

All eyes on Coronavirus—What do we need to know as ophthalmologists

“Of course it is (a pandemic). We’re there. It doesn’t matter what kind of terminology you use. To me, the pandemic is a mindset. We can either use pandemic as a word that makes us all quake with fear or we can use it as a rallying cry to say—This is what we’re going to do to fight it.”—Dr. Michael Osterholm, Director, Center for Infectious Disease Research and Policy, University of Minnesota, MN, USA.

Li Wenliang, a young Chinese ophthalmologist working at the Wuhan Central Hospital in Wuhan, Hubei province, China, tried to alert his colleagues on the social media WeChat on December 30, 2019, about the outbreak of an illness that resembled severe acute respiratory syndrome (SARS).^[1] Wuhan local authorities, however, admonished him for making false comments that would severely disturb the social order—“We solemnly warn you: If you keep being stubborn, with such impertinence, and continue this illegal activity, you will be brought to justice—is that understood?”, the letter from the Wuhan police stated. Underneath Dr. Li meekly wrote: “Yes, I do”. Li returned to work, later contracted the virus from an asymptomatic, infected patient with acute angle-closure glaucoma, manifested disease symptoms on January 10, 2020, and succumbed to the disease on February 7.^[1] Li is considered one of the prime whistleblowers of what is now identified as highly infectious disease COVID-19, caused by a new variant of coronavirus 2019-nCoV. He is also the unfortunate first known case of a patient-to-ophthalmologist transmission of the new strain of coronavirus.

On December 31, 2019, hospitals in Wuhan, a large city with a population of about 11-million, reported a cluster of

cases of pneumonia of unknown cause and the World Health Organization (WHO) was alerted.^[2] On January 1, 2020, Wuhan public health authorities shut down the Huanan Seafood Market, suspecting a link with the outbreak. Two weeks later, a new coronavirus, identified through genomic sequencing, was declared to be the culprit.^[3] But by then, the horse had already bolted from the stable—before the affected cities were locked down, some of the asymptomatic, infected patients from Wuhan had already begun their travel ahead of the Chinese Lunar New Year, (which is said to be the largest human migration in the world with 3 billion passenger-journeys), thus, spreading the virus far and wide. On January 30, 2020, the WHO declared COVID-19 to be a Public Health Emergency of International Concern and declared it as an epidemic.^[4] As on January 21, 2020, there were 282 cases reported from four countries (China, Japan, Republic of Korea, and Thailand), and by March 16, 2020, it has affected 169,610 patients across 157 countries causing 6,518 deaths [Fig. 1].^[4] The disease has now been declared a pandemic by the WHO.^[4] The disease epicenter has shifted to Europe, with Italy contributing to highest number of cases outside China.^[4]

India reported the first case of COVID-19 on January 30, 2020, in the southern coastal state of Kerala in a student who had a travel history to Wuhan, China, followed by two more similar cases on February 2nd and 3rd. Nearly a month later on March 2, 2020, two new cases were reported—one each in New Delhi and Hyderabad. Subsequently, there has been a sharp spurt, with a large group of tourists from Italy and their local contacts and a family with an undisclosed travel history to Italy and some of their contacts having been reported positive, taking the number of cases to 110 across 14 states and Union Territories by March 16 [Fig. 2]. To contain the spread of the disease, the Ministry of Health and Family Welfare (MOHFW) in India has released a travel advisory prohibiting travel from and to China, the

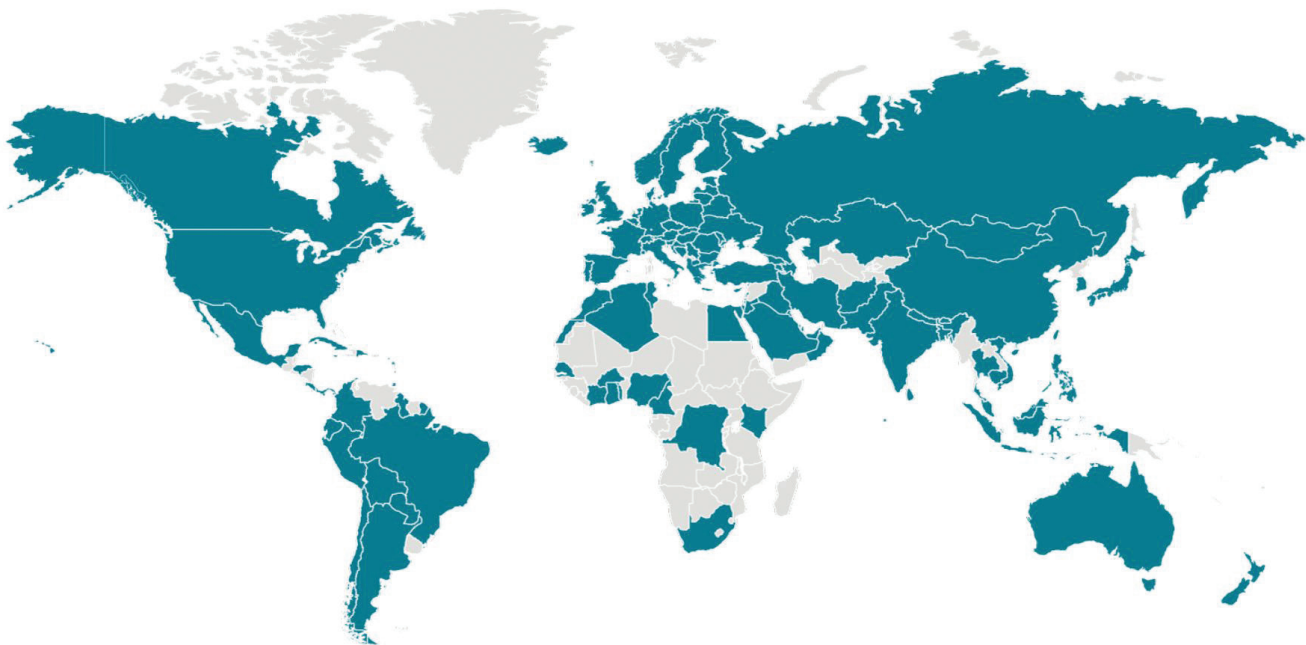


Figure 1: Countries with confirmed COVID-19 Cases - A World Health Organization global map^[4]

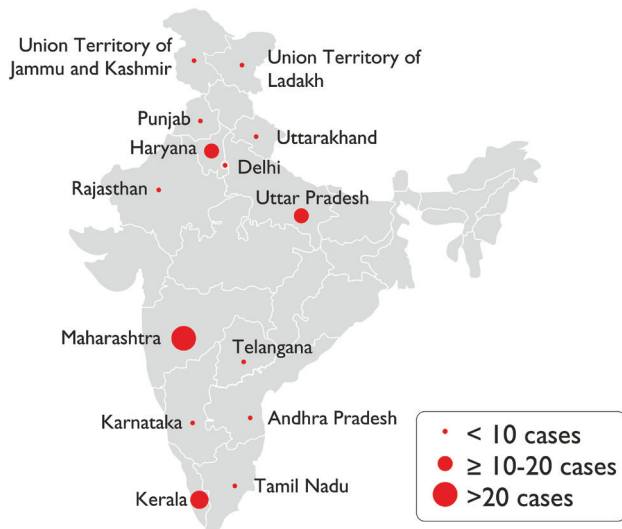


Figure 2: Map of India showing the spread of confirmed coronavirus patients on March 13, 2020

Republic of Korea, Islamic Republic of Iran, Japan, Italy, France, Spain and Germany.^[5] Those having a travel history from these countries are likely to be quarantined for 14 days.^[5] All tourist visas stand suspended until April 15.^[5] An intensive awareness campaign has been rolled out, and guidelines for surveillance, contact tracing, quarantine, diagnosis, laboratory tests, and management have been laid down.^[5] Routine personal hygiene measures suggested by MOHFW include frequent handwashing with soap and water or use of an alcohol-based hand sanitizer, respiratory etiquette (cover the mouth with tissue while coughing and sneezing with safe disposal), avoiding touching eyes, nose, or mouth, avoiding close contact with people who are unwell or showing symptoms of illness with fever, cough, breathlessness, etc.^[5] MOHFW also suggests the use of N95 masks if respiratory symptoms such as cough, fever, or difficulty in breathing, etc., are present.^[5] The suggestion is also not to travel to farms, live animal markets, or where animals are slaughtered and avoid mass gathering.^[5] Potential challenges in containing the infection in India include suboptimal primary health care facilities, dense population, hesitation in voluntary reporting, delayed reporting, difficulty in implementing quarantine, and difficulty in contact tracing. Lockdown, as implemented in China and Italy, seem to be effective. It is, however, challenging to implement lockdown in India, although Kerala has implemented partial lockdown due to a sudden surge in cases. China has seen a decline in a number of cases recently in the Hubei Province as well as in other parts, possibly due to effective lockdowns. Another possible explanation is that the spread of the virus might have peaked and the transmission is slowing down. The effect of increased temperature on virus survival is not clear at this point in time.^[4]

According to the Centers for Disease Control and Prevention (CDC), the 2019-nCoV has an incubation period of 2–14 days, however, studies have also shown a shorter incubation period of 5.2 days.^[6–8] Initial symptoms include fever (90%), cough (75%), and dyspnea (50%). A small subset of patients may have gastrointestinal symptoms.^[9] Although most cases appear to be mild, all admitted in the hospitals

have pneumonia with infiltrates on chest X-ray and computed tomography scans show patchy shadows or ground-glass opacities in the lungs.^[9] About a third of patients, more likely those with comorbidities, develop acute respiratory distress syndrome (ARDS).^[9] The mortality rate reported is 2%, mostly due to ARDS, acute kidney injury, myocardial injury, and septic shock.^[9] The mortality rate has been recently revised to be >3%.^[2] Real-time estimation of mortality rate with two statistical models has been estimated to be 5.3–8.4%.^[10] However, as compared to the other two zoonotic coronavirus infections that have occurred in the last 20 years (SARS and MERS), COVID-19 seems to have higher infectivity but a lower mortality rate.^[11] The median age of the patients is reported to be between 49 and 56 years and cases in children have been rare.^[12]

WHO has suggested that human-to-human transmission of COVID-19 occurs through droplets, contact, and fomites, similar to SARS.^[4] The preliminary estimate of the expected number of cases directly produced by one person in population susceptible to infection for COVID-19 is 2.2% with the epidemic doubling time of 6.4 days.^[8,13] It is not clear when the transmission begins, although cases have been reported that suggest transmission during the asymptomatic incubation phase.^[13] Studies have also shown person-to-person transmission even in the presence of isolation efforts in medical facilities.^[14,15] There is also a risk of environmental contamination.^[16] Hence, there is a need for strict adherence to environmental and hand hygiene.^[16] The virus is also present on the surface of door handles, cell phones, and other residential possessions of confirmed cases.^[17] Touching the eyes, nose, or mouth after contacting the contaminated items is likely to cause human infection.^[17] It has also been reported in the stools of infected persons.^[18] However, vertical transmission has not been confirmed. Neither was it found in the breast milk of infected mothers.^[17]

Transmission via ocular surface is reported.^[19] There are also reports on transmission by aerosol contact with conjunctiva if no eye protection is worn.^[19,20] On January 22nd, Guangfa Wang, a member of the national expert panel on pneumonia, reported that he was infected during an inspection in Wuhan. He wore an N95 mask but with no eye protection. Several days before the onset of pneumonia, Wang manifested conjunctivitis, implying that unprotected exposure of the eyes to the virus in the Wuhan Fever Clinic may have been the source of his systemic infection.^[19]

There are reports on conjunctivitis being the first presenting symptom.^[19,20] Conjunctival congestion has been documented in 9 of 1,099 patients (0.8%) with laboratory-confirmed COVID-19 from 30 hospitals across China.^[12] Ophthalmologists may thus be the first health care providers to evaluate patients potentially infected with 2019-nCoV. Hence, the proximity between ophthalmologists and patients during the slit-lamp examination and most of the ophthalmic evaluation and treatment procedures (which is much within the range of aerosol transmission) may pose a direct risk. As an ophthalmic consultation involves multiple investigations, the patients are likely to stay for a longer duration in the hospital, thus, increasing the risk of cross-infection to other patients as well as to health care workers (HCWs). The risk is higher with unsuspected asymptomatic patients with subclinical infections.^[21] Hence, the American Academy of Ophthalmology (AAO) has issued an alert to ophthalmologists to wear masks for mouth, nose, and

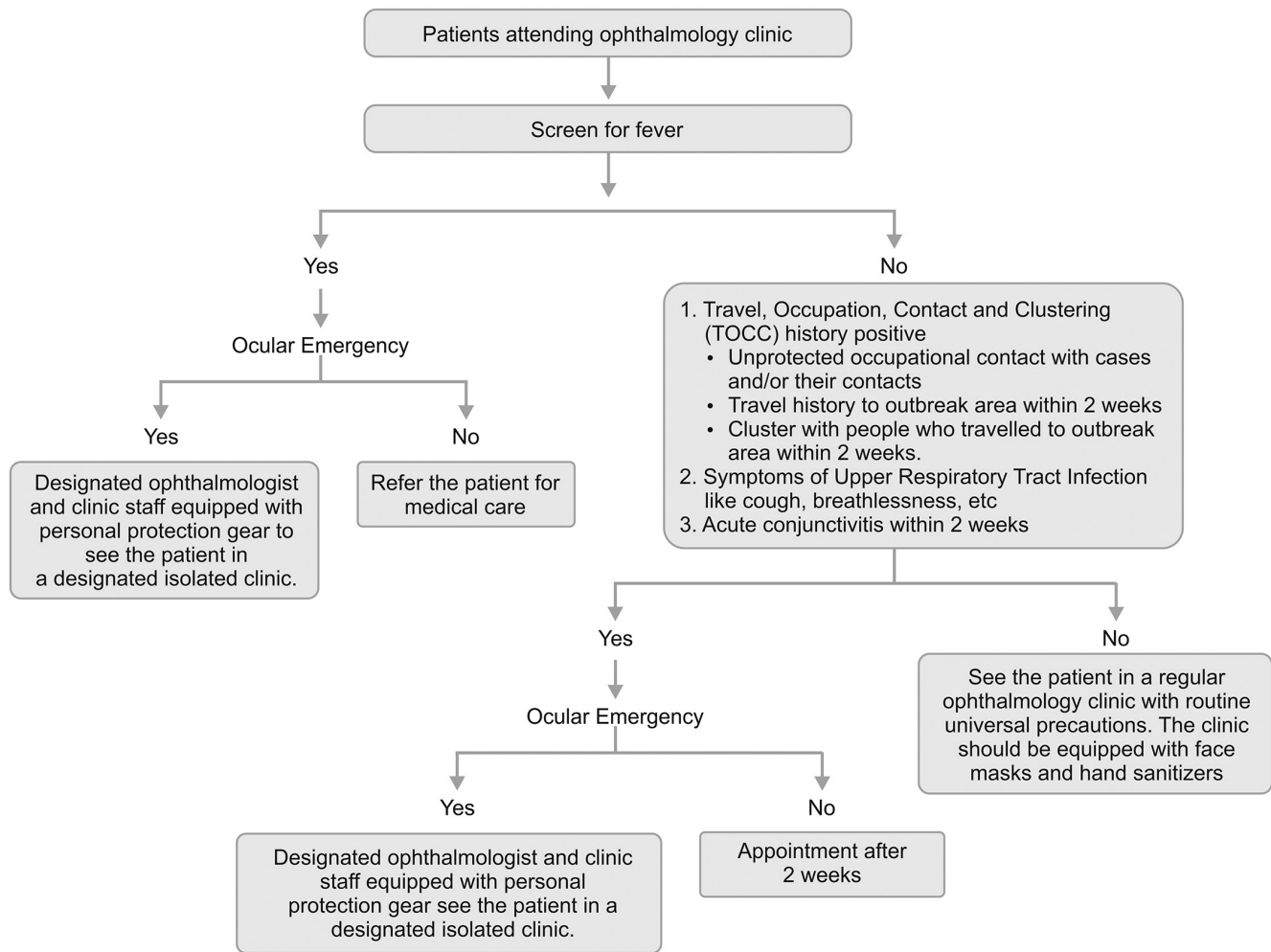


Figure 3: Suggested patient triage in an ophthalmology clinic (adapted from Lai THT, Tang EWH, Chau SKY, Fung KSC, Li KKW. Stepping up control measures in ophthalmology during the novel coronavirus outbreak: an experience from Hong Kong. *Graefes Arch Clin Exp Ophthalmol.* 2020. doi: 10.1007/s00417-020-04641-8)^[24]

eye protection when seeing patients with conjunctivitis with respiratory symptoms and a history of international travel.^[22] While tear samples of COVID-19 cases with conjunctivitis have been documented to carry the virus, the presence of 2019-nCoV in tears of affected individuals without ocular symptoms cannot also be ruled out.^[3,22]

To prevent transmission in the hospital, Hong Kong public hospital system has successfully implemented active and enhanced laboratory surveillance, early airborne infection isolation, rapid molecular diagnostic testing, and contact tracing of HCWs with unprotected exposure in the hospital.^[23] Similarly, to prevent transmission in an eye hospital, Hong Kong has adopted a three-level hierarchy of control measures—administrative, environmental, and use of personal protective equipment (PPE).^[24]

At the administrative level, they took measures to lower patient attendance and suspend elective clinical services.^[24] Patient triage system was introduced and, since fever is the most common symptom, all patients and their attendants were screened with infrared thermometers. Those with fever were asked to seek appropriate medical care and reschedule their

appointments if it was not an emergency. For afebrile patients, a questionnaire to screen for TOCC (travel to affected areas during the incubation period, occupation, contact of suspected or confirmed cases, cluster of cases) was administered by the triage nurse.^[24] Awareness posters for respiratory hygiene and cough etiquette were set up.

Routine aerosol-generating procedures like noncontact tonometry were deferred and cleaning of tonometry tip after each case was practiced.^[24] A suggestion was also to avoid endoscopic dacryocystorhinostomy and general anesthesia. If unavoidable, the suggestion is to use PPE during the procedures.^[25] Finally, all the clinical staff was required to measure and report their temperature before work, as well as report any related symptoms like cough, breathlessness, etc., and their travel history.^[24]

In terms of environmental control, air ventilation in waiting areas was enhanced by putting up HEPA units.^[25] Similarly, to lower the risk of droplet transmission, a protective shield was installed on slit-lamps.^[26] Equipment like slit-lamps, ophthalmoscopes, retinoscopes, computers, and doorknobs that were frequently touched by the staff

were disinfected as per the local disinfection guidelines.^[24] Personal meetings were deferred and replaced by virtual communications. Even for dining, the staff was recommended to sit in one direction.^[24]

As the mode of transmission was by droplet, all personnel in the hospital were asked to use N95 face masks. As the mainstay

Table 1: Five facts about COVID-19 for an ophthalmologist

1. Conjunctivitis may be the first symptom of COVID-19.
2. Patients with COVID-19 conjunctivitis have the transmissible virus in the tears.
3. Transconjunctival aerosol infection is a known mode of disease transmission.
4. Asymptomatic patients with COVID-19 or patients in incubation can transmit the disease.
5. Close contact during ophthalmic procedures has the risk of patient-to-ophthalmologist disease transmission.

Table 2: Five mandatory measures in an ophthalmology clinic

1. Screen for fever at the point-of-entry and elicit a history of travel to affected areas during the incubation period, occupation, contact of suspected or confirmed cases, cluster of cases.
2. Those positive for #1, with no ophthalmic emergency, should be triaged to a designated medical facility.
3. Those positive for #1 with an ophthalmic emergency should be seen by the staff geared in personal protective equipment in an isolated designated examination room with an isolated waiting area.
4. Patients with conjunctivitis, with or without # 1, should be seen by the staff geared in personal protective equipment in an isolated designated examination room with an isolated waiting area.
5. Barrier care including N95 masks for all physically close ophthalmic procedures and universal precautions for all patients; decontamination of applanation prisms, contact gonioscopes, laser contact lenses, B-scan, and ultrasonic biomicroscope probes, etc.

Table 3: Ten reasons why not to panic

1. **We know what it is** - we have identified the virus and have characterized it
2. **We know how to detect** - sensitive and specific tests are in place
3. **The situation is improving in China** - number of cases and deaths are on drastic decline
4. **Most cases are mild** - 81% cases are mild
5. **Patients recover** - of 169,610 cases to date, 77,776 have completely recovered
6. **Symptoms are mild in the young** - only 3% cases occur in those <20 and mortality is only 0.2% in <40
7. **The virus can be wiped clean in a minute** - the virus can be inactivated by ethanol, hydrogen peroxide or sodium hypochlorite
8. **Science is on it, globally** - the international science cooperation is at its peak in tackling COVID-19
9. **Vaccines are in the making** - there are already vaccine prototypes
10. **Antivirals are coming** - Remdesivir, Chloroquine, Oseltamivir and Interferon 1b are under trial.

Adapted from <https://www.weforum.org/agenda/2020/03/coronavirus-keep-things-in-perspective-reasons-not-to-panic>^[27]

for control is handwashing, the staff was instructed to practice hand hygiene as recommended by the WHO.^[26] All clinical staff was suggested to use eye protection glasses. Finally, for examining an infected person, it was suggested to wear full PPE including isolation gowns, gloves, caps, eye protection glasses, and N95 masks.

Similarly, in India at the LV Prasad Eye Institute in Hyderabad, the Hospital Infection control committee has set up a three tier structure for COVID-19 control: a nodal team comprising of the Head of Quality and the Head of Infection Control, a strategy team and an execution team. This structure has helped streamline the information flow and responses. Information posters and awareness messages were set up. Screening and triaging of patients at the front desk was established in compliance with the Government advisory. Waiting room overcrowding was controlled by restricting the number of patient attendants to one each. International patients were advised to reschedule their appointment by 4-6 weeks. The hospital staff were counseled to maintain personal hygiene and protection. HCWs having fever, cough etc were asked to stay home and seek medical care. Monitoring systems and checklists were rolled out to ensure compliance.

Based on the information available currently, we recommend a practical triage system for eye hospitals in India [Fig. 3]. The triage system is being implemented at the Centre for Sight Eye Hospitals in India. The COVID-19 outbreak has just begun in India, and hence, due to the variation in outbreak severity as well as an individual hospital setting, local infection control experts should decide on the specific measures to be taken in each geographic location. It is important not to panic, and be objective in our assessment of the situation and rational in our approach [Tables 1-3].^[27]

What specific intervention will control the COVID-19 outbreak is not yet clear. Currently, there is no vaccine, and the effectiveness of antivirals is not established. We only have fundamental public health measures to follow at this stage. Frontline clinicians and public health authorities are working in tandem to help optimize the outcome of infected patients while containing the risk of human-to-human transmission. Meanwhile, as ophthalmologists, we are bound to follow due diligence and a logical triage system to closely watch out for patients with a possible infection, and take specific measures if found, while continuing to routinely observe universal precautions.

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