Resistant Bugs

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doesn't? This was our attempt to put out what we think is a sensible approach," Dr. Sarwari said in an interview.

Although many hospitals have programs to monitor and reduce antimicrobial resistance, most simply restrict the use of certain agents by having one person who approves or bars their use. But West Virginia University prospectively audits antimicrobial use and resistance every 6 months, and implements changes through educational interventions.

This helps to avoid an "us versus them" phenomenon and should help to sustain the program over the long term, Dr. Sarwari said. "Unless you have a buy-in from the end users, this will not work."

Although it was relatively simple to decide to define antimicrobial use through the measurement of defined daily doses per 1,000 patient-days, it took about 6 months of effort to convert data that are captured for billing purposes into data that can be used longitudinally, he said. To inform hospital administrators, the program also tracked the proportion of the pharmacy budget spent on antimicrobial drugs.

Educational programs were established to encourage or discourage the use of select antimicrobial agents, while strategies to promote the use of alcohol-based hand sanitizers were put in place. In addition, the committee made a pocket-card guide available on an educational Web site. The card featured choices of antimicrobials for various clinical scenarios, listed the susceptible proportion of microorganisms that had been identified for that particular year, and gave the top three choices of antimicrobial agents for a particular pathogen (as perceived by the institution). It also noted if a pathogen had shown a 10% or greater rise in resistance to particular drugs during the past year.

Interventions centered on the principle of cycling the selection of antimicrobial drugs based on local surveillance of resistance rates, and were tailored for different units of the hospital. For example, with help from ICU intensivists, the committee developed a ventilator-assisted pneumonia protocol that incorporated a strategy of de-escalating antibiotic therapy from broader to more specific pathogen coverage, and the bone marrow transplant unit created a febrile neutropenia protocol.

The committee members decided not to keep a very restricted formulary except for quinolones, because more than half of the *Pseudomonas* strains in the ICU were resistant to ciprofloxacin, Dr. Sarwari said.

During the first 5 years of the stewardship program (2003-2007), the number of defined daily doses per 1,000 patient-days of quinolones declined by 81%; the same defined measure of ceftazidime declined by 37%, he said. The committee saw a concomitant rise in the use of agents that were designated to replace quinolones and ceftazidime (aminoglycosides and cefepime, respectively). At the same time, the antimicrobial drug proportion of the pharmacy procurement budget declined from 16% to 8%.

Changes in drug resistance during the period yielded "mixed results," Dr. Sarwari said. During 2004-2006, rates of ciprofloxacin resistance for *Pseudomonas* declined from 38% to 22% and for *Acinetobacter* from 25% to 0%. In 2007, these rates rose again to 34% and 16%, respectively. In the same time period, resistance to ciprofloxacin gradually increased in *Escherichia coli* from 7% to 20%. *Klebsiella* resistance to ceftazidime remained stable at about 5%.

The proportion of nosocomial bacteremia cases caused by methicillin-resistant *Staphylococcus aureus* declined from 20% to 10%, whereas rates for bacteremia caused by vancomycin-resistant enterococci held steady at about 7%.

It is possible that in some cases the replacement agents continued to foster resistance to the antibiotics the hospital had stopped using, Dr. Sarwari suggested. Although this theory to explain the findings is not new, future studies may be able to discern how the use of one antibiotic affects resistance to another drug or class of drugs.

In a separate poster presentation, Dr. Sarwari and his coinvestigators reported that antibiotic use and resistance rates in an ICU were similar to the results for the hospital as a whole.

Dr. Sarwari said he thinks that a program similar to WVU's could work well at small community-based hospitals, especially if they incorporated only the most important elements of the program.

The hospital's antimicrobial stewardship program "appears to be reasonably successful in affecting institutional use and resistance, but I'm not sure it has [had much] influence on the problem of imported resistance," Dr. Sarwari said. "The big thing we want to try to introduce is some form of molecular microbiology to better get a sense of how many resistant bugs are new strains versus the same strains being passed around due to poor infection control."

Dr. Sarwari disclosed no conflicts of interest. ■

Steps for Optimizing Antimicrobial Use

Many potential avenues exist to address antimicrobial resistance through stewardship, Dr. Sara E. Cosgrove said.

But interventions must take into account the fear many clinicians have of inadequate empiric coverage and a general lack of knowledge of antimicrobial classes and activity. The individual prescriber also has a conflict between what is best for the patient and what is best for public health.

"Any time there is an issue at the bedside, the clinician is always going to choose the patient over the public health," said Dr. Cosgrove, director of the antibiotics management program at Johns Hopkins Hospital, Baltimore.

Dr. Cosgrove described the following common interventional strategies that can be used to reduce antimicrobial resistance:

► **Preprescription approval.** This requires a clinician who wants to prescribe an antibiotic to page an infectious diseases fellow or attending physician or pharmacist. The approach guides prescribers to make appropriate empiric choices and helps prevent broad-spectrum antimicrobial use in all patients.

► **Postprescription review.** This strategy involves a review of the choice of antimicrobial agents when clinical and microbiologic data are available 48-72 hours after initial dosing. Phone calls or medical chart notes may be made to the prescriber if the data do not support the use of the agent.

► **Computer-assisted decision support.** An ideal computer support system provides data and recommendations at the time when a prescriber is writing an order. It is best if these recommendations are based on an institution's formulary, local guidelines, and an antibiogram.

► **Education and counterdetailing.** Because it might be difficult to teach hospital staffers about all the antimicrobial agents used at their institution, specific education on the use of particular antimicrobial drugs may be a more feasible way to change inappropriate use. "This may actually be an easier approach to start with in stewardship programs," Dr. Cosgrove said.

► **Antimicrobial switching/cycling/mixing.** The theory behind switching one antimicrobial agent for another (with removal and restriction on the use of the first) is that such action will withdraw the drug's selective pressure.

"The problem with antibiotic switching is when you reduce the use of one drug and usually the resistance associated with that drug, you turn around and develop resistance to the drug you switch to," Dr. Cosgrove said. This may work well during an outbreak, but it is not a good approach for overall stewardship.

The strategy of cycling between empiric antimicrobial agents over prescribed intervals (with an eventual return to each agent over time) relies on the assumption that organisms that have become resistant to an antimicrobial agent will have a growth disadvantage when the selective pressure from that particular agent is removed in the next drug cycle.

Dr. Cosgrove said she is not in favor of this strategy because a study on cycling found that antibiotic use increased without any evidence of the elimination of resistance that had occurred in the previous cycle (Am. J. Respir. Crit. Care Med. 2005;171:480-7).

"My big concern about cycling is that I think it completely disengages prescribers from thinking about appropriate empiric antibiotics," she said.

Mixing all classes of antibiotics is believed to minimize the selective pressure from any one agent. "But this is technically what should be happening if you do nothing," she said.

► **Prediction rules for early discontinuation.** With this method, when stewardship personnel are not available, physicians can use an algorithm about how and when to use particular antibiotics. However, not many prediction rules have been published.

► **Rapid diagnostic testing.** This strategy aims to guide clinicians toward the most appropriate therapy through molecular-based diagnostic tests to provide data about the type of organism or resistance pattern of an organism before the results of microbiologic testing return.

Dr. Cosgrove has received research grants from AdvanDx Inc. and Merck & Co., and financial compensation from Astellas Pharma Inc., Cubist Pharmaceuticals Inc., and Ortho-McNeil Inc.

MRSA Spread Caused in Part by Stressed Health Care Systems

BY DENISE NAPOLI
Associate Editor

Overcrowding and understaffing of hospitals are two of the major underlying factors driving the spread of methicillin-resistant *Staphylococcus aureus* in this setting, according to a review.

"The economic benefits of downsizing health care systems are likely to have been offset by the increased burden of adverse events, such as MRSA," the authors wrote.

Archie Clements, Ph.D., of the division of epidemiology and social medicine at the University of Queensland (Australia), and his colleagues from the fields of mathematics, statistics, infection surveillance, and medicine, cited 140 studies in their review (Lancet Infect. Dis. 2008;8:427-34).

They concluded that the direct mechanisms through which hospital-acquired infections are spread—including a decrease in hand washing, less "cohorting" of patients (meaning patients interact with a large number of health care workers), and closer proximity of infected patients to noninfected patients—are themselves caused by a dearth of health care professionals and a surplus of patients.

For instance, in the case of hand washing—a simple, inexpensive method to reduce the spread of MRSA—overworked health care staff are less likely to wash when indicated, according to several studies cited by the authors. In one, noncompliance was highest in cases of high "intensity of patient care," when there were more than 40 opportunities for hand washing per hour of care, compared with when there were fewer indications per hour (Ann. Intern. Med. 1999;130:126-30).

Also, "a vicious cycle" can occur in which the spread of MRSA within a facility exacerbates overcrowding, as patients' stays are extended, which in turn fuels chronic understaffing. "This contributes to a vicious cycle, where the occurrence of MRSA makes it more difficult to implement effective infection control strategies," the authors wrote.

The authors said they had no conflicts of interest to disclose. ■