World Health Organization

Patient Safety

A World Alliance for Safer Health Care

WHO Guidelines on Hand Hygiene in Health Care

First Global Patient Safety Challenge
Clean Care is Safer Care

11.3 Alcohols

Most alcohol-based hand antiseptics contain either ethanol, isopropanol or n-propanol, or a combination of two of these products. Concentrations are given as either percentage of volume (= ml/100 ml, abbreviated % v/v), percentage of weight (= g/100 g, abbreviated % m/m), or percentage of weight/volume (= g/100 ml, abbreviated % m/v). Studies of alcohols have evaluated either individual alcohols in varying concentrations (most studies), combinations of two alcohols, or alcohol solutions containing small amounts of hexachlorophene, quaternary ammonium compounds (QAC), povidone-iodine, triclosan or CHG.[137,221,267-286]

The antimicrobial activity of alcohols results from their ability to denature proteins.[287] Alcohol solutions containing 60–80% alcohol are most effective, with higher concentrations being less potent.[288,289] This paradox results from the fact that proteins are not denatured easily in the absence of water.[287] The alcohol content of solutions may be expressed as a percentage by weight (m/m), which is not affected by temperature or other variables, or as a percentage by volume (v/v), which may be affected by temperature, specific gravity and reaction concentration.[290] For example, 70% alcohol by weight is equivalent to 76.8% by volume if prepared at 15 ºC, or 80.5% if prepared at 25 ºC.[290] Alcohol concentrations in antiseptic handrubs are often expressed as a percentage by volume.[198]

Alcohols have excellent in vitro germicidal activity against Gram-positive and Gram-negative vegetative bacteria (including multidrug-resistant pathogens such as MRSA and VRE), *M. tuberculosis*, and a variety of fungi.[287-289,291-296] However, they have virtually no activity against bacterial spores or protozoan oocysts, and very poor activity against some non-enveloped (non-lipophilic) viruses. In tropical settings, the lack of activity against parasites is a matter of concern about the opportunity to promote the extensive use of alcohol-based handrubs, instead of handwashing, which may at least guarantee a mechanical removal effect.

Some enveloped (lipophilic) viruses such as herpes simplex virus (HSV), HIV, influenza virus, RSV, and vaccinia virus are susceptible to alcohols when tested in vitro (Table I.11.5).[297] Other enveloped viruses that are somewhat less susceptible, but are killed by 60–70% alcohol, include hepatitis B virus (HBV) and probably hepatitis C virus.[298] In a porcine tissue carrier model used to study antiseptic activity, 70% ethanol and 70% isopropanol were found to reduce titres of an enveloped bacteriophage more effectively than an antimicrobial soap containing 4% CHG.[192]

Numerous studies have documented the in vivo antimicrobial activity of alcohols. Early quantitative studies of the effects of antiseptic handrubs established that alcohols effectively reduce bacterial counts on hands.[63,288,292,299] Typically, log reductions of the release of test bacteria from artificially contaminated hands average 3.5 $\log_{10}$ after a 30-second application, and 4.0–5.0 $\log_{10}$ after a 1-minute application.[48] In 1994, the FDA TFM classified ethanol 60–95% as a generally safe and effective active agent for use in antiseptic hand hygiene or HCW handwash products.[198] Although the TFM considered that there were insufficient data to classify isopropanol 70–91.3% as effective, 60% isopropanol has subsequently been adopted in Europe as the reference standard against which alcohol-based handrub products are compared[201] (see Part I, Section 10.1.1). Although n-propanol is found in some hand sanitizers in Europe,[300] it is not included by the TFM in the list of approved active agents for hand antisepsis and surgical hand preparation in the USA.[58]

Alcohols are rapidly germicidal when applied to the skin, but have no appreciable persistent (residual) activity. However, regrowth of bacteria on the skin occurs slowly after use of alcohol-based hand antiseptics, presumably because of the sub-lethal effect alcohols have on some of the skin bacteria.[301,302] Addition of chlorhexidine, quaternary ammonium compounds, octenidine or triclosan to alcohol-based formulations can result in persistent activity.[48] A synergistic combination of a humectant (octoxyglycerine) and preservatives has resulted in prolonged activity against transient pathogens.[303] Nevertheless, a recent study on bacterial population kinetics on gloved hands following treatment with alcohol-based handrubs with and without supplements (either CHG or mecetronium etilsulfate) concluded that the contribution of supplements to the delay of bacterial regrowth on gloved hands appeared minor.[227]

Alcohols, when used in concentrations present in alcohol-based handrubs, also have in vivo activity against a number of non-enveloped viruses (Table I.11.5). For example, in vivo studies using a fingerpad model have demonstrated that 70% isopropanol and 70% ethanol were more effective than medicated soap or non-medicated soap in reducing rotavirus titres on fingerpads.[257,304] A more recent study using the same test methods evaluated a commercially available product containing 60% ethanol, and found that the product reduced the infectivity titres of three non-enveloped viruses (rotavirus, adenovirus, and rhinovirus) by 3 to 4 logs.[305] Other non-enveloped viruses such as hepatitis A and enteroviruses (e.g. poliovirus) may require 70–80% alcohol to be reliably inactivated.[306,307] It is worth noting that both 70% ethanol and a 62% ethanol foam product with humectants reduced hepatitis A virus titres on whole hands or fingertips to a greater degree than non-medicated soap, and both reduced viral counts on hands to about the same extent as antimicrobial soap containing 4% CHG.[308] The same study found that both 70% ethanol and the 62% ethanol foam product demonstrated greater virucidal activity against poliovirus than either non-antimicrobial soap or a 4% CHG-containing soap.[308] However, depending on the alcohol concentration, time, and viral variant, alcohol may not be effective against hepatitis A and other non-lipophilic viruses. Schurmann concluded that the inactivation of naked (non-enveloped) viruses is influenced by temperature, the ratio of disinfectant to virus volume, and protein load.[309] Various 70% alcohol solutions (ethanol, n-propanol, isopropanol) were tested against a surrogate of norovirus and ethanol with 30-second exposure demonstrated virucidal activity superior to the others.[310] In a recent experimental study, ethyl alcohol-based products showed significant reductions of the tested surrogate for a non-enveloped human virus; however, activity was not superior to non-antimicrobial or tap/faucet water controls[311]. In general, ethanol has greater activity against viruses than isopropanol[70]. Further *in vitro* and *in vivo* studies of both alcohol-based formulations and antimicrobial soaps are warranted to establish the minimal level of virucidal activity that is required to interrupt direct contact transmission of viruses in health-care settings.

Alcohols are not good cleansing agents and their use is not recommended when hands are dirty or visibly contaminated with proteinaceous materials. When relatively small amounts of proteinaceous material (e.g. blood) are present, however, ethanol and isopropanol may reduce viable bacterial counts on hands,[312] but do not obviate the need for handwashing with water and soap whenever such contamination occurs.[179] A few studies have examined the ability of alcohols to prevent the transfer of health care-associated pathogens by using experimental models of pathogen transmission.[74,88,169] Ehrenkranz and colleagues[88] found that Gram-negative bacilli were transferred from a colonized patient's skin to a piece of catheter material via the hands of nurses in only 17% of experiments following antiseptic handrub with an alcohol-based hand rinse. In contrast, transfer of the organisms occurred in 92% of experiments following handwashing with plain soap and water. This experimental model suggests that when HCWs hands are heavily contaminated, alcohol-based handrubbing can prevent pathogen transmission more effectively than handwashing with plain soap and water.

Table I.11.6 summarizes a number of studies that have compared alcohol-based products with plain or antimicrobial soaps to determine which was more effective for standard handwashing or hand antisepsis by HCWs (for details see Part I, Section 11.13).[88,125,137,221,223,273-279,286,313-321]

The efficacy of alcohol-based hand hygiene products is affected by a number of factors including the type of alcohol used, concentration of alcohol, contact time, volume of alcohol used, and whether the hands are wet when the alcohol is applied. Small volumes (0.2–0.5 ml) of alcohol applied to the hands are no more effective than washing hands with plain soap and water.[74,169] Larson and colleagues[151] documented that 1 ml of alcohol was significantly less effective than 3 ml. The ideal volume of product to apply to the hands is not known and may vary for different formulations. In general, however, if hands feel dry after being rubbed together for less than 10–15 seconds, it is likely that an insufficient volume of product was applied. Alcohol-impregnated towelettes contain only a small amount of alcohol and are not much more effective than washing with soap and water.[74,322,323]

Alcohol-based handrubs intended for use in hospitals are available as solutions (with low viscosity), gels, and foams. Few data are available regarding the relative efficacy of various formulations. One small field trial found that an ethanol gel was somewhat less effective than a comparable ethanol solution at reducing bacterial counts on the hands of HCWs.[324] Recent studies found similar results demonstrating that solutions reduced bacterial counts on the hands to a significantly greater extent than the tested gels.[203,325] Most gels showed results closer to a 1-minute simple handwash than to a 1-minute reference antisepsis.[296] New generations of gel formulations with higher antibacterial efficacy than previous products have since been proposed.[70] Further studies are warranted to determine the relative efficacy of alcohol-based solutions and gels in reducing transmission of health care-associated pathogens. Furthermore, it is worth considering that compliance is probably of higher importance, thus if a gel with lower in vitro activity is more frequently used, the overall outcome is still expected to be better.

Frequent use of alcohol-based formulations for hand antsepsis tends to cause drying of the skin unless humectants or other skin conditioning agents are added to the formulations. For example, the drying effect of alcohol can be reduced or eliminated by adding 1–3% glycerol or other skin conditioning agents.[219,221,267,268,273,301,313,326,327]

Moreover, in prospective trials, alcohol-based solutions or gels containing humectants caused significantly less skin irritation and dryness than the soaps or antimicrobial detergents tested.[262,264,328,329] These studies, which were conducted in clinical settings, used a variety of subjective and objective methods for assessing skin irritation and dryness. Further studies of this type are warranted to establish if products with different formulations yield similar results.

Even well-tolerated alcohol-based handrubs containing humectants may cause a transient stinging sensation at the site of any broken skin (cuts, abrasions). Alcohol-based handrub preparations with strong fragrances may be poorly tolerated by a few HCWs with respiratory allergies. Allergic contact dermatitis or contact urticaria syndrome caused by hypersensitivity to alcohol, or to various additives present in some alcohol-based handrubs, occurs rarely (see also Part I, Section 14).[330-332]

A systematic review of publications between 1992 and 2002 on the effectiveness of alcohol-based solutions for hand hygiene showed that alcohol-based handrubs remove organisms more effectively, require less time, and irritate skin less often than handwashing with soap or other antiseptic agents and water.[333] The availability of bedside alcohol-based solutions increased compliance with hand hygiene among HCWs.[60,333-335] Regarding surgical hand preparation, an alcohol-based waterless surgical scrub was shown to have the same efficacy and demonstrated greater acceptability and fewest adverse effects on skin compared with an alcohol-based water-aided solution and a brush-based iodine solution.[336]

Alcohols are flammable, and HCWs handling alcohol-based preparations should respect safety standards (see Part I, Section 23.6). Because alcohols are volatile, containers should be designed so that evaporation is minimized and initial concentration is preserved. Contamination of alcohol-based solutions has seldom been reported. One report documented a pseudo-epidemic of infections resulting from contamination of ethyl alcohol by *Bacillus cereus* spores[337] and in-use contamination by *Bacillus* spp. has been reported.[338]

11.4 Chlorhexidine

CHG, a cationic bisbiguanide, was developed in the United Kingdom in the early 1950s and introduced into the USA in the 1970s.[204,339] Chlorhexidine base is barely soluble in water, but the digluconate form is water-soluble. The antimicrobial activity of chlorhexidine appears to be attributable to the attachment to, and subsequent disruption of cytoplasmic membranes, resulting in precipitation of cellular contents.[48,204] Chlorhexidine's immediate antimicrobial activity is slower than that of alcohols. It has good activity against Gram-positive bacteria, somewhat less activity against Gram-negative bacteria and fungi, and minimal activity against mycobacteria.[48,204,339] Chlorhexidine is not sporicidal.[48,339.] It has in vitro activity against enveloped

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