

NARRATIVE REVIEW

Dealing with the high-risk potential of COVID-19 cross-infection in dental practice

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ABSTRACT

The World Health Organization reported that the SARS-CoV-2 virus has infected more than 5 million people around the world. Dental care providers and health care professionals need to be aware of the high-risk potential of cross-infection since the routes of virus transmission commonly happen through droplets and aerosols. This review aimed at collecting essential knowledge about the COVID-19 needed by dental practitioners. The review focused on the oral involvement in COVID-19, the role of oral transmission as the high-risk potential of cross-infection and recommended strategies to minimize the risk of cross-infection in dental practice. We searched all the published clinical features from PubMed, Google Scholar, Scopus and hand searched library online databases, from January 2015 until May 2020. Keywords used were "COVID-19", "Dentistry", "Dental protection", "Cross-contamination", "Aerosol and non aerosol", and "Povidone-iodine" with their combinations. We identified 52 articles to review after the initial selection with inclusion and exclusion criteria. Results showed use of topical applications of povidone-iodine and viricidal mouthwash could significantly reduce the high-risk of cross-infection from dentistry patients who are asymptomatic with COVID-19 infection. Further safeguards include suspending all non-emergency procedures temporarily and closely screening patients for symptoms which may be suspected to be COVID-19 infection.

Keywords: COVID-19 cross-infection; emergency dental; oral transmission; povidone-iodine; systemic manifestation

INTRODUCTION

Corona Virus Disease 2019 (COVID-19) on March 11, 2020 was determined by the World Health Organization (WHO) as a worldwide pandemic. Based on WHO data up to 24th of May 2020, the number of patients confirmed to be positive of COVID-19 has reached to over 5.17 million cases with 336,430 patients who are have died. The patients confirmed positive with COVID-19 in Indonesia were announced by the Government of Indonesia on March 2, 2020, and subsequently on March 14, 2020, after local transmission was reported, the Corona virus was designated a national disaster. Based on data taken from the COVID-19 Rapid Response and Prevention Cluster up to 24th of May 2020, the number of positive confirmed patients reached 18,496 with more than 1372 mortalities.^{1,2} Considering the source of the spread of COVID-19

tends to be through droplets and aerosols, every patient who has been cared for by dental care providers is at a potential high-risk for the spread of COVID-19.³

In addition, the development of COVID-19 management in the field of dentistry currently focuses on how to handle droplets and aerosols which arise when examinations and treatments are carried out. Dar Odeh (2020)³ and Lo Giudice et al. (2020)⁴ stated that the determination of the service type only in the emergency and elective cases has been established as a form of protection for the spread of COVID-19. However, these present conditions cannot last long, and it is unknown when the pandemic will end and even then, it still retains the potential to re-emerge with a more dangerous form which includes the possibility of mutations of the Severe Acute Respiratory Syndrome

Coronavirus 2 (SARS-CoV-2), the virus which causes COVID-19.⁵

The SARS-CoV-2 virus binds to its receptors, the angiotensin-converting enzyme 2 (ACE2) which are abundant on the surface of the mucosal epithelial cells in the nasal cavity, nasopharynx, oral mucosa, eyes and tongue as well as in the gastro-intestinal tract, kidneys, liver and heart. Accordingly, saliva as a liquid which lubricates the mucosal surface of the oral cavity is a main source of COVID-19 infection. The potential of infection increases in the elderly, people with hypertension, diabetes mellitus, immunocompromised and patients with chronic respiratory problems. Additionally, SARS-CoV-2 infection will stimulate the immune response of IgM and IgG formation, which are very volatile, and currently, there have been no research reports on the formation of adaptive immune responses.⁶ Considering that up to now, there have not been any standardized vaccines and drugs found to prevent and treat COVID-19, then what needs to be especially noticed is that there are some COVID-19 patients who are confirmed to have no symptoms. Regarding these asymptomatic carriers of COVID-19, the dental community needs to be properly alerted and informed of the best practices for prevention of COVID-19 transmission and cross-infection.

This review aims to report any evidence of the high-risk potential of COVID-19 cross-infection in dental practice and strategy to prevent virus transmission in a clinical setting. The focus of this review was the oral involvement in COVID-19, the role of oral transmission as the high-risk potential of cross-infection and recommended strategies for dental care providers and health care professionals to minimize the risk of cross-infection in dental practice. A literature search was performed to find 52 relevant articles published in PubMed, Google Scholar and Scopus during January 2015 until May 2020 according to six search terms which are "COVID-19", "Dentistry", "Dental protection", "Cross-contamination", "Aerosol and non-aerosol", and "Povidone-iodine. Additional references were identified by a manual search from the library online among the references. The inclusion criteria

were all types of articles related to the selection of keywords, full text available and only in human. The grey literature was excluded.

Based on a thorough review of the current selected literatures, the best preventive actions which can be taken now to prevent any further transmission are by closely screening the patients and controlling infection.⁴ Besides these best practices, Flor (2020)⁷ mentioned that the use of antiseptic mouthwash needs to be considered as a national movement to prevent transmission of COVID-19. Along with these recommendations, the review of related articles showed the importance of using povidone-iodine with the right concentration to reduce the spread of SARS-CoV-2 virus infection.⁷

What are the symptoms and mechanisms of COVID-19 in multiple organs?

General pathogenesis

The SARS-CoV-2 viruses are comprised of a spike-shaped cell membrane enveloped with single positive-stranded RNA as their genome which causes symptoms ranging from colds to extreme respiratory, hepatic and neurologic symptoms. Currently, there are six other corona viruses which are reported to attack humans. It is reported that SARS-CoV-2 has closer nucleotide-sequence similarity with SARS-CoV (about 79%) compared with MERS-CoV. The main difference between SARS-CoV-2 and SARS-CoV lies on the ORF1a gene and S-protein gene. The binding of SARS-CoV-2 virus to ACE2 receptors on the surface of the host cells initiating the pathogenesis of COVID-19 is followed with the penetration of the virus into its cytoplasm, starting the cascade of protein synthesis to produce the structural components that the virus needs to form the infectious virions.⁸ Here we propose a schematic mechanism by which the virus infects human cells to initiate inflammation and cell death based on recent published systematic review and research articles from the outstanding journals (9-14). The progress of the disease is schematically illustrated in Figure 1.

The release of IgM and IgG antibodies triggered by activating an immune response becomes the

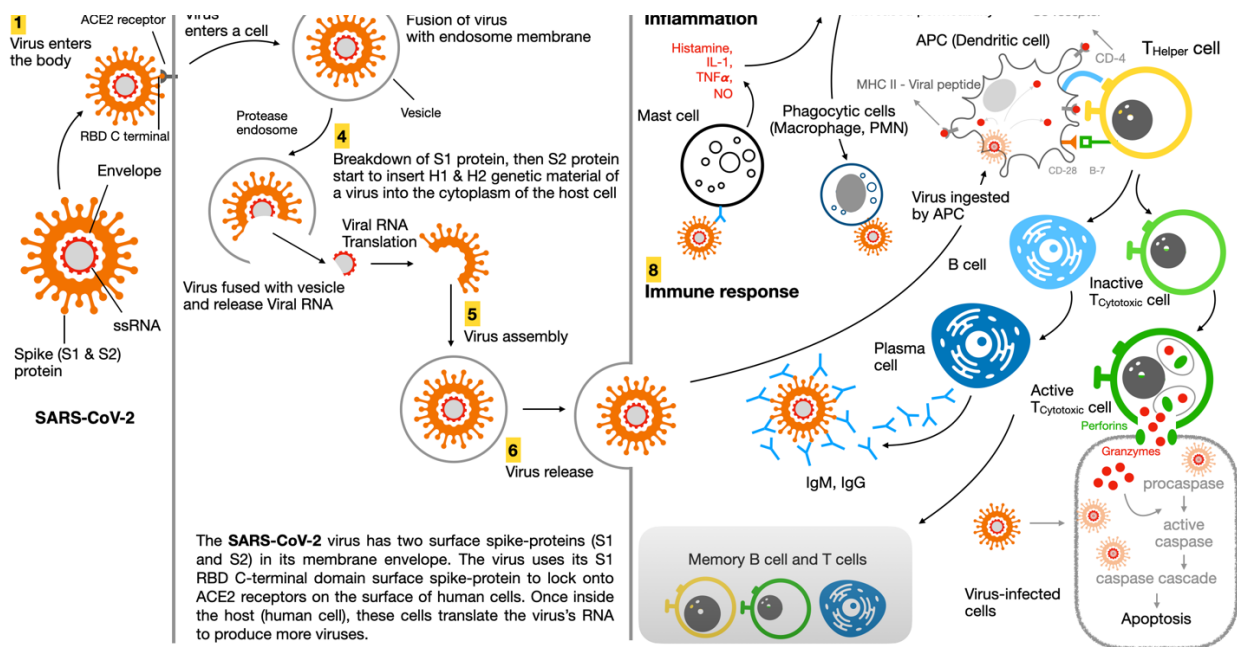


Figure 1. The simplified mechanism which schematically illustrates the infection cascade of SARS-CoV-2. The target cells of this virus are epithelial cells lining the respiratory tract, alveolar, endothelium blood cell and lung macrophage which present ACE2 receptors on its surfaces.⁹ The infection of host cells initiates inflammation and involves a sequence of cellular events to rapidly bring blood-borne host defenses including macrophages and PMN to attack the virus.¹⁰ The dendritic cells phagocytose the virus and the viral peptides are displayed on the surface of MHC class II molecules to be recognized by cell T helpers. The activation of the T cell helpers results in cytokine production and enables other immune responses: Antibodies IgM and IgG released by plasma cells derived from activated B cell can block the virus from infecting cells as well as mark the virus for destruction. Following this, cytotoxic T cells induce apoptosis mechanisms on virus-infected cells.

basis for rapid antibody detection tests on the patients suspected of being positively infected with SARS-CoV-2 virus. The IgM antibodies are first produced by plasma cells on day 3 to day 6, then will disappear after a few weeks. The IgG antibodies are produced a couple of days later as a result of antibody class switching and maturation.¹¹⁻¹³ The immune body response to SARS-CoV-2 infection helps patient to self-recover from the disease. However, a different pathway is likely to occur for the patients who have an immune response disorder, since its excessive immune response may trigger other systemic pathologies. Another harmful condition is pyroptosis which can trigger leakage of blood vessels causing death.¹⁰

The SARS-CoV-2 virus has the advantage of genetic diversity and rapidly mutates and evolves which can affect its pathogenesis.¹⁴ This mutation has implications for future challenges in developing a vaccine.⁵

Manifestations of COVID-19

The incubation periods for COVID-19 are approximately 5-6 days and can be up to 14 days. During this time, the symptoms have not yet appeared, but the infected patient can be contagious.¹⁵ The symptoms of COVID-19 have a wide range from mild or without symptoms to severe respiratory illness accompanied by multiple organ failure. We summarize systemic manifestations of COVID-19 from recent review articles, a clinical case report and research article (Table 1).¹⁶⁻²⁶ These symptoms indicate that COVID-19 not only affects the respiratory system but also involves multiple organs. The damage of organs is not merely by the viral infection itself, but it is largely due to a strong inflammatory response known as a cytokine storm. The previous condition of the patients also significantly contributes as comorbidities including hypertension, cardiovascular disease, diabetes mellitus, malignancy, chronic pulmonary, liver, and

kidney disease.¹⁶ The patients with comorbidities have a higher risk to be infected and have a higher fatality rate.

What is the oral involvement in COVID-19?

The oral cavity is one of the potential port-entries for the SARS-CoV-2 virus into the body through the ACE2 receptor binding sites found in oral epithelial tissues. Furthermore, it was confirmed

that the SARS-CoV-2 virus was present in the saliva of infected COVID-19 patients. A recent case study reported oral manifestations of COVID-19. The oral symptoms that have been reported in patients confirmed positive with COVID-19 include a decreased sense of taste in the early stages, pain, desquamative gingivitis, ulcer, and blistering.²⁷ The decreasing sense of taste is an interesting phenomenon and it may relate with the

Table 1. The manifestation of COVID-19 in multiple organs

Organ	Mechanism	Sign and Symptoms
Respiratory system	The main route of SARS-CoV-2 infection is through the nasal cavity targeting the main respiratory tract. After reaching this area, the virus will bind to several types of non-neuronal cells in the olfactory area which expresses ACE2 and transmembrane protease, serine 2 (TMPRSS2) so that those replicates and accumulate in these cells. This process underlies the reported olfactory disorders (decreasing of smell) in the initial phase of viral infection. ¹⁷	Fever Dry cough Hemoptysis Dyspnea ARDS
Gastrointestinal and liver	In addition, the virus will spread to the surrounding cells in the upper respiratory tract (nasal cavity and pharynx). Then, this virus continues to infect the lower respiratory tract. The greatest damage to the lower respiratory tract is in the apical and distal parts. For that reason, ACE2 is highly expressed in type 2 of pneumocytes cells which are in the alveolar area. Additionally, alveolar areas also contain alveolar macrophages and dendritic cells which will mediate the immune response against the virus. ¹⁸ The severe symptoms of acute respiratory distress syndrome (ARDS) occur due to over-activation of the immune response. Death of epithelial and endothelial cells causes vascular leakage and triggers excessive cytokines production. ¹⁹	Diarrhea Nausea Vomiting Abdominal pain / discomfort
Nervous system	Symptoms in the gastrointestinal system are reported in patients in the early and mild phase of COVID-19 before respiratory symptoms appear. ACE2 is found in the digestive tract namely in the pharynx, esophagus, gastric, and intestines. ²⁰ Viral nucleocapsid proteins are also found in the cytoplasmic epithelium in the gastric, duodenum and rectum. The viral nucleic acids are also found in the stool. These facts may support that the virus directly infected the gastrointestinal system. Liver involvement in COVID-19 is not caused by a direct effect of virus infection to the hepatocytes because ACE2 is only found in bile duct cells and is discovered to be very minimal in hepatocytes. The liver disorder is by an indirect effect due to psychological stress, systemic inflammatory response, and drug toxicity. ²¹	Headache Dizziness Encephalopathy Anosmia Ageusia Impaired consciousness Agitation Stroke Neuralgia Epilepsy ²³
	The involvement of the nervous system in COVID-19 is reported to occur in the periphery and central nervous system (CNS) from mild (anosmia and ageusia) to severe (encephalopathy). The mechanism of anosmia (decreasing sense of smell) and ageusia (decreasing sense of taste) have been explained above. The movement of the virus to the brain may originate from the nasal cavity that may move via the cribriform plate to the area around the olfactory bulb. Thus, the discovery of anosmia must always be followed by examining the possibility of involvement of the SARS-CoV-2 infection in the CNS. The other mechanism of CNS involvement in COVID-19 is via the blood circulation. SARS-CoV-2 presence in circulation interacts with ACE2 expressed in endothelium and damage the endothelial lining. This leads to rupture of the cerebral vascular and bleeding within cerebral tissue. Furthermore, by circulation, the virus reaches the brain and interacts with ACE2 expressed in neuronal tissue and initiates a cycle of viral replication accompanied by neuronal damage. ²²	

Organ	Mechanism	Sign and Symptoms
Cardiovascular	<p>Cardiovascular manifestations in COVID -19 occurs in around 30% of hospitalized patients contributing to approximately 40% of deaths. Although the exact mechanism of cardiac injury is not yet fully understood, the cardiac injury possibly occurs through 3 mechanisms: 1) viral infiltration into myocardial tissue resulting in cardiomyocyte death and inflammation, 2) cardiac stress due to respiratory failure and hypoxemia, and 3) cardiac inflammation secondary to severe systemic hyper inflammation.²⁴</p> <p>The role of ACE2 in cardiovascular disease remains controversial. ACE2 is an ACE homologue, but it acts as a counterbalance in the renin-angiotensin-aldosterone system (RAAS) in maintaining cardiovascular homeostasis. SARS-CoV-2 infection causes downregulation of ACE2 which will further contribute to causing the myocardial dysfunction.²⁴</p>	<p>Tachycardia Hypotensive²⁵ Arrhythmia Cardiogenic shock Thromboembolism²⁶</p>

higher expression of ACE2 on the tongue where most of the taste buds are located.²⁸ The high viral load in saliva (and possibly in the salivary gland) will increase the likelihood of viral attachment and infection to the tongue epithelia.³ By using RNA-seq profiling data analysis Xu et al. (2020) reported that ACE2 receptor found in oral epithelial tissues.²⁸ The SARS-CoV-2 virus may bind and infect gingiva and another oral mucosa through ACE2 receptors which is expressed in this area causing symptoms such as pain and lesions which are very similar to other viral lesions such as foot and mouth disease and herpes.²⁷

What is the role of oral transmission as a high-risk potential of cross-infection?

Previous studies suggested that the oral cavity may play a significant role in COVID-19 transmission and bring a high-risk potency of cross-infection in dental treatment.^{19,29,30} The SARS-CoV-2 can be transmitted directly from person to person through the oral cavity in the form of droplets (when coughing or sneezing), aerosols (due to several dental procedures, nebulizers, and others), and direct contact or indirectly through medical and non-medical equipment. The viral particles in droplets (size of >5 um) can be transmitted at <1-meter distance while in aerosols (size of ≤5 um) can be transmitted through the air (airborne) at a greater distance of >1-meter.²⁹ There is emerging evidence suggesting that the body parts (hand, oral, nasal and eye mucous membrane) or fomites contaminated with the droplets may become a transmitting route of cross-infection.¹⁹ Although there was a report of

patients with conjunctival disorders, the evidence of involvement the conjunctival mucosa in the COVID-19 infection route has not been significant, since the ACE2 expression in the conjunctival is almost non-existent.³⁰

What are the recommended strategies to minimize the risk of cross-infection in dental practice?

Patient screening and comprehensive dental management

The steps of patient dental management are arranged in adherence to a number of infection prevention and dental emergency treatment protocols adopted from the Centers for Disease Control and Prevention (CDC), the Department of Health and Human Services USA, WHO, and the Coronavirus Center for Dentists in the American Dental Association (ADA) as an effort to prevent and minimize the risk of cross-infection. The schematic steps of the screening phase until the management of dental care preparation and the protocols referred to in each stage can be seen in Figure 1. The schematic flowchart describes in detail each stage which is generally divided into two main sequential stages, starting from initial screening (non-contact phase) followed by pre-treatment stage (contact phase).

Initial screening

The initial screening of dental patients is done on a non-contact basis. Patient is directed to fill out an online questionnaire sent via email or on a website. An initial assessment is conducted to determine the

status of the patient's risk level of getting exposed to COVID-19. The evaluation results of initial screening assessment that consists of patient's risk status of COVID-19 exposure and management of dental treatment that is appropriate for the patient's condition are communicated to the patient via tele- or video-consultation.³¹

The follow-up management of the dental care is determined based on the results of the initial stage evaluations. If the results show any indication of a COVID-19 positive suspect, then the patient will be referred to undergo a series of further tests to establish the diagnosis. Elective dental

procedures can be postponed for at least the next 14 days, and urgent cases with pain symptoms can be prescribed with antibiotics and/or analgesics. For suspected COVID-19 patients in an emergency status or whose status has escalated from urgent level, dental procedures can be carried out with strict protocols for handling and preventing cross-infection risk; both the protocol of health facility requirements to be used for treatments and the protocol of emergency treatments. Patients with negative COVID-19 indication can proceed to dental procedures after undergoing a series of pre-treatment procedures (Figure 2).

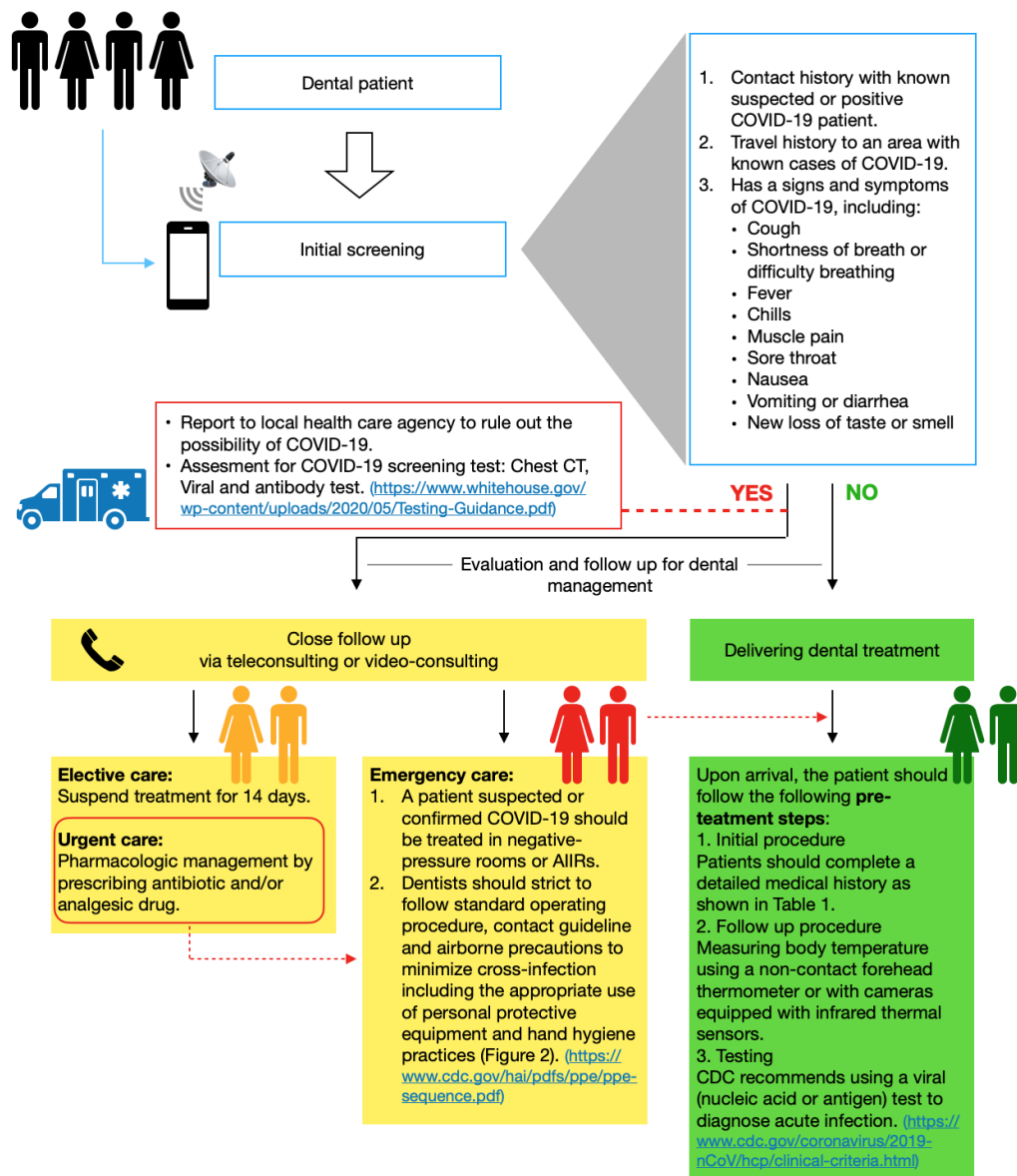


Figure 2. An initial dental patient screening for COVID-19 and follow up plan for dental management

Pre-treatment

Dental treatments on patients with COVID-19 negative indication can be performed by following further screening protocol. At this stage, a subjective examination is done by filling in the patient’s answers into a specific medical record to screen for more accurate possibilities of the risk of being infected with COVID-19 and to conduct an initial evaluation of the possibility of emergency dental status. The list of questions in the specific medical record can be seen in Table 2.

Following complete filling of the medical record data, the patient’s body temperature is then checked using non-contact thermometer or thermometer equipped with an infrared thermal sensor camera²⁹ to identify the risk of body temperature increase that may indicate an infection. Subjective examination procedures and body temperature measurements can be performed by dentists assisted by trained medical staffs with reference to the protocols of COVID-19 emergency prevention and treatment. Dentists and medical staffs must wear personal

Table 2. Detailed medical history form consists of COVID-19 screening questionnaire and assessment of emergency status for the dental patient

1. How old are you:

- < 18 years
- 18 -64 years
- > 65 years

2. In the last 14 days, have you been travelling to the area where COVID-19 is widespread?

- YES, please specify the location:
- NO

3. In the last 14 days, have you had close contact with someone suspected or positive COVID-19?

- YES, please specify your relationship with Him or Her:
- NO

4. In the last 14 days, have you experienced any of these symptoms?
Please select all that apply

- Fever
- Mild or moderate difficulty breathing
- Cough
- Vomiting or Diarrhea
- Nausea
- Body ache
- Loss of taste or smell
- None of above

5. Do you have any of these medical histories?
Please select all that apply

- Asthma or chronic lung disease
- Hypertension or any cardiovascular disorder
- Diabetic
- Kidney failure
- Cirrhosis liver
- Inherited immune suppression
- None of above

6. Have you recently started experiencing any of these signs and symptoms?
Please select all that apply

- Dental or oral pain, please specify:
 - when did it begin:
 - the VAS pain score:

0 1 2 3 4 5 6 7 8 9 10
 No Pain Mild Moderate Severe Very Severe Worst Pain Possible
 0 1-3 4-6 7-9 10

- Dental abscess, please specify:
 - the swollen location: gums face
 - with or without bleeding
 - When did you notice the swelling for the first time?
- Fever
- Trauma, please describe:
- Any trouble of swallowing
- Any restriction of mouth opening

protective equipment (PPE) recommended by CDC standards (Figure 3) and follow hand hygiene procedures.³² During the examination and measurement procedures, the patient is required to wear a mask and follows self-protection protocol by covering the mouth and nose with tissue when sneezing or coughing.³³ Patient suspected of COVID-19 must be placed in a separate room with adequate ventilation and a minimum distance of 6 ft (2 meters) from other patients, according to the guidelines recommended by the CDC.³⁴

If the body temperature is > 100 °F = 38 °C accompanied with symptoms of acute respiratory problems, non-emergency dental treatments can be postponed for at least the next 14 days, and the patient is then referred for an antibody and viral testing,³⁶ followed by infection treatments for COVID-19 suspects at the referral hospital. For emergency cases, further treatments need to be carried out at health facilities that have negative pressure rooms conforming to the regulations

for prevention and management of COVID-19 infectious disease cases.³³

Patient management and prevention of cross-infections in dental clinics

Protocols of infection prevention and control need to be strictly implemented during the clinical treatment of dental patients. Droplets and aerosol sprays from saliva during dental procedures have been reported as sources of SARS-CoV-2 transfer that has the potential to cause cross-infection of COVID-19.²⁹ Several of the strategies that can be applied to minimize the risk of cross-infection during dental treatment, especially for some procedures that have the potential to produce droplets and aerosols, can schematically be seen in Table 3.

The WHO and several other world organizations have issued a number of online guidelines and protocols that are accessible via their websites and are recommended to be implemented by dentists and medical staffs as an

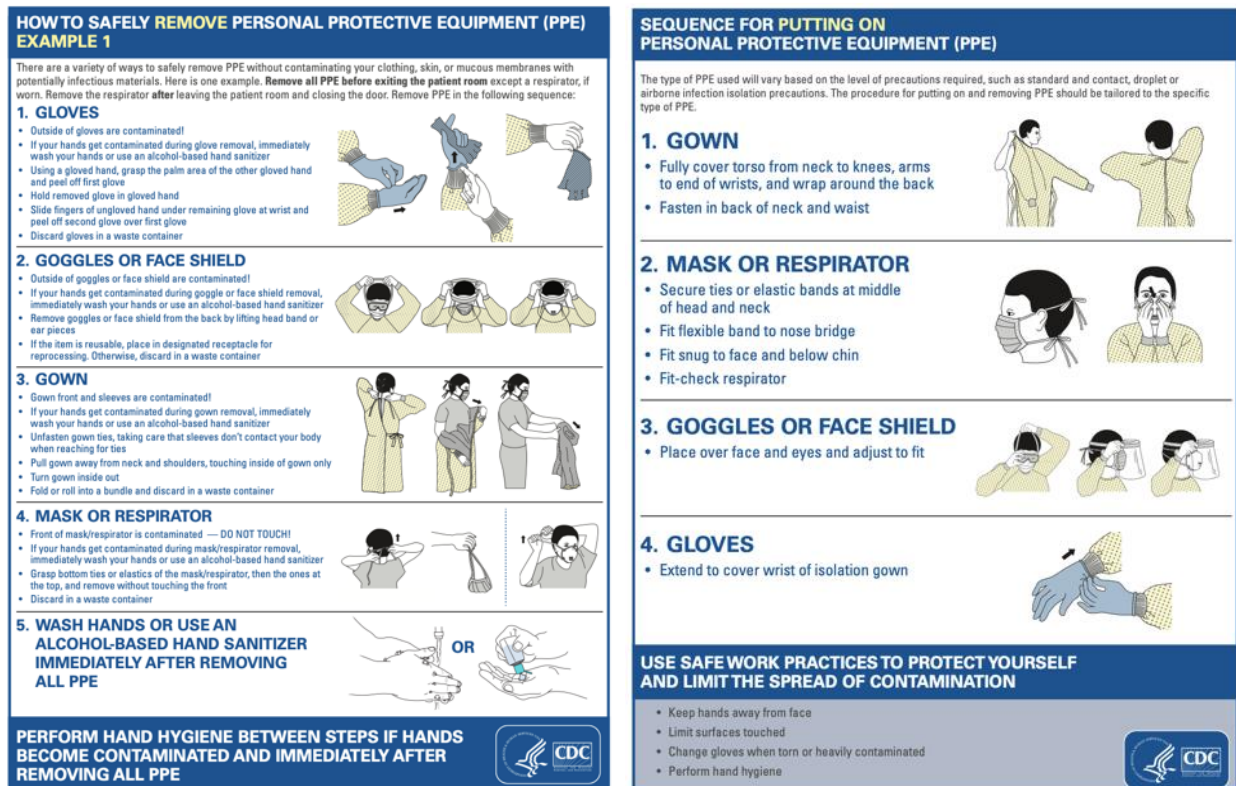


Figure 3. Centers for Disease Control and Prevention recommendations for putting on and removing personal protective equipment (PPE) for treating COVID-19 patients.³⁵

Table 3. Recommended strategies and protocols for preventing cross-infection of COVID-19 in several dental procedures

Prevention Strategies	Treatment precautions
<p>A. Using rotary instruments:</p> <ol style="list-style-type: none"> 1. Place rubber dam³⁷ 2. Use salivary suction³⁷ 3. Use aerosol box for cavity preparation with high speed air-turbine handpiece³⁸ 4. Clean regularly and sterilize the Dental Unit Waterlines (DUWLs) using certain antiseptic³⁹ 	<p>Strategies to prevent cross-infection in using rotary instrument can be implemented in a number of cases such as:</p> <ol style="list-style-type: none"> 1. Treatment of root canals in endodontic cases. This procedure uses many tools that have a potential to be sources of cross-infection from saliva droplets that contaminate the tools and surface of area around the dental unit (inanimate surface)³⁷ 2. Cavity preparation with high speed air-turbine handpiece⁴⁰ 3. Ultrasonic scaling and polishing⁴⁰
<p>B. No-rotary instrumentation</p> <ol style="list-style-type: none"> 1. Using Atraumatic Restorative Techniques (ART) 2. Chemochemical caries removal 	<p>Strategies for using no-rotary instruments can be implemented in the following cases:</p> <ol style="list-style-type: none"> 1. Selected cases of restorative dentistry 2. Pediatric dentistry 3. Manual scaling and polishing

effort to prevent and control cross-infection.^{41–43} On March 16, 2020, the American Dental Association (ADA) released a recommendation to postpone treatment and non-emergency dental procedures.⁴² For emergency cases which require urgent treatments during the COVID-19 pandemic, the possible clinical procedures that can be adopted are elaborated in Table 4. The management of treatments which are summarized in Table 4 are restricted to minimally invasive approaches and could be dynamically adjusted as the COVID-19 outbreak develops in their respective regions. Dental health care professionals should regularly consult their state dental boards and state or local health departments for current local information for requirements specific to their jurisdictions.

During the COVID-19 pandemic, these emergency conditions need to be taken into consideration, especially the conditions of patients suspected of or who have tested positive for SARS-CoV-2. By strictly implementing the protocols, it is expected that the potential risk of cross-infection can be avoided.

It is still uncertain whether a vaccine can be invented in the near future and whether the vaccine will be able to optimally prevent COVID-19 infection. Strategies that can be effectively and immediately implemented as a new protocol for the '**new normal**' era need to be applied as soon as possible during this period in which the risk of SARS-CoV-2 exposure continues. Medical staff and dental care institutions need to be properly prepared because

it has been predicted that the number of patients visiting dental clinics will surge as soon as the restriction of general treatment during the pandemic emergency is lifted.

Recommended strategies applied recently and toward the 'new-normal' future dental management and treatment

Systemic treatment management of COVID-19 cases is still being studied as well as innovations related to curative, rehabilitation, and prevention methods. Additionally, alternative therapies and preventive actions are needed both for patients and healthcare providers.⁴⁵ We analyze important evidences provided in systematic review, research reports, and letter to journal editor to show and recommend the importance of gargling as one treatment and prevention approach.^{7,45–50} Recently, the use of povidone-iodine (PVP-I) has been recommended and discussed due to its potential as an antivirus agent for general and dental care procedures. Closely related to the mechanism of virus infection into the upper respiratory tract through the oral cavity to the nasopharyngeal area, oral hygiene is very important to be maintained by both patients and healthcare providers. Povidone-iodine mouthwash diluted by 1:30 (equivalent to 0.23% PVP-I) is proven to be effective in vitro as an antivirus against MERS-CoV and SARS-CoV-1,⁴⁶ with antivirus ability of $\geq 99.99\%$, and is also recommended as mouthwash or nasal spray for COVID-19 local treatment or prevention.⁴⁷ SARS-

Table 4. Management of acute dental problems during COVID-19 Pandemic⁴⁴

Symptoms	Managements
Acute apical abscess	<ul style="list-style-type: none"> ○ Recommend analgesic, prescribe antibiotic if found an infection symptom ○ Asked patient to call back in 48-72 hours if their symptoms have not resolved
Acute periodontal abscess	<ul style="list-style-type: none"> ○ Recommend analgesic, prescribe antibiotic if found an infection symptom. ○ Asked patient to call back in 48-72 hours if their symptoms have not resolved
Acute pericoronitis	<ul style="list-style-type: none"> ○ Recommend analgesic, prescribe antibiotic if found an infection symptom. ○ Asked patient to call back in 48-72 hours if their symptoms have not resolved ○ Recommend chlorhexidine or warm salt-water mouthwash
Necrotising ulcerative gingivitis/periodontitis	<ul style="list-style-type: none"> ○ Recommend analgesic, consider antibiotic (metronidazole is a drug first choice) ○ Recommended chlorhexidine or hydrogen peroxide mouthwash ○ Advice to maintain good oral hygiene advice
Reversible pulpitis	<ul style="list-style-type: none"> ○ Recommend analgesic ○ Advice to avoid hot and cold foods and beverages ○ Asked patient to call back if the symptoms get worse. ○ Advice patient to use an emergency temporary repair kit (purchase online or at the pharmacy)
Irreversible Pulpitis	<ul style="list-style-type: none"> ○ Recommend analgesic ○ Asked patient to call back if the symptoms get worse
Dentin hypersensitivity	<ul style="list-style-type: none"> ○ Avoid noxious stimuli (cold or acidic foods and beverages) ○ Regularly apply desensitizing toothpaste to the area with a finger
Dry Socket	<ul style="list-style-type: none"> ○ Recommend analgesic ○ Recommend warm salt-water mouthwash ○ Prescribe antibiotics for an immunocompromised patient and patient if emerging signs of spreading infection or systemic infection ○ Refer to urgent dental care for dressing if the pain gets worse
Post-extraction hemorrhage	<ul style="list-style-type: none"> ○ Advise patient not to spit or rinse ○ Washout blood excess by rinsing with warm water ○ Place cotton roll or gauze swab moistened with saline or water over the socket, bite firmly for 20 minutes, check bleeding after 20 minutes and repeat if necessary ○ After bleeding stops, advice patient not to drink alcohol, smoking or exercising for 24 hours
Oral ulceration	<ul style="list-style-type: none"> ○ If ulceration has been present for less than 3 weeks: <ul style="list-style-type: none"> ● Recommend analgesic ● Advice chlorhexidine mouthwash (not for children under 7 years old) ● Take soft diet ○ If ulceration due to denture, remove denture where possible ○ If trauma from an adjacent tooth cause ulceration, advise a patient to use a temporary emergency filling. Suggest a patient purchase at pharmacy or online ○ Prescribe antiviral agents if needed ○ Refer a patient to dental emergency care if ulceration has been present for three weeks or more
Cracked, fractured, loose or displaced tooth fragments and restorations	<ul style="list-style-type: none"> ○ For broken or fractures teeth or filling: <ul style="list-style-type: none"> ● Advice patient to use a temporary emergency filling if a tooth is sensitive. Suggest a patient purchase at pharmacy or online. ● Recommend analgesic ● Advice patient to call back if the symptoms have not been relieved ○ For broken crowns, bridges and veneers: <ul style="list-style-type: none"> ● Advice patient to use a temporary emergency filling. Suggest a patient purchase at pharmacy or online ● Recommend analgesic if a patient has painful symptoms ● Refer to emergency care if a patient has inhaled a piece of tooth

Symptoms	Managements
Ill (pain) fitting or loose denture	<ul style="list-style-type: none"> ○ Recommend analgesic ○ Advice the patient to remove their denture whenever possible ○ Advice patient to visit routine dental care when the service is back to normal
Trauma from fractured or displaced orthodontics appliances	<ul style="list-style-type: none"> ○ Direct patient to www.bos.org.uk website for advice on managing orthodontics problem ○ Refer to emergency care if a patient has inhaled or ingested a large part of an appliance
Dento-alveolar injuries	<ul style="list-style-type: none"> ○ If the patient not in an emergency medical situation: <ul style="list-style-type: none"> ● Consider recommending analgesic ● Advice patient to clean the injury area by rinsing gently with antiseptic ● Remove a foreign object if present in the mouth ● Apply ice packs to soft tissue injury/swelling ● Press with a finger to stop bleedings ● Refer to emergency care if symptoms get worse
Avulsed, displaced or fractured teeth	<ul style="list-style-type: none"> ○ For the permanent tooth: Apply desensitizing-toothpaste on the exposed dentin if the fracture involves only enamel or dentin and advised a patient to use a temporary emergency filling. Suggest a patient purchase at pharmacy or online ○ For the primary tooth: Advice appropriate analgesic and take a soft diet ○ If the permanent tooth has been knocking-out: Advice patient to put a tooth back to the socket by holding its crown part and bite with a handkerchief to hold it in its position ○ Store the tooth in milk or between cheek and molar tooth inside the mouth and advice patient to find the emergency dental care

CoV-2 is known to be susceptible to oxidation, so clinical use of PVP-I 0.2% has been suggested to minimize and anticipate transmission of new variant corona virus.⁴⁸ In addition to these applications, Parhar et al. in 2020⁴⁹ in their literature review suggest dissolving PVP-I up to 0.2% as prophylaxis procedures for upper respiratory mucosa of SARS-CoV-2 cases.

The results of in vitro and in vivo studies as well as previous literature reviews were obtained from the phenomena that occurred in MERS-CoV and SARS-CoV-1 cases. Currently, the results of Halodine antiseptic in vitro tests, which is a polymer-enriched povidone-iodine, have shown a high viricidal power against SARS-CoV-2. The result of in vitro tests on this virus shows Halodine's significant viricidal effect up to 1/20 dilution. This antiseptic is formulated as a nasal spray and mouthwash. It has a very low antiseptic concentration and is safe for mucosal surfaces.⁵⁰

Cytotoxicity of povidone-iodine

The cytotoxic effect of PVP-I in oral cavity is lower than other mouthwash. Result of cytotoxicity tests on L929 fibroblast cells showed that PVP-I is the

safest mouthwash compared to chlorhexidine digluconate (CHex), octenidine dihydrochloride (Oct) and polyhexamethylene biguanide (PHMB).⁵¹ PVP-I 0.23% is effective in vitro as an antiviral agent against SARS and MERS corona viruses, but its in vivo concentration must be controlled. Study conducted by Kim et al. in 2015 revealed that PVP-I at concentrations of 5% and 10% are cytotoxic to respiratory epithelial cells, meaning that the use of mouthwash containing 5% and 10% PVP-I has the potential to harm membrane integrity and accessories of respiratory epithelial cells.⁵²

Treatment approach

The use of PVP-I for oral or oropharyngeal wash is by diluting it in 1:20 of sterile water or distilled water, it is equal a 0.5% final concentration of PVP-I in a solution. Its use varies according to the status of the patient or healthcare providers, with the recommendation to gargle every 2-3 hours or 4x a day. The use of mouthwash can be optional in the treatment of patients without clinical symptoms or health care providers in COVID-19 hotspot.⁴⁵ Supporting the rationale for the use of antiseptic mouthwash, as reported by an otolaryngologist

in Philippines, gargling should be done 3 times a day for 60 seconds each. Mouthwash should be used along with brushing teeth, mucosal surfaces of the palate, tonsils, and basis of tongue. These activities help to minimize the transfer of virus to the lower respiratory tract to lungs. These efforts have helped patients to recover from pneumonia caused by SARS-CoV-2 infection.⁷ In addition, gargling with antiseptic is logical to be recommended as a preventive, prophylactic, or curative measure because it evenly smears antiseptic on the entire mucosal surface which is the target of SARS-CoV-2 attachment, especially the tongue mucosal epithelium as it has the highest number of cells that present ACE2 among other oral mucosal cells.²⁸ As a conclusion, gargling with 0.2% povidone-iodine is a part of strategic preventive, prophylactic, and curative efforts against SARS-CoV-2 infection.

CONCLUSION

Cross-infection of COVID-19 via oral transmission of SARS-CoV-2 virus in the salivary droplets and aerosol has become a '**novel challenge**' for dental professionals. Dental care providers and health care professionals need to be aware and well prepared for preventing the transmission of the virus and its associated systemic manifestations of the disease. In recent predictions toward the future of the 'new normal' in dental practice a shift paradigm is needed in standards of care, habitual oral hygiene and infection control. Strictly applied, the recommendations and protocols of infection prevention and control measures in dental management become a necessity to block the cross-infection routes in dental care facilities and hospitals.

REFERENCES

1. Gugus Tugas Percepatan Penanganan COVID-19. Data sebaran. <https://covid19.go.id/>. Accessed May 27, 2020.
2. Kemenkes. Pedoman pencegahan dan pengendalian corona virus disease (COVID-19).; 2020. Diunduh dari: https://infeksiemerging.kemkes.go.id/downloads/?dl_cat=0&dl_search=pedoman+dan+pencegahan+covid#.Xs1qXGgzblU pada 27 May 2020.
3. Dar Odeh N, Babkair H, Abu-Hammad S, Borzangy S, Abu-Hammad A, Abu-Hammad O. COVID-19: Present and future challenges for dental practice. *Int J Environ Res Public Health*. 2020; 17(9): 3151. doi: 10.3390/ijerph17093151
4. Lo Giudice R. The severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) in dentistry. Management of biological risk in dental practice. *Int J Environ Res Public Health*. 2020; 17(9): 3067. doi: 10.3390/ijerph17093067
5. Dawood AA. Mutated COVID-19 may foretell a great risk for mankind in the future. *New Microbes New Infect*. 2020; 35: 100673. doi: 10.1016/j.nmni.2020.100673
6. Ziegler CGK, Allon SJ, Nyquist SK, et al. SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues. *Cell*. 2020; 181(5): 1016-1035. e19. doi: 10.1016/j.cell.2020.04.035
7. Flor. J. Surviving COVID-19 pneumonia at home: COVID case #1906. *Philipp J Otolaryngol Head Neck Surg*. 2020; 35(1): 78-79. doi: 10.32412/pjohns.v35i1.1259
8. Actor JK. Humoral Immunity. In: Elsevier's Integrated Review Immunology and Microbiology. Elsevier; 2012: 17-24. doi: 10.1016/B978-0-323-07447-6.00003-X
9. Xu X, Chen P, Wang J, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Sci China Life Sci*. 2020; 63(3): 457-460. doi: 10.1007/s11427-020-1637-5
10. Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol*. 2020; 20(6): 363-374. doi: 10.1038/s41577-020-0311-8
11. Li Z, Yi Y, Luo X, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2

- infection diagnosis. *J Med Virol.* 2020; 1-7. doi: 10.1002/jmv.25727
12. Racine R, Winslow GM. IgM in microbial infections: taken for granted? *Immunol Lett.* 2009; 125(2): 79-85. doi: 10.1016/j.imlet.2009.06.003
 13. Shen C, Zhang M, Chen Y, et al. An IgM antibody targeting the receptor binding site of influenza B blocks viral infection with great breadth and potency. *Theranostics.* 2019; 9(1): 210-231. doi: 10.7150/thno.28434
 14. Becerra-Flores M, Cardozo T. SARS-CoV-2 viral spike G614 mutation exhibits higher case fatality rate. *Int J Clin Pract.* 2020. doi: 10.1111/ijcp.13525
 15. World Health Association (WHO). Coronavirus disease 2019 (covid-19) situation report – 73.; 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73-covid-19.pdf?sfvrsn=5ae25bc7_6. Accessed May 28, 2020.
 16. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. *Clin Immunol.* 2020; 215: 108427. doi: 10.1016/j.clim.2020.108427
 17. Butowt R, Bilinska K. SARS-CoV-2: Olfaction, brain infection, and the urgent need for clinical samples allowing earlier virus detection. *ACS Chem Neurosci.* 2020; 11(9): 1200-1203. doi: 10.1021/acscchemneuro.0c00172
 18. Qian Z, Travanty EA, Oko L, et al. Innate immune response of human alveolar type II cells infected with severe acute respiratory syndrome–coronavirus. *Am J Respir Cell Mol Biol.* 2013; 48(6): 742-748. doi: 10.1165/rcmb.2012-0339OC
 19. Jin Y, Yang H, Ji W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses.* 2020; 12(4): 372. doi: 10.3390/v12040372
 20. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Front Med.* 2020; 14(2): 185-192. doi: 10.1007/s11684-020-0754-0
 21. Li J, Fan J-G. Characteristics and mechanism of liver injury in 2019 coronavirus disease. *J Clin Transl Hepatol.* 2020; 8(1): 1-5. doi: 10.14218/JCTH.2020.00019
 22. Das G, Mukherjee N, Ghosh S. Neurological insights of COVID-19 pandemic. *ACS Chem Neurosci.* 2020; 11(9): 1206-1209. doi: 10.1021/acscchemneuro.0c00201
 23. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. *J Clin Neurosci.* 2020. doi: 10.1016/j.jocn.2020.05.017
 24. Akhmerov A, Marbán E. COVID-19 and the heart. *Circ Res.* 2020; 126(10): 1443-1455. doi: 10.1161/CIRCRESAHA.120.317055
 25. Inciardi RM, Lupi L, Zacccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020. doi: 10.1001/jamacardio.2020.1096
 26. Kang Y, Chen T, Mui D, et al. Cardiovascular manifestations and treatment considerations in COVID-19. *Heart.* 2020; heartjnl-2020-317056. doi: 10.1136/heartjnl-2020-317056
 27. Carreras-Presas CM, Sánchez JA, López-Sánchez AF, Jané-Salas E, Pérez MLS. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis.* 2020. doi: 10.1111/odi.13382
 28. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci.* 2020; 12(1): 8. doi: 10.1038/s41368-020-0074-x
 29. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. *Int J Oral Sci.* 2020; 12(1): 1-6. doi: 10.1038/s41368-020-0075-9
 30. Lange C, Wolf J, Auw-Haedrich C, et al. Expression of the COVID-19 receptor ACE2 in the human conjunctiva. *J Med Virol.* 2020. doi: 10.1002/jmv.25981
 31. Ather A, Patel B, Ruparel NB, Diogenes A, Hargreaves KM. Coronavirus Disease 19 (COVID-19): implications for clinical dental care. *J Endod.* 2020; 46(5): 584-595. doi: 10.1016/j.joen.2020.03.008

32. Gerberding JL, Director David Fleming MW, Snider DE, et al. Morbidity and mortality weekly report guideline for hand hygiene in health-care settings recommendations of the healthcare infection control practices advisory committee and the HICPAC/SHEA/APIC/IDSA hand hygiene. Task Force Centers for Disease Control and Prevention. 2002; 51.
33. Centers for Disease Control and Prevention (CDC). Infection control: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). <https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>. Accessed May 29, 2020.
34. Centers for Disease Control and Prevention (CDC). Social Distancing, Quarantine, and Isolation. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html>. Accessed May 29, 2020.
35. Centers for Disease Control and Prevention (CDC). Sequence for putting on personal protective equipment (PPE). <https://www.cdc.gov/hai/pdfs/ppe/ppe-sequence.pdf>. Accessed May 29, 2020.
36. Centers for Disease Control and Prevention (CDC). Interim Guidance: Healthcare Professionals 2019-nCoV | CDC. <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>. Accessed May 29, 2020.
37. Ge Z, Yang L, Xia J, Fu X, Zhang Y. Possible aerosol transmission of COVID-19 and special precautions in dentistry. *J Zhejiang Univ B*. 2020; 21(5): 361-368. doi: 10.1631/jzus.B2010010
38. Babu B, Gupta S, Sahni V. Aerosol box for dentistry. *Br Dent J*. 2020; 228(9): 660. doi: 10.1038/s41415-020-1598-3
39. American Dental Association (ADA). Dental unit water lines. https://success.ada.org/en/practice-management/guidelines-for-practice-success/gps-managing-regulatory/04_dental-unit-water-lines. Accessed June 5, 2020.
40. Harrel SK, Molinari J. Aerosols and splatter in dentistry. *J Am Dent Assoc*. 2004; 135(4): 429-437. doi: 10.14219/jada.archive.2004.0207
41. FDI World Dental Federation. COVID-19 Outbreak: Guidance for Oral Health professionals. <https://www.fdiworlddental.org/covid-19-outbreak-guidance-for-oral-health-professionals>. Accessed May 29, 2020.
42. American Dental Association (ADA). Coronavirus (COVID-19) Center for Dentists. https://success.ada.org/en/-practice-management/patients-infectious-diseases-2019-novel-coronavirus?utm_source=jadaorg&utm_medium=cov19page&utm_content=cv-mvresource-center&utm_campaign=covid-19. Accessed May 29, 2020.
43. World Health Association (WHO). Infection Prevention and Control. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control>. Accessed May 29, 2020.
44. Scottish Dental Clinical Effectiveness Programme (SDCEP). Management of acute dental problems during COVID-19 pandemic. www.sdcep.org.uk. Accessed May 29, 2020.
45. Mady LJ, Kubik MW, Baddour K, Snyderman CH, Rowan NR. Consideration of povidone-iodine as a public health intervention for COVID-19: Utilization as "Personal Protective Equipment" for frontline providers exposed in high-risk head and neck and skull base oncology care. *Oral Oncol*. 2020; 105: 104724. doi:10.1016/j.oraloncology.2020.104724
46. Eggers M, Koburger-Janssen T, Eickmann M, Zorn J. In vitro bactericidal and virucidal efficacy of povidone-iodine gargle/mouthwash against respiratory and oral tract pathogens. *Infect Dis Ther*. 2018; 7(2): 249-259. doi: 10.1007/s40121-018-0200-7
47. Challacombe SJ, Kirk-Bayley J, Sunkaraneni VS, Combes J. Povidone iodine. *Br Dent J*. 2020; 228(9): 656-657. doi: 10.1038/s41415-020-1589-4
48. Pattanshetty S, Narayana A, Radhakrishnan R. Povidone-iodine gargle as a prophylactic intervention to interrupt the transmission of SARS-CoV-2. *Oral Dis*. 2020. doi: 10.1111/odi.13378

49. Parhar HS, Tasche K, Brody RM, et al. Topical preparations to reduce SARS-CoV-2 aerosolization in head and neck mucosal surgery. *Head Neck*. 2020; 42(6): 1268-1272. doi: 10.1002/hed.26200
50. Halodine™ nasal and oral antiseptics show rapid antiviral activity against SARS-CoV-2 (COVID-19). <https://www.prnewswire.com/news-releases/halodine-nasal-and-oral-antiseptics-show-rapid-antiviral-activity-against-sars-cov-2--covid-19-301059003.html>. Accessed May 29, 2020.
51. Müller G, Kramer A. Comparative study of in vitro cytotoxicity of povidone-iodine in solution, in ointment or in a liposomal formulation (Repithel®) and selected antiseptics. *Dermatology*. 2006; 212(1): 91-93. doi: 10.1159/000090102
52. Kim JH, Rimmer J, Mrad N, Ahmadzada S, Harvey RJ. Betadine has a ciliotoxic effect on ciliated human respiratory cells. *J Laryngol Otol*. 2015; 129(S1): S45-S50. doi: 10.1017/S0022215114002746