The Coronavirus Pandemic: Why the Continent of Africa Appears Relatively Spared in Severity – An Immunological Perspective

Introduction

The World Health Organization has rightly coded coronavirus disease as COVID-19 as it started in December 2019 in the city of Wuhan, in Hubei province of China. Coronaviruses are a family of viruses which have always been in existence for millennia and were known to infect mainly animals. Due to the weird social and occupational habits of man, these viruses now have cross infectivity in humans, either intentionally or by accident on the part of man. In the past 20 years, there have been two noted outbreaks of coronaviruses, though of relatively less severity and spread, namely, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[1] SARS and MERS were effectively curtailed, but the COVID-19 is posing a horrendous threat to humankind by virtue of its casualties already experienced, and the casualties appear to mount by the hour in relatively advanced nations and temperate regions of the world. As at this moment, about 4 months into the pandemic, the African continent has 23,207 cases, with 1131 deaths; Europe has 1,011,640 cases with 103, 663 deaths; North America has 824,147 cases with 43,564 deaths; Asia has 389,832 cases with 14,942 deaths; South America has 83,219 cases with 3880 deaths; and Oceania has 8157 cases with 83 deaths.[2]

History

This year, 2020, marks the 100th year of one of the most devastating pandemics on record in man's history. The Spanish Flu pandemic ravaged the world for 3 good years from 1918 to 1920 during the First World War and claimed 50 million lives, with about 500 million individuals affected.[3] This accounts for about one-third of the world's population as at then. It was called the Spanish influenza as it was erroneously thought to have originated from Spain. It took another 80 years before scientists could identify and isolate the H1N1 virus as the causative agent based on the two major proteins, hemagglutinin and neuraminidase, found on its surface.[3]

Trends in the Demographic Distribution of Covid-19

It is obvious that Africa appears relatively spared. This is especially noted in the tropics, sub-Saharan, and Sahelian regions, which span from Morocco through Mali, part of the Sudan to Egypt, even up to the Saudi Arabian Peninsula and the Middle East [Figure 1].[4] Other regions such as the Indian Peninsula, Australia, and New Zealand, which have hotter climates by virtue of their closeness to the Equator, appear also relatively spared in mortality rates.

Immunology

Coronavirus is a single-stranded RNA-enveloped virus. Like all other enveloped viruses, it is heat labile and sensitive to pH changes and solvents by virtue of its lipid bi-layer.[5] It derives this bi-layer from the host's own cell membranes, which it uses as an adaptive mechanism to evade the immune system. This is in contrast to the nonenveloped viruses, whose capsid covering is more resistant to environmental factors. From the principle of vaccine manufacturing where live viruses such as measles, mumps, and rubella are inactivated with heat or formaldehyde, the virulence of COVID-19 appears to be attenuated or get inactivated entirely by heat of the tropical sun, and this may explain why we have many positive cases but relatively less casualties as compared to the temperate zones of the world. Thus, what we are witnessing could be that when the infected individual arrives from the disease ravaged zones of the world and the organism gets deposited on metal surfaces such as aircrafts, car handles or surfaces, and even metal gates and doors, heat either kills it or puts its invasive capability in check. In this sense, the person becomes passively immunized while the organism's pathogenicity becomes mild. Invariably, such a person when tested will be positive but with no disease process.

Immunomodulation

Immunomodulation is the regulation, suppression, or activation of the immune system to achieve a particular set goal. The thermodynamic aspect of immunomodulation is a novel frontier in the future of medicine, both preventive and curative, as it has not really been given proper attention it deserves.[6] It can be seen as a form of immunotherapy, which itself also involves manipulation of the immune system, with its own limitation and side effects. Drugs used in immunotherapy are immunomodulators. For instance, the hydroxychloroquine which is currently being tauted as a treatment of COVID-19 is an immunomodulator. Even though it has its own side effects like that of most drugs, in the desperate situation the world has suddenly found itself, the benefit outweighs its side effects such as optic neuritis and some cardiac conduction defects. As

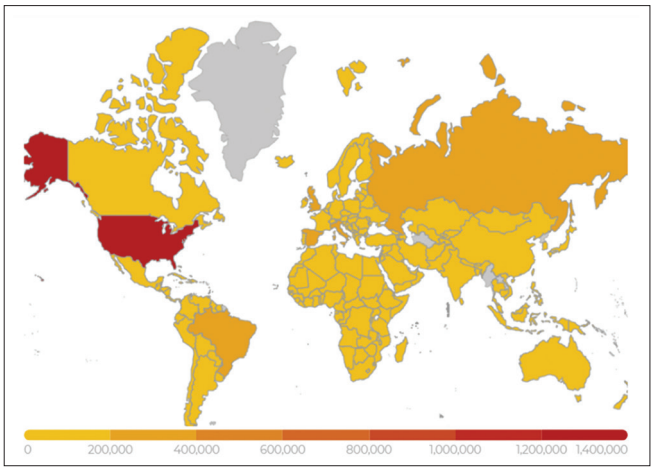

Figure 1: Global trend of confirmed cases of COVID-19 as of May 17, 2020

an immunomodulator, it is said to significantly decrease the serum levels of tumor necrosis factor-alpha and downregulate T-bet, the Th1 transcription factor, while the expression of GATA-3, the Th2 transcription factor, is upregulated.[7] Its immunomodulatory effect on COVID-19 should be an urgent ongoing research question. It has been successfully used to treat cases such as repeated implantation failure (RIF) in women, malaria, and Q fever.

The Pineal Gland – A Major Organ of Immunomodulation

The pineal gland, also called epiphysis cerebri, is a pine-shaped endocrine organ located behind the 3rd cerebral ventricle in the midline between the two cerebral hemispheres in vertebrates. The French Philosopher, Renee Descartes (1594–1650), regarded the pineal gland as the point of contact between the soul and body and where the human thoughts are located. Its immunomodulatory function derives from the hormone melatonin whose precursor serotonin is biosynthesized from the alkaloid, tryptamine. Melatonin is also produced by the retina and the intestines, but one of the pineal gland origins has a circadian rhythm with it peaks at around 2 a.m. and 4 a.m. As an immunomodulator, it enhances both the innate and adaptive immunity and specifically increases T-helper production, especially CD4+ cells.[8] In addition, it was recently found to be a free radical scavenger, acting by transferring electrons directly to detoxify free radicals. It stimulates antioxidative enzymes such as superoxide dismutase and peroxidases. It also increases the efficiency of mitochondrial oxidative phosphorylation as well as reduces electron leakage, thereby lowering free radical generation. Thus, having enough sleep at this period of lockdown has some positive immunological implication as stress itself is a source of free radical generation.

Thermodynamics

Thermodynamic changes in temperature, enthalpy, may have a beneficial role in antigen–antibody binding capacity. This may be due to its effect on the hotspot found in the epitope or antigenic determinant. Immunological hotspots are regions with a certain density of epitope within a given amino acid sequence and with a defined minimum of overlapping peptides in the given region.[9] The identification of hotspots comprising peptides that bind multiple alleles is of particular interest in the design of prophylactic vaccines that can protect the broader population against the pathogen in question.[9] Thus, heat itself has a definite role, perhaps, in the efficient binding of the coronavirus by the antibody. The heat from the sun (solar ultraviolet radiation) damages the genetic material (RNA) of the virus, thereby killing it.[10] The molecular interaction of an antigen epitope and paratope of the antibody can be represented by the following mathematical equation:

$$Ag + Ab \Leftrightarrow AgAb$$

According to the thermodynamics law of mass action, the following association equilibrium constant K_A can be defined:

$$K_A = \frac{[AgAb]}{[Ag][Ab]}$$

Where K_A is dissociation constant, Ag is the antigen, and Ab is the antibody.

Van't Hoff equation relates the temperature-dependent change in association/dissociation constant equilibrium to the reaction temperature (in Kelvin).

$$\frac{\delta In\,(K_D)}{\delta T} = \frac{\Delta H^{\theta}}{RT^2}$$

Where ΔH is enthalpy, change in temperature.

This equation provides a quantitative insight into the complex interrelationship between reaction temperature and antigen–antibody kinetics, both *in vivo* and *in vitro*.

Conclusion

Heat, as seen in the tropics in the COVID-19 pandemic, could be responsible for the lower incidence and relatively lower mortality recorded so far. If this assumption is true, we may experience a rise in the incidence of COVID-19 with rains and lower temperature changes. We also predict that even though cases may rise in tropical regions, there will be some form of passive herd immunity, resulting in less mortalities.

The thermodynamics of the antigen–antibody binding capacity and the COVID-19 pandemic is an area for urgent research and investigation. This inter-relationship has not actually been given the attention it deserves.

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Conflicts of interest

There are no conflicts of interest.

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