

It didn't have to happen this way – what COVID-19 tells us about translational medicine

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Abstract

In this editorial I would like to invite the Readers to look at this situation with broader time frame in mind. I attempt to draw some conclusions from the COVID-19 pandemic that are relevant for the field of translational medicine. My perspective is that it didn't have to happen this way and even worse, the same situation might repeat itself in the near future.

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In December 2019 people who were aware of the *Coronaviridae* family's existence were mostly scientists [1]. Today, or four months later, we all are undergoing practical training in epidemiology, we seek information about the structure of the SARS-CoV-2 virus, non-scientific magazines publish the virus' mortality rate, websites of banks and mobile phone service providers remind us about infection prevention methods and economics experts are convincing us that COVID-19 will not trigger a global recession [2].

In this editorial I would like to look beyond a quick analysis of the rapidly incoming information and invite the Readers to look at this situation with broader time frame in mind. My perspective is that it didn't have to happen this way and even worse, the same situation might repeat itself in the near future.

Several years ago an analysis of parish archives in Gilowice (near Kraków) and Starogard Gdański revealed that 50% of the recorded deaths in the years 1880-1920 were of children < 7 years of age and of

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those 30% were children < 1 year of age [3-4]. At the time the average lifespan in that part of Europe was 25-35 years, there were about 1 billion people living on earth and we had essentially no methods of controlling epidemics of infectious diseases [5]. According to the archives, the leading causes of death were pertussis, tonsillitis, scarlet fever, "cough," pneumonia, dysentery, smallpox. Thanks to vaccinations, antibiotics and hygiene many of these diseases are not found in medical practice anymore, children die sporadically and the average lifespan today is approaching 80 years [6]. In contrast, the leading causes of death around the world today are cardio-vascular diseases, diabetes and cancer [7].

The last global pandemic was the Hong-Kong flu in the years 1968-1970 [8]. Infectious disease specialists could have felt that their mission was completed: pandemics disappeared, almost all of the deadly diseases were eradicated, treatment of the remaining and clinically significant infectious diseases (e.g. HIV, HCV, borreliosis) is so simple that it doesn't require specialized training [8-9]. Some went as far as to say that there is no need for infectious disease specialists anymore.

Unfortunately, in December 2019 in Wuhan (China) cases of a strange pneumonia were noted [10]. You know the rest of the story and we are still part of it today. It is a rather unpleasant feeling to lose control over the events, to be unable to influence the course of the disease (lack of effective treatment, lack of vaccine) and yet at the same time to have to implement drastic limitations of personal freedom in order to stop the pandemic [1, 11]. In practice we are now where we were almost 100 years ago, when the only methods of infection control available were: personal hygiene, isolation, quarantine, sanitary cordon around a city [12-13].

Suddenly the medical world returned to the age when the patient posed a significant danger to the health and life of the physician. In the recent decades we became convinced that our profession is safe and prestigious. Many of us accompany our patients in their agony and death. Indeed this is difficult depressing and may lead to professional burnout, however rarely causes the physician to feel that his/her life is in danger [14]. Now all this has changed and we hear or read about desperate reactions of medical personnel, e.g. trying to strengthen the immune system by using dietary supplements despite the lack of evidence for their effectiveness or seeking pre-exposure prophylaxis guidelines.

It is worth remembering that we witnessed a similar situation in 2002-2003 with the SARS-CoV-1 epidemic [15]. That was also the same time when a new technology became available, the *in silico* method,

which led to the effective and safe anti-viral drugs for HIV and HCV [16]. Despite the availability of this new technology and other research tools neither drug nor vaccine against SARS were created. The reason for this situation is rather simple: it was completely not cost-effective [13].

Fortunately, scientists did not sit idly. Numerous particles and drugs with *in vitro* efficacy were synthesized in laboratories around the world against various viruses, including those from the *Coronaviridae* family. These research projects became stuck in the pre-clinical phases due to the lack of funding, time and volunteer patients. Today these same particles are cleaned of dust and once again re-challenged in terms of their effectiveness against the current biological threat (e.g. remdesivir) [17]. Funding is more likely available now, however for some of the patients there will unfortunately not be enough time [13].

It was predictable that the problem will return. Similar epidemics (MERS, flu virus) occurred as natural events in Southeast Asia and hemorrhagic fevers or retroviruses appeared in Sub-Saharan Africa [13]. Epidemics are somewhat like earthquakes: they do not happen daily and although we know that they will occur again, we are not able to predict when and where. Several years ago our attention was focused on the deadly Ebola virus [18-19]. This virus is known to science since 1976 and although we knew it is deadly, to this day we do not have any treatment or vaccine against it. The reason is once again financial: no government besides perhaps the USA or China is able to finance the costly and lengthy research projects and clinical trials. International pharmaceutical corporations do have the necessary funding, however they function for-profit [20].

A close relative of the Ebola virus is the Marburg hemorrhagic fever [19]. It is named after the central Germany city where the first cases were identified in 1967. The most likely source of the Marburg virus was in Uganda, thus none of us live safely on a lonely island [21].

From the virus' point of view, humans are its host and target. Since the first SARS outbreak in 2003 the global human population has increased by almost 2 billion, mostly in Asia. Today there are almost 9 billion of us on Earth and we travel significantly more often than in 2003, 1967 or 1918 [22]. Patients after organ transplantation also travel, just as those with HIV infection or on chronic immunosuppressive treatment. This is a good sign that patients are returning to their normal daily activity. However after becoming infected, these same patients may potentially replicate viruses for many months without any visible symptoms and therefore infect others. A repetition of the SARS or Marburg scenario is just a matter of time [1, 19].

Let's now draw some conclusions from the COVID-19 pandemic that are relevant for the field of translational medicine:

1. **We need an urgent, fast and non-commercial pathway for implementing medicines and vaccines for new biological threats. Clinical trials should be relatively inexpensive, financed by the taxpayers, not subject to the decisions of shareholders and should last several months (not years).**
2. **We need to initially prepare candidate drugs (therapeutic molecules) against specific, potentially deadly virus families such as flu viruses, Coronaviridae, hemorrhagic fevers, retroviruses, etc. In case of a new outbreak, we need to urgently assess the effectiveness of the candidate drugs and to conduct clinical trials. Clearly this is a significant logistic challenge, however during an epidemic time costs lives.**
3. **Herpes virus eradication using vaccinations is a worthwhile goal. The Herpes endemic has the scope of a pandemic, therefore the lives of many people would be more comfortable and longer.**
4. **We need to prepare for an outbreak of a virus that, in theory, could be synthesized in vitro in order to achieve a political or demographic goal. Unfortunately such bioterrorism is technically feasible, though it is the subject for a completely separate article.**

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