Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: http://ees.elsevier.com

Editorial

# The globe on the spotlight: Coronavirus disease 2019 (Covid-19)

Margarita Brida [a,b], Massimo Chessa [c], Hong Gu [d], Michael A. Gatzoulis [a,]

[a] Adult Congenital Heart Centre and National Centre for Pulmonary Hypertension, Royal Brompton & Harefield NHS Trust, National Heart and Lung Institute, Imperial College, London, UK
[b] Division of Adult Congenital Heart Disease, Department of Cardiovascular Medicine, University Hospital Centre Zagreb, Croatia
[c] ACHD UNIT - Pediatric and Adult Congenital Heart Centre, IRCCS-Policlinico San Donato, Milan, Italy
[d] Department of Pediatric Cardiology, Beijing Anzhen Hospital, Capital Medical University, Chaoyang District, Beijing 100029, China

Throughout history, infectious diseases represent a major global threat to human life and health, knowing neither geographic nor political borders. In 1918 the Spanish flu pandemic, caused by the H1N1 influenza A virus, led to catastrophic consequences with a global mortality toll of more than 50 million people (greater than the two world wars). The impact of this influenza virus was not confined to a single period; to date, three subsequent outbreaks (1957, 1968, and 2009, the last called Swine flu ) resulted from descendants of the initial virus, which acquired one or more genes through reassortment [1].

More recently, coronaviruses (CoVs), named for the crown-like spikes on their surface, have demonstrated similar outbreak patterns with the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) epidemics in 2002 and 2012, respectively [2,3]. The emergence of SARS-CoV and MERS-CoV underscored the threat of cross-species transmission leading in turn to outbreaks in humans. While public health measures contained these outbreaks, scientists identified sequences of closely related SARS-like viruses circulating in bat populations, and warned of this potential future threat as early as 2015 [4]. Our world, however, failed to learn necessary lessons from the SARS-CoV and MERS-CoV outbreaks and to invest on essential global research on ways of preventing the spread of infectious disease. History, as a result repeats itself with the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic of coronavirus disease 2019 (Covid-19) (Fig. 1).

SARS-CoV-2 has 96% of the genome identity of a bat SARS-like coronavirus [5]. Presumably, this virus and its predecessors originated from animals and mutated or recombined in a fashion that permitted it to infect, cause disease, and pass from person to person. The knowledge that the health of humans, animals and of the environment is all interconnected dates back to the ancient world. However, it is only recently, and after evidence that an animal virus could give origin to a devastating human virus (avian influenza, West Nile, Ebola, MERS-CoV and many others zoonotic pathogens), that international health organizations invested on surveillance and animal studies, including livestock, pets and wildlife [6]. Transmission across species and globalization, with the consequent impact of the latter on transcontinental commerce and ease of international travel, makes any nation and any of us susceptible to an infectious disease, new or old, that can spread rapidly, disrespecting borders and becoming global in no time. Furthermore, with the explosion of the world's population, the opportunity for transfer of a microbe from one human to another is higher than ever in history. The majority of the world's population now lives in urban settings, leading to close contacts conducive to the spread of infection. Increase in life expectancy has also amplified the proportion of elderly and of individuals with chronic conditions and/or cancer, all at greater risk of infection and its sometime fatal complications. Last but not least, humans place themselves and others at potential risk of infection through various behaviours [7].

The paper by Tan and Aboulhosn published in the current issue of the Journal, summarizes current knowledge regarding Covid-19 disease pandemic and its potential cardiovascular involvement, with a reference to adult congenital heart disease (ACHD) [8]. Congenital heart disease is the most common and global inborn defect. While the majority of patients had rather effective surgical and/or catheter interventions in childhood, many are afflicted by residual cardiac problems. With an increasing life expectancy amongst them, ACHD patients are susceptible to acquired cardiovascular and other disease and to environmental threats, including infectious diseases discussed herewith, leaving no man immune to them.

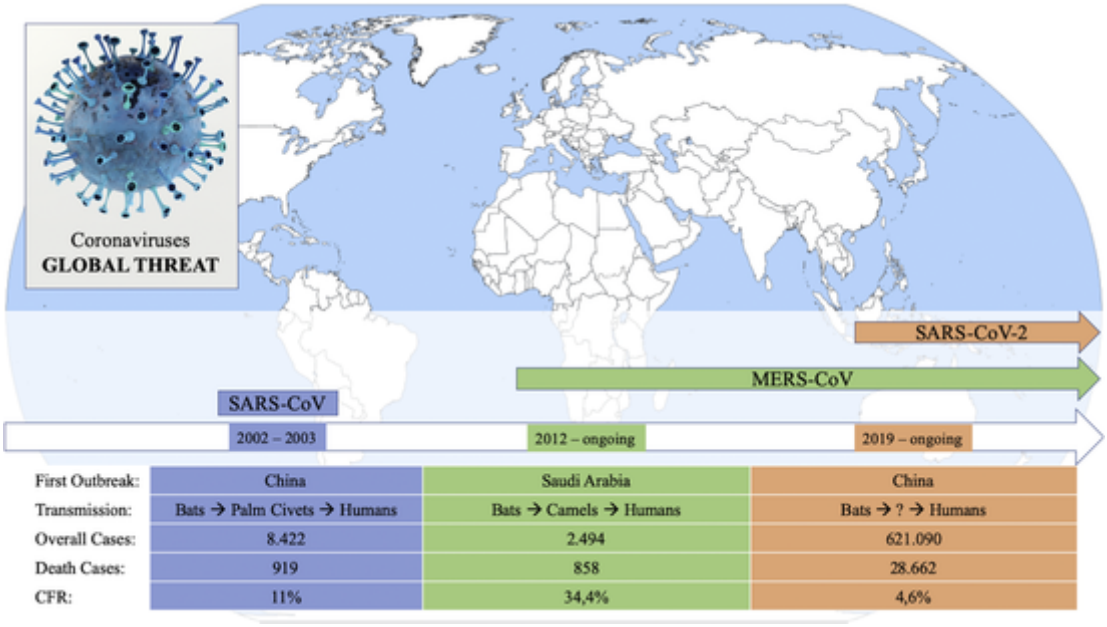
The so far evidence suggests that SARS-CoV-2 is likely to have a more severe clinical presentation in the elderly population, particularly those with comorbidities, and in that sense ACHD patients have an advantage by being relatively younger. The overall case-fatality rate (CFR) (i.e. the proportion of deaths from the disease compared to the total number of people diagnosed) was higher amongst patients with cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer by 10.5%, 7.3%, 6.3%, 6% and 5.6%, respectively [9]. Major complications requiring intensive care treatment amongst hospitalized patients with Covid-19 in turn, included acute respiratory distress syndrome (ARDS), arrhythmias, and cardiogenic shock [10]. Specific data pertaining to ACHD patients and Covid-19 are currently lacking. While awaiting for the evidence, Tan and Aboulhosn propose sensible steps in diagnostics, risk stratification, prevention and management [8]. It stands to reason, as authors clearly point out, that ACHD patients could be considered relatively high risk for complications from Covid-19, especially those with complex underlying cardiac defects, decreased functional reserve, and/or reduced immunity, the last being the case only in a small subset of them [8]. This is further reinforced when arrhythmias are taken into account, being de facto a common complication of ACHD and being reported as one of the main complications requiring intensive care treatment in Covid-19.

What can we do to Support our ACHD Patients through the Covid-19 Pandemic?

Ensure that adequate resources, time and expertise remain in place to provide for the ACHD patient and her/his needs (long-standing or acute [related Covid-19 or not]) and that they do not disappear into the frenzy combat against Covid-19. To affect this, change in ACHD practice is in-

Corresponding author at: Royal Brompton Hospital, London SW3 6NP, UK.
*E-mail address:* m.gatzoulis@rbht.nhs.uk (M.A. Gatzoulis)

https://doi.org/10.1016/j.ijcard.2020.04.006
0167-5273/




| | SARS-CoV | MERS-CoV | SARS-CoV-2 |
|---|---|---|---|
| First Outbreak: | China | Saudi Arabia | China |
| Transmission: | Bats → Palm Civets → Humans | Bats → Camels → Humans | Bats → ? → Humans |
| Overall Cases: | 8.422 | 2.494 | 621.090 |
| Death Cases: | 919 | 858 | 28.662 |
| CFR: | 11% | 34,4% | 4,6% |

**Fig. 1.** Coronaviruses pandemics.Up to present day there are seven human coronaviruses identified; four commonly detected (229E, OC43, NL63 and HKU1) may cause upper respiratory infections; three other strains presented (SARS-CoV, MERS-CoV and SARS-CoV-2) have different pathogenicity and have led to deadly epidemics. CFR = case-fatality rate.

evitable and already taking place. We have, for example instituted teleconference or skype clinics both at our tertiary hub and at the periphery and have replaced our many face-to-face multidisciplinary interactions to digital. This seems to work well at the moment and our patients are relieved and grateful of this ongoing support in the current environment. The distraction of the previous model of health care for chronic conditions, such as ACHD, that is now happening in front of our eyes because of the unprecedented circumstances, is also an opportunity to create an improved 21st century health care model to provide for better ACHD care and better patient journey and experience [11]. This model must utilize technology, including for example artificial intelligence [12] and invest more on education and patient empowerment [13].

ACHD patients should apply social distancing to protect themselves from being infected by SARS-CoV-2 until a vaccine is made available. This may seem as an extreme position as some/many of the ACHD patients would have only marginally increased risk to Covid-19, compared to the general population. However, we are currently lacking ACHD specific data and a strict policy of social distancing employed in other parts of the world, seems to have had a positive response during the first phase of this pandemic in reducing the spread of disease and allowing for health care systems to prepare and somewhat cope with the unprecedented need. There are other countries, such as Sweden where a more relaxed approach to Covid-19 seems to be in place, entrusting social response and shared responsibility, while maximizing public awareness and education. The outcome of such an alternative approach to this global threat would be highly informative to all, as there is uncertainty on when current draconian measures employed in China, Italy, the UK, USA and other parts of the world can and should be relaxed. And, it is deeply concerning for us all on how countries in other parts of the world, such as Africa with poor infrastructure are going to cope with such an aggressive pandemic. We must as a global community, not only survive this major threat but come stronger and better and closer together at the other end.

There are modifiable risk factors related to Covid-19 outcomes such as diabetes, hypertension/obesity that can and should be addressed through this period of social distancing and associated destruction of everybody's day-to-day life. This should apply to patients with cardiovascular disease and all of us; becoming slimmer and more athletic for example will help a) combat Covid-19, should we get infected, b) with the considerable psychosocial burden of all this and c) each one of us longer-term. Technology again and improvisation are here to help us achieve this goal, despite restriction of movements, particularly for those of us living in urban spaces. It is particularly encouraging to see a we are together in it, global spirit emerging out of this global crisis, where people and communities are coming together to support each other and particularly so to support the elderly and more vulnerable in society.

Treatment options for Covid-19 are largely supportive, care being taken to avoid potential complications such as arrhythmias and cardiac injury. The same principles should apply to ACHD, albeit specific issues such pre-existing cyanosis, multi-organ involvement and single or systemic right ventricle circulations are highly relevant and merit attention. It goes without saying that infected patients with complex ACHD will be better cared for in tertiary hospitals with ACHD expertise on site. It is paramount that such specialised ACHD centres secure dedicated space and expertise to continue to support the ACHD population and their urgent needs throughout the pandemic. There are emerging publications regarding models of care of cardiovascular patients with infectious disease, which however are short of specific ACHD experience at present [14,15]. Currently, there is neither effective medical therapy for Covid-19 nor a vaccine for it, albeit both are the subject of extensive research efforts globally. Novel infectious outbreaks naturally trigger off research interest and investment in better understanding of their pathogens, effective therapies and prophylaxis. However, when these outbreaks are contained or eliminated, attention wanes quickly as other priorities take place, leaving us exposed and vulnerable to the next outbreak, with potentially catastrophic impact as we witness today. While our editorial has largely focused on the adverse impact of Covid-19 on global health, loss of life and unprecedented pressures on health care systems, its mid to longer-term effect on economy, security, and overall well-being of the world's population should not be underestimated. In the aftermath of Covid-19, the world will undoubtedly identify the spread of infectious disease as one of the greatest global problems. Now, more than ever, it is paramount to secure resources, enable prompt communication and sharing of information and support and co-ordinate sustained research towards prevention, control, treatment, and eventually eradication of infectious diseases, that is in other words long-due investment in Global Health Security.

## References


[1] J K Taubenberger, D M Morens, The 1918 influenza pandemic and its legacy, Cold Spring Harbor Perspectives in Medicine. (2019).

[2] T G Ksiazek, D Erdman, C S Goldsmith, S R Zaki, T Peret, S Emery, et al., A novel coronavirus associated with severe acute respiratory syndrome, N. Engl. J. Med. 348 (20) (2003) 1953 1966.

[3] A M Zaki, S van Boheemen, T M Bestebroer, A D Osterhaus, R A Fouchier, Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia, N. Engl. J. Med. 367 (19) (2012) 1814 1820.

[4] V D Menachery, B L Yount Jr., K Debbink, S Agnihothram, L E Gralinski, J A Plante, et al., A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence, Nat. Med. 21 (12) (2015) 1508 1513.

[5] Bruce (.W.H.O). Aylward W.(.P.R.C). Liang Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). 2020; 2019(February): 16 24Available from:https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf

[6] I Capua, G Cattoli, One Health (r)Evolution: learning from the past to build a new future, Viruses 10 (12) (2018).

[7] Institute of Medicine Committee on Emerging Microbial Threats to Health in the 21st C, in: M S Smolinski, M A Hamburg, J Lederberg (Eds.), Microbial Threats to Health: Emergence, Detection, and Response, National Academies Press (US) Copyright 2003 by the National Academy of Sciences, Washington (DC), 2003.

[8] W M Tan, J Aboulhosn, Coronavirus disease 2019 (COVID-19) and cardiovascular burden including congenital heart disease, Int. J. Cardiol. (2020).

[9] Z Wu, J M McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention, Jama. 2020 (2019) 3 6.

[10] D Wang, B Hu, C Hu, F Zhu, X Liu, J Zhang, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. Jama. 323 (11) (2020) 1061 1069.

[11] M Brida, M A Gatzoulis, Adult congenital heart disease: past, present and future, Acta Paediatr. 108 (10) (2019) 1757 1764.

[12] G P Diller, A Kempny, S V Babu-Narayan, M Henrichs, M Brida, A Uebing, et al., Machine learning algorithms estimating prognosis and guiding therapy in adult congenital heart disease: data from a single tertiary centre including 10 019 patients, Eur. Heart J. 40 (13) (2019) 1069 1077.

[13] M A Gatzoulis, Adult congenital heart disease: education, education, education, Nature Clinical Practice Cardiovascular Medicine. 3 (1) (2006) 2 3.

[14] Y Han, H Zeng, H Jiang, Y Yang, Z Yuan, X Cheng, et al., CSC expert consensus on principles of clinical management of patients with severe emergent cardiovascular diseases during the COVID-19 epidemic, Circulation. (2020) (Epub ahead of print).

[15] F Romeo, G Calcaterra, F Barilla, J L Mehta, COVID-19 infection and the cardiovascular system, Journal Cardiovascular Medicine (2020).