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# SARS-CoV-2 Disinfection and Potential Overuse Adverse Health Effects

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# INTRODUCTION

The use of surface disinfection products boomed during the COVID-19 pandemic. These products continue to flourish as a mechanism to reduce the transmission of the severe acute respiratory syndrome coronavirus (SARS-CoV-2 that causes COVID-19) in health care settings, workplaces, school environments, businesses, and other public places and transport vehicles.

This white paper provides an overview of the current science regarding SARS-CoV-2 on surfaces, recommended disinfection products, and potential health concerns stemming from overuse of chemical disinfection products. The following information may be of particular interest to individuals, supervisors, and health scientists tasked with establishing adequate facility cleaning protocols.

# SARS-CoV-2 SURFACE-RELATED TRANSMISSION

In May 2021, the United States Centers for Disease Control (CDC) indicated studies to date reflected infectious exposure to SARS-CoV-2 occurs via mechanisms that facilitate exposure to respiratory fluids carrying infectious virus, including:

- Inhalation of infectious virus on very small droplets and aerosol particles
- Deposition of infectious virus onto exposed mucous membranes of the mouth, nose, or eyes (e.g., "splashes and sprays," which can occur when someone is coughed/sneezed on)
- Transfer from hands containing virus to mucous membranes (nose, mouth, or eyes), either through direct deposition on hands (see above) or through touching virus-contaminated surfaces (e.g., "fomite" transmission, where fomite is the term for inanimate object viral transmission)

The dose of SARS-CoV-2 (i.e., amount of infectious virus) needed to cause infection has not been established, which complicates scientific investigations regarding transmission mechanism(s) responsible for observed infections. Animal and epidemiologic studies indicate virus inhalation can cause infection, but these same studies cannot quantitate or differentiate the relative contributions between virus inhalation and deposition onto exposed membranes. A recent CDC brief indicated potential surface transmission of infectious virus is thought to be generally mitigated through adequate hand hygiene and environmental cleaning / disinfection protocols (CDC, 2021), which may explain the lack of scientific support for surface contact mediated transmission in humans (although circumstantial reports have suggested it may occur, the same reports cannot exclude the potential for respiratory transmission and inhalation and/or mucous membrane deposition mediated disease) (Meyerowitz et al., 2021).

# SARS-CoV-2 ON SURFACES

The length of time SARS-CoV-2 can survive on a variety of surfaces has been reported using controlled, scientific experiments. The protocol involves depositing known, high levels of viral loads onto different surfaces (such as aluminum, slick and matte plastics, glass, paper, cardboard, and others) and allowing the virus to age. After known time periods, each material was fully submerged in solution so that any remaining viral load was resuspended and recovered (Chin et al., 2020; Liu et al., 2021; van Doremalen et al., 2020). Although some studies detected intact virus up to 7 days following inoculation on some surfaces, other investigators did not replicate survival times for similar surfaces. At best, these experiments indicate that detectable viral load of SARS-CoV-2 may exist on or in materials for several hours to days following inoculation, provided the material was inoculated with sufficient viral load and any residual viral load was collected through extraction of the submerged material. Using these results to extrapolate to everyday conditions is tenuous because (1) the investigators were unable to replicate findings on the same types of surfaces; (2) it is unclear whether viral survival based on complete immersion and resuspension accurately reflects the potential for the surface-to-surface viral load transfer of real-world conditions; and (3) it is unclear whether survival based on high viral loading will apply to viral loads shed by infected persons.

Finally, the contribution of SARS-CoV-2 surface transmission to human disease is complicated due to the increased hygiene and cleaning that accompanied the pandemic. Recent CDC guidance reflects the complexity and circularity of this issue, stating both that "current evidence strongly suggests transmission from contaminated surfaces does not contribute substantially to new infections," and that "transmission through soiled hands and surfaces can be prevented by practicing good hand hygiene and by environmental cleaning" (CDC, 2021).

## DIFFERENCES BETWEEN CLEANING, DISINFECTION, AND STERILIZATION

The terms cleaning, disinfection, and sterilization describe different but related processes integral in reducing disease transmission.

- **Cleaning** uses detergents/soaps and/or enzymatic products with manual and/or mechanical scrubbing action to remove soil from objects and surfaces. Cleaning is regarded as an essential first step in reducing disease transmission because residual surface soil can interfere with the effectiveness of subsequent disinfection or sterilization processes.

- **Disinfection** uses chemicals to kill/inactivate/eliminate most pathogenic microbes but not necessarily all types (e.g., not bacterial endospores) present on inanimate objects and surfaces.

- **Sterilization** is the most extreme process as it uses chemical and physical agents to eliminate/inactivate/destroy all forms of microbial life (i.e., steam under pressure, dry heat, UV-light, ethylene oxide gas, hydrogen peroxide).

Due to the complexities/limitations associated with sterilization methods, disinfection is more commonly used in healthcare, home (especially kitchens and bathrooms), and outdoor venues (Rai et al., 2020). The global effort to reduce the transmission of SARS-CoV-2 led to unprecedented use of disinfectants in residential settings, essential worker situations (e.g., food production facilities, grocery stores, home improvement stores, and other consumer good factories), and additional scenarios (e.g., restaurants, offices, and indoor arenas) as the nation fully reopens following the pandemic shutdown.

## DISINFECTION INGREDIENTS/PRODUCTS

Governmental agencies in the United States and in many other countries have published guidance documents and/or official lists of recommended disinfecting products with possible or proven viricidal efficacy. Bactericidal and viricidal ingredients include alcohols, quaternary ammonium salts (quats), phenolic compounds, diols, and biguanides which differ substantially in structure, properties, potential human health effects, and environmental behavior. Commercial products based on these chemicals are considered unique and, based on intended use characteristics, must be registered with the US Environmental Protection Agency (US EPA) and/or cleared for use by the United States Food and Drug Administration (FDA). In general, the US EPA reviews and registers the antimicrobial pesticides for use as disinfectants and FDA regulates hand sanitizers.

Disinfecting chemicals are components in a variety of products, including:

- Rinse-off liquid hand soaps,
- Rinse-free hand sanitizers, and
- Pre-saturated wipes or sprays intended for disinfection of impervious surfaces of furniture or high-touch objects (e.g., such as tables, countertops, desks, sinks, toys, and keyboards) in homes or offices

Contact time, usually outlined in directions, is important to understand and fulfill as it defines the amount of time required for a disinfectant to destroy specific pathogenic microbes. Contact times vary based on active ingredients, ingredient concentrations, and target pathogens.

Susceptibility of individual viruses varies based on size, physical properties, and general resistance to inactivation. The easiest to inactivate (i.e., degrade/change to render non-infectious) are enveloped viruses (such as coronaviruses), then large (50 to 100 nanometers, nm) non-enveloped viruses (such as adenovirus and rotavirus); and, finally, small (<50 nm) non-enveloped viruses (such as rhinovirus). SARS-CoV-2 is an enveloped virus, so it is in the class of viruses easiest to inactivate with disinfectants. Cleaning methods also play a role, as detergents/soaps and/or enzymatic products inactivate enveloped viruses such as SARS-CoV-2 through disruption of the virus's lipid membrane envelope.

## DISINFECTANTS FOR SARS-CoV-2

The US EPA maintains a list of disinfectant products registered for efficacy and use against SARS-CoV-2 (referred to as List N) on porous and nonporous surfaces, food contact surfaces and porous laundry surfaces. As of June 2, 2021, there were 554 disinfectants registered for use against SARS-COV-2 associated with contact times that ranged between 0.1 to 30 minutes (US EPA, 2021).

The majority of disinfectant products contain a quaternary ammonium compound as the active ingredient while others may contain single ingredients (or mixtures) of ingredients such as hydrogen peroxide, peroxyacetic acid, isopropanol, ethanol, sodium hypochlorite, octanoic acid, phenolic, triethylene glycol, L-lactic acid, and/or glycolic acid. In most instances, a product is intended for a specific purpose and is to be used in a certain manner. Therefore, the label and use directions should be read carefully to ensure that the right product is selected for the intended use and applied in an appropriate manner.

CDC has indicated when no individuals with confirmed or suspected COVID-19 are known to have been in a space, cleaning once a day sufficiently removes virus that may be on surfaces.

## POSSIBLE HEALTH EFFECTS FROM OVERUSE OF DISINFECTANTS

The pandemic and the associated charge to reduce SARS-CoV-2 transmission has led to unprecedented use of disinfectants. Disinfection products approved for use against SARS-CoV-2 by the US EPA are intended for use on surfaces, not humans. Concerned parties may wonder regarding the human safety for disinfectants, whose sole purpose is the destruction of all encountered microbial pathogens. Acceptable use scenarios, described on the label and in the directions for use, are based on correct handling, use, and storage of disinfectants. Potential adverse health outcomes may occur when humans' exposure occurs at concentrations and durations that exceed those reasonably anticipated with maximum acceptable use characteristics (e.g., when disinfection products are mishandled, used improperly, and/or used in quantities/concentrations beyond anticipated and recommended use characteristics).

A full review of disinfectant toxicology is beyond the scope of this paper. Instead, the following are examples of potential common toxicities that may arise following exaggerated use of common disinfection agents. In general, key factors for assessing potential health risk include the amount of disinfectant involved (concentration and duration of exposure) and the route of exposure (skin, mucous membranes, inhalation). Readers are encouraged to contact the authors directly regarding questions related to specific use scenarios, use of different disinfection products, and/or other adverse effects potentially associated with acute and/or chronic (long-term) use.

- Alcohols used for disinfection include ethanol (the alcohol found in alcoholic beverages) and isopropyl alcohol in concentrations ranging from 60% to 90% in water. Alcohols are dehydrating agents (Rutala et al., 2019). Potential adverse effects associated with overuse include absorption of ethanol (especially in small children using disinfection products over large portions of their bodies). Some toxicities may result from product adulteration with methanol.

- Quaternary ammonium compounds (quats) represent the largest category of the US EPA's approved SARS-CoV-2 disinfectants (List N) and consist of a variety of compounds that all share an organically substituted ammonium compound. In a solution, they can ionize to produce cations. Specific modes of antimicrobial actions vary between chemicals and include denaturing of proteins and disruption of cell membranes. Potential toxicity of benzalkonium chlorides, a class of quaternary ammonium compounds, include irritation to dermal, ocular, and mucosal membranes (Choi et al., 2018; Rutala et al., 2019).

- Sodium hypochlorite, which is also known as "bleach" when diluted to low (e.g., 5 to 8 percent) concentrations in water, is a commonly used surface disinfectant. It has a broad spectrum of antimicrobial activity and acts through oxidizing and denaturing proteins. Potential toxicity includes irritation of skin, eyes and respiratory tract that can progress to more severe effects with increasing concentrations and durations (Benzoni and Hatcher, 2021; Rutala et al., 2019).

Other disinfectants used primarily in healthcare/industrial settings include perioxyacetic acid (peracetic acid), formaldehyde, glutaraldehyde, and phenolic compounds. Because many of the disinfectants are not wiped off following use, disinfectants' physicochemical properties will determine whether they may remain active on the disinfected hard surfaces or objects for long periods of time, either as surface residues or bound to settled dust. For example, quaternary ammonium salts are permanently charged and are involatile, whereas phenolic compounds are generally volatile and more hydrophilic, so they may not remain on hard surfaces for as long as involatile substances. Bleach solutions oxidize relatively quickly and lose efficacy while alcohols generally evaporate and are diluted into the airborne environment.

Mixing of different cleaning products is potentially hazardous because it may, depending on the chemicals, generate hazardous gases. For example, the mixing of bleach with ammonia-based cleaners can produce gaseous chloramines, which decompose to hypochlorous acid and free ammonia gas and cause acute lung injury (Pascuzzi and Storrow, 1998).

## WORKPLACE EXPOSURE LIMITS FOR DISINFECTANTS

Risk of adverse health effects in occupational environments are mitigated by occupational health professionals through controlling exposure concentrations below occupational exposure limits (OELs), which represent the acceptable concentration a worker can be exposed, 40 hours/week over a working lifetime without an appreciable risk of adverse effects.

There are few OELs associated with disinfection products and/or active ingredients, which hinders the ability of health professionals to assess potential worker risk in different use scenarios and environments. Given the use of disinfectants in workplace environments has increased with efforts to reduce the transmission of SARS-CoV-2, OELs associated with products and/or active ingredients have become appropriate/vital to ensure appropriate health and safety conditions of workers. To address the emergent need for OELs, a weight-of-evidence framework was recently developed specifically to derive OELs for disinfection products (Dotson et al., 2020). Alternatively, OELs can be derived using traditional occupational toxicology methodology, which generally relies on available toxicity studies or information regarding chemically similar compounds expected to act through similar mechanisms of action (e.g., read-across methodology).

Facilities implementing large-scale disinfection protocols should consider ensuring occupational exposures do not exceed OELs, which may involve OEL derivation. Readers are encouraged to contact the authors for more information or specific questions regarding establishing and/or interpreting OELs for disinfectant products or active ingredients.

## CONCLUSION

The issue regarding whether surface transmission of SARS-CoV-2 has led (or can lead) to human COVID 19 infection is complicated, because while infectious virus may remain on surfaces, human behavior (increased hand washing and use of disinfectants) likely has prevented (and will prevent) subsequent transmission. This paradigm has led to increased use of disinfection products among all aspects of society, in both commercial and residential scenarios. Numerous options exist for effective disinfection products/active ingredients against SARS-CoV-2. Selection of disinfection products should be based on the intended location (i.e., residential, commercial, school, restaurant) and applied in an appropriate manner consistent with the label and use directions, which are established to avoid adverse health effects.

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