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Wherever the art of medicine is loved,
there is also a love of humanity.
- Hippocrates

Sushruta Medical News

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Editorial

Coping with Mental Health Issues during the COVID-19 Pandemic

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Global pandemics and natural disasters have a negative impact on the mental and physical wellbeing of populations from all backgrounds. However, some groups are disproportionately impacted more, based on age, geographic region, gender, co-morbidities, occupation and socioeconomic status. According to the Johns Hopkins University's Coronavirus Resource Center, COVID-19 has caused death of over one million people and has infected over 35.3 million worldwide in a span of about ten months. Fear of the unknown coupled with mixed messages from the media, global leaders and international and national health organizations; lack of effective medications and treatment protocols; and shortage of personal protective equipment (PPE) for health care providers (HCPs) are some of the reasons for increased stress, anxiety and heightened mental health problems during this crisis. In the current age of constant social media updates, 24-hour news cycles and spread of information and misinformation through group dissemination (e.g., Facebook, Twitter, WhatsApp), it is difficult to stay stress free and with equanimity. It has been reported that social distancing and social isolation can cause an adverse impact on mental health (Pieh et al, 2020). Speculation in the media on treatment options and efficacy and safety of treatment options that are currently available, add to the burden of stress. The onset of flu season in the United States and the impact of the influenza virus on general health during the COVID-19 pandemic is unknown, and it can cause increased anxiety among HCPs and general population alike. The fear of a second wave of the pandemic and its potential impact are viewed with consternation.

Mental Health and the Health Care Provider:

The HCP is the first in line of duty during any health crisis. Maintaining the wellbeing of the HCP is of paramount importance. According to the United States Federal Code §825.125, a HCP is defined as: a doctor of medicine or osteopathy, podiatrist, dentist, chiropractor, clinical psychologist, optometrist, nurse practitioner, nurse-midwife, or a clinical social worker who is authorized to practice by the state and performing within the scope of their practice as defined by state laws. The mental health of HCPs is frequently overlooked in global epidemics and pandemics (Preti et al 2020; Serrano-Ripoll et al, 2020). Due to the high number of COVID-19 patients, medical staff from different backgrounds and specialties were recruited to work in the front line for the treatment of COVID-19 patients in New York City, which was the epicenter of the disease in the early months of the outbreak. During this pandemic, the HCP is at higher risk for overwork, discrimination, isolation from

family and friends, risk of infection and this can lead to anxiety, insomnia and depression (Kang et al, 2020). In countries such as India, HCPs were discriminated against and denied basic facilities that included housing and even the right to a peaceful burial when they lost their lives due to COVID 19 (Bagcchi, 2020; Devi, 2020). Many HCPs in India reported an increase in violence towards them from dissatisfied patients and their family (McKay et al, 2020; Shaktivel et al, 2020) .

The British Medical Association has reported that almost one-third of its doctors have an increase in mental health conditions linked to their work during the COVID-19 pandemic (Torjesen, 2020). Forty-one percent of its doctors reported having depression, anxiety, stress, burnout, emotional distress, or another mental health condition and almost 30% of this population reported that their mental health got worse due to the COVID 19 pandemic. Studies have shown that reduced mental health in HCPs has negative impact on personal wellbeing, lowers productivity, has shown a rise in sick days, increased possibility of human errors and lowers patient satisfaction (Shah et al, 2020). It has been reported that the mental health of HCPs is adversely affected during pandemics based on data from Severe Acute Respiratory Syndrome, Middle East Respiratory Syndromes and Ebola outbreaks (Lee et al, 2018; Park et al, 2018). Published data from these outbreaks suggest that HCPs are at higher risk of developing anxiety, depression and posttraumatic stress (Wu et al, 2005).

Individuals who have been isolated showed functional neurological symptoms, and it is seen in higher numbers in individuals with diagnosed history of mental health illness (Jeong et al, 2016). A study conducted during the COVID-19 pandemic revealed a higher prevalence of anxiety and depressive symptoms among surgical staff (Elhadi and Msherghi, 2020). It is also reported that surgical residents showed higher levels of anxiety. A cross sectional study survey of obstetricians and gynecologists revealed higher rates of depression and anxiety (Shah et al, 2020). This study also reported that women had slightly more anxiety levels than their male counterparts. Family Medicine (Chen, 2020) and Emergency Physicians (Monzani et al, 2020) are at high risk, and have had to deal with an emerging new infectious disease and are constantly working in the front line despite limited and changing knowledge on the disease, changing protocols and guidelines and limited personal PPE. It has been reported that emergency department HCPs have shown more severe PTSD symptoms (Lee et al, 2018). Other groups of HCPs who work in the front line along with specialties that use aerosolized procedures are categorized for higher levels of anxiety, stress, burnout and depression. They also reported higher levels of stress related to fear of infecting their families (Rodriguez et al, 2020).

Dentists have higher exposure to saliva and blood in aerosolized form due to the use of high-speed rotary instruments and ultrasonic scalers. It has been reported that dentists have higher mortality due to COVID-19 (Ing et al, 2020). Reduced visits to the dentist have impacted the income of dental health professionals and has led to increased anxiety and stress. HCPs also reported that use of heavy PPE and N95 masks made communication between co-workers and patients harder leading to associated psychological distress (Lee et al, 2020).

Multi-level Support to the Health Care Provider:

The mental health needs of the HCPs should be at the forefront of all leaders and management professionals at medical and academic institutions. Traditional methods of supporting HCPs by providing support once they have developed mental health pathology (Kinman and Teoh, 2018) should be changed to a more proactive approach with a focus on prevention. Continued mental health support and care should be provided to HCPs that addresses the long-term wellbeing of the HCPs. Priority access to mental health resources should be provided on request to those HCPs with vulnerable mental health status, while maintaining privacy. Early and continuous interventions that have proven to help in reducing stress and anxiety that include in-person and remote counseling services should be provided. As changing medical guidelines and protocols have added to increased stress and anxiety, professional organizations and institutions must make updated clear guidelines readily available. Having easy access to PPE and job security also lead to increase in mental health wellness among HCPs and reduce the fear for personal safety and the safety of family members. Focus on effectively managing shift work, balancing it with the needs of the HCPs family and personal needs might add a sense of increased sense of wellbeing (Walton et al, 2020).

It is necessary to consider multiple stressors that affect the mental health of HCPs and minimize factors that contribute to increased mental health illness. It is vital to ensure that efforts are made at all level of organizations and departments in medical setting to destigmatize access to mental health resources and encourage medical professionals to ask for mental health support when required. Easy secure access, with limited repercussions on their work due to access of mental health support is needed. ***A healthy health care provider leads to increased productivity and increases patient satisfaction.***

Disclosure: Author declared no competing interests.

My Vision for Blockchain in Healthcare: Focus on Preventive Care

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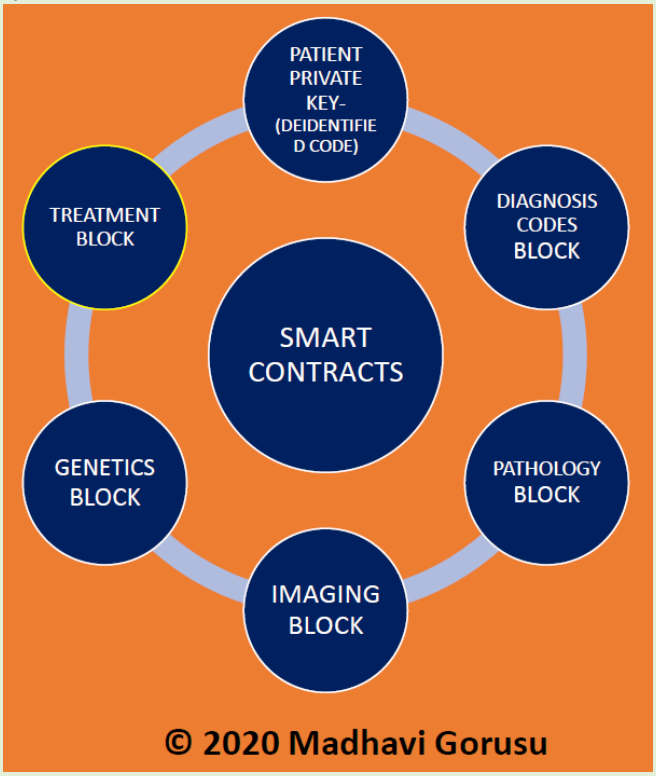
Editor's Note: Originally introduced to record transactions made with cryptocurrencies, such as Bitcoin, blockchain is a foolproof digital record of transactions. The name derives from its structure, consisting of individual records, called blocks, that are linked together in a single list, called chain. Blockchain is a decentralized and open system, distributed across many computers so that any individual block cannot be altered retroactively, without altering all subsequent blocks. This provides a level of security from tampering that is not possible by any other known means. While one can imagine the potential uses of such a system in financial institutes, such as banks, nevertheless, recently blockchain has found many other applications where data integrity is needed and also where recorded data can be accessed securely in real-time. Thus, blockchain is now finding applications in healthcare system. This article by Dr. Madhavi Gorusu presents how the use of blockchain technology can elevate preventive healthcare to new heights and thus can markedly improve healthcare and its costs. Please watch what blockchain is at: https://www.youtube.com/watch?v=SSo_EIwHSd4 **- BK Kishore**

Background: With rising healthcare costs in USA, which are not on par with improvement in healthcare of the population, it is utmost important that value-based care is the model of payment rather than pay per service. The usual culprits of failure of the system resulting in less than optimal healthcare outcomes are the lack of our ability to intercept a problem before it escalates. The lack of adequate usage of aggressive primary/preventive care of patients is the start of many potentially avoidable healthcare problems. In situations with existing health care problems, the lack of robust models to regularly monitor patients' health care issues can lead to worsening of their health due to lack of timely interventions. This can lead to relatively more expensive episodes of hospitalizations, emergency room visits etc. Outpatient surgery centers, infusion centers, dialysis centers are extremely cost-effective options as compared to the hospital where the same services are provided with same quality but at a higher price. Key issues which can significantly affect the revenue of any organization are the lack of timely payment or no payment which can influence accounts receivable and revenue. The implementation of electronic health records (EHR) has benefitted in streamlining health care information of patients. However, the lack of effective intercommunication between EHRs of different healthcare systems i.e. hospitals, physician groups, diagnostics services could block the exchange of healthcare information and can result in increased healthcare expenses by repetition of studies or tests. This lack of exchange of healthcare information can result in sub-optimal care of patients. The other serious concern is the security of patient information. The current encrypted exchange of healthcare information is far from being perfect. The patient private health and financial information with healthcare organizations is not hacker proof either. Is there a viable solution where all parties involved are benefited, and a system that works for the betterment of the patient and reduces the rise of ever escalating healthcare costs?

Proposed Solution to One of the Pain Points in Current Healthcare Ecosystem: One solution that I would like to propose is the use of Blockchain platform P2P ecosystem (Patient-to-Provider). The solution I am offering is a decentralized, blockchain technology. This verification ledger system is meant to increase patient ownership and reduce malpractice claims, help innovative healthcare, and implement effective treatment strategies. This

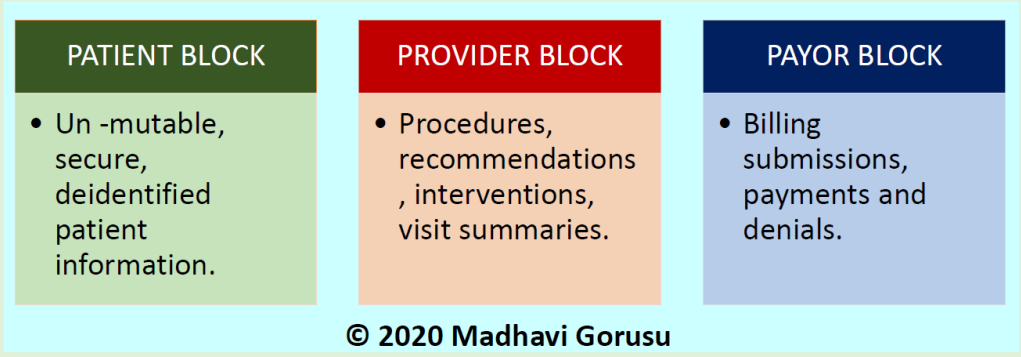
solution is an image of a human being's entire life health record. This model is not proprietary per se but is patient verification of his/her own records, and thus reduces malpractice claims, use of data analytics in clinical trials, and globalized healthcare initiatives through this platform is unique.

P2P: This will be a two-end user platform between providers and payers. Content is the patient's medical history. All healthcare information, and insurance information will be uploaded into this P2P ecosystem once the patient is enrolled into any payor system. The visits to any provider including diagnosis codes, treatment details, hospitalizations, pharmacy, radiology, labs or any new event will be updated in the blockchain system. This decentralized system of blockchain will be peer-reviewed and any change that is made will be recorded and tracks back to who has made the change. The information which is stored in blockchain is extremely difficult to be subjected to security breach as this would cause mutations at the level of several (possibly thousands of systems) at the same time. Provider information updates will save delays in payments from the payors. This P2P ecosystem could be the solution for establishing secure value-based healthcare, and help in the sustainability of organizations. If a patient Mr. X, who has been under the care of a primary care physician, develops early stage colon cancer, then the information on his colonoscopy visit in the gastroenterologist's surgery center, the pathologist's diagnosis, and subsequent visit to surgeon when referred for surgery, gets recorded. The payor now has this information. Subsequent colonoscopy will be quick to be approved and paid for. More importantly, upcoming required standards of care can be implemented in a cost effective manner. This can lead to avoidance of expensive chemotherapy options and potentially save a life. Value based care model can incorporate a reminder system to check on patient's follow ups, scans etc. This information might be relevant for familial syndromes. Consequently, his family members can be enrolled into screening programs and lead to a reduction of morbidity and mortality of cancer. Prevention is the best measure.



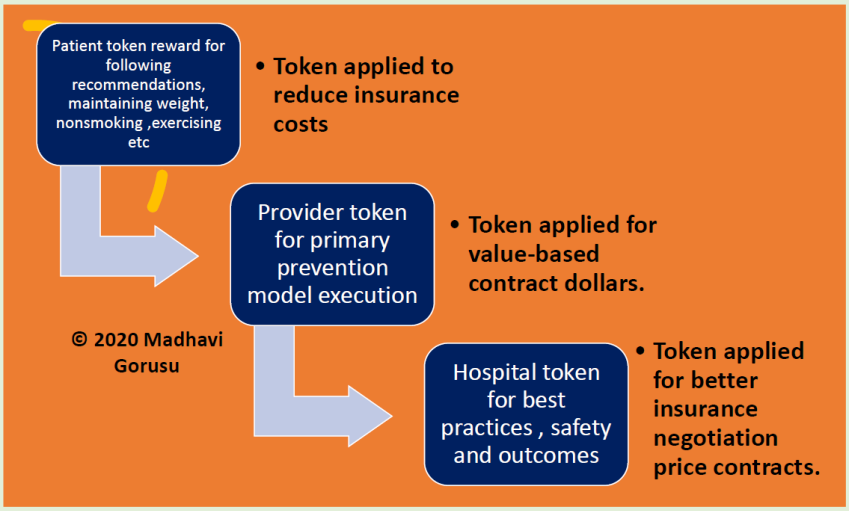
P2P Ecosystem Features:

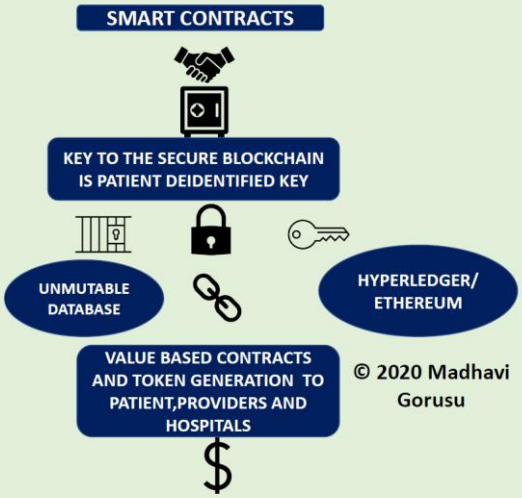
Two-sided Network, Joint venture.
Positive Networks - An increase in providers, leads to betterment of the purpose of the ecosystem.
Cross-side Networks - Multiple stake holders are benefitted from this shared but decentralized platform.



Benefits will be shared by all parties involved. The proportion of sharing of benefits and willingness to pay by customer is a challenging question. The incorporation of P2P ecosystem into the existing health care information

using smart tokens could help in reducing the perceived threat by the health care existing IT. However, it should be an ongoing endeavor to minimize the expenses supporting the expensive healthcare information technology. And the expanding use of blockchain technology hopefully should reduce redundancy and supply the multifaceted uses that it can provide.





Disclosure: The author declares no competing interests. This article is adopted from author's paper submitted for her Blockchain Certification Course from the MIT.

Nobel Prize in Physiology or Medicine 2020

The Nobel Prize in Physiology or Medicine 2020 was awarded jointly to Harvey J. Alter, Michael Houghton and Charles M. Rice "for the discovery of Hepatitis C Virus".

Watch the Announcement at:

https://www.youtube.com/watch?v=BTu6uOWLKR4&feature=emb_logo

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Clinical Dilemma

COVID-19 and Cardiovascular System

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Introduction: COVID-19 and cardiovascular disease (CVD) make literally a deadly combination. Not only do people with pre-existing cardiovascular conditions have predisposition to but also have worse outcomes from COVID-19. COVID-19 (due to SARS Cov-2) was first reported in Wuhan, China in late 2019 and as of September 2020, it has affected nearly 32 million people, causing over 880,000 deaths worldwide. The United States alone has over 7 million confirmed cases and over 200000 deaths. Despite the importance of understanding COVID-19, the novelty of the disease and causative virus, exact mechanistic pathways are not yet clearly elucidated, and much work remains to be done.

COVID-19 Pathogenesis: The SARS-CoV-2 virus is spread primarily via droplet transmission and contact with infected respiratory secretions. Adults may present with a viral pneumonia syndrome characterized by fever, dyspnea, cough, as well as upper respiratory symptoms, loss of smell and taste, myalgias, and gastrointestinal symptoms. The virus enters alveolar epithelial cells through angiotensin converting enzyme 2 (ACE2), a membrane bound aminopeptidase that is expressed in type I and type II pneumocytes as well as other cells such as cardiomyocytes (Long et al, 2020; Ranard et al, 2020; Siripanthong et al, 2020). ACE2 normally metabolizes proinflammatory angiotensin II and its possible inhibition in COVID-19 is postulated to contribute to cytokine release and endothelitis and subsequent systemic coagulopathy. Research over the course of the pandemic has suggested interactions between the cardiovascular system and infection by the SARS-CoV-2 virus. At a clinical level, data suggest a worse COVID-19 outcome for patients with pre-existing cardiovascular disease. Data on specific mechanistic correlations are more limited, however, but offer potential avenues into future areas of research.

Clinical Cardiovascular Impact of COVID-19:

Cardiovascular Manifestations of SARS-CoV-2 Infection: Clinically, COVID-19 results in cardiovascular sequelae that are associated with worse outcomes. Among patients hospitalized for COVID-19, 8-12% experience **acute myocardial injury** with an elevated troponin (Siripanthong et al, 2020). This figure is even higher for patients admitted to the ICU, at 22-31% (Long et al, 2020). Interestingly, this effect is not unique to the SARS-CoV-2 virus – the MERS coronavirus also caused an acute myocardial injury (Long et al, 2020). Postulated mechanisms for this include direct viral entry into cardiomyocytes via the ACE2 receptor or indirect causes such as increased myocardial demand due to active infection and systemic inflammation (Siripanthong et al, 2020). Regardless of cause, however, acute myocardial injury portends a worse prognosis for COVID-19 recovery and has been suggested to increase the risk of fatal arrhythmias (Long et al, 2020; Siripanthong et al, 2020; Ouldali et al, 2020).

In addition, some research suggests possible SARS-CoV-2 **myocarditis** as a potential complication of COVID-19 as identified by mononuclear infiltrates on autopsy. Data on SARS-CoV-2 myocarditis is limited. One case report highlights acute heart failure with global dyskinesia, and left ventricular ejection fraction (LVEF) decreased to 32%, an NT-BNP of 22,600 pg/mL, and acute myocardial injury with a troponin level of 11.4 g/L.

The patient was positive for SARS-CoV-2 and tested negative for other viral causes of myocarditis. After supportive care, his LVEF improved to 68%. The true incidence of COVID-19 myocarditis is unknown, and cases have varied in patient presentations from mild symptoms to fulminant myocarditis (Zhang et al, 2020). Differentiating SARS-CoV-2 myocarditis from acute coronary syndrome and sepsis-related cardiomyopathy requires further imaging, ideally cardiac MRI, though this may not be practical given COVID-19 infection control constraints.

Recent pediatric research has suggested **a Kawasaki Disease-like syndrome** (MIS-C Multi-system inflammatory syndrome in children) as a complication of COVID-19 in children. A 230 patient, single institution French series from 2005-May 2020 found some evidence to suggest an increase in rates of Kawasaki Disease diagnosis correlating with the COVID-19 pandemic and the H1N1 pandemic in late 2009. However, larger cohort studies are needed to establish whether this is indicative of a true clinical trend.

COVID-19 and Pre-existing Cardiovascular Disease: An August 2020 meta-analysis of 25 studies, of which 19 were conducted in China, including over 65,000 patients found the presence of preexisting cardiovascular disease increases COVID-19 mortality by a relative risk (RR) of 2.25 (Ssentongo et al, 2020). Other contributors to COVID-19 mortality were hypertension (RR 1.82), heart failure (RR 2.03), diabetes (RR 1.48), chronic kidney disease (RR 3.25), and cancer (RR 1.47). While the fact that these typically high-morbidity conditions increase the risk of COVID-19 death is not surprising, the high magnitude of the relative risk due to cardiac conditions highlight the need for additional studies that can inform clinical practice.

Safe Management of Acute Coronary Syndrome in COVID-19 Patients: Given the infectivity of SARS-CoV-2 is nearly four times that of influenza (Ouldali et al, 2020), balancing patient treatment with avoiding healthcare worker exposure is difficult, especially in emergency situations such as STEMIs. While all healthcare workers in potential contact with a COVID-19 patient should wear appropriate personal protective equipment, judicious use of the cath lab has also been suggested to limit healthcare worker exposure without compromising patient care. These articles suggest STEMI patients should receive guideline-appropriate percutaneous coronary intervention, though there is discussion regarding the use of tissue plasminogen activators instead in low risk patients. Many NSTEMI patients can undergo conservative management with revascularization deferred to a later date.

COVID-19 and Common Cardiovascular Drugs:

ACE inhibitors and ARBs: Recent mechanistic studies have offered a limited insight into potential interactions between the SARS-CoV-2 virus and common cardiovascular drugs. The rationale for these studies stem from viral use of the ACE2 receptor, which also plays a role in the renin-angiotensin-aldosterone-system (RAAS) and is relevant to the action of ACE inhibitors (ACEi) and angiotensin receptor blockers (ARBs). This has led to discussion about whether the use of ACEi/ARBs potentially worsens active SARS-CoV-2 infection by creating additional receptors for viral entry. Prior animal studies have shown these drugs upregulate ACE2 receptors *in vivo*. Early in the pandemic however, the HFSA, ACC, and AHA released a joint statement dissuading providers from deviating from standard use of ACEi/ARBs.

Multiple studies have evaluated the role of ACEi/ARBs in such patients however and found no such clinical effects. A retrospective cohort study of 174 ACEi/ARB users and 348 propensity-matched patients with hypertension but no ACEi/ARB use conducted in Wuhan, China showed a hazard ratio (HR) of 0.34 (95% CI 0.14-0.83) associated with using the medications in a multivariate Cox proportional hazards model (Zhang et al 2020). The French CORONADO study evaluated 1317 diabetic patients for factors that contributed to intubation for mechanical ventilation or death within 7 days of admission to the hospital (Cariou et al, 2020). An age- and sex-adjusted logistic regression model found only BMI, not ACEi/ARB use or HbA1c, associated with the primary outcome. In light of these studies and the relative risk of hypertension and Covid-19 mortality(Ssentongo et al,

2020), there is at present no convincing reason to deviate from standard clinical use of ACEi/ARBs as noted in the March 2020 combined HFSA/ACC/AHA statement (Bozkurt et al, 2020).

Statins: Concurrent statin use has been proposed to affect COVID-19 patients, though the hypothesized clinical effect is unclear. Beneficial and detrimental effects have both been suggested, the former via decreasing proinflammatory cytokines and the latter by upregulating ACE2 receptors, facilitating viral entry. A study of 861 Covid-19 patients taking statins, of which the vast majority were on atorvastatin (83.2%) with fewer on rosuvastatin (15.6%) found a protective effect of statin on 28-day mortality with a hazard ratio of 0.58 (Zhang et al, 2020). While a single study is insufficient to advocate aggressive statin use in COVID-19 patients otherwise not indicated for statins, this data does suggest a favorable signal associated with statin use.

Conclusion: As the COVID-19 pandemic continues, cardiovascular drug associations and management implications should continue to be active areas of research to elucidate high-quality cardioprotective management strategies. Future studies may suggest an increased role for statins, anti-inflammatory drugs and better-defined management strategies for acute coronary syndrome.

References: Citations shown in the text are hyperlinks to their respective publications.

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- **September 2020** https://www.aapiusa.org/wp-content/uploads/2020/09/SNM_September-2020_081020.pdf

Pathophysiology of Thrombosis in COVID-19:

Possible Remedy through Multiple-Mixed-Strain Probiotic Adjuvant Therapy

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COVID-19 due to the virus SARS-CoV-2 so far infected over 34.2 million people around the world causing the death of over one million people (1.01M), as of the last week of September 2020. In the United States alone, so far there are 7.45 million confirmed COVID-19 patients registered, with a death count of over 211,000 people. The COVID-19 pandemic is not contained and is spreading at a rapid pace throughout the world.

Earlier I wrote several articles on pathophysiology of Coronavirus pandemic mainly concentrating on the overactive immune system, and few ways and means to control it. It has been well established that the death due to COVID-19 virus is primarily linked to the respiratory failure. The SARS-CoV-2 virus infects the human cells (respiratory alveolar cells) through ACE-2 receptor site using its spike protein (S-protein) and then integrates into the cell membrane. The virus multiplies by making virions with the aid of its RNA behaving like mRNA (positive sense) or with the aid of RNA dependent RNA polymerase to make mRNA using their own and host cell enzymes (Reddy, 2020a; Reddy 2020b).

The SARS-CoV-2 virus infects the alveolar tissue and thus collapses the lungs by suppressing the production of surfactant by the type ll pneumocytes. In addition, due to excess stimulation of innate immune system with heavy infiltration of neutrophils and the resultant cytokine storm (due to) production of proinflammatory interleukins), the overactive immune system destroys the alveolar tissue thus causing the glossy appearance of lung with severe pulmonary lesions. Apparently the overactive immune system, due to activation of both innate and adaptive immune pathways, with resultant increase of inflammation provoking interleukins (IL-6 etc.) and effector-T and T-killer cells cause severe damage to alveolar tissue causing severe pulmonary distress and death. Apparently, SARS-CoV-2 significantly decreases the production of T-reg cells as well as inflammation reducing interleukins (IL-10 etc.). This is partly due to dysbiosis in the gastrointestinal microbiota, which is caused by prior comorbid conditions, old age, unscrupulous use of antibiotics, extensive use of medications and stress etc. (Reddy, 2020a; Reddy 2020b).

When once the viral infection spreads to other parts of the body, the following sequence of pathological reactions take place. The virus attaches to the ACE-2 receptors of the endothelial cells in the veins or arteries and thus causes severes inflammation due to viral multiplication followed by cell destruction and apoptosis. The ACE-2 function in the vascular system is to convert angiotensin -ll (AT-ll) to angiotensin 1-7 (AT-1,7). Due to disruption in the function of ACE-2 in the endothelium, the angiotensin-ll accumulates and causes inflammation of the blood vessels with severe vasoconstriction resulting in high blood pressure and damage to the blood vessels. Since angiotensin 1-7 is responsible for vasodilation, reduction of blood pressure and inflammation, the disruption of ACE-2 function due to adhesion and multiplication of SARS-CoV-2 virus significantly reduces the conversion of AT-ll to AT1-7 thus increasing the inflammation, vasoconstriction, uncontrolled activation of NADPH oxidase enzyme with resultant production of superoxide and damage to the endothelium.

This excess inflammation and oxidative damage will further damage the subendothelial layers of the blood vessels leading to the excess production and release of von Willebrand factor (VWF) and clotting factor-VIII into blood, thus ultimately resulting in the formation of thrombus i.e. blood clots. The VWF is a pro-blood clotting protein and clotting factor-VIII is a blood coagulant. Thus, blood clots in veins i.e. venous thromboembolism, which eventually breaks off and gets into systemic circulation and causes pulmonary embolism, leading to the alveolar dysfunction. Whereas,

when the clot forms in the arteries i.e. atherothrombosis, this can lead to heart attack, stroke and multiorgan failure leading to death. The similar mechanism may be taking place in the tissues, where there is an abundant amount of ACE-2 in the human critical organs such as kidneys, heart, and GI tract etc. It has been reported that patients with severe COVID-19 infection had more prothrombin, interleukin-6 (inflammation provoking interleukin), D-dimer, C-reactive protein and other blood clotting factors in their blood, proving the fact that SARS-CoV-2 has a pronounced effect on inducing the thrombosis in the patients (Connors and Levy, 2020).

Angiotensin enzyme converts angiotensin to angiotensin-II. It has been proven that the bioactive peptides and specific and nonspecific immunomodulins and nanotherapeutic bio-compounds produced as by-products of probiotics grown in milk base media, inhibit angiotensin enzyme and thus significantly reduce the formation of AT-II. Apparently, the whey proteins (immunoglobulins) and their hydrolyzed bioactive peptides may have significant effect on inhibiting angiotensin enzymes (Zamel, 2003). In the case of COVID-19, although ACE-2 is rendered non-functional, some of the immunomodulins and bioactive peptides produced by the probiotic bacteria reduce the concentration of angiotensin-II, thus decrease the thrombosis or blood clot formation in COVID-19. Possibly, this can be one of the reasons why in some of the COVID-19 patients the blood clots are not formed. If we analyze and determine the variations in the intestinal microbiota with regards to its individual microbial component composition, perhaps we will have an answer to this puzzle. Under any circumstances, maintenance of the proper intestinal microbiota and microbiome is an essential requisite to override or reduce the death rate in COVID-19.

I conclude that dysbiosis and other comorbid conditions, significantly contribute to the mortality of COVID-19 patients (Reddy, 2020a). Thus, adjuvant multiple mixed strain probiotic therapy coupled with other traditional treatment modalities should significantly help to reduce the mortality in COVID-19 by significantly suppressing the overactive immune system, as well as the Coronavirus induced thrombosis (Reddy and Reddy, 2016a; Reddy and Reddy, 2016b; Reddy and Reddy, 2017; Reddy, 2020a: Reddy 2020b: Reddy, 2020c; Reddy, 2020d).

Disclosure: Author is a scientist heavily involved in probiotic research, has published over 130 research articles, and holds over 150 US and International patients. His company (IMAC, Inc.) manufactures and sell all over the United States, Canada, Europe, and South East Asia and South American countries, food grade microbial cultures and other high tech essential enzyme fortified functional products, which go into the manufacture of cheese and other dairy products.

References: Citations shown in the text are hyperlinks to their respective publications.

Scan QR Code for the Website

A One-Stop Website for COVID-19 Information

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As we are facing this exploding health care crisis of COVID-19 pandemic and inundated with a constant stream of information and misinformation, it is easy to be confounded and confused. It is not easy to navigate through this rapidly spiraling out landscape and timescale. So my approach to this escalating situation is to inform and educate myself as quickly as I can, while also going through daily clinical, family, social and other responsibilities and obligations. As I started collecting and reviewing as much open source information and data as available, it occurred to me that I should share this curated information with peers who are very busy and engaged in the frontline fighting this battle against COVID-19. So, I dedicated my website **RAVIKOLLIMD.COM** and redesigned it, posted numerous links to scientific and medical articles and public health resources. As I will be updating the site daily and frequently, I hope you find it of some value and use to you. Please stay safe and well.

Pioneers in Medicine and Healthcare

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Co-Winner of Nobel Prize in Physiology or Medicine 2007

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Today, knocking out or knocking in or overexpressing or altering a gene in an intact animal is a routine genetic engineering technique. But when it was designed and performed for the first time, it was as sensational as the birth of the first test tube baby or first cardiac transplantation. Behind such groundbreaking and game-changing technological developments, there are great men and women of exceptional abilities, skills, dedication and above all a spirit of human endeavor to conquer the nature and nurture the humanity into a new realm of existence. And some of them might have struggled with innumerable difficulites while they were young. An illustrious personality of that caliber is Prof. Mario Ramberg Capecchi, who was a Co-Winner of Nobel Prize in Physiology or Medicine in 2007, and with whom I have some academic interactions.

Born in Italy in 1937 as the only child of his parents, Dr. Capecchi had a traumatic childhood during World War II. His father, an airman, was reported missing in action. His mother was sent to a concentration camp as punishment for distributing anti-fascist pamphlets. Although she made some arrangements with a peasant family to provide for her son during her absence, after one year the money she gave was exhausted, leaving her son without care. As a child of four-and-half years old, little Mario was left on the streets of Northern Italy fending for himself as an orphan, moving from one orphanage to another, and living with homeless children on the streets for the next four years. He almost died of malnutrition. Finally, his mother, having been released from the camp, found her son in a hospital bed suffering from fever and sustaining on bread crumps. She took him to Rome, where he had his first decent bath after six years. In 1946, Edward Ramberg, the uncle of Mario and an American Physicist at the Radio Corporation of America, sponsored his sister and her son to migrate to the United States. The rest was history. In 1961 Mario Capecchi graduated with B.S. in Chemistry and Physics, and in 1967 obtained his Ph.D. in Biophysics from the Harvard University, working under the mentorship of James D. Watson, the co-discoverer of the structure of DNA. In 1973, Dr. Capecchi joined the faculty at the University of Utah, where he continues his research as a Distinguished Professor of Genetics and Biology even at the age of 83 years.

Dr. Capecchi won the Nobel Prize along with Martin Evans and Oliver Smithies for creating the first gene knockout mouse by genetic engineering and in vitro fertilization, where a selected gene was turned off or inactivated. However, when Dr. Capecchi first proposed this in his NIH grant application, the reviewers apparently turned it down stating “it is impossible”. That speaks volumes on the nature of the task before the young Dr. Capecchi and his determination to knockout a gene. No doubt, genetic engineering has totally changed the way we understand the disease processes and how we treat them. With the advent of CRISPR/Cas9 or gene editing technology, today we are at the verge of entering new horizons of clinical medicine whereby we can treat not only genetic diseases in adults, but also prevent the birth of babies with defective genes due to familial genetic abnormalities. In about a decade or less, genetic engineering becomes part of the Personalized Medicine. All these are possible due to determined scientists, such as Prof. Mario Capecchi, who brought out the best in themselves and gave it to the humanity, despite the harsh conditions they had to face in their early lives. Please watch:

Modeling Neuropsychiatric Disorders in the Mouse | Mario Capecchi | TEDxGeorgeSchool
https://www.youtube.com/watch?v=X_t0_56njGw

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COVID-19 and Diabetes

ADA + META: From the American Diabetes Association

META is a Biomedical Research Discovery Tool that analyzes & connects millions of scientific outputs to give us a comprehensive view of how your field is evolving. Through its customizable feeds, we can easily follow developments, intersections, and emerging trends in science. The following publications using Meta-analysis were indexed by the American Diabetes Association. **Click on the journal names to access the websites of the publications**.

Who is dying from COVID-19 and when? An Analysis of fatalities in Tamil Nadu, India
Asirvathm ES and Lakshmanan J, Clinc Epidemiol Global Health Oct 2020

Type 2 diabetic Asian Indians and COVID-19: Lessons Learnt so Far from the Ongoing Pandemic
Shivane VK and Bandgar TR, J Postgrad Med Oct 2020

Implications of Engaging in Regular Exercise and Reducing Sedentary Behavior During a Global Pandemic: An Immuno-metabolic Perspective in Patients with Obesity and Type 2 Diabetes
Methnani J and Bouhlel E, Preprints.org Oct 2020

Seroprevalence of SARS-CoV-2 IgM and IgG antibodies in an asymptomatic population in Sergipe, Brazil
Pinto Borges et al, Pan American J Public Health, Oct 2020

Vascular Events, Vascular Disease and Vascular Risk Factors-Strongly Intertwined with COVID-19
Scutelnic A and Heldner MR, Curr Treat Options Neurol, Oct 2020

Etiologic Subtypes of Ischemic Stroke in SARS-CoV-2 Patients in a Cohort of New York City Hospitals
Tiwari A and Dmytriw AA, Front Neurol, Oct 2020

Development of a Quantitative Segmentation Model to Assess the Effect of Comorbidity on Patients with COVID-19
Zhang C and Wang J, Eur J Med Res, Oct 2020

Reduced COVID-19 Mortality with Sitagliptin Treatment? Weighing the Dissemination of Potentially Lifesaving Findings Against the Assurance of High Scientific Standards
Nauck MA and Meier JJ, Diabetes Care, Oct 2020

Expression of ACE2, the SARS-CoV-2 Receptor, in Lung Tissue of Patients with Type 2 Diabetes
Wijnant et al, Diabetes Oct 2020

Early Prediction of Level-of-Care Requirements in Patients with COVID-19
Hao et al, eLife, Oct 2020

A Comparative COVID 19 Characterizations and Clinical Course Analysis between ICU and Non ICU Settings
Patel et al, MedRxiv, Oct 2020

A new Imaging Sign in COVID-19 Pneumonia: Vascular Changes and Their Correlation with Clinical Severity of the Disease
Sanli DET and Yildirim D, Diagn Interv Radiol, Oct 2020

The First Case of an HIV Patient Diagnosed with COVID-19 in Korea
Kim et al, J Korean Med Sci, Oct 2020