: 0.9-1.5; P = .16) at admission was not associated with multiple MDRGN colonization. When these risk factors were assessed in multivariate analysis, early gestational age, low birth weight, and length of NICU stay were significantly associated with colonization by multiple species or strains (P < .0005).

Eighty-four (72.4%) of the 116 infants positive for MDRGN were colonized with genetically indistinguishable organisms. These patients were not significantly different from those colonized by unique strains by length of stay (mean, 32.2 days; median, 22 days; range 4-158 vs mean, 25.3 days, median, 14 days; range 3-90, P = .25), even though a positive trend was evident. Exclusive feeding by formula was the only individual factor significantly associated with cross transmission (RR = 1.8; 95% CI: 1.1-3.5; P = .02). The use of central venous catheters (RR = 0.9; 95% CI: 0.4-2.0; P = .36), nasogastric tubes (RR = 1.4; 95% CI: 0.7-5.0; P = .17), endotracheal tubes (RR = 0.7; 95% CI: 0.4-1.4; P = .20), peripheral catheters (RR = 0.9; 95% CI: 0.5-1.7; P = .38), parenteral nutrition (RR = 0.5; 95% CI: 0.2-1.2; P = .06), and administration of ampicillin-sulbactam (RR = 1.1; 95% CI: 0.6-2.0; P = .40) or gentamicin (RR = 1.0; 95% CI: 0.6-1.8; P = .49) at admission were not associated with cross transmission.

Fifty-seven (49.1%) of the 116 MDRGN-positive infants were colonized by ESBL-producing Enterobacteriaceae. These patients significantly differed from those who were colonized by non-ESBL-producing strains by birth weight (mean, 1964.9 g; median, 1850 g; range, 600-3450 vs mean, 2299.7 g; median, 2340 g; range, 350-4500; P = .02) and length of stay (mean, 38.7 days; median, 30 days; range, 5-158 vs mean, 22.1 days; median, 13.0 days; range 3-74; P = .002). By univariate analysis, feeding by formula was the only factor significantly associated with colonization by ESBL-producing Enterobacteriaceae (RR = 1.6, 95% CI: 1.1-2.3, P = .007). On the contrary, feeding by breast milk proved to be protective (RR = 0.5; 95% CI: 0.4-0.8; P = .001). Administration of gentamicin (RR = 1.1; 95% CI: 0.8-1.6; P = .30) and ampicillin-sulbactam (RR = 1.1; 95% CI: 0.7-1.5; P = .43) did not increase significantly the risk of colonization by ESBL-producing strains.

Colonizing strains, PFGE results, and characteristics of the clusters

The species identified were as follows: *Enterobacter cloacae*, 41 patients (35.3%); *Pseudomonas aeruginosa*, 36 patients (31.0%); *Klebsiella oxytoca*, 25 patients (21.6%), *Escherichia coli*, 22 patients (19%); *K pneumoniae*, 21 patients (18.1%); *Serratia marcescens*, 9 patients (7.8%); and others (*Citrobacter freundii*, Morganella morganii, E hermannii, Acinetobacter lwoffii, Stenotrophomonas maltophilia), 15 patients (12.9%).

The 6 most frequent MDRGN species associated with neonatal colonization during the study period were *E cloacae*, *P aeruginosa*, *K oxytoca*, *E coli*, *K pneumoniae*, and *S marcescens* (Table 4). Among the other species, strains of *S maltophilia*, *C freundii*, and *A lwoffii* were isolated from 3, 2, and 2 infants, respectively, but they were genetically unrelated. Of the 153 strains that were biochemically attributed to the 6 most frequently identified species and submitted to PFGE analysis, 101 (66.0%) were isolated from at least 2 patients. In 11 instances, the cluster included 2 or 3 patients. The remaining 7 clusters involved from 4 to 21 patients, the largest being caused by *P aeruginosa* (21 patients) and *K oxytoca* (21 patients) (Table 4). The
mean number of days that a cluster-related MDR organism could be cultured was 60.4 days. In most instances, genetically indistinguishable organisms were isolated from infants whose NICU stay overlapped in time. However, in 3 clusters involving *E. cloacae* (pulsotype C), *P. aeruginosa* (pulsotype A), and *S. marcescens* (pulsotype A), indistinguishable organisms were identified several weeks after the previous positive cases had been discharged.

**Pattern of spread**

The monthly incidence of acquisition of MDRGN and the 6 most frequently identified strains over the 12-month study period are illustrated in Fig 1. The peaks of the overall incidence density of colonization appear to be largely attributable to the cumulative effect of the epidemic cross-transmission phases of the 6 most frequent bacterial clones. Eighteen patients out of 28, which were colonized with MDRGN at the time of entry into the study, proved to be colonized by strains with a PFGE profile previously detected in the NICU, whereas 9 were positive for unique *P. aeruginosa* strains genetically unrelated to each other and to the prevalent one (pulsotype A).

**DISCUSSION**

MDRGN organisms are becoming the prevalent causal agents of infection in NICUs. Described by several authors, who have identified risk factors for colonization and infection and applied molecular tracing as a tool for assessing transmission pathways and cross-transmission burden and addressing drug-resistance control strategies.

Our study showed a colonization rate higher than that reported by some previous studies; indeed, more than 50% of patients proved to be colonized by MDRGN, and approximately one fourth of these were precociously colonized, probably as a consequence of a high prevalence of already colonized patients, a variable previously defined as “colonization pressure.” Moreover, in our study, most patients were colonized by the same strain for prolonged intervals of time and often up to their hospital discharge. Multiple colonization was also more frequent than previous findings. Of particular interest, a very high cross-transmission rate was detected in our study by the application of molecular typing, with several clusters of small size including 2 to 3 patients but also larger size clusters involving up to 21 patients. Moreover, some large size clusters were traced over a long period, suggesting the probable role of a common environmental reservoir interacting with inadequate hygienic practices by the health care providers.

**Table 3. Risk factors for colonization with MDRGN during NICU stay**

<table>
<thead>
<tr>
<th></th>
<th>Colonized with MDRGN n = 116</th>
<th>Colonized with susceptible GN n = 39</th>
<th>Not colonized n = 55</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endotracheal tube*</td>
<td>33 (28.4)</td>
<td>2 (5.1)</td>
<td>9 (16.4)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Central venous catheter*</td>
<td>44 (37.9)</td>
<td>8 (20.5)</td>
<td>15 (27.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Intravenous catheter*</td>
<td>77 (66.4)</td>
<td>19 (48.7)</td>
<td>34 (61.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Nasogastric tube*</td>
<td>33 (28.4)</td>
<td>8 (20.5)</td>
<td>3 (5.5)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Parenteral nutrition*</td>
<td>81 (69.8)</td>
<td>23 (59.0)</td>
<td>37 (67.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Breast milk feeding*</td>
<td>56 (48.3)</td>
<td>22 (56.4)</td>
<td>35 (63.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Formula only*</td>
<td>61 (52.6)</td>
<td>20 (51.3)</td>
<td>22 (40.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Endotracheal tube, days†</td>
<td>7.6 (9.0)</td>
<td>2.0 (1.4)</td>
<td>13.2 (28.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Central venous catheter, days†</td>
<td>12.1 (10.8)</td>
<td>6.0 (3.9)</td>
<td>5.2 (2.2)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Intravenous catheter, days†</td>
<td>6.2 (6.9)</td>
<td>5.6 (2.7)</td>
<td>7.7 (14.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Nasogastric tube, days†</td>
<td>12.7 (12.6)</td>
<td>14.7 (11.7)</td>
<td>16.7 (13.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Parenteral nutrition, days†</td>
<td>9.6 (10.2)</td>
<td>7.3 (11.1)</td>
<td>8.3 (16.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Breast milk feeding, days†</td>
<td>6.6 (5.2)</td>
<td>10.4 (9.8)</td>
<td>5.9 (4.7)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Formula only, days†</td>
<td>12.1 (14.4)</td>
<td>15.5 (9.6)</td>
<td>9.4 (9.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Length of stay, days†</td>
<td>29.7 (27.5)</td>
<td>15.9 (10.8)</td>
<td>11.0 (14.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total exposure to antibiotics, days†</td>
<td>8.0 (13.5)</td>
<td>2.3 (6.2)</td>
<td>5.5 (13.8)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Amoxicillin-sulbactam, days†</td>
<td>4.7 (7.0)</td>
<td>1.7 (3.3)</td>
<td>3.2 (4.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Gentamicin, days†</td>
<td>3.2 (4.3)</td>
<td>1.6 (3.4)</td>
<td>2.3 (3.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

MDRGN, multidrug-resistant gram-negative; GN, gram-negative; NS, not significant.

*Expressed as yes frequency (%).
†Expressed as mean (SD).
§ANOVA test.
predominant circulation of gram-negative bacilli with an enteric ecology could have significantly influenced the peculiar behavior of MDRGN in our study.\textsuperscript{10,11} Furthermore, overcrowding and consequent relative understaffing, by amplifying the chances of cross contamination via hands of health care workers, have likely unleashed the incidence peak of colonization we observed in September. As outlined by Harbarth et al.,\textsuperscript{7} understaffing, overcrowding, and poor hygiene practices are issues of major concern in NICUs and may switch on epidemic chains of transmission, especially in our age of cost containment in health care.\textsuperscript{12,23} However, the concurrent role in promoting epidemic cross transmission of some microorganism properties, like the tenacious resistance to hostile environmental conditions of \textit{P. aeruginosa} or the attitude toward explosive spread of some “particularly fit” ESBL-producing strains, should not be overlooked.\textsuperscript{6,22}

Furthermore, our study identified a high percentage of ESBL- and MBL-producing isolates. Noteworthy, a carbapenem-resistant strain of \textit{Pseudomonas aeruginosa} proved to produce a new metallo-\beta-lactamase identified as VIM11. Such a finding appears alarming because of the increased mortality and cost of hospitalization associated with infections because of these organisms and the poor sensitivity of routine laboratory testing in their detection.

However, in contrast with the very high frequency of MDRGN colonization, infection occurred in only 12\% of patients, accordingly with other studies.\textsuperscript{9} In our setting, the relatively low proportion of VLBW infants, in whom health care-associated infections are most probable to occur after colonization, likely contributed to minimize the risk of infection. Infected and uninfected infants did not significantly differ in their characteristics at admission, except for more frequent malformation in the infected ones. However, it is known that congenital malformation, especially the major ones that often require surgery and very prolonged hospital stay, may play a significant role in neonatal infections.\textsuperscript{1,3}

Both MDRGN colonization and multicolonization proved to be associated with early gestational age, low birth weight, and length of stay, whereas the role of invasive life support procedures as independent risk factors was not confirmed by multivariate analysis. This is consistent with previous observations that, in some cases, have actually described a negative association between the use of invasive equipment and acquisition of MDRGN as a result of more accurate handling and manipulations reserved to more susceptible newborns.\textsuperscript{8} Alternatively, it is probable that, in the NICU under study, the widespread colonization amplified by cross transmission has negatively influenced the strength of association. Although prematurity and low birth weight are not modifiable risk factors, it is imperative to promote among caregivers awareness of risk of acquiring MDRGN isolates among intensive care infants.

Newborn nutrition has been recently emphasized as a critical issue.\textsuperscript{24–27} In the analysis of risk factors, we found that feeding by formula was consistently associated with cross transmission and colonization by ESBL-producing strains, whereas breast-feeding proved to be protective against acquisition of ESBL-producing bacilli. Milk formulas are a well-known vehicle of nosocomial infection in NICUs, and their contamination may be also responsible for cross transmission as a result of inadequate manipulation procedures and handwashing.\textsuperscript{24,27} On the other hand, the absolute protective role of breast-feeding, because of its peculiar nutritional and immunologic properties, is confirmed by several authors.\textsuperscript{25,26}

As expected, MDRGN colonization was associated with total exposure to antimicrobial drugs, but the use as empiric therapy of early onset infections of ampicillin-sulbactam and gentamicin did not result in increased colonization. Indeed, many newborns in our study acquired MDRGN colonization in an early phase of their NICU stay, before induction or selection of resistance mechanisms would likely occur after antibiotic exposure. In other studies, previous antibiotic
exposure has been variably associated with colonization by MDRGN. However, epidemiologic features of these organisms may be peculiar of a given unit, and, in our setting, the strength of association with antecedent antibiotic exposure might be weakened by the extensive cross transmission.

Our study has some potential limitations. The limited data on the organisms responsible for clinical infection cases did not allow for a reliable assessment of the ratio of colonized to infected patients and the cause-effect relationship between risk factors and infection. The NICU patient is a unique host ecosystem because the intestinal microflora develops after admission to the unit and colonization by MDRG organisms from the nosocomial environment could be considered unavoidable. However, most experts agree in believing that colonization is a prerequisite for infection by gram-negative bacilli and that knowledge of their transmission routes in nonepidemic situations may be the key to identify the prevalent mode of transmission in an NICU. Moreover, rectal samples were not obtained at admission and discharge, so time of acquisition and clearing of MDRGN isolates was not thoroughly available. Examination of the formula and environmental flora was not performed during the period under study. Finally, it should be noted that some peculiarities of our setting, such as the high rate of caesarean section and the low frequency of VLBW infants, make problematic a generalization of the results to other NICUs.

The antibiotic usage pattern in ICUs largely contributes to emergence of drug resistance, especially in an NICU in which the spectrum of available antibiotics is more restricted. Variable effects of antibiotic control policies in decreasing the reservoir of resistant gram-negative bacilli have been reported by some authors. In our study, the large proportion of MDRGN colonization acquired through cross transmission identifies infection control instead of antibiotic control as the key issue and urges the identification and application of targeted infection control policies. Assuming that MDRGN are transmitted to the infants mainly via the hands of the caregivers, the importance of limiting overcrowding-understaffing and implementing stringent hand cleansing procedures must be emphasized, along with the adoption of compliance-enhancing strategies and measuring tools. The frequent hand cleansing procedures must be emphasized, along with the adoption of compliance-enhancing strategies and measuring tools. The adoption of targeted infection control strategies and antibiotic stewardship are the approaches most supported by sound scientific evidence to discourage the emergence and diffusion of multidrug-resistant organisms. A greater understanding of the epidemiology of nosocomial organisms and the peculiar features of health care units may greatly contribute to contain the reservoir of MDRGN organisms.

References

17. Tenover FC, Arbet RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, et al. Interpreting chromosomal DNA restriction patterns...
Antimicrobial resistance patterns of colonizing flora on nurses’ hands in the neonatal intensive care unit

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New York, New York, and Philadelphia, Pennsylvania

Background: The Centers for Disease Control and Prevention recommends the use of an alcohol-based handrub for health care worker hand hygiene. The purpose of this study was to examine effects of hand hygiene product and skin condition on the antimicrobial resistance patterns of colonizing hand flora among nurses.

Methods: Colonizing hand flora of 119 nurses working in 2 neonatal intensive care units was compared during a 22-month cross-over study using alcohol handrub or antiseptic soap.

Results: Altogether, 1442 isolates from 834 hand cultures (mean, 7 cultures/nurse) were obtained. In 3 of 9 regression analyses modeling for resistant staphylococcal flora, the use of antiseptic soap was a significant predictor of resistance, and nurses with damaged skin were 2.79 times more likely to carry *Staphylococcus warneri* isolates resistant to gentamicin.

Conclusion: Hand hygiene product and skin condition may influence resistance patterns of hand flora of care providers. (Am J Infect Control 2007;35:231-6.)

The hands of health care workers may serve as reservoirs for organisms causing health care-associated infections, including infections caused by multidrug-resistant strains.1,2 In 2002, the Centers for Disease Control and Prevention revised the recommendations for hand hygiene to include the use of alcohol-based products for standard hand hygiene.3 However, the possible effects of hand hygiene products on the skin flora of personnel hands, including antibiotic resistance patterns, have not been extensively studied. We recently reported that the hands of a small number of new graduate nurses initially harbored methicillin-susceptible strains of staphylococci, which were replaced by methicillin-resistant strains within a few months of employment in the 2 study units.4 The purposes of this study were to describe the types and antimicrobial resistance patterns of hand flora among nurses working in 2 neonatal intensive care units (NICUs) over a 22-month period and to examine risk factors, including the type of hand hygiene product, for antimicrobial resistance in the hand flora.

METHODS

Sample and setting

A substudy was conducted of a larger clinical trial in which a crossover design was used to evaluate the impact of 2 hand hygiene products,5 a detergent-based antiseptic containing 2% chlorhexidine gluconate (Bactoshield; Steris Corporation, St. Louis, MO) and a 61% alcohol-based handrub (Avagard; 3M HealthCare, St. Paul, MN), on health care-associated infections in neonates. The study was conducted in 2 Manhattan NICUs between March 2001 and January 2003. The 2 NICUs are part of the New York Presbyterian Hospital system: a 43-bed unit (NICU 1) and a 50-bed unit (NICU 2).

All full-time nurses working in these units were asked to volunteer for the study; 119 of 155 nurses (76.8%) agreed to participate. Nurses were selected for this study because they were the primary staff members permanently assigned to the study units and they had the most frequent contact with the neonates.6 Throughout the study, all staff on each unit used the same hand hygiene product, including a moisturizer provided by the hospital, and artificial fingernails were prohibited. Nonstoned rings were allowed. The study was approved...
by the institutional review boards of both study sites, and each of the participating nurses signed a consent form. During the 22 study months, the condition of each nurse’s hands was assessed monthly, and a hand culture was obtained quarterly, as described below.

Skin assessment

Nurses’ skin condition was recorded monthly using 2 assessment tools. First, trained research personnel rated the skin on the hands of the participating nurses under ×3 magnification on a scale of 0 to 5, with 0 being extensive cracking of the skin and widespread redness and 5 being normal skin with no observable irritation. Previous studies have confirmed that the ratings generated from this observer assessment tool were consistent with dermatologist ratings of skin condition and had an interrater reliability of ≥90% over a range of skin conditions.

The second assessment tool was a self-rated scale with which participating nurses scored the skin on their hands using 4 criteria: appearance, intactness, moisture content, and sensation. The scale ranged from 4 to 28, with healthier skin having a higher score. Previous studies have demonstrated that this self-rating tool was significantly correlated with other measures of skin condition. The observer-rated and self-rated skin condition scores were collected independently of one another.

Hand culturing and species identification

Hand cultures were obtained every 3 months using a modified glove-juice technique. Nurses cleaned their hands with the available product immediately prior to sampling so that we could identify resident rather than transient flora. Their dominant hand was inserted into a sterile polyethylene bag containing 50 mL sampling solution (0.075 mol/L phosphate buffer, pH 7.9, containing 0.1% polysorbate 80 and 0.1% sodium thiosulfate), and the hand was massaged through the bag for 1 minute. The Clinical Microbiology Service of New York–Presbyterian Hospital, Columbia Campus, performed all microbiologic testing. Undiluted, 10- and 100-fold diluted aliquots of sampling solution were plated onto 5% sheep blood agar plates (BBL; Becton Dickinson Microbiology Systems, Cockeysville, MD). Organisms were identified by the MicroScan Walk Away 96 system (Dade Behring Inc, Newark, DE). Using the clinical laboratory’s standard protocols, a colony of each morphologically distinct colony type was selected for identification.

Antimicrobial susceptibility patterns

Antimicrobial susceptibilities were determined by the MicroScan Walk Away 96 system (Dade Behring Inc). In accordance with the Clinical and Laboratory Standards Institute, the isolates were dichotomized as either susceptible or nonsusceptible based on minimum inhibitory concentration values, with isolates determined to be “intermediate” or “resistant” categorized as nonsusceptible. Further analyses were conducted to examine changes in the staphylococcal flora (Staphylococcus warneri, Staphylococcus epidermidis, Staphylococcus aureus) of each nurse during the study period. For each nurse, we assessed changes in susceptibility of their S epidermidis isolates to oxacillin, rifampin, and gentamicin at each sampling period. We defined a potentially clinically relevant change in resistance as a change from susceptible to resistant or from resistant to susceptible to 2 or more of these agents.

Data analysis

Initially, χ² tests were used to examine differences in the relative proportions of the type of organism (ie, gram negative, gram positive, or fungi) by study unit (NICU 1 or 2) and hand hygiene product in use at the time of the culture (antiseptic soap or alcohol-based rub) as well as the difference in the proportion of isolates susceptible or nonsusceptible to antibiotics during the 2 hand hygiene product periods. Next, logistic regression models were used to examine potential predictors of carrying S warneri, S epidermidis, or S aureus isolates resistant to oxacillin, rifampin, and gentamicin. Models to predict vancomycin resistance were not included because there were too few isolates resistant to vancomycin. Separate regression models were fit for each species and antibiotic combination. In each model, the dependent variable was the presence or absence of resistance, and predictor variables included hand product used (alcohol-based rub or antiseptic soap), number of years worked in the NICU, site (NICU 1 or 2), and observer-rated skin condition. Only observer-rated skin condition was used in the models because observer and self-rating assessments of skin condition were significantly correlated (P < .01). A stepwise procedure with a variable entering the model at P = .1 and retained in the model at P = .05 was used (SAS software; SAS Institute, Cary, NC).

RESULTS

There were 834 hand cultures available for this analysis: 417 during the alcohol-based handrub period and 417 during the antiseptic soap period. An average of 7.0 (range, 1-8) cultures were obtained from each nurse participant (7.1/nurse in NICU 1 and 6.4/nurse in NICU 2). Only 3 of the 119 nurses were male, and the average age of participating nurses was 41.1 years.

Types of flora

During the study period, 1442 isolates were collected from the hands of 119 nurses (Table 1). Most were
gram-positive bacteria (88.8%, 1281/1442), 6.6% were gram-negative bacteria (95/1442), and 4.6% were fungi (66/1442). Of all the isolates, 85.7% (1236/1442) were staphylococci, with *S. epidermidis* and *S. warneri* accounting for 36.3% (524/1442) and 36.1% (520/1442) of isolates, respectively. Because there were no differences in the types of organisms found on the hands of nurses from the 2 units (P = .13), the data from the 2 sites were combined for the subsequent multivariate analyses.

Antibiotic susceptibility patterns

The antibiotic susceptibility profiles of staphylococcal species for which ≥10 isolates were identified during the study period are shown in Table 2. In general, *S. epidermidis* and *S. warneri* isolates were not susceptible to β-lactam agents, including oxacillin, but were susceptible to quinolone agents.

During the 22-month study period, there were 81.5% (97/119) of nurses from whom *S. epidermidis* was isolated more than once, and 70.6% (84/119) of nurses had *S. epidermidis* isolated from at least half of the cultures obtained. The antimicrobial susceptibility profiles of *S. epidermidis* remained the same in 69.2% (63/91) of nurses from whom more than 1 isolate was identified; in 16.5% (15/91), there was 1 change, and, in 14.3% (13/91), there were 2 or more changes in the antibiotic resistance profile over time. However, changes in the resistance patterns of *S. epidermidis* isolates from these 13 nurses had no distinguishable pattern with time.

Hand product, skin condition, and antibiotic resistance

We explored 9 regression models to identify predictors of resistance to oxacillin, rifampin, or gentamicin in *S. warneri*, *S. epidermidis*, and *S. aureus*. In 6 of these models, none of the variables assessed were significant predictors of resistance. In 3 models, the hand product was the only significant predictor of antibiotic resistance; during the period when antiseptic soap was used, there was a significant increase in *S. epidermidis* isolates resistant to oxacillin (relative risk, 1.92; 95% confidence intervals [CI]: 1.08-3.43) and gentamicin (relative risk, 1.50; 95% CI: 1.00-2.27) and a 7.22 times increased risk of rifampin resistance among *S. warneri* isolates (95% CI: 2.97-17.56). Additionally, the relative risk of resistance to gentamicin among *S. warneri* isolates from nurses with damaged skin compared with nurses with healthy skin was 2.79 (95% CI: 1.35-5.81; Table 3).

DISCUSSION

To our knowledge, this is the largest longitudinal study of nurses’ hand flora conducted to date. New and clinically relevant information was identified regarding the types and antimicrobial resistance patterns of nurses’ hand flora, the relationship between hand hygiene product and flora, and the potential role of skin health on antimicrobial resistance of the colonizing flora.

Types and antimicrobial susceptibilities of nurses’ hand flora

As expected, *S. epidermidis* was the most common organism isolated from nurses’ hands. In this sample, however, there was also a higher prevalence of

<table>
<thead>
<tr>
<th>Species</th>
<th>Isolates</th>
<th>Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><em>Micrococcus</em></td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>41</td>
<td>26</td>
</tr>
<tr>
<td><em>Staphylococcus auricularis</em></td>
<td>15</td>
<td>13</td>
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<tr>
<td><em>Staphylococcus capitis</em></td>
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<td>12</td>
</tr>
<tr>
<td><em>Staphylococcus capitis-urealyticus</em></td>
<td>35</td>
<td>24</td>
</tr>
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<td><em>Staphylococcus epidermidis</em></td>
<td>524</td>
<td>118</td>
</tr>
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<td><em>Staphylococcus haemolyticus</em></td>
<td>27</td>
<td>20</td>
</tr>
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<td><em>Staphylococcus hominis</em></td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td><em>Staphylococcus simulans</em></td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td><em>Staphylococcus warneri</em></td>
<td>520</td>
<td>116</td>
</tr>
<tr>
<td><em>Staphylococcus species (other)</em></td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td><em>Streptococcus species</em></td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Other gram-positive organisms</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1281</td>
<td>421</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Isolates</th>
<th>Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td><em>Acinetobacter lwoffii</em></td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td><em>Enterobacter species (other)</em></td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><em>Pseudomonas species (other)</em></td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Other gram-negative organisms</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Subtotal</td>
<td>95</td>
<td>85</td>
</tr>
</tbody>
</table>

| *Candida albicans* | 8 | 5 | 0.6 |
| *Candida parapsilosis* | 41 | 27 | 2.8 |
| *Candida species (other)* | 12 | 9 | 0.8 |
| Other | 5 | 4 | 0.3 |
| Subtotal | 66 | 48 |
| Total | 1442 | 554 |

* N = 119 nurses.

*Some nurses carried >1 isolate of a given species, but were only counted once/ species. This percentage is the percentage of nurses from whom this organism was isolated at least once.
S. warneri than has been noted in other studies, despite the fact that it was not known to be a prevalent organism in the study hospital. This finding is important for 2 reasons. First, it may indicate that the colonizing flora of health care personnel can become modified over time to reflect individual differences by practice site. This was further confirmed by our finding that, although these nurses often retained the same strain of *S. epidermidis* during the study period, they also shared a single clone among each other and among their patients, as previously reported, evidence that this clone was associated with this specific critical care environment.

Our group and others have recently reported decreased susceptibility to vancomycin among neonates. Although *S. warneri* is not known to be of major clinical significance, cases of health care-associated infection with this organism have been reported among neonates. Hence, this “normal flora” may be emerging as yet another multidrug-resistant opportunistic pathogen among high-risk, low-birth-weight neonates.

The majority of the *S. epidermidis* and *S. warneri* isolates from the nurses’ hands were resistant to antibiotics commonly used on the NICU. In previous studies conducted more than a decade ago, rates of oxacillin resistance among coagulase-negative staphylococci from nurses’ hands ranged from 26% to 60%. In our study, 79% of these isolates were resistant to oxacillin. Patient care personnel have been found to be colonized with higher rates of antimicrobial-resistant *S. aureus* isolates than nonmedical personnel. In contrast with the high rates of oxacillin resistance noted in coagulase-negative staphylococci, generally low rates of methicillin-resistant *S. aureus* have been isolated from nurses’ hands in previous studies: 1 of 129 (0.8%) and 3 of 79 (3.8%) nurses. These rates are slightly lower than the rate noted in our study (5/119, 4.2%), although in 1 survey of several hospitals in which MRSA was endemic, the majority of *S. aureus* isolates from staff were methicillin resistant. Clearly, personnel hands are a potential reservoir of resistance that can be transmitted to patients in high-risk environments.

### Table 2. Proportion of staphylococcal isolates susceptible to selected antimicrobial agents

<table>
<thead>
<tr>
<th>Organism</th>
<th>Total No. isolates</th>
<th>Percentage (number of isolates)</th>
<th>Oxacillin</th>
<th>Rifampin</th>
<th>Gentamicin</th>
<th>Levofloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>41</td>
<td>85.4 (35)</td>
<td>92.7 (38)</td>
<td>85.4 (35)</td>
<td>92.7 (38)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus auricularis</td>
<td>15</td>
<td>53.3 (8)</td>
<td>100 (15)</td>
<td>86.7 (13)</td>
<td>80.0 (12)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus capitis-capitis</td>
<td>14</td>
<td>92.9 (13)</td>
<td>92.9 (13)</td>
<td>85.7 (12)</td>
<td>92.9 (13)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus capitis-ureolyticus</td>
<td>35</td>
<td>82.9 (29)</td>
<td>97.1 (34)</td>
<td>82.9 (29)</td>
<td>94.3 (33)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>524</td>
<td>12 (63)</td>
<td>96.6 (506)</td>
<td>27.5 (144)</td>
<td>93.3 (489)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus haemolyticus</td>
<td>27</td>
<td>19.2 (5)</td>
<td>92.6 (25)</td>
<td>55.6 (15)</td>
<td>66.7 (18)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus hominis</td>
<td>27</td>
<td>48.1 (13)</td>
<td>100 (27)</td>
<td>66.7 (18)</td>
<td>96.2 (25)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus simulans</td>
<td>16</td>
<td>60.0 (9)</td>
<td>100 (16)</td>
<td>75.0 (12)</td>
<td>93.8 (15)</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus warneri</td>
<td>520</td>
<td>14.6 (76)</td>
<td>88.6 (459)</td>
<td>21.4 (111)</td>
<td>93.8 (486)</td>
<td></td>
</tr>
</tbody>
</table>

Vancomycin not included in table because most isolates were susceptible.

### Table 3. Predictors of resistance in staphylococcal hand flora of nurses, as analyzed by logistic regression

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antibiotic (No. isolates tested)</th>
<th>Significant variables</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>Oxacillin (n = 478)</td>
<td>Hand product</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Gentamicin (n = 472)</td>
<td>Alcohol</td>
<td>1.92 (1.08-3.43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antiseptic soap</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gentamicin (n = 447)</td>
<td>Hand product</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcohol</td>
<td>1.50 (1.00-2.27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antiseptic soap</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus warneri</td>
<td>Gentamicin (n = 447)</td>
<td>Skin Condition</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Healthy</td>
<td>2.79 (1.35-5.81)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Damaged</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifaxin (n = 463)</td>
<td>Hand product</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcohol</td>
<td>7.22 (2.97-17.56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antiseptic soap</td>
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</tr>
</tbody>
</table>

*Predictor variables included in each model: hand product, skin condition, years worked on unit, and site (NICU 1 or 2).
Factors associated with antimicrobial resistance

We found in this study that antimicrobial resistance was significantly more common for several antibiotics when nurses were using the chlorhexidine-containing soap or when the skin on their hands was damaged. In a 6-year study, Gordin et al reported a decrease in the number of health care-associated methicillin-resistant S. aureus and vancomycin-resistant enterococcus acquired by patients when an alcohol product was used for staff hand hygiene, but we did not examine the rates of clinical infections caused by antibiotic-resistant organisms among neonates in our study.

Although others have reported a higher prevalence of certain potential pathogens such as S. aureus and gram-negative bacteria among nurses with damaged skin, this may be the first report of a possible relationship between hand hygiene product, skin condition, and antimicrobial resistance. Irritant contact dermatitis and other skin problems are prevalent among health care providers, and the detergent base in soaps is one of the primary causes.

To our knowledge, there has been no biologic mechanism identified that could explain our observed association between chlorhexidine use and antibiotic resistance. It is possible that the link may be an intermediary one, ie, that the soap is associated with more skin damage and that it is the damaged skin that facilitates the colonization of hands with hospital-associated resistant flora. We have previously reported, in fact, that skin condition was significantly better when the alcohol product as compared with the antiseptic soap was used among these nurses. An alternative explanation is that microorganisms may develop resistance mechanisms to the chlorhexidine itself, as has been described with triclosan, a bisphenol ingredient used in some antiseptic products. The potential association between the antiseptic soap and increased antibiotic resistance clearly needs further study. In the meantime, the Centers for Disease Control and Prevention's recommendations regarding use of alcohol hand hygiene products and attention to skin health among staff hands may be important for reducing the possibility that the hands of health care personnel could become reservoirs of antimicrobial resistance.

This study had several limitations that must be considered when assessing the relevance of our findings. First, we only obtained cultures every 3 months and did not sample every nurse participant at every sampling interval, although the average number of samples was 7/nurse. Clearly, this represents only a snapshot of changes in skin flora that might occur over time. Second, only a single colony-forming unit of each morphologic type was speciated from each hand sample. Hence, it is possible that several strains or different clones of any organism, in particular the coagulase-negative staphylococci, were present but not detected. Furthermore, we were unable to study multidrug-resistant, gram-negative bacteria on nurses' hands because there were too few isolates. Finally, there may have been unmeasured factors that changed during the periods when the 2 hand hygiene products were used that could have affected resistance patterns.

CONCLUSION

In summary, it appears that the normal skin flora of nurses has become increasingly resistant when compared with earlier studies. Furthermore, in this study hand hygiene product and skin condition were associated with antibiotic resistance in the staphylococcal flora; for some antibiotics, an increased risk of resistance was found when nurses used an antiseptic soap rather than an alcohol product and when their skin was damaged. The potential impact of various hand hygiene products on the numbers, types, and resistance patterns of staff hand flora warrants further research.

References


Implications of the changing face of *Clostridium difficile* disease for health care practitioners

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Recent reported outbreaks of *Clostridium difficile*-associated disease in Canada have changed the profile of *C difficile* infections. Historically, *C difficile* disease was thought of mainly as a nosocomial disease associated with broad-spectrum antibiotics, and the disease was usually not life threatening. The emergence of an epidemic strain, BI/NAP1/027, which produces a binary toxin in addition to the 2 classic *C difficile* toxins A and B and is resistant to some fluoroquinolones, was associated with large numbers of cases with high rates of mortality. Recently, *C difficile* has been reported more frequently in nonhospital-based settings, such as community-acquired cases. The *C difficile* disease is also being reported in populations once considered of low risk (children and young healthy women). In addition, poor response to metronidazole treatment is increasing. Faced with an increasing incidence of *C difficile* infections and the changing profile of patients who become infected, this paper will reexamine the current concepts on the epidemiology and treatment of *C difficile*-associated disease, present new hypotheses for risk factors, examine the role of spores in the transmission of *C difficile*, and provide recommendations that may enhance infection control practices. (Am J Infect Control 2007;35:237-53.)

Recent events have refocused attention on *Clostridium difficile* infections and caused the medical community to reevaluate its assumptions about the virulence, known risk factors, and possible modes of transmission of this important health care-associated pathogen.

*Clostridium difficile*–associated disease (CDAD) is traditionally thought of as a nosocomial pathogen that may cause limited, small outbreaks. The pathogenesis of CDAD involves a triad of factors: (1) disruption of normal intestinal flora (usually by broad-spectrum antibiotics), (2) exposure to *C difficile* (usually during hospitalization), and (3) host factors (comorbidity and advanced age or impaired immune status). The CDAD is not a trivial disease because *C difficile* may have life-threatening complications, such as ileal perforation, fulminant colitis, toxic megacolon, or brain empyema. *Clostridium difficile*-associated disease has also been shown to extend hospital stays a mean of 4 to 14 days, increase the risk of other nosocomial infections, and increase health care costs. Although most patients with an initial episode of CDAD respond well to either metronidazole or vancomycin, 20% develop recurrent episodes of CDAD that occur episodically over years, despite repeated antibiotic treatments.

After more than 20 years of research and experience with *C difficile*, health care providers became complacent that methods of transmission, risk factors, effective infection control practices, and effective therapies were well understood. However, the incidence of CDAD continues to rise despite continued focus on methods to reduce the number of hospital cases, to eradicate the spores of *C difficile* from the environment, and to find effective strategies for treating patients with recurrent CDAD.

In 2002, hospitals in Quebec, Canada, reported outbreaks of high numbers of cases of serious CDAD infections that were health care associated and had a high mortality rate. These outbreaks challenged practitioners to reevaluate diagnosis, treatment, and infection control strategies in light of the changing profile of CDAD. The purpose of this paper is to summarize and integrate these new findings into our understanding of CDAD and to discuss how these new data should influence infection control practices.
INCIDENCE IN NORTH AMERICA

In the United States, rates of CDAD have continued to increase since the 1990s despite established infection control programs and effective treatments (Table 1). Higher CDAD rates are typically reported in teaching hospitals,25 on medical and surgical services or intensive care units, and among elderly patients.15

In December 2002, CDAD outbreaks of an unexpectedly large number of cases were reported in 30 hospitals in the providence of Quebec, Canada. From 2003 through 2005, outbreaks spread to adjacent hospitals.12 These outbreaks were characterized by a 4.5-fold higher incidence (156.3/100,000) over historical rates (35.6/100,000 in 1991), nearly a 5-fold increase in mortality (4.5% in 1991 to 22% in 2004), and a 2.5-fold increase in complicated CDAD cases (7.1% in 1991 to 18.2% in 2003).12,26 An estimated 14,000 cases, including 2000 deaths (28% mortality rate), were reported in Quebec during this outbreak period.27

C difficile was the primary cause of mortality in 3.2% of the 2000 deaths. It was proposed that possible causes for these outbreaks included the emergence of a hypervirulent strain of C difficile, suboptimal infection control practices, or a poor response to the standard treatment for CDAD (metronidazole).12,19,28

CHARACTERIZATION OF THE BI/NAP1/027 STRAIN

The designation of the strain associated with the Canadian outbreaks, BI/NAP1/027, combines the results of several strain typing methods: restriction-endonuclease analysis (REA) group BI, pulsed-field gel electrophoresis (PFGE) type NAP1 (North American PFGE type 1), and ribotype 027.12 This strain is of toxino-type III (presence of binary toxin CDT and contains an 18-base pair [bp] tcdC deletion). As a result of the tcdC deletion, toxin A and B production is not inhibited.29 Strains with the tcdC deletion have been found to produce 16 times more toxin A and 23 times more toxin B than other C difficile strains that do not have this gene deletion.30 Another novel characteristic of this strain is that it is resistant to gatifloxacin and moxifloxacin. This is a recent development because older isolates of BI/NAP1 were not resistant to fluoroquinolones.31 As fluoroquinolones have become one of the most prescribed groups of antibiotics, the development of antibiotic resistance in health care-associated strains of CDAD has become a focus of clinical concern.

Because of the unprecedented increase in the number of cases in Canada caused by this strain, historical C difficile isolate collections were reexamined for the presence of the BI/NAP1 strain. McDonald et al found that 96 (51%) of 187 isolates from 8 United States hospitals collected between 2000 and 2003 were typed as BI/NAP1.31 This strain was found in 2 hospitals in the United States before the appearance of the Canadian outbreaks. This strain is not new because it was first isolated in 1984, although infrequently (14 of 6000 isolates collected before 2001). The difference is that older isolates of BI/NAP1 were not associated with outbreaks or resistant to fluoroquinolones.31 Since the Canadian outbreaks, the BI/NAP1 strain has been found in the United States,32 the United Kingdom,33 and The Netherlands.34

Implications for infection control: Examination of individual clinical cases and incidence rates of CDAD may not reveal the presence of an outbreak caused by hyper-toxigenic-producing strains. Although few hospital laboratories currently assay for C difficile by culture and strain type C difficile isolates, these would be a valuable tool to track the occurrence of specific strains of C difficile and the transmission through an institution. Strain typing methods such as ribotyping or pulsed-field gel electrophoresis are not readily available at most hospital laboratories.

VIRULENCE OF C DIFFICILE STRAINS

The main virulence factors for C difficile are an enterotoxin designated toxin A and a cytotoxin designated toxin B. Both toxins disrupt the actin cytoskeleton of intestinal epithelial cells by the UDP-glucose-dependent glycosylation of Rho and Ras proteins. Usually C difficile isolates from CDAD patients produce both toxin A and B, but nontoxigenic strains (A−B−) or atypical toxin strains (A−B+) may also cause symptoms.4,5,56 Of 153 isolates from CDAD cases at the Chicago Veterans Administration (VA) Medical Center, 123 (80%) were A+B+, 13 (9%) were non-toxigenic (A−B−), and 17 (11%) were toxin variants (A−B+).37 The frequency of toxin variants (A−B+) isolates from CDAD cases was found to be higher in other populations (59% of 77 isolates) in Japan.38 Strains that produce only toxin A and not B (A+B−) have only been reported in 1 patient with recurrent CDAD.39 As shown in Fig 1, the pathogenicity locus (PaLoc) of C difficile contains 2 genes encoding toxin A (tcdA) and toxin B (tcdB) and 3 other important genes: a positive regulator for toxin production (tcdR), a gene producing a holin-like protein involved in membrane disruption (tcdB), and a negative regulator for toxin production (tcdC).29,40

A third toxin, a binary toxin designated CDT (actin-specific ADP-ribosyltransferase), was described in 1988 from the C difficile strain CD196.41 The binary toxin is composed of 2 independent proteins: cdtA (enzymic component that catalyzes the ADP-ribosylation of actin and causes cytoskeleton disorganization) and
cdtB (binding component that recognizes cell-surface receptors and causes the enzymic component to be internalized).42 The location of the binary genes has not been determined, but it is not located within the PaLoc locus. The prevalence of binary toxin in C difficile isolates from human sources ranges from 1% to 16%.36,37,43-45 In some outbreaks, binary toxin isolates were also found in 16% of non-internalized).42 The location of the binary genes has not been determined, but it is not located within the PaLoc locus. The prevalence of binary toxin in C difficile isolates from human sources ranges from 1% to 16%.36,37,43-45 In some outbreaks, binary toxin-positive strains of C difficile are more frequently isolated. Binary toxin was detected in 65% of the C difficile isolates among different REA strain types from a hospital in Pennsylvania during 2001-2002.32 Most of the binary toxin isolates also produce toxins A and B, but binary toxin isolates were also found in 16% of non-toxigenic (A–B–) C difficile isolates37 and in 11% of toxin variant (A–B+) strains.36 Recently, binary toxin strains of C difficile have been found to be resistant to fluoroquinolones, although there is no direct link between the development of antibiotic resistance and the carriage of binary toxin. The association between binary toxin and pathogenicity is still unclear. Binary toxin-positive isolates are cytopathic in cell culture and, when tested in CDAD animal models, A–B–CDT+ strains were found to cause fluid accumulation in rabbit ileal loops but not diarrhea or death in hamster models.46 To determine whether strains carrying binary toxin were associated with increased virulence in humans, 26 CDAD cases of patients who were toxin A+B+CDT+ were compared with 42 CDAD controls who were toxin A+B+CDT−.42 The binary-positive cases reported more abdominal pain (64% vs 39%, respectively) and reported long (>7 days) course of diarrhea (56% vs 29%, respectively). Unfortunately, no data on the strain types were reported in this study. To analyze the influence of binary toxin alone, without the confounding presence of toxin A or B, it would be necessary to compare the severity of CDAD in patients who are A–B–CDT+ with patients who are A–B–CDT−, but this has not been reported.

The presence of 2 major toxins (A or B) is usually more predictive of severe CDAD cases rather than infection with a specific strain or the presence of binary toxin. One study found that the fecal toxin concentration was associated with increasing CDAD severity (0.5 U/g in mild CDAD, 6.8 U/g in moderate, and 149 U/g in severe CDAD (P < .001), but the strain type was not associated with disease severity.47 This was in contrast to an older study that did not find significant differences in toxin presence, toxin amount, or immunoblot strain type in CDAD cases compared with asymptomatic carriers.48 The new BI/NAP1 strain of C difficile appears to be an exception to the rule that strain type does not predict the severity of CDAD. A study in the United States linked an increase in colectomies because of fulminant cases caused by the BI/NAP1 strain.31 It is still unclear whether the apparent increased severity of CDAD cases caused by the BI/NAP1 strain is due to increased toxin A and B production, presence of binary toxin, resistance to gatifloxacin and moxifloxacin, or another undescribed virulence factor.28,30,31

**Table 1. Changes in the frequency of Clostridium difficile-associated disease in various populations**

<table>
<thead>
<tr>
<th>Population</th>
<th>CDAD rate (yr)</th>
<th>References (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secular trends</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized patients, Quebec, Canada</td>
<td>35.6/100,000 (1991)</td>
<td>Pepin et al, 2004 (12)</td>
</tr>
<tr>
<td></td>
<td>156.3/100,000 (2003)</td>
<td></td>
</tr>
<tr>
<td>Veterans Administration Facilities, United States</td>
<td>5.1/1000 (1994)</td>
<td>Perlin, 2005 (13)</td>
</tr>
<tr>
<td>NNIS, United States</td>
<td>4.7/10,000 (1994)</td>
<td>Archibald et al, 2004 (14)</td>
</tr>
<tr>
<td></td>
<td>5.8/10,000 (2000)</td>
<td></td>
</tr>
<tr>
<td>NHDS, United States</td>
<td>31/100,000 (1996)</td>
<td>McDonald et al, 2006 (15)</td>
</tr>
<tr>
<td></td>
<td>61/100,000 (2003)</td>
<td></td>
</tr>
<tr>
<td>Community acquired</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community acquired, United States</td>
<td>7.6/100,000 (2004-2005)</td>
<td>CDC, 2005 (16)</td>
</tr>
<tr>
<td>Community acquired, managed care, United States</td>
<td>3.2/100,000 (1993-1997)</td>
<td>Frost et al, 1999 (17)</td>
</tr>
<tr>
<td>Community acquired, United Kingdom</td>
<td>22/100,000 (1994-2004)</td>
<td>Dial et al, 2000 (19)</td>
</tr>
<tr>
<td>Community acquired, Sweden</td>
<td>25/100,000 (1999-2000)</td>
<td></td>
</tr>
<tr>
<td>High-risk populations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elderly patients, United Kingdom</td>
<td>39.5/100</td>
<td>Settle et al, 1998 (21)</td>
</tr>
<tr>
<td>Adult oncology, France</td>
<td>13.2/100</td>
<td>Blot et al, 2003 (22)</td>
</tr>
<tr>
<td>General medicine ward, United States</td>
<td>7.8/100</td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td>Burn ICU, Kuwait</td>
<td>5.9/100</td>
<td>Rotimi et al, 2002 (24)</td>
</tr>
<tr>
<td>Elderly patients with NAP1 strain</td>
<td>865/100,000</td>
<td>Pepin et al, 2004 (12)</td>
</tr>
</tbody>
</table>

CDAD, Clostridium difficile-associated disease; NNIS, National Nosocomial Infections Surveillance system; NHDS, National Hospital Discharge Survey; ICU, intensive care unit.4

1 NNIS incidence density, cases per 10,000 patient days.

2 NHDS cases per discharges.
Implications for infection control: Surveillance for the BI/NAP strain of C difficile in health care facilities may be of value to predict a possible increase in severe cases of CDAD and define potential outbreaks; therefore, early intervention of infection control measures could prevent potential outbreaks. However, severe cases of CDAD have been reported associated with other strains besides BI/NAP/027. The role of binary toxin and virulence of CDAD is unclear.

COMMUNITY-ACQUIRED CDAD

The preconception that CDAD is mainly a nosocomial disease has been challenged recently by the increasing frequency of community-acquired cases. In the past, rates of community-acquired CDAD have been low (Table 1), ranging from 3.2 to 16.2/100,000. Unfortunately, the definition of community acquired varies. Some studies of community-acquired CDAD in outpatients failed to determine whether there had been recent hospitalization and did not culture for C difficile at admission. One study, which did culture newly admitted patients at admission, found that of the 112 patients who had positive C difficile assays during the study, 74% were negative on admission but acquired C difficile during their stay on the study ward; 21% were admitted with a positive C difficile assay and had a history of hospitalization (≤3 months); and only 5% were community acquired (positive at admission with no history of hospitalization).

Currently, more community-acquired cases of CDAD are being reported (Table 1). Patients admitted into 2 hospitals over 4.5 years in British Columbia with a primary diagnosis of CDAD were reviewed, and 67 (44%) had community-acquired C difficile. In France, significantly more of the 26 C difficile isolates with binary toxins were community acquired (65% vs 36%, respectively, P < .05), however, this study defined community acquired as “onset of symptoms within 3 days after admission, regardless of previous hospitalizations,” which probably overestimated the frequency of community-acquired cases by including cases that may have been previously hospitalized. In the United States, community-acquired cases of the BI/NAP1 strain have been reported in 4 states. These 23 community-acquired CDAD patients were young (48% ≤18 years of age), 35% had no history of recent antibiotic exposure (in the prior 3 months), and 30% were thought to have acquired C difficile from close contacts with diarrheal disease. Of the 23 community-acquired cases, 26% required hospitalization and 35% relapsed.

Implications for infection control: Community-acquired CDAD is becoming a greater problem. The profile of affected patients may be different than health care-associated CDAD cases and should prompt appropriate laboratory investigation in young people with diarrheal disease. If community-acquired cases of CDAD continue to become more frequent, diagnostic algorithms and standard definitions may need to be expanded from including only patients with a recent hospitalization to include the community-acquired cases as CDAD.

SOURCES OF C DIFFICILE

Although the majority of cases of CDAD are reported in the hospital setting, CDAD should be considered a health care-associated disease because it occurs in long-term care facilities, day care facilities, and outpatient clinics. The question of whether the organism is acquired in the hospital or is already present as part of the patient’s indigenous microflora has not been fully answered. Asymptomatic carriers of C difficile may become symptomatic after exposures to specific risk factors in the hospital lead to overgrowth and toxin production, triggering diarrheal symptoms. Unfortunately, few investigators have both cultured patients at admission to a health care facility and asked about prior history of recent hospitalization. It has been accepted that if the newly admitted patient has a negative assay for C difficile and has had no history of prior hospitalization, then if CDAD develops during the hospital stay, the case can be
considered as nosocomial. However, as the specificity of 
*C difficile* toxin assays range from 88% to 99% and 
*C difficile* can be frequently detected after an initial neg-
ative *C difficile* toxin assay, false-negative results may 
occur.\(^{55,56}\) A recent study using a more sensitive poly-
merase chain reaction (PCR) method detected *C difficile*
in 53% of healthy, community-based adults (with no 
history of hospitalization or antibiotic exposure) that 
conventional PCR methods or conventional toxin 
assays did not detect.\(^{57}\) Therefore, low-level, endemic 
carriage of *C difficile* may be more common than previ-
ously thought. Only after patients are exposed to agents 
that disrupt normal intestinal microflora (such as anti-
biotics, surgery, medications) that allows the upsurge 
in the numbers of *C difficile* organisms do laboratory 
assays detect *C difficile* frequently. Other evidence from 
patients who have multiple recurrences of CDAD 
supports endogenous carriage. A study using PCR ribo-
typing of 89 *C difficile* isolates reported that most recur-
rences (90%) were due to the endogenous strain of 
*C difficile* acquisition, whereas only 10% of the recur-
rences were due to a new strain.\(^{20}\) The source of the 
original *C difficile* strain is still in question because 
most (84%) had a prior history of hospitalization in this 
study. In another study of 18 patients with recurrent 
CDAD, 67% of the isolates from the recurrence were 
identical to the isolates from the initial episode, and 
only 33% had been reinfected with a new strain of *C dif-
ficile*.\(^{58}\) Reliance on strain typing to determine epidemi-
ologic spread and source of infection was recently 
called into doubt by a study that found simultaneous 
carriage of multiple types of strains in patients with 
CDAD. Of 23 patients with a primary episode of 
CDAD, 2 (8.7%) carried 2 distinct PCR ribotypes, and, 
of 23 patients with recurrent CDAD, 6 (26%) had differ-
ent *C difficile* strains isolated from the same fecal 
sample.\(^{59}\)

Sources of community-based or nonhealth care set-
tings of *C difficile* may include exposure to spores in the 
soil, carriage by pets (dogs, cats, horses), contaminated 
foods, or exposure to household contacts with diar-
rhea.\(^{60,61}\) In 102 health care visitation dogs in Canada, 
58% were positive for *C difficile*, 71% of those isolates 
produced toxins, and 1 was typed as the hypervirulent 
BI/NAP1 strain.\(^{62,63}\) Although few reports of animal to 
human transmission of *C difficile* have been reported, 
these types of sources may be overlooked, especially 
in community-acquired CDAD.\(^{16}\)

Implications for infection control: As community-
acquired cases are more frequently reported, the 
search for the source of *C difficile* infections needs to 
be expanded to nonhospital vectors. Further research 
with more sensitive *C difficile* assays is needed to deter-
mine the prevalence of endogenous carriage of *C diffi-
cile* to correctly target the preventive measures.

### RISK FACTORS

#### Emerging populations at risk

Reports of CDAD in what has been considered as 
“low risk” populations (young healthy women and 
children) have increased recently. Children are known 
to develop CDAD, but reported outbreaks are less com-
mon than in adult patients.\(^{54}\) Reports from Canada dur-
ing 2000-2003 found that 200 young children (mean 
age, 5.4 years) developed CDAD, of whom 23% were suf-
iciently serious to require hospitalization, and 31% had 
at least 1 recurrence.\(^{64}\) Whether the high rate of hospi-
talization was due to a more virulent *C difficile* strain 
or shifts in other risk factors in the pediatric population 
was not reported. A high frequency (18%) of CDAD was 
detected in 250 children aged 5 to 12 years on antibi-
otics in a hospital in India.\(^{65}\) *Clostridium difficile*-associ-
dated disease was recently found in another population 
traditionally considered of low risk (young peripartum 
women). Ten women developed CDAD, of whom 40% 
were sufficiently severe to require hospitalization, and 50% 
had at least 1 recurrence of disease.\(^{16}\) Of these 10 
cases, 64% had isolates of the recent epidemic strain 
(BiNAP1/027) that carries the binary toxin and is consid-
ered more virulent than other *C difficile* strains.\(^{50}\)

#### Proton pump inhibitors

Association of CDAD with antacid therapy or gastric 
acid-lowering medications remains controversial; sev-
eral studies found a positive association\(^{8,66}\) but an-
other study found no significant association.\(^{67}\)

Recently, 3 studies have shown that proton pump 
inhibitors (PPI) were associated with higher rates of 
CDAD,\(^{19,68,69}\) whereas 2 studies did not find a signifi-
cant association between CDAD and PPIs.\(^{70,71}\) At the 
time of the Canadian outbreaks, a cohort study of 
1187 inpatients at a Montreal teaching hospital from 
August 2002 to May 2003 found CDAD in 81 (68%) of 
the patients, and those who used PPIs had twice the 
risk of CDAD (odds ratio [OR], 2.1; 95% CI: 1.2-3.5).\(^{19}\)

Another study in community-acquired CDAD cases 
found that people taking PPI had nearly 5 times the 
risk for developing CDAD.\(^{68}\) In another study in a 
long-term facility (347 beds) in New York, significantly 
more (60%) of CDAD cases used PPI compared with 
only 32% of control residents.\(^{69}\) The PPIs are fre-
cently used in hospitalized patients (49%-68%), but 
it is apparent that more research is needed before lim-
iting PPI use in hospitals, as was recently suggested.\(^{19}\)

#### Fluoroquinolone therapy

Fluoroquinolones became the most common class of 
antibiotics prescribed to adults in the United States.\(^{72}\)
Historically, fluoroquinolone use was associated with
a 2- to 13-fold risk of CDAD but, because this type of antibiotic was not frequently prescribed, the absolute numbers of quinolone-associated CDAD were low.\textsuperscript{10,73-75}

One of the proposed theories behind the large reported outbreaks in Canada was that a fluoroquinolone-resistant strain (BI/NAP/027) was circulating at the same time when fluoroquinolone use was common in Canadian hospitals. Two studies in Canada found a significantly higher risk of CDAD for patients prescribed fluoroquinolones. In a study of 12 hospitals in Quebec, Canada, during 2004, CDAD case patients had nearly 4 times higher rates of fluoroquinolone use (OR, 3.9; 95% CI: 2.3-6.6) compared with matched controls.\textsuperscript{28} Ciprofloxacin, gatifloxacin, and moxifloxacin were significantly associated with CDAD, whereas levofloxacin was not. A retrospective cohort study performed of 5619 patients admitted to 1 hospital from 2003 to 2004 in Quebec found that use of fluoroquinolones was high (29%). Patients given fluoroquinolones have 3.4 times the risk of developing CDAD than those patients not given this class of antibiotic.\textsuperscript{70}

An opportune time to study the effect of an antibiotic on health care-associated pathogen rates is when a hospital changes its formulary recommendations. Two such studies found a higher incidence of CDAD associated with the switch to gatifloxacin. A formulary replacement of levofloxacin by gatifloxacin occurred at the Atlanta VA long-term care facility in October 2001.\textsuperscript{53} Before the formulary change, the rate of CDAD was 0.4/1000 patient-days and after the switch, the CDAD rate increased to 1.3/1000. After levofloxacin was reintroduced on July 2002, the rate of CDAD fell to pregatifloxacin levels (0.3/1000 patient-days). These results were confounded by a single facility-wide hypochlorite disinfection performed in June 2002. However, because CDAD rates continued to be low for months following the single disinfection process, these results favor a central causative role for the formulary antibiotic change for the increase in CDAD rates. A nested case-control study of CDAD cases at this institution found that gatifloxacin use was significantly more common in CDAD cases than in controls (67% vs 25%, respectively, \textit{P} < .05).\textsuperscript{53} Another study at a 600-bed tertiary-care teaching medical center in Pittsburgh documented an increased rate of CDAD after a formulary change from ciprofloxacin to levofloxacin.\textsuperscript{76} The formulary change occurred March 1999 when the rate of CDAD was 2.7/1000 discharges, and, 9 months after the switch to levofloxacin, the rate of CDAD increased to 6.8/1000 discharges. A nested case-control study of 203 CDAD cases and 203 matched (admission date, type of medical service, and length of stay [LOS]) controls found that levofloxacin use was associated with an increased risk of CDAD (OR, 2.0; 95% CI: 1.2-3.3).

Implications for infection control: Fluoroquinolone use is a major risk factor for CDAD. Although data are preliminary regarding the precise risk for individual members of this antibiotic class, it is clear that changes in hospital formulary preferences among fluoroquinolones have a profound effect on CDAD rates. The role of PPIs as a risk factor for CDAD is not as clear.

**INFECTION CONTROL PRACTICES**

Historically, the control of \textit{C difficile} outbreaks have relied on multiple strategies, including (1) interrupting the routes of transmission by handwashing, patient isolation, enteric precautions; (2) reducing the risk of exposure to \textit{C difficile} spores using environmental disinfectants or disposable medical equipment; (3) reducing the pool of susceptible patients by antibiotic control policies that limit broad-spectrum antibiotic use; and (4) reducing infectious cases by prompt diagnosis and effective treatment.\textsuperscript{51,55} Although the strengths of the evidence-based effectiveness of these different strategies vary (Table 2), infection control policies have relied on a combination of these methods to control CDAD.

With the upsurge in reported CDAD outbreaks and the emergence of an epidemic, hypervirulent strain of \textit{C difficile}, reliance on standard infection control practices may become more important. One explanation for the reported outbreaks in Canada was substandard infection control practices.\textsuperscript{113} The decline of CDAD cases in 2005 (from >40 cases/1000 admissions to <12 cases/1000 admissions) was associated with more stringent infection control and cleaning practices that began in June 2004.\textsuperscript{113} During this same time period, no changes in antibiotic use occurred.\textsuperscript{114} Other clinicians claim that changes in infection control policies did not significantly reduce CDAD rates.\textsuperscript{115} The Quebec provincial surveillance system reported that CDAD rates in late 2004 and early 2005 were similar to the time of preinfection control practice changes.\textsuperscript{116} Regardless of the cause of the upsurge in reported cases in Canada, recent research has focused (Table 3) on the effective control of CDAD in health care settings in 6 strategic areas: (1) surveillance programs, (2) interrupting transmission, (3) reducing exposure to \textit{C difficile} spores, (4) antibiotic stewardship programs, (5) preventive vaccines, and (6) effective treatments. However, the most effective infection control programs are integrated programs that combine all 6 strategies.\textsuperscript{51,55,112}

**Surveillance**

Active surveillance and reporting of CDAD is not required in the United States, but mandatory reporting was started in the United Kingdom in 2004.\textsuperscript{120} The Veterans Health Administration (VHA) is the single largest
provider of health care in the United States, operating 163 hospitals and 130 long-term care facilities. Within the VHA, 93% of the facilities operate periodic or continuous surveillance for \textit{C. difficile}. Hospital surveillance programs have shown to reduce rates of methicillin-resistant \textit{Staphylococcus aureus} but have not been studied specifically to observe its effect on CDAD rates. The value of an active surveillance program includes the documentation of secular trends, the detection of emergent antibiotic-resistant strains, the investigation of outbreaks, and the ability to gather data on the effectiveness of infection control programs.

### Table 2. Historical evidence rating for studies on strategies to limit the transmission of \textit{Clostridium difficile}

<table>
<thead>
<tr>
<th>Recommended strategies</th>
<th>Studies by evidence-based rating, reference (No.)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance</td>
<td></td>
</tr>
<tr>
<td>Secular trend tracking</td>
<td>Frost et al, 1999 (17)</td>
</tr>
<tr>
<td></td>
<td>Rexach et al, 2005 (77)</td>
</tr>
<tr>
<td></td>
<td>Archibald et al, 2004 (14)</td>
</tr>
<tr>
<td></td>
<td>Van den Berg et al, 2004 (78)</td>
</tr>
<tr>
<td></td>
<td>McCoubrey et al, 2003 (79)</td>
</tr>
<tr>
<td></td>
<td>Wult et al, 2003 (80)</td>
</tr>
<tr>
<td></td>
<td>Noren et al, 2004 (20)</td>
</tr>
<tr>
<td></td>
<td>Geric et al, 2004 (37)</td>
</tr>
<tr>
<td></td>
<td>Kato et al, 2005 (81)</td>
</tr>
<tr>
<td></td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
<tr>
<td>Typing of \textit{C. difficile} strains</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McCoubrey et al, 2003 (79)</td>
</tr>
<tr>
<td></td>
<td>Wult et al, 2003 (80)</td>
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<td></td>
<td>Noren et al, 2004 (20)</td>
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<td>Geric et al, 2004 (37)</td>
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<td></td>
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<td></td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
<tr>
<td>Outbreak investigations to reveal weak areas</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
<tr>
<td>Prevent the spread of \textit{C. difficile} organism</td>
<td></td>
</tr>
<tr>
<td>Handwashing with chlorohexidine or use of gloves</td>
<td>Johnson and Gerding, 1990 (83)</td>
</tr>
<tr>
<td></td>
<td>Bettin et al, 1994 (86)</td>
</tr>
<tr>
<td></td>
<td>Pittet et al, 2000 (84)</td>
</tr>
<tr>
<td></td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td></td>
<td>Johnson and Gerding, 1998 (85)</td>
</tr>
<tr>
<td></td>
<td>Boyce and Pittet, 2002 (87)</td>
</tr>
<tr>
<td></td>
<td>Salem et al, 2002 (88)</td>
</tr>
<tr>
<td></td>
<td>Kaatz et al, 1998 (90)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
<tr>
<td></td>
<td>Wilcox and Fawley, 2000 (92)</td>
</tr>
<tr>
<td></td>
<td>Hota, 2004 (94)</td>
</tr>
<tr>
<td>Environmental disinfectants</td>
<td>Wilcox et al, 2004 (89)</td>
</tr>
<tr>
<td></td>
<td>Kaatz et al, 1998 (90)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
<tr>
<td></td>
<td>Wilcox and Fawley, 2000 (92)</td>
</tr>
<tr>
<td>Use of disposable medical equipment</td>
<td>Jernigan et al, 1998 (95)</td>
</tr>
<tr>
<td></td>
<td>Brooks et al, 1992 (96)</td>
</tr>
<tr>
<td></td>
<td>Boone et al, 1998 (97)</td>
</tr>
<tr>
<td></td>
<td>McFarland et al, 1989 (23)</td>
</tr>
<tr>
<td></td>
<td>Verity et al, 2001 (98)</td>
</tr>
<tr>
<td>Patient isolation/cohorting</td>
<td></td>
</tr>
<tr>
<td>Treatment of asymptomatic carriers not effective</td>
<td>Johnson et al, 1992 (99)</td>
</tr>
<tr>
<td></td>
<td>Bender et al, 1986 (100)</td>
</tr>
<tr>
<td></td>
<td>Kerr et al, 1990 (101)</td>
</tr>
<tr>
<td>Reduce clinical burden of disease</td>
<td></td>
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<tr>
<td>Antibiotic restriction programs</td>
<td>Pear et al, 1994 (102)</td>
</tr>
<tr>
<td></td>
<td>Ho et al, 1996 (104)</td>
</tr>
<tr>
<td></td>
<td>McNulty et al, 1997 (105)</td>
</tr>
<tr>
<td></td>
<td>Settle et al, 1998 (21)</td>
</tr>
<tr>
<td></td>
<td>Ludlam et al, 1999 (106)</td>
</tr>
<tr>
<td></td>
<td>Carling et al, 2003 (107)</td>
</tr>
<tr>
<td></td>
<td>Khan and Chessbrough, 2003 (108)</td>
</tr>
<tr>
<td></td>
<td>Thomas et al, 2003 (109)</td>
</tr>
<tr>
<td>Integrated infection control programs</td>
<td></td>
</tr>
<tr>
<td>Combinations of the above</td>
<td>Stone et al, 1998 (110)</td>
</tr>
<tr>
<td></td>
<td>Zafar et al, 1998 (111)</td>
</tr>
<tr>
<td></td>
<td>Apisarnthanarak et al, 2004 (112)</td>
</tr>
<tr>
<td></td>
<td>Struelens et al, 1991 (82)</td>
</tr>
</tbody>
</table>

*A. Evidence from randomized, controlled trials in patients with \textit{C. difficile}-associated disease; B. Evidence from open trials, pre- and postintervention trials, crossover trials in healthy volunteers or uncontrolled trials; C. Observational studies, expert opinion, case reports, anecdotal evidence only.*
or indirectly through contaminated environmental surfaces. *Clostridium difficile* has been cultured from the hands of health care personnel, patients, and visitors in rooms of CDAD patients, and national guidelines recommend thorough handwashing and/or use of disposable gloves. In an effort to reduce CDAD rates at several hospitals, alcohol hand sanitizers were installed, but this infection control practice did not have any significant impact on the rates of CDAD. Alcohol hand gels were introduced at the Veterans Affairs Medical Center in Washington, DC, but had no effect on CDAD rates (3.2/10,000 patient-days before and 3.4/10,000 after). The lack of effectiveness for alcohol in these 2 studies is not surprising because alcohol is used to stimulate *C difficile* spore germination in culture broths. Therefore, handwashing using soap or chlorhexidine or use of disposable gloves is still recommended.

### Reducing environmental contamination

The persistence of *C difficile* in health care settings is largely due to its ability to shed durable spores on a wide variety of environmental sites. The Society of Hospital Epidemiologists of America (SHEA) and the Centers for Disease Control and Prevention (CDC) continue to recommend the use of unbuffered 1:10 hypochlorite solution rather than detergents to disinfect surfaces. Hypochlorite solutions have been found to be more effective than other types of environmental disinfectants, including detergents, glutaraldehyde, combination products of acetic acid and hydrogen peroxide, acidified bleach, regular bleach, and hydrogen peroxide were found to inactivate *C difficile* spores within 15 minutes, but are all strong oxidizers and not recommended for routine use. Wilcox et al recently confirmed the usefulness of hypochlorite disinfectants on a ward that showed a significant reduction in CDAD rates (8.9/100 admissions before and 5.3/100 after, *P* < .05), but a ward using detergents did not show a change in CDAD rates. The continued development of an environmental disinfectant that is sporicidal yet sufficiently nontoxic for routine use is challenging.

### The role of spores

Spores are part of the natural life cycle of *C difficile*. Humans may ingest, inhale, or swallow the spores, which are then passed through the stomach. Fordtran et al showed that, at normal gastric pH (<4.0), vegetative cells of *C difficile* die, but spores are not affected. In the acidic environment, the spores are not killed directly, but germinant binding may be inhibited. Germinants are factors that initiate spore germination and include heat, free bile acids, and lactate. The PPIs, which have been associated with higher CDAD rates, raise gastric pH, allowing germinants to bind more effectively. This may be the mechanism behind the observation that patients given PPI have increased susceptibility to CDAD. Gastric acid acts as a natural defense mechanism, not by directly killing spores, but by inhibiting spore germination. Once the spores reach the small intestine, most germinate within 1 hour. Vegetative cells of *C difficile* may flourish in the intestines only if the normal microbial flora have been disrupted. Normal flora has the ability to inhibit the colonization of opportunistic pathogens through a complex mechanism termed "colonization resistance." Once this normal microflora barrier is disrupted (for example, by broad-spectrum antibiotics, surgery, chemotherapy, or other medications), *C difficile* can colonize, reproduce, and produce toxins. These toxins (toxins A and B) attach to enterocytes, causing cellular disruption and fluid loss, resulting in diarrhea.

As vegetative *C difficile* cells die, new spores are formed and released in the stool into the environment. Some spores may remain lodged in the intestines, acting as seeds for future CDAD episodes.

### Table 3. Recent studies of interventions to limit the transmission of *Clostridium difficile*

<table>
<thead>
<tr>
<th>Strategy</th>
<th>CDAD incidence before intervention</th>
<th>CDAD incidence after intervention</th>
<th>References (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interrupting routes of transmission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol hand sanitizers</td>
<td>2.7/1000 patient-days</td>
<td>6.8/1000 patient-days*</td>
<td>Muto et al, 2005 (76)</td>
</tr>
<tr>
<td>Alcohol hand gel</td>
<td>3.2/10,000 patient-days</td>
<td>3.4/10,000 patient-days, ns</td>
<td>Gordin et al, 2005 (117)</td>
</tr>
<tr>
<td>Reducing exposure to <em>C difficile</em> spores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypochlorite disinfectant</td>
<td>8.9/100 admissions</td>
<td>5.3/100 admissions*</td>
<td>Wilcox et al, 2004 (89)</td>
</tr>
<tr>
<td>Antibiotic stewardship programs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduce cephalosporins</td>
<td>3.9/100 admissions</td>
<td>1.2/100 admissions*</td>
<td>O'Connor et al, 2004 (118)</td>
</tr>
<tr>
<td>Reduce ceftaximes</td>
<td>4.5/100 admissions</td>
<td>2.2/100 admissions*</td>
<td>Wilcox et al, 2004 (119)</td>
</tr>
<tr>
<td>Integrated infection control program</td>
<td>8.0/1000 patient-days</td>
<td>4.2/1000 patient-days*</td>
<td>Apisarntharak et al, 2004 (112)</td>
</tr>
</tbody>
</table>

CDAD, *Clostridium difficile*-associated disease; ns, not significant.

*P* < .05.
Although vegetative forms of *C difficile* die rapidly outside the anaerobic environment of the intestines, *C difficile* spores are stable at a wide range of temperatures from −20°C to 90°C, and can survive brief heating at 100°C (2-35 minutes). Spores facilitate transmission of CDAD within health care settings, and their persistence can lead to subsequent infections and outbreaks. When environmental surfaces are assayed for *C difficile* spores in a room with either an asymptomatic carrier or a symptomatic patient, spores have been found on nearly every type of environmental surface, especially near the patient areas. Several studies have shown persistence of spores of *C difficile* in the environment for 5 months. In 1 study, environmental sites were cultured in rooms with and without CDAD patients. Once a CDAD patient was in the room, 45% of environmental samples were positive for *C difficile* spores, and 82% of those environmental isolates were of the identical strain type as the patient’s (Fig 2). One year later, *C difficile* spores were still detected in the room, and 36% of the isolates were of the original patient’s strain type. As time progressed, not only did the patient’s strain persist, but other types of *C difficile* strains were found on environmental surfaces as other patients transitioned through the room.

Some strains of *C difficile* are hyperproducers of spores, which enables wide spore dissemination. The emerging BI/NAP1/027 strain is one of these hyperproducing spore strains, which might help to explain why outbreaks caused by this strain resulted in a greater number of patients than outbreaks caused by other *C difficile* strains.

Efforts to reduce the dissemination of spores into the environment have been focused on 2 fronts: (1) effective therapies that might reduce spore carriage and (2) environmental disinfectants. Among 163 patients with recurrent CDAD, vancomycin or metronidazole therapy cleared vegetative cells of *C difficile* effectively, but neither antimicrobial was effective in clearing spores by the end of therapy (43% and 56% positive for spores, respectively). To date, there is no effective therapy directed at *C difficile* spore eradication. The search continues for an environmental disinfectant that would be sporicidal for *C difficile* and practical for a wide variety of surfaces and yet be sufficiently nontoxic for routine use by patients and health care workers.

### Antibiotic stewardship programs

One current strategy to retard the increasing incidence of antibiotic-resistant pathogens (such as the BI/NAP1 strain of *C difficile*) focuses on antibiotic utilization programs. Overuse of antibiotics has led to the development of antibiotic-resistant strains by several pathogens, and *C difficile* is no exception to this trend. Clindamycin-resistant strains of *C difficile* have been reported in Sweden, Poland, and the United States. The frequency of macrolide (MLSb)-resistant strains of *C difficile* also has been increasing in Poland and in Germany. Antibiotic stewardship programs, multidisciplinary programs involving physicians, microbiologists, pharmacists, and infection control practitioners, set protocols for prior authorization and concurrently review and give feedback on antibiotic use. There are many reports in the literature that antibiotic restriction has reduced CDAD rates, and a recent review found that 60% of studies found a significant reduction of CDAD with this strategy. Recent investigations have confirmed these earlier findings. A reduction in cephalosporin use at a hospital in Ireland led to a reduction in risk of acquiring CDAD by one third. Cefotaxime use was reduced on a geriatric medical unit in a United Kingdom hospital in favor of piperacillin-tazobactam, resulting in a 52% decrease in CDAD rates (Table 3).

### Vaccines

Vaccines against *C difficile* may be another strategy to reduce the number of susceptible patients and limit
health care-associated outbreaks. Early research into vaccines has shown promise. A toxoid vaccine was tested in 30 healthy volunteers and showed an increased level of antitoxin A immunoglobulin G. A parenteral C difficile vaccine containing toxoid A and toxoid B was tested in 5 patients with recurrent CDAD. Two of the 3 patients showed significant increases in serum IgG for antitoxin A and B, and none reported further recurrences. Currently, clinical trials are ongoing to determine the value of vaccines for the prevention of CDAD.

Effective treatments

The last strategy to control CDAD rates is the prompt treatment of infected cases so that transmission of spores into the environment is shortened and potential transmission to other susceptible patients is limited. Treatments for CDAD include antibiotic therapy, probiotics, prebiotics, immunoglobulin treatment, and toxin-binding polymers.

Antibiotic therapy

Treatment of infected patients is another strategy to reduce health care associated CDAD. Oral vancomycin is the only FDA-approved treatment for CDAD, but metronidazole has also been used. These 2 antibiotics have been considered the “standard” treatments for CDAD and have been considered of equivocal efficacy for decades, but recent data place this opinion into question. In 80% to 90% of patients with CDAD, diarrhea symptoms resolve within a typical 10-day treatment, regardless of antibiotic type. After antibiotics have been discontinued, 20% to 60% of patients may develop at least 1 recurrence of CDAD within 2 to 4 weeks, necessitating additional antibiotic treatments. Some patients may develop “recurrent CDAD” or repeated episodes that occur over a period of years. In these types of patients, vancomycin is usually given for the recurrences, along with another type of adjunctive therapy. In 163 cases of recurrent CDAD, tapering or pulsed doses of vancomycin were significantly more effective than metronidazole. By the end of therapy, vancomycin was more effective at clearing C difficile culture and/or toxins (89%) than metronidazole (59%, P < .001).

Recently, the effectiveness of metronidazole has been questioned because several studies reported high failure rates. Typically, once metronidazole is given, over 95% of patients report that their diarrheal symptoms resolved within 3 to 4 days. Several recent studies have reported higher than expected metronidazole failure rates. Of 207 patients with CDAD treated with metronidazole at the Houston Veterans Administration Medical Center from 2003 to 2004, 46 (22%) did not respond to the initial metronidazole treatment, and 58 (28%) recurred within 90 days. Musher et al examined a small number (18 isolates) from this institution and found that all isolates were sensitive to metronidazole and were of mixed PFGE strain types. In 845 patients treated with metronidazole in Quebec during 2003-2004, 26% failed initial treatment, and 338 (47.2%) recurred within 60 days of treatment. The recurrence rate remained high even after adjusting for the aging population. A retrospective study of 99 cases of CDAD at Temple Hospital in Pennsylvania during 2000-2001 found that 38% failed to respond to metronidazole treatment. Risk factors that predicted metronidazole failure were low albumin level (<2.5 g/L) and stay in an intensive care unit. No recurrence rates were given in this paper. A prospective study at the same hospital in 2005 found that of 27 CDAD patients treated with metronidazole, 17 (59%) did not respond to treatment. All of the 17 patients were still taking the antibiotic that induced CDAD, whereas all the patients that responded well to metronidazole discontinued the inducing antibiotic.

One possible reason why a higher rate of metronidazole treatment failure was observed is antibiotic resistance. Previously, metronidazole resistance has been infrequent in C difficile isolates. No resistance to either metronidazole or vancomycin was found in 186 isolates from patients in the United Kingdom or in 140 isolates from patients in Poland. Of 49 C difficile strains isolated from patients in Israel, none were resistant to vancomycin, but 1 (2%) was resistant to metronidazole. Of 415 C difficile isolates from patients in Spain, 6% of isolates were resistant to metronidazole, and 5% had reduced susceptibility to vancomycin. Several studies analyzed a small number (10-20) of metronidazole failures and did not find any metronidazole-resistant isolates associated with the failures. None of the isolates from patients with metronidazol failure treatment failure in the previous 4 studies were checked for metronidazole resistance nor has it been reported whether the BI/NAP1 strain has developed metronidazole resistance. The reason behind the apparent increase in metronidazole failures has not been explained but may be due to other factors related to the host, such as poor immune status, comorbidities, or intestinal conditions. As recurrent CDAD continues to persist as a clinical problem and the frequency of metronidazole failure increases, the search for more effective treatment strategies continue.

Probiotics

Probiotics (nonpathogenic microbes administered to improve intestinal balance and restore disrupted
normal microflora) are moving into mainstream for the treatment of gastrointestinal disorders. In 1 study, patients with CDAD were randomized to a combination treatment of oral vancomycin (2 g/day for 10 days) and Saccharomyces boulardii (1 g/day for 4 weeks) or vancomycin and placebo. Patients treated with vancomycin and the probiotic had significantly decreased recurrence rates (16.7%) compared with vancomycin and placebo (50%).

A metaanalysis of 6 randomized controlled trials using probiotics combined with 1 of the 2 standard antibiotics to treat CDAD found that probiotics significantly reduced the risk of CDAD (combined relative risk, 0.59; 95% CI: 0.41-0.85; \(P = .005\)).

Prebiotics

Prebiotics are nondigestible food components (starch or fiber) that stimulate the growth of bifidobacteria, a type of bacterium thought to play a major role in inhibiting the establishment of opportunistic pathogens in the intestine. Prebiotics are given alone, without a probiotic organism. A randomized trial of 142 CDAD cases treated with standard antibiotics with or without an adjunctive prebiotic (oligofructose) was conducted. Significantly fewer (8.3%) patients in the prebiotic-treated group had a recurrence within 60 days compared with those on placebo (34.3%, \(P < .001\)).

Immunoglobulin treatment

The host immune response is an important predictor of recurrences of CDAD, and the production of antitoxins A and B antibodies are found in patients who do not develop recurrent CDAD. Unfortunately, no randomized, placebo-controlled trials have been reported. Evidence from uncontrolled trials or case series studies show that increasing the immune response may be beneficial. In a small pilot study of patients with CDAD (9 had recurrent CDAD), all were given bovine antibody-enriched whey for 2 weeks after treatment with standard therapy (usually metronidazole). This enriched whey product has high levels of IgA antitoxin antibodies and has been shown to be protective of CDAD in hamster models.

### Table 4. Proposed changes to established strategies for health care practitioners for Clostridium difficile-associated disease

<table>
<thead>
<tr>
<th></th>
<th>Previous recommendations*</th>
<th>Current proposed recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection control</td>
<td>Use of alcohol-based antiseptics or gloves</td>
<td>Discontinue alcohol-based antiseptics</td>
</tr>
<tr>
<td></td>
<td>Patient isolation precautions if incontinent</td>
<td>Contact precautions, per facility isolation policy guidelines Patient isolation or cohorting during outbreaks for incontinent cases</td>
</tr>
<tr>
<td></td>
<td>Hypochlorite disinfection of surfaces of room with CDAD patient</td>
<td>Hypochlorite disinfectant effectiveness confirmed</td>
</tr>
<tr>
<td></td>
<td>Antibiotic restriction programs</td>
<td>Surveillance for C difficile isolates rates, review of severe CDAD cases, identification of specific strains</td>
</tr>
<tr>
<td></td>
<td>Educational programs stressing transmission, handwashing procedures, and environmental disinfection</td>
<td>Antibiotic stewardship programs established More research for methods to destroy C difficile spores</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Integrated infection control programs during outbreaks heightened (more stringent handwashing, cohorting, contact precautions, environmental disinfection)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Culture or toxin assay for diarrhea stools only</td>
<td>Consider both C difficile culture and toxin assays, rapid assays during outbreaks Inclusion of “low-risk” populations when diagnosing C difficile cases (community acquired, children, peripartum women, recent use of fluoroquinolones)</td>
</tr>
<tr>
<td></td>
<td>Do not assay asymptomatic carriers</td>
<td></td>
</tr>
<tr>
<td>Treatments</td>
<td>Prompt treatment of CDAD</td>
<td>Prompt treatment of CDAD cases confirmed</td>
</tr>
<tr>
<td></td>
<td>Oral metronidazole is treatment of choice</td>
<td>Combine standard antibiotic treatment (vancomycin) with alternative treatments for cases of recurrent C difficile disease</td>
</tr>
<tr>
<td></td>
<td>Retreat recurrences with second course of metronidazole</td>
<td>Discontinue offending antibiotic if possible Metronidazole failures followed until diarrhea resolved</td>
</tr>
</tbody>
</table>

CDAD, Clostridium difficile-associated disease.
*Reference: 2002 Society of Hospital Epidemiologists of America (SHEA) Position Paper.52
patients, 15 cleared *C difficile* toxins by the end of treatment, and none reported further recurrences (median follow-up, 333 days). In another small case series, 5 patients with recurrent CDAD were treated with standard antibiotics (metronidazole and/or vancomycin) and intravenous immunoglobulin (400 mg/kg) given either in single or multiple doses. Two patients died of unrelated causes during the study, 2 patients reported no further recurrences, and 1 patient recurred after 6 weeks. Another study treated 14 patients with refractory CDAD with intravenous immunoglobulin (150-400 mg/kg), and 64% responded within 10 days. This approach seems promising, but requires controlled clinical trials to prove that immunoglobulin is an effective treatment for recurrent CDAD.

**Toxin-binding polymer**

Another approach is to give an agent that would bind *C difficile* toxins within the intestinal lumen. Braunlin et al found that tolevamer, a sodium salt of styrene sulfonate polymer, binds *C difficile* toxin A extensively. In a phase 2 trial of 222 patients with CDAD, a high dose (6 g/day) of tolevamer was found to be equivalent to vancomycin treatment (500 mg/day). Of those treated with vancomycin, 91% were cured by day 10 compared with 85% treated with 6 g/day of tolevamer, and only 67% of those treated with 3 g/day of tolevamer responded. Controlled clinical studies in humans with a higher dose (9 g/day tolevamer) are ongoing.

Implications for infection control: Although newer infection control strategies have recently been tested (alcohol handrubs, different types of disinfectants, vaccines, new treatments), only antibiotic stewardship programs have reduced CDAD rates. Current infection control practices remain in good standing but are only effective if practiced. More research is needed to reduce transmission by *C difficile* spores, to find effective disinfectants and treatments, and to find methods to prevent CDAD outbreaks.

**CONCLUSION**

The emergence of a fluoroquinolone-resistant, hypervirulent strain of *C difficile* resulted in high numbers of patients with severe CDAD and caused several large outbreaks in Canada. These events have renewed focus on infection control practices for this disease. Several recommendations for infection control practitioners are suggested (Table 4). The occurrence of this strain is not unique to North America, and it should be expected to appear at other health care-associated institutions. The need to determine the specific strain type of *C difficile* isolates may be valuable in detecting the arrival of hypervirulent strains and tracking its transmission through health care facilities. However, this requires that hospital laboratories isolate *C difficile* by culture and have strain-typing methods available. These strain-typing assays are not widely available, and greater accessibility is recommended. An increase in the frequency of severe cases of CDAD may herald the arrival of the BI/NAP1/027 strain at an institution. Infection control practitioners and clinicians need to be vigilant for other strains of *C difficile* because a different profile of patients with CDAD is becoming more frequent (community-acquired cases, children, fluoroquinolone-associated cases) that may not be associated with the emergent BI/NAP1/027 strain. Research into more effective treatments for CDAD and recurrent CDAD is warranted. The increasing frequency of metronidazole failures is concerning, and randomized clinical trials are needed to determine whether this observation is due to a failure of the metronidazole itself or to confounders present in the observational studies. It would be prudent for infection control practitioners to have established strategies in place to control CDAD infections. Integrated infection control programs that involve educational programs, handwashing/gloving protocols, appropriate environmental disinfectants, and antibiotic stewardship programs offer the most effective benefits.

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Screening for pulmonary tuberculosis using chest radiography in new employees in an industrial park in Taiwan

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Background: Pulmonary tuberculosis (TB) is prevalent in Taiwan, but it is suspected that its occurrence has been underestimated by the National TB Surveillance Program. A pre-employment health examination is mandated by law in Taiwan, providing a mechanism to assess the occurrence of TB more accurately.

Methods: A pre-employment TB screening program of an industrial park was used to evaluate the performance of the National TB Surveillance Program in Taiwan. The yields of the pre-employment TB screening, using chest radiography from July 2004 to June 2005, were compared with corresponding results of the National TB Surveillance Program.

Results: A total of 17,105 new employees with an even gender distribution (men:women ratio, 50.2%:49.8%) underwent screening during the study period. Among the participants, 22 (128.6 per 100,000) new patients with pulmonary TB were diagnosed, and 7 (31.8%) of the patients had positive bacteriology findings. Compared with the results of the National TB Surveillance Program, the pre-employment screening had a much higher yield (128 vs. 47 per 100,000, \(P < .001\)).

Conclusion: The yield of the active surveillance program through mandatory screening was much higher than that of the National TB Surveillance Program, which is a passive reporting system. The results of this study highlight the need for more active TB surveillance efforts in endemic areas like Taiwan. (Am J Infect Control 2007;35:254-9.)

Pulmonary tuberculosis (TB) has been prevalent in Taiwan for a substantial period of time. The mortality related to TB was reported to be as high as 294.4 per 100,000 individuals in 1947 but has declined gradually and reached a historical low of 4.25 per 100,000 in 2003. Despite this decline in the mortality, TB was still listed as the thirteenth leading cause of death in Taiwan as of 2004. A nationwide survey revealed that the prevalence of bacteriologically confirmed pulmonary TB was 1.02% in 1947, and this figure declined to 0.06% in 1993. On the other hand, owing to the improvement in the notification mechanism, the number of TB cases reported to the National TB Surveillance Program, which is operated by the Department of Health of the central government, has increased in recent years. Such an improvement was achieved by the implementation of the “no-report-no-reimbursement” and “notification-fee” policies. In 1997, the number of newly diagnosed cases reached 15,386, with a reported incidence rate of 71.1 per 100,000 individuals, and the number of newly diagnosed cases remained at approximately 15,000 for each year since that time.

Even so, it has been suspected that the National TB Surveillance Program has underestimated the occurrence of TB in Taiwan because the program assesses the occurrence on the basis of people who participate in various health checkups and people who seek medical help, mostly because of clinical symptoms and signs. In fact, 2 studies have been conducted to evaluate the occurrence of pulmonary TB among certain Taiwanese subpopulations using active case-ascertainment approaches: 1 on prison inmates and the other on military conscripts. Whereas both studies reported higher estimates of the occurrence of TB than the results from the National TB Surveillance Program for corresponding time periods, they were both conducted among very specific subpopulations; inmates are at a higher risk of acquiring pulmonary TB because prisons are crowded confined spaces, and all military conscripts are 19-year-old men.
Therefore, further studies are needed to evaluate the possible underestimation for the whole population.

A preemployment health examination for every new employee is mandated by law in Taiwan. Whereas the main purpose of this examination is to determine whether the newly employed worker is fit for the job, the examination can also serve as a screening for communicable diseases to prevent the spread of such diseases within the workplace. Chest radiography (CXR) is a required item of the examination and can serve as screening for pulmonary TB. In an industrial park in Taiwan, new employees receive the examinations at the clinic located within the park, and such a scenario offers a unique opportunity to assess the occurrence of pulmonary TB in a working population, which can be adopted as a model to evaluate whether the National TB Surveillance Program has underestimated the occurrence of pulmonary TB. We analyzed the data from the preemployment screening and compared those with the corresponding data obtained from the National TB Surveillance Program.

METHODS

We included all new employees who underwent the standard preemployment health examination during the period between July 2004 and June 2005 in an industrial park in Tainan, Taiwan. All the examinations were carried out at the clinic in the park, which is the only health care institute located in the park. According to certain regulations of the Taiwanese government, every new employee of a company must undergo a standard health examination prior to commencing work with that company. This requisite health examination includes a standard 14 × 14-inch CXR film, routine urine sample, complete blood cell count, blood biochemistry, and a general physical examination. Whereas the main purpose of the examination is to determine whether the worker is fit for the job, the CXR also serves as screening for pulmonary TB so as to prevent the spread of this disease within the workplace. As is the case for the National TB Surveillance Program, participants with suspicious lesions on the CXR films were referred for further evaluation to a specialist hospital, the Chest Hospital of the Department of Health (also known as the Tainan TB Center) in this case. The diagnosis of TB was made according to the guidelines implemented by the Taiwan Center for Disease Control (CDC) of the Department of Health, which include follow-up CXR, sputum smears for acid-fast bacilli (AFB), and culture for Mycobacterium tuberculosis. The final diagnosis was made during the weekly staff conference after a review of results of the examinations and was confirmed by the TB specialists of the Taiwan CDC. The Taiwan CDC has adopted the World Health Organization’s case definitions of TB in general, although, because Taiwan is an endemic area of TB and because many physicians are experienced in the diagnosis of TB, a more aggressive approach to the diagnosis of TB is applied to minimize the spread of the disease throughout Taiwan. Therefore, the diagnosis of TB is confirmed for a culture-negative patient who has CXR findings compatible with active TB but fails to respond clinically to a 1-week-treatment regimen with broad-spectrum antibiotics and if the physician deems it appropriate to administer a full course of anti-TB treatment after the treatment with antibiotics. In addition, cases of nontuberculous mycobacteria were excluded as cases of TB.

The extent of the patient’s disease was classified as “minimal” (pulmonary involvement less than the lung parenchyma area demarcated by a horizontal line extending from along the lower end of the second rib), “moderately advanced” (pulmonary involvement of less than a single lung parenchyma), “far-advanced” (pulmonary involvement of more than a single lung parenchyma), and “cavitory” (cavity formation in lung parenchyma). All detected cases of TB were reported to the National TB Surveillance Program and treated with a rifampin-based, short-course anti-TB regimen. All suspicious cases underwent follow-up examinations and were required to complete the treatment course. To prevent the introduction of TB into the workplace, new employees with TB were not allowed to enter the workplace before the completion of their treatment.

The yield of a screening program was calculated using the following equation:

\[
\text{yield} = \frac{\text{number of new TB patients}}{\text{number of new employees examined}}.
\]

Patients who were being treated for TB at the time of screening and participants who had a history of TB were excluded from the study. In addition to the overall yield, we also calculated sex- and age-specific yields.

To evaluate the possible underestimation of TB occurrence by the National Surveillance Program, we obtained data from the program for the year 2003, which was the most updated published data available at the time of study. This program has been and still is operated by the CDC of the Department of Health as apart of the National Notifiable Disease Surveillance System and receives reports of new cases identified through screening programs at all hospitals in Taiwan as well as those identified through mobile CXR screening buses. We compared the gender- and age-specific yields deriving from the national surveillance program to the corresponding data observed in our study and evaluated the differences in the results of the 2 programs using the \( \chi^2 \) test. All statistical analyses were conducted using the Statistical Package for the Social Sciences.
(SPSS for Windows, Version 12.0, Chicago, IL), and all statistical tests were performed at a 2-tailed significance level of 0.05.

To protect patient confidentiality, the database created by our study was password protected, and all personal identifiers were removed from the database. The protocol of this study was determined as not requiring ethical review by the Human Experiment Review Board of the National Cheng Kung University.

RESULTS

During the study period, 17,105 new employees, comprising 8592 women and 8513 men, underwent preemployment health examinations at the clinic. The study participants were aged from 15 to 68 years, with a mean of 27.3 years. Among those, a male patient with previously diagnosed pulmonary TB, who had already commenced treatment for this condition at the time of screening, was identified and excluded from further analyses. Of the remaining 17,104 participants, pulmonary TB was diagnosed for 22, resulting in an overall yield of 128.6 per 100,000 individuals. Half of the 22 newly diagnosed patients were between 25 and 34 years of age, and half of the patients revealed “minimal” disease involvement. Seven patients (31.8%) had at least 1 sputum culture that was positive for *Mycobacterium tuberculosis*, and 2 patients (9.1%) had 1, or more than 1, sputum smear exhibiting the presence of AFB as seen under microscopy. Both of the 2 patients with positive sputum AFB smears also had positive sputum cultures, such that the yield of bacteriologically confirmed pulmonary TB was 40.9 per 100,000 individuals (Table 1).

The overall yield of the National TB Surveillance Program was 47.2 per 100,000 individuals, which was significantly lower than the corresponding figure found in our screening program (Table 2). Furthermore, as compared with the results from the National TB Surveillance Program, our screening program had significantly higher yields for all age groups and for both men and women. However, whereas our program had similar yields between the 2 sexes, the National TB Surveillance Program had a more than 2-fold higher yield for men as compared with women (Table 2).

DISCUSSION

It is generally believed that providing prompt and effective treatment to patients suffering from TB may bring the disease under control globally, but the problem regarding how to identify effectively such patients among an apparently healthy population (the screening for TB) remains a great challenge to both public health practitioners and clinicians. In areas with a relatively low prevalence, the policy of preemployment mass CXR screening for pulmonary TB remains controversial even for health care workers, who are at a higher risk. TB can arise and spread within a regular workplace, and certain mass CXR screening programs have been applied in areas with a relatively low prevalence, this being especially the case when the goal is the elimination of the disease.

The main purpose of the mandated preemployment health examination in Taiwan is to determine whether the worker is fit for the job, although it may be seen to also serve the purpose of screening for communicable diseases. Because this compulsory examination includes a CXR, it can serve effectively as screening for pulmonary TB. The mandatory nature of the health examination offers a unique opportunity to evaluate the performance of the National TB Surveillance Program, which is a combination of various screening programs, including the complimentary Adult Health Examination offered by the National Health Insurance, the pre-recruitment health examination for the military service, the screening using mobile CXR buses, and others. Whereas the reporting to the CDC of all cases of TB as detected by various health care institutes and all physicians is mandated by law in Taiwan, the participation in some of the above-mentioned programs, such as the Adult Health Examination and the mobile bus screening, is voluntary.
Therefore, some previous studies have speculated that the occurrence of pulmonary TB in Taiwan may have been underestimated by the National TB Surveillance Program,⁵,⁶ as has been the cases for a number of other passive public health surveillance systems.¹⁴

In fact, a mass TB survey of all prisons in Taiwan in 1999 screened a total of 51,496 inmates using 70 × 70-mm miniature films and referred 1148 (2%) of these individuals to undergo follow-up examinations using 14 × 14-inch films.⁵ Among the 922 individuals who completed follow-up examinations, pulmonary TB was diagnosed for 107. On the basis of the assumption that the prevalence of TB among those who failed to undergo follow-up examinations was equivalent to that among those who did undergo follow-up examinations, the study obtained an estimated prevalence of 258.7 per 100,000 inmates. Among these 107 patients, 88 (82.2%) were newly diagnosed, resulting in a yield of 212.9 per 100,000 individuals under the similar assumption that the yield of new TB cases among those who failed to undergo follow-up examinations was equal to the yield for those who did undergo follow-up examinations. Contrasting such figures, however, the National TB Surveillance Program's yield was only 61.3 per 100,000 in 1999.¹ Likewise, another survey of TB applied similar approaches to military conscripts in 1997 and 1998 in Taiwan and notified 2969 of the 305,140 19-year-old men (1%) initially examined to undergo follow-up examinations.⁶ Among the 2782 men (94%) who completed follow-up examinations, pulmonary TB was diagnosed for 237, of whom 212 (89%) were newly diagnosed. Accordingly, the estimated yield from this military conscript study was 74.3 per 100,000 individuals, which was similar to the yield of 82 per 100,000 of the National TB Surveillance Program for 19-year-old men conducted in 1998.⁶ For that same year, however, if the 99 cases detected by the military screening were excluded, the yield of the National TB Surveillance Program for 19-year-old men was only 32.7 per 100,000, a figure similar to the corresponding yields for 22-year-old men (31.8 per 100,000) and 23-year-old men (30.6 per 100,000) for the same year. Comparing the data on men with those of the National TB Surveillance Program on women (23 per 100,000 for 19 year olds, 22 per 100,000 for 20 year olds, 25 per 100,000 for 21 year olds, 25 per 100,000 for 22 year olds, and 25 per 100,000 for 23 year olds), the researchers concluded that the peak in the yield for 19-year-old men revealed by the data from the National TB Surveillance Program was due to the military screening and that the relatively low yields for 20-year-old men (25.3 per 100,000) and 21-year-old men (16 per 100,000) might be due to a "post-screening effect" following early case detection by the military screening that resulted in a decrease in detectable cases subsequent to this screening.⁶ In other words, the result of this military conscript study supported the suspicion raised by the prison inmate study that the National TB Surveillance Program tends to underestimate the occurrence of pulmonary TB in Taiwan.

The mandatory preemployment health examination in Taiwan provides a potential mechanism to assess the occurrence of pulmonary TB in a working population, but, to the best of our knowledge, no study using such an approach, as was the case in our study, has been conducted and published in the relevant literature. One previous study reported that, at the time of study, there existed 65 industrial parks in Taiwan, but only 10 of those had an on-site common health care unit.¹⁵ Although all of the other 9 parks were more than 10 years old, the clinic at which we conducted the current study was the most recently established and was still hiring large numbers of new employees; such a scenario, therefore, offered a unique opportunity to assess the occurrence of certain diseases in the general population. In fact, a previous study on the workers in this same park found that the seroprevalence of rubella among employees was compatible with corresponding...
figures observed in studies using representative samples of the general population.16 Using the data from the preemployment screening, the results of the current study confirmed the suspected underestimation of the occurrence of TB by the National TB Surveillance Program.

Of the 22 new pulmonary TB patients identified in our study, half (11 patients; 50.0%) had only “minimal” disease involvement, an outcome that is compatible to the corresponding finding of 51% (120 in 237 individuals) in the military conscript study.6 Both studies applied an active surveillance approach instead of a passive reporting approach, and the results of both have demonstrated that most patients identified by this approach were in the early stage of the disease, an outcome that illustrates the relative effectiveness of such an approach for early diagnosis.

Although HIV infection is a well-known risk factor for TB, none of the patients identified in our study had HIV infection. This is not surprising because HIV is not as prevalent as TB in Taiwan. Because none of our study participants were health care workers, we believe the individuals identified as TB patients acquired the disease in the general community, which is not at all uncommon for endemic area of TB like Taiwan. Although lung malignancy should always be considered as a differential diagnosis for pulmonary TB, no case of lung malignancy was identified among the TB patients diagnosed in our study.

The National TB Surveillance Program had a more than 2-fold higher yield for men as compared with women (91.7 vs 40.7, respectively, per 100,000), whereas the current study has observed similar yields for both sexes (129.2 vs 128.0, respectively, per 100,000). This may be attributable, at least in part, to the fact that men have more opportunities to receive mandatory TB screenings, including the military recruitment screening and preemployment screenings. This finding indicates the need for more active TB surveillance for women in the general population. All of the 22 new patients identified in our study were reported to the National TB Surveillance Program as required by law, and each of these patients received anti-TB therapy. In addition, their starting dates for going to work were postponed to prevent the transmission of TB to their coworkers.

A substantial proportion of the TB patients (31.8%) identified in the current study had positive sputum culture, which indicated that these patients were able to transmit the diseases to others, and they are important cases to both public health and occupational health.17 In particular, patients who are sputum smear-positive for AFB are highly infectious and thus considered as the most important source of the transmission of TB. For the modern industry, almost all of the workers work in air-conditioned buildings, and the presence of such patients in the workplace poses a threat to the health and well-being of other workers. Our study results demonstrate the importance of preemployment screening for TB in endemic areas like Taiwan. The proportion of bacteriologically confirmed pulmonary TB cases constituted approximately 61.4% of all tuberculosis cases reported to the National TB Surveillance Program. It should be noted that a large proportion of cases reported to the program are identified through voluntary participation in various screenings, and many of those individuals are in fact symptomatic or suspect that they have contracted the disease. However, in the current study, participation in the screening was mandated by law, which may explain the relatively smaller proportion of bacteriologically confirmed cases. In the previous study on military conscripts, in which participation in the screening was also mandated by law, the proportion of bacteriologically confirmed cases was even lower (8.9%) than that in our study. Therefore, the yields in our study were not likely to be underestimations.

The preemployment health examination is not designed for screening for TB exclusively, and, therefore, the tuberculin skin test and sputum smear are not included. However, all the participants with suspected pulmonary TB were referred to the Chest Hospital for further diagnostic procedures, although none of them underwent bronchoscopy for diagnosis. Whereas the diagnosis of TB in some of the culture-negative patients might have been inaccurate, such an outcome would not affect the conclusions of our study because the same diagnostic criteria were applied to both the preemployment screening of workers and the National TB Surveillance Program. Because new employees constitute an active working population, they may tend to be somewhat healthier than other people of the same age and thus may not be truly representative of the general population. If that happened to be the case, the rates of TB might have been underestimated in our study. Nonetheless, because our main finding was that the preemployment screening revealed higher rates of TB infection than the National TB Surveillance Program, if the preemployment screening did underestimate the rates, such an outcome would not change our main conclusion. Still, it should be recognized that the accurate diagnosis of pulmonary TB using CXR alone is difficult, and, therefore, other TB screening efforts in addition to the preemployment health examination are needed to identify new cases.

Our study has revealed that the National TB Surveillance Program, which is a passive reporting system, underestimates the occurrence of TB in Taiwan, this being particularly so for women. It has been argued previously that proper coordination between occupational and community health services will give the best results,
and logically, this should lead to a rapid decline of the disease. The results of our study support this argument and demonstrate the importance of preemployment TB screening in endemic areas like Taiwan.

References
Prescription of prophylactic antibiotics for neurosurgical procedures in teaching hospitals in Iran

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Background: To assess the appropriateness of surgical antibiotic prophylaxis in neurosurgical procedures, using the American Society of Health-System Pharmacists (ASHP) guideline as reference, 110 patients were prospectively evaluated. Monitoring surgical antibiotic prophylaxis is crucial in ensuring appropriate use of antimicrobial agents in this setting. This will minimize the consequences of antibiotic misuse such as increased drug antibiotic resistance, adverse events, and higher costs to the institution.

Methods: We recruited 110 consecutive patients undergoing clean neurosurgical treatment in 2 hospitals. Data were collected prospectively from patients’ medical records between February 2004 and April 2004. The data collection forms for each patient included hospital name, patient demographics, type of surgery, and type of antimicrobial prophylaxis regimen (drug name, dose, interval, route of administration, number of doses and time administered, and duration of administration).

Results: Discrepancies about antibiotic selection, duration, and start time of prophylaxis were seen between current administration and the ASHP guideline. The direct cost of prophylactic antibiotics for the 110 procedures was 14 times greater than what it would have cost to administer prophylactic antibiotics adhering to the ASHP guideline (US $802 vs US $59; US $7.29 vs US $0.54 per patient, respectively). This is equivalent to US $6.75 of extra costs per procedure and patient.

Conclusion: This study indicates the need for interventions to improve the rational use of antibiotic prophylaxis in Iran to prevent the complications of inappropriate administration of antimicrobials and decrease unnecessary costs. (Am J Infect Control 2007;35:260-2.)

Surgical site infections (SSIs) are the most common and serious complication among surgically treated patients, resulting in increased rates of morbidity and mortality, length of stay in hospital, and cost.1 Postoperative infection following neurosurgery occurs at a reported incidence of 4%, accounting for a mortality of approximately 14% of the total postoperative deaths.2 Postoperative infection in clean neurosurgery is even lower, with reported frequencies up to 1%.3 Gram-positive Staphylococci are the most common causative pathogens for postoperative infections in neurosurgery patients. Infection can occur in superficial tissues such as skin surrounding the wound, bone flap, or in the deeper tissues; even superficial wound infections may cause complications such as osteomyelitis, meningitis, encephalitis, abscess, or death.4

Although the rate of infection in clean neurosurgical operations is known to be low, the routine use of prophylactic antibiotics has been adopted by many neurosurgeons because of the potentially devastating consequences of infectious complications.5 The effectiveness of antibiotic prophylaxis in preventing postoperative wound infections has been proven in several studies. Therefore, surgical antibiotic prophylaxis accounts for over 30% of antibiotic prescriptions in general hospitals. However, in surgical centers it can be as high as 95%. Monitoring surgical antibiotic prophylaxis is crucial in ensuring appropriate use of antimicrobial agents in this setting. This will minimize the consequences of antibiotic misuse such as increased drug antibiotic resistance, adverse events, and higher costs to the institution.6

The choice of antimicrobial agent, the starting time of administration, and the duration of prophylaxis are factors that can affect the appropriate use of surgical antibiotic prophylaxis. In this study, we used the recommendations made by the American Society of Health-System Pharmacists (ASHP)7 to assess the appropriateness of antibiotic prophylaxis for surgical procedures in 2 teaching hospitals affiliated with Shiraz University of Medical Sciences in Shiraz, Iran.

METHODS

We specifically chose to review adherence to antibiotic prophylaxis in neurosurgical procedures. We recruited 110 consecutive patients undergoing clean neurosurgical treatment from 2 hospitals (57 cases
from hospital "A" and 53 from hospital "B") in Shiraz, the capital of the province Fars. These hospitals are the sole referral centers for neurosurgical treatment for a population of 4 million inhabitants living in this province. Data were collected prospectively from patients' medical records between February 2004 and April 2004. The data collection forms for each patient included hospital name, patient demographics, type of surgery, and type of antimicrobial prophylaxis regimen (drug name, dose, interval, route of administration, number of doses and time administered, and duration of administration). Because of therapeutic use of antibiotics instead of prophylactic, the procedures classified as dirty-infected wound were excluded from the study. Cases for which it was not possible to determine prophylactic or therapeutic use of antibiotics were also excluded. Adherence to the ASHP recommendations was assessed by a clinician. Data were recorded into EPI-INFO 2002 program (Centers for Disease Control and Prevention, Atlanta, GA) and analyzed using SPSS for Windows 11.5 (SPSS Inc., Chicago, IL). Statistical evaluation was conducted by descriptive analysis including frequencies.

RESULTS

Records for 110 patients were collected and reviewed. Sixty-six percent were male. Patients' age ranged between 14 and 76 years (mean, 40.6 years; SD ± 16.3); 15.5% of operations were emergency procedures, and wound classes were clean in 100%.

Only 1 patient (0.9%) received prophylactic antibiotics in accordance with the entire set of recommendations given by the ASHP guidelines. In 81 patients (74.3%), prophylaxis was started at the time of induction of anesthesia as recommended by the ASHP. Prophylaxis was continued in patients for several days (mean, 5 days; SD ± 4.8) rather than the ASHP recommendation of only a single-dose antibiotic.

A total of 9 different antibiotics or combinations thereof were prescribed for 109 patients. One patient received only 1 substance (cefazolin), and up to 5 types of antibiotics were administered for others. The most frequently used antibiotics, alone or in combination, were intravenous gentamicin (in 108 cases; 98%) and cefazolin (in 107 cases; 97%). Some oral agents such as cephalaxin, cloxacillin, and metronidazol were used subsequently after intravenous agents in 52 patients (29%). Vancomycin was prescribed for 3 patients (2.7%) without any evidence of β-lactam allergy.

The direct cost of prophylactic antibiotics for the 110 procedures was 13.6 times greater than what it would have cost to administer prophylactic antibiotics adhering to the ASHP guideline (US $802 vs US $59 or US $7.29 vs US $0.54 per patient, respectively).

DISCUSSION

This study showed discrepancies between current administration of antibiotics for surgical prophylaxis and the ASHP guideline. The major mistakes were antibiotic selection, duration, and start time of prophylaxis. The ASHP recommends a single dose of 1000-mg cefazolin at the time of induction of anesthesia for prevention of SSI. However, most patients received cefazolin but in combination with other antibiotics, including gentamicin or oral antimicrobial compounds. In general, it is debatable whether the concomitant use of oral and parenteral antibiotics has greater efficacy in prevention of postsurgical infections.

The question of why some patients received subsequent oral antibiotics regardless of any postoperative infection in our study was unclear and needs further investigation. The use of vancomycin for prophylaxis is appropriate only when there is a true type I hypersensitivity to β-lactam or when there is a high incidence of SSI because of methicillin-resistant staphylococci. Vancomycin was used in 3% of our patients without any of these situations present.

Aminoglycosides such as gentamicin, which were used for most patients, may be nephrotoxic and ototoxic, even with precise therapeutic doses, and the use of these in prophylaxis may predispose for the emergence of methicillin-resistant staphylococci. This may initiate an unfavorable cascade in which treatment with vancomycin may select for the emergence of vancomycin-resistant enterococci. Therefore, aminoglycosides are not endorsed for systemic prophylaxis.

In light of the ASHP’s recommendations of only 1 time, single-dose antibiotic prophylaxis for neurosurgical procedures, none of the patients in our study received optimal duration of prophylaxis. In fact, the unwarranted prolonged use of antibiotics increases the likelihood of developing infections by antibiotic-resistant bacteria, exposes patients to more adverse drug effects, and increases the overall medical cost.

The initiation time of antibiotic therapy was appropriate for three fourths of the patients. Antibiotic prophylaxis must be initiated early enough to allow the antibiotic to achieve effective tissue concentration. Administration of the antibiotic too early may compromise antibiotic efficacy.

The results of this study show that the direct cost of current surgical antibiotic prophylaxis was approximately 14-fold greater than the cost of a suggested regimen by guideline. This is equivalent to US $6.75 of extra cost per procedure and patient or US $743 for the 110 investigated patients. To put these excess costs in a socioeconomic perspective, it should be noted that the minimum salary of a worker in Shiraz that year was US $120 per month.
Our study has several important limitations. Although most Iranian neurosurgical departments share a close communication and standards are similar, our results represent the situation in the province of Fars and cannot be generalized to the Iranian situation. Second, we have no documented evidence that the ASHP practices would have been any more effective or more economic. We decided to use recommendations published by the ASHP to measure against rational and evidence-based international standards. However, the possibility exists that recommendations given by the ASHP guidelines were not feasible in our patients or for the situation in Iran.

In conclusion, this study indicates the need for interventions to improve the rational use of antibiotic prophylaxis to prevent the complications of inappropriate administration of antimicrobials and decrease unnecessary costs. We suggest that the mistakes in prescribing practice for surgical antibiotic prophylaxis in our study were due to lack of adherence to guidelines among surgical teams.

References
Bacterial contamination of stethoscopes with antimicrobial diaphragm covers

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Antimicrobial stethoscope covers impregnated with silver ions have been developed to prevent surface contamination and potential transmission of bacterial pathogens to patients. To test their practical utility, covers were distributed with the manufacturers’ recommendations to a mixed group of health care professionals in a medical/surgical intensive care unit and an emergency department. Seventy-four clinicians were selected from a convenience sample for surface cultures and standard questioning regarding cleaning and cover use. Surface colony counts were significantly lower for uncovered stethoscope diaphragms (mean, 71.4 colonies) compared with covers used ≤1 week (mean, 246.5 colonies) and those >1 week old (mean, 335.6 colonies). After controlling for type of clinician, frequency of stethoscope cleaning, and method of stethoscope cleaning, only the presence of a stethoscope cover was associated with higher colony counts (P < .0001). We question the practical utility of the antimicrobial diaphragm covers evaluated in this study for reducing the surface colonization of potentially harmful microorganisms. (Am J Infect Control 2007;35:263-6.)

Indirect contact with contaminated patient environment or medical devices has been associated with transmission of nosocomial pathogens and provides the basis for the implementation of current transmission-based isolation guidelines.1 Many nosocomial infections have been demonstrated to be due to cross transmission.2 Many of these infections could potentially be prevented through adequate application of infection control practices.

Medical devices including stethoscopes and otoscopes have been demonstrated to be contaminated with bacterial species and have been implicated as potential vectors of cross transmission.3-10 Other inanimate objects such as pagers,11 toys in the neonatal intensive care unit,12 and hospital surfaces13 have likewise been implicated. The stethoscope represents perhaps the most commonly used medical device in the hospital. Numerous studies have examined the diaphragm surface and earpieces for bacterial contamination and have determined that it occurs at a very high rate (66%-100%).3-10 Among isolated pathogens, staphylococcus species including methicillin-resistant Staphylococcus aureus (MRSA) have been reported.3-8,10,14

Cleaning the diaphragm with alcohol has been demonstrated to reduce surface bacterial counts.3,6-8 Although cleaning does decrease bacterial load, studies show that health professionals may not be committed to the process of routine cleaning. In one study, only 48% of health care providers cleaned their stethoscopes daily or weekly, 37% monthly, and 7% yearly; and 7% had never cleaned their stethoscopes.6

Covering the surface of the stethoscope diaphragm with an antimicrobial cover may prevent contamination and cross transmission of nosocomial pathogens. Diaphragm covers impregnated with silver ions have the potential to suppress growth of bacteria and fungi and thus prevent transmission of nosocomial pathogens. We report our experience of the practical utility of antimicrobial stethoscope diaphragm covers by comparing cultures from the surfaces of covered and uncovered stethoscopes and evaluating clinician’s practices regarding stethoscope cleaning and care. We
discuss the implications of our findings on the potential impact of these antimicrobial covers and stethoscope care in infection prevention.

METHODS

During the fall of 2003, antimicrobial diaphragm covers (≥2 per individual) with the manufacturers’ recommendations about cleaning and routine changing of covers were distributed to a mixed group of health care professionals working in a large medical/surgical/trauma intensive care unit (ICU) and a regional trauma emergency department (ED). All clinicians were instructed that they may be randomly selected to participate in a culture study and to complete a survey regarding their stethoscope care.

During the study period, health care workers were selected from a convenience sample of the ICU and ED staffs as randomly as possible for culture of stethoscope diaphragms. These included equal number of individuals with and without antimicrobial covers. Cultures were obtained by pressing the diaphragm surface for 5 seconds on a blood agar plate and incubating the culture aerobically for 48 hours. After incubation, the total number of colonies of bacterial growth was counted for each sample, but the genus and species of the cultured organisms were not specifically identified. An example of a positive culture is illustrated in Fig 1.

At the time of culture, each health care worker was asked to complete a short written survey. Each clinician indicated whether they were using an antimicrobial cover and whether it was being used beyond the 1-week time frame recommended by the manufacturer. Additionally, clinicians were categorized by role and training (physician, nurse, respiratory therapist, or other), were queried about how often they cleaned the stethoscope (between every patient, several times a day, once daily, once monthly, or rarely if ever), and were asked to identify which cleaning agent was used (alcohol wipes, soap and water, antiseptic wipes, or the alcohol-based handrub). The mean number of colonies was compared between those without covers and those with short-term (<1 week) or long-term cover use (>1 week old). Multiple linear regression modeling was performed to determine predictors of the number of colonies cultured from the diaphragm surface with presence or absence of antimicrobial diaphragm cover, type of clinician, frequency of stethoscope cleaning, and method of stethoscope cleaning as covariates in the model. Surface colony counts, the dependent variables, were transformed to the natural logarithm to satisfy the assumption of homoscedasticity in the linear regression model. All statistical tests were 2-sided, and significance was set at P < .05, with all analyses performed using STATA, version 8 (Stata Corporation, College Station, TX).

RESULTS

One hundred percent of the diaphragms cultured were contaminated. Colony counts were significantly lower for uncovered stethoscope diaphragms (mean, 71.4 colonies) compared with covers less than or equal to 1 week old, as recommended by the manufacturer (mean, 246.5 colonies) and those greater than 1 week old (mean, 335.6 colonies). Health care workers who were surveyed were generally reflective of the distribution of types of clinicians within the institution (36 nurses, 21 respiratory therapists, 14 physicians, and 3 nurse assistants). Mean colony counts by clinician type were highest among nurses (203.1 colonies), followed by nurse assistants (197.7 colonies), physicians (193.1 colonies), and respiratory therapists (169.5 colonies). Viewed differently, the majority of uncovered stethoscopes (91.9%) had colony counts in the 0 to 199 range compared with only 35.1% of covered stethoscopes. Most of the covered stethoscopes had 200 colonies (23, 62.1%) with 14 (37.8%) having 400 to 599 colonies.

Only 11 of 74 (15%) health care workers cleaned their stethoscope between every patient. One third (25/74, 34%) cleaned several times a day, with slightly less (22/74, 30%) cleaning their stethoscopes daily. Fewer (9/74, 12.2%) of those surveyed rarely if ever cleaned their stethoscopes, and 7 of 74 (9.5%) did so once a month. Most surveyed health care workers...
Table 1. Stethoscope colony counts with or without cover stratified by job description

<table>
<thead>
<tr>
<th>Colony counts from culture of stethoscope diaphragm surface</th>
<th>0-199</th>
<th>200-399</th>
<th>400-599</th>
<th>&gt;600</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Job Description</td>
<td>Cover</td>
<td>No Cover</td>
<td>Cover</td>
<td>No Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Physician</td>
<td>2 (33.3)</td>
<td>7 (87.5)</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
<td>4 (66.7)</td>
</tr>
<tr>
<td>Nurse</td>
<td>6 (33.3)</td>
<td>16 (88.9)</td>
<td>4 (22.2)</td>
<td>2 (11.1)</td>
<td>7 (38.9)</td>
</tr>
<tr>
<td>Respiratory Therapist</td>
<td>5 (41.7)</td>
<td>9 (100)</td>
<td>5 (41.7)</td>
<td>0 (0)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td>2 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Totals</td>
<td>13 (35.1)</td>
<td>34 (91.9)</td>
<td>9 (24.3)</td>
<td>3 (8.1)</td>
<td>14 (37.8)</td>
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</tbody>
</table>

Table 2. Stethoscope surface colony counts with or without cover stratified by stethoscope care

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<tr>
<th>Frequency of stethoscope cleaning</th>
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<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
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<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between Every Patient</td>
<td>2 (33.3)</td>
<td>7 (87.5)</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
<td>4 (66.7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (100)</td>
<td>8 (100)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Several Times a Day</td>
<td>6 (33.3)</td>
<td>16 (88.9)</td>
<td>4 (22.2)</td>
<td>2 (11.1)</td>
<td>7 (38.9)</td>
<td>0 (0)</td>
<td>1 (5.6)</td>
<td>0 (0)</td>
<td>18 (100)</td>
<td>18 (100)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Once Daily</td>
<td>5 (71.4)</td>
<td>2 (13.3)</td>
<td>1 (14.3)</td>
<td>7 (46.7)</td>
<td>0 (0)</td>
<td>4 (26.7)</td>
<td>1 (14.3)</td>
<td>2 (13.3)</td>
<td>7 (100)</td>
<td>15 (100)</td>
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<tr>
<td>Once Monthly</td>
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<td></td>
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<tr>
<td>Rarely if Ever</td>
<td>0 (0)</td>
<td>2 (40.0)</td>
<td>3 (75.0)</td>
<td>3 (60.0)</td>
<td>1 (25.0)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (100)</td>
<td>5 (100)</td>
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<td></td>
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<tr>
<td>Totals</td>
<td>6 (16.2)</td>
<td>8 (21.6)</td>
<td>18 (48.7)</td>
<td>18 (48.7)</td>
<td>12 (32.4)</td>
<td>9 (24.3)</td>
<td>1 (2.7)</td>
<td>2 (5.4)</td>
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<table>
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<th>Method of stethoscope cleaning</th>
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<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
<th>Cover</th>
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<th>No Cover</th>
<th>Cover</th>
<th>No Cover</th>
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</thead>
<tbody>
<tr>
<td>Alcohol Wipes</td>
<td>1 (3.5)</td>
<td>6 (22.2)</td>
<td>17 (58.6)</td>
<td>13 (48.2)</td>
<td>10 (34.5)</td>
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<td>1 (3.5)</td>
<td>2 (7.4)</td>
<td>29 (100)</td>
<td>27 (100)</td>
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<td></td>
</tr>
<tr>
<td>Antiseptic wipes</td>
<td>4 (66.7)</td>
<td>2 (22.2)</td>
<td>1 (16.7)</td>
<td>4 (44.4)</td>
<td>1 (16.7)</td>
<td>3 (33.3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (100)</td>
<td>9 (100)</td>
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<td></td>
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<tr>
<td>Alcohol Hand Gel</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Soap and Water</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Totals</td>
<td>6 (16.2)</td>
<td>8 (21.6)</td>
<td>18 (48.7)</td>
<td>18 (48.7)</td>
<td>12 (32.4)</td>
<td>9 (24.3)</td>
<td>1 (2.7)</td>
<td>2 (5.4)</td>
<td>37 (100)</td>
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Table 3. Linear regression model evaluating the predictors of stethoscope surface colony counts*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression coefficient*</th>
<th>p value</th>
<th>95% Confidence Intervals</th>
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</thead>
<tbody>
<tr>
<td>Job Description</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>Reference</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nurse</td>
<td>-0.0054001</td>
<td>0.987</td>
<td>-0.6426102, 0.6318101</td>
</tr>
<tr>
<td>Respiratory Therapist</td>
<td>0.0157252</td>
<td>0.964</td>
<td>-0.6848798, 0.7163302</td>
</tr>
<tr>
<td>Other</td>
<td>0.1543865</td>
<td>0.809</td>
<td>-1.118059, 1.426832</td>
</tr>
<tr>
<td>Frequency of Cleaning</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Rarely, if ever</td>
<td>Reference</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Between every patient</td>
<td>-0.4117073</td>
<td>0.363</td>
<td>-1.310265, 0.4868503</td>
</tr>
<tr>
<td>Once daily</td>
<td>0.0023183</td>
<td>0.995</td>
<td>-0.7746493, 0.779286</td>
</tr>
<tr>
<td>Once monthly</td>
<td>0.3188067</td>
<td>0.503</td>
<td>-0.6277348, 1.265348</td>
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<tr>
<td>Several times a day</td>
<td>-0.2414011</td>
<td>0.519</td>
<td>-0.9859584, 0.5031561</td>
</tr>
<tr>
<td>Method of Cleaning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soap and water</td>
<td>Reference</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Alcohol wipes</td>
<td>-0.4439758</td>
<td>0.660</td>
<td>-2.450394, 1.562442</td>
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<tr>
<td>Antiseptic wipes</td>
<td>-0.1818037</td>
<td>0.856</td>
<td>-2.172516, 1.808909</td>
</tr>
<tr>
<td>Alcohol hand gel</td>
<td>-0.3350889</td>
<td>0.664</td>
<td>-2.988912, 1.918734</td>
</tr>
<tr>
<td>Stethoscope Cover</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cover</td>
<td>Reference</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cover used &lt;1 week</td>
<td>1.66603</td>
<td>&lt;0.0001</td>
<td>0.8939513, 32.438108</td>
</tr>
<tr>
<td>Cover used &gt;1 week</td>
<td>1.615923</td>
<td>&lt;0.0001</td>
<td>1.108545, 2.123301</td>
</tr>
</tbody>
</table>

*Natural logarithmic transformation of colony counts evaluated in this regression model.
(56/74, 76%) used alcohol wipes to clean their stethoscope compared with only 15 of 74 (20%) who used antiseptic wipes. The mean colony counts were not dramatically different between these types of cleaning methods (188.5 and 201.3, respectively). One individual used soap and water as a cleaning method. Data on method of stethoscope cleaning are stratified by clinician type in Table 2.

The relationship between surface colony counts and the presence or absence of stethoscope cover, type of clinician, and frequency and method of cleaning was definitively determined using multiple linear regression modeling (Table 3). When controlling for the type of health care worker and the frequency and method of cleaning the stethoscope, only the presence of an antimicrobial stethoscope cover was associated with higher colony counts ($P < .0001$).

**DISCUSSION**

All stethoscope diaphragm surfaces in this study demonstrated bacterial contamination consistent with the findings of other investigators. Surprisingly, the surface colony counts were higher on the surfaces of the antimicrobial covers, especially if they were being used beyond the manufacturer’s recommended time frame of 1 week. It is speculated that the added surface area in conjunction with the embossing may provide a surface that protects microbes from cleaning agents, thus creating higher colony counts. Furthermore, many of the cultures of the covered diaphragms had colonies in the shape of the embossed lettering on the covers. The method and frequency of cleaning, however, did not appear to impact independently the surface colonization; only the use of the cover was associated with higher colony counts. In addition, at the time of this study, the investigators were not aware of an antimicrobial stethoscope cover impregnated with silver ions that did not have embossing. Therefore, one was not examined.

The practical utility of these covers in preventing surface colonization and potential transmission of organisms to patients is seriously questioned based on the results of this small pilot study. The validity of this study should be confirmed by a larger randomized trial. Using these types of devices may give a false sense of security to health care workers; prolonged use of covers appeared to result in even higher colony counts. Their use may also induce clinicians to clean their stethoscopes less frequently. Although this study failed to show a relationship between cleaning and reduced colony counts, other investigators have demonstrated that cleaning the diaphragm with alcohol reduces surface bacterial counts.5-8

This study has several limitations. Clinicians, although selected in random fashion from a larger convenience sample of ICU staff and ED staff, were not prospectively randomized to either study arm. This may have introduced selection bias. Another limitation was the failure to identify the organisms. This study was initially conceived as an internal performance improvement project, and budgetary restrictions limited extensive microbiologic studies. It is possible that the higher colony counts on the covered stethoscopes were skin organisms representing little risk to patients and that the lower counts on uncovered scopes were serious pathogens. Regardless, it is concerning that silver ion impregnated covers would generally demonstrate significantly higher colonization rates than uncovered stethoscope surfaces. This observation should be considered by others attempting to use these antimicrobial devices as an infection control intervention, and these results should be validated by larger studies.

**References**

Occupationally acquired infectious diseases among health care workers in Brazil: Use of Internet tools to improve management, prevention, and surveillance

Cristiane Rapparini, MD, MSc, a,b Paulo Feijó Barroso, MD, a Valéria Saraceni, MD, PhD, c Alcyone Artioli Machado, MD, PhD, d and Guilherme Córtes Fernandes, MD, MSc e
Rio de Janeiro, São Paulo, and Juiz de Fora, Brazil

Background: Education is a major component of prevention strategies to reduce the risk of occupational transmission of blood-borne pathogens to health care personnel.

Methods: This study describes the results of an Internet-based project, “Projeto Riscobiologico.org”, for which the main objectives are to disseminate information in the Portuguese language about occupational exposures to bloodborne pathogens through a mailing list and Web site as well as to increase case reports of these events in Brazil.

Results: The mailing list expanded quickly with a total of 2078 participants (from 337 different cities and all Brazilian states), and 5613 messages were exchanged over a 5-year period. Mean length of participation was almost 2 years (697 days). Most of the participants (74%) reported that they frequently manage occupational exposures. Nevertheless, results showed an important lack of basic knowledge regarding this issue. In contrast with the high participation in the mailing list, a small number of institutions started to participate in the voluntary surveillance system.

Conclusion: The Internet can be used as a tool to increase knowledge and improve practices in the prevention of occupational bloodborne pathogen exposures. In addition, it may represent a unique opportunity to implement a national surveillance system. (Am J Infect Control 2007;35:267-70.)

Health care workers (HCWs) are at increased risk of acquiring infections by bloodborne pathogens in the health care setting.1,2 A series of prevention strategies can be implemented to reduce this risk. Educational programs for HCWs are extremely important and are among the major components of these strategies.3

The Internet is a worldwide electronic network providing access to millions of resources. The estimated number of active Web sites worldwide was greater than 74 million as of October 2005.4 The use of electronic mail (e-mail) has grown exponentially in recent years. It is estimated that a total of 1.2 billion e-mail mailboxes are in use in 2005 and that the number of person-to-person e-mails sent on an average day exceeds 130 billion.5 Mailing lists are currently used to facilitate online discussions on health issues among health care workers, students, and patients.6,7

“Projeto Riscobiologico.org” (www.riscobiologico.org) was implemented in Brazil in 2000. A Portuguese language mailing list and a Web site were created to allow the discussion of the management and prevention of infectious occupational exposures. In addition, a software program to increase surveillance of occupational exposures to bloodborne pathogens was developed. The purpose of this article is to describe the results of the implementation of “Projeto Riscobiologico.org.”

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Members of Riscobiologico.org Project: M. R. Resende, MD, PhD; R. A. M. Lopes, RN, MSc; C. M. Rosa, MD; R. M. Figueiredo, RN, PhD; E. Gir, RN, PhD; S. M. C. Chaves, MD; and V. Vellozo, PhD.

“Projeto Riscobiologico.org” was partially supported by a grant from Becton, Dickinson and Co; by a grant from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES; to C. R.); and by grants from Fogarty International Center/USNIH (2D43TW00010) and from Fundação Carlos Chagas de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ; to F. B.).

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MATERIALS AND METHODS

Description

‘Projeto Riscobiologico.org’ was initiated in Brazil in 2000. Initially, an e-mail discussion list (listadediscussao@riscobiologico.org) and a Web site (www.riscobiologico.org) were implemented. The main objective was to provide information and to discuss occupational infections among HCWs in the Portuguese language. In addition, software (PSBio) was developed to establish a voluntary surveillance system of occupational exposures to bloodborne pathogens in Brazilian health services.

Invitations to participate in the list and advertisements of the Web site were sent by e-mail to approximately 800 HCWs (infection control professionals [90%] and/or occupational health practitioners [10%]) on August 5, 2000. Simultaneously, the Web site was registered in 40 Web search engines (e.g., Google, Yahoo, Lycos). The project was approved by the Institutional Review Board of the School of Medicine/Hospital Universitário Clementino Fraga Filho of the Universidade Federal do Rio de Janeiro.

Mailing list

Participants subscribed to the list through a form available on the Web site. Variables collected included name, e-mail address, occupation, information about how did he/she learn about the list, experience with occupational exposures to infectious agents, and specialty. E-mail messages are sent to a central address, and a moderator reviewed and approved messages before distribution to subscribers to eliminate advertisements, junk e-mails, and spam. Only registered participants are allowed to send questions and answers through the mailing list. A maximum of 12 messages are sent per day. Health and outbreak alerts are distributed anytime. Since June 2002, the number of e-mails transferred by the server has been measured. This measurement represents the number of different messages sent per day multiplied by the number of participants subscribed in the period.

E-mails sent are classified in 7 major topics: general information and newsletter; health care-related infections and issues; occupational health and infections; medical waste; legislation; emergent disease, health, outbreak alerts; and miscellaneous. All messages are archived on the Web site.

Web site

The Web site was established with approximately 100 pages containing information about occupational exposures to infectious agents and prevention strategies. Educational materials such as international and Brazilian guidelines as well as topic-related articles were included. The Web site, which is regularly updated, includes questions and surveys about several health-related subjects. Web statistics and web log analyses have been collected monthly through WebTrends Software since 2000 (WebTrends Inc., Portland, OR). Data analyzed include page views (refers to the sum total of what a user sees in a browser window), number of visits (a visit begins when a visitor enters the site with an entry click and views a succession of 1 or more page views; the end of a visit is signaled by an exit click or a 10-minute period of inactivity), and duration of the visit.

Surveillance software-PSBio

A surveillance software based on NaSH (National Surveillance System for Health Care Workers) from the Centers for Disease Control and Prevention (CDC, Atlanta, GA)3 was developed within this project. The main objective was to implement a voluntary surveillance system of occupational exposures to bloodborne pathogens among Brazilian health services. Health professionals and institutions may request the software PSBio, which is distributed free of charge, through a form posted on the Web site. At request, information on occupation, experience with occupational exposures to infectious agents, and specialty is collected.

RESULTS

Mailing list: participants

We present data collected between August 2000 and June 2005. As of June 2005, a total of 2078 participants had joined the mailing list, and 1389 (67%) were still participating. The mean length of participation was 697 days (standard deviation [SD] ± 592). For those participants who remained on the list until the end of the evaluation period, the mean length of participation was 887 days (SD ± 576), whereas, for those who dropped from the list, it was 270 days (SD ± 355).

One hundred sixty-five out of 800 (21%) HCWs who were invited to participate by e-mail in August 2000 joined the list, and 103 (62%) of those were still participating as of June 2005. Other users joined the system after being informed by colleagues (46%) and through search engines on the Web (54%). From 2000 to 2005, these last 2 categories increased from 14% to 41% and 5% to 39%, respectively.

Participants from 337 different Brazilian cities joined the list. The mailing list reached 607 HCWs from all 27 Brazilian states within 5 months of its implementation. In addition, participants from 6 other countries (Cuba, 1; Uruguay, 2; Chile, 1; Peru, 2; Portugal, 11; and the United States, 3) joined the list.
Most of the participants were nurses (37%), followed by physicians (19%), occupational health technicians (8%), pharmacists (7%), and biologists (5%). Five hundred fifty-nine participants (559/2078; 27%) were from infection control, and 540 (540/2078; 26%) were from occupational health services. Most of the participants (74%) reported that they frequently managed HCWs exposed to blood and body fluids.

Messages content

During the evaluation period, 5613 messages were sent through the mailing list, with a mean of 4.8 messages/day (SD ± 2.8). From June 2002 to June 2005, 4106 messages sent by participants translated to 4,987,948 e-mails generated by the server.

The main topics of discussion in the list are shown in Table 1. Among 5613 messages, 1312 (23%) were classified as “general information and newsletter,” 1501 (23%) as “health care-related infections and issues,” 880 (16%) as “occupational health and infections,” 817 (15%) as “medical waste management,” 397 (7%) as “legislation,” 170 (3%) as “emergent diseases and outbreaks alerts,” and 736 (13%) as “miscellaneous.”

Web site

The mean monthly number of visits in year 2000 was 787. This number increased to 12,280 in 2005. The mean length of time visitors spend connected to the site ranged from 8 to 11 minutes. During the study period, the number of visitors increased from a mean of 5115 in 2000 to 34,480 page views/month in 2005.

As of June 2005, the Web site had almost 500 pages. These pages included information about occupational exposures among HCWs to several infectious agents. Additionally, a mean of 12 breaking news/month had been included in the first page of the Web site since August 2003. They included mostly health and outbreak alerts (22%) and announcements from the Brazilian Ministry of Health and scientific societies (24%).

An interactive “questions and quiz” tool was also included in the Web site: 3556 answers were sent to 28 questions; 59% of all responses were correct. Questions about basic concepts of management and prevention of occupational infections showed a low proportion of correct answers. For example, only 386 of 646 (60%) participants knew what tests were recommended for screening source patients; 56 of 68 (53%) knew about the safety for use of hepatitis B virus vaccine and hepatitis B immune globulin (HBIG) during pregnancy, and 230 of 498 (46%) knew about interpretation of serologic hepatitis B virus tests (hepatitis B surface antigen, antibody to hepatitis B surface antigen, and antibody to hepatitis B core antigen).

Surveillance software

Since January 2002, 1574 professionals requested the PSBio software. Most of the requests were from nurses (38%), followed by physicians (20%). Most HCWs were from occupational health services (432/1358; 32%) or were from infection control services (399/1358; 29%). This information was not available for all respondents.

One hundred fifty-eight health services have completed registration for the software, but, as of June 2005, only 4 different health care services actually have started sending data to this voluntary surveillance system. Difficulties were identified with the use of software and complexity of data forms. A new version of PSBio software was developed, showing better preliminary results with higher adherence to voluntary participation by the end of 2005.

DISCUSSION

This study describes the results of an Internet-based project, “Projeto Riscobiologico.org,” which included a mailing list, a Web site, and surveillance software for occupational exposures to bloodborne pathogens.

To our knowledge, this is the first mailing list focused on infectious occupational exposures among HCWs in the Portuguese language. A great proportion of Brazilian HCWs do not understand English, the main language in scientific medical literature and Web sites.

### Table 1. Messages topics of Riscobiologico.org mailing list-August 2000 to June 2005

<table>
<thead>
<tr>
<th>Topic</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>General information and newsletter</td>
<td>1312</td>
<td>23</td>
</tr>
<tr>
<td>Information about courses, events, and scientific meetings</td>
<td>713</td>
<td>13</td>
</tr>
<tr>
<td>Bibliography and educative material</td>
<td>438</td>
<td>8</td>
</tr>
<tr>
<td>General reports and contacts</td>
<td>161</td>
<td>3</td>
</tr>
<tr>
<td>Health care-related infections and issues</td>
<td>1301</td>
<td>23</td>
</tr>
<tr>
<td>Sterilization, disinfection, reuse</td>
<td>545</td>
<td>10</td>
</tr>
<tr>
<td>PPE and isolation precautions</td>
<td>304</td>
<td>5</td>
</tr>
<tr>
<td>Support areas (e.g., laundry, pharmacy, housekeeping)</td>
<td>246</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>206</td>
<td>4</td>
</tr>
<tr>
<td>Occupational health and infections</td>
<td>880</td>
<td>16</td>
</tr>
<tr>
<td>Concepts and follow-up procedures</td>
<td>243</td>
<td>4</td>
</tr>
<tr>
<td>Occupational HIV/AIDS Infections</td>
<td>215</td>
<td>4</td>
</tr>
<tr>
<td>Immunizations for HCWs</td>
<td>144</td>
<td>3</td>
</tr>
<tr>
<td>Surveillance systems</td>
<td>71</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>207</td>
<td>4</td>
</tr>
<tr>
<td>Medical waste</td>
<td>817</td>
<td>15</td>
</tr>
<tr>
<td>Legislation</td>
<td>397</td>
<td>7</td>
</tr>
<tr>
<td>Emergent diseases, health, and outbreak alerts</td>
<td>170</td>
<td>3</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>736</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>5613</td>
<td>100.0</td>
</tr>
</tbody>
</table>

PPE, Personal protection equipment.
Brazil and 7 other countries have Portuguese as the official language, with more than 220 million people speaking Portuguese worldwide. This fact supports the need of up-to-date scientific information in Portuguese with easy access via the World Wide Web.

E-mail discussion groups on the Internet are new academic forums in which knowledge and experience can be shared. Lists may be particularly useful to disseminate health and outbreak alerts and also as an early warning system for emerging diseases, such as the example of ProMED-mail from International Society for Infectious Diseases, an electronic outbreak reporting system that monitors infectious diseases globally. Information about emergent diseases, health, and outbreak alerts increased from less than 0.5% of the subjects of the mailing list messages in 2002 to almost 9% in 2005.

Participants subscribed to this list for long periods of time, with a mean duration of almost 2 years, suggesting a high interest and quality of the subjects discussed. Using e-mail to reach the target audience was an efficient strategy at the begging of the project; more than 20% of invited professionals joined the list, and more than 60% of those were still participating after 5 years. This project was initially implemented to discuss and provide information about management and prevention of occupational exposures and infectious diseases among HCWs, but other areas of interest were frequently discussed, such as health care-related infections and medical waste. This may represent a lack of other forums to discuss these issues and the need of additional sources of information for HCWs involved with infection control. Overall, occupational health and infections represented only 16% of messages sent in the list.

Although most of the participants (74%) reported that they frequently manage HCWs exposed to blood and body fluids, the messages in the mailing list and answers to the quizzes showed an important lack of basic knowledge regarding this subject. It was alarming that only nearly half of HCWs were able to give correct answers about serologic screening recommended for source patient testing and about interpretation of serologic HBV tests. Brazil has resources such as antiretroviral drugs for postexposure prophylaxis, guidelines, and standardized protocols to manage exposures in the health care setting. Nevertheless, our results demonstrated an important lack of knowledge among HCWs who manage these exposures. The project expanded quickly, reaching HCWs from several different cities and all Brazilian states in a short period of time. This finding indicates the prospect of using the World Wide Web as an efficient tool to disseminate health-related information and the opportunity to monitor knowledge and practices in specific issues and to target better the topics regarding educational programs. In addition, this model can be expanded to other settings at which Portuguese language infection prevention materials are needed and access to health information is limited. Furthermore, even beyond Portuguese-speaking nations, the experience reported in this study may be adapted for users in countries without existing infection prevention program infrastructure.

This project also aimed to implement a voluntary surveillance system. Although this kind of surveillance system may lead to a biased sample that may not represent the national situation, results obtained from similar systems implemented in developed countries have been useful to help the development of prevention strategies. Presently, no national surveillance system for occupational infections among HCWs is in place in Brazil. In contrast with the high participation in the mailing list, only 4 institutions began to participate in the voluntary surveillance system. In conclusion, this project was successful in functioning as an online discussion group. In addition, several strategies will be tested to increase adherence to this voluntary surveillance system.

The authors thank Dr. Denise Cardo for invaluable assistance in the preparation of this article and for her contribution and participation in “Projeto Riscobiologico.org” since its implementation in 2000 and Dr. Keith Sabin for his comments.

References
10. Worth ER, Patrick TB. Do electronic mail discussion lists act as virtual colleagues? Proc AMIA Annu Fall Symp 1997;97(325-9.)
The infection control audit: The standardized audit as a tool for change

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Vancouver, British Columbia, Canada

Background: Health care workers’ compliance with infection control practices and principles is vital in preventing the spread of disease. One tool to assess infection control practice in clinical areas is the infection control audit; however, many institutions do not approach this in a systematic fashion.

Methods: Key features of the infection control audit were identified by the infection control team and developed into a standardized format for review of clinical areas. The audit incorporates a review of the physical layout, protocols and policies, knowledge of basic infection control principles, and workplace practice review.

Results: Over the last 13 years, the infection control unit has completed 17 audits involving 1525 employees. Four-hundred-one staff members have filled out questionnaires that assessed their understanding of standard precautions. A total of 257 recommendations have been made, and 95% of these have been implemented. The majority of recommendations address separation of clean and dirty supplies, hand hygiene compliance, hand hygiene signage, proper use of barriers, and environmental cleaning.

Conclusion: The infection control audit is an opportunity to implement changes and to introduce remedial measures in collaboration with various departments and services. A standardized approach to the audit allows benchmarking of practices across the institution and enhances standards of care. (Am J Infect Control 2007;35:271-83.)

Consistent adherence to infection control principles is the means by which health care workers can protect themselves and their patients. The infection control audit is an ideal vehicle to assess consistency of approach to infection prevention, and it has proven to be a useful part of infection control programs. The audit is an organized examination of ward or service practices and procedures that provides an opportunity to simultaneously review safety in the workplace and identify and remedy deficiencies. It is also an ideal time to reinforce and acknowledge those procedures and practices that meet high standards of care. The purpose of this paper is to present our institution’s development of a standardized audit form to ensure the consistent and thorough application of key infection control principles.

MATERIALS AND METHODS

Background

Vancouver General Hospital is a 700-bed adult tertiary care facility for British Columbia, Canada, admitting an average of 22,000 patients a year. The hospital is the provincial transplantation center as well as the referral institution for burns, neurosurgery, trauma, and spinal cord injury. The hospital employs, on average, 7000 full-time employees (FTE), and the infection control service is composed of 3.5 FTE medical microbiologists, one of whom is the infection control officer (ICO), and 3.75 FTE infection control professionals (ICP).

The audit structure

The audit tool was designed and developed over a series of meetings with members of the infection control team, consisting of ICPs, ICOs, and medical microbiologists. Audit items were selected based on review of standards and guidelines from the Public Health Agency of Canada (PHAC), the Association for Professionals in Infection Control and Epidemiology, Inc (APIC), and the Hospital Infection Society (HIS) as well as on practical experience. The audit tool was shared with the Community Hospital Infection Control Association-Canada (CHICA-Canada) members, and feedback was requested. Prior to the audit, the patient...
<table>
<thead>
<tr>
<th>ITEM</th>
<th>YES</th>
<th>NO</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td><strong>UNIT:</strong></td>
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<tr>
<td>Patient/Residents Services Manager:</td>
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<tr>
<td>Number of Nurse Clinicians/Supervisory staff:</td>
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<td>Number of staff:</td>
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<td>Number of staff per shift:</td>
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<td>Days:</td>
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<td>Nights:</td>
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<tr>
<td>Number of beds: Single: 2 bed: 3 bed: 4 bed:</td>
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<td>Number of admissions/month:</td>
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<td>Type of admissions:</td>
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<tr>
<td><strong>PHYSICAL ENVIRONMENT</strong></td>
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<tr>
<td><strong>Soiled Utility Room:</strong></td>
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<tr>
<td>1. Does the area have a clean orderly appearance?</td>
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<tr>
<td>2. Is there a sink?</td>
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<td>3. Are there a washer/disinfector and a hopper in place?</td>
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<td>4. If yes to above, are there instructions for its use posted?</td>
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<td>5. Are there containers for confining soiled articles prior to pick-up?</td>
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<td>6. Is there adequate storage for contaminated supplies/equipment?</td>
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<td>7. Are garbage containers covered?</td>
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<tr>
<td>8. Are clean or sterile supplies stored in the room?</td>
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<tr>
<td>9. Are disinfectants or cleaning agents clearly labelled?</td>
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<tr>
<td>10. Is personal protective equipment available?</td>
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<tr>
<td>11. Does traffic move from soiled to clean?</td>
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<tr>
<td><strong>Clean Utility Room:</strong></td>
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<tr>
<td>1. Does the area have a clean orderly appearance?</td>
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<tr>
<td>2. Is there a clear separation of clean and soiled storage areas?</td>
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<tr>
<td>3. Are soiled articles brought into the clean area?</td>
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<tr>
<td>4. Are clean supplies stored above the floor?</td>
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<tr>
<td>5. Is there a handwashing sink?</td>
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<tr>
<td>6. Is there a schedule for cleaning the room?</td>
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<tr>
<td>7. Is there evidence of excessive dust or dampness?</td>
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<tr>
<td><strong>Medication Room:</strong></td>
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<tr>
<td>1. Does the area have a clean orderly appearance?</td>
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<tr>
<td>2. Is there a dedicated handwashing sink?</td>
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<tr>
<td>3. Is there evidence of inappropriate activities such as food preparation/storage?</td>
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<tr>
<td>4. Are open containers of sterile solutions dated?</td>
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<tr>
<td>5. Are multidose vials used?</td>
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<tr>
<td>6. Is a sharps disposal container readily available?</td>
<td></td>
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<tr>
<td>7. Is the refrigerator clean and free of frost build-up?</td>
<td></td>
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<tr>
<td>ITEM</td>
<td>YES</td>
<td>NO</td>
<td>COMMENTS</td>
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<tr>
<td><strong>Tub/Shower Room(s):</strong></td>
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<tr>
<td>1. Does the area have a clean orderly appearance?</td>
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<tr>
<td>2. Is there a policy that designates who cleans the tub between patients?</td>
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<tr>
<td>3. Is there a protocol posted for cleaning tubs and showers?</td>
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<tr>
<td>4. Is there a regular cleaning schedule?</td>
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<tr>
<td>5. Is there a laundry hamper for used towels and shelving for supplies?</td>
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<tr>
<td><strong>Patient/Resident Rooms:</strong></td>
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<tr>
<td>1. Do the rooms have a clean orderly appearance?</td>
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<tr>
<td>2. Are isolation or private rooms for isolation available?</td>
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<tr>
<td>3. Is negative pressure available in these rooms?</td>
<td></td>
<td></td>
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<tr>
<td>4. Are there handwashing sinks accessible in these rooms?</td>
<td></td>
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<tr>
<td>5. If no to the above, are there waterless hand agents available?</td>
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<tr>
<td>6. Can a nurse pass between the beds without touching the adjacent bed?</td>
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<tr>
<td>7. Are sharps containers accessible?</td>
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<tr>
<td>8. Is there a policy on sharing and cleaning of commodes?</td>
<td></td>
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<tr>
<td>9. Is there a urine measuring/discard container for each patient/resident?</td>
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<tr>
<td>10. Is there appropriate storage for urine containers?</td>
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<tr>
<td><strong>SPECIAL EQUIPMENT</strong></td>
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<tr>
<td>1. List any special equipment used in the area:</td>
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<tr>
<td>2. Mechanical lifts: Patient Wheelchairs</td>
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<tr>
<td>3. Oximeters Endoscopes</td>
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<td>4. Laryngoscopes: Ambubags:</td>
<td></td>
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<tr>
<td>5. Glucometers:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6. Other:</td>
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<tr>
<td>7. Is there a regular cleaning schedule for this equipment?</td>
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<tr>
<td>8. Is the cleaning of equipment clearly designated?</td>
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<tr>
<td>9. Is there compliance with the cleaning schedule?</td>
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<tr>
<td><strong>HAND HYGIENE</strong></td>
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<tr>
<td>1. Are health care workers (HCWs) knowledgeable as to how and when to clean their hands?</td>
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<tr>
<td>2. Are HCWs observed to clean hands appropriately?</td>
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<tr>
<td>3. Is antimicrobial soap used on the unit?</td>
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<tr>
<td>4. Are alcohol hand rubs used on the unit?</td>
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<tr>
<td>5. Are alcohol hand rubs readily accessible to HCWs?</td>
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<tr>
<td>6. Are sinks accessible and in adequate number on the unit?</td>
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<tr>
<td>7. Are there dedicated handwashing sinks?</td>
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<tr>
<td>8. Are paper towels and hand cream readily accessible?</td>
<td></td>
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<tr>
<td>9. Are there hand hygiene posters in appropriate areas?</td>
<td></td>
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<tr>
<td>10. Is there an ongoing education on hand hygiene for all HCWs?</td>
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</tr>
</tbody>
</table>

Fig 1. Continued.
<table>
<thead>
<tr>
<th>ITEM</th>
<th>YES</th>
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<th>COMMENTS</th>
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<tbody>
<tr>
<td><strong>BARRIER PROTECTION</strong></td>
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<tr>
<td>1. Is the Infection Control Manual readily available?</td>
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<tr>
<td>2. Do all HCWs know where and how to access Infection Control policies?</td>
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<tr>
<td>3. Are HCWs knowledgeable as to appropriate use of barriers?</td>
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<tr>
<td>4. Is there a protocol on appropriate glove use available?</td>
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<tr>
<td>5. Are gloves being worn for appropriate tasks?</td>
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<tr>
<td>6. Are gloves worn between patient contacts?</td>
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<tr>
<td>7. Are gloves changed as appropriate if they become soiled during a procedure?</td>
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<tr>
<td>8. Are gowns available?</td>
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<tr>
<td>9. Are gowns worn for the appropriate tasks?</td>
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<tr>
<td>10. Is facial barrier protection available?</td>
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<tr>
<td>11. Is facial barrier protection observed to be used when there is a risk of aerosolization of body fluids?</td>
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<tr>
<td>12. Are HCWs knowledgeable about TB precautions/Respiratory isolation?</td>
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<tr>
<td>13. Are particulate respirator masks available?</td>
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<tr>
<td>14. Are HCWs knowledgeable as to the appropriate use of these masks?</td>
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<tr>
<td>15. Are particulate respirator masks observed to be used correctly?</td>
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<tr>
<td><strong>ROUNTE PRECAUTIONS</strong></td>
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<td></td>
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<tr>
<td>1. Do HCWs know what to do in the event of a sharps injury?</td>
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</tr>
<tr>
<td>2. Is a sharps exposure protocol posted in the patient care area?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Are provisions in place for immediate reporting and assessment of a sharps injury?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4. Is there a policy designating responsibility for sharps disposal?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Are sharps containers sealed for disposal when approximately 3/4 full?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Are sharps containers point-of-use?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Are needles used on patients recapped?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. If multidose vials are used, is a separate needle and syringe used for each re-entry?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Is there a protocol prescribing or prohibiting food consumption in patient/resident care areas?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Do HCWs know the difference between biomedical, radioactive, and regular waste?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Is waste segregated appropriately?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Is biomedical waste disposed of appropriately?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITEM</td>
<td>YES</td>
<td>NO</td>
<td>COMMENTS</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----</td>
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<td>----------</td>
</tr>
<tr>
<td><strong>SPECIMEN HANDLING</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Are HCWs knowledgeable about safe handling of body fluid specimens?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Are specimens properly wrapped prior to sending to the laboratory?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3. Are specimens appropriately labelled?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4. Are sharps removed from samples prior to transport?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Is there a written policy for specimen collection and transport available?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DECONTAMINATION OF BODY FLUID SPILLS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Is there a written policy for decontamination of spills of body fluids?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Are supplies readily available for decontamination?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MRSA/VRE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Is there an Antibiotic Resistant Microorganisms Precautions protocol readily available?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Are HCWs knowledgeable about precautions for AROs?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3. Are rooms with ARO patient posted if appropriate?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4. Are HCWs observed to comply with ARO precautions?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Are cleaning staff knowledgeable about cleaning protocols for MRSA/VRE?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Is the appropriate cleaning solution and protocol applied?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Is a different mop head used for MRSA/VRE rooms?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Are patient/resident rooms cleaned in an acceptable manner?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Is there a policy for notifying departments or other institutions when a patient/resident is moved or transferred?</td>
<td></td>
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<tr>
<td><strong>RESPIRATORY CARE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. If applicable, is respiratory protection used when giving respiratory care to ventilated patients?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Are oximeters cleaned between patients?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3. Are respiratory care technologists compliant with hand hygiene?</td>
<td></td>
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<tr>
<td><strong>REHABILITATION THERAPY</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1. Are occupational and physiotherapists observed to be compliant with hand hygiene?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Is special equipment cleaned between residents/patients?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>DRESSING CHANGES</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1. Was the HCW observed to clean their hands prior to gathering supplies?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Was aseptic technique maintained throughout the equipment set-up?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Was &quot;clean to dirty&quot; technique maintained throughout the procedure?</td>
<td></td>
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</tbody>
</table>

Fig 1. Continued.
The audit includes an inspection of the physical plant, a review of workplace infection control practices, an assessment of health care workers’ knowledge and application of infection control principles, and a report documenting deficiencies and required interventions. All documented deficiencies are followed by recommendations that are summarized in a worksheet format with a completion date acceptable to both the audited unit and the infection control team. The review team involves at least 2 ICPs and 1 medical microbiologist.

**Physical environment**

Inspection of the physical environment consists of a general examination of the layout of the unit with emphasis on the soiled and clean utility rooms, medication room, and patient/resident rooms. Special equipment such as oximeters, endoscopes, and glucometers are checked for the presence of a regular cleaning schedule and for compliance. Design flaws that may inhibit good infection control practice are noted. The process requires several visits to assess properly the levels of cleanliness and consistency in cleaning practices.

**Workplace practice review**

The infection control practice of all staff is observed and evaluated using a standardized form to record lapses in accepted practice (Fig 1). The appropriate use of isolation rooms, proper hand hygiene, barrier precautions, and waste disposal are observed and documented on at least 3 occasions, more frequently if deficiencies are initially noted. Policy and procedure manuals are reviewed to determine that all policies conform to current infection control standards. The standard audit form also includes appropriate use of barrier protection, specimen handling, decontamination of body fluid spills, correct use of isolation protocols, and general staff appearance and attire. Other practices assessed when applicable include intravascular line insertion, suctioning, urinary catheter care and insertion, skin and wound care, and unit-related procedures. When practices are unique to a ward/department (eg, the morgue), these are covered with an addendum to the standard form.

Over several visits, a minimum of 75 hand hygiene events are observed by an ICP. Standardized criteria for when hand hygiene is required are used. Episodes are recorded, using personal digital assistant software.
Instructions: Auditors should move around a unit as required to document events rather than targeting one specific area of the unit. Please note that no more than three observations for an individual health care worker should be made. Only those situations where hand hygiene is unequivocally required should be documented:

- Before patient care or contact
- During patient care a) when hands are visibly soiled and b) between procedures involving aseptic technique
- After patient contact
- After removal of all barriers
- Before eating or handling food
- After using the toilet
- Whenever hands appear soiled
- After percutaneous injury to hands
- After sneezing or blowing one’s nose

Assessing knowledge and its application

Prior to any documented observations in the workplace, a questionnaire assessing routine precautions intention of the hand hygiene audit is to primarily provide feedback in a positive manner to the unit and is not intended as a research endeavor.

(Pendragon Forms 3.1, Pendragon Software Corporation, Buffalo Grove, IL) onto a hand hygiene audit form (Fig 2). No more than 3 events are recorded for an individual, and only the profession is documented to maintain anonymity. The ICP is discreet during auditing and generally is on the ward as part of their daily rounds. Sampling is opportunistic because not every individual working on the unit is observed. The

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2 Pendragon Forms 3.1, Pendragon Software Corporation, Buffalo Grove, Illinois

Fig 2. Hand hygiene survey.
The Infection Control Service is conducting a review of your clinical area. It would be greatly appreciated if you could take a few minutes to fill out this questionnaire. Results are anonymous, confidential, and for audit purposes only. Please return your reply to the box in the nursing station or mail it to the Infection Control Unit, LSP 1.

A. **Demographic Information (please circle one response for each question)**
   1) Position: a) Radiologist  b) Radiographer  c) Nurse  d) Resident /MSI  
   e) clerical  (f) Other ________________
   2) Age: a) less than 20 years  b) 20-29 yrs  c) 30-39 yrs  d) 40-49 yrs  e) 50-59 years  f) 60 yrs or older
   3) Sex: a) male  b) female
   4) Years at Vancouver General Hospital:
   5) Total years working in health care:

B. **Routine Precautions (RP) Education Session (circle best response)**
   1) Have you attended an education session on RP at VGH? Yes  No  Unsure
   2) Have you attended an education session on RP? Yes  No  Unsure
   3) When was your last education session on RP? a) < 6 mos  b) 6 mos-2 yrs  c) > 2 yrs
   4) Do you feel you received sufficient information on this subject? Yes  No  Unsure
   5) Was the session(s) clear and understandable? Yes  No  Unsure
   6) Do you feel you understand the principles of RP? Yes  No  Unsure
   7) Are you aware of a hospital policy on sharps (e.g., needle stick) injuries? Yes  No  Unsure
   8) Do you know what to do immediately in the event of a sharps injury? Yes  No  Unsure
   9) Do you understand the appropriate use of gloves, masks, and gowns? Yes  No  Unsure

C. **Knowledge Assessment (circle best response)**
   1) RP advocates the use of gloves for blood or potentially bloody fluids only. True  False
   2) Invasive procedures require hand washing with neutral (non-antiseptic) soap. True  False
   3) Private rooms are still used for potential airborne disease such as TB. True  False
   4) Sharps injuries should be assessed by the Employee Health Unit. True  False
   5) Surgical masks should be used for airborne disease, e.g., Tuberculosis True  False
   6) Hepatitis B immunoglobulin can be given up to one week after an exposure with protection of the individual. True  False
   7) Capped needles may be put into the garbage. True  False
   8) Buffered bleach should be used to clean up blood spills. True  False
   9) The environment is the major source of spread of infections in hospitals. True  False
   10) RP advocates labelling of laboratory requisitions as to risk of bloodborne diseases. True  False

D. **Practical knowledge of RP (circle best response)**
   1) The use of more than one pair of gloves during an invasive procedure with blood spill has been shown to reduce the risk of cutaneous exposure to blood. True  False
   2) Vaccination of staff for influenza is more effective in preventing outbreaks than vaccination of patients. True  False
   3) Passing of sharps in basins during a procedure has been shown to reduce the risk of sharps injuries. True  False
4) The terminal cleaning procedure differs in cases of patients with known bloodborne disease. True False
5) Caring for patients with MRSA requires the routine use of gowns, gloves, and masks. True False

E. **RP in practice (Please circle best response to what you currently practice.)**
   Please leave the answer blank if questions does not pertain to you.
1) Do you wear protective eyewear (other than prescription glasses) during procedures where there is the potential for blood splatter?
   a) always  b) sometimes  c) never
2) Do you double glove when performing invasive procedures with potential for blood spill?
   a) always  b) sometimes  c) never
3) When your gloves come in contact with body fluids, do you discard them when the specific task is complete?
   a) always  b) sometimes  c) never
4) Do you change your personal protection habits if you know the patient has hepatitis B or C?
   a) always  b) sometimes  c) never
5) Do you wash your hands after removing gloves?
   a) always  b) sometimes  c) never
6) Do you wear a respirator when there is a potential to be exposed to respiratory aerosols?
   a) always  b) sometimes  c) never
7) Have you had a sharps injury in the last two years? Yes No
8) Did you report the injury? Yes No
   If no to question 8: Why not?

9) Do you ever recap a needle?
   a) always  b) sometimes  c) never
   Describe the circumstances where you might recap a needle

10) What is the significance of a respirator having an N-95 rating?

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Thank you for your time and cooperation in answering this questionnaire.

Additional comments (or concerns):

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1 Example of questionnaire form from a current Radiology infection control audit

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Fig 3. Infection control standard precautions survey.
(Fig 3), frequency of education sessions and health care worker comprehension, and application of infection control procedures in the workplace is filled in anonymously by staff. The questionnaire contains standard questions as well as questions suitable for that specific work environment. After completion of the audit, education sessions are scheduled to discuss the responses to the knowledge and workplace practice assessment questions.

Report and recommendations

The audit report has a structured format consisting of a description of the unit, number of staff, number of beds, and number of monthly admissions. The report follows the same flow as the review process: (1) description of the unit with its activities, (2) physical environment, (3) workplace practices, and (4) infection control knowledge and its application. Findings are summarized as a list of recommendations that are supported with references and guidelines whenever possible. A checklist of responsibilities and action dates are appended, and a meeting with the clinical area’s multi-disciplinary team is arranged to discuss the findings and the recommendations. Typically, this will include a medical director, patient services manager, nurse representative, unit educator, respiratory therapist, and other ward/department specific staff (eg, morgue attendants). The meeting is an opportunity to discuss any contentious issues prior to the final recommendations. The ICPs then visit the unit at regular intervals (generally 3 and 6 months) to document progress in implementing the various recommendations.

RESULTS

The infection control unit has completed 17 audits at this institution within the last 13 years. The wards and services reviewed included intensive care, emergency department, orthopedic surgery, solid organ transplantation, outpatient clinics, spinal cord injury unit, pathology and clinical laboratory services, morgue, food and nutrition services, occupational therapy kitchens, respiratory services, operating room, radiology, and hemodialysis. On average, each audit occurs over 3 to 6 months and entails approximately 50 to 100 ICP hours. Approximately, 1525 staff members have been contacted during the audit periods. Questionnaires on routine precautions have been completed by 401 staff.

There were 390 forms available for demographic analysis of which 60% were submitted by nursing staff (Table 1). The age range was 20 to 65 years with an average of 14.5 years in health care. Approximately half of respondents had attended an infection control education session; however, the majority felt that they understood basic principles of infection control, particularly barrier use (Table 2). When formal knowledge was assessed, however, deficiencies were noted in application of routine precautions, barrier use for airborne infections, and hand hygiene practice (Table 3).

A total of 257 recommendations have been made, and 95% have been acted on (Table 4). The most common recommendations focused on proper environmental cleaning (11%), proper equipment cleaning protocols (11%), correct use of personal protective equipment (11%), hand hygiene procedures (8%), and separation of clean and soiled supplies (8%).

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**Table 1. Demographic information**

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range</td>
<td>20-65 yr</td>
</tr>
<tr>
<td>Years in health care</td>
<td>&lt;5 to &gt;30 yr (average 14.5)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>234 (60%)</td>
</tr>
<tr>
<td>Male</td>
<td>89 (23%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>67 (17%)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Nurse</td>
<td>187 (48%)</td>
</tr>
<tr>
<td>Physician</td>
<td>34 (9%)</td>
</tr>
<tr>
<td>Technologist/therapist</td>
<td>89 (23%)</td>
</tr>
<tr>
<td>Emergency support staff</td>
<td>43 (11%)</td>
</tr>
<tr>
<td>Other</td>
<td>37 (9%)</td>
</tr>
</tbody>
</table>

*N = 390.

**Table 2. Infection control education**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No. and percentage responding affirmatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attended infection control session</td>
<td>197 (49%)</td>
</tr>
<tr>
<td>Sufficient information received</td>
<td>143 (36%)</td>
</tr>
<tr>
<td>Personal understanding</td>
<td></td>
</tr>
<tr>
<td>of infection control principles</td>
<td>317 (79%)</td>
</tr>
<tr>
<td>Personal understanding</td>
<td></td>
</tr>
<tr>
<td>of correct barrier use</td>
<td>334 (83%)</td>
</tr>
</tbody>
</table>

*N = 401 respondents.

**Table 3. Infection control knowledge assessment**

<table>
<thead>
<tr>
<th>Area of assessment</th>
<th>Correct response, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharps injury policy</td>
<td>321 (85%)</td>
</tr>
<tr>
<td>Sharps exposure management</td>
<td>302 (80%)</td>
</tr>
<tr>
<td>Sharps handling and disposal</td>
<td>310 (82%)</td>
</tr>
<tr>
<td>Routine precautions appropriately applied</td>
<td>177 (47%)</td>
</tr>
<tr>
<td>Personal protection requirements for tuberculosis</td>
<td>185 (49%)</td>
</tr>
<tr>
<td>Body fluid spill cleanup procedure</td>
<td>311 (83%)</td>
</tr>
<tr>
<td>Hand hygiene practice</td>
<td>257 (68%)</td>
</tr>
</tbody>
</table>

*N = 377.
many instances, once a problem or deficiency was identified, it was corrected prior to completion of the audit.

Large scale improvements resulting directly from the audit process include the introduction of standardized orders for antimicrobial prophylaxis (arising from the first operating room audit in 1996); the addition of alcohol handrub dispensers throughout the institution beginning in 1995 (to address observed lack of hand hygiene stations); the introduction of a template in 1998 to address additional costs associated with enhanced infection control measures in the tendering process for new construction and renovations (a response to physical plant design constraints observed in the audits); and, more specifically, the addition of 102 negative-pressure rooms in the new acute care tower (20% of all beds). Other improvements arising from audit recommendations include use of the hands-free technique for passing sharps (2000); enhanced personal protective equipment and new safety protocols in the autopsy suites (1999); revised protocols for cleaning of dialysis machines; and introduction of syndromic surveillance for gastrointestinal and respiratory infections in the emergency department (2003).

DISCUSSION

Audits in infection control have received relatively little attention, although the area should be an ideal subject because of its focus on patient and health care worker safety, the availability of standards by which to measure the quality of care, and the ability to document improvement in practice. Unfortunately, most audits involving infection control focus on environmental cleanliness rather than encompassing unit procedures as they apply to the practice of infection prevention. To be truly effective, an audit must consist of a topic, appropriate practice standards, observation and testing against the selected standards, identification of areas for improvement, and subsequent interventions and demonstration of improvement in practice.3-5

Following completion of the first 3 infection control audits in the early 1990s, it was apparent that there was a need for a more consistent and organized review process. The audit form had been shared with members of CHICA-Canada and feedback requested, but this was not a formal verification or validation process.6 Thus, the audit tool has not been verified, and this is an acknowledged limitation. The infection control services have recently been regionalized, and plans are underway to review the audit document, weight the observations, and develop a scoring system. This will address the urgency of a particular action and the risk to the patient and/or staff. Construct validity and interrater reliability will also be assessed as part of this process.

It must be emphasized that the infection control audit presents an opportunity to promote infection prevention and control improvement activities in partnership with an organization’s multidisciplinary teams. Issues that influence the prioritization of the ward/department to be audited include acuity of patient care, central venous catheter-associated bloodstream infections, surgical wound infection rates and high rates of Clostridium difficile or antibiotic-resistant organisms, and date of last audit.

The audit is comprehensive and includes inspection of the physical plant, review of workplace infection control practices, and assessment of health care workers’ knowledge and application of infection control principles. The observational period is then followed by identification of areas for improvement, involvement of staff in the report writing process, and recommendations for further intervention. Although initially the process may seem daunting, the prolonged period of time for the audit is designed to account for the busy schedule of the ICP and the need to incorporate the audit as part of their routine for the next several months. It is similar to planning a calendar of educational sessions, but instead, unit or ward visits are scheduled into the ICP’s day. In this staged manner, the audit becomes less intimidating, particularly because the ICPs can incorporate some of the observational tasks as part of their daily rounds. The prolonged period of observation likely more accurately reflects true unit practices compared with a set of observations at a single point in time.

An assessment of the physical layout of any unit is necessary to determine the ease or difficulty with which staff can maintain a safe, clean environment.

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**Table 4. Frequency of infection control recommendations**

<table>
<thead>
<tr>
<th>Category of recommendation</th>
<th>Frequency, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environmental cleaning procedures</td>
<td>29 (11)</td>
</tr>
<tr>
<td>Cleaning of equipment</td>
<td>28 (11)</td>
</tr>
<tr>
<td>Use of protective equipment</td>
<td>27 (11)</td>
</tr>
<tr>
<td>Hand hygiene practice</td>
<td>21 (8)</td>
</tr>
<tr>
<td>Separation of clean and soiled supplies</td>
<td>21 (8)</td>
</tr>
<tr>
<td>Accessible protective equipment</td>
<td>16 (6)</td>
</tr>
<tr>
<td>Handling and disposal of sharps</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Multidose vial procedures</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Prohibition of food and drink in work area</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Isolation practices</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Other (eg, traffic flow, untidiness, isolation signage)</td>
<td>84 (33)</td>
</tr>
</tbody>
</table>

*N = 257.*
and prevent cross infection. Good or bad design can affect one’s ability to maintain a clean environment, and clinical areas must be designed to facilitate good work habits. Recommendations for changes to the physical environment are consistent with The American Institute of Architects Academy of Architecture for Health guidelines and are used to assist with future renovations. Consultation between facility planning and infection control is now a regular outcome of the audit process.

Review of workplace practices is evaluated against existing standards and current facility-specific infection control policies and procedures. The most commonly found deficiencies in the areas reviewed include incorrect storage of clean and dirty supplies, poor compliance with handwashing, incorrect use of barriers, inadequate cleaning of shared equipment, and consumption of food and beverages in the work area. Ways in which deficiencies are addressed include review of work practice with staff, reorganization of service areas to improve infection control compliance, and revision of protocols or procedures. For example, confusion over cleaning of electronic equipment such as oximeters and glucometers led to changes in cleaning protocols and assignment of housekeeping personnel to the task. Identification of poor aseptic technique when accessing multidose lidocaine vials on certain wards led to the immediate withdrawal of this item from unit stock. Documentation of inappropriate mask use and review of exposure risk to airborne disease in our institution led to increased promotion of respirators for high-risk respiratory care and training in their use (prior to severe acute respiratory syndrome). The latter intervention was felt to be a high priority because the region accounted for 38% of all newly diagnosed tuberculosis cases in the province and our institution admitted an average of 64 cases of active respiratory tuberculosis a year. These examples of early successes were a direct outcome of the audit process and may have contributed to the facility’s successful infection control management of severe acute respiratory syndrome cases. All of these specific examples were documented as completed on 3- or 6-month follow-up to “close the loop” between observation, recommendation, and implementation.

A recent addition to the audit process is the observation of opportunities for hand hygiene during a 1-hour period on 2 or 3 occasions. Compliance rates for hand hygiene practices vary from 28% to 60% across all professions. Varying compliance rates and hand hygiene practices are highlighted during the postaudit meetings, and staff are invited to provide feedback and suggestions for improving compliance. This component of the audit allows for the opportunity to compare the practice of other units within the same institution and is excellent material for postaudit education sessions. It is difficult to determine whether the hand hygiene audits and feedback have improved health care worker compliance, partly because of the numerous barriers and facilitators that affect intent to comply with this simple yet effective measure and partly because the intent of the audits was for feedback rather than as independent evaluation of compliance over time.

A major component of infection control is education of the health care worker on routine precautions. Comprehension of infection control principles is vital to the protection of both staff and patients. The purpose of the knowledge and practice survey as part of the audit process is to ascertain the level of infection control knowledge, to determine whether perception of knowledge is genuine, and to evaluate whether knowledge is applied in the workplace setting. The questionnaire has been particularly useful in detecting areas that require further attention. Infection control arranges education sessions to review the correct responses with unit personnel and circulates FAQ sheets for each question following collection of all the survey forms.

In retrospect, the behavioral and knowledge components in the knowledge assessment form would have been better if items had been rated on a scale rather than as a simple yes or no question. This is a limitation of the form from an analytical standpoint; however, it must be emphasized that this particular audit tool serves mainly to inform the infection control team of gaps in knowledge and deficiencies in practice, which can then be communicated back to the ward or unit. Future plans for the knowledge assessment form include a factor analysis to verify construct validity and revision to allow for further assessment of changes in knowledge over time. This then would allow for more focused intervention with detailed observations and research questions.

One illustration of the ability of the knowledge and practice assessment form to identify areas for improvement was the disappointing results regarding attendance at infection control education sessions and comments regarding the subject matter presented in the early audits. It clearly documented a need to revise the infection control unit’s approach to content delivery and provided the impetus to create an on-line infection control education module and infection control manual. The latter has recently received funding to assess infection control knowledge retention over time.

Involvement of health care workers from the onset of the audit and review of the audit findings with feedback by staff prior to the final audit draft should be stressed. Participation in the process by the clinical areas facilitates acceptance and completion of recommendations in a timely fashion. The nursing unit
manager, the medical director, the nurse educator, and
the infection control designate on the ward are in-
volved at the beginning of the audit process and are
key participants in the development of action plans.

The goal of the infection control team is to review
each clinical area on a 5- to 7-year cycle, similar to
the hospital accreditation process. Documentation
and consistency of approach should allow the team
to focus on previous deficiencies and to compare infec-
tion control practice over time. This then would com-
plete the audit cycle. The concept of regular review
hopefully will also emphasize the importance of incor-
poration of infection control practices as routine.

The infection control audit can be a daunting task.
A standardized protocol for the audit process provides
a template for an impartial, organized, structured, and
thorough review. Uniformity of approach, front-line
presence of the ICP on the unit, involvement of the
clinical area under review, and documentation of
results have been effective in promoting and improving
standards of infection control in this institution.

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Of viruses, gloves, and crêpes

To the Editor:

Dr. V. Wiwanitkit should be commended for his attempt to estimate some bloodborne viral pathogens’ (HIV, hepatitis B virus, hepatitis C virus, and hepatitis D virus) ability to pass through gloves, based on a consideration at the nanostructure level (AJIC 2006;34;(6):400). Unfortunately, the size of pre-use glove pores in relation to that of the viruses is far from being the main parameter involved in gloves providing adequate protection to personnel and patients during health care.

Most gloves that are used throughout the world, especially sterile ones, are made of latex (others are made of vinyl or nitrile). Latex gloves are manufactured by applying the thinnest possible coating of latex onto hand-shaped forms before drying. Making pancakes—or rather crêpes as the French would have it—provides a suitable illustration: the thinner the desired crêpe (glove layer), the more liquid the crêpe batter (polymer) needs to be, and the more likely it is that holes will appear spontaneously in the crêpe’s structure when the dough is distributed on the surface of the pan so that it is entirely covered. Furthermore, additional micropores may appear during the polymerization stage.

Therefore, gloves are permeable even prior to use, in a varying proportion that depends on their composition, the manufacturer, and the quality of the glove.1,2 The physical properties of gloves are further altered by exposure to body heat, humidity, and mechanical constraints, whether in the surgical setting or while examining patients. Studies on surgeons’ gloves have shown that this proportion increases with use, even in the absence of documented needlestick.3,4 Thus, pre-existing holes or in-use tears in the clinical setting may be significantly larger than are the viruses described by V. Wiwanitkit.

In the clinical, nonsurgical setting, wearing a single layer of quality gloves on intact skin and followed by hand hygiene procedures can be considered to confer a high degree of protection. For the reasons described above, double gloving must be the rule in the surgical setting. Ideally, both layers must be changed at least every hour, to provide protection against leakage, exposure to blood if holes appear spontaneously, and in case of needlestick.5-7

Having access to a sufficient and uninterrupted supply of gloves is a considerable challenge in resource-constrained health care settings.8 Unfortunately, many of these are located in high-prevalence areas, and the scarcity of health care resources further concentrates highly viremic patients in hospital wards. Implementing basic, well-understood, and sustainable infection control measures—including gloving when necessary—should be considered a priority in all developing countries to protect health care workers and patients alike from these pathogens as well as undiscovered ones.9,10

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In response to Silvestri

To the Editor:

We would like to thank Dr. Silvestri and colleagues for their letter and their contributions to the literature related to selective decontamination of the digestive tract.
(SDD). We agree with their assertion that use of SDD, when both enteral and parenteral antibiotics are combined, is associated with lower rates of ventilator-associated pneumonia and improved mortality. We also acknowledge that SDD remains controversial because of the concerns regarding the potential for further emergence of resistant organisms. We believe that individual clinicians and hospitals can make up their own mind on the use of SDD based on their critical appraisal of the literature. However, in our opinion, there are insufficient long-term data on the emergence of resistant organisms to recommend widespread and routine use of selective digestive decontamination. We suspect that, in time, data such as those presented by Dr. Silvestri and colleagues may help resolve this issue.

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Municipal public telephones (n = 100) were selected in the inner Belfast area during the summer period of 2006. Two swabs were taken of each telephone, by premoistening each sterile cotton swab in sterile phosphate-buffered saline solution and by thoroughly swabbing the ear- and mouthpiece of each telephone apparatus. Swabs were transported to a laboratory with 2 hours of sampling, after which they were enriched in both salt-cooked meat broth (Oxoid CM0094; Oxoid Ltd, Basingstoke, United Kingdom) and in MAST MRSA ID broth (MAST Diagnostics Ltd., Merseyside, United Kingdom) for 24 hours at 37°C, in accordance with the manufacturer’s instructions. After this time, a 20-μL inoculum from the salt-cooked meat broth enrichment was plated onto colomycin selective agar for the detection of presumptive MRSA colonies. Appropriate positive and negative controls were established. No MRSA was detected in any public telephone examined by either of the enrichment methods employed.

There have been relatively few studies on the contamination of public telephones with MRSA. Previously, a report from Turkey5 identified several S aureus isolates on a study of 50 phones, but the methods employed were not able to determine whether or not these isolates were resistant to methicillin. Additionally, a report on bacterial contamination on mobile telephones among health care workers6 identified 2 phones (2/105; 1.9%) with MRSA; however, given that mobile phones are used personally and are not commonly shared among workers or from health care workers to patients, the risk of transmission of MRSA from person to person is less likely, which is not the case with municipal public telephones.

In conclusion, although negative in its findings, this study demonstrated that, within the community examined, MRSA contamination of public telephones is not significant. The significance and impact of this study thus helps us in our epidemiologic understanding that public phones are not important reservoirs or vehicles for the transmission of these organisms within the community. There is relatively limited information on the reservoirs and survival kinetics of nosocomially acquired MRSA and, more importantly, community-acquired MRSA in the community outside the health care environment. Further work is urgently required to identify other environmental reservoirs of MRSA in the community, their routes of transmission, and the survival kinetics of these organisms in the community so that we have a better understanding of how they behave/survive occultly in the community.
Letters to the Editor

Assessing vaccination rates at an emergency room

To the Editor:

Vaccination is among the most cost-effective tools to decrease childhood morbidity-mortality. Nonetheless, this effectiveness is dependent on vaccination coverage. Missed opportunities (MO) for vaccinations occur when a vaccine-eligible child does not receive the needed vaccines, and their contribution to under-immunization is significant.1

To assess the vaccination rates among children admitted to the emergency room of a university hospital in Salvador, Brazil, between November 2001 and November 2003, a retrospective cross-sectional study was conducted. The medical records were reviewed. The patients had been evaluated by medical students supervised by the same professor (C. M. Nascimento-Carvalho). A standardized form was used, and inquiry regarding vaccine use was included in the form. The Brazilian Ministry of Health vaccine schedule was used as standard. The study was approved by the Institutional Review Board.

Out of 267 patients, 122 (45.7%) showed the vaccines card, 87 (32.6%) informed on vaccines use, and 58 (21.7%) did not provide any information; overall, 31.6% (66/209) had the vaccination schedule incomplete (42.6% with and 16.1% without card). The median age (years) was 1.7 (mean, 2.6 ± 2.6 years), and 53.9% were males. Overall, association between young age (years) with incomplete vaccination schedule was identified (1.6 ± 1.6 vs 2.7 ± 2.7 years, respectively, 95% CI mean difference, 0.6-1.8; P = .006). This association was also found by analyzing vaccine cardholders or vaccine-use reports separately. The median family income was US $227.30 (mean US, $276.40 ± $166.82). The family income (US $) was greater among children with complete vaccine schedule, by analyzing cardholders ($302.73 ± $167.73 vs $230.45 ± $160.00, respectively, 95% confidence interval mean difference, 8.6-127.3; P = .02). The frequency of delayed vaccines were MMR, 20.8%; Haemophilus influenzae type b first dose, 17.3%; BCG, 11.5%; hepatitis B second dose, polio first dose, HIB second dose, tetra first dose, tetra second dose, 9.6% each; and hepatitis B first dose, polio second dose, and DPT first booster, 7.7% each.

It is noteworthy that almost half (45.7%) of the patients included in this study presented the vaccines card, even looking for health care at an emergency room, and this made accurate assessment for vaccine coverage possible. Another study analyzing data from different settings has reported similar rate for incomplete vaccination schedules: 40.4%.2 Different rates of vaccination coverage have been found by considering vaccine documentation or patients report, with a trend for underestimation for patient report,2 as it was observed herein. The association of young age with incomplete vaccine schedule highlights how important it is to decrease MO because the younger the child the greater is morbidity-mortality, including vaccine-preventable diseases.1 In general, the lower the vaccination coverage and the higher the burden of vaccine-preventable diseases in a population, the greater the need to improve coverage; urban, low-socioeconomic-status populations are particularly vulnerable to vaccine-preventable diseases,3 which is in accordance with the association of lower income and incomplete vaccine schedule found in this study. Improving coverage in impoverished urban communities should be a priority.3

MO was one of the identified barriers that made it difficult to vaccinate fully the young children and contributed to the measles epidemics of 1989 and 1990 in the United States.4 Specific recommendations to eliminate MO have been published in 1993 and included the use of all clinical encounters, including visits for...
mild illnesses, for the provision of needed immunization. In a nationwide study, there was no difference in a state preference for receiving a needed immunization during an illness visit. Expanding access is strongly recommended on the basis that it improves vaccination coverage. The authors propose the screening of the immunization status during health care assistance and the promotion of vaccine use during mild illnesses at emergency rooms as a strategy to reduce MO.

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Phlebitis associated with peripheral intravenous catheters

To the Editor:

Malach et al suggest that presence of an intravenous peripheral catheter longer than 3 days is a risk factor for phlebitis. A point-prevalence research design was used in their study whereby patients with phlebitis were compared with an unmatched control group of patients who did not have phlebitis. There are significant problems with drawing strong conclusions from such a design, which the authors themselves acknowledge. Other prospective, longitudinal studies have found that it is within the first 2 days following peripheral catheter insertion that the patient is at highest risk for infection. These authors surmise that breaching skin integrity, which occurs more frequently with 72-hour changes, may contribute to this result. We have supported their conclusions in a recent randomized controlled trial, in which the incidence of phlebitis was similar in the 3-day change group and the change when clinically indicated group. Among those who had their peripheral catheter removed for phlebitis, the mean length of time that the catheter was in situ was 48.7 hours.

We believe that, if patients are not matched for risk factors that may influence outcomes, incorrect conclusions may be drawn. This could have considerable patient care and economic implications. Consequently, it is important to use the correct study design when trying to understand significant health care questions.

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In response to Webster and Osborne

To the Editor:

We appreciate the comments made by Webster and Osborne. Rather than establish the optimal duration of peripheral intravenous catheters, the purpose of our study was to determine the rate of phlebitis and associated risk factors and, through educational intervention, reduce the rate of phlebitis. These aims were achieved.
Duration of an intravenous catheter of more than 3 days was found to be a risk factor for phlebitis, therefore suggesting that routine replacement before this time limit could help reduce the rate of phlebitis. We agree with Webster and Osborne’s comment that prospective longitudinal studies are superior for determination of the optimal duration of intravenous catheters. Their elegant study\(^2\) seems to confirm the finding of other studies\(^3\) that replacement when indicated is clinically safe and cost-effective. However, their study evidently involved a phlebotomy team, the use of which is associated with a lower rate of complications than elsewhere, such as in our hospital, in which house staff insert intravenous catheters.\(^4,5\)

In such settings, daily examination of the site and scrupulous observation of the 72-hour limit for replacement may be called for, especially if point-prevalence surveys indicate a relatively high rate of phlebitis.

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