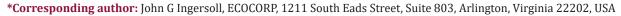


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A Holistic Understanding of the Occurrence and Management of Infectious Diseases Derived from the COVID-19 Pandemic

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ABSTRACT

Three important observations derived from the ongoing COVID-19 pandemic would hopefully allow the development additional approaches to dealing with it and avoid or at least minimize the occurrence and impact of future outbreaks. First, the dramatic increase in pandemics in the past decade alone suggests that the current relationship of humans with the environment is becoming unstable. In order to reduce the toll in life and treasure, we would need to shift our emphasis from control of, to symbiosis with nature. Second, the existence of superspreaders of infection among us in this pandemic requires that we develop objective tests to identify them rather than apply indiscriminate, draconian controls across the board. Leaving superspreaders unidentified could lead this pandemic to turn into a Black Swan event with a catastrophic impact on society. Third, we need to refocus our efforts to deal with this pandemic from the virus to the hosts, that is ourselves. An objective morbidity risk index can be developed such that most of us can go about our daily business without the fear of becoming seriously ill, while measures can be implemented to protect those who are most vulnerable to this virus.

Introduction

Infectious diseases have been around at least since the beginning of the Neolithicera some 12,000 years ago, when humans settled into communities in order to domesticate animals and grow crops [1]. The COVID-19 pandemic demonstrates the power of a tiny organism, the virus SARS-CoV-2, to disrupt the lives of billions of humans across the globe and create economic losses amounting to tens of trillions of dollars and still rising. The response across the board from scientists, to health professionals, to the general public has been almost unanimous and entirely predictable: find ways to control the virus, get rid of it altogether and return to a business as usual existence as soon as possible. It is not uncommon for elected officials and ordinary citizens alike to speak of a war against the virus. And while the current approach to dealing with this virus may or may not succeed, it reveals potentially a deep misunderstanding of the presence of the virus. As is often common in human reasoning cause and effect tend to be reversed. The virus has arrived because we humans have extended unwittingly an invitation to it.Enlightened members of the scientific community and undoubtedly a large number of the public recognize already that aspect of the appearance of this virus [2]. The sooner we realize that across the board the better we will be able to deal with the pandemic situation most effectively at every level, from the individual to the societal. This of course implies that we must refocus our efforts away from the virus and onto us.

Observations

According to the WHO infectious diseases are responsible for 20% of deaths across the globe, amounting to over 11 million annually [3]. The COVID-19 pandemic will increase these figures [4], but it is still nowhere close to the 1918 influenza pandemic that killed an estimated 50 million [2] or to the earlier recorded pandemics of 541 AD (Justinian Plague) and of 1348 AD (Black Death), each of which killed an estimated 1/3 of the populations in Eurasia and the latter being responsible for the death of between 75 to 150 million people [5,6]. The SARS-CoV-2 virus has the potential to

create another major pandemic, because it has not infected humans before in a sustained manner, it has an extremely high degree of transmission, and it has a relatively high rate of mortality [2]. Moreover, if it is found that either this virus never leaves an infected person, but it hides in the body dormant or immunity to infection is very short-lived then the COVID-19 pandemic will be around for a long time. The first observation has to do with the appreciation that all living organisms along with all inanimate objects, i.e., the entire Nature, exist in an interdependent and interconnected state or in a symbiotic manner to use a term from biology. Interconnectedness is the key tenet of our quantum world that has been gradually replacing over the past one hundred years the earlier concept of a mechanistic world [7,8]. Humans can control at will a mechanistic world but they have to live in harmony within the quantum world. And while the mechanistic approach has had a tremendous impact on the well being of humans, particularly in regards to the advances in medicine, it may now be reaching its useful limit.

This is becoming apparent from the explosive increase in potentially pandemic infectious diseases in the 21 century such as SARS (2002), H1N1 (2009), MERS (2012), Chikungunya (2014), Zika (2015), recurrence of Ebola (2014) and now COVID-19 [2]. All these diseases as well as the aforementioned earlier pandemics either have originated in animals or have employed animals for their transmission. Bats and pangolins are believed to be the culpritsof COVID-19. The link of human infection to an animal pathogen was realized scientifically in the middle 19th century by Rudolph Virchow, who coined the term Zoonosis to describe it [9]. Yet more than 150 years later we remain by-and-large oblivious to it as manifested by our human-dominated interaction with the environment. It is reported that the Black Death in its initial phase lasted for about five years and then it kept coming back periodically, albeit not as virulent, for the next 400 years [6]. Depending on how long the COVID-19 pandemic persists and whether an effective vaccine against it can be developed, humans may have to rethink seriously their relationship with nature sooner rather than later. The new relationship may entail among others for people to move away from dense metropolitan centers back into the country, the reduction in commuting for work and for shopping if such activities can be carried out remotely from home, a revision of social interactions whereby families can cluster together, increased efficiency in the use of energy, water and food, more effective recycling and reuse of wastes and local production of food to the extent possible.

The second observation from the COVID-19 pandemic is the realization of the existence of superspreaders of the infection among the population [10,11]. That is to say, while most infected people do not infect anybody, a few infected persons can infect a very large number creating what is called a cluster event. Cluster events have occurred aboard ships, at nursing homes, meetpacking plants, ski resorts, churches, restaurants, hospitals, and prisons. An example is shown in Figure 1. Epidemiologists use the reproduction

number R to describe the average number of new infections caused by each infected person. For most people R will be zero, but for the superspreaders it will be quite high. For SARS-CoV-2 the average value of R without social distancing is estimated to be between 2 and 3 at least in the early stages of the pandemic. In addition to R, a parameter called the dispersion factor k is used to describe how much a disease clusters. The lower the k is the more transmission comes from a small number of people. For example, the estimated value of k was for SARS0.16, for MERS 0.25 and for the 1918 influenza pandemic close to one. For SARS-CoV-2 the current estimates of k vary from a 0.10 to 0.44 [10,12]. This suggests that superspreaders are not important for influenza but they are for SARS-CoV-2. Moreover, if it is conclusively established that most transmissions occur during the pre-symptomatic phase of infection, then SARS-CoV-2 becomes difficult to contain as computer simulations show[13]. The occurrence of superspreaders in the COVID-19 pandemic is indicative of a power law statistical distribution for the occurrence of the disease. In a power law, shown schematically in Figure 2, the functional relationship between two quantities is such that a change in one quantity results in a proportional relative change in the other quantity, independent of the initial size of those quantities.



Figure 1: Example of COVID-19 Cluster Outbreak inLansing, Michigan at a Restaurant and Pub by a few Infected Superspreaders(Source: Ingham County Health Department).

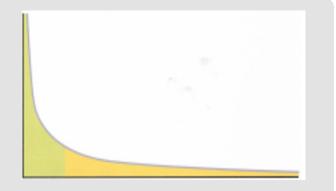


Figure 2: Power Law: Horizontal Axis – Persons; Vertical Axis – No of Infections per Person; GreenArea – Infections by Superspreaders $\sim 80\%$ oftotal; Yellow Area – Infections by 80% of all Persons.

Power laws are ubiquitous in nature from physics (black body radiation, quantum mechanics) to economics (income and wealth distribution, cost of health benefits per person) to finance (business income per client, contribution of taxes per person) to geography (size of cities) to geology (size of lakes and mountains, volcanic eruptions) to environmental quality (emission by cars and power plants) linguistics (occurrence of words and letters) to sociology (criminal charges per convict) to ecology (number of distinct species per ecosystem) and so on. A power law is also known as a Pareto law, because Vilfredo Pareto articulated it first at the turn of the 20th century as descriptive of wealth distribution or as the law of 80/20, because typically 20% of the input is responsible for 80% of the outcome. In the case of the COVID-19 pandemic indications are that between 10 and 20% of those infected generate 80% of subsequent infections [9,11]. A very important characteristic of a power law is that it is scale invariant. This means that depending on the parameters of the power law, it may or may not have a welldefined mean and a finite variance. As it turns out most power laws occurring in nature have a well-defined mean but not a finite variance. A lack of a finite variance can lead to a so-called Black Swan event, an event that is rare, is unexpected, has a huge impact and can be explained in hindsight [14,15]. The values of R and k for COVID-19 will determine whether the current pandemic has can lead into a Black Swan event, but since we may not know that for some time, if ever, it behooves us to take measures to reduce the likelihood of such outcome. These measures would include the identification via objective means, i.e., testing of some type, of the superspreaders such that their contribution to additional infections can be effectively controlled.

We may also note that the reason power laws are so prevalent is that nature confers equal chance of outcome to every actor, animate or inanimate, within a particular situation. In a pandemic everybody is given the same chance of infecting someone else and as a result we obtain the most probable distribution of the majority ofpeople not contributing to the transmission and only a relatively small percentage affecting it. Even though this reason seems counterintuitive, it isborne out of experience in quantum physics whereby the derivation of Planck's Black Body Radiation Law is based on the assumption of the equal access to energy among all oscillators (actors) maximizing (most probable outcome) the system entropy [9,16]. The third observation from the COVID-19 pandemic is that we focus so far too much on the virus and not enough on the person getting infected: the "host." It has already been established that certain characteristics as well as pre-existing conditions of the hosts make them more susceptible to severe illness and increased risk of death: age (85 or older), because of the normally occurring immune system senescence; obesity (body mass index above 30); blood type (type 0 offers increased protection); heart disease (heart failure, coronary artery disease, cardiomyopathies, pulmonary hypertension); cancer; diabetes (type 2); chronic kidney disease; chronic obstructive pulmonary

disease; immune compromised state; sickle cell disease; and perhaps other conditions to be determined as we acquire a better understanding of the virus [2,17]. Thus, the SARS-CoV-2 virus can cause severe disease and even death to those who happen to be afflicted by any of the aforementioned conditions at any age, although the occurrence of such conditions increases with age as the body fails along with the immune system losing some of is potency.

It is interesting to note that the COVID-19 pandemic reconfirms clearly both aspects of the 19th century debate on the causality of disease: Louis Pasteur and Robert Koch demonstrating that a microbe was the necessary agent, while Rudolph Virchow insisting that only those with compromised cells would become ill [10].0f course both sides were correct in understanding the causality of an infectious disease. No one would disagree that each host is unique in so far as his or her immune system and body would respond to the virus. But the complexity of the immune system, which may never be fully understood at the microscopic level, should not stop us from taking action as there are still general markers that can be employed to assign a degree of morbidity and mortality with respect the virus to each individual. These markers comprise the aforementioned macroscopic conditions that SARS-CoV-2 appears to exploit.Based on statistical analysis of the data on the millions of infected people and the hundreds of thousands of them who became severely ill and even succumbed to the disease, even if the data are not perfect, one can develop a quasi-quantitative numerical risk index, say, a number between 0 to 100, of a person's degree of morbidity. Those with a higher risk index would need to be shielded against exposure, while those with a lower risk index could resume normal activities without the fear of getting seriously ill. Such a system could be readily implemented via the internet and through social media at a much faster pace, a much lower cost and most likely higher efficacy than, for example, any vaccine. And even if an efficacious vaccine is developed the proposed focusing on the host will serve well to complement it. We may also note that even in the deadliest pandemics certain percentage of the population manages not to be infected. This would seem to defy the traditional cause and effect mechanistic view of infection. The question then is whether there is a more profound, quantum in nature, connection between humans and the infectious agents that can be ascertained.

Conclusion

In this study, we have briefly addressed three developments derived from the current pandemic and have presented an alternative course of action. First, we would need to reconsider our relationship with nature from that of control to one of symbiosis. Depending on how the current pandemic evolves we may be forced into symbiosis sooner rather than later. After all the popular adage "our actions will destroy nature" is false. Rather, we should realize that "if we do not heed the warnings of nature, we will be destroyed." Second, regarding the existence of superspreaders in

the current pandemic, the present "3 C's" approach to suppress their impact by imposing on everybody the avoidance of closed spaces with poor ventilation, crowded settings, and close contact with others is clearly not a long term solution. Contact tracing could be used to identify superspreaders but they would be found after the facts, i.e., after they have already infected a lot of people. We would need to develop suitable objective tests that would identify who among us are the superspreaders. Third, we should focus much more on the hosts, i.e., us, instead of the agent, i.e., the virus, in order to develop a morbidity risk index for every host. Discriminating policies would then be implemented to protect those at high risk, while those at lower risk can go about their lives without fear and anti-social restrictions.

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