Human Pathogenic Coronaviruses: Understanding their Environmental Survival for better Infection Prevention and Control

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Introduction

Coronaviruses (CoV) are significant pathogens of humans and animals. Though they were first identified as the cause of respiratory infections in humans in 1965, the advent of a new CoV in the etiology of the 2003 pandemic of SARS (severe acute respiratory syndrome) propelled them to international prominence. Then, in 2012, another CoV was identified as the cause of the Middle East respiratory syndrome (MERS-CoV). In December 2019, the Wuhan-CoV (or 2019-nCoV) burst on the scene and has already engulfed over a dozen countries with thousands of clinical cases and dozens of fatalities. An unprecedented global effort is underway to contain its spread. In effect, CoV have emerged as a major threat to human health in the past two decades [1-3]. In the absence of safe and effective vaccines and specific chemotherapy, public education and proper infection prevention and control (IPAC) remain the only viable options to counter the spread of these viruses.

CoV are relatively large (120-160 nm in diameter), enveloped viruses with a single-strand of positive-sense RNA genome. To date, we know of some seven human pathogenic CoV. Many others affect a wide variety of animal species.

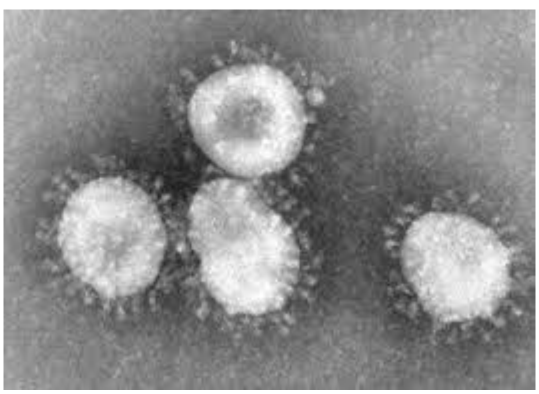

Figure 1. An electron micrograph of CoV particles showing their pleomorphic shape and surface projections. (U.S. National Institutes of Health, Bethesda, Maryland).

CoV are shed from the respiratory and/or gastrointestinal tracts with the nose and the mouth as the portals of virus entry. Susceptible persons normally develop a common cold-like infection, which is self-limiting and often free of any serious sequelae. In contrast, the SARS, MERS, and Wuhan CoV can cause serious and potentially fatal forms of pneumonia and gastroenteritis. The risk of environmental contamination with those three viruses is thus much higher.

The evidence from healthcare settings strongly suggests droplet transmission of CoV and to a much-limited degree by aerosols. We do not know if human pathogenic CoV can enter the body via the mouth and conjunctivae as well; nor do we know if the inhaled virus trapped in the throat can translocate to the gut.

Virus shedding occurs for about 6 days post-infection with a peak around day 4 post-infection. The minimal infective dose for human CoV is unknown.

Environmental survival and spread of CoV

We understand to some degree the environmental survival of CoV. However, and in contrast to animal CoV, we know much less about the nature and relative significance of vehicles in the spread of human pathogenic CoV in the field. The following is a summary of what we know so far.

Droplets and aerosols: Field observations strongly suggest that SARS and MERS CoV spread via droplets, and this may true for Wuhan-CoV as well.

In a rare study [4], when aerosols of the human respiratory CoV 229E (a commonly-used surrogate for human respiratory CoV) were held at the air temperature of 20°C, the virus survived better at low (30%) and med (50%) relative humidity (RH) levels than at the high (80%) RH. Under these conditions, the half-lives of the virus were 27, 67 and 3 hours, respectively. However, when the air temperature was lowered to 6°C, the half-life of the virus at the high RH increased from 3 to over 86 hours! This dramatic influence of lower air temperature and high RH may enhance CoV spread under that set of conditions.

While the droplet spread is more amenable to IPAC via the proper use of masks for example, interrupting the transmission through aerosols can be more challenging.

SARS CoV caused nearly 329 cases in an apartment complex in Hong Kong, China [5]. Retrospective studies suggested viral aerosols emanating from malfunctioning sewers in the building as the likely means of virus spread. However, others have suggested person-to-person transmission or possibly rodents in the building as amplifiers and disseminators of the virus [6].

In one instance, a symptomatic case of SARS is believed to have infected some 22 of 120 airline passengers and crewmembers (18.3%) during a three-hour commercial flight [7]. Those infected included persons seated well beyond the radius (about two meters) for droplet spread. Even though it is extremely difficult to retrospectively prove aerosol spread at the exclusion of other potential vehicles, the generally lower (15-25%) levels of RH on aircraft would be more conducive to CoV survival in air.

A report from Canada suggested that oxygen delivery masks with open vents could promote the dispersal of respiratory pathogens such as SARS-CoV through their enhanced release in mists of exhaled pulmonary gases [8]. The exhaled moist air ejected from such oxygen masks is believed to carry pathogen-laden droplets over longer distances and possibly contribute to an increased risk of spread of respiratory infections in healthcare settings. We need more research to demonstrate that SARS CoV and other similar viruses can remain viable in the warm, moisture-laden air exhaled from such oxygen masks. The findings on the influence of RH and air temperature on the airborne survival of coronavirus 229E would tend to suggest otherwise.

Li et al. [9] conducted a comprehensive but retrospective study of SARS CoV spread at a hospital in Hong Kong and found support for airborne transmission. They also recommend improvements in air handling systems to reduce the risk of such spread.

Skin

Since safety and ethical considerations would not permit the experimental contamination of human subjects with infectious CoV, we have used CoV 229E as a surrogate to study the potential of such viruses to survive on human hands. Preliminary findings from such experiments indicate that nearly 45% of infectious virus remains viable on the hands of adults after 1 hour. Such virus survival is longer than that for other enveloped respiratory viruses (e.g., parainfluenzavirus type 3), which become undetectable in about 10 minutes on human skin.

In a yet to be published study, Sattar et al. used the fingerpads of adult human subjects to show that the viability titer of CoV 229E could be reduced by ~70% by water with a hardness of 200 ppm CaCO3 (mechanical removal) whereas ethanol-based hand sanitizers could inactivate >99.99% of the virus in 30 seconds. This reinforces the importance of oft-emphasized importance of regular and proper hand hygiene in IPAC in general.

Food and water

There are no credible studies on the survival of human CoV in/on foods. One study has found SARS-CoV to survive in water to a very limited degree [10]. There is also no evidence indicating the spread of CoV via food or potable/recreational waters.

Environmental surfaces

CoV are more stable on high-touch environmental surfaces (HITES) as compared to other enveloped viruses [11; 12]. More recently, deposition of respiratory pathogens on HITES at airport was tested using PCR [14]. Even though this study yielded some positive findings, their significance requires careful interpretation because of the limited relevance of molecular approaches to detect pathogens in environmental samples. Such testing has high value when analyzing clinical samples, but detection of infectious virus is essential in testing environmental samples to better assess the potential for infection. Mathematical modelling suggests a role for HITES as fomites in the spread of CoV infections in healthcare settings [13]; this area also needs further investigation.

Microbicides against CoV

In general, enveloped viruses (e.g., influenza- and coronaviruses) are more susceptible to the action of microbicidal chemical as compared to non-enveloped viruses.

Even before the advent of SARS, chemical microbicides were tested against animal and other human pathogenic CoV. The following is a summary of this information relating to human CoV only:

In a comparative study, an animal parvovirus (non-enveloped) required 20- to 500-fold higher concentrations of the tested microbicides than were needed to inactivate an animal coronavirus [14].

The relative resistance of 229E to microbicides was compared to that of coxsackievirus B3, adenovirus type 5, and parainfluenzavirus type 3 using the second tier of a quantitative carrier test (QCT-2) [15]. Stainless steel disks were used as carriers and each one received 10 µL of the test virus, suspended in either faeces or mucin and the inoculum allowed to dry for h under ambient conditions. After a 1-min exposure to 20 µL of the disinfectant, the virus from the disks was eluted and plaque assayed. The efficacy criterion of a >3 log10 reduction in virus infectivity was used. As expected, the coronavirus proved to be generally less resistant to microbicides than the two non-enveloped viruses.

Wood and Payne [16] used a suspension test to assess the activity of chloroxylenol, benzalkonium chloride and cetrimide/chlorhexidine against three types of enveloped viruses (herpesvirus type 1, HIV-I and a human coronavirus). The coronavirus was found to be generally more resistant than the other two enveloped viruses tested. While this observation is of interest, the findings have limited practical significance because the testing was based on a suspension test, which presents the test microbicide with a weaker challenge than a carrier test protocol.

Alcohols: Using a more realistic QCT-2 and an added organic load, ethanol reduced 229E infectivity by >3 log10 over the course of 5 minutes [15].

Aldehydes: Formaldehyde at 4% is used as an overall disinfecting and sterilizing solution although its use as a general disinfectant is not recommended for safety reasons. It is effective against TGEV, reducing it over 5-log10 in under 5 minutes in suspension. At 2%, glutaraldehyde could inactivate 229E by >3 log10 [15] in the QCT-2 test.

Phenolics: The phenolic compounds have a long history as their ancestry dates back to the use of coal tar soaps, whose active ingredients were creosol-based. Although some disinfectants continue to use the same historical active ingredient, creosol, most have developed over time to become more active against various microbes. For example, O-phenylphenol at 200 ppm is highly ineffective against most viruses, including 229E in the QCT-2 test [15]. However, the addition of either a detergent, such as sodium lauryl sulphate, or ethanol, proves highly effective against the virus over 3-log10 reduction is seen after 5 minutes. In the same way, many phenolic compounds rely on the helper effect of other chemicals to work effectively.

Concluding Remarks

Despite the enhanced awareness of the potential of coronaviruses as animal and human pathogens, our understanding of their environmental survival and the exact means of their spread remains weak. Such information would be essential to design and implement rational approaches to prevention and control of outbreaks of CoV infections. This is particularly relevant for the recently discovered causes of SARS, MERS and Wuhan CoV. However, the limited data available indicate that coronaviruses as a group are more stable in the environment than other enveloped viruses.

As is the case with other studies in environmental virology, the use of non-standardized test protocol make it virtually impossible to compare the findings of CoV survival and inactivation within themselves and those with other viruses. There is still a tendency to use molecular approaches (e.g., PCR) when testing for viruses in environmental samples. The findings of such studies require much caution because it is often difficult to correlate the presence of a positive nucleic acid signal with virus infectivity. While such a signal has value in testing clinical samples, it has no relevance in assessing the risk of infection from an environmental source.

Microbicidal chemicals are also assessed against viruses using wide variations in methodology and often in the absence of a suitable and standardized soil load [16]. This is in spite of the fact that well-characterized and field-relevant methods are available for such purposes from well-respected standards-setting bodies such as ASTM International (www.astm.org).

Overall, handling viruses remains relatively expensive and technically demanding, thus limiting the number of laboratories that can perform in vitro studies with them. The use of laboratory animals adds another layer of expense and complexity. There are also strict limitations on the experimental exposure of human subjects to infectious viruses. The only exception here is the use of adult subjects who have given informed consent for placing infectious viruses on the intact skin of their hands. Such studies require prior approval by a properly constituted ethics board.

The above-mentioned factors together with the continuing lack of research funding limit the generation of experimental data for realistic approaches to IPAC. This does not bode in the face of continuing threats from emerging viruses and other types of pathogens.

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CORONAVIRUS UPDATE: SHORTLIST

WHAT IS CORONAVIRUS?

As a large family of viruses, the 2019 novel coronavirus-Wuhan (2019-nCoV) has a tendency to infect bats - which may jump from animals to humans through intermediate animal reservoirs. With many thousands of confirmed cases and hundreds of deaths of the respiratory infection, health officials have confirmed more cases of the novel coronavirus-Wuhan on U.S. soil.

EFFICACY AGAINST CORONAVIRUS?

Similar to Influenza A, coronavirus is an enveloped virus. While this would often serve to protect the virus from possible threats, HYPOCHLOROUS ACID (HOCL) solutions features efficacy against Influenza A and similar, enveloped viral threat including coronavirus. GLP accepted studies show efficacy of HOCL against e.g. norovirus, influenza virus, hiv and parvo virus.

RISK OF CORONAVIRUS INFECTION?

While animal-to-human transmission is thought to be exceedingly unlikely, coronavirus has now demonstrated the ability to mutate and jump from animals to humans prior to person-to-person transmission. With a genome 96% identical to the sequence of a bat coronavirus and similar to a SARS/ MERS-type virus, Chinese officials have stated that patients that have initially contracted the illness have likely eaten an infected animal, possibly a bat, that has come from wet markets in Wuhan, a Chinese city with a population of over 11 million. This virus may spread and evolve into a pandemic, much like the 2003 outbreak of SARS which emerged in China the year prior.

HOW TO AVOID CONTRACTING CORONAVIRUS?

According to the CDC, the best method of coronavirus infection prevention is to wash hands with soap and water, avoid kissing and touching eyes, noses, or mouths, and avoid close contact with those who are sick. Wearing the proper mask and goggles has also shown to possibly assist in the prevention of infection when used properly and consistently. Practicing preventative measures and employing effective disinfection and decontamination methods are essential to helping control the spread of the growing pandemic risk.

ELECTROSTATIC SPRAYING OF HOCL

Electrostatic spraying of HOCL is the most powerful, efficient and cost-effective disinfection treatment available today. Its patented application system places an electrostatic charge to HOCL disinfectants as they leave the spray nozzle, which causes them to cling to virtually any surface and destroy 99.9999% of germs. And because one gallon of solution can cover up to 54,000 square feet of surface area per hour, facility managers can save up to 50% on the cost of solution and 45% on labor.