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SARS-CoV-2 and the Eye: Implications for the Retina Specialist From Human Coronavirus Outbreaks and Animal Models

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Abstract

Purpose: The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has escalated rapidly since December 2019. Understanding the ophthalmic manifestations in patients and animal models of the novel coronavirus may have implications for disease surveillance. Recognition of the potential for viral transmission through tear film has ramifications for patients, physicians, and the public. **Methods:** Information from relevant published journal articles was surveyed using a computerized PubMed search and public health websites. We summarize knowledge of ophthalmic manifestations of SARS-CoV-2 infection in patients and animal models, risk-mitigation measures for patients and providers, and implications for retina specialists. **Results:** SARS-CoV-2 is efficiently transmitted among humans, and although the clinical course is mild in most infected patients, severe complications including pneumonia, acute respiratory distress syndrome, and death can ensue, most often in elderly patients and individuals with comorbidities. Conjunctivitis occurs in a minority of patients with COVID-19, and SARS-CoV-2 RNA has been identified primarily with conjunctivitis. Uveitis has been observed in animal models of coronavirus infection, and cotton-wool spots have been reported recently. **Conclusions:** SARS-CoV-2 and other coronaviruses have been rarely associated with conjunctivitis. Identification of SARS-CoV and SARS-CoV-2 RNA in the tear film of patients and its highly efficient transmission via respiratory aerosols supports eye protection, mask, and gloves as part of infection prevention and control recommendations for retina specialists. Disease surveillance during the COVID-19 pandemic may also include ongoing evaluation for uveitis and retinal disease given prior findings from animal models and a recent report of retinal manifestations.

Keywords

coronavirus, SARS-CoV-2, 2019-nCoV, COVID-19, ophthalmology, retina, uveitis, conjunctivitis, eye, animal models

Introduction

The current pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which causes the clinical disease coronavirus-19 (COVID-19, previously named novel coronavirus-2019, nCoV-2019) was first reported in Wuhan, China, in December 2019.[1] On January 30, 2020, the outbreak was declared a public health emergency of international concern. By March 11, the outbreak was declared a pandemic by the World Health Organization (WHO), prompting keen focus on the public health impact, attention, and resources by regional governments, as well as international public health coordination. The WHO COVID-19 situation report from May 22, 2020, indicated there were 4 993 470 cases with 327 738 deaths globally.[1] Despite the recent decline in cases in China, the outbreak has continued to escalate globally, involving 210 countries or territories as of May 22, 2020.

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In late December 2019, clusters of patients were reported with pneumonia of unknown cause epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, China. Their clinical presentation included fever, cough, and chest discomfort with radiographic confirmation of pneumonia. Some patients subsequently developed rapid-onset acute respiratory distress syndrome (ARDS). Real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of lower respiratory tract samples, including bronchoalveolar lavage fluid, identified a novel betacoronavirus. Subsequent unbiased sequencing and transmission electron microscopy led to the identification of SARS-CoV-2, the seventh coronavirus known to infect humans.[2] The Coronavirus Study Group of the International Committee on Taxonomy of Viruses, responsible for the classification and taxonomy of the Coronaviridae family, identified this virus as a sister virus to severe acute respiratory syndrome (SARS-CoV) based on phylogeny and leading to it being named SARS-CoV-2.[3]

Following this initial report, the number of cases in China quickly escalated to approximately 80 000 cases by late February, and during March the global prevalence escalated to more than 500 000 cases.[1] Although initial cases are thought to be the result of animal-to-person transmission, the person-to-person route is thought to largely be responsible for viral transmission leading to clinical disease.

Other members of the Coronaviridae family have been shown to cause ophthalmic disease, including retinal pathology. In animals, feline coronavirus (FCoV) can cause uveitis, scleritis, and retinitis in cats,[4,5] and murine hepatitis coronavirus (MHV) can cause retinal vasculitis and degeneration in mice.[6-9] Human coronavirus NL63 (HCoV-NL63) can cause conjunctivitis in humans, and the closely related SARS-CoV has been found in the tears of infected patients.[10] Therefore, an understanding of ocular manifestations reported in patients and animal models of coronavirus may guide the recognition of ophthalmic disease phenotypes in patients with COVID-19. In addition, knowledge of the prevalence of SARS-CoV-2 in the tear film and viral transmission dynamics may guide infection prevention and control measures to reduce transmission, particularly during patient visits to physicians.

This review provides an overview of viral pathogenesis and synthesizes the literature regarding pertinent clinical and ophthalmic disease relevant to patients with SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome (MERS-CoV) infection, as well as established animal coronavirus models. Infection prevention and control measures based on our knowledge of SARS-CoV-2 detection in the ocular surface and ramifications for the retina specialist are reviewed.

Methods

Literature Review

A computerized PubMed search was performed for the various journal articles referenced in this review. Searches directly relevant to SARS-CoV-2, for example, clinical features, included its other names: 2019-nCoV and COVID-19. Epidemiological data for MERS-CoV, SARS-CoV, and SARS-CoV-2 were gathered using the virus names. The words *coronavirus*, *ophthalmology*, *eye*, *ocular*, *retina*, *uveitis*, *conjunctivitis*, and *tears* were used when searching for ophthalmic manifestations secondary to Coronaviridae. Search terms used for details on viral taxonomy, replication cycle, and serotypes included *coronavirus*, *taxonomy*, *life cycle*, *structure*, *phylogenetics*, and *serotypes.* Information regarding institutional and public health responses to the virus was collected directly from the WHO, the Centers for Disease Control and Prevention, the American Academy of Ophthalmology (AAO), and the American Society of Retina Specialists (ASRS) websites.

Results

Viral Taxonomy, Structure, Replication Cycle, and Human Coronavirus Serotypes

In 1968, the name *coronavirus* arose following electron microscopic visualization of virions with crown-like spike projections from their membranes, resembling a crown, or *corona* in Latin.[11] In 1975, the Coronaviridae family was added to the taxonomy of viruses and in 2005 was subdivided into 2 subfamilies: toroviruses, causing disease in cattle, and coronaviruses (CoV). Coronaviruses are round, enveloped viruses of approximately 100 nm in diameter, and contain positive-sense, single-stranded RNA with the largest RNA genome reported to date (26-32 kilobases).[12] The viral genome encodes 4 major viral structural proteins—the spike (S), envelope (E), membrane (M), and nucleocapsid (N) protein. The S, E, and M proteins are contained within the viral membrane, and the S protein, specifically, mediates receptor binding and viral entry into host cells, serving as a major therapeutic target.[13]

The replication cycle of coronavirus begins with S protein attachment to the angiotensin-converting enzyme 2 (ACE2) receptor, the likely receptor for SARS-CoV-2, facilitating fusion between the cell and virus membranes.[14] Structural modeling has shown similarities between SARS-CoV and SARS-CoV-2 binding, although SARS-CoV-2 has demonstrated a stronger binding affinity to ACE2.[15] ACE2 expression has been reported in human cornea and aqueous humor as well as the airway epithelia, intestine, kidneys, and testes.[15-17] The nasal mucosa appears to have the highest expression of ACE2 and may be the most important site for SARS-CoV-2 transmission, with oral mucosa and the cornea also being implicated.[16]

By contrast, MERS-CoV infection begins with S protein binding of the cellular receptor dipeptidyl peptidase. For both viruses, the nucleocapsid is released into the cell following binding, whereby RNA genome replication and messenger RNA transcription subsequently begin.[15] Following assembly of viral nucleocapsids in the cytoplasm from genomic RNA and N protein, the virions are released from the infected cell via exocytosis.[13] The S protein of the coronavirus plays a key role in pathogenesis, enabling receptor interaction, fusion, entry, and cell-to-cell spread. However, the available hosts for

Coronaviridae are limited and disease manifestations are dependent on the ability of the virus to interact with cell membranes of specific species (eg, inability of murine coronavirus to replicate in human cells).

There are 7 coronaviruses known to infect humans, referred to as *human coronaviruses* (HCoVs). The 4 most common human serotypes include human coronavirus 229E (alphacoronavirus), NL63 (alphacoronavirus), OC43 (betacoronavirus, lineage A), and HKU1 (betacoronavirus, lineage A).[18] Human coronaviruses 229E and OC43, discovered in 1966 and 1967, respectively, are associated with the common cold and distributed globally.[19,20] HCoV-NL63, an alphacoronavirus, was first discovered in the Netherlands in 2004 and tends to cause respiratory illness in children, who may also develop cojunctivitis.[20,21] Two zoonotic betacoronaviruses, MERS-CoV, the causative virus for Middle East respiratory syndrome, and SARS-CoV, the causative agent of severe acute respiratory syndrome, are ill adapted to humans and occasionally cause human infections and outbreaks.[22,23]

The precise reservoir and transmission dynamics of SARS-CoV-2 are not fully understood. To understand the animal reservoir, 9 patients with confirmed SARS-CoV-2 infection underwent bronchoalveolar lavage for next-generation sequencing and exhibited greater than 99.98% sequence identity. SARS-CoV-2 was closely related to 2 bat-derived SARS-like coronaviruses with 88% identity, albeit more distant from SARS-CoV and MERS-CoV with 79% and 50% identity, respectively.

Phylogenetics classifies SARS-CoV-2 within the subgenus *Sarbecovirus* of the genus *Betacoronavirus*. The novel SARS-CoV-2 genome sufficiently differs from prior strains and was thus classified as a new HCoV.[24] These phylogenetic analyses suggest that bats may be the original host of the virus, whereas an animal sold in Wuhan may have been the intermediate host that facilitated human disease.[24] RaTG13, a betacoronavirus discovered mainly in bats, is very similar to SARS-CoV-2, with genome sequences identical to 96%.[25]

A virus that affects the pangolin, a mammal resembling an anteater with plate-like scales, has also been implicated, with 99% genomic concordance with SARS-CoV-2 and similarities in the S protein region.[26] However, another study investigating a virus in Malayan pangolin found only 90% concordance, making an association less likely.[27] Alternatively, it is possible that recombination between different viruses has occurred, something that has been previously described in coronavirus cross-species transmission.[28]

Severe Acute Respiratory Syndrome, Middle East Respiratory Syndrome, and Severe Acute Respiratory Syndrome Coronavirus 2: Epidemiology and Case Fatality Rate

The 2 other significant human coronavirus strains—SARS-CoV and MERS-CoV—share similar epidemiologic and clinical characteristics to SARS-CoV-2, namely severe worldwide epidemic outbreaks from respiratory illness.[29-31] The SARS-CoV outbreak of 2002 to 2003 resulted in 8098 cases and 774 deaths (an approximately 10% case fatality rate) and spanned 26 countries.[32] The first case was reported in Guangdong Province, China, in November 2002.[23] Although no intermediate animal reservoir was confirmed, studies have suggested animals such as the Himalayan masked palm civet and the Chinese ferret badger may harbor the virus.[33] Bats have been implicated as the potential reservoir both for SARS-CoV and MERS-CoV.[34] Since 2012, MERS-CoV has been responsible for more than 2400 cases and more than 850 deaths, primarily in the Arabian Peninsula, with the majority of cases reported in Saudi Arabia. MERS may also cause ARDS and lead to multiple organ failure, conferring an overall reported case fatality of 34%.[35,36] The 2015 MERS-CoV outbreak in South Korea had a case fatality of 19.4% (36 cases).[37] Dromedary camels have been suggested as a possible source of transmission to humans.[38,39]

Cases of COVID-19 due to SARS-CoV2 infection have greatly exceeded the numbers of SARS-CoV and MERS-CoV combined. The case fatality rate of SARS-CoV-2 approximates 1% to 2%, although these percentages include confirmed cases only and are likely greater than the true rate given the high frequency of asymptomatic, presymptomatic, or mildly symptomatic cases.[40]

Severe Acute Respiratory Syndrome Coronavirus 2: Systemic Disease Features

Following an epidemiological alert by the local authority in Wuhan on December 31, 2019, 59 patients with fever and dry cough were admitted to the hospital and treated for a pneumonia of unknown origin. Of this initial cohort, 41 had laboratory confirmed SARS-CoV-2 infection; 27 (66%) were frequent visitors of the Huanan Seafood Market. The most common signs and symptoms included fever (98%), cough (76%), myalgia or fatigue (44%), as well as sputum production (28%), headache (8%), hemoptysis (5%), and diarrhea (3%). Fifty-five percent developed dyspnea with a median length of duration of 8 days.

Ninety-eight percent of patients had chest computed tomography (CT) abnormalities with bilateral involvement and subsegmental areas of consolidation. Images of patients on intensive care unit (ICU) admission showed multiple lobular and segmental areas of consolidation, whereas non-ICU patient scans showed bilateral ground-glass opacities along with subsegmental areas of consolidation. Thirteen patients (32%) were admitted to the ICU for oxygen therapy to treat hypoxia. All patients had pneumonia, with 29% developing ARDS, 12% with acute cardiac injury, and 10% of patients requiring mechanical ventilation.[41] The typical ground-glass appearance on lung CT scans is a common finding in patients infected with SARS-Cov-2, including in 93% of asymptomatic patients, suggesting a role for early imaging to aid diagnosis.[42]

In another study aiming to establish clinical features, 99 patients with confirmed SARS-CoV-2 admitted to Jinyintan Hospital, Wuhan, which accepted the first cases, were described. Nearly 50% had been exposed to the Huanan

Seafood Market and 51% had chronic illness. Fever, cough, and dyspnea were reported in 83%, 82%, and 31%, of patients, respectively. Other symptoms included muscle ache, headache, diarrhea, sore throat, chest pain, nausea, and vomiting. Seventeen percent developed ARDS and all patients demonstrated pneumonia by CT scan. By January 25, 31% had been discharged and 11% had died. Elderly patients and individuals with comorbidities were more vulnerable to an aggressive disease course.[43]

Shortly thereafter, 2 confirmed cases in Vietnam and 1 US patient who traveled to Wuhan presented with a cough and pneumonia as well as radiological features similar to previously confirmed SARS-CoV-2 patients.[44,45] A study of the transmission dynamics of COVID-10 pneumonia showed that among 425 patients, more than 50% of cases reported before January 1, 2020 were linked with the Huanan Seafood Market compared to only 8.6% of cases following January 1. These data suggest a doubling time of 7.4 days and a reproduction number R_0 of 2.2 (ie, on average, each patient spreads infection to 2.2 others).[46] In comparison to SARS-CoV, SARS-CoV-2 transmits more efficiently and appears less pathogenic than SARS-CoV. This poses a lower health risk to the individual but a greater risk to the population as a whole.[47] In a larger series of 1099 patients with laboratory-confirmed SARS-CoV-2 from 552 hospitals, 6.1% of patients required ICU admission, mechanical ventilation, or died. Conjunctival "congestion" was observed in 9 patients (0.8%).[40]

More recently, case series of critically ill patients have been reported in the United States.[48,49] In a case series of 21critically ill patients from Seattle, Washington, 86% had comorbidities including chronic kidney disease and congestive heart failure. Initial symptoms comprised shortness of breath (76%), fever (53%) and cough (48%). Fifteen of 21 patients (71%) required mechanical ventilation because of ARDS and mortality was 67%.[48] Another series of 24 patients with COVID-19 admitted to ICU settings demonstrated severe morbidity with hypoxemic respiratory failure in 75% of patients and high mortality of 50%. The majority of patients (17) also developed hypotension prompting vasopressor treatment.[49]

Ophthalmic Findings in COVID-19: Conjunctivitis, Viral RNA in Tear Film, and Retinopathy

A 1% rate of conjunctival signs was documented in a large series from China with no elaboration on the clinical features.[40] Another case series assessed conjunctival secretions from 30 patients with confirmed COVID-19. Tear film swabs were collected twice at 2- to 3-day intervals to assess viral RNA by RT-PCR.[50] The single patient with conjunctivitis showed a positive RT-PCR result, whereas the other 29 patients, all without conjunctivitis, had no evidence of viral RNA in their tears. Conjunctivitis was one of the presenting symptoms in 3 patients with laboratory confirmation of COVID-19, 1 of whom was a nurse caring for patients with COVID-19. No further comments on clinical features were reported.[51,52] RT-PCR confirmation of SARS-CoV-2 was identified in 1 patient assessed by conjunctival sampling.[52] More recently, in a series of 17 patients from Singapore, 64 tear film samples were collected from patients without conjunctivitis during their hospitalization for COVID-19 and there was no evidence of viral RNA by RT-PCR or viral culture.[53] Notably, 1 patient from Italy presented with conjunctival hyperemia among her initial presenting signs of COVID-19, and viral RNA was identified in her tear film 3 days after the onset of symptoms and persistently positive until 27 days from symptom onset. Cytopathic effect was observed following inoculation of the first RNA-positive ocular sample in Vero E6 cells.[54] Although conjunctival findings have been observed in adults, recent large series of children with COVID-19 have not specifically reported conjunctivitis or ophthalmic manifestations.[55]

Retinal findings were recently described in 12 adults, 9 of whom tested positive for SARS-CoV-2 by PCR and 2 who were antibody positive. All patients in their series showed hyperreflective lesions within the ganglion cell and inner plexiform layers, which were visualized by optical coherence tomography. Four patients showed cotton-wool spots and hemorrhage along the retinal vascular arcades although these findings did not affect visual acuity. Moreover, no evidence of intraocular inflammation was observed.[56]

Ophthalmic Findings in Other Human Coronaviruses and Animal Models

Ophthalmic Manifestations and Tear Film Assessment in Severe Acute Respiratory Syndrome Coronavirus and Human Coronavirus NL63. Coronaviridae have been reported to cause various ophthalmic manifestations summarized in Table 1. Like SARS-CoV-2, SARS-CoV is a betacoronavirus.[22] The WHO published 2 case definitions for SARS-CoV infection: The first case definition includes a high fever (higher than 38 °C), cough, or dyspnea, and 1 or more exposures during the 10 days prior to symptom onset. The second definition includes unexplained ARDS resulting in death and 1 or more exposures during the 10 days prior to symptom onset.[57]

SARS-CoV RNA was identified with RT-PCR analysis of tear film in the 2003 SARS outbreak. In one study primarily consisting of health care workers with suspected SARS-CoV, 3 of 36 patients (8%) showed evidence of SARS-CoV RNA in their tear film.[62] In another investigation from Hong Kong that used tear swabs and conjunctival scrapings, no evidence of viral RNA was identified on the ocular surface of 17 confirmed and 3 probable SARS patients.[58]

HCoV-NL63, a cause of pediatric respiratory illness, has been reported to cause conjunctivitis in 17% of affected children.[10,21] The case notes of 28 patients admitted to a French hospital with respiratory illness and with confirmed infection were retrospectively examined and no further ophthalmic assessment or features were reported.[10]

Ophthalmic Manifestations in Animal Models of Coronavirus. Two other coronaviruses have been associated with eye disease in animal species: FCoV and MHV. Feline infectious peritonitis

Table 1. Coronaviridae and Their Ophthalmic Disease Associations.

Virus name	Genus	Ophthalmic associations	Affected animal groups
SARS-CoV-2	Betacoronavirus	Conjunctivitis; RT-PCR positive for SARS-CoV-2 in tears[31,41-44]	Humans
SARS-CoV	Betacoronavirus	RT-PCR positive for SARS-CoV in tears.[48,49]	Humans
MERS-CoV	Betacoronavirus	None reported	Humans
FCoV	Betacoronavirus	Pyogranulomatous inflammation and phlebitis in the uvea, sclera, conjunctiva, retina, and optic nerve[56,57]	Cats
MHV	Betacoronavirus	Retinal vasculitis and degeneration, demyelination, and optic neuritis[58-61]	Mice
HCoV-NL63	Alphacoronavirus	Conjunctivitis[53]	Humans

Abbreviations: FCoV, feline coronavirus; HCoV-NL63, human coronavirus NL63; MERS-CoV, Middle East respiratory syndrome; MHV, murine hepatitis coronavirus; RT-PCR, reverse transcriptase–polymerase chain reaction; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

(FIP) is caused by FCoV, which belongs to the family Coronaviridae of the order Nidovirales, the same order as SARS-CoV-2.[59] FIP is a common and often fatal systemic disease of cats that frequently presents with eye involvement. Fibrinous and pyogranulomatous inflammation in multiple organ systems is observed. Pyogranulomatous inflammation and phlebitis have also been found in the uvea, sclera, conjunctiva, retina, and optic nerve. Breakdown of the blood-ocular barrier during systemic viremia allows FCoV-bearing macrophages to access the eye, causing severe uveitis.[60] Bilateral panuveitis due to FCoV has been reported in lions and sphinx cats, and macrophages with FCoV were identified via immunohistochemistry.[4,5]

Murine hepatitis coronavirus (MHV) is also a betacoronavirus and has been found to be the etiology of eye disease in experimental mouse models. Following intraocular inoculation of the virus, early retinal vasculitis (1-7 days) can ensue and is later followed by retinal degeneration (10-14 days).[6,61] Demyelination and optic neuritis have also been observed following intracranial inoculation.[7,8] Interestingly, when mice with differing genetic backgrounds underwent viral inoculation, the retinal degenerative process was triggered only in genetically susceptible hosts.[9] Whether uveitis, retinal vasculitis, or retinal degeneration will be observed in COVID-19 patients during convalescence is unknown. However, animal model systems of RNA viruses in the emerging infectious disease category (ie, ebola, Marburg) have paralleled human disease findings.[63,64]

American Academy of Ophthalmology and American Society of Retina Specialists Guidance

In response to the multitude of implications of the COVID-19 pandemic, the AAO developed a website with guidance for ophthalmologists and the public related to ophthalmic manifestations of COVID-19, scientific evidence related to COVID-19 and the eye, and personal protective equipment (PPE) guidance for providers performing ophthalmic examinations.[65] Full PPE to protect the nose and mouth (eg, N95 mask), gown, gloves, and eyes, along with breath shields are advisable when assessing a patient under investigation or a known COVID-19 patient. Because of concerns about the potential high proportion of individuals with asymptomatic COVID-19, eye protection and masks are recommended for health care providers in the evaluation of asymptomatic patients, and universal masking is recommended for patients. Masking both the patient and provider is thought to decrease the potential for transmission of aerosolized virus. Further evidence is needed regarding whether virus remains sufficiently aerosolized to lead to viral transmission that would prompt the universal need for masks with greater filtration efficiency than surgical masks (eg, N95 or filtering facepiece masks). However, particularly in high-prevalence areas of COVID-19 with the risk of viral transmission through asymptomatic individuals, and during multiple interactions with patients in close proximity (eg, intravitreal injections for retinal vascular disease), N95 masks are a consideration. Institutional protocols, PPE availability, health care provider tolerability, and the provider's ability to perform procedures in different types of PPE also may play a role in PPE decision making in the context of AAO and public health guidance.

Following the Centers for Medicare & Medicaid Services, the US Surgeon General, American College of Surgeons, and AAO recommendations that all elective surgeries and nonessential medical and surgical services be delayed or postponed during the COVID-19 outbreak,[66] the ASRS offered additional guidance regarding emergent, urgent, and nonurgent, nonelective surgical indications.[67] Given the urgent and emergent nature of multiple surgical conditions, as well as the time-sensitive nature of other disease conditions (eg, wet macular degeneration requiring serial antivascular endothelial growth factor injections), ongoing care during the outbreak will be needed for many retinal conditions.

Although the interruption to nonemergent and nonurgent surgeries was needed given global concerns about PPE availability and the capacity of US health systems to handle a COVID-19 surge, we have now moved to the next phase of the pandemic, in which COVID-19 cases remain in the community, threats of second and third waves of infection remain, and vision health care delivery is necessary to avert permanent vision loss, particularly given sight-threatening conditions often treated by retina care providers. Retina specialists remain 1 type of the frontline ophthalmic care providers that will need to mitigate their personal and patient risks in the clinic and operating room.

Important considerations include the high rates of asymptomatic COVID-19 patients who may require surgery, the risk of aerosolized virus during endotracheal intubation, appropriate PPE for the treating ophthalmologist depending on the COVID-19 status of the patient (ie, unknown, COVID-19+ or COVID-19 convalescent), and personnel requirements to reduce overall risk to the operative team. For patients requiring anesthesia, general guidance includes the use of an airborne infection isolation room with a negative-pressure environment for the intubation of COVID-19 patients. Only health care personnel involved with the intubation should be in the room during this time.

Ophthalmologist PPE for patients with known or suspected COVID-19 infection should include an N95 mask, goggles or face shield, gown, and gloves with special care to the doffing portion of the procedure, because this is the most common time contamination may occur. Although COVID-19 testing is not universal at this time as a preoperative measure, universal testing for COVID-19 testing for asymptomatic, COVID-unknown status can help to stratify risk and adjust PPE requirements during the pandemic. Measures to expand preoperative COVID-19 testing have begun nationwide and as testing expands, we will likely see these practices implemented on a greater scale. Whether air-fluid exchange, electrocautery, or tear film aerosols may lead to significant concentrations of aerosolized virus is unknown but further evidence to ascertain risk to ophthalmologists and health care personnel is needed.

Conclusions

COVID-19: Implications for Retina Specialists

As patients will continue to require ophthalmic care during the COVID-19 outbreak, ophthalmologists must continue to use the best-available evidence to guide decision making related to risk-mitigation measures for patients and physicians while balancing the risk of vision loss from postponing medical or surgical care. Although conjunctivitis has been infrequently reported in association with COVID-19, prior coronavirus infections in animal systems have shown uveitis and retinal degeneration. One recent series has described cotton-wool spots and retinal hemorrhage that suggest microvascular disease in COVID-19. Retina specialists should be cognizant of these possibilities for patients with a history of COVID-19 for ongoing ophthalmic surveillance.

As the scientific community learns about the dynamics of potential viral transmission from the tear film and respiratory secretions, emerging data will guide our approaches to retinal surgery for patients (ie, active or convalescent COVID-19 patients; non–COVID-19 patients) who need emergent surgery to avoid vision loss. Preparedness measures will require continued investigation into disease phenotypes, the risk of viral transmission, and more broadly, approaches to retinal medical and surgical care during the COVID-19 and future infectious disease outbreaks.

The current SARS-CoV-2 pandemic has escalated globally, affecting health care providers including ophthalmologists. SARS-Cov2 RNA has been reported in tear film in the setting of conjunctivitis and, although infrequent, underscores its potential transmission risk for ophthalmologists. Uveitis has been reported in animal models of coronavirus infection, but retinal manifestations have rarely been reported, and ongoing surveillance is needed. We assess the current knowledge of ophthalmic manifestations of coronavirus infections, ocular manifestations in animal models, public health measures for patients and providers, and implications for the retina specialist.

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Ethical Approval

This manuscript represents a synthesis of the literature and assessment of published evidence and guidelines. No protected health information related to patients was accessed. Ethical and institutional review board approval was thus not required for this publication.

Statement of Informed Consent

No patient-related material was accessed in the preparation of this manuscript and informed consent was thus not required for this publication.

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