

COVID-19: chronicle of a pandemic foretold

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Wuhan, China, November 2019 - first case of COVID-19. Earth, January 2022 - more than 300 million confirmed infections and around 5.5 million confirmed deaths related to COVID-19.

Between these two phrases a parenthesis of 26 months, a deadly pandemic, and a relevant question: What did we do wrong?

A pandemic is nothing new. Different pandemics have scourged cities, regions, countries or the whole world along human history, with the influenza pandemic of 1918 being by far the most similar to the present COVID-19 pandemic (1). Therefore, the emergence of a new microorganism (viral or not) with a high infectious ability, unknown to our immune system and potentially deadly was absolutely predictable. In fact, this risk has been largely publicly disclosed and systematically ignored.

For decades, the World Health Organization (WHO) has cried out to apparently deaf ears about the risk of new pandemics and has claimed for efforts to expand research outside classical high-income country research scopes. In this sense WHO has identified the microorganisms most likely to cause new pandemics (2). The current version of this webpage includes COVID-19, as well as SARS and MERS (2), two other coronaviruses which produced large outbreaks in 2002-2003 and 2012, respectively (3). These two coronavirus outbreaks were clearly harbingers of the current pandemic. Vaccine efforts were developed, with promising vaccines against SARS-CoV-1, but which were abandoned as soon as the SARS outbreak declined in 2004. Despite MERS having a reported lethality index of ~35% vs.

~1.7% by SARS-CoV-2 (both of which may be misestimated by the non-reporting of mild cases and the weakness of surveillance systems in different affected areas) (4), it is almost restricted to Middle East, mostly affecting disfavored populations (4,5), and thereby not being perceived as a true threat by most fundraisers and producing limited economical interest. These findings have been proposed to explain the limited efforts regarding vaccine development against MERS (3).

Other pathogens / diseases included in the above-mentioned WHO list are: Crimean-Congo hemorrhagic fever, Ebola, Lassa fever, Marburg, Nipah and henipaviral diseases, Rift Valley fever, Zika, and "Disease X". But what are we doing about these diseases?

Ebola and Zika are probably the most studied of these diseases, but this is likely because they expanded outside low- and middle-income endemic regions. Zika was first described in 1952, and Ebola in 1976, but limited studies were performed prior to 2014 (Ebola) and 2016 (Zika) (6). In 2014 a few Ebola patients arrived or were infected in Europe and the USA, while in 2016 the expansion of Zika was related to international travelers with the Olympic Games taking place in Brazil (6,7). Regarding the other listed diseases, they sporadically appear in the press, but mostly fail to attract the interest of fundraisers, who often continue to perceive them as something exotic and distant, remaining almost unknown to most people. But these diseases are not far away from us, they are, in fact, very close.

In the past, the introduction of a new pathogen often had limited local impact because of the time needed to expand to new areas and the deficient and slow communication pathways, but the current globalization allows rapid dissemination worldwide. In 1918 - 1919, the influenza outbreak was mostly disseminated around the world by soldiers, from USA to the battlefronts and from there, those who had been infected on the war front, contributed to spread the disease worldwide (8). COVID-19 was widely disseminated in different waves by international travelers; first by travelers from China to other countries, and thereafter from these countries to others (9). Simply, dissemination became unstoppable, and all measures were taken too late.

Globalization also results in growing and rapid international trade, which also contributes to the dissemination of infectious agents, either directly or indirectly, favoring the installation of disease-vectors in naive areas. For instance, all continents with the exception of Antarctica, have been colonized by *Aedes albopictus*, a mosquito able to be carried and act as a vector for diseases such as dengue, chikungunya, Zika, or yellow fever, among others (10).

The systemic bias of research efforts is the real problem. While funds are limited, and each fundraiser has its own vision and interests, research efforts addressed to fight neglected diseases, mostly affecting low- and middle-income areas, are badly needed. The lack of knowledge about these diseases, the interconnection of the current world and alterations in the climate can facilitate the spread of these diseases, allowing them to propagate outside their current borders and facilitate their installation in naive areas.

Of note, among other potential pandemic diseases, there is the so-called "Disease X". This is a key concept. It refers to any microorganisms for which we have no previous data or currently has not been described as a human pathogen. In other words, we must be made aware of the need to consider that an unexpected microorganism may cross borders, from animals to humans, and transform from being an innocent bystander into a new killer, rising from the oblivion of being a neglected disease to the forefront of the daily press.

The current COVID-19 pandemic is a reality. We cannot return to the past to modify our actions, to enhance the investments on coronavirus research and thereby have more adequate tools to fight current pandemics or to implement effective countermeasures early, but we can and must learn from this experience. We need research approaches that consider the most serious threats suggested by the WHO, including "Disease X". Circulating viruses or bacteria in different environments and wild animals and also the current known neglected infectious diseases need to be considered in research agendas. The recent development of powerful tools such as metagenomics or mRNA vaccines is an opportunity to advance towards the global mapping of microorganisms, which might offer a picture of the real situation as a first step towards this roadmap, and to fight most relevant pandemic threats. The expansion of the application of these tools to low- and middle-income will be key to prevent and mitigate the impact of future pandemics.

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Abstract

COVID-19, neglected diseases, public health, SARS-CoV-2.

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Sole author.

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