Bringing Transmission of SARS-CoV-2 to the Surface: Is there a Role for Fomites?

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Abstract

Understanding the contribution of routes of transmission, particularly the role of fomites in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) transmission is important in developing and implementing successful public health infection prevention and control measures.This article will look at case reports, laboratory findings, animal studies, environmental factors, the need for disinfection, and differences in settings, as they relate to SARS-CoV-2 transmission.

Key words. fomite, surface, transmission, SARS-CoV-2, COVID-19, infection prevention and control, public health

Introduction

The COVID-19 pandemic has evolved into a global public health threat with debate regarding transmission. The initial Wuhan strain and subsequent variants have evolved to become more transmissible and deadly than influenza, with Omicron reaching the R_o (transmissibility) of measles. Infection prevention and control measures have relied on widespread adherence to behavior-based policies including mask-wearing, physical distancing, avoiding crowds, and hand hygiene to reduce virus transmission. Early data suggested that the primary mode of SARS-CoV-2 transmission was respiratory droplets, along with other suggested routes throughout this pandemic including fomites, wastewater, and respiratory aerosols.

Fomites as a mode of SARS-CoV-2 transmission were thought to play a more prominent role at the beginning of the pandemic, with laboratory studies revealing the virus could persist on plastic, stainless steel, and other surfaces for hours to days. Case reports early in the pandemic also suggested fomite transmission. Xie et al. reported five COVID-19 cases where individuals from two separate families in an apartment complex tested positive for SARS-CoV-2. Both families stated that they had no contact with the other family, and the authors hypothesized that transmission likely occurred through touching an elevator button contaminated with nasal discharge [1]. Another study reported on three COVID-19 cases in a managed isolation facility, hypothesizing that transmission may have occurred via the surface of a shared trashcan [2]. The accumulation of this anecdotal data sparked headlines and various guidance measures on how to disinfect everything from door handles to groceries. By May 2020, the World Health Organization (WHO) and other agencies were recommending that everyone carefully and thoroughly wash their hands for 20 seconds and "thoroughly" disinfect all contact surfaces, particularly those frequently touched, such as elevator buttons and door handles.

Data in favor of fomite transmission was first contested in a July 2020 study [3], with literature strengthening this argument in different settings. The Centers for Disease Control and

Prevention (CDC) had stated at the time that "it is possible for people to be infected through contact with contaminated surfaces or objects (fomites), but the risk was generally considered low."[4]

Despite the CDC stating that fomite transmission risk is low, many individuals and institutions expanded their use of disinfection products at home and elsewhere to items beyond frequently touched surfaces (e.g. grocery packaging and food take-out containers, elevator buttons), even leaving delivered food sitting overnight. The overuse and misuse of cleaning and disinfection products can also lead to negative consequences such as added cost and health impact to disinfectors, such as the increased risk of COPD and asthma flares and damage to airways after entering contaminated rooms[5,6] . Some felt the more disinfection the better. Where to actually draw the line on disinfection was never agreed on.

This article will 1) review the data behind the role of fomites in the transmission of SARS-CoV-2 in various settings; 2) discuss the role disinfection and disinfectants play in preventing transmission of COVID-19 as well as other infections; 3) discuss the impact of environmental factors such as type of surface, humidity, and temperature in SARS-CoV-2 transfer to and from surfaces; and 4) review uncertainties and provide recommendations. Due to its inherent predictive uncertainties and ambiguities, as we have witnessed throughout the pandemic, we will not discuss transmission modeling.

Study Selection Criteria

The initial set of studies (N=1206) considered for this systematic literature review was compiled from a search on the PubMed database on December 6, 2021, with the following query: (Covid-19 or SARS-CoV-2) and (Surface Transmission or Fomite). Subsequently, 727 studies were excluded because they were duplicates or completely unrelated. Next, 265 were excluded based on the content of their titles, which were related to fomites but did not touch upon the transmission

risk. Lastly, 143 studies were excluded based on the content of their abstracts. This left 71 studies that were reviewed and included in the paper with 28 additional papers found from other sources. Subsequently, papers were further analyzed for redundant information and the final number of papers discussed became n=50.

Initial Data Review

To evaluate the significance of fomites in SARS-CoV-2 transmission, there have been two approaches: study of viral persistence in controlled laboratory environments, and viral detection in real-world settings. A portion of these research papers is summarized in Table 1 and Table 2, respectively. We will summarize the findings of these two approaches and discuss how they relate to one another.

Studies of viral persistence on surfaces typically involve depositing a set titer of virus onto cut "coupons" of a variety of materials. Subsequently, the surfaces are swabbed at regular intervals and the viral infectivity is measured by observing the cytopathic effect on cultured cells.[3] These studies suggested that SARS-CoV-2 could retain infectivity for as little as 30 minutes on paper to as long as a week on the outer layer of a surgical mask [7-9]. Under laboratory conditions, SARS-CoV-2 had a concerningly long persistence time. These initial findings established that surface transmission of SARS-CoV-2 was indeed possible, but more evidence was needed to determine the nature and magnitude of that risk. That data would come from studies of viral detection in real-world settings.

In a protocol from the World Health Organization (WHO), surface sampling of coronavirus in real-world settings ought to include two steps: detection of RNA and assessment of viable virus present[10]. Due to limited availability of BSL-3 or BSL-4 laboratories looking for live virus, researchers tended to rely more strongly on PCR testing looking for viral fragments rather than live virus[11-13]. The literature for SARS-CoV-2 viral detection studies with PCR is vast, and a large portion of

published studies focused on swabbing areas of perceived risk, such as hospital and laboratory surfaces. These are summarized in Table 2. Compared to community settings, hospital environments see many more infected individuals and are expected to have a higher concentration of SARS-CoV-2 on surfaces. However, other factors are at play as well. Ribaric found that in hospitals, ICU rooms were most frequently contaminated, and the most intense areas of SARS-CoV-2 contamination were near the air vents. In areas with laminar air flow and negative pressure ventilation, contaminants were more likely to be swept out of reach instead of being deposited onto surfaces[14].

There is an extensive body of research focused on swabbing public and community settings. A small minority of SARS-CoV-2 RNA detection studies done in community settings failed to detect any SARS-CoV-2. These were done at a Pennsylvania school[15], and a Brazilian market[16]. In other studies, RNA was found in nearly every conceivable place: commercial boarding residencies (2/428 swabs)[17], playgrounds (2/43 swabs), drinking fountains (1/25 swabs)[18], and supermarket keyboards and handles (13/300)[19].

A small number of the studies that completed procedures of SARS-CoV-2 viral culture and isolation succeeded in observing cytopathic effect (presumed to indicate live virus) from swabs collected in real-world settings. Marcenac swabbed the household surfaces of COVID-19 patients and found 23/150 swabs were positive, including nightstands, and pillows. Only one sample from the nightstand of a high viral load infected patient produced a cytopathic effect[20]. Ahn detected viable virus on the endotracheal tube of one patient and bed handles of another, although researchers noted that the patient had a tendency to spit out sputum frequently, and this may have contributed to the result[21]. Santarpia cultured viable virus only from a windowsill of a patient isolation room.[22]

These illustrate that SARS-CoV-2 surface transmission is possible, but may be the exception rather than the rule. Other studies that completed these viral tests for viability found mRNA failed to have a cytopathic effect on any of their cell cultures (Table 2) [23-29].

These disparities between viral culture, cytopathic effect, and PCR findings have led to thinking that fomite transmission is exaggerated [30]. One prominent explanation is that viral viability drops much faster than mRNA. A positive PCR test might thus be indicative of a non-infectious remnant rather than a viable viral particle[31]. Viable influenza could only be recovered from surfaces for 2 weeks while mRNA was detectable for 7 weeks[32].

There are at least two possible explanations as to why viable SARS-CoV-2 persisted in controlled environments but was largely undetected in the real world. The first is that viral culture assays are not picking up viable virus even when it is present. The development of a rapid viability assay may be able to streamline the laborious process and increase the sensitivity of viral isolation and culture assays[33]. Such innovations may soon give us a better picture of the risk posed by SARS-CoV-2 fomites. The second is that the viral loads used in studies of persistence were unrealistically high. These laboratory studies tend to use high viral loads of 10^5 TCID50/mL or more (Table 1), which corresponds to a PCR cycle threshold (C_t value) of around 16[34]. This is much higher than the typical threshold used in real-world detection studies, which use a cycle threshold of around 40.

The disconnect may also come from the protein-rich liquid media used in experiments. Unrealistic conditions could allow for the virus to remain viable for longer periods of time than they would in real-world settings [30]. Therefore, the mRNA detected with PCR may instead be inactive remnants of the virus rather than a meaningful measurement. Perhaps the detection of SARS-CoV-2 RNA should be treated like wastewater samples: predictors of infection rates in a geographical location instead of a hazard in the individual [35]. The actual dose range of infection has also not been agreed upon.

Animal studies

At the same time as studies of viral persistence on surfaces and studies of environmental detection of SARS-CoV-2 were underway, efforts to identify a suitable model organism were also underway. Rhesus macaques were considered, but available BSL-3 facilities for handling non-human primates were scarce. Transgenic human-ACE2-expressing mice were highly sought after, but their expression was not physiologic and supply was greatly limited[36]. Unlike the other two, the Syrian hamster model and ferret models were both more commonly accessible and appeared to simulate human SARS-CoV-2 infection to an acceptable level.

It's been well known that SARS-CoV-2 could be transmitted between animals that were physically separated. A ferret study found that SARS-CoV-2 can be transmitted between ferrets up to 1 meter apart, although this may be the result of fur, bedding, or other large particles that were blown from one cage to the other[37]. But it took further study to investigate which routes of transmission were greater contributors. One Syrian hamster study investigated three routes of transmission: intranasal, aerosol, and fomite, and concluded that all three resulted in seroconversion of sentinel hamsters by day 14 (N = 12). In a follow-up study, 8 additional sentinel animals were introduced to the soiled cages of intranasally infected animals, and 4 of 8 seroconverted. Hamsters infected intranasally and with aerosol exposure experienced significantly greater disease burden and weight loss than fomite-exposed hamsters[38].

Due to biological differences between humans and animal models, it is unclear what role fomites play in SARS-CoV-2 transmission in humans. However, animal studies do give credence to the possibility that surface transmission occurs between humans but produces minor effects when compared to respiratory routes of transmission.

Disinfectants, disinfection, and handwashing

Several factors impact transfer to and from fomites. First, fomite as viable transmission source requires both transfer to and transfer from a surface within a defined time. Second, transfer from surfaces to humans or to an intermediate host is only important if the virus is viable and not a nucleic acid fragment found by PCR. Third, enough viable virus (measured by viral load or cycle threshold) has to survive this process. The process is complex: human to surface to hand to upper respiratory passage. Only a fraction of infecting virus-containing droplets in a cough or a sneeze are likely to settle on a specific surface or transfer from surface to hand, and subsequently to mucous membranes, causing infection.

There are effective disinfectants, disinfection, handwashing and cleaning processes for rooms, handrails, and corridors. There are personal and institutional hygiene practices. With this in mind, there is still scant literature regarding handwashing and disinfection effectiveness, and how it differs between organisms (i.e. MRSA, VRE, C. difficile, norovirus, and coronaviruses. There is also the nature of the surface characteristics (i.e. wood, metal, paper), and ambient conditions of temperature, and humidity[39].

Since little work has been done with SARS-CoV-2, other enveloped viruses may be a better comparison than bacteria such as Staphylococcus or Pseudomonas. Norovirus, for example, has been extensively studied. Baker used PCR to access the transfer of norovirus from contaminated fecal material via fingers and cloths to hand-contact surfaces. He found that norovirus was consistently transferred via the fingers to melamine surfaces and from there to other typical hand-contact surfaces, such as taps, door handles and telephone receivers, seven clean surfaces in total. With the exception of fecal soiling, he found that detergent-based cleaning with a cloth to produce a visibly clean surface consistently failed to eliminate norovirus contamination.

In situations in which an individual does not have consistent access to soap and water, CDC, WHO, and FDA recommend, for the general public, the use of hand sanitizers containing at least 60% alcohol to reduce microbial burden[40,41]. In vitro studies revealed that hand sanitizers containing 60%-80% ethanol demonstrated 4-6 log reductions in 15-30 seconds against bacterial and fungal species[42]. Alcohol-based sanitizers have been shown to deliver rapid bactericidal activity toward several bacterial pathogens in addition to activity against both enveloped and non-enveloped viruses, including influenza A virus, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-1), Middle Eastern Respiratory Syndrome (MERS) coronavirus, Ebolavirus, Zikavirus, and SARS-CoV-2[43,44]. Handwashing even with soap for 20 seconds, removes sebum, sweat, and microflora from hands while increasing pH and hydrophobicity. Handwashing is effective in preventing certain hospital-associated infections, especially MRSA, C.difficile, norovirus, and vancomycin-resistant enterococcus (VRE) with less data on influenza and even less on SARS-CoV-2.

Another route of possible transmission involves wastewater. SARS-CoV-2 may show up in wastewater for varying periods, but there is no clear evidence it is transmitted person-to-person by this route. This may be similar to PCR positivity on conventional surfaces as described.

Conclusions

We don't know if some variants enhance surface viability more than others, and cause subsequent augmented fomite transmission, as a lack of adequate sequencing had precluded these studies. Will better hand toilet hygiene cut down on wastewater fecal exposure and surface transmission? The inadequtely studied timing, duration, temperature, and quantity of exposure to a surface from an infected individual might be critical in determining the degree of transmission.

It's been estimated by gene sequencing that anywhere from 1-20% of SARS-CoV-2 spreaders may cause 80% of cases[45]. This so-called "Pareto Principle" is getting backing for SARS-CoV-2 transmission. Three studies by Abbott, Miller, and Adam, using three different patient cohorts, showed that a small percent of infections account for a large proportion of spread.

Transmission due to superspreaders and superspreader events have been poorly studied, and are probably multifactorial, especially if there is an outdoor, colder temperature component. The specific contribution of surfaces in this setting has not been adequately studied due to the perceived dominance of respiratory spread by "exchanged air". Further experiments using sequencing and quantification of live virus or cytopathic effect will be helpful especially in small outbreak serttings.

What is the disinfecting role of enzymes such as DNAses on human skin surfaces? Studies on influenza A inactivation on skin suggest that skin appears to have antiviral properties that cause rapid inactivation of viruses on human hands compared to inanimate surfaces[46]. The relevance to fomite transmission here has to be worked out.

There are implications of overdoing handwashing and disinfection. This includes excessive irritation to the skin, the personnel needed, the cost of materials, and the added exposure indoors for those doing the disinfection in a potentially contaminated closed environment that might lead to added respiratory transmission.. Aiello determined the value of hand hygiene for influenza or influenza-like illness prevention, and found "handwashing habits were the same in both face mask–only and control groups, which suggests that mask use alone may provide a reduction in respiratory illness regardless of handwashing practices." Thus, handwashing is important but may be more important in preventing influenza and other respiratory viruses than SARS-CoV-2.

Is SARS-CoV-2 spread primarily by large droplets or by small-particle aerosols? This may well be relevant to fomite transmission. Alford noted that the more likely the virus is transmitted by large

droplets, the more likely hand hygiene will reduce transmission. Hand hygiene may not be beneficial if small particle aerosol is the main route of transmission [47-48].

Sequencing, culture, and viral load measurements of surfaces have been inadequate. In all published definitive outbreaks fomite transmission could not be conclusively proven as the sole or primary vehicle of transmission.

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Table 1: Persistence of SARS-CoV-2 on Surfaces with Starting Viral Load

Surface or fomite	Viral Load (TCID50/mL [log10])	Persistence	Time of complete decay	Temp (°C)	Humidity	Reference
Plastic	5	3 d	4 d	NG	NG	van Doremalen et al. (2020)
Plastic (polystyrene)	4.6	58 hr	5 d	25	45%-55%	Hirose et al. (2020)
Plastic	8-Jul	4 d	7 d	22	65%	Chin et al. (2020)
Copper	5	4 hr	8 hr	NG	NR	van Doremalen et al. (2020)
Stainless steel	5	3 d	4 d	NG	NR	van Doremalen et al. (2020)
Stainless steel	8-Jul	4 d	7 d	22	65%	Chin et al. (2020)
Stainless steel	4.5	84 hr	5 d	25	45%-55%	Hirose et al. (2020)
Glass	8-Jul	2 d	4 d	22	65%	Chin et al. (2020)
Borosilicate glass	4.1	86 hr	10 hr	25	45%-55%	Hirose et al. (2020)
Cloth	8-Jul	1 d	2 d	22	65%	Chin et al. (2020)
Surgical Mask-outer layer	8-Jul	7 d	NR	22	65%	Chin et al. (2020)
Surgical Mask-inner layer	8-Jul	4 d	7 d	22	65%	Chin et al. (2020)
Paper	8-Jul	30 min	3 hr	22	65%	Chin et al. (2020)
Tissue paper	8-Jul	30 min	3 hr	22	65%	Chin et al. (2020)
Banknote paper	8-Jul	2 d	4 d	22	65%	Chin et al. (2020)
Cardboard	5	1 d	2 d	NG	NR	van Doremalen et al. (2020)
Wood	8-Jul	1 d	2 d	22	65%	Chin et al. (2020)
Human skin	4.1	9 hr	10 hr	25	45%-55%	Hirose et al. (2020)

Table 2: Detection of SARS-CoV-2 RNA on Surfaces and Viral Culture in Laboratory and Hospital settings

Setting	Surface or fomite	PCR Technology	PCR Target	Cycle Threshold Value (Ct)	Total PCR Swabs	Positive PCR Swabs	Percentage	Viral culture results	Reference
BSL-2 Laboratory	Building Handles/Buttons	qRT-PCR	ORFab1, N	40	16	0		ND	Lv et al. 2020
BSL-2 Laboratory	Building Handles/Buttons	ddPCR	ORFab1, N	40	16	2	12.5%	ND	Lv et al. 2020
BSL-2 Laboratory	Laboratory Instruments	qRT-PCR	ORFab1, N	40	25	0		ND	Lv et al. 2020
BSL-2 Laboratory	Laboratory Instruments	ddPCR	ORFab1, N	40	25	7	28.0%	ND	Lv et al. 2020
BSL-2 Laboratory	Personal Protective Equipment	qRT-PCR	ORFab1, N	40	14	0		ND	Lv et al. 2020
BSL-2 Laboratory	Personal Protective Equipment	ddPCR	ORFab1, N	40	14	4	28.6%	ND	Lv et al. 2020
Hospital	Patient Isolation Rooms	rRT–PCR	RdRp, E	35	88	15	17.0%	8 cultures showed some cytopathic effect	Ahn et al. 2020
Hospital	Personal Protective Equipment	qRT-PCR	-	40	9	0		No cytopathic effect observed	Wang et al. 2020
Hospital	Objects	qRT-PCR	-	40	36	0		No cytopathic effect observed	Wang et al. 2020
Hospital	Patient Rooms	RT-PCR	RdRp, E	-	26	2	7.7%	No cytopathic effect observed	Colaneri et al. 2020
Hospital	Patient Isolation Rooms	RT-PCR	E	39.2	163	121	74.2%	1 culture showed some cytopathic effect	Santarpia et al. 2020
Personal Environment	Patient Home	RT-PCR	ORFab1, N	37	259	13	5.0%	ND	Luo et al. 2020
Personal Environment	Patient Hotel	RT-PCR	ORFab1, N	37	113	6	5.3%	ND	Luo et al. 2020
Personal Environment	Patient Car	RT-PCR	ORFab1, N	37	5	1	20.0%	ND	Luo et al. 2020

Hospital	Toilet Area	RT-PCR	RdRp, E	-	5	3	60.0%	ND	Ong et al. 2020
Hospital	Personal Protective Equipment	RT-PCR	RdRp, E	-	10	1	10.0%	ND	Ong et al. 2020
Hospital	Patient Isolation Rooms	RT-PCR	ORFab1, E	Median 25.69	102	48	47.1%	ND	Chia et al. 2020
Hospital	Toilet Area	RT-PCR	ORFab1, E	Median 25.69	17	5	29.4%	ND	Chia et al. 2020
Hospital	Air Vents	RT-PCR	ORFab1, E	Median 25.69	5	3	60.0%	ND	Chia et al. 2020
Hospital	Patient Wards	qRT-PCR	ORFab1, N	38	122	2	1.6%	No cytopathic effect was observed	Ge et al. 2020
Hospital	Objects	RT-PCR	ORFab1, N	40	431	60	13.9%	ND	Ye et al. 2020
Hospital	Personal Protection Equipment	RT-PCR	ORFab1, N	40	195	25	12.8%	ND	Ye et al. 2020
Hospital	ICU Ward	qRT-PCR	ORFab1, E	Median 31.22	60	6	10.0%	No cytopathic effect was observed	Ong et al. 2020
Hospital	Pantry	qRT-PCR	ORFab1, E	Median 31.22	15	2	13.3%	No cytopathic effect was observed	Ong et al. 2020