formed on 876 GNB at Pittsburgh. *Proteus* species (261), *E coli* (174), *P aeruginosa* (122), and *Providencia* species (115) were most common. The prevalence of *Providencia* species was significantly higher at Pittsburgh (115 [13.1%] of 876 isolates) than at either Ann Arbor (0/349) or Portland (4/311; $P<.0001$). Of the 754 nonpseudomonal isolates tested, only 5 (0.7%) were ceftriaxone-resistant. Similarly, only 20 (2.3%) of 876 isolates were ceftazidime-resistant. *Enterobacter* species showed the most ceftazidime resistance (7/30 resistant). Ceftriaxone-resistant *Enterobacter* species were less prevalent at Pittsburgh than at Ann Arbor or Portland ($P<.005$).

The epidemiology of cephalosporin resistance in LTCF GNB has been assessed infrequently. Studies of gentamicin-resistant GNB isolates colonizing LTCF residents have been shown to have not only plasmids encoding for gentamicin resistance but also genes for the β-lactamase TEM-1, which hydrolyzes narrow-spectrum cephalosporins and cefoperazone.[1] Spread of GNB resistance to third-generation cephalosporins in hospitals has been associated with admission of LTCF residents colonized with strains of *E coli* or *K pneumoniae* containing plasmids encoding for SHV-7, conferring resistance to cefotaxime, ceftazidime, and aztreonam; TEM-10, conferring ceftazidime resistance, and TEM-26, conferring resistance to ceftazidime and piperacillin-tazobactam.[2,3] During one outbreak of infection, *K pneumoniae* and *E cloacae* containing plasmids encoding for YOU-1 and YOU-2 that confer ceftazidime resistance were detected among residents of a Massachusetts chronic-care facility.[4] Muder et al found resistance to multiple drugs, including ceftazidime, was common among clinical isolates, particularly *Pseudomonas* and *Providencia* species, and found evidence for clonal dissemination of *P aeruginosa*.[5]

In our study of clinical isolates, outbreaks had not occurred. *E coli*, *Proteus* species, *Providencia* species, and *P aeruginosa* were isolated most often, and ceftriaxone resistance and ceftazidime resistance were infrequent. The low prevalence of resistance to third-generation cephalosporins in these more common isolates is similar to that found in studies of GNB isolates from outpatients and community-dwelling older adults.[6] Most resistance to third-generation cephalosporins in our study was found in less commonly isolated bacteria. Although *Enterobacter* species accounted for only 6% of all clinical isolates, 33% and 38% were ceftriaxone-resistant and ceftazidime-resistant, respectively. The proportion of *Enterobacter* species resistant to third-generation cephalosporins exceeds that described in acute-care settings. Differences in third-generation cephalosporin use in referring hospitals and LTCFs or differences in patient populations might explain the differences noted in the rates of resistance among our three LTCFs.

Hospital-acquired multidrug-resistant GNB infections are thought to arise endogenously from a patient's own flora but can be acquired from the environment or a single nosocomial source. LTCF residents could become colonized with resistant GNB acquired in hospitals or in LTCFs and perhaps serve as a reservoir for reintroduction of the organism into acute-care facilities. The prevalence of resistant GNB and the mechanism of their spread need to be defined in LTCFs, so that appropriate infection control practices and antimicrobial-use policies can be developed.

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In Vitro Activity of a Nonmedicated Handwash Product, Chlorhexidine, and an Alcohol-Based Hand Disinfectant Against Multiply Resistant Gram-Positive Microorganisms

To the Editor:

Hands of healthcare workers are, without a doubt, the major source of transmission of nosocomial pathogens. Consequently, treatment of hands with appropriate disinfectants is the most important measure in breaking the chain of transmission, particularly in view of the increasing occurrence of multiply resistant microorganisms.

It still is unclear what kind of measure is the most effective. Whereas alcohol-based hand disinfectants are used predominantly in Europe, Anglo-American countries predominantly use antimicrobial scrubs containing 2% or 4% chlorhexidine or nonmedicated handwash products.

Recently, it was reported that chlorhexidine-containing formulations possess limited effectiveness against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) compared to alcohol-based hand disinfectants.[1,2] Contrary to these results, other investigators demonstrated an adequate antimicrobial efficacy of chlorhexidine.[3] The contradictory results regarding the in vitro activity of chlorhexidine-containing scrubs might be explained by the difficulties in neutralizing chlorhexidine suffi-

ciently.[4] It therefore was the aim of our study to compare the antimicrobial activity of a chlorhexidine-containing scrub (Hibiscrub, AstraZeneca, UK), an alcohol-based hand disinfectant (Desderman N, S&M, Norderstedt, Germany), and a nonmedicated handwash product (S&M Waschlotion, S&M) with multiply resistant gram-positive microorganisms in a model providing sufficient neutralization of chlorhexidine.[4]

Antimicrobial activity was determined by quantitative suspension tests according to the guidelines of the German Society for Hygiene and Microbiology. Since the chlorhexidine-containing scrub and the cleanser are applied to moistened hands, and thus are diluted by water, all products were tested as 1:2 dilutions (50% concentrations). The efficacy was evaluated after contact times of 0.5 and 1 minute. A total of 22 strains were tested. Ten VRE and eight high-level gentamicin-resistant enterococci (HLGRE) isolates from a Pan-European prevalence study and four clinical MRSA isolates from German hospitals were used.

The results are summarized in the Table. The ethanol-based hand disinfectant was highly effective against VRE, with a contact time of 1 minute. Surprisingly, the nonmedicated cleanser showed a higher reduction of VRE than the chlorhexidine-containing scrub and was almost as effective as the alcohol-based disinfectant. The reduction factors (RFs) of HLGRE obtained by using the alcohol-based hand disinfectant and the cleanser were comparable ($\log_{10}$ RF=5.3 and 5.1, respectively). The efficacy of the chlorhexidine-containing scrub was significantly lower ($\log_{10}$ RF=3.3). Against MRSA, the alcoholic hand disinfectant demonstrated the highest activity ($\log_{10}$ RF=5.2), whereas the chlorhexidine-containing scrub and the handwash product were significantly less active, with $\log_{10}$ RF values of 1 and 2.6, respectively. With a contact time of 30 seconds, the alcohol-based hand disinfectant was the only formulation with adequate efficacy against all test organisms, ie, a germ reduction of >5 log steps (data not shown).

Nosocomial infections frequently are caused by multiply resistant microorganisms. In particular, gram-positive pathogens such as MRSA, VRE, and HLGRE are of great clinical significance. It has been demonstrated that MRSA is transmitted primarily from patient to patient by means of contaminated hands. Furthermore, Wade et al reported the first documented outbreak of hospital-acquired infection with VRE-bearing plasmid-mediated vancomycin resistance, in which hand transmission was implicated, in 1991.[3] All of these reports indicate that hygienic hand disinfection is of the utmost importance in preventing the transmission of these pathogens, but Semmelweis was the first to prove that disinfection is better than hand washing.[5] More recently, other studies also have shown that higher infection rates have occurred due to hand washing with nonmedicated soap rather than treating the hands with antimicrobial products.

TABLE
EFFECTIVENESS OF A NONMEDICATED HANDWASH PRODUCT, CHLORHEXIDINE, AND AN ALCOHOL-BASED HAND DISINFECTANT AGAINST MULTIPLY RESISTANT GRAM-POSITIVE MICROORGANISMS IN QUANTITATIVE SUSPENSION TESTS

Preparations	$\log_{10}$ Reduction Factors		
	VRE*	HLGRE†	MRSA‡
Chlorhexidine-containing scrub	3.22±1.22§	3.30±0.73	1.00±0.56
Nonmedicated handwash product	4.80±0.60	5.10±0.74	2.60±0.32
Alcohol-based hand disinfectant	5.10±0.43	5.30±0.30	5.22±0.22

Abbreviations: HLGRE, high-level gentamicin-resistant enterococci; MRSA, methicillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant enterococci.
* Mean of 10 isolates.
† Mean of 8 isolates.
‡ Mean of 4 isolates.
§ Values are expressed as $\log_{10}$ reduction factors.

The effect of chlorhexidine-containing scrubs on microorganisms is controversial. Whereas some investigators demonstrated the antimicrobial efficacy of this active agent, others recorded resistance to chlorhexidine, especially in the case of gram-negative species such as *Serratia marcescens, Escherichia coli,* and *Proteus mirabilis.* More importantly, limited effectiveness of chlorhexidine also has been shown with MRSA. Kampf et al published a report that 4% chlorhexidine was highly effective ($\log_{10}$ RF≥5) against MRSA and methicillin-sensitive *Staphylococcus aureus* at 30 seconds, 60 seconds, and 5 minutes.[1] At a concentration of 2%, $\log_{10}$ RF>5 against MRSA was observed after 60 seconds and 5 minutes. In our model, 2% chlorhexidine was not sufficiently effective against MRSA at the recommended contact time of 1 minute, as was the case with the VRE and HLGRE. The reason for this discrepancy might be that we followed the suggestion for sufficient neutralization of chlorhexidine made by the same investigators at a later stage of their research.[4] In this publication, these authors observed sufficient neutralization only when all dilution steps and the corresponding agar plates were supplemented with the neutralizing agents.

Alcohol-based hand disinfectants have been shown repeatedly to have superior antimicrobial activity to detergent-based preparations. Our own results confirm these data. The diluted ethanol-based formula was highly effective against all test organisms at a contact time of 1 minute, as well as 30 seconds, although in practice it usually is used undiluted on dry hands. Chlorhexidine was significantly less effective against MRSA, VRE, and HLGRE. In the case of the enterococci, Kampf et al published similar results.[2] They showed that chlorhexidine digluconate (4%) was found to be less effective against VRE after 30, 60, and 300 seconds ($\log_{10}$ RF≤2.5) than alcohol-based hand disinfectants. Wade et al showed that chlorhexidine was effective against VRE on contaminated fingertips, but low counts of the test strain still remained on the hands after treatment with the chlorhexidine skin cleanser.[3] It may be that better results would be obtained if the hands were treated with chlorhexidine repeatedly to obtain the persistent effect. However, this is an open question. Hand washing with soap and water was even less reliable; *Enterococcus faecium* was recovered in all posthandwashing samples from two of the three volunteers.

The high RF obtained with the nonmedicated handwash product in our model probably was due to the fact that it contains a preservative that seems to be highly effective against enterococci. The in vitro activity against MRSA was absolutely inadequate, so this handwash product would not pass the test criteria of German or European standards for testing hand rubs or scrubs and never would be used for hand disinfection in hospitals.

To conclude, the results of our study obtained with gram-positive microorganisms show that the antimicrobial potency of chlorhexidine-containing scrubs and nonmedicated handwash products is lower than the potency of alcohol-based preparations. Therefore, scrubs and soaps might not be sufficient for eradication of multiply resistant gram-positive microorganisms from the hands of healthcare workers. The superior in vitro activity of alcohol-based disinfectants in our model indicates that these products should be used for hand disinfection to prevent the transmission of nosocomial pathogens by hands. Of course, this in vitro effect on multiply resistant gram-positive bacteria has to be proven in in vivo studies.

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High Methicillin Resistance of *Staphylococcus aureus* and Coagulase-Negative Staphylococci in Imam Khomeini Hospital of Urmia, Iran

To the Editor:

Staphylococcus aureus is a major pathogen for humans and has long been a cause of nosocomial infections such as bacteremia, wound infections, urinary tract infections, and pneumonia. Coagulase-negative staphylococci (CNS), such as *Staphylococcus epidermidis,* have become important in bloodstream infections, urinary tract infections, and infections of prosthetic devices such as heart valves.[1]

Worldwide, more than 95% of *S aureus* isolates are resistant to first-line antibiotics such as penicillin or ampicillin. In addition, methicillin-resistant strains of *S aureus* (MRSA) are common. The first report of MRSA was in the 1960s, and MRSA now commonly accounts for 20% to 40% of all *S aureus* isolates.[2]

The aim of this study was to estimate the incidence of MRSA in patients hospitalized in Imam Khomeini Hospital of Urmia.

This hospital is a 300-bed university-affiliated teaching center in Urmia, West Azarbayjan, Iran. To do the study, all hospitalized patients were screened for the isolation of MRSA from March 20, 1990, to April 30, 2000. Cultures were obtained after 72 hours. Specimens were plated onto mannitol-salt agar (Merck, Darmstadt, Germany) and incubated for up to 48 hours. Organisms with a yellow color (mannitol fermenters) were identified as *S aureus* by standard methods such as Gram stain, catalase, DNase, and the tube coagulase test. The agar screen test was used to detect MRSA by inoculating 10^4 colony-forming units onto Mueller-Hinton agar supplemented with 4% NaCl containing 6 µg of oxacillin per mL. Strains resistant to oxacillin were confirmed as methicillin-resistant.[3] No changes in the method of identifying MRSA occurred during the study. Antibiogram typing was performed by using the disk-diffusion methods according to the National Committee for Clinical Laboratory Standards guidelines. Other antibiotics used included penicillin, cotrimoxazole, vancomycin, ciprofloxacin, erythromycin, clindamycin, and gentamicin.

During the 1-year study, 200 strains of staphylococci were isolated from clinical samples of hospitalized patients. Of the 200 isolates, 153 strains (76.5%) were identified as *S aureus,* and the remaining 47 strains (23.5%) were CNS.

The frequency of MRSA by the oxacillin screen agar method was 82 strains (53.6%), whereas 26 strains (55.3%) of CNS were methicillin-resistant. Blood cultures were the

TABLE
SOURCES OF *STAPHYLOCOCCUS AUREUS* AND COAGULASE-NEGATIVE STAPHYLOCOCCI

Isolate	Blood	Wound	Catheter	Pleural Fluid	Urine	Urethral Discharge	Infantile Umbilical Cord	Eye	Stool	Total
Staphylococcus aureus	79	12	7	1	37	3	9	4	1	153
CNS	30	1	2	0	11	0	0	3	0	47
Total	109	13	9	1	48	3	9	7	1	200

Abbreviation: CNS, coagulase-negative staphylococci.