Combating SARS-CoV-2: Leveraging microbicidal experiences with other emerging/re-emerging viruses (#49456)

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Combating SARS-CoV-2: Leveraging microbicidal experiences with other emerging/re-emerging viruses

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ABSTRACT

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan City, China, late in December 2019 is another example of an emerging zoonotic virus that threatens public health and international travel and commerce. When such a virus emerges, there is often insufficient specific information available on mechanisms of virus dissemination from animal-to-human or from person-to-person, on the level or route of infection transmissibility or of viral release in body secretions/excretions, and on the survival of virus in aerosols or on surfaces. The effectiveness of available virucidal agents and hygiene practices as interventions for disrupting the spread of infection and the associated diseases may not be clear for the emergent virus. In the present review, we recommend approaches for infection prevention and control for SARS-CoV-2 and future emerging/re-emerging viruses which can be invoked based on pre-existing data on microbicidal and hygiene effectiveness for related and unrelated enveloped viruses.

Keywords 2019-nCoV, Coronavirus, Ebola virus, Enterovirus D68, Hantaan virus; Lassa virus, Microbicides, MERS-CoV, Nipah virus, SARS-CoV, SARS-CoV-2, SFTSV, targeted hygiene

INTRODUCTION

Late in December 2019, cases of pneumonia began appearing in Wuhan City, Hubei Province, China. By early January 2020, these cases were attributed to a novel coronavirus that was temporarily referred to as 2019 Novel Coronavirus (2019-nCoV) (*WHO, 2020a*). This member of the *Coronaviridae* family has now officially been named SARS-CoV-2 (*Gorbalenya et al., 2020*). As of May 27, 2020 (*WHO, 2020c*), there have been over 5,593,631 confirmed cases globally, with 353,334 deaths (mortality rate of ~6.3%). This emerging virus, and the associated disease (COVID-19), are not only impacting public health, but also international commerce and travel. As with the Middle East Respiratory Syndrome coronavirus (MERS-CoV) that emerged in Saudi Arabia in 2012 and the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) that emerged in China in early 2003, SARS-CoV-2 is considered a zoonosis, with bats suspected as the primary host species (Table 1) (*Zhu et al., 2020*).

The *Coronaviridae* family is just one of several families of enveloped viruses that have emerged/re-emerged in recent years (Table 1) (*Zhan et al., 2017; Ang et al., 2018; Brocato and Hooper, 2019; Laenen et al., 2019; Viral Hemorrhagic Fever Consortium, 2019*). While the list of viruses in Table 1 is not intended to be comprehensive, it contains most of the virus families attributed to the World Health Organization (WHO) current list of disease priorities needing urgent R&D attention (*WHO, 2015*) (i.e., MERS and SARS [*Coronaviridae*], Crimean Congo hemorrhagic fever (*Nairoviridae*), Rift Valley fever [*Phenuiviridae*], Ebola virus disease and Marburg virus disease [*Filoviridae*], Nipah and Hendra virus disease [*Paramyxoviridae*], and Lassa fever [*Arenaviridae*]).

To our knowledge, no one has systematically compared the characteristics of the viruses causing the diseases in the WHO current list of disease priorities needing urgent R&D attention (*WHO, 2015*). There may be common characteristics that may favor sustained transmissibility or mortality, and could inform infection prevention and control (IPAC) activities. This review is intended to aid the IPAC community in arriving at strategies for dealing with SARS-CoV-2 as

well as future emerging/re-emerging viruses. In particular, it is our hope that this information may be leveraged to effectively mitigate the health risks associated with SARS-CoV-2 and its associated disease (COVID-19), as well as with future emerging/re-emerging enveloped viruses.

The emerging/re-emerging viruses shown in Table 1, with the exception of enterovirus D68, each are relatively large, enveloped, zoonotic viruses with single-stranded RNA genomes. Enterovirus D68 (EV-D68), a small non-enveloped virus of the *Picornaviridae* family, is an example of a re-emerging virus from that family. While EV-D68, may also be zoonotic (*Bailey et al., 2018; Fieldhouse et al., 2018*), a reservoir species has yet to be identified for that virus.

Aside from the characteristics described in Table 1, what other commonalities exist for these emerging/re-emerging zoonotic viruses? Can we use these commonalities as the basis for proposing approaches for IPAC? In the remainder of this review, we examine various aspects of the emerging/re-emerging viruses that are important in formulating approaches for IPAC, namely transmissibility, infectivity, viral shedding, environmental survival, and expectations regarding microbicidal efficacy for targeted hygiene practices.

SURVEY METHODOLOGY

The review is based upon the WHO list of diseases of concern (*WHO, 2015*) and our search of the literature pertaining to the various virus characteristics considered in Tables 1-3.

TRANSMISSIBILITY OF EMERGING/RE-EMERGING VIRUSES

According to several authors (*Geoghegan et al., 2016; Walker et al., 2018; Munster et al., 2020*), sustained person-to-person transmission of viruses is favored by certain viral characteristics, including lack of a lipid envelope, small particle size, limited genomic segmentation, and low mortality of the associated disease. Tropism of the virus for the liver, central nervous system (CNS), or the respiratory tract, and lack of vector-borne transmission also appear to favor sustained person-to-person transmission (*Geoghegan et al., 2016; Walker et al., 2018*). On the other hand, possession of an RNA vs. a DNA genome was not found to contribute to the likelihood of such sustained transmission (*Geoghegan et al., 2016; Walker et al., 2018*).

It is of interest that many of the viral characteristics mentioned above that are considered predictive of sustained person-to-person transmissibility are not shared by the viruses associated with the WHO diseases of concern. Namely, all of the emerging/re-emerging diseases mentioned in the WHO list (*WHO, 2015*) involve relatively large enveloped viruses with ssRNA genomes, many of which are segmented. Of the emerging/re-emerging viruses listed in Table 1, only EV-D68 is a small, non-enveloped virus. In addition, many of the WHO viruses of concern exhibit high human mortality (Tables 1 and 2). Certain predictive factors (*Geoghegan et al., 2016; Walker et al., 2018; Munster et al., 2020*) that do seem to be shared by the emerging/re-emerging viruses in the list in Table 1 include tropism for the respiratory tract or the CNS, and lack of vector-borne transmission. While most enteroviruses are less susceptible to acid and are disseminated by the fecal-oral route, EV-D68 is acid-labile and has a lower temperature optimum, reflecting its tropism for the upper respiratory tract rather than the gastrointestinal tract (i.e., EV-D68 acts more like a rhinovirus than an enterovirus) (*Sun et al., 2019*).

It is unknown if sustained person-to-person transmissibility necessarily equates to a high level of concern for an emergent zoonotic virus. For instance, there appears to be no evidence that Hendra virus (another zoonotic enveloped virus) has shown person-to-person transmission

(*Paterson et al., 2011*), yet this virus is similar to Nipah virus in many respects and is of concern, due its high mortality rate in humans.

As mentioned in Table 2, the most common modes of transmission for the emerging/re-emerging viruses discussed in this review are contact with infected bodily secretions/excretions and contaminated fomites, especially high-touch environmental surfaces (HITES), and inhalation of respiratory droplets/aerosols containing infectious virus (Fig. 1). The intermediacy of hands in transmission through contact is emphasized in Fig. 1.

The animal-to-human and person-to-person transmission of SARS-CoV-2 and associated COVID-19 disease appears to occur in a manner similar to that described for MERS-CoV and SARS-CoV. That is, the transmission of SARS-CoV-2 (Fig. 1) involves direct contact with infected persons or contaminated HITES, inhalation of large respiratory droplets, and inhalation of small airborne droplets (*Morawska et al., 2020*).

INFECTIVITY AND VIRUS SHEDDING OF EMERGING/RE-EMERGING VIRUSES

The infectivity of a virus refers to its ability to initiate infection of a host cell with production of viral progeny. The infectious $dose_{50}$ (ID_{50}) is the smallest number of infectious virus particles that will lead to infection of 50% of an exposed population (*Westwood and Sattar, 1974*), and is dependent a number of factors, such as the species, age, or race of the host, the receptor, immune, and nutritional status of the host or host tissues, and the portal of entry of the virus. In the case of most viruses, only a percentage of those infected actually develop clinical illness (*Haas et al., 2014*). Those who remain asymptomatic represent subclinical cases of the infection in whom the virus may still replicate and be released into the environment. This has, in fact, been reported to occur in the case of SARS-CoV-2 (*Furukawa et al., 2020; Gandhi et al., 2020*). IPAC may be difficult in the face of such silent disseminators (virus carriers/shedders). Exposure to as low as one infectious viral particle has a probability of causing an infection leading to disease, although that probability varies from virus to virus (*Yezli and Otter, 2011*). Typically, infectious doses are empirically derived and reported in units of 50% infective dose (ID_{50}) values that reflect the doses capable of infecting half of the subjects exposed. As prospective studies in humans of highly pathogenic viral diseases with potentially fatal outcomes (such as SARS-CoV-2) cannot ethically be performed, very limited data exist on the infectivity of the emerging/re-emerging viruses in Table 1. Where studies have been performed using animals, extrapolations of such data to humans must be made with caution.

The estimates that have been reported for viruses listed in Tables 1 and 2 are discussed below, acknowledging the unavoidable variability in literature with regard to such assessments of infectivity. It has been stated that 1-10 infectious aerosolized Ebola virus particles can cause an infection in humans (*Franz et al., 1997; Bibby et al., 2017*). A similar range has been reported for Lassa virus (*Cieslak et al., 2019*). Influenza virus infectivity values specific to the H5N1 and H7N9 strains are not available, but estimates of 100 to 1000 infectious viral particles have been reported (*Yezli and Otter, 2011; Cieslak et al., 2019*). The human infective dose for SARS-CoV has been estimated at 16 to 160 plaque-forming units (*Watanabe et al., 2010*). Data on the human infectious doses for MERS-CoV, severe fever with thrombocytopenia syndrome virus (SFTSV), Nipah virus, EV-D68, and SARS-CoV-2 have not been reported. Until such data become available, it should be assumed that these emerging/re-emerging viruses, including SARS-CoV-2, have relatively low ID_{50} values.

Once infected with one of these emerging/re-emerging viruses, during the prodromal period before actual appearance of symptoms, as well as once symptoms appear, the infected individual may become a shedder of infectious particles, as mentioned above. The extent to which virus shedding might lead to dissemination of the associated disease depends upon a number of factors, including the amount of virus released (shed), the infectivity of the virus within the released matrix (droplets/aerosols, fecal/diarrheal discharge, and other excretions including respiratory secretions), and the survival of the released viruses within such matrices once dried on HITES. Extent of virus shedding, unfortunately, is commonly measured through detection of genomic material (*e.g., Otter et al., 2011; Yezli and Otter, 2011; Hassan et al., 2018; Killerby et al., 2020*), rather than through use of cell-based infectivity assays, so there are only limited data available on infectious SARS-CoV-2 viral shedding (*Francis et al., 2020*).

As displayed in Fig. 1, transmission of respiratory infections commonly involves the intermediacy of the hand. The same can be said about gastrointestinal infections (i.e., through the fecal-oral route). The coronaviruses SARS-CoV, MERS-CoV, and SARS-CoV-2 have been reported (*Otter et al., 2011; Zhang et al., 2020*) to be shed from patients both within respiratory and gastrointestinal secretions/excretions, therefore contaminated HITES and large and small respiratory droplets/aerosols play an important role in dissemination of SARS-CoV-2 (*Morawska et al., 2020*), in many cases through the intermediacy of hands (*Guo et al., 2020*).

VIRAL SURVIVAL ON ENVIRONMENTAL SURFACES AND IN AIR

Knowledge of the transmissibility and infectivity of emerging/re-emerging viruses enables one to assess the risk of spread of a viral disease in the case that infectious virus is shed from an infected individual and is deposited on environmental surfaces/fomites or in droplets/aerosols. Another important factor to consider when assessing risk is the survival (i.e., the continued infectivity) of these viruses on the environmental surfaces/fomites or in air in the form of droplets/aerosols.

There is much more information addressing survival of infectious viruses on environmental surfaces than in aerosols. The data that are available address a number of environmental factors of relevance (*Otter et al., 2011*), including the types and porosities of the surfaces, the matrices in which the viruses have been suspended prior to being deposited onto the surfaces, the temperature and relative humidity (RH), and methods used for measuring survival (e.g., $\log_{10}$ reduction in infectivity per unit time, infectivity half-life, etc., infectious titer after a measured duration, etc.). For Table 3, the results that have been displayed focus on room temperature (ambient) conditions at relatively low and medium RH. Table 3 should not, therefore, be considered to represent a comprehensive review of literature for survival of these viruses on surfaces. For a more systematic review of coronaviruses survival on environmental surfaces under various conditions, see the reviews by Otter et al. (*2011*) and Kampf et al. (*2020*). For certain viruses (e.g., SFTSV), survival data are not yet available, so data for surrogate viruses from the same or similar families are shown in Table 3.

Persistence of SARS-CoV-2 on surfaces and in air has recently been reported by van Doremalen et al. (*2020*) and on surfaces by Chin et al. (*2020*). SARS-CoV-2 was found to remain infectious in aerosols for at least the 3-hour period studied by van Doremalen et al. (*2020*). The survival half-life estimated based on the limited period of observation of that study was 68 minutes. In experiments conducted with HCoV 229E over a 6-day observation period, the survival half-life was found to depend on relative humidity (RH) and temperature (*Ijaz et al.,*

1985). At 20°C, the half-life values observed were 3.3 hours (~80% RH), 67 hours (50% RH), and 27 hours (30% RH). A different pattern of results was obtained at low temperature (6 °C) and high RH (~80~), with the half-life increasing to 86 hours, nearly 30 times that found at 20°C and high RH. The pronounced stabilizing effect of low temperature on the survival of HCoV 229E at high RH indicates that the role of the environment on the survival of coronaviruses in air may be more complex and significant than previously thought (*Ijaz et al., 1985*). This likely is the case for SARS-CoV-2 as well. The survival of SARS-CoV on prototypic HITES has been investigated, and survival of the virus has been reported for up to 24 hours on cardboard and 2 to 4 days on plastic and stainless steel surfaces (*Chin et al., 2020; van Doremalen et al., 2020*).

HIERARCHY OF SUSCEPTIBILITY OF PATHOGENS INCLUDING SARS-COV-2 TO MICROBICIDES

Infectious virus surviving in aerosols/droplets or on HITES represents a source for dissemination of emerging /re-emerging viruses, including SARS-CoV-2. The enveloped viruses listed in Tables 1 and 2 should be relatively susceptible to the virucidal activity of a variety of microbicides, as discussed below. Sattar (*2007*) previously has advanced the concept of utilizing the known knowledge of the susceptibility human viral pathogens to chemical disinfecting agents (microbicides) (*Klein and Deforest, 1983; McDonnell and Russell, 1999; Ijaz and Rubino*, *2008*), to predict the efficacy of such agents for inactivating emerging /re-emerging viral pathogens. This concept, referred to as a hierarchy of susceptibility to microbicides, is portrayed in Fig. 2. As shown, infectious agents can be viewed as displaying a continuum of susceptibilities to microbicides, with enveloped viruses at the bottom of this hierarchy, highlighting their relatively high susceptibilities to formulated microbicides (*Klein and Deforest, 1983; McDonnell and Russell, 1999; Sattar 2007; Ijaz and Rubino*, 2008).

Among pathogens, prions are considered to be the least sensitive to microbicides, requiring highly caustic solutions for inactivation. Bacterial spores and protozoan cysts/oocysts are next on the microbicidal susceptibility spectrum. Small, non-enveloped viruses are considered to be less susceptible to microbicides, although have increased susceptibility to high pH, oxidizers such as sodium hypochlorite, formulated hydrogen peroxide, alcohols, and a variety of microbicidal actives, relative to spores and protozoan cysts/oocysts. Mycobacteria, fungi, vegetative bacteria and enveloped viruses appear to be more susceptible to certain formulated microbicides, such as alcohols, oxidizers, quaternary ammonium compounds (QAC), and phenolics (e.g., p-chloro-m-xylenol) (*Klein and Deforest, 1983; Sattar et al., 1989; McDonnell and Russell, 1999; Rabenau et al., 2005; Sattar 2007; Ijaz and Rubino*, *2008; Geller et al., 2012; Cook et al., 2015; Cook et al., 2016; Cutts et al., 2018, 2019, 2020; Rutala et al., 2019; Weber et al., 2019; Chin et al., 2020; Ijaz et al., 2020; Kampf et al., 2020; O'Donnell et al., 2020;O'Donnell et al., 2020; Senghore et al., 2020; Vaughan et al., 2020;Yu et al., 2020*).

It is of interest that the enveloped viruses are considered to be the most susceptible to a variety of formulated microbicidal actives, even more so than fungi and vegetative bacteria, yeast, and mycobacteria (Fig. 2). Viral envelopes are typically derived from the host cell and therefore comprise host cell phospholipids and proteins (Fig. 3), as well as some virally inserted glycoproteins. Coronaviruses are known to obtain their lipid envelopes from the host cell endoplasmic reticulum Golgi intermediate compartment, after which the particles are transported by exocytosis via cargo vesicles (reviewed in *O'Donnell et al., 2020*). The composition of the coronavirus lipid envelope therefore is determined by the lipid composition of the host cell

endoplasmic reticulum. Since the envelopes contain lipid material, they are readily destroyed by phenolics such as p-chloro-m-xylenol (PCMX), oxidizing agents such as sodium hypochlorite and activated hydrogen peroxide, quaternary ammonium compounds, alcohols, and detergents. Even mild detergents such as soap may inactivate enveloped viruses by denaturing the lipoproteins in the envelope. These include the SARS-CoV-2 spike proteins that interact with the human angiotensin-converting enzyme 2 (ACE2) receptor as a prerequisite event in initiating viral infection (*Letko et al., 2020*). This makes enveloped viruses more susceptible to most of the formulated virucidal microbicides commonly used for IPAC.

It can be assumed as a starting point, therefore, that the enveloped emerging/re-emerging viruses listed in Table 1 should be readily inactivated by a variety of formulated microbicidal actives. This assumption has, in fact, been verified by extensive empirical data (*Klein and Deforest, 1983; Sattar et al., 1989; McDonnell and Russell, 1999; Rabenau et al., 2005; Sattar 2007; Ijaz and Rubino, 2008; Geller et al., 2012; Cook et al., 2015; Cook et al., 2016; Cutts et al., 2018, 2019, 2020; Weber et al., 2019; Chin et al., 2020; Ijaz et al., 2020; Kampf et al., 2020; O'Donnell et al., 2020; O'Donnell et al., 2020; Vaughan et al., 2020; Yu et al., 2020*), and has been embraced by the U.S. Environmental Protection Agency (*U.S. EPA, 2016*). The data for various members of the *Coronaviridae* family, reviewed recently by Kampf et al. (*2020*), support the expectation that SARS-CoV-2 and other coronaviruses of concern (e.g., MERS-CoV, SARS-CoV, mouse hepatitis virus, porcine epidemic diarrhea virus, etc.) should be readily inactivated by commonly employed and commercially available formulated microbicides, including QAC. Virucidal efficacy testing results for SARS-CoV-2 reported by Ijaz et al. (*2020*) also confirm the expectation of susceptibility of this coronavirus to a variety of microbicidal actives. In addition, a European guidance document (*European Centre for Disease Prevention and Control, 2020*) recently has been issued that lists a variety of microbicidal agents that have demonstrated efficacy against a variety of human and animal coronaviruses, and that, therefore, could be applied for decontamination of surfaces in non-healthcare facilities.

Aqueous solutions of the phenolic, PCMX, at concentrations of 0.12 -0.48% by weight were shown to inactivate >4 $\log_{10}$ of infectious Ebola virus - Makona variant (EBOV/Mak) suspended in an organic load and evaluated in liquid virucidal efficacy studies (*Cutts et al., 2018; 2019*) or dried on a steel surface (a prototypic HITES) in a hard surface carrier viricidal efficacy study (*Cutts et al., 2018*). In each case, complete inactivation of ≥6.8 $\log_{10}$ of EBOV/Mak was observed after contact times ≥5 min. In addition, EBOV/Mak dried on prototypic steel carriers was completely inactivated (≥6.5 $\log_{10}$) by aqueous solutions of 70% ethanol or 0.5% or 1% NaOCl (≥0.5%) after contact times ≥2.5 min (*Cook et al., 2015*). Disinfectant pre-soaked wipes containing, as active ingredients, either activated hydrogen peroxide or a QAC were found to have virucidal efficacy (>5 $\log_{10}$) for EBOV/Mak and vesicular stomatitis virus following as little as 5 seconds contact time (*Cutts et al., 2020*)

Microbicidal formulations based on oxidizing agents, QAC, alcohols, phenolics, and aldehydes displaying virucidal efficacy for enveloped viruses and relatively less susceptible non-enveloped viruses (such as human norovirus surrogates) have been recommended for decontaminating environmental surfaces or materials used for food preparation (*Zonta et al., 2016; Scott et al., 2020*). The efficacy of ethanol and QAC actives for inactivating the norovirus surrogate feline calicivirus depends on how the microbicides are formulated. Factors such as the addition of an alkaline agent were found to increase their efficacy (*Whitehead and McCue, 2010*). Microbicides satisfying these requirements can be regarded as effective against

emerging/re-emerging viruses such as SARS-CoV-2. Following this logic, the U.S. EPA has invoked an Emerging Viral Pathogen Policy in the past for pandemic influenza, for the Ebola virus, and most recently for SARS-CoV-2 (*U.S. EPA, 2020*).

In the case of highly pathogenic emerging/re-emerging viruses such as SARS-CoV-2, effective and frequent targeted hygiene using appropriate microbicides is essential for prevention of infectious virus dissemination. Practicing hygiene inappropriately and only once daily may not be sufficient as recontamination of HITES could potentially occur, particularly under healthcare settings where SARS-CoV-2 infected patients are treated. For instance, infectious coronavirus 229E was detected on HITES (e.g., door knobs) in a university classroom in which samples were collected daily over a one-week period (*Bonny et al., 2018*). Vigilant decontamination of HITES becomes of paramount importance when dealing with highly pathogenic viruses with relatively low human infectious doses, as is the case with many of the emerging/re-emerging viruses, including SARS-CoV-2, being discussed in this review.

The enveloped emerging/re-emerging viruses listed in Table 1 display high susceptibility to inactivation by ultraviolet light at 254 nm, an inactivation approach amendable to inactivation of aerosolized viruses (*Ijaz et al., 1985*). For instance, empirical data (*Lytle and Sagripanti, 2005*) for Lassa virus, Hantavirus, and Ebola virus, and for the virus families (*Coronaviridae, Orthomxyoviridae, Paramyxoviridae, Phenuiviridae*) indicate that UV fluencies of 3 to 14 mJ/cm^2 should inactivate 4 log_{10} of the enveloped viruses in Table 1. These fluency values are relatively low, compared to those needed to inactivate 4 log_{10} of the least UV-susceptible viruses, such as those of the *Adenoviridae* (98-222 mJ/cm^2) and *Polyomaviridae* (235-364 mJ/cm^2) families of non-enveloped viruses (*Nims and Plavsic, 2014*).

PERSONAL HYGIENE PRACTICES FOR PREVENTING INFECTIOUS VIRUS ACQUISITION

A 2005 study on SARS-CoV indicated the presence of genomic material for that virus in air and on HITES within a SARS patient's room (*Booth et al., 2005*), indicating the likelihood of airborne droplet transmission for this coronavirus including the air-surface-air nexus (*Ijaz et al., 2016*). This suggests that appropriate respiratory protection, as well as targeted HITES decontamination and hand hygiene, represent important interventional practices for limiting virus dissemination during outbreaks such as that occurring now with SARS-CoV-2 (see also *Morawska et al., 2020*).

The WHO has posted on their website a webpage entitled Coronavirus Disease (COVID-19) advice for the public (*WHO, 2020b*). Basic protective measures against SARS-CoV-2 recommended by the WHO include: frequent hand washing with soap and water or an alcohol-based rub, and maintenance of social distancing (at least 1m; see Fig. 1) especially in the presence of people who are coughing, sneezing, or have a fever (*WHO, 2020b*). The latter recommendation is applicable to any of the viruses listed in Table 2 for which transmission by respiratory aerosols/droplets is expected. Avoidance of touching eyes, nose, mouth, or other mucus membranes with hands post-contact with HITES is also recommended (*WHO, 2020b*). As displayed in Fig. 1, the hands play an important role in transfer of infectious virus from contaminated HITES to susceptible host's mucus membranes, enabling virus-host interactions initiating infection. Following the appropriate hygiene practices described above can potentially help in prevention and control of emerging and re-emerging viruses, including the currently circulating SARS-CoV-2.

DISCUSSION

As Dr. Anthony Fauci eloquently stated in 2005 (*Fauci, 2005*) "Public health officials once suggested that it might someday be possible to 'close the book' on the study and treatment of infectious diseases. However, it is now clear that endemic diseases as well as newly emerging ones (e.g., SARS-CoV-2), reemerging ones (e.g., West Nile virus), and even deliberately disseminated infectious diseases (e.g., anthrax from bioterrorism) continue to pose a substantial threat throughout the world." Recent experience certainly verifies these predictions. Weber et al. (*2019*) have correctly emphasized that "Preventing pathogen acquisition via person-to-person transmission or contact with the contaminated environment depends on rapid and appropriate institution of isolation precautions, appropriate hand hygiene, and appropriate disinfection of medical equipment, devices, and the environmental surfaces. Importantly, once the nature of the emerging infectious agent is known (i.e., enveloped virus, bacteria, fungi, nonenveloped virus, mycobacteria, or non-enveloped virus), it is possible to determine the appropriate hygienic interventions. For example, an enveloped virus (e.g., Ebola, MERS-CoV, SARS-CoV-2, or any of the coronaviruses) or vegetative bacterium (e.g., CRE, MRSA) would be inactivated by any formulated microbicidal active(s) known to be effective against vegetative bacteria, filamentous fungi, mycobacteria, or non-enveloped viruses." (*Weber et al., 2019*).

It is fortunate, though perhaps a little perplexing, that so many of the emerging/re-emerging viruses (examples listed in Table 1 and below) are enveloped viruses. It is not clear why there are not more small, non-enveloped viruses mentioned in the WHO list of viral diseases of concern (*WHO, 2015*). The small non-enveloped viruses are much less susceptible to commonly employed cleaning agents (antiseptics, detergents, microbicidal actives) and, in general, display relatively longer survival on environmental surfaces. According to theoretical modeling of sustained person-to-person transmissibility (*Geoghegan et al., 2016; Walker et al., 2018; Munster et al., 2020*), small non-enveloped viruses are predicted to be more likely to lead to sustained infections within the community. The reality is that the emerging/re-emerging viruses of concern, both in humans and in economically important animals, have more typically included enveloped viruses. Recent examples include porcine epidemic diarrhea virus, MERS-CoV, SARS-CoV and SARS-CoV-2 (*Coronaviridae*), African swine fever virus (*Asfarviridae*), Schmallenberg virus (*Peribunyaviridae*), Crimean-Congo hemorrhagic fever virus (*Nairoviridae*), Rift Valley fever virus (*Phenuiviridae*), West Nile virus and Zika virus (*Flaviviridae*), Hantaviruses (*Hantaviridae*), and Lassa viruses (*Bunyaviridae*).

The fact that the emerging/re-emerging viruses are predominantly RNA viruses might be explained in part by the notion (*Jaijyan et al., 2018*) that RNA viruses can more readily adapt to the rapidly changing global and local environment due to the high error rate of the polymerases that replicate their genomes. The RNA viruses are thought therefore to display higher evolution rates through mutation, genomic reassortment, or recombination.

The likelihood of experiencing future emergent zoonotic viruses is high (*Morens and Fauci, 2013; Paules et al., 2020*, and defining in advance appropriate approaches for limiting the spread of such viruses through IPAC is essential. We now have the sequencing tools necessary for rapidly identifying a novel virus such as SARS-CoV-2, the genetic sequence of which was determined within just over one week (*Zhu et al., 2020*). Provided that a novel emerging virus is found to be a member of a lipid enveloped viral family, it should be possible to leverage IPAC experience for other enveloped viruses of concern, and thereby make predictions as to risk of

viral transmission, virus survival on surfaces, and microbicidal efficacy for the virus and risk mitigation. SARS-CoV-2 is no exception in this regard.

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Declarations

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Not applicable.

Competing Interests

J.R. Rubino and M.K. Ijaz are employed by Reckitt Benckiser LLC, which provided funding for the preparation of the manuscript. The other authors have no financial interest in Reckitt Benckiser LLC. R.W.N.is employed by RMC Pharmaceutical Solutions, Inc. and received a fee from Reckitt Benckiser LLC for his role in authoring and editing the manuscript. The other authors M.K.I, S.A.S., J.R.R, and C. P. Gerba declare no financial or non-financial conflicts of interest in this work.

689 **Figure Legends:**

690 Figure 1 **Modes of transmission of viruses, emphasizing multi-system infections such as**
691 **SARS-CoV, MERS-CoV, and SARS-COV-2** *(modified from Otter et al., 2011*).

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693 Figure 2 **Hierarchy of sensitivity of pathogens to formulated chemical microbicides** (adapted
694 from Sattar (*2007*).

695 Figure 3 **Ultrastructural differences between enveloped and non-enveloped viruses.**
696 Genotypically, these viral genomes may be single-or double-stranded, and segmented or non-
697 segmented (examples are not shown in the figure).

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Table 1(on next page)

. Characteristics of selected emerging/re-emerging viruses including SARS-CoV-2.

Notes ±, ambisense; -, negative sense; +, positive sense; ss, single-stranded. Segments (1) equates to a non-segmented genome. †Now referred to as Huaiyangshan banyangvirus.‡Suspected primary host based on >90% sequence homology to bat coronaviruses (*Zhou et al., 2020*).

Table 1. **Characteristics of selected emerging/re-emerging viruses including SARS-CoV-2.**

Virus	Family	Particle size	Lipid envelope	Genome* (segments)	Reservoir species	References
Lassa virus	*Arenaviridae*	110-130 nm	yes	±ssRNA(2)	rodent	*Viral Hemorrhagic Fever Consortium, 2020; St. Georgiev, 2009*
SFTSV†	*Phenuiviridae*	80-100 nm	yes	-ssRNA(3)	tick	*Zhan et al., 2017*
Hantaan virus	*Hantaviridae*	80-120 nm	yes	-ssRNA(3)	rodent	*Jiang et al., 2016; Brocato and Hooper, 2019; Laenen et al., 2019*
MERS-CoV	*Coronaviridae*	118-136 nm	yes	+ssRNA(1)	bat	*Otter et al., 2011; MERS 2013 ; Gorbalenya et al., 2020*
SARS-CoV	*Coronaviridae*	80-90 nm	yes	+ssRNA(1)	bat	*Otter et al., 2011; MERS 2013 ; Gorbalenya et al., 2020*
SARS-CoV-2	*Coronaviridae*	60-140 nm	yes	+ssRNA(1)	bat‡	*Munster et al., 2020 ; Zhou et al., 2020; Zhu et al., 2020*
Ebola virus	*Filoviridae*	80 × 14000 nm	yes	-ssRNA(1)	bat	*St. Georgiev, 2009*
Influenza H5N1	*Orthomyxoviridae*	80-120 nm	yes	-ssRNA(8)	avian	*Cassidy et al., 2018*
Nipah virus	*Paramyxoviridae*	40-1900 nm	yes	-ssRNA(1)	bat	*Ang et al., 2018*
EV-D68	*Picornaviridae*	~30 nm	no	+ssRNA(4)	unknown	*Cassidy et al., 2018 ; Sun et al., 2019*

Notes

±, ambisense; -, negative sense; +, positive sense; ss, single-stranded. Segments (1) equates to a non-segmented genome. †Now referred to as Huaiyangshan banyangvirus.‡Suspected primary host based on >90% sequence homology to bat coronaviruses (*Zhou et al., 2020*).

Table 2(on next page)

Transmission and mortality of emerging/re-emerging viruses including SARS-CoV-2

Notes: ”Contact” refers to contact with bodily fluids or with fomites; “aerosols/droplets” equates to respiratory aerosols/large or small droplets. CNS, central nervous system, GI, gastrointestinal

Table 2 **Transmission and mortality of emerging/re-emerging viruses including SARS-CoV-2**

Virus	Tropism for organs	Mode of transmission	Mortality	Reference
Lassa virus	Vascular system	Contact, aerosols/droplets	15-20%	*St. Georgiev, 2009; Cieslak et al., 2019*
SFTSV	Vascular system	Vector (tick)	12-30%	*Xing et al., 2016 ; Zhan et al., 2017*
Hantaan virus	Lower respiratory, renal	Contact, aerosols/droplets	1-15%	*Nolte et al., 1995; St. Georgiev, 2009; Krüger et al., 2011 ; Jiang et al., 2016*
MERS-CoV	Lower respiratory, GI	Contact, aerosols/droplets	34-36%	*Cieslak et al., 2019; Weber et al., 2019; Paules et al., 2020 ; van Doremalen et al., 2013*
SARS-CoV	Lower respiratory	Contact, aerosols/droplets	15 ± 11%	*Chan et al., 2011; Cieslak et al., 2019*
SARS-CoV-2	Lower respiratory, GI	Contact, aerosols/droplets	6%	*WHO, 2020c; Morawska et al., 2020; Zhang et al., 2020*
Ebola virus	Vascular system	Contact, aerosols/droplets	41%	*Fischer et al., 2015 ; Cieslak et al., 2019; Weber et al., 2019*
Influenza H5N1	Upper respiratory	Contact, aerosols/droplets	>60%	*U.S. CDC, 2015; Cieslak et al., 2019*
Nipah virus	CNS, respiratory	Contact, ingestion	65 ± 28%	*Ang et al., 2018; Hassan et al., 2018*
EV-D68	Respiratory, CNS	aerosols/droplets, contact	Up to 10%	*Oermann et al., 2015; Cassidy et al., 2018;*

Notes:

”Contact” refers to contact with bodily fluids or with fomites; “aerosols/droplets” equates to respiratory aerosols/large or small droplets. CNS, central nervous system, GI, gastrointestinal

Table 3(on next page)

Environmental survival of emerging/re-emerging viruses including SARS-CoV-2 under ambient conditions.

Notes: †No data for SFTSV are available, the result displayed is for Crimean-Congo virus. *Aerosol data for human coronavirus 229E (*Ijaz et al., 1985*). Survival half-life depended on humidity and temperature. The values ranged from 3.3 h (~80% RH), 67 h (50% RH), to 27 h (30% RH). ‡No data for EV-D68 are available; the result displayed is for human rhinovirus type 14 at 15-55% RH (*Sattar et al., 1987*). ¶The authors only evaluated times up to 3 h (*van Doremalen et al., 2020*).

Table 3 **Environmental survival of emerging/re-emerging viruses including SARS-CoV-2 under ambient conditions.**

Virus	Survival on surfaces	Survival in aerosols	Reference
Lassa virus	0.41 $\log_{10}$/d (glass)	t½ = 0.62 h	*Stephenson et al., 1984; Sagripanti et al., 2010*
SFTSV	t½ = 0.75 h (aluminum)†	No data	*Hardestam et al., 2007*
Hantaan virus	t½ = 1.0 h (aluminum)	No data	*Hardestam et al., 2007*
MERS-CoV	t½ = 0.94 h (steel)	t½ = 27 h*	*Ijaz et al., 1985; van Doremalen et al., 2013*
SARS-CoV	t½ = 10 h (steel), 18 h (plastic)	At least 3 h¶ t½ = 27 h*	*Ijaz et al., 1985; Chan et al., 2011; van Doremalen et al., 2020*
SARS-CoV-2	t½ = 5 min (cloth), 13-14 h (steel), 16 h (plastic), 19 h (mask)	At least 3 h¶ t½ = 27 h*	*Ijaz et al., 1985; Chin et al., 2020; van Doremalen et al., 2020*
Ebola virus	0.68 $\log_{10}$/d (glass) 0.88 $\log_{10}$/d (steel)	t½ = 0.25 h	*Cook et al., 2015; Fischer et al., 2015; Sagripanti et al., 2010; Piercy et al., 2010*
Influenza H5N1	<1 d (glass, metal)	No data	*Wood et al., 2010*
Nipah virus	1 h (plastic)	No data	*US EPA, 2014*
EV-D68	t½ = 0.17 to 0.25 h (steel)‡	No data	*Sattar et al., 1987*

†No data for SFTSV are available, the result displayed is for Crimean-Congo virus.
*Aerosol data for human coronavirus 229E (*Ijaz et al., 1985*). Survival half-life depended on humidity and temperature. The values ranged from 3.3 h (~80% RH), 67 h (50% RH), to 27 h (30% RH).
‡No data for EV-D68 are available; the result displayed is for human rhinovirus type 14 at 15-55% RH (*Sattar et al., 1987*).

6 ¶The authors only evaluated times up to 3 h (*van Doremalen et al., 2020*).

Figure 1

Modes of transmission of viruses, emphasizing multi-system infections such as SARS-CoV, MERS-CoV, and SARS-COV-2 *(modified from Otter et al., 2011*).

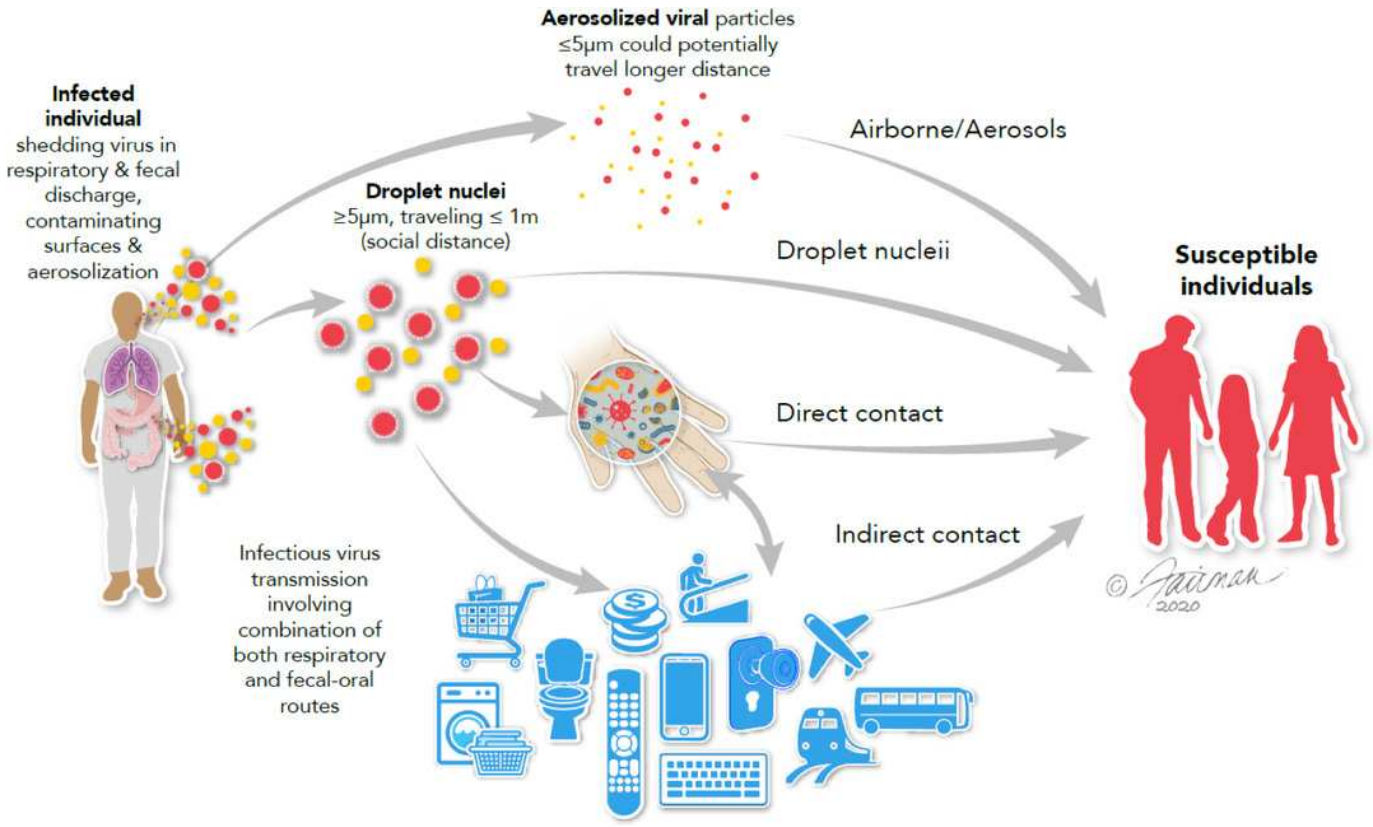

Figure 2

Hierarchy of sensitivity of pathogens to formulated chemical microbicides (adapted from Sattar (*2007*).

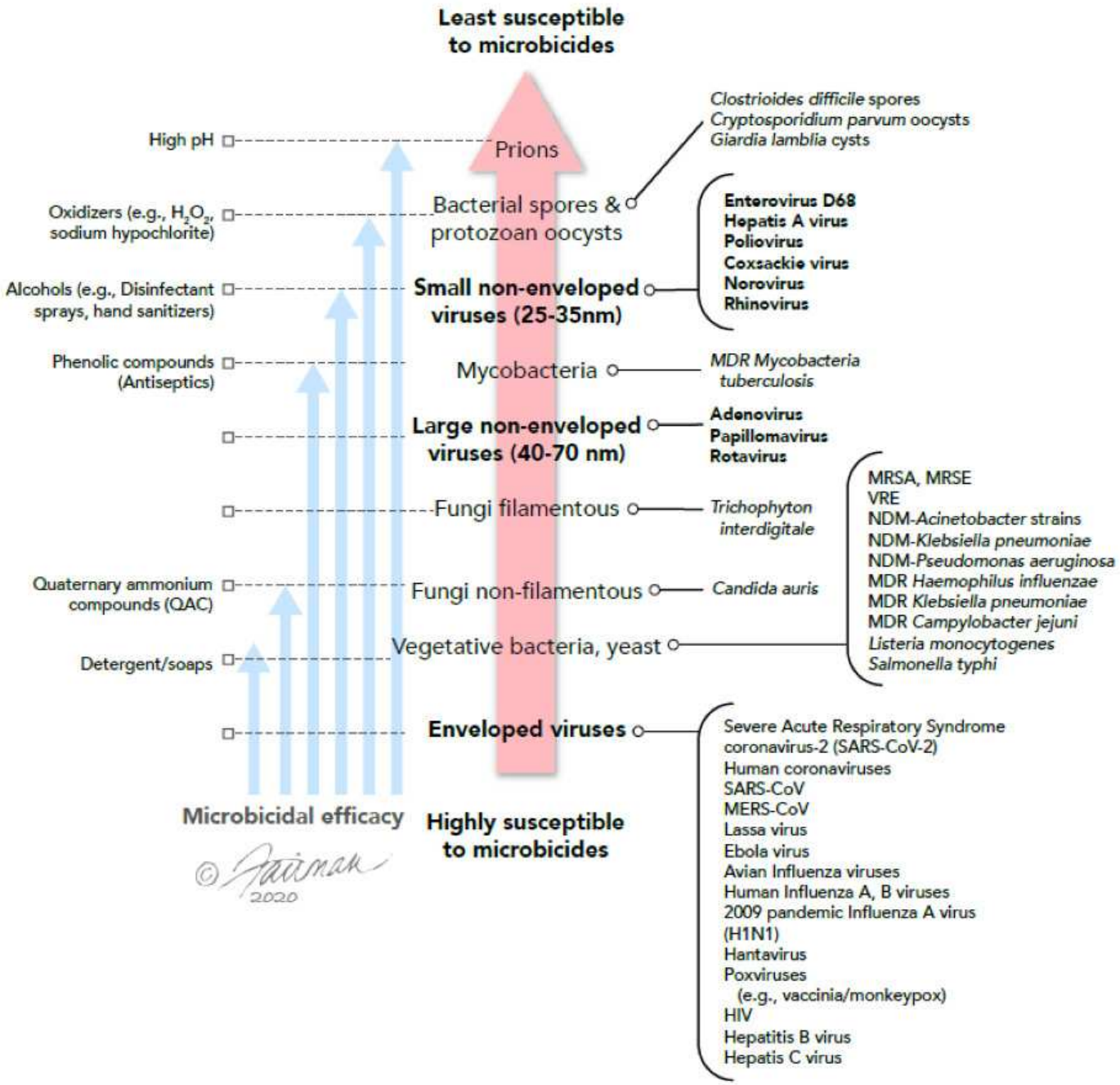

Figure 3

Ultrastructural differences between enveloped and non-enveloped viruses. Genotypically, these viral genomes may be single-or double-stranded, and segmented or non-segmented (examples are not shown in the figure).