

COMMENT

The COVID-19 pandemic as a scientific and social challenge in the 21st century

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Abstract. The coronavirus disease-2019 (COVID-19) pandemic, caused by the new coronavirus SARS-CoV-2, has spread around the globe with unprecedented consequences for the health of millions of people. While the pandemic is still in progress, with new incidents being reported every day, the resilience of the global society is constantly being challenged. Under these circumstances, the future seems uncertain. SARS-CoV-2 coronavirus has spread panic among civilians and insecurity at all socio-political and economic levels, dramatically disrupting everyday life, global economy, international travel and trade. The disease has also been linked to the onset of depression in many individuals due to the extreme restriction measures that have been taken for the prevention of the rapid spreading of COVID-19. First, the socio-economic, political and psychological implications of the COVID-19 pandemic were explored. Substantial evidence is provided for the consequences of the pandemic on all aspects of everyday life, while at the same time we unravel the role and the pursuits of national regimes during this unforeseen situation. The second goal of this review is related to the scientific aspect of the pandemic. Hence, we explain why SARS-CoV-2 is not a so-called 'invisible enemy', and also attempt to give insight regarding the origin of the virus, in an effort to reject the conspiracy theories that have arisen during the pandemic. Finally, rational strategies were investigated for successful vaccine development. We are optimistic that this review will complement the knowledge of specialized scientists and inform

non-specialized readers on basic scientific questions, and also on the social and economic implications of the COVID-19 pandemic.

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1. Introduction

What we have experienced during the current pandemic is an unprecedented situation with World War characteristics. For younger generations who have heard about the World War II only through the stories of our parents and grandparents, books, movies and documentaries, the current situation will be recorded in our memories as a modern form of a new World War.

2. Death and the solitude of the dead

For many people, this period of the pandemic will be recorded in their memory as a tragedy, as they have lost either loved ones or their jobs and look forward to the future with great uncertainty. *'Everyone dies like dogs, like pigs, I'm not ashamed to admit that. It's not fair that dad died like that. People say they were old, they were sick. But he was my father, he was not old and he was not sick [...]. Here in Val Seriana you can only hear the sirens of ambulances and the bells of mourning'* (1). This was the testimony of a young lady from the tormented Italian city of Bergamo. Italy is one the seven largest International Monetary Fund (IMF)-advanced economies in the world, which comprise the Group of 7 (G7). Such a 'major advanced economy' could not provide its doctors with safe masks, such a 'great industrial power' ran out of gloves and consumables, like most other affluent countries in the world, resulting in the infection and death of doctors and nurses, the frontline fighters who had been discredited and insulted before the pandemic and praised and applauded during its progression. Tragedies were the suicides of nurses due to their inability to cope with the insurmountable pressure and the burden of many patient deaths. Furthermore, lamentable news of unclaimed dead people in USA and Italy reminded the inhumanity of the society. The sense of unbearable solitude has been overwhelming as if their death did not matter to anyone. No one cared, at least not enough to pay their last respects to the dead.

3. Many questions arise from the words 'cost-profit'

There are many questions concerning the frequency of zoonotic virus-related epidemics and pandemics in the last twenty years, the strengths and weaknesses of various health systems around the world and the weakness of the 'developed' world to cope with the 'invisible viral invaders - enemies' of public health, in the 21st century and during the so-called 4th industrial revolution. However, if one was to take into account all of these questions together, one basic question would emerge; how much is the life or death of a fellow human worth in the 21st century? In the era of the current pandemic, the answer to such a question, and all types of questions related to it, is defined by a 'cost-benefit' assessment, entangled with the existing social system. The current prevailing approach of minimising expenditure and maximising profit, limits the potential of the public health sector, with consequences that have become evident during the current pandemic.

The Latin-American revolutionary Ernesto 'Che' Guevara, physician by training, stated that *'the life of a single human being is worth a million times more than all the property of the richest man on earth'* and he continued: *'medicine will have to convert itself into a science that serves to prevent disease and orients the public toward carrying out its medical duties. Medicine should only intervene in cases of extreme urgency, to perform surgery or something else which lies outside the skills of the people'* (2).

In the antipodes of these views, lie the statements made by the Bundestag president and former finance minister, Wolfgang Schäuble. While Germany was mourning the deaths of more than 5,600 people from the new coronavirus, and was yet to calculate the damage caused by the quarantine to the state's

economy, Schäuble warned that the state cannot solve all the problems and argued that he did not consider politics obliged to plan everything out in order to protect human life. Referring to the relaxation of restrictive measures, Schäuble stated that *'we cannot trust the decision exclusively to epidemiologists, but we must also weigh the significant economic, social, psychological or other consequences. If we close everything for two years, the consequences will be terrible'*. And he concluded: *'When I hear that everything is receding in front of the protection of human life, I must say that this is not absolute. The basic human rights have to be restricted on both sides. If there is one absolute value in our Constitution, it is human dignity. This is inviolable. But that doesn't rule out that one day we will die'* (3).

4. The 'invisible enemy' from a scientific perspective

The two-month confinement due to the restrictive measures, formed the basis for us to reflect on ourselves our friends and family and society, and appreciate the concepts of solidarity, volunteering and sacrifice. Member of the scientific community were also concerned about news reports describing the new coronavirus as an 'invisible enemy'.

The phrase 'invisible enemy' sounds almost metaphysical to scientists. In a way it takes us back to the dark ages, when mankind lacked scientific knowledge and technological tools. Such expressions deconstruct rational thinking when one tries to identify the causality of a phenomenon, reinforcing conspiracy theories about new biological weapons or secret and uncontrollable forces. They support the idea that the world is falling apart and that we are unable to reverse this process and, most importantly, to envision a new world that has mankind in its focal point. They give us the impression that invisible enemy forces are conspiring against us, while the confinement measures which isolate us from the community, reinforce these existential crises. Terrifying television news reports are enhancing these effects: In Russia, civilians have been monitored by cameras in every building block and the offenders have been tracked down in real time by the nearby police (4). Dozens of robots have been released in the centre of Tunis, patrolling and checking whether civilians comply with the COVID-19 restrictive measures (5): pedestrians are no longer inspected by police officers, but by robots, the so-called P-Guards, which behave exactly like officers, stopping pedestrians and asking for personal documents. Robots, of course, function through an intercom system. The officers at the Ministry of Interior are the ones giving the orders that are executed by the robots. In the streets of Israel, armed soldiers have been inspecting whether the measures against the coronavirus are being followed by the residents (6). To many, the coronavirus pandemic serves as an excuse for a global-scale exercise, aiming to control social consciousness. A variety of weapons from the quiver are used: conspiracy theories regarding the construction of SARS-CoV-2 in a secret laboratory in Wuhan, China, a special phraseology regarding an 'invisible enemy', which is unfortunately adopted by some science spokesmen, the constant display of images that reinforce fear and panic by the media, the presentation of the state as consistent with its duties, and most importantly, the notion that the course of the pandemic is being defined by the responsibility of the individuals instead of the establishment of

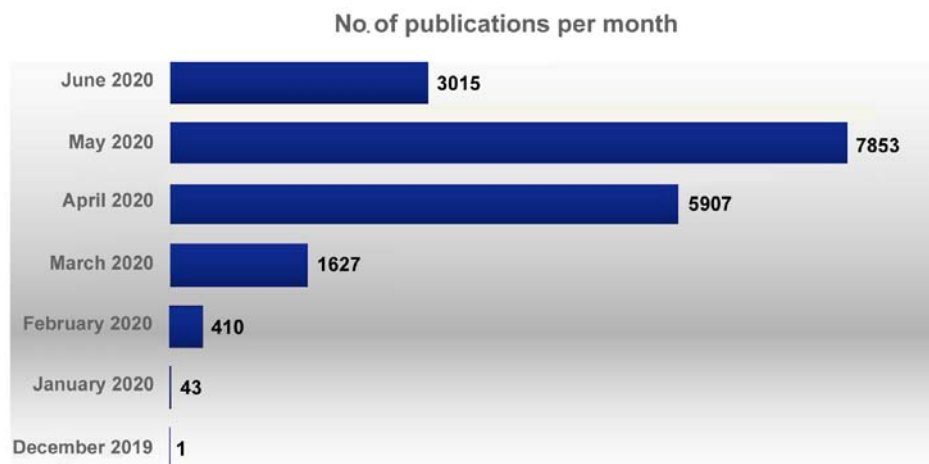


Figure 1. Graphic presentation of the total number of publications per month regarding SARS-CoV-2 and the COVID-19 pandemic. Presentation is of the monthly number of publications that were recorded in PubMed, from the 1st of December 2019, i.e., the first recorded case, until the 16th of June 2020.

a robust public health system. The results of this exercise will be manifested in the post-epidemic era and in the context of a new global economic recession that is already taking place.

The dynamics and connotations of words and images, can influence or even transform the consciousness of each individual to a certain extent and, consequently, affect social consciousness. Rarely is a word neutral. It carries our energy and our aim with it. Modern science (neurology, biology, anthropology, linguistics, etc.) can confirm this notion, as every single word is a process of thoughts that are the result of hormonal, biochemical and metabolic alterations, and electrical charges or discharges of our neurons (7). We should not forget that the main goal of the targeter is to look indeterminable, incomprehensible, inaccessible, powerful, invincible, and invisible if possible (here we are not referring to SARS-CoV-2, but to the economic elite that define global social policies). When the root of the problem is traced within the DNA of the targeter, in our attempt to defend ourselves to survive the attack and to confront the enemy, we must come up with a plan for its total elimination. It is important to first record and then analyze the targeter's plan. We must study its purpose, what it seeks from its target, which in this case is us. Marx has already answered these questions as early as mid-19th century, with the phrase *'The philosophers have only interpreted the world in various ways; the point, however, is to change it'* (8). For such a change it is necessary for the targeter to become the target and for the target to become the targeter, in the context of a scientific plan for social transformation that will move us, excite us and, as a shining star, guide us into the future. And in these imprinted thoughts we must search where they come from and where they may lead us to. Only then will we be able to understand whether they are good or bad. As Hölderlin wrote in 'Patmos': *'But where there is danger, Salvation also grows'*. It is a nice expression of the Heraclitean struggle of the opposites (9), which at the socio-political level may be translated as the struggle of the social classes.

5. Is SARS-CoV-2 indeed invisible?

The total number of publications on the new coronavirus (nCoV-2019) since the first reported case in China, is impres-

sive. Notably, until the 16th June 2020, 22,792 articles related to COVID-19 had been published in PubMed-indexed journals (Fig. 1), as well as 5,244 pre-prints in medRxiv and bioRxiv. These numbers give a very important message: The scientific community is alert, and most importantly, that SARS-CoV-2 is not 'invisible' and, hopefully, not invincible for too long.

Surely, when it first emerged, the virus was unknown, and so was its relation to the human immune system, and its general pathophysiology. Today, however, following the identification of more than 11 million cases through the use of specific molecular tests and the recovery of millions of patients, we know that the immune system reacts adequately in the vast majority of the cases. The clinical manifestations of the virus and its unique behaviour towards various vulnerable groups have been recorded in detail. There are asymptomatic and slightly symptomatic people who do not get sick, but act as carriers and reservoirs for the disease. A large number of data already exists on the genetic identity of the various strains of the virus. The genomes of many thousand different viral strains have been sequenced. SARS-CoV-2 is the 7th coronavirus to be historically recorded and using bioinformatic tools, it has been classified as a member of the Coronaviridae β family (10). The coronaviruses responsible for the SARS and MERS epidemics (10-12), that were discovered in 2002 and 2012, respectively, also belong to the group of β -coronaviruses; SARS-CoV-2 genome is composed of 30,000 bases, harbouring approximately 10 genes, with functions that are implicated in viral structure and function (10). Viral spike proteins interact with their receptors on the surface of epithelial cells (10-12). A study including SARS-CoV-2 genomes from 7,666 patients with COVID-19 from around the world, identified 198 recurrent genetic mutations of the virus, which appear to have occurred independently, more than once (13). The main conclusions from this study highlight the following: i) A large portion of the global gene diversity of the new coronavirus has been recorded in all countries affected by the pandemic. This finding indicates that there has been an extensive transmission of the virus on a global scale since the very early stages of the epidemic, which also means that in most countries there has not been a single 'patient

zero', but more likely, the virus has intruded independently several times and via different routes. ii) New phylogenetic findings confirm that the virus emerged towards the end of 2019, before it began its rapid global transmission. iii) All coronavirus genomes from patients around the world appear to have originated from a common ancestor that seemed to emerge between 6th October and 11th December 2019. At that point, the new coronavirus must have been transmitted from an animal to the first human and to have caused an infection in that human. iv) Researchers believe it is highly unlikely that the coronavirus had been circulating among humans for a long time before it was detected in Wuhan, China, last December. v) Although the number of the detected mutations is large, this cannot thus far be correlated to the virulence and the severity of the virus. Several research teams around the world, including Greece, are conducting similar studies (14). The collection of a large number of genomic data and its correlation with the clinical manifestations of COVID-19 will lead to more accurate conclusions regarding the possibility of increased virulence due to frequent mutations, to the design of safe vaccines and therapeutics, as well as to our preparation for the possibility of an impending second wave of the pandemic. vi) A large number of mutations (15 in total) have been identified in the gene that encodes for the spike protein S (the protein that comes into contact with the target cell, e.g., lung epithelial cells), while other sites are far less frequently mutated and could, according to researchers, be much better targets for the development of effective therapeutics and vaccines (15).

6. The right strategy for vaccine development

Genomic analyses and the identification of highly conserved sequences will determine the right strategy for the design of vaccines and drugs with long lasting effects, which will not be easily evaded by the virus. For this purpose, Academic professionals of various scientific expertise (Molecular Biologists, Doctors, Epidemiologists, Statisticians, Pharmacists, Immunologists, Structural Biologists, Bioinformaticians, etc.) must work together in harmony in order to achieve the best possible result, i.e., an effective treatment against the new coronavirus. It is important to determine whether the already known viral mutations are beneficial or neutral or whether they contribute to the aggressiveness of the disease. This information can be reliably deduced from collaborative studies that combine clinical and demographic data with the type of mutations, the dynamics of mutations in the structure of the S protein, and the correlation of the altered S protein structure with the receptor protein of the host cell (15). Of particular interest are the 15 already known mutations in the gene that encode for the viral spike protein S which is essentially regarded as the tip of the viral spear, the first to come in contact with the receptor of the host cell. In this battle for viral replication, i.e., in the battle of 'opposite pursuits', some will be victorious and some will be defeated. For the patient, this is phenotypically translated into being asymptomatic, slightly symptomatic and symptomatic (diseased). Evolutionary Biology has taught us that mutations can be either beneficial, neutral, or harmful to the organism. This depends on how the mutation affects the survival and reproduction of each organism, including the new coronavirus. A more aggressive type of the new coronavirus has been found to account for approximately 70% of

the 30 analysed strains, while only 30% of the analysed strains were associated with a less aggressive viral subtype. The most aggressive and deadly strain was identified in the early stages of the Wuhan epidemic, the Chinese city that the coronavirus first appeared in, and now scientists are trying to decode all possible mutations and to determine which strains have emerged in each geographic area (16).

Based on these data, the statement that the virus is 'unknown' or, even worse, an 'invisible enemy', is at the very best a statement made out of habit or, in the worst case scenario, a statement which could become offensive to the research scientists that are working on it.

Interestingly, more than 1,000,000 scientists are currently estimated to be involved in basic and clinical-epidemiological research on the new coronavirus worldwide. Plenty of information regarding the biology and the pathophysiology of the virus has already become available and this is perhaps the most optimistic message for a rational and effective design of therapeutics and vaccines against COVID-19. At least 40 putative drugs are currently under evaluation in 500 clinical trials worldwide. Remdesivir and two immunomodulatory antibodies used in other diseases are already being tested against the coronavirus, and ongoing clinical trials will undoubtedly shed more light on the effectiveness of these drugs. The clinical trials on monoclonal antibodies that target the viral proteins (mainly the S protein) and inactivate the virus are also of significant interest, as they have been proven to be effective in many pre-clinical studies.

Based on the existing experience, it seems that one cannot apply the same anti-COVID-19 treatment to all patients; the type of treatment is highly dependent on the stage of the disease. In the early stages, antiviral factors that inhibit the viral reproduction enzymes, such as remdesivir, favipiravir, EIDD-2801, as well as antibodies against the viral proteins or the viral cellular receptor, ACE2, play a major role in effectively clearing the disease before it can progress to more advanced stages. In the advanced stages of the disease, however, immunomodulatory drugs, such as antibodies against IL-6, CCR5, and C5a receptors, as well as anti-coagulation drugs and drugs used in microvascular inflammatory disease, appear to be more effective (17).

In addition to the above therapeutic approaches, immunotherapy may also constitute another effective means against COVID-19, with significant research experience already gained in this field. People who have recovered from a coronavirus infection are being encouraged to donate their plasma for the treatment of other patients. Such studies are being conducted all over the world (17).

The high degree of initiative of a significant number of companies around the globe for the development of an effective vaccine against the new coronavirus is impressive. The very form of this pandemic, with its especially devastating consequences for global economy, the uncertainty of a new disease outbreak, and the small percentage of recorded immunity in the world's population (18), have put several companies of the most developed countries in a race of relentless competition. In such cases, there can only be one winner to receive the gold medal, although the rest may actually not lose too much, as the majority of these 'losers' will have received state funding; in this case the tax payers' money will have been

used to 'cushion' the imminent recession they themselves will have caused with their laws of economy. The demand for the vaccine will be huge, the profit will exceed every expectation, and will therefore provide a secure investment 'for the sake of humanity'.

Today, on 28th June 2020, there are as many as 40 programs on vaccine development, out of which 7 vaccines are already being tested in humans all over the world. Among the leading companies are CanSino Biologics (Beijing), which uses an adenoviral vector, and Sinovac (Beijing), which uses an inactivated virus (PiCoVacc). In the United Kingdom, researchers at the University of Oxford are testing the ChAdOx1 nCoV-19 vaccine which includes an adenoviral vector and the spike protein S. In the United States, Inovio Pharmaceuticals is testing a DNA type vaccine. The American company Moderna has also developed an RNA vaccine in collaboration with NIH. There is also BNT162, a four-vaccine program developed by the German biotechnological company BioNTech and Pfizer pharmaceuticals; the four vaccines represent different viral mRNA antigens that are used as targets (17). In addition, in early April, Veronika Skvortsova, the head of Russia's Federal Biomedical Agency (FMBA), announced that Russia had created seven novel anti-coronavirus vaccines ready to enter clinical trials (19). Experience with influenza virus has shown that vaccines are usually effective for 40-60% of the people who get vaccinated, but this rate is sufficient to control the infection fully within the community. In addition, anti-flu vaccines are modified yearly, in an effort to effectively protect against new strains.

7. The 'competitive nature' of man and reality

Those who dream of another, humanistic world, know very well that if all scattered scientific forces that are currently dealing with the vaccine against the coronavirus were united for a common purpose, i.e., to serve the supreme good of human health, in a continuous exchange and sharing of scientific knowledge, the goal of the vaccine would be realised much sooner, spending much less effort and funds. Others believe that competition acts as a catalyst for the realisation of the ultimate goal, which in this case is the production of the vaccine. Many also believe that competition is a basic characteristic of human nature. But there is another apprehension. Competition is not a characteristic of human nature as projected by certain socio-biologists who like to compare, and even equate, human societies with animal communities. Competition is not something that man carries since birth as a biological evolutionary trait. It appears only when the necessary social structures and relationships are formed, when a person or a group of people may possess materials of nature and means of production and the rest of the people act as their employees. Therefore, competition should be looked for within the social structures and in the relationships between people and the means of production. In other words, competition among people is a relationship that, if it were to be ablated, the 'original' non-competitive intellectual man, the Nietzschean superhuman, would emerge in a course of civilisation that would allow the realisation of one Utopia after another.

The hominization process of *Homo sapiens* was a huge leap forward in evolution. The conquest of nature by man

began with the development of manual workmanship. The development of labour helped to strengthen the bonds of mutual assistance and joint activity. Mutual working activity has contributed to the need to communicate with articulated speech and language, which has been recorded in human history as culture. Therefore, because of work, humans were able to conquer the forces of nature, obliging them to serve their purpose. On the contrary, the animals adapt to the forces of nature and are not able to consciously influence them, to tame them. This is the most essential feature that distinguishes humans from animals.

To be in the position that he is today, Man has fought against the immense forces of nature, he has managed to subdue them and emerge victorious, because he had to respond to something deeper. He responded to the necessity to improve his life, to create culture. It is not by coincidence that many inventors who defined the course of humanity through their discoveries, apart from possessing scientific knowledge, they were inspired people, devoted to the common good. After all, the great meaning of life is for all humanity to enjoy the discoveries and inventions of the inspired creators. This is now known to require another social organisation plan that people will understand, believe in and fight for its realisation.

9. The extreme rivalries among the powerful of the world may have an economic basis

In the context of the 'invisible enemy', extreme rivalries have emerged among the powerful of the world. Some politicians, led by the US president, have insisted that the virus is a fabrication of China's secret laboratories (20,21). Such statements can be taken as seriously as those made by the President of the United States... solarium and disinfectant injections to treat the coronavirus infection. Respectively, China insists on denying allegations by the US government that it has been negligent in dealing with the epidemic and in not notifying the global community early enough (22). More specifically, through the newspaper 'People's Daily', China poses a series of questions to the US government, substantiated as follows: they accuse the US government that after 'inadequately dealing with the outbreak', they are now 'shifting the responsibilities' to China. In particular, they provoke the US government to provide answers regarding the sudden closure of the US Army's biological weapons laboratory in Fort Detrick, Maryland, USA, following a pneumonia outbreak and a simultaneous H1N1 virus epidemic last July. The Chinese also point out that two months after the exercise event 201 for a global pandemic, held by various US organizations in October 2019, the first case of COVID-19 was identified in Wuhan, wondering as to a possible relevance between these events (22). They report that Robert Redfield, head of the CDC (US Infectious Diseases Center), also acknowledged that some of the COVID-19 victims had been diagnosed with the seasonal flu, which has killed more than 20,000 people since last September (23). The majority know from personal experience that 'when the buffaloes fight, the frogs pay for it', the frogs being the humble people around the world. It is certain that in the near future the economic rivalries among the most powerful will intensify, as can be understood from the information presented in Table I.

Table I. Estimated global ranking by GDP in PPP terms (2 billion US dollars at fixed 2016 prices) (24).

| Ranking by GDP (PPP) | 2016 Ranking | | 2030 Ranking | | 2050 Ranking | |
|----------------------|--------------|------------|--------------|------------|--------------|------------|
| | Country | GDP in PPP | Country | GDP in PPP | Country | GDP in PPP |
| 1 | China | 21,269 | China | 38,008 | China | 58,499 |
| 2 | USA | 18,562 | USA | 23,475 | India | 44,128 |
| 3 | India | 8,721 | India | 19,511 | USA | 34,102 |
| 4 | Japan | 4,932 | Japan | 5,606 | Indonesia | 10,502 |
| 5 | Germany | 3,979 | Indonesia | 5,424 | Brazil | 7,540 |
| 6 | Russia | 3,745 | Russia | 4,736 | Russia | 7,131 |
| 7 | Brazil | 3,135 | Germany | 4,707 | Mexico | 6,863 |

GDP, gross domestic product; PPP, purchasing power parity.

John Hawksorth, chief economist at PwC and one of the authors of the relevant report, states the following: *'We will continue to see a shift in the global economic power from the advanced economies to the emerging economies in Asia and elsewhere. By 2050, the E7 countries (Brazil, China, India, Indonesia, Mexico, Russia and Turkey) will produce approximately 50% of the world GDP, while the share of the G7 countries (Canada, France, Germany, Italy, Japan, UK and USA) will marginally exceed 20%'* (Table I) (24).

10. There is irrefutable evidence that SARS-CoV-2 is not only contagious but also highly related to social class

While the pandemic was still in its infancy in the United States, with a reported 400,000 cases and 13,000 deaths from the new coronavirus, statistical analyses revealed the following: In Chicago, African Americans make up 30% of the population, but they seem to account for 70% of the total number of people who have died from COVID-19 in this large city. In Illinois, the African-American population is 14%, yet the death toll in this sub-group is 41%. Similarly, in Milwaukee, African-Americans make up 26% of the population but the victims exceed 80%. Surely this picture is not unrelated to the social inequalities that reflect the material basis of racism in a country where the financially less-privileged cannot have access to either (private) insurance or healthy living conditions. According to the UN's International Labor Organization, 1.25 billion workers out of the world's 3.3 billion are at high risk of suffering 'drastic and catastrophic' consequences, such as layoffs and pay cuts, as a result of the economic measures taken during the pandemic (25).

According to a report published in Lancet which includes tens of thousands COVID-19 cases from China, depicting mortality rates per region of the country, it appears that in areas where the population had substantial access to satisfactory health care services, the mortality rate (deaths in % of patients) was 0-0.3%, while in areas where for various reasons there was no such possibility, the mortality rate was more than tenfold higher (3-5%) (26). In an ideal situation, however, if 10% of the 7 trillion (!) monetary funds held by the 500 Croesuses who make up 0.0000066% of the world's population were committed to helping those who are less-privileged financially,

we would all feel that the pandemic was just an annoying nightmare that would go away the moment we opened our eyes. The virus is therefore contagious and social class-related as the effects of the various economic measures undertaken globally have been unequally distributed on existing social class territory (27).

A recent report from the National Records of Scotland (NRS) includes statistics on the number of coronavirus-related deaths (COVID-19) and the total number of deaths recorded in Scotland in the weeks 1 to 19 of 2020. Regarding COVID-19 deaths recorded in March and April 2020, it was observed that people in the most deprived areas were 2.3 times more likely to die of COVID than those living in the least deprived areas. If an area is recognized as deprived, this may be related to low-income, but it may also mean fewer resources or opportunities, such as employment, education, health, access to services, crime and housing. In week 19 (4 to 10 May), the Health Board area with the highest number of deaths involving COVID-19 was Greater Glasgow and Clyde with 126 deaths (also the highest number of COVID-19 deaths to date: 1,038). The Health Board area with the highest rate of COVID-19 deaths to date has also been Greater Glasgow and Clyde with 8.8 deaths per population of 10,000 (Fig. 2) (28).

11. The conspiracy theories as an antidote to the scientific truth

The struggle for the 'paternity' of the new SARS-CoV-2 coronavirus between US and Chinese officials is indicative of the contradictions that exist between these two very powerful economic forces in the world (23).

Regardless of such statements made by political officials with powerful economic status, scientists must first and foremost use strict scientific criteria and, based on published scientific data, form an opinion as to the possibility, or not, of a laboratory construction of the virus with biological warfare purposes. Having acquired enough information on the new coronavirus, we dispel such myths and conspiracy theories.

Scenarios for a laboratory construction of the virus are based on the work entitled 'A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence' (26). In this report, the authors point out that the 2002-2003 emer-

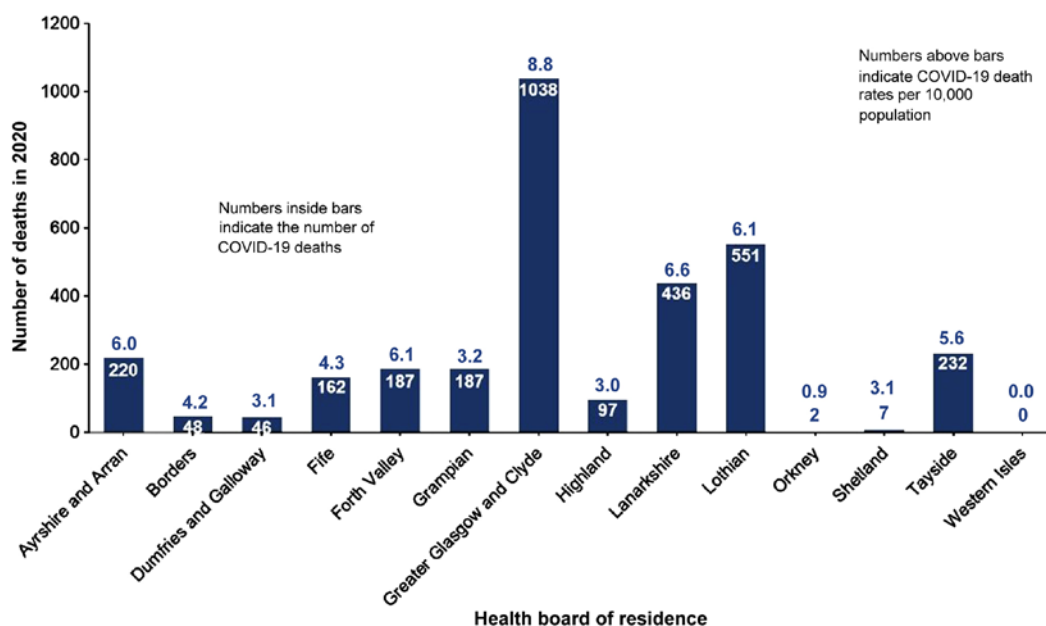


Figure 2. Deaths involving COVID-19 in Scotland. Registered between weeks 1 and 19 (beginning of year to 10th of May 2020), by the Health Board of residence, Scotland (28).

gence of SARS-CoV introduced the possibility of epidemics in human populations by viruses of animal origin and opened up a new topic for discussion in the scientific community. They also refer to influenza viruses (H5N1, H1N1, H7N9) and the MERS-CoV coronavirus, and point out that previous studies have demonstrated the existence of closely related SARS-like viral genes in Chinese bat populations. However, the authors conclude that the presence of SARS-like genes in bats alone does not mean that these are indeed SARS viruses, nor does it mean that they can infect humans. Based on these concerns, they introduced the question of whether these potentially SARS horseshoe bat viruses (mainly found in China) are capable of infecting humans and thereby of causing a new SARS epidemic (26).

The first approach, which included electronic simulation experiments, showed that no spike of the bat virus is predicted to attach to the human cell receptor. They then performed pseudotyping experiments; that is, they stripped a murine SARS virus of its genetic material, and re-coated it with the nucleocapsid of a horseshoe bat virus. In all cases, the pseudotyped viruses failed to infect both mouse and human cells. The latest experimental approach involved the use of chimeric viruses consisting of a SARS-CoV mouse-adapted backbone and a novel spike protein isolated from Chinese horseshoe bats, that is both the genetic material of a murine SARS virus with a bat spike protein encoding gene and a complete murine SARS virus capsid-enclosure (minus the bat spike protein). The recombinant viruses successfully managed to infect both mouse and human cells *in vitro*. In this case, the *in vitro* approaches served as an indication of what can happen *in vivo*. Following this, the researchers infected mice with the recombinant viruses and managed to cause SARS disease in these animals, with profound related symptoms. Young infected mice showed 10% weight loss with no reported deaths, whereas older mice presented with greater weight loss and low mortality rates. This way the research team managed

to create an *in vivo* model to use as a platform for testing various therapeutic protocols. Antibodies to SARS-CoV (2002-2003 virus) had little or no effect on alleviating the disease in mice infected with the recombinant virus. In addition, the vaccine, developed against SARS-CoV (DIV), did not seem to offer any protection, but it produced significant side effects in these animals (26).

In their Nature Medicine report, the researchers also describe the experiments performed on the horseshoe bat virus. This virus infects both mouse and human cells but with a profound delay in viral replication. Infection of mice with the horseshoe bat virus did not seem to induce weight loss and viral replication was slow as compared to SARS-CoV. If we were to take into account all of the above experiments, i.e., the experiments with recombinant viruses and the experiments with the horseshoe bat virus, we could reach the following conclusion: in order for the horseshoe bat virus to become more infectious and to be able to infect humans, it would need to undergo additional adaptations or adjustments. Viruses can acquire these adaptations selectively, as for example when a bat virus crosses the species barrier and is passed on to an intermediate host. In the new host, the spike protein acquires the necessary adaptive mutations to facilitate improved infection and eventually the ability to infect humans. Another possibility is that humans are directly infected by the horseshoe bat virus and human contact with other animals that also carry the virus eventually leads to continuous human re-infections until, due to random mutational events, the deadly variant emerges (26).

Most likely, however, horseshoe bat viruses have the potential to infect humans. And since coronaviruses are well-known for their ability to easily recombine in nature, this recombination is suggested to take place in an intermediate host and to pass on to humans thereafter. In all cases, the best and perhaps most ideal place for this to happen is in the markets of the Far East, as indicated by the metagenomics data analysis of this review. In these places thousands of people gather in front of

Notably, new evidence suggests that a significant proportion of the population, mostly people who tend to be more dependent on social media for information, are more likely to believe in conspiracy theories and less likely to follow official health advice and restriction measures (32). While the majority of extreme conspiracies have been banned from a significant number of electronic platforms, a wealth of conspiratorial material still exists on the big social media sites and continues to misinform and mislead the general public. In this context,

unregulated social media misinformation may pose as a significant health risk to the general public by creating a negative association between health-protective behaviours and the spreading of COVID-19 (33).

In addition to the conspiracy theories on the nature and origins of the pandemic, two major study retractions have recently left scientists skeptical not only as to the quality of scientific research, but also regarding the efficacy of the peer review process and the credibility of respected medical journals (34). The first article, which was published in the *New England Journal of Medicine*, promised that commonly prescribed blood-pressure medication was safe to use by people infected by the new coronavirus, whereas the second article, published in the *Lancet*, issued a warning that the anti-malarial drugs chloroquine and hydroxychloroquine endangered the lives of coronavirus patients. Notably, the second retracted paper claimed to rely on detailed medical records from 96,000 COVID-19 patients at nearly 700 hospitals on six continents (35), yet the scientific community had not heard of this enormous international registry. Despite claims that these admissions, which in the space of one month turned into hasty retractions, were due to an eagerness to publish helpful information during the pandemic, the editor in chief of *The Lancet*, Dr Richard Horton, called the paper retracted by his journal a 'fabrication' and a 'monumental fraud' (34).

It appears that research during the pandemic is taking place at an unprecedented pace, with both journal editors and research scientists who donate time in the peer reviewing process being overwhelmed with new information, trying to understand the pathophysiology of the coronavirus, or to elucidate effective treatments and vaccines. And it is during this time, when the academic system has stretched its capacity thin, that political motivation seizes the opportunity to step in. Indeed, the politicization of the pandemic is suspected to have played a role in the article published in *The Lancet*, if only to rebuke the US President, Mr Donald Trump, who vigorously endorsed hydroxychloroquine as both preventive and curative treatment for COVID-19 (34). This study resulted in the WHO and other health organizations halting clinical trials before substantial reviews could be conducted on the safety of these anti-malarial drugs, with immediate repercussions for many thousand patients worldwide.

12. Thoughts regarding international research on the viral origins

Ahead of the General Assembly of the WHO on May 20-28, 2020, it seems that several proposals are being reviewed as part of an international research conduct on the origins of SARS-CoV-2. On the 30th of April 2020, the Swedish Health Minister Lena Hallengren said that Sweden is planning to ask the European Union to push for the probe, stating '*When the global situation of COVID-19 is under control, it is both reasonable and important that an international, independent investigation be conducted to gain knowledge about the origin and spread of the coronavirus*' (36). Accordingly, the UN envoy to China Chen Xu expressed backing for the WHO but said an invitation for the agency's experts to visit Wuhan to look into the origins of the coronavirus must wait until after the pandemic is beaten (37).

Specifically, he said: '*First things first: The top priority for the time being is to focus on the fight against the pandemic. We need the right focus and allocation of our resources*'. All of the above can be seen as positive messages in a coordinated global effort to tackle COVID-19. In the end, it seems that of the few things that can unite the world, even if only temporarily, are the issues relating to the consequences of the current pandemic or the pandemics that will follow with 'mathematical precision'

13. The lack of prevention strategies against the SARS-CoV-2 pandemic

The reactions of the economically powerful countries of Europe and the United States to the upcoming pandemic have seemed rather surprising, and rather disappointing, to many of us Biomedical Scientists. After the first case in Wuhan, China, Chinese scientists isolated the virus and, with the help of high-tech RNA sequencing technology, classified it as a beta-coronavirus. Therefore, both the Global Scientific Community and the political powers of this world had in their hands two important elements: i) the sequence identity of the coronavirus; and ii) previous experience in dealing with epidemics caused by similar coronaviruses of the beta-coronavirus group (SARS-CoV-1 and MERS-CoV). In addition, we have all been witnesses to the strict and vertical isolation measures taken in China, in the city of Wuhan with its population of 11 million people, since January 23, 2020 (38). There was detailed daily media coverage of how an entire city was quarantined and how the Chinese government managed to build an entire hospital within 2 weeks as well as a mask manufacturing facility. Apparently, the country that was first hit by the pandemic was faced with the most difficulties. However, the Chinese government seems to have reacted with incredible speed, possibly owing to its past communist experience and centralized powers. In the Western world we have watched with admiration how well the Chinese have reacted to prevent the spreading of SARS-CoV-2, which is reflected on the relatively small number of victims. It is also worth mentioning that China's National Health Committee had acknowledged from the start that the virus can be transmitted from one person to another, as well as that the new coronavirus is similar to the virus causing SARS, but that it does not seem to be as deadly, also stressing what is already known for viruses, that they sometimes mutate and become more dangerous to human health.

The WHO, via Director-General Tedros Adhanom Ghebreyesus, declared the coronavirus pandemic on March 11, 2020, when the number of infected cases already exceeded 118,000 in 114 countries and 4,291 people had already lost their lives worldwide (39). It was also noted that the pandemic was expected to cause additional problems in a larger number of countries. From that moment on, the whole planet was and still remains alert and anxious as to the emergence of a second wave of the pandemic.

14. Critical remarks

The WHO's decision to name the disease caused by the new coronavirus COVID-19 may have been unfortunate: this description

(coronavirus disease 19) is indicative of previous coronaviruses and it therefore does not represent the dangerousness of SARS-CoV-2. They may have had the noblest of intentions not to cause panic, for example, but it seems now that we are in the 6th month of the pandemic since its outbreak in China that it did not help in the preparation of the states against it.

The delay by WHO in announcing the pandemic somehow acted reassuringly for all the countries of the world. With the announcement of the pandemic, panic spread across Europe and America (40). The feeling at that point was that the virus had entered many homes and would enter many more without as much as a warning or a 'knock on the door'.

The worst scenario in such a situation (pandemic) is to be unprepared and disorganized, and the whole developed world was blatantly unprepared for such a serious problem. This is mainly due to the tremendous downgrading of the public health system worldwide. In our country this translates to i) a shortage of 30,000 doctors and auxiliary nursing staff; ii) Greece being the third country in the EU with the worst ratio of ICUs in relation to its population (41). According to EU data, Greece has only 6 ICU beds per 100,000 residents! iii) the downgrading and closure of Primary Health Care units and hospitals during the memorandum period; iv) the lack of protective material for nursing staff (e.g., appropriate masks) and respiratory equipment for patients; and v) the lack of staff and technological equipment for molecular tests.

Asian countries have reacted more efficiently in the face of the pandemic than the rest of the world. Hong Kong, for example, has slowed down the spreading of SARS-CoV-2 through a combination of intensive monitoring, quarantine and social distancing, and not by relying solely on the strict measures employed elsewhere. In January, authorities in Wuhan, where the coronavirus epidemic began, prohibited traveling outside the city in an effort to control the spreading of COVID-19. However, Hong Kong was based on a program that included extensive testing, isolation of those who had come in contact with infected people, and distancing measures such as closing schools. When Peng Wu at Hong Kong University and her colleagues conducted a residential survey in early March, 99% said that they wore a mask in public and 85% said that they avoided crowds. Public compliance with government measures kept viral spreading relatively low in Hong Kong until the end of March 2020.

Despite the fact that the WHO insisted on extensive molecular testing for the detection of the virus, much to the surprise of us Molecular Biologists, the whole of Europe and America seemed unable to respond. Indeed, it has been extremely difficult to perform these tests on a larger scale. Nonetheless, people working in the sectors of Biological Research and Biomedical Sciences know that it may not have been as hard to perform large scale molecular testing on the virus, if the following had been put to good use: i) In January and February 2020, the existing accredited laboratories could have been employed and organized in such a way as to be fully competent in performing the tests, with the addition of more such facilities in all the major reporting hospitals and wherever else it was deemed necessary; ii) the personnel capable of performing these tests should be selected; in this respect, PhD students, postdoctoral fellows and researchers in permanent employment positions could be selected even on a voluntary basis; iii) from the moment that the coronavirus

RNA sequence was submitted to a public database there was enough time to organize these in-house tests. Postgraduate and PhD students in research laboratories throughout the country could have prepared these tests reliably. iv) PCR machines do not come at a high cost, which means that additional purchases could have been made. In Greece, for example, the 30 million euros that were given to private diagnostic companies to perform these tests, and who were unable to do so, and the samples were eventually sent to the Pasteur Institute and the Medical School of Athens, could have been used to purchase 1,000 state-of-the-art PCR machines, translating to a minimum dynamic testing of 1,000 samples by each machine daily. v) Primary health services and reference hospitals could aid in the development of a network of human resources that would ensure the efficient collection of samples and their rapid transport and testing in accredited laboratories.

Seventeen years have passed since the SARS epidemic and we still do not know what makes these coronaviruses so dangerous. It is unfortunate that there have been no funding policies for the coronaviruses, both at the European level and globally. We would be much better prepared to deal with the SARS-CoV-2 pandemic if, with dedication and consistency, and provided that the appropriate funds were available, there was sufficient research on this type of virus after the SARS epidemic in 2003. Significant experience has been obtained on a global scale by the research community from research conducted against the virus that causes AIDS. Characteristically, in the context of the sustainable development set by the WHO, the European Union has set a goal to eliminate AIDS and tuberculosis by the year 2030 and to continue research on hepatitis (42). Let's not forget that AIDS has left 35 million dead in its path since its appearance in 1981. Due to lack of investment in research and vaccine production for SARS, we should not overlook a defining aspect set out by the strict laws of capitalist economy. Pharmaceutical companies are often a major part of this system and often show no interest in investing in vaccines. Many of the vaccines in circulation cost between \$600 million and \$1 billion. The major profits in pharmaceutical companies come from drugs that cure long-term illness. For example, the sales of a single drug for hepatitis C have exceeded \$10 billion in one year (43). One must also bear in mind that the vaccine market (\$24 billion today) appears to be extensive, but it represents only 2.4% of the global pharmaceutical industry, which is worth \$1 trillion per year (44). Vaccines, in particular, are therefore not major sources of profit for the pharmaceutical companies that specialize in them. Based on this logic one should also not overlook the lack of large investments in the production of a SARS vaccine. With the confinement of the SARS epidemic in 2003 and 2004 in some Asian countries, companies estimated that a vaccine investment would not translate to a corresponding profit margin due to the small customer market. The consequences of such a decision to public health have become more realistic during the current SARS-CoV-2 epidemic. If there had been research on SARS in the last 17 years since its original outbreak, we would certainly be better prepared and equipped against SARS-CoV-2.

The genetic material of both SARS and SARS-CoV-2 encodes approximately 20 proteins. Apart from the protein that looks like a crown under the microscope and which is

responsible for binding to the host cell, three other proteins that structure the viral shell (nucleocapsid) and cover its genetic material, as well as a multi-protein that is responsible for the transcription and reproduction the virus, we have very little information on what the rest of the viral proteins do. Therefore, research on SARS for the appropriate characterization of these proteins should help to obtain a better understanding of SARS-CoV-2 and to determine the appropriate treatment strategy.

Therefore, the inaction of the global community and the lack of funding to conduct biomedical research on the first SARS virus have provided the ideal environment for the new coronavirus to reach pandemic status. The field of Molecular Virology has produced prominent scientific personalities who have been and still are dedicated to the study of RNA viruses. Columbia University professor David Ho, who has saved countless lives with the antiviral therapy for AIDS, applied for \$20 million funding in order to test antivirals against SARS in his laboratory, but his request has never been met (45). It seems that various government officials and pharmaceutical companies, as we have explained above, regarded the previous epidemics as cases only pertaining to the East. Thus, in an attempt to justify the unjustified, the majority of institutional officials, with the help of several scientists, often refer to the new coronavirus as an invisible enemy and to the battle against it as an unequal war. These words sound like a cover-up of our inability to effectively deal with the pandemic and of the fact that we are ill-equipped in terms of vaccines, drugs and scientific equipment to deal with a virus that, despite being called new, is highly related to the previous SARS disease. We probably have no excuse as there have been many warnings from the scientific community in the first two decades of the 21st century about the increased incidence of epidemics and the need to fund coronavirus research. Unfortunately, the institutions chose inaction and now it appears that we must make up for the lost ground in a very short time, and suffer all the consequences that this pandemic will leave behind. Despite the delays, however, the devaluation of research on SARS since 2003 shows that the Biomedical Science Community, as we speak and as the pandemic is still ongoing, are doing their best to turn the tables in favor of humanity in the battle against COVID-19.

15. Conclusions and thoughts for a better relationship between man and the environment

Many notable scientists such as Professor Michael Greger, former director of Public Health and Animal Husbandry at the Humane Society of the United States, and Professor Rob Wallace, evolutionary biologist and Public Health Phylogeographer, collaborator of the Institute of International Studies at the University of Minnesota, author of *Big Farms Make Big Flu* and former adviser to the Food and Agriculture Organization of the United Nations, have touched the basis of the root cause of the latest epidemics and the current pandemic of SARS-CoV-2. The message from this pandemic is that unequal access to natural resources must be brought to an end, so as to prevent the next pandemic that is expected to occur with mathematical accuracy (46,47).

The protection of public health requires a review of the relationship between man and all biological ecosystems,

especially animals, and the environment in general. Available genomic data now make it clear that behind the global COVID-19 pandemic lies a virus that has most likely entered the human population via human interaction with bats or another intermediate host (48).

It seems that dealing with such pandemics requires a holistic approach that focuses on causality, i.e., the generator cause, and not solely relying on the restriction/distancing measures that should be undertaken anyway in order to prevent loss of human life. In order to achieve this, we need to redefine our relationship with the environment and the inequalities that lead to its destruction. It is estimated that 75% of all new infectious diseases are the result of contact between humans and animals (49). We have all heard of at least some of them in the last twenty years, such as Zika, Ebola, SARS, bird flu, MERS and, more recently of course, COVID-19.

The United Nations Environment Program (UNEP) emphasizes on the main factors that are implicated in the transmission of viruses to humans: i) deforestation; ii) intensive cultivation; and iii) climate change (49). A number of studies have ascertained that the universal approach to food production, including basic agricultural and livestock products such as beef, palm oil, coffee and cocoa, makes it easier to deplete resources in poorer countries than in countries with affluent economies. The production of such goods leads to i) deforestation and ii) loss of biodiversity. These are the main factors for the transmission of diseases among species. In the majority of nations producing coffee and cocoa (sub-Saharan Africa, Southeast Asia and Latin America), 95% of production is exported to the North, mainly to North America and Europe.

In terms of climate change, the economically developed world bears the highest responsibility for the global emissions causing the greenhouse effect and for the production of other harmful pollutants. Under developed countries, being far less responsible for the greenhouse effect, suffer to a much greater extent the consequences of climate change-related diseases that are transmitted by mosquitoes. Even very small increases in temperature seem to currently make it easier for mosquitoes to spread to new areas where people are not immune to the diseases they carry (50).

In the oppressed ecosystems of less developed countries, large predators are becoming extinct. This creates biosystem imbalances that favor the reproduction of certain species, such as bats, rats and mosquitoes, i.e., those species that usually transmit zoonoses to humans. The lack of food for these animal species in ecosystems where they lived in harmony before the violent human interventions strengthens the competition for food among them, in an attempt to meet their nutritional needs. The increased competition for food for these animals leads to their migration to more densely populated areas and to closer contact with humans (51).

COVID-19 should ring like a very loud bell to the ears of the global financial elite and of every single consumer. If global environmental, health and development issues are not addressed holistically, new pandemics will continue to emerge. Priority should be given to reducing consumption levels, eliminating trade and economic inequalities, and creating sustainable production systems for both the people and the environment, and all of this in a different socio-political system.

The current crisis brought on by the coronavirus pandemic has provided us with a unique opportunity to very seriously reconsider our relationship with the environment. This practically means that large agri-food companies and global policies should be immediately concerned about the current industrial environment producing our food products. The current food production process is often modified by the introduction of new technologies that essentially lead to significant violations of the balance in natural ecosystems. This approach undoubtedly increases the rate of production and the size of the total product, but at the same time it greatly promotes and strengthens the necessary conditions for viral replication, so that new mutations are produced at a higher rate and with greater infectious power. Many warnings can be deduced from the pandemics that have occurred so far, yet the course of our future lies in the hands of humanity.

Despite the numerous warnings that can be derived from pandemics, as Professor Rob Wallace points out '*agribusiness is so focused on profits that selecting for a virus that might kill a billion people is treated as a worthy risk*' (52). If we were to use molecular biology terminology to describe this phenomenon, it would translate as follows: the world's financial elite owning the agri-food companies are self-designated by the dominant gene of profit that determines their phenotype and their aggressive behavior both to the environment and to other people. This gene is so powerful, 'dominant' in the language of Biology, that no effort to convince them otherwise has had any result so far. Therefore, as is the case with the numerous work-related problems being faced on a global scale, in the emergence of every pandemic we will be faced with the same clear-cut question: is there an alternative? Of course there is, this can be easily deduced by reading Brecht's poem (53, Brecht B: In Praise of Dialectics).

In Praise of Dialectics

Today injustice goes with a certain stride,
The oppressors move in for ten thousand years.
Force sounds certain: it will stay the way it is.
No voice resounds except the voice of the rulers.

And on the markets, exploitation says it out loud:

I am only just beginning.

But of the oppressed, many now say:

What we want will never happen.

Whoever is alive must never say 'never'!

Certainty is never certain.

It will not stay the way it is.

When the rulers have already spoken

Then the ruled will start to speak.

Who dares say 'never'?

Who's to blame if repression remains? We are.

Who can break its thrall? We can.

Whoever has been beaten down must rise to his feet!

Whoever is lost must fight back!

Whoever has recognized his condition -
how can anyone stop him?

Because the vanquished of today will be tomorrow's victors
And 'never' will become: 'already today'!

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