



## Hand-sanitizer Usage During COVID-19 Outbreak: A Case of 'Better Safe than Sorry' or 'excess of Anything is Bad'?

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### Abstract

In 2019, the world saw the emergence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic which is claiming lives globally on a large scale. Different medical advisories were issued to slow down the transmission of the virus including the recommendation of using alcohol-based hand-sanitizers. Approximately a century ago, we saw the advent of antibiotics and anti-microbials which were termed as 'magic bullets'. These were elevated to the pedestal as an answer to majority of human infections which had plagued our society for centuries. This was followed by years of mass production and usage of antibiotics. Selection pressure created by excessive antibiotic usage stroked the selection 'itch' amongst susceptible microbial species and carved out a phenomenon known as 'antibiotic resistance'. If history has a habit of repeating itself, then excessive use of hand-sanitizers these days has the potential to become a major health problem in the near future. Through this review, we aim to remind the medical community and our society that the use of hand-sanitizers must be judicious and should not replace the common practices of traditional hand hygiene, safe distancing and wearing a mask. We also attempt to highlight other potential side effects associated with excessive use of hand-sanitizers.

**Keywords:** Antimicrobial Resistance; Covid-19; Hand-sanitizer; Normal Microflora; Side Effects

### Introduction

Hand hygiene, a routine practice today, was unheard of just two centuries ago. In the mid-1800s, a Hungarian doctor Ignaz Semmelweis, now known as the father of hand hygiene, was the first person to identify and reform the spread of fatal infections via contaminated hands in a hospital in Vienna [1]. He introduced the practice of hand washing with chlorinated lime solution to prevent transmission of infections by doctors from autopsy tables to maternity wards [1]. During the same time, Oliver Wendell Holmes

in the USA also established a link between hospital acquired infections and poor hand hygiene. However, despite achieving a low mortality rate and curtailing the spread of infections, this procedure was shunned even by the medical fraternity of those times [2]. A renewed interest in this area developed in the 1980s when the first ever hand hygiene guidelines were published and have since been followed by many amendments and awareness campaigns by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC, USA). In the last few decades, the

importance of hand hygiene has been highlighted and significant progress has been achieved in this regard [2].

On March 11, 2020, the WHO declared that the infection caused by SARS-CoV-2 had reached a pandemic scale with more than 5.85 million individuals infected and more than 359,000 deaths globally [3]. SARS-CoV-2 spreads from person-to-person through close contact and through aerosols from respiratory droplets [4]. This has brought upon emergency lockdowns globally and its effects on health, wellbeing, business, and other aspects of daily life are felt throughout the society. There has been a direct detrimental impact to the global economy, raising concerns about the financial sustainability with effects predicted to continue as the virus fails to be contained [5,6]. Without effective pharmacological intervention or vaccine in sight for the near future, the priority is to reduce the rate of infection and prevention of infection seems to be the best approach [7]. The basic measures adopted worldwide include maintenance of hand hygiene, avoiding close contact, using face masks, disinfection and monitoring health [8].

The ongoing COVID-19 pandemic has once again brought the benefits of appropriate hand hygiene (hand washing and use of alcohol-based hand-sanitizers) to the centerstage. Since hand washing is not a feasible and available option at all times, the use of alcohol-based hand-sanitizers (hand rubs) has been recommended by health organizations, when hands are not visibly soiled. These sanitizers act as a powerful, fast acting and effective solution with broad antimicrobial range [8]. Their efficacy against pathogens is well documented [8], however, on the flip side, the usage of these agents in excess has the potential to cause after-effects, the information of which remains veiled from the general public. This write-up is therefore an attempt by the authors to play devil's advocate and provoke a debate in the medical community, forcing us to re-think whether usage of hand-sanitizers is a boon or bane.

### Hand hygiene

Hands act as a medium for exchange of microbes between the organism and its environment. The skin of the hands harbors a variety of organisms ranging from commensals to potential pathogens. Therefore, adequate hand hygiene can greatly reduce disease transmission. Hand hygiene comprises various processes such as hand washing, cleansing or disinfection. While hand washing is done with soap and water and aims at mechanical removal of

dirt and microorganisms, hand disinfection reduces or inhibits the growth of microbes with the use of an antiseptic solution [2]. The most commonly used agents for hand disinfection are hand-sanitizers. There are two major types of preparations available: alcohol-based and alcohol-free. The alcohol-based ones, known as alcohol-based hand rubs (ABHRs), typically have ethyl alcohol (ethanol), isopropanol, or n-propanol at concentrations between 60 to 95% alcohol [9]. The alcohol-free preparations usually contain quaternary ammonium compounds (benzalkonium chloride or benzethonium chloride). However, these have been found to be less effective and have a risk of contributing to antimicrobial resistance (AMR), hence are not recommended by CDC [10].

Even the ABHRs are not 100% effective and to achieve the best results, certain criteria need to be met. The appropriate amount of product has to be spread on the surface of a clean hand, coating it and then allowed to air dry for at least 20-30s, while rubbing properly all over including the interdigital space. Any laxity, either in the product formulation, application dose, application procedure or the contact time can significantly decrease its efficiency. Alcohol concentrations >80% can work with contact times as low as 10s but for complete efficacy, the product has to spread all over the hand surface. Also, the anti-microbial effect is compromised against some microorganisms when the hands are even slightly greasy or soiled [10]. Also, presence of microdroplets of mucus as a result of coughing may offer protection to the encased microorganisms against the product [11].

### COVID-19 outbreak and usage of hand-sanitizers

The CDC has recommended the use of ABHRs and hand washing to fight the COVID-19 pandemic. This is due to the structural characteristics of coronaviruses, which are enveloped viruses with lipid bilayer and are easily inactivated by alcohol. The guidelines suggest the use of ABHRs over hand washing where the hands appear clean to ensure greater compliance [10]. Following this, the sales of hand-sanitizers have skyrocketed along with its usage. A market research conducted by Nielsen has reported an expected spike in the global sale of hand sanitizers by 300% and 470% in the last week of February and first week of March 2020, respectively, *vis a vis* the previous year [12,13]. Most of this usage is paranoia driven and can be categorized as overuse or abuse. With most of the supermarket shelves going empty as a result of panic buying, the USFDA has allowed mass production of hand-sanitizers by vari-

ous distilleries and local companies while asking them to adhere to specific guidelines [9]. But not all of these preparations have been meeting the expected/required quality standards. Recently, the USFDA has issued a warning about the presence of varying concentrations of methanol in products labeled to contain ethanol only, and certain brands have been taken off the shelves with this list ever growing. Deceptive marketing during this time of chaos means the general public is inadvertently using these substandard products with lower alcohol content, or with non-alcoholic formulations which have a narrow spectrum and are ineffective against SARS-CoV-2 [12]. The side-effects resulting from using these substandard products are being discussed in the following section.

#### Potential consequences of excessive hand-sanitizer usage

A combination of factors such as inappropriate formulations, excessive/repeated usage of hand-sanitizers during this pandemic will have far reaching consequences. These may range from emergence of alcohol tolerance and antimicrobial resistance (AMR), disturbance of normal microflora, and product toxicity.

A few years ago, the scientific community was amazed at the discovery of fungal species feeding on the radiation at abandoned Chernobyl nuclear reactor. This fungal species was reported to manifest melanin pigment proposed to be involved in utilizing radiations as an energy source [14]. It is a perfect example of nature outdoing itself when presented with a challenge. This discovery is pertinent to the present scenario as nuclear radiation similar to alcohol was once considered the most hostile environment with no species capable of surviving it. As pointed above, there is a tremendous surge in the sale and usage of ABHRs to curb COVID-19 transmission [12]. Widespread usage of alcohol-based hand-sanitizers is, without a doubt, a fast track method of converting our hands into an abattoir for SARS-CoV-2 and other microbes. What could be the consequence of this overuse? Similar to antibiotics, excessive or repetitive application of alcohol through hand-sanitizers has the potential to act as a selection pressure for the emergence of new microbial species tolerant to high alcohol concentrations [18]. A recent publication by Pidot, *et al.* reported emergence of alcohol tolerance amongst hospital isolates of *Enterococcus faecium* in Australia [16]. This group of bacteria are opportunistic pathogens capable of causing severe urinary tract infection, endocarditis and bacteremia [17]. These *E. faecium* strains were not only resistant to 70% isopropanol but also had increased capability to colonize

the murine intestinal tract [16]. Emergence of strains resistant to alcohol is already a concern in the medical community given its implications in hospital settings. Another example is *Acinetobacter baumannii*, an opportunistic pathogen and causal agent of ventilator-associated pneumonia, bacteremia and sepsis in immunosuppressed patients. Supplementation of minimal media with 1% of commercially available ABHRs resulted in enhanced bacterial growth and triggered the secretion of outer membrane protein (Omp)-A. OmpA is important for bacterial growth due to its ability to scavenge carbon from complex hydrocarbons [18,19]. One might argue that the concentration of alcohol used by the group was way less than present in conventional hand-sanitizers. However, one should not forget that microbes have short-term response elements enabling their survival under environmental stress [20]. These short-term responses often form the basis for long-term adaptations aiding in survival and multiplication in otherwise inhospitable conditions. Nevertheless, the above examples demonstrate the potential of alcohol to confer enhanced pathogenicity to microbes.

Taking note of the repetitive use of ABHRs, Professor Tim Stinear from the Peter Doherty Institute for Infection and Immunity remarked "anywhere we repeat a procedure over and over again, whether it's in a hospital or at home or anywhere else, you're giving bacteria an opportunity to adapt, because that's what they do, they mutate. The ones that survive the new environment better then go on to thrive." He further added that the risk increases when appropriate guidelines are not followed [21]. Thus, while ABHRs in the short run might be working effectively to combat SARS-CoV-2 virus, these might be driving the other microflora on the skin into an unprecedented stress which could trigger their survival instincts in the long run. Is it a far-fetched notion to assume that alcohol tolerance could fuel another cycle of AMR? Considering the hospital setting where the burden of controlling microbial spread relies on alcohol-based disinfection, this might not seem impossible. Any breach in the protection offered by alcohol-based disinfectants may lead to increased spread of pathogens with subsequent surge in prescription and usage of antibiotics. The very weapon on which the medical community relies today to combat AMR spread might become an unintentional driving force for it.

ABHRs also hold the potential to tilt the host-microbe balance in favor of the pathogens. The skin in general, is a niche for a large

variety of microorganisms. The permanent microflora lives as commensals with their presence dictated by the skin pH and secretions of the sebaceous glands [22]. The transient microflora whose presence is determined by the surfaces touched or places visited, include mainly pathogenic species such as *Escherichia coli* or methicillin-resistant *Staphylococcus aureus*; particularly within high risk environments, such as healthcare and food-handling settings [23]. The commensals compete with the pathogens for same ecological niche and metabolites thus, creating a hostile environment which prevents pathogen colonization [24,25]. Besides, the production of antimicrobial peptides directly inhibits pathogen growth as exemplified by the skin commensal *Staphylococcus epidermidis* which limits biofilm formation by *S. aureus* [26,27]. Therefore, eliminating the normal microflora of the skin by repeated use of hand-sanitizers may eventually deprive the skin of the protection offered by these commensals.

Besides hand-sanitizers, stress is being laid on conventional hand hygiene which includes proper washing of hands with soap. However, the human mind tends to gravitate towards things which are easy to use and marketed as effective. Seldom do we remember to pay close attention to the potential side effects. A recent article by Shetty, *et al.* highlighted a lesser known health hazard associated with ABHR usage. Given its dehydrating capacity, alcohol has the tendency to cause desiccation stress and dryness of ocular surface, known as dry eye disease [28,29]. An ophthalmology unit in India reported high number of red-eye cases with chemosis associated with chemical components of hand-sanitizers during mandatory home stay to curb COVID-19 transmission [30]. With no check on the composition of hand-sanitizers during this desperate time, it is highly possible that some of these brands contain mixtures of alcohols with some substandard components. Repeated exposure to the irritants and components of soaps or solvents occasionally end up removing essential skin lipids and induce alterations in keratinocytes [31,32]. The denaturation of stratum corneum proteins and decreased corneocyte cohesion is long known to be caused by hand hygiene products [33]. This occurrence of skin pathology is also evident through a recent survey done in China to assess the prevalence and risk factors of skin reaction of medical workers during COVID-19 pandemic. Long term use of personal protective equipment along with frequent hand hygiene was responsible for high rate of skin damage in 97% of respondents while frequent hand hygiene was attributed with increased risk of hand skin damage [33].

Then there is another category of side effect linked with usage of substandard sanitizers. Currently, the market is flooded with products containing various concentrations of methanol. This is a dangerous situation; exposure to methanol is known to cause toxic effects as it is readily absorbed by the skin and can cause methanol poisoning [11]. Methanol poisoning leads to nausea, blurred vision, permanent blindness, damage to the nervous system and death [11]. Besides methanol, even isopropanol is toxic towards certain age groups. The American Academy of Pediatrics has warned against the potential toxicity of ABHRs containing isopropanol on children, if accidentally ingested [34]. Guidelines have been issued to add bitter tasting compounds to discourage accidental ingestion. Still, there is a need for vigorous awareness campaigns to educate the public about potential consequences of their use. Parents need to be vigilant about reading labels before applying such products on children. Caution needs to be exercised while giving complete control of these preparations to children, such as putting travel packs and pocket-sized bottles in their backpacks. Health organizations need to present a complete picture to the general public about the appropriate usage of hand-sanitizers as well as the potential side effects of non-compliance.

In a nutshell, we feel that the effects of incomplete information reaching the masses might outweigh the expected benefits of hand sanitization. Both, improper usage and overuse of hand-sanitizers can have detrimental effects at different levels. Sole reliance on hand-sanitizers with laxity in hand washing will not only reduce its efficacy but would also end up creating an environment suitable for emergence of tolerant microbes. Besides, overuse of hand-sanitizers could create a breach in the skin barrier as well as disturb the normal microflora, thereby, creating a niche apt for potential pathogens.

## Conclusion

The aim of this review is not to oppose the recommendation of the scientific community regarding the use of hand-sanitizers during this pandemic. Hand hygiene was and should always be the priority of every individual in order to remain safe and healthy. However, being part of the scientific community, we feel that it is also our responsibility to make everyone aware of the difference between appropriate usage and abuse. It was the same rampant usage of antibiotics which has brought mankind to a position where we are running out of options. Pressure created by excessive an-

tibiotic usage catapulted many of the lesser known microbes to research hot topics. Restraint shown while empirically prescribing the antibiotics along with public awareness regarding potential side effects of antibiotic abuse could have slowed down the evolution of AMR. Short-term solutions when not properly regulated have the capacity to become long-term problems. In addition to recommending hand-sanitizers to the public, the medical community should also create awareness that this is not a one-stop shop and should not replace conventional hand washing and hygiene. By-passing hand washing for hand-sanitizers should not become a 'new normal'. Unintentional creation of new environments for species capable of surviving harsh conditions will only drive a new cycle of virulence and pathogenesis. It is the responsibility of the Government to collaborate with the medical fraternity to open effective communication channels and ensure judicious use of hand-sanitizers. Elimination of life with overuse of hand-sanitizers is in our hands but what kind of life will then replace it is literally "not in our hands".

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### Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

### Authors' Contributions

All authors contributed equally in planning and drafting the manuscript. All authors approve the final version.

### Ethics Approval

Not applicable.

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