Review

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What every orthopaedic surgeon should know about COVID-19: A review of the current literature

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Abstract

The coronavirus (COVID-19) pandemic has severely affected the medical community and stopped the world in its tracks. This review aims to provide the basic information necessary for us, orthopaedic surgeons to prepare ourselves to face this pandemic together. Herein, we cover the background of COVID-19, presentation, investigations, transmission, infection control and touch upon emerging treatments. It is of paramount importance that we should stay vigilant for our patients, our families and ourselves. Adequate infection control measures are necessary during day-to-day clinical work.

Keywords

coronavirus, COVID-19, infection control, SARS-CoV-2

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Introduction

The topic of coronavirus (COVID-19) may seem alien to many orthopaedic surgeons. It is not easy for us to handle something so deeply removed from our field, yet so closely affecting our daily lives. The best strategy to combat is to first know your enemy. This review aims to provide the basic information for orthopaedic surgeons, to converse and to inform. Rather than being passive, we are preparing ourselves in the wake of the COVID-19 pandemic.

Background

Corona is crown in Latin. The large protrusions from the spike proteins on the surface give the appearance of having crowns under electron microscopy.[1] They are large, enveloped, positive-strand RNA viruses. They are relatively large in the family of viruses and contain the largest genome among RNA viruses. However, they are much smaller than other microbes, approximately 10 times smaller than a *Streptococcus* bacterium. Coronaviruses are surrounded by a lipid bilayer derived from the host, hence enveloped. This lipid bilayer makes it difficult for the host immune system to target.[2] On the other hand, it is less stable in the environment and can be destroyed effectively by alcohol and other antiseptic solutions.[3] The term positive-strand RNA means they are readily translated to protein without the need for transcription. The surface protein is recognized by human angiotensin-converting enzyme 2 (ACE2) receptor, which is predominantly found in the lower respiratory tract.

There are four groups of coronaviruses: α, β, γ and δ.[4] They are found in warm-blooded flying vertebrates including bats for α and β, and birds for γ and δ. The α and β coronaviruses are known to infect humans and there are currently four coronaviruses (HCoV 229E, NL63, OC43 and HKU1) that are endemic globally, accounting for

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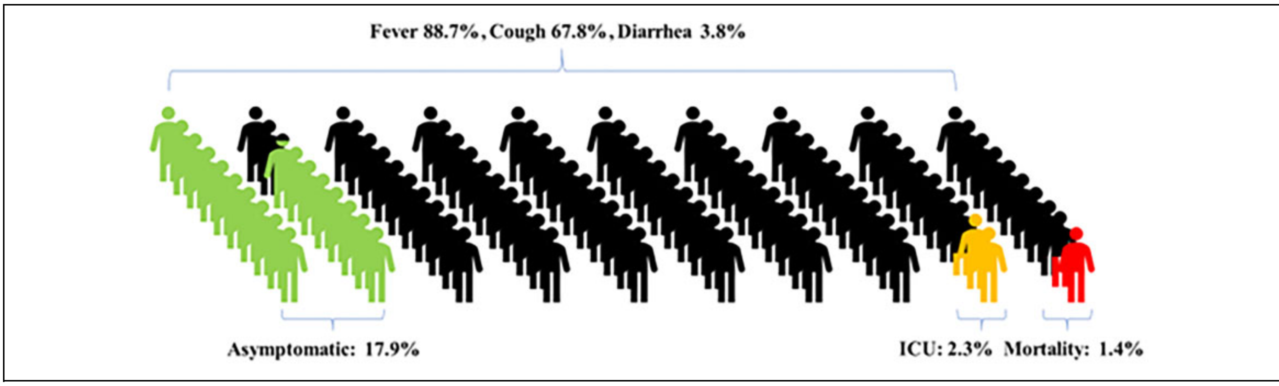

Figure 1. Distribution of symptomatology in COVID-19.

10–30% of upper respiratory tract infections in adults.[5] The virus responsible for the recent pandemic coronavirus disease (COVID-19) is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), belonging to the β group of coronaviruses. Its genome is closest related to a virus that was first found in horseshoe bats with a similarity of 89%.[6] This suggests that the origin of the COVID-19 pandemic is likely from an animal source transmitting to humans. However, bats were not the only hosts for this SARS-CoV-2 virus – there were reports that the virus was also found in other mammals such as pangolins and pet dogs.[7,8]

How infectious is COVID-19?

Epidemiology studies help us to predict how the viral disease will spread, and the most important value is the term 'basic reproduction number' or 'R_0'. It is defined as the number of cases that one infected patient is capable of generating, or in other words infecting, when all individuals are susceptible to the same infection. If the value is greater than 1, the disease starts to spread; R_0 has to be smaller than 1 in order to control spreading of infection. The basic reproduction number R_0 is affected by environmental conditions and behaviour of the population, such as the use of masks, hand hygiene, social distance and quarantine measures. In the early stage of the COVID-19, the R_0 was 2.68. Hence, with one positive patient, he or she transmits the virus to 2.68 susceptible people on average, which is similar to early phase of SARS in 2003.[9]

Presentation

Symptomatology

The clinical features of patients infected with SARS-CoV-2 have unfolded gradually as the pandemic evolves. At the start of the outbreak of COVID-19 in Wuhan, only severely infected patients with pneumonia were reported. Hence, the most common presentation was fever (98%) and cough (76%) – all with radiological pneumonia. There was a high ICU admission rate (32%) and high mortality rate of up to 15%.[10] With more patients screened by contact tracing and symptoms evaluation, the percentages of symptoms, ICU admission and mortality rates came down. In the largest series in China involving more than 1000 patients, the most common presentation on admission was cough (67.8%) followed by fever (43.8%). Diarrhoea was an uncommon presentation (3.8%). The mean incubation period was 4 days and 88.7% of patients developed fever during hospitalization (Figure 1). This may reflect the effectiveness of screening and contact tracing policies that allow detection of virus before the onset of symptoms. With a much larger sample size for analysis, the ICU admission rates (2.3%) and mortality (1.4%) were lower than earlier reports.[11]

Asymptomatic carriers pose a serious threat to the society. One example is the Diamond Princess cruise ship outbreak in February, where 634 (20%) people were tested positive among 3063 passengers. Three hundred and twenty-eight (51.7%) cases were reported to be asymptomatic at the time of diagnostic testing. Statistical models were employed to perform real-time outbreak analysis and the estimated asymptomatic proportion was 17.9%, which is the probability an individual will never develop symptoms.[12] This probability estimated by statistical modelling was consistent with clinical data from China that 17.9% of patients did not have any X-ray or computed tomography (CT) abnormalities.[11] The virus was also found to be present in stool samples even after the nasopharyngeal tests were negative. Hence, the viral shedding in the digestive system lasted longer than in the respiratory tract.[13] These findings bring out the importance of a good isolation policy to contain asymptomatic carriers that may shed the virus in the community.

Investigations

Virological diagnosis of COVID-19 is based on reverse transcription polymerase chain reaction on patient respiratory tract samples. Nasopharyngeal swab, oropharyngeal swab or saliva sample are common upper respiratory tract

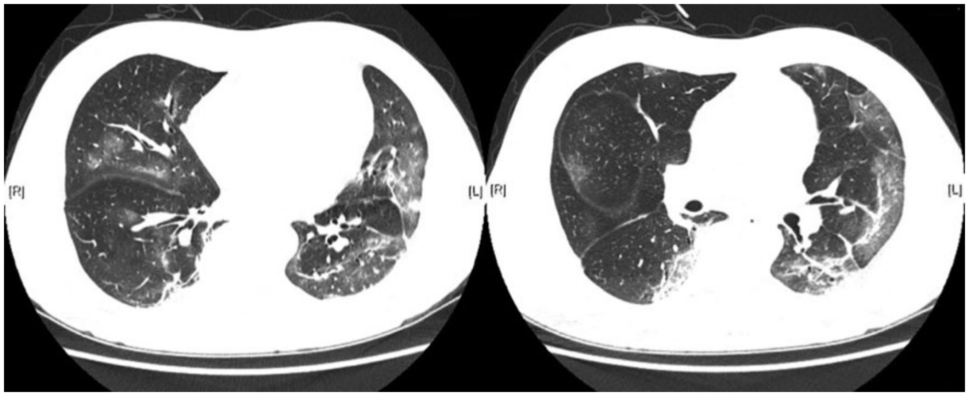

Figure 2. High-resolution CT images of a 51-year-old gentleman with COVID-19. There are diffuse subpleural ground-glass opacities with peribronchovascular distribution. Minimal pleural effusion is observed. Focal consolidations can be seen with collapse of alveoli. CT: computed tomography.

samples used for diagnosis, whereas lower respiratory tract samples are recommended when upper respiratory tract samples return negative despite significant clinical and epidemiological suspicion.[14] Quantitative monitoring of viral load may correlate with disease progression.[15]

Laboratory findings vary depending on clinical severity of the patient. In mild to moderate cases, there is normal to decreased white cell count and normal to elevated C-reactive protein. In severe cases, there are raised procalcitonin and elevated liver parenchymal enzymes. Patients may develop renal impairment when in circulatory shock. The creatine kinase level is also reported to be elevated in severe cases.[16,17] Children are observed to have less severe laboratory findings with usually near normal white cell count and normal C-reactive protein.[18,19]

Imaging

Chest radiographs in COVID-19 patients evolve with clinical presentation. It is worth noting that 18% of asymptomatic patients were reported to have normal chest radiograph findings.[20] Typical findings are patchy ground-glass opacities and focal consolidation. There is a preponderance for the right lower lobe to be affected. However, most patients present with bilateral lower zone involvements with a peripheral distribution. With progression, the patchy lesions may become confluent, leading to diffuse bilateral involvement.[17,19,21]

In CT scans, subpleural nodular or patchy ground-glass opacities can be found in peripheral zones of the lungs, extending towards the hilum (Figure 2). There may be interlobular thickening and pleural thickening. Findings are typically bilateral.[20] Late signs such as reversed halo sign (central ground-glass opacity surrounded by denser consolidation), batwing sign (large symmetrical shadows around bilateral hilum) and blizzard lung (white out of lung fields) occur with progressive involvement.[20,22–26] Sensitivity of CT scans for COVID-19 is reported at 97% with a specificity of 25% in a retrospective analysis of 1014 cases of COVID-19.[22]

Transmission

Viral transmissions can occur via direct contact, respiratory droplets or airborne transmissions. The transmission of COVID-19 is predominantly by respiratory droplets.[27] There is no gold standard methodology to study the transmission routes of viruses. Hence, there is a constant debate on the relative contribution of each route; contact, droplet and airborne.[28,29] Droplet transmission occurs from person-to-person contact within 1 m, where infective droplets from sneezing or coughing can contact mucosal surfaces including the nose, mouth and conjunctiva. Airborne transmissions are more difficult to prove and are dictated by particulate size usually less than 5 μm in diameter, which allows it to be suspended in air for longer durations. Smaller size particulates can travel further and deposit lower down in the respiratory tract. Airborne transmissibility also depends on the time the pathogen can remain infectious and its biological decay. A case study evaluated environmental air samples from the first confirmed case of COVID-19 in Hong Kong, which were obtained while the patient performed various tasks without a surgical mask and were subsequently analysed for viral RNA.[30] The study revealed no detectable SARS-CoV-2 RNA in the obtained air samples; furthermore, the healthcare worker involved in collecting the samples did not get infected despite prolonged exposure, albeit wearing full personal protective equipment (PPE) and an N95 respirator. Nonetheless, other studies have shown COVID-19 to be present in experimental aerosol generation, raising the possibility of nosocomial infections of healthcare workers from in-hospital aerosol-generating procedures similar to the events from SARS in 2003.[31]

Apart from respiratory droplets, COVID-19 has also been found in nasal, pharyngeal swabs, throat saliva, bronchoalveolar lavage fluid, faecal specimens and blood samples.[7] Thus, faecal–oral transmission and blood transmission from patients with active viremia can technically also occur. However, not all patients become viremic. Positive blood samples for viral RNA were only found in 1–10.5% of patients.[7,32] Other routes of infection include mucocutaneous contact with inadvertent transfer of viruses from infected surfaces onto mucous membranes, that is, contact transmission. It was shown that viable viruses were detectable on plastic surfaces, stainless steel and copper for 72 h, 48 h and 4 h, respectively.[31] With the majority of patients being asymptomatic or with mild symptoms, unintentional exposure to confirmed cases can occur in day-to-day practice and hence the importance of hand hygiene, masks, social distancing, screening and infection control.[33]

Transmission in orthopaedic surgery

Orthopaedic surgeons have an increased occupational risk of mucocutaneous exposure and blood-borne contamination due to sharp injuries and bony debris during operative procedures.[34] Certain procedures have been speculated to generate aerosols intraoperatively. These include high-speed cutting devices (6 mm ball cutting burr) in spinal surgeries and ultrasound devices (Ultradrive; Biomet, Warsaw, Indiana, USA) used in revision arthroplasty, which have been implicated in creating an aerosol cloud of up to 5 $\times$ 7 m radius with positive bacterial cultures detected from air sampling.[35,36] These aerosols containing a mixture of blood, bony debris, tissue and irrigation fluid could potentially harbour infected viruses and bacteria posing a contamination risk to surgical personnel. The use of body exhaust suits reduces the amount of splash contamination to the surgeon by 30% in one study with simulation arthroplasty procedures.[37] However, this is insufficient for airborne precautions with previous studies showing that surgical helmet systems were inferior to respirators with face mask and shield combination for reduction of airborne particulate counts.[38]

Moreover, the risk of infection can go both ways and patients undergoing elective or emergency orthopaedic procedures can become infected from asymptomatic healthcare personnel. Parvizi et al. speculated that aerosols released including textile fibres and respiratory aerosols from the surgical team members can be spread by convective airflow in the operating theatre settling onto surgical wounds or instrument surfaces.[39] These can lead to microbial surgical site infections and periprosthetic joint infections. However, viral transmissions from healthcare workers to patient can only be extrapolated and mitigated with implementation of proper infection control measures including dilution with air changes up to 15–20 per hour, high-efficiency particulate air (HEPA) filtration, limiting traffic in theatre and ensuring sterilization of instruments and surgical field.[39]

Infection control

Healthcare setting: Screening

Strategies in controlling an epidemic can be divided into infection control measures in healthcare, local and global settings. In the healthcare setting, the World Health Organization (WHO) provided guidelines on infection control which involves early detection and screening of suspected COVID-19 cases.[40] They also suggest applying standard precautions to all patients and additional droplet and contact precautions for suspected patients with COVID-19. Airborne precautions are reserved for aerosol-generating procedures. For orthopaedic surgery in Hong Kong, surgical cases undergoing elective or emergency surgeries are preoperatively screened for COVID-19 if they have either fever or upper respiratory tract symptoms, overseas travel or strong epidemiological history such as close contact with a confirmed case. Patients with community-acquired pneumonia on presentation or suggestive chest X-ray imaging will also be screened. Although most cases are asymptomatic or exhibit only mild symptoms, the ability to screen all patients will be dependent on individual centre's capability to cope with such demand.

PPE and hand hygiene

The conscientious use of PPE for contact, droplet and airborne precautions has been a hot topic with inadequate supply and high global demand. The WHO published recommendations on rational use of PPE, optimization and appropriate usage.[41] It is best to follow local authorities' recommendations on PPE usage due to the need for prudent resource allocation to those healthcare workers who are in greater need for PPE. The Centers for Disease Control and Prevention (CDC) suggests the use of eye protection, N95 respirator, gloves and isolation gown for dealing with COVID-19 patients. Successful usage of PPE is dependent on proper training, technical difficulties and tolerability as more sophisticated PPE become more cumbersome.[42] Users can develop heat stress and more steps required during doffing can increase the risk of self-contamination.[43] Tomas et al. used fluorescent lotion to highlight contamination with PPE usage and showed that doffing led to contamination in 46% of episodes.[44] This occurred most commonly in the hands when removing gloves and at the neck during gown removal. Similar to the orthopaedic practice of double gloving, Casanova et al. performed a study on hand contamination after PPE doffing with either one or two layers of gloves and showed that their protocol using double gloves significantly reduced the contamination episodes to the hand by 55%.[45] Removal of the first layer of gloves followed by other PPE items and removing the second layer of gloves last ensured the potential contamination was transferred to the inner gloves rather than the hand. Double glove adds another layer of defence, but most importantly, this highlights the necessity of proper hand hygiene accompanied with appropriate PPE usage.[42] Given the austerity of the SARS-CoV-2 pandemic, the orthopaedic specialty in Hong Kong has cut back on elective surgeries and reduced personnel in operating theatre to the bare minimum in order to reduce the usage of PPE. Day surgical cases, operations under spinal, local or regional anaesthesia are the preferred elective surgeries in order to reduce in-hospital time and avoid aerosol generation associated with intubation along with the utilization of appropriate protective gear. Out-patient clinics have reduced patient flow and routine follow-up cases are deferred or managed via telemedicine whenever possible. This helps decrease hospital exposure and contact with asymptomatic carriers along with the reduced use of surgical face masks.

Administrative, environmental and engineering controls

In addition, other administrative policies such as monitoring compliance of PPE usage, adequate training and ensuring infection surveillance of healthcare personnel are also recommended by the WHO to prevent nosocomial spread of infection. Contingency plans for unintentional contact with COVID-19 patients and ready access to COVID-19 testing for healthcare workers should be made available. Orthopaedic surgeons should undergo training on COVID-19 diagnosis, PPE usage, triage procedures and local reporting guidelines in preparation for crisis management.[46] Environmental and engineering controls are also important to reduce the spread of infection, including inpatient bed spacing of at least 1 m distance, disinfection protocols, laundry and food management. The most important engineering control during a pandemic such as COVID-19 could be argued as the presence of airborne infection isolation rooms (AIIRs), which houses patient(s) in a negative pressure room that has individual bathroom, at least 6–12 air changes per hour and circulation of air through a HEPA filter. Due to limited space and number, AIIRs become hospital's most priced commodity. In Hong Kong, the rapid conversion of general wards to negative pressure ventilation with 12 air changes per hour is the strategy employed to tackle saturated AIIRs and reduce nosocomial spread of infection. Ideally, all positive COVID-19 cases should be placed in AIIRs. However, the CDC suggests placing COVID-19 patients in individual rooms and reserving AIIRs for aerosol-generating procedures. Though not ideal, this may become a necessary measure; with the rapid community spread and exponential growth of COVID-19 caseload compared to the recovery rate, these AIIRs become saturated and the hospital system becomes overloaded. Nosocomial infections eventually spread, worsening the already dire situation.

Local infection control measures

Social distancing and community mitigation. In order to prevent the overburdening of the healthcare system, local and global infection control measures need to be implemented in a timely manner to stem the spread of disease. Public health measures include isolation of confirmed cases, contact tracing and quarantining of exposed persons as well as social distancing, such as school closures and avoiding mass gatherings.[47] These measures were effective interventions in reducing the spread of infection during the US 1918 influenza pandemic.[48] An epidemiological modelling study was performed in Singapore with the effects of quarantining, school closures and workplace distancing on infection spread.[49] With a R_0 of 2.5, similar to numbers reported in Wuhan, the combined approach of incorporating all non-pharmaceutical interventions reduced the caseload by 78.2% compared to baseline. A peak in incidence occurring at 9 weeks was observed. Nonetheless, there would still be over 250,000 confirmed cases in Singapore under this model. Similarly, in Wuhan, a simulation model was performed with the ongoing outbreak trajectory adapted to the presence of school and workplace closures as well as social distancing.[50] These measures reduce the magnitude of the epidemic peak and shorten the duration. However, these physical distancing measures may in fact increase household clustering and more sophisticated modelling is required. In addition, a staggered rather than universal uplifting of interventions is suggested to prevent a second peak of infections due to imported cases or community transmission.

Public use of face masks. The public use of surgical masks is a highly contentious topic. It has highlighted cultural disparities and even stigmatization.[51] The WHO advice on mask usage in the community states that only people with respiratory symptoms or people who are taking care of, or in the same room as, a person with suspected COVID-19 infection should wear masks. They state that the use of masks *alone* is insufficient for prevention.[52] Moreover, the use of masks increases the global shortage and has led to increased prices and constraint on front-line medical staff.[53] A review of face mask use in the community identified nine randomized controlled trial (RCT) with mask usage, hand hygiene or a combination of the two for prevention of infection spread.[54] The studies were heterogeneous. However, six out of nine RCTs demonstrated a reduction in risk when masks were used in combination with hand hygiene or started early within 36 h of illness and with good compliance. Nonetheless, the WHO is correct in that the use of masks should only be one part of the personal protection regimen and combination with hand hygiene is essential. Feng et al. described different country's policies and response to face masking.[53] Places such as Hong Kong, China, Japan and South Korea have policies allowing some form of public masking especially in high

	Minimum Performance	ASTM Level 1	ASTM Level 2	ASTM Level 3	N95 Respirators
Performance Level and Testing Standards	No performance level e.g. utility mask, tissue/tissue or cloth as a physical barrier	**FDA Testing –** PFE: Non-neutralized aerosol of 0.1-5µm latex spheres at a flow rate of 28.3L/min; BFE: Non-neutralized 3±0.3-µm *Staphylococcus Aureus* aerosol at a flow rate of 28.3L/min			**NIOSH Testing –** Collect >95% of NaCl aerosols with median aerodynamic diameter of 0.3 µm at 85L/min, 85% humidity at 38°c
Fluid Resistance	Physical barrier	Resistant at 80mmHg	Resistant at 120mmHg	Resistant at 160mmHg	Resistant at 160mmHg
Filtration Efficacy	N/A	BFE ≥ 95% PFE ≥ 95% @ 0.1µm	BFE ≥ 98% PFE ≥ 98% @ 0.1µm	BFE ≥ 98% PFE ≥ 98% @ 0.1µm	PFE ≥ 99.9% at 0.1µm
Breathability – Delta P	N/A	< 4.0 mm H_2O/cm^2	< 5.0 mm H_2O/cm^2	< 5.0 mm H_2O/cm^2	> 5.0 mm H_2O/cm^2
Flame Spread	N/A	Class 1	Class 1	Class 1	Class 1

Figure 3. Standards of respiratory protective equipment. Different testing standards and filtration efficiency between levels of common surgical masks and N95 respirators. FDA: Food and Drug Administration; NIOSH: National Institute for Occupational Safety and Health; BFE: bacterial filtration efficiency; PFE: particulate filtration efficiency.

population density areas, while countries such as the United Kingdom, the United States and Germany dissuade public masking unless symptomatic and instead, those with mild symptoms should stay at home. Unfortunately, as previously mentioned, there is a significant proportion of COVID-19 patients that are asymptomatic and viral shedding can occur prior to the onset of symptoms. We must also trust the moral integrity of citizens to wear masks when they do in fact develop symptoms. Hence, cultural differences and perceptions come into play. Increased production and banned exportation of face masks along with innovative ways such as make-shift alternatives and reusable masks are strategies to tackle the lack of supply.[53] Note that not all surgical masks are created equal and proper testing such as following the American Society for Testing and Materials (ASTM) international standards set out by Food and Drug Administration should be sought in order to offer the basic level of protection against respiratory droplets (Figure 3). In comparison, the National Institute for Occupational Safety and Health (NIOSH) testing standards are more stringent and used for N95 respirators (Figure 3). Oberg and Brosseau performed a study comparing the penetration of aerosol-sized particulates using NIOSH testing standards on different types of surgical masks despite being the same ASTM level and similar filtration efficiency.[55] A significant amount of aerosol penetration was found, varying from 4% to 37% in surgical- and procedural-based masks, but these fared better than dental masks with 53–90% penetration. In addition, tie-on masks provided improved facial fitting compared to masks with ear loops. Despite this, the use of N95 respirators in the community is inappropriate. Several high-level studies including randomized control trials have shown that there is no difference between N95 respirators compared to surgical masks for the prevention of influenza.[56,57] Hence, it is universally agreed that N95 respirators should be reserved for high-risk medical staff in close contact with suspected cases.

Global infection control measures

Lastly, the global measures implemented, including limiting human traffic and travel bans, have been implicated in reducing the spread of infection at the cost of economic turbulence. Imposing the lockdown of Wuhan significantly prolonged the doubling time of infection from 2 days to 4 days.[58] Travel restriction modelling showed modest reduction in infection spread and delay in the peak of the epidemic. But these restrictions should be coupled with other public health measures.[59] By the time Wuhan restrictions were in place on 23 January 2020, many exposed and asymptomatic COVID-19 individuals were already travelling unhindered. The economic impact, however, is immense with China expected to lose US$62 billion in the first quarter and is expected to erase 0.5% of the world GDP.[60]

Emerging treatment

Currently, the recommendations from WHO for treatment of COVID-19 focus on early diagnosis, infection control, isolation and supportive treatment. Caution should be taken in particular in elderly patients with medical co-morbidities for possible complications.[61]

There are myriad therapies proposed and in trial for COVID-19. Different therapeutic agents are proposed which target different points in the viral cell entry and replication pathways. Host immune response is also studied for potential therapeutic targets. Repurposing of existing antiviral medications has been studied and yielded potential results. Lopinavir and ritonavir, used in the treatment of human immunodeficiency virus, have shown preliminary effects in reducing disease severity and shortening the length of hospitalization. Conjunctive use of interferon-α may also be beneficial.[62–64] Antimalarial drug hydroxychloroquine or chloroquine was shown *in vitro* to suppress viral replication.[65,66] Its clinical application has also shown to have radiological improvement and possible reduction in viral load.[66–70] Convalescent plasma is potentially beneficial, but its efficacy and efficiency are still under study.[71,72] Therapeutic agents targeting the renin–aldosterone–angiotensin axis including ACE inhibitors and angiotensin receptor blockers are now under study. However, there is no evidence yet to support any of these agents in clinical application for COVID-19.[73,74] Other potential pharmaceutical agents include ribavirin, tocilizumab and remdesivir.[75,76] As many clinical trials are still underway, new treatments may emerge along with improved understanding of the disease.

Conclusions

COVID-19 is a rapidly evolving pandemic. It is of paramount importance that we should stay vigilant for our patients, our families and ourselves. Adequate infection control measures are necessary during day-to-day clinical work.

Key points

- COVID-19 is a rapidly evolving pandemic.
- Transmission is mainly by respiratory droplet and contact, but there is potential for airborne transmission particularly in aerosol-generating procedures.
- Orthopaedic operations such as those requiring intubation for general anaesthesia, high-speed cutters and other aerosol-generating procedures should be reduced in the short term given the global scarcity of PPE.
- Cough and fever are the commonest symptoms, but a significant proportion are asymptomatic, and a minority present with diarrhoea.
- Patients pending elective operations who develop fever, upper respiratory tract symptoms or diarrhoea should be tested for COVID-19 before undergoing surgery.
- Prevention of nosocomial transmission requires the prudent use of PPE, combined with hand hygiene and environmental measures such as AIIRs.
- Prevention of community transmission requires systematic screening and early detection, hand hygiene, appropriate use of masks, social distancing, avoiding mass gatherings and government policies to enact travel restrictions.

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