Research Article

Journal of
Experimental Stroke and
Translational Medicine

Microbiome - an omitted thread in the COVID-19 discussion

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Received date: March 02, 2021
Accepted date: March 09, 2021
Published date: March 24, 2021

Abstract:

This publication continues the author's previous publication from 2020 on mental barriers hindering a more accurate interrogation of the COVID 19 pandemic phenomenon and which focused on an analysis from sociological, philosophical and anthropological perspectives. The current publication completes this trajectory of inquiry by presenting a biological perspective which demonstrates the human organism as one in which viruses are a co-host in the fullest sense. The publication continues to document the author's hypothesis that the essence of the COVID-19 pandemic is reduced effectiveness of those evolutionarily born defensive mechanisms which are integral to humans. Such a situation has resulted from the plundering of natural resources (including those of health) which characterised the industrial era.

Keywords: COVID-19 pandemic; natural resources destruction; mental barriers to understanding; biological mechanisms in COVID-19

Introduction

This publication retains the theme of the author's previous publications [1] which analysed barriers to a fuller understanding of the COVID-19 pandemic. That analysis generated results derived mainly from sociological, philosophical and anthropological perspectives whereas the current publication considers the role of significant microbiological, microecological and ethnotoxicological factors.

The hermetic nature of biological disciplines and the great mass of new, detailed and inadequately ranked information generated by the rapid advancement of knowledge in relevant fields, are significant challenges to coherence in assimilating new information. This problem about which I have written in earlier publications is compounded by mental/psychological mechanisms which inhibit optimal processing of new information on the epidemic, in brief- our perception of the problem is too narrow if not simplistic. Consider the following: how we are responding to the phenomenon, how we discuss it, how we manage our social relationships and how we muster our defences. Military tropes dominate the narrative, the virus must be defeated, or we shall be the victims. We need in a way to look at the virus differently and be aware that our body is a community where viruses, prions and bacteria exist in numbers vastly in excess of the number of cells constituting our bodies.

The evolution that led to the creation of man in his present form was mainly based on the blending of the preceding evolutionary form into that which followed, supplemented only by a functional enhancement. This process has existed since that period when only the simplest organisms (those not yet with constituted as cells) existed and in numerical terms, they still dominate the composition of our planet's biosphere. The next stage of evolution was the formation of cellular organisms that integrated with subcellular organisms, using them as permanent functional elements. These enriched cellular structures gradually organized into more and more complex colonies, the most complex of which is man.

This treatise centres on the author's hypothesis that the essence of the COVID-19 pandemic is reduced effectiveness of evolutionarily born mechanisms integral to humans. These have permitted coexistence with the world of viruses both in an endogenous form - and as such are part of our human makeup and an exogenous form with which we permanently interface including those we might regard as pathogenic. The author attempts to provide an outline of the complexity and interrelationships of cellular and subcellular organisms that make up the human body and their sensitivity to the toxic effects of an industrial world.

The publication is directed mainly to a small group of experts who attempt to analyse facts which may encroach on the domains (or silos) of other scientific disciplines. It recognises that such experts still possess the mental and physical resilience required to critically interrogate novel and often threatening hypotheses, unlike the general public-now overwhelmed and exhausted by the immanence of COVID 19.

In order to discuss the hypothesis this focusses on the disturbed coexistence of man and viruses, the author moves outside the commonly accepted boundaries of his own specific medical practice. He sketches the COVID-19 phenomenon as a microcosm of the human body, demonstrating the influence of the pathogenic virus on its function. At the same time, the author accepts the possibility of imperfections within this text but opines that its content will be expanded, corrected, and further developed by virologists and biologists.

Despite significant technological advances, we stubbornly view the world through increasingly opaque lenses, and if we want to understand the phenomena of the present, we must recognize its precedence. Including some that we will mention later. It is difficult to banish this ever-present and powerful image that dominates our cortex - a symbol of our superiority that mistakenly suggests that our bodies are unique to the creation of the world. Our body is a multicellular structure analogous to other organisms on our planet and as such is only a link in the evolution of our planet's biosphere. Our body embraces the transfer phenomenon in this constantly flowing stream of matter within the biosphere, both in its corpuscular wave form and in its organic and inorganic manifestations.

Information passes through us and energy exchange within us constantly operates connecting Man with the biosphere of which we are but an element. Our body components are thus constantly exchanging within our liminal structures and are coeval with integrally related living organisms, including viruses. Constant change defines our bodily existence, the life of our epithelial cells is only a few hours and within a few years we exchange almost all of our body's atoms. We constantly exchange the atoms which compose us with the stock of matter limited only by the shells of our body but also exchange them in an ever-expanding environment facilitated by globalization and the movement of people and goods.

Until recently, we treated atoms as the lifeless building material of our bodies but now recognise that regardless of the distance between them, spin-paired atoms remain in constant contact with each other enabling transmission of information. From the perspective of the exchange of atoms within the Earth's biosphere, we are one large community of which the biosystem of the body is a microcosm. The same pool of atoms within our bodies circulates in a rotational way, encompassing both human and bacterial cells, as well as viral and prion microorganisms, all of which together combine uniquely to constitute Man.

The scientific facts available today challenge the anthropocentric belief that only humans are capable of thinking, animals guided only by instincts and the rest of organic matter passive building blocks. The ability to think is not only the ability to comprehend abstract phenomena, a faculty that is now being reduced in humans, but also mainly the ability to collect information, process it and apply it in practice. In this sense, thinking is a common feature of living organisms and not unique to Man. The cells of the human body in the process of evolution have lost many of the features necessary for independent existence in exchange for the ability to perform highly specialized functions, but still remain living, thinking organisms. We know today that the chromatin nucleic acids of each cell, apart from storing the genetic code, have capabilities similar to efficient computers for storing and processing information, a property also possessed by proteins. I discuss this issue in a recent publication [2] and include references to newer scientific works/researches by others including [3, 4].

If now we return to the topic of the human-virus conflict, an important fact to accept is that we intimately cohabit as it were with viruses that are a vital integral part of our body and (in a sense) we cooperate with these same entities. In the case of a viral infection, it is not so much about contamination of the supposedly sterile space of our body, but rather about disturbing the homeostasis of our body's biocenosis, which opens the door to the pathological

activity of exogenous viruses. The multi-component barrier that protects our body, evolving over billions of years and enabling us to survive thanks to its protective effects, has been severely damaged by the influence of a toxic industrial civilization that has accelerated throughout our planet over the past 200 years (and especially the last decades).

We should recall that from the moment of inception as a species, organisms in the earlier stages of their evolution adapted to cooperate and functionally integrate with existing endogenous viruses. The ability of the organism to defend itself against the emergence of new and/or pathogenic viral strains is the result! This is especially true of the RNA virus family which is the only virus group (it includes SARS-CoV-2) known to have left a fossil record of endogenous proviruses dating back over 100 million years -it makes up approximately 8% of the human genome. Research by Horie Masayuki and his team [5] provided evidence of the endogenization of viral elements within the genomes of mammals. This work is evidence of the mechanism which propagates endogenous viral elements and describes the role of endogenous RNA virus as a source of generating genetic variation in its host. Subsequent phylogenetic analyses have demonstrated that the presence of endogenous RNA viruses in the primate genome has persisted for 40 million years. Endogenous ancient viral sequences (EBLs), analogous to the Bornavirus family viruses (now widespread in the animal and plant world) were integrated into the genomes of animals nearly 100 million years ago. This knowledge emerged from the work of scientists using molecular fossil records to track past Bornavirus infections, especially in primates. Phylogenetic analyses indicated that the ancestors of primates were repeatedly contaminated with different strains of Bornaviruses during their evolution and that these viruses underwent repeated endogenization over several million years. Moreover, the viral lineage that was endogenized in primate ancestors was also endogenized in some bat ancestors [6]. In particular, it was found that the geographic distribution of these bat ancestors coincided with the migration route of non-human primates, suggesting that long-term virus-host coexistence may have extended the geographic distribution of the virus lineage and may have spread their infection to new hosts. These findings reveal a latent co-evolutionary history of virus-host relationships across geological timescales, including chronological change in the epidemic Bornavirus lineages, long-term virus-host coexistence, and the geographic spread of a potential source of viral infection. The above information is particularly important in the context of our knowledge that the current COVID-19 pandemic is a zoonotic disease transmitted from bats [7]. This suggests the existence of a potential phylogenetic link between humans and tropical forest bats, both in terms of the endogenous existence of RNA viruses and the possibility of interspecies transfer. Professor Jean-Jacques Muyembe-Tamfum, the discoverer of the Ebola virus, currently working at the Institut National de la Recherche Biomédicale in Congo (INRB), believes that still unknown viruses, whose natural habitats in tropical forests are currently being violated, may pass to humans and in the near future will prove to be much more dangerous and lethal than the SARS-CoV-2 we are currently facing.

The doubling of the human population in a short period of 60 years (currently approximately 7.7 billion individuals) has radically reduced and often eliminated many "wild animals" (who hosted such protective viruses) and dangerously impacted on the surrounding biotope. Human living conditions have also changed radically, facilitating penetration and mutation of viruses, large population clusters have arisen (e.g., Wuhan) and in tandem there is increased contact with large numbers of people in artificially ventilated rooms. Given the high prevalence of viral infections, the presence of minimally symptomatic or asymptomatic vectors and the persistence of viruses on shared items, the constant transmission of viruses in workplaces or other sites of human interaction is inevitable. As a reminder, I quote from [8] a summary of the viral survivability (and infectivity) in a typical office environment : Coronaviruses (Coronaviridae) durability up to 3 hours; influenza virus (Orthomyxoviridae) up to 48 hours; human papillomavirus (Papillomaviridae) up to 8 days, human parvovirus (B19) (Parvoviridae) with a proclivity for infecting children and pregnant women persists for over 1 year.

Conditions conducive to the transmission of infection include overcrowding of both animals and people. Animals bred for meat in industrial farms create a particularly dangerous epidemiological threat, due to the situation in which the host cell is simultaneously infected by two different viruses, leading to the emergence of new, more mutational variants, which are better at extending their range and infectivity. Animals in confined and crowded conditions are often in very close contact with people (e.g., immigrants) working in meat processing plants who themselves live in poor and overcrowded living conditions. This reduces the resistance of both man and animal to viral transfer and creates fertile conditions for the emergence of pathogenic strains and further epidemics. It also creates the enabling environment for the animal virus to transfer

and colonise a new host namely man. Eating animals such as bats is an example of how viral transfer is facilitated and in which the mechanism of endogenization of RNA viruses occurs, as previously seen in the case of human phylogenetic protoplasts.

An understanding of how the human body's microbiotope functions and in particular the role of viruses in these processes, requires an explanation of new and relevant scientific findings relating to function. The mass of new information in that field threatens to overwhelm the reader, but it is both necessary and useful to reflect on the complexity of mechanisms that determine our susceptibility to SARS-CoV-2 infection. To repeat: there are many viral sequences are integrated into the human genome such as EVE (Engogennous Viral Elements), which are passed on in heredity. Archaic forms of endogenous retroviruses found in human DNA are responsible for the regulation of several genes, most of which are inactive or are only activated at certain times. One such is the HERV-W / Syncytin-1, which supports the implantation of the embryo into the placenta and endogenous retroviruses are suspected to be involved in the pathogenesis of neurodegenerative diseases. The role of these significant elements of our genome (about 1/10) is still unclear, although it is known that the integration of RNA viruses (which include the coronavirus family) facilitates their penetration of the human body. Recent studies [9] show a more complete understanding of how cell community function when they are constantly exposed to agents (including viruses) that damage the structures of DNA strands. The presence of duplicate homologous DNA chains in cells allows them, with the support of auxiliary proteins, to have an effective repair apparatus that enables the repair of damaged genetic material on an ongoing basis. This facilitates the permanent elimination of threats to DNA, including those caused by viruses. Thus, in order to maintain homeostasis in the organism, the key is not so much sterile isolation from potentially pathogenic viruses as the effectiveness of the organism's defence mechanisms in restraining their destructive potential.

In general, the role of the viral component of the human body (the virome) is still not fully understood and our information on its composition and function is still incomplete. Research indicates great variability in the virome, which depends on various factors, including diet, climate, infection, immunity status and age. It is estimated that one gram of intestine contains 109-1015 virus particles and 106 per 1 cm^2 of skin and indeed completely healthy people can be infected chronically or temporarily with several types of viruses. Virological research carried out in areas where people inhabit tropical forests, biocenoses unchanged by human influence confirm the endemic occurrence of zoonotic viruses in humans. Such research also includes those viruses transmitted from bats, which may be the source of further pandemics comparable to COVID-19. Violation of the naive biotope (not yet damaged by civilization) resulting in the elimination of existing animal hosts, forces viruses to search for a new host and thus spawn another pandemic, as was the case with the Ebola virus. Currently exploitation of tropical forests continues apace and huge areas are destroyed every year, this includes most of the jungles in Sumatra and Borneo for example, or the Amazon region which loses an average of 20 thousand. sq. km of forest per year. The rate of extinction is accelerating and is now 100-1000 times faster than would occur naturally. According to experts, this heralds the arrival of the sixth mass extinction of wildlife as part of human-induced geological and biological changes - the Anthropocene epoch.

The usual perception of our body is one in which we identify different organs, (mainly when they do not function as expected) and imagine it to be composed of passive material. In fact, the human body is the most intensely inhabited and most dynamic biosystem on our planet with an interior resembling the bustling, crowded centre of a large cosmopolitan city. The cells of our body together with the bacteria and subcellular organisms inhabiting them, constantly communicate with each other, exchange information and participate in the circulation of matter.

Cell communication is affected by means of "packet mail" entities called exosomes which consist of protein substances with information transmitting ability (or DNA) surrounded by microbubbles. These are spherical membrane nanobubbles, released by almost all cell types and contain a rich panel of bioactive molecules. This complex transport package mechanism mediates the exchange of information, transports components between cells and initiates (or modulates) specific physiological as well as pathological processes.

Another form of information exchange that crosses the intercellular space are known as plasmids - extra-chromosomal DNA molecules found in the cytoplasm of a cell and capable of autonomous replication. Plasmids usually enclose several genes (often including those governing antibiotic resistance) whose classification is based on gene identity and the properties they impart to the host cells. The following types of plasmids have been identified:

- R-type plasmids – these contain genes that develop bacterial resistance to antibiotics (e.g. ampicillin)
- F-type plasmids - enable the transfer of genes between bacterial cells in a process called conjugation
- Tin colic plasmids – these contain genes that code for proteins called colicins that kill bacteria

- Degradation plasmids - encode proteins that allow the host cell to metabolize unusual compounds, such as toluene or salicylic acid
- Virulence plasmids – which confer disease-causing capacity on bacteria

It should be remembered that one bacterial cell can contain several types of plasmids, each possessing up to hundreds of copies. Plasmids may constitute nearly half of the genetic material of bacteria and are key investigative entities contributing to the armamentarium of biotechnology laboratories.

Transposons have a role similar to that of plasmids with entities such as jumping genes, wandering genes and moving DNA segments that carry genetic information with repeated fragments of the same or inverted sequence at both ends (border sequences or inverted terminal repeats). The last named can move independently within the host's genome or (much less frequently) between genomes, without the aid of any vectors ("carriers") such as phages or plasmids. They exist in many forms, occasionally as multiple copies within the chromosomes of bacteria, plants and animals. When copies of transposons are moved (transposed) to new places in the genome, various genetic changes such as gene mutations as well as chromosome aberrations can occur.

Another very widespread group of subcellular organisms are prions (proteinaceous infectious particles) formed from harmless proteins found in many organisms and only become "infectious" when they change their natural conformation. Prions are present in great numbers in the endogenous human biotope and in the surrounding "living" environment. They have many features similar to the RNA viruses from which the SARS-CoV-2 virus is derived and are an important part of the human microbiome. Recognition of this entity was long delayed because its existence violates a dogma of molecular biology, namely the obligatory participation of nucleic acids in the transfer of genetic information. They were first detected in yeast and subsequently identified in several animal species and humans. Prions have a simple protein structure and analogous to more complex viruses, can be endogenized, bind functionally to a cell and change to an infectious pathogenic form -resistant to enzymes that break down proteins. An example is the PrP prion, the synthesis of which is controlled by a gene located on the 20 chromosome and is found throughout the nervous system and in many other tissues. When a cell divides, the DNA is copied into the two emerging cells, the prions copy each other independently, introducing the halves of the prion's division into the two new cells. Here they complete the missing part, forcing the emerging cells to add their own protein. In this way, they support their existence on their own. The basic physiological function of the PrP prion protein is not yet fully understood, it may play a role in the neuronal development and plasticity of synapses and may be necessary for the maintenance of the neuronal myelin sheath.

"Infectious" prions attack healthy cells and multiply to form new PrPsc protein structures by their ability to temporarily associate with the healthy prion protein with subsequent transformation into the β structure. This results in the appearance of a new infectious protein which triggers a chain reaction whereby the cell continues to synthesize normal proteins. However, these are immediately transformed to a β structure - a new protein construct that does not disintegrate, break down, but continues to infect new nerve cells. The role of prions in our body's functioning is not yet fully understood, but current evidence suggests that prions are actively involved in maintaining the body's biocenotic homeostasis.

The other organisms that inhabit our body are known as bacteriophages (or "phages"), and the pattern and colony composition of these individuals varies from person to person. They change with age and react to changes in the state of the body, just like the bacteria that inhabit this niche. Phages are viruses that parasitize bacteria, have the ability to destroy them, and have protective properties against viral infections. Penetrating into our body in great amounts, they compete with pathogenic viruses in the places of their entry into the cell.

The average human body absorbs 3.1 x 1010 phages per day through our body's cell membranes and this continuous stream of endogenous phages spreading through the blood and organs is believed to provide us with antibacterial and antiviral protection [10]. Each human organism has a specific constellation of phages in their habitat, although currently we have little information on the factors determining their composition and interaction within the human body. We know they can penetrate lung epithelial cells and muster a defence against viral infections. The competitive activity of phages against the angiotensin II converting enzyme (ACEII) has been demonstrated and is considered to be the method of penetration of the SARS-CoV and SARS-CoV-2 coronaviruses [11, 12]. The functional state of our body's phage population is therefore one of the determinants of resistance (immunity) to COVID-19.

Fungi tend to colonise the digestive tract and the skin and becomes pathogenic only when the ecosystem steady state is disturbed, and protozoa (behaving analogously) proceed to colonize up to 80% of the population in countries with inadequate sanitation. However, the most significant fellow inhabitants of our body are bacteria, which need to be discussed separately.

We still have only partial information on the interaction of organisms that make up the biotope community in our body. To date, we have only fragmentary knowledge of how the chains of connections serving homeostasis function in humans, in contrast to our more comprehensive knowledge of this phenomenon in plants and other animals. Examples include the symbiotic relationships of plants with fungi (mycorrhiza) and bacteria (bacteriorosis), or the interaction of aphids with viruses carrying genes necessary for the periodic growth of wings needed for the transmission of the aphids to the new host.

The human microbiome and in particular the role of the gut microbiome in human immune mechanisms (with significance for COVID-19) requires further discussion. The intestinal tract prevents pathogen access to the sensitive interior of our body by a specific barrier composed of a mucous membrane which has a huge surface area of about 400 m2. However, the human immune system operating from and within the tract itself constitutes the core of the human immune system and plays a significant role in maintaining tissue homeostasis. The human intestine is home to many microorganisms (intestinal microbiota) and has also the largest clusters of immune cells in the body which constitute part of gut associated lymphoid tissue (GALT). It is estimated that 8% of people suffer from impaired physical integrity of this barrier, while functional disorders of the barrier components and in particular the composition and derangements of the intestinal microflora (Microbiota), are more frequent.

The framework of this study does not allow for an in-depth discussion on the consequences of a poorly functioning microbiota, including its significance for the body's immunity and the prevention and combating of viral infections. The tightness or integrity of the intestinal barrier is closely related to the condition of the intestinal microbiota, as in the example of the interactions of a bacterial strain - Escherichia Coli Nissle 1917. This strain increases the sealing of intestinal wall porosities by increasing the expression of ZO-1 and ZO-2 proteins. At the same time, the presence of excess Escherichia coli, together with a reduction in the amount of Clostridium leptum and the genus Bifidobabacterium, may lead to the development of irritable bowel syndrome-a significant and widespread disturbance of intestinal function. The gastrointestinal microbiota is composed of about 1,500 known species of such entities and has been in existence for millions of years, as evidenced by archaic forms of bacteria which exist in hydrothermal vents on the ocean floor [13]. Microbiota is a very sensitive entity (organ) that analyses the condition of the external environment through ingested food, but this renders it very sensitive to toxic substances in food, as discussed later in this article.

It is worth remembering that the combined genomes of human microbiota encode over 10 million genes, outnumber our own body's genetic potential by 2 to 3 orders of magnitude and facilitate the numerous biochemical and metabolic operations necessary for effective body function. It is estimated that as much as 10% of all gene transcriptions, especially those related to immunity, cell proliferation and metabolism, are regulated by the intestinal microflora [14]. Because intestinal epithelial cells recognize and transmit signals from intestinal bacteria, our microbiota can be regarded as the "brain" of our immune system. It constantly communicates with the surrounding biotope to be further updated and primed and deserves to be a key target of research dedicated to combating the COVID-19 pandemic.

Bearing in mind the current level of knowledge about the human immune system, our actions to optimise immunity could be compared to the crass attempt to boost computer performance by increasing the voltage. While there are still major gaps in our knowledge of the immune system with regard to its functions and interactions, we are now acutely aware of the on-going progressive destruction of natural immune mechanisms and are forced to ever more radical action to compensate for this loss. Thus, we are increasingly dependent upon an uninterrupted series of artificial immunizations and repetitive administration of antibacterial substances. Apropos antibiotics, non-selective administration of biocides destroys our microbiota and exposes us to common diseases such as diabetes, obesity, atherosclerosis and inflammatory bowel disease [15]. Previously the observed dysbiosis was considered either a cause or a consequence of the above diseases but recent research using more sophisticated techniques confirm that dysbiosis of the intestinal microflora primarily leads to the development of type 1 diabetes [16], a similar relationship was found in relation to Alzheimer's disease [17].

An important element of the human microbiome are microorganisms bound by mucous membranes lining the respiratory, digestive and urinary tracts. The dominant form of bacterial existence on mucous membranes exists within a membrane structure complex called biofilm. This fixes the bacterial colony to the substrate, protects it from destruction and is thought to consist of one or more species of microorganisms surrounded by a layer of extracellular polysaccharides. Biofilm is formed as a result of the multi-layered or single-layered growth of microorganisms that arrange themselves in orderly, complicated structures composed of bacterial microcolonies and comprises countless microcolonies, separated by a network of open channels. The liquid circulating in the tubules flows around the microcolonies provides nutrients, oxygen and removes waste products, demonstrating a water

and sewage system working at the edge of the microcolony, while the bacteria inside are partially isolated. Dense clusters of bacteria connected by extracellular substance inhibit the flow of fluid circulating in the tubules and the cells living inside use nutrients that migrate to reach the interior of the microcolony. Therefore, bacterial cells located in deeper layers are alive, but are in the state of anabiosis - "dormant". The formation of a biofilm matrix, functionally reminiscent of a parasitic organism, aims to protect microorganisms (which make up the biofilm) against the degradative activity of environmental factors including the action of antibiotics. Biofilm is involved in the pathogenesis of chronic diseases and is also the spore of antibiotic-resistant bacteria involved in an unfavourable course of COVID-19. J. W. Costerton from Montana State University, a leading researcher in this field noted that biofilm occurs in 65% of chronically ill Western patients, including 80% of those with chronic lung and sinus infections. Little is known about the effect of biofilm on virus penetration across the mucosal barrier, but it is known that biofilm impairs the protective function of the mucosa.

Respiratory viral infections are seasonal in nature, particularly evident in the winter peak of respiratory infections caused by influenza virus, human orthopneumovirus (RSV), and coronavirus family viruses. Coronaviruses functionally pave the way for SARS-CoV-2, have been present in humans since childhood, and typically cause only mild infections in children between the ages of three and four. In Western countries, antibodies to coronaviruses are found in most children up to the age of 10, and there are as many as seven species of coronaviruses that infect humans, most often with symptoms similar to the common cold. The reasons for the recent emergence of new coronavirus species with very serious consequences, such as MERS and SARS, have now been discussed.

The argument supporting the thesis of the author, which posits the main cause of the COVID-19 pandemic as the decline of immunity resulting from the adverse impact of industrial civilization, is derived from the analysis of mortality rates related to the COVID-19 pandemic. Current observations indicate that although the number of infected people per 1 million population in Asian countries with an uncontrolled pandemic is not lower than in the countries of Western civilization, the number of deaths per 1 million is significantly lower. On March 5th the death rate from COVID 19 infection in the US was 1 578 / million, as opposed to India where it was 114 and Pakistan where it was 62. It is worth noting that in another Asian country, Japan (population 126 million), the number of precisely recorded deaths related to Covid is also low (67 deaths / 1 million people) [18].

Mortality is probably lowered when there is an effective counter to the "cytokine storm" reducing deaths due to the pulmonary complications of Covid -19 and other possible civilization-related immune disorders discussed later in this publication. A thesis occasionally presented links these effects with the high consumption of the spice turmeric which stimulates the immune system in the above-mentioned Asian countries. However, a more convincing argument suggests that the lowered incidence of Covid 19 results from less industry -related disturbance of the Biom's functionality. Another possible protective factor is thought to be linked to the fact that the peoples living in the areas from the Amur to the Don, including Buryatia and Mongolia, developed a unique set of microflorae over the ages which exhibits considerable resistance to negative environmental factors. Nevertheless, industrial civilization as it advances, similarly disturbs the composition and functioning of the intestinal microflora of these people. The corollary of industrial civilization is also air pollution which have a detrimental effect on human health and acute exposures to high concentrations of air pollutants exacerbate cardiopulmonary disorders in human population [19]. The recently published results analysing the course of the COVID 19 pandemic in Italy [20] showed that acceleration of transmission dynamics of COVID-19 has a high association with air pollution of cities measured with days exceeding the limits set for PM10 or ozone. The results of this work prove that in Italian cities where air pollution (measured by exceeding the PM 10 limit) lasted over 100 days, the daily number of infected people was on average 3,350 people, while the number of infected people in cities where the level of air pollution measured in an analogous manner remained below 100 days, the number of infected was 1014 people (data as of April 7, 2020). Mario Coccia - The author of the cited work (National Research Council of Italy and Yale School of Medicine, USA) puts forward the thesis, based on the analyses, that the dynamics of COVID 19 spread to a greater extent the degree depends on the degree of air pollution than on the frequency of human-human contact. This explains the higher virulence of the virus in industrialized regions and higher COVID 19 deaths in the most industrialized western countries, despite better-equipped health care and better financial and organizational resources.

Barriers and their effectiveness in protecting the human body:

Most people believe that the integrity of their bodies is maintained and protected by natural barriers created by the skin and epithelium of the respiratory and digestive systems. This is not altogether correct, viruses easily overcome the various barriers mentioned and thoroughly saturate our bodies, including those potentially pathogenic and a threat to life. As long as the defence and repair

mechanisms referred to earlier (and later) function effectively, these are neutralised, and we remain healthy.

There are three intestinal tract defensive barriers which protect us: The physical barrier (epithelium, tight junctions, mucus, commensal bacteria), the biomedical barrier [21] and an immunological barrier (lymphocytes and IgA). Although all three are functionally related, the microbiological has the most dominant role which includes that of the vortex discussed earlier. It is estimated that 109–1015 viral particles exist in one gram of intestine, although the function of such a highly represented intestinal virome is not yet fully understood. From our current and admittedly incomplete knowledge we can reasonably conclude that the endogenous population of viruses compete with exogenous viruses and inhibit or neutralise forms unfavourable to our bodies. Likewise, we know from phage research that the intestinal barrier does not block penetration of a large number of viral phages and their subsequent spread through the circulation to provide antibacterial and antiviral protection. It should be recalled that the number of human cells is greatly exceeded by those of the microbiome in which the most numerous are the bacteria. More recent studies conducted in Israel [22] compare the number of bacteria in the human body (3.9 x 1013) to the number of nucleated human cells (0.3 x 1013) showing a tenfold quantitative advantage of bacteria.

The mental barrier that hampers the perception of the organism from a microbiological perspective is the traditional belief that our physical bodies are subordinate to our divine souls. This makes it difficult to accept multi-centred logical management of the body and its functions. The concept of a body directed by an immortal soul and created by God in his own image, is completely different from that of a cell community, which in effect is the human organism. An example of the simplest form of an organized community is the biofilm (composed of bacterial cells) which enables better survival of the individuals possessing it and the biofilm aggregate is a link in the evolutionary trajectory leading to complex multicellular organisms such as animals. Diverse cellular participants of such a community, despite narrow specialization, still retain the basic characteristics of independent organisms, including the ability to analyse conditions of the surrounding environment and adapt to changing conditions.

The human brain is mainly responsible for operational functions at the level of the social macro-organism, but it is not only an effector and regulator of biological functions of the organism, including immunity. It also acts as a centre cooperating with the local peripheral "brains" of the autonomic nervous system, which modify the functioning of self-steering systems, affecting cells throughout the human body. The homeostasis of our body's biotope is the combined result of the cooperation existing between the groups of cells that make up the organs of our body and their co-habiting bacterial and subcellular organisms. The groups of cells that make up the human organism and other animal organisms are able to analyse microenvironmental changes and take appropriate adaptive actions and this faculty also exists within simple cellular and subcellular organisms. The independent, self-steering mechanisms of both human cells and those of separate species (co-inhabitants of our body), contest the common human belief that our body is subject only to our will.

More than two-thirds of the human genome is non-coding extragenomic DNA, which according to more recent studies [23], is capable of replicating computer function-i.e. the ability to accumulate and process information. Almost half of the human genome is made up of mobile sequences- DNA, RNA and transposons. An important group of such entities in the human genome are ERVs, which are human endogenous retroviruses (HERVs) which constitute 1 - 8% of the human genome and comprise about 450,000 copies. It is about 35- 40 million years since older copies were incorporated into the DNA of reproductive cells of human ancestors while more recent copies followed suit about 200 - 400 thousand years ago. Since then they have been amplified within the genome, most belong to highly repeatable retro-elements and their integration into the genome is irreversible. Currently no new forms of HERV are emerging which contrast with Alu and L1 elements, in which retro transposition to the human genome is on-going at present.

When the genome was discovered, it appeared to be a stable structure, but later research demonstrates that it undergoes a series of changes and rearrangements over the years of its evolutionary journey and also during each individual's lifetime. The moving parts of the genome can be considered a tool of evolution found in the genomes of all living organisms at all stages, from bacteria to humans.

As the facts cited above show, our body resembles masses of independent entities gathered within man's physical cloak- his body! There are many indications (as already mentioned) that he does not fully control or guide it, although he has the conviction that only he- unique within creation- possesses and is distinguished by the gift of thought. Unfortunately, we must smash the pedestal of man's monumental conceit as thinking is not only a human proclivity and privilege, all living matter "thinks". Bacteria, viruses and proteins, are able to store information, process it and implement changes in their structures and functioning modes. Man has only an indirect and usually negative influence on the

biocenosis that constitutes his body and the current frontal clash between man and the SARS-CoV-2 virus attacking him is the culmination of a guerrilla war. This has raged between man, viruses and related macrobiotic microorganisms since our entry into this epoch of an industry-based civilisation. An unfortunate outcome is the systematic destruction of interactive links connecting the ecosystem of the human body with the native external ecosystem, another is the havoc created by a conflict-generated toxic chemistry on both internal and external ecosystems. In addition, constant conflict has provoked interventions of biocenotic activity, which has led to a disturbed homeostasis and disruption of the finely balanced functioning of the system as a whole. This has resulted in an increased pathogenicity of viruses and bacteria and decreased immunity to the resultant infections.

The flagship achievement of the industrial age is the extension of life expectancy, especially evident in Western civilization. This has been achieved mainly by the elimination of hunger and reduction of perinatal mortality, but also by controlling and treating infectious diseases. Preventive vaccinations programmes were started, antibiotic therapy was introduced, and the use of biocides was widely hailed and advocated. The "golden" period of antibiotic therapy resulted in the discovery of new compounds with antibacterial properties, existing compounds were then modified to improve their pharmacological effect and newer properties continued to be identified. The aggregate result of all such initiatives was to incrementally increase activity against strains becoming resistant to preceding generations of drugs. Unfortunately, this situation has changed since the mid-1980s as the development of newer biocidal agents has slowed dramatically. Ominously and in tandem, an increase and spread of different or newer forms of pathogenic organisms has been increasingly observed and these are armed with boosted resistance mechanisms and decreased sensitivity to previously effective drugs. As the rate of pathogen emergence and resistance increases, the effectiveness of existing biocides is reduced, and further development of such drugs is slowed or indeed halted. Bacteria have adapted to this new scenario by creating pathogens such as the New Delhi bacterium which is resistant to all antibiotics and is an analogue of Klebsiella pneumoniae, which co-habits with most people without causing disease symptoms. The SARS-CoV-2 virus which is the progenitor of the COVID 19 emerged from similar adaptational prompts. This new virus belongs to the group of coronaviruses with which we have co-habited for millions of years but is now capable of breaching the biological protective barriers we had evolved over the aeons.

Before birth, the foetus (or indeed the embryo) is often exposed directly and indirectly to chemical substances which may alter or damage the developing immune system. Shortly after delivery and in subsequent months and years, the infant is confronted with a prescribed number of numerous vaccinations which force the immune system to develop differently from how it would otherwise develop i.e. naturally and in lock-step with the complementary ecosystem of the biosphere. This altered trajectory to achieve immune competence is associated with progressive dystrophy of that system and signals again the progressive extinction of our species [24]. The scenario is as follows: Man is now engaged in an intrinsically disabling sequence of steps starting with the enforced wearing of a protective shield, followed by mandatory cocoonization and isolation from that complementary part of the biocenosis which originally constituted the source of his immunity. I would not like to be understood as an uncritical supporter of the anti-vaccine movement, I am in favour of a more rational use of vaccines in a situation where there will be more and more needs for their use, and our natural defense mechanisms will gradually reduce their efficiency. Science increasingly reveals the weaknesses of our immune system, which in essence is the cause of our susceptibility to the COVID 19 pandemic. The current acceleration and intensification of research to counter the virus clearly illustrates the research gaps and the omissions of investigations over the past decades. In particular the patchy information on the Biocenosis/Man complex and its interaction with the external Biocenosis that complements it has been amply demonstrated. With such fragmented knowledge, we are not in a position at present to comprehensively and systematically describe the many causes of vulnerability to the COVID-19 pandemic. One of the identified causes, however is a deficiency in the production of type I interferon, currently recognized as an important component of the immune response, the lack of which does not bode well for an effective COVID-19 cure. It has been shown that mutations in the genes responsible for its production of interferon I [25] and the presence of "autoantibodies" inhibiting the activity of type I interferon occur in more than 10% of people suffering from the unfavourable course of COVID-19, while in contrast they are found in only 0.3% of the general population [26].There are as yet no comparative studies to determine the extent to which these factors are responsible for the more unfavourable course of SARS-CoV-2 infection in Westerners. It is reasonable however to assume that the increased levels of congenital defects of the immune system, is largely the result of controlling the hitherto high mortality of children (due mainly to infectious diseases) through the extensive use of antibiotics. Such indiscriminating use (particularly in the West) has maintained health in a cohort of individuals with immune system defects who in the past would have died or been

seriously and chronically ill. Another enabling factor for the COVID 19 pandemic results from widespread use of biocides which favour activation of adaptive mechanisms within bacteria. These include the permanent implantation in mucous membranes using biocide-resistant biofilm structures which facilitate greater porosity of the mucosal barrier thus permitting viral penetration. The irresponsible use of chemicals in the last century is another factor which impacts negatively on the microflora of the digestive system, a community of microorganisms which interact with GALT - the intestinal lymphoid tissue. This can synthesize over 20,000 antibiotic-like substances, deactivate toxins and perform a number of other functions necessary for the body.

In reviewing significant research initiatives, we can mention extensive Microbiome research projects such as: The Human Microbiome Project sponsored by the National Institutes of Health and the Metagenomics of the Human Intestinal Tract program sponsored by the European Commission. Other valuable work is emerging from research centres specializing in microbiome research [27]. For a detailed review of the currently available literature on the role of the microbiome in human immune mechanisms the reader is referred to research by scientists from the Kashan University of Medical Sciences in Iran [28]. Their work also interrogates the influence of the microbiome on the course and susceptibility to COVID 19 and pays particular attention to the role of flagellin-a structural protein of the flagellum of Gram-positive and Gram-negative bacteria and found in the gut microbiome. Flagellin stimulates immune pathways such as the Toll-like 5 (TLR5) receptor pathway making implantation of viruses difficult.

The scope and structure of this review allows only a superficial and selective treatment of the impact the numerous synthetic chemical substances impregnating the body and environment, have on the human microbiome. Examples of these substances are the degradation products of plastics - bisphenols, the presence of which is already found in the urine of young children. Bisphenol A (BPA) is a common toxic substance with an acceptable concentration level of 0.05 mg / kg body weight, easily penetrating the skin, digestive and respiratory systems. BPA is found in many substances including food and it binds to estrogen receptors in both animals and humans and mimicking a natural compound it accumulates in the tissues of the body from which it is gradually released. Its production in 2013 was estimated at 6.8 million tons, most of which are polycarbonates.

Many plastics contain heavy metals that are used as stabilizers and have strong properties to absorb and attract other contaminants, including toxic heavy metals, other endocrine disruptors and long-lasting organic pollutants. Today, about 70 years after the introduction of plastics into general use their annual production is over 300 million tons. Almost all plastic waste begins its "journey" on land, is carried by rivers and ends in the ocean, where huge floating islands of waste accumulate and increase every year. The expanding garbage patch in the Pacific Ocean has been termed the eighth continent and over time (and as a result of sunlight), its plastic content degrades into micro- and nanoparticles that remain in constant circulation-entering inevitably into our water and food supplies. Toxic products of plastic degradation and combustion of organic substances (mostly affecting urban settings) increasingly constitute some of the most toxic air pollutants by accessing the body's interior through the respiratory tract. Environmental pollution as described above contributes to the mass extinction of animals and bacteria, including those producing oxygen and as yet we do not have sufficient data of the effect on viruses, virons, phages and other subcellular organisms. However, it is a reasonable assumption that effects at micro level, mimic or are analogous to those observed at the macro level.

Another group of biocidal compounds damaging the microbiome (biocides) are produced and used in a wide range of industries to eliminate living organisms such as viruses, bacteria, fungi, insects and animals. Examples include disinfectants, wood preservatives and insect repellents, which when used excessively or inappropriately facilitate the development of antimicrobial resistance, unaffected by currently available antibiotics. In addition, the widespread use and production of biocides promotes the spread of genes that facilitate and regulate antimicrobial resistance. Transmission between bacteria of the same or different species of genes responsible for drug resistance is facilitated by urbanization and the agricultural use of products obtained from sewage and waste. A similar mechanism can be used for transmission of RNA viruses, including COVID 19 [29, 30].

Biocenosis of the human body developed during several million years of its phylogeny, a fact confirmed by the presence of intercellular fluid in our body which has a proto-oceanic composition and the presence of bacteria, whose phylogeny dates back billions of years . Maintained over the aeons, the stable internal homeostasis of our body has been overwhelmed by the challenge of managing the exposure of our body to over 100,000 chemicals synthesized within the last 150 years. The body cannot mount a timely defence and adapt effectively in the face of what from a historical perspective was such a precipitous assault. Many highly reactive and powerful chemicals were introduced and used (sometimes on a global scale) without any research of the effects on the functional competence of the human body and the surrounding biotope. Too often the only

method used to verify safety from a health perspective, the newly manufactured substances and new technologies, was to observe the basic health parameters of those exposed to them. This observation did not often include the delayed and cumulative negative effects we are currently experiencing. The impact of such materials on the efficiency of our defence and adaptation mechanisms was rarely studied. Standard investigation of toxicity in the newly introduced chemical substances mainly involved observation schedules (for acute and sub-acute poisoning) and monitoring of mortality or morbidity and significant organ (or organism) dysfunction, following administration of high doses. The effects of chronic administration of the test substances were examined piece-meal and superficially and the micro-ecological and ethnotoxicological analyses were conducted inconsistently and with little scientific rigour.

The COVID 19 pandemic has disabused man of the widespread and naïve belief that civilization's greatest achievement in the 19th and 20th centuries- that of overcoming the scourge of infectious diseases and doubling human life expectancy- is sustainable. But as with other "achievements" of the industrial age, the cost of this objective is the near exhaustion of natural resources (including health). Increasing longevity was achieved primarily by improving the health status of the richer part of the earth's population while neglecting health hazards which continue to plague the masses in the poorer section of the globe, which is further aggravated by the COVID 19 pandemic [31].

The programs of preventive vaccination and comprehensive infectious disease treatment, both of which promote increased longevity, are almost at the point of collapse. The effectiveness of the antibiotic shield is almost completely lost and our body's natural immunity, upon which preventive vaccination builds, continues to weaken. We neglect measures to prevent further pandemics and fail to address comprehensively the problem of antibiotic resistance. The emphasis remains on the profitable duplication and molecular tweaking of drugs for symptomatic self-treatment of trivial ailments instead of focusing on scientific research and organizational strategies to develop new antibiotics. We do not sufficiently promote research in the disciplines of biology, medicine and ecology and as a result we cannot defend ourselves against a bacteria whose resistance to antibiotics strengthens by the hour. The introduction of a new antibiotic is a billion-dollar expense item for a pharmaceutical company, which often however is written off as a loss, because resistance emerges after a few years or indeed earlier. The so-called market mechanism of the pharmaceutical industry inherited from the industrial era fails in this case.

In the fight against viruses, including the SARSS-CoV-2 virus, we rely on stimulating natural immune mechanisms in addition to current, well known protective measures such as mask wearing, social distancing etc. In fact, we imitate a "natural" contact with the virus by administering a vaccine. Being "civilized" and separated from contact with viruses and bacteria of the biocenosis in which we "naturally" lived for millions of years; we have become susceptible to microorganisms to which we formerly had immunity. As a result of civilization and its complex interactions, we have created conditions for the emergence of highly pathogenic microorganisms, resistant to currently available antibiotics. Key sites for the generation of such pathological entities are industrial farms and slaughterhouses with unfavourable working, processing and storing conditions. This constellation of factors combined with the violation of natural ecological niches of animals and related microorganisms has opened a Pandora's box of potential biological plagues. Main in pursuit of what he terms civilizational progress has gradually separated himself from his natural environment by means of mechanical and chemical screening, a technology which mimics our former naïve state. Additionally, he damages his internal biotope with chemicals used for "disinfecting" the environment and the food he eats. It is not an exaggeration to state in sum, that modern man exists in an environment which constantly generates life-damaging effects through massive chemicalization of the environment.

Summary:

This publication complements the author's previous publications analysing the phenomenon of the COVID-19 pandemic from sociological, philosophical and anthropological perspectives, but now links such reflections to new thinking in biology. Popular views on the COVID 19 pandemic tend to treat it as a temporary phenomenon, similar to previously occurring epidemics in that we can expect it to run its course. In addition, there exists a flourishing growth in conspiracy theories with narratives that treat the pandemic as a weapon, wielded in a planet-wide struggle for power in which billionaires secretly manipulate global forces and are the sinister puppet masters in the background. An avalanche of negative and frequently difficult to understand information is now being delivered to a society petrified with fear of the pandemic and anticipating the most extreme negative effects on our lives. When combined with high levels of societal anxiety and depression, such information significantly constrains a substantive discussion on the nature of COVID-19.

The key to understanding COVID 19 is the rational interpretation of the pandemic as a powerful impetus to accelerate the evolutionary change of the human species. It involves promoting the transition

of our species from an individual, loosely bound existence to one in which the individual human becomes a fully integral part of the macro-organism in which it plays a specific role. The arguments for this approach are supported by the results of studies of previous evolutionary phases of the Earth's crust, in which the form of loose, independent existence of cells was transformed into a form of existence within plant and animal organisms.

A similar phase of the evolution of the earth's shell biotope in which loosely living subcellular organisms created a more perfect form of cellular existence, in which they were integrated while retaining the elements of independence. Subcellular organisms, such as viruses or prions, although integrated with cellular life forms, still remain quantitatively dominant in the Earth's biosphere, maintaining the ability to penetrate the barriers that isolate the forms of cellular existence.

The rapid development of cellular life forms has been achieved by securing its internal homeostasis with a cell membrane. A similar process took place in multicellular organisms, the functional stability of their interior was preserved, as was the body shell, by lining the body cavities with mucous membranes.

The author believes that as we enter the post-industrial era, we also progressively morph into a state of collective existence within a supporting framework of macro-organisms, that he designates the POLIS. This is protected by inner and outer shells equipped with respiratory, detoxification and defence systems, to combat infection and other threats to the macro-organism. Societal development logically requires such protection in the event of breached shell structures and lowered efficiency of the existing defence systems. So as cells have adapted to collective life within multicellular organisms, people today must adapt to life within the POLIS.

An objective of this publication was to analyse the basic facts describing the biocenosis of the human body, including the mechanisms to secure the homeostasis of the internal environment and defend against viral pathogens predisposing to infection. Recent research has demonstrated the close functional connections between the biocenosis of the human organism and the biocenosis of the surrounding natural environment. This relationship has been disrupted by the impact of humans on much of the biosphere of our planet's crust and has included the irresponsible impregnation of its ecosystem (including the human body) by chemical substances. The four-billion-years period of sustainable development of the biosphere has been facing a massive assault through human agency over the last 200 years. It has unfortunately resulted in a major breach of its functional integrity and the consequence include the emergence of the COVID-19 pandemic and the high probability of others following in its train.

Within the container of his skin, man stores an aquatic environment that preserves the composition of the primordial ocean in which life on earth was born. Thus, human and bacterial cells, viruses and prions, function as in the early stages of evolution billions of years ago. Man is now planning to establish a colony on Mars replicating the living conditions of our body cells (which are similarly congregated in colonies) by creating ever more artificial conditions for them to live and reside in a space increasingly isolated from the environment. Our civilization has accelerated this isolation by what I have designated cocoonization and it replaces the natural mechanisms of maturation, immunity maintenance and homeostasis with artificially designed technical devices (and activities). These are integrated within our body in a process I term- the progressive cyborgization of man.

To balance the tsunami of doom-laden information, lets discuss the possibilities of constructive, positive action. The damage resulting from the exploitation of our planet's natural and biological resources is almost incalculable, however there is still a window for effective action to slow the pace of climate change and reduce the rate of environmental degradation. As a priority it is necessary (and possible) to conduct in-depth, more comprehensive investigations of how our body functions within its complementing biosphere. In tandem with this project, an ecotoxicological analysis of commonly used chemicals and the dynamics of their effects on health and the biosphere itself, is a pressing necessity and should be instituted at the earliest opportunity. An opportunity exists to fully protect and research those still intact shelters of the natural environment which contain minimally disturbed human populations and whose existence is more akin to that of refugees sheltering from external chaos. Knowledge obtained in this way will allow for at least a partial restoration of natural immune mechanisms and the more effective introduction of artificial substitutional mechanisms. The current achievements of research on the establishment of a colony on Mars should also be used to build analogous structures adapted to human life on the planet Earth in conditions of isolation from adverse environmental influences, which becomes a more urgent task than the conquest of other planets.

The scale of the necessary and urgently required actions warrants transnational agreements to effect orderly scheduling of the required tasks and ensure maximum cooperation in implementing them. This is far from an easy task when we consider that the first phase of the present crisis has deepened divisions and exacerbated existing conflicts. Dialogue has all but disappeared from political discourse which at present is dominated by the language of

confrontation. Unfortunately, this is due to the persistence of nationalist, xenophobic and conservative trends in national and international politics.

Conflict of Interest

We hereby confirm that there is no conflict of interest associated with publication.

Acknowledgement

The author would like to thank Dr. Eugene Egan from Cork in Ireland for significant help in editing this publication, in particular for language consultations.

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