



COVID-19 from mysterious enemy to an environmental detection process: a critical review

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Abstract

The recent global emergence of an unusual viral pneumonia of COVID-19 epidemic was firstly started in Wuhan city, Hubei province in China in December 2019. Regrettably, it is still sweeping the planet, and it cannot be controlled up till now. By May 2020, the unexpected spread of this disaster had caused more than 3,759,967 cases and 259,474 deaths in 114 countries from Asia to the Middle East, Europe, and the USA. Considering its fatal nature, it has evolved as a major challenge for the world. This is necessitating a quick and steep intervention in order to save millions of people's lives across the globe. The knowledge about the nature and evolution of the COVID-19 virus in water, soils, and other environmental compartments can be addressed through wastewater and sewage. Wastewater-based epidemiology approach can be used as an early indicator of the infection within a specific population. The basic aim of this review article is trying to provide a prompt, and valuable reference guides about COVID-19. Some important questions were addressed, such as, its origin, transmission, clinical symptoms, diagnosis, environmental aspects, and the possible indoors and outdoors airborne transmission minimization strategies that may benefit specialists.

Keywords Coronavirus · COVID-19 · Transmission · Emerging infection · Prevention strategies · Environmental aspects · Wastewater-based epidemiology

Introduction

Coronaviruses (CoVs) are enveloped, non-segmented, positive-sense RNA viruses ranging from 60 to 140 nm in diameter. Its name is attributing to their distinctive shape under the electron microscope examination as they are characterized by possessing spikes like projections on their external surface providing them with a crown-like appearance [1]. Taxonomically, they are members of the subfamily of *Orthocoronavirinae*, the family of *Coronaviridae*, the order of *Nidovirales*. Generally, CoVs are categorized into four

main genera including α - β - γ - δ -COV. α - and β -COV have the abilities to infect mammals, whereas γ - and δ -COV can infect birds [2, 3]. Additionally, they have shown a similar ability to infect humans in previous decades [4–9]. Historically, before 2019, six-known human CoVs types were causing respiratory diseases with various severities; four common CoVs types identified as HKU1, NL63, 229E, and OC43; and two highly pathogenic CoVs types identified as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [10]. For instance, the lethality of CoVs was demonstrated considering the emergence of SARS in 2002 [5] and MERS in 2012 attributing to their rapid spread across intermediary hosts (i.e., bats) [11] up to the final host (i.e., humans) [12, 13]. On December 31, 2019, a series of unexplained 27 pneumonia cases were recorded in Wuhan city, China. Given the commercial nature of Wuhan, as the main transportation center in central China, it is considered one of the most over crowded cities with a population exceeding 11 million [14]. Pathologically, these patients suffered from dry cough, dyspnea, myalgia, fever, and bilateral lung infiltrates. Whereas the less common symptoms are headache, sputum production, hemoptysis,

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and diarrhea [15]. A temporary name was originally given to this coronavirus as 2019-novel coronavirus (2019-nCoV) and was subsequently named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses (ICTV) [16]. World Health Organization (WHO) named this newly identified flu-like β -coronavirus as COVID-19 and on January 30, 2020 WHO declared that COVID-19 outbreak as “public health emergency of international concern” and a pandemic on March 11 [17, 18]. Until May 8, 2020, a total of 3,759,967 cases of COVID-19 have been confirmed in globally including 259,474 deaths. Figure 1 presents an illustration of the COVID-19 spread worldwide from 30 December 2019 through May 8, 2020. The major aim of this review is to provide a prompt, and valuable reference guides about COVID-19. Some important questions will be addressed, such as, its origin, transmission, clinical symptoms, diagnosis, environmental aspects, and the possible indoors and outdoors airborne transmission minimization strategies.

Structure of coronavirus (SARS-CoV)

Typically, SARS-CoV comprises four variable types of proteins including spike (S) protein, envelope (E) protein, nucleocapsid (N) protein, and membrane (M) protein (i.e., accessory proteins, RNA polymerase, papain-like protease, helicase, 3-chymotrypsin-like protease, and glycoprotein) [19] as presented in Fig. 2a. The S protein plays a major role in infecting the host body as it binds with the host’s receptors, reach the target cells, and consequently initiate the infection process. Despite the structural variations of S protein’s amino acids between SARS and COVID-19, the latter can cling to the human angiotensin-converting enzyme 2 (ACE2), representing the same host’s receptors of SARS [20]. Figure 2b shows the linear ssRNA(p) genome of SARS-CoV2 [21].

Transmission and spread of COVID-19

Unfortunately, few studies were published up till now to clarify the pathophysiological characters of COVID-19 and its mysterious spread mechanism. The current exceptions are largely derived from the similar CoVs transmissibility behaviors, which are based on human-to-human transmission scenario [22]. In general, respiratory viruses are most contagious when the patient is symptomatic; however, some studies demonstrate the possibility of SARS-CoV-2 transmission during the asymptomatic incubation period, i.e., between 1 and 14 days [23–25]. The common transmission ways of SARS-CoV-2 include contact transmission (i.e., oral, nasal, and eye mucous membranes), and direct transmission (i.e., cough, sneeze, and droplet inhalation) [26].

CONTACT TRANSMISSION can occur by skin-to-skin contact with an infected person, or by touching contaminated items from a patient’s room (i.e., fomites, equipment, telephones, countertops, and bed sheets, etc.). The risk of contact transmission increases if a person exposed to wound drainage, secretions, or fluids (i.e., vomitus, diarrhea, etc.) of an infected person. Some of the notable pathogens transmitted by contact include MRSA, CRE (carbapenem-resistant enterococcus), SARS, and MERS [27].

DIRECT TRANSMISSION can occur when people with certain infections talk, laugh, cough, sneeze, and/or sing in the presence of others. There are two main types of direct transmission: droplet and airborne [27]. DROPLET TRANSMISSION occurs when an infected person is coughed, sneezed, or spoken, which in turn creates contaminated droplets that can reach other persons’ eyes, nose, and/or mouth. These droplets are quite large, not long suspended in the air and settle down rather fast [28]. Simply placing a disposable mask on the patient reduces infection transmission to healthcare workers [29]. Droplet-borne diseases are influenza, meningococcal disease, mycoplasma, whooping

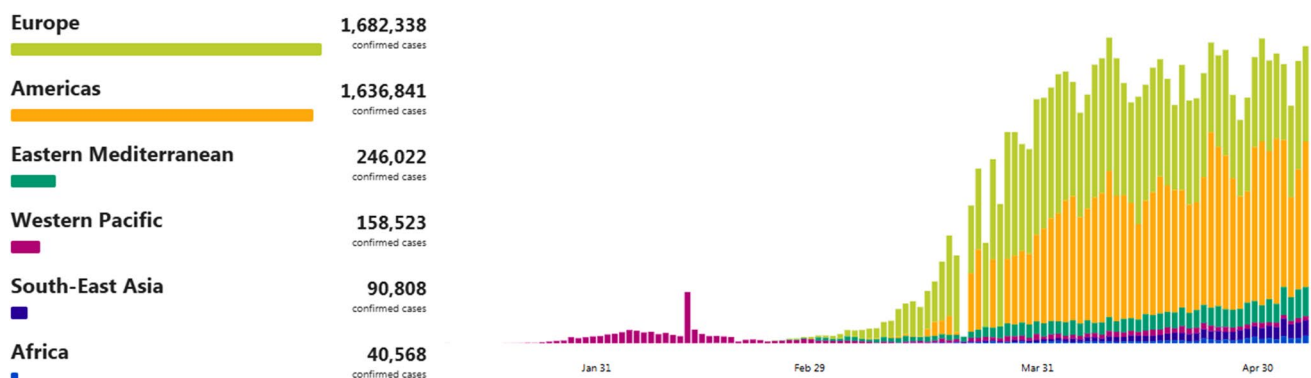


Fig. 1 Illustration of global confirmed COVID-19 cases from 30 December 2019 through May 8, 2020. (Reproduced from [95])

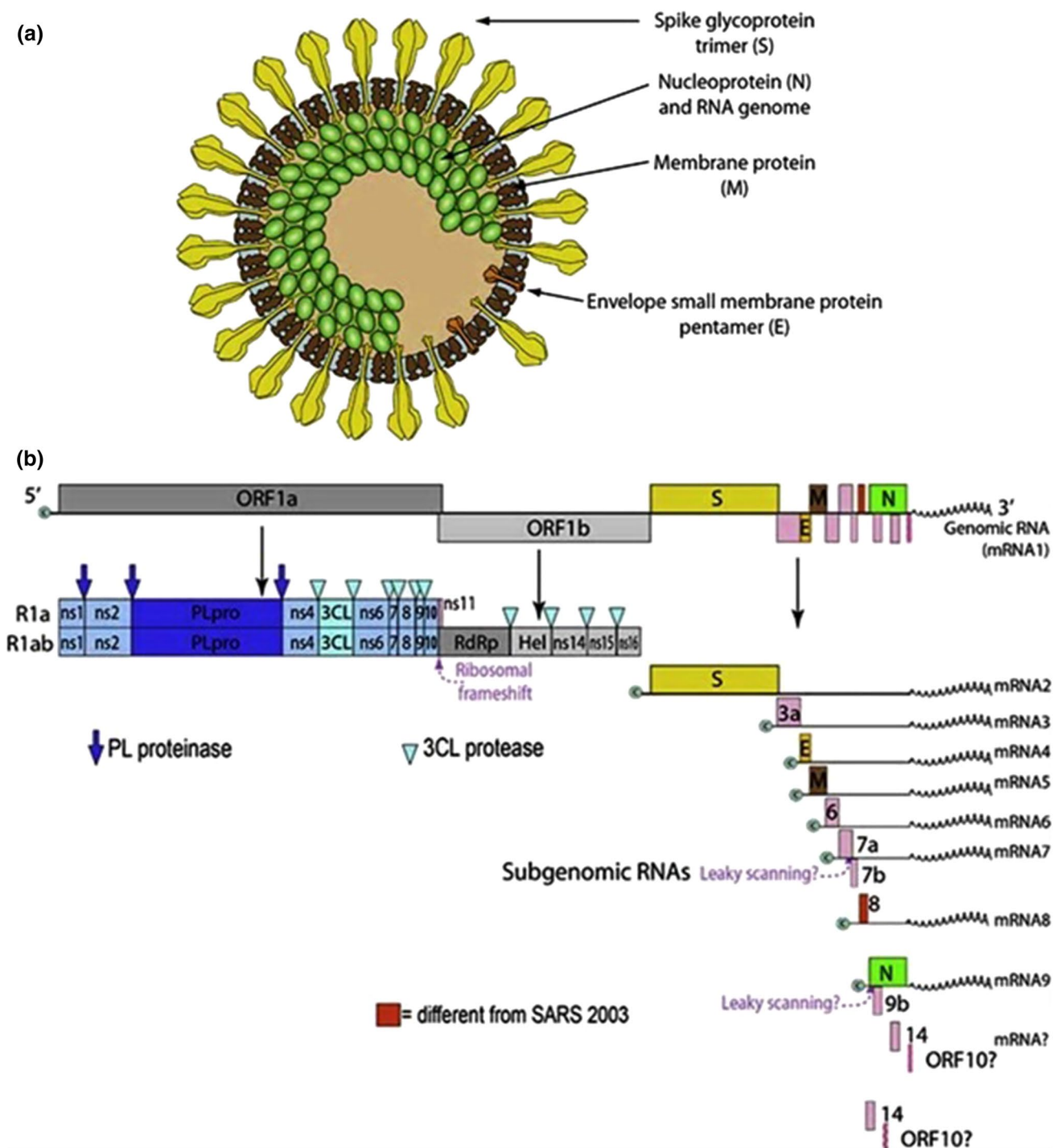


Fig. 2 a Schematic illustration of SARS-CoV-2 structure. It has four structural proteins, S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and

the S, E, and M proteins together create the viral envelope; b genome structure of SARS-CoV-2. (Reproduced from [21])

cough, rubella, and mumps [27]. AIRBORNE TRANSMISSION refers to situations where small droplets and/or dust particles containing the pathogen may remain suspended in the air for long (2 h or more) and can travel a much greater distance from the patient [28]. Furthermore, the samples

of conjunctiva obtained from confirmed and suspected COVID-19 cases showed that its spread is not limited to the respiratory tract [30]. Eye exposure may be considered as a way of getting infected with viruses as well [31]. Other study stated that the susceptibility of SARS-CoV-2

to transmit directly and/or indirectly through saliva during medical procedures [32]. Moreover, SARS-CoV-2 was detected in fecal swabs of patients, indicating the possibility of fecal–oral route transmission [33–35]. The risk related to dental care settings is invariably not less than the mentioned routes referring to its procedures specificity involving face-to-face communication with patients and frequent contact with saliva, blood, and other fluids [36–38]. Figure 3 shows a hypothesized origin of the virus and a generalized path of transmission of the epidemic zoonotic coronavirus.

Patient evaluation and clinical symptoms of COVID-19

First of all, the proper identifying of a suspected COVID-19 case represents a suitable route to distinguish between doubt and certainty. If anyone has fears to be infected with SARS-CoV-2, the first thing they should do is to go to the nearest local health care center where the medical representative should do the following scenario; the body temperature should be examined by a contact-free forehead thermometer. Then, a questionnaire should be given to the patient, which would include some typical questions like the following: (1) In the past fortnight, did you have or experience a fever? (2) Have you recently experienced respiratory problems, such as a cough or difficulty in breathing within the past fortnight?

(3) In the past fortnight, have you travelled to Wuhan city or its surroundings, or visited any area with documented COVID-19 transmission? (4) Have you physically contacted with a COVID-19 patient within the past fortnight? (5) In the past fortnight, have you physically contacted with people who come from Wuhan city or its surroundings, or people from areas with recently documented fever or respiratory problems? (6) In the past fortnight, were there at least two people with documented experience of fever or respiratory problems having close contact with you? (7) Have you recently attended meetings, gatherings, or had close contact with many people? [26]. The body temperature will be the controlling parameter in these conditions. If a person replies “yes” to any question and their body temperature is below 37.3 °C, the physician can postpone the treatment until 14 days after the exposure. The person should be instructed to self-quarantine at home and report any fever experience to the local health department. If a person replies “yes” to question and their body temperature is over 37.3 °C, they should be immediately quarantined. If a person replies “no” to all questions, and their body temperature is below 37.3 °C, the physician can treat them with extra-protection measures and avoids spatter or aerosol-generating procedures to the best [26].

The Center for Disease Control and Prevention (CDC), and the World Health Organization (WHO) have distributed a brief on important clinical conclusions regarding the SARS-CoV-2 infection [39] (Table 1). The clinical

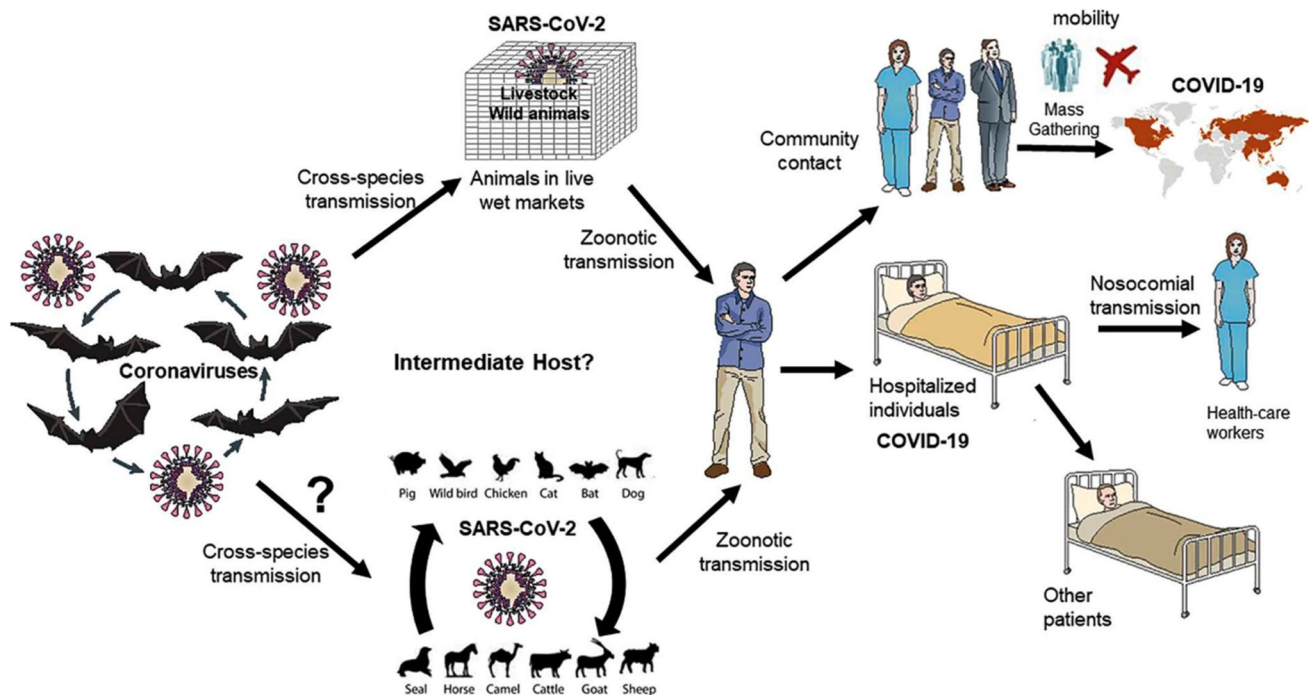


Fig. 3 A hypothesized origin of the virus and a generalized route of transmission of the epidemic zoonotic coronavirus [52]

Table 1 A comparison of CDC versus WHO symptoms

	CDC	WHO
Clinical features	<p>People with COVID-19 have had a wide range of symptoms reported ranging from mild symptoms to severe illness</p> <p>These symptoms may appear 2–14 days after exposure to the virus:</p> <p>Fever—cough—shortness of breath or difficulty breathing—chills—repeated shaking with chills—muscle pain—headache—sore throat—new loss of taste or smell</p>	<p>Acute respiratory infection (ARI)—fever or measured temperature $\geq 38\text{ }^{\circ}\text{C}$—cough—onset within the last ~10 days—requires hospitalization</p>

symptoms include dry cough, diarrhea, vomiting, fever, and myalgia. Some patients may have other complications including; acute respiratory distress syndrome, acute heart injury, and secondary infection with bacteria [15]. However, cases may be asymptomatic or even without fever [40]. Based on 1099 cases, Guan et al. [41] team found that the common clinical signs included headache (13.6%), sore throat (13.9%), shortness of breath (18.6%), sputum production (33.4%), fatigue (38.1%), cough (67.8%), and fever (88.7%). These findings have been supported by a meta-analysis study involved 3600 patients and found that fever (83.3%), cough (60.3%), and fatigue (38.0%) were the most common clinical symptoms [42]. Furthermore, a number of patients had gastrointestinal symptoms, with vomiting (5.0%), and diarrhea (3.8%). The clinical signs matched the data of 41.99 patients in Hubei province. Cough and fever were the main signs, while gastrointestinal signs were rare, reflecting the differences in the virus tropism compared to SARS, MERS, and influenza [43]. Cases of aged people and those with chronic disorders like diabetes, hypertension, cardiovascular disease, or chronic obstructive pulmonary disease were quickly developed into acute respiratory distress syndrome, septic shock, metabolic acidosis, and coagulation dysfunction, leading to unavoidable death [30].

Diagnosis of COVID-19

The Institute of Virology in China has done preliminary classification of the SARS-CoV-2 through Koch’s postulates and observed its morphology through electron microscopy [14]. When the SARS-CoV-2 genetic sequence was published, the national laboratory networks in Japan, Singapore, and Hong Kong initiated diagnostic tests [44]. The clinical diagnostic method known so far is nucleic acid detection in the throat and nasal swab sampling by real-time PCR [3]. Patients with suspected infection may present an elevated C-reactive protein, erythrocyte sedimentation rate, lactate dehydrogenase, creatinine, prolonged prothrombin time, and lymphopenia has been associated with severe cases. Additionally, chest X-ray (CXR) imaging generally shows bilateral infiltrates, ground glass opacities in the lungs of infected patients [45]. Furthermore, the full genomic sequencing from bronchoalveolar lavage fluid can confirm SARS-CoV-2 infection [46]. Efforts are still exerted to reach a vaccine that is hoped to be an essential tool to contain this epidemic [47].

Guangdong Second Provincial General Hospital plans to integrate artificial intelligence image recognition in order to improve the accuracy of immediate detection [48]. Moreover, Chinese experts relied on the IoT-aided diagnosis. The ultimate goal is to diagnose COVID-19 at an early stage and to improve its treatment by applying medical technology. This

could help in reducing disease transmission and physician infection [49].

Minimization of COVID-19 outbreak

To confront this sudden public health crisis, and to reduce the complications and death rate, CDC and WHO have pointed out guiding advice on preventing further spread of COVID-19 [50, 51]. Basically, the CDC defines standard precautions as common-sense utilization of practices, and personal protective equipment (PPE) to seize the spread of infection. These practices include proper patient isolation, cough etiquette, proper handling and cleaning of patient equipment, laundry, and so forth [50]. Basic hygiene measures are highly recommended as well, like frequent hand washing and the use of PPE such as face masks (N95 and 3M respirators) [52]. Systematically, we can divide the prevention plan into three stages to reduce the risk of the new COVID-19 as follow [52, 53]:

- (i) Reducing the danger of transmission from the natural host. This necessitates more awareness of the natural environment of the virus. Similarly, it is important to consider transmission dangers when new interactions occur, e.g., when human residences extend into bat habitats. Finally, important social measures are conveying the message to the public that interactions with bats should be avoided (based on disease ecology knowledge).
- (ii) Reducing the danger of transmission from the intermediate host. Basically, such danger could be evaded through entirely isolating bats away from the intermediate host. However, this may be more or less difficult based on the virus intermediate hosts(s). Live-animal markets play a central role in this route, and they need to be strictly addressed. However, the cultural context of these markets should be wisely considered.
- (iii) Reducing the human-to-human transmission. This is obviously a vital measure to seize the current outbreak.

While much can be collected from our general understanding of corona virus biology and some early studies on SARS-CoV-2, many pertinent questions still exist, which will be outlined here.

What were the necessary steps organizations have taken?

The international response of governments across the globe has adopted extreme procedures to curb the outbreak of COVID-19. First, travel restrictions to China were declared, and people returning/evacuated from China were being examined, isolated,

and tested for COVID-19 for 2 weeks [22]. With the rapid spread of the virus globally, these travel restrictions have been extended to other countries as well [1]. For instance, Italy, Greece, and the Czech Republic have recently suspended issuing visas [54]. US airlines have suspended their flights till early spring as well [55]. The WHO is currently recommending local exit screening by healthcare professionals at airports [56]. Several countries worldwide (Australia, Thailand, Japan, India, Italy, UK, USA, and Singapore) have initiated temperature and symptom screening protocols and quarantining citizens who have been recently evacuated from Wuhan [57–60]. Additionally, some countries have banned public gatherings to seize the spread of the virus. France has banned crowds of more than 1000 to contain coronavirus [61], and Saudi Arabia has temporarily stopped religious pilgrims (both foreign and local) from visiting Mecca and Medina [62]. Spain and Italy have declared the entire country in quarantine; travel and all commercial activities have been halted, except for pharmacies and food shops [63]. Germany has closed its borders in coordination with other EU countries. Canada has enacted varying measures; Alberta had indefinitely closed child daycares and schools, and Quebec had announced the closure of all public and private entertainment facilities, while Ontario banned jail visits and postponed court trials. Iran has released 85,000 prisoners as a precautionary measure [64].

Other countries have fought back coronavirus without such strict procedures. South Korea, for instance, has reported confirmed infections decrease from 909 persons on February 29–74 on March 16. The success of their strategy relied on a well-structured testing process, along with exerted efforts to separate infected people, trace their contacts, and quarantine them. By March 16, South Korea had tested more than 270,000 persons [65].

The Egyptian government hastened the exerted efforts to curb the spread of the virus. The authorities have declared a nationwide curfew from 7 p.m. till 6 a.m., and the suspension of all governmental services except for health care services [66]. In mid-March, Egypt suspended international flights to and from the country and returned Egyptians locked in other countries who could not return home after imposing the travel ban. Those who returned were quarantined to protect them, their families, and the society at large. The authorities also closed schools and universities, banned mass gatherings, and temporarily paused communal prayers at mosques and churches [67].

What were the positive (economic/medical) steps against the COVID-19 disaster?

In less than a 2-week period, a 1 billion Chinese finance fund was used to build two new hospitals in Wuhan [68]. The EU collected a €10,000,000 research fund to contribute to more efficient clinical management of infected

patients [69]. Some important medical companies, such as, Co-Diagnostics, the Novacyt's molecular diagnostics division, and Primerdesign Ltd., have launched COVID-2019 testing kits for use in the research studies [70, 71]. In order to help in the development of vaccine, the UK government has assigned a budget of £20,000,000 [72].

The Egyptian government has followed a number of procedures, such as the allocation of EGP 1 billion to finance the COVID-19 response plan, as well as sending medical aids and food to a number of countries haunted by the pandemic, like Italy, China, Lebanon, and the Gaza Strip [67].

In the absence of a specific antiviral drug, anecdotal use of drugs like protease inhibitors lopinavir/ritonavir, hydroxychloroquine, and azithromycin as an RNA polymerase inhibitor as well as remdesivir, favipiravir, ribavirin, and interferon-1 beta has been reported. The other antibiotics worth mentioning are glycopeptides and teicoplanin which were used to prevent the entry of Ebola envelope pseudo-typed viruses into the cytoplasm. These antibiotics have an inhibitory effect on transcription/replication of competent virus-like particles with low micromolar range [73]. SARS-CoV-2 receptor binding site has a strong affinity with angiotensin-converting enzyme 2 (ACE2) and using inhibitors of the rennin angiotensin system may have a great role in treating severe respiratory disease [74, 75]. Similarly, zinc nanoparticles were shown to have inhibitory effects on H1N1; however, their effect on COVID-19 still needs more evaluation [76]. Vitamin C supplementation has some role in the prevention of pneumonia; yet, its effect on COVID-19 is still unknown [77]. Furthermore, the usage of traditional Chinese herbs has been recommended in the Chinese guidelines [47]. It has been reported that Ivermectin, a previously FDA-approved anti-parasitic drug, can act as an inhibitor of SARS-CoV-2 in vitro in Vero-hSLAM cells. Thus, Ivermectin needs further research on possible benefits in vivo [78]. However, more clinical studies are still required before these drugs are used in the battle against SARS-CoV-2. As a last resort, Convalescent plasma—or immunoglobulins—has been used to improve the survival rate of patients with deteriorated conditions [79]. Probably, this is because the immunoglobulin antibodies in the plasma of patients recovering from viral infection might suppress viremia [73].

What can be done to protect the life of the doctors treating COVID-19 infected persons?

To prevent the transmission of the infection to others, and to ensure the continuity of care-providing, it is fundamental to protect healthcare workers. Other transmission modes, such as airborne, are likely given the virus is found in higher

concentrations in the lungs than the upper respiratory tract [80]. Therefore, gasmasks were recommended during the 2002–2003 outbreak of SARS [81].

Droplet particles are larger than those exhibiting airborne transmission; thus, keeping a distance of at least 6 feet away from the patient may be sufficient. Though negative pressure rooms are not necessary, patients should be quarantined in single rooms. The surfaces and equipment should be decontaminated regularly. Airborne transmission safety measures should be followed during aerosol-generating processes [1]. A recent study stated the presence of coronavirus in anal swabs from infected patients, and the possibility of transmission through the fecal–oral route [35]. Therefore, personal protective equipment (PPE), including N95 respirators, protective suits, goggles, gloves, caps, and face shields, should be offered to medical staff and healthcare providers who are working at the frontlines [27].

Vulnerable healthcare ancillary staff (such as nursing assistants, cleaners, food service workers, ambulance drivers, medics, and techs/aids who help move patients onto stretchers) should wear all the above-recommended PPE [27].

Intra-hospital and inter-hospital transfer of patients may be required; therefore, accompanying staff must wear PPE [82]. In addition, clinicians should exercise caution if an aerosol-generating procedure, such as bag valve mask (BVM) ventilation, oropharyngeal suctioning, endotracheal intubation, or nebulizer treatment is necessary [27]. Though a confirmed SARS-CoV-2 patient is rare to be treated in the dental clinic, the dentist, who by default cannot avoid close contact with the infected patient, should wear special protective attire. In addition to the PPE, a coat with extra one-use protective clothing, disposable doctor cap, and impermeable shoe cover should be worn [26].

Guangdong Second Provincial General Hospital outlined an advanced infection control system to provide real-time monitoring and to avoid nosocomial infection [83]. All infection control observers have been trained to become familiar with the infection-control requirements in the isolation zones. They monitor medical staff in the actual time via computer monitors in a separate area using cameras that cover the entire zone except for the privacy area. The main responsibilities of the observer are to maintain the operation of the isolation zones, supervise the procedure of disinfection, ensure a sufficient supply of protective supplies, prepare specimens for examination and observe the care provider during treating patients and also while wearing or taking the PPE off when entering or leaving the zone [48].

COVID-19 in the environment

La Rosa et al. reviewed research data on SARS-CoV-2 in water environments [21]. The available data suggested that: (i) SARS-CoV-2 appears to have low environmental stability

and is highly sensitive to oxidants, such as chlorine; (ii) SARS-CoV-2 appears to be inactivated significantly faster in water than non-enveloped human enteric viruses with known waterborne transmission; (iii) Temperature is an important factor affecting viral survival (the titer of infectious virus decreases more rapidly at 23–25 °C compared to 4 °C; (iv) there is no current evidence that SARS-CoV-2 is present in surface or groundwater or is transmitted through contaminated drinking water [21].

The knowledge about the nature and evolution of the SARS-CoV-2 virus in water, soils, and other environmental compartments can be addressed through wastewater and sewage sludge [84]. Several studies have shown the advantages of environmental surveillance by controlling sewage for the evaluation of viruses that circulate within a specific population (wastewater-based epidemiology; WBE) [85, 86]. Concentrations of the Covid-19 genetic material in wastewater samples collected every week accurately reflect the infection in the watershed, suggesting that this approach can serve as a warning of a public outbreak. Cheaper and faster monitoring tools need to be developed to detect Covid-19 in wastewater by biosensors, chemical sensors or paper-based indicator methods. This will allow revealing true scale of Covid-19 outbreak associated with population link to a specific wastewater treatment plant. COVID-19 virus may be shed into wastewater at insufficiently high rates, and that both the virus itself and its RNA may be too labile to facilitate detection in wastewater.

Can a paper-based device trace COVID-19 sources with WBE?

The analysis of the genetic material of COVID-19 virus in wastewater could give warning of an epidemic outbreak. Recent analysis carried out by Water Quality and Health Department of the Italian National Institute of Health (ISS) examined eight samples of wastewater collected from February 3 to 28 in Milan and from March 31 to April 2 in Rome [87]. The presence of COVID-19 RNA has been confirmed in two of the sewage system samples collected in the western and central-eastern area of Milan. While the integrated water cycle, which includes water purification and sewage, is certainly safe and controlled for this virus and other pathogens as stated in a recent ISS report, the presence of COVID-19 in wastewater has made it possible to use urban sewage systems as a noninvasive tool for early detection of virus spread [84].

In Paris, on April 19, traces of COVID-19 were found in the non-drinkable street cleaning water. Time course quantitative analysis (PCR) was performed in 23 raw and eight treated wastewater samples from three major treatment plants, from 5 March to 7 April 2020 [88]. All raw wastewater samples proved positive for SARS-CoV-2, as did six of eight samples from treated wastewater. The viral

load of treated wastewater was 100 times less than that of raw wastewater. Drinking water, separately treated, had no traces of the virus [88]. These data confirm that WBE has the potential to be applied to SARS-CoV-2 as a sensitive tool to study spatial and temporal trends of virus circulation in the population.

This environmental surveillance data can be compared to declare COVID-19 cases at municipality level, revealing that members of the community were shedding SARS-CoV-2 RNA in their stool even before the first cases were reported by local or national authorities in many of the cities where wastewaters have been sampled. The estimated viral RNA copy numbers observed in the wastewater can be used to estimate the number of infected individuals in the catchment via Monte Carlo simulation.

The WBE approach to testing for COVID-19 has potential advantages over testing the public. First, virus concentrations in wastewater represent the overall status of the watershed, while the number of COVID-19 cases involving infected people is possibly biased. Testing of the public seldom involves complete enumeration or even randomized sampling, because these sampling methods tend to overwhelm or collapse the medical care system, have the disadvantage of false-positives, and are time and labor intensive. The WBE approach is effective in identifying temporal changes in the infection status in the watershed without selection bias. Its second advantage relates to the issue of the stigma that can result from an outbreak. Infected people, or those diagnosed with a false-positive, together with their families, are potentially harmed by stigma and discrimination as well as social isolation [89]. Moreover, WBE minimizing domino effects such as unnecessarily long stay-at-home policies that stress humans and economies alike. WBE measures chemical signatures in sewage, such as fragment biomarkers from the severe acute respiratory syndrome from SARS-CoV-2, simply by applying the type of clinical diagnostic testing (designed for individuals) to the collective signature of entire communities.

The disadvantages of WBE approach are incomplete enumeration or randomized sampling of the entire population. So far, WBE may not have been preferred due to potential regional stigma; however, WBE has proved its value by avoiding individual stigmatization. By contrast, in the current context of a worldwide outbreak of COVID-19, details of the number of cases in a particular region, and sometimes identifying details of infected individuals, are already being broadcast.

How can airborne transmission of COVID-19 indoors be minimized?

The effect of weather on COVID-19 spread is poorly understood. Recently, few studies have claimed that warm weather may possibly slowdown the global pandemic.

It is essential to know the environmental parameters within which the severe acute respiratory syndrome SARS-CoV-2. The results of Huang et al. (2020) showed that 60.0% of the confirmed cases of SARS-CoV-2 occurred in places where the air temperature ranged from 5 to 15 °C, with a peak in cases at 11.54 °C [90]. Moreover, approximately 73.8% of the confirmed cases were concentrated in regions with absolute humidity of 3 to 10 g/m³. SARS-CoV-2 appears to be spreading toward higher latitudes. These findings suggest that there is an optimal climatic zone in which the concentration of SARS-CoV-2 markedly increases in the ambient environment (including the surfaces of objects). These results strongly imply that the COVID-19 pandemic may spread cyclically and outbreaks may recur in large cities in the mid-latitudes in autumn 2020 [90].

Biktasheva proposed that a habitat's air humidity negatively correlate with Covid-19 morbidity and mortality and supported this hypothesis on the example of publicly available data from German federal states [91].

Inhaling small airborne droplets is probable as a route of infection, in addition to more widely recognized transmission via larger respiratory droplets and direct contact with infected people or contaminated surfaces [92]. While uncertainties remain regarding the relative contributions of the different transmission pathways, we argue that existing evidence is strong enough to warrant engineering controls aimed at airborne transmission as part of a comprehensive indoor infection risk reduction strategy. Suitable building engineering controls include adequate and effective ventilation, possibly enhanced by particulate filtration and air disinfection, avoiding recirculation of air and avoiding overcrowding. These interventions can also be introduced quickly and at no expense, but only if they are regarded as important in contributing to the objectives of infection control. We believe that the use of engineering controls in public buildings, including hospitals, schools, restaurants, kindergartens, shops, libraries, offices, conference, cruise ships, elevators, rooms or public transport, in parallel with the effective application of other controls (including isolation and quarantine, social distance, and hygiene of hands) would be an additional significant global measure to reduce the risk of transmission and thereby shielding healthcare staff, patients, and the general public.

How to increase the global awareness?

Governments and public health authorities alone cannot succeed in combating the outbreak. People need to protect themselves and others from COVID-19 by following public health advice, adopting the suggested preventive measures, and complying with the guidance issued by health authorities [63]. Testing and isolating of the infected and their

recent contacts are considered one way to solve the problem of the outbreak. The population should be properly educated of who to isolate themselves to help them to deal with the matter when got infected [65]. In addition to the exerted efforts to battle the disease, special attention should be paid to the mental health issues of the community. Screening of psychiatric disorders including anxiety, depression, and mental stress among patients and the medical staffs are vital to ensure the stable psychological status quo [93]. Governments should provide health care services to patients without health insurance benefits. The government can create a hotline for citizens to report suspected coronavirus cases and to provide medical advice via specialized doctors for non-emergency cases. Community organizations that deal with anyone experiencing food, medication, or housing insecurity should receive additional governmental support. Employment rights, including paid sick-leave policies, should be applied for the individuals who act in the interest of communal health to support themselves and their families [94].

Compared with the SARS outbreak, the international response to COVID-19 was more straightforward and effective. However, some learnings points should be taken into consideration in case of future COVID-19 outbreaks (Table 2).

Conclusion

In the last 3 months, a viral infectious disease namely COVID-19 has emerged and quickly spread all over the world. It is a fatal disease that is turned out to be a massive load on the global health systems. COVID-19 infection is not limited to vulnerable persons (i.e., children, health care providers, and the elderly), but it can infect the youth as well. Therefore, combating this epidemic requires robust and rigorous protocols to curb its accelerated transmission. Considering the absence of an approved and effective vaccine for COVID-19 up till now, epidemiological changes, such as, transmissibility, pathogenicity, phylogeny, clinical manifestation, diagnosis, and fatality rate, should be cautiously observed. Most of the countries around the world have adopted effective control and preventive measures, like stopping domestic and international flights, and nationwide curfew, so as to face the viral spread. To sum up, with the current status of this pandemic, more scientific investigations are carried out to reduce its deadly consequences. The detection of SARS-CoV-2 in wastewater in early stages of the spread of COVID-19 highlights the relevance Wastewater-based epidemiology (WBE) approach as an early indicator of the infection within a specific population. International cooperation between environmental researchers, wastewater workers, and public health specialists is suggested, aimed at preventing the spread of COVID-19. Surprisingly, this tool

Table 2 A tabular presentation of the issues of the current response verses lessons to be learned from COVID-19 outbreak [22]

Issues with the current response	Event	Consequence	Key learning points
Lack of transparency	Intimidation of clinicians who initially identified COVID-19	Delay in the release of information pertaining to COVID-19 cases	Establish clear whistleblowing policies for possible global health emergencies
Travel restriction delay	Aviation services operated for over a month following the initial outbreak with minimal health screening at international borders	Citizens traveling from high-risk areas were able to freely pass through large airports without a health screening	Precautions such as screening citizens returning from high-risk countries should be implemented earlier
Quarantine delay	On 31 December 2019, the first report of COVID-19 was released. Wuhan began to quarantine on 23 January 2020, nearly a month later	Allowed individuals potentially infected with COVID-19 to spread the infection both nationally and internationally	Quarantine high-risk areas as soon as a possible health threat is identified
Public misinformation	Lack of transparency allows rumors, speculation, and misinformation to be spread among the public	Racism, incorrect public precautions, and unprecipitated fear surrounding COVID-19	Transparency and open access to all information are essential to avoid misinformation
Emergency announcement delay	Public Health Emergency of International Concern declared by WHO on 30 December 2019, a month following the initial outbreak	The severity of the outbreak was not widely broadcasted or acknowledged. This may have delayed containment measures	A framework should be developed for fast-spreading diseases in order to escalate a threat status earlier
Research and development	Lack of funding in initial stages of research and development of vaccine and treatment of COVID-19	Over 3000 patients worldwide have died due to COVID-19, and the death toll continues to rise weekly	Further investment is required to produce effective treatments and to establish robust methods to contain future outbreaks of communicable diseases

has not been widely embraced by epidemiologists or public health officials.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

References

- Singhal T (2020) A review of coronavirus disease-2019 (COVID-19). *Indian J Pediatr* 87:281–286
- Yin Y, Wunderink RG (2018) MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology* 23:130–137
- Guo Y-R, Cao Q-D, Hong Z-S et al (2020) The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—an update on the status. *Mil Med Res* 7:1–10. <https://doi.org/10.1186/s40779-020-00240-0>
- Vabret A, Mourez T, Gouarin S et al (2003) An outbreak of coronavirus OC43 respiratory infection in Normandy, France. *Clin Infect Dis* 36:985–989. <https://doi.org/10.1086/374222>
- Zhong NS, Zheng BJ, Li YM et al (2003) Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. *Lancet* 362:1353–1358. [https://doi.org/10.1016/S0140-6736\(03\)14630-2](https://doi.org/10.1016/S0140-6736(03)14630-2)
- Gerna G, Campanini G, Rovida F et al (2006) Genetic variability of human coronavirus OC43-, 229E-, and NL63-like strains and their association with lower respiratory tract infections of hospitalized infants and immunocompromised patients. *J Med Virol* 78:938–949. <https://doi.org/10.1002/jmv.20645>
- Gerna G, Percivalle E, Sarasini A et al (2007) Human respiratory coronavirus HKU1 versus other coronavirus infections in Italian hospitalised patients. *J Clin Virol* 38:244–250. <https://doi.org/10.1016/j.jcv.2006.12.008>
- Vabret A, Dina J, Gouarin S et al (2008) Human (non-severe acute respiratory syndrome) coronavirus infections in hospitalised children in France. *J Paediatr Child Health* 44:176–181. <https://doi.org/10.1111/j.1440-1754.2007.01246.x>
- Owusu M, Annan A, Corman VM et al (2014) Human coronaviruses associated with upper respiratory tract infections in three rural areas of Ghana. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0099782>
- Lim Y, Ng Y, Tam J, Liu D (2016) Human coronaviruses: a review of virus–host interactions. *Diseases* 4:26. <https://doi.org/10.3390/diseases4030026>
- Woo PCY, Lau SKP, Lam CSF et al (2012) Discovery of seven novel mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. *J Virol* 86:3995–4008. <https://doi.org/10.1128/jvi.06540-11>
- Birmingham A, Chand MA, Brown CS et al (2012) Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012. *Eurosurveillance*. <https://doi.org/10.2807/ese.17.40.20290-en>
- Zaki AM, Van Boheemen S, Bestebroer TM et al (2012) Isolation of a novel coronavirus from a man with pneumonia in Saudi

- Arabia. *N Engl J Med* 367:1814–1820. <https://doi.org/10.1056/NEJMoa1211721>
14. Lu H, Stratton CW, Tang YW (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. *J Med Virol* 92:401–402
 15. Chen N, Zhou M, Dong X et al (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 395:507–513. [https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)
 16. Gorbalenya AE, Baker SC, Baric RS et al (2020) The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* 5:536–544
 17. World Health Organisation (WHO) (2020) Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). WHO, Geneva, pp 1–6
 18. World Health Organisation (WHO) (2020) WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020. WHO Dir Gen speeches 4
 19. Chen Y, Liu Q, Guo D (2020) Emerging coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol* 92:418–423
 20. Wu A, Peng Y, Huang B et al (2020) Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. *Cell Host Microbe* 27:325–328. <https://doi.org/10.1016/j.chom.2020.02.001>
 21. Rosa GL, Bonadonna L, Lucentini L et al (2020) Coronavirus in water environments: occurrence, persistence and concentration methods—a scoping review. *Water Res* 179:115899
 22. Sohrobi C, Alsafi Z, O'Neill N et al (2020) World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). *Int J Surg* 76:71–76
 23. Centers for Disease Control and Prevention (2020) How coronavirus spreads|CDC. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covidspreads.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fprepare%2Ftransmission.html. Accessed 3 May 2020
 24. Li Q, Guan X, Wu P et al (2020) Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 382:1199–1207
 25. Rothe C, Schunk M, Sothmann P et al (2020) Transmission of 2019-NCOV infection from an asymptomatic contact in Germany. *N Engl J Med* 382:970–971
 26. Peng X, Xu X, Li Y et al (2020) Transmission routes of 2019-nCoV and controls in dental practice. *Int J Oral Sci* 12:9
 27. Holland M, Zaloga DJ, Friderici CS (2020) COVID-19 personal protective equipment (PPE) for the emergency physician. *Vis J Emerg Med* 19:100740. <https://doi.org/10.1016/j.visj.2020.100740>
 28. Center for Disease Control and Prevention (CDC) (2016) Transmission-based precautions|basics|infection control|CDC. CDC. <https://www.cdc.gov/infectioncontrol/basics/transmission-based-precautions.html>. Accessed 5 April 2020
 29. Radonovich LJ, Simberkoff MS, Bessesen MT et al (2019) N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. *JAMA - J Am Med Assoc* 322:824–833. <https://doi.org/10.1001/jama.2019.11645>
 30. Lu CW, Liu XF, Jia ZF (2020) 2019-nCoV transmission through the ocular surface must not be ignored. *Lancet* 395:e39
 31. Belser JA, Rota PA, Tumpey TM (2013) Ocular tropism of respiratory viruses. *Microbiol Mol Biol Rev* 77:144–156. <https://doi.org/10.1128/mmb.00058-12>
 32. To KK-W, Tsang OT-Y, Chik-Yan Yip C et al (2020) Consistent detection of 2019 novel coronavirus in saliva. *Clin Infect Dis*. <https://doi.org/10.1093/cid/ciaa149>
 33. Holshue ML, DeBolt C, Lindquist S et al (2020) First case of 2019 novel coronavirus in the United States. *N Engl J Med* 382:929–936. <https://doi.org/10.1056/NEJMoa2001191>
 34. Xiao F, Tang M, Zheng X et al (2020) Evidence for Gastrointestinal Infection of SARS-CoV-2. *Gastroenterology* 158:1831–1833.e3. <https://doi.org/10.1053/j.gastro.2020.02.055>
 35. Zhang W, Du RH, Li B et al (2020) Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 9:386–389. <https://doi.org/10.1080/22221751.2020.1729071>
 36. Harrel SK, Molinari J (2004) Aerosols and splatter in dentistry: a brief review of the literature and infection control implications. *J Am Dent Assoc* 135:429–437. <https://doi.org/10.14219/jada.archive.2004.0207>
 37. Liu L, Wei Q, Alvarez X et al (2011) Epithelial cells lining salivary gland ducts are early target cells of severe acute respiratory syndrome coronavirus infection in the upper respiratory tracts of *Rhesus macaques*. *J Virol* 85:4025–4030. <https://doi.org/10.1128/jvi.02292-10>
 38. Cleveland JL, Gray SK, Harte JA et al (2016) Transmission of blood-borne pathogens in US dental health care settings: 2016 update. *J Am Dent Assoc* 147:729–738. <https://doi.org/10.1016/j.adaj.2016.03.020>
 39. Elsevier (2020) Novel coronavirus information center. Elsevier Connect, Amsterdam
 40. Center for Disease Control and Prevention (CDC) (2019) Symptoms of coronavirus|CDC. Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>. Accessed 6 May 2020
 41. Guan WJ, Ni ZY, Hu Y et al (2020) Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 382:1708–1720. <https://doi.org/10.1056/NEJMoa2002032>
 42. Fu L, Wang B, Yuan T et al (2020) Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. *J Infect*. <https://doi.org/10.1016/j.jinf.2020.03.041>
 43. Huang C, Wang Y, Li X et al (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395:497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
 44. Chan JFW, Kok KH, Zhu Z et al (2020) Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect* 9:221–236. <https://doi.org/10.1080/22221751.2020.1719902>
 45. Wang D, Hu B, Hu C et al (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan. *JAMA - J Am Med Assoc*, China. <https://doi.org/10.1001/jama.2020.1585>
 46. Zhu N, Zhang D, Wang W et al (2020) A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 382:727–733. <https://doi.org/10.1056/NEJMoa2001017>
 47. Gupta R, Ghosh A, Singh AK, Misra A (2020) Clinical considerations for patients with diabetes in times of COVID-19 epidemic. *Diabet Metab Syndr Clin Res Rev* 14:211–212
 48. Chen X, Tian J, Li G, Li G (2020) Initiation of a new infection control system for the COVID-19 outbreak. *Lancet Infect Dis* 20:397–398. [https://doi.org/10.1016/S1473-3099\(20\)30110-9](https://doi.org/10.1016/S1473-3099(20)30110-9)
 49. Bai L, Yang D, Wang X et al (2020) Chinese experts' consensus on the Internet of Things-aided diagnosis and treatment of coronavirus disease 2019 (COVID-19). *Clin eHealth* 3:7–15. <https://doi.org/10.1016/j.ceh.2020.03.001>
 50. Center for Disease Control and Prevention (CDC) (2020) How to protect yourself|CDC. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>. Accessed 8 May 2020
 51. World Health Organisation (WHO) (2020) Advice for public. WHO, Geneva

52. El Zowalaty ME, Järhult JD (2020) From SARS to COVID-19: a previously unknown SARS-related coronavirus (SARS-CoV-2) of pandemic potential infecting humans—call for a one health approach. *One Health*. <https://doi.org/10.1016/j.onehlt.2020.100124>
53. Lu J, Milinovich GJ, Hu W (2016) A brief historical overview of emerging infectious disease response in China and the need for a one health approach in future responses. *One Health* 2:99–102. <https://doi.org/10.1016/j.onehlt.2016.07.001>
54. Shengen Visa Info (2020) Italy suspends visa issuance and all air traffic from China
55. The Wall Street Journal (2020) U.S. imposes entry restrictions over coronavirus. <https://www.wsj.com/articles/u-k-reports-first-coronavirus-cases-as-china-allies-limit-ties-11580467046>. Accessed 8 May 2020
56. World Health Organisation (WHO) (2020) Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Geneva, pp 1–6
57. BBC (2020) Coronavirus: which countries have evacuated their citizens? <https://www.bbc.com/news/world-asia-china-51312378>. Accessed 8 May 2020
58. BBC (2020) Coronavirus: more Britons evacuated from Wuhan on French flight. <https://www.bbc.com/news/health-51345279>. Accessed 8 May 2020
59. The Wall Street Journal (2020) U.S. plans to evacuate more Americans by aircraft from Wuhan. <https://www.wsj.com/articles/u-s-plans-another-wuhan-evacuation-flight-as-soon-as-next-week-11580380747>. Accessed 8 May 2020
60. Phelan AL, Katz R, Gostin LO (2020) The novel coronavirus originating in Wuhan, China: challenges for Global Health Governance. *JAMA - J Am Med Assoc* 323:709–710
61. France24 (2020) France bans gatherings of more than 1000 people to contain coronavirus. *Fr. 24*. <https://www.france24.com/en/20200308-france-bans-gatherings-of-more-than-1-000-people-to-contain-coronavirus>. Accessed 8 May 2020
62. Ebrahim SH, Memish ZA (2020) COVID-19: preparing for super-spreader potential among Umrah pilgrims to Saudi Arabia. *Lancet* 395:e48
63. Purcell LN, Charles AG (2020) An Invited Commentary on “World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19)”: emergency or new reality? *Int J Surg* 76:111. <https://doi.org/10.1016/j.ijso.2020.03.002>
64. Tanne JH, Hayasaki E, Zastrow M et al (2020) Covid-19: how doctors and healthcare systems are tackling coronavirus worldwide. *BMJ* 368:m1090. <https://doi.org/10.1136/bmj.m1090>
65. Cohen J, Kupferschmidt K (2020) Countries test tactics in “war” against COVID-19. *Science* (80-.) 367:1287–1288
66. Amin S (2020) Egyptian government’s anti-virus plan met with mixed reactions. *Al-Monitor*. <https://www.al-monitor.com/pulse/originals/2020/03/egypt-coronavirus-curfew-sisi-measures-protects.html#ixzz6Ixo0qtBO>. Accessed 7 April 2020
67. Online A (2020) Egypt’s SSCHR reviews national response towards coronavirus pandemic—politics—Egypt—Ahrām Online. *Ahrām Online*. <http://english.ahrām.org.eg/NewsContent/1/64/366717/Egypt/Politics-/Egypt's-SSCHR-reviews-national-response-towards-co.aspx>. Accessed 8 April 2020
68. France-Presse A (2020) New 1000-bed Wuhan hospital takes its first coronavirus patients|World news|The Guardian. *Guard*
69. Innovation R and (2020) Coronavirus: EU mobilises €10 million for research|European Commission. *European Commission*. https://ec.europa.eu/info/news/coronavirus-eu-mobilises-eur10-million-for-research-2020-jan-31_en. Accessed 8 May 2020
70. Devices VM (2020) Co-diagnostics launches RUO test for novel coronavirus. *Verdict Medical Devices*. <https://www.medicaldevice-network.com/news/co-diagnostics-ruo-test/>. Accessed 8 May 2020
71. Devices VM (2020) Primerdesign launches new molecular test for novel coronavirus. *Verdict Medical Devices*. <https://www.medicaldevice-network.com/news/primerdesign-molecular-test-coronavirus/>. Accessed 8 May 2020
72. BBC (2020) Coronavirus: UK donates £20 m to speed up vaccine. *BBC News*
73. Jean S-S, Lee P-I, Hsueh P-R (2020) Treatment options for COVID-19: the reality and challenges. *J Microbiol Immunol Infect*. <https://doi.org/10.1016/j.jmii.2020.03.034>
74. Gurwitz D (2020) Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res*. <https://doi.org/10.1002/ddr.21656>
75. Sun ML, Yang JM, Sun YP, Su GH (2020) Inhibitors of RAS might be a good choice for the therapy of COVID-19 pneumonia. *Zhonghua Jie He He Hu Xi Za Zhi* 43:219–222. <https://doi.org/10.3760/cma.j.issn.1001-0939.2020.03.016>
76. Ghaffari H, Tavakoli A, Moradi A et al (2019) Inhibition of H1N1 influenza virus infection by zinc oxide nanoparticles: another emerging application of nanomedicine. *J Biomed Sci*. <https://doi.org/10.1186/s12929-019-0563-4>
77. Hemilä H (1997) Vitamin C intake and susceptibility to pneumonia. *Pediatr Infect Dis J* 16:836–837
78. Caly L, Druce JD, Catton MG et al (2020) The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Res*. <https://doi.org/10.1016/j.antiviral.2020.104787>
79. Chen L, Xiong J, Bao L, Shi Y (2020) Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 20:398–400
80. World Health Organisation (WHO) (2020) Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected. *WHO* 38:71–86. <https://doi.org/10.1016/j.ccm.2016.11.007>
81. McKinney KR, Gong YY, Lewis TG (2006) Environmental transmission of SARS at Amoy Gardens. *J Environ Health* 68:26–30
82. Liew MF, Siow WT, Yau YW, See KC (2020) Safe patient transport for COVID-19. *Crit Care* 24:94
83. Peng J, Ren N, Wang M, Zhang G (2020) Practical experiences and suggestions on the eagle-eyed observer, a novel promising role for controlling nosocomial infection of the COVID-19 outbreak. *J Hosp, Infect*
84. Lapolla P, Lee R, Mingoli A (2020) Wastewater as a red flag in COVID-19 spread. *Public Health* 185:26
85. Randazzo W, Truchado P, Cuevas-Ferrando E, Simon P, Allende A, Sanchez G (2020) SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area. *Water Res* 181:115942
86. Ahmed W, Angel N, Edson J et al (2020) First confirmed detection of SARS-CoV-2 in untreated wastewater in Australia: a proof of concept for the wastewater surveillance of COVID-19 in the community. *Sci Total Environ* 728:138764
87. Italian National Institute of Health (ISS). CS N 30/2020—wastewater can be an in-dicator of Covid-19 outbreaks. https://www.iss.it/web/guest/primario-piano/-/asset_publisher/o4oGR9qmvUz9/content/id/5344257. Accessed 1 May 2020 (in Italian)
88. Wurtzer S, Marechal V, Mouchel JM, Moulin L (2020) Time course quantitative detection of SARS-CoV-2 in Parisian waste waters correlates with COVID-19 confirmed cases. *medRxiv*. <https://doi.org/10.1101/2020.04.12.20062679>
89. Murakami M, Hata A, Honda R et al (2020) Letter to the editor: wastewater-based epidemiology can overcome representativeness and stigma issues related to COVID-19. *Environ Sci Technol* 54:5311

90. Huang Z, Huang J, Gu Q et al (2020) Optimal temperature zone for the dispersal of COVID-19. *Sci Total Environ* 736:139487
91. Biktasheva IV (2020) Role of a habitat's air humidity in Covid-19 mortality. *Sci Total Environ* 736(2020):138763
92. Buonanno G, Stabile L, Morawska L (2020) Estimation of airborne viral emission: Quanta emission rate of SARS-CoV-2 for infection risk assessment. *Environ Int* 141:105794
93. Zandifar A, Badrfam R (2020) Iranian mental health during the COVID-19 epidemic. *Asian J, Psychiatry*, p 51
94. Berger ZD, Evans NG, Phelan AL, Silverman RD (2020) COVID-19: control measures must be equitable and inclusive. *BMJ* 368 (2020) M No1141
95. World Health Organisation (WHO) (2020) COVID-19 situation reports. WHO. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>. Accessed 9 May 2020