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TITLE:
Back to basics: hand hygiene and isolation

ABSTRACT:
PURPOSE OF REVIEW: Hand hygiene and isolation are basic, but very effective, means of preventing the spread of pathogens in healthcare. Although the principle may be straightforward, this review highlights some of the controversies regarding the implementation and efficacy of these interventions. RECENT FINDINGS: Hand hygiene compliance is an accepted measure of quality and safety in many countries. The evidence for the efficacy of hand hygiene in directly reducing rates of hospital-acquired infections has strengthened in recent years, particularly in terms of reduced rates of staphylococcal sepsis. Defining the key components of effective implementation strategies and the ideal method(s) of assessing hand hygiene compliance are dependent on a range of factors associated with the healthcare system. Although patient isolation continues to be an important strategy, particularly in outbreaks, it also has some limitations and can be associated with negative effects. Recent detailed molecular epidemiology studies of key healthcare-acquired pathogens have questioned the true efficacy of isolation, alone as an effective method for the routine prevention of disease transmission. SUMMARY: Hand hygiene and isolation are key components of basic infection control. Recent insights into the benefits, limitations and even adverse effects of these interventions are important for their optimal implementation.

INTRODUCTION:
Hand hygiene and patient isolation are two basic principles that have long been recognized as effective methods of reducing hospital-acquired infections. However, the optimal methods for implementation and monitoring of such programmes are not straightforward.
The WHO Global Patient Safety Challenge: ‘Clean Care is Safer Care’ campaign was launched in 2005 with the aim of reducing healthcare-associated infections worldwide [1]. Consensus guidelines on hand hygiene in healthcare were subsequently published in 2009 [2,3] after the early success of the WHO hand hygiene multimodal implementation strategy and toolkit [4,5▪▪,6]. Ongoing research and experience from other programmes worldwide is helping in guiding the optimal implementation of these interventions.
Recent experience with emerging infectious diseases has highlighted the role of isolation in outbreak settings. However, new studies have also emphasized the limitations, and even negative effects, of isolation under certain circumstances.

THE CLINICAL IMPACT OF HAND HYGIENE PROGRAMMES:
Since the early initiatives by the WHO, hand hygiene campaigns have been initiated worldwide [7,8,9▪]. The countries participating in the WHO CleanHandsNet [10], a global network of coordinators or leaders involved in the promotion of hand hygiene in healthcare, are shown in Fig. 1. In many countries, hand hygiene has been incorporated as a measure of quality of care at the national or subnational level [11▪,12▪].
Until recently, the preponderance of data demonstrating the clinical benefits of improved hand hygiene compliance came from single-centre or multicentre before-and-after studies [13–15], including the landmark study from Pittet et al.[16]. In the last few years, the clinical evidence for hand hygiene has strengthened in two ways. First, the outcomes of several major national and subnational programmes have been reported [17–20]. Second, a number of recent studies have incorporated more advanced study designs in their assessment of hand hygiene efficacy.
The Cleanyourhands campaign was instituted in all acute National Health Service (NHS) hospital trusts in England and Wales commencing in 2004. In the first 4 years of this initiative, rates of Clostridium difficile and methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia declined significantly [18]. In addition, when consumption of hand hygiene products by individual trust was reviewed, procurement of soap was independently associated with reduction in C. difficile rates, and alcohol-based hand rub (ABHR) was independently associated with reduction in MRSA bacteraemia, although only in the last four quarters of the study period. Notably (and somewhat disappointingly), formal surveillance of hand hygiene compliance rates was not assessed, with consumption data used as a surrogate for compliance.
The Australian National Hand Hygiene Initiative (NHHI) commenced in 2009, following a number of successful state-based programmes, which were associated with reductions in rates of MRSA

bacteraemia [13,21,22]. The aim was to implement a standardized hand hygiene culture change programme on the basis of the WHO multimodal hand hygiene improvement strategy throughout all Australian public and private hospitals. Hand hygiene compliance increased from 63.6 to 68.3% in the first 2 years of this programme [17]. The NHHI now involves data submission from more than 740 hospitals three times annually, with the national hand hygiene compliance rate improving to 79% in late 2013 [12▪]. Public reporting of hand hygiene compliance and healthcare-associated S. aureus bacteraemia (SAB) rates for individual hospitals is a mandatory component of Federal Government hospital accreditation [12▪,23]. Subsequently, the national rates of healthcare-associated SAB have continued to decrease [24].

Although these longitudinal studies demonstrate a temporal relationship between increases in hand hygiene compliance and reductions in hospital acquired infection rates, few controlled, prospective studies have been performed until recently. Two multicentre cluster-randomized trials conducted in long-term care facilities in Hong Kong demonstrated the efficacy of multimodal interventions in both improving hand hygiene compliance, and reducing infection rates (respiratory outbreaks or infections requiring hospitalization) [25,26].

In comparison, a single-centre cluster-randomized trial (RCT) in Canada failed to demonstrate a reduction in hospital-acquired MRSA colonization in their hand hygiene intervention arm compared with the control arm [27]. However, this was not unexpected, as hand hygiene adherence improved in both the intervention arm (15.9–48.2%) and the control arm (15.9–42.6%) during the intervention. This ‘contamination’ of the control group demonstrates one of the challenges of implementing a randomized controlled study involving behaviour change within a single institution. To improve on the simple before-and-after study design, Kirkland et al.[28] performed an interrupted time-series study in which interventions were introduced sequentially at a rural hospital in New Hampshire to provide insights into the temporal associations between interventions, hand hygiene performance and clinical outcomes. Notably, they observed that although improvement in hand hygiene was temporally associated with a significant decline in healthcare-associated infections, there was an increase in (nonclonal) S. aureus infections attributable to the operating room (where improvements in routine hand hygiene would not be expected to impact).

Lee et al.[29▪▪] recently published an ambitious prospective, multicentre, interventional cohort study comparing interventions aimed at reducing rates of MRSA clinical isolates across 10 hospitals in Europe. Hospitals were assigned to enhanced hand hygiene (using the WHO multimodal hand hygiene promotion programme), screening for colonization with contact precautions and decolonization (if needed), or both. The individual interventions were not effective in reducing MRSA rates during the study period. However, the combination of hand hygiene promotion and target screening resulted in a reduction of MRSA isolates of 12% per month. Importantly, these hospitals had relatively low baseline rates of MRSA infection – thus, whether these findings can be generalized to other settings with high MRSA rates is less clear. Furthermore, the brief intervention period of only 12 months may have contributed to the failure of enhanced hygiene to reduce MRSA rates, as a number of studies have demonstrated a time lag between hand hygiene improvement and changes in infection rates [16,18,28].

WHAT IS THE OPTIMAL APPROACH TO IMPROVING HAND HYGIENE COMPLIANCE?:

Allegranzi et al.[5▪▪] recently reported a quasiexperimental study to assess the effect of the WHO multimodal hand hygiene promotion programme on hand hygiene compliance and healthcare worker knowledge at six sites in Costa Rica, Italy, Mali, Pakistan and Saudi Arabia. Implementation of the WHO strategy led to an improvement in hand hygiene compliance from 51% to 67.2%, with healthcare worker knowledge about hand hygiene and infection prevention also improving. After adjustment for key confounders, the intervention was significantly associated with improved hand hygiene compliance (adjusted odds ratio 2.15, 95% confidence interval 1.99–2.32). This study represents an important proof of concept for the WHO multimodal strategy, demonstrating that it can be successfully implemented in a diverse range of clinical and socio-economic settings.

Which components of the WHO multimodal strategy are the most important and how they should be combined for optimal impact remains uncertain. Schweizer et al.[30▪▪] addressed this issue in a recent meta-analysis of hand hygiene promotion interventions. Importantly, this meta-analysis differed from the earlier Cochrane review [31] by including quasiexperimental studies – a pragmatic decision that has particular importance in the field of infection control and quality improvement in which randomized controlled studies are particularly challenging, and often unfeasible. Thus, 46 studies (including six randomized controlled trials) were included [30▪▪]. This

analysis suggested that two bundled interventions were associated with an increase in hand hygiene compliance – namely, the WHO bundle comprising feedback, education, reminders, access to ABHR and administrative support [3], and a bundle that only included feedback, education and reminders (although, healthcare settings using the later approach almost certainly had preexisting access to ABHR). Pooled effect measures for these two interventions were calculated, further supporting the impact of the WHO multimodal strategy.
The Feedback Intervention Trial (FIT) [32] used a stepped wedge cluster randomized controlled trial design conducted across 16 trusts in the United Kingdom to evaluate the impact of feedback at group and individual levels. The intervention was designed using goal setting, control and operant learning theories. In the intention to treat analysis, hand hygiene compliance rose postrandomization (odds ratio 1.44; 95% CI 1.18, 1.76; $P < 0.001$) in the intensive therapy units, but not aged care wards.
The use of personality profiling techniques, similar to those routinely used in advertising to better determine and target the most effective hand hygiene education strategies for various healthcare workers, has undergone preliminary assessment in Australia [33] and will be used in a forthcoming multicentre trial to improve hand hygiene compliance.

ASSESSING THE ACCURACY OF VARIOUS APPROACHES TO HAND HYGIENE SURVEILLANCE:

Approaches to the monitoring of hand hygiene include direct observation, self-reporting, measurement of product consumption and use of various automated devices; each approach has strengths and weaknesses [34]. Although no method is ideal, direct monitoring is generally considered the gold standard, although limitations include resource intensity, observer bias and the potential of a Hawthorne effect [35,36]. In fact, multiple factors can affect results (Table 1), including the type of hand hygiene compliance audit tool used. Use of a standardized tool, such as the WHO 5 Moments tool, allows valid comparability between sites, although standardization of assessors and wards surveyed requires careful attention [37]. For example, approximately 80% of the current Hand Hygiene Australia (HHA) budget is required solely to maintain appropriate auditor (and therefore data) standardization to allow valid interhospital comparisons (Grayson ML, personal communication). Standardized hand hygiene auditing tools for nonacute settings, such as long-term care facilities, day surgical centres and psychiatry units, need to be defined and validated. When various surveillance methodologies have been directly compared [38–40], there has not always been a strong correlation. Table 2 summarizes the monitoring methods used in recent publications on hand hygiene programmes [41,42▪,43–45].
Measuring consumption of ABHR as a surrogate for hand hygiene behaviour has been used widely across Europe [46], including Germany [42▪] and Britain [18]. The benefits of this approach are objectivity, the availability of quantitative data and in some cases, an indication of daily use. However, this measure does not take into account variability in the amount of product used by an individual or differential use by family members and staff. More importantly, consumption data does not take into account the frequency of occasions when hand hygiene should have been performed, nor the appropriateness of ABHR usage. Similar limitations occur when using automated ABHR dispenser counters.
Automated wireless systems for monitoring hand hygiene behaviour are an emerging area of interest [47,48▪▪]. These systems generally involve the healthcare worker carrying an electronic identifying badge or tag, with sensors installed at various locations in the healthcare setting to record use of ABHR by individual healthcare workers. Several recent studies have evaluated these systems, reporting varying levels of accuracy [49–51]. Nevertheless, some systems provide an automated mechanism for performance feedback, which may assist individuals in improving compliance. Second, they may be useful in single rooms in which direct unobtrusive observation may be impractical. Unfortunately, current systems are unable to detect all WHO 5 Moments, and significant financial investment is generally required if an institution commits to one of these systems.

HAND HYGIENE PREPARATIONS AND THEIR COMPARABLE EFFICACY:

Current guidelines recommend the use of ABHR when hands are not visibly soiled, but recommendations vary in terms of the concentration of required alcohol (60–95%), the type of alcohol and the formulation (solution or rinse vs. gel vs. foam) [3,52]. The WHO has created simple formulations for ABHR solutions for use in settings in which commercial products may not be readily available [3].

Factors that can affect results include in-vitro vs. in-vivo testing methodology (e.g., European Norm 1500 vs. ASTM E1174 vs. glove juice techniques), the species and inoculum of pathogens tested, the volume of ABHR utilized and the time between ABHR application and assessment of pathogen kill. Overall, the optimum ABHR formulation has not been clearly established [53–58]. Edmonds et al.[55] evaluated 12 different ABHR formulations and did not find that alcohol content (within the WHO recommended range) influenced efficacy. Contrary to previous reports, gel or foam ABHR preparations were not shown to be inferior to solutions or rinses, although design flaws have subsequently been highlighted with this study [56]. A key issue with all these studies is that they utilize in-vivo models to extrapolate to clinical effectiveness, whereas multiple other factors, including healthcare worker product preference, ease or accuracy of various dispensers and hand hygiene compliance, are also critical factors in this equation. Gels and foams appeared to be equally acceptable to healthcare workers in one study [59], whereas solutions were preferred in others [13,14,16,17].
Novel approaches to hand hygiene, such as nonalcohol-based products [60], cold plasma systems [61] and photodynamic therapy [62], have recently been investigated, but there is insufficient efficacy or safety data to recommend their use.

ALCOHOL-BASED HAND RUB EFFICACY AGAINST SPECIFIC PATHOGENS:

A number of ABHR preparations have demonstrated virucidal and bactericidal activity [63,64]. The effectiveness of ABHR against norovirus remains controversial [65]. Although the WHO favours the use of ABHR during norovirus outbreaks [66], the Centre for Disease Control (CDC) continues to recommend handwashing with soap and water [67]. Paulmann et al.[68] recently demonstrated that two WHO ABHR solutions were effective against murine norovirus (a surrogate for human norovirus) both in vitro and in vivo, although the efficacy of other formulations remains unclear. Further research is required in this area. A variety of ABHR formulations appeared to have equivalent efficacy to soap and water handwashing in reducing hand contamination with H1N1 influenza [63]. A study from Taiwan [69▪] demonstrated poor activity of existing ABHR formulations against human enterovirus 71, a nonenveloped virus of public health significance in the Asia-Pacific region.
Despite these in-vivo studies, the clinical utility of ABHR for preventing respiratory virus infections in the community remains less certain. Turner et al.[70] conducted a randomized trial in young adult volunteers on the ability of ABHR to prevent rhinovirus infection or rhinovirus-associated illness. Despite the earlier promise in experimental models [71], they were not able to demonstrate a benefit. Wong et al.[72▪▪] performed a meta-analysis on the efficacy of hand hygiene interventions in preventing influenza virus transmission in the community. Although subgroup analysis from developed countries suggested that a combined intervention of hand hygiene with facemasks is a beneficial strategy, the efficacy of hand hygiene alone was not demonstrated.
It has previously been demonstrated that washing with soap and water is more effective than ABHR in removing C. difficile spores from the hands of healthcare workers [73]. Edmonds et al.[74] evaluated 10 different test products in their ability to remove C. difficile spores from the hands of test subjects. The only substances that were able to achieve significantly higher log10 reductions than tap water were not suitable for routine use in healthcare environments. This reinforces the current recommendation of handwashing with soap and water and contact precautions for care of patients with C. difficile.
One formulation of ABHR (70% isopropanol and 0.5% chlorhexidine) effectively reduced the density of vancomycin-resistant enterococci (VRE) contamination by approximately 104 in a detailed assessment of 20 healthcare workers who had their hands heavily contaminated (108 cfu/ml) with two strains of VRE [75].

CURRENT GUIDELINES ON ISOLATION AND RECENT EXPERIENCES:

Guidelines for isolation precautions were published by the Healthcare Infection Control Practices Advisory Committee (HICPAC) in 2007 [76]. Recently, guidelines on the control of multidrug-resistant Gram-negative infections have been published by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) [77▪▪], the CDC [78] and the Australian Commission on Safety and Quality in Healthcare [79]; all recommend isolation.
Recent experience with emerging pathogens has highlighted the importance of isolation precautions in preventing the spread of various infections during outbreaks. During the severe acute respiratory syndrome (SARS) outbreak in Hong Kong [80], overcrowding of medical wards, suboptimal air processing and inadequate isolation facilities were some of the key factors associated with transmission. Similarly, the description of nosocomial transmission of the Middle

East respiratory syndrome (MERS) coronavirus highlighted the importance of isolation precautions in the outbreak setting [81].
During the 2009 influenza A (H1N1) pandemic, Lee et al.[82] conducted a prospective, observational study to evaluate the impact of public health measures in the control of pandemic influenza among military personnel in Singapore. Healthcare workers and military units considered ‘essential’ were subject to additional public health measures, including enhanced surveillance, isolation via home medical leave and segregation. This intervention bundle was effective in decreasing H1N1 pandemic influenza infection with 17% in the ‘essential’ worker cohort developing serologically confirmed infection compared with 44% in the standard cohort.
Finally, the worldwide dissemination of carbapenem-resistant enterobacteriaceae (CRE) has provided some insights into effective infection control strategies. These strategies, usually instituted as bundles, include patient isolation, active surveillance, geographic cohorting, standards for detection and reporting, monitoring of adherence and environmental control initiatives. These bundles have proven to be successful in multiple settings worldwide [83▪,84▪,85,86], with early identification and isolation of asymptomatic carriers appearing to be a key component of successful interventions [85,87].

IS ISOLATION ALWAYS NEEDED OR EFFECTIVE? WHAT ARE THE LIMITATIONS?:
Recent progress into the molecular epidemiology of infections due to VRE and C. difficile has provided new insights into modes of pathogen acquisition and the limitations of patient isolation in preventing new infections.
Eyre et al.[88▪▪] performed whole genome sequencing of all C. difficile isolates from symptomatic patients over a 3-year period in Oxfordshire, in the United Kingdom. They found that 45% of the cases were due to transmission from either environmental reservoirs, or transmission from asymptomatic carriers, rather than previous symptomatic hospital cases. Asymptomatic carriage (and presumably shedding) is known to be relatively common [89,90]. These findings support a greater emphasis on improved antimicrobial stewardship to minimize emergence of clinical disease, in addition to prevention of cross-transmission [88▪▪].
The epidemiology of VRE transmission may not be dissimilar. Using large-scale comparative genomics, Howden et al.[91▪] demonstrated that the epidemiology of hospital vanB VRE was more complex than previously thought. They and others [92,93] have proposed a model in which silent circulation of closely related vancomycin-susceptible Enterococcus faecium isolates acquires the vanB operon via lateral gene transfer from anaerobic bacteria in the gastrointestinal tract. Hence, hospital-acquired vanB VRE may also be driven by de-novo generation rather than solely nosocomial transmission via direct contact. This is in keeping with previous work by Johnson et al.[94], in which it was observed within an institution that each time a new vancomycin-resistant E. faecium (VREfm) sequence type appeared, it was observed first as vancomycin-sensitive E. faecium (VSEfm). This may explain why the incidence of VRE has continued to rise in many countries despite strict patient isolation, effective infection control measures and significant reduction rates of nonenteric pathogens, such as MRSA [94,95].

NEGATIVE EFFECTS OF ISOLATION:
The potential adverse outcomes of contact precautions have been recently reviewed [96]. In addition, a single-centre retrospective cohort study by Karki et al.[97] compared the incidence rate of documented adverse events in patients before and after initiation of contact precautions for VRE. They found that the overall rate of adverse events was not significantly different, but that there was an increase in medication administration errors and nonpressure-related injuries. The same group also observed that the waiting time for patients to obtain a CT scan, whereas under contact precautions for VRE colonization, was 46% longer than those who were not isolated [98].
In a prospective cohort study by Mehrotra et al.[99], patients who were managed under contact precautions perceived problems with care twice as frequently as those not under precautions. Although this difference may be attributable to bias, it appears that patient perception of care is negatively impacted by isolation.
Dhar et al.[100▪▪] conducted a multicentre, prospective cohort study that evaluated whether the proportion of patients in isolation is a determinant of compliance with contact isolation precautions. They observed a stepwise increase in noncompliance as the overall proportion of patients in isolation in a unit increased, with an apparent ‘tipping point’ when 40% of patients was reached. They hypothesized that at this point ‘compliance fatigue’ became more common, particularly for hand hygiene prior to gloving.

The evidence to support isolation in the intensive care unit is limited. In a 2011 cluster randomized controlled trial involving 10 intensive care units [101], surveillance for MRSA and VRE and expanded barrier precautions for colonized patients was not effective in reducing transmission rates. In a recent post-hoc analysis of a large cohort encompassing three intensive care units, a number of medical errors and adverse events were observed more frequently in the patients under contact isolation [102▪]. This occurred despite the higher staffing ratios in the ICU compared with other wards. Despite these issues, isolation in ICU is still recommended.

CONCLUSION:

Hand hygiene and isolation remain key components of the infection control ‘toolkit’ to reduce cross-transmission of key viral and multiresistant bacterial pathogens. Future research should focus on the optimal methods for implementation and monitoring of these strategies as well as ways to mitigate any potential negative effects.

Conflicts of interest ::: Acknowledgements:
None declared.

REFERENCES AND RECOMMENDED READING:

Papers of particular interest, published within the annual period of review, have been highlighted as:▪ of special interest▪▪ of outstanding interest