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Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs

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INTRODUCTION

Nosocomial infections (NIs) remain a major global concern. Approximately 2 million NIs occur annually in the United States (232). Overall national prevalence rates have been described as ranging between 3.5 and 9.9% (160), but they vary significantly between departments, patient groups, types of surgical procedures, and the use of indwelling medical devices, etc. (20, 162). The most common NIs are urinary tract infections, lower respiratory tract infections, surgical-site infections, and primary septicemia (27, 159, 528, 532). They lead to additional days of treatment (146, 232, 411, 431, 605), increase the risk of death (27, 157), and increase treatment costs (217, 232, 234, 414, 431, 440, 460, 489, 605). The overall financial burden incurred by NIs has been estimated to be $4.5 billion per year in the United States alone (232). Approximately one-third of all NIs are regarded as preventable (193).

In 2002, a new Centers for Disease Control and Prevention (CDC) guideline for hand hygiene in health care settings, entitled *Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force*, was published (71). It provides health care workers with a review of data on hand washing and hand antisepsis in health care settings and provides specific recommendations to promote improved hand hygiene practices and reduce the transmission of pathogenic microorganisms to patients and personnel in health care settings. As a clinical guideline, its chief aim is to reduce the incidence of NIs by providing detailed recommendations on two main aspects of hand hygiene: (i) choice of the most appropriate agents for hand hygiene in terms of efficacy and dermal tolerance and (ii) different strategies to improve compliance in hand hygiene, including hand hygiene practices among health care workers, behavioral theories, and methods for reducing adverse effects of agents. Our review is intended to support the CDC guideline by presenting specific additional aspects of the various agents, such as a broader evaluation of the in vitro and in vivo efficacy in various test models and their mode of action, resistance potential, and effect on compliance in hand hygiene.

Hand hygiene has been considered to be the most important tool in NI control (403, 462) ever since Semmelweis observed its immense effect on the incidence of childbed fever (473). Health care workers have three opportunities for the postcontamination treatment of hands: (i) the social hand wash, which is the cleaning of hands with plain, nonmedicated bar or liquid soap and water for removal of dirt, soil, and various organic substances; (ii) the hygienic (Europe) or antiseptic (United States) hand wash, which is the cleaning of hands with antimicrobial or medicated soap and water ("scrub"); most antimicrobial soaps contain a single active agent and are usually available as liquid preparations; and (iii) the hygienic hand disinfection (Europe), which normally consists of the application of an alcohol-based hand rub into dry hands without water.

For the preoperative treatment of hands two options are available: (i) the surgical hand wash (Europe) or surgical hand scrub (United States) which is the cleaning of hands with antimicrobial soap and water; and (ii) the surgical hand disinfection (Europe), which is the application of an alcohol-based hand rub into dry hands without water.

Three main types of preparations can be used for the different procedures of hand hygiene. (i) The first is plain, nonmedicated soap (social hand wash). (ii) The second is medicated soap (antiseptic and surgical hand wash). The most commonly used agent is chlorhexidine, usually at a concentration of 4 or 2%. Triclosan can also be found in medicated soaps, usually at a concentration of 1%. Hexachlorophene has now been banned worldwide because of its high rate of dermal absorption and subsequent toxic effects, especially among newborns (84, 98). Levels of 0.1 to 0.6 ppm in blood were found among health care workers who regularly used a 3% hexachlorophene preparation for hand washing (323). These findings speak strongly against the topical use of this active agent. The Food and Drug Administration classifies this agent as not being generally recognized as safe and effective for use as an antiseptic hand wash (21). Hexachlorophene is therefore not included in this review. Other active agents such as povidone iodine have rarely been used for the postcontamination treatment of hands and therefore are also not addressed in this review. (iii) The final type is the alcohol-based hand rub (hygienic and surgical hand disinfection). This is a leave-on preparation and this applied to the skin without the use of water.

In addition, non-alcohol-based waterless antiseptic agents are available for use by health care workers. Some of these contain quaternary ammonium-type compounds. They were not discussed in the CDC hand hygiene guideline because

TABLE 1. Contamination rates of health care workers' hands with nosocomial pathogens and their persistence on hands and inanimate surfaces[a]

Pathogen	Contamination rate(s) of health care workers' hands (%) (references)	Duration of persistence on hands (references)	Duration of persistence on inanimate surfaces (references)
Acinetobacter spp.	3–15 (132, 335, 519)	≥150 min (33)	3 days–5 mo (166, 233, 387, 393, 596, 598)
B. cereus	37 (569)	Unknown	Unknown
C. difficile	14–59 (362, 491)	Unknown	≥24 h (vegetative cells), up to 5 mo (spores) (363)
E. coli	Unknown	6–90 min (33, 151)	2 h–16 mo (3, 111, 190, 350, 376, 393, 509)
"Gram-negative bacteria"	21–86.1 (4, 7, 166, 187, 271, 302, 378)	Unknown	Unknown
Influenzavirus, parainfluenzavirus	Unknown	10–15 min (25, 46)	12–48 h (46, 72, 433, 614)
HAV	Unknown	Several hours (354, 355)	2 h–60 days (1, 2, 356)
HCV	8–23.8 (11)	Unknown	Unknown
Klebsiella spp.	17 (81)	Up to 2 h (33, 81, 151, 514)	2 h–30 mo (111, 190, 376, 393, 509)
MRSA	Up to 16.9 (378, 412, 542)	Unknown	4 wk–7 mo (114, 581)
P. vulgaris	Unknown	≥30 min (33)	1–2 days (376)
Pseudomonas spp.	1.3–25 (53, 119, 144, 420, 607)	30–180 min (33, 119)	6 h–16 mo (111, 178, 190, 393, 509)
Rhinovirus	Up to 65 (191, 457)	Unknown	2 h–7 days (456, 497)
Rotavirus	19.5–78.6 (490)	Up to 260 min (22)	6–60 days (1, 2, 24)
Salmonella spp.	Unknown	≤3 h (427)	6 h–4.2 yr (209, 376, 467)
S. marcescens	15.4–24 (90, 492)	≥30 min (33)	3 days–2 mo (111, 376)
S. aureus	10.5–78.3 (90, 101, 179, 359, 378, 412, 546)	≥150 min (33)	4 wk–7 mo (190, 394, 509, 581, 582)
VRE	Up to 41 (202)	Up to 60 min (402)	5 days–4 mo (39, 393, 394, 402, 599)
"Yeasts," including *Candida* spp. and *Torulopsis glabrata*	23–81 (90, 112, 221, 378, 541)	1 h (79, 564)	1–150 days (65, 452, 564)

[a] Persistance of nosocomial pathogens on inanimate surfaces is important because of the high rate of acquisition of these pathogens on the hands after contact with environmental surfaces (58).

there was insufficient evidence at the time to promote their use; therefore, they are not further evaluated here.

This review provides an in-depth comparison of the several options for hand hygiene, with the aim of further supporting the CDC guideline on hand hygiene.

TYPES OF SKIN FLORA

Three principal types of skin flora have been described. The resident and transient flora were already distinguished in 1938 (447, 470). In addition, the infectious flora was described, with species such as *Staphylococcus aureus* or beta-hemolytic streptococci, which are frequently isolated from abscesses, whitlows, paronychia, or infected eczema (475).

The resident flora consists of permanent inhabitants of the skin. They are found mainly on the surface of the skin and under the superficial cells of the stratum corneum (379). These bacteria are not regarded as pathogens on intact skin but may cause infections in sterile body cavities, in the eyes, or on nonintact skin (292). Resident skin bacteria survive longer on intact skin than do gram-negative transient species (325). The protective function of the resident flora, so-called colonization resistance, has been demonstrated in various in vitro and in vivo studies. Its purpose is twofold: microbial antagonism and the competition for nutrients in the ecosystem (12). Nevertheless, the interactions between bacteria and fungi on the skin are still inadequately understood. Many such interactions have been demonstrated experimentally. Their contribution—which is thought to be a major mechanism of preventing the adherence of pathogens—to the stability of the dermal ecosystem, however, remains unclear (375).

The dominant species is *Staphylococcus epidermidis*, which is found on almost every hand (311, 454, 522). The incidence of oxacillin resistance among isolates of *S. epidermidis* is up to 64.3% (311) and is higher among health care workers who have direct contact with patients than in those who do not (522). Other regular residents are *Staphylococcus hominis* and other coagulase-negative staphylococci, followed by coryneform bacteria such as propionibacteria, corynebacteria, dermabacteria, and micrococci (137, 315, 401). Among fungi, the most important genus of the resident skin flora is *Pityrosporum* (*Malassezia*) (201). Viruses are usually not resident on the skin but can proliferate within the living epidermis, where they may induce pathological changes (361).

Total counts of bacteria on the hands of medical staff have ranged from 3.9×10^4 to 4.6×10^6 (294, 309, 338, 447). Their number increases with the duration of clinical activities, on average by 16 cells per min (438). Some clinical situations are associated with a higher bacterial load on the hands of health care workers: direct contact with patients, respiratory tract care, contact with body fluids, and after being interrupted while caring for a patient (438). In general, however, it is difficult to clearly assign a specific risk of hand contamination to certain patient care activities. Nurses can contaminate their hands with 100 to 1,000 CFU of *Klebsiella* spp. during "clean activities" (81), while 10 to 600 CFU/ml can be found on nurses' hands after touching the groins of patients heavily contaminated with *Proteus mirabilis* (129). In intensive care units (ICU), the number of direct contacts between the hands of the health care workers and the patients is particularly high, leading to a higher risk of NI (148).

The transient skin flora consists of bacteria, fungi, and viruses that may be found on the skin only at times (447). They usually do not multiply on the skin, but they survive and occasionally multiply and cause disease (15). They may come from patients or inanimate surfaces. Between 4 and 16% of the hand surface is exposed by a single direct contact, and after 12 direct contacts, up to 40% of the hand surface may have been touched (74). The transmissibility of transient bacteria depends on the species, the number of bacteria on the hand, their survival on skin, and the dermal water content (230, 344, 418).

In addition, there is the temporary resident skin flora, which

TABLE 2. Overview of NIs traced to the hands of an individual health care worker or another relevant point source and analysis of the main reason for transmission

Pathogen	Type and no. of NIs	Department	Source	Reason for transmission	Reference
Adenovirus	Epidemic keratoconjunctivitis, 126	Ophthalmology	Infected doctor	Carrier (hand)	235
C. tropicalis	Surgical site infections, 8	Cardiothoracic surgery	Surgical nurse	Carrier (hand), use of nonmedicated soap before surgery due to intolerance of the antiseptic soap	226
HCV	Hepatitis C, 5	Orthopedic and general surgery	Infected anesthesist	Wound on finger during incubation	469
K. aerogenes	Urinary tract infections, 17	Urology	Nurse	Carrier (hand)	82
MRSA	Diarrhea, 8	Orthopedic surgery	Health care worker	Carrier (nose and hands)	507
MRSA	Surgical-site infections, 3	Pediatric cardiovascular surgery	Surgeon	Carrier (nose and hands)	595
MRSA	Surgical-site infections, 5	Cardiac surgery	Hand of assisting surgeon	Dermatitis on hand of surgeon	589
S. liquefaciens	Bloodstream infections, 15	Hemodialysis	Contaminated medicated soap	Transient hand carriage, leading to contamination of epoetin alpha	183
S. marcescens	Septicemia, meningitis, pneumonia, 14	Neonatal ICU	Contaminated triclosan-based liquid soap	Use of soap, resulting in transient hand carriage	574
S. marcescens	Septicemia, meningitis, 15	Neonatal ICU	Contaminated brush	Use of the brush, probably resulting in transient hand carriage	16
S. marcescens	Pneumonia, septicemia, urinary tract infection, surgical-site infection, 83	11 different units	Contaminated liquid soap	Use of soap, resulting in transient hand carriage	492
S. marcescens	Surgical-site infections, 5; septicemia, 2	Cardiovascular surgery	Surgical nurse	Highly contaminated nail cream	417
S. aureus	Dermatitis exfoliativa, 42	Obstetrics	Midwife	Hand eczema	102
S. epidermidis	Surgical-site infections with mediastinitis, 7	Cardiovascular surgery	Hand of assisting surgeon	Chronic dermatitis on hand of surgeon	292

persists and multiplies for a limited period on the skin. The definition is more or less identical to that of transient skin flora, because the duration of residence on human skin is uncertain and variable but never permanent (5). In addition, the temporary resident skin flora often includes nosocomial bacteria and fungi (5, 201, 399, 400).

MICROBIAL AND VIRAL FLORAS OF HANDS AND THEIR EPIDEMIOLOGIC ROLE

Gram-Positive Bacteria

Role in NIs. *S. aureus* is the most common gram-positive bacterium causing NIs (353, 533). Its frequency among all pathogens in NIs varies between 11.1 and 17.2% (265, 484, 493, 583). Methicillin resistance in *S. aureus* (MRSA) is increasing worldwide (113, 503, 578), leading not only to NIs but recently also to community-acquired infection. In 139 ICUs in Germany, 14.3% of all 1,535 NIs due to *S. aureus* have been caused by MRSA. This proportion is highest for urinary tract infections (26.4%), followed by primary septicemia (23.3%), and lower respiratory tract infection (12.9%) (161). The most common type of NI caused by *S. aureus* is the surgical-site infection (245, 259, 422).

Enterococcus spp. are isolated in up to 14.8% of patients with NI (484). The most common species are *Enterococcus faecium* and *E. faecalis* (385), which frequently cause urinary tract infections (533). The emergence of vancomycin resistance among enterococci (VRE) has led to an increased recognition of cross-transmission of VRE, including the role of health care workers' hands (29, 347).

Coagulase-negative staphylococci, such as *S. epidermidis*, mainly cause catheter-associated primary bloodstream infections. In ICUs, approximately one-third of all blood culture isolates from patients with nosocomial bloodstream infections were found to be coagulase-negative staphylococci (463, 533).

Frequency of colonized hands. Colonization of health care workers' hands with *S. aureus* has been described to range between 10.5 and 78.3% (Table 1). Up to 24,000,000 cells can be found per hand (33). The colonization rate with *S. aureus* was higher among doctors (36%) than among nurses (18%), as was the bacterial density of *S. aureus* on the hands (21 and 5%, respectively, with more than 1,000 CFU per hand) (101). The carrier rate may be up to 28% if the health care worker contacts patients with an atopic dermatitis which is colonized by *S. aureus* (608, 609). MRSA has been isolated from the hands of up to 16.9% of health care workers. VRE can be found on the hands of up to 41% of health care workers (Table 1).

Role of hand colonization in cross-transmission. Hand carriage of pathogens such as *S. aureus*, MRSA, or *S. epidermidis* has repeatedly been associated with different types of NI (Table 2) (212, 455). The analysis of outbreaks revealed that dermatitis on the hands of health care workers was a risk factor for colonization or for inadequate hand hygiene, resulting in various types of NI (Table 2).

Transmissibility of VRE has also been demonstrated. The hands and gloves of 44 health care workers were sampled after

care of VRE-positive patients. Gloves were VRE positive for 17 of 44 healthcare workers, and hands were positive for 5 of 44, even though they had worn gloves (553). One health care worker was even VRE positive on the hands although the culture from the glove was negative (553).

Survival on hands and surfaces. *S. aureus* can survive on hands for at least 150 min; VRE survives on hands or gloves for up to 60 min (Table 1). On inanimate surfaces, *S. aureus* and MRSA may survive for 7 months, with wild strains surviving longer than laboratory strains (Table 1). VRE may survive on surfaces for 4 months. The long survival on surfaces, together with the relatively short survival on hands, suggests that contaminated surfaces may well be the source of transient colonization despite negative hand cultures.

Gram-Negative Bacteria

Role in NIs. *Escherichia coli* is the most common gram-negative bacterium, causing mainly urinary tract infections (265, 463). *Pseudomonas aeruginosa* is also very common, chiefly causing lower respiratory tract infections (265, 463). In the majority of cases, both types of infection are device associated (364, 463, 531) and are often found among patients in ICUs (260). Manual handling of devices such as urinary catheters, ventilation equipment, and suction tubes emphasizes the importance of the hands of health care workers in possible cross-transmission of gram-negative bacteria. Overall, gram-negative bacteria are found in up to 64% of all NIs (463).

Frequency of colonized hands. Colonization rates of gram-negative bacteria on the hands of health care workers have been described as ranging from 21 to 86.1% (Table 1), with the highest rate being found in ICUs (271). The number of gram-negative bacteria per hand may be as large as 13,000,000 cells (33). The colonization may be long-lasting (302). Even in nursing homes, a rate of 76% has been described for nurses hands (610). Colonization with gram-negative bacteria is influenced by various factors. For example, it is higher before patient contact than after the work shift (187). Hands with artificial fingernails harbor gram-negative bacteria more often than those without (207). Higher colonization rates with gram-negative bacteria also occur during periods of higher ambient temperature and high air humidity (358).

Different species of gram-negative bacteria exhibit different colonization rates. For instance, the colonization rate is 3 to 15% for *Acinetobacter baumannii*, 1.3 to 25% for *Pseudomonas* spp., and 15.4 to 24% for *Serratia marcescens* (Table 1). *Klebsiella* spp. were found on the hands of 17% of the ICU staff sampled, with up to 10,000 bacteria per hand (81). Artificial fingernails have been associated with a higher risk for colonization with *P. aeruginosa* (144).

Role of hand colonization in cross-transmission. Transient hand carriage of various gram-negative bacterial species has quite often been suspected to be responsible for cross-transmission during outbreaks resulting in various types of NI (155, 426, 514, 571). Most reports of cross-transmission of specific gram-negative bacteria come from critical-care areas, such as neonatal ICUs and burn units. Contaminated hands (Table 1), brushes, contaminated plain soap, and contaminated antiseptic soap have been associated with various types of NI, which were quite often caused by *S. marcescens* (Table 2).

Survival on hands and surfaces. Most gram-negative bacteria survive on the hands for 1 h or more. Survival on inanimate surfaces has been reported to be different for the different gram-negative species, with most of them surviving for many months (Table 1). In general, gram-negative bacteria survive for longer on inanimate surfaces than on human skin (151).

Spore-Forming Bacteria

Role in NIs. The main spore-forming bacterium causing NIs is *Clostridium difficile*. It is estimated that between 15 and 55% of all cases of nosocomial antibiotic-associated diarrhea are caused by *C. difficile* (40, 374, 567, 613). Patients with diarrhea caused by *C. difficile* have on average 3.6 additional hospital days attributable to the NI, which in the United States costs approximately $3,669 per case or $1.1 billion per year (289). The overall mortality is 15% (381). Extraintestinal manifestations are very uncommon (≤1%) (156). Patients can be contaminated from, for instance, the hands of hospital personnel and from inanimate surfaces (40).

Frequency of colonized hands. In one study, the hands of 59% of 35 health care workers were *C. difficile* positive after direct contact with culture-positive patients. Colonization was found mainly in the subungual area (43%), on the fingertips (37%), on the palm (37%), and under rings (20%) (362). In another study, 14% of 73 health care worker were culture positive for *C. difficile* on their hands. The presence of *C. difficile* on the hands correlated with the density of environmental contamination (491). During a third outbreak, caused by *Bacillus cereus* in a neonatal ICU, 11 (37%) of 30 fingerprints from health care workers were positive for *Bacillus* spp. (569).

Role of hand colonization in cross-transmission. Transmission of *C. difficile* in an endemic setting on a general medical ward has been shown to occur in 21% of patients, with 37% of them suffering from diarrhea (362). An outbreak of necrotizing enterocolitis among neonates was associated with clostridial hand carriage in four of seven health care workers (173). Another spore-forming bacterium has been described as well: *B. cereus* was transmitted to the umbilicus in 49% of newborns on a maternity ward; the hands of 15% of the health care workers were found to be culture positive (62).

Survival on hands and surfaces. Vegetative cells of *C. difficile* can survive for at least 24 h on inanimate surfaces, and spores survive for up to 5 months (Table 1).

Fungi

Role in NIs. Fungi are less commonly found than bacteria as the causative agent of NIs, but their frequency and importance are increasing (216, 502, 527). In Germany and New Zealand, 6% of all NIs were caused by fungi (397, 484). In Spain, the overall rate was found to be 2.4% in 1990 and 3.2% in 1999, indicating a higher clinical relevance for NIs in the more recent study (26). In the United States, an increase in isolation of yeasts from 7.6 to 10.6% has been noted over a period of 10 years in patients with NIs (593). The most important fungus with respect to NIs is *Candida albicans*. Fungi may cause septicemia, urinary tract infections, or surgical-site infections (463, 500). Device-associated bloodstream infections caused by *Can-*

TABLE 3. Transmissibility of nosocomial pathogens from contaminated hands

Type of pathogen	Contact time (s)	Target	Transmission rate (%)	Reference
C. albicans	Unknown	Hands	69	452
Feline calicivirus	10	Food	18–46	60
		Steel surface	13	
HAV	10	Lettuce	9.2	59
HSV-1	Unknown	Hands	100 (moist skin), 60 (dry skin)	41
Rhinovirus	10	Hands	71	191
Rotavirus	10	Hands	6.6	22
Salmonella spp.	5	Meat	16 (inoculum of 7 cells per fingertip), 100 (inoculum of ≥600 cells per fingertip)	427

dida spp. have become more common among critically ill patients in the last decades (89, 128, 163, 342); the contribution of non-*albicans Candida* spp. is increasingly significant (216). It has also been reported that 21% of all urinary tract infections among ICU patients are caused by *C. albicans* (463).

Frequency of colonized hands. In an ICU, 67 (46%) of the hands of 146 health care workers were colonized with a yeast. The most common species were *Candida* and *Rhodotorula* spp. Respiratory therapists were found to have the highest colonization rate (69%) (221). In another study of nurses and other hospital staff, 75% of the nurses and 81% of the other hospital staff were colonized with a yeast (541). In a long-term-care facility, 41% of 42 health care workers were found to have *Candida* spp. on their hands (378). Yeasts quite often also colonize artificial fingernails (207). Acquisition of *C. albicans* on the hands of health care workers immediately after attending systemically infected patients was reported to occur in 2 of 17 nurses (79).

Role of hand colonization in cross-transmission. Only a few studies are found in the literature which demonstrate the role of hands in cross-transmission (Table 2), sometimes despite negative hand cultures (572). The analysis of an outbreak revealed that caring for a patient who is colonized with *Candida parapsilosis* can lead to positive hand cultures and finally to severe infections or colonization among patients (501). The transmissibility of yeasts from hand to hand is high (Table 3).

Survival on hands and surfaces. On fingertips, only 20% of viable cells of *C. albicans* and *C. parapsilosis* remain detectable after 1 h (79, 564). *Candida* spp. can survive on surfaces for up to 150 days (452, 564). During this period of survival, most yeast cells die within the first few minutes (452).

Viruses

Role in NIs. Viruses account for approximately 5% of all NIs. On pediatric wards, the proportion is higher at 23% (6). Five main groups of viruses have been identified with respect to their nosocomial transmission: blood-borne viruses (e.g., hepatitis B virus [HBV], hepatitis C virus [HCV], and human immunodeficiency virus [HIV]), respiratory route viruses (e.g., respiratory syncytial virus [RSV], influenza virus, rhinovirus, coronavirus, and adenovirus), fecal-oral route viruses (e.g., rotavirus, small round structured viruses [noroviruses], enteroviruses, and hepatitis A virus [HAV]), herpesviruses obtained from direct contact with skin, mucous membranes, or wounds (e.g., herpes simplex viruses, varicella zoster virus, cytomegalovirus, and Epstein-Barr virus), and exotic viruses such as viral hemorrhagic fever viruses (Ebola virus, Marburg virus, Lassa fever virus, and Congo Crimean hemorrhagic fever virus) and rabies virus (8). The fingers, especially the pads and tips, are the most likely areas to come into contact with viruses while touching infected people and their bodily substances as well as other contaminated materials (499, 576).

Frequency of contaminated hands. The risk of direct contact with blood and thereby with blood-borne viruses is variable. In general, it must be assumed that a health care worker wears protective gloves if contact with blood is expected. However, there are still clinical situations in which contamination with blood is unexpected. Health care workers in invasive radiology have blood contact in 3% of clinical activities, surgeons have blood contact in 50%, and midwives have blood contact in 71% (48). Surgical gloves should protect from direct contact with blood, but perforations are found on average in 17% of gloves, which correlates with the detection of blood under surgical gloves in 13% of surgeons (392). Perforations in most gloves (83%) remain undetected by the surgeon (557). Up to 82.5% of protective gloves have invisible perforations (276). In an acute viremic state, HBV may be present in blood at a concentration of 5×10^8 IU per ml of blood (623). A 1-μl volume of blood, which is hardly visible on a hand, may still contain 500 IU of HBV. For HCV, a concentration of 10^4 to 10^7 IU was found in blood (105). Virus detection on the hands has been investigated in a few studies. In a dialysis unit, 23.8% of samples obtained from health care workers' hands were positive for HCV RNA after treatment of HCV-positive patients despite the use of standard precautions, whereas the rate was 8% after treatment of HCV-negative patients (11).

Viruses from the respiratory tract are often found on hands, e.g., rhinoviruses in up to 65% from persons with a common cold (191, 457). Adenovirus has been found on the hands of healthcare workers during outbreaks of keratoconjunctivitis (380) and was isolated from the hands of 46% of patients with epidemic keratoconjunctivitis (35), which emphasizes the potential of virus transfer to hospital personnel through casual hand contact. No data were available regarding the detection of severe acute respiratory syndrome (SARS) virus on hands during the outbreaks in Asia and Canada in 2003.

Rotaviruses can be found on the hands in up to 78.6% of individuals sampled (Table 1) and also on surfaces with frequent hand contact, e.g., TV sets, toys, and patient charts (9). At the peak of a bout of rotavirus gastroenteritis, every gram of

TABLE 4. Spectrum of antimicrobial activity of procedures for hand hygiene derived from the etiology of NIs, data on the transient flora of health care workers' hands, and their role in the transmission of nosocomial pathogens

Type of antimicrobial activity	Required activity	Optional activity[a]
Bactericidal	+	
Mycobactericidal		+
Sporicidal		+
Fungicidal (yeasts)	+	
Fungicidal		+
Virucidal (enveloped viruses)	+	
Virucidal (including nonenveloped viruses)		+

[a] May be relevant in special patient care or during outbreaks.

feces may contain more than 10^7 to 10^8 infectious viral particles (590).

Cytomegalovirus has been isolated from the hands of day care workers (224), but exotic viruses such as hemorrhagic fever viruses have to date not been detected on health care workers' hands.

Role of hand colonization in cross-transmission. Hands play a major role especially in the transmission of blood-borne, fecal, and respiratory tract viruses. The transmission of some viruses from the hands of health care workers has been described (Table 2). In addition, transient hand carriage is associated with the transmission of many viruses, such as rhinovirus (99, 191), RSV (194, 488), astrovirus (136), and cytomegalovirus (109). For the SARS virus, a similar correlation has been described, since hand hygiene was found to be the second most effective measure to prevent cross-transmission of the SARS virus in a hospital (510). Most viruses are easily transmitted from hand to hand, food, or surfaces (Table 3).

Persistence of infectivity on hands and surfaces. Persistance of viruses on the hands has been investigated mainly for fecal and respiratory tract viruses. Artificial contamination of hands with HAV led to an immediate-recovery rate of 70.5% (59). HAV persisted for several hours on human hands (354, 355). With poliovirus, the immediate-recovery rate was 22% but the whole inoculum was recovered after 150 min, indicating an almost complete persistence of poliovirus on hands (505). Rotavirus has been described as persisting on hands for up to 260 min, with 57% recovery after 20 min, 42.6% recovery after 60 min, and 7.1% recovery after 260 min (22). It can be transferred from contaminated hands to clean hands, with 6.6% of the viral contamination transferred 20 min after contamination (Table 3), and 2.8% of the viral contamination transferred 60 min after contamination (22). Rotavirus has been described to persist better on hands than rhinovirus or parainfluenzavirus (24).

Many enveloped viruses such as influenza virus, parainfluenza virus (Table 1), and cytomegalovirus (139) may survive on the hands for 10 to 15 min or even up to 2 h (herpes simplex virus type 1 [Table 1]). Adenoviruses have been described to persist on human skin for many hours (499).

Only a few studies of the persistence of viruses on surfaces have been performed. Rotavirus and HAV can persist for up to 60 days (Table 1) depending on the room temperature, air humidity, and type of surface (495). HIV remains infective on surfaces for up to 7 days, depending on the inoculum and the type of preparation (cell-associated virus or cell-free virus). HIV obtained from clinical specimens remains infective for a few days (568). Influenza A virus may persist on steel for up to 48 h; on other materials, such as paper or handkerchiefs, the virus persists for up to 12 h (46). Rhinovirus may persist for up to 7 days (Table 1).

MINIMUM SPECTRUM OF ANTIMICROBIAL ACTIVITY

The new CDC guideline on hand hygiene does not suggest a specific minimum spectrum of antimicrobial activity of a suitable hand hygiene agent (71). However, it can be derived from the etiology of NIs as well as the data on the skin flora of the hands of health care workers and their role in the transmission of nosocomial pathogens (Table 4). A procedure for the postcontamination treatment of hands must have at least bactericidal, fungicidal (yeasts), and virucidal (coated viruses) activity.

The spectrum of activity can be substantiated in suspension tests (474). In principle, suspension tests are suitable to substantiate the spectrum of antimicrobial activity (474). The suggested activity against coated viruses is based on the frequent contamination of health care workers' hands with blood during routine patient care and thereby possibly with blood-borne viruses, such as HCV or HIV, where neither patients nor health care workers can be protected by vaccination. The contamination of hands with blood may not be visible but may still be infective with HCV or HIV for the health care worker or the next patient (123). That is why activity against coated viruses should be included in the minimum spectrum of activity for an active agent for hand hygiene. Uncoated viruses, however, are usually spread from patients with infective gastroenteritis (e.g., caused by noroviruses or rotaviruses), upper and

TABLE 5. Effect of alkali- and detergent-based nonmedicated soaps on human skin[a]

Type of effect	Effect observed with:	
	Alkaline-based soap	Detergent-based soap
Formation of lime soaps	Yes	No
Swelling	Substantial	Small
Dehydration	Moderate	Moderate to strong
Degreasing	Pronounced	Pronounced, depending on the amount of detergent
pH shift to alkaline	Substantial	Preventable
Neutralization capacity	Noticeably retarded	Somewhat retarded
Regeneration of skin pH	Strongly impaired	Slightly impaired
Surfaction	No	Possible

[a] Reprinted from reference 283 with permission of the publisher.

TABLE 6. Effect of a simple hand wash with water alone on various types of artificial transient hand flora

Microorganism	Duration of hand wash	Mean removal rate (log_{10})	Reference
E. coli	10 s	1.0	23
	1 min	2.99	377
	2 min	3.08	377
	4 min	3.39–3.67	377
Klebsiella spp.	20 s	1.7	81
VRE	5 s	0	402
	30 s	0	402
Rotavirus	10 s	0.79	23
	30 s	1.26–1.57	47

lower respiratory tract infections, or keratoconjunctivitis (e.g., caused by adenoviruses). These infections often have typical and visible symptoms. The activity against uncoated viruses can be restricted to a specific clinical area, e.g., in ophthalmology (adenovirus), pediatrics (rotavirus), or oncology (parvovirus) or to outbreaks of specific infectious diseases caused by uncoated viruses. Additional activity against the whole spectrum of fungi (including molds), mycobacteria, and bacterial spores may be relevant in special patient care situations (e.g., in bone-marrow transplant units) or during outbreaks. A procedure for the preoperative treatment of hands should be at least bactericidally and fungicidally (yeasts) effective, since the hands of most health care workers' hands carry yeasts and since surgical-site infections have also been associated with hand carriage of yeasts during an outbreak.

AGENTS FOR REDUCTION OF THE NUMBERS OF PATHOGENS ON HANDS

Nonmedicated Soap (Social Hand Wash)

Normally, nonmedicated soaps are detergent-based products. Those based on esterified fatty acids and sodium or potassium hydroxide are less skin compatible (Table 5). They are available in various forms including bar soaps, tissue, leaflet, and liquid preparations. This cleaning activity can be attributed to the detergent properties.

TABLE 7. Effect of a simple hand wash with plain soap and water on various types of artificial transient hand flora

Microorganism	Duration of hand wash	Mean removal rate (log_{10})	Reference(s)
E. coli	10 s	0.5	23
	15 s	0.6–1.1	406
	30 s	1.37–3	34, 326, 330
	1 min	2.6–3.23	257, 377, 478, 480
	2 min	3.27	377
P. aeruginosa	30 s	2–3	330
Klebsiella spp.	20 s	1.7	81
S. aureus	30 s	0.52–3	34, 318, 330
S. saprophyticus	30 s	2.49	34
Rotavirus	10 s	0.14	23
	30 s	1.17–1.19	47
C. difficile	10 s	2.0–2.4	57
B. atrophaeus	10 s	2.4	594
	30 s	2.3	594
	60 s	2.1	594

TABLE 8. Effect of various agents for hand hygiene on the resident hand flora

Type of agent	Concn (%)	Duration of treatment (min)	Mean removal rate (log_{10})	Reference(s)
Plain soap	NA	2	−0.05	36
	NA	3	0.3–0.57	96
	NA	5	0.3–0.4	208, 305, 326, 471
Chlorhexidine	4	2	0.35–1.0	36, 317, 329
	4	3	0.68–1.75	96, 218, 341, 471, 472
	4	5	0.9–1.6	49, 305, 404, 471
	4	6	1.2	153
	4	10	2.29	404
Triclosan	1	5	0.6	305
	2	2	0.3	36
	2	5	0.8	49
Ethanol	70	2	1.0	328
	70	3	1.32	326
	80	2	1.5	475
	85	3	2.1–2.5	251
	95	2	2.1	317, 320
Isopropanol	60	5	1.7	472
	70	0.5	1.5	36
	70	1	0.7–0.8	475
	70	2	1.2–1.65	36, 328
	70	3	1.5–2.0	475
	70	5	2.1–2.4	475
	80	3	2.3	483
	90	3	2.4	483
n-propanol	60	1	1.1	475
	60	3	0.8–2.9	213, 240, 251, 341
	60	5	2.05–2.9	208, 213, 471, 479

[a] NA, not applicable.

Effect on microorganisms and viruses. (i) Spectrum of activity. Nonmedicated soaps do not contain any active ingredient with an antimicrobial activity apart from preservatives. That is why in vitro data on the antimicrobial activity of nonmedicated soap rarely exist. The first experiments with soft alkaline soap were carried out by Robert Koch. He found out that multiplication of the vegetative cells of *Bacillus anthracis* was completely (dilution of 1:1,000) or partly (dilution of 1:5,000) inhibited (273). A more recent study described a fungistatic effect of a tenside-based soap at dilutions between 1:64 and 1:1,000 against *Trichosporon cutaneum*, *C. albicans*, *Trichophyton rubrum*, *Trichophyton schönleinii*, *Microsporum audouinii*, and *Microsporum canis* (277). With one plain soap, even limited fungicidal activity was described and largely explained by the presence of preservatives (603).

(ii) Testing under practical conditions. The use of plain soap and water reduces the numbers of microorganisms and viruses by mechanical removal of loosely adherent microorganisms from the hands. Many studies are available which address the reduction of the transient hand flora. The most common type of artificial contamination of hands for test purposes in the United States is *S. marcescens* (21), whereas *E. coli* is the main contaminant used in Europe (115). Regarding the transient flora, a reduction between 0.5 and 2.8 log_{10} units can be found within 1 min for *E. coli* (Table 6). Other types of artificial contamination have been used as well, such as VRE, rotavirus, *Klebsiella* spp., or spores of *Bacillus atrophaeus*. A simple hand wash still leads to a mean reduction of up to 2.4 log_{10} units within 1 min (Table 7). There is basically no effect on resident hand flora after a 2-min hand wash; after a 5-min hand wash, a reduction of 0.4 log_{10} unit was found, and after

3 h of wearing gloves, no reduction at all was observed (Table 8).

(iii) In-use tests. The effect of a social hand wash "in real life" has also been studied. Among 224 healthy homemakers, a single hand wash had little impact on microbial counts (mean log counts before hand wash, 5.72 ± 0.99; mean log counts after hand wash, 5.69 ± 1.04) (307). In a study with 11 volunteers who washed their hands for 15 s with water alone 24 times per day for a total of 5 days, a slight increase of the bacterial counts was observed (mean log bacterial counts: prewash, 4.91 ± 0.46; postwash, 5.12 ± 0.44); when bar soap was used, a similar result was found (mean log bacterial counts: prewash, 4.81 ± 0.46; postwash, 5.07 ± 0.47) (299). Other authors, too, have found paradoxical increases in bacterial counts on the skin after hand washing with plain soap (299, 371, 611). In contrast, another study showed that a 5-min hand wash with regular bar soap reduced the resident hand flora by 0.33 $\log_{10}$ units (326). The use of a nonmedicated soap by a surgical nurse for the preoperative treatment of hands even led to eight cases of surgical-site infection after cardiac surgery, which underscores the limited efficacy of nonmedicated soap (226).

Some studies have examined only microorganisms that are left on the hands after a hand wash. Washing hands with soap and water has been described to be ineffective in eliminating adenovirus from the culture-positive hands of a physician and patients, indicating that mechanical removal was incomplete (235). Transient gram-negative bacteria remained on the hands of health care workers in 10 of 10 cases despite five successive hand washes with soap and water (187). Furthermore, transmission of gram-negative bacteria from hands has been shown to occur 11 of 12 cases when a simple hand wash is carried out (129).

(iv) Risk of contamination by a simple hand wash. One risk of using soap and water is the contamination of hands by the washing process per se. This has been reported for *P. aeruginosa* (143). A possible source is the sink itself, when splashes of contaminated water come in contact with the hand of the health care worker (119). The reason is that the microorganisms are not killed during the hand wash but only removed and distributed in the immediate surroundings of the person, including the clothes. Nonmedicated soaps may also become contaminated and lead to colonization of the hands of personnel and to NIs, e.g., with *S. marcescens* (492) or *Serratia liquefaciens* (183).

Although the data involving nonmedicated soap suggest that a simple hand wash has some effect on the transient hand flora, it must be borne in mind that, in reality, a simple hand wash often does not last longer than 10 s (121, 145, 176, 177, 180, 300, 334, 450, 552).

Effect on human skin. Each hand wash detrimentally alters the water-lipid layer of the superficial skin, resulting in a loss of various protective agents such as amino acids and antimicrobial protective factors. Regeneration of the protective film may be insufficient if many hand washes are carried out in a row. This may lead to damage of the barrier function of the stratum corneum by inhingement of intercellular putty substances. The transepidermal water loss (TEWL) increases, and the skin becomes more permeable for toxic agents. At the same time, the superficial skin cells dry out, resulting in dehiscence of the stratum corneum, initially on the microscopic level and in due course on the macroscopic level (280).

The incidence with which simple soaps and detergents affect the condition of the skin of health care workers' hands varies considerably (407). For years, natural soaps that have high pH values were thought to be more irritating to the skin than synthetic detergents with neutral or acidic pHs. However, subsequent studies have found that pH is less important than other product characteristics as a cause of skin irritation (200). In some studies, plain soaps have caused less skin irritation than synthetic detergents, while in others, plain bar soap caused greater skin irritation than did a synthetic antimicrobial-containing detergent (299, 565). Synthetic detergents also vary in their propensity to cause skin irritation (200, 407). The incidence of detergent-related-irritant contact dermatitis is affected by various factors: the concentration of the compound, the type of detergent (anionic, cationic, amphoteric, or nonionic) and its quantity, the refattening, the vehicle, the time of exposure, and area exposed (50, 133, 283, 565). For example, it has been shown in vivo that higher concentrations of sodium lauryl sulfate (a detergent) caused greater skin irritation than lower concentrations did (133). In addition, anionic detergents are known to cause greater skin irritation than amphoteric or nonionic detergents (565).

Another factor is the temperature of the water that is used for the hand wash. Hot water leads to greater skin irritation, as reflected by in vivo measurements of TEWL and in vitro measurements of the penetration of detergent through the skin (50, 133, 405). This is explained by an increased penetration of detergents into the epidermis (405). In addition, scaling of the skin is greater when hands are washed with hot water (50). Only skin hydration does not appear to be affected by higher water temperatures (50, 405).

Frequent hand washing induces irritative contact dermatitis (ICD) and dry skin (70, 275, 525, 611), which may become colonized with nosocomial pathogens. ICD can be found in 18.3% of nursing staff in hospitals and is a major occupational health concern (523). A single hand wash already significantly reduces the dermal sebum content; the reduction lasts for 1 h. Skin hydration drops at the same time (280). If hands are washed four times within 1 h, the skin does not recover to its normal state within this period (337). In a study with 52 volunteers who washed their hands 24 times per day for a total of 5 days, a significant increase of the TEWL was observed, indicating that the skin barrier function is impaired (299). The prevalence of ICD caused by hand washing with antimicrobial soaps (detergents) is related to the factors listed above (540). The hardness of water may also affect the incidence of ICD due to frequent hand washing (591).

In summary, plain soap has basically no antimicrobial activity. A simple hand wash can reduce transient bacteria by 0.5 to 3 $\log_{10}$ units but has no real effect on the resident hand flora. The dermal tolerance is rather poor (Table 9).

Chlorhexidine

Chlorhexidine is a cationic biguanide (485) and was first established as an antimicrobial agent in 1954 (104). It exists as acetate (diacetate), gluconate, and hydrochloride salts (485). Chlorhexidine gluconate is commonly used either at 0.5 to

TABLE 9. Comprehensive evaluation of the most important agents for hand hygiene[a]

Criterion for evaluation	Effect for:					
	Plain soap (hand wash)	Chlorhexidine (2–4%) (hand wash)	Triclosan (1–2%) (hand wash)	Ethanol (60–85%) (hand rub)	Isopropanol (60–80%) (hand rub)	*n*-Propanol (60–80%) (hand rub)
Spectrum of activity						
Bacteria	−	++	++	+++	+++	+++
Mycobacteria	−	(+)	Unknown	+++	+++	+++
Bacterial spores	−	−	−	−	−	−
Yeasts	−	++	++	+++	+++	+++
Dermatophytes	−	−	+	++	Unknown	Unknown
Coated viruses	−	++	Unknown	+++	+++	+++
Uncoated viruses[b]	−	+	Unknown	+[c]	(+)[d]	(+)[d]
Effect on hand flora (mean $\log_{10}$ reduction)						
Transient bacteria (≤1 min)	0.5–3	2.1–3	2.8	2.6–4.5	4.0–6.81	4.3–5.8
Resident bacteria (≤3 min)	≤0.4	0.35–1.75	0.29–0.8	2.4	1.5–2.4	2.0–2.9
Potential for acquired bacterial resistance	−	Moderate	Low	None	None	None
Effect on skin						
Skin hydration	Decrease	Decrease	Decrease	No change	No change	No change
Skin barrier	Impaired	Impaired	Impaired	No change	No change	No change
Skin irritation	Likely	Likely	Possible	Very uncommon	Very uncommon	Very uncommon
Allergy	Uncommon	Possible	Uncommon	Extremely uncommon[e]	None	None
Effect on compliance with hand hygiene	(↓)	(↓)	(↓)	(↑)	↑	↑

[a] +++, effective within 30 s; ++, effective within 2 min; +, effective in >2 min; (+), partially effective; −, not effective.
[b] Poliovirus and adenovirus, test viruses of prEN 14476.
[c] Ethanol at 95% has virucidal activity within 2 min.
[d] Results largely dependent on the test virus.
[e] Individual cases, possibly due to impurities.

0.75% in aqueous solution or in some detergent preparations or at 2 to 4% in other detergent preparations (327, 328). Its activity is greatly reduced in the presence of organic matter (485), natural corks (321), and hand creams containing anionic emulsifying agents (586). Inactivation of chlorhexidine may result in contamination of solutions containing 0.1% chlorhexidine, e.g., with *Pseudomonas* spp. (78).

The main target is the bacterial cytoplasmic membrane (360, 464). After chlorhexidine has caused extensive damage to the cytoplasmic inner membrane, precipitation or coagulation of protein and nucleic acids occurs (487). Damage also occurs to the outer membrane in gram-negative bacteria and the cell wall in gram-positive cells (131, 142, 227, 228, 236). Chlorhexidine also damages the cytoplasmic membrane of yeasts (588) and prevents the outgrowth, but not the germination, of bacterial spores (511). If chlorhexidine is hydrolyzed, small amounts of carcinogenic *para*-chloraniline may develop (87); this chemical has been found even in manufactured chlorhexidine solutions (274). At temperatures above 70°C, chlorhexidine is not stable and may degrade to *para*-chloraniline (171). An upper limit for *para*-chloraniline has been set in the British Pharmacopoeia at 0.25 mg per 100 mg of chlorhexidine (17).

Effect on microorganisms and viruses. (i) Spectrum of activity. The antimicrobial activity of chlorhexidine is dependent on its concentration. At lower concentrations, chlorhexidine has a bacteriostatic effect against most gram-positive bacteria (e.g., at 1 μg/ml), many gram-negative bacteria (e.g., at 2 to 2.5 μg/ml) (100, 195), and bacterial spores (513). At chlorhexidine concentrations of 20 μg/ml or more, a bactericidal effect can be expected as well as activity against yeasts (487). The actual effective concentration against *Burkholderia cepacia* and *S. aureus* varies with different supplements from 0.004 to 0.4% (factor 100), and the actual killing time also varies with different supplements (phenylethanol or edetate disodium) from <15 min to >360 min (465). In most studies, concentrations for rapid inactivation are well in excess of MICs, e.g., for *S. aureus* (103), *E. coli*, *Vibrio cholerae* (237), and yeasts (214). When used in a liquid soap, chlorhexidine usually has a concentration of 4% and exhibits a bactericidal activity against various gram-negative (130) and gram-positive (249) bacteria. In some comparative studies using suspension tests chlorhexidine (4%) was found to be less effective against MRSA than against methicillin-susceptible *S. aureus*, which has raised concerns about the suitability of the active agent in the prevention of transmission of MRSA (93, 192, 249). This concern has been confirmed with enterococci. Against *Enterococcus* species and VRE, chlorhexidine (4%) was found to be essentially ineffective in suspension tests if neutralization of residual activity is excluded (247). In a comparison with a nonmedicated hand wash product, a chlorhexidine-based scrub yielded a lower reduction of different antibiotic-resistant test bacteria such as MRSA, VRE, or high-level gentamicin-resistant enterococci (175). Chlorhexidine has no sporicidal activity (513). The data on mycobactericidal activity are not unambiguous but do indicate the relevance of a threshold concentration of chlorhexidine. In one report, 4% chlorhexidine was described as having very good activity against *Mycobacterium smegmatis* (reduction of >6 $\log_{10}$ units within 1 min) (54), whereas another study

with *Mycobacterium tuberculosis* suggested a low activity of 4% chlorhexidine (reduction of <3 $\log_{10}$ units within 1 min) (55). Chlorhexidine at 1.5% did not reveal sufficient activity against *Mycobacterium bovis* (56), and chlorhexidine at 0.5% had no activity against *Mycobacterium avium*, *Mycobacterium kansasii*, or *M. tuberculosis* within 120 min (466).

Against dermatophytes such as *Trichophyton mentagrophytes*, chlorhexidine (1.5%) has been described as having no activity (56).

Antiviral activity has been described as good against most enveloped viruses, such as HIV, cytomegalovirus, influenza virus, RSV, and herpes simplex virus (284, 441), but the virucidal activity of chlorhexidine against naked viruses such as rotavirus, adenovirus, or enteroviruses is low (391, 498).

In comparison to other active agents, chlorhexidine has been described to be less effective in vitro against various nosocomial pathogens than is benzalkonium chloride or povidone iodine (517).

Overall, chlorhexidine seems to have good residual activity (13, 34, 305, 328, 423, 468, 476), but the residual activity must be assessed with caution. It may be false positive due to insufficient neutralization of chlorhexidine in the test design, leading to bacteriostatic concentrations beyond the actual exposure time. Significant difficulties in effective neutralization in in vitro tests have been described, and may yield false-positive activity data for this active agent (246, 516, 517, 600). In addition, the clinical benefit of such a residual effect has never been shown.

(ii) Testing under practical conditions. A 1-min hand wash with soap containing 4% chlorhexidine has been reported to lead to a mean reduction of *E. coli* of 3.08 $\log_{10}$ units on artificially contaminated hands (478). In a study with 52 volunteers who washed their hands 24 times per day for a total of 5 days, a significant decrease in the number of resident skin bacteria was observed with a 4% chlorhexidine liquid soap (mean reduction of 0.76 $\log_{10}$ unit) compared to nonmedicated bar soap (mean increase of 0.21 $\log_{10}$ unit) and a povidone-iodine soap (mean reduction of 0.32 $\log_{10}$ unit) (299). Under practical conditions with hands artificially contaminated by MRSA, chlorhexidine-based liquid soap was equally effective as simple soap (188, 220). A similar result was reported after contamination of hands with *S. aureus* (577). A reduction of 2.1 to 3 $\log_{10}$ units was found on hands contaminated with *Klebsiella* spp. after a 20-s hand wash with a soap based on 4% chlorhexidine (81). If hands were contaminated with rotavirus and treated with chlorhexidine soap for 10 s, the number of test viruses was reduced by 86.9%, which was significantly lower than the reductions achieved with 70% ethanol (99.8%) and 70% isopropanol (99.8%) (23). Treatment with 4% chlorhexidine soap for 30 s on hands contaminated with rotavirus leads to a similar effect of only 0.27 to 0.5 $\log_{10}$ unit (47). Under practical conditions and in terms of removal rate from hands, the efficacy against bacterial spores (e.g., *B. atrophaeus*) of an antiseptic liquid soap based on chlorhexidine was similar to that of nonmedicated soap, indicating that within 10 s or 60 s, chlorhexidine does not exhibit a significant sporicidal activity (57, 594). The effect of 4% chlorhexidine on the resident hand flora was found to be a reduction of between 0.35 and 2.29 $\log_{10}$ units, depending on the application time (Table 8).

(iii) In-use tests. The in-use studies yield a heterogeneous picture of the efficacy of chlorhexidine. One of the first studies with chlorhexidine was performed in 1955. A hand cream containing 1% chlorhexidine was rubbed into dry hands and led to a substantial reduction is the number of resident skin bacteria after 30 min (386). In another clinical study, 74 health care workers evaluated plain soap and a liquid soap based on 4% chlorhexidine over 4 months in a neurosurgical unit and a vascular surgery ward. Overall hand contamination was found to be significantly lower after the use of plain soap (mean number of CFU, 125) than after the use of chlorhexidine (mean number of CFU, 150) (343). A hand wash with 4% chlorhexidine was reported to be more effective on the total bacterial count under clinical conditions than was a 1% triclosan hand wash (140). In a prospective crossover study over 4 months with plain soap and a 4% chlorhexidine soap among health care workers in two surgical units, plain soap was found to be significantly more effective than chlorhexidine in reducing bacterial counts from the hands of health care workers (343). After contamination of hands with *Klebsiella* spp., a 98% reduction was described in 19 of 23 experiments in which a soap based on 4% chlorhexidine was used (81); this is an almost 2 $\log_{10}$ unit reduction. Chlorhexidine failed to eliminate MRSA from the hands (140). In contrast, gram-negative bacteria were more likely to be eliminated after the use of chlorhexidine (140, 357, 573, 580). The mean resident flora of the hands of surgeons was reduced by a 3-min application of 4% chlorhexidine from 3.5 $\log_{10}$ units (preoperatively) to 3.15 $\log_{10}$ units (postoperatively) in operations lasting less than 2 h. It has been shown that for operations lasting more than 3 h, 4% chlorhexidine was unable to keep the resident skin bacteria below the baseline value (4.5 preoperatively and 5.2 postoperatively) (76).

(iv) Resistance. The definition of chlorhexidine resistance is often based on a report from 1982 in which the MICs of chlorhexidine for 317 clinical isolates of *P. aeruginosa* were analyzed, leading to the suggestion that resistance to chlorhexidine should be reported if the MIC is $\geq$50 mg/liter (390).

Resistance to chlorhexidine among gram-positive bacterial species is rather uncommon. Among *Streptococcus* and *Enterococcus* species, no chlorhexidine resistance has been demonstrated (42, 231). However, gram-negative bacteria, such as *E. coli* (389), *Proteus mirabilis* (100, 536), *Providencia stuartii* (227, 228, 554), *P. aeruginosa* (390, 556), *P. cepacia* (348), and *S. marcescens* (291), have frequently been reported to be resistant to chlorhexidine. The frequency of resistance for the different species is variable. A total of 84.6% of clinical isolates of *P. mirabilis* must be considered resistant to chlorhexidine (536). Among other gram-negative bacteria, the rate is lower (42, 195). *C. albicans* was found to have a resistance rate of 10.5% (42, 231).

Acquired resistance to chlorhexidine has been reported to occur in *S. aureus* (249) and among many gram-negative bacteria (37, 38, 434) which were isolated after recurrent bladder washouts using 600 mg of chlorhexidine per liter (537, 538) or after addition of chlorhexidine to catheter bags for paraplegic patients (584). Some of the isolates were highly resistant, with chlorhexidine MICs of $\geq$500 mg/liter (538). The chlorhexidine resistance is quite clearly linked to hospital isolates only. A

selection of 196 environmental gram-negative isolates did not reveal a resistance to chlorhexidine (147).

High chlorhexidine MICs correlate with poor reduction in the number of test bacteria in suspension tests, which highlights the potential hazard (555). The MIC may be as high as 1600 μg/ml and correlates well with a slow and insufficient bacterial reduction in suspension tests, as shown with strains of *Providencia* (539). The resistance may be single (83), but cross-resistance to other anti-infective agents can also occur. Among isolates of *P. aeruginosa* from industry and hospitals, an association between resistance to antibiotics and chlorhexidine has been described (290). The potential for cross-resistance between antiseptic agents and antibiotics must be given careful consideration (443). Various nonfermenting gram-negative bacteria which were isolated from blood cultures of oncology patients were inactivated only with >500 mg of chlorhexidine per liter (210).

Different mechanisms of resistance have been found. The acquired resistance is probably linked to the inner (227) or the outer (551) membrane of bacterial cells, the cell surface (131), or the cell wall (549). It may also be explained by the presence of plasmids which code for chlorhexidine resistance (269) and may therefore be transfered to other bacterial species (486, 619). A change in lipid content or a reduced adsorption of the antiseptic can be excluded as the main mechanism of resistance, as shown with isolates from urinary tract infections caused by *P. mirabilis* (554) and *S. marcescens* (410).

Recurrent exposure of bacteria to chlorhexidine may lead to adaptation and may enhance their resistance. This phenomenen was shown with *S. marcescens*. One example involves repeated exposure to various contact lens solutions containing between 0.001 and 0.006% chlorhexidine, which enabled *S. marcescens* to multiply in the disinfectant solution (154). Repeated exposure of *P. aeruginosa* to 5 mg of chlorhexidine per liter was shown to increase the MIC from <10 to 70 mg/liter within 6 days (556). A similar result was reported with *Pseudomonas stutzeri*, which became resistant (MIC, 50 mg/liter) after 12 days of exposure to chlorhexidine (550). Even with *Streptococcus sanguis*, a clear increase of the chlorhexidine MIC during permanent chlorhexidine exposure was observed (601). In general, higher exposures to chlorhexidine in hospitals were reported to be associated with higher rates of resistance (67). Recently, some isolates of *P. aeruginosa*, *K. pneumoniae*, and *A. baumannii* isolated from soap dispensers were reported to multiply in a 1:2 dilution of a 2% chlorhexidine liquid soap; ATCC strains of *K. pneumoniae* and *A. baumannii* multiplied only at higher dilutions (73). The latter report highlights the potential danger for the hospital.

Resistance to chlorhexidine may even result in nosocomial infections. Occasional outbreaks of NIs have been traced to contaminated solutions of chlorhexidine (345). There is one report that a 0.5% chlorhexidine solution which was used to disinfect plastic clamps for Hickman lines and was handled by health care workers who transmitted the adapted bacteria to intravenous lines led to 12 cases of bacteremia with three fatalities (357). In another outbreak, contamination of a disinfectant solution with *Burkholderia multivorans* led to nine cases of surgical site infection (45). Especially when chlorhexidine resistance is endemic in gram-negative bacteria, the use of chlorhexidine-based hand antiseptics may lead to an increase of NIs by the chlorhexidine-resistant species (100).

Effect on human skin. Chlorhexidine gluconate is among the most common antiseptics causing ICD (540). However, the frequency of hand dermatitis associated with chlorhexidine-containing detergents is concentration dependent; products containing 4% chlorhexidine cause dermatitis much more frequently than do those containing lower concentrations (540). However, even preparations with the same concentration of chlorhexidine (4%) may cause skin irritation at different frequencies (398, 508). The differences are presumably due to other components of the various formulations. The relatively large number of reports of dermatitis related to chlorhexidine gluconate was partly explained by the fact that it was one of the most widely used antiseptics. In a survey of over 400 nurses working in several hospitals, detergents containing chlorhexidine were reported to cause skin damage less frequently than was nonantimicrobial soap or other detergents containing antimicrobial agents (298). In one 5-day prospective clinical trial, a detergent containing 4% chlorhexidine gluconate caused less irritation than did plain bar soap (300). Nonetheless, dry skin may occur with repeated exposure to preparations containing 4% chlorhexidine gluconate (339, 398).

The potential for contact allergy has been studied as well. Among eczema patients, 5.4% were found to have a positive skin reaction after a single patch test with 1% chlorhexidine, indicating the presence of an allergic contact dermatitis. Repeated exposure resulted in a sensitization rate of ca. 50% (310). In another study, 15 (2.5%) of 551 patients showed a strong and obviously relevant skin reaction in a single patch test with 1% chlorhexidine (415). Although these studies were carried out with patients and not with health care workers, the results nevertheless indicate the potential for sensitization and allergic contact dermatitis during frequent use. Allergic reactions to the use of detergents containing chlorhexidine gluconate on intact skin have been reported and can be severe, including dyspnea and anaphylactic shock (30, 92, 124, 138, 158, 270, 409, 425, 430, 468, 526, 563). Some cases of contact urticaria have also occurred as a result of chlorhexidine use (141, 617).

In summary, chlorhexidine (2 to 4%) has good activity against most vegetative bacteria, yeasts, and enveloped viruses but limited activity against mycobacteria, dermatophytes, and naked viruses. It has a moderate potential for acquired bacterial resistance. A hand wash with a chlorhexidine-based soap can reduce the number of transient bacteria by 2.1 to 3 $\log_{10}$ units; the effect on the resident hand flora is smaller, with a mean reduction between 0.35 and 2.29 $\log_{10}$ units. The dermal tolerance is rather poor, and anaphylactic reactions have been reported (Table 9).

Triclosan

Triclosan is one of many phenol derivatives (diphenoxyethyl ether) which have been used as a group of active agents since 1815, when coal tar was used for disinfection (222). Ever since, many different derivatives, such as thymol, cresol, and hexachlorophene, have been isolated and synthesized. Some of them have been used in antiseptic soaps for health care workers. Triclosan was introduced in 1965 and has been marketed

as cloxifenol, Irgasan CH 3565, and Irgasan DP 300. It has very good stability (585) and resists diluted acid and alkali (453). The commonly used concentration in antiseptic soaps is 1%.

The mode of action of triclosan was identified some years ago. For decades, it has been assumed that triclosan attacks the bacterial cytoplasmic membrane (372, 458). Since 1998, we have known that it blocks lipid synthesis by inhibition of the enzyme enoyl-acyl carrier protein reductase, which plays an essential role in lipid synthesis (367). Mutation and overexpression of the *fabI* gene—which encodes the enoyl-acyl carrier protein reductase—are able to abolish the blockage of lipid synthesis caused by triclosan (205, 312). The *fabI* gene was first found in *E. coli* (366) and was subsequently also found in various other bacterial species such as *P. aeruginosa* (215), *S. aureus* (203, 520), and *M. smegmatis* (365). Some other bacteria, such as *Bacillus subtilis*, contain orthologous enoyl-acyl carrier protein reductases, namely those encoded by *fabI* and *fabK*, which are not inhibited by triclosan (204, 206). A genetic sequence coding for broad-spectrum resistance to triclosan has been identified (239).

The identification of the specific mode of action has raised concerns about the development of resistance to triclosan (313, 366, 506). A recent study has shown that this concern is valid. Strains of *P. aeruginosa* were exposed to triclosan and subsequently developed multiresistance to various antibiotics, including ciprofloxacin (86). Particular care should be taken in the use of triclosan in ICUs, where *P. aeruginosa* is the most common nosocomial pathogen, causing lower respiratory tract infection (260).

Effect on microorganisms and viruses. (i) Spectrum of activity. In vitro, triclosan exhibits a bacteriostatic effect at lower concentrations (575); at higher concentrations, it has bactericidal activity (560). The activity of triclosan is greater against gram-positive organisms than against gram-negative bacteria, particularly *P. aeruginosa* (238). MIC of triclosan generally range between 0.025 and 4 mg/liter among isolates of *S. aureus* and MRSA (94, 459, 543). The fungicidal activity of triclosan is good and includes yeasts and dermatophytes (459).

(ii) Testing under practical conditions. For artificially contaminated hands, a 1-min hand wash with 0.1% triclosan has been shown to reduce the number of test bacteria by 2.8 $\log_{10}$ units (475), which is essentially identical to the results obtained with nonmedicated soap (257). A soap based on 1% triclosan was found to reduce the resident hand flora within 5 min by 0.6 $\log_{10}$ unit (305). A 2% concentration yielded no major difference at 0.8 $\log_{10}$ unit (49). If hands were contaminated with rotavirus and treated with 2% triclosan for 30 s, the number of test viruses was reduced by 2.1 $\log_{10}$ units (47). On the resident hand flora, 1 or 2% triclosan has only a small effect, showing a mean reduction between 0.29 and 0.8 $\log_{10}$ unit within 5 min (Table 8).

(iii) In-use tests. In comparison to plain soap, at 0.2% triclosan does not further reduce bacterial counts on the hands (295). Under clinical conditions, a hand wash with 1% triclosan was reported to be less effective on the total bacterial count than a 4% chlorhexidine hand wash (140). Triclosan was able to eliminate MRSA from the hands (140). In contrast, gram-negative bacteria were less likely to be eliminated after the use of triclosan (140).

(iv) Resistance. One *S. aureus* isolate for which the triclosan MIC is >6,400 mg/liter has been described (494). Some isolates of gram-negative bacteria have been found with triclosan MICs of >100 mg/liter as well (459). This high resistance was not transferable and was probably chromosomal (494). Exposure of *S. aureus* to 0.01% triclosan over 28 days did not result in a change of the triclosan MIC (543). Using *S. epidermidis* in a similar test, however, resulted in an increase of the MIC from 2.5 to 20 mg/liter, indicating a high potential for adaptation of the bacterium (545). Exposure of *P. aeruginosa* to 25 mg of triclosan per liter yielded multiresistant mutants which exhibited resistance to triclosan (MIC, >128 mg/liter) and some antibiotics, e.g., tetracycline (MIC, >256 mg/liter), trimethoprim (MIC, >1,024 mg/liter), and erythromycin (MIC, >1,024 mg/liter) (86).

An antiseptic hand wash preparation based on 1% triclosan was found to be contaminated with *S. marcescens* in an operating theater and a surgical ICU (43). This involved 4 (17%) of 23 bottles and 5 (28%) of 18 wall dispensers, but no association with a higher rate of NIs was found (43).

The widespread use of triclosan in antibacterial household products such as liquid soaps is cause for concern that selection for bacteria with an intrinsic resistance to triclosan may be occurring (314). Triclosan can be found in 76% of antibacterial liquid soaps in the United States (424), which has led to the recommendation that it should not be used in consumer products (547). It is therefore not surprising that highly resistant bacteria were detected in compost, water, and soil (369). Two species, *Pseudomonas putida* and *Alcaligenes xylosoxidans*, were even capable of metabolizing triclosan and thereby of actively "digesting" the active agent (369).

Effect on human skin. Detergents containing less than 2% triclosan are generally well tolerated. In one laboratory-based study of surgical hand disinfectants, a detergent containing 1% triclosan caused fewer subjective skin problems than did formulations containing an iodophor, 70% ethanol plus 0.5% chlorhexidine gluconate, or 4% chlorhexidine gluconate (305). Allergic reactions to triclosan-based handwash products are uncommon (616).

In summary, triclosan (1 to 2%) has good activity against vegetative bacteria and yeasts but limited activity against mycobacteria and dermatophytes. The activity against viruses is unknown. Triclosan has a low potential for acquired bacterial resistance. A hand wash with a triclosan-based soap can reduce the number of transient bacteria by 2.8 $\log_{10}$ units; the effect on the resident hand flora is lower, yielding a mean reduction between 0.29 and 0.8 $\log_{10}$ unit. The dermal tolerance is rather poor (Table 9).

Ethanol, Isopropanol, and *n*-Propanol

The general antimicrobial activity of alcohols has been described to increase with the length of the carbon chain and reaches a maximum at six carbon atoms (548). Solubility in water has led to a preference for ethanol and the two propanols. Alcohols have a nonspecific mode of action, consisting mainly of denaturation and coagulation of proteins (241). Cells are lysed (229, 428), and the cellular metabolism is disrupted (360).

Ethanol is a well-known antimicrobial agent, which was first

recommended for the treatment of hands in 1888 (473). The antimicrobial activity of isopropanol (equivalent to propan-2-ol) and *n*-propanol (equivalent to propan-1-ol) was first investigated in 1904 (612). Many studies followed and supported the use of the two propanols for hand disinfection (52, 85, 322, 395).

Both the alkyl chain length and branching affect the antimicrobial activity (562). The following ranking regarding the bactericidal activity has been generally established: *n*-propanol > isopropanol > ethanol (95, 476, 548). The bactericidal activity is also higher at 30 to 40°C than at 20 to 30°C (561). In terms of virucidal activity, ethanol is superior to the propanols.

Effect on microorganisms and viruses. (i) Spectrum of activity. *(a) Ethanol.* Ethanol has a strong immediate bactericidal activity (297) that is observed at 30% and higher concentrations (383, 444, 448, 449). Against *S. aureus*, *E. faecium*, or *P. aeruginosa*, its bactericidal activity seems to be slightly higher, at 80% than at 95% (110). According to the tentative final monograph for health care antiseptic products, ethanol is considered to be generally effective at between 60 and 95% (21). The spectrum of bactericidal activity of ethanol is broad (198).

Ethanol is also effective against various mycobacteria. Ethanol at 95% killed *M. tuberculosis* in sputum within 15 s, 70% ethanol required a contact time of 30 s, and 50% ethanol required 60 s (524), which was also required against *M. smegmatis* (54). Similar results were obtained with 70% ethanol and *M. tuberculosis* (55). For *Mycobacterium terrae*, the surrogate test strain for *M. tuberculosis*, a $\log_{10}$ reduction of >4 was found with 85% ethanol within 30 s (258). Very good activity was also shown with 70% ethanol against *M. bovis* (56).

In addition, ethanol has broad activity against most fungi—including yeasts and dermatophytes—at different exposure times and under different test conditions (56, 134, 258, 285, 286, 331).

The spectrum of virucidal activity is largely dependent on the concentration of ethanol. Higher concentrations of ethanol (e.g., 95%) generally have better virucidal activity than do lower concentrations, such as 60 to 80%, especially against naked viruses (127, 244, 534). A hand rub based on 95% ethanol has been described to have broad virucidal activity within 2 min, even against the most common nonenveloped viruses such as poliovirus and adenovirus (19). A gel based on 85% ethanol was still effective with a reduction factor (RF) of >4 against poliovirus within 3 min and against adenovirus within 2 min (258). Most naked viruses such as poliovirus (258, 262, 268, 535, 566), astroviruses (288), feline calicivirus (164), rotaviruses (258, 288), and echoviruses (287, 288) are inactivated by ethanol as well. HAV may be the only virus which is not fully inactivated; however, a higher RF of 3.2 was found with 95% ethanol whereas the RF was only 1.8 with 80% ethanol (615). Preparations containing less than 85% ethanol are usually less effective against viruses (570), although they may reveal sufficient activity within 10 min against various nonenveloped viruses such as adenovirus, poliovirus, echovirus, or Coxsackie virus (268). Under variable test conditions and at different exposure times, ethanol has broad general activity against the enveloped viruses, such as vaccinia virus (61, 184, 185, 268), influenza A virus (185, 268), togaviruses (77), Newcastle disease virus (97), HIV (346, 529), HBV (68, 272), and herpes simplex viruses (268).

Ethanol is known to have virtually no sporicidal activity (56, 165). This was first described over a century ago (135, 199, 395, 461). A pseudo-outbreak was reported due to contamination of ethanol with spores of *B. cereus*. The ethanol was used in the hospital pharmacy for preparation of skin antiseptics without spore filtration (219). Another report described contamination of 70% ethanol with spores of *Clostridium perfringens*, which was eliminated by addition of 0.27% hydrogen peroxide over 24 h (602).

(b) Isopropanol. The bactericidal activity of isopropanol begins at a concentration of 30% (445) and increases with increasing concentration but is lower again at 90% (544). It is similar to the bactericidal activity of *n*-propanol (612). In suspension tests, a hand rub based on propanols (total of 75%, wt/wt) had a comprehensive bactericidal activity against 13 gram-positive species, 18 gram-negative species, and 14 emerging pathogens within 30 s. Test bacteria included both ATCC strains and clinical isolates (248). Variations of the test conditions (e.g., with organic load) usually have no effect on the overall result in suspension tests (253). A tuberculocidal activity was found with isopropanol between 50 and 70% (150). The virucidal activity against naked viruses is limited and usually does not include enteroviruses such as astrovirus or echovirus (287, 288). If the exposure time is extended, sufficient activity against some nonenveloped viruses—such as echovirus (90% isopropanol for 10 min), feline calicivirus (50 to 70% isopropanol for ≥3 min), or adenovirus (50% isopropanol for 10 min)—can be achieved (164, 268). Isopropanol alone has no sporicidal activity, as shown with spores of *B. subtilis* and *Clostridium novyi* (445).

(c) n-Propanol. As early as 1904, *n*-propanol was described as an alcohol with a very strong bactericidal effect (548, 612) starting at a concentration of 30% (250). Compared to isopropanol, the activity against feline calicivirus seems to be better (164). In general, however, the antimicrobial activity of *n*-propanol is thought to be similar to that of isopropanol (475).

(ii) Testing under practical conditions. *(a) Ethanol.* On hands artificially contaminated with *E. coli*, ethanol at concentrations between 70 and 80% caused a reduction in the number of test organisms of between 3.8 and 4.5 $\log_{10}$ units within 60 s (475–477), and 1.96 $\log_{10}$ units within 10 s (23). Significant differences may be observed among alcohol-based gels. Up to an ethanol concentration of 70%, gels have been described to be significantly less effective than the reference hand disinfection (282, 432). A preparation with 85% ethanol, however, was found to be as effective as the reference hand disinfection, with 3 ml within 30 s (258).

Other types of artificial contamination of hands have only rarely been tested. Using *S. aureus*, a 30-s application of 70% ethanol achieved a 2.6 or 3.7 $\log_{10}$ unit reduction (34, 318). A similar result was found with 79% ethanol against *Micrococcus luteus* (mean RF, 3.2 after 30 s) (174). If hands were contaminated with rotavirus and treated with 70% ethanol for 10 s, the number of test virus was reduced by 2.05 $\log_{10}$ units (23). A longer application time of 30 s revealed a similar reduction of 2.72 $\log_{10}$ units (47). Low ethanol concentrations, e.g., 70 or 62%, did not even achieve a 1 $\log_{10}$-unit reduction of HAV on contaminated hands (355) but achieved a 2.9 to 4.2 $\log_{10}$-unit reduction within 20 s against adenovirus, rhinovirus, and rotavirus (496). Contamination with poliovirus was reduced by only

TABLE 10. Baseline compliance rates in hand hygiene, according to the agent

Type of ward(s)	Type of agent(s)[a]	Baseline compliance rate (%)	Reference(s)
Pediatric ICU	Soap	30.1	118
All wards	Soap	30.2	592
Long-term care	Soap	31.9	558
All wards	Soap	32	334
Pediatric ICU	Soap	34	196
Medical ICU	Soap	38.1	10
All wards	Soap	45	293
Surgical ICU	Soap	45	429
ICU and oncology ward	Soap	56	515
Medical ICU	Soap	60.7	266
ICU	Soap	61.4	530
ICU	Soap	63.1	261
Neonatal ICU and infant rehydration unit	Plain soap	29	308
ICU	Medicated soap (4% chlorhexidine)	42	117
ICU	Plain soap and alcohol	38[b]	117
ICU	Plain soap and alcohol	40.2	622
Emergency department	Plain soap and isopropanol (60%)	32.3	370
All	Plain soap and isopropanol (70%)	48	439
ICU	Medicated soap (chlorhexidine) and alcohol	28.7	176
ICU	Alcohol	55.2	126

[a] "Soap" was always assumed to be meant when "hand washing" was mentioned in a study; it may include plain and medicated soap.
[b] Low compliance was explained by incorrect and rare use of alcohol.

1.6 $\log_{10}$ units within 10 s by use of 70% ethanol (534). A solution of 80% ethanol reduced the carriage of poliovirus on fingers by only 0.4 $\log_{10}$ unit within 30 s (106). A higher concentration of ethanol (95%) reduced different naked viruses, such as adenovirus (RF, >2.3), poliovirus (RF, between 0.7 and 2.5), and coxsackievirus (RF, 2.9), significantly better on the hands (504). Against feline calicivirus, a sufficient efficacy (RF $\geq$ 3.83) was observed with 70% ethanol within 1 min without an organic load (164). Experiments with 5% fecal test suspension as the organic load, however, demonstrated a lowered efficacy of ethanol. Within 30 s, ethanol at 70% revealed a mean $\log_{10}$ reduction between 1.27 and 1.56 (244) and ethanol at 95% was more effective (mean RF between 1.63 and 2.17) (244).

The lack of sporicidal efficacy has been recently confirmed under practical conditions of hand contamination, using spores of *B. atrophaeus*, a surrogate for *B. anthracis* (594).

The effect on the resident hand flora depends on the ethanol concentration and the application time. A reduction between 1.0 and 1.5 $\log_{10}$ units has been found with ethanol at 70 and 80% within 2 min; higher concentrations (80 and 85%) and longer application times led to mean reductions between 2.1 and 2.5 $\log_{10}$ units (Table 8).

Comparison to antimicrobial soaps or nonmedicated soaps usually reveals the superior efficacy of ethanol on the resident hand flora or on artificial contamination of hands with *E. coli* or *S. marcescens* (32, 34, 66, 80, 267, 318, 377, 406, 419, 476). To date, there is only one study with a 2-min application time, yielding the opposite result (319). Other test models have been investigated as well. Compared to washing hands with plain soap, a 30-s hand disinfection using 70% ethanol was significantly more effective in reducing the transfer of *Staphyloccocus saprophyticus* (344). The higher bactericidal efficacy of ethanol than of antimicrobial soaps is even more pronounced in the presence of blood (296, 297).

Comparison to other alcohols reveals only minor differences. Using *S. marcescens* as a test organism, 70% ethanol with 0.5% chlorhexidine was described to be more effective under practical conditions than was 70% isopropanol, which may be explained by the different type of alcohol, the additional chlorhexidine, or both (14).

(b) Isopropanol. Isopropanol (60%) has been chosen as the reference agent for testing the efficacy of hygienic hand disinfection in European standard EN 1500 (116). With the reference treatment on hands which were artificially contaminated with *E. coli* and treated with two 3-ml doses for a total of 60 s, a mean reduction of 4.6 $\log_{10}$ units was achieved (256, 257). In other studies, similar results of 4.0 to 4.4 $\log_{10}$ units within 60 s were found (472, 475, 480, 482). The reduction with 70% isopropanol after 10 s, however, is 2.15 $\log_{10}$ units (23). In contrast, a gel based on 60% isopropanol was found to be significantly less effective than three liquid rinses against three test bacteria at 15 and 30 s (110). Using bacteria other than *E. coli* to artificially contaminate hands, similar mean reductions were found after 30 s in *S. aureus* (mean RF, 6.36), *E. faecalis* (mean RF, 6.07), and *P. aeruginosa* (mean RF, 6.81) (110). After 15 s, mean RFs were only marginally lower in *S. aureus* (mean RF, 5.90), *E. faecalis* (mean RF, 5.03), and *P. aeruginosa* (mean RF, 6.05) (110). If hands were contaminated with rotavirus and treated with 70% isopropanol for 10 s, the number of test viruses was reduced by 99.8% (RF, 2.7). The number of *E. coli* cells is reduced to a similar extent (99%; RF, 2.0) (23). A similar result was obtained when hands were contaminated with rotavirus and treated with 70% isopropanol for 30 s. The number of test viruses was reduced by 3.1 $\log_{10}$ units (47). Contamination with poliovirus was reduced only by 0.8 $\log_{10}$ units within 10 s after use of 70% isopropanol (534). The efficacy against feline calicivirus is also quite low, with a mean reduction of 0.76 $\log_{10}$ unit (90% isopropanol) or 2.15 $\log_{10}$ units (70% isopropanol) within 30 s (164).

TABLE 11. Compliance rates in hand hygiene, according to the agent and intervention

Type of ward(s)	Agent(s)[a] (baseline)	Main active agent(s)[a] (new)	Intervention(s)	Compliance rate (%)		Main reason(s) for change	Reference
				Baseline	After intervention		
ICU	Soap	Soap	Lectures, feedback, demonstrations	5	63	Lectures, feedback, demonstrations	51
ICU	Soap	Soap	New design of ICU	16	30	More convenient sink location	446
ICU	Soap	Soap	Education	22.0	29.9	Education	518
ICU	Soap	Soap	Lectures and reminder labels on ventilators	46 (before patient contact), 83 (after patient contact)	92 (before patient contact), 92 (after patient contact)	Lectures and reminder labels on ventilators	264
Pediatric ambulatory setting	Soap	Soap	Use of reminders	49	49	Use of reminders	324
Pediatric wards	Soap	Soap	Educational program	52	74	Educational program	31
Emergency department	Soap	Soap	Posting of signs, education	54	64	Posting of signs, education	120
Neonatal ICU	Soap	Soap	Use of gowns	62	60	Use of gowns	421
ICU	Soap	Soap	Performance feedback and new soap	63	92	Performance feedback	352
ICU	Soap	Soap	Education and feedback	81	92	Education and feedback	122
Surgical ICU	Plain and medicated soap (chlorhexidine)	Plain and medicated soap (chlorhexidine)	Automatic hand-washing machines available	22	38	Availability of hand-washing machines	618
New-burn nurseries	Medicated soap	Medicated soap	Feedback	28	63	Feedback	451
Medical ICU	Medicated soap	Medicated soap	Routine wearing of gowns and gloves, educational meetings	40.8	58.2	Routine wearing of gowns and gloves, educational meetings	521
ICU	Medicated soap (*para*-chloro-metaxylenol)	Medicated soap (*para*-chlorometaxylenol)	Teaching and reminders (buttons)	22	29.9	Reminders	518
Medical ICU	Medicated soap (4% chlorhexidine)	Medicated soap (4% chlorhexidine)	Education	26% (before patient contact), 23% (after patient contact)	38% (before patient contact), 60% (after patient contact)	Education	91
Pediatric ICU	Soap (plain and medicated), ethanol (70%), aqueous povidone iodine	Soap (plain and medicated), ethanol (70%), aqueous povidone iodine	Overt observation and feedback	12% (before patient contact), 11% (after patient contact)	68% (before patient contact), 65% (after patient contact)	Overt observation and feedback	559
ICU	Soap	Ethanol (60%)	Quality improvement and introduction of hand gel	42.5	35.1	"Sticky uncomfortable feeling" of product	197
ICU and medical ward	Plain and medicated soap (4% chlorhexidine)	Ethanol (60%)	Education program followed by introduction of hand rub	16.3	20.9 (after education), 33.2 (after introduction of hand rub)	Easy access of hand rub	63
Medical ICU and ward	Soap	Ethanol (62%)	Introduction of hand rub with an educational and motivational campaign; wall dispensers	Overall, 60%; medical ICU, 70.3%; ward, 46.2%	Overall, 52%; Medical ICU, 58%; ward, 48%	Physicians as role models	388
Plastic surgery department	Soap	Ethanol (70%)	Performance feedback	62	61.3	Performance feedback	336
Neonatal ICU	Plain soap	Ethanol (79%)	Introduction of hand rub and quality improvement	44	48	Unknown	75
ICU	Soap	Isopropanol (60%)	Introduction of hand rub and teaching	32	45	Accessability of hand rub	180
ICU	Plain soap	Isopropanol (75%)	Promotion campaign for hand hygiene	38.4	54.5	Campaign on benefits of alcohol-based hand rubs	223
All		Isopropanol (75%)	Promotion campaign for hand hygiene	48	66	Campaign on benefits of alcohol-based hand rubs	439
Medical ICU	Plain soap	Isopropanol (45%) and *n*-propanol (30%)	Introduction of hand rub and education	42.2	60.9	Availability of hand rub; short time for hand rub procedure	351
All	Soap (plain and medicated)	Isopropanol (45%) and *n*-propanol (30%)	Introduction of hand rub and education	62.2	66.5	Better dermal tolerance of hand rub	167
All	Soap (plain and medicated)	Isopropanol (45%) and *n*-propanol (30%)	Introduction of hand rub and education	52	66	Dermal tolerance and accessibility	169

[a] "Soap" was always assumed to be meant when "hand washing" was mentioned in a study; it may include plain and medicated soap.

Isopropanol at 60 and 70% has a rather low efficacy against the resident hand flora within 2 min (RF, between 0.7 and 1.2). With longer application times (3 and 5 min) and higher concentrations of isopropanol (80 and 90%), the mean reduction of the resident hand flora is between 1.5 and 2.4 (Table 8).

Comparison of isopropanol with nonmedicated soaps and antimicrobial soaps reveals the better efficacy of isopropanol, both on the resident hand flora (129, 316) and on hands which were artificially contaminated (33, 44, 472), with only one study showing discrepant results (306).

(c) n-Propanol. On hands which were artificially contaminated with *E. coli*, n-propanol at 100, 60, or 50% reduced the number of test bacteria within 1 min by 5.8, 5.5, or 5.0 $\log_{10}$ units, respectively (482, 604). Lower concentrations, e.g., 40%, still reduce the test bacteria by 4.3 $\log_{10}$ unit within 1 min (475). The efficacy against feline calicivirus seems to be quite good, with a mean RF between 1.9 (80% *n*-propanol) and $\geq$ 4.13 (50% *n*-propanol) within 30 s (164). Against the resident hand flora, 60% *n*-propanol is quite effective, with a mean reduction of 1.1 after 1 min and of 2.05 to 2.9 after 5 min (Table 8). A combination of isopropanol (45%) with *n*-propanol (30%) is significantly more efficacious than *n*-propanol (60%) on the resident hand flora in two studies; yielding a mean RF of 4.61 versus 2.9 in one study (240) and a mean RF of 1.45 versus 0.83 in the other (341).

(iii) In-use tests. *(a) Ethanol.* During an outbreak of gentamicin-resistant *Klebsiella aerogenes*, a health care worker was found to carry the strain on her hand. *K. aerogenes* was still detectable on two occasions after use of 95% ethanol for hand disinfection. The nurse continued to carry the strain for almost 4 weeks on her hand (82). Especially among health care workers wearing artificial fingernails, ethanol (60%) was found to be more effective in the removal of nosocomial pathogens than was an antimicrobial soap (368).

(b) Isopropanol. Under clinical conditions, a combination of isopropanol, *n*-propanol, and mecetronium etilsulfate was found to be significantly more effective than a chlorhexidine-based liquid soap (168). Isopropanol at 60% was found to have a better bactericidal efficacy on the resident hand flora than do antiseptic soaps based on chlorhexidine or triclosan (382). The higher bactericidal efficacy of isopropanol compared to antimicrobial soaps is even more pronounced in the presence of blood (296, 297).

Isopropanol at 60 to 70% was found to be necessary for removal of aerobic gram-negative bacteria from hands, whereas a simple hand wash with soap was inadequate (125). Transmission of gram-negative bacteria was also significantly better interrupted by propanol than by a social hand wash following brief contact with a heavily contaminated patient source (129).

(c) n-Propanol. Comparisons of *n*-propanol with nonmedicated soaps and antimicrobial soaps consistently reveal the greater efficacy of *n*-propanol on hands which were artificially contaminated (33, 480, 482). Comparison between *n*-propanol and isopropanol reveals a slightly greater efficacy of *n*-propanol (33). The efficacy of 60% *n*-propanol was found to be similar to that of 90% isopropanol on the resident bacteria (483).

(iv) Resistance. No acquired resistance to ethanol, isopropanol, or *n*-propanol has been reported to date.

Effect on human skin. Alcohols are considered to be among the safest antiseptics available and generally have no toxic effect on human skin (332). One of the first studies was carried out in 1923 and found that isopropanol had no noticeable harmful effect on human skin (181). This has been confirmed in a repetitive occlusive patch test with *n*-propanol at various concentrations (333). In addition, different formulations based on various alcohols were tested on intact skin for 6 days and 4 weeks and were well tolerated (279). The skin barrier remains intact, dermal hydration does not change significantly, and the dermal sebum content remains unchanged (279). A similar result was found in a repetitive occlusive patch test with an ethanol-based hand gel (255) and a propanol-based hand rub (254). Even on preirritated skin, the potential for irritation by commonly used alcohols is very low (333). Repeated exposure to alcohol or a moderately formulated product can cause or maintain skin dryness and irritation (108, 197, 475). Ethanol is less cytotoxic (278) and may be less irritating than *n*-propanol or isopropanol (108, 281, 423). Adding 1 to 3% glycerol, humectants, emollients, or other skin-conditioning agents can reduce or eliminate the drying effects of alcohol (34, 182, 306, 328, 396, 408, 481, 587).

Various studies have addressed the question whether alcohol-based hand rubs have a dermal tolerance that is similar to or better than that of nonmedicated or antimicrobial soaps. Several prospective trials have demonstrated that alcohol-based hand rubs containing emollients may cause significantly less skin dryness and irritation than washing hands with liquid detergents (70, 303, 304, 378, 611). For example, a prospective, randomized clinical trial with crossover design was conducted with nurses working on several hospital wards in order to compare hand washing with a nonantimicrobial liquid detergent and hand disinfection using a commercially available alcohol hand gel. The condition of the skin of nurses' hands was determined at the beginning, midpoint, and end of each phase of the trial by using participants' self-assessment, visual assessment by an observer, and objective assessment of skin dryness via measurements of the electrical capacitance of the skin on the dorsal surface of the hands. Self-assessments and visual assessments by the observer both found that skin irritation and dryness occurred significantly less often when nurses routinely used the alcohol-based hand gel between attending to patients, and electrical skin capacitance readings demonstrated that skin dryness occurred significantly less often when the alcohol hand gel was used (70). A questionnaire study conducted at the end of the trial found that more than 85% of nurses felt that the alcohol hand rub caused less skin dryness than did washing with soap and water and that they would be willing to use the product routinely for hand hygiene (69). In another study of 77 operating-room staff who used either an alcohol-based hand rub or an antiseptic liquid soap for surgical hand disinfection, skin dryness and skin irritation decreased significantly in the group using the alcohol rub whereas they both increased in the group using soap (416). In another clinical trial, nurses were randomly assigned to use either a nonantimicrobial liquid detergent or an alcohol-based hand rinse, and skin tolerance was studied by using a combination of self-assessments, evaluations by a dermatologist, and measurements of TEWL. Self-assessments and those of the dermatologist found that the alcohol hand rinse was tolerated significantly better than the liquid

detergent (611). There was no significant difference in TEWL readings with the two regimens. In a prospective, randomized trial conducted with ICU personnel, the effects on skin condition of a detergent containing 2% chlorhexidine were compared to those of an alcohol-based hand rub. Both the skin scaling scores and self-assessments found that the alcohol-based hand rub was tolerated better than the detergent containing 2% chlorhexidine (303). In a similar randomized, prospective trial in a neonatal ICU, the alcohol-based hand rinse regimen was tolerated significantly better than a detergent containing 2% chlorhexidine (301).

In a prospective intervention trial designed to study the impact of introducing an alcohol hand rinse on hand hygiene compliance among health care workers, dermatologist-assessed skin dryness and irritation revealed that the alcohol hand rinse was tolerated better than the traditional antiseptic hand-washing preparation (167). Measurements of skin hydration improved (although not significantly) after the alcohol hand rinse was introduced. Other clinical studies have also shown that alcohol-based hand rubs are tolerated well by health care workers (351). Furthermore, in a laboratory-based study of hand disinfection which compiled observations by an expert, self-assessments, and TEWL measurements, an alcohol-based hand rub caused less skin irritation than did a detergent containing 2% chlorhexidine (186).

Another trial based only on self-assessments to determine the impact on skin condition of an alcohol hand rub versus a detergent containing 4% chlorhexidine gluconate also found that the alcohol-based product was better tolerated (384).

In health care facilities where hand washing with plain soap or antimicrobial soap and water has been the rule, switching (particularly in the winter) to an alcohol-based hand rub may cause some personnel to complain of burning or stinging of the skin when applying alcohol. This is usually due to the presence of underlying, detergent-associated ICD among personnel (252). Skin that has been damaged by preexisting exposure to detergents may be more susceptible to irritation by alcohols than are nondamaged skin areas (333). As the skin condition improves with continued use of alcohol-based hand rubs, the burning and stinging associated with applying alcohol invariably disappears.

Allergic contact dermatitis or contact urticaria syndrome induced by exposure to alcohol-based hand rubs occurs rarely (88), and the cause is not clear. For example, surveillance at a large hospital where a commercial alcohol hand rub has been used for more than 10 years has not identified a single case of well-documented allergy to the product (606). In the few observed cases, however, it remains unclear whether the allergic reaction to the product is caused by the ethanol or by any of the auxiliary agents of the formulation (88). When reactions do occur, they may be caused by hypersensitivity to the alcohol itself, to aldehyde metabolites, or to some other additive (413). Allergic reactions to ethanol or isopropanol have been reported, are extremely rare (413), and depend on the chemical purity of the tested alcohol. Other ingredients in alcohol-based hand rubs that could be responsible for allergic reactions include fragrances, stearyl or isostearyl alcohol, benzyl alcohol, myristyl alcohol, phenoxyethanol, propylene glycol, parabens, and benzalkonium chloride (28, 107, 152, 189, 413, 442, 620).

In summary, ethanol (60 to 85%), isopropanol (60 to 80%) and *n*-propanol (60 to 80%) have very good activity against vegetative bacteria, mycobacteria, yeasts, dermatophytes, and enveloped viruses. Ethanol is more effective against naked viruses than are isopropanol and *n*-propanol. None of the alcohols has a potential for acquired bacterial resistance. Hand disinfection with an alcohol-based hand rub can reduce transient bacteria by 2.6 to 6.8 $\log_{10}$ units, but the effect on the resident hand flora is lower, with a mean reduction between 1.5 and 2.9 $\log_{10}$ units. The dermal tolerance is good (Table 9).

EFFECT ON NOSOCOMIAL INFECTIONS

Plain Soap (Social Hand Wash)

Compared with no hand washing at all, a simple hand wash reduces the transmission of nosocomial pathogens. Enforcement of a simple hand wash together with other infection control measures on a neonatal ICU led to a significant reduction of rectal colonization with VRE among newborns (40.2 versus 7%) (340). The simple hand wash has also been shown to be effective after direct contact with contaminated objects and before meals for prevention of infectious enteritis caused by *Salmonella enterica* servar Enteritidis (149). A similar effect on the incidence of diarrhea has been reported from India, although the hand wash had no effect on diarrhea caused by rotaviruses (512). One study exists which shows an effect even on the transmission of respiratory tract viruses. More frequent hand washing by health care workers in combination with cohorting of patients with respiratory tract infections caused by RSV has been found to reduce the nosocomial spread of RSV (225). Although these studies indicate that hand washing can reduce the transmission of nosocomial pathogens, especially during outbreak investigations involving multiple control measures, it is impossible to determine the individual contribution made by hand hygiene in preventing transmission.

Overall, wet hands have been described to significantly increase the risk of cross-transmission, indicating that hands should always be thoroughly dried (373).

Chlorhexidine and Triclosan (Hygienic Hand Wash)

Only a few studies were available which examined the impact of antimicrobial soaps on NIs. One study looked at the colonization and infection rate with *Klebsiella* spp. in an ICU. The annual rate was reduced from 22% in 1972 and 22.6% in 1973 to 15.5% in 1974, which was explained mainly by the introduction of a chlorhexidine-based liquid soap (81). In another study, NIs were less frequent when personnel performed antiseptic hand washing instead a simple hand wash (339). Antiseptic hand washing was also associated with lower NI rates in some ICUs but not in others (349). Some investigators have found that nosocomial acquisition of MRSA was reduced when the antimicrobial soap used for hand washing was changed (597, 621).

Ethanol, Isopropanol, and *n*-Propanol

The use of alcohol-based hand rubs in regular patient care and its promotion over the years resulted in an increase of compliance in hand hygiene from 48 to 66% and a decreased in the rate of NIs from 16.9 to 9.9% at the same time. This is

a significant decrease, of 41.1% in the NI rate (439). A comparative study of ICUs was carried out to determine the efficacy of a chlorhexidine-based soap (4%) and an isopropanol-based hand rub (60%) with the optional use of bland soap in reducing NIs. Washing hands with the chlorhexidine-based soap resulted in a lower rate of NIs, but the difference was not significant. However, it has been stated that this study does not indicate which of the two hand hygiene treatments is superior in ICUs. The personnel used much smaller volumes of isopropanol than of chlorhexidine and washed their hands more often than they used the hand rub (117). The data should therefore be regarded as resulting from a comparison between a social hand wash and chlorhexidine rather than a comparison between isopropanol and chlorhexidine (170). On a single ward in a 498-bed acute-care facility, use of an alcohol-based hand preparation over a 10-month period resulted in a 36% decrease in the incidence of two indicator NIs (urinary tract infections and surgical-site infections), expressed as the infection rate per 1,000 patient-days (211). In another study with an ethanol-based hand gel, the incidence of *C. difficile*-associated diarrhea decreased from 11.5 to 9.5 cases per 1,000 admissions within 1 year, but the difference was not significant (172). At the same time, the incidence of hospital-acquired MRSA decreased from 50 to 39% (172). Introduction of an ethanol-based hand disinfectant in a neonatal ICU significantly reduced cross-transmission of *K. pneumoniae* within 3 months from 21.5 to 4.7 cases of nosocomial colonization per 1,000 patient-days (75). Cross-transmission of *E. faecium* and *C. albicans* decreased as well, while rates for *E. coli*, *Enterobacter agglomerans*, and *E. faecalis* remained low and almost unchanged (75). The use of a virucidal hand rub based on 95% ethanol was part of an effective outbreak management of gastroenteritis caused by norovirus which involved 63 patients and health care workers (263).

EFFECT ON COMPLIANCE WITH HAND HYGIENE PRACTICES

Compliance with hand hygiene practices is known to be low. Compliance rates have been described to vary between 16 and 81% (437), with an overall average of 40% (71). One of the main goals of the new CDC guideline on hand hygiene is to provide evidence-based recommendations for improvement of compliance with hand hygiene (71). It is known that strategies to improve compliance with hand hygiene practices should be multimodal and multidisciplinary (435). Many individual parameters with a proven effect on hand hygiene compliance, however, have been identified in the new CDC guideline (71). These are efficacy, dermal tolerance, accessibility, time required for the procedure education, and personal perception; they are discussed below.

Hospital personnel should be provided with efficacious hand hygiene products, such as alcohol-based hand rubs. A change of the hand hygiene agent has been described to be particularly beneficial in institutions or hospital wards with a high workload and a high demand for hand hygiene (71).

Hand-washing agents are known to cause irritation and dryness, resulting in lower compliance rates (71). Hand hygiene products should have a low irritancy potential, particularly when these products are used multiple times per shift. A change to alcohol-based hand rubs should be made with great care, especially during winter, when hand skin is more irritable (252). Provision of skin care products may help (71, 437). However, they should not impair the efficacy of agents applied to the hands (71).

Easy access to a fast-acting hand hygiene agents should be viewed as the main tool of the strategy (71, 435, 437). Hand hygiene should be made possible, easy, and convenient. In areas with high workload, alcohol-based hand rubs should be made available at the entrance to the patient's room or at the bedside, in other convenient locations, or in individual pocket-sized bottles to be carried by health care workers (71).

Insufficient time to carry out the procedure, e.g., caused by high workload or understaffing, is associated with poor compliance (71). The time required for nurses to leave a patient's bedside, to to a sink, and wash and dry their hands before attending the next patient is a deterrent to a high compliance rate (71). A hand wash may take 62 s, whereas only one-fourth that time is required to use an alcohol-based hand rub placed at the bedside (579).

Ongoing education and promotion of hand hygiene should accompany the introduction of alcohol-based hand rubs in order to achieve long-lasting improvement in hand hygiene practices. Educational elements should include topics such as the rationale for hand hygiene, indications for hand hygiene, techniques of hand hygiene, methods to maintain hand skin health, and the correct use of gloves (71).

The smell, consistency ("feel"), and color may be important characteristics of the hand hygiene preparation that can influence the compliance rate by affecting the personal perception of those who use it (71). Differences in the acceptability of various agents have been described (258, 279, 349).

As well as the above parameters, the choice of the agent and the contents of a preparation may well have an impact on the compliance rate (242, 349, 481). The choice of a hand hygiene agent has been described to be one of many factors contributing to a strategy to successfully promote hand hygiene in hospitals (436). Baseline compliance rates in different departments vary between 30 and 63% for any soap, including plain and medicated soap, and sometimes even with the optional use of alcohol-based hand rubs if no intervention is done (Table 10). Several other studies have been conducted to measure the effect of various interventions on compliance rates with hand hygiene practices. In many studies the agent for hand hygiene remained unchanged. A higher compliance rate could be achieved by educational and training. In other studies, introduction of an alcohol-based hand rub or gel was accompanied by an educational and motivational campaign. Compliance rates could also be increased, often to a higher rate compared with the rate associated with no change of the hand hygiene agent (Table 11). Introduction of ethanol-based hand rubs sometimes revealed lower compliance rates and sometimes revealed higher compliance rates, with a trend toward the higher rates. The acceptability of the preparation and the role model function of physicians apparently have considerable influence. Preparations based on isopropanol or a combination of isopropanol and *n*-propanol revealed consistently higher compliance rates if education and promotion are carried out during introduction of the preparation and if the preparation has a superior dermal tolerance (Table 11). A 25% increase of

compliance with hand hygiene is possible (64) with the right choice of agent (which should have an excellent dermal tolerance and a high acceptability among users) and with an intensive educational and promotional campaign. These data very much support the recommendation of the CDC guideline to choose hand hygiene products with a low irritance potential and with a maximum acceptability by health care workers (71). The acceptability includes an assessment of the feel, fragrance, and subjective skin tolerance of the product (71). In this respect, well-formulated preparations based on propanol have been shown to have a better acceptability in terms of skin tolerance and skin dryness (279).

CONCLUSION

The social hand wash has only a few indications in hospitals and community medicine (243): mechanical cleaning when hands are visibly soiled with blood or other body fluids, before eating and after using the restroom, and if contamination of hands with bacterial spores is suspected (71). In these clinical situations, the simple hand wash reveals the best results compared with other possible hand treatments.

In the CDC guideline, a hygienic hand disinfection with an alcohol-based hand rub is the preferred treatment to be carried out after patient care activities that could lead to contamination of the hands of the health care workers, e.g., after contact with the patient's intact skin, body fluids or excretions, mucous membranes, nonintact skin, and wound dressings (if hands are not visibly soiled), when moving from a contaminated body site to a clean body site, after contact with environmental surfaces in the immediate vicinity of patients, and after glove removal (71). Hands should also be treated before having direct contact with patients, before donning sterile gloves when inserting devices such as vascular lines, indwelling urinary catheters, or peripheral vascular catheters (71). Hand hygiene is also indicated after using the restroom in cases of diarrhea and after blowing the nose in cases of an upper respiratory tract infection (18). The use of antimicrobial soaps in all these situations will probably be less effective in preventing cross-transmission of nosocomial pathogens and also has the risk of inducing occupational ICD.

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