Profiling severe acute respiratory syndrome coronavirus 2 and its relevance to otolaryngologic examinations during the coronavirus disease 2019 pandemic

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Purpose of review
The WHO announced the coronavirus disease 2019 (COVID-19) outbreak as a pandemic in February 2020 with over 15 million confirmed cases of COVID-19 globally to date. Otolaryngologists are at a high risk of contracting COVID-19 during this pandemic if there is inadequate and improper personal protective equipment provision, as we are dealing with diseases of the upper-aerodigestive tract and routinely engaged in aerosol-generating procedures.

Recent findings
This article discusses the background and transmission route for severe acute respiratory syndrome coronavirus 2, its viral load and temporal profile as well as precaution guidelines in outpatient and operative setting in otorhinolaryngology.

Summary
As it is evident that COVID-19 can be transmitted at presymptomatic or asymptomatic period of infections, it is essential to practice ear, nose, and throat surgery with high vigilance in a safe and up-to-standard protection level during the pandemic. This article provides a summary for guidelines and recommendations in otorhinolaryngology.

Keywords
aerosol-generating procedures, coronavirus disease 2019, ear, nose, and throat, personal protective equipment, viral load

INTRODUCTION

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first noted in Wuhan, China in December 2019 with isolation of a novel coronavirus (2019-nCoV). In February 2020, the WHO announced the coronavirus disease 2019 (COVID-19) outbreak as a pandemic [1]. To date, there have been over 15 million confirmed cases of COVID-19 globally and almost 620 000 deaths [2].

Back in 2003, the Hong Kong Special Administrative Region experienced an epidemic of SARS associated coronavirus (SARS-CoV-1) between March and June that resulted in a total of 1755 cases and 300 deaths [3]. Not only did the SARS-CoV-1 result in mortalities, survivors were reported to have suffered from the sequelae of receiving high-dose steroid treatment regimens. The wider effect on society also involved decimation of the economy, resulting in a long-lasting economic depression.

The waves of COVID-19 have spread across the globe for more than half of a year. The memory of the devastation and lessons learned from SARS-CoV-1 has taught the medical practitioners and citizens of Hong Kong to stay extremely vigilant on hand hygiene, masking, and social distancing during the current pandemic. Resulting in a low infection rate in Hong Kong and a three-week streak of zero local cases in June 2020 [4].

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KEY POINTS

- SARS-CoV-2 can be transmitted in asymptomatic or presymptomatic period.
- High viral loads in nasopharynx and oropharynx.
- PPE is essential when carrying out AGPs in outpatient and operative settings.

Although there are ongoing clinical trials for the treatment of COVID-19, there is so far no effective therapy available. With the third wave of COVID-19 attacking Hong Kong since July, we have been experiencing hundreds of cases every day, overloading isolation wards in public hospitals, consuming our limited resources of personal protective equipment (PPE). Within our discipline, Otolaryngologists are at a high risk of contracting COVID-19 during this pandemic if there is inadequate and improper PPE provision, as we are dealing with diseases of the upper-aerodigestive tract and routinely engaged in aerosol-generating procedures (AGPs).

In this article, we will review on how the general outpatient procedures and ear, nose, and throat (ENT)-related surgeries put ENT surgeons at risk and discuss our current practice to reduce the potential exposure to COVID-19.

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 VIRAL LOAD AND KINETICS

SARS-CoV-2 is an enveloped and single-stranded RNA virus under the family Coronaviridae and order Nidovirales, *which is under the same genera with SARS-CoV-1 and* the Middle Eastern respiratory syndrome coronavirus (MERS-CoV) [5]. SARS-CoV-2 is believed to have transformed from a zoonotic transmission to a novel human-transmitting coronavirus, with a similar genetic sequence to bat-derived coronaviruses, suggesting bats as the original host of the virus [6].

SARS-CoV-2 seems to infect predominantly middle-age male adults with a poor prognosis and higher mortality associated with chronic comorbidities such as diabetes mellitus [7]. On the other hand, there have been fewer pediatric cases of COVID-19 and majority of the cases were asymptomatic or only minimal symptoms. In spite of the milder presentation of COVID-19 in most of the pediatric cases, there has been a concern of a hyperinflammatory syndrome with features of Kawasaki disease called 'Paediatric Inflammatory Multisystem Syndrome-temporally associated with SARS-CoV-2' associated with current or prior COVID-19 infection with development of shock, multisystem inflammation and coronary artery abnormality in this population [8,9].

Compared with the SARS in 2003 and the Middle East respiratory syndrome (MERS), COVID-19 behaves similarly with initial presenting symptoms including a fever, flu-like symptom, and dry cough. All of the three viral infections may result in lower respiratory diseases such as pneumonia with severe inflammatory response in the host, resulting in pulmonary injury and respiratory failure requiring ventilator support [7,10]. It has however been observed that the transmission pattern of SARS-CoV-2 differs from SARS-CoV-1 and MERS-CoV. Whilst similar to influenza, SARS-CoV-2 has the highest viral load at the onset of symptoms, a time when symptoms appear mild or asymptomatic but the infected patients are the most infective [10–12]. SARS-CoV-1 and MERS-CoV conversely have their peak viral load occurring at the seventh to tenth day after symptoms onset, when these patients are most infective and most likely already isolated [10,13,14]. However, SARS-CoV-2 also differs from the former viruses by having a longer incubation period with peak viral load at the onset of symptoms when patients are not aware nor isolated, hence community-acquired transmission during asymptomatic or presymptomatic period in the general public is more likely [15▪]. To understand the viral shredding kinetics of SARS-CoV-2, studies focusing on the site of viral load detected in COVID-19 patients reveal that higher viral load is detected in the upper-respiratory tract than in lower respiratory tract, and higher concentration of viral load in the nose than in the throat at onset of symptoms [15▪,16]. Wölfel *et al.* [17] analyzed virus replication in specific sites suggesting a much higher concentration in nasopharyngeal and oropharyngeal swab than sputum by at least two log-folds at the first week of onset of symptoms in COVID-19 (7.11×10^8 RNA copies per throat swab versus 7.00×10^6 copies/ml of sputum of SARS-CoV-2 viral load). A summary of transmission pattern of different respiratory viruses is shown in Table 1.

Traditionally, viral samples are obtained by means of nasopharyngeal aspiration and throat swabs. WHO recommended screening for the SARS-CoV-2 with nucleic acid amplification tests, such as reverse-transcription polymerase chain reaction for confirmation of suspected cases of COVID-19 [23]. As these testing kits need to be inserted through the nostril to nasopharynx or through orally to oropharynx, it often induces reflex coughing and sneezing, potentially shredding the virus to

Table 1. Comparison of the transmission pattern of the viruses [10,18–22]

	SARS-CoV-2	Influenza	SARS-CoV-1	MERS-CoV
Route of transmission	Contact, droplets, fomites, potentially airborne	Contact, droplets, fomites	Close contact, droplets, airborne	Close contact, zoonotic airborne
Incubation period	4–12 days	2 days	2–7 days	2–14 days
Peak viral load from the symptoms onset	4–5th days	4–7th days	7th–10th days	14th day
Mortality rate	0–6% below 45 years old 15–52% above 45 years old	1.9–4.1%	14.7–63.9%	14.5–69.2%

MERS-CoV, Middle Eastern respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

healthcare staff. Newly proposed deep throat saliva to detect and monitor viral load by a Hong Kong group suggested that this noninvasive sample collection performed by patients is feasible and sensitive [16]. The Centre for Health Protection (CHP) in Hong Kong has developed a comprehensive enhanced laboratory surveillance scheme for COVID-19 with multiple tier levels for triage and investigation. A brief summary of testing recommended by CHP is listen in Table 2.

THE TRANSMISSION ROUTE OF CORONAVIRUS DISEASE 2019

Similar to other respiratory viral infections, respiratory droplets have a size of 5–10 μm in diameter, produced when infected patients cough or sneeze, travel a limited distance (within 3 ft/1 m) because of the weight of the particles [25].

WHO reported that SARS-CoV-2 could be contacted via droplet and fomite transmission in March 2020 [26]. There is evidence that the virus survives on mucosal surfaces or external surfaces that can be transmitted to other uninfected people by direct contact from person to person or indirectly through touching contaminated external surfaces [27]. Experiments were conducted to assess the durability and surface stability on various materials of the SARS-CoV-2 and compared it with the similar family class – SARS-CoV-1 virus. Doremalen's group observed similar pattern of viral durability and stability in these two viruses [28]. They reported that SARS-CoV-2 remained viable on plastic and stainless steel after 72 and 48 h, respectively. However, the virus is not viable on copper after 4 h. SARS-CoV-2 appears to have similar viral load persistence when tested on plastic and stainless steel whereas it survives much longer on a cardboard surface, 3 times longer as compared with SARS-CoV-1 (24 h versus 8 h).

Given the relatively short stability of SARS-CoV-2 on external surfaces under experimental situations, close contact from person-to-person was

Table 2. Laboratory Surveillance and Monitoring Programs in Hong Kong [24]

Tier	Inclusion criteria	Laboratory test
1	CHP's reporting criteria of severe respiratory disease associated with a novel infectious agent under Cap 599	NPA and throat swab RT-PCR for SARS-CoV-2
2	Enhanced laboratory surveillance: any pneumonia case Irrespective of their travel history Requiring intensive care support Occurring in clusters A healthcare worker	NPA and throat swab RT-PCR for SARS-CoV-2
3	Extended laboratory surveillance: Any inpatients with pneumonia other than Tier 2 Any inpatients presented with influenza like illness symptoms (e.g., fever or cough or sore throat); or Any inpatients presented with new loss of taste/smell, shortness of breath or gastrointestinal symptoms	NPA and throat swab RT-PCR for SARS-CoV-2
4	Patient with fever or acute onset of mild respiratory symptoms in emergency department or general outpatient clinics	Deep throat saliva collection
5	Patient with fever or acute onset of mild respiratory symptoms in private outpatient clinics	Deep throat saliva collection
6	Asymptomatic returned travellers	Deep throat saliva collection

CHP, Centre for Health Protection; NPA, nasopharyngeal aspiration; RT-PCR, reverse-transcription polymerase chain reaction.

highlighted by Centers for Disease Control and Prevention (CDC) as the most important mode of transmission for spreading of COVID-19 [29]. Airborne transmission is attributed to infectious droplet nuclei, defined by the size of 5 μm or small in diameter [30]. For example, *Mycobacterium tuberculosis* and chickenpox virus are classified as airborne transmittable diseases. Previously recognized as transmitting by droplets, on July 9th, 2020, the WHO updated the mode of transmission of SARS-CoV-2, recognizing that airborne transmission can occur during aerosol-generating procedures [31,32]. However, the CDC in Aug 2020 cited that there is still currently lack of data to illustrate that SARS-CoV-2 has long-range aerosol transmission but short-range aerosol transmission is possible [33].

As the research on mode of SARS-CoV-2 transmission is ongoing, possible nosocomial infection particularly during AGPs cannot be overlooked. Strong emphasis on measures to contain the spread of COVID-19 should be advocated including the proper use of PPE and enhancing hand hygiene. The Korea Centres for Disease Control and Prevention (KCDC) also highlights the key to preventing transmission of COVID-19 by active screening, early diagnosis, contact tracing and rapid isolation [34].

PERSONAL PROTECTIVE EQUIPMENT GUIDELINES FOR UPPER AIRWAY EXAMINATION AND AEROSOL GENERATING PROCEDURES IN THE OUTPATIENT CLINIC

WHO considers coughing as an aerosol generating action and studies also suggest that 'pursed lip' breathing generates small droplet nuclei [35]. AGPs refer to medical procedures that could create and disperse aerosol droplets mechanically or indirectly via the induction of patients to cough or sneeze [36]. Tracheostomy, endotracheal intubation, airway care, and cardiopulmonary resuscitation are examples of AGP that have been shown to represent significant risks of transmission of viral respiratory infections in healthcare workers [37].

One in 10 patients with COVID-19 presents with ENT symptoms such as sore throat [38]. Many countries have also reported a sudden increase in isolated anosmia cases seen in ENT clinics. Currently, anosmia or hyposmia are recognizable symptoms in up to 30% positive COVID-19 cases [39]. As an otolaryngologist, it is inevitable that we encounter patients presenting with ear, nose, and throat symptoms irrespective of whether they have COVID-19 or not during an outpatient clinic visit. Although head and neck physical examination is not classified as an AGP, some guidelines suggest otolaryngologists to undertake airborne precautions when performing head and neck examinations on patients who have suspected or known COVID-19 [35]. Nasopharyngoscopy and flexible laryngoscopy through the nasal cavities are regarded as 'probably AGPs' as these are essentially to a flexible bronchoscopy without suctioning [40].

To date, COVID-19 is still affecting people around the world and is not yet containable. Postponement of elective surgeries and triaging nonurgent cases has already been implemented in Hong Kong since early March 2020. The American Academy of Otolaryngology Head and Neck Surgery suggested the need to prioritize and limit the provision of care to only patients requiring urgent ENT interventions [41]. However, it implies that we might delay seeing patients with early malignancies being misdiagnosed to have benign ENT diseases. A cautious comprehensive well thought triage system would be the first step to utilize the limited resources during COVID-19 crisis in addition to protecting healthcare staff from the exposure of extra risks from unnecessary AGP [42].

It is not recommended to perform routine head and neck examination during COVID-19 pandemic so as to reduce the number of patients in the clinic as well as to spare the valuable protective equipment for infectious disease control purposes [43▪]. Caution and special arrangements should be made for ENT clinics during this pandemic. Patients and accompanying relatives should be screened for typical symptoms, travel, and contact history at the entrance of outpatient clinics through questionnaires and body temperature measurements. In our locality, the government has made public announcements advising patients with stable diseases (e.g., rhinitis, indolent chronic suppurative otitis media, or obstructive sleep apnea syndrome) to postpone their follow-up appointment until the resolution of the pandemic disease and attend a drug refill clinic to replenish their stock of medication instead. Telehealth consultations have been used for selective head and neck cancer patients amid the pandemic that avoids excessive rescheduling of appointments and permits the monitoring of possible recurrence or posttreatment complications [44▪▪]. Secondly, otolaryngologists dealing with transoral and transnasal examinations should treat every patient with high vigilance as if dealing with asymptomatic COVID-19 cases and adhere with universal and standard precautions by wearing surgical masks, disposable gloves, and eye shields. In Hong Kong, CHP recommends wearing an N95 respirator, eye protection, gown, and gloves, if an AGP is undertaken [45]. The National Health and Family Planning Commission (NHFPC) from China

Table 3. China NHFPC recommendation for precaution of viral droplet transmission [46]

Level of precaution	Setting	Recommended PPE
Basic precaution	General outpatient clinic, general ward medical staff	Surgical masks, hand hygiene, working uniform ± latex gloves
Grade I precaution	Fever or infectious ward medical staff	Surgical masks, hand hygiene, working uniform, latex gloves, waterproof medical cap, disposable gown
Grade II precaution	General examination for Airborne transmitting disease suspect	N95 masks, hand hygiene, working uniform, latex gloves, waterproof medical cap, antipenetration isolation gown, shoe covers and wearing antifog protective goggles or a protective face shield
Grade III precaution	AGPs in suspected or confirmed disease	All Grade II PPE as well as PAPRs

AGPs, Aerosol generating procedures; PAPRs, powered air-purifying respirators; PPE, personal protective equipment.

suggests four levels of precaution during the COVID-19 pandemic as shown in Table 3 [46]. Recommendations by various organization in different regions are listed in Table 4.

Otolaryngologic examinations should be targeted and purposeful specific for presenting symptoms during this COVID-19 pandemic. Patients followed up for otologic disease who do not require transoral or transnasal examination could be allocated to a non-AGP room in which staff could practice standard precautions during examination whereas patients who require to have endoscopic examination of the upper-respiratory tract could be reviewed in a negative pressure room by a designated otolaryngologist and healthcare assistance with full personal protective equipment. Topical local anesthetic in the form of aerosolized spray for ENT examination should also be avoided and be replaced by pledgets [43▪].

Some ENT specific but least-mentioned AGPs in the literature that were routinely performed in the outpatient clinic should be performed in a negative pressure procedural room with airborne precaution level of PPE during the current pandemic. These procedures could induce forceful coughing and generate aerosol droplets from the respiratory tract. Moreover, otolaryngologists often require to perform these procedures in close proximity with patient's upper-respiratory tract. Therefore, we recommend otolaryngologists and nursing assistance to obtain airborne precaution PPE when carrying out these procedures. Lists of the General and ENT-specific AGPs is provided in Table 5 [45,51].

PERSONAL PROTECTIVE EQUIPMENT IN EAR, NOSE, AND THROAT OPERATIONS

Beyond adaptations in the ENT outpatient clinic, operative arrangement has also been significantly

Table 4. Comparison of recommendations of precaution for AGPs in suspected/ confirmed COVID-19

Organizations/ Lists of PPE	China NHFPC [46]	CHP (Hong Kong) [47]	NHS (UK) [48]	AAO-HNS (USA) [49]	CDC (USA) [50]
N95 respirator	Y	Y	FRSM-type IIR	Y	Y
Hand hygiene	Y	Y	Y	Y	Y
Working uniform	Y	–	–	–	–
Disposable gloves	Y	Y	Y	Y	Y
Cap	Y	Optional	Not routinely required	–	–
Gown	Antipenetration isolation gown	AAMI level 1	Full body or fluid-repellent coveralls	Y	Y
Shoe covers	Y	Not recommended	Not required	–	–
Goggles	Y	Y	Y	Y	Y
Face shield	Y	Y	Y	–	Y
Powered air-purifying respirators	Y	–	–	Y	Y

AGPs, Aerosol generating procedures; AAMI, Association for the Advancement of Medical Instrumentation; AAO-HNS, American Academy of Otolaryngology – Head and Neck Surgery; CHP, Centre for Health Protection; CDC, Centers for Disease Control and Prevention; FRSM, fluid resistance surgical face masks; NHS, National Health Service, United Kingdom; UK, The United Kingdom; USA, United States of American; '–', not mentioned; 'Y', mentioned.

Table 5. List of general and ENT specific AGPs

Recommended PPE	General high-risk procedures	ENT-specific procedures
N95 respirator	Endotracheal intubation	Open suctioning of respiratory tract
Eye shield	Cardiopulmonary resuscitation	Exchange of tracheostomy tubes
Gown	Bronchoscopy	Exchange of tracheoesophageal puncture voice prothesis
Gloves	Noninvasive positive pressure ventilation (BiPAP and CPAP)	Tracheostoma care and toileting
Cap		Removal of foreign body from the upper respiratory tract
		Incision and drainage of peritonsillar abscess
		Nasopharyngeal biopsy
		Oral cavity and oropharyngeal biopsy

AGPs, Aerosol generating procedures; ENT, ear, nose, and throat.

modified during the COVID-19 outbreak. In view of the increasing number of confirmed SARS-CoV-2 cases in Hong Kong, overloading isolation facilities in public hospitals, depleting the limited amount of protective equipment and need of deployment of staff to COVID-19 temporary care units, ENT-related operative services have been restricted to provide emergency and urgent elective operations since February 2020 [44▪▪]. The postponement of elective surgery has been detrimental to patients who are waiting for elective surgeries, such as functional endoscopic sinus surgeries for chronic rhinosinusitis or tympanoplasties for chronic secretory otitis media. Nevertheless, the limited provision of the ENT operative service has put additional stress on patients in particularly those with head and neck cancers as this implies a longer waiting time for their curative surgery, potentially leading to disease progression and affecting disease management. Prior to COVID-19 pandemic, the average waiting time in our center in Hong Kong for a curative head and neck cancer surgery was four weeks from the time of diagnosis, not including the waiting time of referral, ENT consultation, and initial diagnostic investigations [44▪▪]. During the COVID-19 period, the waiting time for operation has been lengthened to six months. A cautious stratification to balance between the infectious disease control measures during COVID-19 and risks of delaying the head and neck cancer and other timely urgent ENT surgeries is essential. Our head and neck center recommends a three-tier stratification for head and neck cancer operations with target time of surgery, comparable with the international consensus among 20 national clinical trial groups for head and neck cancer management during COVID-19 pandemic [44▪▪,52▪▪].

A systemic review evaluating risks of SARS-CoV-1 transmission through AGPs found endotracheal intubation and tracheostomy carry the highest risk with odds ratio of 6.6 and 4.2, respectively [37]. When performing endotracheal intubation, only essential anesthetic staff wearing full airborne level protection with N95 masks and face shields should be allowed in the operative theater. Surgeons, scrubbed nurses and operative assistance should not enter the operative theater until the patient is intubated and the mechanical ventilation is connected in a closed-circuit system. For emergency and urgent elective cases, the SARS-CoV-2 polymerase chain reaction test should be taken and surgery should be proceeded after obtaining a negative test should time allow. In the case of suspicious or confirmed COVID-19 cases, intubation and ENT operations should be performed in a dedicated negative pressure operative theater room.

Specific maneuvers and precautions to minimize aerosol generation during tracheostomy are also recommended. For example, complete muscle paralysis with intubation if permitted is preferable. Should the patient require an awake tracheostomy, measures including adequate local anesthesia, low-flow oxygen administration via nasal cannula, and putting facemasks on patients could help reduce the large droplet particle transmission when coughing [53].

Postoperatively, patient with tracheostomy or laryngectomy should be provided with a closed tracheal suction system with a viral filter to minimize droplet transmission during sputum suction in the ward. Laryngectomy apron and heat moisture exchanger help to reduce lower respiratory symptoms and sputum retention, thus it is highly recommended during the COVID-19 situation [51].

Although a commonly cited case of transsphenoidal skull base surgery has been postulated to transmit SARS-CoV-2 to fourteenth healthcare workers in China, it was reported that none participated in the surgery [54]. Experts are still recommending at least standard airborne-level PPE should be warrant when undergoing endoscopic transnasal procedures with suctioning and mucosal instrumentation [55].

An autopsy study testing mastoid and middle ear viral loads in three confirmed COVID-19

deceased cases has shown positivity in viral isolation in these regions [56]. Therefore, PPE for otologic operations and skull base procedures requiring the use of powered instrument such as high-speed bone drills require eye protection with tight-fitting goggles and N95 masks.

In theory, the best measure of minimizing the risks of contacting the SARS-CoV-2 is by minimizing the physical exposure to the virus. During operation on a confirmed COVID-19 case involving the mucosal surfaces, it is best to perform the procedure with the bare essential number of staff with well-trained anesthetists and surgeons carry out the operation efficiently. The routine exchange of the scrubbed team and anesthetists would increase number of exposed staff and hence is not recommended.

WAY FORWARD IN MEDICAL AND SURGICAL SETTINGS

With the experience of SARS 2003 and COVID-19 outbreak, markets focusing on reducing aerosol generation for ENT examination are expected to boom in the near future. For instance, a disposable flexible laryngoscope with digital camera, a one-way valve device punctured through the mask to allow endoscopic examination without taking off patient's masks and transparent protective shields on the devices or covering patient's surgical field are all innovative and aiming to ensure provide additional barrier to reduce transmission of the infectious disease [57].

Amidst the COVID-19 pandemic with ongoing effort of vaccination development, otolaryngologists are combating the disease at frontline in various setting. We should remain highly vigilant and be responsible to practice ENT surgery in a safe and up-to-standard protection level. We should be prepared to face these immense challenges in caution and be reminded that another wave of novel infectious disease or natural disasters could resurrect even after the resolution of COVID-19 pandemic.

CONCLUSION

Otolaryngologists will inevitably be exposed to SARS-CoV-2 in the hospital, in the outpatient clinic, in the wards and in operation theaters because of the nature of the droplet and airborne transmission of COVID-19 and our work on the upper-aerodigestive tract. Being the 'airway specialists,' we should anticipate to take part in a crucial role for airway protection management in this COVID-19 pandemic.

This article summarizes and reviews the current state of art concerning the upper-aerodigestive tract assessment and the management of otorhinolaryngology and head and neck oncological diseases during the COVID-19 pandemic.

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Conflicts of interest

There are no conflicts of interest.

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- ■ of special interest
- ■■ of outstanding interest

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