On the nature of the alcohol-based hand rub and its use for hand hygiene in medicine and healthcare

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Having personally witnessed cases of inadequate hand hygiene practices amongst health professionals, Adrian was inspired to write this article as a means of raising awareness of the issue amongst future health professionals. The idea to focus on alcohol-based hand rubs came from observing an increase in their presence over the last decade. His other general interests include clinical immunology.

Hand hygiene (HH) is today recognised as being the most important factor in preventing the spread of infections; however, adequate compliance with this remains unacceptably low amongst healthcare workers (HCWs). One of the leading products in the push for successful HH is the alcohol-based hand rub (ABHR), which currently exists as a ubiquitous item in healthcare facilities. This review amalgamates the current understanding of ABHRs, presenting an overview of important issues including its correct usage and insights into HH. Aimed at Australian HCWs and students, a small yet significant amount of attention is devoted to Hand Hygiene Australia – one of the leading authorities in this subject area. It may be concluded that the ABHR is an effective hand disinfectant that also improves HH compliance, and is thus highly recommended for use in healthcare settings.

Hand hygiene beginnings

Since the late nineteenth century, hand hygiene (HH) in medicine and healthcare has emerged as a significant concept in the prevention of infection. The basic notion has been present for a considerable time; yet it was chiefly the observations of the Hungarian obstetrician, Ignaz Semmelweis (1818-65), that highlighted the implications of HH upon patient health. Whilst at the General Hospital of Vienna in 1846, Semmelweis noted that parturient women who were attended to by physicians and medical students had a significantly higher mortality rate of puerperal fever - an endemic of which was present at the time - than those who were attended to solely by midwives. [1]

Through his series of meticulous observations, he noticed that the basis of this was the fact that physicians and students attended autopsies and midwives did not; hence, he hypothesised, the causative agent was transmitted from the autopsy rooms to the obstetric wards, mostly likely via the hands. Despite soap and water handwashing already being required for physicians and students, Semmelweis ordered that they sanitise their hands with 4% chlorinated lime solution before and in between seeing patients. This notion was initially not well-received by his peers; yet its practice was marked with the considerable decrease in mortality from puerperal fever amongst the antepartum patients. [1,2] His discovery thus marked the beginnings of modern HH practice, and along with the work of the English surgeon Joseph Lister (1827-1912), who highlighted the need for antisepsis in medicine, [1,3] a thorough understanding of its importance was born.

Hand flora

Thorough HH is recognised today as being the most important factor in preventing nosocomial infections, [4] with an estimated 4.9×10^4 Colony Forming Units (CFU)/cm^2 bacteria on the hands of HCWs [5] compared to 10^2-10^3 CFU/cm^2 on normal skin. [6] Micro-organisms, particularly when referred to in terms of the hands, have categorically been broken down into two groups: transient flora and resident flora. Transient flora reside in outer layers of the skin and are acquired through direct patient contact or through contaminated surfaces. They are not "consistently present in the majority of persons" [7] and may easily be removed by careful handwashing. Continued removal on a long-term basis, however, is not desirable since it alters normal flora and, hence, may give rise to proliferation of potentially pathogenic flora. Resident flora, in comparison, reside in the deeper layers of the

skin and are considered to be relatively permanent and not usually removed by routine handwashing. Of most concern are the transient flora which are associated with nosocomial infections, [2,6,8] although resident flora may be implicated in some infections that involve the alteration of host immunity with, for example, catheterisation. [6]

Handwashing versus hand hygiene

'Handwashing' is defined by The Centers for Disease Control and Prevention (CDC) as the "vigorous, brief rubbing together of surfaces of lathered hands, followed by rinsing under a stream of water." [4] Whilst the precise definition of 'handwashing' varies across the globe, [6] the process fundamentally involves two methods of cleaning: mechanical and chemical. The physical removal of pathogens through frictional scrubbing is termed 'mechanical cleaning.' Plain (non-antimicrobial) soaps and detergents are generally also utilised. These are chemically composed of hydrophobic and hydrophilic components, consisting of a long, non-polar hydrocarbon tail, and a polar and typically ionic head. As a result, micro-organisms - mostly transient flora - and other particles are suspended in solution to be washed away by excess water. Chemical methods of handwashing employ specialised antimicrobial soaps that kill and/or inhibit the growth of micro-organisms through various means, depending on the active chemical(s) present. [4] A routine handwash, according to various leading authorities, involves use of plain or anti-microbial soaps and vigorous scrubbing for some time before hand-drying on paper towels. [2,4,7]

Whilst sometimes used synonymously with handwashing, HH generally encompasses a broader scope of coverage than handwashing with plain or medicated soap and water; including also "antiseptic hand rub, antiseptic hand wash or surgical hand antisepsis." [2] According to Hand Hygiene Australia (HHA), these procedures have different products and durations compared to handwashing. [9] HHA also associates HH with general hand care (such as the use of moisturisers to prevent skin cracking). [9] Indeed, the precise distinction and definition of HH, much like the definition of handwashing, varies amongst the literature.

Alcohol-based hand rubs

Although strong evidence exists to support HH in the reduction of nosocomial infections, full compliance with HH in the healthcare setting remains surprisingly low, with some studies reporting no more than 40% compliance amongst staff. [6,8,10] Thus, one of the leading products in the push for adequate HH is the alcohol-based hand

rub (ABHR) which emerged prominently in recent times. [11] ABHR dispensers are fast becoming a ubiquitous item in the healthcare setting owing to the convenience of ABHRs. Compared to handwashing with soap and water, they are antimicrobially more effective in vitro and in vivo [6,12] and the application time is significantly less. Consequently, compliance with proper HH methodology has been reported to be significantly higher when ABHRs are introduced, far more effective than education intervention programmes. [13]

Mode-of-action

ABHRs contain ethanol, n-propanol, isopropyl alcohol or mixtures of these. [14-16] The alcohols exhibit both bacteriostatic and bactericidal activity, and whilst their mechanisms are not well-understood, it is widely accepted that the primary mode-of-action is the denaturation and precipitation of proteins. [7,14-17]

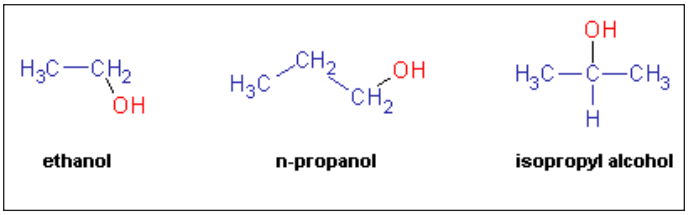

Figure 1. *The three alcohols that can be found in ABHRs. Polar, hydroxyl ends are marked in red; non-polar, aliphatic ends are in blue.*

Due to the hydrophilic and hydrophobic properties at the hydroxyl group (–OH) and aliphatic ends respectively (Figure 1), these alcohols facilitate the denaturation of proteins by first disrupting the lipid bilayer membrane of various micro-organisms, [15] permitting exposure of cellular proteins. Protein unravelling and destruction occur by the disruption of intermolecular bonding or forces. For the tertiary structure of proteins, the disruption of such bonding between the 'tucked-in' hydrophobic amino acid side chains and the surface hydrophilic side chains leads to significant unfolding of the polypeptide backbone and hence, denaturation of the protein (Figure 2). [18]

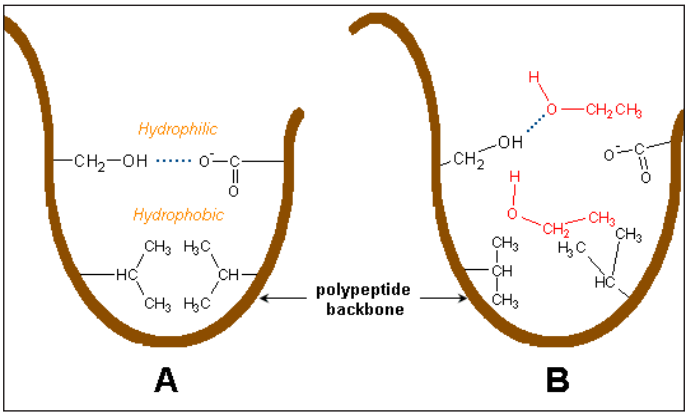

Figure 2. *Examples of tertiary interactions of hydrophilic and hydrophobic side chains (A) and the disruption caused by adding an alcohol (ethanol, for this diagram) (B). Note how the hydrophobic side chains are 'tucked in', away from the external, aqueous environment in Figure A.*

Proteins susceptible to denaturation are reportedly found at the cell wall and cell membrane, thereby compromising the micro-organisms' membrane and cytoplasmic integrity from the resultant disruptions. [17] However, in order for these effects to occur, it is necessary for the alcohols to be present at certain concentrations in aqueous solutions. Many ABHRs contain 60-80% v/v alcohol which represent the concentrations that deliver the most effective antimicrobial activity. Each alcohol, however, has its own unique, optimal concentration – ethanol, for instance, appears to be most effective at 80% v/v. [19,20] The dilution of alcohol is thought to be necessary as high concentrations coagulate proteins on the exterior of the cell wall, therefore preventing entry of the alcohol. [18] However, some antimicrobial activity may still be observed at these levels. [21] In similar concentrations, n-propanol appears to be the most effective alcohol, followed by isopropyl alcohol. [20]

Activity

ABHRs have been shown to possess antiseptic action across a range of micro-organisms. Against most gram-positive and gram-negative vegetative bacteria, the alcohols are highly effective, killing within several seconds. [7,10] In addition, ABHRs have shown promise against drug-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), [22] and other resilient bacteria such as *Mycobacterium tuberculosis*. [7]

There are, however, examples of bacteria where ABHRs are ineffective; one of the more prominent examples being *Clostridium difficile*. [23,24] This is an issue as *C. difficile* diseases are increasing in the healthcare setting and therefore, other methods must be used to combat it. Recent research indicates that handwashing with warm water and soap is an effective alternative in removing C. difficile spores. [25] Having said this, ABHR activity against bacterial spores has often been reported as poor; [10] yet, there are exceptions. Research by Morton in 1983, cited by Ali *et al.* [17] found that Bacillus anthracis spores could be killed by isopropyl alcohol in a few minutes. From a practical view-point, however, ABHRs should not be used against spores until they are at least supplemented with 1% hydrogen peroxide which may confer better sporicidal activity. [10]

Against parasites and protozoan oocytes, ABHRs are poor. [2,26] Conversely, the alcohols have been found to have excellent activity against a range of fungi and enveloped viruses, (such as human immunodeficiency, herpex simplex, influenza and hepatitis B viruses), [15,17] and some non-enveloped viruses (for instance, rhinovirus and rotavirus). [2,27] Apart from enveloped viruses, ethanol is generally more potent against viruses than isopropyl alcohol. [2,28]

Issues

ABHRs are highly effective and versatile antimicrobial agents which have emerged as a chief tool against nosocomial infections. They are widely available, safe, do not require a sink or additional water, and have a quick application time thus not compromising the quality of patient care. [29] These important benefits have helped to promote ABHRs and proper HH amongst HCWs. Furthermore, ABHRs are generally less irritating to the skin than many other antiseptic products and soap and water, making it an attractive alternative. [8,30] Despite this, alcohol does have an inherent drying effect on the skin which may cause some irritation; thus many ABHRs contain emollients, such as glycerol, and humectants which can prevent such irritation and dermatitis. [31]

An increasingly prominent issue for HCWs is antibiotic resistance amongst bacteria, and therefore, extra vigilance is exercised with the utilisation of antibiotic and antiseptic agents. [32,33] As previously mentioned, ABHRs have proven to be effective against such resistant bacteria, and, currently, no evidence yet exists to suggest that topical antimicrobial agents, such as ABHRs, contribute to antibiotic resistance. [10,34] From a scientific point-of-view, this conclusion is certainly sound as ABHRs, in contrast to antibiotics, cause widespread physical damage to micro-organisms by the non-specific denaturation of many proteins. Mutation, and therefore resistance, is extremely unlikely, if not impossible. Moreover, it has been suggested that insufficient exposure time to the alcohol due to rapid evaporation reduces the risk of resistance developing. [10]

ABHRs, of course, are not free from their limitations and disadvantages. Whilst they display excellent antimicrobial activity, residual activity is not present and flora grows back hours after use. Consequently, some ABHRs have added antiseptics, such as chlorhexidine gluconate, for synergistic bactericidal effects and possible prolonged activity. [10,15] In addition, ABHRs are highly flammable and therefore pose a fire hazard; however, fires as a result of these products are thought to

be rare. [6,35] One measure of their flammability is the 'flash point,' defined as the lowest temperature needed for a volatile liquid to produce an ignitable vapour. For the 'diluted' alcohol in ABHRs, flash points range from approximately 21°C to 24°C. [6] Thus, care should be taken with naked flames and sparks around ABHR dispensers, which should be well-designed to minimise unwarranted evaporation or exposure of the product.

Further concerns identified include the fragrances of certain volatile ABHRs which may upset people with respiratory sensitivity or allergies. [16,36] Additional costs to install ABHR dispensers and provide education has been highlighted as a minor issue which prevented the more widespread usage of ABHRs. [28] However, the cost to the hospital system resulting from nosocomial infections is far greater than the costs to supply ABHRs, [37] thus making these products financially worthwhile. Table 1 summarises the main advantages and disadvantages of ABHRs.

Table 1. *Main advantages and disadvantages of ABHRs.*

Advantages
Highly effective against a range of micro-organisms
Relatively non-toxic
Fast application with no water, sinks or paper towels needed
Improves hand hygiene compliance
Disadvantages
May cause skin and respiratory irritation
Flammable (fire hazard)
Poor residual activity

Correct procedure

ABHRs are not designed to physically clean one's hands. Hands that are visibly or obviously contaminated with debris, proteinaceous and/or organic material should be washed with soap and water and dried. [2,32] Before use of the ABHR, HHA states that jewellery should be removed and artificial nails should not be worn. [9] This is consistent with research that these objects significantly harbour pathogens. [38-40] Following this, any lesions or abrasions on the hands must be covered appropriately with water-proof material to minimise the chances of pathogen cross-transmission. [32] A sufficient amount of undiluted hand rub should then be squirted into the open palm. Depending on the manufacturer's instructions, this amount will vary, [2] though between 2mL and 3mL is the volume often used. [8,20]

The ABHR should be rubbed in completely with both hands until dry, [32] covering all surfaces of the hands, and following the authoritative procedure outlined by the World Health Organisation's (WHO) 'How to Handrub?' poster. [41] To benefit from the full antimicrobial effect of the alcohol, the process should last for at least 30 seconds; [19,31,42] however, HHA only suggests ten to fifteen seconds. [9] Importantly, they recommend ABHRs have the approval of the Therapeutic Goods Administration and meet the European Committee for Standardisation (EN1500) standard for bactericidal activity. [9]

The use of ABHRs and general HH is indicated in a variety of healthcare situations – many of these are listed in the HHA manual. [9] However, most notably, the WHO lists five critical occasions when HH is essential as the so-called 'Five Moments for Hand Hygiene' (FMHH): (1) before touching a patient; (2) before aseptic procedures; (3) after contact with bodily fluids; (4) after patient contact; and (5) after touching a patient's environment. [16] Indeed, these indications were "created to bridge the gap between the results of scientific studies and evidence-based guidelines and the necessity to provide user-centred, practical tools." [43]

One of the many reasons why HH compliance is low is due to the belief that wearing disposable gloves negates the need for proper HH. [44,45] This assumption is false, and studies have shown that gloves contain microscopic pores, exacerbated by normal clinical use, that may permit entry of viruses. [46-48] Widmer [6] mentions a 1988 study by Doebbeling *et al.* where certain micro-organisms handled by gloves were able to be isolated on the hands themselves. Therefore, adequate HH must be followed with glove use, and it is currently recommended people follow HH practices before donning and after removing gloves. [9,10] Despite this, the WHO reports that HH upon de-gloving is still an unresolved issue. [16]

Discussion

It is clear that ABHRs have proven to be highly effective and convenient, and are becoming increasingly accepted amongst HCWs. There are, undeniably, disadvantages with their use; but by far the biggest barrier to more prevalent and proper usage is not any intrinsic limitation, rather it lies with the users of the hand rub themselves. The lack of time, misconceptions, inaccessible handwashing supplies, forgetfulness, few role-models, lack of institutional HH protocols and skin irritation are some of the issues that stand in the way of better compliance amongst HCWs. [8,31,45] Therefore, these barriers must be recognised and addressed appropriately in order to improve compliance.

A relatively unexplored barrier includes religious beliefs. Most notably, the religion of Islam forbids the consumption of alcohol and hence, contact with it through ABHRs by Muslim HCWs is a cause of concern. [49] However, the amount of alcohol systemically absorbed is negligible and any absorbed amount quickly declines after several minutes. [50,51] In addition, the use of alcohol as a medicinal agent to improve health is, in actual fact, permitted under Islam. This was reinforced by the World Muslim League in 2002. [49] Thus, an increased appreciation and awareness of the concerns of HCWs with religious beliefs that ban contact with alcohol is fundamental to improving HH compliance. [49] Further research is suggested to holistically address this matter. [52]

The main challenge with ABHR use lies in maintaining HCWs' adherence to the product and protocols. [53] The introduction of systematic, hospital- and discipline-wide programmes with HH education, promotion and feedback have proven successful and instrumental in combating this issue and many of the aforementioned barriers. [54-56] At the heart of these programmes, multimodal and multidisciplinary strategies should be employed to maximise success in ensuring optimal compliance. [2,8,45,53]

Kampf [57] identified 'six golden rules' of improving compliance which, in the first two rules, advocated the use of accessible and acceptable ABHRs. His other recommendations included the implementation of education and promotion, creating budgets to cover associated costs, creating role models and having a balanced staff-patient ratio. A suggested approach by Apisarnthanarak *et al.* [58] also adds performing audits, providing feedback and identifying and addressing individual obstacles; for example, combating 'forgetfulness' with promotional posters. In fact, HHA asserts that "ensuring ABHR is readily available at the point-of-care…can reduce many of the potential barriers to good HH." [9] The National Health and Medical Research Council (NHMRC) goes on to suggest automated ABHR dispensers and computerised voice prompts to increase compliance. [32] Hence, whilst different approaches are taken, multimodal programmes demonstrate fitting responses to some existing barriers.

Without doubt, the FMHH is a key constituent of various multimodal strategies, employing the use of simple visuals for the successful delivery of these critical moments. [43] These visuals can be placed in multiple locations, thereby encouraging and reminding HCWs of safe HH practices. The protocol also allows for suitable monitoring with its clearly defined indications, which is a necessary and vital step in ensuring the continued success of the programme, and certainly a step that is advocated by WHO. [32,59] Hence, owing to its value, the FMHH is an integral component in the HHA's National Hand Hygiene Initiative (NHHI) for Australian HCWs. [60]

*Table 2. A list of selected prominent guidelines and protocols for HH and the use of ABHRs. *URLs are correct as of January 2011.*

Guideline	Source*
NHMRC: Australian Guidelines for the Prevention and Control of Infections in Healthcare (2010)	http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/ CD33_ InfectionControlGuidelines2010.pdf
Hand Hygiene Australia Manual (2009)	http://www.hha.org.au/UserFiles/file/Manual/ManualJuly2009v2(Nov09).pdf
WHO Guidelines on Hand Hygiene in Health Care (2009) & 'Five Moments for Hand Hygiene' (2009)	http://whqlibdoc.who.int/publications/2009/9789241597906_eng.pdf
CDC (MMWR): Guideline for Hand Hygiene in Health-Care Settings (2002)	Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/ IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. MMWR Recomm Rep. 2002;51(RR-16):1-45, quiz CE1-4.
APIC Guideline for Handwashing and Hand Antisepsis in Health Care Settings (1995)	Larson E. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995;23(4):251-69.

The guidelines listed in Table 2, along with all other HH protocols, should form the basis of HH practices today. Amongst HCWs, it is simply unacceptable to disregard such protocols, particularly knowing the potential consequences of non-compliance. Certainly, it is not suggested that HH practices ought to be replaced entirely by ABHRs - and in fact, the efficacy of solely using ABHRs has been doubted. [19,61] Rather, ABHRs should be used in conjunction with HH procedures as products to improve the standard of HH. With this in mind, and current HCWs and students alike being instrumental in pushing for better HH practices, the future certainly looks more promising for modern healthcare.

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Conflicts of Interest

None declared.

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