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CORONAVIRUS: WHAT DO YOU NEED TO KNOW AS AN OPHTHALMOLOGIST?

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ABSTRACT

Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been previously identified in humans. On 11th February 2020, the WHO formally named the disease triggered by 2019-nCoV now better identified as SARS-CoV-2, as coronavirus disease 2019 (COVID-19). On 11th March 2020, WHO declared COVID-19 as a pandemic. As of 10th April, 2020 more than 1.71 million confirmed cases of COVID-19 have been reported in over 210 countries and territories, resulting in approximately 103,000 deaths and 389,000 recoveries. This article gives a brief review about the microbiology, epidemiology, diagnosis, impact in the field of Ophthalmology and its management & prophylaxis.

INTRODUCTION

Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been previously identified in humans.

- ✓ Since December 2019, there has been a series of unexplained cases of pneumonia reported in Wuhan, China.
- ✓ On 31st December 2019 China notified World Health Organization (WHO).
- ✓ On 12 January 2020, WHO tentatively named this new virus as the 2019 novel coronavirus (2019-nCoV).
- ✓ On 30 January 2020, WHO announced the 2019-nCoV epidemic a public health emergency of international concern.
- ✓ On 11 February 2020, the WHO formally named the disease triggered by 2019-nCoV as coronavirus disease 2019 (COVID-19).
- ✓ On the same day, the coronavirus study group of the International Committee on Taxonomy of Viruses named 2019-nCoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
- ✓ On 11th March 2020, WHO declared COVID-19 as a pandemic (A **pandemic** is the worldwide spread of a new disease as per WHO).
- ✓ India on March 14, 2020 declared Covid-19 as a "notified disaster" which would enable the country to provide assistance and spend more funds to fight the pandemic.

SARS-CoV-2 belongs to the β-coronavirus cluster. COVID-19 is the third known zoonotic coronavirus disease after Severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory syndrome (MERS). Several known coronaviruses are circulating in animals that have not yet infected humans.

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. As of 10th April, 2020 more than 1.71 million confirmed cases of COVID-19 have been reported in over 210 countries and territories, resulting in approximately 103,000 deaths and 389,000 recoveries.[1]

HISTORY

SARS-CoV-2 belongs to the β-coronavirus cluster. COVID-19 is the third known zoonotic coronavirus disease after Severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory syndrome (MERS) (Table 1). Several known coronaviruses are circulating in animals that have not yet infected humans.

	SARS-CoV[2]	MERS-CoV[3]
Causative agent	Outbreak of Severe Acute Respiratory Syndrome	Outbreak of Middle East Respiratory Syndrome
Year	2002-2003	2012
originating area	Guangdong Province of China	Saudi Arabia and other countries in the Middle East
Morbidity and mortality	Approximately 8098 cases occurred with 774 deaths, resulting in a mortality rate of 9%. This rate was much higher in elderly individuals, with mortality rates approaching 50% in individuals over 60 years of age	855 cases with 333 deaths and a case fatality rate of nearly 40%, according to the European Center for Disease Prevention and Control
Primary Host	Chinese horseshoe bats	Bats
Intermediate hosts	Civet cats	Dromedary camels
Mode of transmission	Transmission via direct contact with infected individuals after the onset of illness. Thus, the outbreak was largely contained within households and healthcare settings	Direct contact with infected individuals after onset of illness Thus, the outbreak was largely contained within households and healthcare settings

CONTRIBUTION OF DR LI WENLIANG AND CORONAVIRUS (Figure 1)

Li Wenliang, a young 33 year old 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 SARS. Local authorities, however, admonished him for making false comments that would severely disturb the social order. Li later contracted the virus from an asymptomatic, infected patient with acute angle-closure glaucoma. He manifested the symptoms on January 10, 2020, and succumbed to the disease on February 7, 2020. He is considered one of the prime whistleblowers of COVID-19. He is also the first known case of a patient-to-ophthalmologist transmission of coronavirus. A subsequent Chinese official inquiry exonerated him and the Communist Party formally offered a "solemn apology" to his family.[4]

Figure 1: Dr. Li Wenliang: ophthalmologist who is considered as the whistleblower for coronavirus

MICROBIOLOGY[5]

Coronaviruses (CoVs) are the largest group of viruses belonging to the *Nidovirales* order, which includes *Coronaviridae, Arteriviridae, and Roniviridae* families. The *Coronavirinae* comprise one of two subfamilies in the *Coronaviridae* family, with the other being the *Torovirinae*. The *Coronavirinae* are further subdivided into four groups, the alpha, beta, gamma and delta coronaviruses out of which only alpha and beta groups can affect humans. SARS-CoV-2 are β coronaviruses.

These are enveloped, non-segmented positive-sense RNA viruses and have the largest identified RNA genomes, containing approximately 30 kilobase (kb) genomes. The genome contains a 5′ cap structure along with a 3′ poly (A) tail, allowing it to act as a mRNA for translation of the replicase polyproteins. Nonstructural proteins (Nsps) occupy two-thirds of the genome, about 20 kb, as opposed to the structural and accessory proteins, which make up only about 10 kb of the viral genome.

Coronavirus virions are spherical with diameters of approximately 125 nm as depicted in recent studies by cryo-electron tomography and cryo-electron microscopy. The most prominent feature of coronaviruses is the club-shape spike projections emanating from the surface of the virion which give them the appearance of a solar corona, thus prompting the name, coronaviruses. Within the envelope of the virion is the nucleocapsid. Coronaviruses have helically symmetrical nucleocapsids, which is uncommon among positive-sense RNA viruses, but far more common for negative-sense RNA viruses. (Figure 2).

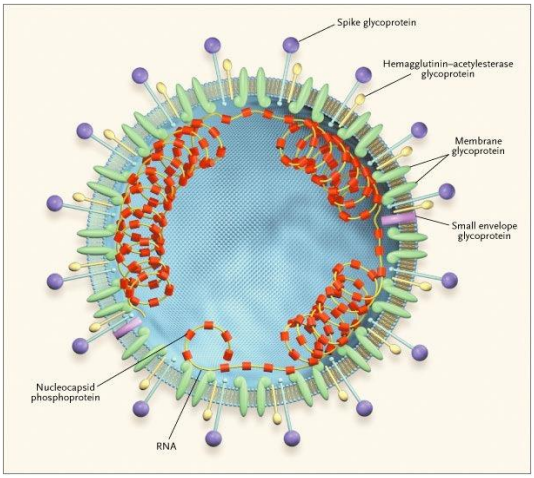

Figure 2: Structure of sars-cov2.

Angiotensin-Converting Enzyme 2 (ACE2) is the receptor for SARS-CoV-2. In the normal human lung, ACE2 is expressed on type I and II alveolar epithelial cells. Among them, 83% of the type II alveolar cells have ACE2 expression. The binding of SARS-CoV-2 on ACE2 causes an elevated expression of ACE2, which can lead to damages on alveolar cells. Damage to alveolar cells can, in turn, trigger a series of systemic reactions stimulating autoimmune responses and thus killing our own body healthy cells mainly by neutrophils and CD8 T-Killer cells, thus causing complications and ultimately death. Men have a higher ACE2 level in their alveolar cells than women. Asians have a higher level of ACE2 expression in their alveolar cells than the White and African American populations. The receptor-binding ability of SARS-CoV-2 is 10 to 20 times stronger than that of SARS-CoV thus making SARS-CoV-2 more potent than SARS-CoV.

EPIDEMIOLOGY[1,6]

- Attack rate: 30-40%
- Case fatality rate (CFR) ranges from 0.25% to 10% (worldwide as on 26th March 2020 was 4.49%).
- Incubation period was found to be 2-14 days thus supporting current 14-day quarantine recommendations.
- Viral shedding period was 20 days (maximum 37 days).
- The ratio of male to female deaths was 3.25:1.
- The median age of death was 75 years
- The median time from the first symptom to death was 14 days, and the median time from early symptoms to death in people aged 70 or older (11.5 days) was shorter than than in people under 70 years old (20 days). These findings suggest the disease may progress faster in the elderly than in the young.
- The CFR for people with underlying health conditions is higher than for those without. One possible reason why the elderly might be most at risk is that they are also those who are most likely to have underlying health conditions such as cardiovascular diseases, respiratory diseases, hypertension, diabetes or cancer. (Figure 3)
- Comparison of case fatality rates among other viral outbreaks (TABLE 2)

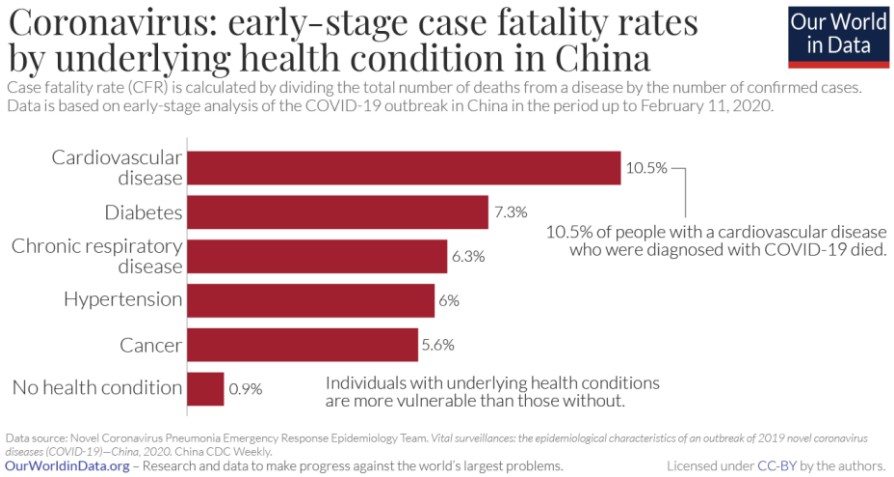

Figure 3: Case fatality rates in patients with different systemic co-morbidities.

Table 2: Comparison of case fatality rates among other viral outbreaks.

Disease/viral outbreak	Case fatality rate
SARS-CoV	10%[7,8]
MERS-CoV	34%[8]
Seasonal Flu	0.1%(US CDC)[9]
Ebola virus	50%, 40% in the 2013-16 outbreak[10,11]

- **Mode of transmission[6]**

✓ Infection via fomites- surface of door handles, cell phones, and other residential possessions of confirmed cases

✓ Droplet infection by aerosolisation from infected cases

✓ Tears in conjunctival sac of an infected person also harbor the virus

- ✓ Stool and urine have also been implicated as the possible media in harboring the infective agent.

Transmission occurs during the asymptomatic incubation phase.

SYMPTOMS[12-16]

- Fevers 98%, of which 78% had a temperature higher than 38°C
- Coughs 76%
- Fatigue and muscle pain 44%
- Dyspnea 55%
- Expectoration (28%),
- Headaches (8%),
- Hemoptysis (5%)
- Diarrhea (3%).

Laboratory tests had the following findings[17-18]

- ✓ CBC: Leucopenia (25% of patients) and lymphocytopenia (63%) on peripheral blood smear evaluation.
- ✓ LFT: The level of aspartate aminotransferase, alkaline amiotransferase and total bilirubin was elevated in 37% of the patients.
- ✓ Increased BUN/ Serum creatinine
- ✓ Increased D-dimer, CRP and LDH.
- ✓ Increased IL-6, IL-10, Tumor Necrosis Factor (TNF) and ferritin
- ✓ Decreased procalcitonin
- ✓ Myocarditis was diagnosed in 12% of the patients, and the level of hypersensitive Troponin I was significantly increased in these patients.
- ✓ Hazy bilateral peripheral opacities on chest X-ray
- ✓ Abnormalities in chest computed tomography (CT) images were found in 100% of the patients. Ground glass opacities and consolidation areas were found in 98% of the infected patients' bilateral lungs. (rarely may be unilateral)

OPHTHALMOLOGY AND COVID-19[6]

- ✓ There have been reports on **conjunctivitis (follicular conjunctivitis)** being the first although umcommon, presenting symptom with tears in the conjunctival sac being a potential source of transmission.

Two published reports suggest the virus can cause conjunctivitis. Thus, it is possible that SARS-CoV-2 is transmitted by aerosol contact with the conjunctiva.

In a *Journal of Medical Virology* study of 30 patients hospitalized for COVID-19 in China, 1 had conjunctivitis. That patient—and not the other 29—had SARS-CoV-2 in their ocular secretions. This suggests that SARS-CoV-2 can infect the conjunctiva and cause conjunctivitis, and virus particles are present in ocular secretions.

In a larger study published in the *New England Journal of Medicine*, researchers documented "conjunctival congestion" in 9 of 1,099 patients (0.8%) with laboratory-confirmed COVID-19 from 30 hospitals across China.

- ✓ Ophthalmologists may thus be the first health care providers to evaluate potentially infected patients. 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).
- ✓ Hence, the American Academy of Ophthalmology (AAO) has issued an alert to ophthalmologists to wear masks for mouth, nose, and eye protection when seeing patients with conjunctivitis with respiratory symptoms, fever, shortness of breath and a history of international travel particularly to areas with known outbreaks or with family members recently back from one of these areas, could represent cases of COVID-19.
- ✓ The coronavirus is very likely susceptible to the same alcohol- and bleach-based disinfectants those ophthalmologists commonly use to disinfect ophthalmic instruments and office furniture.
- ✓ To prevent SARS-CoV-2 transmission, the same disinfection practices already used to prevent office-based spread of other viral pathogens are recommended before and after every patient encounter.
- ✓ Slit-lamp breath shields are helpful for protecting both health care workers and patients from respiratory illness. All the slit lamps to have acrylic/plastic/ X ray sheets as slit lamp breath shields. These barriers do not, however, prevent contamination of equipment and surfaces on the patient's side of the barrier, which may then be touched by staff and other patients and lead to transmission. Homemade barriers may be more difficult to sterilize and could be a source of contamination. In general, barriers are not a substitute for careful cleaning of equipment between patients and asking those patients who cough, sneeze, or have flu-like symptoms to wear masks during examination.
- ✓ Clinicians should postpone those outpatient visits and procedures that can be safely delayed, particularly in elderly patients and those with co-morbidities. Postpone all elective procedures.
- ✓ Reschedule appointments for patients with non-urgent ophthalmic problems.
- ✓ If the office setup permits, patients who come to an appointment should be asked *prior to* entering the waiting room about respiratory illness and whether they or a family member have traveled to a high-risk area in the past 14 days. If they answer yes to either

question, they should be sent home and told to speak to their primary care physician.

- ✓ Keep the waiting room as empty as possible, advice seated patients to remain at least 6 feet from one another. Keep open as many doors as possible in waiting area to avoid touching door knobs. As much as prudent, reduce the visits of the most vulnerable patients.
- ✓ If a patient with known COVID-19 infection needs urgent ophthalmic care, they should be sent to a hospital or center equipped to deal with COVID-19 and urgent eye conditions, ideally in a hospital setting under hospital infection control conditions.
- ✓ If a patient with urgent ophthalmic problem with respiratory illness symptoms, but no fever or other COVID-19 risk factor, he should be examined immediately and asked to wear a surgical mask. The treating ophthalmologist and health care personnel require Personal Protective Equipments (PPE) such as surgical masks, gowns, gloves and eye protection. An N-95 mask should be worn if a procedure is planned that will result in aerosolized virus. The examining room must be cleaned after examination. A protocol which can be followed up in ophthalmology clinics is highlighted in Figure 4.
- ✓ To further decrease the risk of any virus transmission, ophthalmologists should inform their patients that they will speak as little as possible during the slit-lamp examination, and request that the patient also refrain from talking.
- ✓ Rooms and instruments should be thoroughly disinfected after each patient encounter. Wear disposable gloves when cleaning and disinfecting surfaces, and discard the gloves after use. Slit lamps, including controls and accompanying breath shields, should be disinfected, particularly wherever patients put their hands and face.

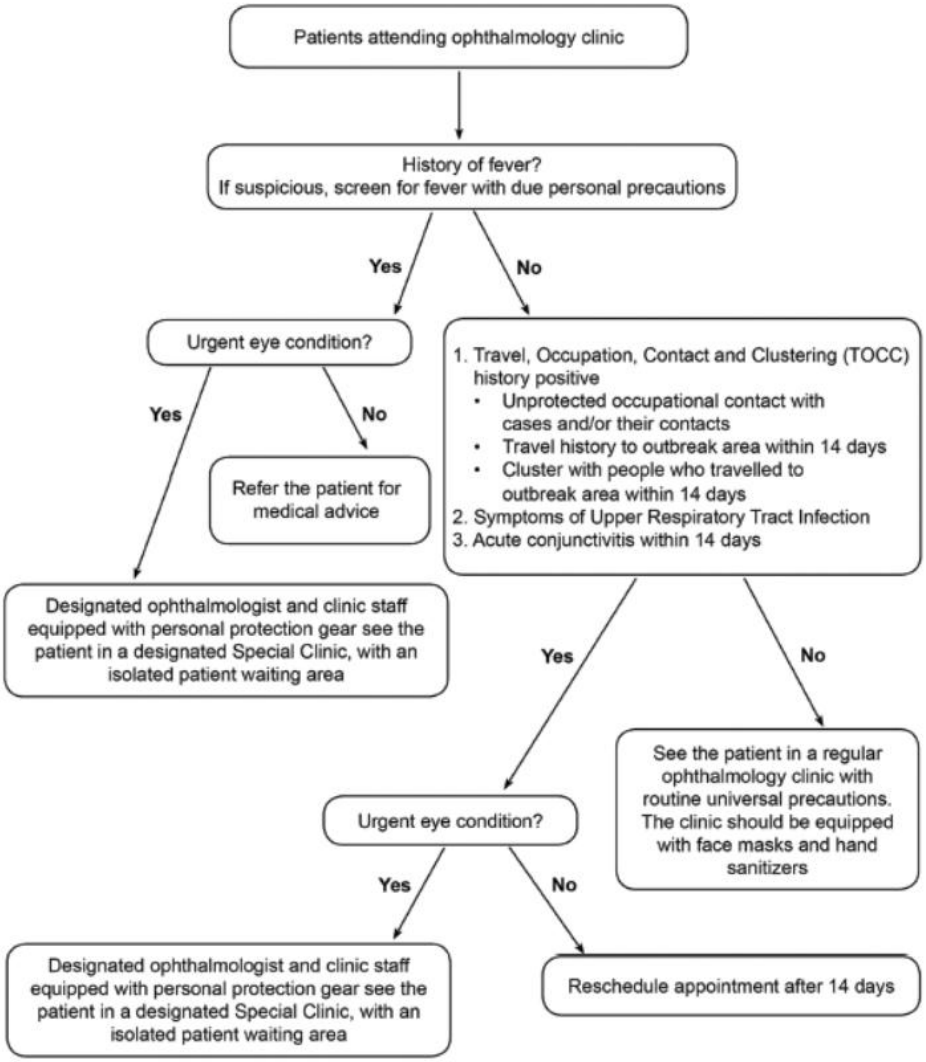

Figure 4: Protocol which can be followed in ophthalmology clinics adopted from Lai THT, Tang EWH, Chau SKY, Fung KSC, Li KKW.Stepping up control measures in ophthalmology during the novel coronavirus outbreak: an experience from Hong Kong. Graefes Arch Exp Ophthalmol.2020.doi:10.1007/s00417-020-04641-8.

The current CDC recommendations for disinfectants specific to COVID-19 include

1. Diluted household bleach (5 tablespoons bleach per gallon of water)
2. Alcohol solutions with at least 70% alcohol (alcohol swabs)
3. Common EPA-registered household disinfectants currently recommended for use against SARS-CoV-2 include Clorox brand products (e.g., disinfecting wipes, multi-surface cleaner + bleach, clean up cleaner + bleach), Lysol brand products (e.g., professional disinfectant spray, clean and fresh multi-surface cleaner, disinfectant max cover mist), Purell professional surface disinfectant wipes and more.

- ✓ 70% alcohol solutions should be effective at disinfecting tonometer tips from SARS-CoV-2. However, alcohol will not effectively sterilize the tip against adenoviruses. Use single-use, disposable tonometer tips if available. Tips cleaned with diluted bleach remain a safe and acceptable practice.
- ✓ Use Telemedicine services- telephone services, internet-based consultation or telemedicine exam
- ✓ Avoid using contact lenses as they involve touching the eyes and face repeatedly. Use spectacles instead on contact lenses.
- ✓ All the OPDs to have hand sanitizer for staff and patient use
- ✓ Disposable OT gowns to be used in OT for emergency surgeries
- ✓ While performing any contact procedure like Tonometry, gonioscopy, keratometry, A- scan, B scan, visual fields, thoroughly clean the instruments before and after every new case
- ✓ Trial frames, lenses, to be wiped with alcohol swabs after doing refraction for each case
- ✓ Special handling of conjuctivitis patient with gloves and cotton buds after triaging from any COVID risk factors
- ✓ Avoid direct ophthalmoscopy, routine refraction, naso-lacrimal syringing and all aerosol based procedure including NCT.
- ✓ Faculty and senior fellows should preferably do emergency surgeries-quick and safe surgery warranted
- ✓ Choose the quickest possible surgical procedure
- ✓ Try to avoid GA unless mandatory, prefer topical over local anaesthesia
- ✓ Minimum number of staff in OT. Stop positive ventilation in OT during the surgery and for atleast 20 mins after patient has left the OT.

Table 3 gives important working definations for COVID-19.

Table 3: Important working definations for COVID-19[19]

SARI (Severe Acute Respiratory Infection)	**An ARI with history of fever or measured temperature ≥38 C° and cough; onset within the last ~10 days; and requiring hospitalization.**
Suspect COVID-19 case	**1.** SARI in a person, with history of fever and cough requiring admission to hospital, with no other etiology that fully explains the clinical presentation (clinicians should also be alert to the possibility of atypical presentations in patients who are immune-compromised); **AND** any of the following: A history of international travel in 14 days prior to symptom onset; or **the disease occurs in a health care worker who has been working in an environment where patients with severe acute respiratory infections are being cared for, without regard to place of residence or history of travel** within 14 days before onset of illness**; or** close physical contact with a confirmed case of COVID - 19 infection within 14 days before onset of illness, while that patient was symptomatic; or the person develops an unusual or unexpected clinical course, especially sudden deterioration despite appropriate treatment, without regard to place of residence or history of travel, even if another etiology has been identified that fully explains the clinical presentation
Close contact	Health care associated exposure, including providing direct care for COVID – 19 patients, working with health care workers infected with COVID – 19**,** visiting patients or staying in the same close environment of a COVID - 19 patients. Working together in close proximity or sharing the same classroom environment with a COVID - 19 patient Travelling together with COVID - 19 patient in any kind of conveyance. Living in the same household as a COVID - 19 patients.

Points to be remembered while sample collection from suspected patients[20]

- Trained health care professionals to wear appropriate personal protective while collecting the sample from the patient. Maintain proper infection control when collecting specimens.
- Restricted entry to visitors or attenders during sample collection.
- Specimens should be collected as soon as possible once a suspected case is identified regardless of time of symptom onset.
- It is recommended that testing of multiple clinical specimens from different sites, including two specimen types—lower respiratory and upper respiratory must be done.
- Transport immediately to the lab which tests for Corona virus
- Label each specimen container with the patient's serial number, name, ward, specimen type and the date the sample was collected. Complete the requisition form for each specimen submitted.
- Proper disposal of all waste generated.

SAMPLE TO BE COLLECTED IN A COVID-19 SUSPECT[20]

- Collect blood cultures for bacteria, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures
- Collect specimens of upper respiratory tract-nasopharyngeal and oropharyngeal swab for RT - PCR.
- Clinicians may also collect Lower Respiratory Tract (LRT) samples such as Bronchoalveolar lavage, tracheal aspirate- Collect when these are readily available (for example, in mechanically ventilated patients). Do not induce sputum.
- *Nasopharyngeal swab:* Tilt patient's head back 70 degrees. Insert flexible swab through the nares parallel to the palate (not upwards) until resistance is encountered or the distance is equivalent to that from the ear to the nostril of the patient. Gently, rub and roll the swab. Leave the swab in place for several seconds to absorb secretions before removing
- *Oropharyngeal swab (e.g., throat swab):* Tilt patient's head back 70 degrees. Rub swab over both tonsillar pillars and posterior oropharynx and avoid touching the tongue, teeth, and gums.
- When collecting URT samples, use viral swabs (sterile Dacron or rayon, not cotton) and viral transport media. Use only synthetic fiber swabs with plastic shafts. Nasopharyngeal and Oropharyngeal specimens should be kept in separate vials. Do not use calcium alginate swabs or swabs with wooden shafts. Place swabs immediately into sterile tubes containing 2-3 ml of viral transport media.
- In a patient with suspected COVID - 19, especially with pneumonia or severe illness, a single URT sample does not exclude the diagnosis, and additional URT and LRT samples are recommended. Sputum induction should be avoided due to increased risk of increasing aerosol transmission.
- Dual infections with other respiratory viral infections have been found in SARS and MERS cases. Both URT and LRT specimens can be tested for other respiratory viruses, such as influenza A and B (including zoonotic influenza A), respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, enteroviruses (e.g. EVD68), human metapneumovirus, and endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E). LRT specimens can also be tested for bacterial pathogens, including *Legionella pneumophila*.
- In hospitalized patients with confirmed COVID - 19 infections, repeat URT samples should be collected to demonstrate viral clearance. The frequency of specimen collection will depend on local circumstances but should be done at least every 2 to 4 days until there are two consecutive negative results (of URT samples) in a clinically recovered patient at least 24 hours apart.
- Additional clinical specimens may be collected as COVID-19 virus has been detected in blood and stool, however duration and frequency of shedding of COVID-19 virus in stool and potentially in urine is unknown.
- In case of patients who are deceased, consider autopsy material including lung tissue.
  Causes of a false negative result[20] (The WHO's guidelines for laboratory testing of COVID-19 say that negative results "do not rule out the possibility of COVID-19 virus infection)
- They may be in the early stage of the disease with a viral load that is too low to be detected.
- They may have no major respiratory symptoms, so there could be little detectable virus in the patient's throat and nose.
- There may have been a very little sample to test.
- There may have been poor handling and shipping of samples and test materials.
- There may have been technical issues inherent in the test, e.g. virus mutation.
  The WHO suggests that these issues should be taken into account and that for a patient with a high index of suspicion, tests should be carried out several times and lower respiratory tract sample if possible, should be collected and tested.

Current testing strategy as per guidelines laid by Indian Council of Medical Research (ICMR)[21]

- All symptomatic individuals who have undertaken international travel in the last 14 days.
- All symptomatic contacts of laboratory confirmed cases.
- All symptomatic health care workers (HCW)
- All hospitalized patients with severe acute respiratory illness (fever and cough and/or shortness of breath)

- Asymptomatic direct and high risk contacts of a confirmed case should be tested once between day 5 and day 14 of coming in his/her contact.

Prevention and treatment of COVID-19[22]

- As of 26th March 2020, no COVID-19 vaccine has been successfully developed. But on March 5, mRNA coronavirus vaccine trials began enrollment at Kaiser Permanente Washington Health Research Institute in Seattle, and at Emory Children's Center in Decatur. Both institutions are members of the Infectious Diseases Clinical Research Consortium, a clinical trials network supported by the National Institute of Allergy and Infectious Diseases (NIAID).[4]
- At present, the treatments of patients with SARS-CoV-2 infection are mainly symptomatic treatments. The most common complications in patients with 2019-nCoV infection were acute respiratory distress syndrome, followed by anemia, acute heart injuries, and secondary infections.
- Currently, there are no proven agents for prophylaxis or therapy for SARS-CoV-2. An investigational drug, remdesivir, has shown activity in vitro and is currently in clinical trials. [6]
- In the absence of effective treatments, the best way to deal with the SARS-CoV-2 epidemic is to control the sources of infection. Preventive strategies include:

✓ Screening, reporting, isolation, and supportive treatment
✓ Timely release of epidemic information;
✓ Maintenance of social orders
✓ Improving personal hygiene
✓ Wearing medical masks
✓ Adequate rest
✓ Keeping rooms well ventilated
✓ Contact tracing
✓ Social distancing
✓ Flatten the curve by converting it into a slow pandemic rather than a fast pandemic

What is meant by flattening the curve? (Figure 5)

- The intention is to lower the rate of infection so that the epidemic is spread out over time such that the peak demand on the healthcare system is lower.
- Containment measures are intended to avoid an outbreak trajectory in which a large number of people get sick *at the same time*.
- Health systems can care for more patients across an outbreak when the number of cases is spread out over a long period rather than condensed in a very short period.

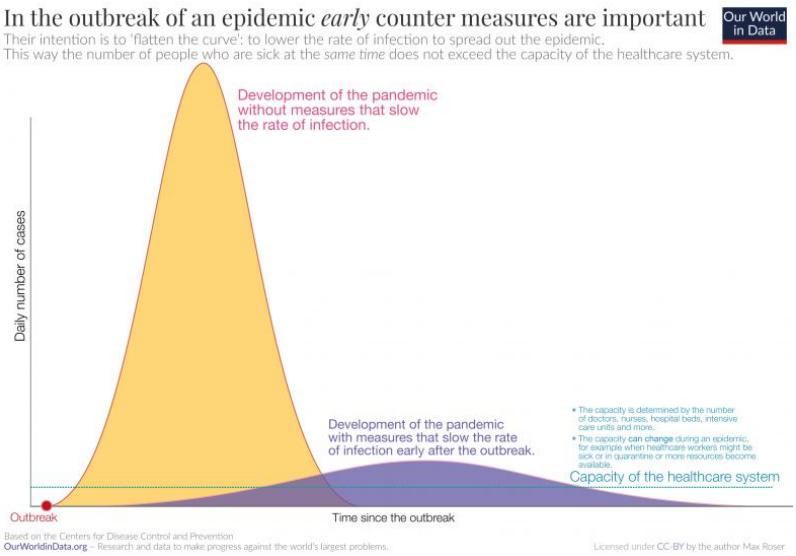

Figure 5: Flattening the curve: fast and slow pandemics.

Preventing transmission of COVID-19 between employees

✓ Implement remote work practices (tele-working)
✓ Social distancing measures in the workplace when on-site presence is required (at least 1 metre)
✓ Hold fewer in- person meetings
✓ Restrict the number of visitors entering the workplace
✓ Limit travel beyond non-essential travel
✓ Ensure people with symptoms or with family members with symptoms self-quarantine for 14 days
✓ Check the body temperature of employees daily so that employees with fever don't come to work
✓ Facilitate access to reliable information for employees to promote understanding of the disease and its symptoms and the personal preventative measures (respiratory etiquette, hand washing, self-isolation if sick)
✓ Check and follow the advice from the authorities in the community before holding a meeting or event; follow all necessary precautions, protective and self-isolation measures, should a meeting go ahead.

Droplet precautions prevent large droplet transmission of respiratory viruses.

- Use a triple layer surgical mask if working within 1-2 metres of the patient.
- Place patients in single rooms, or group together those with the same etiological diagnosis.
- If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation.
- When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection (face-mask or goggles), because sprays of secretions may occur.

Limit patient movement within the institution and ensure that patients wear triple layer surgical masks when outside their rooms

- all patients' beds should be placed at least 1 metre apart regardless of whether they are suspected to have COVID-19;
- Where possible, a team of HCWs should be designated to care exclusively for suspected or confirmed cases to reduce the risk of transmission

Droplet and contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces).

- Use PPE (triple layer surgical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving.
- If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers).
- If equipment needs to be shared among patients, clean and disinfect between each patient use.
- Ensure that health care workers refrain from touching their eyes, nose, and mouth with potentially contaminated gloved or ungloved hands.
- Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches).
- Ensure adequate room ventilation.
- Perform hand hygiene.

USE OF CHOROQUIN OR HYDROXYCHLOROQUIN[6]

- Chloroquine and hydroxycholoquine are oral agents approved for malaria and autoimmune disorders, respectively. Both drugs showed promise in nonrandomized trials and are under further study to evaluate their safety and efficacy in the treatment of COVID-19.
- In a review of published guidelines for the use of these 2 drugs as treatment for COVID-19, a working group from the Asia-Pacific Vitreo-retina Society found that proposed doses in many of the ongoing studies worldwide exceeded the maximum daily dose considered safe for long-term therapy (generally <5mg/kg of real weight for hydroxychloroquine) for rheumatic and other chronic diseases. The risk of irreversible maculopathy at these higher doses for short periods of time is unknown.
- Patients should be informed of the potential for macular toxicity before starting therapy.
- The need for baseline fundus examination and/or imaging is also unknown in cases with high doses over a relatively short duration.
- Additional diagnostic testing, such as an ERG, prior to placing a patient on hydroxychloroquine for treatment of COVID-19 is likely unnecessary due to the short treatment duration. Additionally, performing an ERG in this setting carries an unnecessary risk of virus transmission.
- Until more is learned about the toxicity associated with current regimens, decisions should be made on an individual basis, taking into consideration any pre-existing retinal disease.

Prophylaxis for HCW for SARS-COV-2 infection as per Ministry of Health and Family welfare[23]

- At present there is no substitute for infection prevention methods. Any prophylaxis is purely conincidental
- An option of following prophylactic regimen may be given to HCW who are designated as first line workers in accordance with Ministry of Health and Family Welfare (MoHFW) guidelines after obtaining consent and with contraindications
- The regimen which can be followed can be: Tab Hydroxychloroquine 400mg BD on day 1 followed by 400mg once a week for 7 weeks.
- Besides this, HCW may be given an option for participating in multicentric chemoprophylaxis trial of Chloroquine/ Hydroxychloroquine.
- In either case a written consent will be obtained and HCW will need to be in follow up for monitoring of adverse effects

Administration of Lopinavir/ Ritonavir to be considered in Laboratory confirmed cases of COVID – 19 when the following criteria are met[19]

Symptomatic patients with any of the following

i. Hypoxia,

ii. Hypotension,

iii. New onset organ dysfunction (one or more)

- Increase in creatinine by 50% from baseline, GFR reduction by >25% from baseline or urine output of <0.5 ml/kg for 6 hours.
- Reduction of GCS by 2 or more
- Any other organ dysfunction

iv. High Risk Groups:

- Age> 60 yrs
- Diabetes Mellitus, Renal Failure, Chronic Lung disease
- Immuno – compromised persons

WHEN THE PATIENT CAN BE DISCHARGED

- If the laboratory results for 2019-nCoV are negative, discharge is to be decided as per discretion of the treating physician based on his provisional/confirmed diagnosis
- In case of high suspicion of 2019-nCoV repeat samples are to be sent

  Confirmed case- Resolution of symptoms, radiological improvement with a documented virological clearance in 2 samples at least 24 hours apart

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
- ✓ Difficulty in contact tracing

FUTURE DEVELOPMENTS

In response to the COVID-19 epidemic, the focus of future studies will still be on the development of COVID-19 vaccines and effective drugs to treat COVID-19. With the progress of diagnostic technology, potential super-spreaders may be discovered in the future.

REFERENCES

1. Available from: https://en.wikipedia.org/ 2019-20 Coronavirus pandemic. [Last accessed on 2020 April 11].
2. Peiris JSM, Yuen KY, Osterhaus ADME, et al. The severe acute respiratory syndrome. N Engl J Med, 2003; 349: 2431–41.
3. Killerby ME, Biggs HM, Midgley CM, et al. Middle East respiratory syndrome coronavirus transmission. Emerg Infect Dis, 2020; 26: 191–8.
4. Available from: https://en.wikipedia.org/wiki/Li_Wenliang. [Last accessed on 2020 Mar 13].
5. Coronaviruses: An Overview of Their Replication and Pathogenesis. Fehr, Perlman: Methods Mol Biol, 2015; 1282: 1–23.
6. Available from: https://www.aao.org/headline/Alert:Important Coronavirus updates for ophthalmologists. [Last accessed on 2020 Mar 26].
7. Venkatesh, S. & Memish, Z.A. SARS: the new challenge to international health and travel medicine. *EMHJ – Eastern Mediterranean Health Journal*, 2004; 10(4-5):, 655-662.
8. Munster, V. J., Koopmans, M., van Doremalen, N., van Riel, D., & de Wit, E. (2020). A novel coronavirus emerging in China—key questions for impact assessment. *New England Journal of Medicine*, *382*(8), 692-694.
9. US Centers for Disease Control and Prevention (CDC). Influenza Burden, 2018-19.
10. Shultz, J. M., Espinel, Z., Espinola, M., & Rechkemmer, A. Distinguishing epidemiological features of the 2013–2016 West Africa Ebola virus disease outbreak. *Disaster Health*, 2016; 3(3): 78-88.
11. World Health Organization (2020). Ebola virus disease: Factsheet.
12. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2002032.
13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 2020; 395(10223): 497–506.
14. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 2020; 395: 507–13.
15. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020. https://doi.org/10.1001/jama.2020.1585.
16. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ, 2020; 368:m606.
17. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus [2019-nCoV] infected pneumonia [standard version]. Mil Med Res, 2020; 7: 4.
18. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J. 2020. https://doi.org/10.1097/CM9.0000000000000744
19. Available from https://www.mohfw.gov.in. Guidelines of clinical management of COVID -19. Ministry of health and family welfare, directorate general of health services (EMR division), Government of India. Last updated on 17th March 2020.
20. WHO (2020). Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases. World Health Organization.
21. Available from icmr.nic.in/node/39071. Indian council of medical research, department of health research: revised strategy of COVID19 testing in India (version 3, dated 20/3/2020).
22. WHO (2020). Infection prevention and control during health care when COVID-19 is suspected: Interim guidance 19th March 2020. World Health Organization.
23. Available from: https://www.mohfw.gov.in/pdf/advisory on the use of hydroxychloroquine as prophylaxis for SARS COV2 infection.