Draft Guideline for Hand Hygiene in Healthcare Settings

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ABSTRACT

Background: Although handwashing has been considered one of the most important measures for reducing transmission of microorganisms in healthcare facilities, adherence of healthcare personnel to recommended handwashing practices is poor.

Objective: Develop evidence-based hand hygiene guideline designed to promote new strategies for improving hand hygiene practices in healthcare facilities and reduce healthcare-acquired infections.

Search strategy for identification of studies: Medline searches of English-language articles published from 1966 through early 2001, review of bibliographies of retrieved articles, and review of abstracts from selected scientific meetings.

Criteria for selecting studies for this review: Articles dealing with handwashing, hand antisepsis, hand hygiene agents, adherence of healthcare personnel to recommended hand hygiene practices, and other aspects of hand hygiene in healthcare facilities were reviewed.

Types of studies: In vitro and in vivo laboratory-based studies, prospective controlled clinical trials, prospective intervention trials, epidemiologic investigations of healthcare-acquired infections, and questionnaire surveys were included.

Outcome measures: Log_{10} reductions in bacterial counts achieved in vitro and in vivo by hand hygiene agents, percent adherence of healthcare personnel to recommended hand hygiene practices, and prevalence and incidence rates of healthcare-acquired infections.

Main results: There is convincing evidence that hand antisepsis can reduce transmission of healthcare-acquired microorganisms. Alcohol-based handrubs reduce bacterial counts on the hands of personnel more effectively than plain or antimicrobial soaps, can be made more accessible than sinks and other handwashing facilities, and require less time to use and cause less skin irritation and dryness than washing hands with soap and water. Long-term multimodal, multidisciplinary programs that address individual and institutional barriers are necessary to achieve enduring improvements in hand hygiene adherence.

Reviewers' conclusions: Promoting increased use of alcohol-based handrubs, when combined with multidisciplinary educational and motivational programs, can lead to improved hand hygiene practices among healthcare personnel. Limited studies suggest that improving adherence to recommended hand hygiene practices can reduce rates of healthcare-acquired infections.

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EXECUTIVE SUMMARY

The "Guideline for Hand Hygiene in Healthcare Settings" provides healthcare practitioners with a thorough review of evidence dealing with handwashing and hand antisepsis in healthcare settings, and specific recommendations to promote improved hand hygiene practices and reduce transmission of pathogenic microorganisms to patients and personnel in healthcare settings.

The present guideline reviews studies published since the 1985 CDC guideline and the 1995 APIC guideline were issued, and provides an in-depth review of hand hygiene practices of healthcare personnel, levels of adherence of personnel to recommended handwashing practices, and factors adversely affecting adherence. New studies of the in vivo efficacy of alcohol-based handrubs 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 handrubs in improving hand hygiene practices are summarized. Recommendations dealing with related issues such as the use of hand lotions or creams and wearing of artificial fingernails are included.

Part I: Review of Scientific Data on Hand Hygiene Practices in Healthcare Settings reviews in detail the efficacy of agents used for handwashing and hand antisepsis and factors adversely affecting adherence of healthcare personnel to recommended hand hygiene practices, including poor access to sinks and handwashing materials, the time required to perform conventional handwashing with soap and water, irritant contact dermatitis associated with frequent exposure to detergents and water, high workloads among personnel, knowledge deficits among care givers regarding when hand contamination occurs and proper hand hygiene techniques, and failure of administrative leaders to make hand hygiene an institutional priority. Using a waterless antiseptic agent such as an alcohol-based handrub minimizes many of the factors adversely affecting adherence to hand hygiene protocols. Alcohol-based handrubs are more effective compared to washing hands with a non-antimicrobial or antimicrobial soap, can be made much more accessible, require less time to use, and are less prone to cause irritant contact dermatitis. Several recent studies suggest that having personnel decontaminate their hands with an alcohol-based handrub between most patient contacts can lead to improved adherence of healthcare workers to hand hygiene policies and reduce infection rates. Part II: Recommendations provides consensus recommendations of the Healthcare Infection Control Practices Advisory Committee (HICPAC) and other professional societies that participated in development of this guideline.

PART I. REVIEW OF THE SCIENTIFIC DATA REGARDING HAND HYGIENE

1. 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 part of the 19th century. As early as 1822, Labarraque, 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, he stated that physicians and others attending patients with contagious diseases would benefit from moistening their hands with liquid chloride solution.[2]

In 1846, Ignaz Semmelweis observed that women whose babies were delivered by students and physicians in the First 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 suggesting that cleansing heavily contaminated hands with an antiseptic agent between patient contacts may reduce healthcare-acquired transmission of contagious diseases more effectively than handwashing with plain soap and water.

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 of 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 healthcare facilities.

In 1961, the U. S. Public Health Service produced a training film that demonstrated handwashing techniques recommended for use by healthcare workers.[4] At the time, it was recommended that personnel wash their hands with soap and water for 1 to 2 min 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 (CDC).[5,6] These guidelines recommended handwashing with non-antimicrobial soap between most patient contacts and washing with antimicrobial soap before and after performing invasive procedures or caring for high-risk patients. Use of waterless antiseptic agents such as 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 waterless antiseptic agents and supported their use in more clinical settings than had been recommended in earlier guidelines. In 1995 and 1996, HICPAC recommended that either antimicrobial soap or a waterless antiseptic agent be used for cleaning hands upon leaving the rooms of patients with multi-drug resistant pathogens such as vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA).[9,10] These guidelines also included useful recommendations for handwashing and hand antisepsis in other clinical settings, such as those for routine patient care. Although the APIC and HICPAC guidelines have been adopted by most hospitals, adherence of healthcare workers to recommended handwashing practices has remained unacceptably 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. The current literature review and accompanying recommendations have been prepared by a task force comprised of representatives from HICPAC, the Society for Healthcare Epidemiology of America (SHEA), APIC, and the Infectious Diseases Society of America (IDSA).

2. Normal Bacterial Skin Flora

In order 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, with total aerobic bacterial counts ranging from more than 1 x 10^6 CFU/cm^2 on the scalp, 5 x 10^5 CFU/cm^2 in the axilla and 4 x 10^4 CFU/cm^2 on the abdomen to 1 x 10^4 CFU/cm^2 on the forearm.[13] Total bacterial counts on the hands of medical personnel have ranged from 3.9 x 10^4 to 4.6 x 10^6.[14-17] In 1938, Price[14] established that bacteria recovered from the hands could be divided into two categories, i.e., transient and resident. Transient flora, which colonize the superficial layers of the skin, are more amenable to removal by routine handwashing. They are often acquired by healthcare workers during direct contact with patients or contaminated environmental surfaces adjacent to the patient, and are the organisms most frequently associated with healthcare-acquired infections. Resident flora, which are attached to deeper layers of the skin, are more resistant to removal. In general, resident flora such as coagulase-negative staphylococci and diphtheroids are less likely to be associated with such infections. The hands of some health personnel may become persistently colonized with pathogenic flora such as *S.aureus*, gram-negative bacilli, or yeast. Price and subsequent investigators documented that although the number of transient and resident flora varies considerably among individuals, it is often relatively constant for any given individual.[14,18]

3. Physiology of Normal Skin

The primary function of the skin is to reduce water loss, provide protection against abrasive action and microorganisms, and generally act as a permeability barrier to the environment. Its basic structure is as follows: the superficial region, termed the stratum corneum or horny layer, is between 10 and 20 μm thick; underlying this region is the viable epidermis (50-100 μm), dermis (1-2 mm), and hypodermis (1-2 mm). The barrier to percutaneous absorption lies within the stratum corneum, the thinnest and smallest compartment. The stratum corneum contains the corneocytes or horny cells, which are flat polyhedral-shaped non-nucleated cells, remnants of the terminally differentiated keratinocytes found 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 such as 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, composed primarily of 10-20 layers of keratinizing epithelial cells, which are responsible for the synthesis 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 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. There is now substantial evidence that the formation of the skin barrier is under homeostatic control. This is illustrated by the epidermal response to barrier perturbation by skin stripping or solvent extraction. There is circumstantial evidence that the rate of keratinocyte proliferation directly influences the integrity of the skin barrier. A general increase in the rate of proliferation will result in a decrease in the time available for (i) uptake of nutrients, such as essential fatty acids; (ii) protein and lipid synthesis; and (iii) processing of the precursor molecules required for skin barrier function. It remains unclear if chronic but quantitatively smaller increases in rate of epidermal proliferation also lead to changes in skin barrier function. Thus, the extent to which the decreased barrier function caused by irritants is due to an increased epidermal proliferation also remains unclear.

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 (i) extraction of skin lipids with apolar solvents; (ii) physical stripping of the stratum corneum using adhesive tape; and (iii) chemically induced irritation. All of these experimental manipulations lead to a decreased skin barrier as determined by transepidermal water loss (TEWL). Perhaps the most studied experimental system is the treatment of mouse skin with acetone. This leads to a marked and immediate increase in TEWL, indicating a decrease in skin barrier function. Since acetone treatment selectively removes glycerolipids and sterols from the skin, this suggests that these lipids are necessary though perhaps not sufficient in themselves for a barrier function. Detergents (see below) act similarly as acetone on the intercellular lipid domain. The return to normal barrier function is biphasic: 50-60% of barrier recovery is typically seen by 6 hours but complete normalization of barrier function requires 5-6 days.

4. Definition of Terms

Antimicrobial soap. Soap containing an antiseptic agent.

Antiseptic agent. Antiseptics are antimicrobial substances that are applied to the skin to reduce the number of microbial flora. Examples include alcohols, chlorhexidine, chlorine, hexachlorophene, iodine, para-chloro-meta-xylenol, quaternary ammonium compounds, and triclosan.

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

Antiseptic handrub. Applying a waterless antiseptic agent to all surfaces of the hands to reduce the number of microorganisms present.

Decontaminate hands. Reducing bacterial counts on hands by performing antiseptic handrub or antiseptic handwash.

Detergent. Detergents (surfactants) are compounds that possess a cleaning action. They are composed of a hydrophilic part and a lipophilic part and can be divided into four groups: anionic, cationic, amphoteric, and non-ionic detergents. Although products used for handwashing or antiseptic handwash in healthcare settings represent various types of detergents, they are usually referred to as soaps.

Hand antisepsis. Refers to either antiseptic handwash or antiseptic handrub.

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

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

Persistent activity. Antimicrobial activity that persists after the agent has been rinsed off the skin or has dried. This property, which is due to binding of the antiseptic agent to the stratum corneum, is also referred to as *residual activity* or *substantivity*.

Plain soap. Plain soap refers to products that do not contain antimicrobial agents, or contain very low concentrations of antimicrobial agents that are effective solely as preservatives. Plain bar soap is comprised of alkyl carboxylate salts, a form of anionic detergent.

Surgical hand antisepsis. Antiseptic handwash or antiseptic handrub 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 body substances (e.g., blood, fecal material, urine).

Waterless antiseptic agent. An antiseptic agent that does not require use of exogenous water. After applying such an agent, the individual rubs the hands 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 divides products into three categories.[19] *Patient preoperative skin preparations* are products applied to a patient's skin to reduce the number of microorganisms on the skin at the site of anticipated surgery. *Antiseptic handwash* or *healthcare personnel handwash* preparations are fast-acting products designed to reduce the number of transient microorganisms on the hands of healthcare workers. A persistent effect is considered desirable, but not necessary. *Surgical hand scrub* refers to antiseptic-containing preparations that significantly reduce the number of microorganisms on the hands of healthcare personnel and have a persistent effect.

5. Evidence of Transmission of Pathogens on Hands

Transmission of healthcare-acquired pathogens from one patient to another via the hands of healthcare workers requires four elements. One, organisms present on the patient's skin, or that have been shed onto inanimate objects immediately surrounding the patient, must be transferred to the hands of healthcare workers. Two, organisms must be capable of surviving for at least several minutes on the hands of personnel. Three, handwashing or hand antisepsis by the worker must be inadequate or omitted altogether, or the agent used for hand hygiene inappropriate. Four, the contaminated hands of the care giver must come in direct contact with another patient, or with an inanimate object that will come in contact with the patient. Evidence supporting each of these elements is given below.

Healthcare-acquired 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 tend to be 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 such as *S. aureus, Proteus mirabilis, Klebsiella* and *Acinetobacter* spp. present on intact areas of the skin of some patients can vary from 100 to 10^6 /cm^2.[25,29,31,33] Diabetics, patients undergoing dialysis for chronic renal failure, and those with chronic dermatitis are particularly likely to have areas of intact skin that are colonized with *S. aureus*.[34-41] Because nearly 10^6 skin squames containing viable microorganisms are shed daily from normal skin,[42] it is not surprising that patient gowns, bed linen, bedside furniture, and other objects in the immediate environment of the patient become contaminated with patient flora.[30,43-46] Such contamination is particularly likely to be due to staphylococci or enterococci, which are resistant to dessication.

Relatively few data are available 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. More recently, Casewell and Phillips[48] demonstrated that nurses could contaminate their hands with 100 to 1000 CFU of *Klebsiella* spp. during such "clean" activities as lifting patients, taking the patient's pulse, blood pressure, or oral temperature; or touching the patient's hand, shoulder, or groin. Similarly, Ehrenkranz et al.[25] cultured the hands of nurses who touched the groin of patients heavily colonized with *P. mirabilis*, and found 10 to 600 CFU/ml in glove juice samples from nurses' hands. Recently, Pittet and colleagues[51] studied contamination of healthcare workers' hands during activities that involved direct patient contact, wound care, intravascular catheter care, respiratory tract care, or handling patient secretions. Using agar fingertip impression plates, they found that the number of bacteria recovered from fingertips ranged from 0 to 300 CFU. Direct patient contact and respiratory tract care were most likely to contaminate the fingers of care givers. Gram-negative bacilli accounted for 15% of isolates and *S. aureus* for 11%. Importantly, duration of patient care activity was strongly associated with the intensity of bacterial contamination of healthcare worker hands in this study.

Several other studies have documented that personnel can contaminate their hands with gram-negative bacilli, *S. aureus*, enterococci, or *Clostridium difficile* by performing "clean procedures" or touching intact areas of skin of hospitalized patients.[26,45,46,53] Furthermore, personnel caring for infants with respiratory syncytial virus (RSV) infections have acquired RSV by performing activities such as feeding infants, changing diapers, and playing with the infant.[49] Personnel who had contact only with surfaces contaminated with the infants' secretions also acquired RSV. In the above studies, personnel contaminated their hands with RSV and inoculated their oral or conjunctival mucosa. Other studies also have documented that healthcare workers may contaminate their hands (or gloves) merely by touching inanimate objects in patient rooms.[46,53,54] Also, laboratory-based studies have documented that touching contaminated surfaces can transfer *S. aureus* or gram-negative bacilli to the fingers.[55] Unfortunately, none of the studies dealing with hand contamination of hospital personnel were designed to determine if the contamination resulted in transmission of pathogens to susceptible patients.

Many other studies have documented contamination of healthcare workers' hands with potential healthcare-acquired pathogens, but did not relate their findings to the specific type of preceding patient contact.[15,17,56-61] For example, in studies conducted before glove use was common among healthcare personnel, Ayliffe et al.[60] found that 15% of nurses working in an isolation unit carried a median of 1 x 10^4 CFU of *S. aureus* on their hands. Twenty-nine percent of nurses working in a general hospital had *S. aureus* on their hands (median count, 3,800 CFU), while 78% of those working in a hospital for dermatology patients had the organism on their hands (median count, 14.3 x 10^6 CFU). The same survey revealed that 17% to 30% of nurses carried gram-negative bacilli on their hands (median counts ranged from 3,400 CFU to 38,000 CFU). Daschner[58] 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 >1000 CFU of the organism on their hands. Maki[16] 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. Serial cultures revealed that 100% of healthcare personnel carried gram-negative bacilli at least once, and 64% carried *S. aureus* at least once.

6. Models of Hand Transmission

Several investigators have studied transmission of infectious agents using different experimental models. Ehrenkranz et al.[25] asked nurses to touch a patient's groin for 15 seconds, as though they were taking a femoral pulse. The patient was known to be heavily colonized with gram-negative bacilli. 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 so that subsequent transmission to catheter material occurred despite handwashing with plain soap and water.

Marples et al.[62] studied transmission of organisms from artificially contaminated "donor" fabrics to clean "recipient" fabrics via hand contact and found that the number of organisms transmitted was greater if the donor fabric or the hands were wet. Overall, only 0.06% of the organisms obtained from the contaminated donor fabric were transferred to recipient fabric via hand contact. Using the same experimental model, Mackintosh et al.[63] found that *S. saprophyticus, P. aeruginosa,* and *Serratia* spp. were transferred in greater numbers than was *Escherichia coli* from a contaminated fabric to a clean one following hand contact. Patrick et al.[64] found that organisms were transferred to various types of surfaces in much larger numbers (>10^4) from wet hands than from hands that had been dried carefully.

7. Relation Between Hand Hygiene and Acquisition of Healthcare-Acquired Pathogens

Despite a paucity of appropriate randomized, controlled trials, there is substantial evidence that hand antisepsis reduces the incidence of healthcare-acquired infections.[65,66] In what would be considered an intervention trial using historical controls, Semmelweis[3] demonstrated in 1847 that the mortality rate among mothers delivered in the First Obstetrics Clinic at the General Hospital of Vienna was significantly lower when hospital staff cleaned their hands with an antiseptic agent than when they washed their hands with plain soap and water. In the 1960s, a prospective, controlled trial compared the impact of *no* handwashing versus antiseptic handwashing on acquistion of *S. aureus* among infants in a hospital nursery.[67] The investigators 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 significantly more often, and more rapidly, than did infants cared for by nurses who used hexachlorophene to clean their hands between infant contacts.

Several trials have studied the effect on healthcare-acquired infection rates of handwashing with plain soap and water versus some form of hand antisepsis.[68,69] Maki[68] found that healthcare-acquired infection rates were when antiseptic handwashing was performed by personnel. Massanari and Hierholzer[69] found that antiseptic handwashing was associated with lower healthcare-acquired infection rates in some intensive care units, but not others. Doebbeling et al.[70] compared antiseptic handwashing using a chlorhexidine-containing detergent to a combination regimen that permitted either handwashing with plain soap or use of an alcohol-based hand rinse. Healthcare-acquired infection rates were lower when the chlorhexidine-containing product was in use. However, because relatively little of the alcohol rinse was utilized during periods when the combination regimen was in use, and adherence to policies was higher when chlorhexidine was available, it was difficult to tell whether the hand hygiene regimen used or differences in adherence of personnel was responsible for lower infection rates. Several investigators have found that healthcare-acquired acquisition of MRSA was reduced when the antimicrobial soap used for hygienic handwashing was changed.[71,72]

Casewell and Phillips[48] reported that increased handwashing frequency among hospital staff was associated with a decrease in transmission of *Klebsiella* spp. among patients, but did not quantitate the level of handwashing among personnel. More recently, Pittet et al.[73] reported that the frequency of acquisition of various healthcare-acquired pathogens was reduced when hand antisepsis was performed more frequently by hospital personnel. The latter study and another by Larson et al.[74] documented that the prevalence of healthcare-acquired infections decreased as adherence of healthcare workers to recommended hand hygiene measures improved.

In addition to these quasi-experimental studies, outbreak investigations have suggested an association between infections and understaffing or overcrowding that was consistently linked with poor adherence to hand hygiene. During an outbreak, Fridkin[75] investigated risk factors for central venous catheter-associated bloodstream infections. After adjustment for confounding factors, the patient-to-nurse ratio remained an independent risk factor for bloodstream infection, suggesting that nursing staff reduction below a critical threshold may have contributed to this outbreak by jeopardizing adequate catheter care. More recently, Vicca[76] demonstrated the relationship between understaffing and the spread of MRSA in intensive care. These findings tend to show indirectly that an imbalance between workload and staffing leads to relaxed attention to basic control measures, such as hand hygiene, and spread of microorganisms. Harbarth and colleagues[77] investigated an outbreak of *Enterobacter cloacae* in a neonatal intensive care unit, and showed that the daily number of hospitalized children was above the maximal capacity of the unit, resulting in an available space per child well below current recommendations. In parallel, staff on duty was significantly below the number required by the workload, and this 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. Continuous surveillance showed that being hospitalized during this period carried a 4-fold increased risk of acquiring a healthcare-acquired infection. This study not only shows the association between workload and infections, but highlights also the intermediate step, which is poor adherence to hand hygiene policies.

8. Methods Used to Evaluate the Efficacy of Hand Hygiene Products

8.1 Current methods

Direct comparison of studies of the in vivo efficacy of handwashing, antiseptic handwash, and surgical hand antisepsis protocols is complicated by the fact that methods used by investigators have varied a great deal. Important differences between 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 (percent reduction in bacteria recovered from the skin, or log reduction of bacteria released from the skin). Despite these differences, most studies fall into one of two major categories. Studies designed to evaluate products that will be used by healthcare workers for handwashing or antiseptic handwashs between patient contacts are tested for their ability to remove "transient" flora from the hands. A majority of such studies include 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 potential use for pre-operative cleansing of surgeons' hands (surgical hand antisepsis protocols) are tested for their ability to remove "resident" flora from the hands, without preceding artificial contamination of the volunteer's hand.

In the United States, antiseptic handwash products intended for use by healthcare personnel are regulated by the FDA's Division of OTC Drug Products. Requirements for in vitro and in vivo testing of healthcare personnel handwash products and surgical hand scrubs are outlined in the FDA Tentative Final Monograph for Healthcare Antiseptic Drug Products.[19] Such products must be evaluated by using a standardized method (E 1174-94) published by the American Society of Testing and Materials.[78] After hands are artificially contaminated with a defined inoculum of a test organism (usually *S. marcescens* or *E. coli*), 5 ml or an amount specified by the manufacturer of the test formulation is applied to the hands, a small amount of tap water is added, hands are completely lathered for 30 sec, and then rinsed with tap water for 30 sec. After washing, test volunteers don rubber gloves, 75 ml of sampling solution is added to each glove, hands are massaged for 1 min, 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.

The method most widely used in Europe to evaluate the efficacy of hand hygiene agents is the European Standard 1500 – 1997 (EN 1500- Chemical disinfectants and antiseptics. Hygienic handrub - Test method and requirements).[79] Briefly, this method requires 12 to 15 test volunteers, and a 24-hr growth of broth culture of *E. coli* K12. Hands are washed with a soft soap and dried, then immersed half-way to the metacarpals in the broth culture for 5 sec. Hands are removed, excess fluid is drained off, and hands are dried in the air for 3 min. Bacterial recovery for the initial value is by kneading the fingertips of each hand separately for 60 sec in 10 ml of Tryptic soy broth (TSB) without neutralizers. The hands are removed and disinfected with 3 ml of the handrub agent for 30 sec in a set design. The same operation is repeated with a total disinfection time not exceeding 60 sec. Both hands are rinsed in running water for 5 sec and excess 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) and the test product. Colony counts are carried out after 24 and 48 hrs 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 there is a difference, then the results are analyzed statistically (Wilcoxon test).

Several other methods have been utilized to measure the efficacy of antiseptic agents against a variety of viral pathogens.[80-82]

8.2 Shortcomings of traditional methodologies

Currently accepted methods of evaluating hand hygiene products intended for use by healthcare workers require that test volunteers wash their hands with a plain or antimicrobial soap for 30 sec or 1 min, despite the fact that the average duration of handwashing by hospital personnel has been observed to be less than 15 sec in a majority of studies.[52,83-88] A few investigators have used 15-sec handwashing or hygienic hand wash protocols.[89-93] Therefore, almost no data exist regarding the efficacy of plain or antimicrobial soaps under conditions in which they are actually used by healthcare workers. Similarly, some accepted methods for evaluating waterless antiseptic agents for use as antiseptic handrubs require that 3 ml of alcohol be rubbed into the hands for 30 sec, followed by a repeat application of the same type. This type of protocol also does not reflect actual usage patterns among healthcare personnel. Further studies should be conducted at the bedside using standardized protocols to obtain more realistic views of microbial colonization and risk of bacterial transfer and cross-transmission.[51]

9. Review of Preparations Used for Hand Hygiene

9.1. 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, leaf and liquid preparations. Their cleaning activity is due to their detergent properties, which result in removal of dirt, soil, and various organic substances from the hands. Plain soaps have little 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 sec reduces bacterial counts on the skin by 0.6 to 1.1 log_{10}, whereas washing for 30 sec reduces counts by 1.8 to 2.8 log_{10}.[1] However, in a number of studies, handwashing with plain soap failed to remove pathogens from the hands of hospital personnel.[25,45] Handwashing with plain soap may sometimes result in paradoxical increases in bacterial counts on the skin.[91,94-96] Although non-antimicrobial soaps are often assumed to have low irritancy potential because they do not contain antiseptics, some formulations may be associated with considerable skin irritation and dryness.[91,95,97] Occasionally, plain soaps have become contaminated, which may lead to colonization of hands of personnel with gram-negative bacilli.[98]

9.2. Alcohols

Most alcohol-based hand antiseptics contain either isopropanol, ethanol, n-propanol, or a combination of two of these products. Studies of alcohols have evaluated either individual alcohols in varying concentrations (a majority of studies), combinations of two alcohols, or alcohol solutions containing small amounts of hexachlorophene, quaternary ammonium compounds, povidone-iodine, triclosan, or chlorhexidine gluconate.[60,92,99-118]

The antimicrobial activity of alcohols is due to their ability to denature proteins.[119] Alcohol solutions containing 50% to 80% alcohol are most effective, with higher concentrations being less potent.[120,121] This paradox is due to the fact that proteins are not denatured easily in the absence of water.[119]

Alcohols have excellent in vitro germicidal activity against gram-positive and gram-negative vegetative bacteria (including multi-drug resistant pathogens such as MRSA and VRE), *Mycobacterium tuberculosis*, and a variety of fungi.[119-127] However, they have very poor activity against bacterial spores. Herpes simplex virus, human immunodeficiency virus (HIV), influenza virus, respiratory syncytial virus, and vaccinia virus are quite susceptible to alcohols.[119,128,129] Other viruses that are somewhat less susceptible, but are killed by 50% to 70% alcohol, include hepatitis B virus, enteroviruses, rotavirus, and adenovirus.[80,119] In general, ethanol has greater activity against viruses than isopropanol.

Numerous studies have documented the *in vivo* antimicrobial activity of alcohols. Early quantitative studies of the effects of antiseptic handrubs established that alcohols effectively reduce bacterial counts on the hands.[14,120,123,130] Typically, log reductions of the release of test bacteria from artificially contaminated hands average 3.5 $\log_{10}$ after a 30-sec application, and 4.0 to 5.0 $\log_{10}$ after a 1-min application.[1] Alcohols are rapidly germicidal when applied to the skin, but have no appreciable persistent (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.[131,132] Addition of chlorhexidine, quaternary ammonium compounds, octenidine, or triclosan to alcoholic solutions can result in persistent activity.[1]

A few studies have examined the ability of alcohol to prevent the transfer of healthcare-acquired pathogens by using experimental models of pathogen transmission.[25,62,63] Ehrenkranz et al.[25] found that 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 following antiseptic handrub with an alcohol-based hand rinse. In contrast, transfer of the organisms occurred in 92% of experiments following handwashing with plain soap and water. This experimental model suggests that when the hands of healthcare personnel are heavily contaminated, an antiseptic handrub using an alcohol-based rinse can prevent pathogen transmission more effectively than can handwashing with plain soap and water. Table 1 summarizes a number of studies that have compared alcohol-based products to plain soap or antimicrobial soaps to determine which was more effective for standard handwashing or hand antisepsis by health personnel.[25,53,60,92,105-111,118,133-142] In all studies that included plain soap, alcohols were more effective than plain soap. In all but one of the trials that compared alcohol-based solutions to antimicrobial soaps or detergents, alcohol was superior to washing hands with soaps or detergents containing hexachlorophene, povidone-iodine, 4% chlorhexidine, or triclosan. In studies dealing with antimicrobial-resistant organisms, alcohol-based products reduced the number of multi-drug- resistant pathogens recovered from the hands of healthcare workers more effectively than did handwashing with soap and water.[143-145]

The effectiveness of alcohols for pre-operative cleaning of the hands of surgical personnel has been addressed in numerous studies.[1,100,103,112-118,131,133,137,146-149] In many of these studies, bacterial counts on the hands were determined immediately after using the product and again 1 to 3 hr later. The delayed testing is performed to determine if regrowth of bacteria on the hands is inhibited during operative procedures. The relative efficacy of plain soap, antimicrobial soaps, and alcohol-based solutions to reduce the number of bacteria recovered from hands immediately after use is shown in Table 2. Alcohol-based solutions were more effective than washing hands with plain soap in all studies, and were more effective than antimicrobial soaps or detergents in most experiments.[100,103,112-118,131,133,137,147-149] Table 3 shows the $\log_{10}$ reductions in the release of resident skin flora from clean hands immediately and 3 hr after use of surgical handrub products. Alcohol-based preparations proved more effective than plain soap and water and, with most formulations, were superior to povidone-iodine or chlorhexidine.

The efficacy of alcohol-based hand hygiene products is affected by a number of factors, including the type of alcohol used, the concentration of alcohol, the contact time, the volume of alcohol used, and whether the hands are wet when the alcohol is applied. Small volumes (0.2 – 0.5 ml) of alcohol applied to the hands are not more effective than washing hands with soap and water.[62,63] Larson et al.[90] documented that 1 ml of alcohol was significantly less effective than 3 ml. Because alcohol-impregnated towelettes contain a small amount of alcohol, they are not much more effective than washing with soap and water.[62,150,151]

Alcohol-based waterless antiseptics intended for use in hospitals are available as rinses (with low viscosity), gels, and foams. Few data are available regarding the relative efficacy of various formulations. One small field trial found that an ethanol gel was somewhat more effective than a comparable ethanol solution at reducing bacterial counts on the hands of healthcare workers.[152] However, further studies are warranted to determine the relative efficacy of alcohol-based rinses and gels.

Frequent use of alcohol-based formulations for hand antisepsis tends to cause drying of the skin unless emollients, humectants, or other skin conditioning agents are added to the formulations. For example, the drying effect of alcohol can be reduced or eliminated by adding 1% to 3% glycerol or other skin conditioning agents.[89,92,99,100,105,131,133,153,154] Recently, several prospective trials have demonstrated that alcohol-based rinses or gels containing emollients may cause less skin irritation and dryness than do commonly used detergents.[95,97,155,156] These studies, which were conducted in clinical settings, used a variety of subjective and objective methods for assessing skin irritation and dryness. Importantly, despite the fact that different commercially available products were tested, the alcohol-based handrub in each trial caused significantly less skin irritation and dryness than did washing hands with soap and water.

Even well-tolerated alcohol handrubs containing emollients may cause a transient stinging sensation at the site of any broken skin (cuts, abrasions). Alcohol handrub preparations with strong fragrances may be poorly tolerated by a few healthcare workers with respiratory allergies. Allergic contact dermatitis or contact urticaria syndrome caused by hypersensitivity to alcohol, or to various additives present in some alcohol handrubs, occurs rarely.[157,158] Alcohols are flammable and require that products be stored away from high temperatures or flames. Because alcohols are volatile, containers should be designed so that evaporation is minimized. Contamination of alcohol-based solutions has seldom been reported. One report documented a pseudoepidemic of infections due to contamination of ethyl alcohol by *Bacillus cereus* spores.[159]

9.3. Chlorhexidine

Chlorhexidine gluconate, a cationic bisbiguanide, was developed in England in the early 1950s and introduced into the United States in the 1970s.[8,160] Chlorhexidine base is barely soluble in water, but the digluconate form is water-soluble. The antimicrobial activity of chlorhexidine appears to be attributable to attachment to, and subsequent disruption of cytoplasmic membranes, resulting in precipitation of cellular contents.[1,8] Chlorhexidine's immediate antimicrobial activity is slower than that of alcohols. Chlorhexidine has good activity against gram-positive bacteria, somewhat less activity against gram-negative bacteria and fungi, and minimal activity against tubercle bacilli.[1,8,160] Chlorhexidine is not sporocidal.[1,160] It has in vitro activity against enveloped viruses such as herpes simplex virus, HIV, cytomegalovirus, influenza and respiratory syncytial virus, but significantly less activity against non-enveloped viruses such as rotavirus, adenovirus and enteroviruses.[128,129,161] The antimicrobial activity of chlorhexidine is not seriously affected by the presence or organic material, including blood. Because chlorhexidine is a cationic molecule, its activity can be reduced by natural soaps, various inorganic anions, non-ionic surfactants, and hand creams containing anionic emulsifying agents.[8,160,162] 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 are less effective than antiseptic detergent preparations containing 4% chlorhexidine gluconate.[131,163] Preparations with 2% chlorhexidine gluconate are slightly less effective than those containing 4% chlorhexidine.[164]

Chlorhexidine has significant residual activity.[105,113-115,117,131,136,163] Addition of low concentrations (0.5 to 1%) of chlorhexidine to alcohol-based preparations results in significantly greater residual activity than alcohol alone.[115,131] When used as recommended, chlorhexidine has an excellent safety record.[160] Little, if any, absorption of the compound occurs through the skin. Care must be taken to avoid contact with the eyes when using preparations with 1% chlorhexidine or greater as the agent can cause conjunctivitis. The frequency of skin irritation is concentration-dependent, with products containing 4% most likely to cause dermatitis when used frequently for antiseptic handwashing.[165] True allergic reactions to chlorhexidine gluconate are very uncommon.[117,160]

9.4. Hexachlorophene

Hexachlorophene is a bisphenol composed of two phenolic groups and 3 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 is related to 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.[53,133,166] Hexachlorophene has residual activity for several hours after use and gradually reduces bacterial counts on hands after multiple uses (cumulative effect).[1,100,166,167] In fact, 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 to 0.6 ppm hexachlorophene.[168] In the early 1970s, infants bathed with hexachlorophene sometimes developed neurotoxicity (vacuolar degeneration).[169] As a result, in 1972, the Food and Drug Administration 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, a number of investigators noted that the incidence of healthcare-acquired *S. aureus* infections in hospital nurseries increased substantially.[170,171] In several instances, the frequency of infections decreased when hexachlorophene bathing of infants was reinstituted. However, current guidelines recommend against routine bathing of neonates with hexachlorophene because of its potential neurotoxic effects.[172] Hexachlorophene should not be used to bathe patients with burns or extensive areas of abnormal, sensitive skin. Soaps containing 3% hexachlorophene are available by prescription only.[7]

9.5. Iodine and iodophors

Iodine has been recognized as an effective antiseptic since the 1800s. However, because iodine often causes irritation and discoloring of skin, pain when applied to open wounds, and allergic reactions, 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.[173] Iodophors are composed of elemental iodine, iodide or triiodide, and a polymer carrier (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.[174] Typical 10% povidone-iodine formulations contain 1% available iodine, and yield free iodine concentrations of 1 ppm.[174] 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 (povidone) and ethoxylated nonionic detergents (poloxamers).[173,174] 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 some spore-forming bacteria and are active against mycobacteria, viruses, and fungi.[8,173,175-178] In vivo studies have demonstrated that iodophors reduce the number of viable organisms that may be recovered from the hands of personnel.[112,135,138,142,145] The extent to which iodophors exhibit persistent antimicrobial activity once they have been washed off the skin is a matter of some controversy. In several studies, persistent activity was found 30 to 60 min after washing hands with an iodophor.[60,116,179] However, in studies where bacterial counts were obtained after individuals wore gloves for 1 to 4 hr after washing, iodophors demonstrated poor persistent activity.[1,103,114,167,180-185] The in vivo antimicrobial activity of iodophors is significantly reduced in the presence of organic substances such as blood or sputum.[8]

Most iodophor preparations used for hand hygiene contain 7.5% to 10% povidone-iodine. However, formulations with lower concentrations also have good antimicrobial activity because dilution tends to increase free iodine concentrations.[186] Iodophors cause less skin irritation and fewer allergic reactions than iodine, but more irritant contact dermatitis than other antiseptics commonly used for hand hygiene.[91] 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.[174]

9.6. Para-chloro-meta-xylenol (PCMX)

PCMX is a halogen-substituted phenolic compound that has been used widely as a preservative in cosmetics and other products and as an active agent in antimicrobial soaps. It was developed in Europe in the late 1920’s and has been used in the United States since the 1950s.[187]

The antimicrobial activity of PCMX is apparently due 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 some viruses.[1,7,187] PCMX is less active against *P. aeruginosa*, but addition of ethylene-diaminetetraacetic acid (EDTA) increases its activity against *Pseudomonas* spp. and other pathogens.

Relatively few articles dealing with the efficacy of PCMX-containing preparations intended for use by healthcare personnel have been published in the last 25 years, and the results of studies have sometimes been contradictory. For example, in experiments where antiseptics were applied to abdominal skin, Davies et al. found that PCMX had the weakest immediate and residual activity of any of the agents studied.[188] However, when 30-sec hand washes 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/day for 5 days, PCMX had less cumulative activity than did chlorhexidine gluconate.[189] When PCMX was used as a surgical scrub, Soulsby et al.[190] reported that 3% PCMX had immediate and residual activity comparable to 4% chlorhexidine gluconate, while two other studies found that the immediate and residual activity of PCMX was inferior to both chlorhexidine gluconate and povidone-iodine.[164,191] The disparity between published studies may be due in part to the various concentrations of PCMX included in the preparations evaluated, and to other aspects of the formulations tested, including the presence or absence of EDTA.[7,187] Larson concluded that PCMX is not as rapidly active as chlorhexidine gluconate or iodophors, and that its residual activity is less pronounced than that observed with chlorhexidine gluconate.[7,187]

The antimicrobial activity of PCMX is minimally affected by the presence of organic matter, but is neutralized by non-ionic surfactants. Although PCMX is absorbed through the skin, it appears to be safe.[7,187] PCMX is generally well-tolerated, and allergic reactions are relatively uncommon. PCMX is available in concentrations ranging from 0.5% to 3.75%. In-use contamination of a PCMX-containing preparation has been reported.[192]

9.7. Quaternary ammonium compounds

Quaternary ammonium compounds are composed of a nitrogen atom linked directly to four alkyl groups, which may vary considerably in their structure and complexity.[193] Of this large group of compounds, alkyl benzalkonium chlorides have been the most widely used as antiseptics. Other compounds that have been used as antiseptics include benzathonium 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 pre-operative cleaning of surgeons' hands was used as early as 1935.[193] The antimicrobial activity of this group of compounds appears to be due to adsorption to the cytoplasmic membrane, with subsequent leakage of low molecular weight cytoplasmic constituents.[193]

Quaternary ammonium compounds are primarily bacteriostatic and fungistatic, although they are microbicidal against some organisms at high concentrations.[1] 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.[1,193]

In general, quaternary ammonium compounds are relatively well tolerated. Unfortunately, because of weak activity against gram-negative bacteria, benzalkonium chloride is prone to contamination by these organisms. A number of outbreaks of infection or pseudoinfection have been traced to quaternary ammonium compounds contaminated with gram-negative bacilli.[194-196] For this reason, in the United States, these compounds were seldom used for hand antisepsis during the last 15-20 years. However, newer handwashing products containing benzalkonium chloride or benzathonium chloride have recently been introduced for use by healthcare workers. Further experience with such products is necessary to determine if newer formulations are less prone to contamination.

9.8. 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 healthcare personnel and the public, and into a variety of other consumer products. Concentrations ranging from 0.2% to 2% have antimicrobial activity. Triclosan enters bacterial cells and affects the cytoplasmic membrane and synthesis of RNA, fatty acids, and proteins.[197] Recent studies suggest that this agent's antibacterial activity is due in large part to binding to the active site of enoyl-acyl carrier protein reductase.[198,199] 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. Of additional concern, exposing

Pseudomonas strains containing the MexAB-OprM efflux system to triclosan may select for mutants that are resistant to multiple antibiotics, including fluoroquinolones.[200].

Triclosan has a fairly broad range of antimicrobial activity, but tends to be bacteriostatic.[1] Minimum inhibitory concentrations range from 0.1 to 10 ug/ml, while minimum bactericidal concentrations are 25 to 500 ug/ml. Triclosan's activity against gram-positive organisms (including MRSA) is greater than against gram-negative bacilli, particularly *P. aeruginosa*.[1,197] The agent possesses reasonable activity against mycobacterial and *Candida* spp., but has little activity against filamentous fungi. Triclosan (0.1%) reduces bacterial counts on hands by 2.8 $\log_{10}$ after a one-minute hygienic hand wash.[1] In a number of studies, log reductions achieved have been lower than with chlorhexidine, iodophors, or alcohol-based products.[1,60,139,189,201] Like chlorhexidine, triclosan has persistent activity on the skin. Its activity in handcare products is affected by pH, the presence of surfactants, emollients, or humectants; and the ionic nature of the particular formulation.[1,197] Triclosan's activity is not substantially affected by organic matter, but may be inhibited by sequestration of the agent in micelle structures formed by surfactants present in some formulations. Most formulations containing less than 2% triclosan are well-tolerated and seldom cause allergic reactions. A few reports suggest that providing hospital personnel with a triclosan-containing preparation for hand antisepsis has led to decreased infections caused by MRSA.[71,72] Triclosan's lack of potent activity against gram-negative bacilli has resulted in occasional reports of contaminated triclosan.[202]

9.9. Others agents

More than 100 years after Semmelweis demonstrated the impact of rinsing hands with a hypochlorite solution on maternal mortality related to puerperal fever, Lowbury et al.[203] studied the efficacy of rubbing hands for 30 sec with an aqueous hypochlorite solution. They found that the solution was not more effective than rinsing with distilled water. Rotter[204] subsequently studied the regimen used by Semmelweis, which called for rubbing hands with a 4% [w/w] hypochlorite solution until the hands were slippery (approx. 5 min). He found that the regimen was 30 times more effective than a 1-min rub using 60% isopropanol. However, because hypochlorite solutions tend to be very irritating to the skin when used repeatedly and have a strong odor, they are seldom used for hand hygiene today.

In addition to the antiseptic preparations listed above, products that utilize 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 healthcare personnel. For example, preliminary studies have demonstrated that adding silver-containing polymers to an ethanol carrier (Surfacine) results in a preparation that has persistent antimicrobial activity on animal and human skin.[205] 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 personnel.

9.10. 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 (surgical scrub) with an antiseptic detergent or a waterless antiseptic agent has been an accepted practice.[206] Although there are no randomized controlled trials demonstrating that surgical site infection rates are signficantly lower when preoperative scrubbing is performed with an antiseptic agent rather than a non-antimicrobial soap, a number of factors provide a strong rationale for this practice. There is compelling evidence that bacteria on the hands of surgeons may cause wound infections if introduced into the operative field during surgery.[207] Rapid multiplication of skin bacteria occurs under surgical gloves if hands are washed with a non-antimicrobial soap, whereas bacterial growth occurs more slowly following preoperative scrubbing with an antiseptic agent.[14,208] 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.[1,146,209]. Finally, at least one outbreak of surgical site infections occurred when surgeons who normally used an antiseptic surgical scrub preparation switched to a non-antimicrobial product.[210]

Antiseptic preparations intended for use as surgical scrubs are evaluated for their ability to reduce the number of bacteria released from hands (a) immediately after scrubbing, (b) after wearing surgical gloves for one to 6 hrs (persistent activity), and (c) after multiple applications over 5 days (cumulative activity). Immediate and persistent activity are considered the most important. Current guidelines in the United States recommend that agents used for surgical scrubs should significantly reduce microorganisms on intact skin, contain a non-irritating antimicrobial preparation, have broad-spectrum activity, and be fast-acting and/or have a persistent effect.[211]

Numerous studies have demonstrated that formulations containing 50% - 95% alcohol, either alone or combined with small amounts of hexachlorophene or chlorhexidine gluconate, lower bacterial counts on the skin immediately post-scrub more effectively than do other agents (Table 2). The next most active agents (in order of decreasing activity) are chlorhexidine gluconate, iodophors, triclosan, and plain soap.[103,118,166,180,181,183,185,191,212] 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 to that of the above agents.[164,190,191]

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 to 6 hr seldom exceed baseline (pre-scrub) values.[1] Alcohol-based preparations containing 0.5% chlorhexidine gluconate have persistent activity that, in some studies, has equaled or exceeded that of chlorhexidine gluconate-containing detergents.[1,117,131].

Persistent antimicrobial activity of detergent-based surgical scrub formulations is generally greatest for those containing 2% or 4% chlorhexidine gluconate, followed by hexachlorophene, triclosan, and iodophors.[1,101,112-114,149,167,180,181,183-185,212] Because hexachlorophene is absorbed into the blood after repeated use, it is seldom used as a surgical scrub.

For many years, surgical staff frequently scrubbed their hands for 10 min pre-operatively, which frequently led to skin damage. Several studies have demonstrated that scrubbing for 5 min reduces bacterial counts as effectively as a 10-min scrub.[116,213,214] In other studies, scrubbing for 2 or 3 min reduced bacterial counts to acceptable levels.[146,182,184,215,216]

A few studies have suggested that two-stage surgical scrubs utilizing an antiseptic detergent, followed by application of an alcohol-containing preparation, is effective. For example, an initial 1-min or 2-min scrub with 4% chlorhexidine gluconate or povidone-iodine followed by application of an alcohol-based product was as effective as a 5-min scrub with an antiseptic detergent.[113,217]

For many years, preoperative handwashing protocols required personnel to scrub with a brush. However, this practice may damage the skin of personnel and can result in increased shedding of bacteria from the hands.[94,218] Scrubbing with a disposable sponge or combination sponge-brush has been shown to reduce bacterial counts on the hands as effectively as scrubbing with a brush.[219-221] However, several studies suggest 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.[101,116,149,155,208,222-224]

9.11. Relative efficacy of plain soap, antiseptic soap/detergent, and alcohols

Comparing studies dealing with the in vivo efficacy of plain soap, antimicrobial soaps, and waterless antiseptic agents is problematic because some studies express efficacy as the percent reduction in bacterial counts achieved, while others give $\log_{10}$ reductions in counts achieved. However, summarizing the relative efficacy of agents tested in each study can provide a useful overview of the *in vivo* activity of various formulations intended for handwashing, hygienic hand wash, antiseptic handrub, or surgical hand antisepsis (see Tables 1-3).

10. Irritant Contact Dermatitis due to Hand Hygiene

10.1 Frequency and pathophysiology of irritant contact dermatitiis

In some surveys, about 25% of nurses have reported symptoms or signs of dermatitis involving their hands, and as many as 85% give a history of having skin problems.[225] Frequent and repeated use of hand hygiene products, particularly soaps and other detergents, is an important cause of chronic irritant contact dermatitis among health personnel.[226] 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.[226,227] Damage to the skin also changes skin flora, resulting in more frequent colonization by staphylococci and gram-negative bacilli.[17,89] Although alcohols are among the safest antiseptics available, they can cause dryness and irritation of the skin.[1,228] Ethanol tends to be less irritating than n-propanol or isopropanol.[228]

In general, dermatitis is more commonly reported with iodophors.[91] Other antiseptic agents that may cause dermatitis, in order of decreasing frequency, include chlorhexidine, PCMX, triclosan, and alcohol-based products. The irritancy potential of commercially prepared hand hygiene products, which is often determined by measuring transepidermal water loss of persons using the preparation, may be available from the manufacturer. Other factors that may 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 perhaps the quality of paper towels.[229,230] Shear forces associated with wearing or removing gloves and allergy to latex proteins may also contribute to dermatitis of the hands of healthcare personnel.

10.2 Proposed methods for reducing adverse effects of agents

Potential strategies for minimizing hand hygiene-related irritant contact dermatitis among healthcare workers 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 about the risks of irritant contact dermatitis, and providing care givers with moisturizing skin care products or barrier creams.[95,97,227,231-233] Reducing the frequency of exposure of healthcare personnel to hand hygiene products would prove difficult, and it is not desirable, given the low levels of adherence to hand hygiene policies in most institutions. Although many hospitals have provided personnel with “mild”, non-antimicrobial soaps in hopes of minimizing dermatitis, frequent use of such products may cause greater skin damage, dryness and irritation than some antiseptic preparations.[91,95,97] One strategy for reducing the exposure of personnel to irritating soaps and detergents is to promote the use of waterless antiseptic agents containing alcohol and various emollients. Several recent prospective, randomized trials have demonstrated that alcohol-based handrubs containing emollients were tolerated better by healthcare personnel than was washing hands with non-antimicrobial soaps or with an antimicrobial soap.[95,97,156] Routinely washing hands with soap and water immediately after using an alcohol handrub may lead to dermatitis. For this reason, personnel should be reminded that it is neither necessary nor recommended to routinely wash hands after each application of an alcohol handrub.

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.[227,231] Several controlled trials have shown that regular use (e.g., twice/day) of such products can help prevent (and treat) irritant contact dermatitis caused by hand hygiene products.[232,233] Importantly, in the trial by McCormick et al.,[233] improved skin condition resulting from frequent and scheduled use of an oil-containing lotion led to a 50% increase in handwashing frequency among healthcare workers. The investigators who conducted these trials emphasized 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. Of interest, two recent randomized, controlled trials that evaluated skin condition of care givers found that barrier creams did not yield better results that did the control lotion or vehicle utilized.[232,233] As a result, the role of barrier creams in preventing irritant contact dermatitis among healthcare workers remains to be defined.

In addition to evaluating the efficacy and acceptibility 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.[8,212]

Factors to Consider When Selecting Hand Hygiene Products

When evaluating hand hygiene products for potential use in healthcare facilities, administrators or product selection committees need to consider numerous factors that can affect the overall efficacy of such products. These include the relative efficacy of antiseptic agents against various pathogens (see Appendix for brief summary), and acceptance of hand hygiene products by personnel.[234,235] Soap products that are not well-accepted by nurses can be an important deterrent to frequent handwashing.[236] Characteristics of a product (either soap or alcohol handrub) that can affect acceptance by personnel include its smell, consistency (feel), and color.[91,237,238] For soaps, ease of lathering also may affect user preference.

Because healthcare workers may wash their hands from a few times per shift to as many as 40 to 50 times per shift, the tendency of products to cause skin irritation and dryness is a major factor that influences acceptance, and ultimate usage, by healthcare personnel.[60,97,234,235,237,239] For example, concern about the drying effects of alcohol was a major cause of poor acceptance of alcohol-based hand hygiene products in hospitals in the United States.[5,133] However, a number of studies have shown that alcohol-based handrubs containing emollients are acceptable to healthcare workers.[89,92,97,99,100,105,133,153,154,156] With alcohol-based products, the time required for drying may also affect user acceptance.

Several studies suggest that the frequency of handwashing or antiseptic handwashing by personnel is affected by how accessible hand hygiene facilities are.[240-243] In some healthcare 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 such as ventilators or intravenous infusion pumps. In contrast to sinks used for handwashing or antiseptic handwash, dispensers for alcohol-based handrubs 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 handrub solutions together with availability of bedside dispensers has been associated with significant improvement in adherence of personnel to hand hygiene protocols.[73,244] In order to avoid any confusion between soap and alcohol handrubs, alcohol handrub dispensers preferably should not be placed adjacent to sinks. Inservice programs for personnel should comment on the fact that washing hands with soap and water after each use of an alcohol handrub is not necessary and is not recommended because it may lead to dermatitis. However, because some 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 some manufacturers. Automated handwashing machines have been tested by several investigators, usually for the purpose of improving the quality or the frequency of handwashing, but have not been proven to improve hand hygiene practices.[87,245]

Dispenser systems provided by manufacturers or vendors also need to be considered when evaluating hand hygiene products. Dispensers that become blocked or partially blocked and do not deliver the product when accessed by personnel, or do not deliver the product onto the individual's hand appropriately, may discourage use by health personnel. In one recent survey, only 50% of dispensers delivered product onto the care givers' hands with one press of the dispenser lever, and 10% of dispensers were totally occluded (Boyce JM, SHEA Hand Hygiene Workshop, Atlanta). In addition, the volume delivered was often suboptimal, and the product was sometimes squirted onto the wall instead of the care giver's hand.

Little published information is available regarding the cost of hand hygiene products used in healthcare facilities.[155,246] Boyce[246] recently evaluated these costs in patient care areas at a 450-bed community-teaching hospital and found that the hospital spent $22,000 ($0.72 per patient-day) on 2% chlorhexidine-containing preparations, plain soap, and an alcohol hand rinse. 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 (about $1 per patient-day). Annual hand hygiene product budgets at other institutions vary considerably, due to differences in usage patterns and varying product prices. Boyce[246] determined that if non-antimicrobial liquid soap was assigned arbitrarily relative cost of 1.0, the cost per liter was 1.7 times as much for 2% chlorhexidine gluconate detergent, 1.6 to 2.0 times higher for alcohol-based handrub 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 handrub revealed that costs and time required for preoperative scrubbing were less with the alcohol-based product.[155] In a trial conducted in two critical care units, Larson et al.[156] found that the cost of using an alcohol handrub was half as much as using an antimicrobial soap for handwashing ($0.025 vs $0.05 per application, respectively).

To put expenditures for hand hygiene products into perspective, healthcare facilities should consider comparing their budget for hand hygiene products to estimated excess hospital costs associated with healthcare-acquired infections. The excess hospital costs associated with only four or five healthcare-acquired 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 infection, or bloodstream infection may cost the hospital more than the entire annual budget for antiseptic agents used for hand hygiene.[246] Two studies provided some quantitative estimates of the benefit of hand hygiene promotion programs.[71,73] Webster and colleagues[71] reported a cost saving of approximately $17,000 resulting from reduced use of vancomycin following the observed decrease in MRSA incidence in a 7-month period. Including both direct costs associated with the intervention (increased use of handrub solution and poster reproduction and implementation) and indirect costs associated with healthcare personnel time, Pittet and colleagues[73] estimated the costs of the program to be less than $57,000 per year, an average of $1.42 per patient admitted. Supplementary costs associated with the increased use of alcohol-based handrub solution averaged $6.07 per 100 patient-days. Based on conservative estimates of $2,100 saved per infection averted, and assuming that only 25% of the observed reduction in the infection rate has been associated with improved hand hygiene practice, the program was largely cost-effective. Thus, hospital administrators need to consider the fact if purchasing more effective or more acceptable hand hygiene products improves hand hygiene practices, preventing only a few additional healthcare-acquired infections per year will lead to savings that will exceed any incremental costs of better hand hygiene products.

12. Hand Hygiene Practices Among HCWs

In observational studies conducted in hospitals, healthcare workers washed their hands an average of 5 times per shift to as much as 30 times per shift (Table 4).[17,60,89,97,234,247] Some nurses may wash their hands up to 100 times per shift.[89] Hospital-wide surveillance of hand hygiene revealed that the average number of opportunities varies markedly between hospital wards; for example, nurses in pediatric wards had an average number of 8 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 hand wash episodes by healthcare personnel has averaged from as low as 6.6 sec to 21 sec in observational studies (Table 5).[17,52,58,83-86,88,225,239] In addition to washing their hands for very short time periods, personnel often fail to cover all surfaces of their hands and fingers.[247]

13. Adherence of healthcare workers to recommended hand hygiene practices

13.1 Observational studies of hand hygiene adherence

Adherence of healthcare workers to recommended hand hygiene procedures has been unacceptably poor, with mean baseline rates ranging from 5% to 81%, with an overall average of about 40% (Table 6).[70,73,80,85,86,236,240,241,243,245,248-271] It should be pointed out that the methods for defining adherence (or non-adherence) and the methods for conducting observations varied considerably among reported studies, and many articles did not include detailed information about the methods and criteria used. Most studies were conducted with hand hygiene adherence as the major outcome measure, while a few measured adherence as part of a broader investigation. A number of investigators reported improved adherence after implementing various interventions, but most studies had short follow-up periods and did not establish if improvements were long-lasting. Studies by Pittet et al.[73] and Larson et al.[74] established that sustained improvements occurred during a long-term program to improve addherence to hand hygiene policies.

13.2 Factors affecting adherence

Factors that may influence hand hygiene include risk factors for non-adherence identified in epidemiologic studies, as well as reasons reported by healthcare workers 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.[11,12,234,251,254,272-275] Among these, being a physician or a nursing assistant, rather than a nurse, was almost consistently associated with reduced adherence. Table 7 lists the major factors identified in observational studies of hand hygiene behavior in the healthcare setting.

In the largest survey conducted so far,[11] the authors identified predictors of poor adherence to recommended hand hygiene measures during routine patient care using a hospital-wide survey. 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, non-adherence was lowest among nurses compared with other healthcare workers and during weekends (Odds Ratio [OR] 0.6, 95% confidence interval [CI_{95}] 0.4-0.8). It was higher in intensive care units compared with internal medicine (OR 2.0, CI_{95} 1.3-3.1) during procedures that carry a high risk of bacterial contamination (OR 1.8, CI_{95} 1.4-2.4), and when intensity of patient care was high (compared with 0-20 opportunities, 21-40 opportunities, OR 1.3, CI_{95} 1.0-1.7; 41-60 opportunities, OR 2.1, CI_{95} 1.5-2.9; >60 opportunities, OR 2.1, CI_{95} 1.3-3.5). In other words, 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 hr when the intensity of patient care exceeded 10 opportunities per hour. Similarly, the lowest adherence rate (36%) was found in intensive care units (ICUs) 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 where the average intensity of patient care was lower than elsewhere (on average, 8 opportunities per patient-hour). The results of this study suggest that full adherence to previous guidelines may be unrealistic, and that a facilitated access to hand hygiene could help improve adherence.[11,12,276]

Perceived barriers to adherence with hand hygiene practice recommendations include skin irritation caused by hand hygiene agents, inaccessible hand hygiene supplies, interference with healthcare worker-patient relation, patient needs perceived as a priority over hand hygiene, wearing of gloves, forgetfulness, lack of knowledge of guidelines, insufficient time for hand hygiene, high workload and understaffing, and the lack of scientific information showing a definitive impact of improved hand hygiene on healthcare-acquired infection rates.[11,234,251,254,273-275] Some of the perceived barriers to adherence with hand hygiene guidelines have been assessed, or quantified in observational studies.[12,234,251,254,272-275] Table 7 lists the most frequently reported reasons that are possibly, or effectively, associated with poor adherence. Some of these barriers are discussed below.

Skin irritation by hand hygiene agents constitutes an important barrier to appropriate adherence.[277] Because soaps and detergents can damage skin when applied on a regular basis, healthcare workers need to be better informed about the possible effects of hand hygiene agents. Lack of knowledge and education on this topic is a key barrier to motivation. In particular, it is extremely important to recall that (i) alcohol-based formulations for hand disinfection (whether isopropyl, ethyl, or n-propanol, in 60-90% vol/vol) are less irritating to skin than any antiseptic or nonantiseptic detergents; (ii) alcohols with the addition of appropriate emollients are at least as tolerable and efficacious as detergents; (iii) emollients on healthcare workers' hand skin are recommended and may even be protective against cross-infection by keeping the resident skin flora intact; and (iv) hand lotions help to protect skin and may reduce microbial shedding.[66,232,233]

Easy access to hand hygiene supplies, whether sink, soap, medicated detergent, or waterless alcohol-based handrub 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 antisepsis.[11,276] Engineering controls could facilitate adherence, but careful monitoring of hand hygiene behavior should be conducted to exclude the possible negative effect of newly introduced devices.[87]

The impact of wearing gloves on adherence to hand hygiene policies has not been definitively established, since published studies have yielded contradictory results.[86,249,260,278] It is important to recognize that 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 has to be regarded as nonadherence to hand hygiene recommendations.[11] Furthermore, Doebbeling and colleagues[279] concluded from their experimental conditions close to clinical practice that it may not be prudent to wash and reuse gloves between patient contact and hand washing or disinfection should be strongly encouraged after glove removal. The authors cultured the organisms used for artificial contamination from 4 to 100% of the gloves and observed counts between 0 and 4.7 log on the hands after glove removal.

Lack of knowledge of guidelines for hand hygiene, lack of recognition of hand hygiene opportunities during patient care, and lack of awareness of the risk of cross-transmission of pathogens are barriers to good hand hygiene practices. Furthermore, some healthcare workers believed that they washed their hands when necessary even when observations indicated they did not.[88,91,254,255,280]

Additional perceived barriers to hand hygiene behavior are listed in Table 7. These are linked not only to the institution but, also, to the healthcare worker's own particular group. Therefore, both institutional and small group dynamics need to be considered when implementing a system change to secure an improvement in healthcare workers' hand hygiene practice.

14. Possible Targets for Hand Hygiene Promotion

Targets for the promotion of hand hygiene are derived from studies assessing risk factors for non-adherence, reported reasons for the lack of adherence to recommendations, and additional factors perceived as important to facilitate appropriate healthcare worker behavior. Although some factors cannot be modified (Table 7), others are definitely amenable to change.

One factor that must be addressed is the time required for healthcare personnel to clean their hands. The results of the large, hospital-wide study on the epidemiology of hand hygiene adherence reported above[11] suggest that time required for traditional handwashing may make full adherence to previous guidelines unrealistic[11,12,276] and that more rapid access to hand hygiene could help improve adherence. One study conducted in an ICU found that it took nurses an average of 62 sec to leave a patient's bedside, walk to a sink, wash their hands, and return to patient care.[276] In contrast, the authors estimated it would require about one fourth as much time to use an alcohol-based handrub placed at each patient's bedside. Providing easy access to hand hygiene materials is mandatory for appropriate hand hygiene behavior, and should be achievable in most healthcare facilities.[281] In particular, in high demand situations (such as in most critical care units), in high stress working conditions, and at times of overcrowding or understaffing, healthcare workers may be more likely to use an alcohol-based handrub than to wash their hands.[281] Further, alcohol-based handrub may be superior to traditional handwashing with plain soap and water or antiseptic hand wash because it not only requires less time,[156,276] but acts faster,[1] irritates hands less often,[1,66,95,97,156] and was used in the only program that reported a sustained improvement in hand hygiene adherence associated with decreased infection rates.[73] However, it must be emphasized that making an alcohol-based handrub available to personnel without ongoing educational and motivational activities may not result in long-lasting improvement in hand hygiene practices.[271] Because increased use of hand hygiene agents might be associated with skin dryness, the availability of free skin care lotion is appropriate and recommended by most experts.

Education is as a cornerstone for improvement with hand hygiene practices. Important topics that must be addressed by educational programs are the lack of scientific information for the definitive impact of improved hand hygiene on healthcare-acquired infection and resistant organism(s) transmission rates, the lack of awareness of guidelines for hand hygiene and insufficient knowledge about indications for hand hygiene during daily patient care, the lack of knowledge about the very low average adherence rate to hand hygiene of most healthcare workers, and the lack of knowledge about the appropriateness, efficacy, and understanding of the use of hand hygiene and skin care protection agents.

Healthcare workers necessarily evolve within a group which functions within an institution. It appears that possible targets for improvement in hand hygiene behavior not only include factors linked to the individual, but also those related to the group(s) and the institution as a whole.[275,281] 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 role model from key staff in the unit. At the institutional level, the lack of written guidelines, available/suitable hand hygiene agents, skin care promotion/agent or hand hygiene facilities, the lack of culture or tradition of adherence as well as the lack of administrative leadership, sanction, rewarding, or support are targets for improvement. Several studies, conducted in different types of institutions, reported modest and even low levels of adherence to recommended hand hygiene practices and showed that it varied by hospital ward and by type of healthcare worker, thus suggesting that targeted educational programs may be useful.[11,248,249,253] Importantly, education should be targeted at individual, group, and institutional levels.[275,281]

15. Lessons from Behavioral Theories

In 1998, Kretzer and Larson[275] revisited the major behavioral theories and their applications with regard to the health professions in an attempt to better understand how to target more successful interventions. They 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.

Behavioral theories and secondary interventions have primarily targeted individuals. But this might be insufficient to effect sustained change.[275,282,283] Interventions aimed at improving hand hygiene practices must consider the various levels of behavior interaction.[12,275,284] Thus, the interdependence of individual factors, environmental constraints, and the institutional climate need to be taken into account in the strategic planning and development of hand hygiene promotion campaigns. Interventions to promote hand hygiene in hospitals should consider variables at all these levels.

The dynamic of behavioral change is complex.[74,281] It involves a combination of education, motivation, and system change. Various factors involved in hand hygiene behavior include intention, attitude towards the behavior, perceived social norm, perceived behavioral control, perceived risk of infection, habits of hand hygiene practices, perceived model role, perceived knowledge, and motivation; they have been discussed in the review by Kretzer and Larson.[275] The factors necessary for change include (i) dissatisfaction with the current situation, (ii) the perception of alternatives, and (iii) the recognition, both at the individual and institutional level, of one’s ability and potential to change. While the latter implies education and motivation, the former two necessitate primarily a system change.

Among the reported reasons for poor adherence with hand hygiene recommendations (Table 7), some are clearly related to the institution (i.e., the system) such as the lack of institutional priority for hand hygiene, the lack of administrative sanctions for noncompliers or rewards for compliers, and the lack of an institutional safety climate. Whereas all three reasons would require a system change in most institutions, the latter would also involve top management commitment, visible safety programs, an acceptable level of work stress, a tolerant and supportive attitude towards reported problems, and the belief in the efficacy of preventive strategies.[12,275,283,285] Importantly, an improvement in infection control practices requires (i) questioning basic beliefs; (ii) continuous assessment of the group (or individual) stage of behavioral change; (iii) intervention(s) with an appropriate process of change; and (iv) supporting individual and group creativity.[275] Because of the complexity of the process of change, it is not surprising that single interventions often fail. Thus, a multimodal, multidisciplinary strategy seems necessary.[73,74,275,281,284]

16. Methods Used to Promote Improved Hand Hygiene

Hand hygiene promotion has been a major challenge for more than 150 years. In-service education, information leaflets, workshops and lectures, automated dispensers, and performance feedback on hand hygiene adherence rates have been associated with, at best, transient improvement.[250,253-255,264,272]

Table 8 reviews published strategies for the promotion of hand hygiene in hospitals and indicates whether the strategies require education, motivation, or system change. Some of the strategies are based on epidemiologic evidence, others on the authors' and other investigators' experience and review of the current knowledge. Some 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 waterless handrub is not available.[11,72,77,286] However, a change in the recommended hand hygiene agent could be deleterious if introduced during winter, at a time of higher hand skin irritability, and in particular if not accompanied by skin care promotion and protective cream/lotion availability. Specific elements that should be considered for inclusion in educational and motivational programs are listed in Table 9.

Several strategies that could potentially be associated with successful promotion of hand hygiene require a system change (Table 8). 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 major challenges that go well beyond the current perception of the infection control professional's common role.

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,[12,275,287,288] or combinations of these factors would improve healthcare workers' adherence with hand hygiene needs more research. Ultimately, adherence to recommended hand hygiene practices should become part of a culture of patient safety where a set of interdependent elements of quality interact to achieve a shared objective.[289]

Based on the above considerations and successful experiences in some institutions, it appears that strategies to improve adherence to hand hygiene practices should be multimodal and multidisciplinary. It is important to note, however, that the strategies proposed in Table 8 need further research before implementation.

17. Efficacy of Promotion and Impact of Improved Hand Hygiene

The lack of scientific information of the definitive impact of improved hand hygiene on healthcare-acquired infection rates has been reported as a possible barrier to appropriate adherence with hand hygiene recommendations (Table 7). However, members of this Task Force believe that there is convincing evidence that improved hand hygiene can reduce healthcare-acquired infection rates. Failure to perform appropriate hand hygiene is considered the leading cause of healthcare-acquired infections and spread of multi-resistant organisms, and has been recognized as a significant contributor to outbreaks.

Nine quasi-experimental hospital-based studies of the impact of hand hygiene on the risk of healthcare-acquired infections have been published between 1977 and 2000 (Table 10).[48,68-74,255] Despite study limitations, most reports showed a temporal relation between improved hand hygiene practices and reduced infection rates.

In one of these studies, endemic MRSA was eliminated in 7 months in a neonatal ICU following the introduction of a new hand antiseptic.[71] Another study reported an MRSA outbreak involving 22 infants in a neonatal unit.[72] Despite intensive efforts, the outbreak could not be controlled until an antiseptic new to the unit was introduced.

The effectiveness of a longstanding, hospital-wide program to promote hand hygiene at the University of Geneva hospitals has been recently reported.[73] Overall adherence to hand hygiene guidelines during routine patient care was monitored during hospital-wide observational surveys conducted biannually from December 1994 to December 1997, before and during implementation of a hand hygiene campaign, with special emphasis on bedside, alcohol-based hand disinfection. Healthcare-acquired infection rates, attack rates of MRSA cross-transmission, and consumption of handrub disinfectant were measured in parallel. Adherence to recommended hand hygiene practices improved progressively from 48% in 1994 to 66% in 1997 ($p<0.001$). While recourse to handwashing with soap and water remained stable, frequency of hand disinfection markedly increased over the study period ($p<0.001$). This result was unchanged after adjustment for known risk factors of poor adherence. During the same period, both overall healthcare-acquired infection and MRSA transmission rates decreased (both $p<0.05$), and the consumption of alcohol-based handrub solution increased from 3.5 to 15.4 litres per 1000 patient-days between 1993 and 1998 ($p<0.001$). Individual bottles of handrub solution were distributed in large amount to all wards, and custom-made holders were mounted on all beds to facilitate access to hand disinfection. Healthcare workers were also encouraged to carry a bottle in their pocket, 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 healthcare workers, the use of wall posters, the promotion of bedside, antiseptic handrubs throughout the institution and regular performance feedback to all healthcare workers (see www.hopisafe.ch for further details on methodology). The experience from the University of Geneva hospitals constitutes the first report of a hand hygiene campaign with a sustained improvement over several years, since most experiences in the literature are limited to 6 to 9 months. The multimodal program implemented by Larson et al.[74] also yielded sustained improvements in hand hygiene practices over an extended period.

The beneficial effects of hand hygiene promotion on the risk of cross-transmission also have been reported in surveys conducted in schools or day care centers,[290-295] as well as in a community setting.[296-298] All studies in the literature fail to establish the relative importance of hand hygiene in the prevention of healthcare-acquired infections because they fail to show a causal relationship because of the lack of statistical significance, the presence of confounding factors, or the absence of randomization. Nevertheless, although it remains important to generate additional scientific and causal evidence for the impact of enhanced adherence with hand hygiene on infection rates, these results indicate that improved hand hygiene practices reduce the risk of transmission of pathogenic microorganisms.

18. Other Policies Related to Hand Hygiene

18.1. Fingernails and Artificial Nails

Numerous 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.[14,299,300] 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.[301,302] Even after careful handwashing or surgical scrubs, personnel often harbor substantial numbers of potential pathogens in the subungual spaces.[303-305]

Whether artificial nails contribute to transmission of healthcare-acquired infections has been a matter of debate for several years. However, a growing body of evidence suggests that wearing artificial nails may contribute to transmission of certain healthcare-acquired pathogens. Healthcare workers 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.[304-306] It is not clear if the length of natural or artificial nails is an important risk factor, since most bacterial growth occurs along the proximal 1 mm of the nail, adjacent to subungal skin.[302,304,305] 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.[307] Case patients were significantly more likely than controls to have been cared for by the two nurses during the exposure period, suggesting that colonization of long or artifical nails with *Pseudomonas* spp*.* may have had a role in causing the outbreak. Personnel wearing artificial nails also have been epidemiologically implicated in several other outbreaks of infection caused by gram-negative bacilli or yeast.[308-310] Although the above reports provide the best evidence to date that wearing artificial nails poses an infection hazard, additional studies of this issue are warranted.

18.2. Gloving policies

For many years, authorities have recommended that healthcare personnel wear gloves for three reasons: to reduce the risk of personnel acquiring infections from patients, to prevent healthcare worker flora from being transmitted to patients, and to reduce transient contamination of the hands of personnel by flora that can be transmitted from one patient to another.[311] Prior to the emergence of the 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 healthcare workers.[312] 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.[313]

The effectiveness of gloves in preventing contamination of healthcare worker hands has been confirmed in several clinical studies.[45,51,57] One study found that healthcare workers who wore gloves during patient contact contaminated their hands with an average of only 3 CFUs per minute of patient care, compared to 16 CFUs per minute for those not wearing gloves.[51] Two other studies, of personnel caring for patients with *C. difficile* or VRE, found that wearing gloves prevented hand contamination among a majority of those having direct contact with patients.[45,57] Wearing gloves also prevented personnel from acquiring VRE on their hands when touching contaminated environmental surfaces.[57] Preventing gross contamination of the hands is considered important because handwashing or hand antisepsis may not remove all potential pathogens when hands are heavily contaminated.[25,110]

Several studies provide evidence that wearing gloves can help reduce transmission of pathogens in healthcare 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/1000 patient discharges before the intervention to 1.5 cases/1000 discharges during the intervention.[314] The prevalence of asymptomatic *C. difficile* carriage also decreased significantly on "glove" wards, but not on control wards. In intensive care units where VRE or MRSA have been epidemic, requiring all healthcare workers to wear gloves to care for all patients in the unit (universal glove use) appeared to contribute to control of outbreaks.[157,196]

The influence of glove use on 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.[249,278] In contrast, two other studies found that personnel who wore gloves were significantly *more* likely to wash their hands following patient care.[86,260]

A few caveats regarding use of gloves by healthcare personnel are in order. 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 up to 30% of healthcare workers who wear gloves during patient contact.[50,57] Further, wearing gloves does not provide complete protection against acquisition of infections caused by hepatitis B virus and herpes simplex virus.[315,316] In such instances, pathogens presumably gain access to the care giver's hands via small defects in gloves or by contamination of the hands during glove removal.[50,279,315,317]

The integrity of gloves varies considerably based on type of glove material (latex, low-latex, non-latex), the manufacturer, whether gloves are tested before or after use, the intensity of use, and the method used to detect glove leaks.[315,317-322] Vinyl gloves have defects more frequently than do latex gloves, the difference being greatest after use.[315,317,320,323] However, vinyl gloves that are intact provide protection comparable to latex gloves.[315] Limited studies suggest that nitrile gloves have leakage rates that are close to those of latex gloves.[324-327] Although recent studies suggest improvements have been made in the quality of gloves,[322] the laboratory and clinical studies cited above provide strong evidence that hands should be decontaminated or washed after removing gloves.[8,50,57,279,317] Gloves should not be washed or reused.[279,317] Personnel should be reminded that failure to remove gloves between patients may contribute to transmission of organisms.[157,328]

Following use of powderless gloves, some alcohol handrubs may interact with residual powder, resulting in a gritty feeling on the hands. In facilities where powderless gloves are commonly used, a variety of alcohol handrubs should be tested following removal of powdered gloves in order to avoid selecting a product that causes this undesirable reaction.

18.3 Jewelry

Several studies have shown that skin underneath rings is more heavily colonized than comparable areas of skin on fingers without rings.[205,329,330] A study by Hoffman et al.[205] found that 40% of nurses harbored gram-negative bacilli such as *E. cloacae*, Klebsiella, and

Acinetobacter on skin under rings and that some nurses carried the same organism under their rings for months. In a more recent study involving more than 60 ICU nurses, multivariable analysis revealed that rings were the only significant 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 (RA Weinstein, personal communication) Whether the wearing of rings results in greater transmission of pathogens is not known. Two studies found that mean bacterial colony counts on hands after handwashing were similar among individuals wearing rings and those not wearing rings.[330,331] Further studies are needed to establish if wearing rings poses an increased risk of transmission of pathogens in healthcare settings.

19. Hand hygiene research agenda

Although the number of published studies dealing with 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. Table 11 lists a number of issues that should be addressed by researchers in industry and by clinical investigators.

Table 1. Studies comparing the relative efficacy (based on log_{10} reductions achieved) of plain soap or antimicrobial soaps versus alcohol-based antiseptics in reducing counts of viable bacteria on hands.

REF #	YEAR	SKIN CONTAMINATION	ASSAY METHOD	TIME (min)	RELATIVE EFFICACY
133	1965	existing hand flora	finger tip agar culture	60	plain soap < HCP < 50% EA foam
118	1975	existing hand flora	handrub broth culture	--	plain soap < 95% EA
105	1978	artificial contamination	finger tip broth culture	30	plain soap < 4% CHG < P-I < 70% EA = alc. CHG
134	1978	artificial contamination	finger tip broth culture	30	plain soap < 4% CHG < 70% EA
106	1979	existing hand flora	handrub broth culture	120	plain soap < 0.5% aq. CHG < 70% EA < 4% CHG < alc.CHG
135	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
107	1982	artificial contamination	glove juice test	15	P-I < alc. CHG
108	1983	artificial contamination	finger tip broth culture	120	0.3-2% triclosan = 60% IPA = alc. CHG < alc. triclosan
136	1984	artificial contamination	finger tip agar culture	60	phenolic < 4% CHG < P-I < EA < IPA < n-P
137	1985	existing hand flora	finger tip agar culture	60	plain soap < 70% EA < 95% EA
109	1986	artificial contamination	finger tip broth culture	60	phenolic = P-I < alc. CHG < n-P
92	1986	existing hand flora	sterile broth bag technique	15	plain soap < IPA < 4% CHG = IPA-E = alc. CHG
60	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
138	1991	existing hand flora	agar plate/image analysis	30	plain soap < 1% triclosan < P-I < 4% CHG < IPA
110	1992	artificial contamination	finger tip agar culture	60	plain soap < IPA < EA < alc. CHG
139	1992	artificial contamination	finger tip broth culture	60	plain soap < 60% n-P
111	1994	existing hand flora	agar plate/image analysis	30	plain soap < alc. CHG
140	1999	existing hand flora	agar plate culture	N.S.	plain soap < commercial alcohol mixture
141	1999	artificial contamination	glove juice test	20	plain soap < 0.6% PCMX < 65% EA
142	1999	artificial contamination	finger tip broth culture	30	4% CHG < plain soap < P-I < 70% EA

Existing hand flora = without artificially contaminatiing 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 = para-chloro-meta-xylenol detergent
P-I = povidone-iodine detergent
N.S. = not stated

Table 2. 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#	YEAR	ASSAY METHOD	RELATIVE EFFICACY
133	1965	Finger tip agar culture	HCP < 50% EA foam
147	1969	Finger tip agar culture	HCP < P-I < 50% EA foam
100	1973	Finger tip agar culture	HCP soap < EA foam + 0.23% HCP
131	1974	broth culture	plain soap < 0.5% CHG < 4% CHG < alc. CHG
118	1975	hand broth test	plain soap < 0.5% CHG < 4% CHG < alc. CHG
117	1976	glove juice test	0.5% CHG < 4% CHG < alc. CHG
113	1977	glove juice test	P-I < CHG < alc. CHG
116	1978	finger tip agar culture	P-I = 46% EA + 0.23% HCP
112	1979	broth culture of hands	plain soap < P-I < alc. CHG < alc. P-I
115	1979	glove juice test	70% IPA = alc. CHG
137	1985	finger tip agar culture	plain soap < 70% - 90% EA
114	1990	glove juice test, modified	plain soap < triclosan < CHG < P-I < alc. CHG
103	1991	glove juice test	plain soap < 2% triclosan < P-I < 70% IPA
148	1998	finger tip broth culture	70% IPA < 90% IPA = 60% n-P
149	1998	glove juice test	P-I < CHG < 70% EA

alc. CHG = alcoholic chlorhexidine gluconate
CHG = chlorhexidine gluconate detergent
EA = ethanol
HCP = hexachlorophene detergent
IPA = isopropanol
P-I = povidone-iodine detergent

Table 3. Efficacy of surgical handrub solutions in reducing the release of resident skin flora from clean hands (Rotter M[6]) Reprinted with permission.

STUDY	RUB	CONCENTRATION[a] (%)	TIME (min)	MEAN LOG REDUCTION	
				Immediate	Sustained (3hr)
1	n-Propanol	60	5	2.9[b]	1.6[b]
2			5	2.7[b]	NA
3			5	2.5[b]	1.8[b]
4			5	2.3[b]	1.6[b]
5			3	2.9[c]	NA
4			3	2.0[b]	1.0[b]
4			1	1.1[b]	0.5[b]
6	Isopropanol	90	3	2.4[c]	1.4[c]
6		80	3	2.3[c]	1.2[c]
7		70	5	2.4[b]	2.1[b]
4			5	2.1[b]	1.0[b]
6			3	2.0[c]	0.7[c]
5			3	1.7[c]	NA
4			3	1.5[b]	0.8[b]
8			2	1.2	0.8
4			1	0.7[b]	0.2
9			1	0.8	NA
10		60	5	1.7	1.0
7	Isopropanol + chlorhexidine gluc. (w/v)	70+ 0.5	5	2.5[b]	2.7[b]
8			2	1.0	1.5
11	Ethanol	95	2	2.1	NA
5		85	3	2.4[c]	NA
12		80	2	1.5	NA
8		70	2	1.0	0.6
13	Ethanol + chlorhexidine gluc. (w/v)	95+0.5	2	1.7	NA
14		77+0.5	5	2.0	1.5[d]
8		70+0.5	2	0.7	1.4
8	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[b]	0.8[b]
16	Peracetic acid (w/v)	0.5	5	1.9	NA

NA, not available
[a] volume/volume unless otherwise stated
[b] Tested according to Deutsche Gesellschaft fur Hygiene, and Mikrobiologic (DGHM)-German Society of Hygiene and Microbiology method
[c] Tested according to European Standard prEN
[d] After 4 h

Table 4. Handwashing frequency among healthcare workers.

REF #	YEAR	FREQUENCY OF HANDWASHING EPISODES		
		AVERAGE NO./ TIME PERIOD	RANGE	AVER. NO./HR.
60	1988	5/8 hr	N.S.	
88	1984	5-10/shift	N.S.	
95	2000	10/shift	N.S.	
233	2000	12-18/day	2-60	
97	2000	13-15/8 hr	5-27	1.6-1.8/hr
89	1977	20-42/8 hr	10-100	
332	2000	21/12 hr	N.S.	
232	2000	22/day	0-70	
87	1991			1.7-2.1/hr
17	1998			2.1/hr
239	1978			3/hr
333	1994			3.3/hr

N.S. = Not Stated

Table 5. Average duration of handwashing by healthcare workers.

REF #	YEAR	MEAN / MEDIAN TIME
334	1997	4.7 - 5.3 sec
333	1994	6.6 sec
52	1974	8 - 9.3 sec
84	1984	8.6 sec
85	1994	< 9 sec
86	1994	9.5 sec
87	1991	< 10 sec
253	1990	10 sec
88	1984	11.6 sec
259	1992	12.5 sec
58	1988	15.6 – 24.4 sec
17	1998	20.6 sec
239	1978	21 sec
252	1989	24 sec

Table 6. Handwashing adherence of healthcare workers.

REF #	YEAR	SETTING	BEFORE /AFTER CONTACT	ADHERENCE BASELINE	ADHERENCE AFTER INTERVENTION	INTERVENTION
240	1981	ICU	A	16%	30%	More convenient sink locations
248	1981	ICU	A	41%	--	
		ICU	A	28%	--	
249	1983	All wards	A	45%	--	
241	1986	SICU	A	51%	--	
		MICU	A	76%	--	
236	1986	ICU	A	63%	92%	Performance feedback
250	1987	PICU	A	31%	30%	Wearing overgown
251	1989	MICU	B/A	14%/28% *	73%/81%	Feedback, policy reviews, memo, posters
		MICU	B/A	26%/23%	38%/60%	
252	1989	NICU	A/B	75%/50%	--	
253	1990	ICU	A	32%	45%	Alcohol rub introduced
254	1990	ICU	A	81%	92%	Inservices first, then group feedback
255	1990	ICU		22%	30%	
256	1991	SICU	A	51%	--	
257	1991	Pedi OPDs	B	49%	49%	Signs, feedback, verbal reminders to physicians
258	1991	Nursery & NICU	B/A **	28%	63%	Feedback, dissemination of literature, results of environmental cultures
259	1992	NICU/ others	A	29%	--	
70	1992	ICU	N.S.	40%	--	
260	1993	ICUs	A	40%	--	
86	1994	Emerg Room	A	32%	--	
85	1994	All wards	A	32%	--	
245	1994	SICU	A	22%	38%	Automated HW machines available
261	1994	NICU	A	62%	60%	No gowning required
333	1994	ICUs Wards	A A	30% 29%	--	
263	1995	ICU Oncol Ward	A	56%	--	
335	1995	ICU	N.S.	5%	63%	Lectures, feedback, demonstrations
264	1996	PICU	B/A	12%/11%	68%/65%	Overt observation, followed by feedback
265	1996	MICU	A	41%	58%	Routine wearing of gowns and gloves
266	1996	Emerg Dept	A	54%	64%	Signs/distributed review paper
267	1998	All wards	A	30%	--	
268	1998	Pediatric wards	B/A	52%/49%	74%/69%	Feedback, movies, posters, brochures
336	1999	MICU	B/A	12%/55%	--	
73	2000	All wards	B/A	48%	67%	Posters, feedback, administrative support, alcohol rub
270	2000	MICU	A	42%	61%	Alcohol handrub made available
243	2000	MICU CTICU	B/A B/A	10%/22% 4%/13%	23%/48% 7%14%	Education, feedback, alcohol gel made available
271	2000	Medical wards	A	60%	52%	Education, reminders, alcohol gel made available

ICU = intensive care unit, SICU = surgical ICU, MICU = medical ICU, PICU = pediatric ICU, NICU = neonatal ICU, Emerg = emergency, Oncol = oncology, CTICU = cardiothoracic ICU

***** Percent compliance Before/After patient contact

** After contact with inanimate objects

Table 7. Factors influencing adherence to hand hygiene practices. *

A. 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 gender
Working in an intensive care unit
Working during the week (vs. week-end*)*
Wearing gowns/gloves
Automated sink
Activities with high risk of cross-transmission
High number of opportunities for hand hygiene per hour of patient care

B. Self-reported factors for poor adherence with hand hygiene

Handwashing agents cause irritations and dryness
Sinks are inconveniently located/shortage of sinks
Lack of soap, paper, towel
Often too busy/insufficient time
Understaffing/overcrowding
Patient needs take priority
Hand hygiene interferes with healthcare worker-patient relation
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 about the value of hand hygiene
Disagreement with the recommendations
Lack of scientific information of definitive impact of improved hand hygiene on healthcare-acquired infection rates

C. 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 non-compliers/rewarding of compliers
Lack of institutional safety climate

* Adapted from reference [281]

Table 8. Stategies for successful promotion of hand hygiene in hospitals.

Strategy	Tool for change*	Selected references†
1. Education	E (M, S)	73,254,264,284,337
2. Routine observation and feedback	S (E, M)	73,253,264,284,337
3. Engineering control		
Make hand hygiene possible;easy;convenient	S	73,241,284,337
Make alcohol-based handrub available	S	73
(at least in high-demand situations)	S	73,243,270
4. Patient education	S (M)	243,338
5. Reminders in the workplace	S	73,339
6. Administrative sanction/rewarding	S	12,275
7. Change in hand hygiene agent	S (E)	11,66,70,243,270
8. Promote/facilitate skin care for HCW hands	S (E)	66,73,234,235
9 . Obtain active participation at individual and institutional level	E, M, S	73,74,275
10. Improve institutional safety climate	S (M)	73,74,275
11. Enhance individual and institutitional self-efficacy	S (E, M)	73,74,275
12. Avoid overcrowding, understaffing, excessive workload	S	11,73,77,256,340
13. Combine several of above strategies	E, M, S	73,74,254,264,275,284

*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.[1,8,275,281,341]

Table 9. Elements of healthcare worker educational and motivational programs.

Rationale for hand hygiene, including:

a. potential risks of transmission of microorganisms to patients
b. potential risks of healthcare worker colonization or infection caused by organisms acquired from the patient
c. morbidity, mortality, and costs associated with healthcare-acquired infections

Indications for hand hygiene, including those patient contacts for which potential contamination is not readily apparent to the healthcare worker, such as:

a. 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]
b. contact with environmental surfaces in the immediate vicinity of patients[46,51,53,54]
c. following glove removal[50,57,70]

Techniques for hand hygiene, including:

a. amount of hand hygiene solution
b. duration of hand hygiene procedure
c. selection of hand hygiene agents
    1. Alcohol-based handrubs 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.[1,158]
    2. soap and water are recommended for visibly soil hands.
    3. waterless antiseptic agents 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:

a. lotions and creams can prevent or minimize skin dryness and irritation due to irritant contact dermatitis
b. acceptable lotions or creams to use
c. recommended schedule for applying lotions or creams

Expectations of patient care managers/administrators as evidenced by:

a. written statements regarding the value of, and support for, adherence to recommended hand hygiene practices
b. role models demonstrating adherence to recommended hand hygiene practices[342]

Indications for, and **limitations** of, glove use:

a. hand contamination may occur as a result of small, undetected holes in examination gloves[279,317]
b. contamination may occur during glove removal[50]
c. wearing gloves does not replace the need for hand hygiene[57]
d. failure to remove gloves after caring for a patient may lead to
e. transmission of microorganisms from one patient to another[328]

Table 10. Association between improved adherence with hand hygiene practice and healthcare-acquired infection rates.

Year	Authors	Hospital setting	Significant results	Duration of follow-up
1977	Casewell and Philips	Adult ICU	Reduction in healthcare-acquired infections due to endemic *Klebsiella* spp.	2 years
1982	Maki and Hecht	Adult ICU	Reduction in healthcare-acquired infection rates	N.S.
1984	Massanari and Heirholzer	Adult ICU	Reduction in healthcare-acquired infection rates	N.S.
1990	Simmons et al.	Adult ICU	No effect (Average hand hygiene adherence improvement did not reach statistical significance)	11 months
1992	Doebbeling et al.	Adult ICU	Significant difference between rates of healthcare-acquired infection between two different hand hygiene agents	8 months
1994	Webster et al.	NICU	Elimination of MRSA Reduction of vancomycin use	9 months
1995	Zafar et al.	Newborn nursery	Elimination of MRSA	3.5 years
2000	Larson et al.	MICU/NICU	Significant reduction of VRE rates in the intervention hospital	8 months
2000	Pittet et al.	Hospital-wide	Significant reduction in the annual overall prevalence of healthcare-acquired infections and MRSA cross-transmission rates	5 years

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

Table 11. Hand hygiene research agenda

Education and promotion

- Provide healthcare workers with better education regarding the types of patient care activities that can result in hand contamination and cross-transmission.
- Develop and implement promotion programs in pre-graduate 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 healthcare workers to clean their hands after every patient contact with the patient).
- Assess the key determinants of hand hygiene behavior and promotion among the different populations of healthcare workers.
- Develop methods to obtain top 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 hand hygiene agents.
- 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 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 eventual toxic impact of 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 healthcare 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.

PART II. RECOMMENDATIONS

These recommendations are designed to improve hand hygiene practices of healthcare workers and to reduce transmission of pathogenic microorganisms to patients and personnel in healthcare settings.

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 some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

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

Category II. Suggested for implementation and supported 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.

I. Indications for handwashing and hand antisepsis

A. Wash hands with a non-antimicrobial soap and water or an antimicrobial soap and water when hands are visibly dirty or contaminated with proteinaceous material. (IA) [65]
B. If hands are not visibly soiled, use an alcohol-based waterless antiseptic agent for routinely decontaminating hands in all other clinical situations described in items I.C. through I.K. listed below. (IA) [73,92,156,158,209,243,253,270]
C. On nursing units where an alcohol-based waterless antiseptic agent is available, provide personnel with a non-antimicrobial soap for use when hands are visibly dirty or contaminated with proteinaceous material. It is not necessary, and may be confusing to personnel, to have both an alcohol-based waterless antiseptic agent and an antimicrobial soap available on the same nursing unit. (II)
D. Although waterless antiseptic agents are highly preferable, hand antisepsis using an antimicrobial soap may be considered in settings where time constraints are not an issue and easy access to hand hygiene facilities can be ensured, or in rare instances when a care giver is intolerant of the waterless antiseptic product used in the institution. (IB)
E. Decontaminate hands after contact with a patient's intact skin (as in taking a pulse or blood pressure, or lifting a patient). (IB) [25,45,48,67]
F. Decontaminate hands after contact with body fluids or excretions, mucous membranes, non-intact skin, or wound dressings, as long as hands are not visibly soiled. (IA) [343]
G. Decontaminate hands if moving from a contaminated body site to a clean body site during patient care. (II) [25,53]
H. Decontaminate hands after contact with inanimate objects (including medical equipment) in the immediate vicinity of the patient. (II)[46,53,54]
I. Decontaminate hands <u>before</u> caring for patients with severe neutropenia or other

forms of severe immune suppression. (II)

J. Decontaminate hands before donning sterile gloves when inserting a central intravascular catheter. (IB)[344-348]
K. Decontaminate hands before inserting indwelling urinary catheters or other invasive devices that do not require a surgical procedure. (IB) [25]
L. Decontaminate hands after removing gloves. (IB)[50,57,70]
M. To improve hand hygiene adherence among personnel in units or instances where high workloads and high intensity of patient care are anticipated, make an alcohol-based waterless antiseptic agent 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 healthcare workers. (IA)[11,73,156,243,244,270,276]

II. Hand hygiene technique

A. When decontaminating hands with a waterless antiseptic agent such as an alcohol-based handrub, apply product to palm of one hand and rub hands together, covering all surfaces of hands and fingers, until hands are dry. (IB)[247,349] Follow the manufacturer's recommendations on the volume of product to use. If an adequate volume of an alcohol-based handrub is used, it should take 15 to 25 seconds for hands to dry.
B. When washing hands with a non-antimicrobial or antimicrobial soap, wet hands first with warm water, apply 3 to 5 ml of detergent to hands and rub hands together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers. Rinse hands with warm water and dry thoroughly with a disposable towel. Use towel to turn off the faucet. (IB)[89-91,93,350]

III. Surgical hand antisepsis

A. Surgical hand antisepsis, using either an alcohol-based handrub or an antimicrobial soap, is recommended before donning sterile gloves when performing surgical procedures. (IB)[114,207,210,224]
B. To reduce the number of bacteria that may be released from the hands of surgical personnel, while minimizing skin damage related to surgical hand antisepsis, decontaminate hands without using a brush. (IB) [94,114,116,149,218,222-224]

IV. Selection of hand hygiene agents

A. Provide personnel with efficacious hand hygiene products that have low irritancy potential, particularly when used multiple times per shift. (IB)[89,91,97,156,225]
B. To maximize acceptance of hand hygiene products by health personnel, solicit input from care givers 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)[91,92,156,234,236-238]
C. Prior to 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)
D. Do not add soap to a partially empty soap dispenser. This practice of "topping off" dispensers may lead to bacterial contamination of soap. (IA)[192,351]

V. Skin care

A. Provide healthcare workers with hand lotions or creams in order to minimize the occurrence of irritant contact dermatitis associated with hand antisepsis or handwashing. (IA)[232,233]
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)[162,269,352]

VI. Other Aspects of Hand Hygiene

A. Do not wear artificial fingernails or extenders when providing patient care. (IA)[307-310]
B. Keep natural nails less than ¼ inch long. (II)
C. Wear gloves when it can be reasonably anticipated that contact with blood or other potentially infectious materials, mucous membranes, and non-intact skin will occur. (IC)[313]
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 patients. (IB)[50,57,279,328]
E. Change gloves during patient care if moving from a contaminated body site to a clean body site. (II)[50,51,57]
F. No recommendation on wearing rings in healthcare settings. Unresolved issue.

VII. Healthcare worker educational and motivational programs

A. As part of an overall program to improve hand hygiene practices of healthcare workers, 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)[73,251,254,258] Include elements listed in Table 11.
B. Monitor healthcare workers' adherence with recommended hand hygiene practices and provide personnel with information regarding their performance. (IA)[73,236,251,254,258,264,268]
C. Encourage patients and their families to remind healthcare workers to decontaminate their hands. (II)[338,353]

VIII. Administrative measures

A. Make improved hand hygiene adherence an institutional priority and provide appropriate administrative support and financial resources. (IB) [73,74]
B. Implement a multidisciplinary program designed to improve adherence of health personnel to recommended hand hygiene practices. (IB)[73,74]
C. As part of a multidisciplinary program to improve hand hygiene adherence, provide healthcare workers with a readily accessible waterless antiseptic agent such as an alcohol-based handrub product. (IA)[73,156,243,253,270,354]

IX. Outcome or process measurements

A. Develop and implement a system for measuring improvements in adherence of healthcare workers to recommended hand hygiene practices. Examples are listed below.
   1. 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.
   2. Monitor the volume of alcohol-based handrub (or detergent used for handwashing or hand antisepsis) used/1000 patient-days.
   3. Monitor adherence to policies dealing with wearing of artificial nails.
   4. When outbreaks of infection occur, assess the adequacy of healthcare worker hand hygiene.

APPENDIX

Anti-microbial 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 60-90%; 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 non-ionic surfactants
Triclosan	+++	++	+	-	+++	intermediate	acceptability on hands varies
Quaternary ammonium compounds	+	++	-	-	+	slow	used only in combination with alcohols; ecologic concerns

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

REFERENCES

1. Rotter M. Hand washing and hand disinfection. In: Mayhall, C. G., eds. *Hospital epidemiology and Infection control*. Philadelphia: Lippincott Williams & Wilkins, 1999:1339-1355.
2. Labarraque A. G. The use of the chloride of soda and lime. Translated by Porter, J. New Haven, CT: Baldwin and Treadway, 1829:1-32.
3. Carter K. C. *Ignaz Semmelweis. The etiology, concept, and prophylaxis of childbed fever.* Madison: University of Wisconsin Press; 1983.
4. Coppage C. M. *Handwashing in patient care.* United States Public Health Service; Washington, D.C., 1961.
5. Steere A. C. and Mallison G. F. Handwashing practices for the prevention of nosocomial infections. Ann Intern Med 1975;83:683-690.
6. Garner J. S. and Favero M. S. CDC guideline for handwashing and hospital environmental control, 1985. Infect Control 1986;7:231-243.
7. Larson E. Guideline for use of topical antimicrobial agents. Am J Infect Control 1988;16:253-266.
8. Larson E. L. and APIC Guidelines Committee. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995;23:251-269.
9. Hospital Infection Control Practices Advisory Committee (HICPAC). Recommendations for preventing the spread of vancomycin resistance. Infect Control Hosp Epidemiol 1995;16:105-113.
10. Garner J. S. and Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. Infect Control Hosp Epidemiol 1996;17:53-80.
11. Pittet D., Mourouga P., Perneger T. V., and members of the Infection Control Program. Compliance with handwashing in a teaching hospital. Ann Intern Med 1999;130:126-130.
12. Boyce J. M. It is time for action: Improving hand hygiene in hospitals. Ann Intern Med 1999;130:153-155.
13. Selwyn S. Microbiology and ecology of human skin. The Practitioner 2000;224:1059-1062.
14. Price P. B. The bacteriology of normal skin: a new quantitative test applied to a study of the bacterial flora and the disinfectant action of mechanical cleansing. J Infect Dis 1938;63:301-318.
15. Larson E. Effects of handwashing agent, handwashing frequency, and clinical area on hand flora. Am J Infect Control 1984;11:76-82.
16. Maki D. Control of colonization and transmission of pathogenic bacteria in the hospital. Ann Intern Med 1978;89 (Part 2):777-780.
17. Larson E. L., Norton Hughes C. A., Pyrak J. D., Sparks S. M., Cagatay E. U., and Bartkus J. M. Changes in bacterial flora associated with skin damage on hands of health care personnel. Am J Infect Control 1998;26:513-521.
18. Sprunt K., Redman W., and Leidy G. Antibacterial effectiveness of routine hand washing. Pediatrics 1973;52:264-271.
19. Food and Drug Administration. Tentative final monograph for healthcare antiseptic drug products; proposed rule. Federal Register 1994;59:31441-31452.
20. Lowbury E. J. L. Gram-negative bacilli on the skin. Br J Dermatol 1969;81:55-61.
21. Noble W. C. Distribution of the Micrococcaceae. Br J Dermatol 1969;81:27-31.
22. McBride M. E., Duncan W. C., Bodey G. P., and McBride C. M. Microbial skin flora of selected cancer patients and hospital personnel. J Clin Microbiol 1976;3:14-20.
23. Casewell M. W. The role of hands in nosocomial gram-negative infection. In: Maibach, H. I. and Aly, R., eds. *Skin Microbiology Relevance to Clinical Infection*. New York: Springer-Verlag, 1981:192-202.
24. Larson E. L., McGinley K. J., Foglia A. R., Talbot G. H., and Leyden J. J. Composition and antimicrobic resistance of skin flora in hospitalized and healthy adults. J Clin Microbiol 1986;23:604-608.
25. Ehrenkranz N. J. and Alfonso B. C. Failure of bland soap handwash to prevent hand transfer of patient bacteria to urethral catheters. Infect Control Hosp Epidemiol 1991;12:654-662.
26. Sanderson P. J. and Weissler S. Recovery of coliforms from the hands of nurses and patients: activities leading to contamination. J Hosp Infect 1992;21:85-93.
27. Coello R., Jiminez J., Garcia M., Arroyo P., Minguez D., Fernandez C., Cruzet F., and Gaspar C. Prospective study of infection, colonization and carriage of methicillin-resistant *Staphylococcus aureus* in an outbreak affecting 990 patients. Eur J Clin Microbiol 1994;13:74-81.
28. Sanford M. D., Widmer A. F., Bale M. J., Jones R. N., and Wenzel R. P. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. Clin Infect Dis 1994;19:1123-1128.
29. Bertone S. A., Fisher M. C., and Mortensen J. E. Quantitative skin cultures at potential catheter sites in neonates. Infect Control Hosp Epidemiol 1994;15:315-318.
30. Bonten M. J. M., Hayden M. K., Nathan C., VanVoorhis J., Matushek M., Slaughter S., Rice T., and Weinstein R. A. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. Lancet 1996;348:1615-1619.
31. Larson E. L., Cronquist A. B., Whittier S., Lai L., Lyle C. T., and Della Latta P. Differences in skin flora between inpatients and chronically ill patients. Heart Lung 2000;29:298-305.
32. Polakoff S., Richards I. D. G., Parker M. T., and Lidwell O. M. Nasal and skin carriage of *Staphylococcus aureus* by patients undergoing surgical operation. J Hyg (Camb) 1967;65:559-566.
33. Leyden J. J., McGinley K. J., Nordstrom K. M., and Webster G. F. Skin microflora. J Invest Dermatol 1987;88:65s-72s.
34. Tuazon C. U., Perez A., Kishaba T., and Sheagren J. N. *Staphylococcus aureus* among insulin-injecting diabetic patients. JAMA 1975;231:1272-1272.
35. Kaplowitz L. G., Comstock J. A., Landwehr D. M., Dalton H. P., and Mayhall C. G. Prospective study of microbial colonization of the nose and skin and infection of the vascular access site in hemodialysis patients. J Clin Microbiol 1988;26:1257-1262.
36. Aly R., Maibach H. I., and Shinefield H. R. Microbial flora of atopic dermatitis. Arch Dermatol 1977;113:780-782.
37. Kirmani N., Tuazon C. U., Murray H. W., Parrish A. E., and Sheagren J. N. *Staphylococcus aureus* carriage rate of patients receiving long-term hemodialysis. Arch Intern Med 1978;138:1657-1659.
38. Goldblum S. E., Ulrich J. A., Goldman R. S., and Reed W. P. Nasal and cutaneous flora among hemodialysis patients and personnel: quantitative and qualitative characterization and patterns of staphylococcal carriage. Am J Kidney Dis 1982;11:281-286.
39. Boelaert J. R., Van Landuyt H. W., and Gordts B. Z. Nasal and cutaneous carriage of *Staphylococcus aureus* in

hemodialysis patients: the effect of nasal mupirocin. Infect Control Hosp Epidemiol 1996;17:809-811.
40. Zimakoff J., Pedersen F. B., Bergen L., Baago-Nielsen J., and Daldorph B. *Staphylococcus aureus* carriage and infections among patients in four haemo- and peritoneal-dialysis centres in Denmark. J Hosp Infect 1996;33:289-300.
41. Bibel D. J., Greenbert J. H., and Cook J. L. *Staphylococcus aureus* and the microbial ecology of atopic dermatitis. Can J Microbiol 1997;23:1062-1068.
42. Noble W. C. Dispersal of skin microorganisms. Br J Dermatol 1975;93:477-485.
43. Walter C. W., Kundsin R. B., Shilkret M. A., and Day M. M. The spread of staphylococci to the environment. Antibiotics Annual 1959;952-957.
44. Boyce J. M., Opal S. M., Chow J. W., Zervos M. J., Potter-Bynoe G., Sherman C. B., Romulo R. L. C., Fortna S., and Medeiros A. A. Outbreak of multidrug-resistant *Enterococcus faecium* with transferable *vanB* class vancomycin resistance. J Clin Microbiol 1994;32:1148-1153.
45. McFarland L. V., Mulligan M. E., Kwok R. Y. Y., and Stamm W. E. Nosocomial acquisition of *Clostridium difficile* infection. N Engl J Med 1989;320:204-210.
46. Samore M. H., Venkataraman L., Degirolami P. C., Levin E., and Karchmer A. W. Clinical and molecular epidemiology of sporadic and clustered cases of nosocomial *Clostridium difficile* diarrhea. Am J Med 1996;100:32-40.
47. Lidwell O. M., Towers A. G., Ballard J., and Gladstone B. Transfer of micro-organisms between nurses and patients in a clean air environment. J Appl Bacteriol 1974;37:649-656.
48. Casewell M. and Phillips I. Hands as route of transmission for *Klebsiella* species. Br Med J 1977;2:1315-1317.
49. Hall C. B. and Douglas G. Modes of transmission of respiratory syncytial virus. J Pediatr 1981;99:100-102.
50. Olsen R. J., Lynch P., Coyle M. B., Cummings J., Bokete T., and Stamm W. E. Examination gloves as barriers to hand contamination in clinical practice. JAMA 1993;270:350-353.
51. Pittet D., Dharan S., Touveneau S., Sauvan V., and Perneger T. V. Bacterial contamination of the hands of hospital staff during routine patient care. Arch Intern Med 1999;159:821-826.
52. Fox M. K., Langner S. B., and Wells R. W. How good are hand washing practices? Am J Nursing 1974;74:1676-1678.
53. Ojajarvi J. Effectiveness of hand washing and disinfection methods in removing transient bacteria after patient nursing. J Hyg (Camb) 1980;85:193-203.
54. Boyce J. M., Potter-Bynoe G., Chenevert C., and King T. Environmental contamination due to methicillin-resistant *Staphylococcus aureus*: possible infection control implications. Infect Control Hosp Epidemiol 1997;18:622-627.
55. Scott E. and Bloomfield S. F. The survival and transfer of microbial contamination via cloths, hands and utensils. J Appl Bacteriol 1990;68:271-278.
56. Bauer T. M., Ofner E., Just H. M., Just H., and Daschner F. D. An epidemiological study assessing the relative importance of airborne and direct contact transmission of microorganisms in a medical intensive care unit. J Hosp Infect 1990;15:301-309.
57. Tenorio A. R., Badri S. M., Sahgal N. B., Hota B., Matushek M., Hayden M. K., Trenholme G. M., and Weinstein R. A. Effectiveness of gloves in preventing personnel handcarriage of vancomycin-resistant enterococcus (VRE) after patient care. Clin Infect Dis 2001;32:826-829.
58. Daschner F. D. How cost-effective is the present use of antiseptics?. J Hosp Infect 1988;11(Suppl A):227-235.
59. Knittle M. A., Eitzman D. V., and Baer H. Role of hand contamination of personnel in the epidemiology of gram-negative nosocomial infections. J Pediatr 1975;86:433-437.
60. Ayliffe G. A. J., Babb J. R., Davies J. G., and Lilly H. A. Hand disinfection: a comparison of various agents in laboratory and ward studies. J Hosp Infect 1988;11:226-243.
61. Strausbaugh L. J., Sewell D. L., Ward T. T., and Pfaller M. A. High frequency of yeast carriage on hands of hospital personnel. J Clin Microbiol 1994;32:2299-2300.
62. Marples R. R. and Towers A. G. A laboratory model for the investigation of contact transfer of micro-organisms. J Hyg (Camb) 1979;82:237-248.
63. Mackintosh C. A. and Hoffman P. N. An extended model for transfer of micro-organisms via the hands: differences between organisms and the effect of alcohol disinfection. J Hyg 1984;92:345-355.
64. Patrick D. R., Findon G., and Miller T. E. Residual moisture determines the level of touch-contact-associated bacterial transfer following hand washing. Epidemiol Infect 1997;119:319-325.
65. Larson E. A causal link between handwashing and risk of infection? Examination of the evidence. Infect Control Hosp Epidemiol 1988;9:28-36.
66. Larson E. Skin hygiene and infection prevention: more of the same or different approaches? Clin Infect Dis 1999;29:1287-1294.
67. Mortimer E. A., Lipsitz P. J., Wolinsky E., and et al. Transmission of staphylococci between newborns. Am J Dis Child 1962;104:289-295.
68. Maki D. G. The use of antiseptics for handwashing by medical personnel. J Chemother 1989;1 (Suppl):3-11.
69. Massanari, R. M. and Hierholzer, W. J., Jr. A crossover comparison of antiseptic soaps on nosocomial infection rates in intensive care units. Am J Infect Control 1984;12:247-248.
70. Doebbeling B. N., Stanley G. L., Sheetz C. T., Pfaller M. A., Houston A. K., Annis L., Li N., and Wenzel R. P. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. N Engl J Med 1992;327:88-93.
71. Webster J., Faoagali J. L., and Cartwright D. Elimination of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit after hand washing with triclosan. J Paediatr Child Health 1994;30:59-64.
72. Zafar A. B., Butler R. C., Reese D. J., and Gaydos L. A. Use of 0.3% triclosan (Bacti-Stat*) to eradicate an outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal nursery. Am J Infect Control 1995;23:200-208.
73. Pittet D., Hugonnet S., Harbarth S., Mourouga P., Sauvan V., and Touveneau S. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Lancet 2000;356:1307-1312.
74. Larson E. L., Early E., Cloonan P., Sugrue S., and Parides M. An organizational climate intervention associated with increased handwashing and decreased nosocomial infections. Behavioral Medicine 2000;26:14-22.
75. Fridkin S., Pear S. M., Williamson T. H., Galgiani J. N., and Jarvis W. R. The role of understaffing in central venous catheter-associated bloodstream infections. Infect Control Hosp Epidemiol 1996;17:150-158.
76. Vicca A. F. Nursing staff workload as a determinant of methicillin-resistant *Staphylococcus aureus* spread in an adult intensive therapy unit. J Hosp Infect 1999;43:109-113.
77. Harbarth S., Sudre P., Dharan S., Cadenas M., and Pittet D. Outbreak of *Enterobacter cloacae* related to understaffing, overcrowding and poor hygiene practices. Infect Control Hosp Epidemiol 1999;20:598-603.
78. American Society for Testing Materials. Standard test method for evaluation of health care personnel handwash

formulation. American Society for Testing Materials, West Conshohocken, PA, 1994.
79. European Committee for Standardization. Chemical disinfectants and antiseptics - hygienic handrub - test method and requirements. CEN 1997;
80. Sattar S. A., Abebe M., Bueti A. J., Jampani H., Newman J., and Hua S. Activity of an alcohol-based hand gel against human adeno-, rhino-, and rotaviruses using the fingerpad method. Infect Control Hosp Epidemiol 2000;21:516-519.
81. Wolff M. H. Hepatitis A virus: a test method for virucidal activity. J Hosp Infect 2001;48(Suppl A):S18-S22.
82. Steinmann J. Some principles of virucidal testing. J Hosp Infect 2001;28(Suppl A):S15-S17.
83. Gould D. and Ream E. Assessing nurses' hand decontamination performance. Nursing Times 1993;89:47-50.
84. Quraishi Z. A., McGuckin M., and Blais F. X. Duration of handwashing in intensive care units: a descriptive study. Am J Infect Control 1984;11:178-182.
85. Lund S., Jackson J., Leggett J., Hales L., Dworkin R., and Gilbert D. Reality of glove use and handwashing in a community hospital. Am J Infect Control 1994;22:352-357.
86. Meengs M. R., Giles B. K., Chisholm C. D., Cordell W. H., and Nelson D. R. Hand washing frequency in an emergency department. J Emerg Nurs 1994;20:183-188.
87. Larson E., McGeer A., Quraishi A., Krenzischek D., Parsons B. J., Holdford J., and Hierholzer W. J. Effect of an automated sink on handwashing practices and attitudes in high-risk units. Infect Control Hosp Epidemiol 1991;12:422-428.
88. Broughall J. M. An automatic monitoring system for measuring handwashing frequency. J Hosp Infect 1984;5:447-453.
89. Ojajarvi J., Makela P., and Rantasalo I. Failure of hand disinfection with frequent hand washing: a need for prolonged field studies. J Hyg 1977;79:107-119.
90. Larson E. L., Eke P. I., Wilder M. P., and Laughon B. E. Quantity of soap as a variable in handwashing. Infect Control 1987;8:371-375.
91. Larson E., Leyden J. J., McGinley K. J., Grove G. L., and Talbot G. H. Physiologic and microbiologic changes in skin related to frequent handwashing. Infect Control 1986;7:59-63.
92. Larson E. L., Eke P. I., and Laughon B. E. Efficacy of alcohol-based hand rinses under frequent-use conditions. Antimicrob Agents Chemother 1986;30:542-544.
93. Larson E. L. and Laughon B. E. Comparison of four antiseptic products containing chlorhexidine gluconate. Antimicrob Agents Chemother 1987;31:1572-1574.
94. Meers P. D. and Yeo G. A. Shedding of bacteria and skin squames after handwashing. J Hyg (Camb) 1978;81:99-105.
95. Winnefeld M., Richard M. A., Drancourt M., and Grobb J. J. Skin tolerance and effectiveness of two hand decontamination procedures in everyday hospital use. Br J Dermatol 2000;143:546-550.
96. Maki, D., Zilz, M. A., and Alvarado, C. J. Evaluation of the antibacterial efficacy of four agents for handwashing. Current Chemotherapy and Infectious Disease 1979;II:1089-1090.
97. Boyce J. M., Kelliher S., and Vallande N. Skin irritation and dryness associated with two hand hygiene regimens: soap and water handwashing versus hand antisepsis with an alcoholic hand gel. Infect Control Hosp Epidemiol 2000;21:442-448.
98. Sartor C., Jacomo V., Duvivier C., Tissot-Dupont H., Sambuc R., and Drancourt M. Nosocomial *Serratia marcescens* infections associated with extrinsic contamination of a liquid nonmedical soap. Infect Control Hosp Epidemiol 2000;21:196-199.
99. Walter C. W. Disinfection of hands. Am J Surg 1965;109:691-693.
100. Gravens D. L., Butcher H. R., Jr., Ballinger W. F., and Dewar N. E. Septisol antiseptic foam for hands of operating room personnel: an effective antibacterial agent. Surgery 1973;73:360-367.
101. Eitzen H. E., Ritter M. A, French M. L. V., and Gioe T. J. A microbiological in-use comparison of surgical hand-washing agents. J Bone Joint Surg 1979;61-A:403-406.
102. Minakuchi K., Yamamoto Y., Matsunaga K., Hayata M., Yasuda T., Katsuno Y., Takada H., Iriyama J., Ishigo S., and Asano Y. The antiseptic effect of a quick drying rubbing type povidone-iodine alcoholic disinfectant solution. Postgrad Med J 1993;69:S23-S26.
103. Babb J. R., Davies J. G., and Ayliffe G. A. J. A test procedure for evaluating surgical hand disinfection. J Hosp Infect 1991;18:41-49.
104. Bellamy K., Alcock R., Babb J. R., Davies J. G., and Ayliffe G. A. A test for the assessment of "hygienic" hand disinfection using rotavirus. J Hosp Infect 1993;24:201-210.
105. Ayliffe G. A. J., Babb J. R., and Quoraishi A. H. A test for "hygienic" hand disinfection. J Clin Pathol 1978;31:923-928.
106. Lilly H. A., Lowbury E. J. L., and Wilkins M. D. Detergents compared with each other and with antiseptics as skin 'degerming' agents. J Hyg (Camb) 1978;82:89-93.
107. Ulrich J. A. Clinical study comparing hibistat (0.5% chlorhexidine gluconate in 70% isopropyl alcohol) and betadine surgical scrub (7.5% povidone-iodine) for efficacy against experimental contamination of human skin. Curr Ther Res 1982;31:27-30.
108. Bartzokas C. A., Gibson M. F., Graham R, and Pinder D. C. A comparison of triclosan and chlorhexidine preparations with 60 per cent isopropyl alcohol for hygienic hand disinfection. J Hosp Infect 1983;4:245-255.
109. Rotter M. L., Koller W., Wewalka G., Werner H. P., Ayliffe G. A. J., and Babb J. R. Evaluation of procedures for hygienic hand-disinfection: controlled parallel experiments on the Vienna test model. J Hyg (Camb) 1986;96:27-37.
110. Kjolen H. and Andersen B. M. Handwashing and disinfection of heavily contaminated hands--effective or ineffective? J Hosp Infect 1992;21:61-71.
111. Namura S., Nishijima S., and Asada Y. An evaluation of the residual activity of antiseptic handrub lotions: an "in use" setting study. J Dermatol 1994;21:481-485.
112. Jarvis J. D., Wynne C. D., Enwright L., and Williams J. D. Handwashing and antiseptic-containing soaps in hospital. J Clin Path 1979;32:732-737.
113. Pereira L. J., Lee G. M., and Wade K. J. An evaluation of five protocols for surgical handwashing in relation to skin condition and microbial counts. J Hosp Infect 1997;36:49-65.
114. Larson E. L., Butz A. M., Gullette D. L., and Laughon B. A. Alcohol for surgical scrubbing? Infect Control Hosp Epidemiol 1990;11:139-143.
115. Aly R. and Maibach H. I. Comparative study on the antimicrobial effect of 0.5% chlorhexidine gluconate and 70% isopropyl alcohol on the normal flora of hands. Appl Environ Microbiol 1979;37:610-613.
116. Galle P. C., Homesley H. D., and Rhyne A. L. Reassessment of the surgical scrub. Surg Gynecol Obstet 1978;147:215-218.
117. Rosenberg A., Alatary S. D., and Peterson A. F. Safety and efficacy of the antiseptic chlorhexidine gluconate. Surg

Gynecol Obstet 1976;143:789-792.
118. Ayliffe G. A. J., Babb J. R., Bridges K., Lilly H. A., Lowbury E. J. L., Varney J., and Wilkins M. D. Comparison of two methods for assessing the removal of total organisms and pathogens from the skin. J Hyg (Camb) 1975;75:259-274.
119. Larson E. L. and Morton H. E. Alcohols. In: Block, S. S., eds. *Disinfection, Sterilization and Preservation*. Philadelphia: Lea & Febiger, 1991:191-203.
120. Price P. B. Ethyl alcohol as a germicide. Arch Surg 1939;38:528-542.
121. Harrington C. and Walker H. The germicidal action of alcohol. Boston Medical and Surgical Journal 1903;148:548-552.
122. Coulthard C. E. and Sykes G. The germicidal effect of alcohol with special reference to its action on bacterial spores. Pharmaceutical Journal 1936;137:79-81.
123. Pohle W. D. and Stuart L. S. The germicidal action of cleaning agents - a study of a modification of Price's procedure. J Infect Dis 1940;67:275-281.
124. Gardner A. D. Rapid disinfection of clean unwashed skin. Lancet 1948;760-763.
125. Sakuragi T., Yanagisawa K., and Dan K. Bactericidal activity of skin disinfectants on methicillin-resistant *Staphylococcus aureus*. Anesth Analg 1995;81:555-558.
126. Kampf G., Jarosch R., and Ruden H. Limited effectiveness of chlorhexidine based hand disinfectants against methicillin-resistant *Staphylococcus aureus* (MRSA). J Hosp Infect 1998;38:297-303.
127. Kampf G., Hofer M., and Wendt C. Efficacy of hand disinfectants against vancomycin-resistant enterococci in vitro. J Hosp Infect 1999;42:143-150.
128. Platt J. and Bucknall R. A. The disinfection of respiratory syncytial virus by isopropanol and a chlorhexidine-detergent handwash. J Hosp Infect 1985;6:89-94.
129. Krilov L. R. and Harkness S. H. Inactivation of respiratory syncytial virus by detergents and disinfectants. Pediatr Infect Dis 1993;12:582-584.
130. Pillsbury D. M., Livingood C. S., and Nichols A. C. Bacterial flora of the normal skin. Arch Dermatol 1942;45:61-80.
131. Lowbury E. J. L., Lilly H. A., and Ayliffe G. A. J. Preoperative disinfection of surgeon's hands: use of alcoholic solutions and effects of gloves on skin flora. Br Med J 1974;4:369-372.
132. Lilly H. A., Lowbury E. J. L., Wilkins M. D., and Zaggy A. Delayed antimicrobial effects of skin disinfection by alcohol. J Hyg (Camb) 1979;82:497-500.
133. Dineen P. and Hildick-Smith G. Antiseptic care of the hands. In: Maibach H. I. and Hildick-Smith G., eds. *Skin Bacteria and their Role in Infection*. New York: McGraw-Hill, 1965:291-309.
134. Lilly H. A. and Lowbury E. J. L. Transient skin flora: their removal by cleansing or disinfection in relation to their mode of deposition. J Clin Path 1978;31:919-922.
135. Rotter M., Koller W., and Wewalka G. Povidone-iodine and chlorhexidine gluconate-containing detergents for disinfection of hands. J Hosp Infect 1980;1:149-158.
136. Rotter M. L. Hygienic hand disinfection. Infect Control 1984;1:18-22.
137. Blech M.-F., Hartemann P., and Paquin J.-L. Activity of non antiseptic soaps and ethanol for hand disinfection. Zbl Bakt Hyg 1985;181:496-512.
138. Leyden J. J., McGinley K. J., Kaminer M. S., Bakel J., Nishijima S., Grove M. J., and Grove G. L. Computerized image analysis of full-hand touch plates: a method for quantification of surface bacteria on hands and the effect of antimicrobial agents. J Hosp Infect 1991;18:13-22.
139. Rotter M. L. and Koller W. Test models for hygienic handrub and hygienic handwash: the effects of two different contamination and sampling techniques. J Hosp Infect 1992;20:163-171.
140. Zaragoza M., Salles M, Gomez J., Bayas J. M., and Trilla A. Handwashing with soap or alcoholic solutions? A randomized clinical trial of its effectiveness. Am J Infect Control 1999;27:258-261.
141. Paulson D. S., Fendler E. J., Dolan M. J., and Williams R. A. A close look at alcohol gel as an antimicrobial sanitizing agent. Am J Infect Control 1999;27 (4):332-338.
142. Cardoso C. L., Pereira H. H., Zequim J. C., and Guilhermetti M. Effectiveness of hand-cleansing agents for removing *Acinetobacter baumannii* strain from contaminated hands. Am J Infect Control 1999;27(4):327-331.
143. Casewell M. W., Law M. M., and Desai N. A laboratory model for testing agents for hygienic hand disinfection: handwashing and chlorhexidine for the removal of klebsiella. J Hosp Infect 1988;12:163-175.
144. Wade J. J., Desai N., and Casewell M. W. Hygienic hand disinfection for the removal of epidemic vancomycin-resistant *Enterococcus faecium* and gentamicin-resistant *Enterobacter cloacae*. J Hosp Infect 1991;18:211-218.
145. Huang Y., Oie S., and Kamiya A. Comparative effectiveness of hand-cleansing agents for removing methicillin-resistant *Staphylococcus aureus* from experimentally contaminated fingertips. Am J Infect Control 1994;22:224-227.
146. Lowbury E. J. L. and Lilly H. A. Disinfection of the hands of surgeons and nurses. Br Med J 1960;1445-1450.
147. Bernard E. and Knight R. A. Evaluation of hand antisepsis. Arch Environ Health 1969;18:781-783.
148. Rotter M. L., Simpson R. A., and Koller W. Surgical hand disinfection with alcohols at various concentrations: parallel experiments using the new proposed european standards method. Infect Control Hosp Epidemiol 1998;19:778-781.
149. Hobson D. W., Woller W., Anderson L., and Guthery E. Development and evaluation of a new alcohol-based surgical hand scrub formulation with persistent antimicrobial characteristics and brushless application. Am J Infect Control 1998;26:507-512.
150. Jones M. V., Rowe G. B., Jackson B., and Pritchard N. J. The use of alcoholic paper wipes for routine hand cleasing: results of trials in two hospitals. J Hosp Infect 1986;8:268-274.
151. Butz A. M., Laughon B. E., Gullette D. L., and Larson E. L. Alcohol-impregnated wipes as an alternative in hand hygiene. Am J Infect Control 1990;18:70-76.
152. Ojajarvi J. Handwashing in Finland. J Hosp Infect 1991;18:35-40.
153. Newman J. L. and Seitz J. C. Intermittent use of an antimicrobial hand gel for reducing soap-induced irritation of health care personnel. Am J Infect Control 1990;18:194-200.
154. Rotter M. L., Koller W., and Neumann R. The influence of cosmetic additives on the acceptability of alcohol-based hand disinfectants. J Hosp Infect 1991;18 (suppl B):57-63.
155. Larson E. L., Aiello A. E., Heilman J. M., Lyle C. T., Cronquist A., and Stahl J. B. Comparison of different regimens for surgical hand preparation. AORN J 2001;73:412-420.
156. Larson E. L., Aiello A. E., Bastyr J., Lyle C., Stahl J., Cronquist A., Lai L., and Della-Latta P. Assessmant of two hand hygiene regimens for intensive care unit personnel. Crit Care Med 2001;29;944-951.
157. Maki D. G., McCormick R. D., Zilz M. A., Stolz S. M., and Alvarado C. J. An MRSA outbreak in a SICU during universal precautions: new epidemiology for nosocomial MRSA: downside for universal precautions. Program and abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta 1990;Abstr. 473.

158. Boyce J. M. Scientific basis for handwashing with alcohol and other waterless antiseptic agents. In: Rutala, W. A., eds. *Disinfection, sterilization and antisepsis: principles and practices in healthcare facilities*. Washington, DC: Association for Professionals in Infection Control and Epidemiology, Inc, 2001:140-151.
159. Hsueh P. R., Teng L. J, Yang P. C., Pan H. L., Ho S. W., and Luh K. T. Nosocomial pseudoepidemic caused by *Bacillus cereus* traced to contaminated ethyl alcohol from a liquor factory. J Clin Microbiol 2000;37:2280-2284.
160. Denton G. W. Chlorhexidine. In: Block, S. S., ed. *Disinfection, Sterilization, and Preservation*. Philadelphia: Lea and Febiger, 1991:274-289.
161. Narang H. K. and Codd A. A. Action of commonly used disinfectants against enteroviruses. J Hosp Infect 1983;4:209-212.
162. Walsh B., Blakemore P. H., and Drubu Y. J. The effect of handcream on the antibacterial activity of chlorhexidine gluconate. J Hosp Infect 1987;9:30-33.
163. Lowbury E. J. L. and Lilly H. A. Use of 4% chlorhexidine detergent solution (hibiscrub) and other methods of skin disinfection. Br Med J 1973;1:510-515.
164. Paulson D. S. Comparative evaluation of five surgical hand scrub preparations. AORN J 1994;60:246-256.
165. Stingeni L., Lapomarda V, and Lisi P. Occupational hand dermatitis in hospital environments. Contact Dermatitis 1995;33:172-176.
166. Lowbury E. J. L., Lilly H. A., and Bull J. P. Disinfection of hands: removal of resident bacteria. Br Med J 1963;1:1251-1256.
167. Kundsin R. B. and Walter C. W. The surgical scrub - practical consideration. Arch Surg 1973;107:75-77.
168. Lockart J. How toxic is hexachlorophene? Pediatrics 1972;50:229-235.
169. Shuman R. M., Leech R. W., and Alvord E. C. Jr. Neurotoxicity of hexachlorophene in humans. II. A clinicopathological study of 46 premature infants. Arch Neurol 1975;32:320-325.
170. Dixon R. E., Kaslow R. A., and Mallison G. F. Staphylococcal disease outbreaks in hospital nurseries in the United States - December 1971 through March 1972. Pediatrics 1973;51:413-416.
171. Kaslow R. A., Dixon R. E., and Martin S. M. Staphylococcal disease related to hospital nursery bathing practices - a nationwide epidemiologic investigation. Pediatrics 1973;51:418-429.
172. American Academy of Pediatrics and American College of Obstetricians and Gynecologists. *Guidelines for perinatal care.* Elk Grove Village, IL: The Academy; Washington, DC: The College, c1997: American Academy of Pediatrics; 1997.
173. Gottardi W. Iodine and iodine compounds. In: Block, S. S., ed. *Disinfection, Sterilization and Preservation* . Philadelphia: Lea & Febiger, 1991:152-166.
174. Anderson R. L. Iodophor antiseptics: intrinsic microbial contamination with resistant bacteria. Infect Control Hosp Epidemiol 1989;10:443-446.
175. Goldenheim P. D. In vitro efficacy of povidone-iodine solution and cream against methicillin-resistant *Staphylococcus aureus*. Postgrad Med J 1993;69 (suppl 3):S62-S65.
176. Traore O., Fournet Fayard, and Laveran H. An in-vitro evaluation of the activity of povidone-iodine against nosocomial bacterial strains. J Hosp Infect 1996;34:217-222.
177. McLure A. R. and Gordon J. In-vitro evaluation of povidone-iodine and chlorhexidine against methicillin-resistant *Staphylococcus aureus*. J Hosp Infect 1992;21:291-299.
178. Davies J. G., Babb J. R., and Bradley C. R. Preliminary study of test methods to assess the virucidal activity of skin disinfectants using poliovirus and bacteriophages. J Hosp Infect 1993;25:125-131.
179. Wade J. J. and Casewell M. W. The evaluation of residual antimicrobial activity on hands and its clinical relevance. J Hosp Infect 1991;18:23-28.
180. Aly R. and Maibach H. I. Comparative evaluation of chlorhexidine gluconate (hibiclens) and povidone-iodine (E-Z scrub) sponge/brushes for presurgical hand scrubbing. Curr Ther Res 1983;34:740-745.
181. Herruzo-Cabrera R., Vizcaino-Alcaide M. J., and Fdez-Acinero M. J. Usefulness of an alcohol solution of N-duopropenide for the surgical antisepsis of the hands compared with handwashing with iodine-povidone and chlorhexidine: clinical essay. J Surgical Research 2000;94:6-12.
182. Hingst V, Juditzki I, and Heeg P. Evaluation of the efficacy of surgical hand disinfection following a reduced application time of 3 instead of 5 min. J Hosp Infect 1992;20:79-86.
183. Faoagali J., Fong J., and George N. Comparison of the immediate, residual, and cumulative antibacterial effects of Novaderm R, Novascrub R, betadine surgical scrub, Hibiclens, and liquid soap. Am J Infect Control 1995;23:337-343.
184. Pereira L. J., Lee G. M., and Wade K. J. The effect of surgical handwashing routines on the microbial counts of operating room nurses. Am J Infect Control 1990;18:354-364.
185. Peterson A. F. and Rosenberg A. Comparative evaluation of surgical scrub preparations. Surg Gynecol Obstet 1978;146:63-65.
186. Berkelman R. L., Holland B. W., and Anderson R. L. Increased bactericidal activity of dilute preparations of povidone-iodine solutions. J Clin Microbiol 1982;15:635-639.
187. Larson E. and Talbot G. H. An approach for selection of health care personnel handwashing agents. Infect Control 1986;7:419-424.
188. Davies J., Babb J. R., Ayliffe G. A. J., and Wilkins M. D. Disinfection of the skin of the abdomen. Br J Surg 1978;65:855-858.
189. Larson E., Mayur K., and Laughon B. A. Influence of two handwashing frequencies on reduction in colonizing flora with three handwashing products used by health care personnel. Am J Infect Control 1988;17:83-88.
190. Soulsby M. E., Barnett J. B., and Maddox S. Brief report: the antiseptic efficacy of chlorxylenol-containing vs. chlorhexidine gluconate-containing surgical scrub preparations. Infect Control 1986;7:223-226.
191. Aly R. and Malbach H. I. Comparative antibacterial efficacy of a 2-minute surgical scrub with chlorhexidine gluconate, povidone-iodine, and chloroxylenol sponge-brushes. Am J Infect Control 1988;16:173-177.
192. Archibald L. K., Corl A., Shah B., Schulte M., Arduino M. J., Aguero S., Fisher D. J., Stechenberg B. W., Banerjee S. N., and Jarvis W. R. *Serratia marcescens* outbreak associated with extrinsic contamination of 1% chlorxylenol soap. Infect Control Hosp Epidemiol 1997;18:704-709.
193. Merianos J. J. Quaternary ammonium antimicrobial compounds. In: Block, S. S., ed. *Disinfection, Sterilization, and Preservation*. Philadelphia: Lea and Febiger, 1991:225-255.
194. Dixon R. E., Kaslow R. A., Mackel D. C., Fulkerson C. C., and Mallison G. F. Aqueous quaternary ammonium antiseptics and disinfectants. JAMA 1976;236:2415-2417.
195. Sautter R. L., Mattman L. H., and Legaspi R. C. *Serratia marcescens* meningitis associated with a contaminated benzalkonium chloride solution. Infect Control 1984;5:223-225.

196. Hartstein A. I., Denny M. A., Morthland V. H., LeMonte A. M., and Pfaller M. A. Control of methicillin-resistant Staphylococcus aureus in a hospital and an intensive care unit. Infect Control Hosp Epidemiol 1995;16:405-411.
197. Jones R. D., Jampani H. B., Newman J. L., and Lee A. S. Triclosan: a review of effectiveness and safety in health care settings. Am J Infect Control 2000;28:184-196.
198. Ward W. H., Holdgate G. A., and Rowsell S. Kinetic and structural characteristics of the inhibition of enoyl (acyl carrier protein) reductase by triclosan. Biochemistry 1999;38:12514-12525.
199. Heath R. J., Li J., and Roland G. E. Inhibition of the *Staphylococcus aureus* NADPH-dependent enoyl-acyl carrier protein reductase by triclosan and hexachlorophene. J Biol Chem 2000;275:4654-4659.
200. Chuanchuen R., Beinlich K., and Hoang T. T. Cross-resistance between triclosan and antibiotics in *Pseudomonas aeruginosa* is mediated by multidrug efflux pumps: exposure of a susceptible mutant strain to triclosan selects nfxB mutants overexpressing MexCD-OprJ. Antimicrob Agents Chemother 2001;45:428-432.
201. Faoagali J. L., George N., Fong J., Davy J., and Dowser M. Comparison of the antibacterial efficacy of 4% chlorhexidine gluconate and 1% triclosan handwash products in an acute clinical ward. Am J Infect Control 1999;27 (4):320-326.
202. Barry M. A., Craven D. E., Goularte T. A., and Lichtenbert D. A. *Serratia marcescens* contamination of antiseptic soap containing triclosan: implications for nosocomial infection. Infect Control 1984;5:427-430.
203. Lowbury E. J. L., Lilly H. A., and Bull J. P. Disinfection of hands: removal of transient organisms. Br Med J 1964;2:230-233.
204. Rotter M. L. Semmelweis' sesquicentennial: a little-noted anniversary of handwashing. Current Opinion in Infectious Diseases 1998;11:457-460.
205. Manivannan, G., Brady, M. J., Cahalan, P. T., Lisay, C. M., Hale, D. A., Hamberger, J. F. et al. Immediate, persistent and residual antimicrobial efficiency of surfacine hand sanitizer. Infect Control Hosp Epidemiol 2000;21:105.
206. Groschel D. H. M. and Pruett T. L. Surgical antisepsis. In: Block, S. S., ed. *Disinfection, Sterilization, and Preservation*. Philadelphia: Lea and Febiger, 1991:642-654.
207. Boyce J. M., Potter-Bynoe G., Opal S. M., Dziobek L., and Medeiros A. A. A common-source outbreak of *Staphylococcus epidermidis* infections among patients undergoing cardiac surgery. J Infect Dis 1990;161:493-499.
208. Dewar N. E. and Gravens D. L. Effectiveness of septisol antiseptic foam as a surgical scrub agent. Appl Microbiol 1973;26:544-549.
209. Widmer A. F. Replace hand washing with use of a waterless alcohol hand rub? Clin Infect Dis 2000;31:136-143.
210. Grinbaum R. S., de Mendonca J. S., and Cardo D. M. An outbreak of handscrubbing-related surgical site infections in vascular surgical procedures. Infect Control Hosp Epidemiol 1995;16:198-202.
211. Association of Operating Room Nurses Recommended Practices Committee. Recommended practices for surgical hand scrubs. AORN J 1999;69:842-850.
212. Larson E., Anderson J. K., and Baxendale L. Effects of a protective foam on scrubbing and gloving. Am J Infect Control 1993;21:297-301.
213. Dineen P. An evaluation of the duration of the surgical scrub. Surg Gynecol Obstet 1969;129:1181-1184.
214. O'Farrell D. A., Kenny G., O'Sullivan M., Nicholson P., Stephens M., and Hone R. Evaluation of the optimal hand-scrub duration prior to total hip arthroplasty. J Hosp Infect 1994;26:93-98.
215. O'Shaughnessy M., O'Maley V. P., and Corbett G. Optimum duration of surgical scrub-time. Br J Surg 1991;78:685-686.
216. Wheelock S. M. and Lookinland S. Effect of surgical hand scrub time on subsequent bacterial growth. AORN J 1997;65:1087-1098.
217. Deshmukh N., Kjellberg S. I., and Kramer J. W. A comparison of 5-minute povidone-iodine scrub and 1-minute povidone-iodine scrub followed by alcohol foam. Military Medicine 1998;163:145-147.
218. Kikuchi-Numagami K., Saishu T., and Fukaya M. Irritancy of scrubbing up for surgery with or without a brush. Acta Derm Venereol 1999;79:230-232.
219. Dineen P. The use of a polyurethane sponge in surgical scrubbing. Surg Gynecol Obstet 1966;123:595-598.
220. Bornside G. H., Crowder V. H., Jr., and Cohn I., Jr. A bacteriological evaluation of surgical scrubbing with disposable iodophor-soap impregnated polyurethane scrub sponges. Surgery 1968;64:743-751.
221. McBride M. E., Duncan W. C., and Knox J. M. An evaluation of surgical scrub brushes. Surg Gynecol Obstet 1973;137:934-936.
222. Berman R. E. and Knight R. A. Evaluation of hand antisepsis. Arch Environ Health 1969;18:781-783.
223. Loeb M. B., Wilcox L., Smaill F., Walter S., and Duff Z. A randomized trial of surgical scrubbing with a brush compared to antiseptic soap alone. Am J Infect Control 1997;25:11-15.
224. Larson E., Aiello A. E., and Heilman J. M. Comparison of different regimens for surgical hand preparation. AORN J 2001;73:412-432.
225. Larson E., Friedman C., Cohran J., Treston-Aurand J., and Green S. Prevalence and correlates of skin damage on the hands of nurses. Heart Lung 1997;26:404-412.
226. Tupker R. A. Detergents and cleansers. In: van der Valk, P. G. M. and Maibach, H. I., eds. *The Irritant Contact Dermatitis Syndrome*. New York: CRC Press, 1996:71-76.
227. Wilhelm K.-P. Prevention of surfactant-induced irritant contact dermatitis. In: Elsner, P., Lachapelle, J. M., Wahlberg, J. E., and Maibach, H. I., eds. *Prevention of Contact Dermatitis. Curr Probl Dermatol*. Basel: Karger, 1996:78-85.
228. de Haan P., Meester H. H. M., and Bruynzeel D. P. Irritancy of alcohols. In: van der Valk P. G. M. and Maibach H. I., eds. *The Irritant Contact Dermatitis Syndrome*. New York: CRC Press, 1996:65-70.
229. Ohlenschlaeger J., Friberg J., Ramsing D., and Agner T. Temperature dependency of skin susceptibility to water and detergents. Acta Derm Venereol 1996;76(4):274-276.
230. Emilson A., Lindbert M., and Forslind B. The temperature effect of in vitro penetration of sodium lauryl sulfate and nickel chloride through human skin. Acta Derm Venereol 1993;73:203-207.
231. Hannuksela M. Moisturizers in the prevention of contact dermatitis. In: Elsner, P., Lachapelle, J. M., Wahlberg, J. E., and Maibach, H. I., eds. *Prevention of Contact Dermatitis. Curr Probl Dermatol*. Basel: Karger, 1996:214-220.
232. Berndt U., Wigger-Alberti W., Gabard B., and Elsner P. Efficacy of a barrier cream and its vehicle as protective measures against occupational irritant contact dermatitis. Contact Dermatitis 2000;42:77-80.
233. McCormick R. D., Buchman T. L., and Maki D. Double-blind, randomized trial of scheduled use of a novel barrier cream and an oil-containing lotion for protecting the hands of health care workers. Am J Infect Control 2000;28:302-310.
234. Larson E. and Killien M. Factors influencing handwashing behavior of patient care personnel. Am J Infect Control 1982;10:93-99.
235. Zimakoff J., Kjelsberg A. B., Larsen S. O., and Holstein B. A multicenter questionnaire investigation of attitudes toward hand hygiene, assessed by the staff in fifteen hospitals in Denmark and Norway. Am J Infect Control 1992;20:58-64.

236. Mayer J. A., Dubbert P. M., Miller M., Burkett P. A., and Chapman S. W. Increasing handwashing in an intensive care unit. Infect Control 1986;7:259-262.
237. Ojajarvi J. The importance of soap selection for routine hand hygiene in hospital. J Hyg (Camb) 1981;86:275-283.
238. Scott D., Barnes A., Lister M., and Arkell P. An evaluation of the user acceptability of chlorhexidine handwash formulations. J Hosp Infect 1991;18:51-55.
239. Taylor L. J. An evaluation of handwashing techniques-2. Nursing Times 1978;108-110.
240. Preston G. A., Larson E. L., and Stamm W. E. The effect of private isolation rooms on patient care practices, colonization and infection in an intensive care unit. Am J Med 1981;70:641-645.
241. Kaplan L. M. and McGuckin M. Increasing handwashing compliance with more accessible sinks. Infect Control 1986;7:408-410.
242. Freeman, J. Prevention of nosocomial infections by location of sinks for hand washing adjacent to the bedside. Program and Abstracts of the 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, 1993, abstr 60.
243. Bischoff W. E., Reynolds T. M., Sessler C. N., Edmond M. B., and Wenzel R. P. Handwashing compliance by health care workers. The impact of introducing an accessible, alcohol-based hand antiseptic. Arch Intern Med 2000;160:1017-1021.
244. Pittet D. Compliance with hand disinfection and its impact on nosocomial infections. J Hosp Infect 2001;28(Suppl A):S40-S46.
245. Wurtz R., Moye G., and Jovanovic B. Handwashing machines, handwashing compliance, and potential for cross-contamination. Am J Infect Control 1994;22:228-230.
246. Boyce J. M. Antiseptic techology: access, affordability and acceptance. Emerg Infect Diseases 2001;7:231-233.
247. Taylor L. J. An evaluation of handwashing techniques-1. Nursing Times 1978;54-55.
248. Albert R. K. and Condie F. Hand-washing patterns in medical intensive-care units. N Engl J Med 1981;24:1465-1466.
249. Larson E. Compliance with isolation technique. Am J Infect Control 1983;11:221-225.
250. Donowitz L. G. Handwashing technique in a pediatric intensive care unit. Am J Dis Child 1987;141:683-685.
251. Conley J. M., Hill S., Ross J., Lertzman J., and Loule T. J. Handwashing practices in an intensive care unit: the effects of an educational program and its relationship to infection rates. Am J Infect Control 1989;17:330-339.
252. DeCarvalho M., Lopes J. M. A., Pellitteri M., Neonatal Department, Fernandes Figueira Institute, and Mininstry of Health. Frequency and duration of handwashing in a neonatal intensive care unit. Pediatr Infect Dis J 1989;8:179-180.
253. Graham M. Frequency and duration of handwashing in an intensive care unit. Am J Infect Control 1990;18:77-80.
254. Dubbert P. M., Dolce J., Richter W., Miller M., and Chapman S. W. Increasing ICU staff handwashing: effects of education and group feedback. Infect Control Hosp Epidemiol 1990;11:191-193.
255. Simmons B., Bryant J., Neiman K., Spencer L., and Arheart K. The role of handwashing in prevention of endemic intensive care unit infections. Infect Control Hosp Epidemiol 1990;11:589-594.
256. Pettinger A. and Nettleman M. D. Epidemiology of isolation precautions. Infect Control Hosp Epidemiol 1991;12:303-307.
257. Lohr J. A., Ingram D. L., Dudley S. M., Lawton E. L., and Donowitz L. G. Hand washing in pediatric ambulatory settings. An inconsistent practice. Am J Dis Child 1991;145:1198-1199.
258. Raju T. N. K. and Kobler C. Improving handwashing habits in the newborn nurseries. Am J Med Sci 1991;302:355-358.
259. Larson E. L., McGinley K. J., Foglia A., Leyden J. J., Boland N., Larson J., Altobelli L. C., and Salazar-Lindo E. Handwashing practices and resistance and density of bacterial hand flora on two pediatric units in Lima, Peru. Am J Infect Control 1992;20:65-72.
260. Zimakoff J., Stormark M., and Olesen Larsen S. Use of gloves and handwashing behaviour among health care workers in intensive care units. A multicentre investigation in four hospitals in Denmark and Norway. J Hosp Infect 1993;24:63-67.
261. Pelke S., Ching D., Easa D., and Melish M. E. Gowning does not affect colonization or infection rates in a neonatal intensive care unit. Arch Pediatr Adolesc Med 1994;148:1016-1020.
262. Julich W. D. and Woedtke T. Reprocessing of thermosensitive materials - efficacy against bacterial spores and viruses. Journal of Hospital Infection 2001;48(suppl A):S69-S79.
263. Shay D. K., Maloney S. A., Montecalvo M., Banerjee S., Wormser G. P., Arduino M. J., Bland L. A., and Jarvis W. R. Epidemiology and mortality risk of vancomycin-resistant enterococcal bloodstream infections. J Infect Dis 1995;172:993-1000.
264. Tibballs J. Teaching hospital medical staff to handwash. Med J Aust 1996;164:395-398.
265. Slaughter S., Hayden M. K., Nathan C., Hu T.-C., Rice T., VanVoorhis J., Matushek M., Franklin C., and Weinstein R. A. A comparison of the effect of universal use of gloves and gowns with that of glove use alone on acquisition of vancomycin-resistant enterococci in a medical intensive care unit. Ann Intern Med 1996;125:448-456.
266. Dorsey S. T., Cydulka R. K., and Emerman C. L. Is handwashing teachable?: failure to improve handwashing behavior in an urban emergency department. Acad Emerg Med 1996;3:360-365.
267. Watanakunakorn C., Wang C., and Hazy J. An observational study of hand washing and infection control practices by healthcare workers. Infect Control Hosp Epidemiol 1998;19:858-860.
268. Avila-Aguero M. L., Umana M. A., and Jimenez A. L. Handwashing practices in a fertiary-care, pediatric hospital and the dffect on an educational program. Clin Perform Qual Health Care 1998;6:70-72.
269. Heeg P. Does hand care ruin hand disinfection? J Hosp Infect 2001;48(Suppl A):S37-S39.
270. Maury E., Alzieu M., Baudel J. L., and Haram N. Availability of an alcohol solution can improve hand disinfection compliance in an intensive care unit. Am J Respir Crit Care Med 2000;162:324-327.
271. Muto C. A., Sistrom M. G., and Farr B. M. Hand hygiene rates unaffected by installation of dispensers of a rapidly acting hand antiseptic. Am J Infect Control 2000;28:273-276.
272. Jarvis W. R. Handwashing--the Semmelweis lesson forgotten? Lancet 1994;344:1311-1312.
273. Larson E. and Kretzer E. K. Compliance with handwashing and barrier precautions. J Hosp Infect 1995;30 (suppl):88-106.
274. Sproat L. J. and Inglis T. J. A multicentre survey of hand hygiene practice in intensive care units. J Hosp Infect 1994;26:137-148.
275. Kretzer E. K. and Larson E. L. Behavioral interventions to improve infection control practices. Am J Infect Control 1998;26:245-253.
276. Voss A. and Widmer A. F. No time for handwashing!? Handwashing versus alcoholic rub: can we afford 100% compliance? Infect Control Hosp Epidemiol 1997;18:205-208.
277. Larson E. Handwashing and skin physiologic and bacteriologic aspects. Infect Control 1985;6:14-23.
278. Thompson B. L., Dwyer D. M., Ussery X. T., Denman S., and Vacek P. Handwashing and glove use in a long-term care facility. Infect Control Hosp Epidemiol 1997;18:97-103.

279. Doebbeling B. N., Pfaller M. A., Houston A. K., and Wenzel R. P. Removal of nosocomial pathogens from the contaminated glove. Ann Intern Med 1988;109:394-398.
280. McLane C., Chenelly S., Sylwestrak M., and Kirchhoff K. T. A nursing practice problem: failure to observe aseptic technique. Am J Infect Control 1983;11:178-182.
281. Pittet D. Improving compliance with hand hygiene in hospitals. Infect Control Hosp Epidemiol 2000;21:381-386.
282. Teare E. L., Cookson B., French G., Gould D., and Jenner E. Hand washing - a modest measure-with big effects. BMJ 1999;318:686-686.
283. Teare E. L., Cookson B., French G. L., and Jenner E. A. UK handwashing initiative. J Hosp Infect 1999;43:1-3.
284. Larson E. L., Bryan J. L., Adler L. M., and Blane C. A multifaceted approach to changing handwashing behavior. Am J Infect Control 1997;25:3-10.
285. Weeks A. Why I don't wash my hands between each patient contact. BMJ 1999;319:518-518.
286. Webster J. Handwashing in a neonatal intensive care nursery: product acceptability and effectiveness of chlorhexidine gluconate 4% and triclosan 1%. J Hosp Infect 1992;21:137-141.
287. Kelen G. D., Green G. B., Hexter D. A., and Fortenberry D. C. Substantial improvement in compliance with universal precautions in an emergency department following institution of policy. Arch Intern Med 1991;151:2051-2056.
288. Lundberg G. D. Changing physician behavior in ordering diagnostic tests. JAMA 1998;280:2036-2036.
289. Phillips D. F. "New look" reflects changing style of patient safety environment. JAMA 1999;281:217-219.
290. Early E., Battle K., Cantwell E., English J., Lavin J., and Larson E. Effect of several interventions on the frequency of handwashing among elementary public school children. Am J Infect Control 1998;26:263-269.
291. Butz A. M. Occurrence of infectious symptoms in children in day care homes. Am J Infect Control 1990;6:347-353.
292. Kimel L. S. Handwashing education can decrease illness absenteeism. J Sch Nurs 1996;12:14-16.
293. Master D., Hess Longe S. H., and Dickson H. Scheduled hand washing in an elementary school population. Fam Med 1997;29:336-339.
294. Roberts L., Smith W., Jorm L., Patel M., Douglas R. M., and McGilchrist, C. Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomized, controlled trial. Pediatrics 2000;105:738-742.
295. Roberts L., Jorm L., Patel M., Smith W., Douglas R. M., and McGilchrist C. Effect of infection control measures on the frequency of diarrheal episodes in child care: a randomized, controlled trial. Pediatrics 2000;105:743-746.
296. Khan M. U. Interruption of shigellosis by handwashing. Trans R Soc Trop Med Hyg 1982;76:164-168.
297. Shahid N. S., Greenough W. B., Samadi A. R., and Huq M. I. Hand washing with soap reduces diarrhoea and spread of bacterial pathogens in a bangladesh village. J Diarrhoeal Dis Res 1996;14:85-89.
298. Stanton B. F. and Clemens J. D. An educational intervention for altering water-sanitation behaviors to reduce childhood diarrhea in urban Bangladesh. Am J Epidemiol 1987;125:292-301.
299. McGinley K. J., Larson E. L., and Leyden J. J. Composition and density of microflora in the subungual space of the hand. J Clin Microbiol 1988;26:950-953.
300. Hedderwick S. A., McNeil S. A., and Kauffman C. A. Pathogenic organisms associated with artificial fingernails worn by healthcare workers. Infect Control Hosp Epidemiol 2000;21:505-509.
301. Baumgardner C. A., Maragos C. S., and Larson E. L. Effects of nail polish on microbial growth of fingernails. AORN J 1993;58:84-88.
302. Wynd C. A., Samstag D. E., and Lapp A. M. Bacterial carriage on the fingernails of OR nurses. AORN J 1994;60:796-805.
303. Gross A., Cutright D. E., and D'Allessandro S. M. Effect of surgical scrub on microbial population under the fingernails. Am J Surg 1979;138:463-467.
304. Pottinger J., Burns S., and Manske C. Bacterial carriage by artificial versus natural nails. Am J Infect Control 1989;17:340-344.
305. McNeil S. A., Foster C. L., and Hedderwick S. A. Effect of hand cleansing with antimicrobial soap or alcohol-based gel on microbial colonization of artificial fingernails worn by health care workers. Clin Infect Dis 2001;32:367-372.
306. Rubin D. M. Prosthetic fingernails in the OR. AORN J 1988;47:944-948.
307. Moolenaar R. L., Crutcher M., San Joaquin V. H., Sewell L. V., Hutwagner L. C., Carson L. A., Robison D. A., Smithee L. M., and Jarvis W. R. A prolonged outbreak of *Pseudomonas aeruginosa* in a neonatal intensive care unit: did staff fingernails play a role in disease transmission? Infect Control Hosp Epidemiol 2000;21:80-85.
308. Passaro D. J., Waring L., Armstrong R., Bolding F., Bouvier B., Rosenberg J., Reingold A. W., McQuitty M., Philpott S. M., Jarvis W. R., Werner S. B., Tompkins L. S., and Vugia D. J. Postoperative *Serratia marcescens* wound infections traced to an out-of-hospital source. J Infect Dis 1997;175:992-995.
309. Foca M., Jakob K., Whittier S., Della Latta P., Factor S., Rubenstein D., and Saiman L. Endemic *Pseudomonas aeruginosa* infection in a neonatal intensive care unit. N Engl J Med 2000;343:695-700.
310. Parry M. F., Grant B., Yukna M., Adler-Klein D., McLeod G. X., and Taddonio R. Candida osteomyelitis and diskitis after spinal surgery: an outbreak that implicates artificial nail use. Clin Infect Dis 2001;32:352-357.
311. Garner J. S. and Simmons B. P. CDC guideline for isolation precautions in hospitals. Infect Control 1983;4:245-325.
312. Centers for Disease Control and Prevention. Recommendations for prevention of HIV transmission in health-care settings. MMWR 1987;36 suppl 2S:3S-18S.
313. Occupational Safety and Health Admininstration. Occupational exposure to bloodborne pathogens: final rule. Federal Register 1991;29CFR Part 1910:1030.
314. Johnson S., Gerding D. N., Olson M. M., Weiler M. D., Hughes R. A., Clabots C. R., and Peterson L. R. Prospective, controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. Am J Med 1990;88:137-140.
315. Kotilainen H. R., Brinker J. P., Avato J. L., and Gantz N. M. Latex and vinyl examination gloves. Arch Intern Med 1989;149:2749-2753.
316. Reingold A. L., Kane M. A., and Hightower A. W. Failure of gloves and other protective devices to prevent transmission of hepatitis B virus to oral surgeons. JAMA 1988;259:2558-2560.
317. Korniewicz D. M., Laughon B. E., and Butz A. Integrity of vinyl and latex procedures gloves. Nurs Res 1989;38:144-146.
318. DeGroot-Kosolcharoen J. and Jones J. M. Permeability of latex and vinyl gloves to water and blood. Am J Infect Control 1989;17:196-201.
319. Korniewicz D. M., Kirwin M., and Cresci K. In-use comparison of latex gloves in two high-risk units: surgical intensive care and acquired immunodeficiency syndrome. Heart Lung 1992;21:81-84.
320. Korniewicz D. M., Kirwin M., and Cresci K. Barrier protection with examination gloves: double versus single. Am J Infect Control 1994;22:12-15.
321. Sistrom, M. G., Muto, C. A., Neal, J., and Strain, B. A. Glove leakage rates as a function of latex content and brand.

Presented at the 10th Annual Meeting of Society of Healthcare Epidemiology of America, Orlando, FL, 1998;abstr 24.
322. Flanagan, H. and Farr, B. Continued evaluation of glove leakage rates at the University of Virginia. Presented at the 11th Annual Meeting of the Society for Healthcare Epidemiology of America, Toronto, 2001;abstr 5.
323. Korniewicz D. M., Laughon B. E., and Cyr W. H. Leakage of virus through used vinyl and latex examination gloves. J Clin Microbiol 1990;28:787-788.
324. Rego A. and Roley L. In-use barrier integrity of gloves: latex and nitrile superior to vinyl. Am J Infect Control 1999;27:405-410.
325. Fisher M. D., Reddy V. R., Williams F. M., and Lin K. Y. Biomechanical performance of powder-free examination gloves. J Emerg Med 1999;17:1011-1018.
326. Edlich R. F., Suber F., Neal J. G., and Jackson E. M. Integrity of powder-free examination gloves to bacteriophage penetration. J Biomed Mater Res 1999;48:755-758.
327. Murray C. A., Burke F. J. T., and McHugh S. An assessment of the incidence of punctures in latex and non-latex dental examination gloves in routine clinical practice. Br Dental Journal 2001;190:377-380.
328. Patterson J., Vecchio J., Pantelick E. L., Farrel P., Mazon D., Zervos M. J., and Hierholzer W. J., Jr. Association of contaminated gloves with transmission of *Acinetobacter calcoaceticus* var. *antitratus* in an intensive care unit. Am J Med 1991;91:479-483.
329. Lowbury E. J. L. Aseptic methods in the operating suite. Lancet 1968;1:705-709.
330. Jacobson G., Thiele J. E., McCune J. H., and Farrell L. D. Handwashing: ring-wearing and number of microorganisms. Nurs Res 1985;34:186-188.
331. Salisbury D. M., Hutfilz P., Treen L. M., Bollin G. E., and Gautam S. The effect of rings on microbial load of health care workers' hands. Am J Infect Control 1997;25:24-27.
332. Larson E., Silberger M., Jakob K., Whittier S., Lai L., Della Latta P., and Saiman L. Assessment of alternative hand hygiene regimens to improve skin health among neonatal intensive care unit nurses. Heart Lung 2000;29:136-142.
333. Gould D. Nurses' hand decontamination practice: results of a local study. J Hosp Infect 1994;28:15-30.
334. Gould D. and Chamberlain A. The use of a ward-based educational teaching package to enhance nurses' compliance with infection control procedures. J Clin Nursing 1997;6:55-67.
335. Berg D. E., Hershow R. C., and Ramirez C. A. Control of nosocomial infections in an intensive care unit in guatemala city. Clin Infect Dis 1995;21:588-593.
336. Kirkland K. B. and Weinstein J. M. Adverse effects of contact isolation. Lancet 1999;354:1177-1178.
337. Aspock C. and Koller W. A simple hand hygiene exercise. Am J Infect Control 1999;27:370-372.
338. McGuckin M., Waterman R., Porten L., Bello S., Caruso M., Juzaitis B., Krug E., Mazer S., and Ostrawski S. Patient education model for increasing handwashing compliance. Am J Infect Control 1999;27:309-314.
339. Khatib M., Jamaleddine G., Abdallah A., and Ibrahim Y. Hand washing and use of gloves while managing patients receiving mechanical ventilation in the ICU. Chest 1999;116:172-175.
340. Haley R. W. and Bregman D. The role of understaffing and overcrowding in recurrent outbreaks of staphylococcal infection in a neonatal special-care unit. J Infect Dis 1982;145:875-885.
341. Pittet D. and Boyce J. M. Hand hygiene and patient care: pursuing the Semmelweis legacy. Lancet Infectious Diseases 2001;April:9-20.
342. O'Boyle C. A., Henly S. J., and Duckett L. J. Nurses' motivation to wash their hands: a standardized measurement approach. Applied Nursing Research 2001;14:136-145.
343. Semmelweis, I. *The etiology, concept and prophylaxis of childbed fever [excerpts]. The challenge of epidemiology - Issues and selected readings.* Washington, DC: PAHO Scientific Publication; 1988.
344. Mermel L. A., McCormick R. D., Springman S. R., and Maki D. G. The pathogenesis and epidemiology of catheter-related infection with pulmonary artery swan-ganz catheters: a prospective study utilizing molecular subtyping. Am J Med 1991;91(suppl 3B):197S-205S.
345. Raad I., Hohn D. C., Gilbreath B. J., Suleiman N., Hill L. A., Bruso P. A., Marts K., Mansfield P. F., and Bodey G. P. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. Infect Control Hosp Epidemiol 1994;15:231-238.
346. Sherertz R. J., Ely E. W., Westbrook D. M., Gledhill K. S., Streed S. A., Kiger B., Flynn L., Hayes S., Strong S., Cruz J., Bowton D. L., Hulgan T., and Haponik E. F. Education of physicians-in-training can decrease the risk of vascular catheter infection. Ann Intern Med 2000;132:641-648.
347. Eggimann P., Harbarth S., Constantin M. N., Touveneau S., Chevrolet J. C., and Pittet D. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. Lancet 2000;355:1864-1868.
348. Bull D. A., Neumayer L. A., Hunter G. C., Sethi G. K., McIntyre K. E., Bernhard V. M., and Putnam C. W. Improved sterile technique diminishes the incidence of positive line cultures in cardiovascular patients. J Surgical Research 1992;52:106-110.
349. Ojajarvi J. An evaluation of antiseptics used for hand disinfection in wards. J Hyg (Camb) 1976;76:75-82.
350. Mermel L. A., Josephson S. L., Dempsey J., Parenteau S., Perry C., and Magill N. Outbreak of *Shigella sonnei* in a clinical microbiology laboratory. J Clin Microbiol 1997;35:3163-3165.
351. Grohskopf L. A., Roth V. R., Feikin D. R., Arduino M. J., Carson L. A., Tokars J. I., Holt S. C., Jensen B. J., Hoffman R. E., and Jarvis W. R. *Serratia liquefaciens* bloodstream infections form contamination of epoetin alfa at a hemodialysis center. N Engl J Med 2001;344:1491-1497.
352. Dharan S., Hugonnet S., Sax H., and Pittet D. Evaluation of interference of a hand care cream with alcohol-based hand disinfection. Occup Environ Dermatol 2001;49:81-84.
353. McGuckin M., Waterman R., Storr J., Bowler I. C. J. W., Ashby M., Topley K., and Porten L. Evaluation of a patient-empowering hand hygiene programme in the U.K. J Hosp Infect 2001;48:222-227.
354. Girou, E., Oppein, F., Cizeau, F., Ducellier, D., Dupil, A., and Brun-Buisson, C. Increased compliance with hand cleansing after implementation of hand rubbing with an alcohol-based solution in a French university hospital. 11th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America, Toronto 2001;abstr 13.