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The Pandemic and the 'Techno-fix'

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Abstract

The current pandemic was an announced possibility. Its potential causes were known: destroyed ecosystem niches, declining biological diversity, intensive farming, abuse of genetics, and biological manipulations. This paper deals with some aspects of the biological (and social) history of the ongoing COVID-19 pandemic but also with the history of previous epidemics, including the AIDS epidemics, which all have in common to be highly linked, enhanced or even the result of human activities. But now, the myth is setting in that an innovative technique for fast production of vaccines is the only *and sufficient* response to the crisis in the ecosystem and in health structures, of which this pandemic is a symptom. The reductionist and mechanistic approaches to the ecosystem and human biology are feeding the idea that the natural world may be fully manipulated and controlled ("the power to control Evolution" as in a recent book by a Nobel Award winner). This article calls for a critical thinking about the interfaces between the technosphere and the biosphere, their limits as well as for new frameworks for biology and medicine.

Keywords: pandemics, vaccine "techno-fix", technocracy, DNA-centric vision, human and ecosystems

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Introduction

The world and our lives have been turned upside down by an expected pandemic. In fact, experts have been denouncing an "epidemic of epidemics" since 1993. A well-documented 2015 book (Morand, Figuié & Coord 2018) and numerous articles have subsequently updated the data on this phenomenon, which is summarized in Figure 1: about 70% are zoonoses.

Surveillance of epidemics, epizootic and zoonoses has increased since the 2000s when the One Health's approach started to be promoted (Stephen & Karesh 2014). Governments are aware of the threat posed by this increase in epidemics, some of which have the potential to turn into a pandemic nightmare at lightning speed due to the huge, rapid and now very hard to control human travel and flows. They have taken seriously previous WHO warnings about the risk of an influenza pandemic.

First, in 2005, an epizootic of H5N1 avian influenza in intensive poultry farms in Asia caused a zoonosis that infected 114 people, 59 of whom died. Fearing that this zoonosis could lead to the emergence of a human-to-human transmission influenza virus, 120 million birds died in three months, most of them suffering from flu or having been sacrificed as a precaution (Ligon, 2005). States have adopted prevention plans and stockpiled antivirals, in particular tamiflu®, and masks. They were also prepared in 2009, when the WHO announced a risk of a human flu pandemic due to the H1N1 influenza virus, by prioritizing the production of new vaccines on an emergency basis (Mereckiene *et al.* 2012).

The dreaded pandemic finally arrived in 2020. It took the whole world by surprise because it did not

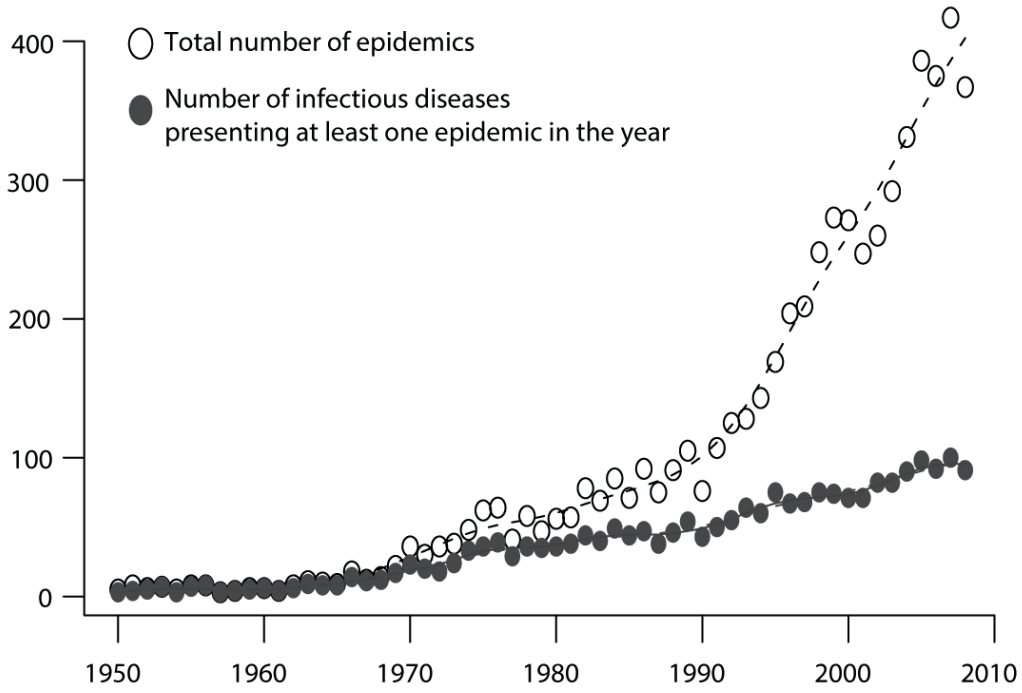

Figure 1: Evolution of the number of epidemics of infectious diseases in the world from 1950 to 2010: total number of epidemics in the year (upper curve in gray) and number of infectious diseases presenting at least one epidemic in the year—thus iterating (lower curve in black). Adapted from (Morand, 2015), upon kind permission by the Author.

come from the flu virus as expected, but from a new Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) that emerged at the end of 2019 in China. The states were not prepared for this pandemic (not enough masks, issues with PCR reagents, etc.). They accelerated the pace of research and focused essentially on vaccines, in particular on mRNA vaccines. This challenging technology, which consists in having the body produce a therapeutic protein of interest, was little studied after the early research in the 1990s but has undergone new developments recently, in particular as an alternative to conventional vaccine approaches (Pardi *et al.* 2018). The production of COVID-19 mRNA vaccines has been compressed in time thanks to a fast-track development in a public health emergency and a conditional marketing authorization allowing their large-scale use without the need to wait for full scientific knowledge in accordance with evidence-based medicine (Guyatt *et al.* 1992).

This gave the illusion of being able to control the circulation of a virus already dispersed throughout the world. Unfortunately, the mass vaccination failed to eradicate the virus but this does not seem to taint the logic of huge and repetitive vaccination by mRNA as a unique solution to face this health crisis in many countries and as recommended by WHO. This attitude ignores the causes of these repeated outbreaks, the limits of their unimodal solution, and their possible consequences for the future. In fact, it chooses to ignore fundamental knowledge in medical virology spanning from the history of coronaviruses, which we will recall, to the different severity of its various forms. Rather, the European Union as well as North America, Israel, Australia and many other countries focused on the quick and miracle technical solution of the mRNA vaccine. This technology is relatively easy to produce but its potential harmful effects are unknown, due to the lack of controlled clinical trials and sufficient follow-up time. In the urgency of the first waves of the epidemic, protecting the elderly or those vulnerable because of comorbidities *via* a vaccine with conditional marketing authorization was certainly justified. Unfortunately, the effectiveness of vaccines seems short-lived, with boosts mandated

every three months. Despite this, the main or only medical solution adopted for adult population remains the vaccine as a "techno-fix" (a technical shortcut with little scientific knowledge of its effects), which is proposed as a perfect technology that definitively solves the problem. This also contributed to disregarding the analysis of causes, which are rooted in a distorted relationship among the ecosystem and human beings, as well in the role of the health systems. In many cases, the failure in protecting lives was due to the unpreparedness of medical structures to face the largely predicted emergency.

We now need measured scientific and medical responses that do not rely on techno-science alone as many countries around the world have chosen to do. In this regard, see the review on the global turn towards mandatory COVID-19 vaccination policies by Bardosh and colleagues (Bardosh *et al.* 2022). It is typical of techno-science to deny its own limits, which are precisely based on a reductionist vision of the living world, including the reduced medical attention to the specificities of individuals ("one [vaccine] fits all") and the manipulation of DNA—seen as a context-free combinatorics of alphabetical signs—in order to "control evolution" (Doudna & Sternberg 2017). We also need to address urgently the actual causes of these repeated outbreaks and transform our relationship with nature, while embedding fantastic techniques to manipulate molecules into still missing scientific frames, as we will argue below. Governments must empower themselves to act according to the concept of One Health (WHO 2017) beyond the buzzword.

The direct contribution of humans to this inflation of epidemics is already a reality, as shown by examples mentioned in this article. We will first briefly survey some major epidemics or pandemics that affected humanity and their possible origins, including medical activities and laboratory experiments. Further, the health systems of many countries failed to provide adequate services in the expected emergency. Therefore, only extensive PCR tests and mass vaccination helped to maintain the impression of very active answers by governments, which avoided discussing the ecosystemic, technical, and healthcare failures. These shortcomings call for a critical thinking about the technosphere and its relation to the biosphere, while going beyond the dominant explanatory frameworks in biology and medicine.

1. Infectious Diseases and Epidemics: Brief Historical and Ecological Perspectives

Most major human infectious diseases are caused by pathogens transmitted by wild or domestic animals (Taylor, Latham & Woolhouse, 2001). The emergence of several of them is consecutive to the recent development—11,000 years ago—of agriculture accompanied by new cohabitations between human and animal populations, in particular domesticated ones. This is most likely the case for diphtheria, influenza A, measles, mumps, pertussis, rotavirus, smallpox, and tuberculosis (Diamond 1999). These new proximities between human and animal populations were unprecedented compared to the previous world of human hunters and gatherers. This multiplied the opportunities for transmitting pathogens as well as to ensuring their endemic persistence in human populations (Wolfe, Dunavan & Diamond 2007). The authors describe five steps necessary to transform an exclusively animal pathogen into a pathogen whose only host is human, as this is the case for measles, rubella, smallpox and syphilis for example. But the transition from one stage to the next one is not a fatality. In fact, some pathogens such as anthrax or West Nile virus do not cause secondary human infections while others, such as viral zoonoses like the Marburg virus disease or monkeypox only generate a few cycles of secondary human-to-human infections that lead to micro-epidemics (Wolfe, Dunavan & Diamond 2007).

Dobson and Carper focused on the settlement of infectious disease during human civilizations and identified three factors for understanding the impact, persistence, and spread of pathogens: the size and spatial distribution of the host population, the movement of infected and susceptible hosts and vectors, and the nutritional status of the human host population (Dobson & Carper 1996). The elements that may shed light on the epidemics of the past, which these authors studied based on numerous documented examples, are as diverse as malnutrition consecutive to a reduction in diet diversity associated with urbanization, diversity of herd immunities, number of siblings, human displacement, wars, access to health care, etc.

Thus, the causes of epidemics are multifactorial and span from natural history to human activities. Epidemics can be analyzed as resulting from interactions between

infectious agents and their hosts, whether they are single or multiple, and of ecological competition processes (Karesh *et al.* 2012). For example, the emergence of the Lyme disease, induced by the tick-borne *Borrelia burgdorferi* bacteria, in Northeastern United States during the 20th century, was largely facilitated by partial reforestation in fragmented forest landscapes, resulting in new prey-predator/host-pathogen balances (Allan, Keesing & Ostfeld 2003; Kilpatrick & Randolph 2012). Host-pathogen relationships can be affected locally, as in the example of Lyme, but also by a multitude of social, physical, chemical, and biological factors involving larger scales that require a holistic analysis.

In their review calling for a new paradigm of interdisciplinary biocomplexity, Wilcox and Colwell adopted such a framework. They integrated different scales and their reciprocal influence dynamics from regional ecosystems affected by environmental and anthropological variations (urbanization, agriculture, habitat) to the dynamics of host-pathogen interactions leading to emerging diseases (Wilcox & Colwell 2005).

In summary, epidemics have always existed and the emergence of infectious diseases is a complex phenomenon that only a societal and ecosystemic approach—including analyses of zoonoses—can clarify. Today, they are more frequent and more easily turn into pandemics.

2. Epi/Pandemics and their Zoonotic Origin in the Past 50 years: The Case of AIDS

What happened over the last 50 years after a century of very significant decline in the number of epidemics, particularly but not only in Europe? World population doubled and there was an eight or nine-fold increase in epidemics (Morand & Figuié 2018). As mentioned in Figure 1, about 70% of these recent epidemics have been the result of "zoonoses", *i.e.* they are due to microorganisms passing from animals to humans (more generally called "spill-overs"). Among the many causes of this astonishing "spill-over" growth, deforestation and human encroachment on natural habitats associated with an unprecedented loss of biodiversity in human history top the list. Often, this is worsened by the creation of huge intensive livestock farms near critical areas, which serve as perfect incubators for diseases or novel mutations thereof (Daszak, Cunningham & Hyatt 2000; Wilcox & Colwell 2005; Karesh *et al.* 2012)). Finally, laboratory accidents, medical procedures, and human genetic manipulations are also responsible for these outbreaks (Heymann, Aylward & Wolff 2004).

The last major pandemic, *i.e.* AIDS, is still raging around the world, since the early 1980s. AIDS is caused by two emerging viruses, HIV-1 and HIV-2, that are the product of several independent zoonotic transmissions of the simian immunodeficiency virus (SIV) occurred from monkeys to humans in the early 20th century (Hillis 2000; Korber *et al.* 2000). These zoonoses are not directly pathogenic for humans who have lived closed to several species of monkeys in the depths of the jungle for thousands of years (Poulsen *et al.* 2000; Lemey *et al.* 2003; Keele *et al.* 2006). However, the monkey's pathogens alone do not explain the origin of the AIDS pandemic, since emerging HIV viruses subsequently acquired human-to-human transmission properties (Marx, Apetrei & Drucker 2004). Several simian viruses transmitted separately and simultaneously to humans in African colonies at the beginning of the 20th century and led to the various groups of HIV-1 and HIV-2 (Hahn *et al.* 2000; Korber *et al.* 2000; Damond *et al.* 2004; Santiago *et al.* 2005). Large-scale colonial construction projects and crop development leading to deforestation, massive population displacements, urbanization and rapid socio-cultural changes have contributed to diffuse the virus also out of its natural forest habitat (Pepin 2011). Colonial medicine organized massive vaccination campaigns and antibiotic treatments by injection, or carried out blood transfusions with reusable syringes, including in SIV reservoir places (Schneider & Drucker 2006). This medicalization was most probably a determining factor in the cross-species transmission of simian viruses and their iatrogenic spread by blood contamination through syringes that were used for many consecutive people without intermediate sterilization (Lachenal *et al.* 2010). All these factors, which have contributed to the adaptation of the simian's SIV to humans over a short period of time are the result of human activities, including medical and altruistic ones (Chitnis, Rawls & Moore 2000; Drucker, Alcabes & Marx 2001; Marx, Alcabes & Drucker 2001; Apetrei *et al.* 2006; Schneider & Drucker 2006; Pépin 2021). In conclusion, the emerging AIDS disease is caused by the human immunodeficiency virus HIV, whose origin is the simian virus SIV transmitted by zoonosis to humans and which has evolved to acquire a strictly human tropism through the five intermediate stages mentioned above (Wolfe,

Dunavan & Diamond 2007). The example of the AIDS pandemic illustrates the complex origin of a pandemic combining natural, human, situational and historical factors, which cannot be reduced to a single cause.

Hepatitis C is a disease caused by a virus transmitted only by blood. Its epidemic in Central Africa is simpler case, since it has an essentially iatrogenic origin linked to the massive non-sterile injections practiced to fight trypanosomiasis and by colonial mass medicine between 1920 and 1960 (Njouom *et al.* 2007; Pépin *et al.* 2010).

Other epidemic episodes have become more and more frequent since these emergent diseases in the 20th century. Among them, the coronaviruses have been on alert for two decades with several appearances under close surveillance. First in 2002, a major epidemic of SARS-CoV caused great concern with the death of 800 people out of 8,000 cases recorded in about thirty countries (Drosten *et al.* 2003; Fouchier *et al.* 2003; Ksiazek *et al.* 2003; Zhong *et al.* 2003). This new epidemic came from an emerging coronavirus transmitted by small carnivores, civets, sold in southern China bushmeat markets (Guan *et al.* 2003; Song *et al.* 2005). However, the wild reservoirs of the virus were most likely bats (Hu *et al.* 2015).

A first human case of infection with a new coronavirus occurred in the Arabian Peninsula in 2012. This caused the Middle east respiratory syndrome (MERS) with cases of human-to-human transmission imported into Europe, in Asia and the United States (Zaki *et al.* 2012; Hemida *et al.* 2013). The virus was transmitted to humans by camels contaminated by bats, which are the reservoir of the virus (Alagaili *et al.* 2014; Sabir *et al.* 2016).

These examples highlight the role of many changes caused by humankind at unprecedented speed and scale over the last century, threatening biodiversity (Vitousek *et al.* 1997) and spreading by badly handled technologies. This set ideal situations for the emergence of new pathogens and enhanced the probability of their spreading, outpacing medicine (Keesing *et al.* 2010; Morand, Krasnov & Littlewood 2015).

3. Accidental Outbreaks of Pathogens Escaping from Laboratories

Numerous pathogens have accidentally escaped laboratories. This phenomenon is documented worldwide and has been regularly denounced (Furmanski 2014).

The Marburg virus, which belongs to the same family as the highly lethal Ebola virus, infected a few people in Germany during a micro-epidemic in 1967. Most of the infected people were working in research laboratories and handled tissue from grivet monkeys imported from Africa (Martini *et al.* 1968). Fortunately, only few nosocomial infections occurred in the hospitals where sick employees had been admitted. Retrospective studies have assessed the ratio of primary to secondary contaminations, outside the laboratories, at 21:3 in Marburg, 4:2 in Frankfurt and 1:1 in Belgrade (Slenczka & Klenk 2007; Ristanović *et al.* 2020). Many other accidental episodes involving a wide range of pathogens have been reported (Heymann, Aylward & Wolff 2004; Furmanski 2014). These laboratory leaks have killed hundreds of people in total, but none of them have gone beyond the geographically circumscribed outbreak, with the exception of the 1976–1977 flu.

This H1N1 pandemic originated from a virus strain that circulated in the 1950s and had disappeared (Kung *et al.* 1978). Since the 1950 and 1977 influenza viruses are genetically very similar, the hypothesis of an escape of the 1950 viral strain, preserved in a laboratory, is highly probable (Nakajima, Desselberger & Palese 1978; Scholtissek, von Hoyningen & Rott 1978; Furmanski 2015). The re-emergence of the H1N1 virus was first detected in Russia and China, but analysis of frozen biological samples and subsequent phylogeny methods showed that it was present some months earlier, making it impossible to trace back to the countries where the accidental re-introduction of the virus took place (Wertheim 2010). Fortunately, this pandemic, which mainly affected young people, was no more deadly than seasonal flu thanks to the collective immune memory of the epidemics of the 1950s (Kilbourne 2006).

This short history illustrates that human error can turn into a nightmare if more virulent pathogens escape and that science-fiction disaster scenarios could become reality (Klotz & Sylvester 2012). Among them, coronaviruses gained attention in 2002 with the emergence of SARS-CoV, which was placed under close surveillance with monitoring of highly pathogenic infections. Its zoonotic origin as well as the animal reservoirs that harbor it have been established (Cui, Li & Shi 2019). Most of the 8,000 cases identified are the result of a human-to-human transmission chain. However, at least four laboratory accidents resulting in human infections with the same virus were reported

in Asia in 2002 and 2003. One of these resulted in secondary infections, including one fatal (Heymann, Aylward & Wolff 2004). Following this SARS outbreak and the identification of the high pandemic risk of coronaviruses, the G20 countries reacted with a patchy and inconsistent investment in basic research, which turned to be relatively limited, considering the relevance of the SARS epidemics (Head *et al.* 2020).

In early 2020, governments around the world were helpless when faced with a devastating pandemic that rapidly became global. The pathogen, an emerging SARS-CoV, was quickly identified, related to SARS-CoV and named SARS-CoV-2. Its origin was soon officially declared to be a zoonotic virus. Its animal reservoir was the bat, with the pangolin as an intermediate host, in which it would have acquired its human-to-human transmission properties. On March 26, 2020, the WHO "dismissed" the non-natural origin of SARS-CoV-2: "However, all available evidence suggests that SARS-CoV-2 has a natural animal origin and is not a manipulated or constructed virus. SARS-CoV-2 virus most probably has its ecological reservoir in bats" (WHO 2020). A few days later, a scientific publication ruled out the hypothesis of an accidental origin of the virus by leak of a research laboratory and opened the track of the pangolin (Andersen *et al.* 2020).

However, many elements are missing from this explanatory puzzle and the examination of the artificial origin hypothesis involves geopolitical issues that complicate the work of experts on site (Harrison & Sachs 2022). In the case of COVID-19 pandemic, "accidental laboratory leakage" moved higher on the list of possible origins of SARS-CoV-2 (Decroly, Claverie & Canard 2021; Sallard *et al.* 2021). Some authors even consider since long time that the most imminent danger today comes more from the laboratory manipulation of this type of virus than from the new natural and recurrent zoonoses, which are most often dead-end infections (Klotz & Sylvester 2012; Lipsitch & Bloom 2012).

Finally, the origin of HIV AIDS viruses that are at the origin of the pandemic started in the 1970s has been established in the depths of Central Africa in the 1920s (Pépin 2013). However, the emergence of a new virus in China only two years ago has still not been elucidated despite the vastly improved technological sequencing capabilities available over the last decade.

4. Moratorium on "Gain-of-Function" Experiments and Scientific Precautionary Principle

If the hypothesis of an accidental escape of a laboratory virus were to be confirmed, then the question of whether the SARS-CoV-2 strain that caused the 2020 pandemic is natural or not is still open. In particular, the presence of a furin site, which is absent in other SARS-CoVs (Coutard *et al.* 2020), raises the question of whether this site could have been introduced by humans through genetic manipulation as part of gain-of-function genetic research (Sallard *et al.* 2020).

This type of experiment consists in increasing the virulence or the infectivity, or both, of a pathogen. It has divided scientists for a decade, after genetic manipulations involving H5N1 avian viruses were carried out to allow airborne transmission from mammal to mammal (ferret to ferret) in several laboratories (Imai *et al.* 2012; Russell *et al.* 2012). Opponents of these experiments consider that the benefit/risk ratio is very unfavorable and that by playing with fire, with the intention to be prepared for a pandemic, researchers risk producing precisely the pandemic they fear, like a "self-fulfilling prophecy" (Zimmer & Burke 2009; Klotz & Sylvester 2012; Lipsitch & Bloom 2012; Wain-Hobson 2013). In 2012, the US government listed 15 pathogens and toxins for which certain types of research are subject to new safety rules. The aim is to better control experiments on these pathogens for their dual-use research potential (United States Government 2012). Scientists' warnings about the danger of gain-of-function experiments reached the highest political levels, including in Europe (Enserink 2013).

In 2014, following three separate laboratory incidents reported by the CDC, over 200 scientists signed the Cambridge Working Group declaration asking for a cessation of experiments on potential pandemic pathogens (Cambridge Working Group 2014). Indeed, President Obama administration imposed a moratorium on gain-of-function studies on influenza, SARS, and MERS (United States Government 2014; NIH 2015). This moratorium, which was relatively respected (Lentzos & Koblentz 2022), lasted only three years (NIH 2017) and new funds and funding procedures, framing the gain-of-function experiments (United States Department of Health and Human

Services 2017), were enacted in January 2017 (Burki 2018; Klotz & Koblentz 2018).

We know now that laboratory manipulation of this type of virus implies a high risk of spillover. Therefore, risky manipulations should be conceivable only under severe restrictions and in scientific frames. Instead, for example, CRISPR-Cas9 toolkits can be easily bought and handled by any biology laboratory to be then extensively used under the pressure of "publish or perish" and "patent" logics. Further, this happens within a reprehensible mechanistic conceptual frame that, in our views, misses the organismal and ecosystemic interactions of DNA and its functions. In view of the power of the existing technical tools, a "scientific precautionary principle"—*i.e.* no more actions without an open critical reflection on fundamental principles—should govern science, as we will further hint below. Fundamental research should be at the core of a scientific approach also when dealing with these emergent but expected phenomena.

Finally, two non-minor, yet neglected issues emerge. Correctness of programs or their possible manipulation under cyber-attacks are far from being remote challenges. Computer driven DNA manipulation is a widespread technology, often based on piling up of programs working in immense databases. This may easily lead to inconsistencies, hence to incorrect programs. Correctness is an undecidable property at the core of major research work and applications, e.g. in Flight Control Systems where it has been closely studied for decades (Henzinger & Sifakis 2006), while the authors of this paper could never see this issue mentioned in reference to genetic manipulations. As for the computer systems' vulnerability to attacks, "the risks of using gene sequencing technologies to corrupt databases by altering sequences or annotations" and the work of computer scientists who "designed a DNA sample that, when sequenced, resulted in a file that allowed the hacker to remotely control the sequencing computer and make changes to DNA sequences" have been described (Baumann *et al.* 2022; Mueller 2021). The myth of cell and computer as exact Cartesian Machine (Monod 1970) fails even more blatantly when the two interact in open networks. In short, techniques show their limits, and more science seems required, at least as much as it is applied in Flight Control Systems.

5. Technology as the Only Solution to Recurring Pandemic Threats?

The emergence of an acute infectious disease in human population is a transitory phenomenon leading to a new dynamic equilibrium between pathogens and their hosts in a prey-predator type relationship (Wilcox & Colwell 2005), also known as homeorhesis, as it continually changes (Waddington 1953). The endemization of the new pathogen is one of these possible evolutions as it is regularly the case with the variants of influenza virus—carriers of antigenic shifts that explain the particularly deadly nature of certain flu pandemics (Kilbourne 2006). Four known strains of coronaviruses are endemic in the human population (Kahn & McIntosh 2005). Nasopharyngeal swabs and sera from 466 patients with upper respiratory tract disease collected between 1962 and 1967 were analyzed in an epidemiological study. This showed that endemic coronavirus infections accounted for up to 35% of total respiratory viral activity during epidemics (Mcintosh *et al.* 1970).

The emergence of the OC43 coronavirus strain was most probably at the origin of the deadly "Russian" flu of 1889 and 1894, the symptomatology of influenza and coronavirus infection being similar (Vijgen *et al.* 2005; Korsia-Meffre 2020). After a few deadly waves and the acquisition of immunity in the human population, this strain is now circulating without any particular harm, except for some vulnerable persons (Kistler & Bedford 2021). The same process is occurring today with SARS-CoV-2, which after several highly lethal epidemic waves, continues to circulate in an endemic way, without unusual severity, thanks to a host-virus coevolution leading to a peaceful equilibrium (del Rio & Malani 2022). The notion that such a pathogen could be completely eradicated by any sort of intervention in such an integrated world as ours was simplistic or even an illusion (Wilcox & Colwell 2005).

How these iatrogenic and laboratory accidents are being addressed? And what about their various anthropic causes, which have a common origin in a techno-science that destroys both the ecosystem and science? The aggressive use of powerful combinatorial techniques with little scientific content—see below and (Longo 2021) for more—increases the chances of disaster. Yet, on these grounds, some have—once again—proposed a technical solution, a quick "techno-

fix" serving as a molecular "magic bullet", allegedly successful in the short term, but not viable in the long run. However, causes are rooted in a distorted, anti-scientific, and mechanistic relationship with the ecosystem, following in the footsteps of Francis Bacon and treating plants and animals as machines through the early bio-technologies (Hartley 1937). The consequences are zoonoses following unlimited deforestations and intensive animal breeding as well as abusive experiments with no theoretical frames, but the myth of "re-programming life" like a computer.

In itself, the invention of messenger RNA vaccines is an innovative and very interesting technical possibility (Zhang *et al.* 2019). However, the scientific understanding of RNA and its "independent" functions in the proteome has long been delayed by the dominant geno-centric vision, according to which everything is played out at the level of DNA. In particular, this narrow vision has prevented for too long the funding of heterodox research, coined by many as "epigenetics", which has been proposed since the 1990s, for example by the pioneer of RNA studies, Katalin Karikó in the USA (Sahin, Karikó & Türeci 2014) and by Bruno Canard in France (Canard 2020). Moreover, it did not promise anything profitable in the short term. However, in face of the pandemic and once corporate actors understood the potential financial gains of this technology, gigantic pharmaceutical companies such as Pfizer grasped the value of the possible role of RNA-based tools. Then they quickly repurposed the RNA intervention platforms towards a vaccine against COVID-19, whose technical basis had been developed by a few small start-up-style laboratories that were in fact, so far, unsuccessfully working on cancer mono-antigenic immunotherapies (BioNTech). This was only possible due to very substantial public funding that was never repaid to date despite corporate record profits. These technical interventions, *i.e.* vaccines, applied first and urgently on elderly or fragile individuals, may have saved hundreds of thousands of lives, according to many government and health authorities. But… now what? Will we reflect on the causes of this dramatic increase of epidemics, which are now easily becoming pandemics? Will we resume the commitments made to the public health infrastructure in the early months of its spreading?

Everyone should remember that many governments, for example, France and Italy, acknowledged the needs of hospitals that had been so long neglected and turned into business enterprises, where every "act of care" had to be evaluated first financially and in the short term, mask storage included. More than 1000 head of intensive or urgent care hospital services had resigned in France before COVID-19, as they considered impossible to handle safely the "normal" incoming flu epidemics (Zéau 2020). We also remember how health care workers took control of their core business by adapting to the situation during the first lock-down. This was done at great personal cost and against the financial priorities imposed on them. Some of them died from COVID-19, often for lack of a sufficient, standard protection. For a few months, hospitals prioritized medicine before financial optimization and governments recognized the needs of community medicine, which was unable to provide care on an outpatient basis or at home. Since long, this has been forgotten: only "the vaccine" is mentioned. Any critical discussion on the subject is conveniently condemned and labeled as "anti-vax" whereas the criticisms stressing the limits of COVID-19 mRNA vaccination is based more on rational arguments than on *a priori* irrational positions (Schwarzinger *et al.* 2021), acknowledging its effectiveness in the short term for elderly or fragile people.

6. Technoscience's Denial of its Own Limitations

The effectiveness of messenger RNA vaccines in protecting the elderly or the vulnerable has been soundly stressed and pointed out by many colleagues and institutions (Joshi *et al.* 2021; Bardosh *et al.* 2022; WHO 2022). Notwithstanding, techno-science is blind to its own limitations, as spelling them out requires a broader scientific understanding based on principles (Longo 2019).

In fact, since mid-2021, the dominant political trend pushed for vaccinating everyone, including children who are almost never at risk of becoming seriously ill from SARS-CoV-2 (French National Academy of Medicine, 2021). In spite of this, the whole world should receive these short-lived vaccines as the only way out. An absurd idea that billions of people could be vaccinated on a tri-annual basis or even more frequently. Moreover, in the absence of data consolidated by time and sufficient hindsight, only limited considerations of the benefit/risk balance seem reasonable. The potential benefit

for people who are vulnerable because of their age or comorbidities, even in the absence of such data, may justify the governments' incentives to vaccinate them before the final FDA or EMA approval of the vaccines. This approval is still awaited, as it is conditioned by a methodology established to provide a sufficient level of scientific evidence (Doshi, Godlee & Abbasi 2022). For other people, those for whom the chances of serious consequences of SARS-CoV-2 infection are very low—and we know this since May 2020 through confirmed observations (Ioannidis 2021)—the benefit of the vaccine is questionable, especially when its related risks are still unknown. This holds more true as, today, the Omicron variant of SARS-CoV-2 is in the process of becoming endemic (del Rio & Malani 2022): more contagious but less pathogenic, it tends to be similar to the four endemic coronaviruses that have already been in circulation for decades or centuries (Lavine, Bjornstad & Antia 2021; Sonigo, Petit & Arhel 2021; Murray 2022).

To develop and devise future sustainable strategies in light of the soon-to-be endemic nature of SARS-CoV-2, it is mandatory to consider the success of these vaccines in the context of their limitations. Some scientific articles have shed light in vain on the fact that even vaccinated people can efficiently transmit SARS-CoV-2 infection also to fully vaccinated people (Singanayagam *et al.* 2021). Thus, sanitary passes or "certifications" are barely, if at all, effective against the spread of the virus, whereas hygiene measures, including masks, are helpful in protecting against SARS-CoV-2. Prevention around food and beverage handling is very important too. Unfortunately, too often politicians and journalists have been confusing the speed of contagion with pathogenicity and the effectiveness of the vaccine with its lack of protection against infection (Nainu *et al.* 2020; Brouqui *et al.* 2021). Ireland reached the highest rate of adult vaccinations in Europe in September 2021 (BBC 2021). However, it presented the highest rate of infection (Worldometer 2022). Indeed, "The epidemiological relevance of the COVID-19-vaccinated population is increasing", as soon observed in The Lancet, November 2021 (Kampf 2021). Sanitary passes based on vaccination may favor risky behaviors, thus the spreading of the virus.

Our human collective is falling into the fallacy of deeming ourselves in control of viruses if only the whole world, regardless of their vulnerability, participates in the technical solution (a "techno-fix")—this time an experimental vaccine. So, many politicians, while insisting on the vague notion of "herd immunity" for months (at 70% of the population?), suddenly started to accuse the unvaccinated 10% for the continuing crisis. And this focus on vaccines only makes us forget the multiplication of zoonoses following deforestation and persistent encroachment of natural habitats as well as laboratories carrying out gain-of-function research with potential pandemic pathogens.

Similarly, the degradation of our health systems, for example in France, continues unabated, with decreasing human and financial resources. Instead of facing these problems, the answer is then based on new vaccines, or even on a "universal vaccine", whose aim is to make all diseases disappear, including those of the future triggered by unknown and non-existent pathogens. The international Coalition for epidemic preparedness innovations (CEPI) was launched in 2017 with the ambitious goal of creating "a world in which epidemics are no longer a threat to humanity". It called for "platform technologies to enable rapid vaccine development against unknown pathogens", and released major funding "to develop a transformative rapid-response technology to create vaccines", with a special interest in early 2019 for "the RNA Printer™—a mRNA vaccine platform that can rapidly combat multiple diseases" (CEPI 2019).

The advantages of mRNA vaccine technology, since it can be quickly manufactured, is that it can be easily implemented in large-scale emergencies, as was done massively in 2020 to stop the COVID-19 pandemic. Moreover, it can be adapted in near real time to protect against variants that follow each other in quick succession due to the rapid evolution of the virus during the period of its emergence (Zhang *et al.* 2019). In the meanwhile, we compensate for the ephemeral efficacy of the current vaccine by repeated injections, which is the reason for the multiple boosters recommended in many countries. This perfect business model is also an ideal solution in theory. However, it is difficult to be satisfied with it in the current state of our knowledge.

Never has a vaccine been developed so quickly or delivered so massively in the absence of any pharmacovigilance data on possible long-term adverse effects, due to the lack of hindsight. Even the efficacy of COVID-19 mRNA vaccines raises questions as it is unclear whether they prevent severe forms of

the COVID-19 or not, in the absence of the raw data underlying the clinical trials (Doshi, Godlee & Abbasi 2022). Before the start of the vaccination campaigns, Peter Doshi, associate editor of the British Medical Journal, explained how the methodology of the clinical trials did not allow to know the protective value of vaccines against serious and deadly forms of SARS-CoV-2 infection (Doshi 2020). The randomized controlled trials (RCT) are considered as the gold standard for decision making but post-hoc modifications of some key elements of the trial plan have been shown to be frequent and worrisome (Eichler & Rasi 2020; Shepshelovich *et al.* 2020). However, adherence to the original trial design is fundamental to ensuring its scientific validity intended to address a precise medical purpose. In the absence of robust epidemiological data and sufficient hindsight, it seems fundamental to us to remain aware of the limits of technology without being classified as "anti-vax" people for this. Enough health scandals have warned us about it (Nature 1992; Mullard 2011; Fénichel, Brucker-Davis & Chevalier 2015; Wise 2015; The Lancet 2021). In particular, the precautionary principle is not an irrational attitude. It is especially relevant for those subjects who are not at risk of severe forms of the disease, such as children and young people. This awareness is a scientific attitude.

As a matter of fact, the first precaution must be scientific, as we hinted above: strongly needed research on "epigenetic" activities of RNA have been delayed for more than twenty years by the geno-centric perspective. In turn, this denied, a priori, the possibility of any side effect of the mRNA vaccine during the pandemic, on the grounds that... the RNA does nothing, alone, in the proteome (except in the case of retroviruses, of course, as they act on DNA). This response is grounded on the same anti-scientific attitude, which, through its action on ecosystems or by molecular manipulations based on the flawed vision that organisms are Baconian mechanisms programmed by Lego-like DNA segments, is at the origin of almost all the epidemics of the last decades, sometimes transformed into pandemics. And the techno-scientific "solution" keeps making promises on the basis of the same lack of scientific knowledge.

Indeed, the engines that may generate pandemics continue at full speed and, undoubtedly, the next pandemic is already in the making. In fact, we will be lucky if it does not break out before this one has finally become endemic.

7. A Failed Conception of the Living World

As stressed above, from the scientific point of view, most of these manipulations (intensive destruction of ecosystems as well as laboratory experiments) are based on a techno-scientific vision of organisms. Let us now analyze this vision. It is based on an "alphabetical combinatorial" approach to DNA, which is seen as a "computer program" or "code" of life that can be manipulated at will—with little if any understanding about the organism, its ecosystem, and its history.

The book *A crack in creation: The new power to control evolution* by 2020 Nobel Award winner, J. Doudna (Doudna & Sternberg 2017) offers a good example of such an anti-scientific attitude. The book focuses on a very relevant technique that has allowed to transfer to the laboratory bench the "mechanism" used by bacteria to detect and destroy the DNA of invading bacteriophages. This remarkable invention *per se* certainly deserves a Nobel Award. Unfortunately, the technical advance is framed in a totally wrong or vague theoretical frame. As for the wrong part, the Central Dogma of molecular biology (CD) is advocated explicitly, a statement claiming that "the genetic/hereditary information is completely contained in the DNA", or that the DNA fully guides the embryogenesis and the ontogenesis. In spite of several rephrasing, this assumption is at the core of the CD, as long as the usual "information/programming" language is used: since "information goes from DNA to RNA to proteins" and proteins cannot reverse the information back to the DNA, no other source of "information/programming" has to be found. Some sort of essentialist-Thomist view frames this perspective, like in the reference, since 2001, to the "decoding of human DNA": once known the chemico-physical structure of DNA (a major advance) we know its *essence*. Now, the DNA matters also, or mostly, for what it does. And this depends on the context (Longo 2021)). As for the "vague" part of the assumptions, the wording of "information" and "program" are referred to in the usual sloppy way proper to molecular biology, where it is not clear if the first refers to discrete data types information, Shannon's or Turing's approaches, which significantly differ concerning entropy and complexity (Longo 2020). These precise but wrong assumptions plus vague notions, such as genetic information and genetic

program, make a vast and powerful community take strong stances: by editing, acting on, and modifying DNA we can drive, program, and control organisms, species... and even evolution.

However, if we change perspective and see the DNA as the (amazingly important) physico-chemical trace of a history (evolution) and as a constraint to macromolecular, largely stochastic, flows, then we may aim at understanding its fundamental role both in phylogenesis and ontogenesis (Soto, Longo & Noble 2016). Further, we may get rid of the myth of driving/programming them by editing DNA-alphabetic sequences.

Coupled to the mechanistic insensitivity to the ecosystemic issues, *i.e.* unlimited extractivism and the use of plants and animals as machines, this "editing/programming" attitude prevails in too many laboratories, where powerful techniques are used with no scientific grounds. The "publish or perish" criteria further encourage all sorts of manipulations with no scientific knowledge, hoping for any output that may justify a publication.

In summary, in either case—zoonosis or loss of control over genetically manipulated pathogens—the root "cause" is our relationship with nature. Many of us (Association of Friends of the Thunberg Generation, the European Network of Scientists for Social and Environmental responsibility, and the Cardano Group), are calling for a radical change in order to prevent future pandemics, and more generally, to preserve a viable life on the planet. We need to understand biology in its evolutionary and historical context including all its diversity and singularities (Sonigo & Stengers, 2003). Instead, we treat plants, forests, animals, and humans as machines constructed by the gears of Descartes and Bacon's clocks, which still serve as the main reference for the founding fathers of mainstream molecular biology (Monod, 1970) and bio-technologies (Hartley, 1937). The pupils of the latter consider organisms as driven by a software written in the DNA, which can be programmed and reprogrammed at will. In a recent talk, Nobel Laureate Jennifer Doudna announced that the new CRISPR-based gene editing techniques will allow to "cure (all) diseases" (Doudna 2022). Jointly to the other speakers, Andrea Crisanti from Imperial College London, bioethicist Françoise Baylis from Dalhousie University, and WHO Chief Scientist Soumya Swaminathan, she conjectured that CRISPR will help facing the ongoing ecosystemic changes by driving animal and plants towards viable evolutionary paths.

Possibly the current pandemic and certainly many previous failures or unrealized promises illustrate that this is not only a scientifically flawed assumption but also a dangerous project (Longo 2018). Just consider the fifty-year old, iterated promises to cure or even eliminate cancer by acting on genes within... 2015 (von Eschenbach 2003). The financial support of this enterprise was opposed to the search for environmental causes of cancer, in spite of its doubling incidence in forty year. This increase, a paradigmatic case for our analysis, is largely due to human/ecosystem interactions (Soto & Sonnenschein 2010). We introduced 80,000 new molecules in the biosphere in less than a century. The current paradigm gets rid of this fact stating that most of these new molecules are small and not (stereo-) specific to organismal macromolecules (Zoeller *et al.* 2012), so they cannot act as "key-lock" in the cellular "cartesian mechanisms", thus it is impossible that they interfere with the genetic program. Instead, they do interfere with hormone cascades in varying probabilities and kill people. Corporate interests once more meet a view of nature that, in turn, is kept alive by those interests and their financial support.

Conclusions

We need to think better, and collectively, about the current and future possible debacles. There is an urgent need for more expertise than that currently showed in the debate about COVID-19. In particular, more knowledge is needed in the disciplines that understand the ecosystem or laboratory origins of epidemics to propose countermeasures and new research guidelines and directions. Rapid technical responses are only palliatives, which confirm a flawed logic. Unfortunately, they are financially hegemonic. Even in urgency, investments and research on medical care and multi-antigenic vaccines must proceed in parallel. Precautionary, broad measures taken ahead of time addressing the root causes of pandemics will allow us to avoid the hasty and risky emergency actions we have seen during this pandemic. Building on the theoretical and practical knowledge of a broad range of experts and actors, who aim to look after the biosphere while fostering critical thinking about the technosphere, seems to us the way forward to avoid a repetition of the current debacle.

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