COVID-19: What do we know?

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Coronavirus disease 2019 (COVID-19) is a global pandemic caused by the pathogen severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Preliminary assessments suggest the virus is highly transmittable and infectious,[2-7] with similarities in nosocomial and super-spreading events seen with severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) in 2003.[8] Patients infected with SARS-CoV-2 display a wide range of host responses including no symptoms, mild nonrespiratory symptoms, severe respiratory illness, or organ dysfunction and death.[1,5] The American Association of Orthodontists Council on Scientific Affairs was charged with examining the literature to determine the best evidence for questions pertaining to COVID-19 and its impact on the practice of orthodontics.

HOW IS SARS-COV-2 TRANSMITTED?

Transmission of SARS-CoV-2 is not fully understood, but preliminary evidence supports transmission of the virus between humans by (1) *direct* inhalation of airborne virus contained in infectious bioaerosol produced from an infected patient (ie, bioaerosol from coughing, sneezing, talking, exhaling breath, or mechanical aerosolization of infected salivary or respiratory secretions are potential routes of transmission), or (2) *indirect* transfer to the mouth, nose, or eyes from surfaces contaminated with virus-laden salivary or respiratory secretions or the settling of the airborne virus.[1,9]

Recent evidence suggests that transmission of SARS-CoV-2 is possible from presymptomatic, symptomatic, and asymptomatic patients.[10-26] The proportion of asymptomatic patients to symptomatic patients varies with age, and children are less likely to exhibit clinical symptoms than adults.[27] Estimates of infected asymptomatic patients range from 6% to 41%.[14] The mechanism of asymptomatic transmission (direct or indirect) is not clear, and the extent of this phenomena is not exactly known, but is estimated to be low compared with transmission from symptomatic patients.[18,24,28,29] Viral shedding, detected by viral RNA assay of nasopharyngeal secretions, has been reported in patients fully recovered from SARS-CoV-2 infection,[30-33] however it is not known how the detection of viral RNA is related to transmissible (replication-competent) virus,[34,35] and no studies have reported transmission from patients fully recovered from COVID-19.[36]

Proximity to symptomatic patients appear to be the most significant risk factor for contracting the virus, and prolonged close contact with a symptomatic individual increases the risk.[37,38] Although there is not yet a consensus on the mode of transmission during close contact, studies indicate indoor venues with crowded spaces requiring prolonged close personal contact (ie, *high-risk* spaces) appear to be the source of super-spreading events and suggest airborne transmission is likely under these conditions.[39]

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Even though airborne transmission is strongly suspected, we lack an understanding of exactly how this occurs.[40] Airborne virus (~0.1 μm) travels in droplets produced by coughing, sneezing, talking, exhaling, or by bioaerosol generated during certain medical and dental procedures (aerosol-generating procedures [AGPs]). Airborne droplets from a respiratory or salivary origin are distinguished by size, from large (>5 μm) to small (<5 μm). Large droplets (eg, from sneezing, AGPs) tend to settle on surfaces or unprotected mucosa of close contacts and may be the source of direct or indirect virus transmission (also termed droplet transmission).[41] In experimentally simulated aerosolization of SARS-CoV-2, the virus maintains viability on surfaces for up to 72 hours, indicating indirect (droplet) transmission can occur long after droplets establish contact with surfaces.[42-44] In contrast, small droplets (eg, from coughing, talking, exhaling, or AGPs) produced by similar experimental aerosolization can evaporate into "droplet nuclei" and remain in the air for many hours.[42,43,45-47] The amount of viable SARS-CoV-2 in droplet nuclei remains unclear, but in subjects infected with other respiratory viruses, such as influenza, experiments comparing coughing and breathing suggest an equivalent production of viral RNA and replication-competent virus, detected at close range (<12-in).[48,49] Although this has not been adequately studied for SARS-CoV-2, similar findings might be anticipated.[50-52] Moreover, saliva can be aerosolized during AGPs and is a known source of SARS-CoV-2 in infected patients.[53]

A timeline suggesting when infected patients are most contagious has been informed by studies assessing viral shedding of COVID-19 patients by 2 methods: detection of SARS-CoV-2 RNA and SARS-CoV-2 replication in cultured cells.[54] Viral RNA can be detected 1-3 days before the onset of COVID-19 symptoms, with the highest viral load in the upper respiratory tract occurring near the onset of symptoms followed by a decreasing viral load that is time-dependent based on disease severity. Viral RNA is shed for 1-2 weeks in asymptomatic cases and 3 or more weeks for mild to moderate cases of COVID-19.[11,15,31,55-61] More severe symptoms require a longer time to reduce viral load.[11,15,19,56,62-65] Reduction in viral load is accompanied by increases in neutralizing antibodies.[11] The findings from a limited number of studies evaluating virus viability during the course of COVID-19 illness suggest it is rare to find infected symptomatic patients shedding viable virus after 9 days of symptom onset.[11,17,57,66-68] A study of nursing home residents found viral RNA and viable virus in presymptomatic and asymptomatic subjects.[17] Taken together, these data suggest viral shedding, detected by viral RNA, may be an indicator of SARS-CoV-2 transmissibility before the onset of COVID-19 symptoms, but not later in the course of COVID-19 illness. However, measuring virus viability is more complex and may not be as sensitive as RNA detection.[11,69] It is clear that additional studies are needed to correlate viral RNA detection and transmissibility of viable virus.[68]

Important factors characterizing airborne SARS-CoV-2 transmission remain unknown: (1) the presence of the virus within the spectrum of droplet sizes contained within the human bioaerosol of infected subjects; (2) the proportion of small bioaerosol droplets that evaporate to droplet nuclei; (3) the half-life of viable virus in droplet nuclei; (4) the inhalation dose of the virus required to cause infection; (5) the timeline of when infected patients are most contagious; and (6) the role of environmental conditions play in airborne transport and virus viability.[70]

WHAT DO WE KNOW ABOUT AIRBORNE TRANSMISSION OF SARS-COV-2 IN HEALTH CARE SETTINGS?

Studies evaluating airborne transmission from patients with COVID-19 illness undergoing medical care that includes AGPs and medical care without AGPs (non-AGPs) have not revealed a clear consensus on the risk of airborne transmission of SARS-CoV-2.[71] Airborne transmission of viable SARS-CoV-2 virus during medical AGPs on infected patients is suggested from previous studies of SARS-CoV-1 but has not been confirmed.[71] In situations where health care workers wearing personal protective equipment (PPE) attend to patients with COVID-19 and do not perform medical AGPs, direct airborne transmission of replication-competent SARS-CoV-2 has not been confirmed.[72]

The results of hospital studies evaluating aerosolization of body fluids and respiratory droplets of SARS-CoV-1 infected patients generated during certain medical AGPs (tracheal intubation, noninvasive ventilation, bronchoscopy, etc.), suggest that airborne transmission of SARS-CoV-2 may be possible during these procedures.[72] However, the "possibility" is not clearly defined. High-quality studies using consistent methodology to assess virus transmissibility during medical AGPs are lacking.[71] A 2012 systematic review of 5 case-control studies and 5 retrospective cohort studies on the transmissibility of SARS-CoV-1 during medical AGPs found a weak association with tracheal intubation across multiple studies and could draw no conclusions regarding other medical AGPs.[73] Subsequent studies

on SARS-CoV-1 transmissibility during medical AGPs produced variable results.[41,74] Similar controversial findings were found for Influenza A H1N1.[75] To date, although there is evidence suggesting that SARS-CoV-2 is likely transmitted via bioaerosol,[76] there is no direct evidence of airborne transmission of SARS-CoV-2 during medical AGPs when health care workers are wearing appropriate PPE, the risk of airborne transmission is not clearly defined.[71] Using precaution as the guiding principle in risk management, the Centers for Disease Control and Prevention (CDC) and World Health Organization have adopted guidelines for barrier and environmental protection based on the hypothesis that airborne transmission can occur, even though a detailed understanding remains to be elucidated. From the CDC guidelines:

> *Development of a comprehensive list of AGPs for healthcare settings has not been possible, due to limitations in available data on which procedures may generate potentially infectious aerosols and the challenges in determining if reported transmissions during AGPs are due to aerosols or other exposures.*
>
> *There is neither expert consensus, nor sufficient supporting data, to create a definitive and comprehensive list of AGPs for healthcare settings.*[77]

Scientific consensus on the transmission of SARS-CoV-2 during medical non-AGPs is not yet available. Results from studies designed to sample air for SARS-CoV-2 RNA, in hospital rooms where infected patients were cared for without medical AGPs, produced variable results.[78-89] The studies finding the presence of viral RNA reported very low amounts.[78-83] This experimental design assesses the presence of SARS-CoV-2 RNA but does not assess virus viability. Currently, there are no studies reporting airborne viable (replication-competent) SARS-CoV-2 virus in hospital settings where infected patients are cared for, but not subjected to medical AGPs, by health care workers wearing surgical masks.[74]

WHAT IS KNOWN ABOUT THE RISKS OF DIRECT AIRBORNE INFECTION FROM BIOAEROSOL IN THE TREATMENT OF ORTHODONTIC PATIENTS?

In contrast to medical procedures in the hospital and clinical settings, the risk of airborne SARS-CoV-2 infection during the treatment of orthodontic patients has not been studied. In addition, there are no reports of transmission of the virus in an orthodontic setting to elucidate clues regarding risk and transmission. Guidelines to mitigate the risk of SARS-CoV-2 airborne transmission during orthodontic treatment must be inferred

from studies of SARS-CoV-2 infected patients during AGPs and non-AGPs in other health care settings. However, the extent to which AGPs and non-AGPs differ between the practice of medicine and the practice of orthodontics and the impact of these differences on the risk of SARS-CoV-2 transmission has not been adequately addressed. As potential SARS-CoV-2 transmission from presymptomatic and asymptomatic patients remains a possibility, COVID-19 screening procedures will not prevent the unintentional treatment of some contagious patients. This poses an unknown risk of airborne transmission for both AGPs (mechanically-generated bioaerosol) and non-AGPs (patient sneezing, coughing, talking, exhaling) in orthodontic practice.

WHICH ORTHODONTIC PROCEDURES ARE CONSIDERED AEROSOL-GENERATING (AGPS)?

In orthodontic practice, AGPs include the use of rotary instruments (high-speed and slow-speed handpiece), air-water syringes (produce both splatter and aerosol), ultrasonic scalers, or air abrasion/polishing instrumentation on the tissues within the oral cavity. The use of these instruments generates aerosolized particles, including particulates from dental materials and bioaerosol from aerosolized saliva and respiratory droplets. The particles/droplets generated range from 0.1-50 μm. The bioaerosol contents include live bacteria, fungus, and viruses that increase the contamination of the air and surfaces in the area of patient treatment.[90-93] Many reports have characterized the bacterial content of this bioaerosol, but there is a lack of research characterizing the production of viable airborne viruses from AGPs used in orthodontic practice.[92,94] Of particular importance is the size difference between viruses and bacteria. For example, Bennett et al[95] found that bacteria (oral streptococci) in aerosols generated during dental AGPs dissipate within 30 minutes of their peak concentration. However, streptococci are 10-fold larger in diameter compared with SARS-CoV-2, which may limit their maintenance in aerosol compared with that seen for coronaviruses.[42,43,45-47,96]

HOW MUCH AEROSOL IS GENERATED DURING ORTHODONTIC DEBONDING?

Although the composition of particulates and bioaerosol generated during debonding of fixed orthodontic appliances has been widely studied (viruses excluded), the amount of bioaerosol generated during orthodontic debonding is not exactly known and remains unknown for virus and virus particles[91,92,97-102] (for a comprehensive review, see Zemouri et al[92] and Eliades

and Koletsi[94]). Evaluating various dental procedures in situ, Polednik[91] established that compared with background levels, airborne particulates increase approximately 6-fold for composite grinding, compared with a 2.5-fold increase for ultrasonic scaling. Composite grinding produced the most particulate aerosol of any dental AGP tested. Levels of bacterial aerosolization compared with background were ~1.5-fold greater across dental AGPs tested.

DOES AEROSOL GENERATION DIFFER WHEN DEBONDING IS PERFORMED WITH A SLOW-SPEED VS HIGH-SPEED HANDPIECE, OR WHEN DEBONDING IS PERFORMED WITH WATER VS WITHOUT WATER?

There are no studies addressing this question in situ, and no studies quantifying the amounts of bioaerosol generated during orthodontic debonding. The production of aerosol containing bonding adhesive and enamel particulates has been measured during the removal of orthodontic adhesive from human teeth under laboratory conditions.[97,98,100,102] One study suggests particle size differs between slow-speed and high-speed handpieces, and the addition of water spray to the procedure results in a reduction of particle size generated during debonding. Slow-speed handpieces, with or without water spray, produced particles ~5-15 μm. High-speed handpieces without and with water spray produced particles ~3 μm and ~0.5-1.3 μm, respectively.[98] A second study by the same research group suggests debonding with a high-speed handpiece and water spray generates approximately 2-fold more adhesive and enamel particulates compared with debonding with a slow-speed handpiece without water spray.[100] Results from another research group evaluating smaller diameter particulates suggests the addition of water spray during slow-speed handpiece reduction of bulk composite reduces, by one half, the amount of airborne particulates smaller than 0.1 μm in diameter.[103] Taken together, these studies suggest that slower speed and water spray may reduce the amount of particulate aerosol produced. Additional studies are needed to confirm this finding.

It has been proposed that the use of water spray during orthodontic debonding improves debonding efficiency and thereby reduces the time that bioaerosol is produced.[94] Additional studies are needed to confirm this hypothesis.

At present, we cannot extrapolate from these laboratory studies to understand the amount of viable SARS-CoV-2 present in bioaerosol produced by various permutations of handpiece use during orthodontic debonding.

ARE HIGH-VOLUME EXTRAORAL EVACUATION UNITS EFFECTIVE IN REDUCING AEROSOLS GENERATED DURING ORTHODONTIC DEBONDING?

By and large, the clinical evidence for the reduction of aerosols by the use of high-volume extraoral evacuation (HVE) comes from studies detecting the bacterial load produced during ultrasonic scaling.[104] Results from these studies have not been consistent. Significant bacterial load reductions (83%-94%)[105,106] or no reduction[107] have been reported depending on the orientation of the HVE tip to the ultrasonic scaler. There are no studies assessing the effect of HVE on bacterial load reduction in aerosols generated during orthodontic debonding. Laboratory studies generating aerosol by various dental AGPs have suggested aerosol is reduced by the use of HVE.[100,108,109] However, the generalizability of findings from laboratory ultrasonic scaling studies to orthodontic debonding in situ is not fully understood.

In addition, a recent meta-analysis of randomized and nonrandomized trials assessing interventions to reduce bacterial aerosolization during dental AGPs suggests the use of HVE is not more effective than preprocedural rinses with chlorhexidine or chlorine dioxide.[104] However, it is uncertain how this pertains to a viable aerosolized virus.

At present, no studies have assessed the effectiveness of HVE during orthodontic debonding on the reduction of transmissible SARS-CoV-2. The use of HVE should be considered a prudent adjunctive measure to reduce the risk of virus transmission via bioaerosol during orthodontic debonding, but the efficacy of HVE use remains unclear. New evacuation instrumentation (eg, high-flow extractor[110]) are being developed and studied for their efficacy in reducing mechanically-generated bioaerosol. Ongoing research will determine the benefit of their use during dental AGPs.[107]

Currently, CDC recommendations for reducing the risk during AGPs in a dental setting include:[35] (1) 4-handed dentistry, (2) use of HVE, (3) dental dams when practical, (4) PPE including N95 mask, face shield, gown, gloves, and (5) portable high-efficiency particulate air (HEPA) filtration system properly situated.

ARE AIR FILTRATION/AIR PURIFICATION SYSTEMS EFFECTIVE IN REDUCING AEROSOLS GENERATED DURING ORTHODONTIC DEBONDING? ARE HEPA FILTERS REQUIRED IN AIR FILTRATION/AIR PURIFICATION SYSTEMS FOR EFFECTIVE REDUCTION OF AEROSOLS GENERATED DURING ORTHODONTIC DEBONDING?

To lessen the risk of airborne transmission of SARS-CoV-2 from the bioaerosol produced during

dental AGPs, portable HEPA filtration systems (known as high-efficiency particulate air, high-efficiency particulate absorbing, and high-efficiency particulate arrestance systems) are recommended by the CDC as a supplement to the barrier protection of PPE.[35] There is ample evidence that HEPA air purification reduces the concentration of airborne particles in the size range associated with airborne SARS-CoV-2,[88,111-113] but direct evidence for reduction of the viable virus has not yet been reported. CDC guidelines suggest best practices for the positioning and use of portable HEPA systems in the operatory during dental AGPs, which is a subject of ongoing research.[35,114]

THE USE OF PPE DURING ORTHODONTIC PROCEDURES

As previously discussed, the infective potential of patient bioaerosol is not fully understood. Bioaerosol generated from coughing, sneezing, exhaling, or by mechanical aerosolization of saliva during patient procedures occurs as a range of drop and droplet sizes, all of which are potentially infective, by direct or indirect droplet contact with uncovered mucosal surfaces, or by inhalation of droplets or droplet nuclei. PPE is an important part of a system protecting doctors, staff, and other patients by reducing the spread of viral respiratory infection. Other parts of that system are equally important: patient prescreening, patient isolation from other patients, minimizing the number of staff caring for a patient, appropriate donning, doffing, and disposal of PPE, appropriate decontamination of surfaces and equipment, and appropriate biohazard waste management.[115] The World Health Organization and CDC have recommended the use of PPE to match the potential mode of SARS-CoV-2 transmission during patient care.[35,116] High-filtration masks (N95 or equivalent) are recommended as protection during AGPs because of their barrier capability. However, in practice, uncertainty remains regarding the effect mask training, mask type, and the reuse of masks and gowns on the true nature of protection.[115,117,118] Reports of headache among health care personnel during prolonged use of N95 respirators[119,120] has prompted the investigation of powered air-purifying respirators as a possible improvement in potential side effects of N95 respiratory use.[121]

ARE N95 MASKS MORE EFFECTIVE IN FILTERING VIRUSES COMPARED WITH LEVEL 2 OR LEVEL 3 SURGICAL MASKS?

There is a lack of high-quality research comparing the effectiveness of the N95 respirator and the surgical mask in preventing transmission of SARS-CoV-2 to a health care worker under conditions of varying transmission risk. A recent systematic review and meta-analysis of 4 randomized trials compared protection from respiratory illness for surgical masks vs N95 respirators in health care workers potentially exposed to patients with acute viral respiratory illness (influenza).[122] Because of the heterogeneity of methods and outcome measures, the findings of no difference between surgical masks and N95 respirators are weakly supported with low or very low levels of evidence. Comparing surgical masks and N95 respirators for protection from other respiratory viruses have produced similar findings.[118,123] No trials have tested N95 respirator protection against SARS-CoV-2 transmission directly.

This evidence should be interpreted with caution. Laboratory studies indicate N95 respirators are far superior in blocking penetration of 10-80 nanometer virions than surgical masks.[124] Trials conducted in health care settings suffer from variation in mask training, mask fitting, mask use, and mask removal that is absent in well-controlled laboratory studies.[117,125] It is not yet clear that surgical masks offer equivalent protection to N95 respirators in situ.

WHAT PPE IS MOST APPROPRIATE DURING AEROSOL-GENERATING PROCEDURES VS NONAEROSOL-GENERATING PROCEDURES?

The CDC recommends the use of face shields, gowns, and gloves during both AGPs and non-AGPs.[35] The CDC recommends the use of an N95 respirator, or a respirator offering equivalent or greater barrier protection to the inhalation of bioaerosol, during dental AGPs, and a surgical facemask during dental non-AGPs.[35] N95 respirators are recommended to limit the inhalation of potentially infectious aerosol. Surgical facemasks offer a more limited "protection for the wearer against exposure to splashes and sprays of infectious material from others."[126]

WHEN SHOULD PPE BE DISCARDED AND REPLACED DURING PATIENT CARE?

The CDC recommends discarding gloves, gowns, and surgical masks between successive patients.[127] The CDC recommends N95 respirators be disposed of after each use, but have provided guidance for extended use, or reuse after decontamination, during periods of reduced N95 availability.[127] Limited reuse is defined as using the same N95 respirator for multiple patients, but removing (doffing) after each patient encounter. The respirator is stored between encounters. Extended use is defined as using the same N95 respirator continuously

during encounters with multiple patients. There are strict guidelines for extended use and limited reuse of N95 respirators.[127]

WHAT ARE THE GUIDELINES FOR DECONTAMINATING PPE?

The CDC has issued strategies for dealing with supply shortages of PPE that include decontaminating the National Institute for Occupational Safety and Health-approved N95 filtering facepiece respirators (FFRs) without exhalation valves. Although knowledge gaps remain in the efficacy of FFR decontamination, moist heat, ultraviolet germicidal irradiation, and vaporous hydrogen peroxide appear to be appropriate decontamination methods. However, FFR decontamination is meant to be implemented under strict guidelines. These guidelines should be thoroughly understood before implementing this strategy.[127]

ARE PREPROCEDURAL RINSES EFFECTIVE AGAINST SARS-COV-2?

Two recent meta-analyses of randomized controlled trials, studying the effect of preprocedural mouth rinses on bacteria produced during dental AGPs, concluded that there is moderate evidence that preprocedural mouth rinses (chlorhexidine, cetylpyridinium chloride, povidone-iodine, or essential oils) significantly reduce aerosolized bacteria.[108,128]

There is no direct evidence for a similar effect of these oral antiseptics on aerosolized viruses. According to the CDC,

> There is no published evidence regarding the clinical effectiveness of PPMRs to reduce SARS-CoV-2 viral loads or to prevent transmission. Although SARS-CoV-2 was not studied, PPMRs with an antimicrobial product (chlorhexidine gluconate, essential oils, povidone-iodine or cetylpyridinium chloride) may reduce the level of oral microorganisms in aerosols and spatter generated during dental procedures.[35]

A number of narrative reviews suggest selected oral antiseptic rinses, including 1.0% hydrogen peroxide, have antiviral activity in vitro, but this indirect evidence requires well-designed trials to evaluate clinical efficacy in situ.[129-133]

HOW MUCH TIME SHOULD BE ALLOCATED BETWEEN PATIENTS WHEN AEROSOL-GENERATING PROCEDURES ARE PERFORMED?

Currently, there is not enough information to answer this question directly. CDC guidelines for performing AGPs on patients known to be infected with SARS-CoV-2 require treatment in an airborne infection isolation room with a minimum of 6 air changes per hour and a minimum waiting time of 69 minutes to reduce potentially infectious aerosol by 99.9%.[33,134] Aerosol-generating treatment of asymptomatic or presymptomatic orthodontic patients poses a risk that is not quantifiable. The CDC has suggested evaluating heating, ventilation, and air conditioning systems for airflow patterns, rates of air exchange, and increased filtration, and the addition of portable HEPA filtration systems to reduce this risk.[35]

IS THE PLACEMENT OF PHYSICAL PARTITIONS BETWEEN CHAIRS, IN AN OPEN OPERATORY, EFFECTIVE IN REDUCING SARS-COV-2 TRANSMISSION DURING ORTHODONTIC APPOINTMENTS?

There is no direct evidence for the efficacy of physical partitions reducing the risk of SARS-CoV-2 transmission in and open operatory facility. As part of engineering controls to reduce the risk of transmission associated with the potential treatment of asymptomatic or presymptomatic orthodontic patients, the CDC recommends floor to ceiling barriers between open operatory chairs to enhance the effectiveness of portable HEPA filtration units dedicated to each operatory chair.[35]

EPILOGUE

COVID-19 is a novel disease. Evidence for COVID-19 management and best practices is being generated rapidly. Although we have assembled the best available current evidence to this series of questions, it must be considered interim information and guidance. As the safe practice of orthodontics is our collective responsibility, the American Association of Orthodontists' task force on COVID-19 will continue to update our understanding of this disease and the impact of new information on the provision of orthodontic care.

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