

Viral Infections of the Upper Airway in the Setting of COVID-19: A Primer for Rhinologists

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Abstract

Background: Viral respiratory tract infections are associated with a significant burden of disease and represent one of the leading causes of mortality worldwide. The current Coronavirus Disease 2019 (COVID-19) pandemic highlights the devastating toll that respiratory viruses have on humanity and the desperate need to understand the biological characteristics that define them in order to develop efficacious treatments and vaccines. To date, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has infected nearly 600 times more people and resulted in 200 times more deaths relative to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) combined.

Objective: Through this review, we aim to summarize the key characteristics of respiratory viruses that hold global significance, with a focus on SARS-CoV-2. Our goal is to disseminate our current knowledge of these infectious agents to otolaryngologists, in particular rhinologists, practicing in the COVID-19 era.

Methods: The general and clinical characteristics of selected respiratory viruses along with available viral treatments and vaccines are reviewed.

Results: There has been significant progress in our understanding of the epidemiology and pathogenesis of various respiratory viruses. However, despite the advancement in knowledge, efficacious vaccines and antiviral treatments remain elusive for most respiratory viruses. The dire need for these scientific discoveries is highlighted by the recent COVID-19 pandemic, which has prompted investigators worldwide to conduct clinical trials at an accelerated timeline in an effort to reduce the morbidity and mortality associated with SARS-CoV-2 infection. Rhinologists will continue to remain on the front-lines of pandemics associated with respiratory viruses.

Conclusion: In light of these unprecedented times, the need to understand the nuances of these viral respiratory pathogens, especially SARS-CoV-2, cannot be overemphasized. This knowledge base is of particular importance to otolaryngologists, whose expertise in the upper airway coincides with the anatomic tropism of these infectious agents.

Keywords

COVID-19, viral, respiratory infection, coronavirus, SARS-CoV-2, upper airway, otolaryngologists, SARS-CoV, MERS-CoV, antivirals

Introduction

Most viral respiratory tract infections (VRTI) are self-limited. However, acute respiratory infections kill an estimated 3.9 million people annually and represent one of the top five causes of mortality worldwide. In developing countries, they represent the leading cause of death in children under five years of age.¹ VRTIs are associated with tremendous societal economic costs

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related to medical expenses and productivity losses.² Fendrick et al. estimated that in the United States, non-influenza-related VRTIs were associated with \$40 billion annually in direct and indirect costs.³ Although VRTIs typically cause non-specific symptoms that resolve spontaneously without treatment, they may predispose vulnerable populations to secondary bacterial infections or exacerbate chronic diseases.⁴

The causal agents of VRTIs differ with respect to epidemiology, temporal appearance throughout the year, age distribution, and severity. The WHO estimates that annual influenza epidemics cause 1 billion cases and result in 290,000 to 650,000 deaths worldwide.⁵ In comparison, as of early June 2020, there are over 6.5 million cases and 380,000 deaths globally due to the novel coronavirus.⁶ However, due to variable testing capacity and reliability across the world, these figures may be vastly underreported. While the true mortality rate has yet to be determined, available data suggests that the crude mortality ratio of COVID-19, defined as the number of reported deaths divided by the reported cases, is between 3-4%, at least 30 times greater than that of influenza.⁷ Given the gravity of the impact of VRTIs on the population as a whole, it is imperative that otolaryngologists understand nuances of various respiratory viruses that they are likely to face, including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 virus particles are present in extremely high concentrations in the nasal cavity and nasopharynx, placing otolaryngologists at increased risk of transmission through mucus, blood, and aerosolized particles when examining or operating in these areas.⁸ Early evidence from China, Italy, and Iran suggests that otolaryngologists are at extremely high risk of contracting the virus when performing routine procedures if proper personal protective equipment is not utilized.⁸ Additionally, the symptoms of COVID-19, including fever, cough, rhinorrhea, sore throat, nasal congestion, and sneezing, overlap with those of common diseases that are typically evaluated by an otolaryngologist, and patients with sino-nasal inflammation may be more likely to harbor upper respiratory viral infections.^{9,10} Anosmia, a symptom of unique interest to the specialty, can also be a clinical manifestation of SARS-CoV-2, potentially from primary infection of olfactory sustentacular cells.¹¹

Respiratory viruses have caused three outbreaks in the past 18 years, suggesting many otolaryngologists will face a new viral respiratory pathogen at some point in their careers. Therefore, understanding the fundamental virology of VRTIs is critical for the practicing otolaryngologist. In this review, we summarize the key characteristics and tropism of respiratory viruses of global significance for the otolaryngologist, specifically those practicing rhinology, in the era of COVID-19 (Tables 1 and 2).

Coronaviridae

Coronaviridae is a family of enveloped, single-stranded, positive-sense RNA viruses that cause respiratory and gastrointestinal infections in humans and animals.¹² They are typically 100-160 nanometers (nm) in diameter.¹² Within the subfamily *Coronavirinae*, there are four genera but only two include human coronaviruses (HCoVs): *Alphacoronavirus* and *Betacoronavirus*. The *Alphacoronavirus* genus includes HCoV-229E and HCoV-NL63. The *Betacoronavirus* genus includes HCoV-OC43, HCoV-HKU1, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV), and SARS-CoV-2.¹³ Common HCoVs (229E, NL63, OC43, and HKU1) typically cause mild to moderate upper respiratory tract infections, similar to the common cold, in immunocompetent individuals, with severe cases present in infants, the elderly, and the immunocompromised.¹³ Viral entry into target cells is mediated by the interaction between the Spike (S) glycoprotein, which requires proteolytic processing at specific cleavage sites by host cell proteases, present on the viral envelope and the host cell receptor. Priming induces conformational changes in the S glycoprotein that ultimately allows for membrane fusion and release of the viral package into the host cell.^{12,13} In other words, the S glycoprotein determines the viral tropism and host spectrum. The specific host receptor targeted by each HCoV, along with other key characteristics, are listed in Table 2.

SARS-CoV

In 2002, SARS-CoV emerged in southern China and was responsible for an epidemic that infected over 8,000 people across 26 countries with a fatality rate of approximately 10%.¹⁴ It is hypothesized that SARS-CoV originated from bats, with masked palm civets serving as intermediate hosts between an animal reservoir and humans.¹² After an incubation period of 2-7 days, influenza-like symptoms are typically present in the first two weeks of illness. Most patients develop pneumonia, which in severe cases can progress rapidly to respiratory distress requiring intensive care.^{12,13} In addition to airway epithelium and alveolar cells, SARS-CoV can infect vascular endothelial cells, lymphocytes, and lung macrophages by binding its S glycoprotein to host receptors Angiotensin-converting enzyme 2 (ACE2) and L-SIGN (CD209L).^{12,15,16} Interestingly, ACE2 is expressed in many cell types throughout the body, including airway epithelium, lung parenchyma, vascular endothelium, kidney cells, and small intestine cells, thereby accounting for the virus's multi-organ involvement.¹⁷

MERS-CoV

In 2012, the first MERS outbreak was identified, with the majority of reported cases originating from Saudi Arabia. Epidemiological studies suggest that bats are the natural hosts while camelids act as the intermediary.¹² Most confirmed cases presented with severe respiratory distress associated with fever, cough, and dyspnea 2-14 days following exposure. Gastrointestinal symptoms were also reported. Severe complications included pneumonia and kidney failure.¹⁸ Among the 2494 laboratory-confirmed cases of MERS, 35% have died.¹⁹ Consistent with these clinical findings and the involved anatomical subsites, MERS-CoV has been demonstrated to infect a range of host cell types in *ex vivo* human cultures, including airway epithelium, vascular endothelium, and hematopoietic cells, via the dipeptidyl peptidase 4 (DPP4) receptor.²⁰ Kidney and intestinal cells are also known to express DPP4 on their surfaces.²⁰

SARS-CoV-2

In December 2019, SARS-CoV-2 emerged from Wuhan, China and rapidly disseminated to other countries, resulting in a global outbreak. On March 11, 2020, WHO declared for the first time a pandemic caused by a coronavirus. Two to fourteen days following infection, patients typically complain of fever, cough, and dyspnea.²¹ Studies suggest loss of smell and/or taste are early symptoms of infection.²² The clinical spectrum ranges from asymptomatic infection to mild symptoms to severe illness. In the last case, acute respiratory distress syndrome (ARDS), coagulation dysfunction, and septic shock can develop.²¹ In the setting of the significant inflammatory response elicited by the infection and resultant airway damage, ARDS may culminate in respiratory failure, which is the cause of death in 70% of fatal COVID-19 cases.^{21,23} In addition, there is growing evidence that SARS-CoV-2 is associated with neurological alterations in patients presenting with severe clinical manifestations through unknown mechanisms.²⁴ The inflammatory response may trigger or accelerate processes that contribute to various neurodegenerative disorders.

Similar to SARS-CoV and CoV-NL63, SARS-CoV-2 targets host cells expressing the surface receptor ACE2,¹² a metalloproteinase ectoenzyme that primarily functions in the regulation of angiotensin II, but also has non-catalytic roles such as intestinal neutral amino acid transport. Along with the ACE2 receptor, the cellular serine protease TMPRSS2 is required to properly process the S glycoprotein and facilitate viral entry into host cells.²¹ In humans, ACE2 protein is broadly expressed in the lung, kidney, and small intestines.¹⁷ Multiple studies

have also demonstrated ACE2 receptor expression in the nasal olfactory epithelium,^{11,25} and postmortem analysis of patients with COVID-19 demonstrates substantial damage in the lung, suggesting that the airway is the principal entry and target of SARS-CoV-2.²⁶

Paramyxoviridae

The *Paramyxoviridae* family consists of enveloped, single-stranded, negative-sense RNA viruses that are responsible for many acute respiratory diseases in infants and children. Respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), and human metapneumovirus (HMPV) are three members known to infect the upper and lower respiratory tract, causing significant morbidity and mortality globally.²⁷ These viruses vary in size, typically from 150 to 350 nm in diameter.²⁷ All members of this family encode two transmembrane glycoproteins, the attachment and fusion (F) proteins that mediate viral entry into host cells following attachment to their surface receptors.²⁷ There are currently no approved antivirals to treat these viruses.

Respiratory Syncytial Virus

RSV is a common respiratory virus that typically causes mild, cold-like symptoms that self-resolve within 1-2 weeks in healthy children and adults. Prevalent in the late fall through early spring, virtually all children are infected once prior to two years of age.²⁸ However, premature, low-birth weight, and less than 6-month-old infants and older adults are at higher risk for severe RSV infection that may require hospitalization.²⁸ In the United States, RSV is the most common cause of bronchiolitis and pneumonia in children less than 1 year of age.²⁸ Ciliated cells of the small bronchioles and Type 1 alveolar cells are the main targets of infection in the lower airway.²⁹ Although the host receptors that facilitate viral attachment and fusion are unclear, candidates have been proposed (Table 2).³⁰ Despite the lack of effective antivirals, passive immunoprophylaxis of high-risk infants with a humanized monoclonal antibody, palivizumab, is available.

Human Parainfluenza Virus

HPIV Types 1-4 represent a group of viruses that circulate at different times of the year, commonly causing upper and lower respiratory tract illnesses in all age groups. After an incubation period of 2-7 days, infected individuals will display symptoms similar to those of the common cold, recovering without sequelae 1-2 weeks later.³¹ In contrast, infants, children, older adults, and the immunocompromised are most at risk for severe parainfluenza symptoms. HPIV-1 and HPIV-2 both cause laryngotracheobronchitis (croup), with HPIV-1

Table 1. Clinical Characteristics of Selected Respiratory Viruses.

Virus	Incubation Period	Additional Signs and Symptoms ^a	Typical Illness Duration	Attack Rate	Fatality Rate	Vaccine	Antivirals with Demonstrated Efficacy
Human Coronavirus 229E	2–14 d	None	7–10 d	7.2%	22.7% (in hospitalized patients)	None	None
Human Coronavirus NL63	2–14 d	Croup (in children)	7–10 d	12.6%	NR	None	None
Human Coronavirus HKU1	2–14 d	Febrile convulsions	7–10 d	8.6%	20% (in hospitalized patients)	None	None
Human Coronavirus OC43	2–14 d	Necrotizing enterocolitis (newborns), diarrhea (infants), gastroenteritis, encephalitis	7–10 d	10.6%	8%–11.6% (in hospitalized patients)	None	None
SARS-CoV	2–7 d	None	14 d	10.3%–60%	14%–15%	None	None
MERS-CoV	2–14 d	Pericarditis, disseminated intravascular coagulation, acute kidney injury, neurologic symptoms with wide-spread intracranial white matter lesions	Median ICU length of stay: 30 days	0.42%–4% (Saudi Arabia); 3.7%–15.8% (South Korea)	34.3%	None	None
SARS-CoV-2	2–14 d	Taste and/or smell disturbances, neurologic alterations	Mild: 1–2 weeks, Severe/Critical: 3–6 weeks	0.09%–0.34% (Western countries), 3%–10% (China)	Highly variable ^b	In development	None
Respiratory syncytial virus	2–8 d	Bronchiolitis and pneumonia (infants, young children), apnea (infants), wheezing	1–2 weeks	3–20%	<1%–1.4%	None	None
Parainfluenza virus 1	2–7 d	Croup	7–10 d	40%–80%	0.9% (in the elderly (age ≥ 65))	None	None
Parainfluenza virus 2	2–7 d	Croup	7–10 d			None	None
Parainfluenza virus 3	2–7 d	Bronchitis, bronchiolitis, pneumonia	7–10 d			None	None
Parainfluenza virus 4	2–7 d	None	7–10 d			None	None
Human metapneumovirus	3–6 d	Wheezing, bronchiolitis, croup, encephalitis	2–5 d	5%–16.4%	4%–10% (in immunocompromised patients)	None	None
Human rhinovirus/enterovirus	12–72 hrs	None	5–7 d	25%–70%	3% (in hospitalized patients)	None	None

Table 1. Continued.

Virus	Incubation Period	Additional Signs and Symptoms ^a	Typical Illness Duration	Attack Rate	Fatality Rate	Vaccine	Antivirals with Demonstrated Efficacy
Influenza A and B	1–4 d	Musculoskeletal (myositis, rhabdomyolysis), cardiac (acute myocardial infarction, myocarditis, pericarditis), neurologic (encephalitis, aseptic meningitis, transverse myelitis), toxic shock syndrome	1–2 weeks	5%–10% (adults), 20–30% (children)	0.1%	Seasonal trivalent or quadrivalent	Oseltamivir phosphate, zanamivir, peramivir, baloxavir marboxil

^aSymptoms common among all viral respiratory tract infections include fever, cough, rhinorrhea, headache, sore throat, dyspnea, and gastrointestinal manifestations (anorexia, nausea, vomiting, diarrhea).
^bCountries have reported vastly different fatality rates, possibly due to variable resource availability (e.g. testing), demographics, and other unknown factors. The case-fatality rate ranges from 0.1% (Singapore) to 6.0% (United States) to 31.2% (Nicaragua).
 NR: Not Reported; d: days; hrs: hours.

identified as the most common etiology in children.³¹ HPIV-3 is more often associated with bronchiolitis, bronchitis, and pneumonia.³¹ HPIV-4 is less well characterized but may cause mild to severe respiratory illnesses.³¹ HPIVs' infectivity is based on recognizing sialic acid-containing receptors on host cells.³²

Human Metapneumovirus

Although HMPV was first identified in 2001, evidence suggests that the virus has been responsible for respiratory tract infections worldwide for at least 60 years.³³ HMPV is most active during late winter and spring. Similar to RSV and HPIV, HMPV typically causes mild symptoms that resolve in 2–5 days with supportive measures. Children, the immunocompromised, and the elderly are most susceptible to developing complications, including bronchitis, bronchiolitis, and pneumonia.³⁴ To establish infection in the respiratory epithelium, HMPV interacts with heparan sulfate proteoglycans on host cell surfaces to gain entry.³⁵

Picornaviridae

Human rhinoviruses (HRVs) and enteroviruses (EVs) are leading causes of human infection worldwide, both belonging to the *Enterovirus* genus within the *Picornaviridae* family.³⁶ These pathogens are small (25–30 nm), non-enveloped, single-stranded RNA viruses.³⁶ Despite sharing common genomic features, these two groups of viruses possess different phenotypic characteristics. Although HRV infection is largely restricted to the upper respiratory tract, EV infection can occur in various cell types, producing diverse clinical syndromes.³⁶ However, some EVs, appropriately named respiratory EVs, exhibit specific respiratory tropism and therefore cause HRV-like symptoms.³⁶ Due to the absence of efficacious antivirals, treatment remains palliative.

Human Rhinovirus

HRVs, consisting of over 100 serotypes classified into three species (A, B, and C), account for over 50% of upper respiratory tract infections.^{36,37} While most cases cause self-limited cold-like symptoms that resolve in 5–7 days, HRV infection can result in severe pneumonia and exacerbations of chronic obstructive pulmonary disease and asthma in susceptible patients.³⁷ These complications highlight the potential for HRVs to cause greater morbidity than previously recognized. The nasal mucosa is the primary site of infection, where ciliated epithelial cells with the cognate receptors are accessible.³⁷ Intercellular adhesion molecule-1 (ICAM-1) represents the target host receptor for most HRVs but members of the low-density lipoprotein (LDL) receptor family and CDHR3 are also candidates.³⁷

Table 2. General Characteristics of Selected Respiratory Viruses.

Virus	Virion Size (nm)	Airway Host Cells	Airway Host Receptor Molecule	Protein Coating	Mode of Transmission
Human Coronavirus 229E	100–160	Alveolar macrophages, dendritic cells, non-ciliated airway epithelium	Aminopeptidase N (CD13)	Enveloped	Droplet, Contact, Airborne
Human Coronavirus NL63		Ciliated cells of nasal and tracheobronchial airway epithelium	ACE2		
Human Coronavirus HKU1		Ciliated airway epithelium, Type II pneumocytes	9-O-acetylated sialic acid		
Human Coronavirus OC43		Ciliated airway epithelium, astrocytes, oligodendrocytes, neurons, microglia	9-O-acetylated sialic acid		
SARS-CoV	100–160	Airway epithelial cells, alveolar epithelial cells, vascular endothelial cells, T lymphocytes, lung macrophages	ACE2, L-SIGN (CD209L)	Enveloped	Droplet, Contact, Airborne (possibly)
MERS-CoV	100–160	Bronchial, bronchiolar, and alveolar epithelial cells, pulmonary endothelial cells, macrophages, dendritic cells, T cells, gastrointestinal tract	DPP4 (CD26)	Enveloped	Droplet, Contact, Airborne (possibly)
SARS-CoV-2	60–140	Goblet and ciliated cells (nasal passages), type II pneumocytes, absorptive enterocytes (intestines)	ACE2, TMPRSS2 for S glycoprotein priming	Enveloped	Droplet, Contact, Airborne (possibly)
Respiratory syncytial virus	150–250	Ciliated airway epithelium, Type I pneumocytes	TLR4, CX3CR1, EGFR, ICAM-1, heparin sulfated proteoglycans, nucleolin	Enveloped	Droplet, Contact, Airborne (possibly)
Parainfluenza virus 1	150–200	Ciliated epithelial cells of the upper- >lower respiratory tract	Sialic acid residues	Enveloped	Droplet, Contact, Airborne
Parainfluenza virus 2	150–200	Ciliated epithelial cells of the upper- >lower respiratory tract	Sialic acid residues	Enveloped	
Parainfluenza virus 3	150–200	Ciliated epithelial cells of the lower- >upper respiratory tract	Sialic acid residues	Enveloped	
Parainfluenza virus 4	150–200	Ciliated epithelial cells of the respiratory tract	Sialic acid residues	Enveloped	
Human metapneumovirus	150–600	Ciliated airway epithelial, alveolar epithelial cells	Heparan Sulfate Proteoglycans	Enveloped	Droplet, Contact
Human rhinovirus/enterovirus	25–30	Ciliated airway epithelium	ICAM-1, LDL receptor, CDHR3	Nonenveloped	Droplet, Contact, Airborne (possibly)
Influenza A and B	80–120	Ciliated columnar epithelium of the respiratory tract	2-6-linked sialic acids	Enveloped	Droplet, Contact, Airborne (possibly)

nm: nanometers.

Influenza

Influenza A and B are responsible for seasonal human flu epidemics each year in the United States. They are 80–120 nm in diameter and have an incubation period of 1–4 days. Although influenza is usually a self-limited infection with symptom resolution in 1–2 weeks, the burden of disease is substantial. CDC estimates that influenza has caused 9–45 million illnesses, 140,000–810,000 hospitalizations, and 12,000–61,000 deaths annually since 2010 in the United States.³⁸ Furthermore, at risk individuals may develop severe flu-related complications that can be life-threatening, including pneumonia, multi-organ failure, sepsis, and exacerbation of chronic diseases.³⁸

Influenza A viruses are classified into subtypes based on two surface glycoproteins—hemagglutinin (H) and neuraminidase (N).³⁹ These viruses are capable of undergoing periodic changes in the antigenic characteristics of their envelope glycoproteins. In contrast, Influenza B viruses are divided into two lineages—B/Yamagata and B/Victoria.³⁹ To infect the respiratory tract epithelium, Influenza A and B utilize hemagglutinin to bind sialic acid residues on host cell surfaces.⁴⁰ There are currently four FDA-approved antivirals for the treatment of Influenza A and B. Zanamivir, oseltamivir, and peramivir are neuraminidase inhibitors that block the release of progeny virus; baloxavir is a polymerase endonuclease inhibitor that targets viral replication.⁴¹ When initiated within 2 days of symptom onset, these antivirals can reduce the severity of influenza complications, length of hospital stay, and influenza-associated mortality.⁴¹

Viral Treatments and Vaccines

Therapies for VRTIs include both antiviral treatments for active infections and preventative vaccines to induce immunity and thus prevent infection. Antivirals are a class of medications that ameliorate symptoms, minimize infectivity, and reduce the duration of illness by arresting the viral replication cycle at various stages. Most antivirals target key enzymes involved in the replication process. However, because viruses are obligate intracellular pathogens that hijack and exploit the host cell machinery to propagate, developing medications that disrupt the viral replication cycle without damaging host cells has proved to be challenging. To date, antivirals are available for the treatment of only a limited number of infectious pathogens, including human immunodeficiency virus (HIV), herpes viruses, hepatitis B and C viruses, and influenza A and B viruses.

In response to the COVID-19 pandemic, efforts to develop efficacious therapies are well underway. In China, a randomized controlled trial was conducted to evaluate the efficacy of lopinavir-ritonavir, two HIV

protease inhibitors, in 199 hospitalized adults with confirmed SARS-CoV-2 infection.⁴² In addition, the efficacy of remdesivir, a viral RNA polymerase inhibitor, in the treatment of SARS-CoV-2 is currently under investigation. Preliminary results from a randomized controlled trial sponsored by the National Institutes of Health (NIH) suggested that remdesivir helped patients recover 31% faster and conferred a survival benefit compared to placebo.⁴³ On May 1, 2020 the Food and Drug Administration issued an emergency use authorization for remdesivir for the treatment of adults and children hospitalized with severe COVID-19 disease.⁴⁴

Vaccination is the most effective medical intervention against viral illnesses. Vaccines prevent or attenuate the severity of disease and interrupt or reduce the transmission of pathogens to susceptible individuals. Although there is currently no vaccine for SARS-CoV-2, countries across the globe are employing different vaccine technologies with the hope of developing one that can halt the pandemic. To date, there are over 100 candidate vaccines in various stages of development, nine of which are now being evaluated in human clinical trials.⁴⁵

While vaccine investigations are underway for SARS-CoV-2, novel treatment approaches are also under investigation. As the virus appears in high concentrations in the nasal and upper airway epithelium, strategies to decrease the viral load and likelihood of transmission may be explored. For example, povidine-iodine has been shown to be effective against SARS-CoV-2 homologues SARS-CoV and MERS-CoV in topical preparations,⁴⁶ and recent reports explore its efficacy and safety for topical nasal application.^{47–49} The concept of “nasal sterilization” for SARS-CoV-2 may be explored as a therapeutic strategy for patients actively infected or as a prophylactic strategy for high-risk exposures, such as healthcare workers or patients undergoing aerosol-generating procedures. Various other treatment options may include the use of topical therapies such as surfactants or novel medications targeting the ACE2 receptor, given its accessibility in the apical membrane of the respiratory mucosa.

Future Rhinologic Practice Directions

In an effort to flatten the curve of COVID-19 transmission, numerous international groups have issued safety recommendations relevant to the care of otolaryngologic patients during the pandemic.^{50–53} Although general practice guidelines are valuable, there is an urgent need to address rhinology-specific concerns during the acute phase of the pandemic and in preparation for upcoming “waves” that may occur in the future. Best-practice recommendations for ambulatory and surgical encounters will guide safe and effective clinical care during such conditions. Although there is evidence that telemedicine

can be effectively used to triage patients with ear-related complaints,^{54,55} guidelines to select candidates who are evaluated remotely and require further endoscopic examination are lacking. Due to the potential risk of aerosolization associated with otolaryngology encounters, reevaluating the role of computed tomography (CT) as a substitute for office procedures such as nasal endoscopy merits further consideration as well.⁵⁶

To assist otolaryngologists operating in the COVID-19 era in prioritizing rhinologic procedures, the American Academy of Otolaryngology—Head and Neck Surgery designated specific surgical interventions as emergent/urgent, time-sensitive, and routine priority.⁵⁵ However, as there is currently no definitive evidence of transmission associated with specific otolaryngologic procedures, further research to ascertain these risks and an improved understanding of aerosol generation in otolaryngic procedures is warranted. Furthermore, as rhinologists can perform a diverse array of sinonasal procedures in the office, guidance on the same safety measures as for operating room cases would be beneficial. Whether different procedures are associated with different risks of viral transmission to the rhinologist and staff remains unknown. Without a doubt, rhinology will remain on the “front-lines” of pandemics associated with VRTIs given their unique risk of aerosol-generating procedures, as well as their insight on the development of novel treatment strategies that directly target the site of human host entry.

Conclusion

VRTIs are a leading cause of mortality and disability worldwide. There has been significant progress in our understanding of the epidemiology and pathogenesis of various respiratory viruses. The unique implications of COVID-19 on the otolaryngic patient and otolaryngologist alike necessitate increased understanding of SARS-CoV-2 in the otolaryngology community. Though there is a feverish race for discovery of effective treatment strategies and a vaccine, the otolaryngologist may be uniquely situated to aid in development and implementation of novel management strategies to mitigate further outbreaks.

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