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Management of Neovascular Age-Related Macular Degeneration during the COVID-19 Pandemic

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The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified first in Wuhan, China, by Dr. Wenliang Li, a fellow ophthalmologist. Dr. Li warned his medical school alumni of a possible “SARS-like” epidemic disease at the end of 2019, after seeing patients with a severe atypical respiratory illness, anticipating the global health crisis by more than 3 weeks.¹ The disease rapidly spread worldwide to more than 190 countries with, 7 273 958 infected and more than 413 372 deaths to date.² The World Health Organization initially declared a Public Health Emergency of International Concern and officially confirmed COVID-19 as a pandemic outbreak on March 11, 2020.³ As of today, June 11, 2020, the United States counts 1 968 331 cases of COVID-19 and 111 978 deaths, and thus represents the country most severely hit by the pandemic.²

The government of the United States responded to this deadly crisis by releasing trillions of dollars to fight the virus, funding research for a vaccine and new therapeutics, attempting to provide first-line healthcare workers with necessary personal protective equipment, producing critical care medical equipment, providing unemployment payment checks, forgiving loans for businesses, and providing social security tax relief. Given the uncontrolled spread of the virus, state and federal authorities responded by locking down cities and states, declaring safer-at-home orders and limiting nonessential businesses, including nonelective procedures. Schools and universities transferred their academic activities online, and research centers started working remotely. Scientific meetings were cancelled and their contents transferred online through webinars. All specialties of medicine have been affected. Physician practitioners were advised to use telemedicine tools to screen and evaluate patients when possible.

Currently, with the exception of remdesivir, which shows modest benefits,⁴ no proven therapies to treat or prevent the COVID-19 disease have been found, nor has a vaccine been developed to achieve herd immunity.⁵ If the virus is contracted, patients can experience severe respiratory insufficiency associated with multiorgan failure, which can

result in death. Severe outcomes occur more frequently in elderly, immunocompromised individuals, and those with comorbid health conditions, but even younger, healthy patients can succumb to the disease.^{6,7} The American Academy of Ophthalmology and the American College of Surgeons, as early as March 13, 2020, warned hospitals, health systems, and surgeons to prepare to manage only elective and urgent surgeries and visits during the COVID-19 outbreak to minimize the risk of infections for patients and physicians. On April 17, 2020, the American Academy of Ophthalmology made national recommendations to guide ophthalmologists and their staff on the process of reopening to a more normal practice situation, based on local and regional conditions and rules, public health authority communications, and institutional policies, given the large variations in prevalence of COVID-19 across the United States.

The requirement for ophthalmologists to be in close physical proximity to a patient’s eyes during an ophthalmologic evaluation has led to a perception that there may be a higher risk of infection, a problem exacerbated by a shortage of personal protective equipment and high patient volumes in the

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clinic. However, retina specialists are a particular group of practitioners in ophthalmology who are called to manage a significant number of conditions, such as proliferative diabetic retinopathy, diabetic macular edema, and neovascular macular degeneration, that can lead to permanent vision loss if not treated in a timely manner. Thus, these patients generally cannot have their visits postponed for an extended period. The American Society of Retina Specialists, according to the guidelines of the American Academy of Ophthalmology related to COVID-19, provided guidelines supporting retina specialists to continue to perform intravitreal injections to avoid vision loss in these patients, particularly those with macular neovascularization manifesting signs of activity and exudation. This creates a significant challenge during the COVID-19 health crisis in which ophthalmologists need to balance the benefits of providing sight-saving therapies against the risks to staff, physicians, and patients (and, in particular, high-risk elderly patients in the case of age-related macular degeneration

[AMD]) of contracting the potentially fatal COVID-19 during the in-person interactions required to deliver therapy. Consequently, creating a safe environment for patients and providers to deliver this vital care to patients is of paramount importance.

We report our recent experience at the Doheny-University of California, Los Angeles eye centers (in Los Angeles and Orange County, California) in the management of patients affected by neovascular AMD during the COVID-19 pandemic. We focus specifically on considerations relevant to a retina or ophthalmic practice, and not the broader public health implications or concerns of having individuals leave their homes to come to a medical facility.

Retinal imaging, especially OCT, has become a critical diagnostic technology in the clinical management of AMD. For patients with neovascular AMD, OCT is used to assess the activity of the neovascular lesion, based on the presence of intraretinal or subretinal fluid, and to evaluate the progression of the disease.⁸ In addition, the final therapeutic decision often is based on a detailed examination of the retina and the anterior segment (e.g., to exclude inflammation before treatment). Although telemedicine has been an option in some subspecialty areas, retina specialists generally have not been able to take advantage of the innovative telemedicine approaches. Although home-based OCT diagnostics are under evaluation, they are not yet available. The current anti-vascular endothelial growth factor therapeutics are highly effective for preventing disease progression and improving vision in patients with neovascular AMD, but they must be given at appropriate intervals to control disease activity.^{9–11} This requires careful monitoring with imaging and examination. Unfortunately, because patients affected by AMD are by definition older than 50 years of age, they are at a higher risk of morbidity and mortality as a result of COVID-19.⁶ Given that the risk of permanent vision loss is very high in untreated eyes with active neovascular AMD, patients at the Doheny-University of California, Los Angeles eye centers are prescreened via telephone to assess the risk of COVID-19 based on presence of upper respiratory symptoms or fever or exposure to other persons affected by COVID-19. The risk of a patient of being infected by COVID-19 or being an asymptomatic carrier is stratified as low, moderate, or high based on the exposure to those infected by COVID-19, in accordance with Centers for Disease Control and Prevention guidelines.¹²

In case of low or moderate COVID-19 risk, patients in need of a retina evaluation can be admitted to the clinic. At the entrance to the clinic, patients are requested to wear a mask (surgical or cloth facial covering), which they keep in place throughout their time in the clinic. The clinic will provide a mask to the patient in case he or she is not equipped with one at the entrance. Temperature measurement from all individuals accessing the clinic is carried out to identify and exclude febrile patients. Accompanying visitors are encouraged to wait outside unless their presence is strictly necessary. Waiting times are minimized, and each patient is moved to an examination room as quickly as possible to avoid sharing common spaces with other patients. A longer interval between appointment slots also

has been instituted. Social distancing is maintained between patients in the waiting room, providing a minimum space of 6 feet between each patient. Examination rooms, chairs, and all instruments, shields, and lenses are sanitized and disinfected with alcohol wipes after each patient encounter. All ophthalmologists and eye care technicians wear surgical masks (but not N95 masks), wash their hands before and after each examination, limit conversation with the patient to essential items, and maintain a secure distance of 6 feet when the proximity to the patient is not required by the examination or procedure. Examination times are minimized to perform only those essential components of the examination (including dilation and extended ophthalmoscopy) as determined by the physician. Procedures also have been implemented to manage potential shortages in personal protective equipment. At least 1 new surgical mask is made available to each staff member and physician every day. Ultraviolet sterilization devices also have been procured and used to sterilize surgical masks as needed.¹³ Gloves also are used when contact with the patient or the patient's eyes are required, because tears are known to harbor the virus. Because SARS-CoV-2 is a respiratory coronavirus, transmission is believed to occur primarily through respiratory droplets from either symptomatic or asymptomatic patients, and given the proximity to patients' faces during a retina examination, larger slit-lamp shields have been applied to all devices in the clinic. The patient leaves the room only briefly for OCT imaging and returns to the same room for further care, including intravitreal injection. This minimizes the patient's movement through the clinic. Patients in need of injection are treated on the same day as the examination to minimize travel and reduce patient exposure. Safe injection practices are followed according to the Centers for Disease Control and Prevention and the World Health Organization guidelines minimizing exposure to the physician and the patient. Conversations are limited, masks and glasses are in place at all times, and the time spent in close proximity (less than the social distancing guideline of 6 feet) is minimized during the injection procedure. Gloves must be worn for injections and all procedures involving any direct physical contact with the patient.

Patients who are known to be positive for SARS-CoV-2, who are symptomatic, or who have a high COVID-19 risk based on exposure may be evaluated if the physician deems this to be urgent. Examples may be a patient with suspected retinal detachment or with significant vision loss. Such patients are seen in a physically separate clinic space. The number of staff interacting with such patients is minimized to the maximum extent possible, and all interacting staff wear gowns, N95 respirator masks, gloves, and face shields (or safety goggles) during these encounters.

Adherence to these rules and principles is essential to create a safe environment for patients, staff, and physicians. Although we consider every individual to be potentially infected, the strategy that we use also includes a risk stratification process to ensure that we provide as safe an environment as possible while balancing resources such as personal protective equipment. It is important to recognize that the current procedures represent a point in time base on current knowledge of SARS-CoV-2 and current available

resources. In addition, because the goal is to optimize the risks and benefits for the patient, individual patient factors may need to be considered when deciding to bring a patient in or when determining the interval between visits. Patients who are very old or with numerous comorbid conditions may need to be seen less frequently at the expense of potential risk of vision loss. These are difficult decisions we will need to make as physicians. Also, the considerations for retinal practice detailed in this letter are by no means exhaustive. For example, one might consider further mitigation of the exposure of staff and physicians who are elderly or have other comorbidities, possibly by having them avoid seeing patients at high risk for COVID-19 or by implementing more stringent protective gear (e.g., N95 respirators), even while seeing patients at low risk for COVID-19. As the pandemic crisis continues to evolve, we expect that procedures and protocols also will evolve in parallel. We also recognize that although these protocols work in our practice environment, they may need to be refined or modified based on the specific characteristics of a particular practice. In addition, we may need to modify our practice approaches based on broader public health considerations. For example, having patients leave their home to come for frequent medical appointments may increase the spread of infection in the community. These are important issues that may extend beyond our expertise as retinal specialists, but may need to be considered as more data become available.

The COVID-19 pandemic has impacted the practice of medicine dramatically in all specialties and has impacted public health profoundly. As retina specialists, we continue to strive to provide the best standard of care to patients affected by neovascular AMD and other retinal diseases, while maintaining a safe environment for all.

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Footnotes and Financial Disclosures

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