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Commentary

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A Personalized and precision medicine framework in the treatment of pre-existing conditions in coronavirus disease

Abstract

In healthy individuals, the immune system processes pathogens with a natural immune response that is mild and non-lethal; however in those that are immune-compromised-elderly and those with pre-existing conditions- diabetes, high blood pressure, dysbiosis and chronic liver disease etc., their immune system may overreact; and in the case of COVID-19, attacking lung epithelial cells and tissues resulting in vitamin A deficiency which shrinks the epithelial cells. Continuous exposure to this chemical stressor by the virus will result in squamous keratinization of the skin, digestive tract, respiratory tract, genitourinary system etc. leading to symptoms of dry skin, diarrhoea, coughing, keratomalacia associated with coronavirus leading to hospitalization and mortality. The immune cells notably the macrophages, neutrophils, natural killer cells etc. become weakened and dysfunctional especially among the elderly with chronic diseases. Boosting the immune system holds sway for infectious diseases (COVID-19) and non-communicable diseases rather than the reductionist science of modern allopathic medicine.

Keywords: COVID-19, cytokine storm, vitamin A, hypertension, personalized medicine

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Commentary

Introduction

The continuing emergence and re-emergence of novel and dangerous pathogens of epidemic potential (Coronavirus) is a permanent threat to the health of populations around the world and a major challenge to global health security. Basic biology, epidemiology, clinical presentation and the bases, to the extent it is understood, of how coronavirus disease and the compounding effects on non-communicable diseases notably high blood pressure, diabetes, chronic liver disease etc. have emerged and the current risk they represent will be succinctly outlined.

From basic biology, it is understood that cells are the basic unit of life, and the combination of cells results in tissues. When two or more tissues aggregate it results in organs and combination of organs results in a system. It is pertinent to mention that organelles are precursors of cells and the combination of molecules give rise to these organelles. These conceivable molecules are nucleic acid (RNA and DNA), proteins, carbohydrates and lipids. When the Human Genome Project got underway in 1993, there were two key assumptions that the complexity between a Human Being and other lower organisms, such as a worm, was the number of genes in DNA; and, that if the entire human genome could be mapped, then manipulating the DNA could control all aspects of life. Eventually, it was revealed that we have the about the same number of genes as the lowly earthworm somewhere in the neighbourhood of 25,000. Yet, we are so different. So clearly, the number of genes is not a measure of complexity.

The underlining denominator is the interactions of the molecules or parts that make up the system. The body is an integrated system and not a reductionist entity that has to be treated in parts. The body doesn't work in parts, if you change one part, it will change something else; and whatever is changed goes on to affect other parts. So the body is a system and should be looked at as so. A reductionist approach to treat the body rather than a précised or personalised approach is tantamount to adopting a one chance fits all approach. Personalised medicine involves designing the right drug for the right person at the right time.

These molecules are incapable of metabolising or replicating on their own as such are considered not alive. A virus cannot replicate on its own; it needs the help of a host cell's duplicating equipment, borrowing enzymes and other molecules to concoct more viruses. Succinctly put, viruses are not living organisms but well-organized molecular parasites. Coronavirus (COVID-19) is not a living entity.

You are more microbes than human

We are a walking ecosystem of microorganisms with 383 trillion viruses, 60 trillion bacteria and tons of fungi and parasites in and on our skin/intestines/ mucus membranes etc. Ninety-nine per cent of what makes us human is microbes. The presents of a virus does not mean it is the cause of the illness. Viruses are residing in our body for a purpose and a good purpose at that. Up to 45% of the genetic information in our DNA is viral.[1] The double-stranded DNA is a little virus hotel and viruses are responsible for two critically important functions in nature: variation and adaptation. It is the virus that is behind much of what is termed evolution. Many viruses can change in response to their environment.[2]

Aetiology and disease progression

Coronavirus disease (COVID-19) is caused by SARS-COV2- a positive-sense single-stranded RNA virus and represents the causative agent of a potentially fatal disease that is of great global public health concern today.[3] Coronavirus (COVID-19) is thought to be a mutated form of SARS-COV1, but after matching the nucleotide sequence with viruses in the data bank through BLASTN, it was discovered that the virus exhibit 100% amino acid similarity in the nsp7 and E-protein.[4] Nevertheless, it has been said that it is difficult to see a

100% similarity of amino acid sequence when a virus jumps a species. This has been the basis of the speculation that the virus must have been engineered in the laboratory and it can't possibly be a natural mutation.

Coronavirus essentially targets the human respiratory system which encompasses the lungs, pharynx, larynx, trachea and bronchi. These organs of the respiratory system are lined by epithelial cells fuelled by vitamin A. vitamin A plays a crucial role in the morphological function of the epithelium, epithelial keratinization, stratification, differentiation, and functional maturation of epithelial cells. Vitamin A is an integral part of the mucus layer of both the respiratory tract and intestine. Vitamin A improves mucin secretion; it improves the antigen non-specific immunity function of these tissues.[5]

Another unique addendum is vitamin D which is essential in creating CAMPs. Antimicrobial peptides eg cathelicidins AMP (CAMPs) are evolutionarily conserved across several species and is the oldest mechanism of action towards microbial pathogens, it is involved in pathogen cell wall/membrane disruption of bacteria and viruses. Vitamin D sources are sunlight, dietary supplements, fatty fish and cod liver oil.

Pathogenesis

The first step of the coronavirus infection is the binding of the receptor expressed by the host cells with the S-protein which inactivate the ACE2 followed by fusion with the cell membrane.[6] Human Angiotensin-converting enzyme 2 (hACE 2) is believed to be the receptor that is attached to the outer membranes of most of the respiratory organs and other organs of the body notably heart, kidney, and intestines. hACE 2 serves as the entry point into cells for some coronaviruses notably COVID-19.[7] It is pertinent to mention that the hACE 2 is a vasoconstrictor and stimulates aldosterone secretion it is always in parasympathetic dominant phase reason for its ability to lower blood pressure by catalysing the cleavage of angiotensin II into angiotensin (1-7). It equally stimulates the immune system, repairs tissues, increases blood supply to the gut and repairs mechanisms. Upon the binding of the coronavirus to the hACE2, the enzyme is neutralised and invariably neutralising all the functions of the hACE 2 just to provide the entry point for the virus to gets into the cell. Once the virus is in the cell, the body will not sit idly and watch its devastating effects. The innate immune system is the first line of defence in the form of macrophages, neutrophils etc will be called into play. The efficacies of this innate immunity notably the macrophages are fuelled by Cathilicidin Antimicrobial Particles (CAMPs) which is highly antivirals.[8] The surviving strategies of the body amid the infection is a function of Vitamin A which forms a scald folds around the respiratory organs and vitamin D which among other functions is essential in creating CAMPs.

Pre-existing conditions (Hypertension) and COVID-19

The severity of COVID-19 depends on the immune health and the underlining pre-existing conditions. An active immune system will naturally not result in cytokine storm which is a major culprit in the death of COVID-19 cases. Our exposure to the sun in generating vitamin D3 and D2 as a supplement essential in creating CAMPs and sulphate which prevent a no-flow situation in the blood is yet another factor. The age of the client is undoubtedly another defining factor as it is believed that children and the elderly are immune-compromised.

High blood pressure is a physiological adaptive response based on physical, emotional and chemical stressors, and never a disease. Disease can be treated with medications but an adaptive response can be fixed by fixing the stressors.

When at rest, the parasympathetic nervous system is activated and when under emotional, physical and chemical stress, the sympathetic nervous system is activated. The nervous system regulates everything, controls, and coordinates every function of the body including hormone production. If you are in a sympathetic dominant state, the blood supply to the gut shuts down, the immune system weakens, and blood supply to the digestive tract shuts down leading to inflammatory bowel disease, digestive disorder, reflux, and chronic immune system dysfunction, all from a stress adaptation of a sympathetic nervous system. Several cardinal features of chronic critical illness regardless of the aetiology support the assertion that autonomic dysfunction is a core mechanism underlying the development and perpetuation of multi-organ failure. Gut microbiota is reported to have a positive impact on key host functions related to the immune and nervous systems, in the prevention of disease and also in development and behaviour.[9–12] The structures of gut microbial populations are shaped by foodstuffs, in particular.[13,14] Fixing the gut which is linked to the neural system through the vagus nerve will program the body automata.

Symptoms of COVID-19

The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days. The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days.[15] The most common symptoms at the onset of COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, head-ache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia.

Transmission of COVID-19

It has been hypothesized that 90% of those that are infected with coronavirus are asymptomatic, only about 10 % of those infected are symptomatic and 1% of those that are symptomatic end up dying. Transmission of COVID-19 is not airborne but can move from one person to another through droplet spread. The U.S Centres for Disease Control and Prevention (CDC) states that to practice social distancing, you must stay at least six feet (two meters) away from other people, not gather in large groups and avoid crowded places and mass gatherings.[16] According to the CDC, 'Limiting face-to-face contact with others is the best way to reduce the spread of COCID-19 pandemic.[16] Being a non- living entity which can survive on our body surfaces, inanimate objects like desks, workbenches, clothes etc, it becomes imperative to adopt good personal hygiene. Personal hygiene encompasses covering of mouth when coughing, frequent bathing, washing of hands, not picking the nose, avoid transmitting of organisms from the mouth to the nose and vice versa etc. When you suspect you have come in contact with someone tested positive for the disease, the best option is to self- quarantine while you boost your immune system by taking cocktails of vitamins notably vitamins A, C and D for 5-14 days being the incubation period of the virus.[17] If after the expiration of the quarantine period and there is no symptom of COVID-19, then you can go about your business while still maintaining your hygiene or shelter-in-place (staying indoor to limit transmission, not because you tested positive for coronavirus or came in contact with someone who tested positive for coronavirus). Finally,

if you have glaring symptoms of COVID-19 confirmed by RT-PCR, then you can self-isolate to limit the spread of the virus to others while the undergoing treatment.

Non- pharmaceutical approach in the treatment of Covid-19

Science is not settled, doctors are not infallible and medical interventions come with risks. Nevertheless, this treatment is organised into three groups.

Group 1: - **Shelter-in-place**

Group 2: - **Self-quarantine**

Group 3: - **Self-isolated**

Group 1 are a healthy individual who chose to stay at home just to limit the spread of the virus.

For children:

i. 1,000 IU vitamin A palmitate per day ongoing

ii. 2,000 IU of vitamin D per day ongoing

iii. 500mg of vitamin C per day

iv. Iodine/iodide- eg Brand Lugols-3 drops per drink, once per day

For Adults:

i. 10, 000 IU vitamin A palmitate per day

ii. 5,000 IU of vitamin D per day

iii. 1,000mg of vitamin C per day

iv. Iodine/iodide- eg. Brand Lugols- 6 drops per drink once per day

Group 2: -Self-quarantine are those that must have come in contact with someone who tested positive for coronavirus. They may be immune active or immunocompromised.

For children:

i. 400,000 IU vitamin A palmitate per day for 2 days

ii. 50,000 IU of vitamin D per day for 2 days

iii. 500mg of vitamin C per day on going

iv. Iodine/iodide- eg Brand Lugols-6 drops per drink, once per day

For Adults:

i. 400,000 IU vitamin A palmitate per day for 2 days

ii. 50,000 IU of vitamin D per day for 2 days

iii. 1000mg of vitamin C per day on going

iv. Iodine/iodide- eg Brand Lugols-6 drops per drink, once per day

Group 3: Self-isolated:

Those who tested positive for COVID-19 but are not critically ill

i. 400, 000IU of vitamin A palmitate per day for 2 days

ii. 50,000 IU of vitamin D per day for two days

Those who tested positive for COVID-19 and are critically ill

i. 400,000 IU of vitamin A palmitate per day for two days

ii. 50,000 IU of vitamin D per day for two days

iii. Deliver intravenous vitamin C-100g drip per day until they are back to normal

Treatment of hypertension complicated by COVID-19

The best initial treatment strategy for controlling or reducing the physiology adaptive response induced hypertension is a modification of lifestyle. Lifestyle modifications should include eating a nutritionally balanced diet rich in vitamins A, C, D, reducing sodium intake, limiting alcohol and caffeine; not smoking; controlling weight; getting regular exercise, and managing stress. Such self-care measures may make drug therapy unnecessary. But if they do not significantly improve blood pressure within three to six months, medication may be required.

Scientists found the risk of stroke went up by a third for each blood pressure medication taken. People who needed three or more medication were at a 248 per cent higher risk than those whose normal systolic blood pressure was less than 120mmHg. You are in as much trouble by the time you are on three medications that achieve excellent control as you are when you have hypertension and it is untreated, which is amazing' Howard said. According to the American College of Cardiology, relying solely on pharmaceutical approach despite its great advances is going to come at a dear price of people's lives. [18]

Conclusion

In conclusion, the sun gives us the reason to be fast and the energy to do that, for that energy to be efficient, the human cells must be healthy. The human body uses sunlight to make sulphate, which maintains gelled water surrounding cells. Gelled water reduces charge separation that supplies electricity to tissues and that sulphate is essential to prevent a no-flow situation in the blood. Endothelial nitric oxide synthetase (eNOS) is a magical protein that makes sulphate in response to sunlight. In the same vein, in response to sunlight, 7-dehydrocholesterol (Vitamin D receptor) makes cholecalciferol vitamin D3 (Not an active form but in circulation). This vitamin is further hydroxylated in the liver to 25-hydroxyvitamin D3 (Most abundant but not the active form), this undergo second hydroxylation to become 125-dihydroxy vitamin D3 in the liver. This vitamin maintains calcium balance in the body.

Vitamin D is both a hormone and natural antibiotics (Cathelicidins and Defensins). It is part of the innate immune response against the S or spike protein. It is known to suppress renin gene and renin which otherwise would activate the RAS and Angiotensin II. Vitamin D deficiency leads to overexpression of Renin and RAS. Feeding the gut with these vitamins- A, C, D will reprogram the whole system automata.

Author's contributions

Ewaoche Sunday ITODO, B.Sc.; AMLSCN; M.Sc.; PhD conceptualized, did the literature search, typed, grammar checked and came up with the final article. Yibala Ibor and Tolutope Alade read and approved the final manuscript.

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Conflicts of interest

The authors declare no Conflicts of interest.

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