

GUIDELINE FOR HAND HYGIENE IN HEALTH-CARE SETTINGS: RECOMMENDATIONS OF THE HEALTHCARE INFECTION CONTROL PRACTICES ADVISORY COMMITTEE AND THE HICPAC/SHEA/APIC/IDSA HAND HYGIENE TASK FORCE

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SUMMARY

The Guideline for Hand Hygiene in Health-Care Settings provides health-care workers (HCWs) with a review of data regarding handwashing and hand antisepsis in health-care settings. In addition, it provides specific recommendations to promote improved hand-hygiene practices and reduce transmission of pathogenic microorganisms to patients and personnel in health-care settings. This report reviews studies published since the 1985 CDC guideline (Garner JS, Favero MS. CDC guideline for handwashing and hospital environmental control, 1985. *Infect Control* 1986;7:231-43) and the 1995 APIC guideline (Larson EL, APIC Guidelines Committee. APIC guideline for handwashing and hand antisepsis in health care settings. *Am J Infect Control*

1995;23:251-69) were issued and provides an in-depth review of hand-hygiene practices of HCWs, levels of adherence of personnel to recommended handwashing practices, and factors adversely affecting adherence. New studies of the in vivo efficacy of alcohol-based hand rubs and the low incidence of dermatitis associated with their use are reviewed. Recent studies demonstrating the value of multidisciplinary hand-hygiene promotion programs and the potential role of alcohol-based hand rubs in improving hand-hygiene practices are summarized. Recommendations concerning related issues (e.g., the use of surgical hand antiseptics, hand lotions or creams, and wearing of artificial fingernails) are also included (*Infect Control Hosp Epidemiol* 2002;23[suppl]:S3-S40).

PART I. REVIEW OF THE SCIENTIFIC DATA REGARDING HAND HYGIENE

HISTORICAL PERSPECTIVE

For generations, handwashing with soap and water has been considered a measure of personal hygiene.¹ The concept of cleansing hands with an antiseptic agent probably emerged in the early 19th century. As early as 1822, a French pharmacist demonstrated that solutions containing chlorides of lime or soda could eradicate the foul odors associated with human corpses and that such solutions could be used as disinfectants and antiseptics.² In a paper published in 1825, this pharmacist stated that physicians and other persons attending patients with contagious diseases would benefit from moistening their hands with a liquid chloride solution.²

In 1846, Ignaz Semmelweis observed that women whose babies were delivered by students and physicians in the First Obstetrics Clinic at the General Hospital of Vienna

consistently had a higher mortality rate than those whose babies were delivered by midwives in the Second Clinic.³ He noted that physicians who went directly from the autopsy suite to the obstetrics ward had a disagreeable odor on their hands despite washing their hands with soap and water upon entering the obstetrics clinic. He postulated that the puerperal fever that affected so many parturient women was caused by "cadaverous particles" transmitted from the autopsy suite to the obstetrics ward via the hands of students and physicians. Perhaps because of the known deodorizing effect of chlorine compounds, as of May 1847, he insisted that students and physicians clean their hands with a chlorine solution between each patient in the clinic. The maternal mortality rate in the First Clinic subsequently dropped dramatically and remained low for years. This intervention by Semmelweis represents the first evidence indicating that cleansing heavily contaminated hands with an antiseptic agent between patient contacts may reduce health-care-associated transmission of contagious diseases more effectively than handwashing with plain soap and water.

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In 1843, Oliver Wendell Holmes concluded independently that puerperal fever was spread by the hands of health personnel.¹ Although he described measures that could be taken to limit its spread, his recommendations had little impact on obstetric practices at the time. However, as a result of the seminal studies by Semmelweis and Holmes, handwashing gradually became accepted as one of the most important measures for preventing transmission of pathogens in health-care facilities.

In 1961, the U.S. Public Health Service produced a training film that demonstrated handwashing techniques recommended for use by health-care workers (HCWs).⁴ At the time, recommendations directed that personnel wash their hands with soap and water for 1–2 minutes before and after patient contact. Rinsing hands with an antiseptic agent was believed to be less effective than handwashing and was recommended only in emergencies or in areas where sinks were unavailable.

In 1975 and 1985, formal written guidelines on handwashing practices in hospitals were published by the Centers for Disease Control and Prevention (CDC).^{5,6} These guidelines recommended handwashing with non-antimicrobial soap between the majority of patient contacts and washing with antimicrobial soap before and after performing invasive procedures or caring for patients at high risk. Use of waterless antiseptic agents (e.g., alcohol-based solutions) was recommended only in situations where sinks were not available.

In 1988 and 1995, guidelines for handwashing and hand antisepsis were published by the Association for Professionals in Infection Control (APIC).^{7,8} Recommended indications for handwashing were similar to those listed in the CDC guidelines. The 1995 APIC guideline included more detailed discussion of alcohol-based hand rubs and supported their use in more clinical settings than had been recommended in earlier guidelines. In 1995 and 1996, the Healthcare Infection Control Practices Advisory Committee (HICPAC) recommended that either antimicrobial soap or a waterless antiseptic agent be used for cleaning hands upon leaving the rooms of patients with multidrug-resistant pathogens (e.g., vancomycin-resistant enterococci [VRE] and methicillin-resistant *Staphylococcus aureus* [MRSA]).^{9,10} These guidelines also provided recommendations for handwashing and hand antisepsis in other clinical settings, including routine patient care. Although the APIC and HICPAC guidelines have been adopted by the majority of hospitals, adherence of HCWs to recommended handwashing practices has remained low.^{11,12}

Recent developments in the field have stimulated a review of the scientific data regarding hand hygiene and the development of new guidelines designed to improve hand-hygiene practices in healthcare facilities. This literature review and accompanying recommendations have been prepared by a Hand Hygiene Task Force, comprising representatives from HICPAC, the Society for Healthcare Epidemiology of America (SHEA), APIC, and the Infectious Diseases Society of America (IDSA).

NORMAL BACTERIAL SKIN FLORA

To understand the objectives of different approaches to hand cleansing, a knowledge of normal bacterial skin flora is essential. Normal human skin is colonized with bacteria; different areas of the body have varied total aerobic bacterial counts (e.g., 1×10^6 colony forming units (CFUs)/cm² on the scalp, 5×10^5 CFUs/cm² in the axilla, 4×10^4 CFUs/cm² on the abdomen, and 1×10^4 CFUs/cm² on the forearm).¹³ Total bacterial counts on the hands of medical personnel have ranged from 3.9×10^4 to 4.6×10^6 .^{14–17} In 1938, bacteria recovered from the hands were divided into two categories: transient and resident.¹⁴ Transient flora, which colonize the superficial layers of the skin, are more amenable to removal by routine handwashing. They are often acquired by HCWs during direct contact with patients or contact with contaminated environmental surfaces within close proximity of the patient. Transient flora are the organisms most frequently associated with health-care-associated infections. Resident flora, which are attached to deeper layers of the skin, are more resistant to removal. In addition, resident flora (e.g., coagulase-negative staphylococci and diphtheroids) are less likely to be associated with such infections. The hands of HCWs may become persistently colonized with pathogenic flora (e.g., *S. aureus*), gram-negative bacilli, or yeast. Investigators have documented that, although the number of transient and resident flora varies considerably from person to person, it is often relatively constant for any specific person.^{14,18}

PHYSIOLOGY OF NORMAL SKIN

The primary function of the skin is to reduce water loss, provide protection against abrasive action and microorganisms, and act as a permeability barrier to the environment. The basic structure of skin includes, from outer- to innermost layer, the superficial region (i.e., the stratum corneum or horny layer, which is 10- to 20- μ m thick), the viable epidermis (50- to 100- μ m thick), the dermis (1- to 2-mm thick), and the hypodermis (1- to 2-mm thick). The barrier to percutaneous absorption lies within the stratum corneum, the thinnest and smallest compartment of the skin. The stratum corneum contains the corneocytes (or horny cells), which are flat, polyhedral-shaped nonnucleated cells, remnants of the terminally differentiated keratinocytes located in the viable epidermis. Corneocytes are composed primarily of insoluble bundled keratins surrounded by a cell envelope stabilized by cross-linked proteins and covalently bound lipid. Interconnecting the corneocytes of the stratum corneum are polar structures (e.g., corneodesmosomes), which contribute to stratum corneum cohesion.

The intercellular region of the stratum corneum is composed of lipid primarily generated from the exocytosis of lamellar bodies during the terminal differentiation of the keratinocytes. The intercellular lipid is required for a competent skin barrier and forms the only continuous domain. Directly under the stratum corneum is a stratified epidermis, which is composed primarily of 10–20 layers of keratinizing epithelial cells that are responsible for the synthe-

sis of the stratum corneum. This layer also contains melanocytes involved in skin pigmentation; Langerhans cells, which are important for antigen presentation and immune responses; and Merkel cells, whose precise role in sensory reception has yet to be fully delineated. As keratinocytes undergo terminal differentiation, they begin to flatten out and assume the dimensions characteristic of the corneocytes (i.e., their diameter changes from 10–12 μm to 20–30 μm , and their volume increases by 10- to 20-fold). The viable epidermis does not contain a vascular network, and the keratinocytes obtain their nutrients from below by passive diffusion through the interstitial fluid.

The skin is a dynamic structure. Barrier function does not simply arise from the dying, degeneration, and compaction of the underlying epidermis. Rather, the processes of cornification and desquamation are intimately linked; synthesis of the stratum corneum occurs at the same rate as loss. Substantial evidence now confirms that the formation of the skin barrier is under homeostatic control, which is illustrated by the epidermal response to barrier perturbation by skin stripping or solvent extraction. Circumstantial evidence indicates that the rate of keratinocyte proliferation directly influences the integrity of the skin barrier. A general increase in the rate of proliferation results in a decrease in the time available for (1) uptake of nutrients (e.g., essential fatty acids), (2) protein and lipid synthesis, and (3) processing of the precursor molecules required for skin-barrier function. Whether chronic but quantitatively smaller increases in rate of epidermal proliferation also lead to changes in skin-barrier function remains unclear. Thus, the extent to which the decreased barrier function caused by irritants is caused by an increased epidermal proliferation also is unknown.

The current understanding of the formation of the stratum corneum has come from studies of the epidermal responses to perturbation of the skin barrier. Experimental manipulations that disrupt the skin barrier include (1) extraction of skin lipids with apolar solvents, (2) physical stripping of the stratum corneum using adhesive tape, and (3) chemically induced irritation. All of these experimental manipulations lead to a decreased skin barrier as determined by transepidermal water loss (TEWL). The most studied experimental system is the treatment of mouse skin with acetone. This experiment results in a marked and immediate increase in TEWL, and therefore a decrease in skin-barrier function. Acetone treatment selectively removes glycerolipids and sterols from the skin, which indicates that these lipids are necessary, though perhaps not sufficient in themselves, for barrier function. Detergents act like acetone on the intercellular lipid domain. The return to normal barrier function is biphasic: 50%–60% of barrier recovery typically occurs within 6 hours, but complete normalization of barrier function requires 5–6 days.

DEFINITION OF TERMS

Alcohol-based hand rub. An alcohol-containing preparation designed for application to the hands for reducing the number of viable microorganisms on the hands. In the

United States, such preparations usually contain 60%–95% ethanol or isopropanol.

Antimicrobial soap. Soap (i.e., detergent) containing an antiseptic agent.

Antiseptic agent. Antimicrobial substances that are applied to the skin to reduce the number of microbial flora. Examples include alcohols, chlorhexidine, chlorine, hexachlorophene, iodine, chloroxylenol (PCMX), quaternary ammonium compounds, and triclosan.

Antiseptic handwash. Washing hands with water and soap or other detergents containing an antiseptic agent.

Antiseptic hand rub. Applying an antiseptic hand-rub product to all surfaces of the hands to reduce the number of microorganisms present.

Cumulative effect. A progressive decrease in the numbers of microorganisms recovered after repeated applications of a test material.

Decontaminate hands. To reduce bacterial counts on hands by performing antiseptic hand rub or antiseptic handwash.

Detergent. Detergents (i.e., surfactants) are compounds that possess a cleaning action. They are composed of both hydrophilic and lipophilic parts and can be divided into four groups: anionic, cationic, amphoteric, and nonionic detergents. Although products used for handwashing or antiseptic handwash in health-care settings represent various types of detergents, the term “soap” is used to refer to such detergents in this guideline.

Hand antiseptics. Refers to either antiseptic handwash or antiseptic hand rub.

Hand hygiene. A general term that applies to either handwashing, antiseptic handwash, antiseptic hand rub, or surgical hand antiseptics.

Handwashing. Washing hands with plain (i.e., non-antimicrobial) soap and water.

Persistent activity. Persistent activity is defined as the prolonged or extended antimicrobial activity that prevents or inhibits the proliferation or survival of microorganisms after application of the product. This activity may be demonstrated by sampling a site several minutes or hours after application and demonstrating bacterial antimicrobial effectiveness when compared with a baseline level. This property also has been referred to as “residual activity.” Both substantive and nonsubstantive active ingredients can show a persistent effect if they substantially lower the number of bacteria during the wash period.

Plain soap. Plain soap refers to detergents that do not contain antimicrobial agents or contain low concentrations of antimicrobial agents that are effective solely as preservatives.

Substantivity. Substantivity is an attribute of certain active ingredients that adhere to the stratum corneum (i.e., remain on the skin after rinsing or drying) to provide an inhibitory effect on the growth of bacteria remaining on the skin.

Surgical hand antiseptics. Antiseptic handwash or antiseptic hand rub performed preoperatively by surgical personnel to eliminate transient and reduce resident hand

flora. Antiseptic detergent preparations often have persistent antimicrobial activity.

Visibly soiled hands. Hands showing visible dirt or visibly contaminated with proteinaceous material, blood, or other body fluids (e.g., fecal material or urine).

Waterless antiseptic agent. An antiseptic agent that does not require use of exogenous water. After applying such an agent, the hands are rubbed together until the agent has dried.

Food and Drug Administration (FDA) product categories. The 1994 FDA Tentative Final Monograph for Health-Care Antiseptic Drug Products divided products into three categories and defined them as follows¹⁹:

- *Patient preoperative skin preparation.* A fast-acting, broad-spectrum, and persistent antiseptic-containing preparation that substantially reduces the number of microorganisms on intact skin.
- *Antiseptic handwash or HCW handwash.* An antiseptic-containing preparation designed for frequent use; it reduces the number of microorganisms on intact skin to an initial baseline level after adequate washing, rinsing, and drying; it is broad-spectrum, fast-acting, and if possible, persistent.
- *Surgical hand scrub.* An antiseptic-containing preparation that substantially reduces the number of microorganisms on intact skin; it is broad-spectrum, fast-acting, and persistent.

EVIDENCE OF TRANSMISSION OF PATHOGENS ON HANDS

Transmission of health-care-associated pathogens from one patient to another via the hands of HCWs requires the following sequence of events:

- Organisms present on the patient's skin, or that have been shed onto inanimate objects in close proximity to the patient, must be transferred to the hands of HCWs.
- These organisms must then be capable of surviving for at least several minutes on the hands of personnel.
- Next, handwashing or hand antisepsis by the worker must be inadequate or omitted entirely, or the agent used for hand hygiene must be inappropriate.
- Finally, the contaminated hands of the caregiver must come in direct contact with another patient, or with an inanimate object that will come into direct contact with the patient.

Health-care-associated pathogens can be recovered not only from infected or draining wounds, but also from frequently colonized areas of normal, intact patient skin.²⁰⁻³¹ The perineal or inguinal areas are usually most heavily colonized, but the axillae, trunk, and upper extremities (including the hands) also are frequently colonized.^{23,25,26,28,30-32} The number of organisms (e.g., *S. aureus*, *Proteus mirabilis*, *Klebsiella* spp., and *Acinetobacter* spp.) present on intact

areas of the skin of certain patients can vary from 100 to 10⁶/cm².^{25,29,31,33}

Persons with diabetes, patients undergoing dialysis for chronic renal failure, and those with chronic dermatitis are likely to have areas of intact skin that are colonized with *S. aureus*.³⁴⁻⁴¹ Because approximately 10⁶ skin squames containing viable microorganisms are shed daily from normal skin,⁴² patient gowns, bed linen, bedside furniture, and other objects in the patient's immediate environment can easily become contaminated with patient flora.^{30,43-46} Such contamination is particularly likely to be caused by staphylococci or enterococci, which are resistant to desiccation.

Data are limited regarding the types of patient-care activities that result in transmission of patient flora to the hands of personnel.^{26,45-51} In the past, attempts have been made to stratify patient-care activities into those most likely to cause hand contamination,⁵² but such stratification schemes were never validated by quantifying the level of bacterial contamination that occurred. Nurses can contaminate their hands with 100–1,000 CFUs of *Klebsiella* spp. during "clean" activities (e.g., lifting a patient; taking a patient's pulse, blood pressure, or oral temperature; or touching a patient's hand, shoulder, or groin).⁴⁸ Similarly, in another study, hands were cultured of nurses who touched the groins of patients heavily colonized with *P. mirabilis*⁵²; 10–600 CFUs/mL of this organism were recovered from glove juice samples from the nurses' hands. Recently, other researchers studied contamination of HCWs' hands during activities that involved direct patient-contact wound care, intravascular catheter care, respiratory-tract care, and the handling of patient secretions.⁵¹ Agar fingertip impression plates were used to culture bacteria; the number of bacteria recovered from fingertips ranged from 0 to 300 CFUs. Data from this study indicated that direct patient contact and respiratory-tract care were most likely to contaminate the fingers of caregivers. Gram-negative bacilli accounted for 15% of isolates and *S. aureus* for 11%. Duration of patient-care activity was strongly associated with the intensity of bacterial contamination of HCWs' hands.

HCWs can contaminate their hands with gram-negative bacilli, *S. aureus*, enterococci, or *Clostridium difficile* by performing "clean procedures" or touching intact areas of the skin of hospitalized patients.^{26,45,46,53} Furthermore, personnel caring for infants with respiratory syncytial virus (RSV) infections have acquired RSV by performing certain activities (e.g., feeding infants, changing diapers, and playing with infants).⁴⁹ Personnel who had contact only with surfaces contaminated with the infants' secretions also acquired RSV by contaminating their hands with RSV and inoculating their oral or conjunctival mucosa. Other studies also have documented that HCWs may contaminate their hands (or gloves) merely by touching inanimate objects in patient rooms.^{46,53-56} None of the studies concerning hand contamination of hospital personnel were designed to determine if the contamination resulted in transmission of pathogens to susceptible patients.

Other studies have documented contamination of HCWs' hands with potential health-care-associated pathogens, but did not relate their findings to the specific

type of preceding patient contact.^{15,17,57-62} For example, before glove use was common among HCWs, 15% of nurses working in an isolation unit carried a median of 1×10^4 CFUs of *S. aureus* on their hands.⁶¹ Of nurses working in a general hospital, 29% had *S. aureus* on their hands (median count: 3,800 CFUs), whereas 78% of those working in a hospital for dermatology patients had the organism on their hands (median count: 14.3×10^6 CFUs). Similarly, 17%–30% of nurses carried gram-negative bacilli on their hands (median counts: 3,400–38,000 CFUs). One study found that *S. aureus* could be recovered from the hands of 21% of intensive care unit personnel and that 21% of physician and 5% of nurse carriers had >1,000 CFUs of the organism on their hands.⁵⁹ Another study found lower levels of colonization on the hands of personnel working in a neurosurgery unit, with an average of 3 CFUs of *S. aureus* and 11 CFUs of gram-negative bacilli.¹⁶ Serial cultures revealed that 100% of HCWs carried gram-negative bacilli at least once, and 64% carried *S. aureus* at least once.

MODELS OF HAND TRANSMISSION

Several investigators have studied transmission of infectious agents by using different experimental models. In one study, nurses were asked to touch the groins of patients heavily colonized with gram-negative bacilli for 15 seconds—as though they were taking a femoral pulse.²⁵ Nurses then cleaned their hands by washing with plain soap and water or by using an alcohol hand rinse. After cleaning their hands, they touched a piece of urinary catheter material with their fingers, and the catheter segment was cultured. The study revealed that touching intact areas of moist skin of the patient transferred enough organisms to the nurses' hands to result in subsequent transmission to catheter material, despite handwashing with plain soap and water.

The transmission of organisms from artificially contaminated "donor" fabrics to clean "recipient" fabrics via hand contact also has been studied. Results indicated that the number of organisms transmitted was greater if the donor fabric or the hands were wet upon contact.⁶³ Overall, only 0.06% of the organisms obtained from the contaminated donor fabric were transferred to recipient fabric via hand contact. *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa*, and *Serratia* spp. were also transferred in greater numbers than was *Escherichia coli* from contaminated fabric to clean fabric after hand contact.⁶⁴ Organisms are transferred to various types of surfaces in much larger numbers (i.e., $>10^4$) from wet hands than from hands that are thoroughly dried.⁶⁵

RELATION OF HAND HYGIENE AND ACQUISITION OF HEALTH-CARE-ASSOCIATED PATHOGENS

Hand antisepsis reduces the incidence of health-care-associated infections.^{66,67} An intervention trial using historical controls demonstrated in 1847 that the mortality rate among mothers who delivered in the First Obstetrics Clinic at the General Hospital of Vienna was substantially lower

when hospital staff cleaned their hands with an antiseptic agent than when they washed their hands with plain soap and water.³

In the 1960s, a prospective, controlled trial sponsored by the National Institutes of Health and the Office of the Surgeon General demonstrated that infants cared for by nurses who did not wash their hands after handling an index infant colonized with *S. aureus* acquired the organism more often and more rapidly than did infants cared for by nurses who used hexachlorophene to clean their hands between infant contacts.⁶⁸ This trial provided evidence that, when compared with no handwashing, washing hands with an antiseptic agent between patient contacts reduces transmission of health-care-associated pathogens.

Trials have studied the effects of handwashing with plain soap and water versus some form of hand antisepsis on health-care-associated infection rates.^{69,70} Health-care-associated infection rates were lower when antiseptic handwashing was performed by personnel.⁶⁹ In another study, antiseptic handwashing was associated with lower health-care-associated infection rates in certain intensive-care units, but not in others.⁷⁰

Health-care-associated infection rates were lower after antiseptic handwashing using a chlorhexidine-containing detergent compared with handwashing with plain soap or use of an alcohol-based hand rinse.⁷¹ However, because only a minimal amount of the alcohol rinse was used during periods when the combination regimen also was in use and because adherence to policies was higher when chlorhexidine was available, determining which factor (i.e., the hand-hygiene regimen or differences in adherence) accounted for the lower infection rates was difficult. Investigators have determined also that health-care-associated acquisition of MRSA was reduced when the antimicrobial soap used for hygienic handwashing was changed.^{72,73}

Increased handwashing frequency among hospital staff has been associated with decreased transmission of *Klebsiella* spp. among patients⁴⁸; these studies, however, did not quantitate the level of handwashing among personnel. In a recent study, the acquisition of various health-care-associated pathogens was reduced when hand antisepsis was performed more frequently by hospital personnel⁷⁴; both this study and another⁷⁵ documented that the prevalence of health-care-associated infections decreased as adherence to recommended hand-hygiene measures improved.

Outbreak investigations have indicated an association between infections and understaffing or overcrowding; the association was consistently linked with poor adherence to hand hygiene. During an outbreak investigation of risk factors for central venous catheter-associated bloodstream infections,⁷⁶ after adjustment for confounding factors, the patient-to-nurse ratio remained an independent risk factor for bloodstream infection, indicating that nursing staff reduction below a critical threshold may have contributed to this outbreak by jeopardizing adequate catheter care. The understaffing of nurses can facilitate the spread of MRSA in intensive-care settings⁷⁷ through relaxed attention to basic control measures (e.g., hand hygiene). In an outbreak of

Enterobacter cloacae in a neonatal intensive-care unit,⁷⁸ the daily number of hospitalized children was above the maximum capacity of the unit, resulting in an available space per child below current recommendations. In parallel, the number of staff members on duty was substantially less than the number necessitated by the workload, which also resulted in relaxed attention to basic infection-control measures. Adherence to hand-hygiene practices before device contact was only 25% during the workload peak, but increased to 70% after the end of the understaffing and overcrowding period. Surveillance documented that being hospitalized during this period was associated with a fourfold increased risk of acquiring a health-care-associated infection. This study not only demonstrates the association between workload and infections, but it also highlights the intermediate cause of antimicrobial spread: poor adherence to hand-hygiene policies.

METHODS USED TO EVALUATE THE EFFICACY OF HAND-HYGIENE PRODUCTS

Current Methods

Investigators use different methods to study the in vivo efficacy of handwashing, antiseptic handwash, and surgical hand antisepsis protocols. Differences among the various studies include (1) whether hands are purposely contaminated with bacteria before use of test agents, (2) the method used to contaminate fingers or hands, (3) the volume of hand-hygiene product applied to the hands, (4) the time the product is in contact with the skin, (5) the method used to recover bacteria from the skin after the test solution has been used, and (6) the method of expressing the efficacy of the product (i.e., either percent reduction in bacteria recovered from the skin or log reduction of bacteria released from the skin). Despite these differences, the majority of studies can be placed into one of two major categories: studies focusing on products to remove transient flora and studies involving products that are used to remove resident flora from the hands. The majority of studies of products for removing transient flora from the hands of HCWs involve artificial contamination of the volunteer's skin with a defined inoculum of a test organism before the volunteer uses a plain soap, an antimicrobial soap, or a waterless antiseptic agent. In contrast, products tested for the preoperative cleansing of surgeons' hands (which must comply with surgical hand-antisepsis protocols) are tested for their ability to remove resident flora without artificially contaminating the volunteers' hands.

In the United States, antiseptic handwash products intended for use by HCWs are regulated by the Food and Drug Administration's (FDA) Division of Over-the-Counter Drug Products (OTC). Requirements for in vitro and in vivo testing of HCW handwash products and surgical hand scrubs are outlined in the FDA Tentative Final Monograph for Healthcare Antiseptic Drug Products (TFM).¹⁹ Products intended for use as HCW handwashes are evaluated by using a standardized method.¹⁹ Tests are performed in accordance with use directions for the test material. Before baseline bacterial sampling and before each

wash with the test material, 5 mL of a standardized suspension of *Serratia marcescens* are applied to the hands and then rubbed over the surfaces of the hands. A specified volume of the test material is dispensed into the hands and is spread over the hands and lower one third of the forearms. A small amount of tap water is added to the hands, and hands are completely lathered for a specified time, covering all surfaces of the hands and the lower third of the forearms. Volunteers then rinse hands and forearms under 40°C tap water for 30 seconds. Ten washes with the test formulation are required. After the first, third, seventh, and tenth washes, rubber gloves or polyethylene bags used for sampling are placed on the right and left hands, and 75 mL of sampling solution is added to each glove; gloves are secured above the wrist. All surfaces of the hand are massaged for 1 minute, and samples are obtained aseptically for quantitative culture. No neutralizer of the antimicrobial is routinely added to the sampling solution, but if dilution of the antimicrobial in the sampling fluid does not result in demonstrable neutralization, a neutralizer specific for the test formulation is added to the sampling solution. For waterless formulations, a similar procedure is used. TFM criteria for efficacy are as follows: a 2-log₁₀ reduction of the indicator organism on each hand within 5 minutes after the first use, and a 3-log₁₀ reduction of the indicator organism on each hand within 5 minutes after the tenth use.¹⁹

Products intended for use as surgical hand scrubs have been evaluated also by using a standardized method.¹⁹ Volunteers clean under fingernails with a nail stick and clip their fingernails. All jewelry is removed from hands and arms. Hands and two thirds of forearms are rinsed with tap water (38°C–42°C) for 30 seconds, and then they are washed with a non-antimicrobial soap for 30 seconds and are rinsed for 30 seconds under tap water. Baseline microbial hand counts can then be determined. Next, a surgical scrub is performed with the test formulation using directions provided by the manufacturer. If no instructions are provided with the formulation, two 5-minute scrubs of hands and forearms followed by rinsing are performed. Reduction from baseline microbial hand counts is determined in a series of 11 scrubs conducted during 5 days. Hands are sampled at 1 minute, 3 hours, and 6 hours after the first scrubs on day 1, day 2, and day 5. After washing, volunteers wear rubber gloves; 75 mL of sampling solution are then added to one glove, and all surfaces of the hands are massaged for 1 minute. Samples are then taken aseptically and cultured quantitatively. The other glove remains on the other hand for 6 hours and is sampled in the same manner. TFM requires that formulations reduce the number of bacteria 1 log₁₀ on each hand within 1 minute of product application and that the bacterial cell count on each hand does not subsequently exceed baseline within 6 hours on day 1; the formulation must produce a 2-log₁₀ reduction in microbial flora on each hand within 1 minute of product application by the end of the second day of enumeration and a 3-log₁₀ reduction of microbial flora on each hand within 1 minute of product use by the end of the fifth day when compared with the established baseline.¹⁹

The method most widely used in Europe to evaluate the efficacy of hand-hygiene agents is European Standard 1500–1997 (EN 1500—Chemical disinfectants and antiseptics. Hygienic hand-rub test method and requirements).⁷⁹ This method requires 12–15 test volunteers and an 18- to 24-hour growth of broth culture of *E. coli* K12. Hands are washed with a soft soap, dried, and then immersed halfway to the metacarpals in the broth culture for 5 seconds. Hands are removed from the broth culture, excess fluid is drained off, and hands are dried in the air for 3 minutes. Bacterial recovery for the initial value is obtained by kneading the fingertips of each hand separately for 60 seconds in 10 mL of tryptic soy broth (TSB) without neutralizers. The hands are removed from the broth and disinfected with 3 mL of the hand-rub agent for 30 seconds in a set design. The same operation is repeated with total disinfection time not exceeding 60 seconds. Both hands are rinsed in running water for 5 seconds and water is drained off. Fingertips of each hand are kneaded separately in 10 mL of TSB with added neutralizers. These broths are used to obtain the final value. \log_{10} dilutions of recovery medium are prepared and plated out. Within 3 hours, the same volunteers are tested with the reference disinfectant (60% 2-propanol [isopropanol]) and the test product. Colony counts are performed after 24 and 48 hours of incubation at 36°C. The average colony count of both left and right hand is used for evaluation. The log-reduction factor is calculated and compared with the initial and final values. The reduction factor of the test product should be superior or the same as the reference alcohol-based rub for acceptance. If a difference exists, then the results are analyzed statistically using the Wilcoxon test. Products that have log reductions substantially less than that observed with the reference alcohol-based hand rub (i.e., approximately 4 \log_{10} reduction) are classified as not meeting the standard.

Because of different standards for efficacy, criteria cited in FDA TFM and the European EN 1500 document for establishing alcohol-based hand rubs vary.^{1,19,79} Alcohol-based hand rubs that meet TFM criteria for efficacy may not necessarily meet the EN 1500 criteria for efficacy.⁸⁰ In addition, scientific studies have not established the extent to which counts of bacteria or other microorganisms on the hands need to be reduced to minimize transmission of pathogens in health-care facilities^{1,8}; whether bacterial counts on the hands must be reduced by 1 \log_{10} (90% reduction), 2 \log_{10} (99%), 3 \log_{10} (99.9%), or 4 \log_{10} (99.99%) is unknown. Several other methods also have been used to measure the efficacy of antiseptic agents against various viral pathogens.^{81–83}

Shortcomings of Traditional Methodologies

Accepted methods of evaluating hand-hygiene products intended for use by HCWs require that test volunteers wash their hands with a plain or antimicrobial soap for 30 seconds or 1 minute, despite the observation in the majority of studies that the average duration of handwashing by hospital personnel is <15 seconds.^{52,84–89} A limited number of investigators have used 15-second handwashing or hygienic hand-

wash protocols.^{90–94} Therefore, almost no data exist regarding the efficacy of plain or antimicrobial soaps under conditions in which they are actually used by HCWs. Similarly, certain accepted methods for evaluating waterless antiseptic agents for use as antiseptic hand rubs require that 3 mL of alcohol be rubbed into the hands for 30 seconds, followed by a repeat application for the same duration. This type of protocol also does not reflect actual usage patterns among HCWs. Furthermore, volunteers used in evaluations of products are usually surrogates for HCWs, and their hand flora may not reflect flora found on the hands of personnel working in health-care settings. Further studies should be conducted among practicing HCWs using standardized protocols to obtain more realistic views of microbial colonization and risk of bacterial transfer and cross-transmission.⁵¹

REVIEW OF PREPARATIONS USED FOR HAND HYGIENE

Plain (Non-antimicrobial) Soap

Soaps are detergent-based products that contain esterified fatty acids and sodium or potassium hydroxide. They are available in various forms including bar soap, tissue, leaflet, and liquid preparations. Their cleaning activity can be attributed to their detergent properties, which result in removal of dirt, soil, and various organic substances from the hands. Plain soaps have minimal, if any, antimicrobial activity. However, handwashing with plain soap can remove loosely adherent transient flora. For example, handwashing with plain soap and water for 15 seconds reduces bacterial counts on the skin by 0.6–1.1 \log_{10} , whereas washing for 30 seconds reduces counts by 1.8–2.8 \log_{10} .¹ However, in several studies, handwashing with plain soap failed to remove pathogens from the hands of hospital personnel.^{25,45} Handwashing with plain soap can result in paradoxical increases in bacterial counts on the skin.^{92,95–97} Non-antimicrobial soaps may be associated with considerable skin irritation and dryness,^{92,96,98} although adding emollients to soap preparations may reduce their propensity to cause irritation. Occasionally, plain soaps have become contaminated, which may lead to colonization of hands of personnel with gram-negative bacilli.⁹⁹

Alcohols

The majority of alcohol-based hand antiseptics contain either isopropanol, ethanol, n-propanol, or a combination of two of these products. Although n-propanol has been used in alcohol-based hand rubs in parts of Europe for many years, it is not listed in TFM as an approved active agent for HCW handwashes or surgical hand-scrub preparations in the United States. The majority of studies of alcohols have evaluated individual alcohols in varying concentrations. Other studies have focused on combinations of two alcohols or alcohol solutions containing limited amounts of hexachlorophene, quaternary ammonium compounds, povidone-iodine, triclosan, or chlorhexidine gluconate.^{61,93,100–119}

The antimicrobial activity of alcohols can be attributed to their ability to denature proteins.¹²⁰ Alcohol solutions containing 60%–95% alcohol are most effective, and higher concentrations are less potent^{120–122} because pro-

TABLE 1
VIRUCIDAL ACTIVITY OF ANTISEPTIC AGENTS AGAINST ENVELOPED VIRUSES

Ref. No.	Test Method	Viruses	Agent	Results
(379)	Suspension	HIV	19% EA	LR = 2.0 in 5 minutes
(380)	Suspension	HIV	50% EA	LR > 3.5
			35% IPA	LR > 3.7
(381)	Suspension	HIV	70% EA	LR = 7.0 in 1 minute
(382)	Suspension	HIV	70% EA	LR = 3.2B 5.5 in 30 seconds
(383)	Suspension	HIV	70% IPA/0.5% CHG	LR = 6.0 in 15 seconds
			4% CHG	LR = 6.0 in 15 seconds
(384)	Suspension	HIV	Chloroxylenol	Inactivated in 1 minute
			Benzalkonium chloride	Inactivated in 1 minute
(385)	Suspension	HIV	Povidone-iodine	Inactivated
			Chlorhexidine	Inactivated
(386)	Suspension	HIV	Detergent/0.5% PCMX	Inactivated in 30 seconds
(387)	Suspension/dried plasma chimpanzee challenge	HBV	70% IPA	LR = 6.0 in 10 minutes
(388)	Suspension/plasma chimpanzee challenge	HBV	80% EA	LR = 7.0 in 2 minutes
(389)	Suspension	HSV	95% EA	LR > 5.0 in 1 minute
			75% EA	LR > 5.0
			95% IPA	LR > 5.0
			70% EA + 0.5% CHG	LR > 5.0
(130)	Suspension	RSV	35% IPA	LR > 4.3 in 1 minute
			4% CHG	LR > 3.3
(141)	Suspension	Influenza	95% EA	Undetectable in 30 seconds
		Vaccinia	95% EA	Undetectable in 30 seconds
(141)	Hand test	Influenza	95% EA	LR > 2.5
		Vaccinia	95% EA	LR > 2.5

Note: HIV = human immunodeficiency virus, EA = ethanol, LR = Log₁₀ reduction, IPA = isopropanol, CHG = chlorhexidine gluconate, HBV = hepatitis B virus, RSV = respiratory syncytial virus, HSV = herpes simplex virus, HAV = hepatitis A virus, and PCMX = chloroxylenol.

teins are not denatured easily in the absence of water.¹²⁰ The alcohol content of solutions may be expressed as percent by weight (w/w), which is not affected by temperature or other variables, or as percent by volume (vol/vol), which can be affected by temperature, specific gravity, and reaction concentration.¹²³ For example, 70% alcohol by weight is equivalent to 76.8% by volume if prepared at 15°C, or 80.5% if prepared at 25°C.¹²³ Alcohol concentrations in antiseptic hand rubs are often expressed as percent by volume.¹⁹

Alcohols have excellent *in vitro* germicidal activity against gram-positive and gram-negative vegetative bacteria, including multidrug-resistant pathogens (e.g., MRSA and VRE), *Mycobacterium tuberculosis*, and various fungi.^{120-122,124-129} Certain enveloped (lipophilic) viruses (e.g., herpes simplex virus, human immunodeficiency virus [HIV], influenza virus, RSV, and vaccinia virus) are susceptible to alcohols when tested *in vitro*.^{120,130,131} (Table 1). Hepatitis B virus is an enveloped virus that is somewhat less susceptible but is killed by 60%–70% alcohol; hepatitis C virus also is likely killed by this percentage of alcohol.¹³² In a porcine tissue carrier model used to study antiseptic activity, 70% ethanol and 70% isopropanol were found to reduce titers of an enveloped bacteriophage more effectively than an antimicrobial soap containing 4% chlorhexidine gluconate.¹³³ Despite its effectiveness

against these organisms, alcohols have very poor activity against bacterial spores, protozoan oocysts, and certain nonenveloped (nonlipophilic) viruses.

Numerous studies have documented the *in vivo* antimicrobial activity of alcohols. Alcohols effectively reduce bacterial counts on the hands.^{14,121,125,134} Typically, log reductions of the release of test bacteria from artificially contaminated hands average 3.5 log₁₀ after a 30-second application and 4.0–5.0 log₁₀ after a 1-minute application.¹ In 1994, the FDA TFM classified ethanol 60%–95% as a Category I agent (i.e., generally safe and effective for use in antiseptic handwash or HCW hand-wash products).¹⁹ Although TFM placed isopropanol 70%–91.3% in category III (i.e., insufficient data to classify as effective), 60% isopropanol has subsequently been adopted in Europe as the reference standard against which alcohol-based hand-rub products are compared.⁷⁹ Alcohols are rapidly germicidal when applied to the skin, but they have no appreciable persistent (i.e., residual) activity. However, regrowth of bacteria on the skin occurs slowly after use of alcohol-based hand antiseptics, presumably because of the sublethal effect alcohols have on some of the skin bacteria.^{135,136} Addition of chlorhexidine, quaternary ammonium compounds, octenidine, or triclosan to alcohol-based solutions can result in persistent activity.¹

TABLE 2
VIRUCIDAL ACTIVITY OF ANTISEPTIC AGENTS AGAINST NONENVELOPED VIRUSES

Ref. No.	Test Method	Viruses	Antiseptic	Result
(390)	Suspension	Rotavirus	4% CHG 10% povidone-iodine 70% IPA/0.1% HCP	LR < 3.0 in 1 minute LR > 3.0 LR > 3.0
(141)	Hand test	Adenovirus Poliovirus Coxsackie	95% EA 95% EA 95% EA	LR > 1.4 LR = 0.2–1.0 LR = 1.1–1.3
	Finger test	Adenovirus Poliovirus Coxsackie	95% EA 95% EA 95% EA	LR > 2.3 LR = 0.7–2.5 LR = 2.9
(389)	Suspension	ECHO virus	95% EA 75% EA 95% IPA 70% IPA + 0.5% CHG	LR > 3.0 in 1 minute LR < 1.0 LR = 0 LR = 0
(140)	Finger pad	HAV	70% EA 62% EA foam Plain soap 4% CHG 0.3% triclosan	87.4% reduction 89.3% reduction 78.0% reduction 89.6% reduction 92.0% reduction
(105)	Finger tips	Bovine Rotavirus	n-propanol + IPA 70% IPA 70% EA 2% triclosan Water (control) 7.5% povidone-iodine Plain soap 4% CHG	LR = 3.8 in 30 seconds LR = 3.1 LR = 2.9 LR = 2.1 LR = 1.3 LR = 1.3 LR = 1.2 LR = 0.5
(137)	Finger pad	Human Rotavirus	70% IPA Plain soap	98.9% decrease in 10 seconds 77.1%
(138)	Finger pad	Human Rotavirus	70% IPA 2% CHG Plain soap	99.6% decrease in 10 seconds 80.3% 72.5%
(81)	Finger pad	Rotavirus Rhinovirus Adenovirus	60% EA gel 60% EA gel 60% EA gel	LR > 3.0 in 10 seconds LR > 3.0 LR > 3.0
(139)	Finger pad	Poliovirus	70% EA 70% IPA	LR = 1.6 in 10 seconds LR = 0.8
(200)	Finger tips	Poliovirus	Plain soap 80% EA	LR = 2.1 LR = 0.4

Note: HIV = human immunodeficiency virus, EA = ethanol, LR = Log₁₀ reduction, IPA = isopropanol, CHG = chlorhexidine gluconate, HBV = hepatitis B virus, RSV = respiratory syncytial virus, HSV = herpes simplex virus, and HAV = hepatitis A virus.

Alcohols, when used in concentrations present in alcohol-based hand rubs, also have in vivo activity against several nonenveloped viruses (Table 2). For example, 70% isopropanol and 70% ethanol are more effective than medicated soap or nonmedicated soap in reducing rotavirus titers on fingerpads.^{137,138} A more recent study using the same test methods evaluated a commercially available product containing 60% ethanol and found that the product reduced the infectivity titers of three nonenveloped viruses (i.e., rotavirus, adenovirus, and rhinovirus) by >3 logs.⁸¹ Other nonenveloped viruses such as hepatitis A and enteroviruses (e.g., poliovirus) may require 70%–80% alcohol to be reliably inactivated.^{82,139} However, both 70% ethanol and a 62% ethanol foam product with emollients reduced hepatitis A virus titers on whole hands or finger-

tips more than nonmedicated soap; both were equally as effective as antimicrobial soap containing 4% chlorhexidine gluconate in reducing reduced viral counts on hands.¹⁴⁰ In the same study, both 70% ethanol and the 62% ethanol foam product demonstrated greater virucidal activity against poliovirus than either non-antimicrobial soap or a 4% chlorhexidine gluconate-containing soap.¹⁴⁰ However, depending on the alcohol concentration, the amount of time that hands are exposed to the alcohol, and viral variant, alcohol may not be effective against hepatitis A and other nonlipophilic viruses. The inactivation of nonenveloped viruses is influenced by temperature, disinfectant–virus volume ratio, and protein load.¹⁴¹ Ethanol has greater activity against viruses than isopropanol. Further in vitro and in vivo studies of both alcohol-based formulations

TABLE 3

STUDIES COMPARING THE RELATIVE EFFICACY (BASED ON LOG₁₀ REDUCTIONS ACHIEVED) OF PLAIN SOAP OR ANTIMICROBIAL SOAPS VERSUS ALCOHOL-BASED ANTISEPTICS IN REDUCING COUNTS OF VIABLE BACTERIA ON HANDS

Ref. No.	Year	Skin Contamination	Assay Method	Time (sec)	Relative Efficacy
(143)	1965	Existing hand flora	Finger-tip agar culture	60	Plain soap < HCP < 50% EA foam
(119)	1975	Existing hand flora	Hand-rub broth culture	—	Plain soap < 95% EA
(106)	1978	Artificial contamination	Finger-tip broth culture	30	Plain soap < 4% CHG < P-I < 70% EA = alc. CHG
(144)	1978	Artificial contamination	Finger-tip broth culture	30	Plain soap < 4% CHG < 70% EA
(107)	1979	Existing hand flora	Hand-rub broth culture	120	Plain soap < 0.5% aq. CHG < 70% EA < 4% CHG < alc. CHG
(145)	1980	Artificial contamination	Finger-tip broth culture	60–120	4% CHG < P-I < 60% IPA
(53)	1980	Artificial contamination	Finger-tip broth culture	15	Plain soap < 3% HCP < P-I < 4% CHG < 70% EA
(108)	1982	Artificial contamination	Glove-juice test	15	P-I < alc. CHG
(109)	1983	Artificial contamination	Finger-tip broth culture	120	0.3%–2% triclosan = 60% IPA = alc. CHG < alc. triclosan
(146)	1984	Artificial contamination	Finger-tip agar culture	60	Phenolic < 4% CHG < P-I < EA < IPA < n-P
(147)	1985	Existing hand flora	Finger-tip agar culture	60	Plain soap < 70% EA < 95% EA
(110)	1986	Artificial contamination	Finger-tip broth culture	60	Phenolic = P-I < alc. CHG < n-P
(93)	1986	Existing hand flora	Sterile-broth bag technique	15	Plain soap < IPA < 4% CHG = IPA-E = alc. CHG
(61)	1988	Artificial contamination	Finger-tip broth culture	30	Plain soap < triclosan < P-I < IPA < alc. CHG < n-P
(25)	1991	Patient contact	Glove-juice test	15	Plain soap < IPA-E
(148)	1991	Existing hand flora	Agar-plate/image analysis	30	Plain soap < 1% triclosan < P-I < 4% CHG < IPA
(111)	1992	Artificial contamination	Finger-tip agar culture	60	Plain soap < IPA < EA < alc. CHG
(149)	1992	Artificial contamination	Finger-tip broth culture	60	Plain soap < 60% n-P
(112)	1994	Existing hand flora	Agar-plate/image analysis	30	Plain soap < alc. CHG
(150)	1999	Existing hand flora	Agar-plate culture	N.S.	Plain soap < commercial alcohol mixture
(151)	1999	Artificial contamination	Glove-juice test	20	Plain soap < 0.6% PCMX < 65% EA
(152)	1999	Artificial contamination	Finger-tip broth culture	30	4% CHG < plain soap < P-I < 70% EA

Note: Existing hand flora = without artificially contaminating hands with bacteria, alc. CHG = alcoholic chlorhexidine gluconate, aq. CHG = aqueous chlorhexidine gluconate, 4% CHG = chlorhexidine gluconate detergent, EA = ethanol, HCP = hexachlorophene soap/detergent, IPA = isopropanol, IPA-E = isopropanol + emollients, n-P = n-propanol, PCMX = chloroxylenol detergent, P-I = povidone-iodine detergent, and N.S. = not stated.

and antimicrobial soaps are warranted to establish the minimal level of virucidal activity that is required to interrupt direct contact transmission of viruses in health-care settings.

Alcohols are not appropriate for use when hands are visibly dirty or contaminated with proteinaceous materials. However, when relatively small amounts of proteinaceous material (e.g., blood) are present, ethanol and isopropanol may reduce viable bacterial counts on hands more than plain soap or antimicrobial soap.¹⁴²

Alcohol can prevent the transfer of health-care-associated pathogens.^{25,63,64} In one study, gram-negative bacilli were transferred from a colonized patient's skin to a piece of catheter material via the hands of nurses in only 17% of experiments after antiseptic hand rub with an alcohol-based hand rinse.²⁵ In contrast, transfer of the organisms occurred in 92% of experiments after handwashing with plain soap and water. This experimental model indicates that when the hands of HCWs are heavily contaminated, an antiseptic hand rub using an alcohol-based rinse can prevent pathogen transmission more effectively than can handwashing with plain soap and water.

Alcohol-based products are more effective for standard handwashing or hand antisepsis by HCWs than soap or antimicrobial soaps (Table 3).^{25,53,61,93,106-112,119,143-152} In all but two of the trials that compared alcohol-based solutions

with antimicrobial soaps or detergents, alcohol reduced bacterial counts on hands more than washing hands with soaps or detergents containing hexachlorophene, povidone-iodine, 4% chlorhexidine, or triclosan. In studies examining antimicrobial-resistant organisms, alcohol-based products reduced the number of multidrug-resistant pathogens recovered from the hands of HCWs more effectively than did handwashing with soap and water.¹⁵³⁻¹⁵⁵

Alcohols are effective for preoperative cleaning of the hands of surgical personnel^{1,101,104,113-119,135,143,147,156-159} (Tables 4 and 5). In multiple studies, bacterial counts on the hands were determined immediately after using the product and again 1–3 hours later; the delayed testing was performed to determine if regrowth of bacteria on the hands is inhibited during operative procedures. Alcohol-based solutions were more effective than washing hands with plain soap in all studies, and they reduced bacterial counts on the hands more than antimicrobial soaps or detergents in the majority of experiments.^{101,104,113-119,135,143,147,157-159} In addition, the majority of alcohol-based preparations were more effective than povidone-iodine or chlorhexidine.

The efficacy of alcohol-based hand-hygiene products is affected by several factors, including the type of alcohol used, concentration of alcohol, contact time, volume of alcohol used, and whether the hands are wet when the alcohol is applied. Applying small volumes (i.e., 0.2–0.5 mL) of alco-

TABLE 4

STUDIES COMPARING THE RELATIVE EFFICACY OF PLAIN SOAP OR ANTIMICROBIAL SOAP VERSUS ALCOHOL-CONTAINING PRODUCTS IN REDUCING COUNTS OF BACTERIA RECOVERED FROM HANDS IMMEDIATELY AFTER USE OF PRODUCTS FOR PRE-OPERATIVE CLEANSING OF HANDS

Ref. No.	Year	Assay Method	Relative Efficacy
(143)	1965	Finger-tip agar culture	HCP < 50% EA foam + QAC
(157)	1969	Finger-tip agar culture	HCP < P-I < 50% EA foam + QAC
(101)	1973	Finger-tip agar culture	HCP soap < EA foam + 0.23% HCP
(135)	1974	Broth culture	Plain soap < 0.5% CHG < 4% CHG < alc. CHG
(119)	1975	Hand-broth test	Plain soap < 0.5% CHG < 4% CHG < alc. CHG
(118)	1976	Glove-juice test	0.5% CHG < 4% CHG < alc. CHG
(114)	1977	Glove-juice test	P-I < CHG < alc. CHG
(117)	1978	Finger-tip agar culture	P-I = 46% EA + 0.23% HCP
(113)	1979	Broth culture of hands	Plain soap < P-I < alc. CHG < alc. P-I
(116)	1979	Glove-juice test	70% IPA = alc. CHG
(147)	1985	Finger-tip agar culture	Plain soap < 70% - 90% EA
(115)	1990	Glove-juice test, modified	Plain soap < triclosan < CHG < P-I < alc. CHG
(104)	1991	Glove-juice test	Plain soap < 2% triclosan < P-I < 70% IPA
(158)	1998	Finger-tip broth culture	70% IPA < 90% IPA = 60% n-P
(159)	1998	Glove-juice test	P-I < CHG < 70% EA

Note: QAC = quaternary ammonium compound, alc. CHG = alcoholic chlorhexidine gluconate, CHG = chlorhexidine gluconate detergent, EA = ethanol, HCP = hexachlorophene detergent, IPA = iso-propanol, and P-I = povidone-iodine detergent.

TABLE 5

EFFICACY OF SURGICAL HAND-RUB SOLUTIONS IN REDUCING THE RELEASE OF RESIDENT SKIN FLORA FROM CLEAN HANDS

Study	Rub	Concentration* (%)	Time (min)	Mean log Reduction	
				Immediate	Sustained (3 hr)
1	n-propanol	60	5	2.9 [†]	1.6 [†]
2			5	2.7 [†]	NA
3			5	2.5 [†]	1.8 [†]
4			5	2.3 [†]	1.6 [†]
5			3	2.9 [§]	NA
4	Isopropanol	90	3	2.0 [†]	1.0 [†]
4			1	1.1 [†]	0.5 [†]
6			3	2.4 [§]	1.4 [§]
6			3	2.3 [§]	1.2 [§]
7			5	2.4 [†]	2.1 [†]
4			5	2.1 [†]	1.0 [†]
6			3	2.0 [§]	0.7 [§]
5			3	1.7 ^c	NA
4			3	1.5 [†]	0.8 [†]
8			2	1.2	0.8
4	1	0.7 [†]	0.2		
9	1	0.8	NA		
10	Isopropanol + chlorhexidine gluc. (w/v)	60	5	1.7	1.0
7			5	2.5 [†]	2.7 [†]
8			2	1.0	1.5
11	Ethanol	95	2	2.1	NA
5			3	2.4 [§]	NA
12			2	1.5	NA
8	Ethanol + chlorhexidine gluc. (w/v)	70	2	1.0	0.6
13			2	1.7	NA
14			5	2.0	1.5 [¶]
8	Ethanol + chlorhexidine gluc. (w/v)	70 + 0.5	2	0.7	1.4
8			2	0.4	1.2
15	Chlorhexidine gluc. (aq. Sol., w/v)	0.5	2	0.4	1.2
15	Povidone-iodine (aq. Sol., w/v)	1.0	5	1.9 [†]	0.8 [†]
16	Peracetic acid (w/v)	0.5	5	1.9	NA

Note: NA = not available.

Source: Rotter M. Hand washing and hand disinfection [Chapter 87]. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999. Table 5 is copyrighted by Lippincott Williams & Wilkins; it is reprinted here with their permission and permission from Manfred Rotter, M.D., Professor of Hygiene and Microbiology, Klinisches Institut für Hygiene der Universität Wien, Germany.

*Volume/volume unless otherwise stated.

[†]Tested according to Deutsche Gesellschaft für Hygiene, and Mikrobiologie (DGHM)-German Society of Hygiene and Microbiology method.

[§]Tested according to European Standard prEN.

[¶]After 4 hours.

hol to the hands is not more effective than washing hands with plain soap and water.^{63,64} One study documented that 1 mL of alcohol was substantially less effective than 3 mL.⁹¹ The ideal volume of product to apply to the hands is not known and may vary for different formulations. However, if hands feel dry after rubbing hands together for 10–15 seconds, an insufficient volume of product likely was applied. Because alcohol-impregnated towelettes contain a limited amount of alcohol, their effectiveness is comparable to that of soap and water.^{63,160,161}

Alcohol-based hand rubs intended for use in hospitals are available as low viscosity rinses, gels, and foams. Limited data are available regarding the relative efficacy of various formulations. One field trial demonstrated that an ethanol gel was slightly more effective than a comparable ethanol solution at reducing bacterial counts on the hands of HCWs.¹⁶² However, a more recent study indicated that rinses reduced bacterial counts on the hands more than the gels tested.⁸⁰ Further studies are warranted to determine the relative efficacy of alcohol-based rinses and gels in reducing transmission of health-care-associated pathogens.

Frequent use of alcohol-based formulations for hand antisepsis can cause drying of the skin unless emollients, humectants, or other skin-conditioning agents are added to the formulations. The drying effect of alcohol can be reduced or eliminated by adding 1%–3% glycerol or other skin-conditioning agents.^{90,93,100,101,106,135,143,163,164} Moreover, in several recent prospective trials, alcohol-based rinses or gels containing emollients caused substantially less skin irritation and dryness than the soaps or antimicrobial detergents tested.^{96,98,165,166} These studies, which were conducted in clinical settings, used various subjective and objective methods for assessing skin irritation and dryness. Further studies are warranted to establish whether products with different formulations yield similar results.

Even well-tolerated alcohol hand rubs containing emollients may cause a transient stinging sensation at the site of any broken skin (e.g., cuts and abrasions). Alcohol-based hand-rub preparations with strong fragrances may be poorly tolerated by HCWs with respiratory allergies. Allergic contact dermatitis or contact urticaria syndrome caused by hypersensitivity to alcohol or to various additives present in certain alcohol hand rubs occurs only rarely.^{167,168}

Alcohols are flammable. Flash points of alcohol-based hand rubs range from 21°C to 24°C, depending on the type and concentration of alcohol present.¹⁶⁹ As a result, alcohol-based hand rubs should be stored away from high temperatures or flames in accordance with National Fire Protection Agency recommendations. In Europe, where alcohol-based hand rubs have been used extensively for years, the incidence of fires associated with such products has been low.¹⁶⁹ One recent U.S. report described a flash fire that occurred as a result of an unusual series of events, which included an HCW applying an alcohol gel to her hands, immediately removing a polyester isolation gown, and then touching a metal door before the alcohol had evaporated.¹⁷⁰ Removing the polyester gown created a sub-

stantial amount of static electricity that generated an audible static spark when the HCW touched the metal door, igniting the unevaporated alcohol on her hands.¹⁷⁰ This incident emphasizes the need to rub hands together after application of alcohol-based products until all the alcohol has evaporated.

Because alcohols are volatile, containers should be designed to minimize evaporation. Contamination of alcohol-based solutions has seldom been reported. One report documented a cluster of pseudoinfections caused by contamination of ethyl alcohol by *Bacillus cereus* spores.¹⁷¹

Chlorhexidine

Chlorhexidine gluconate, a cationic bisbiguanide, was developed in England in the early 1950s and was introduced into the United States in the 1970s.^{8,172} Chlorhexidine base is only minimally soluble in water, but the digluconate form is water-soluble. The antimicrobial activity of chlorhexidine is likely attributable to attachment to, and subsequent disruption of, cytoplasmic membranes, resulting in precipitation of cellular contents.^{1,8} Chlorhexidine's immediate antimicrobial activity occurs more slowly than that of alcohols. Chlorhexidine has good activity against gram-positive bacteria, somewhat less activity against gram-negative bacteria and fungi, and only minimal activity against tubercle bacilli.^{1,8,172} Chlorhexidine is not sporicidal.^{1,172} It has in vitro activity against enveloped viruses (e.g., herpes simplex virus, HIV, cytomegalovirus, influenza, and RSV) but substantially less activity against nonenveloped viruses (e.g., rotavirus, adenovirus, and enteroviruses).^{130,131,173} The antimicrobial activity of chlorhexidine is only minimally affected by the presence of organic material, including blood. Because chlorhexidine is a cationic molecule, its activity can be reduced by natural soaps, various inorganic anions, nonionic surfactants, and hand creams containing anionic emulsifying agents.^{8,172,174} Chlorhexidine gluconate has been incorporated into a number of hand-hygiene preparations. Aqueous or detergent formulations containing 0.5% or 0.75% chlorhexidine are more effective than plain soap, but they are less effective than antiseptic detergent preparations containing 4% chlorhexidine gluconate.^{135,175} Preparations with 2% chlorhexidine gluconate are slightly less effective than those containing 4% chlorhexidine.¹⁷⁶

Chlorhexidine has substantial residual activity.^{106,114-116,118,135,146,175} Addition of low concentrations (0.5%–1.0%) of chlorhexidine to alcohol-based preparations results in greater residual activity than alcohol alone.^{116,135} When used as recommended, chlorhexidine has a good safety record.¹⁷² Minimal, if any, absorption of the compound occurs through the skin. Care must be taken to avoid contact with the eyes when using preparations with $\geq 1\%$ chlorhexidine, because the agent can cause conjunctivitis and severe corneal damage. Ototoxicity precludes its use in surgery involving the inner or middle ear. Direct contact with brain tissue and the meninges should be avoided. The frequency of skin irritation is concentration-

dependent, with products containing 4% most likely to cause dermatitis when used frequently for antiseptic handwashing¹⁷⁷; allergic reactions to chlorhexidine gluconate are uncommon.^{118,172} Occasional outbreaks of nosocomial infections have been traced to contaminated solutions of chlorhexidine.¹⁷⁸⁻¹⁸¹

Chloroxylenol

Chloroxylenol, also known as parachlorometaxylenol (PCMX), is a halogen-substituted phenolic compound that has been used as a preservative in cosmetics and other products and as an active agent in antimicrobial soaps. It was developed in Europe in the late 1920s and has been used in the United States since the 1950s.¹⁸²

The antimicrobial activity of PCMX likely is attributable to inactivation of bacterial enzymes and alteration of cell walls.¹ It has good in vitro activity against gram-positive organisms and fair activity against gram-negative bacteria, mycobacteria, and certain viruses.^{1,7,182} PCMX is less active against *P. aeruginosa*, but addition of ethylenediaminetetraacetic acid (EDTA) increases its activity against *Pseudomonas* spp. and other pathogens.

A limited number of articles focusing on the efficacy of PCMX-containing preparations intended for use by HCWs have been published in the last 25 years, and the results of studies have sometimes been contradictory. For example, in studies in which antiseptics were applied to abdominal skin, PCMX had the weakest immediate and residual activity of any of the agents studied.¹⁸³ However, when 30-second handwashes were performed using 0.6% PCMX, 2% chlorhexidine gluconate, or 0.3% triclosan, the immediate effect of PCMX was similar to that of the other agents. When used 18 times per day for 5 consecutive days, PCMX had less cumulative activity than did chlorhexidine gluconate.¹⁸⁴ When PCMX was used as a surgical scrub, one report indicated that 3% PCMX had immediate and residual activity comparable to 4% chlorhexidine gluconate,¹⁸⁵ whereas two other studies demonstrated that the immediate and residual activity of PCMX was inferior to both chlorhexidine gluconate and povidone-iodine.^{176,186} The disparity between published studies may be associated with the various concentrations of PCMX included in the preparations evaluated and with other aspects of the formulations tested, including the presence or absence of EDTA.^{7,182} PCMX is not as rapidly active as chlorhexidine gluconate or iodophors, and its residual activity is less pronounced than that observed with chlorhexidine gluconate.^{7,182} In 1994, FDA TFM tentatively classified PCMX as a Category III SE active agent (i.e., insufficient data are available to classify this agent as safe and effective).¹⁹ Further evaluation of this agent by the FDA is ongoing.

The antimicrobial activity of PCMX is minimally affected by the presence of organic matter, but it is neutralized by nonionic surfactants. PCMX, which is absorbed through the skin,^{7,182} is usually well-tolerated, and allergic reactions associated with its use are uncommon. PCMX is available in concentrations of 0.3%–3.75%. In-use contamination of a PCMX-containing preparation has been reported.¹⁸⁷

Hexachlorophene

Hexachlorophene is a bisphenol composed of two phenolic groups and three chlorine moieties. In the 1950s and early 1960s, emulsions containing 3% hexachlorophene were widely used for hygienic handwashing, as surgical scrubs, and for routine bathing of infants in hospital nurseries. The antimicrobial activity of hexachlorophene results from its ability to inactivate essential enzyme systems in microorganisms. Hexachlorophene is bacteriostatic, with good activity against *S. aureus* and relatively weak activity against gram-negative bacteria, fungi, and mycobacteria.⁷

Studies of hexachlorophene as a hygienic handwash and surgical scrub demonstrated only modest efficacy after a single handwash.^{53,143,188} Hexachlorophene has residual activity for several hours after use and gradually reduces bacterial counts on hands after multiple uses (i.e., it has a cumulative effect).^{1,101,188,189} With repeated use of 3% hexachlorophene preparations, the drug is absorbed through the skin. Infants bathed with hexachlorophene and personnel regularly using a 3% hexachlorophene preparation for handwashing have blood levels of 0.1–0.6 ppm hexachlorophene.¹⁹⁰ In the early 1970s, certain infants bathed with hexachlorophene developed neurotoxicity (vacuolar degeneration).¹⁹¹ As a result, in 1972, the FDA warned that hexachlorophene should no longer be used routinely for bathing infants. However, after routine use of hexachlorophene for bathing infants in nurseries was discontinued, investigators noted that the incidence of health-care-associated *S. aureus* infections in hospital nurseries increased substantially.^{192,193} In several instances, the frequency of infections decreased when hexachlorophene bathing of infants was reinstated. However, current guidelines still recommend against the routine bathing of neonates with hexachlorophene because of its potential neurotoxic effects.¹⁹⁴ The agent is classified by FDA TFM as not generally recognized as safe and effective for use as an antiseptic handwash.¹⁹ Hexachlorophene should not be used to bathe patients with burns or extensive areas of susceptible, sensitive skin. Soaps containing 3% hexachlorophene are available by prescription only.⁷

Iodine and Iodophors

Iodine has been recognized as an effective antiseptic since the 1800s. However, because iodine often causes irritation and discoloring of skin, iodophors have largely replaced iodine as the active ingredient in antiseptics.

Iodine molecules rapidly penetrate the cell wall of microorganisms and inactivate cells by forming complexes with amino acids and unsaturated fatty acids, resulting in impaired protein synthesis and alteration of cell membranes.¹⁹⁵ Iodophors are composed of elemental iodine, iodide or triiodide, and a polymer carrier (i.e., the complexing agent) of high molecular weight. The amount of molecular iodine present (so-called “free” iodine) determines the level of antimicrobial activity of iodophors. “Available” iodine refers to the total amount of iodine that can be titrated with sodium thiosulfate.¹⁹⁶ Typical 10% povidone-iodine formulations contain 1% available iodine and

yield free iodine concentrations of 1 ppm.¹⁹⁶ Combining iodine with various polymers increases the solubility of iodine, promotes sustained release of iodine, and reduces skin irritation. The most common polymers incorporated into iodophors are polyvinyl pyrrolidone (i.e., povidone) and ethoxylated nonionic detergents (i.e., poloxamers).^{195,196} The antimicrobial activity of iodophors also can be affected by pH, temperature, exposure time, concentration of total available iodine, and the amount and type of organic and inorganic compounds present (e.g., alcohols and detergents).

Iodine and iodophors have bactericidal activity against gram-positive, gram-negative, and certain spore-forming bacteria (e.g., clostridia and *Bacillus* spp.) and are active against mycobacteria, viruses, and fungi.^{8,195,197-200} However, in concentrations used in antiseptics, iodophors are not usually sporicidal.²⁰¹ In vivo studies have demonstrated that iodophors reduce the number of viable organisms that are recovered from the hands of personnel.^{113,145,148,152,155} Povidone-iodine 5%–10% has been tentatively classified by FDA TFM as a Category I agent (i.e., a safe and effective agent for use as an antiseptic handwash and an HCW handwash).¹⁹ The extent to which iodophors exhibit persistent antimicrobial activity after they have been washed off the skin is unclear. In one study, persistent activity was noted for 6 hours¹⁷⁶; however, several other studies demonstrated persistent activity for only 30–60 minutes after washing hands with an iodophor.^{61,117,202} In studies in which bacterial counts were obtained after gloves were worn for 1–4 hours after washing, iodophors have demonstrated poor persistent activity.^{1,104,115,189,203-208} The in vivo antimicrobial activity of iodophors is substantially reduced in the presence of organic substances (e.g., blood or sputum).⁸

The majority of iodophor preparations used for hand hygiene contain 7.5%–10% povidone-iodine. Formulations with lower concentrations also have good antimicrobial activity because dilution can increase free iodine concentrations.²⁰⁹ However, as the amount of free iodine increases, the degree of skin irritation also may increase.²⁰⁹ Iodophors cause less skin irritation and fewer allergic reactions than iodine, but more irritant contact dermatitis than other antiseptics commonly used for hand hygiene.⁹² Occasionally, iodophor antiseptics have become contaminated with gram-negative bacilli as a result of poor manufacturing processes and have caused outbreaks or pseudo-outbreaks of infection.¹⁹⁶

Quaternary Ammonium Compounds

Quaternary ammonium compounds are composed of a nitrogen atom linked directly to four alkyl groups, which may vary in their structure and complexity.²¹⁰ Of this large group of compounds, alkyl benzalkonium chlorides are the most widely used as antiseptics. Other compounds that have been used as antiseptics include benzethonium chloride, cetrimide, and cetylpyridium chloride.¹ The antimicrobial activity of these compounds was first studied in the early 1900s, and a quaternary ammonium compound for preoperative cleaning of surgeons' hands was used as early as 1935.²¹⁰ The antimicrobial activity of this group of com-

pounds likely is attributable to adsorption to the cytoplasmic membrane, with subsequent leakage of low molecular weight cytoplasmic constituents.²¹⁰

Quaternary ammonium compounds are primarily bacteriostatic and fungistatic, although they are microbicidal against certain organisms at high concentrations¹; they are more active against gram-positive bacteria than against gram-negative bacilli. Quaternary ammonium compounds have relatively weak activity against mycobacteria and fungi and have greater activity against lipophilic viruses. Their antimicrobial activity is adversely affected by the presence of organic material, and they are not compatible with anionic detergents.^{1,210} In 1994, FDA TFM tentatively classified benzalkonium chloride and benzethonium chloride as Category IIISE active agents (i.e., insufficient data exists to classify them as safe and effective for use as an antiseptic handwash).¹⁹ Further evaluation of these agents by FDA is in progress.

Quaternary ammonium compounds are usually well tolerated. However, because of weak activity against gram-negative bacteria, benzalkonium chloride is prone to contamination by these organisms. Several outbreaks of infection or pseudoinfection have been traced to quaternary ammonium compounds contaminated with gram-negative bacilli.²¹¹⁻²¹³ For this reason, in the United States, these compounds have been seldom used for hand antiseptics during the last 15–20 years. However, newer handwashing products containing benzalkonium chloride or benzethonium chloride have recently been introduced for use by HCWs. A recent study of surgical intensive-care unit personnel found that cleaning hands with antimicrobial wipes containing a quaternary ammonium compound was about as effective as using plain soap and water for handwashing; both were less effective than decontaminating hands with an alcohol-based hand rub.²¹⁴ One laboratory-based study reported that an alcohol-free hand-rub product containing a quaternary ammonium compound was efficacious in reducing microbial counts on the hands of volunteers.²¹⁵ Further studies of such products are needed to determine if newer formulations are effective in health-care settings.

Triclosan

Triclosan (chemical name: 2,4,4'-trichloro-2'-hydroxydiphenyl ether) is a nonionic, colorless substance that was developed in the 1960s. It has been incorporated into soaps for use by HCWs and the public and into other consumer products. Concentrations of 0.2%–2% have antimicrobial activity. Triclosan enters bacterial cells and affects the cytoplasmic membrane and synthesis of RNA, fatty acids, and proteins.²¹⁶ Recent studies indicate this agent's antibacterial activity is attributable to binding to the active site of enoyl carrier protein reductase.^{217,218}

Triclosan has a broad range of antimicrobial activity, but it is often bacteriostatic.¹ Minimum inhibitory concentrations (MICs) range from 0.1 to 10 µg/mL, whereas minimum bactericidal concentrations are 25–500 µg/mL. Triclosan's activity against gram-positive organisms (including MRSA) is greater than against gram-negative bacilli, particularly *P*

aeruginosa.^{1,216} The agent possesses reasonable activity against mycobacterial and *Candida* spp., but it has limited activity against filamentous fungi. Triclosan (0.1%) reduces bacterial counts on hands by 2.8 log₁₀ after a 1-minute hygienic handwash.¹ In several studies, log reductions have been lower after triclosan is used than when chlorhexidine, iodophors, or alcohol-based products are applied.^{1,61,149,184,219} In 1994, FDA TFM tentatively classified triclosan ≤1.0% as a Category IIISE active agent (i.e., insufficient data exist to classify this agent as safe and effective for use as an antiseptic handwash).¹⁹ Further evaluation of this agent by the FDA is under way. Like chlorhexidine, triclosan has persistent activity on the skin. Its activity in hand-care products is affected by pH, the presence of surfactants, emollients, or humectants, and by the ionic nature of the particular formulation.^{1,216} Triclosan's activity is not substantially affected by organic matter, but it can be inhibited by sequestration of the agent in micelle structures formed by surfactants present in certain formulations. The majority of formulations containing <2% triclosan are well-tolerated and seldom cause allergic reactions. Certain reports indicate that providing hospital personnel with a triclosan-containing preparation for hand antiseptics has led to decreased MRSA infections.^{72,73} Triclosan's lack of potent activity against gram-negative bacilli has resulted in occasional reports of contamination.²²⁰

Other Agents

Approximately 150 years after puerperal-fever-related maternal mortality rates were demonstrated by Semmelweis to be reduced by use of a hypochlorite hand rinse, the efficacy of rubbing hands for 30 seconds with an aqueous hypochlorite solution was studied once again.²²¹ The solution was demonstrated to be no more effective than distilled water. The regimen used by Semmelweis, which called for rubbing hands with a 4% [w/w] hypochlorite solution until the hands were slippery (approximately 5 minutes), has been revisited by other researchers.²²² This more current study indicated that the regimen was 30 times more effective than a 1-minute rub using 60% isopropanol. However, because hypochlorite solutions are often irritating to the skin when used repeatedly and have a strong odor, they are seldom used for hand hygiene.

Certain other agents are being evaluated by FDA for use in health-care-related antiseptics.¹⁹ However, the efficacy of these agents has not been evaluated adequately for use in handwashing preparations intended for use by HCWs. Further evaluation of these agents is warranted. Products that use different concentrations of traditional antiseptics (e.g., low concentrations of iodophor) or contain novel compounds with antiseptic properties are likely to be introduced for use by HCWs. For example, preliminary studies have demonstrated that adding silver-containing polymers to an ethanol carrier (i.e., Surfacine®) results in a preparation that has persistent antimicrobial activity on animal and human skin.²²³ New compounds with good in vitro activity must be tested in vivo to determine their abilities to reduce transient and resident skin flora on the hands of HCWs.

ACTIVITY OF ANTISEPTIC AGENTS AGAINST SPORE-FORMING BACTERIA

The widespread prevalence of health-care-associated diarrhea caused by *Clostridium difficile* and the recent occurrence in the United States of human *Bacillus anthracis* infections associated with contaminated items sent through the postal system has raised concern regarding the activity of antiseptic agents against spore-forming bacteria. None of the agents (including alcohols, chlorhexidine, hexachlorophene, iodophors, PCMX, and triclosan) used in antiseptic handwash or antiseptic hand-rub preparations are reliably sporicidal against *Clostridium* spp. or *Bacillus* spp.^{120,172,224,225} Washing hands with non-antimicrobial or antimicrobial soap and water may help to physically remove spores from the surface of contaminated hands. HCWs should be encouraged to wear gloves when caring for patients with *C. difficile*-associated diarrhea.²²⁶ After gloves are removed, hands should be washed with a non-antimicrobial or an antimicrobial soap and water or disinfected with an alcohol-based hand rub. During outbreaks of *C. difficile*-related infections, washing hands with a non-antimicrobial or antimicrobial soap and water after removing gloves is prudent. HCWs with suspected or documented exposure to *B. anthracis*-contaminated items also should be encouraged to wash their hands with a non-antimicrobial or antimicrobial soap and water.

REDUCED SUSCEPTIBILITY OF BACTERIA TO ANTISEPTICS

Reduced susceptibility of bacteria to antiseptic agents can either be an intrinsic characteristic of a species or can be an acquired trait.²²⁷ Several reports have described strains of bacteria that appear to have acquired reduced susceptibility (when defined by MICs established in vitro) to certain antiseptics (e.g., chlorhexidine, quaternary ammonium compounds, and triclosan).²²⁷⁻²³⁰ However, because the antiseptic concentrations that are actually used by HCWs are often substantially higher than the MICs of strains with reduced antiseptic susceptibility, the clinical relevance of the in vitro findings is questionable. For example, certain strains of MRSA have chlorhexidine and quaternary ammonium compound MICs that are several-fold higher than methicillin-susceptible strains, and certain strains of *S. aureus* have elevated MICs to triclosan.^{227,228} However, such strains were readily inhibited by the concentrations of these antiseptics that are actually used by practicing HCWs.^{227,228} The description of a triclosan-resistant bacterial enzyme has raised the question of whether resistance to this agent may develop more readily than to other antiseptic agents.²¹⁸ In addition, exposing *Pseudomonas* strains containing the MexABOprM efflux system to triclosan may select for mutants that are resistant to multiple antibiotics, including fluoroquinolones.²³⁰ Further studies are needed to determine whether reduced susceptibility to antiseptic agents is of epidemiologic significance and whether resistance to antiseptics has any influence on the prevalence of antibiotic-resistant strains.²²⁷

SURGICAL HAND ANTISEPSIS

Since the late 1800s, when Lister promoted the application of carbolic acid to the hands of surgeons before procedures, preoperative cleansing of hands and forearms with an antiseptic agent has been an accepted practice.²³¹ Although no randomized, controlled trials have been conducted to indicate that surgical-site infection rates are substantially lower when preoperative scrubbing is performed with an antiseptic agent rather than a non-antimicrobial soap, certain other factors provide a strong rationale for this practice. Bacteria on the hands of surgeons can cause wound infections if introduced into the operative field during surgery²³²; rapid multiplication of bacteria occurs under surgical gloves if hands are washed with a non-antimicrobial soap. However, bacterial growth is slowed after preoperative scrubbing with an antiseptic agent.^{14,233} Reducing resident skin flora on the hands of the surgical team for the duration of a procedure reduces the risk of bacteria being released into the surgical field if gloves become punctured or torn during surgery.^{1,156,169} Finally, at least one outbreak of surgical-site infections occurred when surgeons who normally used an antiseptic surgical scrub preparation began using a non-antimicrobial product.²³⁴

Antiseptic preparations intended for use as surgical hand scrubs are evaluated for their ability to reduce the number of bacteria released from hands at different times, including (1) immediately after scrubbing, (2) after wearing surgical gloves for 6 hours (i.e., persistent activity), and (3) after multiple applications over 5 days (i.e., cumulative activity). Immediate and persistent activity are considered the most important in determining the efficacy of the product. U.S. guidelines recommend that agents used for surgical hand scrubs should substantially reduce microorganisms on intact skin, contain a nonirritating antimicrobial preparation, have broad-spectrum activity, and be fast-acting and persistent.^{19,235}

Studies have demonstrated that formulations containing 60%–95% alcohol alone or 50%–95% when combined with limited amounts of a quaternary ammonium compound, hexachlorophene, or chlorhexidine gluconate, lower bacterial counts on the skin immediately postscrub more effectively than do other agents (Table 4). The next most active agents (in order of decreasing activity) are chlorhexidine gluconate, iodophors, triclosan, and plain soap.^{104,119,186,188,203,204,206,208,236} Because studies of PCMX as a surgical scrub have yielded contradictory results, further studies are needed to establish how the efficacy of this compound compares with the other agents.^{176,185,186}

Although alcohols are not considered to have persistent antimicrobial activity, bacteria appear to reproduce slowly on the hands after a surgical scrub with alcohol, and bacterial counts on hands after wearing gloves for 1–3 hours seldom exceed baseline (i.e., prescrub) values.¹ However, a recent study demonstrated that a formulation containing 61% ethanol alone did not achieve adequate persistent activity at 6 hours postscrub.²³⁷ Alcohol-based preparations containing 0.5% or 1% chlorhexidine gluconate have persistent activity that, in certain studies, has equaled

or exceeded that of chlorhexidine gluconate-containing detergents.^{1,118,135,237*}

Persistent antimicrobial activity of detergent-based surgical scrub formulations is greatest for those containing 2% or 4% chlorhexidine gluconate, followed by hexachlorophene, triclosan, and iodophors.^{1,102,113-115,159,189,203, 204,206-208,236} Because hexachlorophene is absorbed into the blood after repeated use, it is seldom used as a surgical scrub.

Surgical staff have been traditionally required to scrub their hands for 10 minutes preoperatively, which frequently leads to skin damage. Several studies have demonstrated that scrubbing for 5 minutes reduces bacterial counts as effectively as a 10-minute scrub.^{117,238,239} In other studies, scrubbing for 2 or 3 minutes reduced bacterial counts to acceptable levels.^{156,205,207,240,241}

Studies have indicated that a two-stage surgical scrub using an antiseptic detergent, followed by application of an alcohol-containing preparation, is effective. For example, an initial 1- or 2-minute scrub with 4% chlorhexidine gluconate or povidone-iodine followed by application of an alcohol-based product has been as effective as a 5-minute scrub with an antiseptic detergent.^{114,242}

Surgical hand-antiseptic protocols have required personnel to scrub with a brush. But this practice can damage the skin of personnel and result in increased shedding of bacteria from the hands.^{95,243} Scrubbing with a disposable sponge or combination sponge-brush has reduced bacterial counts on the hands as effectively as scrubbing with a brush.²⁴⁴⁻²⁴⁶ However, several studies indicate that neither a brush nor a sponge is necessary to reduce bacterial counts on the hands of surgical personnel to acceptable levels, especially when alcohol-based products are used.^{102,117,159,165,233,237,247,248} Several of these studies performed cultures immediately or at 45–60 minutes postscrub,^{102,117,233,247,248} whereas in other studies, cultures were obtained 3 and 6 hours postscrub.^{159,237} For example, a recent laboratory-based study using volunteers demonstrated that brushless application of a preparation containing 1% chlorhexidine gluconate plus 61% ethanol yielded lower bacterial counts on the hands of participants than using a sponge/brush to apply a 4% chlorhexidine-containing detergent preparation.²³⁷

RELATIVE EFFICACY OF PLAIN SOAP, ANTISEPTIC SOAP/DETERGENT, AND ALCOHOLS

Comparing studies related to the in vivo efficacy of plain soap, antimicrobial soaps, and alcohol-based hand rubs

**In a recent randomized clinical trial, surgical-site infection rates were monitored among patients who were operated on by surgical personnel who cleaned their hands preoperatively either by performing a traditional 5-minute surgical hand scrub using 4% povidone-iodine or 4% antiseptic antimicrobial soap, or by washing their hands for 1 minute with a non-antimicrobial soap followed by a 5-minute hand-rubbing technique using an alcohol-based hand rinse containing 0.2% mectronium etilsulfate. The incidence of surgical-site infections was virtually identical in the two groups of patients. (Source: Parienti JJ, Thibon P, Heller R, et al. for Members of the Antiseptie Chirurgicale des Mains Study Group. Hand-rubbing with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates: a randomized equivalence study. JAMA 2002;288:722–7).*

is problematic, because certain studies express efficacy as the percentage reduction in bacterial counts achieved, whereas others give \log_{10} reductions in counts achieved. However, summarizing the relative efficacy of agents tested in each study can provide an overview of the *in vivo* activity of various formulations intended for handwashing, hygienic handwash, antiseptic hand rub, or surgical hand antisepsis (Tables 2–4).

IRRITANT CONTACT DERMATITIS RESULTING FROM HAND-HYGIENE MEASURES

Frequency and Pathophysiology of Irritant Contact Dermatitis

In certain surveys, approximately 25% of nurses report symptoms or signs of dermatitis involving their hands, and as many as 85% give a history of having skin problems.²⁴⁹ Frequent and repeated use of hand-hygiene products, particularly soaps and other detergents, is a primary cause of chronic irritant contact dermatitis among HCWs.²⁵⁰ The potential of detergents to cause skin irritation can vary considerably and can be ameliorated by the addition of emollients and humectants. Irritation associated with antimicrobial soaps may be caused by the antimicrobial agent or by other ingredients of the formulation. Affected persons often complain of a feeling of dryness or burning; skin that feels “rough”; and erythema, scaling, or fissures. Detergents damage the skin by causing denaturation of stratum corneum proteins, changes in intercellular lipids (either depletion or reorganization of lipid moieties), decreased corneocyte cohesion, and decreased stratum corneum water-binding capacity.^{250,251} Damage to the skin also changes skin flora, resulting in more frequent colonization by staphylococci and gram-negative bacilli.^{17,90} Although alcohols are among the safest antiseptics available, they can cause dryness and irritation of the skin.^{1,252} Ethanol is usually less irritating than n-propanol or isopropanol.²⁵²

Irritant contact dermatitis is more commonly reported with iodophors.⁹² Other antiseptic agents that can cause irritant contact dermatitis (in order of decreasing frequency) include chlorhexidine, PCMX, triclosan, and alcohol-based products. Skin that is damaged by repeated exposure to detergents may be more susceptible to irritation by alcohol-based preparations.²⁵³ The irritancy potential of commercially prepared hand-hygiene products, which is often determined by measuring TEWL, may be available from the manufacturer. Other factors that can contribute to dermatitis associated with frequent handwashing include using hot water for handwashing, low relative humidity (most common in winter months), failure to use supplementary hand lotion or cream, and the quality of paper towels.^{254,255} Shear forces associated with wearing or removing gloves and allergy to latex proteins may also contribute to dermatitis of the hands of HCWs.

Allergic Contact Dermatitis Associated With Hand-Hygiene Products

Allergic reactions to products applied to the skin (i.e., contact allergies) may present as delayed type reac-

tions (i.e., allergic contact dermatitis) or less commonly as immediate reactions (i.e., contact urticaria). The most common causes of contact allergies are fragrances and preservatives; emulsifiers are less common causes.²⁵⁶⁻²⁵⁹ Liquid soaps, hand lotions or creams, and “udder ointments” may contain ingredients that cause contact allergies among HCWs.^{257,258}

Allergic reactions to antiseptic agents, including quaternary ammonium compounds, iodine or iodophors, chlorhexidine, triclosan, PCMX, and alcohols have been reported.^{118,167,172,256,260-265} Allergic contact dermatitis associated with alcohol-based hand rubs is uncommon. Surveillance at a large hospital in Switzerland, where a commercial alcohol hand rub has been used for >10 years, failed to identify a single case of documented allergy to the product.¹⁶⁹ In late 2001, a Freedom of Information Request for data in the FDA’s Adverse Event Reporting System regarding adverse reactions to popular alcohol hand rubs in the United States yielded only one reported case of an erythematous rash reaction attributed to such a product (John M. Boyce, M.D., Hospital of St. Raphael, New Haven, Connecticut, personal communication, 2001). However, with increasing use of such products by HCWs, true allergic reactions to such products likely will be encountered.

Allergic reactions to alcohol-based products may represent true allergy to alcohol, allergy to an impurity or aldehyde metabolite, or allergy to another constituent of the product.¹⁶⁷ Allergic contact dermatitis or immediate contact urticarial reactions may be caused by ethanol or isopropanol.¹⁶⁷ Allergic reactions can be caused by compounds that may be present as inactive ingredients in alcohol-based hand rubs, including fragrances, benzyl alcohol, stearyl or isostearyl alcohol, phenoxyethanol, myristyl alcohol, propylene glycol, parabens, and benzalkonium chloride.^{167,256,266-270}

PROPOSED METHODS FOR REDUCING ADVERSE EFFECTS OF AGENTS

Potential strategies for minimizing hand-hygiene-related irritant contact dermatitis among HCWs include reducing the frequency of exposure to irritating agents (particularly anionic detergents), replacing products with high irritation potential with preparations that cause less damage to the skin, educating personnel regarding the risks of irritant contact dermatitis, and providing caregivers with moisturizing skin-care products or barrier creams.^{96,98,251,271-273} Reducing the frequency of exposure of HCWs to hand-hygiene products would prove difficult and is not desirable because of the low levels of adherence to hand-hygiene policies in the majority of institutions. Although hospitals have provided personnel with non-antimicrobial soaps in hopes of minimizing dermatitis, frequent use of such products may cause greater skin damage, dryness, and irritation than antiseptic preparations.^{92,96,98} One strategy for reducing the exposure of personnel to irritating soaps and detergents is to promote the use of alcohol-based hand rubs containing various emollients. Several recent prospective, randomized trials have

demonstrated that alcohol-based hand rubs containing emollients were better tolerated by HCWs than washing hands with non-antimicrobial soaps or antimicrobial soaps.^{96,98,166} Routinely washing hands with soap and water immediately after using an alcohol hand rub may lead to dermatitis. Therefore, personnel should be reminded that it is neither necessary nor recommended to routinely wash hands after each application of an alcohol hand rub.

Hand lotions and creams often contain humectants and various fats and oils that can increase skin hydration and replace altered or depleted skin lipids that contribute to the barrier function of normal skin.^{251,271} Several controlled trials have demonstrated that regular use (e.g., twice a day) of such products can help prevent and treat irritant contact dermatitis caused by hand-hygiene products.^{272,273} In one study, frequent and scheduled use of an oil-containing lotion improved skin condition, and thus led to a 50% increase in handwashing frequency among HCWs.²⁷³ Reports from these studies emphasize the need to educate personnel regarding the value of regular, frequent use of hand-care products.

Recently, barrier creams have been marketed for the prevention of hand-hygiene-related irritant contact dermatitis. Such products are absorbed to the superficial layers of the epidermis and are designed to form a protective layer that is not removed by standard handwashing. Two recent randomized, controlled trials that evaluated the skin condition of caregivers demonstrated that barrier creams did not yield better results than did the control lotion or vehicle used.^{272,273} As a result, whether barrier creams are effective in preventing irritant contact dermatitis among HCWs remains unknown.

In addition to evaluating the efficacy and acceptability of hand-care products, product-selection committees should inquire about the potential deleterious effects that oil-containing products may have on the integrity of rubber gloves and on the efficacy of antiseptic agents used in the facility.^{8,236}

FACTORS TO CONSIDER WHEN SELECTING HAND-HYGIENE PRODUCTS

When evaluating hand-hygiene products for potential use in health-care facilities, administrators or product-selection committees must consider factors that can affect the overall efficacy of such products, including the relative efficacy of antiseptic agents against various pathogens (Appendix) and acceptance of hand-hygiene products by personnel.^{274,275} Soap products that are not well-accepted by HCWs can be a deterrent to frequent handwashing.²⁷⁶ Characteristics of a product (either soap or alcohol-based hand rub) that can affect acceptance by personnel include its smell, consistency (i.e., "feel"), and color.^{92,277,278} For soaps, ease of lathering also may affect user preference.

Because HCWs may wash their hands from a limited number of times per shift to as many as 30 times per shift, the tendency of products to cause skin irritation and dryness is a substantial factor that influences acceptance, and ultimate

usage.^{61,98,274,275,277,279} For example, concern regarding the drying effects of alcohol was a primary cause of poor acceptance of alcohol-based hand-hygiene products in hospitals in the United States.^{5,143} However, several studies have demonstrated that alcohol-based hand rubs containing emollients are acceptable to HCWs.^{90,93,98,100,101,106,143,163,164,166} With alcohol-based products, the time required for drying may also affect user acceptance.

Studies indicate that the frequency of handwashing or antiseptic handwashing by personnel is affected by the accessibility of hand-hygiene facilities.²⁸⁰⁻²⁸³ In certain health-care facilities, only one sink is available in rooms housing several patients, or sinks are located far away from the door of the room, which may discourage handwashing by personnel leaving the room. In intensive-care units, access to sinks may be blocked by bedside equipment (e.g., ventilators or intravenous infusion pumps). In contrast to sinks used for handwashing or antiseptic handwash, dispensers for alcohol-based hand rubs do not require plumbing and can be made available adjacent to each patient's bed and at many other locations in patient-care areas. Pocket carriage of alcohol-based hand-rub solutions, combined with availability of bedside dispensers, has been associated with substantial improvement in adherence to hand-hygiene protocols.^{74,284} To avoid any confusion between soap and alcohol hand rubs, alcohol hand-rub dispensers should not be placed adjacent to sinks. HCWs should be informed that washing hands with soap and water after each use of an alcohol hand rub is not necessary and is not recommended, because it may lead to dermatitis. However, because personnel feel a "build-up" of emollients on their hands after repeated use of alcohol hand gels, washing hands with soap and water after 5-10 applications of a gel has been recommended by certain manufacturers.

Automated handwashing machines have not been demonstrated to improve the quality or frequency of handwashing.^{88,285} Although technologically advanced automated handwashing devices and monitoring systems have been developed recently, only a minimal number of studies have been published that demonstrate that use of such devices results in enduring improvements in hand-hygiene adherence among HCWs. Further evaluation of automated handwashing facilities and monitoring systems is warranted.

Dispenser systems provided by manufacturers or vendors also must be considered when evaluating hand-hygiene products. Dispensers may discourage use by HCWs when they (1) become blocked or partially blocked and do not deliver the product when accessed by personnel, and (2) do not deliver the product appropriately onto the hands. In one hospital where a viscous alcohol-based hand rinse was available, only 65% of functioning dispensers delivered product onto the caregivers' hands with one press of the dispenser lever, and 9% of dispensers were totally occluded.²⁸⁶ In addition, the volume delivered was often suboptimal, and the product was sometimes squirted onto the wall instead of the caregiver's hand.

Only limited information is available regarding the cost of hand-hygiene products used in health-care facilities.^{165,287} These costs were evaluated in patient-care areas at a 450-bed community teaching hospital²⁸⁷; the hospital spent \$22,000 (\$0.72 per patient-day) on 2% chlorhexidine-containing preparations, plain soap, and an alcohol hand rinse.²⁸⁷ When hand-hygiene supplies for clinics and non-patient care areas were included, the total annual budget for soaps and hand antiseptic agents was \$30,000 (approximately \$1 per patient-day). Annual hand-hygiene product budgets at other institutions vary considerably because of differences in usage patterns and varying product prices. One researcher²⁸⁷ determined that if non-antimicrobial liquid soap were assigned an arbitrary relative cost of 1.0, the cost per liter would be 1.7 times as much for 2% chlorhexidine gluconate detergent, 1.6–2.0 times higher for alcohol-based hand-rub products, and 4.5 times higher for an alcohol-based foam product. A recent cost comparison of surgical scrubbing with an antimicrobial soap versus brushless scrubbing with an alcohol-based hand rub revealed that costs and time required for preoperative scrubbing were less with the alcohol-based product.¹⁶⁵ In a trial conducted in two critical-care units, the cost of using an alcohol hand rub was half as much as using an antimicrobial soap for handwashing (\$0.025 versus \$0.05 per application, respectively).¹⁶⁶

To put expenditures for hand-hygiene products into perspective, health-care facilities should consider comparing their budget for hand-hygiene products to estimated excess hospital costs resulting from health-care-associated infections. The excess hospital costs associated with only four or five health-care-associated infections of average severity may equal the entire annual budget for hand-hygiene products used in inpatient-care areas. Just one severe surgical-site infection, lower respiratory tract infection, or bloodstream infection may cost the hospital more than the entire annual budget for antiseptic agents used for hand hygiene.²⁸⁷ Two studies provided certain quantitative estimates of the benefit of hand-hygiene-promotion programs.^{72,74} One study demonstrated a cost saving of approximately \$17,000 resulting from reduced use of vancomycin after the observed decrease in MRSA incidence in a 7-month period.⁷² In another study that examined both direct costs associated with the hand-hygiene promotion program (increased use of hand-rub solution and poster production) and indirect costs associated with health-care-personnel time,⁷⁴ costs of the program were an estimated \$57,000 or less per year (an average of \$1.42 per patient admitted). Supplementary costs associated with the increased use of alcohol-based hand-rub solution averaged \$6.07 per 100 patient-days. Based on conservative estimates of \$2,100 saved per infection averted and on the assumption that only 25% of the observed reduction in the infection rate was associated with improved hand-hygiene practice, the program was substantially cost-effective. Thus, hospital administrators must consider that by purchasing more effective or more acceptable hand-hygiene products to improve hand-hygiene practices, they will avoid the occurrence of

TABLE 6
HANDWASHING FREQUENCY AMONG HEALTH-CARE WORKERS

Ref. No.	Year	Avg. No./ Time Period	Range	Avg. No./Hr
(61)	1988	5/8 hours	N.S.	
(89)	1984	5–10/shift	N.S.	
(96)	2000	10/shift	N.S.	
(273)	2000	12–18/day	2–60	
(98)	2000	13–15/8 hours	5–27	1.6–1.8/hr
(90)	1977	20–42/8 hours	10–100	
(391)	2000	21/12 hours	N.S.	
(272)	2000	22/day	0–70	
(88)	1991			1.7–2.1/hr
(17)	1998			2.1/hr
(279)	1978			3/hr
(303)	1994			3.3/hr

Note: N.S. = not stated.

nosocomial infections; preventing only a limited number of additional health-care-associated infections per year will lead to savings that will exceed any incremental costs of improved hand-hygiene products.

HAND-HYGIENE PRACTICES AMONG HCWS

In observational studies conducted in hospitals, HCWs washed their hands an average of five times per shift to as many as 30 times per shift (Table 6)^{17,61,90,98,274,288}; certain nurses washed their hands ≤ 100 times per shift.⁹⁰ Hospital-wide surveillance of hand hygiene reveals that the average number of handwashing opportunities varies markedly between hospital wards. For example, nurses in pediatric wards had an average of eight opportunities for hand hygiene per hour of patient care compared with an average of 20 for nurses in intensive-care units.¹¹ The duration of handwashing or hygienic handwash episodes by HCWs has averaged 6.6–24.0 seconds in observational studies (Table 7).^{17,52,59,84-87,89,249,279} In addition to washing their hands for limited time periods, personnel often fail to cover all surfaces of their hands and fingers.²⁸⁸

Adherence of HCWs to Recommended Hand-Hygiene Practices

Observational Studies of Hand-Hygiene Adherence. Adherence of HCWs to recommended hand-hygiene procedures has been poor, with mean baseline rates of 5%–81% (overall average: 40%) (Table 8).^{71,74,86,87,276,280,281,283,285,289-313} The methods used for defining adherence (or nonadherence) and those used for conducting observations vary considerably among studies, and reports do not provide detailed information concerning the methods and criteria used. The majority of studies were conducted with hand-hygiene adherence as the major outcome measure, whereas a limited number measured adherence as part of a broader investigation. Several investiga-

TABLE 7
AVERAGE DURATION OF HANDWASHING BY HEALTH-CARE WORKERS

Ref. No.	Year	Mean/Median Time
(392)	1997	4.7–5.3 seconds
(303)	1994	6.6 seconds
(52)	1974	8–9.3 seconds
(85)	1984	8.6 seconds
(86)	1994	<9 seconds
(87)	1994	9.5 seconds
(88)	1991	<10 seconds
(294)	1990	10 seconds
(89)	1984	11.6 seconds
(300)	1992	12.5 seconds
(59)	1988	15.6–24.4 seconds
(17)	1998	20.6 seconds
(279)	1978	21 seconds
(293)	1989	24 seconds

tors reported improved adherence after implementing various interventions, but the majority of studies had short follow-up periods and did not confirm whether behavioral improvements were long-lasting. Other studies established that sustained improvements in handwashing behavior occurred during a long-term program to improve adherence to hand-hygiene policies.^{74,75}

Factors Affecting Adherence. Factors that may influence hand hygiene include those identified in epidemiologic studies and factors reported by HCWs as being reasons for lack of adherence to hand-hygiene recommendations. Risk factors for poor adherence to hand hygiene have been determined objectively in several observational studies or interventions to improve adherence.^{11,12,274,292,295,314-317} Among these, being a physician or a nursing assistant, rather than a nurse, was consistently associated with reduced adherence (Box 1).

In the largest hospitalwide survey of hand-hygiene practices among HCWs,¹¹ predictors of poor adherence to recommended hand-hygiene measures were identified. Predictor variables included professional category, hospital ward, time of day/week, and type and intensity of patient care, defined as the number of opportunities for hand hygiene per hour of patient care. In 2,834 observed opportunities for hand hygiene, average adherence was 48%. In multivariate analysis, nonadherence was lowest among nurses and during weekends (Odds Ratio [OR]: 0.6; 95% confidence interval [CI] = 0.4–0.8). Nonadherence was higher in intensive-care units compared with internal medicine wards (OR: 2.0; 95% CI = 1.3–3.1), during procedures that carried a high risk of bacterial contamination (OR: 1.8; 95% CI = 1.4–2.4), and when intensity of patient care was high (21–40 handwashing opportunities — OR: 1.3; 95% CI = 1.0–1.7; 41–60 opportunities — OR: 2.1; 95% CI = 1.5–2.9; >60 opportunities — OR: 2.1; 95% CI = 1.3–3.5). The higher the demand for hand hygiene, the lower the adherence; on average, adherence decreased by 5% (\pm 2%) for each

increase of 10 opportunities per hour when the intensity of patient care exceeded 10 opportunities per hour. Similarly, the lowest adherence rate (36%) was found in intensive-care units, where indications for hand hygiene were typically more frequent (on average, 20 opportunities per patient-hour). The highest adherence rate (59%) was observed in pediatrics wards, where the average intensity of patient care was lower than in other hospital areas (an average of eight opportunities per patient-hour). The results of this study indicate that full adherence to previous guidelines may be unrealistic, and that facilitated access to hand hygiene could help improve adherence.^{11,12,318}

Perceived barriers to adherence with hand-hygiene practice recommendations include skin irritation caused by hand-hygiene agents, inaccessible hand-hygiene supplies, interference with HCW–patient relationships, priority of care (i.e., the patients' needs are given priority over hand hygiene), wearing of gloves, forgetfulness, lack of knowledge of the guidelines, insufficient time for hand hygiene, high workload and understaffing, and the lack of scientific information indicating a definitive impact of improved hand hygiene on health-care-associated infection rates.^{11,274,292,295,315-317} Certain perceived barriers to adherence with hand-hygiene guidelines have been assessed or quantified in observational studies (Box 1).^{12,274,292,295,314-317}

Skin irritation by hand-hygiene agents constitutes a substantial barrier to appropriate adherence.³¹⁹ Because soaps and detergents can damage skin when applied on a regular basis, HCWs must be better informed regarding the possible adverse effects associated with hand-hygiene agents. Lack of knowledge and education regarding this subject is a barrier to motivation. In several studies, alcohol-based hand rubs containing emollients (either isopropanol, ethanol, or n-propanol in 60%–90% vol/vol) were less irritating to the skin than the soaps or detergents tested. In addition, the alcohol-based products containing emollients that were tested were at least as tolerable and efficacious as the detergents tested. Also, studies demonstrate that several hand lotions have reduced skin scaling and cracking, which may reduce microbial shedding from the hands.^{67,272,273}

Easy access to hand-hygiene supplies, whether sink, soap, medicated detergent, or alcohol-based hand-rub solution, is essential for optimal adherence to hand-hygiene recommendations. The time required for nurses to leave a patient's bedside, go to a sink, and wash and dry their hands before attending the next patient is a deterrent to frequent handwashing or hand antiseptics.^{11,318} Engineering controls could facilitate adherence, but careful monitoring of hand-hygiene behavior should be conducted to exclude the possible negative effect of newly introduced handwashing devices.⁸⁸

The impact of wearing gloves on adherence to hand-hygiene policies has not been definitively established, because published studies have yielded contradictory results.^{87,290,301,320} Hand hygiene is required regardless of whether gloves are used or changed. Failure to remove gloves after patient contact or between "dirty" and "clean" body-site care on the same patient must be regarded as non-adherence to hand-hygiene recommendations.¹¹ In a study in

TABLE 8
HAND-HYGIENE ADHERENCE BY HEALTH-CARE WORKERS (1981–2000)

Ref. No.	Year	Setting	Adherence			Intervention
			Before/ After	Adherence Baseline	After Intervention	
(280)	1981	ICU	A	16%	30%	More convenient sink locations
(289)	1981	ICU	A	41%	—	
		ICU	A	28%	—	
(290)	1983	All wards	A	45%	—	
(281)	1986	SICU	A	51%	—	
		MICU	A	76%	—	
(276)	1986	ICU	A	63%	92%	Performance feedback
(291)	1987	PICU	A	31%	30%	Wearing overgown
(292)	1989	MICU	B/A	14%/28%*	73%/81%	Feedback, policy reviews, memo, and posters
		MICU	B/A	26%/23%	38%/60%	
(293)	1989	NICU	A/B	75%/50%	—	
(294)	1990	ICU	A	32%	45%	Alcohol rub introduced
(295)	1990	ICU	A	81%	92%	Inservices first, then group feedback
(296)	1990	ICU	B/A	22%	30%	
(297)	1991	SICU	A	51%	—	
(298)	1991	Pedi OPDs	B	49%	49%	Signs, feedback, and verbal reminders to physicians
(299)	1991	Nursery and NICU	B/A†	28%	63%	Feedback, dissemination of literature, and results of environmental cultures
(300)	1992	NICU/others	A	29%	—	
(71)	1992	ICU	N.S.	40%	—	
(301)	1993	ICUs	A	40%	—	
(87)	1994	Emergency Room	A	32%	—	
(86)	1994	All wards	A	32%	—	
(285)	1994	SICU	A	22%	38%	Automated handwashing machines available
(302)	1994	NICU	A	62%	60%	No gowning required
(303)	1994	ICU Wards	AA	30%/29%	—	
(304)	1995	ICU Oncol Ward	A	56%	—	
(305)	1995	ICU	N.S.	5%	63%	Lectures, feedback, and demonstrations
(306)	1996	PICU	B/A	12%/11%	68%/65%	Overt observation, followed by feedback
(307)	1996	MICU	A	41%	58%	Routine wearing of gowns and gloves
(308)	1996	Emergency Dept	A	54%	64%	Signs/distributed review paper
(309)	1998	All wards	A	30%	—	
(310)	1998	Pediatric wards	B/A	52%/49%	74%/69%	Feedback, movies, posters, and brochures
(311)	1999	MICU	B/A	12%/55%	—	
(74)	2000	All wards	B/A	48%	67%	Posters, feedback, administrative support, and alcohol rub
(312)	2000	MICU	A	42%	61%	Alcohol hand rub made available
(283)	2000	MICU	B/A	10%/22%	23%/48%	Education, feedback, and alcohol gel made available
		CTICU	B/A	4%/13%	7%/14%	
(313)	2000	Medical wards	A	60%	52%	Education, reminders, and alcohol gel made available

Note: ICU = intensive care unit, SICU = surgical ICU, MICU = medical ICU, PICU = pediatric ICU, NICU = neonatal ICU, Emerg = emergency, Oncol = oncology, CTICU = cardiothoracic ICU, and N.S. = not stated.

*Percentage compliance before/after patient contact.

†After contact with inanimate objects.

which experimental conditions approximated those occurring in clinical practice,³²¹ washing and reusing gloves between patient contacts resulted in observed bacterial counts of 0–4.7 log on the hands after glove removal. Therefore, this practice should be discouraged; handwashing or disinfection should be performed after glove removal.

Lack of (1) knowledge of guidelines for hand hygiene, (2) recognition of hand-hygiene opportunities during patient care, and (3) awareness of the risk of cross-transmission of pathogens are barriers to good hand-hygiene practices. Furthermore, certain HCWs believe they have washed their hands when neces-

BOX 1**FACTORS INFLUENCING ADHERENCE TO HAND-HYGIENE PRACTICES***

Observed risk factors for poor adherence to recommended hand-hygiene practices

- Physician status (rather than a nurse)
- Nursing assistant status (rather than a nurse)
- Male sex
- Working in an intensive-care unit
- Working during the week (versus the weekend)
- Wearing gowns/gloves
- Automated sink
- Activities with high risk of cross-transmission
- High number of opportunities for hand hygiene per hour of patient care

Self-reported factors for poor adherence with hand hygiene

- Handwashing agents cause irritation and dryness
- Sinks are inconveniently located/shortage of sinks
- Lack of soap and paper towels
- Often too busy/insufficient time
- Understaffing/overcrowding
- Patient needs take priority
- Hand hygiene interferes with healthcare worker relationships with patients
- Low risk of acquiring infection from patients
- Wearing of gloves/beliefs that glove use obviates the need for hand hygiene
- Lack of knowledge of guidelines/protocols
- Not thinking about it/forgetfulness
- No role model from colleagues or superiors
- Skepticism regarding the value of hand hygiene
- Disagreement with the recommendations
- Lack of scientific information of definitive impact of improved hand hygiene on health-care-associated infection rates

Additional perceived barriers to appropriate hand hygiene

- Lack of active participation in hand-hygiene promotion at individual or institutional level
- Lack of role model for hand hygiene
- Lack of institutional priority for hand hygiene
- Lack of administrative sanction of noncompliers/rewarding compliers
- Lack of institutional safety climate

*Source: Adapted from Pittet D. Improving compliance with hand hygiene in hospitals. *Infect Control Hosp Epidemiol* 2000;21:381-6.

sary, even when observations indicate they have not.^{89,92,295,296,322}

Perceived barriers to hand-hygiene behavior are linked not only to the institution, but also to HCWs' colleagues. Therefore, both institutional and small-group dynamics need to be considered when implementing a system change to secure an improvement in HCWs' hand-hygiene practice.

Possible Targets for Hand-Hygiene Promotion

Targets for the promotion of hand hygiene are derived from studies assessing risk factors for nonadherence, reported reasons for the lack of adherence to recommendations, and additional factors perceived as being important to facilitate appropriate HCW behavior. Although certain factors cannot be modified (Box 1), others can be changed.

One factor that must be addressed is the time required

for HCWs to clean their hands. The time required for traditional handwashing may render full adherence to previous guidelines unrealistic^{11,12,318} and more rapid access to hand-hygiene materials could help improve adherence. One study conducted in an intensive-care unit demonstrated that it took nurses an average of 62 seconds to leave a patient's bedside, walk to a sink, wash their hands, and return to patient care.³¹⁸ In contrast, an estimated one fourth as much time is required when using alcohol-based hand rub placed at each patient's bedside. Providing easy access to hand-hygiene materials is mandatory for appropriate hand-hygiene behavior and is achievable in the majority of healthcare facilities.³²³ In particular, in high-demand situations (e.g., the majority of critical-care units), under hectic working conditions, and at times of overcrowding or understaffing, HCWs may be more likely to use an alcohol-based hand rub than to wash their hands.³²³ Further, using alcohol-based hand rubs may be a better

option than traditional handwashing with plain soap and water or antiseptic handwash, because they not only require less time^{166,318} but act faster¹ and irritate hands less often.^{1,67,96,98,166} They also were used in the only program that reported a sustained improvement in hand-hygiene adherence associated with decreased infection rates.⁷⁴ However, making an alcohol-based hand rub available to personnel without providing ongoing educational and motivational activities may not result in long-lasting improvement in hand-hygiene practices.³¹³ Because increased use of hand-hygiene agents might be associated with skin dryness, the availability of free skin-care lotion is recommended.

Education is a cornerstone for improvement with hand-hygiene practices. Topics that must be addressed by educational programs include the lack of (1) scientific information for the definitive impact of improved hand hygiene on health-care-associated infection and resistant organism transmission rates; (2) awareness of guidelines for hand hygiene and insufficient knowledge concerning indications for hand hygiene during daily patient care; (3) knowledge concerning the low average adherence rate to hand hygiene by the majority of HCWs; and (4) knowledge concerning the appropriateness, efficacy, and understanding of the use of hand-hygiene and skin-care-protection agents.

HCWs necessarily evolve within a group that functions within an institution. Possible targets for improvement in hand-hygiene behavior not only include factors linked to individual HCWs, but also those related to the group(s) and the institution as a whole.^{317,323} Examples of possible targets for hand-hygiene promotion at the group level include education and performance feedback on hand-hygiene adherence; efforts to prevent high workload, downsizing, and understaffing; and encouragement and provision of role models from key members in the work unit. At the institutional level, targets for improvement include (1) written guidelines, hand-hygiene agents, skin-care promotions and agents, or hand-hygiene facilities; (2) culture or tradition of adherence; and (3) administrative leadership, sanction, support, and rewards. Several studies, conducted in various types of institutions, reported modest and even low levels of adherence to recommended hand-hygiene practices, indicating that such adherence varied by hospital ward and by type of HCW. These results indicate educational sessions may need to be designed specifically for certain types of personnel.^{11,289,290,294,317,323}

LESSONS LEARNED FROM BEHAVIORAL THEORIES

In 1998, the prevailing behavioral theories and their applications with regard to the health professions were reviewed by researchers in an attempt to better understand how to target more successful interventions.³¹⁷ The researchers proposed a hypothetical framework to enhance hand-hygiene practices and stressed the importance of considering the complexity of individual and institutional factors when designing behavioral interventions.

Although behavioral theories and secondary interventions have primarily targeted individual workers, this

practice might be insufficient to produce sustained change.^{317,324,325} Interventions aimed at improving hand-hygiene practices must account for different levels of behavior interaction.^{12,317,326} Thus, the interdependence of individual factors, environmental constraints, and the institutional climate must be taken into account in the strategic planning and development of hand-hygiene campaigns. Interventions to promote hand hygiene in hospitals should consider variables at all these levels. Various factors involved in hand-hygiene behavior include intention, attitude towards the behavior, perceived social norm, perceived behavioral control, perceived risk for infection, hand-hygiene practices, perceived role model, perceived knowledge, and motivation.³¹⁷ The factors necessary for change include (1) dissatisfaction with the current situation, (2) perception of alternatives, and (3) recognition, both at the individual and institutional level, of the ability and potential to change. Although the latter implies education and motivation, the former two necessitate a system change.

Among the reported reasons for poor adherence with hand-hygiene recommendations (Box 1), certain ones are clearly associated with the institution or system (e.g., lack of institutional priority for hand hygiene, administrative sanctions, and a safety climate). Although all of these reasons would require a system change in the majority of institutions, the third requires management commitment, visible safety programs, an acceptable level of work stress, a tolerant and supportive attitude toward reported problems, and belief in the efficacy of preventive strategies.^{12,317,325,327} Most importantly, an improvement in infection-control practices requires (1) questioning basic beliefs, (2) continuous assessment of the group (or individual) stage of behavioral change, (3) intervention(s) with an appropriate process of change, and (4) supporting individual and group creativity.³¹⁷ Because of the complexity of the process of change, single interventions often fail. Thus, a multimodal, multidisciplinary strategy is likely necessary.^{74,75,317,323,326}

METHODS USED TO PROMOTE IMPROVED HAND HYGIENE

Hand-hygiene promotion has been challenging for >150 years. In-service education, information leaflets, workshops and lectures, automated dispensers, and performance feedback on hand-hygiene adherence rates have been associated with transient improvement.^{291,294-296,306,314}

Several strategies for promotion of hand hygiene in hospitals have been published (Table 9). These strategies require education, motivation, or system change. Certain strategies are based on epidemiologic evidence, others on the authors' and other investigators' experience and review of current knowledge. Some strategies may be unnecessary in certain circumstances, but may be helpful in others. In particular, changing the hand-hygiene agent could be beneficial in institutions or hospital wards with a high workload and a high demand for hand hygiene when alcohol-based hand rubs are not available.^{11,73,78,328} However, a change in the recommended hand-hygiene agent could be deleterious

TABLE 9
STRATEGIES FOR SUCCESSFUL PROMOTION OF HAND HYGIENE IN HOSPITALS

Strategy	Tool for Change*	Selected References†
Education	E (M, S)	(74,295,306,326,393)
Routine observation and feedback	S (E, M)	(74,294,306,326,393)
Engineering control		
Make hand hygiene possible, easy, and convenient	S	(74,281,326,393)
Make alcohol-based hand rub available (at least in high-demand situations)	S S	(74) (74,283,312)
Patient education	S (M)	(283,394)
Reminders in the workplace	S	(74,395)
Administrative sanction/rewarding	S	(12,317)
Change in hand-hygiene agent	S (E)	(11,67,71,283,312)
Promote/facilitate skin care for health-care-workers' hands	S (E)	(67,74,274,275)
Obtain active participation at individual and institutional level	E, M, S	(74,75,317)
Improve institutional safety climate	S (M)	(74,75,317)
Enhance individual and institutional self-efficacy	S (E, M)	(74,75,317)
Avoid overcrowding, understaffing, and excessive workload	S	(11,74,78,297,396)
Combine several of above strategies	E, M, S	(74,75,295,306,317,326)

*The dynamic of behavioral change is complex and involves a combination of education (E), motivation (M), and system change (S).

†Only selected references have been listed; readers should refer to more extensive reviews for exhaustive reference lists.^{1,8,317,323,397}

if introduced during winter, at a time of higher hand-skin irritability, and if not accompanied by the provision of skin-care products (e.g., protective creams and lotions). Additional specific elements should be considered for inclusion in educational and motivational programs (Box 2).

Several strategies that could potentially be associated with successful promotion of hand hygiene require a system change (Box 1). Hand-hygiene adherence and promotion involve factors at both the individual and system level. Enhancing individual and institutional attitudes regarding the feasibility of making changes (self-efficacy), obtaining active participation of personnel at both levels, and promoting an institutional safety climate represent challenges that exceed the current perception of the role of infection-control professionals.

Whether increased education, individual reinforcement technique, appropriate rewarding, administrative sanction, enhanced self-participation, active involvement of a larger number of organizational leaders, enhanced perception of health threat, self-efficacy, and perceived social pressure,^{12,317,329,330} or combinations of these factors can improve HCWs' adherence with hand hygiene needs further investigation. Ultimately, adherence to recommended hand-hygiene practices should become part of a culture of patient safety where a set of interdependent quality elements interact to achieve a shared objective.³³¹

On the basis of both these hypothetical considerations and successful, actual experiences in certain institutions, strategies to improve adherence to hand-hygiene practices should be both multimodal and multidisciplinary. However, strategies must be further researched before they are implemented.

EFFICACY OF PROMOTION AND IMPACT OF IMPROVED HAND HYGIENE

The lack of scientific information of the definitive impact of improved hand hygiene on health-care-associated infection rates is a possible barrier to appropriate adherence with hand-hygiene recommendations (Box 1). However, evidence supports the belief that improved hand hygiene can reduce health-care-associated infection rates. Failure to perform appropriate hand hygiene is considered the leading cause of health-care-associated infections and spread of multiresistant organisms and has been recognized as a substantial contributor to outbreaks.

Of nine hospital-based studies of the impact of hand hygiene on the risk of health-care-associated infections (Table 10),^{48,69-75,296} the majority demonstrated a temporal relationship between improved hand-hygiene practices and reduced infection rates.

In one of these studies, endemic MRSA in a neonatal intensive-care unit was eliminated 7 months after introduction of a new hand antiseptic (1% triclosan); all other infection-control measures remained in place, including the practice of conducting weekly active surveillance by obtaining cultures.⁷² Another study reported an MRSA outbreak involving 22 infants in a neonatal unit.⁷³ Despite intensive efforts, the outbreak could not be controlled until a new antiseptic was added (i.e., 0.3% triclosan); all previously used control measures remained in place, including gloves and gowns, cohorting, and obtaining cultures for active surveillance.

The effectiveness of a long-standing, hospital-wide program to promote hand hygiene at the University of Geneva hospitals was recently reported.⁷⁴ Overall adher-

BOX 2

ELEMENTS OF HEALTH-CARE WORKER EDUCATIONAL AND MOTIVATIONAL PROGRAMS

Rationale for hand hygiene

- Potential risks of transmission of microorganisms to patients
- Potential risks of health-care worker colonization or infection caused by organisms acquired from the patient
- Morbidity, mortality, and costs associated with health-care-associated infections

Indications for hand hygiene

- Contact with a patient's intact skin (e.g., taking a pulse or blood pressure, performing physical examinations, lifting the patient in bed)^{25,26,45,48,51,53}
- Contact with environmental surfaces in the immediate vicinity of patients^{46,51,53,54}
- After glove removal^{50,58,71}

Techniques for hand hygiene

- Amount of hand-hygiene solution
- Duration of hand-hygiene procedure
- Selection of hand-hygiene agents
 - Alcohol-based hand rubs are the most efficacious agents for reducing the number of bacteria on the hands of personnel. Antiseptic soaps and detergents are the next most effective, and non-antimicrobial soaps are the least effective.^{1,398}
 - Soap and water are recommended for visibly soiled hands.
 - Alcohol-based hand rubs are recommended for routine decontamination of hands for all clinical indications (except when hands are visibly soiled) and as one of the options for surgical hand hygiene.

Methods to maintain hand skin health

- Lotions and creams can prevent or minimize skin dryness and irritation caused by irritant contact dermatitis
- Acceptable lotions or creams to use
- Recommended schedule for applying lotions or creams

Expectations of patient care managers/administrators

- Written statements regarding the value of, and support for, adherence to recommended hand-hygiene practices
- Role models demonstrating adherence to recommended hand hygiene practices³⁹⁹

Indications for, and limitations of, glove use

- Hand contamination may occur as a result of small, undetected holes in examination gloves^{321,361}
- Contamination may occur during glove removal⁵⁰
- Wearing gloves does not replace the need for hand hygiene⁵⁸
- Failure to remove gloves after caring for a patient may lead to transmission of microorganisms from one patient to another³⁷³

ence to hand-hygiene guidelines during routine patient care was monitored during hospital-wide observational surveys. These surveys were conducted biannually during December 1994–December 1997, before and during implementation of a hand-hygiene campaign that specifically emphasized the practice of bedside, alcohol-based hand disinfection. Individual-sized bottles of hand-rub solution were distributed to all wards, and custom-made holders were mounted on all beds to facilitate access to hand disinfection. HCWs were also encouraged to carry bottles in their pockets, and in 1996, a newly designed flat (instead of round) bottle was made available to further facilitate pocket carriage. The promotional strategy was multimodal and involved a multidisciplinary team of HCWs, the use of wall posters, the promotion of antiseptic hand rubs located at bedsides throughout the institution, and regular performance feedback to all HCWs (see <http://www.hopisafe.ch> for further details on methodology). Health-care-associated infection rates, attack rates of

MRSA cross-transmission, and consumption of hand-rub disinfectant were measured. Adherence to recommended hand-hygiene practices improved progressively from 48% in 1994 to 66% in 1997 ($P < .001$). Whereas recourse to handwashing with soap and water remained stable, frequency of hand disinfection markedly increased during the study period ($P < .001$), and the consumption of alcohol-based hand-rub solution increased from 3.5 to 15.4 liters per 1,000 patient-days during 1993–1998 ($P < .001$). The increased frequency of hand disinfection was unchanged after adjustment for known risk factors of poor adherence. During the same period, both overall health-care-associated infection and MRSA transmission rates decreased (both $P < .05$). The observed reduction in MRSA transmission may have been affected by both improved hand-hygiene adherence and the simultaneous implementation of active surveillance cultures for detecting and isolating patients colonized with MRSA.³³² The experience from the University of Geneva hospitals con-

TABLE 10

ASSOCIATION BETWEEN IMPROVED ADHERENCE WITH HAND-HYGIENE PRACTICE AND HEALTH-CARE-ASSOCIATED INFECTION RATES

Year	Ref. No.	Hospital Setting	Results	Duration of Follow-up
1977	(48)	Adult ICU	Reduction in health-care-associated infections caused by endemic <i>Klebsiella</i> spp.	2 years
1982	(69)	Adult ICU	Reduction in health-care-associated infection rates	N.S.
1984	(70)	Adult ICU	Reduction in health-care-associated infection rates	N.S.
1990	(296)	Adult ICU	No effect (average hand-hygiene adherence improvement did not reach statistical significance)	11 months
1992	(71)	Adult ICU	Substantial difference between rates of health-care-associated infection between two different hand-hygiene agents	8 months
1994	(72)	NICU	Elimination of MRSA, when combined with multiple other infection-control measures. Reduction of vancomycin use	9 months
1995	(73)	Newborn nursery	Elimination of MRSA, when combined with multiple other infection-control measures	3.5 years
2000	(75)	MICU/NICU	85% relative reduction of VRE rate in the intervention hospital; 44% relative reduction in control hospital; no change in MRSA	8 months
2000	(74)	Hospital wide	Substantial reduction in the annual overall prevalence of health-care-associated infections and MRSA cross-transmission rates. Active surveillance cultures and contact precautions were implemented during same period	5 years

Note: ICU = intensive care unit, NICU = neonatal ICU, MRSA = methicillin-resistant *Staphylococcus aureus*, MICU = medical ICU, and N.S. = not stated.

stitutes the first report of a hand-hygiene campaign with a sustained improvement over several years. An additional multimodal program also yielded sustained improvements in hand-hygiene practices over an extended period⁷⁵; the majority of studies have been limited to a 6- to 9-month observation period.

Although these studies were not designed to assess the independent contribution of hand hygiene on the prevention of health-care-associated infections, the results indicate that improved hand-hygiene practices reduce the risk of transmission of pathogenic microorganisms. The beneficial effects of hand-hygiene promotion on the risk of cross-transmission also have been reported in surveys conducted in schools and day care centers,³³³⁻³³⁸ as well as in a community setting.³³⁹⁻³⁴¹

OTHER POLICIES RELATED TO HAND HYGIENE

Fingernails and Artificial Nails

Studies have documented that subungual areas of the hand harbor high concentrations of bacteria, most frequently coagulase-negative staphylococci, gram-negative rods (including *Pseudomonas* spp.), Corynebacteria, and yeasts.^{14,342,343} Freshly applied nail polish does not increase the number of bacteria recovered from periungual skin, but chipped nail polish may support the growth of larger numbers of organisms on fingernails.^{344,345} Even after careful handwashing or the use of surgical scrubs, personnel often harbor substantial numbers of potential pathogens in the subungual spaces.³⁴⁶⁻³⁴⁸

Whether artificial nails contribute to transmission of health-care-associated infections is unknown. However, HCWs who wear artificial nails are more likely to harbor

gram-negative pathogens on their fingertips than are those who have natural nails, both before and after handwashing.³⁴⁷⁻³⁴⁹ Whether the length of natural or artificial nails is a substantial risk factor is unknown, because the majority of bacterial growth occurs along the proximal 1 mm of the nail adjacent to subungual skin.^{345,347,348} Recently, an outbreak of *P. aeruginosa* in a neonatal intensive care unit was attributed to two nurses (one with long natural nails and one with long artificial nails) who carried the implicated strains of *Pseudomonas* spp. on their hands.³⁵⁰ Patients were substantially more likely than controls to have been cared for by the two nurses during the exposure period, indicating that colonization of long or artificial nails with *Pseudomonas* spp. may have contributed to causing the outbreak. Personnel wearing artificial nails also have been epidemiologically implicated in several other outbreaks of infection caused by gram-negative bacilli and yeast.³⁵¹⁻³⁵³ Although these studies provide evidence that wearing artificial nails poses an infection hazard, additional studies are warranted.

Gloving Policies

CDC has recommended that HCWs wear gloves to (1) reduce the risk of personnel acquiring infections from patients, (2) prevent HCW flora from being transmitted to patients, and (3) reduce transient contamination of the hands of personnel by flora that can be transmitted from one patient to another.³⁵⁴ Before the emergence of the acquired immunodeficiency syndrome (AIDS) epidemic, gloves were worn primarily by personnel caring for patients colonized or infected with certain pathogens or by personnel exposed to patients with a high risk of hepatitis B. Since 1987, a dramatic increase in glove use has occurred in an effort to prevent transmission of HIV and

other bloodborne pathogens from patients to HCWs.³⁵⁵ The Occupational Safety and Health Administration (OSHA) mandates that gloves be worn during all patient-care activities that may involve exposure to blood or body fluids that may be contaminated with blood.³⁵⁶

The effectiveness of gloves in preventing contamination of HCWs' hands has been confirmed in several clinical studies.^{45,51,58} One study found that HCWs who wore gloves during patient contact contaminated their hands with an average of only 3 CFUs per minute of patient care, compared with 16 CFUs per minute for those not wearing gloves.⁵¹ Two other studies, involving personnel caring for patients with *C. difficile* or VRE, revealed that wearing gloves prevented hand contamination among the majority of personnel having direct contact with patients.^{45,58} Wearing gloves also prevented personnel from acquiring VRE on their hands when touching contaminated environmental surfaces.⁵⁸ Preventing heavy contamination of the hands is considered important, because handwashing or hand antisepsis may not remove all potential pathogens when hands are heavily contaminated.^{25,111}

Several studies provide evidence that wearing gloves can help reduce transmission of pathogens in health-care settings. In a prospective controlled trial that required personnel to routinely wear vinyl gloves when handling any body substances, the incidence of *C. difficile* diarrhea among patients decreased from 7.7 cases/1,000 patient discharges before the intervention to 1.5 cases/1,000 discharges during the intervention.²²⁶ The prevalence of asymptomatic *C. difficile* carriage also decreased substantially on "glove" wards, but not on control wards. In intensive-care units where VRE or MRSA have been epidemic, requiring all HCWs to wear gloves to care for all patients in the unit (i.e., universal glove use) likely has helped control outbreaks.^{357,358}

The influence of glove use on the hand-hygiene habits of personnel is not clear. Several studies found that personnel who wore gloves were less likely to wash their hands upon leaving a patient's room.^{290,320} In contrast, two other studies found that personnel who wore gloves were substantially more likely to wash their hands after patient care.^{87,301}

The following caveats regarding use of gloves by HCWs must be considered. Personnel should be informed that gloves do not provide complete protection against hand contamination. Bacterial flora colonizing patients may be recovered from the hands of $\leq 30\%$ of HCWs who wear gloves during patient contact.^{50,58} Further, wearing gloves does not provide complete protection against acquisition of infections caused by hepatitis B virus and herpes simplex virus.^{359,360} In such instances, pathogens presumably gain access to the caregiver's hands via small defects in gloves or by contamination of the hands during glove removal.^{50,321,359,361}

Gloves used by HCWs are usually made of natural rubber latex and synthetic nonlatex materials (e.g., vinyl, nitrile, and neoprene [polymers and copolymers of chloroprene]). Because of the increasing prevalence of latex sensitivity among HCWs and patients, FDA has approved several powdered and powder-free latex gloves with reduced protein contents, as well as synthetic gloves that can be made avail-

able by health-care institutions for use by latex-sensitive employees. In published studies, the barrier integrity of gloves varies on the basis of type and quality of glove material, intensity of use, length of time used, manufacturer, whether gloves were tested before or after use, and method used to detect glove leaks.^{359,361-366} In published studies, vinyl gloves have had defects more frequently than latex gloves, the difference in defect frequency being greatest after use.^{359,361,364,367} However, intact vinyl gloves provide protection comparable to that of latex gloves.³⁵⁹ Limited studies indicate that nitrile gloves have leakage rates that approximate those of latex gloves.³⁶⁸⁻³⁷¹ Having more than one type of glove available is desirable, because it allows personnel to select the type that best suits their patient-care activities. Although recent studies indicate that improvements have been made in the quality of gloves,³⁶⁶ hands should be decontaminated or washed after removing gloves.^{8,50,58,321,361} Gloves should not be washed or reused.^{321,361} Use of petroleum-based hand lotions or creams may adversely affect the integrity of latex gloves.³⁷² After use of powdered gloves, certain alcohol hand rubs may interact with residual powder on the hands of personnel, resulting in a gritty feeling on the hands. In facilities where powdered gloves are commonly used, various alcohol-based hand rubs should be tested after removal of powdered gloves to avoid selecting a product that causes this undesirable reaction. Personnel should be reminded that failure to remove gloves between patients may contribute to transmission of organisms.^{358,373}

Jewelry

Several studies have demonstrated that skin underneath rings is more heavily colonized than comparable areas of skin on fingers without rings.³⁷⁴⁻³⁷⁶ One study found that 40% of nurses harbored gram-negative bacilli (e.g., *E. cloacae*, *Klebsiella*, and *Acinetobacter*) on skin under rings and that certain nurses carried the same organism under their rings for several months.³⁷⁵ In a more recent study involving >60 intensive care unit nurses, multivariable analysis revealed that rings were the only substantial risk factor for carriage of gram-negative bacilli and *S. aureus* and that the concentration of organisms recovered correlated with the number of rings worn.³⁷⁷ Whether the wearing of rings results in greater transmission of pathogens is unknown. Two studies determined that mean bacterial colony counts on hands after handwashing were similar among persons wearing rings and those not wearing rings.^{376,378} Further studies are needed to establish if wearing rings results in greater transmission of pathogens in health-care settings.

HAND-HYGIENE RESEARCH AGENDA

Although the number of published studies concerning hand hygiene has increased considerably in recent years, many questions regarding hand-hygiene products and strategies for improving adherence of personnel to recommended policies remain unanswered. Several concerns must still be addressed by researchers in industry and by clinical investigators (Box 3).

BOX 3**HAND-HYGIENE RESEARCH AGENDA****Education and promotion**

- Provide healthcare workers (HCWs) with better education regarding the types of patient care activities that can result in hand contamination and cross-transmission of microorganisms.
- Develop and implement promotion hand-hygiene programs in pregraduate courses.
- Study the impact of population-based education on hand-hygiene behavior.
- Design and conduct studies to determine if frequent glove use should be encouraged or discouraged.
- Determine evidence-based indications for hand cleansing (considering that it might be unrealistic to expect HCWs to clean their hands after every contact with the patient).
- Assess the key determinants of hand-hygiene behavior and promotion among the different populations of HCWs.
- Develop methods to obtain management support.
- Implement and evaluate the impact of the different components of multimodal programs to promote hand hygiene.

Hand-hygiene agents and hand care

- Determine the most suitable formulations for hand-hygiene products.
- Determine if preparations with persistent antimicrobial activity reduce infection rates more effectively than do preparations whose activity is limited to an immediate effect.
- Study the systematic replacement of conventional handwashing by the use of hand disinfection.
- Develop devices to facilitate the use and optimal application of hand-hygiene agents.
- Develop hand-hygiene agents with low irritancy potential.
- Study the possible advantages and eventual interaction of hand-care lotions, creams, and other barriers to help minimize the potential irritation associated with hand-hygiene agents.

Laboratory-based and epidemiologic research and development

- Develop experimental models for the study of cross-contamination from patient to patient and from environment to patient.
- Develop new protocols for evaluating the in vivo efficacy of agents, considering in particular short application times and volumes that reflect actual use in health-care facilities.
- Monitor hand-hygiene adherence by using new devices or adequate surrogate markers, allowing frequent individual feedback on performance.
- Determine the percentage increase in hand-hygiene adherence required to achieve a predictable risk reduction in infection rates.
- Generate more definitive evidence for the impact on infection rates of improved adherence to recommended hand-hygiene practices.
- Provide cost-effectiveness evaluation of successful and unsuccessful promotion campaigns.

WEB-BASED HAND-HYGIENE RESOURCES

Additional information regarding improving hand hygiene is available at

<http://www.hopisafe.ch>

University of Geneva Hospitals, Geneva, Switzerland

<http://www.cdc.gov/ncidod/hip>

CDC, Atlanta, Georgia

<http://www.jr2.ox.ac.uk/bandolier/band88/b88-8.html>

Bandolier journal, United Kingdom

<http://www.med.upenn.edu/mcguckin/handwashing>

University of Pennsylvania, Philadelphia, Pennsylvania

<http://www.handhygiene.org>

Hospital of Saint Raphael, New Haven, Connecticut

PART II. RECOMMENDATIONS**CATEGORIES**

These recommendations are designed to improve hand-hygiene practices of HCWs and to reduce transmission of pathogenic microorganisms to patients and person-

nel in health-care settings. This guideline and its recommendations are not intended for use in food processing or food-service establishments, and are not meant to replace guidance provided by FDA's Model Food Code.

As in previous CDC/HICPAC guidelines, each recommendation is categorized on the basis of existing scientific data, theoretical rationale, applicability, and economic impact. The CDC/HICPAC system for categorizing recommendations is as follows:

Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

Category IB. Strongly recommended for implementation and supported by certain experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

Category IC. Required for implementation, as mandated by federal or state regulation or standard.

Category II. Suggested for implementation and sup-

ported by suggestive clinical or epidemiologic studies or a theoretical rationale.

No recommendation. Unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exist.

RECOMMENDATIONS

1. Indications for handwashing and hand antisepsis
 - A. When hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or other body fluids, wash hands with either a non-antimicrobial soap and water or an antimicrobial soap and water (IA).⁶⁶
 - B. If hands are not visibly soiled, use an alcohol-based hand rub for routinely decontaminating hands in all other clinical situations described in items 1C–J (IA).^{74,93,166,169,283,294,312,398} Alternatively, wash hands with an antimicrobial soap and water in all clinical situations described in items 1C–J (IB).^{69-71,74}
 - C. Decontaminate hands before having direct contact with patients (IB).^{68,400}
 - D. Decontaminate hands before donning sterile gloves when inserting a central intravascular catheter (IB).^{401,402}
 - E. Decontaminate hands before inserting indwelling urinary catheters, peripheral vascular catheters, or other invasive devices that do not require a surgical procedure (IB).^{25,403}
 - F. Decontaminate hands after contact with a patient's intact skin (e.g., when taking a pulse or blood pressure, and lifting a patient) (IB).^{25,45,48,68}
 - G. Decontaminate hands after contact with body fluids or excretions, mucous membranes, nonintact skin, and wound dressings if hands are not visibly soiled (IA).⁴⁰⁰
 - H. Decontaminate hands if moving from a contaminated-body site to a clean-body site during patient care (II).^{25,53}
 - I. Decontaminate hands after contact with inanimate objects (including medical equipment) in the immediate vicinity of the patient (II).^{46,53,54}
 - J. Decontaminate hands after removing gloves (IB).^{50,58,321}
 - K. Before eating and after using a restroom, wash hands with a non-antimicrobial soap and water or with an antimicrobial soap and water (IB).⁴⁰⁴⁻⁴⁰⁹
 - L. Antimicrobial-impregnated wipes (i.e., towelettes) may be considered as an alternative to washing hands with non-antimicrobial soap and water. Because they are not as effective as alcohol-based hand rubs or washing hands with an antimicrobial soap and water for reducing bacterial counts on the hands of HCWs, they are not a substitute for using an alcohol-based hand rub or antimicrobial soap (IB).^{160,161}
 - M. Wash hands with non-antimicrobial soap and water or with antimicrobial soap and water if exposure to *Bacillus anthracis* is suspected or proven. The physical action of washing and rinsing hands under such circumstances is recommended because alcohols, chlorhexidine, iodophors, and other antiseptic agents have poor activity against spores (II).^{120,172,224,225}
 - N. No recommendation can be made regarding the routine use of non-alcohol-based hand rubs for hand hygiene in health-care settings. Unresolved issue.
2. Hand-hygiene technique
 - A. When decontaminating hands with an alcohol-based hand rub, apply product to palm of one hand and rub hands together, covering all surfaces of hands and fingers, until hands are dry (IB).^{288,410} Follow the manufacturer's recommendations regarding the volume of product to use.
 - B. When washing hands with soap and water, wet hands first with water, apply an amount of product recommended by the manufacturer to hands, and rub hands together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers. Rinse hands with water and dry thoroughly with a disposable towel. Use towel to turn off the faucet (IB).^{90-92,94,411} Avoid using hot water, because repeated exposure to hot water may increase the risk of dermatitis (IB).^{254,255}
 - C. Liquid, bar, leaflet, or powdered forms of plain soap are acceptable when washing hands with a non-antimicrobial soap and water. When bar soap is used, soap racks that facilitate drainage and small bars of soap should be used (II).⁴¹²⁻⁴¹⁵
 - D. Multiple-use cloth towels of the hanging or roll type are not recommended for use in health-care settings (II).^{137,300}
3. Surgical hand antisepsis
 - A. Remove rings, watches, and bracelets before beginning the surgical hand scrub (II).^{375,378,416}
 - B. Remove debris from underneath fingernails using a nail cleaner under running water (II).^{14,417}
 - C. Surgical hand antisepsis using either an antimicrobial soap or an alcohol-based hand rub with persistent activity is recommended before donning sterile gloves when performing surgical procedures (IB).^{115,159,232,234,237,418}
 - D. When performing surgical hand antisepsis using an antimicrobial soap, scrub hands and forearms for the length of time recommended by the manufacturer, usually 2–6 minutes. Long scrub times (e.g., 10 minutes) are not necessary (IB).^{117,156,205,207,238-241}
 - E. When using an alcohol-based surgical hand-scrub product with persistent activity, follow the manufacturer's instructions. Before applying the alcohol solution, prewash hands and forearms with a non-antimicrobial soap and dry hands and forearms completely. After application of the alcohol-based product as recommended, allow hands and forearms to dry thoroughly before donning sterile gloves (IB).^{159,237}
4. Selection of hand-hygiene agents
 - A. Provide personnel with efficacious hand-hygiene products that have low irritancy potential, particularly when these products are used multiple times per shift (IB).^{90,92,98,166,249} This recommendation applies to products used for hand antisepsis before and after patient care in clinical areas and to prod-

- ucts used for surgical hand antisepsis by surgical personnel.
- B. To maximize acceptance of hand-hygiene products by HCWs, solicit input from these employees regarding the feel, fragrance, and skin tolerance of any products under consideration. The cost of hand-hygiene products should not be the primary factor influencing product selection (IB).^{92,93,166,274,276-278}
 - C. When selecting non-antimicrobial soaps, antimicrobial soaps, or alcohol-based hand rubs, solicit information from manufacturers regarding any known interactions between products used to clean hands, skin care products, and the types of gloves used in the institution (II).^{174,372}
 - D. Before making purchasing decisions, evaluate the dispenser systems of various product manufacturers or distributors to ensure that dispensers function adequately and deliver an appropriate volume of product (II).²⁸⁶
 - E. Do not add soap to a partially empty soap dispenser. This practice of "topping off" dispensers can lead to bacterial contamination of soap (IA).^{187,419}
5. Skin care
 - A. Provide HCWs with hand lotions or creams to minimize the occurrence of irritant contact dermatitis associated with hand antisepsis or handwashing (IA).^{272,273}
 - B. Solicit information from manufacturers regarding any effects that hand lotions, creams, or alcohol-based hand antiseptics may have on the persistent effects of antimicrobial soaps being used in the institution (IB).^{174,420,421}
 6. Other aspects of hand hygiene
 - A. Do not wear artificial fingernails or extenders when having direct contact with patients at high risk (e.g., those in intensive-care units or operating rooms) (IA).³⁵⁰⁻³⁵³
 - B. Keep natural nails tips less than 1/4-inch long (II).³⁵⁰
 - C. Wear gloves when contact with blood or other potentially infectious materials, mucous membranes, and nonintact skin could occur (IC).³⁵⁶
 - D. Remove gloves after caring for a patient. Do not wear the same pair of gloves for the care of more than one patient, and do not wash gloves between uses with different patients (IB).^{50,58,321,373}
 - E. Change gloves during patient care if moving from a contaminated body site to a clean body site (II).^{50,51,58}
 - F. No recommendation can be made regarding wearing rings in health-care settings. Unresolved issue.
 7. HCW educational and motivational programs
 - A. As part of an overall program to improve hand-hygiene practices of HCWs, educate personnel regarding the types of patient-care activities that can result in hand contamination and the advantages and disadvantages of various methods used to clean their hands (II).^{74,292,295,299}
 - B. Monitor HCWs' adherence with recommended hand-hygiene practices and provide personnel with information regarding their performance (IA).^{74,276,292,295,299,306,310}
 - C. Encourage patients and their families to remind HCWs to decontaminate their hands (II).^{394,422}
 8. Administrative measures
 - A. Make improved hand-hygiene adherence an institutional priority and provide appropriate administrative support and financial resources (IB).^{74,75}
 - B. Implement a multidisciplinary program designed to improve adherence of health personnel to recommended hand-hygiene practices (IB).^{74,75}
 - C. As part of a multidisciplinary program to improve hand-hygiene adherence, provide HCWs with a readily accessible alcohol-based hand-rub product (IA).^{74,166,283,294,312}
 - D. To improve hand-hygiene adherence among personnel who work in areas in which high workloads and high intensity of patient care are anticipated, make an alcohol-based hand rub available at the entrance to the patient's room or at the bedside, in other convenient locations, and in individual pocket-sized containers to be carried by HCWs (IA).^{11,74,166,283,284,312,318,423}
 - E. Store supplies of alcohol-based hand rubs in cabinets or areas approved for flammable materials (IC).

PART III. PERFORMANCE INDICATORS

The following performance indicators are recommended for measuring improvements in HCWs' hand-hygiene adherence:

- A. Periodically monitor and record adherence as the number of hand-hygiene episodes performed by personnel/number of hand-hygiene opportunities, by ward or by service. Provide feedback to personnel regarding their performance.
- B. Monitor the volume of alcohol-based hand rub (or detergent used for handwashing or hand antisepsis) used per 1,000 patient-days.
- C. Monitor adherence to policies dealing with wearing of artificial nails.
- D. When outbreaks of infection occur, assess the adequacy of HCW hand hygiene.

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APPENDIX

ANTIMICROBIAL SPECTRUM AND CHARACTERISTICS OF HAND-HYGIENE ANTISEPTIC AGENTS*

Group	Gram-positive bacteria	Gram-negative bacteria	Mycobacteria	Fungi	Viruses	Speed of action	Comments
Alcohols	+++	+++	+++	+++	+++	Fast	Optimum concentration 60%–95%; no persistent activity
Chlorhexidine (2% and 4% aqueous)	+++	++	+	+	+++	Intermediate	Persistent activity; rare allergic reactions
Iodine compounds	+++	+++	+++	++	+++	Intermediate	Causes skin burns; usually too irritating for hand hygiene
Iodophors	+++	+++	+	++	++	Intermediate	Less irritating than iodine; acceptance varies
Phenol derivatives	+++	+	+	+	+	Intermediate	Activity neutralized by nonionic surfactants
Tricolsan	+++	++	+	-	+++	Intermediate	Acceptability on hands varies
Quaternary ammonium compounds	+	++	-	-	+	Slow	Used only in combination with alcohols; ecologic concerns

Note: +++ = excellent; ++ = good, but does not include the entire bacterial spectrum; + = fair; - = no activity or not sufficient.
* Hexachlorophene is not included because it is no longer an accepted ingredient of hand disinfectants.

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