Antimicrobial-drug resistance in hospitals is driven by failures of hospital hygiene, selective pressures created by overuse of antibiotics, and mobile genetic elements that can encode bacterial resistance mechanisms. Attention to hand hygiene is constrained by the time it takes to wash hands and by the adverse effects of repeated handwashing on the skin. Alcohol-based hand rubs can overcome the time problem and actually improve skin condition. Universal glove use could close gaps left by incomplete adherence to hand hygiene. Various interventions have been described to improve antibiotic use. The most effective have been programs restricting use of antibiotics and computer-based order forms for health providers.

Hand Hygiene

In a survey in four U.S. medical centers (a public hospital, a community hospital, a long-term care facility, and a university hospital), 85% of 424 physicians noted that antimicrobial-drug resistance was a major national problem; 55% thought that resistance was an issue for their patients (6). At the root of the resistance problem are health-care workers, who, although generally willing to do the right thing to control antimicrobial-drug resistance, undervalue the problem, do not know what the “right thing” is, or need an easier way to do it. This review summarizes a “facilitated right thing” approach to the problems of failed hygiene and antibiotic pressures.

Hand Hygiene

In a recent survey of physicians (6), 45% considered poor handwashing practices an important cause of antimicrobial-drug resistance in hospitals, perhaps a reflection of health-care workers’ markedly inflated view of their attention to hand hygiene (Table 1) (7). In fact, in most surveys of handwashing adherence, in various patient-care settings, personnel have practiced appropriate hand hygiene in only 25% to 50% of opportunities. As we pass the sesquicentennial of Semmelweis’ seminal observations on the importance of hand hygiene in reducing the incidence of nosocomial childbed fever, why does handwashing remain the most breached infection control measure in hospitals? Two frequently cited reasons are the large time commitment (up to

Table 1. Hospital personnel self-reported and observed handwashing rates

<table>
<thead>
<tr>
<th>Handwashing after patient contact</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported rate (n=123)</td>
<td>104 (85)</td>
</tr>
<tr>
<td>Estimate of co-workers' rate</td>
<td>63 (51)</td>
</tr>
<tr>
<td>Observed rate (n=173)</td>
<td>48 (28)</td>
</tr>
</tbody>
</table>

Note: S. aureus = Staphylococcus aureus; CNS = coagulase-negative staphylococci; 3rd Ceph = resistance to third-generation cephalosporins (ceftriaxone, cefotaxime, or ceftazidime); P. aeruginosa = Pseudomonas aeruginosa; Quinolone = resistant to either ciprofloxacin or ofloxacin.

Address for correspondence: Robert A. Weinstein, Division of Infectious Diseases – Suite 129 Durand, Cook County Hospital, 1835 W. Harrison St., Chicago, IL 60612, USA; fax: 312-572-3523; e-mail: rweinste@rush.edu

Figure 1. Rates of resistance in nosocomial infections reported in ICU patients, National Nosocomial Infections Surveillance System, CDC. Comparison of data from January-December 1999 with historical data.

1 = Vancomycin/enterococci
2 = Methicillin/S. aureus
3 = Methicillin/CNS
4 = 3rd Ceph/E. coli**
5 = 3rd Ceph/K. pneumoniae**
6 = Imipenem/P. aeruginosa
7 = Quinolone/P. aeruginosa
8 = 3rd Ceph/P. aeruginosa
9 = 3rd Ceph/Enterobacter spp.

Note: S. aureus = Staphylococcus aureus; CNS = coagulase-negative staphylococci; 3rd Ceph = resistance to third-generation cephalosporins (ceftriaxone, cefotaxime, or ceftazidime); P. aeruginosa = Pseudomonas aeruginosa; Quinolone = resistant to either ciprofloxacin or ofloxacin.

*Percentage (%) increase in resistance rate of current period (January-December 1999) compared to mean rate of resistance over previous 5 years (1994 through 1998): [(1999 rate - previous 5-year mean rate)/previous 5-year mean rate] X 100.

**Resistance for Escherichia coli or Klebsiella pneumoniae is the rate of nonsusceptibility of these organisms to either 3rd Ceph group or aztreonam.
90 minutes per work shift if performed as recommended by
the Centers for Disease Control and Prevention (CDC) and
the adverse effects of repeated handwashing on the skin (8).

**Alcohol-Based Hand Rubs**

If given a choice of changing human behavior (e.g.,
improving attention to hygiene and asepsis) or designing a
technologically foolproof device to control infections, go for the
device. For hand hygene, we have the opportunity to fulfill
the infection control “prime directive”: use technologic advances to improve behavior. How? Alcohol-based sinkless
hand rubs (Table 2) can overcome the time problems of
handwashing (9) and actually improve skin condition (10).
Handwashing requires approximately 45 to 90 seconds to
access and use a sink with running water, soap, and hand-
drying facilities; an alcohol-based hand rub can degerm hands
in less than 30 seconds and enhance killing of transient hand
flora.

Although use of alcohol for handwashing or scrubbing is
perceived as leading to dry skin, use of alcohol hand rubs,
without rinsing, is beneficial to skin, presumably because the
protective fats and oils remain on the hands as the alcohol
dries and because alcohol rubs contain emollients. In a study
comparing an alcohol gel hand rub to soap and water
handwashing, Boyce et al. reported that health-care workers
found that alcohol hand rubs cause less skin dryness, is
accessible and convenient to use, and has a pleasant odor.
After the study, 92% of test participants agreed to use the
hand rub routinely (11).

<table>
<thead>
<tr>
<th>Time required</th>
<th>Soap and water handwashing</th>
<th>Alcohol hand rub</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy in degeming</td>
<td>Good to very good</td>
<td>Excellent</td>
</tr>
<tr>
<td>Acceptance by personnel</td>
<td>Historically poor</td>
<td>Good to excellent</td>
</tr>
</tbody>
</table>

**Colonization Pressure and Universal Glove use**

While alcohol-based hand rubs appear promising,
maintaining adherence may require ongoing educational
reinforcement, compliance monitoring, and feedback to
personnel. With such aggressive campaigns, hand hygiene
rates of 60% to 80% can be achieved. But is this enough? For
uncommon pathogens that may colonize or infect only a small
proportion of patients, indirect patient-to-patient cross-
transmission by the hands of health-care workers may be
interrupted readily by such adherence rates. However, when
“colonization pressure” is greater because of a large number of
colonized patients, such rates may not be sufficient. For
example, when 30% to 50% of patients are colonized with
vancomycin-resistant enterococci (VRE), even occasional
lapses in hand hygiene may be enough to sustain cross-
transmission (Figure 2) (12,13).

A “belt and suspenders” approach to the colonization
pressure dilemma has been to encourage use of disposable
examination gloves during contacts with patients and their
environment (2,14,15). In one study, the rate of nosocomial

**Clostridium difficile-associated diarrhea** was threefold lower
on “universal glove use” wards than on control wards (16). In
a study of VRE, 39% of personnel had contamination of
examination gloves by VRE after even brief contact with
infected or colonized patients; personnel hand contamination
was reduced 71% by use of gloves (17). Because even intact
upper body skin may be colonized by resistant bacteria such as
VRE (18) and environmental contamination by VRE is
common (19), we recommend that disposable examination
gloves be worn for all contact, even with intact skin or the
environment of at-risk patients. Gloves must be changed and
hands disinfected by an alcohol hand rub between patients,
because gloves are not a total barrier (17,20). In one
observational study of universal glove use, 96% of gloved
personnel removed gloves after leaving the patient’s room
(21). In that study, personnel cited a marked preference for
universal glove use over traditional contact precautions.

Because of the huge resistance iceberg (Figure 3), with as
many as 5 to 10 patients colonized with resistant bacteria for
every patient known to be infected, universal glove use may be
a more preferable infection control strategy than contact
precautions, which are applied only to the tip of the iceberg.
With universal glove use, gowning of personnel is
recommended only for self-protection, e.g., from blood and
body fluid exposures. In a study of the epidemiology and
control of VRE in a medical ICU; prevalence of VRE (“colonization pressure”) exerted a
greater effect on acquisition than did antibiotic use, i.e., time to
acquisition of VRE was shorter with high colonization pressure and
low antibiotic use than with the converse conditions (13).

**Prescription of Antibiotics**

Antibiotic pressures may be more amenable to
intervention than hygiene practices. Prescribers want to do
Figure 3. The dynamics of nosocomial resistance. Resistance iceberg floating in an epicenter (2).

the right thing but may not always remember recommendations. Even though most health-care workers see inappropriate use of antibiotics as an important cause of drug resistance, many consider use of broader-spectrum antibiotics for longer periods the way to stamp out resistant bacteria (6).

To simplify prescription of antibiotics, most hospitals use “closed” formularies that limit prescribing options, often based on competitive bidding, to one or two drugs per antibiotic class. Clinical guidelines have become popular, especially for common infections, such as community-acquired pneumonia. Such guidelines may improve antibiotic use, especially if results are audited, and feedback is provided to prescribers. Use of order forms (24) and concurrent feedback to prescribers or next-day review of antibiotic appropriateness (25) also can improve prescriptions. The most effective antibiotic interventions have been restriction programs and computer-based order forms (so-called provider-order entries).

Restrictions to Use of Antibiotics
Restricting use of antibiotics has been especially effective in reducing cost and excess empiric use of broad-spectrum drugs (26). In one large study of the effect of prior authorization for selected drugs, a 32% decrease in expenditure for parenteral antibiotics was accompanied by increased susceptibility of bacterial isolates to beta-lactam and quinolone antibiotics. There were no adverse effects on clinical outcomes as measured by time to receipt of appropriate antibiotics, survival, and discharge from hospital for patients with bacteremia caused by gram-negative bacilli (27).

Computer Order Entry
Computer-based order entry for medical providers uses technology to direct and improve prescription behavior and thus fulfills the infection control prime directive (28). Order entry systems for antibiotics (and other drugs) provide simple messages to prescribers, such as the hospital’s suggested indications for, or the local resistance patterns of, a selected antibiotic. More sophisticated systems integrate results of microbiology and other laboratory tests into decision-support algorithms (29). Because they provide prescribing information when it is needed, in a neutral, nonjudgmental, fact-based format, computer order forms are efficient and well accepted and can change prescribing behavior dramatically, almost overnight.

Rotating Use of Antibiotics
The most recent intervention in antibiotic prescribing has been renewed interest in rotating use, or cycling, of antibiotics (30). Over 20 years ago, in a series of studies at the Minneapolis Veterans’ Administration Hospital, the substitution of amikacin for gentamicin and tobramycin as the aminoglycoside of choice produced sustained decreases in the prevalence of aminoglycoside-resistant gram-negative bacilli (31). The higher serum levels of amikacin, and the infrequent appearance in U.S. hospitals of amikacin-modifying enzymes that could confer amikacin resistance in gram-negative bacilli, were the underpinnings of the success of this strategy.

The more recent reports on cycling describe replacement (or switch) therapy for empiric antibiotic choices (30,32-34). Replacing ceftazidime with ciprofloxacin for empiric treatment of suspected gram-negative bacterial infections in a cardiac surgery ICU was associated with decreased incidence of ventilator-associated pneumonia and bacteremia caused by antibiotic-resistant gram-negative bacilli (33). In another hospital, use of beta-lactam/beta-lactamase inhibitor combinations to replace use of third-generation cephalosporins and clindamycin was associated with decreased rates of colonization by VRE (34); a follow-up study reported that these formulary manipulations were associated with decreasing numbers of patients from whom methicillin-resistant S. aureus and ceftazidime-resistant K. pneumoniae were cultured but increased rates of resistance of Acinetobacter (35). Rotating use of fourth-generation cephalosporins, quinolones, carbapenems, and beta-lactam/beta-lactamase inhibitor combinations is being studied in several hospital ICUs.

Cycling of antibiotics is most likely to be effective for limited periods in closed environments, such as ICUs, but this approach requires careful microbiologic monitoring because of the monotonic selective pressure of a single agent and the possible emergence of resistance to unrelated classes of drugs caused by genetic linkage of resistance mechanisms (30,36). As the size of the patient population under study increases, availability of various classes of drugs may be more effective at reducing the risk of emergence of resistance and may be a better strategy than cycling (37).

Conclusions
Control of antibiotic resistance requires aggressive implementation of several strategies (2): ongoing surveillance of resistance; molecular typing of isolates, usually using pulsed-field gel electrophoresis (38,39) when rates of resistance increase; using hygiene controls to limit spread of single (clonal) strains and antibiotic controls to limit spread of multiple (polyclonal) strains of resistant bacteria; and enlisting administrative support. Monitoring adherence of health-care workers to control measures and feedback of individual and ward rates of hygiene adherence and antibiotic resistance are central components of health-care worker education and motivation. Mathematical modeling has been used to judge the value of infection control activities. In these calculations, screening and cohorting of infected and colonized patients are the most effective control measures (11), although creating and maintaining cohorts are often logistically and technically difficult.

Current infection control strategies are aimed at the hygiene and antimicrobial engines that drive resistance. To fulfill the infection control prime directive, we must harness technology to improve and direct adherence to these
strategies. Future approaches may control or eliminate the bacterial events that underlie evolution of resistance.

Dr. Weinstein is chair, Division of Infectious Diseases, Cook County Hospital; director of Infectious Disease Services for the Cook County Bureau of Health Services; and professor of medicine, Rush Medical College. He also oversees the CORE Center for the Prevention, Care and Research of Infectious Disease and directs the Cook County Hospital component of the Rush/Cook County Infectious Disease Fellowship Program. His areas of research include nosocomial infections (particularly the epidemiology and control of antimicrobial resistance and infections in intensive care units) and health-care outcomes for patients with HIV/AIDS.

References


