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# Are the Most Simple Methods Still Useful in Preventing Respiratory Infections?

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## Introduction

Pathogens causing nosocomial pneumonia, such as Gram-negative bacilli and *Staphylococcus aureus*, are ubiquitous in healthcare settings, especially in intensive or critical care areas [1]. Transmission of these microorganisms to patients frequently occurs via the hand of healthcare personnel that become contaminated or transiently colonized with the microorganisms [2]. Procedures such as tracheal suctioning and manipulation of ventilator circuit or endotracheal tubes increase the opportunity for cross-contamination. The risk of cross-contamination can be reduced by using aseptic technique and sterile or disinfected equipment when appropriate and eliminating pathogens from the hands of personnel [3].

Hand hygiene is widely recognized as an important but underused measure to prevent nosocomial infections [2]. Even if hand hygiene seems the simplest method of prevention, all studies that have examined handwashing practices for 20 years report great difficulties in obtaining good compliance with this measure. New guidelines that promote the use of handrubbing with a waterless alcohol-based product have been recently published and may increase personnel compliance and decrease incidence of hand-transmitted infections [4].

In this chapter, hand hygiene will refer to the three following techniques: handwashing with a nonmedicated soap or an antiseptic soap, and handrubbing with a waterless alcohol-based product.

## Hand Hygiene Reduces Hand Contamination (Category A)

Hand hygiene aims at reducing or eradicating transient flora acquired during patient care activities to avoid cross transmission and thus nosocomial infections. The majority of experimental studies of products for removing transient flora from the hands of healthcare workers involve artificial contamination of the volunteer's skin with a defined inoculum of a test organism before the volunteer uses a plain soap, an antimicrobial soap, or a waterless antiseptic agent. No scientific study has established the extent to which counts of bacteria or other microorganisms on the hands need to be reduced to minimize transmission of pathogens in healthcare facilities; whether bacterial counts on the hands must be

reduced by 1 log<sub>10</sub> (90% reduction), 2 log<sub>10</sub> (99%), 3 log<sub>10</sub> (99.9%), or 4 log<sub>10</sub> (99.99%) is unknown.

Accepted methods of evaluating hand-hygiene products intended for use by healthcare workers require that test volunteers wash their hands with a plain or antiseptic soap for 30 seconds or 1 minute, despite the observation in the majority of studies that the average duration of handwashing by hospital personnel is <15 seconds [5, 6]. A limited number of investigators have used 15-second handwashing or hygienic hand-wash protocols (Table 1) [4]. Therefore, few data exist regarding the efficacy of hand hygiene under conditions in which they are actually used by healthcare workers. Similarly, certain accepted methods for evaluating waterless antiseptic agents for handrubbing require that 3 ml of alcohol be rubbed into the hands for 30 seconds, followed by a repeat application for the same duration. This type of protocol also does not reflect actual usage patterns among healthcare workers. Furthermore, volunteers used in evaluations of products are usually surrogates for healthcare workers, and their hand flora may not reflect flora found on the hands of personnel working in health-care settings.

As summarized in Table 1, several experimental assays approaching real conditions of use have examined the relative efficacy of hand hygiene techniques to remove micro-organisms from the hands. All showed a poor bactericidal activity of handwashing with nonmedicated soap as compared with hand hygiene with antiseptic agents. To date, only five clinical studies (Table 2) have evaluated the efficacy of hand hygiene procedures in routine practice [7–11].

In a prospective, randomized clinical trial, Zaragoza et al. compared the efficacy of an alcoholic solution with handwashing with nonmedicated soap during regular work in clinical wards and intensive care units (ICUs) of a large public university hospital in Barcelona [11]. Healthcare workers were randomly assigned to handwashing or handrubbing with the alcoholic solution by using a crossover design. The number of colony-forming units (cfu) on agar plates from hand printing in three different samples was counted (before and after hand hygiene procedure, 10 to 30 minutes after hand hygiene procedure). A total of 47 healthcare workers were included. The average reduction in the number of cfu from samples before handwashing to samples after handwashing was 50% for handwashing and 88% for handrubbing. When both methods were compared, the average number of cfu recovered after the procedure showed a statistically significant difference in favor of the alcoholic solution ( $p < 0.001$ ). The investigators did not interfere with any healthcare worker during the study. Thus the results reflect the real practice of hand hygiene during care activities.

Pittet et al. performed an uncontrolled observational study to examine the process of bacterial contamination of health care workers' hands during routine patient care in a large teaching hospital. Structured observations of 417 episodes of care were conducted by trained external observers. Each observation period started after a hand hygiene procedure and ended when the healthcare worker proceeded to clean his or her hands or at the end of a coherent episode of care. At the end of each period of observation, an imprint of the five fingertips of the dominant hand was taken and bacterial colony counts were quantified. Regression methods were used to model the intensity of bacterial contamination as a function of method of hand hygiene, duration and type of care, with time of ungloved hands

**Table 1.** Experimental studies comparing the relative efficacy of nonmedicated soap or medicated soaps versus alcohol-based antiseptics in reducing hand contamination

Authors [Ref]	Year	Skin contamination	Hand sampling method	Time	Relative efficacy
Ayliffe et al. [20]	1978	Artificial contamination	Finger-tip broth culture	30"	UM soap < M soap < ABP
Lilly et al. [21]	1978	Artificial contamination	Finger-tip broth culture	30"	UM soap < M soap < ABP
Ojajarvi et al. [22]	1980	Artificial contamination	Finger-tip broth culture	15"	UM soap < M soap < ABP
Ulrich et al. [23]	1982	Artificial contamination	Glove juice test	15"	M soap < ABP
Larson et al. [24]	1986	Existing hand flora	Sterile-broth bag technique	15"	UM soap < M soap = ABP
Ayliffe et al. [25]	1988	Artificial contamination	Finger-tip broth culture	30"	UM soap < M soap < ABP
Ehrenkranz et al. [26]	1991	Patient contact	Glove-juice test	15"	UM soap < ABP
Leyden et al.[27]	1991	Existing hand flora	Agar-plate/image analysis	30"	UM soap < M soap < ABP
Namura et al.[28]	1994	Existing hand flora	Agar-plate/image analysis	30"	UM soap < ABP
Paulson et al. [29]	1999	Artificial contamination	Glove-juice test	20"	UM soap < M soap < ABP
Cardoso et al. [30]	1999	Artificial contamination	Finger-tip broth culture	30"	UM soap < M soap < ABP

UM: unmedicated; M: medicated; ABP: alcohol-based product for handrubbing.

during patient care. Respiratory care was a care activity independently associated with higher contamination levels. Simple handwashing with nonmedicated soap before patient care, without hand antiseptics, was also associated with significantly higher colony counts. The major limitation of this study is that observation bias may have accounted for earlier hand hygiene than during routine patient care in the absence of an external observer.

Larson et al. performed a randomized clinical trial to compare skin condition and skin microbiology among 50 ICU personnel using one of two randomly assigned hand hygiene regimens: handwashing with an antiseptic soap or handrubbing with an alcohol-based gel.[8] Each hand hygiene regimen was assigned for four consecutive weeks. Hand cultures (n=193) were obtained four times: at baseline, during the first day of week 1, and as late as possible on the subject's last workday of weeks 2 and 4. For the handwashing group, there were no significant differences between baseline mean log counts and mean log counts from day 1, week 2, or week 4. For the handrubbing group, counts were significantly lower than baseline at day 1 and week 2, but not week 4. The microbial counts on hands of participants using handwashing increased slightly in weeks 2 and 4, whereas the counts decreased slightly at each time interval among those using handrubbing. However, the timing of hand cultures was questionable in this study whose primary endpoint was not to assess hand hygiene efficacy. In a similarly designed randomized clinical trial, Lucet et al. did not find a significant difference in bacterial counts between antiseptic handwashing and handrubbing [9].

In a randomized controlled trial, Girou et al. compared the efficacy of handrubbing with an alcohol based solution versus conventional handwashing with antiseptic soap in reducing hand contamination during routine ICU patient care [7]. During daily nursing sessions of 2 to 3 hours, 23 healthcare workers were randomly assigned to either handrubbing with alcohol based solution or handwashing with antiseptic soap when hand hygiene was indicated before and after patient care. Imprints were taken of fingertips and palm of dominant hand before and after hand hygiene procedure. Bacterial counts were quantified blindly and 114 patient care activities were evaluated. With handrubbing, the median percentage reduction in bacterial contamination was significantly higher than with handwashing (83 v 58%,  $P=0.012$ ), with a median difference in the percentage reduction of 26% (95% confidence interval, 8 to 44%). The major limitation of this trial is that the sampling method may have underestimated the degree of contamination in both groups.

With regard to this body of data coming from experimental and clinical studies, handrubbing with an alcohol-based product appears to be the best method to achieve hand disinfection.

## **Hand Hygiene Reduces Nosocomial Infections (Category C)**

Studies evaluating the impact of hand hygiene on nosocomial infection rates examine generally all sites of infection together. Therefore, no study has measured specifically the impact of hand hygiene on respiratory infections. In some studies, the results are detailed according to the site of infection, but, usually, they are not powered enough to evidence significant differences by site of infection. Most of

**Table 2.** Clinical studies assessing the effectiveness of hand hygiene to reduce hand contamination

Authors [Ref]	Year	Study design	Study location	Main results
Zaragoza et al. [11]	1999	Randomized controlled study	Hospital	Handrubbing > Handwashing with NMS
Pittet et al. [10]	1999	Uncontrolled observational study	Hospital	Handrubbing > Handwashing with NMS
Larson et al. [8]	2000	Randomized controlled study	Adult ICU	Handrubbing = Handwashing with AS
Lucet et al. [9]	2002	Randomized controlled study	Adult ICU	Handrubbing = Handwashing with AS
Girou et al. [7]	2002	Randomized controlled study	Adult ICU	Handrubbing > Handwashing with AS

NMS: nonmedicated soap; AS: antiseptic soap.

the studies presented below took advantage of the discovery of poor hand hygiene practices to evaluate interventions aimed at increasing hand hygiene compliance, and monitored nosocomial infection rates in parallel. Such studies are very difficult to perform because the duration of follow-up has to be long to see both increase in compliance and decrease in infections.

An intervention trial using historical controls demonstrated in 1847 that the mortality rate among mothers who delivered in the First Obstetrics Clinic at the General Hospital of Vienna was substantially lower when hospital staff cleaned their hands with an antiseptic agent than when they washed their hands with nonmedicated soap and water [12]. Semmelweis observed that the mortality rate of puerperal fever was substantially higher in the First Clinic (16%) where doctors and medical students provided care to women in labor as compared with the Second Clinic (7%) where midwives assisted at all deliveries. He postulated that the high rate of puerperal fever was caused by “cadaverous particles” transmitted from the autopsy rooms to the obstetrics ward via the hands of students and doctors despite washing them with unmedicated soap and water. In May 1847, Semmelweis insisted that students and doctors scrub their hands in a chlorinated lime solution before every physical examination. The maternal mortality rate in the First Clinic subsequently dropped dramatically to 3% in the 7 remaining months of 1847 and remained low for years. This intervention by Semmelweis represents the first evidence that cleansing heavily contaminated hands with an antiseptic agent between patient contacts can reduce nosocomial transmission of contagious diseases more effectively than handwashing with nonmedicated soap and water.

In 1977, Casewell et al. found that 70% of the staff of an adult ICU had their hands contaminated with *Klebsiella* [13]. These strains could be related to serotypes infecting or colonizing patients in the ward on the same day. They identified ward

procedures that resulted in contamination of nurses' hands with  $10^2$  to  $10^3$  *Klebsiella* per hand with a survival on hands for up to 150 minutes. Handwashing with an antiseptic agent reliably gave 98–100% reduction in hand counts, and the introduction of routine handwashing by staff before moving from one patient to the next was associated with a significant and sustained reduction in the number of patients colonized or infected with *Klebsiella*. However, the investigators did not quantitate the level of handwashing compliance among personnel.

In a sequential comparative trial of three handwashing agents in a surgical ICU (i.e., nonmedicated soap and two antiseptic soaps, each regimen used exclusively for approximately six weeks), the incidence of nosocomial infection was 50% lower during the use of the antiseptic handwashing products than during the use of nonmedicated soap ( $p < 0.001$ ) [14].

With a sequential intervention study in an ICU, Conly et al. demonstrated that poor handwashing practices were associated with a high nosocomial infection rate, whereas good handwashing practices were associated with a low nosocomial infection rate [15]. An educational program designed to improve handwashing procedures significantly reduced endemic nosocomial infection rates. Before the educational program, the nosocomial infection rate (number of infections per 100 patient discharges) was greater than 30% with handwashing compliances of 14 and 28% before and after patient contact, respectively. After the institution of the first educational program, the infection rate decreased dramatically to 12% meanwhile handwashing compliance rates reached 73 and 81% before and after contact. The infection rates were maintained low during the three subsequent years. The fourth year, nosocomial infection rates increased to 33% with poor handwashing practices (26 and 23% before and after contact, respectively). A second educational program was implemented, and nosocomial rates dropped again to 9% with average handwashing compliance of 60%.

Handwashing and infection rates were studied in two ICUs of a community teaching hospital [16]. Handwashing rates were monitored secretly throughout the study. After six months of observation, educational interventions were started to increase handwashing. Handwashing increased gradually, but overall compliance rates before (22%) and after (30%) interventions were not significantly different ( $p = 0.07$ ) whereas infection rates per 100 admissions remained stable (22% and 23%).

For eight months, Doebbeling et al. conducted a prospective multiple-crossover trial involving 1894 adult patients in three ICUs [17]. In a given month, the ICU used a hand-washing system involving either chlorhexidine or alcohol, with the optional use of a nonmedicated soap; in alternate months the other system was used. Rates of nosocomial infection and handwashing compliance were monitored prospectively. When chlorhexidine was used, there were 152 nosocomial infections, as compared with 202 when the combination of alcohol and soap was used (adjusted incidence-density ratio [IDR], 0.73; 95% confidence interval, 0.59 to 0.90). The largest reduction with chlorhexidine was in gastrointestinal infections. However, because only a minimal amount of the alcohol rinse was used during periods when the combination regimen also was in use and because compliance with handwashing instructions was higher when chlorhexidine was available (48

versus 30%,  $p=0.002$ ), determining which factor (i.e., the hand-hygiene regimen or differences in adherence) accounted for the lower infection rates was difficult.

Webster et al. evaluated hand wash products in terms of user acceptability and effectiveness against methicillin-resistant *S. aureus* (MRSA) as part of a long-term strategy to eliminate endemic MRSA from the neonatal ICU at an Australian hospital [18]. Following the introduction of a new hand wash disinfectant, new cases of MRSA colonization were monitored for 12 months. In addition, the use of antibiotics, the incidence of multi-resistant Gram-negative cultures, and neonatal infections were noted. No changes were made to any procedures or protocols during the trial. All babies colonized with MRSA were discharged from the nursery within 7 months of the introduction of triclosan and in the subsequent 9 months no new MRSA isolates were reported. Compared with the previous 12 months, fewer antibiotics were prescribed and fewer nosocomial infections recorded ( $p<0.05$ ).

Zafar et al. described nosocomial infections due to MRSA of 22 male infants in a neonatal nursery during a 7-month period and the infection control procedures that effectively brought this outbreak under control and eliminated recurrence for more than 3 years [19]. After a single index case of bullous impetigo caused by MRSA in a neonate discharged from the nursery 2 weeks previously, an additional 18 cases of MRSA skin infections were clustered in a 7-week period. Aggressive infection control measures were instituted, including changes in umbilical cord care, circumcision procedures, diapers, handwashing, gloves, gowns, linens, disinfection, placement in cohorts of neonates and staff, surveillance, and monitoring. These measures were not effective in slowing the outbreak. The single additional measure of changing handwashing and bathing soap to a preparation containing an antiseptic (0.3% triclosan) was associated with the immediate termination of the acute phase of the MRSA outbreak.

### **Impact of Hand Hygiene Promotion on Nosocomial Infection Rates (Table 3)**

Pittet et al. attempted to promote hand hygiene by implementing a hospital-wide program, with special emphasis on bedside, alcohol-based hand disinfection and measuring nosocomial infections in parallel. The overall compliance with hand hygiene during routine patient care in a teaching hospital in Geneva, was monitored before and during implementation of a hand-hygiene promoting campaign. Seven hospital-wide prevalence surveys were done twice yearly from December, 1994, to December, 1997. Secondary outcome measures were nosocomial infection rates, attack rates of MRSA, and consumption of handrub disinfectant. Compliance with hand hygiene improved progressively from 48% in 1994, to 66% in 1997 ( $p<0.001$ ). During the same period, overall nosocomial infection decreased (prevalence of 17% in 1994 to 10% in 1998;  $p=0.04$ ), MRSA transmission rates decreased (2.16 to 0.93 episodes per 10,000 patient-days;  $p<0.001$ ), and the consumption of alcohol-based handrub solution increased from 3.5 to 15.4 l per 1000 patient-days between 1993 and 1998 ( $p<0.001$ ).

**Table 3.** Clinical studies evaluating the impact of hand hygiene promotion on nosocomial infection rates

Authors [Ref]	Year	Study design	Study location	Impact on Hand Hygiene Compliance	Impact on nosocomial infections rates
Casewell et al. [13]	1977	Non-randomized controlled study	Adult ICU	NM	↘ Klebsiella infections
Maki et al. [14]	1989	Non-randomized controlled study	Adult ICU	NM	↘ infections
Conly et al. [15]	1989	Non-randomized controlled study	Adult ICU	↗	↘ infections
Simmons et al. [16]	1990	Non-randomized controlled study	Adult ICU	No effect	No effect
Doebbeling et al. [17]	1992	Non-randomized controlled study	Adult ICU	↗	↘ infections
Webster et al. [18]	1994	Non-randomized controlled study	Neonatal ICU	NM	↘ MRSA cross transmission
Zafar et al. [19]	1995	Non-randomized controlled study	Neonatal ICU	NM	↘ MRSA cross transmission
Pittet et al. [31]	2000	Non-randomized controlled study	Hospital	↗	↘ infections ↘ MRSA cross transmission
Larson et al. [32]	2000	Non-randomized controlled study	Hospital	↗	↘ VRE cross transmission

NM: not monitored; MRSA: methicillin-resistant *Staphylococcus aureus*; VRE: vancomycin-resistant enterococci. ↗ significant increase; ↘ significant decrease.

Larson et al. conducted a quasi-experimental intervention trial to assess the impact of an intervention to change behavior on frequency of staff handwashing (as measured by counting devices inserted into soap dispensers on four ICUs) and nosocomial infections associated with MRSA and vancomycin-resistant enterococci (VRE). All staff in one of two hospitals received an intervention with multiple components designed to change behavior; the second hospital served as a comparison. Over a period of 8 months, 860,000 soap dispensings were recorded, with significant improvements in the study hospital after 6 months of follow-up. Rates of MRSA were not significantly different between the two hospitals, but rates of VRE were significantly reduced in the intervention hospital during implementation.



## Conclusion

In conclusion, there is a good level of evidence showing that hand hygiene with antiseptic products is effective to reduce hand contamination significantly during patient care activities. Surely, the best technique is handrubbing with an alcohol-based solution. This measure should decrease the risk of cross transmission of microorganisms and thus decrease the risk of acquiring an infection, especially in ICU patients. However, the level of evidence demonstrating a link between an increased compliance to hand hygiene and low rates of nosocomial infections is low according to the classification used in this chapter. Good evidence for effect of a procedure should be obtained from placebo-controlled, double-blind, crossover studies. For obvious reasons, no such studies on the effect of hand hygiene in ICUs ever have been or will be performed. Hand hygiene has been general practice in medical care since the days of Semmelweis. No ethics committee would accept a study where some intensive care patients intentionally received care from staff with dirty hands!

The hand hygiene research agenda should certainly include valid epidemiological research generating more definitive evidence for the impact of improved compliance with hand hygiene on infection rates [2]. But also, and maybe as a priority, the key determinants of hand-hygiene behavior must be assessed and the evidence-based indications for hand cleansing must be promoted among the different populations of healthcare workers, (considering that it might be unrealistic to expect healthcare workers to clean their hands after every patient contact), the necessary percentage increase in hand-hygiene compliance resulting in a predictable risk reduction in infection rates.

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