Stability and transmissibility of SARS-CoV-2 in the environment

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Abstract
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing the ongoing global coronavirus disease 2019 (COVID-19) pandemic, is believed to be transmitted primarily through respiratory droplets and aerosols. However, reports are increasing regarding the contamination of environmental surfaces, shared objects, and cold-chain food with SARS-CoV-2 RNA and the possibility of environmental fomite transmission of the virus raises much concern and debate. This study summarizes the current knowledge regarding potential mechanisms of environmental transmission of SARS-CoV-2, including the prevalence of surface contamination in various settings, the viability and stability of the virus on surfaces or fomites, as well as environmental factors affecting virus viability and survival such as temperature and relative humidity. Instances of fomite transmission, including cold-chain food transmission, and the importance of fomite transmission in epidemics, are discussed. The knowledge gaps regarding fomite transmission of SARS-CoV-2 are also briefly analyzed.

KEYWORDS
cold-chain transmission, environmental stability, fomite transmission, SARS-CoV-2, surface contamination, survivability

1 INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, family Coronaviridae, genus Betacoronavirus, species severe acute respiratory syndrome-related coronavirus) is the causative agent of coronavirus disease 2019 (COVID-19). SARS-CoV-2 is highly contagious as evidenced by its spread to nearly all countries worldwide within a very short time.1 However, the viral determinants for the high transmissibility of SARS-CoV-2 are still unclear, and routes by which the virus can effectively spread through the population remain debating.

Respiratory viruses are transmitted between individuals when virus is released from the respiratory tract of infected individuals and is transferred to the environment, leading to infection of the respiratory tract of exposed and susceptible people.2 It is recognized that respiratory viruses spread via four transmission routes: droplet, aerosol, direct contact, and indirect transmission.3,4 SARS-CoV-2 was initially recognized to transmit mainly via respiratory droplets from an infected host. Aerosol transmission of SARS-CoV-2 was subsequently proven to be the predominant transmission mode.4-6 Transmission through droplets and aerosols are both classified as airborne transmission.3 Droplets and aerosols are conventionally distinguished by size (5 μm), delineating distinct characteristics such as dispersion efficiency, residence time in the air, and deposition patterns along the human respiratory tract.5 Direct contact transmission refers to direct virus transfer from an infected to a susceptible individual
(e.g., via contaminated hands), and indirect transmission occurs via contaminated environmental surfaces or fomites that serve as vectors for virus transmission.\textsuperscript{2,3} Direct transmission of SARS-CoV-2 has been confirmed after tracing case clusters. However, the role of indirect SARS-CoV-2 transmission through intermediate surfaces or fomites remains under discussion, with considerable controversy.\textsuperscript{7,8}

For contaminated surfaces or fomites to play a role in transmission, a respiratory pathogen must be shed into the environment, possess the capacity to survive on surfaces, be transferred to hands or other objects at a concentration above the minimum infective dose, and be able to initiate infection through contact with the eyes, nose, mouth or by re‐inhalaion into the respiratory tract.\textsuperscript{2,9} In this study, we review current new evidence on these topics, including the shedding of SARS-CoV-2, contamination of environmental surfaces in various settings, stability and viability of SARS-CoV-2 on environmental surfaces and objects including cold foods, and current evidence for and against the importance of fomite transmission. We aim to summarize the findings regarding the transmissibility of environmental SARS-CoV-2 and relative importance of indirect environmental transmission in COVID‐19 spread. We also identify ongoing research gaps and opportunities. The information provided herein will help in establishing practical and effective protocols to interrupt indirect environmental transmission of SARS-CoV-2 and mitigate its associated risks.

2 SHEDDING AND DISSEMINATION OF SARS-CoV-2 FROM INFECTED INDIVIDUALS

Viral shedding is the first step of virus transmission from infected to susceptible individuals. Respiratory virus shedding occurs after airway epithelial cells excrete virions to extracellular fluid in the respiratory tract, especially the upper respiratory tract, through sneezing, breathing, talking, singing, coughing, and other aerosol‐generating activities.\textsuperscript{2}

Studies show that shedding of SARS-CoV-2 can begin before symptom onset,\textsuperscript{10–13} peak in the first week of illness,\textsuperscript{12,13} in contrast to SARS and MERS but similar to influenza, COVID‐19 exhibits high viral shedding at an early stage of infection, when virus carriers display no or mild symptoms.\textsuperscript{14,15} Most studies attempting virus isolation from respiratory samples have also successfully cultured viable virus within the first week of illness whereas live virus is rarely isolated from patients beyond 9 days of symptomatic illness.\textsuperscript{15} When SARS-CoV-2 RNA screening was carried out in communities, more than half of the residents with positive test results were asymptomatic at the time of testing.\textsuperscript{16–19} The rapid dissemination of COVID‐19 may be attributed to the existence of presymptomatic and asymptomatic patients with active virus shedding, as these patients are harder to identify and control. The relative contribution of asymptomatic transmission was much higher in regions where case‐based interventions were stringent.\textsuperscript{20}

The viral load in infected individuals is an important factor affecting their transmissibility. Studies found that the viral load in patients’ nasopharyngeal swabs is positively correlated with viral loads emitted in both droplets and aerosols, and with environmental contamination.\textsuperscript{21–23} Multivariate analyses have identified that viral load (viral RNA) larger than $10^7$ copies/ml (OR = 14.7) is independently associated with isolation of infectious virus from respiratory tract samples.\textsuperscript{11} Numerous studies have demonstrated that higher SARS-CoV-2 viral load in the upper airway of an infected person is associated with increased infectivity.\textsuperscript{24–26}

Using quantitative RT‐PCR assay, Pan et al. determined viral loads in sputum and throat swab samples of 80 patients. The median viral load was $7.52 \times 10^5$ copies/ml and $7.99 \times 10^4$ copies/ml; the highest load was $1.34 \times 10^{11}$ copies/ml and $>10^8$ copies/ml, respectively.\textsuperscript{12} Studies have found that SARS-CoV-2 viral load in respiratory samples is similar in symptomatically and asymptotically infected persons. Yang et al. showed that the distribution of SARS-CoV-2 viral load in 1405 asymptomatic individuals fits under a log‐normal distribution centered around the mean of $2.1 \times 10^7$ virions/ml, while the highest viral load found in saliva was $6.1 \times 10^{12}$ copies/ml.\textsuperscript{27} Comparing with H1N1 influenza A, the standard deviation of the overall respiratory viral load distribution for COVID‐19 was significantly higher, showing that the heterogeneity in viral load was indeed broader for SARS-CoV-2 infected persons.\textsuperscript{28} This indicates that some patients shed virions at very high concentrations, for example, the highest viral load found in H1N1 influenza A patients was $1 \times 10^{15}$ copies/ml, while the highest viral load in SARS-CoV-2 infected individuals can reach $6.1 \times 10^{12}$ copies/ml.\textsuperscript{28} Approximately 2% of individuals with SARS-CoV-2 have a viral load $>10^{10}$ copies/ml.\textsuperscript{27} Further analysis found that just these 2% of individuals carry 90% of the virions circulating within communities, serving as viral “super carriers.”\textsuperscript{27}

The heterogeneity in transmissibility among infected individuals may be associated with dissimilarity of viral shedding. The super‐carriers shed virions at very high concentrations, making them highly infectious and more likely to contaminate the environment. Analyses of such individuals suggest heterogeneity associated with super‐spreading events as an intrinsic viral factor facilitating greater overdispersion of SARS-CoV-2 during the COVID‐19 pandemic than influenza A during the 2009 influenza pandemic.\textsuperscript{27,28}

In addition to respiratory tract specimens, viable SARS-CoV-2 has been detected in other biological samples, including stool and urine.\textsuperscript{29} The detection of viable SARS-CoV-2 in diverse bodily fluids and secretions indicates various other potential sources of environmental contamination.

3 ENVIRONMENTAL CONTAMINATION OF SARS-CoV-2

SARS-CoV-2 environmental contamination occurs through the release of nasal mucus, sputum, saliva, and other biological fluids by infected individuals into their surroundings. Infected individuals can contaminate surfaces and objects to create fomites by either shedding onto their hands and then touching a surface or by expelling respiratory particles when coughing, speaking,
or even breathing, which then fall onto a surface.\textsuperscript{6,30,31} Aerosolized droplets from an infected person can easily settle and persist on immediate surfaces for extended periods, especially in poorly ventilated indoor spaces with a continual affluence of people.\textsuperscript{6,32}

### 3.1 | Presence of SARS-CoV-2 in clinical settings

Studies have found extensive SARS-CoV-2 contamination of surfaces in hospitals dedicated to patients with COVID-19. In airborne infection isolation rooms where COVID-19 patients were hospitalized in Singapore, 56.7% of rooms were found have at least one contaminated environmental surface, and high-touch surface contamination was found in the rooms of 10 (66.7%) of 15 patients during the first week of their illness.\textsuperscript{33} In a study at six acute care hospitals in Toronto, 125 (26%, 125/474) surface samples from 42 (57%, 42/74) patient rooms were positive for SARS-CoV-2 RNA.\textsuperscript{34} In another study, swabs taken from hospital air exhaust outlets yielded positive test results, suggesting that small virus-laden droplets may be displaced by airflows and deposited on equipment, such as vents.\textsuperscript{22}

Some patients with SARS-CoV-2 infection appear to cause more extensive environmental contamination than others. In addition to higher viral load in respiratory samples, multivariable analysis indicates that hypoxia at admission, higher Charlson comorbidity score, and the time from illness onset to the sampling date are significantly associated with the presence of SARS-CoV-2 RNA on surface samples.\textsuperscript{23,34}

In outpatient health care facilities, surface contamination has also been found, including on dental chairs, sinks, keyboards, ophthalmoscopes, laboratory equipment, and door handles. Places with greater contact had higher positive rates.\textsuperscript{30,33} Toilet bowl and sink samples have tested positive for SARS-CoV-2, suggesting possible viral shedding in stool.\textsuperscript{22}

### 3.2 | Presence of SARS-CoV-2 on surfaces in households

Households have been important sites of transmission throughout the COVID-19 pandemic. SARS-CoV-2 has been detected in the household environment of individuals with COVID-19, notably on surfaces in areas where there is close, prolonged contact with persons who have recently tested positive for SARS-CoV-2.\textsuperscript{35,36} SARS-CoV-2 RNA appears to be able to sustain on environmental surfaces for a long time. One study found that a month after symptom subsidence, 46% of surfaces in the home had detectable levels of SARS-CoV-2.\textsuperscript{36} Some surfaces found to be SARS-CoV-2 positive, such as home HVAC filters, floors, and the top of televisions, are common reservoirs for dust build-up and might be infrequently touched.\textsuperscript{36} In contrast to hospitals and health care settings, there are limited data on environmental contamination with SARS-CoV-2 in households.

### 3.3 | Prevalence of SARS-CoV-2 on high-touch surfaces in community settings

During the ongoing pandemic, emerging evidence shows that SARS-CoV-2 is present in different community environments. Longitudinal monitoring of SARS-CoV-2 RNA on high-touch surfaces was carried out in Massachusetts, United States during a COVID-19 outbreak. SARS-CoV-2 RNA was found on various surfaces in 10 of 12 locations sampled; the overall positive rate among surface samples was 8.3% (29/348).\textsuperscript{37} In a densely populated urban area of Brazil, SARS-CoV-2 RNA was detected in 5.3% (49/933) of swab samples collected from public surfaces, including metal and concrete, and in distinct places, mainly around hospital care units and public squares.\textsuperscript{38}

The viral RNA concentrations detected on surfaces in both studies ranged between <0.1 and 40 gc/cm\textsuperscript{2} (gene copies per cm\textsuperscript{2}) and 2.5-102 gc/cm\textsuperscript{2}, respectively.

SARS-CoV-2 viral RNA has also been detected on environmental surfaces in playgrounds,\textsuperscript{39} supermarkets,\textsuperscript{40} cruise ship surfaces,\textsuperscript{41} public transport vehicles,\textsuperscript{42} tourist recreational facilities,\textsuperscript{43} retail stores, and workplaces.\textsuperscript{37} Surfaces in public areas that are exposed to human crowding or that are frequently touched by the hands (e.g., ATMs in public facilities) are frequently found to be positive for SARS-CoV-2 RNA contamination.\textsuperscript{30}

### 3.4 | Presence of SARS-CoV-2 in cold foods

During the pandemic, workers in labor-intensive workplaces such as seafood processing and food manufacturing plants or slaughterhouses, have had high COVID-19 infection rates.\textsuperscript{44,45} Processed foods and their packaging can be contaminated by infected workers with mild or no symptoms through falling respiratory droplets or hand contact. SARS-CoV-2 RNA has been detected many times in cold-chain aquatic products imported to China and their packaging materials.\textsuperscript{46} In September 2020, the contamination status of imported frozen seafood from a cargo ship in Qingdao was investigated; the positive rate of SARS-CoV-2 RNA in frozen seafood was 11.53% (106/919).\textsuperscript{47}

### 4 | Viability and Stability of SARS-CoV-2 in the Environment

Assessment of the risks posed by SARS-CoV-2 on surfaces requires data on viability and stability of the virus on environmental surfaces as well as how virus viability is affected by environmental variables, such as air temperature and relative humidity.

#### 4.1 | Viability of SARS-CoV-2 isolated from surface samples in natural settings

Many studies have attempted to assess the viability and infectivity of SARS-CoV-2 present on surfaces or objects. Using cell culture
TABLE 1 Viable severe acute respiratory syndrome coronavirus 2 isolated from various surfaces

| Settings                       | Sample source                                                                 | Culture cell | Virus Ct (or concentration) of the swab from surface | References |
|--------------------------------|-------------------------------------------------------------------------------|--------------|-----------------------------------------------------|------------|
| Patient room                   | Bathroom door, bed and switch, phone, table and chair, toilet and sink        | Vero E6      | NA                                                  | [34]       |
| Household                      | Nightstand                                                                    | Vero CCL-81  | 26.4                                                | [35]       |
| Quarantine unit                | Windowsill                                                                    | Vero E6      | 0.65 copies/μl                                       | [48]       |
| Patient room                   | Windowsill                                                                    | Vero E6      | >102 copies/μl                                       | [48]       |
| Negative-pressure isolation rooms| Endotracheal tube, floor, bed rails, bedsheet, ambulance mask/NIV, bedside table, remote controller | Vero E6      | 30.9-34.3                                           | [49]       |
| Imported food                  | Frozen cod package                                                            | Vero E6      | NA                                                  | [50]       |

Abbreviations: Ct, cycle threshold of real-time PCR; NA, not available; NIV, noninvasive ventilation.

systems, viable SARS-CoV-2 virus has been isolated from various environmental settings, as well as from frozen food packaging (Table 1). These studies provide direct evidence supporting SARS-CoV-2 survival in fomites for a length of time consistent with the possibility of onward transmission.

4.2 | Stability of SARS-CoV-2 on skin, environmental surfaces, and in cold foods

4.2.1 | Stability of SARS-CoV-2 on the skin

Human hands are considered critical vectors in direct contact and indirect transmission of SARS-CoV-2. To understand how long SARS-CoV-2 can remain viable on the hands and evaluate the importance of hand hygiene, two experimental studies evaluated SARS-CoV-2 stability on the skin. In one study, 50 μl of SARS-CoV-2 virus at a starting titer of 4.5 ± 0.5 log10 PFU (plaque-forming unit) was deposited onto swine skin with the hair removed. The virus remained viable on skin samples for 8 h at 37°C, at least 96 h at 22°C, and for 14 days at 4°C. In another study on human skin, Hirose et al. compared the stability of SARS-CoV-2 and influenza A virus and found that SARS-CoV-2 could survive approximately 9 h on skin, significantly longer than the survival time of influenza A virus (approximately 1.8 h), indicating that the stability of SARS-CoV-2 is markedly higher. However, the survival and half-life times of both SARS-CoV-2 and influenza A virus were significantly shorter on human skin than on other surfaces, indicating that the hands are less suitable for virus survival.

4.2.2 | Stability of SARS-CoV-2 on inanimate surfaces

Several in-vitro studies have evaluated the survivability of SARS-CoV-2 when inoculated onto dry surfaces and shown that SARS-CoV-2 is relatively stable. Using large initial viral concentrations and under optimized environmental conditions, SARS-CoV-2 can remain viable on solid surfaces such as plastic, glass, stainless steel, and polymer banknotes for up to 28 days at 20°C (Table 2).

Some researchers have controverted the results because of much higher amount of virus used in these studies than that in actual contamination. Considering that a portion of infected individuals have a viral load >10^10 copies/ml in saliva, and the most infectious saliva and cough specimens exhibited viral loads approaching 10^6 PFU/ml, the initial viral concentrations used in these studies are plausible. In fact, SARS-CoV-2 shows an exponential decay in virus titer across all experimental conditions, as indicated by a linear decrease in the log10 TCID50/ml (50% tissue-culture infectious dose per ml) on surfaces over time. When decimal reduction time (D value), the time of a 1-log reduction in viability (or infectivity), was used to gauge the stability of SARS-CoV-2, the virus inactivation rate on environmental surfaces was independent of initial loading. Paton et al. compared the viability of SARS-CoV-2 on stainless steel coupons between two starting titers, and found that the virus could be recovered after 4 days at the lower titer of 4 × 10^3 PFU/ml and 7 days at the higher titer of 4 × 10^5 PFU/ml, suggesting that the virus can remain viable on stainless steel for several days even with a lower initial viral load. Sun et al. also reported that at 22°C the virus with a low starting titer of 10^3 TCID50 on stainless steel and plastic bag maintained infectious for 3 days. These findings suggest high stability of SARS-CoV-2 on certain surfaces.

A comparison of SARS-CoV-2 and SARS-CoV-1 showed that these viruses have similar levels of stability on dry surfaces under the same experimental circumstances. However, the survival and half-life of SARS-CoV-2 was significantly longer than that of influenza A virus across different inanimate surface types, suggesting that SARS-CoV-2 is more stable. Therefore, SARS-CoV-2 may pose a higher risk of transmission through fomites than influenza A virus.

4.2.3 | Stability of SARS-CoV-2 in cold foods

Unlike regular surfaces or fomites, cold foods are generally characterized by conditions that promote viral particle survival, such as high protein and moisture levels, temperatures below 4°C, and a lack of exposure to direct sunlight. Numerous studies have found that
in cold foods contaminated with SARS-CoV-2 RNA, the viability and stability of virions within the foods, as a marker for transmission, raises much concern.

A laboratory study demonstrated that SARS-CoV-2 on contaminated fish with a titer of $3.16 \times 10^6$ TCID50/ml can survive for 2 days at 25°C and for 8 days at 4°C.59 In an experiment involving contamination of pork, beef, and salmon meat with low virus concentrations close to the actual concentration in respiratory secretions, SARS-CoV-2 retained viability for 3 days at 4°C and for 7 days at −20°C.63

Similar to raw meats and seafood, deli foods that are high in protein, fats, and moisture can maintain infectivity of SARS-CoV-2 for up to 3 weeks when stored at refrigeration temperature (4°C).64,65 However, processed meat, such as salami, and some fresh produce have exhibited antiviral effects.65

Under refrigeration (4°C) and freezing (−10°C to −80°C) conditions, the virus can remain infectious for more than 21 days in some foods.59,66 Because under globalized logistics networks, imported and exported cold foods are usually transported in a low-temperature (e.g., 0°C to −4°C) environment from one country or region to another within a few days, contaminated food may serve as a vector for international transmission of SARS-CoV-2.

### 4.3 Environmental factors affecting the viability of SARS-CoV-2

The survival and persistence of SARS-CoV-2 on surfaces appears to be influenced by many environmental factors, of which the following are particularly important.

1. **Types of surface and medium or metrics**

   The stability and viability of SARS-CoV-2 on surfaces is highly dependent on surface materials (Table 2). In general, coronaviruses are inactivated more rapidly on porous materials (i.e., containing pores/cavities) than nonporous materials. Longer persistenre is observed on less absorbent or hydrophobic porous surfaces, particularly hydrophobic synthetic items, such as surgical masks, compared with hydrophilic natural fibers like cotton. It is hypothesized that dryness accelerates the inactivation of SARS-CoV-2 on paper and other porous solids; conversely, droplets of water remaining on waterproof surfaces protects the virus from dryness.54,67

   Experimental studies show that the stability of SARS-CoV-2 on surfaces is also affected by its surrounding matrix; the suspending medium used to dry the virus onto surfaces is another important factor influencing survival times.53,68 Several studies have demonstrated that the addition of a moderate amount of protein, like bovine serum albumin or mucus, to the inoculating suspension when loading onto a surface increases SARS-CoV-2 infectivity, indicating that additional protein provides a protective effect for the virus during and after drying on
surfaces.\textsuperscript{55–58} These results suggest that a protein-rich medium, like airway secretions, could protect the virus when it is expelled and may enhance its persistence and transmission via contaminated fomites.

(2) Temperature

Temperature is a critical environmental factor that affects SARS-CoV-2 survival. Like other known viruses, the stability of SARS-CoV-2 either in solution or on a dry surface is inversely correlated with temperature.

The half-life of SARS-CoV-2 infectivity is 1.7–2.7 days at 20°C and decreases to a few hours at 40°C on common surfaces.\textsuperscript{57} SARS-CoV-2 can persist for 14 days in Dulbecco’s modified Eagle medium at 4°C whereas the persistence time is dramatically reduced to 10 min and 1 min when the temperature is increased to 56°C and 70°C, respectively.\textsuperscript{58} Because viruses are sensitive to temperature, heating is one method used for virus inactivation, including for SARS-CoV-2.

Using low virus concentrations close to the actual concentration of viral particles in the environment, SARS-CoV-2 has been shown to be more stable and infectious after storage at −20°C than at 4°C.\textsuperscript{69} Infectious SARS-CoV-2 can persist for at least 60 days on cold-chain food packaging (kept at less than −18°C).\textsuperscript{70} These foods are produced, transported, stored, and sold in a cold chain to keep them fresh, which also helps the virus to retain its viability and infectivity for a longer time.

(3) Humidity and moisture status

In contrast to dry surfaces, moist surfaces are more likely to be positive for SARS-CoV-2 RNA, and the duration of environmental surface contamination is associated with the moisture status of the sampling site.\textsuperscript{23,64} Studies have found that water cups are the most frequently contaminated site in the hospital rooms of patients with COVID-19, and SARS-CoV-2 RNA can be detected in the water cup in room-temperature environments for 48 days after the infected patient has left the room, suggesting that water in the cup may play an important role in virus persistence.\textsuperscript{23,70}

Relative humidity is associated with viability of airborne respiratory viruses. Biryukov and colleagues\textsuperscript{71} found that SARS-CoV-2 on dry surfaces can decay more rapidly with increased humidity. However, contradictory findings have been obtained regarding SARS-CoV-2 viability and relative humidity. One study found that the rate of viral decay was most rapid at 65% relative humidity and slower with either lower (40%) or higher (75%) humidity.\textsuperscript{72} Further studies found that there is an interaction effect between temperature and humidity on viral viability on surfaces. When the relative humidity was increased from 20% to 80%, the virus half-life changed from 18.6 to 6.3 h at room temperature (24°C) and from 8.9 to 1.0 h at 35°C.\textsuperscript{71} The rate of inactivation increases with increased temperature and shows a U-shaped dependence on relative humidity.\textsuperscript{72}

5 | OCCURRENCE OF SARS-CoV-2 INFECTIONS THROUGH INDIRECT TRANSMISSION

Extensive surface contamination of SARS-CoV-2 around asymptotically and symptomatically infected individuals has been documented, and increasing evidence shows that SARS-CoV-2 can remain viable on surfaces, from several hours to 21 days. Thus, contaminated surfaces and fomites may result in exposing a larger number of susceptible individuals to potential infection.

5.1 | Fomite transmission estimated using mathematical models

Several mathematical model-based epidemiological investigations have evaluated the relative importance of different modes of virus transmission. Modeling of the Diamond Princess Cruise ship outbreak suggested that short-range (droplets), long-range (aerosols), and fomite transmission modes contributed to 35%, 35%, and 30% of infected cases, respectively, across the entire simulation period. The estimated contribution of fomite transmission before the start of quarantine on the cruise ship was higher than that after quarantine began.\textsuperscript{73} Higher relative risks associated with SARS-CoV-2 fomite transmission were also reported in studies modeling child daycare centers\textsuperscript{74} and hospital and health care settings.\textsuperscript{75,76} However, studies of the infection risk via fomites using different mathematical models have had surprisingly divergent outcomes, with extremely low substantial risk estimates being reported.\textsuperscript{37,77} This discrepancy could be explained by bias introduced from data on viral exposure and persistence generated in simulated laboratory conditions and those observed in naturally contaminated real-life scenarios.

5.2 | Fomite transmission demonstrated in animal experiments

Direct evidence for fomite transmission is still lacking because of difficulty in distinguishing between cases arising from fomite transmission and those involving droplet and aerosol transmission. A hamster model provided robust evidence to support fomite transmission, although airborne transmission was found to be more efficient. Hamsters were infected after being exposed to 40 μl of 8 × 10^4 TCID50 viruses in a propylene dish for 24 h.\textsuperscript{78} Hamsters exposed to fomite SARS-CoV-2 displayed delayed replication kinetics in the respiratory tract and less severe lung pathology in comparison with hamsters exposed via aerosol inoculation.\textsuperscript{78} Other studies using hamster models also demonstrated SARS-CoV-2 transmission via fomites in the absence of direct contact, droplets, and aerosols, in which naïve hamsters were placed in cages where infected hamsters had lived and became infected.\textsuperscript{79,80}
Rhesus macaques can be infected with SARS-CoV-2 through direct conjunctival inoculation but develop less severe pulmonary disease than macaques inoculated via an intra-tracheal route, implying that an extra-respiratory route of SARS-CoV-2 infection and hand contamination pose an increased risk of virus infection.81

5.3 | Occurrence of COVID-19 through fomite and cold-chain transmission

Because conventional epidemiologic studies cannot distinguish between competing transmission pathways (e.g., droplet, aerosol, direct, or fomite) acting simultaneously, reports on COVID-19 related to the transmission of SARS-CoV-2 from contaminated surfaces are rare.82,83 Even in the few instances that appear to have been caused by surface transmission, aerosol transmission cannot be ruled out, and debate continues regarding the importance of fomite transmission of SARS-CoV-2.7,8

However, several outbreaks and sporadic cases in China have been demonstrated to be associated with transmission from imported cold-chain foods (Table 3).46,50,84–86 The first outbreak speculated to originate from contaminated imported cold-chain foods occurred at Xinfadi Market in Beijing in June 2020. The index case emerged after 56 days with no community transmission in Beijing, and the possibility of contact with overseas personnel was ruled out based on epidemiological investigations. Subsequent field investigations and an on-site simulation experiment suggested that the virus spread from contaminated foods to humans in the market.84 In September 2020, an outbreak occurred among dock workers in Qingdao, Shandong Province.50 Apart from epidemiological evidence that the index case had no exposure to any COVID cases, more convincing evidence involved viable SARS-CoV-2 isolated from the outer packaging of frozen cod to which the workers were exposed.50 Similar connections have been found in re-emerged COVID-19 outbreaks in the Chinese coastal cities of Dalian, Tianjin, and Guangzhou (Table 3).

Investigation results documented the possibility that imported cold foods and their packaging can serve as vectors for the reintroduction of SARS-CoV-2 into areas with controlled transmission. The evidence from these outbreaks supports that cold-chain logistics transmission of SARS-CoV-2 is biologically plausible.

However, it has been nearly impossible to identify cases of infection via cold-chain food transmission during the pandemic when infections are primarily attributed to close-proximity transmission. Fomite transmission can be easily identified during the period of epidemic near-eradication, with the absence of explanatory source cases in the community.87 With the near elimination of SARS-CoV-2 in China during 2020–2021, it became possible to exclude transmission via close contact with a known case and to distinguish unusual transmissions from single cases.

6 | IMPLICATION OF SARS-CoV-2 INFECTIONS VIA INDIRECT TRANSMISSION AND KNOWLEDGE GAP

Although it is estimated that the transmission of SARS-CoV-2 via fomites is rare, the possibility of fomite transmission cannot be ruled out. The debate over fomite transmission has shifted to the implications of this transmission mode.7

6.1 | Implication of SARS-CoV-2 infections via indirect transmission

During 2020–2021, although most Western countries were gradually lifting their border controls and quarantine measures, the Western Pacific Region, including in China, retained the elimination strategy aiming for “zero COVID-19.” When stringent quarantine measures were implemented for travelers to control the introduction of infectious diseases, several outbreaks occurred in cities where COVID-19 was close to elimination via imported frozen foods or Table 3  COVID-19 outbreak or sporadic infection initiated by cold chain food

| Location, China | Starting date | Related cold chain food (COVID-19 RNA positive) | Period since the last infection (consecutive days) | References |
|-----------------|---------------|-----------------------------------------------|-----------------------------------------------|------------|
| Beijing         | June, 2020    | Imported salmon                               | 59                                            | [84]       |
| Dalian          | July, 2020    | Frozen seafood products                       | 111                                           | [85]       |
| Qingdao         | September, 2020| Frozen cod packages                           | 151                                           | [50]       |
| Tianjin         | November, 2020| Frozen pork packages                          | 125                                           | [86]       |
| Dalian          | December, 2020| Imported cold food                            | NA                                            | [46]       |
| Yingkou         | May, 2021     | Frozen cod                                    | NA                                            | [46]       |
| LiuAn           | May, 2021     | Frozen cod                                    | NA                                            | [46]       |

Abbreviation: NA, not available.
Another concern is that some items contaminated with the virus, such as food products, have been stockpiled in cold storage during the global pandemic. These frozen items will likely be thawed and consumed over the next years, releasing the viable virus and posing the risk of human re-infection.

6.2 Knowledge gaps in environmental transmission of COVID-19

The debate over the risks and control measures of fomite transmission is expected to continue until the mechanisms involved are fully understood. Among the many knowledge gaps regarding this transmission mode, the following are of greatest concern: (1) the way via which virus deposited on surfaces is re-transferred to humans is unknown. In addition to transferring virus from fomites to the hands and subsequently to mucous membranes of the mouth, nose, or eyes, there may be alternative routes via which the virus is transferred to humans from fomites. A plausible route could be via “aerosolized fomites,” in which live virus on surfaces is taken up into the air and inhaled. In living and workplace settings, contaminated objects can generate aerosols, such as when transporting and processing frozen foods. (2) The minimum infective dose required to cause an infection via a specific transmission mode is unknown. Recent studies report that respiratory tract samples from COVID-19 with only 14–30 PFU or a minimum infective dose as low as 1 TCID50 caused illness in Syrian hamsters. Nevertheless, it remains a challenge to identify the minimum infective dose of fomite transmission, making it difficult to quantitatively estimate the risks associated with exposure to fomites. (3) Emergence of the SARS-CoV-2 Omicron strain has raised concerns about whether its increased infectivity is owing to altered contamination/persistence on surfaces and/or a gain in airborne transmissibility. Currently, viral factors provide inadequate explanation for its high transmissibility. Further molecular epidemiologic data may help to address this question.

7 Conclusion

There is now extensive evidence supporting the contamination of surfaces and objects caused by individuals infected with SARS-CoV-2. SARS-CoV-2 showed high stability and viability in environment, surviving for hours to days depending on the surface, temperature, and humidity as key factors in viral survival. Studies have isolated viable viroms from contaminated surfaces, including dry surfaces and frozen fish. Experimental animal models proved that infections can occur via the fomite transmission route. More importantly, several outbreaks and sporadic cases in China have been demonstrated to be associated with transmission from imported cold-chain foods. It is worth noting for international community that indirect transmission of SARS-CoV-2 through fomite may constitute problems by posing the risks of long distance transmission, reintroducing the virus into an area that achieved local epidemic elimination, and extending the duration of the pandemic. Strengthening the inspection and quarantine of cold-chain foods from high-epidemic areas should be an effective measure for COVID-19 prevention. Personal protective measures including washing hands and regular disinfection practices should reduce environmental contamination and the possibilities of environmental transmission of the virus.

Author Contributions

Yansheng Geng and Youchun Wang conceived and wrote the manuscript. Youchun Wang contributed to the modification and revision of the manuscript. Both authors approved the submitted versions.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

Data are available on request from the authors.

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