SARS-Cov-2: The Relevance and Prevention of Aerosol Transmission

Coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), has claimed many victims worldwide due to its high virulence and contagiousness. The person-to-person transmission of SARS-Cov-2 when in close contact is facilitated by respiratory droplets containing the virus particles, and by skin contact with contaminated surfaces. However, the large number of COVID-19 infections cannot be explained only by droplet deposition or contact contamination. It seems very plausible that aerosols are important in transmitting SARS-Cov-2. It has been demonstrated that SARS-CoV-2 remains viable in aerosols for hours, facilitating rapid distribution of the virus over great distances. Aerosols may, therefore, also be responsible for so-called super-spreader events. Indirect evidence points to a correlation between ventilation and the transmission and spread of SARS-Cov-2, supporting ventilation as an important factor in preventing airborne transmission. Further actions to avoid transmission of COVID-19 include social distancing, hygiene measures, and barrier measures, such as face-coverings. Professional masks offer better protection than cloth masks. These protection measures are especially relevant to health care workers, when performing endotracheal intubation, but the risk from non-invasive ventilation and nebulizing treatment seems to be moderate.

Keywords: aerosols, COVID-19, prevention, SARS-CoV-2, transmission

The Coronavirus disease (COVID-19), first emerging in Wuhan in late 2019, and caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) has claimed many victims worldwide due to its high virulence and contagiousness. The person-to-person transmission of SARS-Cov-2 in close contact is facilitated by respiratory droplets containing the virus particles, and by skin contact with contaminated surfaces. Another route is airborne transmission by aerosols (Fig. 1). COVID-19 is transmitted by both symptomatic patients and asymptomatic carriers.[2] Measures to prevent transmission of SARS-Cov-2 are absolutely necessary to curb the pandemic, and to relieve the heavy burden on society and hospitals. Knowledge of and respect for the route of transmission is pivotal to taking precautions.

EVIDENCE OF VIRUS TRANSMISSION

Droplet Transmission

Virus transmission of SARS-Cov-2 from person to person (direct transmission) is facilitated by respiratory droplets containing virus particles. The German bacteriologist Carl Flügge (1847–1923) demonstrated as far back as 1894 that "speaking"—patients in a study emitted droplets that showed bacterial growth on a culture medium close by. An American health scientist, William Wells (1887–1963), exposed the interplay between gravity and evaporation. Droplets larger than a humidity-determined threshold fall to the ground due to gravity and smaller droplets evaporate to become aerosols that drift in the air and remain airborne (Fig. 2). Droplets released by coughing/speaking do not spread further than approximately 3 ft due to gravity.[3,4]

The current government social distancing measures were based on these historical data of William Wells: the 5 foot distancing in, for example, the Netherlands, the stricter 6.5 foot distancing in Switzerland and Sweden, and less strict measures of 3 foot distancing in France and Austria. The study by Chen et al[5] demonstrated that droplet deposition by gravity only dominates when the droplets are larger than 100 μm and when the subjects are within 0.2 m while talking, or 0.5 m while coughing.

To get more insight into transmission routes, in 1981 Breese Hall et al performed experiments with Respiratory Syncytial Virus in infected infants. Volunteers were exposed to the infected infants in three ways: (1) the cuddlers (caring for the infants in the usual manner; feeding, playing, cleaning a diaper), (2) touchers (contact with surfaces contaminated by the infants), and (3) sitters (sitting at a distance from the infants). The most, and most severely infected volunteers were seen in the cuddler group, followed by the toucher group.[6]

The findings of the most clinically relevant systematic review and meta-analysis by Chu et al on COVID-19, SARS, and Middle East Respiratory Syndrome (MERS) (44 comparative studies; $n = 25{,}697$ patients) suggest evidence that the current policies of at least 1 m distancing were associated with a large reduction in infections, but a distance of 2 m might be even more effective. However, the studies on droplets transmission continue to be debated, because there is not full transparency about the measurement of transmission distance and the time of remaining exposed to the virus.

Surface Transmission

The person-to-person transmission of SARS-Cov-2 is also facilitated by direct skin contact or indirect contact via contaminated surfaces. Van Doremalen et al[7] demonstrated that SARS-Cov-2 may be viable for days on surfaces, a precondition for contact contamination. A Japanese video showed using a fluorescent substance, only visible under black light, how easily viruses can spread by contact transmission in restaurants from one infected person (weblink 1). However, it is noteworthy that in home measurements with COVID-19 patients, the virus was detectable on less than 5% of the tested surfaces.[8] The large numbers of simultaneous COVID-19 group infections, the so-called super-spreader events (SSEs) cannot be explained solely by droplet deposition or contact contamination. It is very plausible that aerosols may be important in transmitting SARS-Cov-2.[9]

Weblink 1

https://edition.cnn.com/2020/05/13/health/japan-black-light-experiment-coronavirus-trnd-wellness/index.html

Aerosol Transmission

Aerosols are fine solid particles or droplets dispersed in gas. Aerosols containing virus particles are released when infected persons cough, or even talk or breathe. The number of particles expelled

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Clinical significance: Aerosol transmission is one of the dominant ways of spreading of SARS-Cov-2. SARS-CoV-2 remains viable in aerosols for hours, facilitating rapid virulent distribution. Adequate ventilation, with avoidance of air and thus virus recirculation, is pivotal in preventing virus transmission next to barrier measurements in the public domain as well in health care setting.
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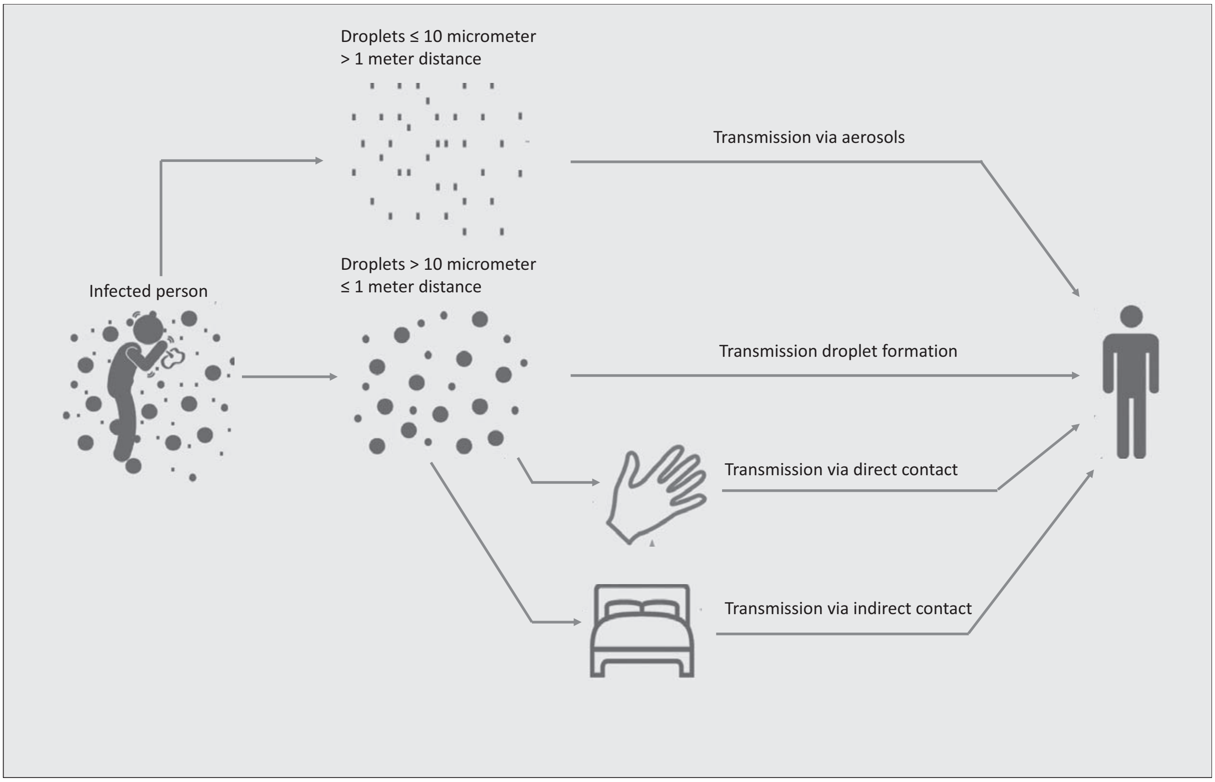

FIGURE 1. Routes of virus transmission. This figure is reproduced and modified from Otter et al (2016).[1]

from the airways when talking varies from person to person and can be as much as 300,000 particles at a time, with an average size of 0.7 to 10 μm, but range in size in the flume of patients. Wang et al[10] showed that a single cough by a person with a high viral load in their respiratory fluid (2.35 × 109 copies per mL) may generate as many as 1.23 × 105 copies of viruses. This aerosol transmission is well demonstrated in Japanese micro-droplet spreading experiments (weblink 2).

Previously, evidence indicated that aerosols were an important mode of transmission for Influenza A virus and SARS-CoV-1.[11,12] The small aerosols (less than 5 μm) with virus material can be inhaled and directly transported deep into the airways and alveolar compartment.[13] For Influenza A, it has been demonstrated that transmission via aerosols was associated with more severe illness.[14] Larger droplets (greater than 5 μm) are more likely to infect the upper airways.[13] The potential for droplet transmission also depends on environmental conditions. The study by Xie et al investigated using numerical computations, among other things, the effects of humidity on large droplet evaporation to aerosols, with subsequent dispersion. They demonstrated that at lower humidity, more droplets suspended in the air increase the probability of subsequent inhalation.[3] In contrast, sunlight rapidly inactivates SARS-CoV-2 in small-particle aerosols.[15]

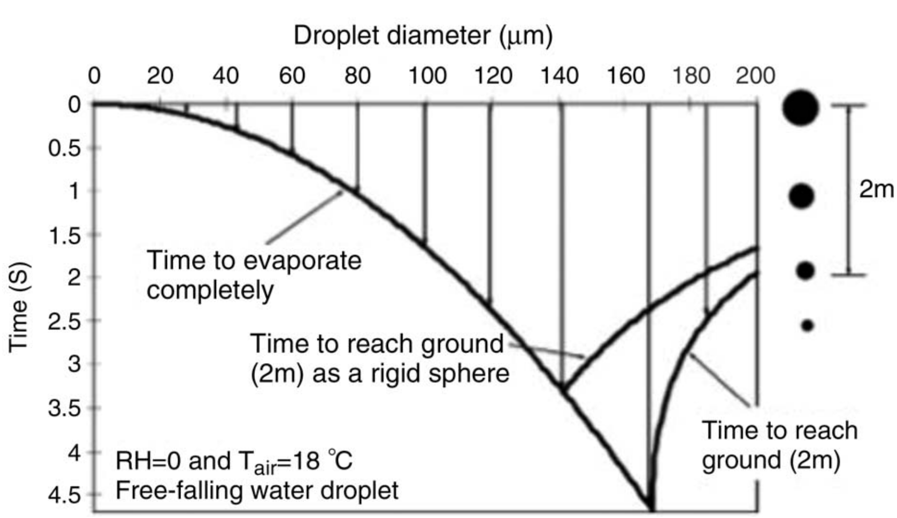

FIGURE 2. The Wells evaporation-falling curve. This figure is reproduced and modified from Wells and Xie.[3,4]

William Wells demonstrated in his book (1955) that all laboratory animals exposed to aerosols containing influenza die quickly compared to animals who were inoculated with large droplets containing influenza.[4] A study by Yu et al[12] showed during the SARS-COV-1 outbreak using an airflow simulation model how the airborne spread of the SARS-COV-1 takes place in different buildings, and supported the probability of airborne spread.

Aerosols may also be important in transmitting SARS-Cov-2 and it has been demonstrated that SARS-CoV-2 remains viable in aerosols for hours, facilitating rapid distribution of the virus over great distances.[7,9] Several other model studies made it likely that SARS-CoV-2 airborne transmission is even more relevant than large droplets or contact transmission.[16,17] An illustrative example is contamination with SARS-CoV-2 in a Chinese restaurant: only people who were in the index patient's airflow were infected. The air flow was passing continuously through a recirculating cooling system without a filter, while the basic ventilation system for fresh air supply was switched off.[18] Another example is the outbreak in a nursing home in the Netherlands that was likely the result of aerosol transmission due to inadequate ventilation. SARS-CoV-2 RNA was detected in dust present on the air conditioners and in four block filters from 3 of the 8 ventilation cabinets.[19]

Weblink 2

https://www.youtube.com/watch?v=vBvFkQizTT4

ATTENTION TO ROUTES OF TRANSMISSION

The World Health Organization and governments focus mainly on the prevention of droplet and surface transmission through hygiene measures, limiting human contact and social distancing. The third route, aerosol transmission, has been underestimated for a long time. However, this airborne route may be a plausible transmission route for SARS-CoV-2, facilitating its fast spread all over the world. Knowledge and awareness of all routes of transmission is pivotal to managing the pandemic.

Throughout the pandemic, we have seen that SARS-CoV-2 follows a cluster super-spreader pattern, generating a disproportionately large number of infections. SARS-CoV-2 spread for example at après-ski bars, choirs, concert rehearsals, naval and cruise ships, gyms, nursing homes, restaurants, slaughterhouses, festivals, and weddings. SARS-CoV-2 has an estimated basic reproduction (R)-number of 3.49 in the early stage of the epidemic, which only partly explains the high contamination rate.[20] The R-number reflects the average transmission number in a population, while in COVID-19 only 10% of the population is responsible for 80% of the infections and can be defined by the co-called dispersion K factor of 0.1. This skewing phenomenon can only be explained by aerosol transmission during SSEs.[21] Another observation that SSEs occur almost exclusively indoors in poorly ventilated areas is consistent with the role of aerosol transmission.[22]

PREVENTION OF TRANSMISSION

Ventilation

The correlation between ventilation and the transmission and spread of several infectious diseases has previously been extensively demonstrated.[23] A study in the Netherlands analyzed the droplet size distribution, travel distance, and velocity from coughing and speaking, and the airborne time in relation to the level of air ventilation. They applied a laser diffraction measurement, using a spray droplet measurement system and performed the experiment in three rooms with different levels of ventilation: no ventilation, mechanical ventilation only and mechanical ventilation supported by the opening of an entrance door and a small window. The droplets halved in the best ventilated room after 30 s, whereas with no ventilation this took about 5 min and in a poorly ventilated room, the number of droplets was halved in 14 min.[24] This supports the argument that ventilation is an important factor in preventing airborne transmission.

More recently, focus on improving ventilation, not only in government institutions and hospitals, but also in nursing homes, general practices, offices, restaurants, and schools has become urgent. It must be stressed that fresh air supply by using windows that can be opened, mechanical ventilation systems, avoiding central recirculation (reintroduction of return air) may be a key factor in diminishing aerosols and so the spread of the virus. The high concentration of infection droplets in aerosols around infectious individuals highlights the importance of personalized ventilation.[5]

It is demonstrated in an experimental setting that Mobile High-Efficiency Particulate Air (HEPA) filters have added value if there is no ventilation option.[25] Ventilation systems with ultra violet light to disinfect air may be helpful, although no published studies have demonstrated efficacy, and these methods are currently not recommended in the infection prevention guidelines from the World Health Organization.[26]

Masks

Face coverings act as a source control measure to prevent aerosol transmission by infected patients who sneeze, cough and speak.[27] The use of a face covering in public indoor areas is advised to prevent large droplet transmission. Aerosols are more difficult to block with a face covering. The added value of wearing a face mask in addition to social distancing for the prevention of SARS-CoV-2 transmission is, therefore, still under debate.

The first in vivo experimental study supported a significant benefit of surgical masks in preventing SARS-CoV-2 transmission in a hamster model.[14] The use of masks by humans suggested beneficial effects on the course of the pandemic in several countries immediately at the start of the lockdown.[17] The University of Kansas found a 50% reduction in the spread of COVID-19 in countries that had compulsory masks, compared to those without. Leffler et al[28] demonstrated in a univariate analysis of 198 countries that the duration of mask-wearing in general by the public was significantly negatively correlated with mortality, and also international travel controls are independently associated with lower per-capita mortality from COVID-19. The findings of a systematic review and meta-analysis identified 172 observational studies across 16 countries, supporting face mask use being able to result in a large reduction in risk of infection.[29] Serial cross-sectional data from approximately 7000 German participants demonstrate that implementing a mandatory policy increased actual compliance despite moderate acceptance. An obligation to wear a face mask appears to be an effective solution to curb transmissions of airborne viruses.[30] Therefore, government policies in many countries make properly worn masks mandatory in public areas.[28] If approximately 40% of the population wore a mask that filters out particles ranging from 0.3 to 10 mm in diameter, it would be possible to curb the pandemic.[31]

There are many differences in face covering methods such as the professional Filtering Face Pieces (FFP, Europe)/N-95 Mask (USA)/KN95 (China), surgical mask (simpler 3-layer nose-mouth) and (homemade) cloth masks, neck gaiters, and face shield. Protection by these masks varies considerably.[32] Professional masks offer better protection than simpler surgical masks, although the latter may also offer protection.[13,31] At least a professional mask should be used during airborne precaution situations.[33] The filtration efficiency and air flow resistance of cloths mask vary strongly depending on the different textiles used.[34,35] A variety of commonly available homemade mask types were tested in a proof-of-principle study and this study demonstrated that some mask types approach the performance of standard surgical masks.[32] Clapp et al[36] demonstrated also that simple modifications as nylon hosiery sleeve placed over the procedure mask can improve medical mask fit and can substantially improve filtration efficiency. However, it is not recommended that cloth masks should be used by health care workers.[37]

Face shields and neck gaiters are more comfortable and, therefore, may be worn more consistently. However, face shields only protect against large drops and not against aerosols.[38] Several studies demonstrated that aerosols from the infected person whirl around the face shield and enter the environment.[39] Neck gaiters also offer very little protection.[32] The Technical University in Delft, the Netherlands, developed a detection method for objective mask leakage on a plastic head. They demonstrated that the homemade masks give the least protection, because of their poor fit and showed that mask protection is not fool proof (weblink 3).

Notwithstanding all these studies, which in summary show the benefit of using masks, this preventive measure is still under debate. A randomized study of more than 6000 people in Denmark from April to June showed that wearing a face mask did not significantly reduce the SARS-CoV-2 infection at 1 month by antibody testing.[40] Their results were however heavily criticized because of the design of the study.

Weblink 3

https://innovationorigins.com/nl/kunststofhoofd-maakt-lekkage-bij-mondkapjes-zichtbaar/

Furthermore, there are some general disadvantages of face coverings, such as low compliance due to discomfort, and incorrect use of the face covering from re-use or by physical contact with the infected parts of the mask. The study MacIntyre et al warned against the use of cloth masks, because moisture retention, reuse of cloth masks and poor filtration may result in increased risk of infection. In contrast, face coverings can optically increase fear of approach and act as a reminder of infection risks, and it demonstrated that mask wearing correlated positively with other protective behaviors.[40,41]

In conclusion, it is plausible that appropriately wearing a surgical mask has an added value, especially when good ventilation measures are lacking or cannot be guaranteed (Fig. 3).[42]

Toilet Flushing

An underestimated source of infection may be flushing a toilet used by SARS-CoV-2 infected patients. Kang et al[17] demonstrated that faecal transmission may have caused the community outbreak of COVID-19 in a high-rise building.[17] The study by Döhla et al[43] showed that in 21 households under quarantine conditions, surfaces in the domestic environment as well as the wastewater from washbasins, showers and toilets showed SARS-CoV-2 contamination.[43] Preventive measures in the public domain are flushing the toilet with the lid closed and leaving the toilet door open between toilet visits to improve ventilation. Another option is disposable toilet seat covers to ensure a more hygienic toilet visit.

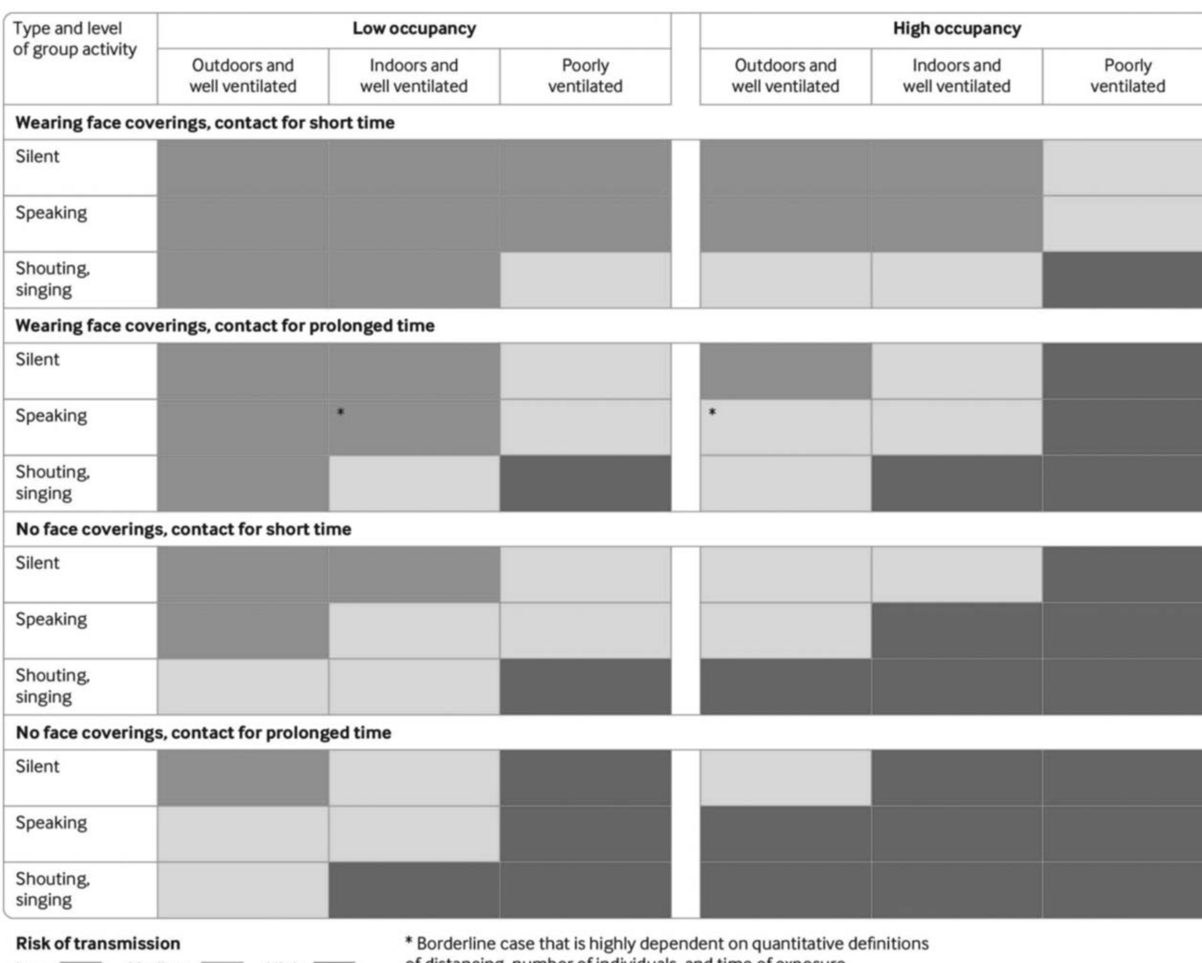

FIGURE 3. Transmission risk of SARS-CoV-2 in different settings and different occupation times, venting, and crowding levels. This figure is from Jones NR.[42] SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

HEALTH CARE

The disproportionately large number of infections among health care workers, especially in nursing homes, suggest super-spreader patterns. Health care institutions have high transmission rates due to high exposure to SARS-CoV-2, crowding, gathering in common areas and bad ventilation. Furthermore, the care homes' supply of personal protective equipment was suboptimal at the beginning of the COVID-19 pandemic because of scarcity and reuse of materials.[44] In addition, the quality of ventilation is often inadequate in hospitals and nursing homes due to recirculation. A prospective, observational cohort study in the UK and the USA noted that compared to the general community, front-line health-care workers show approximately a threefold increase in the risk of COVID-19, even after accounting for other risk factors.[45] In addition, there are several specific medical procedures that generate aerosols that may increase the risk of SARS-CoV-2 transmission among health care workers.[3,46]

Nebulized Medication

There are contradictory study outcomes concerning the increased risk of virus transmission by nebulizer treatment.[47] Nebulizers create aerosols, nonetheless it is uncertain whether these aerosols contain infectious viral particles. The nebulized medication is also relevant to generating aerosols: for example, saline has been shown to decrease aerosol formation.[48]

Non-Invasive Ventilation

There is no strong evidence that non-invasive ventilation (NIV) increases the risk of viral diseases.[47] Therefore, NIV is not considered as an aerosol-generating procedure for virus transport.[49] It has been demonstrated that NIV results in more aerosol dispersion, but the viral load appeared lower than without NIV.[50] A possible explanation might be that NIV may provide a protective benefit by limiting dispersal of droplets from coughing by the patients.[51] The use of specific full-face mask/helmet NIV reduces SARS-CoV-2 transmission.[52,53]

There is also insufficient evidence to conclude that nasal high flow (NHF) therapy should be considered an aerosol generating procedure.[47] NHF therapy use does not increase the risk of dispersing aerosols over the risk from patient breathing with violent exhalation or standard oxygen mask.[54,55] Vianello et al performed an NHF study in SARS-CoV-2 infected patients. None of the staff members tested positive for COVID-19 during this study, which supports the limited risk of airborne transmission by NHF.[56] Previous studies also showed a low risk of airborne transmission with NHF therapy when good interface fitting is achieved.[57]

Intubation and Bronchoscopy

Endotracheal intubation of SARS CoV-1-infected patients has been consistently associated with viral transmission to health care workers. Four cohort studies showed that the tracheal intubation procedure is a significant risk factor for transmission of SARS CoV-1 to health care workers.[46]

There is little data about the risk of virus transmission by bronchoscopy. In two studies performed during the SARS CoV-1 outbreak, bronchoscopy was not associated with infection transmission.[58,59] Bronchoscopy of influenza A H1N1 infected patients demonstrated an increased detection of viral aerosols.[50] The extrapolation of SARS CoV-1 data is complicated by the fact that presymptomatic spread of SARS CoV-1 appears to be rare. Therefore, the aerosolizing procedures are not the greatest danger for the transmission of SARS-CoV-2, it is the daily breathing and talking to someone who is asymptomatically or pre-symptomatically infected, whilst recording the patient's history or talking to colleagues during the lunch break.

There are also several general options to reduce the risk of aerosol transmission during aerosol generating procedures. Negative-pressure rooms, high-energy particulate accumulator (HEPA) filters, and adequate personal protective equipment (PPE) are effective in protecting staff from aerosol transmission.[60,61] PPE for health care workers during aerosol-generating procedures are a waterproof long-sleeved gown, double non-sterile gloves, eye protection and a respirator that ensures a level of protection equal to or greater than professional masks.[62]

In conclusion, clinicians should be aware of distancing, ensure correct use of equipment, use protection material and guarantee treatment of the patient in an airborne infection isolation or negative pressure room during aerosol generating procedures.[57] The greatest risk of aerosol transmission is during endotracheal intubation, the risk with non-invasive ventilation seems to be moderate.

Nonetheless, it is important to realize that, in addition to aerosol generating procedures such as risk for SARS-CoV-2 transmission, the greatest likelihood of SARS-CoV-2 contamination occurs during regular contact with speaking, singing, laughing, and breathing.

CONCLUSION

The evidence for transmission via aerosols containing SARS-CoV-2 seems to be at least as strong as the evidence for transmission via deposition of droplets on surfaces. It is plausible that virus transmission via aerosols plays an important role in SSEs in the COVID-19 pandemic. Knowledge and awareness of all routes, including aerosol transmission, is pivotal for taking precautions. This is absolutely necessary to curb the pandemic and to relieve the heavy burden on society and hospitals. Important preventive measures for aerosol transmission are face protection using masks and good quality ventilation. These preventive measures are definitely needed for health care workers, especially during intubation, while the risk with non-invasive ventilation seems to be moderate.

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