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OCULAR IMMUNOLOGY AND INFLAMMATION
2020, VOL. 28, NO. 5, 714–720
https://doi.org/10.1080/09273948.2020.1755442

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ORIGINAL ARTICLE

COVID-19: Limiting the Risks for Eye Care Professionals

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ABSTRACT

After the outbreak of the disease COVID-19, it has reached pandemic proportions within a very short time. It is mainly transmitted human-to-human through direct contact with secretions from an infected person or through inhalation of droplets containing SARS-CoV-2. It is controversial whether the virus may be transmitted via tears. Exposed ocular surface can serve as a gateway in transmission and acquiring respiratory diseases. Considering the reported cases on healthcare workers indicating nosocomial transmission and the anatomical and physiological aspects it is perceived that ophthalmic healthcare professionals are at higher risk of contracting the virus by virtue of their job. In this narrative review we discuss current evidence around detection of SARS-CoV-2 in human tears and forms of transmissions reported to date. We also provide a comprehensive approach that may be implemented in an ophthalmic care facility to protect healthcare personnel, as well as patients, from contracting the virus.

ARTICLE HISTORY
Received 30 March 2020
Revised 9 April 2020
Accepted 9 April 2020

KEYWORDS
Coronavirus disease 2019; COVID-19; severe acute respiratory syndrome coronavirus 2; SARS-CoV-2; infection control

Coronaviruses (CoV) are a family of enveloped positive-sense single-stranded RNA viruses that are known to cause the common cold, influenza, and acute severe respiratory illness.[1,2] A new strain of the coronavirus family was identified in December 2019, causing severe pneumonia. World Health Organization (WHO) named the disease, coronavirus disease 2019 (COVID-19), and the coronavirus, Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2).[1,2] In the 3 months following its identification, COVID-19 has spread across the globe reaching pandemic proportions. On March 14, the Director-General of WHO announced that Europe was the epicenter of the pandemic. By April 7, 2020, there were nearly 30,000 deaths in Europe caused by COVID-19. Most deaths occurred in Italy, with Spain a close second. On April 7, the number of cases in the United States has surpassed the reported numbers in China, despite limited testing.[3] Most developing countries were still anticipating the spread of the virus to their nations at this time. From the ocular perspective, there have been reports suggesting implications of SARS-CoV-2 and its ocular involvement.[4]

A study published in January 2020 indicated that the number of infections in health-care professionals has been increasing since the outbreak of COVID-19.[1] In one recent retrospective, single-center case series of 138 consecutive hospitalized patients in China with confirmed COVID-19, 57 (41.3%) of infections were judged to be hospital-acquired, and 40 of 57 were in health-care professionals working in close proximity with patients who had attended the hospital.[2] This raises significant concern not only among ophthalmologists but among all the health-care professionals, and hence the use of appropriate personal protective equipment (PPE) in health-care facilities was strongly warranted.

The outbreak was first reported on December 30, 2019, by Dr. Li Wenliang, an ophthalmologist, who critically determined the significance of seven patients quarantined at his hospital. Unfortunately, Dr. Li himself contracted the virus, most likely from one of his patients, and possibly from one who was asymptomatic at the time and presenting for care of an unrelated eye problem. In early February Dr. Li passed away, and the ophthalmic community has paid tribute in many obituaries.[5] In a report by the World Health Organization (WHO) in early February 2020, the Director-General said that 1716 health-care workers had been infected with the SARS-CoV-2 virus and 6 had died.[6] In a previous observational study published in 2004, aimed at detecting coronavirus in the tears by PCR, the investigators emphasized that the virus could be transmitted in tears – putting the ophthalmologist at risk of acquiring the infection.[7]In this

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context, we have reviewed the current literature and understanding of ocular implications and transmission of coronaviruses based on the limited and rapidly expanding knowledge regarding the recent pandemic COVID-19. We have provided a comprehensive approach that can be implemented in an ophthalmic facility.

Transmission of SARS-CoV-2

SARS-CoV-2 is believed to be zoonotically transmitted,[8] as are other coronaviruses, including those responsible for SARS and MERS (Middle Eastern Respiratory Syndrome). There is a strong sequence homology between SARS-CoV, which causes SARS, and COVID-19 (almost 80%), and hence the SARS pandemic is often used to model the course of COVID-19.[9] SARS-CoV-2 is a crown-shaped virus with a diameter between 60 and 140 nm, capped by quite distinctive spikes, about 9 to 12 nm in length.[1] As applies to other airborne viruses, it can be transmitted from an infected person via aerosolized droplets when talking, sneezing, or coughing or via contaminated surfaces by body fluids (like door handles).[9] The ability of the virus to survive in the environment is dependent on temperature, relative humidity, and the nature of the surfaces on which fomites land. On some inanimate surfaces, such as plastic, it can survive for multiple days, on cardboard for 24 hours, and as aerosol particles for several hours.[10,11]

SARS-CoV-2 enters a cell following binding with the human angiotensin-converting enzyme (ACE) 2 protein, which is expressed in the epithelial cells in lungs and other tissues such as intestines and kidney. Increased expression of ACE-2 has been found in patients with hypertension and/or diabetes mellitus, who are treated with ACE inhibitors and angiotensin II type-I receptor blockers (ARBs).[12] By now, an increased perceptibility has not been demonstrated. The human eye has its own intraocular renin-angiotensin system (RAS), a system that has been of interest for developing antiglaucomatous drugs.[13] The expression of ACE2 in more anterior tissues, such as the conjunctiva or cornea, has yet to be established, though it has been reported in aqueous and vitreous humor. At this time, there is no information on SARS-CoV-2 infection of ocular tissues through ACE2.[4] However, the receptors of some species of adenovirus and avian influenza (α-2-3-linked sialic acid, CD46, desmoglein-2) and the human influenza virus (α-2-6-linked sialic acid) are abundantly present in corneal, conjunctival epithelium as well as nasal and tracheal mucosal lining.[14,15]

The transfer of microorganisms along with the tears from the ocular surface into the nasal cavity and the upper part of respiratory tissues is because of the continuation of the mucous membrane via the puncta into the nasolacrimal duct and into the nasopharyngeal space can eventually deliver the virus into the lungs and the gastrointestinal tract, when swallowed, where it can bind to the ACE2 receptors.

Clinical Signs and Symptoms

Many individuals infected with SARS-CoV-2 may remain asymptomatic or have very mild symptoms, while remaining highly contagious. The incubation period varies between 2 and 24 days. The basic reproduction number or R0 (i.e., average number of secondary infections per case) is reported to be between 1.4 and 2.5 according to the WHO on January 23, 2020, but this number may vary based on season and geographic location.[16] Almost 85% of patients will have mild-to-moderate illness and symptoms and will recover from the disease. Fever is the most common symptom; 97% of patients with clinical disease will have fever[1,2] and show symptoms within approximately 2 weeks. Apart from fever, some of the clinical features include dry cough, sputum production, fatigue, arthralgia, diarrhea, shortness of breath along with chest radiographic abnormalities.[1,2]

Ocular Manifestations of SARS-CoV-2

Mucous membranes of the mouth, eyes, and tears are potential sources of microbial transmission and detection.[7,17] In a recent prospective interventional case series study of 30 confirmed cases of novel coronavirus pneumonia (NCP), tear samples collected for RT-PCR assay tested positive for SARS-CoV-2 in only one patient with conjunctivitis.[18] In a large study of 1099 confirmed NCP patients, conjunctival congestion was observed in 9 (0.8%) patients.[2] In a retrospective study of 63 NCP patients, conjunctival swabs were positive for 3 patients and negative for 1 patient with conjunctivitis.[19] In an observational study, 17% of pediatric patients infected with similar coronavirus named NL63 had conjunctivitis,[20] whereas, in 2004, 3 of 36 patients with confirmed SARS yielded positive conjunctival swabs for coronavirus RNA.[7] All these results suggest that the presence of the virus on the ocular mucosa in minimally 25% of eyes with COVID-19 associated conjunctivitis which is expected in approximately 10% of all COVID-19 cases. Contact with tears may thus can principally lead to transmission of the virus.,[4,5,9,21] In line, in a new study, performed in Singapore, Seah et al. could not find any conclusive evidence of virus shedding in the tears on RT-PCR or culture at different time points following SARS-CoV-2 infection (in press, Ophthalmology journal). In this study, the authors recruited a total of 17 SARS-CoV-2 patients and took tear samples. SARS-CoV-2 is known to have a disease course of approximately 2 weeks. The sampling done eventually provided the authors a good coverage of patients at different phases of the infection (Day 3–Day 20). The authors then tried to culture and run RT-PCR on these samples for SARS-CoV-2 and samples also were studied for cytopathic effect (CPE), in addition to RT-PCR and viral culture. None of the patients had any evidence of viral particles in the tears, and the authors concluded that there was a low risk of transmission of SARS-CoV-2 from the tears. The results from this study suggest that the risk of transmission through ocular fluids is low. In the ophthalmology practice, we come into close contact with the patient. This study suggests that transmission through droplets from the respiratory tract was a more likely mechanism to explain the currently circulating reports.

Limiting Transmission During Eye Care Practice

Eye care professionals are in close proximity to patients during various ophthalmic procedures, including the basic ophthalmic examination, and therefore may face a relatively

increased risk of contracting SARS-CoV-2. The WHO, Centers for Disease Control and Prevention (CDC), and Occupational Safety and Health Administration (OSHA) have given interim recommendations on standards and PPE to prevent infection among health-care providers and patients.[22–26] Strategies and recommendations for ophthalmologists to reduce transmission are described below.[22–26]

Minimizing Exposures

Opportunities for exposure to SARS-CoV-2 can be reduced by postponing all the elective appointments and routine ophthalmic surgery. The attendants to strictly observe social distancing and particularly for emergency eye patients where the family members can wait in the waiting area. If the patient must be seen, it is appropriate to take an initial history of fever and respiratory symptoms prior to the patient's arrival in the waiting area. This may be done by telephone prior to the patient's arrival or by making use of triage personnel on arrival. Administration of screening questionnaires like TOCC (**T**ravel to affected areas during the incubation period, **O**ccupation, **C**ontact of a suspected or confirmed case, **C**luster of cases) (Figure 1) may be helpful.[5] Patients and accompanying persons should be questioned for any recent personal or family travel history, as well as for symptoms of COVID-19. Travel history is less important in countries where the pandemic has become mostly by local transmission.

Individuals with symptoms suspicious for COVID-19 must be evaluated in an isolated area and send for further investigations to rule out infection. If patients have an eye emergency, then the ophthalmologist should see them in an isolation room with appropriate PPE. If they do not have an eye emergency, then they should not be seen by the ophthalmologist, but rather referred for medical workup. The health-care facility should supply surgical masks, instructions on cough etiquette and physical distancing, alcohol-based hand rub at entrances and patient check-in areas, and in waiting rooms.[22–26]

Standard and Transmission-Directed Precautions

Health-care professionals examining patients with suspected COVID-19 should follow strict precautions, including for a suspected COVID case.

"Social distancing" practice in ophthalmology can include reducing patient number and turnover time. Patients arriving from the so-called hot spots can be identified at the time of registry itself and they can be kept in different zones. Such patients may also travel in groups – especially in developing countries. Eye centers in such instances also have an important role to identify these patients for contact tracing and certain scenarios in notifying concerned authorities.

Contact time with the patients should also be kept minimal. If longer durations or investigations mandating longer time required, the urgency of the indication must be kept in mind and be done as a part of strict medical need. The same holds true for many procedures which would require contact with the ocular surface and the skin – e.g. Applanation tonometry, Visual evoked potentials, and Electroretinograms. These should be kept in minimum and done only if medically justified. There is no solid data available till date to suggest the spread via sweat or skin, but until proven, every bodily secretion must be dealt with precaution.

Standard hand hygiene practice during the pandemic includes hand-rub containing 70–90% ethanol or 0.1% sodium hypochlorite, which effectively inactivates coronaviruses,[22–25] or washing hands with soap and warm water for at least 20 seconds before and after examining patients. Disposable hand gloves should be immediately discarded into the trash. A face mask should be donned. The US Food and Drug Administration reviews and approves face masks under 21 CFR 878.4040 as Class II medical devices, which may be designated as surgical mask, surgical mask with an antimicrobial/antiviral agent, or pediatric/child face mask.

Many centers are not able to comply with the guidelines due to the shortages, particularly of face masks. Hence, CDC has provided additional guidance according to the capacity of a facility to accommodate demand.[27,28] For conventional capacity, patient care continues without any change in contemporary practice. These centers are often well stocked and/or supplied. They are advised to continue with surgical face masks or use masks such as N95, which filters 95% of the particles with dimensions up to 0.3 microns (Figure 2). For contingency capacity, some changes are made to standard practice, which may not have any significant impact on the care. Examples include extended use of the masks and changing them only in case of soiling or other damage. For crisis capacity, with severe shortages or unavailability, the masks may be continued beyond the manufacturer-designated shelf life, but with limited use. Limited re-use of facemasks is the practice of using the same facemask by one health-care provider for multiple encounters with different patients, removing it after each encounter. Since the potential for contact transmission of SARS-CoV-2 is still unclear, it is important not to touch the outer surface of the mask during care, and mask removal and replacement must be performed carefully and deliberately. It must be noted that not all facemasks can be re-used. Facemasks that fasten to the provider via ties may tear when undone and should be considered only for extended use, rather than re-use. Facemasks with elastic ear hooks may be more suitable for re-use.

Aerosol-Generating and Contact or Invasive Diagnostic Procedures

Ophthalmologists are placed at risk of contracting SARS-CoV-2 when positioned ata short distance from the patient at a slit-lamp bio-microscope and during direct ophthalmoscopy. The need to touch the eyelids also favors transmission of the virus though the risk seems relatively low according to the above-mentioned data so that standard skin and surface disinfection measure will be sufficient to protect patient and care provider. Instruments that use high-speed air, such as the air-puff tonometer can theoretically cause aerosolization and can pose risk to health-care professionals and the next patient due to generation of aerosol from the ocular surface.[29] A slit-lamp barrier-breath shield should be installed. A simple slit-lamp barrier can be easily made by using a clean discarded X-ray, CT, or MRI

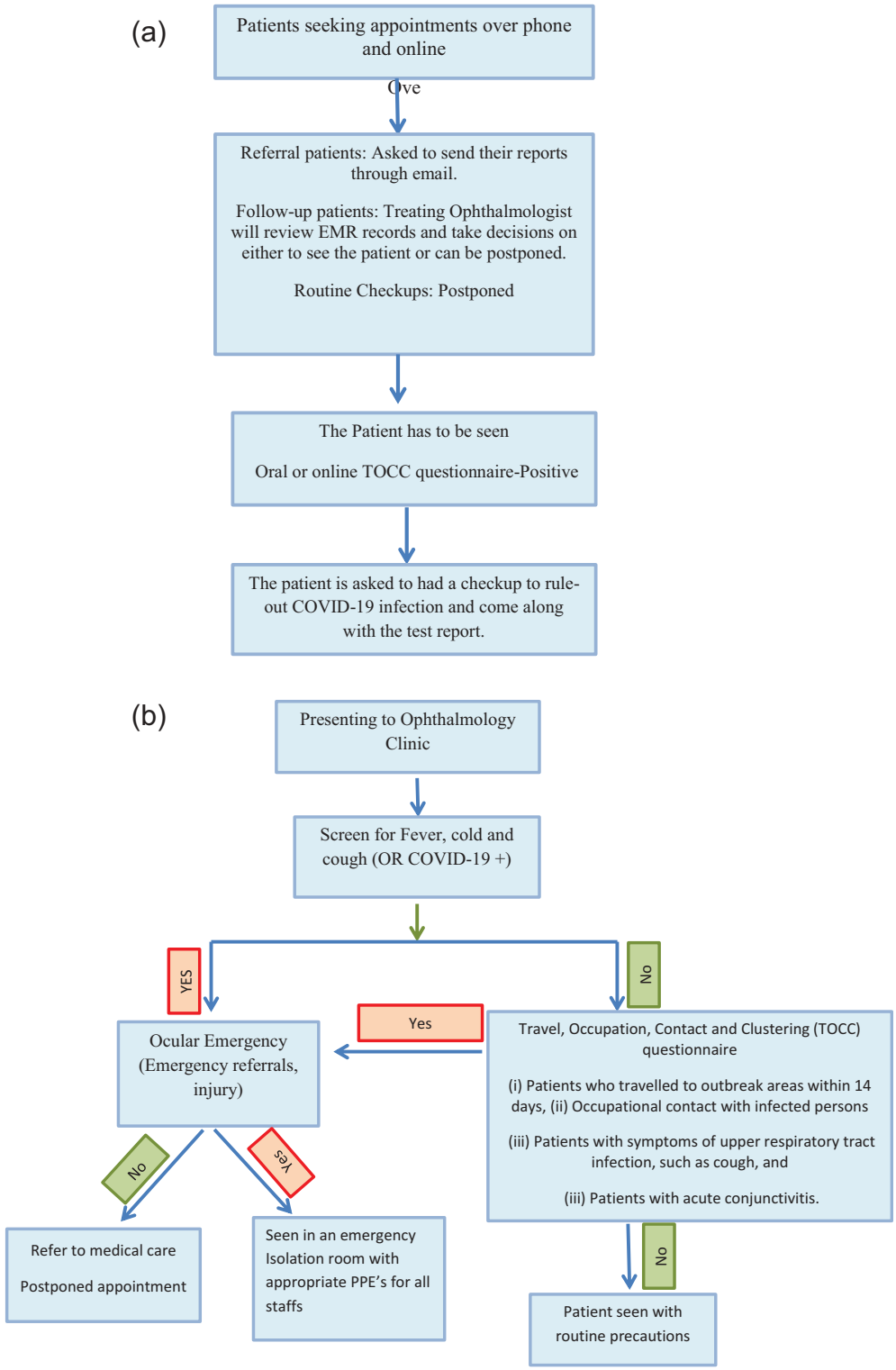

Figure 1.: A and B: Flowchart of the patient triage protocol. Adapted from: Lai THT.[4]

film that can be placed on every slit-lamp biomicroscope, a step by step guide has been provided (Figure 3). Diagnostic machines may be fomites for SARS-CoV-2. Non-disposable contact equipment, as is used in applanation tonometry, gonioscopy, pachymetry, ultrasound biomicroscopy, and electrophysiology, should be disinfected with ethanol-based solutions, and use of disposable attachments, such as tonometry probes, is recommended. Collection of ocular samples, such as conjunctival swabs and biopsies, and aqueous or vitreous aspirates, and other minor procedures, such as tear tests, lacrimal

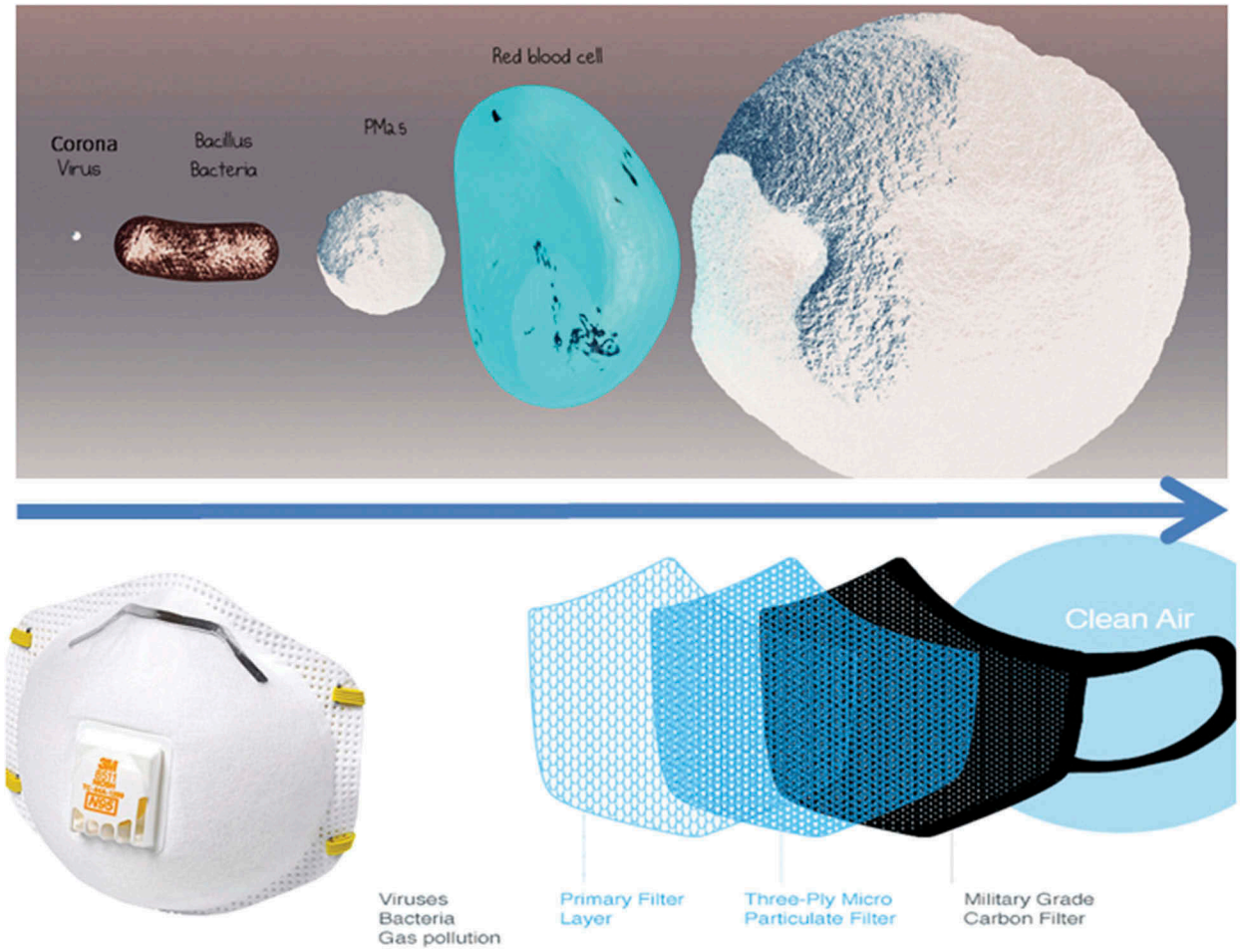

Figure 2. The minimum average range of sneezed droplets containing microorganisms is 1 to 100 microns. A 3-layered mask or a respirator filter particles as small as 0.3 microns.

syringing, and subconjunctival injection should be carried in PPE according to local PPE guidelines.[5,22-26]

Non-Emergency Surgery

Reduction in the number of surgical procedures reduces the risk of exposure to SARS-CoV-2. If surgery must be done, appropriate PPE and disinfection and sterilization procedures are required.[22–26] Vacating operating rooms equipped for general anesthesia also increases the number of respirators that are available for management of persons with acute respiratory distress syndrome. Sight-threatening conditions that are urgent and emergency surgical procedures should be carried out. Some of the recommendations given by the American Academy of Ophthalmology (AAO) for non-emergency surgery and outpatient clinics are listed in https://www.aao.org/headline/alert-important-coronavirus-context.

Infection Control at the Hospital

The CDC recommends that areas which may harbor SARS-CoV-2, such as doorknobs and handles, equipment such as trial frames and slit-lamp bio-microscopes, and all surroundings, should be disinfected. Environmental protection agency (EPA)-registered hospital-based disinfectant cleaning solution for SARS-CoV-2 should be used, following the manufacturer's recommendations.[8,22-25] Frequent cleaning of hospital premises area with these solutions can reduce transmission. High-efficiency particulate air filter (HEPA) units are useful to reduce levels of SARS-CoV-2 in the air. A missed infected patient entering an operating theater poses an infection risk for all members of the medical team. Although the risk of spread of infection is always present, we hypothesize that eye drapes have the highest risk for contamination, given the proximity to the mouth and the nose, and the fact that these cover the whole face during the surgical procedure. These drapes need to be handled carefully and appropriately discarded at the end of the procedure. Beyond these steps, other recommendations include keeping the hospital's inventory current, periodic training of health-care professionals, requiring employees who are unwell to not attend work, and staying up-to-date on the latest information on epidemiology and management of COVID-19.

Conclusion

Current knowledge around COVID-19 is rapidly increasing. Preliminary evidence suggests that SARS-CoV-2 may be transmitted by tears, although the risk may be low. Negative PCR report in ocular samples does not fully exclude the risk of transmission of the virus. Conjunctivitis is the only

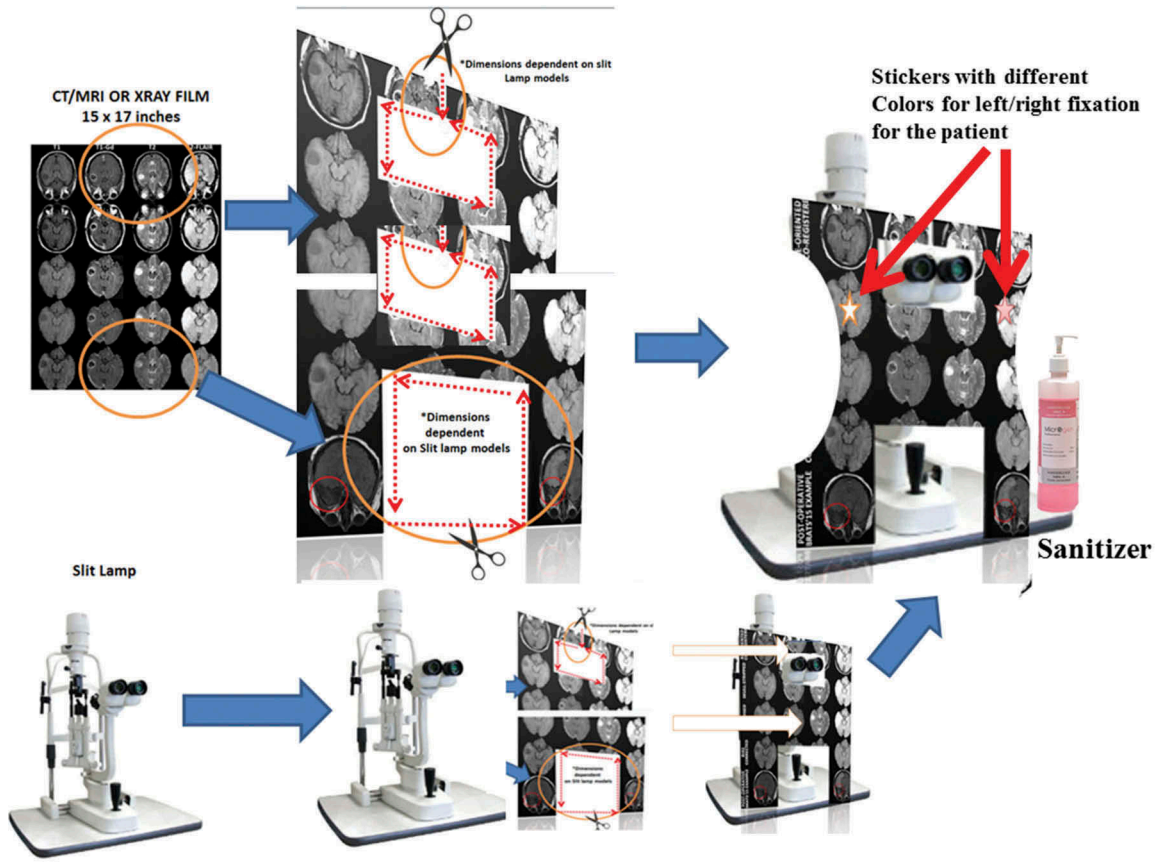

Figure 3. A Do-It-Yourself (DIY) diaphragm can be easily made using a clean discarded X-ray, CT, or MRI film. A vertical slit of approximately 3 cm is made at the top center, and a rectangular opening is created with size dependant on the model of the slit-lamp biomicroscope. A similar opening is made in the bottom to allow comfortable toggling of the joystick. The film can be easily attached using a small piece of double-sided adhesive tape.

reported ocular complication of COVID-19 to date, and an association between conjunctivitis and SARS-CoV-2 is still unclear. Recommendations of WHO and CDC are important to ensuring protection of ophthalmic personnel and their patients. Ophthalmologists should pool resources and work collaboratively in a focused and scientific manner to address the current COVID-19 pandemic.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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