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COVID-19: Do's and Don'ts

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In December 2019, Wuhan, China, was faced with a new type of coronavirus, i.e. 2019 novel coronavirus (COVID-19).¹ Since then, the disease has affected most of the world by pushing healthcare systems to their breaking points, taking human lives, and causing financial losses. The aim of the present article is to provide an overview of the disease for eye health professionals and to provide strategies for protecting clinicians and patients.

Coronaviruses

Coronavirus (CoV) is a group of enveloped positive-strand RNA viruses for which there are four genera: a- and b-CoV, which typically cause infections in human and mammalian respiratory, gastrointestinal, and central nervous systems, and g- and d-CoV, which mainly infect birds.²⁻⁶

Previously, other types of coronavirus have affected the world, such as severe acute respiratory

syndrome (SARS) and Middle East respiratory syndrome (MERS) in 2003 and 2012, respectively.^{7,8}

Spread of the disease, diagnosis, and the clinical features of patients

Despite the fact that SARS and MERS have much higher mortality rates than COVID-19,⁹ the potential of spreading COVID-19 is much higher¹⁰ and it can have fatal consequences, especially for

at-risk patients, including the elderly and people with chronic diseases.⁹ At this point, the spread of the disease is not well understood, but it is believed that the virus is transmitted through direct contact, indirect contact, or by droplets.¹¹ Indirect contact includes contact with different kinds of surfaces in the surroundings. Coronavirus has been shown to live for days on surfaces.¹⁰



Table 1. Personal protective equipment

COVID-19 diagnosis is confirmed with a positive real-time reverse transcriptase-polymerase chain reaction analyses of a mucous sample.¹² The sensitivity and specificity of the test are not well established, however; there might be up to 15-30% false negative results, causing problems in hospitals, as the test is typically used to decide whether or not to isolate patients or health workers.¹³

Diagnosis is important for lowering the risk of COVID-19 spread. A person infected with COVID-19 is likely to transmit the disease to 2.2 people, including men at increased risk of contracting the disease.¹⁴ Ground-glass opacities are typical findings on chest X-rays and computed tomography (CT) scans, observed as a slight increase in lung density with sustained visibility of vascular structures and bronchial walls, and which is also observed in patients with lung cancer and diffuse pulmonary infiltrative disease.^{15,16} The laboratory findings include lymphopenia (23.8%) and increased C-reactive protein (22.2%), and approximately one in every five patients admitted to hospital will need admission to the intensive care unit.¹² Currently, ongoing clinical trials are investigating potential treatment options, including chloroquine and antiviral drugs such as remdesivir, lopinavir, and ritonavir. However, it is important to emphasize that there are

no evidence-based treatments at this time.^{9,17,18}

Containing the disease

To contain the disease and protect individuals, the World Health Organization has issued recommendations for healthcare professionals that include postponing all non-urgent visits to the hospital and the use of personal protective equipment, including protective glasses, face masks, and disposable gloves (Table 1).^{19,20} All patients presenting with COVID-19 symptoms (Table 2) are advised to stay home and self-isolate as long as symptoms have not progressed and put the patient at risk.¹⁰ Early in the pandemic, Dr. Li Wenliang, a Chinese whistleblower and ophthalmologist, lost his life after treating a patient with glaucoma who was infected with COVID-19 but who did not present any symptoms.¹¹ This case emphasizes the fact that ophthalmologists are in close contact with patients and mucous membranes, and therefore ophthalmologists are

prone to be infected by patients. More importantly, if doctors are infected, patients would be easily infected with COVID-19 as well.^{11,21} To prevent doctors from spreading the disease to patients, health workers in the Capital Region of Denmark are offered testing to determine if they have developed antibodies against COVID-19. The test

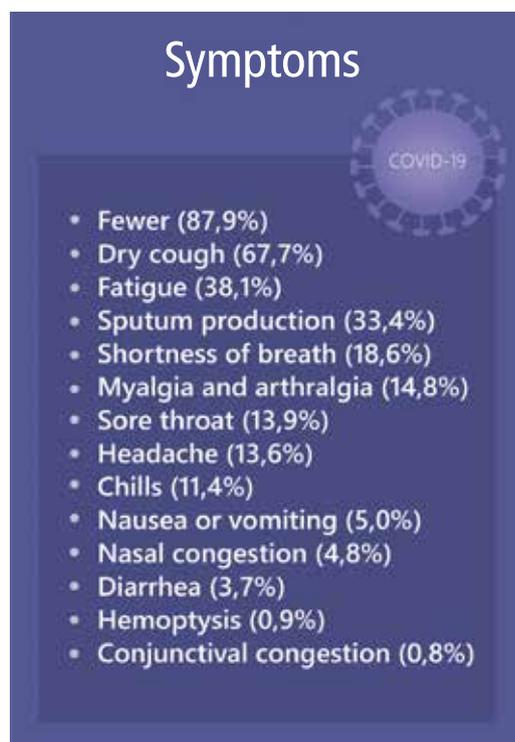


Table 2. Symptoms of COVID-19

Preclinical studies on previously identified coronaviruses

Animal species	Anatomical structure	Disease	Subgroup of coronavirus
Feline	Conjunctiva	Conjunctivitis	Feline infectious peritonitis virus
	Iris, ciliary body	Anterior uveitis	Feline infectious peritonitis virus
	Retina	Retinal vasculitis	Feline infectious peritonitis virus
	Retina	Choroiditis	Feline infectious peritonitis virus
Murine	Retina	Retinopathy	Mouse hepatitis virus – JHM virus
	Optic nerve	Optic neuritis	Mouse hepatitis virus – A59
Ferret	Multiple structures	Panophthalmitis	Ferret systemic coronavirus

Table 3. Animal studies on previous coronaviruses

includes both immunoglobulin M, typically produced over weeks, and immunoglobulin G, typically produced over months.²² However, the sensitivity and specificity of the test has not been evaluated.

In March 2020, a Hong Kong-based ophthalmologist published an article focusing on how to act responsibly during the crises. The article highlights that non-urgent visits must be postponed, which includes most cases in ophthalmology.¹¹ Previous experience from SARS and MERS further supports this statement, as the risk of contracting coronavirus is greatest during hospital visits.¹⁴ Furthermore, the fact that most patients with eye disease are elderly, and thus more vulnerable to COVID-19, emphasizes that consultations with ophthalmologists should be postponed until further notice.^{23,24} The main reason for avoiding the healthcare system is the risk of being infected by a COVID-19 carrier, who is possibly a doctor, a nurse, or other hospital staff, as healthcare workers maintain close human contact and pose a high risk of spreading the disease.

Eye disease induced by COVID-19 Preclinical studies

Animal studies have reported

vision-threatening eye disease after infection with coronavirus subgroups. In this context, studies on cats (i.e., feline studies) have reported that coronavirus causes several ocular

manifestations, including anterior uveitis, choroiditis, and retinal vasculitis, as part of the feline infectious peritonitis (FIP) complex, the term for coronavirus infection in cats.²⁵



Figure 1. Slit-lamp examination of patients during COVID-19

Severe eye complications due to coronavirus have also been found in mice. Retinopathy and optic neuritis have been shown in mice infected with two coronaviruses: coronavirus mouse hepatitis virus JHM and A59, respectively.^{26,27} Finally, a case report on a female ferret explained how a coronavirus infection, i.e., ferret systemic coronavirus, caused pyogranulomatous panophthalmitis in addition to other systemic manifestations.²⁸ Table 3 presents an overview of the existing animal studies.

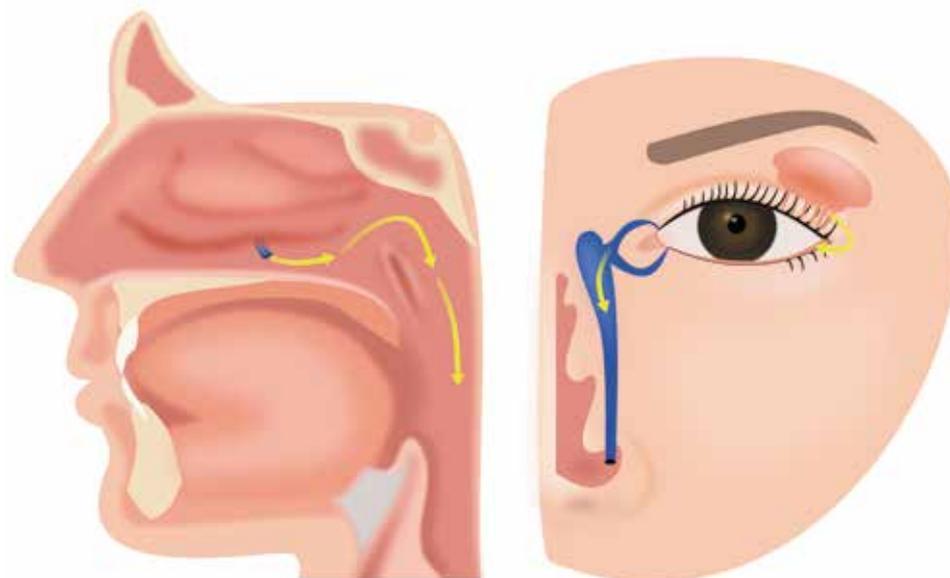


Figure 2. Spread of COVID-19 through the tear fluid drainage system

Clinical studies

Apart from conjunctivitis, there are, to our knowledge, no known COVID-19-induced eye diseases in humans. Among the less specific symptoms, eye pain has been reported. Currently, conjunctivitis caused by COVID-19 is a matter of dispute in the literature. However, this statement is supported by the American Academy of Ophthalmology and the European Society of Cataract & Refractive Surgeons.^{29,30} Additionally, clinical cases support the possibility of COVID-19-induced conjunctivitis, as a healthcare professional who wore a face mask but not goggles while treating a patient infected with COVID-19 contracted the disease and reported conjunctivitis as the primary symptom.³¹ In another study, the tear fluid of 30 patients with COVID-19 was analyzed. Among the 30 patients, only one patient complained of eye irritation. The tear fluid sample from this patient tested positive for COVID-19 bilaterally.

Apparently, COVID-19 enters the cell by interacting with the ACE2 (angiotensin I converting enzyme 2) receptor.^{10,14,19} Compared to SARS and MERS, COVID-19 has a higher affinity for the receptor, which explains the aggressive behavior in the spread of the disease.³² The ACE2 receptor has been found in the lower respiratory system but has not been identified in the oral or nasal cavity, which may be why

patients rarely show upper respiratory system symptoms when infected with COVID-19 only.³³⁻³⁵ Whether ACE2 receptors are found in the conjunctiva or cornea warrants further research.³⁶

At present, we do not know whether COVID-19 can replicate in the conjunctival cells, and theoretically, COVID-19 can also spread to the upper and lower respiratory system through drainage of tear fluid (Figure 2).¹⁹ Since conjunctivitis may be the first symptoms of COVID-19 and given the present knowledge gap, it is essential to wear personal protective equipment, including protective glasses. The American Academy of Ophthalmology has issued recommendations that are divided into “standard” and “transmission-based” precautions. Standard precautions include the use of face masks, disposable gloves, and protective glasses when examining a patient without COVID-19 symptoms in addition to cleaning and disinfecting environmental surfaces. When examining patients with symptoms of COVID-19 transmission-based precautions are recommended. In addition to standard precautions, these include equipping the patient with a surgical mask, appropriately positioning the patient unrelated to other people

who are not properly equipped, limiting patient transport, and using of disposable or dedicated patient care equipment.³⁷ If aerosol producing procedures are performed, staff are advised to use special masks (N95 or better) instead of standard surgical masks, and pre-operative testing of asymptomatic patients are advised. Ophthalmologists should equip slit lamps with breath shields to prohibit speech during slit lamp examination and other close contact procedures.³⁸ In addition, the American Academy of Ophthalmology supports only urgent and emergent eye care during the crisis, which includes suspected or confirmed malignancy and sight- or life-threatening infections.³⁰

In conclusion, COVID-19 has proven to be highly contagious and could have fatal consequences, especially for at-risk patients. The sensitivity and specificity of available testing methods have not been evaluated, and there may be up to 30% false negative results, leading to a false sense of security. To protect both clinicians and patients, the use of recommended protective personal equipment is advised, especially because we, as eye care professionals, are in close contact with patients who are typically elderly.

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