Literature Review: Evidence for SARS-CoV-2 and MERS-CoV as Aerosol Transmissible Pathogens and the Role of Ventilation in Reducing Transmission

Prepared for Cal/OSHA by HESIS, OHB/CDPH

Knowledge of the transmission mechanisms for SARS-Cov-2 and MERS-CoV viruses is essential for designing effective infection prevention measures to protect health care and non-health care workers.[1] Transmission of these viruses via the airborne route in health care and other settings is sufficiently likely that this mode of transmission must be controlled.[2-4] Ventilation and air filtration are measures used to contain and reduce the airborne concentration of respiratory aerosol particles containing SARS-CoV-2 and MERS-CoV viruses, and therefore are important tools to reduce the risk of transmission through the air.[4-11]

Summary Points on Transmission

1. Aerosol particles are emitted during normal exhalation, talking, coughing, and sneezing. In a person with an infectious viral respiratory tract infection, viruses are contained in particles emitted from the respiratory tract. The aerosol particles contain viable virus and are small enough to remain airborne for minutes to hours.[12]
2. Most particles emitted are 5 micrometers (µm) or smaller which are in the respirable size range (Leung 2020) [13-15] and SARS-CoV-2 viral RNA has been detected in particles smaller than 5 µm.[16] These particles can deposit throughout the respiratory tract.
3. The following studies support the likelihood of transmission via aerosols for SARS-CoV-2 and Middle East respiratory syndrome coronavirus (MERS-CoV).

Researchers have found SARS-CoV-2 RNA in aerosol samples in patients' room air during childbirth [17] and in hospitalized COVID-19 patients' rooms and in the corridors outside hospitalized patients' rooms.[18] In a recent literature review of air sampling for SARS-CoV-2, Borges described eight studies in health care settings in which SARS-CoV-2 RNA was detected in air samples.[19] In two of these studies, viable airborne virus was also isolated. In one, air samplers collected viable virus 2 to 4.8 meters from a COVID-positive patient inside the patient's room [20] and, in a second study, viable airborne virus was collected in a hallway outside patients' rooms.[21] In a recently published study in a hospital, researchers used size-selective air sampling and found viable SARS-CoV-2 virus in aerosols that were smaller than 5 µm; this result shows the potential for transmission via the airborne route.[22] SARS-CoV-2 viruses in experimentally generated aerosols remain viable for up to 3 hours.[23]

Airborne transmission of SARS-CoV-2 has also been demonstrated in an experimental animal (ferret) model where the only exposure source was by inhalation of air from an infectious ferret that passed through an air duct more than one meter long.[24] It was also demonstrated in Syrian hamsters that were housed separately in two compartments. When the direction of airflow was reversed, to flow from uninfected to infected hamster, no infection occurred providing experimental evidence of the importance of directional airflow.[25]

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In epidemiological studies, COVID infections at distances greater than six feet from an infectious person have been documented in several indoor settings including in a poorly ventilated restaurant,[26] in a hotel quarantine center,[27] in a church,[28] and during choir practice.[29] Such transmission at a distance is most reasonably explained by an airborne route of exposure.

Several researchers have stated that there is sufficient evidence that indoor airborne transmission associated with small, micron-scale aerosol droplets plays a dominant role in the spread of COVID-19.[6,13,30,31]

In a study of MERS-CoV infections in Saudi Arabia and South Korea between 2015-2017, researchers found that most cases of MERS were due to transmission in health care settings and 25% of cases were in health care professionals.[32] South Korean researchers confirmed the presence of viable MERS-CoV from cultured samples of air taken from hospitalized patients' rooms where the patients had MERS. With the likelihood of airborne transmission and extensive environmental presence and stability of virus found, they concluded that MERS is easily spread in health care settings.[33]

In a study from South Korea that included 31 hospitals, researchers found the incidence of MERS infection in health care workers was higher among study participants who didn't wear appropriate personal protective equipment (PPE). The definition of appropriate PPE included (a) an N95 respirator or powered air-purifying respirator (PAPR), (b) isolation gown (coverall), (c) goggles or face shield and (d) gloves. Additionally, the risk of infection of health care workers was found to be higher if the health care worker performed an aerosol-generating procedure (AGP) without a PAPR compared to performing an AGP with a PAPR.[34]

MERS or MERS-CoV is not listed in Appendix A of the ATD Standard; however, CDPH has recommended the use of airborne infection isolation and contact precautions, as well as standard precautions, for hospitalized patients with MERS.[35] Therefore, under the ATD Standard, this disease must be considered an airborne disease requiring airborne infection isolation.

Ventilation: Rates, Filtration, and Directional Flow

Ventilation in Health Care and Non-Health Care Settings

Scientists have recognized for decades the importance of ventilation and filtration in reducing the airborne concentration of virus particles involved in disease transmission.[8,36,37] Evidence that COVID-19 transmission occurs in poorly ventilated indoor spaces, and that it is more likely to occur in indoor rather than outdoor spaces, are arguments for airborne transmission since only small-sized aerosols, and not large droplets, are affected by ventilation.[38,39]

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Research studies have demonstrated that the higher the rate of ventilation, the faster the removal of exhaled virus particles which reduces the dose inhaled by occupants.[40,41] (Yin 2011)[42] Data from a study by Horve (preprint), confirmed that the higher the ventilation rate in air changes per hour (ACH), the lower the detectable aerosolized viral load within the enclosed spaces of isolation dormitory rooms.[43]

An article by Michael C. Jarvis describes ways researchers have calculated the transmission risk as a function of ventilation rate.[44] Zhang estimated the risk reduction factors for selected control strategies such as increasing ventilation rates, improving filtration efficiency within the HVAC system, and using a room air cleaner. He emphasized that implementing a combination of several controls would be most effective at controlling exposure to SARS-CoV-2.[10]

The literature review by Li et al. (2007) demonstrated the importance of unidirectional flow for the reduction of cross-infection.[36] ASHRAE (formerly the American Society of Heating, Refrigerating and Air-Conditioning Engineers but now just "ASHRAE") has recommended negative pressure relative to other areas for bathrooms, process areas, custodial areas, and commercial kitchens.

Using airflow modeling for a health care setting that had a large nosocomial SARS outbreak, researchers found air exchange due to temperature differences played a significant role in SARS transmission and directional airflow was demonstrated to reduce the risk of airborne infection.[45]

Ventilation in Health Care Settings

ASHRAE provides guidance for hospitals and residential care facilities on ventilation rates, pressure relationships between isolation areas and surrounding areas, and directional airflow.[46] For example, for hospitals, ASHRAE recommends a minimum of 6 ACH for emergency department exam/treatment rooms (with minimum of two ACH of outdoor air) and 12 ACH for airborne infection isolation rooms (with a minimum of 2 ACH of outdoor air), which is consistent with Centers for Disease Control and Prevention (CDC) Guidelines for Environmental Infection Control in Health-care Facilities.[47] For comparison, for regular, non-airborne infection isolation patient rooms, ASHRAE specifies 4 ACH (or 6 ACH if have Group D diffusers, with a minimum of two ACH of outdoor air) for hospitals and only two total ACH (both outdoor air ACH) for nursing home resident rooms.

Since the pandemic began, ASHRAE has also provided additional guidance on their website specific to these health care settings and based on the existing evidence of airborne transmission of SARS-CoV-2.[48-50]

Airborne Infection Isolation:

Currently, ASHRAE recommends that airborne infection isolation rooms (AIIRs) used for persons with diagnosed or suspected airborne infectious diseases in health care facilities be engineered to provide 1) more than 12 ACH (with two air changes outdoor); 2) an air supply and exhaust rate sufficient to maintain a 2.5 Pa (0.01-inch water gauge) negative pressure difference with respect to all surrounding spaces; and 3) air exhausted directly outside away from air intakes and traffic or exhausted after HEPA filtration before recirculation.[46]

Characteristics of an Airborne Infection Isolation Room:
Within an infection isolation room, Cho 2019 found that "that the airflow paths, induced SA (supply air) flow paths, and EA (exhaust air) grille placement can be coordinated to establish effective contaminant control. Locations of the SA and EA openings are the most important elements that directly affect the pollutants dispersion in the room." The researcher recommended that facilities "Arrange EA grilles and SA diffusers to allow clean SA to move from the clean area (HCW) to the contaminated area (patient), and exhausted from the AIIR." Cho found that air supply and exhaust diffuser placement had a significant effect on health care worker exposure to an airborne contaminant generated at the head of the bed.[51]

Few skilled nursing facilities in California have well-designed airborne infection isolation rooms (personal communication with staff in the CDPH Healthcare-Associated Infections Program). To achieve airborne infection isolation without a well-designed airborne infection isolation room, ASHRAE and the National Institute for Occupational Safety and Health (NIOSH) have recommended use of expedient patient isolation control measures, ventilated headboards, and patient tents with HEPA filters.[49,50,52-54] Researchers at the University of Colorado, Boulder created a negative pressure isolation area in a skilled nursing facility by modifying an existing HVAC system during the COVID pandemic. Over the course of their study, the isolation space consistently maintained a population of between 2 and 6 known COVID-19-positive residents and no transmission occurred between positive residents and non-positive residents or between positive residents and health care workers. The researchers concluded that this retrofitted negative pressure isolation space was successfully implemented in a reasonable time frame and in a cost-effective manner to minimize airborne disease transmission within that space.[55]

Local Exhaust Ventilation Devices
Ventilated headboards provide near-instant capture of most infectious aerosols released by a patient at the source while the patient is in bed. They provide an affordable way to protect staff and other residents and continuously maintain clean air in the patient's/resident's room. The ventilated headboard is a special inlet system designed to provide improved air intake and particle capture when coupled with a high-efficiency particulate air (HEPA) fan/filter unit. Together, the ventilated headboard and HEPA system can provide surge isolation capacity

in either traditional health care facilities or alternate care sites.[53] In a laboratory setting, the NIOSH-designed headboard successfully captured/removed over 99% of airborne infectious-sized aerosols using the NIOSH droplet nuclei test protocol.[56]

Another local exhaust ventilation device used in health care facilities in California is the Peace Demistifier tent. The tent vinyl canopy provides an isolation enclosure by fitting over the patient's bed. Air is drawn from under the canopy near the floor and is exhausted by a 220 cubic foot per minute fan through a HEPA filter. The Peace Demistifier tent has been used for aerosol generating procedures such as nubulizer treatments. NIOSH tested the efficacy of this tent during pentamidine administration to a patient and found that none of the area air samples collected outside the tent had detectable pentamidine aerosol, thereby indicating that the tent and filter effectively captured the aerosol.[57] According to the manufacturer, the tents have also been used for patient isolation during the COVID-19 pandemic to contain infectious aerosols.

Alternate Care Sites (health care setting):

For **non-COVID emergency surge spaces outside of a licensed hospital**, ASHRAE recommends the following general parameters for air changes per hour, temperature, filtration, and relative humidity:

- Minimum 2 ACH Outdoor air and 2 ACH Total air, though higher total air is desired (basis is patient room from FGI 1997).
- For large volume spaces with high ceilings, such as conference centers, air changes may be calculated based on a ceiling height of 10 feet, however for supply air temperatures above room temperature, minimum OA and total ACH may be calculated as 2 ACH Outdoor divided by 0.8 ACH, or 2.5 Total air, (ASHRAE 62.1 ventilation effectiveness) and supply air temperatures kept no more than 15 degrees F above room temperature to minimize stratification and short circuiting of air within the space.
- No less than MERV 13 and MERV 14 preferred for systems that are not serving specialized environments that may require even higher efficiency filtration.
- Refer also to Minnesota Department of Health, "Methods for Temporary Negative Pressure Isolation".[49]

Ventilation and Transmission Risk in Ambulances and other Vehicles

NIOSH researchers studied the effectiveness of ambulance ventilation systems at reducing emergency medical service (EMS) worker exposure to airborne particles (aerosols). They found that the ambulance ventilation system reduced but did not eliminate worker exposure to infectious aerosol particles. Aerosol exposures were not significantly different at different locations within the compartment, including locations behind and beside the patient.[58]

An air sampling study in a car driven by a COVID patient with mild illness found SARS-CoV-2 in respirable size ranges by PCR and was cultured from the section of the sampler collecting particles in the 0.25-0.50 micrometer (µm) size range. The study highlighted the potential risk of SARS-CoV-2 transmission by minimally symptomatic persons in the closed space inside of a car and suggested that a substantial component of that risk was via aerosolized virus.[59]

Ventilation for Non-Health Care Settings

Several guidance documents recommend a minimum ventilation rate of 6 ACH in non-health care environments to reduce the spread of airborne SARS-CoV-2.[60-62] In addition, where occupant density cannot be limited to fewer than 1 person per ~30 ft^2 (i.e., 6-foot radius), or where there is likelihood that infected persons are present, the AIHA (formerly the American Industrial Hygiene Association) has recommended that facilities deliver air change rates higher than 6 ACH.[63] Recirculating air within a building having a single infectious person without adequate filtration can result in increasing the risk of airborne infection in areas that otherwise would not have been contaminated.[42] Consequently, the CDPH, "Interim Guidance for Ventilation, Filtration, and Air Quality in Indoor Environments" recommends 100% outside air be provided if feasible.

The California Department of Public Health/Cal/OSHA/OSHPD "Interim Guidance for Ventilation, Filtration, and Air Quality in Indoor Environments"[64] and ASHRAE guidance[65] recommends the following steps to 1) increase the delivery of clean air and 2) remove or dilute concentrations of COVID-19 or other contaminants in the building air.

1. Increase outdoor air ventilation (use caution in highly polluted areas); with a lower population in the building, this increases the effective dilution ventilation per person.
2. In buildings with a mechanical ventilation (HVAC) system, disable demand-controlled ventilation (DCV) and occupancy sensors so that fans operate continuously.
3. Further open minimum outdoor air dampers, as high as 100%, thus eliminating recirculation. Set economizers at 100% outdoor air.
4. Improve central air filtration to MERV-13 or higher, or the highest compatible with the filter rack and without significantly diminishing design airflow, and seal edges of the filter to limit bypass.
5. Keep systems running longer hours, if possible 24/7, to enhance the two actions above. Continuous operation of the HVAC system is required regardless of COVID-19 when employees are present under CCR Title 8, Section 5142.

6. Consider adding portable room air cleaners with HEPA filters.
7. Note that (regardless of COVID-19) CCR Title 8, Section 5142, requires that mechanical ventilation systems be maintained and operated to provide at least the quantity of outdoor air required by the State Building Standards Code, Title 24, Part 2, California Administrative Code, in effect at the time the building permit was issued.

Schools

For schools, the California Department of Public Health has posted guidance for schools at "COVID-19 Public Health Guidance for K-12 Schools in California, 2021-22 School Year" (September 22, 2021) and specifically on ventilation on the topic page: Aerosol Transmission and Airborne Diseases including the document, Ventilation and Filtration to Reduce Long-Range Airborne Transmission of COVID-19 and Other Respiratory Infections: Considerations for Reopened Schools (2021) (PDF) and Information for School Districts on Purchase of Filtration/Air Cleaning Devices (2021) (PDF).

A modeling study demonstrated that increasing natural ventilation was the most effective COVID-19 mitigation measure in schools compared with the alternatives of portable HEPA filtration devices and masking, and that combining interventions can significantly reduce estimates of inhaled doses per person.[66]

More information on school ventilation and air filtration can be found at:
CDC's Guidance for Ventilation in Schools and Childcare Programs
EPA's Program for Healthy Indoor Air Quality in Schools

Offices and Laboratories

For offices and laboratories, Augenbraun developed guidelines to result in occupants' risk of contracting COVID-19 to less than 1% over 6 months.[67]

Recommendations for Filtration

Ventilation system filters are assigned a Minimum Efficiency Reporting Value (MERV) based on their filtration efficiency per the ASHRAE 52.2 test. MERV values range from 1 to 16; the higher the MERV, the higher the efficiency. HEPA filters are more efficient than MERV 16. Most residential and commercial buildings utilize MERV-5 to MERV-11 filtration. MERV 13 filters remove ≥85% of 1-3 µm particles. Based on the aerodynamic size of aerosolized particles containing SARS-CoV-2 virus measured in hospitals in the range of 0.25 to 0.5 µm by Liu et al.(2020),[68] Dietz et al. recommended high efficiency filtration to reduce the transmission potential of pathogens such as SARS-CoV-2.[69] AIHA stated that installing MERV 13 or higher filters in central HVAC systems can reduce infectious aerosol concentrations of SARS-CoV-2 in recirculated air.[63]

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ASHRAE recommends no less than MERV-13, and MERV 14 preferred, in health care settings although specialized environments may require a higher level of filtration.[48] Gola et al. recommended MERV-13 or higher filtration in health care settings as well.[9] To avoid leakage of contaminated air through and around the filter, Gola et al recommended leakage tests after each filter replacement and periodically, according to ISO 14644 be performed to verify that no damage to the filter occurred during installation and that no leaks are occurring at the perimeter.[9] In November 2020, ASHRAE specified MERV 14 (or ISO equivalent) filters for skilled nursing facilities and other residential health care environments in Addendum r of ANSI/ASHRAE/American Society for Health Care Engineering (ASHE) Standard 170-2017, Table 9.1.[4]

For schools, Zhang et al. recommended MERV 14 filters in ventilation systems if any air is recirculated in schools to minimize cross contamination between different rooms. MERV 14 filters can typically be accommodated by existing HVAC system fans and can reduce the risk by a factor of 4 compared to a factor of 2-3 for filtration with MERV 9-13 filters. A higher grade MERV 16 or HEPA filter is likely to require a major system modification while the risk reduction benefit is marginal.[10]

One concern often raised about increasing the filtration efficiency in an existing building ventilation system is the potential increase in energy required with the use of MERV 13 or higher filters.

In 2018, the California Energy Commission prepared for 2019 Title 24, Part 6, Building Energy Efficiency Standards Rulemaking. The California Energy Commission staff arranged for testing of residential ventilation system air filters to compare the pressure drop characteristics of MERV rated filters in the range of MERV 6 through MERV 13 from several manufacturers. Residential type filters might be used in small skilled nursing facilities. Staff tested one and two-inch filters. The results of the testing indicated that:

1. "The pressure drop characteristics of these air filters varied widely, and there was no significant or useful correlation between MERV rating and pressure drop for the observed filter models, which ranged from MERV 6 to MERV 13."
2. Three 2" depth MERV 13 filters were tested, and two of those had the lowest pressure drop performance over all others in the dataset, thus indicating that 2" depth filters, which are readily available, provide improved pressure drop performance compared to 1" depth filters. The best performing 2" depth filter provided approximately 30% greater airflow at 0.1 inch water column (w.c.) as compared to the best performing 1" depth MERV 13 filter at 0.1 inch w.c. in this dataset.

3. MERV 13 rated models with clean filter pressure drop performance below 0.1 inch w.c. at 150 ft/min are readily available from multiple manufacturers.

Faulkner et al. found that changing to ASHRAE-recommended MERV 13 filtration reduced the average virus concentration by about 10% when compared to MERV 10 filtration, with negligible additional operational cost.[70]

Portable Air Cleaners

Implementing portable air cleaners having HEPA filtration is another effective method of reducing the concentration infectious aerosols in a room. They provide a cost-effective way to increase the filtration of aerosol particles from a room without modifying the existing building ventilation system.[10] In addition to filtering the air, portable HEPA filters are used to:

- temporarily recirculate air in rooms with no general ventilation,
- augment ventilation systems that cannot provide adequate airflow, and
- provide increased effectiveness in airflow.

NIOSH researchers reported on two recent studies that found that HEPA air cleaners in classrooms could reduce overall aerosol particle concentrations by ≥80% within 30 minutes. In their experimental study in a conference room, NIOSH found that portable air cleaners were able to reduce aerosol concentrations by 65% when the portable air cleaner was in a center floor location. When the portable air cleaner with HEPA filter was combined with universal masking, the combined mean concentrations for the receivers was decreased by 90% in 60 minutes.[71]

For health care settings, CDC's Guidelines for Environmental Infection Control in Health-Care Facilities (2003) recommended using portable, industrial-grade HEPA filter units capable of filtration rates in the range of 300–800 ft^3/minute to augment removal of respirable particles with the goal of achieving the equivalent of ≥12 ACH for airborne infection isolation rooms.

CDPH also recommends that facilities consider adding portable air cleaners in areas where mechanical and passive ventilation cannot be improved. CDPH guidelines provide recommendations on purchasing portable air cleaners that are certified for ozone emissions and that are appropriately sized for the room or area they are deployed in.[64]

Ren et. al evaluated the mechanical ventilation rates of dental treatment rooms and assessed the effectiveness of aerosol removal by mechanical ventilation and a portable air cleaner (PAC). The addition of a PAC with a HEPA filter improved aerosol removal in rooms with low ventilation rates.[72]

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Partial List of Guidelines and Standards for Ventilation in Health Care Settings:

1. California Building Standards Code, Part 4, California Mechanical Code: Title 24, California Code of Regulations Chapter 4. (https://up.codes/viewer/california/ca-mechanical-code-2019/chapter/4/ventilation-air#402.0 or http://epubs.iapmo.org/2019/CMC/index.html#p=114)
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14. CDC, Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition; (www.cdc.gov/labs/BMBL.html).

Partial List of Guidelines and Standards for Ventilation in Non-Health Care Settings:

1. CDPH/Cal/OSHA/OSHPD, Interim guidance for Ventilation, Filtration, and Air Quality in Indoor Environments, February 26, 2021 (accessed on September 23, 2021); (www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Interim-Guidance-for-Ventilation-Filtration-and-Air-Quality-in-Indoor-Environments.aspx).
2. CDPH, Indoor Air Quality Section, The Role of Building Ventilation and Filtration in Reducing Risk of Airborne Viral Transmission in Schools, Illustrated with SARS-CoV-2, September 1, 2020; (www.cdph.ca.gov/Programs/CCDPHP/DEODC/EHLB/IAQ/Pages/Airborne-Diseases.aspx).
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4. CDPH, Indoor Air Quality Section, Information for School Districts on Purchase of Filtration/Air Cleaning Devices (2021)(PDF); (www.cdph.ca.gov/Programs/CCDPHP/DEODC/EHLB/IAQ/CDPH Document Library/Information_for_School_Districts_on_Purchase_of_Air_Cleaning_Devices-logo_date_ADA.pdf).
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resources/coronavirus_outbreak_resources/aiha-covid-19-pandemic-efforts/free-covid-19-public-resources).

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5. ASHRAE Environmental Health Committee (EHC). Emerging Issue Brief: Pandemic COVID-19 and Airborne Transmission, 2020; (www.ashrae.org/technical-resources/covid-19-one-page-guidance-documents).
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