

Coronavirus and other airborne agents with pandemic potential

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Abstract

The recent emergence of a novel coronavirus (severe acute respiratory syndrome coronavirus 2) has caused a pandemic, which is the most severe infectious disease outbreak in many decades. Other infective agents such as influenza as well as other neglected viruses such as Lassa virus, Nipah virus or poxviruses are also a cause for concern owing to their attack rate and potential for global spread. Drug-resistant bacteria, such as *Mycobacterium tuberculosis*, are already a significant public health issue in many countries, and it is expected that they will be expanding in the near future. Finally, airborne bioterrorism agents have high morbidity and mortality rates and should be looked with concern in the current international unrest.

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Introduction

Traditionally, the respiratory transmission of infective agents has been classified into different categories depending on the size of the inhaled particles. While airborne transmission is defined by the inhalation of small particles (<5 μm), droplet transmission involves larger

particles [1]. A further route of transmission, aerosols, is defined as the presence of solid or fluid particles in a gas, such as air. This has significant implications not only in terms of transmission prevention—larger particles tend to travel longer distances—but also in pathophysiological terms because airborne particles tend to deposit on the lung alveoli and droplet transmission tends to involve contact with mucosae [2].

Aerosol or airborne pathogens are particularly concerning owing to their high infection rate, which if linked with significant mortality rates, can lead to global health crises. The current collusion of several factors (population movements, natural catastrophes, climate change, wars, deprivation and so on) is causing a globalisation of infections and public health issues, with significant clinical, social and economic repercussions, as the current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is showing.

Coronavirus

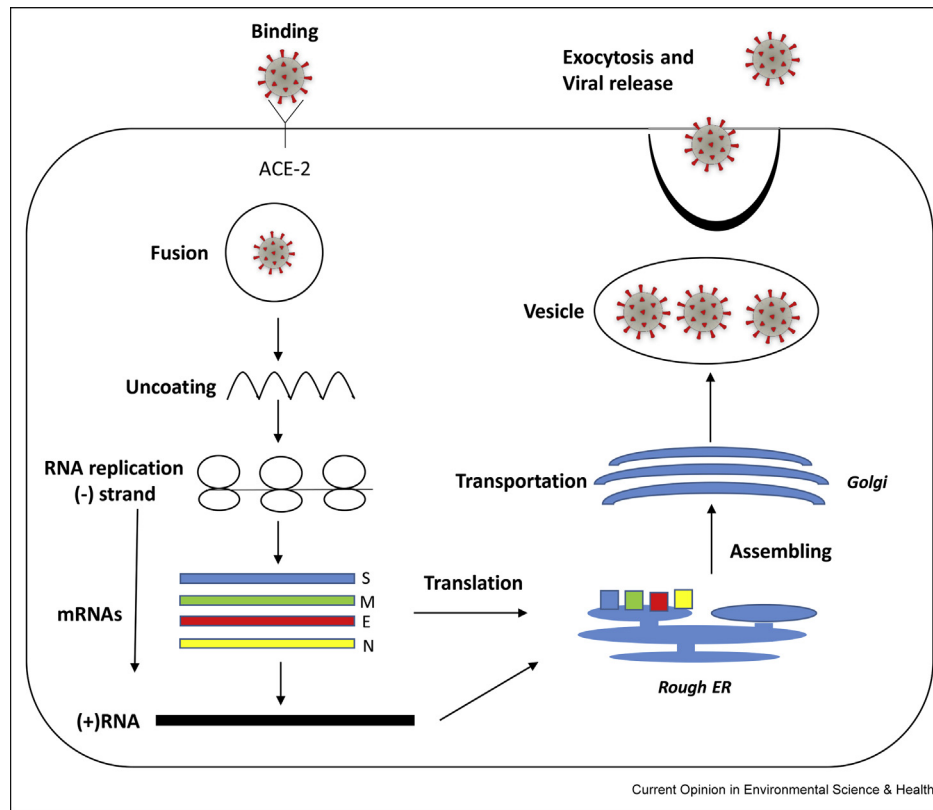
Severe acute respiratory syndrome coronavirus 2

In December 2019, an outbreak of pneumonia of unknown cause was reported in Wuhan, China. Samples from bronchial lavages in patients diagnosed with this pneumonia revealed the existence of a new beta-coronavirus (SARS-CoV-2), which is found to be the causative agent of this respiratory syndrome [3]. In March 2020, the World Health Organization declared the worldwide expansion of the SARS-CoV-2 pandemic, and as of June 2020, more than 26 million cases have been diagnosed, causing more than 800,000 deaths in 188 countries [4]. In epidemiological terms, this is the largest outbreak of an infectious disease since the 2009 H1N1 influenza pandemic [5].

Coronaviruses (CoVs) are a family of single-stranded RNA viruses, with a genome of 30 kB. Beta-CoVs have a phospholipid envelope, with several surface proteins, such as the spike, haemagglutinin esterase, nucleocapsid and the membrane proteins [6] (Figure 1). SARS-CoV-2 binds to the cell through the ACE-2 enzyme, which is used as the receptor [7].

Initial cases of SARS-CoV-2 infections, clinically named coronavirus disease 2019 (COVID-19), were linked with exposures to wet markets [9]. The genomic

Figure 1



SARS-COV-2 replication cycle. E, esterase; M, membrane; N, nucleocapsid; S, spike; SARS-COV-2, severe acute respiratory syndrome coronavirus 2; ER, Endoplasmic reticulum.

characterisation of SARS-CoV-2 showed similarities to that of two bat CoVs (bat-SL-CoVZC45 and bat-SL-CoVZXC21) and, to a lesser extent, to that of SARS-CoV and Middle Eastern respiratory syndrome coronavirus (MERS-CoV) [7]. Initial reports confirmed an early zoonotic or environmental transmission, followed by sustained person-to-person transmission in the community [8]. Further reports confirmed cluster transmission of SARS-CoV-2 [10], in keeping with droplet transmission. SARS-CoV-2 is considered to be transmitted mostly by small respiratory droplets (<5- μ m diameter), through the respiratory tract or eye mucosae after close contact (<1 m) with an infected individual [11]. Transmission through fomites has also been described because SARS-CoV-2 can remain viable and infective in droplets for over 3 h and up to 72 h on other surfaces [12]. Faecal-oral transmission has also been considered. Studies have reported positive faecal SARS-CoV-2 PCR results in 36–53% of patients [13], whereas vertical transmission [14] is less plausible because there is no solid evidence with regard to the presence of SARS-CoV-2 in amniotic fluid, cord blood or breast milk [15]. Parenteral transmission is unlikely due to the low prevalence of detectable viraemia in patients

with COVID-19 [16] along with generally low serum viral loads [17]. However, further research in this area is warranted.

SARS-CoV-2 has an incubation period of 14 days from exposure, with most patients developing symptoms after 4–5 days [18]. Most patients present with mild coryzal symptoms (mostly fever, fatigue and cough), anosmia, dysgeusia as well as occasional vomiting and diarrhoea. Severe diseases occur in approximately 20% of cases, and admission to intensive care units is required in 5% of patients owing to respiratory distress, heart ischaemia, arrhythmias or immune hyperreactivity [19]. Mortality rates range from 1.5% to 13% depending on the series [20]. Severe presentations and mortality have been associated with factors such as age, previous comorbidities, male gender or obesity. Of note, there are a significant proportion of asymptomatic patients [21], which pose a public health threat, particularly for vulnerable patients [22].

The treatment of COVID-19 is based on supportive measures because no drugs have proven their efficacy against SARS-CoV-2 in large clinical trials, and a vaccine

is not yet available. Several drugs have been proposed as plausible treatment for SARS-CoV-2 infection. Chloroquine and hydroxychloroquine could be efficacious owing to their immunomodulatory effects as well as inhibition of viral entry and endocytosis. However, their efficacy as treatment or prophylaxis in patients with COVID-19 is still unclear, and their safety profile is controversial owing to the high dose used and the association with other drugs with which adverse effects are shared (mainly QT prolonging effect) [23]. HIV protease inhibitors have also been proposed as possible treatments for SARS-CoV-2 infection. Lopinavir and darunavir could also inhibit SARS-CoV-2 protease, as found in *in vitro* studies. However, early clinical data in patients with severe COVID-19 did not show a benefit in adding lopinavir to supportive management [24]. Further studies with darunavir are ongoing. A study on patients with Acute respiratory distress syndrome (ARDS) secondary to SARS-CoV-2 receiving methylprednisolone [25] showed a decrease in mortality, and early results from the RECOVERY trial have shown that dexamethasone reduces mortality in severely ill patients [26]. Monoclonal antibodies aimed at decreasing interleukin-6 activation and signalling have also been assessed. Tocilizumab has shown some efficacy in severely ill patients, particularly in those with raised interleukin-6 levels [27]. Finally, remdesivir, a prodrug of an adenosine analogue, has displayed *in vitro* activity against SARS-CoV and MERS-CoV polymerases [28]. A randomised study in patients with severe COVID-19 did not show significant differences in mortality, clinical improvement or length of hospitalisation [29]. Further trials, particularly in patients with milder disease, are warranted. Other treatment strategies such as the use of interferon, hepatitis C NS5B polymerase inhibitors, ivermectin or plasma from recovered patients are being assessed. In addition, several clinical trials on vaccines are ongoing (Table 1).

Other CoVs

In 2003, an outbreak of a novel CoV causing the so-denominated SARS was reported initially in China, with further cases described mostly in South-east Asia and Canada [30]. Horseshoe bats have been found to be the main reservoir of SARS-CoV-2, with other species such as civets acting as intermediate hosts. Human-to-human transmission through respiratory droplets is the main transmission route, as well as through respiratory secretions in healthcare settings. Transmission through fomites has also been reported [31]. SARS-CoV-1 has an incubation period of 2–7 days, and symptoms appear within 10 days after exposure. Fever, cough and coryzal symptoms are the most common clinical features of SARS-CoV-1 infection, which, particularly in patients in high-risk groups, such as older age individuals or those with previous comorbidities, can progress to respiratory distress and multiorgan failure. Case–fatality ratio was

estimated around 16%, increasing up to 50% in patients older than 65 years [32]. At the time of the outbreak, no treatment or vaccine was available, and supportive treatment was the only possible option for patients with SARS-CoV-1 infection. After the implementation of containment measures, the first wave of the epidemic was controlled. Since the mid 2000s, no cases of SARS-CoV-1 infection have been notified. However, the 2003–2005 SARS epidemic showed the pandemic potential of CoVs as well as the need for improving hygiene and public health standards worldwide.

In 2012, several cases of viral pneumonia were reported in patients in Saudi Arabia and other Middle Eastern countries, resulting in the identification of a novel CoV, the MERS-CoV [33]. MERS-CoV is another beta-CoV transmitted from camels to humans through contact with respiratory droplets or consumption of camel products. Transmission between humans happens mostly through respiratory secretions in the context of close contact, households or nosocomial environments [34]. MERS-CoV uses Dipeptidyl peptidase-4 (DPP-4) receptors as the binding site. In clinical terms, MERS-CoV has an incubation period of 5 days, although in some cases, it can be as long as 2 weeks. Fever, cough and coryzal symptoms are the commonest presentations, whereas patients with comorbidities or older age tend to develop complicated pneumonias and ARDS. Overall mortality rates range from 30% to 45% [35]. No efficacious treatments against MERS-CoV have been identified, making hygiene and risk reduction the only current approach to prevent infection. Owing to its low transmission rate, MERS-CoV has not yet shown an actual pandemic potential, although mutations or transmission between humans in the setting of travels to risk areas could increase its incidence in the future.

Influenza

Different strains of influenza viruses circulate worldwide every year during winter months, causing significant morbidity and mortality despite being a vaccine-preventable disease.

Influenza viruses are enveloped, RNA viruses. The envelope contains several glycoproteins, particularly haemagglutinin (HA) and neuraminidase (NA). Both HA and NA undergo mutations, leading to two different processes. First, antigenic drifts due to point mutations in HA or NA cause outbreaks of variable severity and extension. Besides, reassortments between animal and human influenza strains can lead to the development of viral shifts, which create new strains with a pandemic potential. Because influenza viruses are transmitted through droplets, further influenza pandemics can be expected, as has happened in previous occasions [36]. In recent times, two outbreaks of newer influenza viruses have been reported. First, an outbreak of avian influenza

Table 1

Main clinical trials for COVID-19 therapies.

Trial	Study type	n	Intervention	Findings
Hung et al. [56]	Phase 2, multicentric RCT	127	LPV/r + IFN β -1b + RBV vs LPV/r	Shorter time to undetectable PCR and length of hospitalisation in the combination group
Wang Y [29]	Double-blind, placebo-controlled, multicentric RCT, severe COVID-19	237	Remdesivir vs placebo	No clinical differences. Higher rate of adverse events in the remdesivir arm
Beigel JH [57]	Phase 2, double-blind, placebo-controlled, RCT, COVID-19 pneumonia	1059	Remdesivir vs placebo	Shorter time to recovery in the the remdesivir arm. No differences in mortality rates.
Tang W [58]	Multicentric, open-label, RCT, mild/moderate COVID-19	150	Hydroxychloroquine + SOC vs SOC	No differences in time to negative conversion
RECOVERY [26]	Multicentric, RCT	1542	Hydroxychloroquine vs SOC	No differences in mortality or in length of hospitalisation
Campochiaro C [59]	Single-centre, retrospective, severe COVID-19	65	Tocilizumab + SOC vs SOC	No differences in mortality or in length of admission
Li L [60]	Open-label, multicentric RCT	103	Convalescent plasma vs SOC	Higher clinical improvement and negative conversion rates on the intervention arm
RECOVERY [6]	Multicentric RCT	2104	Dexamethasone vs SOC	Decreased mortality in patients with moderate/severe COVID-19

COVID-19, coronavirus disease 2019; RBV, ribavirin; LPV, Lopinavir; RCT, Randomised Clinical Trial; SOC, Standard of Care.

A H7N9 was described in China [37], with further cases reported worldwide. Although cases were associated with exposure to poultry products, several clusters of human-to-human transmission have been identified [38]. NA inhibitors have shown to be efficacious against H7N9 influenza. Owing to poor human-to-human transmission efficiency and also owing to hygiene interventions in Chinese markets, H7N9 influenza was not widely spread.

Influenza C is a lesser known influenza virus, mostly causing mild upper respiratory infections in children. Influenza C has a worldwide distribution, with a higher seroprevalence in individuals in the third decade of life and progressive decrease in older adults [39]. Despite being known as a cause of mild respiratory infections in young children, it has also been described as a causative agent of severe respiratory infections in adults, particularly among immunocompromised patients [40]. Hence, besides influenza A and B viruses, influenza C virus might be a respiratory pathogen associated with outbreaks, particularly among children and young adults.

Tuberculosis

Tuberculosis (TB) is the infection caused by *Mycobacterium tuberculosis*, an acid-fast bacillus, which can cause respiratory and systemic infections. It is estimated that 1 in 4 people worldwide are infected or have been in contact with *M. tuberculosis* in the past [41]. It is estimated that 10 million people develop TB every year, mostly in developing countries, causing 1.5 million

deaths per year [42] (Figure 2). The association of poverty, population density and deficient healthcare systems in many of these countries contributes to the transmission of the disease. *M. tuberculosis* is transmitted through respiratory droplets, after which 10% of individuals will develop active TB and about 50% will develop it within 3 years from exposure. Other clinical scenarios are spontaneous mycobacterial elimination or the development of latent forms of infection.

Currently, isoniazid (INH), rifampicin (RIF), pyrazinamide and ethambutol remain as first-line antimicrobials for TB [43]. Second-line drugs, such as respiratory quinolones (levofloxacin, moxifloxacin), injectable aminoglycosides (amikacin, kanamycin, streptomycin) and other antimicrobials, such as capreomycin, cycloserine and ethionamide, have also shown their efficacy against *M. tuberculosis* and are indicated in cases of drug-resistant TB.

Antimicrobial resistance is a significant health issue for patients with TB. Multidrug-resistant TB (MDR-TB), defined as the resistance to INH and RIF, and extensively drug-resistant TB, applying to isolates resistant to INH, RIF, quinolones and either aminoglycosides or capreomycin, are becoming more common, posing a significant public health threat not just in areas with high prevalence but also worldwide owing to globalisation, migrations or refugee exodus. Currently, around 500,000 people are infected with drug-resistant TB worldwide, particularly in Eastern Europe, Central Asia,

the Middle East and China [44]. Risk factors for the development of drug-resistant TB are suboptimal adherence to previous TB treatments, with 20% of patients previously treated developing resistances, age <65 years, institutionalisation, alcohol abuse, injection drug use and homelessness [45]. Hence, the confluence of higher prevalence of MDR-TB and extensively drug-resistant TB in densely populated countries, deprivation, lack of access to public healthcare along with globalisation and major population movements give MDR-TB a potential for further expansion, seriously putting at risk the achievement of the World Health Organization 'End-TB' initiative [46].

Lassa and Nipah virus

Lassa virus (LASV) is the agent responsible for Lassa haemorrhagic fever, an endemic disease in Western Africa. Its seroprevalence is variable in different areas in that region, ranging from 8% to 52% depending on the series [47]. Although mostly a rodent-borne virus, LASV has also a potential for human-to-human transmission through contact with body fluids and aerosol droplets, particularly in healthcare settings in some developing countries in Africa. It is estimated that 100,000–300,000 people are infected with LASV every year in endemic areas [48]. Lassa fever symptomatology is highly variable, including multiorgan damage, haemorrhage, central nervous system involvement, kidney damage or gastrointestinal symptoms. Mortality rates can be as high as 39% in vulnerable groups [49]. There are no

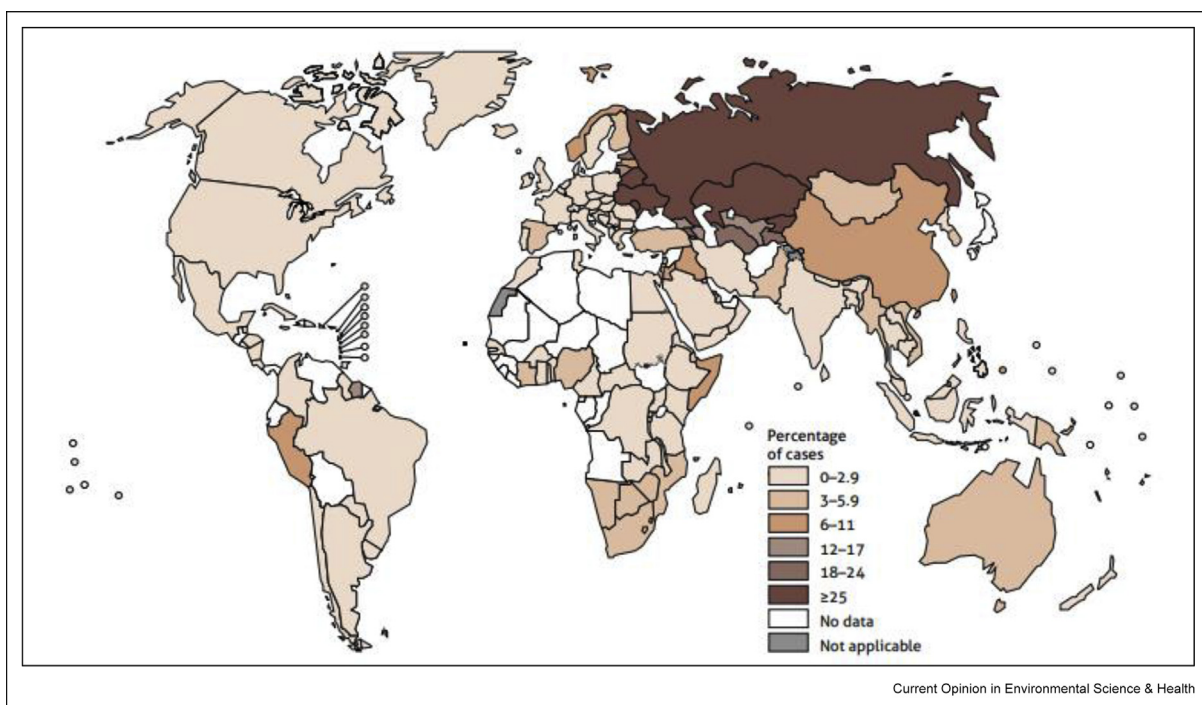
vaccines available against LASV. Ribavirin has shown to reduce mortality and is the treatment of choice along with supportive therapy [50]. Even when being a rodent-borne virus, the risk of human-to-human transmission, particularly in limited resource settings, along with an increased mobility in the setting of globalisation, confers LASV a potential for severe regional outbreaks and also for further transmission outwith endemic areas [51].

Nipah virus (NiV) is a zoonotic pathogen, prevalent in Asia and the Pacific. Fruit bats are the main zoonotic reservoir of NiV, and although initial transmission to humans is due to exposure to bats' or intermediate hosts' (i.e. pigs) secretions, human-to-human transmission has been well documented [52], both after contact with body fluids or through respiratory secretions. Of note, a minority of NiV infections present in an asymptomatic manner, although severe encephalitic syndromes are the most significant presentations. Neither efficacious treatment nor vaccine against NiV is available yet. Despite its high mortality, the reproduction number of NiV is low [52], hence limiting its pandemic potential. Contact and respiratory precautions are necessary to avoid transmission from source patients to their carers and healthcare workers.

Airborne bioterrorism agents

Infective agents have been and can be used as weapons of mass destruction. To be effective, these agents need

Figure 2



Incidence of drug-resistant TB worldwide. TB, tuberculosis [44].

Table 2

WHO priorities for research and development in infectious diseases.

- COVID-19
- Crimean-Congo haemorrhagic fever
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV)
- Severe acute respiratory syndrome (SARS)
- Nipah and heniparviral disease
- Rift Valley fever
- Zika
- 'Disease X' (future global pandemics caused by novel infectious agents)

COVID-19, coronavirus disease 2019; WHO, World Health Organization.

to show high morbidity or mortality, need to be easily transmittable, particularly on a human-to-human manner, need to cause social disruption and require special actions in terms of preparedness.

Anthrax is a potentially airborne disease, cause by *Bacillus anthracis*, a sporulating, gram-positive rod, which can cause a broad spectrum of conditions in humans. Inhalation of spores of anthrax causes a biphasic disease, starting with a prodromal phase, consisting of flu-like symptoms, that 4–5 days later can progress to a bacteraemic phase, with haemorrhagic mediastinitis, necrotising pneumonia or shock, with high rates of mortality despite antibiotic therapy [53]. *B. anthracis* spores can be viable for a very long period of time and are resistant to some disinfectants, thus prolonging the risk of transmission. Human-to-human transmission has not been documented, thus limiting the pandemic potential of anthrax. However, its persistent sporulating form makes anthrax a potential source of large outbreaks in the setting of a bioterrorist attack.

Poxviruses are also potential bioterrorism agents with a potential for affecting large numbers of victims. Variola virus, the causative agent of smallpox, can be transmitted through respiratory secretions, as well as through contact with cutaneous lesions from infected patients. Smallpox has a high reproduction number, with a high case fatality rate. It has been estimated that smallpox caused 300 million deaths in the 20th century, until its eradication in 1977 [54]. Smallpox had an incubation period of 10–14 days, with a further pre-eruptive phase (2–4 days) characterised by the development of coryzal symptoms and the appearance of an exanthema 1–2 days later. Although smallpox has been eradicated, it has been found to be a potential agent for bioterrorism owing to its high transmission rates and mortality and its stability in the environment. Although not generally included in routine vaccination schemes anymore, there is a potential to escalate the production of smallpox

vaccine should an outbreak develop. Furthermore, tecovirimat, a smallpox virion maturation inhibitor has shown its efficacy [55]. Other poxviruses, such as monkeypox, although not having a significant potential for airborne transmission, could also be modified to make it a potential bioterrorism agent.

Conclusions

The ongoing SARS-CoV-2 pandemic is arguably the most severe health threat the world has faced in decades. The emergence of this new CoV, with a high transmission rate and significant mortality rates, has had a significant impact on many public healthcare systems and has brought the attention to the risk of further pandemics caused by airborne agents. CoVs or influenza viruses might be the virus species with a higher potential for future pandemics, as has been shown in the past. Although the spread of drug-resistant TB might happen at a slower rate, it is arguably a major health problem issue and can be a more common problem in low prevalence areas owing to globalisation and population movements. Other viruses, such as MERS-CoV, Lassa virus, Nipah virus or poxviruses, might be present just in some geographical areas, but have shown the potential of causing local outbreaks that can lead to a wider spread of the disease (Table 2). Finally, bioterrorism attacks involving airborne agents such as anthrax or smallpox are a security threat. Hence, a global public health control, along with a more strict control and improvement in hygiene measures, is needed to prevent global spread of airborne infectious diseases.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Papers of particular interest, published within the period of review, have been highlighted as:

- * of special interest
- ** of outstanding interest

1. Jones RM, Brosseau LM: **Aerosol transmission of infectious disease.** *J Occup Environ Med* 2015, **57**:501–508.
2. Kutter JS, Spronken MI, Fraaij PL, et al.: **Transmission routes of respiratory viruses among humans.** *Curr Opin Virol* 2018, **28**: 142–151.
3. **Zhu N, Zhang D, Wang W, et al.: A novel coronavirus from patients with pneumonia in China, 2019.** *N Engl J Med* 2020, **382**:727–733.
- ** First report describing SARS-CoV-2
4. Johns Hopkins University Coronavirus resource centre. <https://coronavirus.jhu.edu/map.html>. Last accessed 23rd of July 2020.
5. Dawood FS, Iuliano AD, Reed C, et al.: **Estimated global mortality associated with the first 12 Months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study.** *Lancet Infect Dis* 2012, **12**:687–695.

6. Jin Y, Yang H, Ji W, *et al.*: **Virology, epidemiology, pathogenesis, and control of COVID-19.** *Viruses* 2020, **12**:E372, <https://doi.org/10.3390/v12040372>. Published 2020 Mar 27.
7. Zhou P, Yang X, Wang X, *et al.*: **A pneumonia outbreak associated with a new coronavirus of probable bat origin.** *Nature* 2020, **579**:270–273.
8. Li Q, Guan X, Wu P, *et al.*: **Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia.** *N Engl J Med* 2020, **382**:1199–1207.
9. Lu R, Zhao X, Li J, *et al.*: **Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding.** *Lancet* 2020, **395**:565–574.
**
First study describing SARS-CoV-2 genome
10. Chan JF-W, Yuan S, Kok K-H, *et al.*: **A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster.** *Lancet* 2020, **395**:514–523.
11. World Health Organisation: **Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations.** *Scientific brief* 29 March 2020.
12. van Doremalen N, Bushmaker T, Morris DH, *et al.*: **Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1.** *N Engl J Med* 2020, **382**:1564–1567.
13. Tian Y, Rong L, Nian W, *et al.*: **Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission.** *Aliment Pharmacol Ther* 2020, **51**:843–851.
14. Dong L, Tian J, He S, *et al.*: **Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn.** *J Am Med Assoc* 2020 Mar 26, e204621, <https://doi.org/10.1001/jama.2020.4621>. in press.
15. Dashraath P, Jing Lin, Jeslyn W, *et al.*: **Coronavirus disease 2019 (COVID-19) pandemic and pregnancy.** *Am J Obstet Gynecol* 2020 Mar 23, **S0002-9378**:30343–30344, <https://doi.org/10.1016/j.ajog.2020.03.021>. in press.
16. Wang W, Yu Y, Gao R, *et al.*: **Detection of SARS-CoV-2 in different types of clinical specimens.** *J Am Med Assoc* 2020 Mar 11, e203786, <https://doi.org/10.1001/jama.2020.3786>. in press.
17. Chang L, Yan Y, Wang L: **Coronavirus disease 2019: coronaviruses and blood safety.** *Transfus Med Rev* 2020 Feb 21, <https://doi.org/10.1016/j.tmr.2020.02.003>. In press.
18. Guan WJ, Ni ZY, Hu Y, *et al.*: **Clinical characteristics of coronavirus disease 2019 in China.** *N Engl J Med* 2020, **382**:1708–1720, <https://doi.org/10.1056/NEJMoa2002032>. NEJMoa2002032.
19. Zhou F, Yu T, Du R, *et al.*: **Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.** *Lancet* 2020, **395**:1054–1062.
20. World Health Organisation: **Coronavirus disease 2019 (COVID-19) situation report 92.** April 21st 2020.
21. Jiang XL, Zhang XL, Zhao XN, *et al.*: **Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China.** *J Infect Dis* 2020, **221**:1948–1952, <https://doi.org/10.1093/infdis/jiaa206>. jiaa206.
*
First report of human-to-human transmission of SARS-CoV-2 in asymptomatic patients
22. Kimball A, Hatfield KM, Arons M, *et al.*: **Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility - king county, Washington, march 2020.** *MMWR Morb Mortal Wkly Rep* 2020, **69**:377–381.
23. Hernandez AV, Roman YM, Pasupuleti V, *et al.*: **Hydroxychloroquine or chloroquine for treatment or prophylaxis of COVID-19: a living systematic review.** *Ann Intern Med* 2020, **173**:287–296.
24. Cao B, Wang Y, Wen D, *et al.*: **A trial of lopinavir-ritonavir in adults hospitalized with severe covid-19.** *N Engl J Med* 2020, **382**:1787–1799.
25. Wu C, Chen X, Cai Y, *et al.*: **Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China.** *JAMA Intern Med* 2020, **180**:934–943.
26. https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_v2final.pdf. First randomised clinical trial reporting decreased mortality in CoVid-19 patients treated with dexamethasone
27. Luo P, Liu Y, *et al.*: **Tocilizumab treatment in COVID-19: a single center experience.** *J Med Virol* 2020:1–5.
28. McCreary EK, Pogue JM: **Coronavirus disease 2019 treatment: a review of early and emerging options.** *Open Forum Infect Dis* 2020, **7**, ofaa105, <https://doi.org/10.1093/ofid/ofaa105>. Published 2020 Mar 23.
29. Wang Y, Zhang D, Du G, *et al.*: **Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial.** *Lancet* 2020, **395**:1569–1578.
30. Booth TF, Kournikakis B, Bastien N, *et al.*: **Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units.** *J Infect Dis* 2005, **191**:1472–1477.
31. Xiao S, Li Y, Wong TW, Hui DSC: **Role of fomites in SARS transmission during the largest hospital outbreak in Hong Kong.** *PLoS One* 2017, **12**, e0181558.
32. World Health Organisation: **Severe acute respiratory syndrome (SARS): status of the outbreak and lessons for the immediate future.** Geneva. 2003. 20th of May.
33. Zumla A, Hui DS, Perlman S: **Middle East respiratory syndrome.** *Lancet* 2015, **386**:995–1007.
34. Hui DS, Azhar EI, Kim YJ, *et al.*: **Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission.** *Lancet Infect Dis* 2018, **18**. e217–e227.
35. Azhar EI, Hui DSC, Memish ZA, *et al.*: **The Middle East respiratory syndrome (MERS).** *Infect Dis Clin* 2019, **33**:891–905.
36. Pavia A: **One hundred years after the 1918 pandemic: new concepts for preparing for influenza pandemics.** *Curr Opin Infect Dis* 2019, **32**:365–371.
37. Gao R, Cao B, Hu Y, *et al.*: **Human infection with a novel avian-origin influenza A (H7N9) virus.** *N Engl J Med* 2013, **368**:1888–1897.
38. Wang X, Wu P, Pei Y, *et al.*: **Assessment of human-to-human transmissibility of avian influenza A (H7N9) virus across 5 waves by analyzing clusters of case patients in Mainland China, 2013–2017.** *Clin Infect Dis* 2019, **68**:623–631.
39. Sederdahl BK, Williams JV: **Epidemiology and clinical characteristics of influenza C virus.** *Viruses* 2020, **12**:89, <https://doi.org/10.3390/v12010089>.
40. Nesmith N, Williams JV, Johnson M, *et al.*: **Sensitive diagnostics confirm that influenza C is an uncommon cause of medically attended respiratory illness in adults.** *Clin Infect Dis* 2017, **65**:1037–1039.
41. Houben RM, Dodd PJ: **The global burden of latent tuberculosis infection: a Re-estimation using mathematical modelling.** *PLoS Med* 2016, **13**, e1002152.
42. Furin J, Cox H, Pai M: **Tuberculosis.** *Lancet* 2019, **393**:1642–1656.
*
Updated, comprehensive review of the current situation of tuberculosis worldwide
43. Nahid P, Dorman SE, Alipanah N, *et al.*: **Official American thoracic society/centers for disease control and prevention/infectious diseases society of America clinical practice**

- guidelines: treatment of drug-susceptible tuberculosis.** *Clin Infect Dis* 2016, **63**:e147–e195.
44. World Health Organisation: *Global tuberculosis report*. 2019.
 45. Dheda K, Gumbo T, Maartens G, *et al.*: **The Lancet Respiratory Medicine Commission: 2019 update: epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant and incurable tuberculosis.** *Lancet Respir Med* 2019, **7**:820–826.
 46. Treatment Action Group, Stop TB Partnership: *Tuberculosis research funding trends 2005–2017*. New York: Treatment Action Group; 2018.
 47. Fichet-Calvet E, Rogers DJ: **Risk maps of Lassa fever in West africa.** *PLoS Neglected Trop Dis* 2009, **3**:e388, <https://doi.org/10.1371/journal.pntd.0000388>.
 48. Safronetz D, Sogoba N, Diawara SI, *et al.*: **Annual incidence of Lassa virus infection in southern Mali.** *Am J Trop Med Hyg* 2017, **96**:944–946.
 49. Okokhere P, Colubri A, Azubike C, *et al.*: **Clinical and laboratory predictors of Lassa fever outcome in a dedicated treatment facility in Nigeria: a retrospective, observational cohort study.** *Lancet Infect Dis* 2018, **18**:684–692.
 50. Asogun DA, Günther S, Akpede GO, *et al.*: **Lassa fever: epidemiology, clinical features, diagnosis, management and prevention.** *Infect Dis Clin* 2019, **33**:933–951.
 51. Kofman A, Choi MJ, Rollin PE, *et al.*: **Lassa fever in travelers from west africa, 1969-2016.** *Emerg Infect Dis* 2019, **25**: 245–248.
 52. Nikolay B, Salje H, Hossain MJ, *et al.*: **Transmission of Nipah virus - 14 Years of investigations in Bangladesh.** *N Engl J Med* 2019, **380**:1804–1814.
 53. Inglesby TV, O'Toole T, Henderson DA, *et al.*: **Anthrax as a biological weapon, 2002: updated recommendations for management.** *J Am Med Assoc* 2002, **287**:2236–2252.
 54. Meyer H, Ehmann R, Smith GL: **Smallpox in the post-eradication Era.** *Viruses* 2020, **12**:138, <https://doi.org/10.3390/v12020138>. Published 2020 Jan 24.
 55. Grosenbach DW, Honeychurch K, Rose EA, *et al.*: **Oral tecovirimat for the treatment of smallpox.** *N Engl J Med* 2018, **379**: 44–53.
 56. Hung IF, Lung KC, Tso EY, *et al.*: **Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial.** *Lancet* 2020, **395**: 1695–1704.
 57. Beigel JH, Tomashek KM, Dodd LE, *et al.*: **Remdesivir for the treatment of covid-19 - preliminary report.** *N Engl J Med* 2020 Oct 8, **NEJMoa2007764**, <https://doi.org/10.1056/NEJMoa2007764>.
 58. Tang W, Cao Z, Han M, *et al.*: **Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial.** *BMJ* 2020 May 14, **369**, m1849, <https://doi.org/10.1136/bmj.m1849>.
 59. Campochiaro C, Della-Torre E, Cavalli G, *et al.*: **Efficacy and safety of tocilizumab in severe COVID-19 patients: a single-centre retrospective cohort study.** *Eur J Intern Med* 2020, **76**: 43–49.
 60. Li L, Zhang W, Hu Y, *et al.*: **Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial.** *JAMA* 2020, **324**:460–470.