The mother of all battles: Viruses vs. humans. Can humans avoid extinction in 50-100 years?

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Abstract

The recent SARS-CoV-2 pandemic, which is causing COVID 19 disease, has taught us unexpected lessons about the dangers of human extinction through highly contagious and lethal diseases. As the COVID 19 pandemic is now being controlled by various isolation measures, therapeutics and vaccines, it became clear that our current lifestyle and societal functions may not be sustainable in the long term. We now have to start thinking and planning on how to face the next dangerous pandemic, not just overcoming the one that is upon us now. Is there any evidence that even worse pandemics could strike us in the near future and threaten the existence of the human race? The answer is unequivocally yes. It is not necessary to get infected by viruses of bats, pangolins and other exotic animals that live in remote forests in order to be in danger. Creditable scientific evidence indicates that the human gut microbiota harbor billions of viruses which are capable of affecting the function of vital human organs such as the immune system, lung, brain, liver, kidney, heart etc. It is possible that the development of pathogenic variants in the gut can lead to contagious viruses which can cause pandemics, leading to destruction of vital organs, causing death or various debilitating diseases such as blindness, respiratory, liver, heart and kidney failures. These diseases could result n the complete shutdown of our civilization and probably the extinction of human race. In this essay, I will first provide a few independent pieces of scientific facts and then combine this information to come up with some (but certainly not all) hypothetical scenarios that could cause human race misery, even extinction. I hope that these scary scenarios will trigger preventative measures that could reverse or delay the projected adverse outcomes.

Keywords: pandemics; contagious diseases; human race extinction; viruses; microbiome; COVID-19; blindness

Introduction

Le Chatelier's Principle: Named after the French chemist, Le Chatelier's principle posits that *"When an external stress (change in pressure, temperature or concentration) is applied to a system in chemical equilibrium, the equilibrium will change in such a way as to reduce the effect of the stress*". In other words, a change in a system will evoke a counter-change, which will bring the equilibrium to a new point. This principle operates with almost every human or other activity. For example, it is known that when fruit production in the Serengeti ecosystem is reduced, the number of elephants, who feed on these fruits, is reduced proportionally. In the context of this essay, I hypothesize that human-made changes in climate, the atmosphere, waters, soil and all other planet-living organisms, will likely evoke counter-changes that may be highly consequential to human life. Due to the complexity of our ecosystem, humans do not know exactly how these dramatic changes will affect them in the long run. Consequently, they choose to disregard them because adjustments cost money and convenience or loss of well-established pleasures.

The earth is changing rapidly

What is changing on earth that could induce a potentially catastrophic counter-change? The answer is everything is changing*, from the living inhabitants (humans, other species and plants), to the atmosphere, water, soil, climate, etc.

**Greek Philosopher Heraclitus (c. 535-475 BC) famously said πάντα ῥεῖ (panta rhei) "all is flux" or "everything flows."*

The changes caused by human activity are sometimes dramatic. It has been estimated that about 1 million out of 8.5 million species of plants, animals and other organisms are in imminent

danger of extinction (1). Other estimates show that 50% of the organisms that existed 50 years ago have already gone extinct, not to take into account additional species that are gone before we even identify them. Soon, we will likely be losing more than 80% of the world's species due to human overdevelopment and its associated consequences. The major reasons for species extinction are habitat destruction, pesticide poisoning and illegal hunting.

Global Warming

You may choose to believe what the politicians are debating about; that climate change is a fact or fiction; but the data say that the last 6 years were the warmest on record (2). Overall, the planet was 1.25 ^{o}C warmer than in pre-industrial times (in the 1950s). Warmer oceans are melting ice sheets and raising sea levels by almost 5 mm per year. In Australia, record-setting heat and draught was responsible for the bushfires that destroyed almost 25% of southeastern Australia's forests and their living inhabitants, such as koalas. If we cannot slow down earth's heating by reducing emissions, the current increase of about 0.2 ^{o}C per decade will likely be rapidly surpassed. How will the planet react? Likely with more catastrophic fires, tsunamis, earthquakes and floods. The homeostatic changes of a human to increased temperatures are very complex and include many vital organs (3). Global warming may also cause changes in the biology of our candidate foes, the viruses, bacteria and parasites that live in our gut and skin (see below).

How much human-made environmental damage has been done already?

Humans are now the undisputed masters of the planet and cannot be easily stopped from actively destroying it, consciously or unconsciously. An interesting question is how much damage has been done already and do we have the data to support these claims? Elhacham et al have recently

compared the natural biomass that exists on earth with the human-made (anthropogenic) mass (4). They found that each person on the globe produces a mass that is about equal to their body weight every week! Is that too little or too much? Let us first define biomass and anthropogenic mass. The majority of earth's biomass is represented by trees and bushes. The majority of man-made mass is represented by buildings and infrastructure such as roads, and consists of concrete, bricks, asphalt, metals and plastic. Just consider that the total global mass of produced plastic so far is greater than the overall mass of all terrestrial and marine animals combined!

So, how do we fare when comparing biomass to anthropogenic mass production? In the 1900s the latter represented only 3% of global biomass; but now, in the 2020s, the two masses are about equal. The projection is that if we go on with more deforestation, buildings, streets, plastics, cars etc., by 2040, it is likely that anthropogenic mass will almost triple the earth's biomass. Will then be enough resources and clean air and water to sustain the life of the projected 9 billion inhabitants? Anthropogenic mass production is difficult to slow down since this activity is considered part of our evolving civilization and way of living.

Human microbiome

The human body consists of approximately 30 trillion cells but the microbiota population in human gut is estimated to be 300 trillion! (5). There is additional microbiota in the skin. It was originally thought that these microbiota act locally (only in the gut or skin) but new evidence suggests that the effects of microbiota may be global, reaching every cell in the body. This can be achieved with various mechanisms, one being transmission of signals mediated by proteins that can travel through anatomically distinct structures such as the vagus nerve. For example, a protein called curli can travel through the vagus nerve and reach the brain, where it can promote

abnormal aggregation of proteins such as a-synuclein, one major player in Parkinson disease (5, 6). Another, and even more likely mechanism, includes diffusion of bacterial or viral proteins (some could be toxins to various organs) or pathogenic viruses into the blood stream. From there, they can travel around the body. One piece of evidence for that happening is that about half of the human metabolome (the collection of all metabolites in blood) is derived by host bacteria (5). Bacteria or virus-derived metabolites could also pass through the placenta and reach the fetus, including the fetal brain, possibly causing diseases such as autism.

Despite skin not being as hospitable to microorganisms as the gut, a typical person may have about 1,000 species of bacteria on their skin (7). These microbial communities continue to grow and diversify until puberty, when hormonal and developmental changes reach a plateau. The balance between bacteria and host in the skin is determined by production of skin-derived microbial nutrients, microbiome-derived skin nutrients, skin and microbiome-derived antimicrobial peptides and by the interaction of the microbiome with the host's immune system. Like in the gut, there is a delicate balance between beneficial and potentially harmful bacteria and the host immune system. We should expect that our future enemies may derive from either the gut or the skin. The latter is more sensitive to environmental changes such as climate change since it is directly exposed to the environment.

In conclusion, bacterial, viral and parasite-derived proteins or pathogenic viruses are produced locally (in the gut or skin) but are able of acting globally.

Human viruses and how they could cause disease

Many strains of gut bacteria are harmless but they can become dangerous pathogens under certain conditions, such as antibiotic use (8). It is well-known that the gut bacteria can harbor

many viruses (bacterial phages) (9). If they do not immediately kill the infected bacteria, these viruses incorporate into the bacterial genome and stay latent for long periods (they are known as “prophages”). Under certain environmental or other factors, these prophages can be reactivated and act like pathogenic viruses. You will be surprised to know that in general, viruses are so many, they qualify as the most abundant biological entities on the planet. Sometimes, gut bacteria are using their activated prophages as weapons to gain an advantage and kill other, competing bacteria. Phages could also assist in bacterial evolution in their way to become more virulent (10). The gut bacteria seem to interact with the host immune system as well and can influence the efficacy of cancer immunotherapy (11-13). The microbiome has been blamed to play direct or indirect roles in many human diseases including cancer, metabolic syndrome, diabetes, dementias, etc. (14).

So, it is all about the balance of powers between the gut/skin viruses, the gut/skin microbiome and the host immune system. If this balance is disturbed, a war between these players will be initiated and the outcome will be unpredictable.

In conclusion, scientific evidence supports the idea that phages in the mammalian intestine or skin not only can be engulfed by certain eucaryotic cells, but also might escape from the gut or skin, enter the bloodstream and make their way in other parts of the body, with as yet undiscovered consequences.

Viral variants

Viruses evolve continuously, eventually leading to variants that are more transmissible and some times more lethal than the original strains. The SARS-CoV-2 is a good contemporary example. Multiple variants of SARS-CoV-2 are rapidly spreading and are becoming dominant in certain

geographic areas (15, 16). For example, the B.1.1.7 variant (United Kingdom) has 23 mutations and 17 amino acid changes; variant 501Y.V2 (South Africa) has 23 mutations and 17 amino acid changes and P.1 variant (Brazil) has approximately 35 mutations with17 amino acid changes. New variants with additional mutations could become able to evade our currently available vaccines by weakening the ability of vaccine-induced antibodies to neutralize/block viral entry, and by strengthening the ability of the virus to enter the cells via surface receptors.

How CoVID-19 and possibly other viruses affect the brain

In general, viral invasion of the central nervous system may be achieved by several routes, including transsynaptic transfer across infected neurons, entry via the olfactory nerve, infection of vascular endothelium, or leukocyte migration across the blood-brain barrier. SARS-CoV-2 invades endothelial cells via transmembrane angiotensin-converting enzyme 2 (ACE2) receptor binding and a subsequent proteolytic event, facilitated by transmembrane protease serine 2 (TMPRSS2) (17). Is there evidence that SARS-CoV-2 can enter the brain? The answer is yes (18). One route is by migrating from the cribriform plate along the olfactory tract (19) or through vagal pathways, as already mentioned. Another route may include viral entry into brain capillary endothelial cells via the ACE2 pathway. Viral RNA was detected in medulla and cerebellum by reverse transcription polymerase chain reaction. However, viral proteins seem to be absent from neurons and glial cells. Consequently, the adverse events of the virus on the brain, including altered neurotransmission and neuronal damage are likely mediated by neuroinflammation and hypoxic injury through cytokines and other pro-inflammatory mediators.

SARS-CoV-2 and possibly other viruses can affect the senses

Viruses can affect our senses. For example, SARS-CoV-2 causes anosmia (loss of smell) and ageusia (loss of taste) in 40-70% of COVID-19 patients (20). Other neurological symptoms include headache, stroke, impairment of consciousness, seizure, anxiety and encephalopathy.

Current evidence suggests that SARS-CoV-2-related anosmia may be a new viral syndrome specific to COVID-19. This syndrome is likely mediated by intranasal inoculation of SARS-CoV-2 into the olfactory neural circuitry. Since the olfactory sensory neurons do not express

ACE2 receptor, the likely explanation for the loss of smell is damage of accessory cells supporting these neurons.

Although anosmia is not lethal or a severe disease, other neurological damage such as blindness could be devastating (21, 22).

Adverse Senarios

Fifty years ago, one adverse scenario was presented in the film “the Andromeda strain”, which describes a pandemic caused by a pathogen of extraterrestrial origin (23). Here, is an alternative scenario that involves a hypothetical endogenous virus.

A prophage, which was residing dormant for years in the genome of the commensal gut bacterium *Bifidobacterium infantis* suddenly, and without an apparent reason, has undergone induction and started to produce viral proteins, which were subsequently assembled into whole phages. After cell lysis, these phages infected other, neighboring cells. This cycle was repeated many times and millions of free virions were released, some entering the systemic circulation (viremia). Some virions were able to reach the lung endothelium and through an as yet unknown receptor, entered the endothelial cells and started replicating and lysing these cells. The resulting

mucous caused the host to cough, thus facilitating transfer of the virus to other humans through aerosol droplets. Soon, the virus was able to infect, first hundreds, then thousands, then millions of other unsuspected people through coughing and sneezing. The virus was able to travel all over the world, since the pulmonary manifestations were mild and most infected individuals thought it was a common flu or a similar ailment.

Scientists isolated the virus that caused this flu-like disease and determined from its genomic sequence that it was a novel member of influenza virus B, which usually causes seasonal flu. Despite the pandemic nature of the infection, nobody died and governmental bodies were not highly concerned.

Six months later, one individual reported weakening of his of vision, which, within3 months progressed to total blindness. This unusual form of blindness quickly spread to other people until scientists performed epidemiological studies, which linked the blindness to the previously mentioned mild flu. Soon afterwards, scientists isolated and identified the virus from brains of blind and subsequently succumbed individuals and confirmed that the sequence matched the virus that caused the unusual flu. More elaborate studies had shown that there was an unusual and very severe neuroinflammation around the occipital lobe of the brain (Brodmann area 17), an area that is responsible for interpretation of visual signals arriving from the optic nerve. Several therapeutics were tried but none was proven to be effective. Twelve months into the pandemic, 10 million people lost their vision and within 18 months, and without any success in developing therapies or a vaccine, the blindness had spread to whole nations.

Blindness

The selection of blindness as a chronic consequence of an acute pandemic was deliberate. In 1995, Portuguese author Jose Saramago published a fictional novel entitled “Blindness” (ISBN:9780151002511) which contributed to him winning the Nobel Prize in literature in 1998.

Blindness is a highly detailed story of a mysterious mass epidemic that caused blindness of a whole nation, and the social breakdown that followed. The blindness pandemic, in many respects, is reminiscent of the COVID-19 pandemic. Blindness caused widespread panic, anarchy and government lock-downs. The life of the blind people was characterized by filthiness, aggressive manners, disrespect of others and a struggle to survive by any possible means. The breakdown of society was near total. Law and order, social services, government, schools, etc., could no longer function. Families have been separated and cannot find one another. People squat in abandoned buildings and scrounge for food. Violence, disease, and despair threaten to overwhelm human coping. One of Saramago’s quotes, describing life after blindness, is reproduced here “*Perhaps humanity will manage to live without eyes, but then it will cease to be humanity, the result is obvious...”.*

Other ailments

Acute pandemics could cause many other chronic diseases that can threaten the sustainability of our present society. Although COVID-19 causes loss of smell and taste, these are considered non- life-threatening ailments. However, in the long run, permanent absence of smell and taste will mean loss of innumerable current pleasures associated with consumption of food and drinks. Clearly, loss of hearing will not be compatible with current societal functions or human achievements. Acute viral diseases are also associated with innumerable organ-specific diseases such as heart, kidney and reproductive failures, and disturbance of other vital functions that can

paralyze our current society economy and culture. Even a minor weakening of our memory (mild cognitive impairment) could result in chaotic situations that authors of fiction, like Saramago, can attempt to describe in detail before this happens.

Epilogue

Humans take for granted what they currently have and enjoy. Perhaps we did not realize that the spectacular advances of the human race are dependent of a number of potentially volatile abilities (senses, brain function etc.) and that even one loss, or diminution of such abilities, could be detrimental, causing collapse of our civilization. The COVID019 pandemic helped us to realize that we may be sitting on a time bomb which may explode, if we continue disturbing the current equilibrium between humans and our other planetary partners. In addition to viruses of rather exotic origin, like SARS-CoV-2, billions of other viruses and other infectious agents in our gut and skin are waiting for the right time to attack us. The lessons learned from COVID-19 should be a wake -up call for humans to stop disturbing the equilibrium with actions that favor the well-being of humans, but put in danger the existence of other inhabitants of planet earth. Last but not least. Artists are always ahead of scientists in seeing things coming. On this occasion, the rock band R.E.M. released a song 30 years ago entitled “It's the end of the world as we know it (and I feel fine)”. They are likely not far off their prediction!

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