GLOBAL SCIENCE LIBRARY

Frontiers in Infectious diseases and Microbiology

Review Article ISSN: 2771-1838

SARS Wars: The aerosols versus the fomites

Emanuel Goldman*

Department of Microbiology, Biochemistry & Molecular Genetics, Rutgers New Jersey Medical School, USA

Abstract

Early in the pandemic, there was great worry about SARS-CoV-2, the causative agent of COVID-19, spreading via fomites, that is inanimate surfaces and objects. People were disinfecting their mail, their groceries, and everything else, in the mistaken belief that this was the way to prevent transmission of the virus.

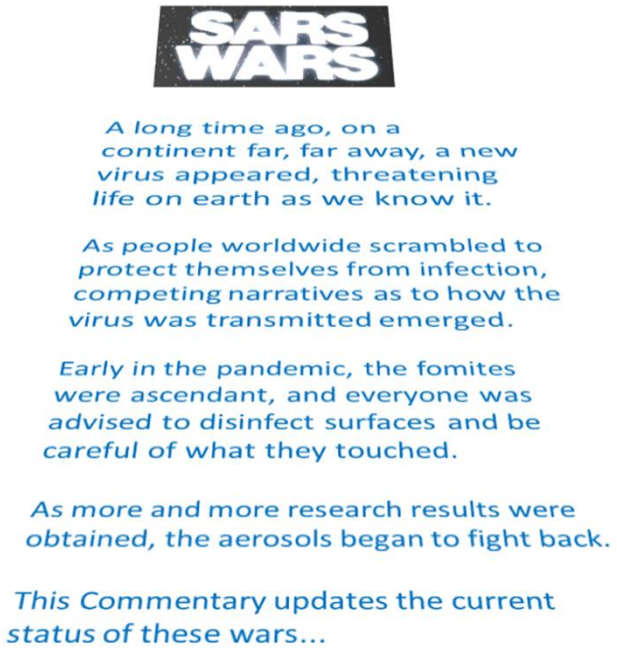
In July 2020, I published online a Comment in *Lancet Infectious Diseases* challenging this presumption. The title of the Comment was "Exaggerated risk of transmission of COVID-19 by fomites". The crux of the argument was that the concentrations of virus used were way too high in experiments showing long survival of the virus on surfaces. Since the virus decays with a defined half-life, the more you start with, the more half-lives you have to go through before reaching an endpoint of less than one infectious virus particle on the surface. In other words, the experiments that were the basis for concern about fomite transmission of COVID-19 were unrelated to real-world conditions.

It turns out to be even worse than I originally thought. Experiments recently published in *Applied and Environmental Microbiology* show that an enveloped virus, bacteriophage Phi6, protects itself from environmental decay at higher virus concentrations. Phi6 has been suggested for use as a non-pathogenic surrogate for SARS-CoV-2, which is also an enveloped virus. Therefore, the design flaw in experiments measuring surface survival of SARS-CoV-2 is not just that too much inoculum requires more half-lives to go through -- the larger inoculums extend the half-lives as well.

The *Lancet ID* Comment was picked up by the press. A columnist from the *Atlantic* coined the term "hygiene theater" in an interview about the *Lancet ID* Comment. Other research corroborated the assertions in the Comment, and finally, *Nature* posted an editorial citing the *Lancet ID* Comment, calling on Public Health agencies to emphasize aerosols and stop warning about fomites.

Nevertheless, publications continue to appear promoting fomite transmission as a risk. This article describes why these publications should not raise concern over the possibility of fomite transmission in the real world.

Graphic abstract



Part 1: The phantom menace

In keeping with the analogy to the popular Star Wars series of movies, part one of this article is entitled "The Phantom Menace" (which is also the title of episode 1 in the Star Wars series of films). The battle lines are drawn between fomites and aerosols in the quest to achieve scientific consensus on the mode of transmission of COVID-19.

Early in the pandemic, like everyone else, I was concerned with fomites (inanimate surfaces and objects) as sources of infection with this new disease. People were disinfecting groceries and the mail and anything else that may have come into their homes.

Public health authorities were pushing the notion that fomites were a menace. The World Health Organization website from March 29, 2020 [1], urged environmental cleaning and disinfection. They advised to avoid touching surfaces, to clean surfaces regularly with standard disinfectants, to carry an alcohol-based rub with you and use it often [1].

The United States Centres for Disease Control (CDC) likewise promoted this view. On April 8, 2020, the CDC website advised the public to provide tissues, no-touch trash cans, hand soap, alcohol-based sanitizer containing at least 60% alcohol, disinfectants, and disposable towels for workers to clean their work surfaces [2]. And on March 30, 2020, Healthline.com displayed this headline: "Here's How to Clean Your Groceries During the COVID-19 Outbreak" [3].

This is what we were dealing with early in the pandemic. But what was the scientific basis for these concerns about objects and surfaces? Why did the WHO and the CDC make these recommendations?

In April 2020, there wasn't a whole lot of literature yet on SARS-CoV-2, the causative agent of COVID-19. There was, however, considerable literature about the original SARS virus, renamed SARS-CoV-1, the virus that caused the epidemics of 2002, 2003, 2004. One paper from the time of the original SARS outbreak found a very long survival of the SARS virus on surfaces of six days [4]. But this paper used a very large titer of virus at the outset, 10^7, 10 million virus particles, which clearly is excessive.

Another paper even earlier with the original SARS virus reported a long survival of 4 days on surfaces, but similarly used a large input titer of a million, 10^6 infectious virus particles on the surface [5].

In March 2020, the New England Journal of Medicine published online a study that was very influential in shaping how the world approached fomites. This paper was titled "Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1." The authors reported survival of up to two days on surfaces and three days in aerosols that they generated in a laboratory [6]. But as was the case with the papers on the original SARS virus, they used fairly high titers of virus as their inoculum. The aerosols experiments used between 10^5 to 10^7, and 10^4 particles were used for the surfaces.

One good thing that they did in this paper was that they gave half-lives of the viruses on the various surfaces [6]. When a virus decays in the environment, it decays with a predictable half-life that varies depending on the surface, the virus, and other conditions. In this paper, they measured half-lives for both the original SARS virus and SARS-CoV-2, the COVID-19 virus. On copper, the virus was killed very quickly. That's been observed by others as well. On cardboard, they reported about a 3-hour half-life; on stainless steel, about a 6-hour half-life.

Scientists usually think of half-life in relation to radioactive decay: half of the decay takes place in the first half-life and then after that, each subsequent half-life removes half of what had been left after the previous decay.

The same applies to virus decay in the environment. With a half-life of about three hours for SARS-CoV-2 on cardboard, if you inoculate with 10,000 virus particles, it takes about 40 hours until you get less than one virus particle remaining. But if you inoculated with 50 virus particles, it would only take about 17 hours until you got less than one virus particle remaining. With SARS-CoV-1, the half-life on cardboard was about one hour, and so even with a 10,000-virus particle inoculum, the virus would be gone in half a day. The larger the inoculum, the longer virus will survive on the surface because you have more half-lives to go through.

So, what is the appropriate inoculum size? There wasn't anything in the literature in early 2020, and actually, there still isn't anything for SARS-CoV-2 for this question, but there was in the literature measurements of how much influenza virus was present in coughs and airborne droplets [7]. Those measurements led to a concentration equivalent of 10 to 100 viral particles in droplets for influenza, on the basis of viral RNA present; actual infectious virus in droplets was even less than that, more in the neighbourhood of around 10. Therefore, it seems that there was a vast overkill in laboratory experiments of the amount of SARS-CoV-2 that was being used, and that the proper amount should be much less.

Further, there was an actual experiment done with the original SARS virus where the workers went into hospitals with SARS patients and took smears from the patients and placed the smears on surfaces, and then looked on the surface to see if they had any virus.

They didn't find any live virus. There was no viable SARS virus on the surfaces, even after taking smears from patients with SARS. They did find viral RNA on the surface, which means they actually made a transfer from the patient to the surface, but the virus died very, very quickly [8].

Part 2: Solo: A SARS war story

The *Star Wars* series also includes some “anthology films”, and the next part of this story is titled after one of those anthology films, because I published a “solo” Comment in *Lancet Infectious Diseases* online July 2020 [9] arguing that the possibility of fomite transmission was exaggerated.

The manuscript was first offered to the *New England Journal of Medicine*, since they had published the misleading study that was the basis for all those warnings about fomite transmission. *NEJM* quickly rejected the article without comment, which was then submitted to *Lancet Infectious Diseases* on 5/4/2020, the unofficial annual *Star Wars* Day (“May the 4th be with you”). *Lancet ID* didn't respond for a long time, and I was thinking that the article must have been rejected again, so which is the next journal to try?

After 6 weeks, *Lancet ID* finally responded with a surprise message that they were going to publish the Comment after all. They then worked very assiduously to verify all the numbers and published the Comment [9] (Figure 1).

Figure 1

The article is titled "Exaggerated risk of transmission of COVID-19 by fomites." One of the key take-home messages from that article: "In my opinion, the chance of transmission through inanimate surfaces is very small, and only in instances where an infected person coughs or sneezes on the surface and someone else touches that surface soon after the cough or the sneeze (within an hour or two)."

This article actually went out on a limb somewhat because up to that time, no reputable scientist had challenged in print the conventional wisdom about the risk of fomite transmission. One colleague communicated that he thought the article should have been more cautious and he hoped it wouldn’t be noticed.

But it was noticed and began to be reported on by the lay press. An enterprising young columnist, Derek Thompson, in *The Atlantic*, published a piece that became fairly influential. On July 27, 2020, he coined the phrase, "Hygiene Theater" (Figure 2) to describe all of the disinfection that was going on in businesses and airports and everywhere else that was intending to have the effect of making people feel safer, but really had very little impact in protection from COVID-19.

Figure 2

One of the points Thompson included was that as many as 100 people would need to sneeze in the same area of a table at the same time in order to mimic the kind of inoculum that was used in the experiments reported in NEJM, for a risk of fomite transmission. The article by Thompson magnified the visibility of the Lancet ID comment and increased lay press interest, with coverage coming from

major news organizations and publications including *NBC, ABC, Public Broadcasting System, National Public Radio, Associated Press, New York Times, Washington Post, Time Magazine* and others. Considerable international coverage also followed, for example from the BBC, *the Sunday Times (London), and the Guardian*.

One of the most comprehensive articles in the lay press on this subject appeared October 20, 2020, in *Wired.com*, by Gregory Barber (Figure 3). In his article, he made the comment that the focus on fomites has waned and it's been replaced by a focus on person-to-person transmission through respiration. He also talked about gradual improvement in the latest CDC guidance.

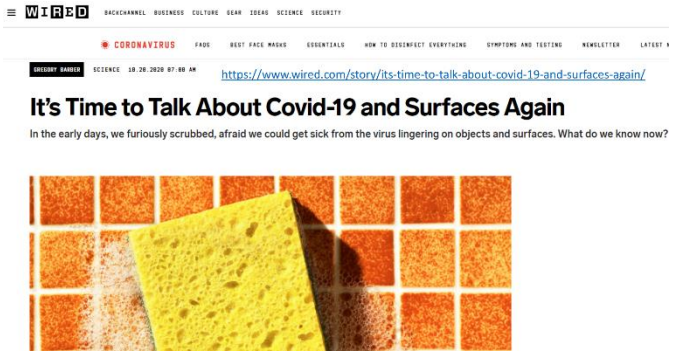


Figure 3

Ultimately, in February 2021, the journal *Nature* published an editorial calling for public health authorities to stop the focus on fomites and shift attention to airborne transmission [10]. The Comment in *Lancet ID* was the only cited article in this editorial. Two months later, the CDC did just that [11], estimating that the chance of transmission through fomites was less than 1 in 10,000.

For a brief respite, it began to appear that maybe the proper balance of where infectivity of COVID-19 comes from had achieved a scientific consensus, and maybe we could relax a little bit. But that was not to be the case, because articles continued to be published warning of the danger of fomite transmission. I shall examine the validity of these in the next section.

Part 3: The fomites strike back

Another *Star Wars* movie in the series was titled "The Empire Strikes Back" (episode 5). In this section, I shall deal with how advocates for fomite transmission have struck back, challenging hard-won scientific consensus on the unimportance of fomite transmission.

A paper in October 2020 from Australia in *Virology Journal* made headlines all around the world [12]. The authors reported up to 28 days survival of infectious SARS-CoV-2 on some surfaces.

A comprehensive review article from Canada published in November 2020 [13] came to the conclusion that there was a high potential for SARS-CoV-2 transmission through contaminated surfaces.

Studies in China looked at SARS-CoV-2 on food packaging and reported a number of times the presence of viral RNA on the packaging, but not infectious virus. A report was finally published in November 2020 [14] about isolating infectious SARS-CoV-2 from frozen cod packaging in Qingdao Port.

Modeling the Diamond Princess cruise ship outbreak suggested that 30% of the cases were from fomites, in an analysis published in February 2021 [15]. However, a modelling study is only as good as the data it is based on, and in this case, the underlying data came from reference 6, which used artificially elevated levels of virus deposited on surfaces not representative of real-life conditions.

Nonetheless, the fomites are still around, and the controversy continues.

Most studies to date of survival of the virus on surfaces are misleading (Figure 4). The first problem is that inoculums are way too large, already discussed and the crux of the argument in the *Lancet ID* Comment [9]. In the paper from Australia the authors argue that the levels are comparable to what you would find in secretions from actual patients in hospitals [12]; however, those levels were determined by assays for viral RNA, not by assays for infectious virus. These are not the same thing. Viral RNA could be considered the equivalent of the corpse of the virus. Although it may reflect a live virus, it most often reflects the fact that the virus was there and died. One study that did assay for infectious virus, as well as viral RNA, couldn't come up with a formula relating the amounts, but they did comment that the virus could not be isolated after eight days, in spite of high viral loads of 10^5 RNA copies per ml [16]. Thus, the presence of viral RNA is not a valid surrogate for the presence of infectious virus.

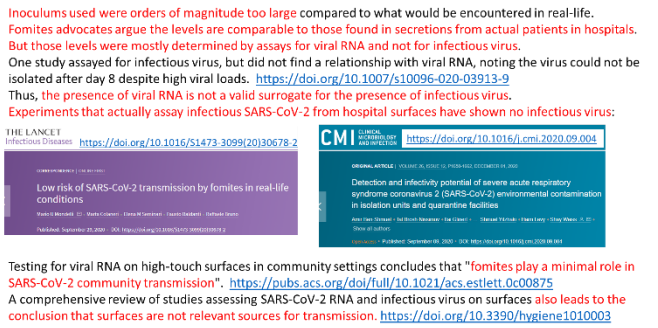


Figure 4: why studies showing long-term survival of virus on surfaces in lab settings are misleading

By contrast, experiments assaying for SARS-CoV-2 in hospitals with COVID-19 patients have shown no infectious virus despite plenty of viral RNA [17,18]. This is comparable to that study mentioned earlier with the original SARS virus where they took the smears from patients placed on surfaces and didn't find any infectious virus [8].

Further, a study was published where authors looked at viral RNA on high touch surfaces in community settings, and although they did find viral RNA, it was of low quality; the authors concluded that “fomites play a minimal role in SARS-CoV-2 community transmission” [19]. A review of published studies of SARS-CoV-2 RNA or infectious virus on surfaces also leads to the conclusion that surfaces are not relevant sources for transmission [20], and a recent study from Brazil similarly concludes that fomites have no role in virus transmission in the real world [21].

It turns out that the high inoculum of virus at the beginning of surface survival studies may be even more specious than originally suspected. The original argument was that you just had more half-lives to go through, so if you start with more virus, it will take longer to get rid of it. It's actually worse than that because it now appears that the virus at high concentrations protects itself from decay.

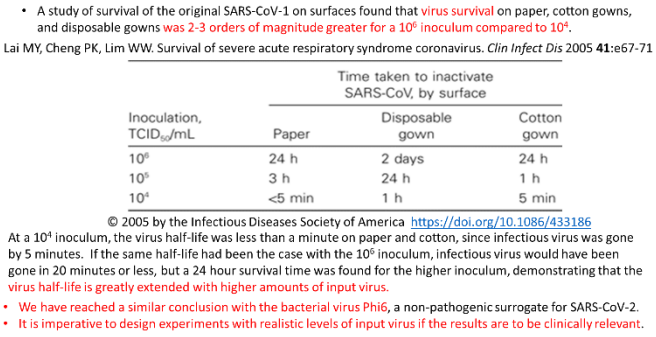


Figure 5: SARS-CoV-1 protects itself at higher concentrations

There were actually data suggesting this with the original SARS virus, inexplicably ignored by the field. A table from a paper [22] on the original SARS virus reports "Tissue Culture Infectious Dose" (TCID), which is the virus concentration that causes infection in 50% of samples tested. With a 10^6 inoculum, the authors observed 24-hour virus survival on paper, but with only a 10^4 inoculum of infectious virus at the start, viable virus was gone in less than 5 minutes. Similarly, with a cotton gown, even with disposable gowns, tremendous differences between the half-lives were found when the inoculum was higher compared to when it was lower (Figure 5). The half-life for the lower inoculum has to be less than a minute on paper and cotton in this experiment because it's gone by 5 minutes. If that same half-life applied with the 10^6 inoculums, virus would have been gone in 20 minutes, not 24 hours. So, the virus half-life was greatly extended with higher amounts of input virus.

This was the only result like this in the literature, and it hadn't been followed up. My lab pursued this finding with the bacterial enveloped virus Phi6 and its host, *Pseudomonas syringae*. Bacteriophage Phi6 has been reported in the literature as a potential non-pathogenic surrogate for SARS-CoV-2 [23-25].

These experiments were done by a very talented master's graduate student, Ron Bangiyev, and he also had help from a senior researcher, Maxim Chudaev. We dried 5 microliters of a saline suspension of Phi6 in plastic Eppendorf tubes at room temperature and let them sit for varying amounts of time, after which we added back 0.1 ml saline solution to the Eppendorf tubes, vortexed and assayed to see how much virus was left (Figure 6).

Sample	Time dry (min)	Inoculum	Recovered	% Recovered	Half-life (min)
1	0	6×10^3	5.6×10^3	93	
2	0	6×10^2	4.2×10^2	70	
3	0	60	1	2	
4	0	6	0	0	
5	15	1.2×10^4	1×10^4	83	57
6	15	1.2×10^3	3.2×10^2	27	8
7	15	1.2×10^2	13	11	5
8	15	12	0	0	
9	30	4.7×10^4	2×10^4	43	24
10	30	4.7×10^3	7.6×10^2	16	11
11	30	4.7×10^2	18	4	6
12	30	47	0	0	
13	60	3.2×10^4	1.2×10^4	38	42
14	60	3.2×10^3	1.4×10^2	4	13
15	60	3.2×10^2	0	0	
16	60	32	0	0	

Figure 6: Extent of survival of Phi6 on plastic is dependent on input amount

The results were described as follows [26]: "The simple act of drying the phage led to the loss of nearly all viable phage at the lower phage input concentrations (samples 3 and 4) while having no significant effect (93% recovery) on the highest phage concentration tested (sample 1) and a small effect (70% recovery) on a 10-fold-lower initial phage concentration (sample 2). Similar patterns of protection by higher initial phage concentrations were also seen for all subsequent lengths of time that the phage remained dry in the tube. At 15 min of dry time, we began to see some loss of survival from the most concentrated initial virus input (sample 5, 83% recovery) compared to a 10-fold-lower virus input (sample 6, 27% recovery). As was seen for the samples dried and assayed immediately, the lowest virus inputs led to the loss of almost all viable phage (sample 7, 11% recovery; sample 8, none recovered).

"After 30 or 60 min of dry time, the highest initial phage inputs began to show significant environmental decay, with just 43% recovery after 30 min (sample 9) and 38% recovery at 60 min (sample 13). But even more substantial environmental decay was observed for the lower-input virus samples (samples 10 to 12 for the 30-min dry time and samples 14 to 16 for 60 min). For those samples with measurable virus survival, we were able to calculate the half-lives of virus in those samples (Table 1), which were commensurate with the percent survival observed. That is, at higher initial phage input levels, the half-lives were much longer than the half-lives at lower initial phage input levels, e.g., compare sample 5 (57-min half-life) to sample 6 (8-min half-life), sample 9 (24-min half-life) to sample 11 (6-min half-life), or sample 13 (42-min half-life) to sample 14 (13-min half-life). The results in (Table 1) show that the higher phage input concentrations delay and protect dried phage from environmental decay compared to lower phage input concentrations."

A similar result was found even for phage that were not dried but left in solution. However, LB (Luria-Bertani) growth medium protected and delayed environmental decay of dried phage even at low concentrations of phage [26].

Thus, at least for a potential surrogate for SARS-CoV-2, the bacterial enveloped virus Phi6, we see a protective effect of higher concentrations of the virus on virus resistance to environmental decay. The mechanism may involve some kind of association of the phage particles together in a protective array or a lattice at the higher concentrations.

Whatever the mechanism, these results underscore that it's even more imperative to design the survival experiments with realistic amounts of virus, if the results are to be clinically relevant.

Aside from the concentration of the virus, there are other reasons that make published laboratory studies on fomites unreliable for a real-world application (Figure 7). Most lab studies chose conditions that favour the survival of the virus, such as optimal humidity and temperature, while in the real world, humidity and temperature are variables.

- Samples were kept under optimal humidity and temperature whereas humidity and temperature are variables in the real world, and the virus is killed when it is fully dried out.
- In one study (https://doi.org/10.1186/s12985-020-01418-7) samples were kept in the dark to avoid ultraviolet light, which is known to rapidly kill SARS-CoV-2.
- Also in the same study, samples were placed in a medium containing Bovine serum albumen (BSA) and other proteins, whereas BSA specifically has been shown to protect SARS-CoV-2 from environmental decay. https://dx.doi.org/10.3201/eid2609.201788
  We have obtained similar results with phage Phi6 in LB medium.
- Defending this choice, fomite advocates argue they were trying to mimic an environment similar to human secretions.
  However, respiratory mucous is actually a hostile environment for virus survival.
- Measurements of SARS-CoV-2 survival in actual mucous show half-life of ~3 hours at room temperature in 40% humidity. https://dx.doi.org/10.3201/eid2609.202267

Figure 7: Laboratory conditions used in the fomite's studies chose conditions that favor virus survival

In the study that reported up to 28 days survival [12], the authors actually kept their samples in the dark to avoid ultraviolet light whereas it's been shown that ultraviolet light rapidly kills SARS-CoV-2 [27]. Also in that study, they put their samples into a medium containing bovine serum albumen and other proteins, whereas it was already published that bovine serum albumen specifically protects SARS-CoV-2 from environmental decay [28]. In the paper where that was reported, the authors said, "Our data showed that SARS-CoV-2 infectivity was remarkably preserved in the presence of proteins, regardless of the type of surface." We have also had similar results for Phi6 with LB medium (mentioned above), which contains tryptone and yeast extract; tryptone is a tryptic digest of casein.

The reason why they said they used these proteins is they were trying to mimic an environment similar to human secretions. However, respiratory mucus is actually a hostile environment for virus survival because it not only doesn't have much if any proteins, but it also has nonspecific immunity factors in them, and other unfavorable (for the virus) components [29,44]. Measurements of SARS-CoV-2 survival in mucus shows a half-life of about 3 hours at room temperature and 40% humidity [30].

What about the report from China finding live virus on frozen cod packaging [14]? This may be the most persuasive argument for the potential importance for fomite transmission. However, this doesn't

really change anything for us in the real world because very few people will deal with imported frozen packaging directly upon receipt of the shipments. Furthermore, all the other tests performed in China have found no live virus downstream after the imported packages were received, and they've looked very hard for that. They find viral RNA, but they do not find live virus. Their report is more like a proof of principle. Yes, virus survival on fomites could happen, but it's still very rare.

The recovery of live virus from imported packaging raised the possibility that the virus didn't originate in Wuhan. However, this seems highly unlikely because that would require some worker elsewhere in the world to have been infected with the virus, deposit it on the package, and not infect anybody else at a time when were no other outbreaks elsewhere in the world.

If fomite transmission were really an issue in this pandemic, we would have seen cases of it in other venues. One particularly persuasive example was a situation in South Korea where a call center had a COVID-19 outbreak. Almost everyone in this call center gets infected with COVID-19, but it was a mixed-use building with almost 1,000 other occupants, including residences alongside that call center, and almost no one else in that building caught the disease [31]. There were three additional infections and those could easily have been explained by aerosol contamination. If fomite contamination had been a real issue with everyone in that call center being infected, we would have seen far more cases in that building.

Another reason arguing that fomites are not a significant factor are experiments with another respiratory virus. There was a wonderful experiment done with rhinoviruses, the major cause (65-70%) of the common cold. This is a non-enveloped virus; the experiment proved that the transmission was by aerosols and not by fomites, to at least a first approximation.

The study in 1987 at the University of Wisconsin was published in the *Journal of Infectious Diseases* [32]. Two groups of subjects played poker, the card game, for many hours. One group was sick with the common cold -- coughing, sneezing, runny noses -- and the other group was healthy. The healthy group wore some kind of restraint so that the participants could not touch their faces. After many hours, the contaminated cards and the chips used in the game were transferred to a different room with another group of all-healthy volunteers to play with, and these healthy volunteers were instructed to touch their faces every 15 minutes.

The results of this experiment were that the healthy volunteers that could not touch their faces but were exposed to the aerosols got sick, and the healthy volunteers that played with the fomites (the contaminated cards and the chips) and touched their faces did not get sick. Pretty definitive experiment that you do not transmit the common cold by surfaces, but you do transmit it by what you breathe.

Of course, this was not the coronavirus. We can't do this with the coronavirus because it's a potentially lethal virus, but there's no reason to think that it would behave differently. It's a respiratory virus, and if anything, as an enveloped virus, it's more fragile in the environment compared to the rhinovirus, which is a non-enveloped virus.

By contrast, there's good evidence for the transmission by aerosols, for example, see a review article about the size of infectious aerosols [33], and a paper reporting isolating infectious SARS-CoV-2 in the air of a hospital room with COVID-19 patients [34].

Part 4: A new hope

Another *Star Wars* movie in the series was titled "A New Hope" (episode 4). This final section updates the current status of the war between the aerosols and the fomites with the hope that this war, and the pandemic, will soon be behind us.

To get infected from a fomite, it is believed that several steps need to occur in sequence: 1) the surface has to be freshly contaminated with live virus (for example, a sneeze or cough from an infected person). 2) In a relatively short period of time after the contamination (a few hours at most), a person has to touch that contamination. 3) Without washing hands, that person has to touch either their eyes, nose, or mouth, again in a relatively short period of time after having touched the contamination (a few hours at most). If all of these steps are fulfilled, a person may have a small chance of self-infecting from the surface.

The level of risk drops with each step. One could ask why to recommend not worrying about an item bought at a store but still recommend washing hands. If you look at the chain of events in the sequence described above, the answer is obvious. The store-bought item may fulfill step 1 (although note the limit of the time interval). But someone can ignore disinfecting the item because the chain of transmission will end there after a few hours at most. The virus is fragile and dies quickly on the surface in the real world. If by some bad luck, the contamination gets past steps 2 and 3, there is presumed to be a small chance of self-infecting. Washing one's hands breaks the chain of transmission at step 3. It is a simple, cost-effective method that is not much of an inconvenience or imposition, and therefore an easy way to eliminate even that small hypothetical chance of infection from a surface. There is also a big drop in risk once the virus is on your fingers (step 2), as transfer of the virus by fingers is inefficient [35], nor does the virus survive very well on fingers [36]. Finger transfer rates for Phi6, an enveloped virus surrogate for SARS-CoV-2, have been reported as 17%, but even this low rate is an overestimate because the researchers excluded ~10% of their data samples when there were no viable viruses recovered [37].

Handwashing is something everyone should be doing anyway, pandemic or no pandemic. The risk of COVID-19 doesn't affect that recommendation. Our mothers taught us, if you want to prepare food, wash your hands. If you go to the bathroom, wash your hands. If you touch something dirty, wash your hands. This general policy applies even if there were no pandemic. Doing so is normal, common sense, proper hygiene. We shouldn't need a pandemic to know this.

To beat the pandemic, vaccination is of course the weapon of choice. But even with this weapon in our arsenal, we need to focus on what we breathe to protect ourselves, particularly since this virus has the potential to mutate to partially vaccine-resistant forms, already observed to some extent with the Delta variant [38] and apparently even more so with Omicron [39].

Now that we know that surfaces are not significant sources of infection, treatment of the air, specifically indoor air, is the next frontier. Various devices and filtration systems have been put forth, but these have a significant weakness: there is a critical gap, window of opportunity between when the virus is expelled by an infected person before the air gets filtered or treated. During this window, an infection could be transmitted.

What is needed instead is a pre-deployed virus-killing treatment in the air to protect us as soon as virus is introduced, but one that is nevertheless safe for humans to breathe. Amazingly, such a product exists, and will hopefully soon be widely approved for this purpose.

The product is triethylene glycol (TEG), marketed as "Grignard Pure" by the Grignard Company. This reagent is a non-toxic, FDA approved aerosol dispersed in the air that's been safely used for years in the theater for special effects, also used in some air sanitizers. It was found a long time ago to kill viruses, including influenza [40]; the Grignard Company has shown that it inactivates a variety of airborne

viruses [41]. This potential indoor air treatment may allow safe resumption of indoor activities even during a pandemic.

In conclusion, I contend that transmission of SARS-CoV-2 by fomites in the pandemic is virtually negligible (Figure 8). This is a virus that you catch almost exclusively by breathing and not by touching. The design of laboratory experiments showing long-term survival of SARS-CoV-2 on fomites render those results irrelevant for real-life scenarios [42]. This is not to deny a remote possibility of transmission by surfaces, but that route of infection remains hypothetical. It is a terrible waste to continue expensive, time-consuming, and potentially dangerous [43] surface disinfection procedures beyond normal routine hygiene. Surface transmission is at most a very minor component of COVID-19 infections.

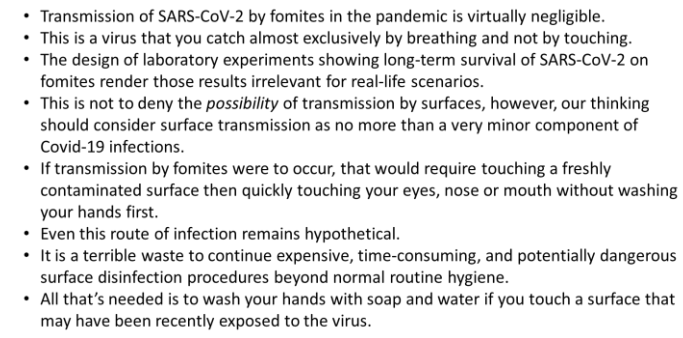


Figure 8: Conclusions

References

1. https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations
2. https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-covid-19-client-interaction.html#
3. https://www.healthline.com/health-news/worried-about-contaminated-groceries-how-to-be-safe
4. Rabenau HF, Cinatl J, Morgenstern B, Bauer G, Preiser W, et al. Stability and inactivation of SARS coronavirus. *Med Microbiol Immunol*. 2005; 194: 1-6.
5. Duan SM, Zhao XS, Wen RF, Huang JJ, Pi GH, et al. SARS Research Team. Stability of SARS coronavirus in human specimens and environment and its sensitivity to heating and UV irradiation. *Biomed Environ Sci*. 2003; 16: 246-255.
6. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020; 382: 1564-1567.
7. Lindsley WG, Blachere FM, Thewlis RE, Vishnu A, Davis KA, et al. Measurements of airborne influenza virus in aerosol particles from human coughs. *PLoS One*. 2010; 5: e15100.
8. Dowell SF, Simmerman JM, Erdman DD, Wu JS, Chaovavanich A, et al. Severe acute respiratory syndrome coronavirus on hospital surfaces. *Clin Infect Dis*. 2004; 39: 652-657.
9. Goldman E. Exaggerated risk of transmission of COVID-19 by fomites. *Lancet Infect Dis*. 2020; 20: 892-893.
10. Coronavirus is in the air—there's too much focus on surfaces. *Nature*. 2021; 590:7.
11. Centers for Disease Control and Prevention. 2021. Science brief: SARS-CoV-2 and surface (fomite) transmission for indoor community environments. Department of Health and Human Services, Washington, DC. https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/surface-transmission.html
12. Riddell S, Goldie S, Hill A, Eagles D, Drew TW. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. *Virol J*. 2020; 17: 145.
13. Bueckert M, Gupta R, Gupta A, Garg M, Mazumder A. Infectivity of SARS-CoV-2 and other coronaviruses on dry surfaces: potential for indirect transmission. *Materials (Basel)*. 2020; 13: 5211.
14. Liu P, Yang M, Zhao X, Guo Y, Wang L, et al. Cold-chain transportation in the frozen food industry may have caused a recurrence of COVID-19 cases in destination: successful isolation of SARS-CoV-2 virus from the imported frozen cod package surface. *Biosaf Health*. 2020; 2: 199–201.
15. Azimi P, Keshavarz Z, Cedeno Laurent JG, Stephens B, Allen JG. Mechanistic transmission modeling of COVID-19 on the Diamond Princess cruise ship demonstrates the importance of aerosol transmission. *Proc Natl Acad Sci USA*. 2021; 118: e2015482118.
16. La Scola B, Le Bideau M, Andreani J, Hoang VT, Grimaldier C, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis*. 2020; 39: 1059-1061.
17. Mondelli MU, Colaneri M, Seminari EM, Baldanti F, Bruno R. Low risk of SARS-CoV-2 transmission by fomites in real-life conditions. *Lancet Infect Dis.* 2021; 21: E112.
18. Ben-Shmuel A, Brosh-Nissimov T, Glinert I, Bar-David E, Sittner A, et al. Detection and infectivity potential of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) environmental contamination in isolation units and quarantine facilities. *Clin Microbiol Infect.* 2020; 26: 1658-1662.
19. Harvey AP, Fuhrmeister ER, Cantrell ME, Pitol AK, Swarthout JM, et al. Longitudinal monitoring of SARS-CoV-2 RNA on high-touch surfaces in a community setting. *Environ Sci Technol Lett.* 2021; 8: 168-175.
20. Kampf G, Pfaender S, Goldman E, Steinmann E. SARS-CoV-2 Detection Rates from Surface Samples Do Not Implicate Public Surfaces as Relevant Sources for Transmission. *Hygiene.* 2021; 1: 24-40.
21. Rocha ALS, Pinheiro JR, Nakamura TC, da Silva JDS, Rocha BGS, et al. Fomites and the environment did not have an important role in COVID-19 transmission in a Brazilian mid-sized city. *Sci Rep.* 2021; 11: 15960.
22. Lai MYY, Cheng PKC, Lim WWL. Survival of severe acute respiratory syndrome coronavirus. *Clin Infect Dis.* 2005; 41: e67-e71.
23. Lin K, Schulte CR, Marr LC. Survival ofMS2 and Phi6 viruses in droplets as a function of relative humidity, pH, and salt, protein, and surfactant concentrations. *PLoS One*. 2020; 15: e0243505.
24. Fedorenko A, Grinberg M, Orevi T, Kashtan N. Survival of the enveloped bacteriophage Phi6 (a surrogate for SARS-CoV-2) in evaporated saliva microdroplets deposited on glass surfaces. *Sci Rep.* 2020; 10: 22419.
25. Whitworth C, Mu Y, Houston H, Martinez-Smith M, Noble-Wang J, et al. Persistence of bacteriophage phi 6 on porous and nonporous surfaces and the potential for its use as an Ebola virus or coronavirus surrogate. *Appl Environ Microbiol.* 2020; 86: e01482-20.
26. Bangiyev R, Chudaev M, Schaffner DW, Goldman E. Higher concentrations of bacterial enveloped virus Phi6 can protect the virus from environmental decay. *Appl Environ Microbiol.* 2021; 87: e0137121.
27. Ratnesar-Shumate S, Williams G, Green B, Krause M, Holland B, et al. Simulated sunlight rapidly inactivates SARS-CoV-2 on surfaces. *J Infect Dis.* 2020; 222: 214-222.
28. Pastorino B, Touret F, Gilles M, de Lamballerie X, Charrel RN. Prolonged infectivity of SARS-CoV-2 in fomites. *Emerg Infect Dis*. 2020; 26: 2256-2257.
29. Eccles R. Respiratory mucus and persistence of virus on surfaces. *J Hosp Infect.* 2020; 105: 350.
30. Matson MJ, Yinda CK, Seifert SN, Bushmaker T, Fischer RJ, et al. Effect of environmental conditions on SARS-CoV-2 stability in human nasal mucus and sputum. *Emerg Infect Dis.* 2020; 26: 2276-2278.
31. Park SY, Kim Y-M, Yi S, Lee S, Na B-J, et al. Coronavirus disease outbreak in call center, South Korea. *Emerg Infect Dis.* 2020; 26: 1666-1670.
32. Dick EC, Jennings LC, Mink KA, Wartgow CD, Inborn SL. Aerosol transmission of rhinovirus colds. *J Infect Dis*. 1987; 156: 442-448.
33. Fennelly KP. Particle sizes of infectious aerosols: implications for infection control. *Lancet Respir Med.* 2020; 8: 914-924.
34. Lednicky JA, Lauzardo M, Fan ZH, Jutla A, Tilly TB, et al. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *Int J Infect Dis.* 2020; 100: 476-482.
35. Todt D, Meister TL, Tamele B, Howes J, Paulmann D, et al. A realistic transfer method reveals low risk of SARS-CoV-2 transmission via contaminated euro coins and banknotes. *iScience.* 2021; 24: 102908.
36. Weber TP, Stilianakis NI. Fomites, hands, and the transmission of respiratory viruses. *J Occup Environ Hyg*. 2021; 18: 1-3.
37. Anderson CE, Boehm AB. Transfer rate of enveloped and non-enveloped viruses between fingerpads and surfaces. *Appl Environ Microbiol.* 2021; 87: e0121521.
38. Farinholt T, Doddapaneni H, Qin X, Menon V, Meng Q, et al., Transmission event of SARS-CoV-2 Delta variant reveals multiple vaccine breakthrough infections. *medRxiv*. 2021; 2021.06.28.21258780.
39. Liu L, Iketani S, Guo Y, et al. Striking Antibody Evasion Manifested by the Omicron Variant of SARS-CoV-2. *Nature*. 2021.
40. Rudnick SN, McDevitt JJ, First MW, Spengler JD. Inactivating influenza viruses on surfaces using hydrogen peroxide or triethylene glycol at low vapor concentrations. *Am J Infect Control*. 2009; 37: 813-819.
41. https://grignardpure.com/
42. Goldman E. SARS Wars: the Fomites Strike Back. *Appl Environ Microbiol*. 2021; 87: e0065321.
43. Chang A, Schnall AH, Law R, Bronstein AC, Marraffa JM, et al. Cleaning and disinfectant chemical exposures and temporal associations with COVID-19—National Poison Data System, United States, January 1, 2020–March 31, 2020. *MMWR Morb Mortal Wkly Rep.* 2020; 69: 496-498.
44. Wardzala CL, Wood AM, Belnap DM, Kramer JR. Mucins Inhibit Coronavirus Infection in a Glycan-Dependent Manner. *ACS Cent Sci.* 2022; 8: 351-360.

*Correspondence: Emanuel Goldman, Department of Microbiology, Biochemistry & Molecular Genetics, Rutgers New Jersey Medical School, Newark, NJ 07103, USA, E-mail: egoldman@njms.rutgers.edu

Received: 10 Dec 2021; **Accepted:** 16 Jan 2022; **Published:** 19 Jan 2022

Citation: Goldman E. SARS Wars: The aerosols versus the fomites. *Front Infect Diseases Microbiol.* 2022; 2: 107.