



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



# COVID-19 and emerging infectious diseases: The society is still unprepared for the next pandemic

Roger Frutos<sup>a,\*</sup>, Laurent Gavotte<sup>b</sup>, Jordi Serra-Cobo<sup>c,d</sup>, Tianmu Chen<sup>e</sup>, Christian Devaux<sup>f</sup>

<sup>a</sup> Cirad, UMR 17, Intertryp, Montpellier, France

<sup>b</sup> Espace-Dev, Université de Montpellier, Montpellier, France

<sup>c</sup> Department of Evolutionary Biology, Ecology and Environmental Sciences, University of Barcelona, Barcelona, Spain

<sup>d</sup> Institut de Recerca de la Biodiversitat, Faculty of Biology, University of Barcelona, Spain

<sup>e</sup> State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics, Xiamen University, Xiamen, PR China

<sup>f</sup> IHU-Méditerranée Infection and CNRS, Marseille, France

## ARTICLE INFO

### Keywords:

COVID-19  
Pandemics  
Preparedness  
Society  
Emerging diseases

## ABSTRACT

The whole human society was caught unprepared by the emergence of SARS-CoV-2 and the related COVID-19 pandemic. This should have not been. We already had on hand all information to organize properly and prevent this emergence. However, this information was never translated into preparedness because the current system of sanitary crises management is not adapted. We keep implementing a medical, symptomatic, post-emergence approach which cannot stop an emerging pandemic. The only preventive action considered is the screening for viruses in the wild but it is not efficient since pandemic viruses do not exist in the wild, and indeed, have never been found. The emergence of a viral pandemic is the result of a double accident: the in-host evolution of the causative virus and its amplification to the epidemic threshold by societal factors. To be prepared the society should target this societal dimension of emerging diseases and organize accordingly. Unfortunately, the society is not organized that way and is still unprepared and vulnerable.

## 1. Introduction

In December 2019, the world has been surprised by the COVID-19 epidemic which soon became a pandemic (Zhu et al., 2019; Guan et al., 2020). The main problem is not really that a new disease emerged. It happened many times in the past and it will happen again in the future. The main problem is that the world was surprised and was caught unprepared. This should not have been because we had on hands all the information needed to be prepared. The question is why this information was not translated into preparedness. The answer is because we use the wrong “software”, in other words our system of response to sanitary crises is not adapted.

### 1.1. A belated reaction

An emerging infectious disease is indeed a disease and this is the origin of the problem because as such it is considered only a medical issue. What is a disease? A disease is a physiological disorder characterized by a specific pattern of symptoms to which a name is given. The

art of the physician is to recognize this pattern of symptoms, recognize the disease and propose an adequate treatment to cure the patient. However, an emerging infectious disease is by definition a disease with no associated specific pattern of symptoms and name. Physicians only recognize that there is an unknown disease outbreak when confronted to a flow of patients displaying the same unknown pattern of symptoms or unresponsive to recognized treatments. There is by definition no established treatment and vaccine for an emerging infectious disease and at that stage, physicians can only experiment. By the time a treatment or a vaccine is developed the disease may have caused a high number of casualties. Until now, we have been lucky because with the exception of the Spanish flu in 1918–1920 all pandemics since the beginning of the XX<sup>th</sup> Century have been mild or moderate. COVID-19 is no exception and is a mild to moderate disease with a fatality rate currently estimated at 2.07% (Johns Hopkins University, 2021) but which will most likely be lower since asymptomatic cases are not considered in the calculation. The high number of deaths is only due to its very important diffusion within human populations throughout the world and to the high size of the human population (Coelho et al., 2020;

\* Corresponding author. Intertryp – UMR 17, CIRAD, TA A17/G Campus International de Baillarguet, 34398 Montpellier, Cedex 5, France.

E-mail address: [roger.frutos@cirad.fr](mailto:roger.frutos@cirad.fr) (R. Frutos).

<https://doi.org/10.1016/j.envres.2021.111676>

Received 9 June 2021; Received in revised form 6 July 2021; Accepted 8 July 2021

Available online 9 July 2021

0013-9351/© 2021 Elsevier Inc. All rights reserved.

Iacus et al., 2020; Sigler et al., 2021). However, what will happen if the next pandemic to occur is caused by a virus with at least the same virulence and transmissibility as the Spanish flu? Consequences on a population of 7.7 billion people will be cataclysmic if we are not adequately prepared. Facts are that we are not. All nations worldwide as well as WHO are basing their strategy of emerging disease control on the same medical approach. All actions are triggered only after the disease has been recognized and the outbreak alert has been given. This is exactly what happened with COVID-19. No actions were taken outside China when WHO released the information about a new emerging disease in Wuhan in late December 2020. National actions were considered only after WHO has declared COVID-19 a pandemic in March 2020. Nevertheless, these reactions were based on detection of cases, intensive care and attempts to prevent the virus circulation within populations but it was too late, the virus has already spread widely. The strategies applied by the different countries were meant to manage the disease once it was recognized. All have relied on the capacity of their health systems to manage the epidemic and their administrative systems to coordinate the detection and isolation of patients. The outcome, while all countries in the world are facing a second, or even a third, epidemic wave, is disastrous: 185 million cases, 4 million deaths and more than 700 thousand daily cases. This situation can then be summarized in two words: too late. This approach leaves mankind vulnerable to any further pandemic.

### 1.2. "Change the software"

In a metaphorical way, we must quickly "change the software". We must reorganize our epidemic/pandemic warning and prevention system to act upstream of the disease emergence event. We must see things objectively and step away from corporatist behavior and preconceived ideas. What options are being brought today? First, the whole medical approach implemented nowadays with COVID-19 is inefficient and not adapted to counteract emerging pandemics. Not only it is too late to do anything when the disease is declared but it simply does not stop the pandemic despite impressive economic and societal impacts. Medicine cannot stop any emerging pandemic, simply because its framework of action is not adapted. Medicine takes care of patients and manages the disease by limiting the number of deaths, but this is not what allows for an effective prevention. By definition, medicine acts at the symptomatic level which is of the utmost importance but does not stop a pandemic. COVID-19 showed that the only way to avoid the saturation of hospitals was to strictly lockdown entire populations at a very high societal and economic cost. The most effective way to minimize human, economic and societal costs is thus to manage the emergence of the disease, not the disease itself. Another option brought today is the search for viruses in the wild to identify them before they emerge as a threat to human health. Projects like PREDICT or Global Virome are being set for that purpose (Jonas and Seifman, 2019; Carroll et al., 2018). However, as per today, no viruses responsible for epidemics nor pandemics have ever been found in the wild, including SARS-CoV-2 responsible for COVID-19 or the less spread coronaviruses SARS-CoV (SARS) or MERS-CoV (MERS). The viruses found in the wild are not those causing the disease in the human populations. They only are related viruses. The viruses causing the pandemics in humans only represent the human evolution of a group of viruses which in other hosts will evolve differently. This is what we regularly see when doing screening in the wild: related viruses but never the same virus as in the human population. The exception is animals in rearing or captivity which are contaminated by humans and can contaminate humans back. The theory behind this search, called "spillover" (Power and Mitchell, 2004), is also claiming that intermediate species transmitted the virus to humans from reservoirs (pangolins or minks have been targeted as intermediaries in the case of SARS-CoV-2). Here again, no intermediate or reservoir species have ever been found, despite numerous investigations. This model, although widely used, has so far received no conclusive validation for

emerging viruses. It is in fact an intellectual construction that has never been confirmed by field observations. This lack of detection of viruses, reservoir species and intermediate species in nature, and the lack of understanding of the reason for this absence, unfortunately fuels many conspiracy theories and flawed conclusions. These simplistic narratives assume that since the virus cannot be found in nature, it must be man-made and coming from a voluntarily release or a laboratory accident. There is simply not a single evidence to support such ultra-simplistic narratives. Since we cannot find the viruses before they emerge in humans, the choice of remaining options is very simple: the medical approach. However, the medical approach can only limit pathological effects in human populations and save as many people as possible. The worst part is that both options leave humanity totally vulnerable to any future emerging pandemic.

### 1.3. The middle way

A third option is offered but it requires to change the software and rely on prevention rather than reaction. An evidence-based model, the circulation model, was built to replace the spillover model and explain how viruses like SARS-CoV-2 can emerge through well-known natural evolutionary processes (Frutos et al., 2021). No need to resort to fantasy and science-fiction to explain the origin of SARS-CoV-2. There is a simpler natural way. Viruses simply circulate between susceptible hosts, including humans, and evolve within these hosts (Frutos et al., 2021; Bonneaud and Longdon, 2020). A poorly adapted virus can infect humans and transmit itself without being identified. Natural processes of mutation and selection of new viral variants will lead, little by little, to a virus well adapted to human hosts which will thus be able to "emerge" as a disease (Bonneaud and Longdon, 2020). Such processes are fairly frequent and well described in RNA viruses. Many viruses circulating in the wild have already been described but none ever corresponded to the virus causing the new human disease having emerged. This is normal since "zoonotic viruses" are almost all RNA viruses evolving in-hosts, therefore in humans as well, through the quasispecies model (Frutos et al., 2021). The human disease will be new but the presence of the virus in the human population is not. A large part of the problem lies in this confusion between disease and infection. However, this evolution of the virus is not sufficient to trigger a pandemic. It takes a second accident, from anthropogenic nature this time, to really start the pandemic. The presence of a highly transmissible and infective virus is not sufficient to trigger an epidemic. Indeed, the virus population must quickly increase, a phenomenon allowed by human societal conditions like meetings, gathering, events, etc., to the point where the size of the virus population reaches the outbreak threshold or epidemic threshold. This is the point when there are enough infected individuals in a population to start an exponential expansion of the epidemic. Before that threshold the virus is in a stochastic phase influenced by multiples factors where it can also disappear from the population. By crossing that threshold, the virus passes into a deterministic phase where the epidemic is rapidly progressing. Exceeding this threshold depend on anthropogenic events. Said differently, it is the accidental combination of societal factors which potentiates the capacity of a virus adapted to humans to become epidemic or even pandemic. They constitute the virus population amplification loops needed to reach the epidemic threshold. A major problem is the confusion between the primary case and the index case. The primary case is the first human individual to be infected by the pathogen. It corresponds to the primo-infection. The index case is the first case corresponding the described disease. It corresponds to the first medical case. These are very different concepts. Between the primary case and the index case lies a whole area of societal events and mechanisms which are the real drivers of the disease emergence. Comparing SARS-CoV-2, a pandemic virus, and Ebola, a virus with no pandemic potential, can well demonstrate the importance of this phase. Pandemic viruses display very specific traits. They are highly transmissible but with low to moderate virulence. The mortality rate is

low. They have a rather long period of incubation, generate a very high proportion of asymptomatic cases and when symptoms occur they can be easily confused with those of other diseases. This novel disease is characterized at the clinical level starting with the index case. All these traits allow the virus to spread widely in the human population before any suspicion of epidemic outbreak and emergence of a novel disease. The primary case is never found. Conversely, a virus like Ebola displays very high virulence and mortality rates. Symptoms are very strong, disabling and very quickly visible. The primary case cannot be ignored and is also easily recognized as the index case. There is no time for the virus to spread in the population and there is no possibility to misdiagnose or miss the presence of the disease. Ebola spread widely in 2014 in West Africa but only because of poor outbreak management and active transportation of the virus over large distances. This kind of virus has no potential for pandemic. Confusing the primary case and the index case when a pandemic virus is involved leads to ignoring the most important factors in pandemic disease emergence, the societal events leading to the epidemic.

#### 1.4. An accident

The occurrence of a pandemic is an accidental process involving both evolutionary and societal (amplification loops) events (Frutos et al., 2020). To control future emergences nothing can be done with respect to evolution, mutations and genetic accidents. It is a natural process totally out of reach. However, a lot can be done with regards to the society-driven factors involved. Since the emergence of a disease is an accidental event, it is not possible to predict it or to identify in advance which series of events will occur and be determinant. But these events being societal and thus man-made, it is possible to model and analyze the different ways this accidental coincidence of events may occur and identify the potential nodes of the process that can be effectively controlled. Like for the prevention of industrial accidents, it is possible to identify the actors involved in these anthropogenic events and the links connecting them, and thus to determine how to interrupt the chains of events potentially leading to the emergence of a disease. Whatever the pathogen, it will have to go through these specific societal amplification loops.

#### 1.5. A shift in philosophy

The only way for the society to ensure her protection against future pandemics is to change her approach, her way of addressing the risk of emergence of infectious diseases. The society must stop considering that an emerging infectious disease is exclusively a medical issue. Simply because when it has become a medical issue, it is already too late to properly control the epidemic at a bearable human and economic cost. Indeed, it becomes a medical issue only at the end, when symptoms are visible and an epidemic is already under way. A better approach is to consider that an emerging infectious disease is first of all a societal issue and to treat it as such. The right approach is to focus on the societal dimension of the process of emergence of an infectious disease and to manage the emergence of the disease, not to try to manage the disease itself when it is too late or to search for viruses in the wild with no success since they do not exist yet. The first objective should be to prevent this disease emergence instead of only searching for treatments to cure an already declared diseased. Treatments are essential but the society should invest for the non-event, for the emergence of the disease not to occur. The society should address emerging infectious diseases like it addresses industrial risks and, first, recognize its intrinsic anthropogenic and societal nature. What causes the disease is biological, the pathogen, but what causes the disease to emerge is societal. This is worsened by the growth of the human population. What is needed is to develop novel regulations of human activities potentially involved in the emergence of infectious diseases.

## 2. Conclusion

Societies are diverse and it is impossible to implement the same international regulations everywhere. Besides, anthropogenic factors leading to disease emergence vary from one society to another. They vary depending on culture, history and geography but they can all lead to an accidental coincidence of events opening the way to the emergence of a disease. However, the chain of events might be different depending on the society. The only way to prevent future pandemics from happening is to properly organize each society to block the chain of events and prevent the accidental event of emergence to occur, based on their respective traits. This endeavor must be coordinated at the international level but actions must be designed and implemented locally to match national and local specificities. WHO will open in September 2021 in Berlin, a Hub for Pandemic and Epidemic Intelligence which will, according to WHO, be in charge of “quickly analyze data to predict, prevent, detect, prepare for, and respond to risks worldwide” and “be able to detect pandemic signals earlier than current systems” (WHO, 2021). However, these early pandemic signals are, according to UNO and WHO, mostly climate changes, early case detection and fast communication (UNO, 2021). Diseases have always emerged in human populations, long before the current issue of climate change. Climate change is only marginally affecting the potential for disease emergence mostly by influencing animal species movements and geographic range. The influence of climate change is on the circulation of pathogens through host mobility and replacement not on the process of emergence itself. On the other hand, as previously said, the early detection of cases is particularly complicated since the pathogens involved are not known, the associated pathologies have not been identified yet and the rate of asymptomatic cases is usually high. Early detection of emerging pathogens could be envisioned at two levels: a search for the pathogen in i) animal species or ii) human populations. An exhaustive and permanent screening of every human or wild animal populations for viruses is non-realistic. It would not only be logistically impossible and economically extremely costly, but it does not yield any information since it is impossible to identify a potential threat before it has spread through the population and already went out of control. International regulations and measures against epidemics taken after Influenza, SARS, MERS or even Ebola did not help preventing the emergence of COVID-19. This hub might well be unable to prevent the next pandemic if relying only on the speed of relaying information and signs of epidemics because when these signs become visible it is already too late. Actions, i.e. proper organization, must be taken before these signs become visible. Furthermore, there is also a risk of deleterious effect as it will direct all efforts and attention on reactions instead of prevention, leaving thus the society totally vulnerable and unprepared for the next emerging virus.

#### Credit author statement

All authors contributed equally to the manuscript. RF, LG, JSC, TC and CD participated equally in the development, writing and correction of the manuscript.

#### Ethics declarations

No human samples or clinical data were used.

#### Authors' contributions

All authors contributed equally to the manuscript. RF, LG, JSC, TC and CD participated equally in the writing and correction of the manuscript.

#### Funding

Partial financial support is acknowledged from the CoNVat project of

the H2020 Research and Innovation Programme of the European Commission (H2020-SC1-PHE-CORONAVIRUS-2020, Project No. 101003544), the Science and Technology Program of Fujian Province (No: 2020Y0002), and the Xiamen New Coronavirus Prevention and Control Emergency Tackling Special Topic Program (No: 3502Z2020YJ03). The only other funding sources involved are the institutions of affiliation of each author: CIRAD for RF, University of Montpellier for LG, University of Barcelona for JSC, Xiamen University for TC and CNRS for CD. The involvement of the institutions was limited to the salaries of the authors, with no other role or involvement. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### 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

- Bonneaud, C., Longdon, B., 2020. Emerging pathogen evolution: using evolutionary theory to understand the fate of novel infectious pathogens. *EMBO Rep.* 21, e51374.
- Coelho, M.T.P., Rodrigues, J.F.M., Medina, A.M., Scalco, P., Terribile, L.C., Vilela, B., Diniz-Filho, J.A.F., Dobrovolski, R., 2020. Global expansion of COVID-19 pandemic is driven by population size and airport connections. *PeerJ* 8, e9708.
- Frutos, R., Lopez Roig, M., Serra-Cobo, J., Devaux, C.A., 2020. COVID-19: the conjunction of events leading to the Coronavirus pandemic and lessons to learn for future threats. *Front. Med.* 7, 223.
- Frutos, R., Gavotte, L., Devaux, C.A., 2021. Understanding the origin of COVID-19 requires to change the paradigm on zoonotic emergence from the spillover model to the viral circulation model. *Infect. Genet. Evol.*, 104812.
- Guan, W., Ni, Z., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X., et al., 2020. Clinical characteristics of Coronavirus disease 2019 in China. *N. Engl. J. Med.* 382, 1708–1720. <https://doi.org/10.1056/NEJMoa2002032> 575.
- Iacus, S.M., Santamaria, C., Sermi, F., Spyrtatos, S., Tarchi, D., Vespe, M., 2020. Human mobility and COVID-19 initial dynamics. *Nonlinear Dynam.* 101, 1901–1919.
- Jonas, O., Seifman, R., 2019. Do we need a global Virome project? *The Lancet Global Health* 7, e1314–e1316.
- Johns Hopkins University, 2021. <https://coronavirus.jhu.edu/map.html>.
- Power, A.G., Mitchell, C.E., 2004. Pathogen spillover in disease epidemics. *Am. Nat.* 164, S79–S89.
- Sigler, T., Mahmuda, S., Kimpton, A., Loginova, J., Wohland, P., Charles-Edwards, E., Corcoran, J., 2021. The socio-spatial determinants of COVID-19 diffusion: the impact of globalisation, settlement characteristics and population. *Glob. Health* 17, 1–14.
- WHO, 2021. Early-warning 'pandemic Hub' Plan Unveiled by WHO's Tedros and Germany's Merkel. <https://news.un.org/en/story/2021/05/1091332>.
- WHO, 2021. WHO, Germany Launch New Global Hub for Pandemic and Epidemic Intelligence. <https://www.who.int/news/item/05-05-2021-who-germany-launch-new-global-hub-for-pandemic-and-epidemic-intelligence>.
- Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., et al., 2019. A novel Coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* 382, 727–733.