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May
2020

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

Sushruta Medical News

A Medical Newsletter of the

American Association of Physicians of Indian Origin

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Editorial

As Healthcare Heroes, Are We Falling Short of Our Duty?

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May is Women's Health Month and a time to reflect on healthy choices. With the unforeseen impact of COVID-19 on young and old, a healthy lifestyle is more important than ever. COVID-19 data are still quite sparse. For example, we don't currently have clear gender data. Some data tend to imply more women are impacted; other sources say the infection rate between genders are equal. Early data does seem to indicate that men may have a higher mortality rate.

However, one factor does seem to continue to show in all the early studies: "pre-existing conditions" portend a worse prognosis. That seems obvious and some younger members of the healthcare community may be relieved by that, however it's not quite that simple. As we hear about more and more young people dying, we must begin to wonder. As physicians we're used to thinking of more significant illnesses like COPD, CHF, DM, or Renal Failure as the mortality indicators. We take obesity and hypertension for granted. "Everyone has that." The reality is obesity and/or hypertension is enough. In many cases, that was all COVID-19 needed. Various sites have shown that elevated BMI significantly increased the rate of ventilatory need and mortality.

This should come as a wakeup call to all of us. These are **preventable** diseases. Nearly 50% of adults in America have hypertension and **less than 25%** are adequately controlled *in the United States!* The obesity epidemic is

so problematic that it has birthed entire specialties, e.g. Bariatric Surgery. Over 40% of Americans are obese and the rates continue to rise, despite the increasing popularity of various fad diets. The average American adult consumes 3400 mg sodium (cf. 1500 mg recommended) and 17 tsp of added sugar (cf. 6 tsp/female and 9 tsp/male recommended) daily. For those that are dubious about the impact of sodium on obesity, data shows that less 400mg additional sodium per day increased obesity risk by almost 30%. Fortunately, the converse is also true. I just saw a patient who lost 45 pounds in 6 weeks (intentionally, no malignancy) from simply cutting out added salt in her diet! She's not an exception. We see this often. If you're thinking our Indian diet is better than the average American, think again. The average Indian adult consumes 4400 mg sodium. This is a double whammy for Indian Americans. We eat a lot more processed food than our Indian predecessors/counterparts, but even when we eat at home we are used to unhealthy preparations.

We can't afford to be complacent anymore. Not with our patients and not with ourselves. Our patients and communities look to us to lead, especially regarding health issues. If not us, then who? When we condone unhealthy habits we become part of the problem. Now, when it seems harder than ever, it's *more important* than ever. Opt for fresh immune boosting fruits and vegetables rather than a processed meal. Snack on unsalted nuts instead of chips. Drink water instead of soda. Ask a favorite restaurant to make that takeout meal without salt and hold the cheese. It can be surprising how accommodating they can be. As we know, what we eat is the most critical aspect of our physical health. Exercise is an important aspect of a healthy immune boosting lifestyle, but no amount of exercise can compensate for poor dietary choices. These changes are not only important to stay strong in the fight against COVID, they're critical for what comes next. Heart disease and other complications of hypertension are still the biggest health problems in America and the World. It would be a shame to survive the COVID pandemic only to succumb to that which we have known about and failed to prevent.

We must lead by example, making healthier choices ourselves, but also in reminding our patients that they need to work on those same issues as well. In these stressful times, it's easy to take or give free passes for dietary splurges. Those splurges add up and they have consequences. Eating healthy helps build the foundation for a better immunity. Complementing healthy diet with good exercise and sleep habits is now more crucial than ever. Meditation and Yoga is our cultural inheritance. We have the tools. So let's encourage ourselves and our patients to swap an hour of Netflix for exercise. Think about what healthy substitutes can be incorporated in our diet. When the world seems like a crazy place, it's sometimes hard to be strong and make these choices, but that is why we are Healthcare Heroes. After all, there is no more important time than now.



Scan QR Code for the Website

A One-Stop Website for COVID-19 Information Ravi Kolli, M.D.

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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.



Call to Action

Turning the Clock Back on South Asian Heart Disease Epidemic

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While we are in the grip of the COVID-19, there has been another epidemic of cardiovascular diseases (CVD) taking a toll on us. Everyone knows someone who has had heart attack or worse, died from it, so this is a personal issue for many of us. Yet, we wake up only when it is too late. It is about time we embark on a multi-year global campaign of education and awareness involving physicians, patients and the South Asian community in general. We all know prevention is the best intervention. So, there is urgent need for action and future road map to combat this hidden epidemic amongst South Asians.

South Asians constitute 2% of US or about 25% of the world population but account for 60% of global cardiovascular burden. We are the highest risk prone ethnic group for developing cardio-metabolic disorders. The American Heart Association has finally recognized this fact and issued guidelines in November 2019 urging physicians to consider ethnicity when determining cardiovascular risk as conventional models underestimate our risk. While there is consensus about the higher risk, there is no single "smoking gun". Most experts think South Asian cardio-metabolic epidemic is mainly mediated by visceral obesity-induced insulin resistance but genetic/epigenetics factors and inflammation also play their role.

For starters, coronary atherosclerosis in South Asians strikes a decade earlier and many times sudden death could be the first sign. The nature of this atherosclerosis is also unique in that it is diffuse and progresses rapidly in relatively smaller caliber vessels making them less amenable to percutaneous or surgical interventions resulting in less than optimal outcomes. If we are serious about fighting this epidemic effectively then we all need to detect it before it strikes.

First, we need to raise more awareness and take the message to the grass root levels through community outreach programs. Second, educating our community about early check-up is crucial given our phenotype as we tend to develop cardio-metabolic disease at lower BMI and HbA1c levels. Third, we need to promote the value of early imaging of heart, such as coronary calcium score/CTA as appropriate to detect subclinical atherosclerosis. Fourth, we need a national registry of premature South Asian CVD and put it on our webpage and keep it updated with latest research. Fifth, we should participate in our own ongoing cohort studies like MASALA to build our database whether clinical, biological or genetic to advance science. Sixth, let us train every South Asian household in basic "Hands only CPR" to rescue our loved ones in crucial first few minutes before any help arrives. Finally let us use our clout and join efforts to advocate for funding the research on South Asian CVD at legislative level.

We realize the task is daunting and will need the entire AAPI village including all stakeholders, local and regional chapters as well other like-minded associations. So, let us begin and learn as we go forward. To paraphrase JFK "If not us, who? If not now, when?" Looking forward to working with you all. Please write to Brahmasharma102@gmail.com for any interest or suggestions.



A Piece of My Mind

Dietary Salt and Immune System

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"We are able to uncover complex control circuits that lead from salt intake to immune deficiency"

...with these words, on March 25, 2020 Prof. Christian Kurts from the University of Bonn joined a long list of scientists who have raised the alarm yet again to the dangers of dietary salt. This warning is especially timely in the context of the present pandemic of COVID-19. As we all want to reduce the chances of contacting or dying from COVID-19, one area that deserves more focus is the understanding of the interplay between dietary salt and the immune system.

Presence of comorbidities, especially hypertension, a very important salt linked health problem, has been the hallmark of the mortalities from COVID-19. This also explains why Black Americans, who are among the most salt sensitive groups, have had a disproportionately high mortality from COVID-19.

One of the landmark publications from which we drew the attention in our writing in 2013 "Salt: Friendly Fire Aimed at You" was based on research jointly published from the prestigious universities of Yale, MIT and Harvard. In this publication the interplay between table salt and the immune system was shown to result in incremental production of autoimmune protein in response to salt. Special thymic lymphocytes labeled Th17 cells proliferated and produced more autoimmune proteins in vitro and in experimental animals. Mice genetically engineered to get multiple sclerosis manifested the disease quicker and more aggressively in response to salt. This pathway is likely responsible for the more rigorous autoimmune response to COVID-19 which affects multi-organ systems once infected with Coronavirus. This phenomenon would explain higher mortality from COVID-19 among the hypertensive, especially the salt-sensitive Black Americans.

Writing on the relationships between salt and dementia, we also reported in 2015 the finding of these autoimmune proteins causing neuronal degeneration which is a key feature of Alzheimer's dementia. In a subsequent writing, we reported on a landmark study linking dietary salt to excess production of glucocorticoids. This study published from Vanderbilt University shows the pathway from table salt to metabolic syndrome, including development of type 2 diabetes mellitus.

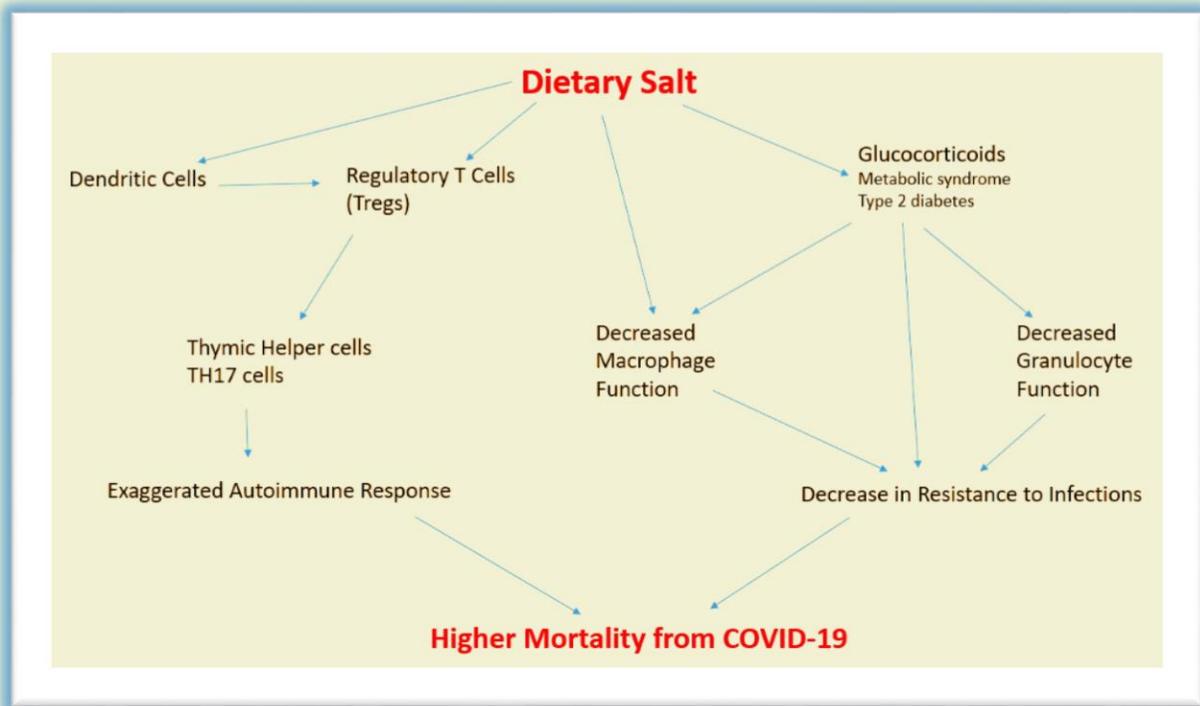
Several published reports also established the relationship of excess production of glucocorticoids in response to dietary salt. The interaction between the immune system and salt is in part mediated via excess glucocorticoids, which are known to decrease the immune response. The current research from University of Bonn and other institutions is summarized in the following scheme.

In addition to the known effect of salt on Th17 cells, dietary salt impacts the immune system in many other pathways. The entire family of white blood cells, the soldiers of defense against external aggression by microorganisms, is impacted by dietary salt. Recently it was shown that the dendritic cells and regulatory cells (Tregs) carry messages to the granulocytes and macrophages. The defense function of both these cells has been demonstrated to be decreased, which means increased vulnerability to infections.

In the currently reported research from University of Bonn, human volunteers and experimental animals demonstrated higher susceptibility to infections following increase in dietary salt. On a high salt diet consisting of merely two hamburgers, the white blood cells in these volunteers demonstrated less antibacterial function. In mice, pyelonephritis by *E. coli* was persistent and aggravated in one experiment. In another experiment, *Listeria* infection was systemically induced and bacterial counts in the liver and spleen were measured to be dramatically higher in mice fed with salt.

In summary, research across the Globe from several prestigious institutions raises concerns regarding the impact of dietary salt on the human immune response causing decrease in resistance to a variety of infections including COVID-19. To further

aggravate the problem, once infected, the exaggerated autoimmune response is also influenced by dietary salt, leading to higher mortality. There is however good news. If we engage in salt reduction in our diet aggressively and sincerely, there is hope for reduction of many salt-related health problems affecting everyone.



Recommended Further Reading:

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Bench-to-Bedside

ACE2: Did we Miss the Boat after SARS-CoV of 2003?

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A devastating earthquake is often preceded by several tremors. So also, experts believe that major pandemics are preceded by less severe in spread, but distinct outbreaks of deadly related infections. No doubt, the current pandemic of SARS-CoV-2 virus outbreak was preceded by SARS-CoV of 2003 and MERS of 2012, which are also fatal respiratory illnesses caused by zoonotic viruses. But, apparently we did not realize that they were the pre-tremors for the current SARS-CoV-2 pandemic that virtually paralyzed the entire world. More than that, the SARS-CoV of 2003 offered clues for a potential remedy to combat the COVID-19. COVID-19 has brought out ACE2 (Angiotensin Converting Enzyme 2) on to the stage. ACE2 is not a textbook name as the ACE of the decades-old classical renin-angiotensin system (RAS). (Donoghue et al, 2000, PMID: 10969042; Huang et al, 2003, PMID: 12606557; Riordan, 2003, PMID: 12914653). Soon after the outbreak of SARS-CoV in 2003, i.e., much before the physiological role of ACE2 was understood, it was found that ACE2 is the functional receptor for the SARS-CoV (Li et al, 2003, PMID: 14647384; Jia et al, 2005, PMID: 16282461). Subsequently it was established that ACE2 is a key modulator of the RAS in health and disease. The main role of ACE2 is degradation of Ang II resulting in the formation of angiotensin 1-7 (Ang 1-7), which opposes the action of Ang II (Tikellis and Thomas, 2012, PMID: 22536270). Thus, by virtue of its opposing action on RAS, ACE2 has a beneficial role in many diseases, such as hypertension, diabetes, and cardiovascular diseases where its expression is decreased (Jiang et al, 2014, PMID: 24776703). The attractive idea of enhancing the expression of ACE2 to treat the above diseases of modern lifestyle has blinded our vision to the potential uses of blocking the ACE2 to overcome pandemics like the COVID-19. The milder tremor of SARS-CoV also did not draw our serious attention. But, in the hindsight, had we taken that tremor seriously, today we could have a remedy for COVID-19 by effectively blocking the ACE2, the receptor for SARS-CoV-2. One could argue that approach may be harmful in patients with hypertension, who are on ACE inhibitors or ARBs (angiotensin receptor blockers). But, the position statements issued by the American Heart Association, American College of Cardiology, Heart Failure Society of America, American Society of Nephrology, as well as the Council on Hypertension of the European Society of Cardiology are very clear that the use of ACE inhibitors or ARBs in hypertensive COVID-19 patients should not be discontinued. A comprehensive literature survey of human and animal studies published recently also did not find any evidence of ACE inhibitors or ARBs having an effect on ACE2 protein expression (Sriram and Insel, 2020, PMID: 32320478). Hence, it should not be a problem to treat COVID-19 patients with potential ACE2 blockers (such as monoclonal antibodies directed to extracellular domain), as such therapy is limited to the duration of COVID-19 treatment. Hopefully, the scientific community will pay more attention to ACE2 now.

Call for Contributors

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- **Pioneers in Medicine and Healthcare** (300 words)

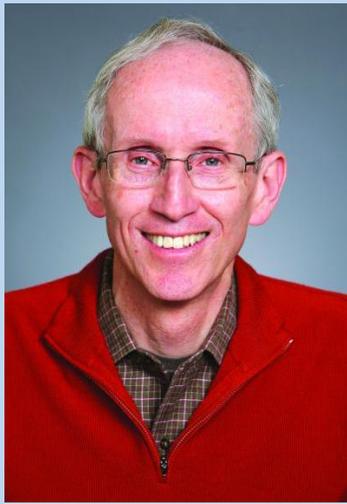


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ASN Kidney News

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Passed away on April 24, 2020 due to complications of COVID-19.

COVID-19 Cytokine Storm: The Interplay between Inflammation and Coagulation

Ricardo J. Jose and Ari Manuel *The Lancet Respiratory Medicine* April 27, 2020

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30216-2/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30216-2/fulltext)

Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized with Severe Acute Respirator Syndrome Coronavirus 2 (SARS-CoV-2) Infection. A Randomized Clinical Trial

Mayla Gabriela Silva Borba et al, *JAMA Network Open* April 24, 2020

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765499>

Risks of ACE Inhibitor and ARB Usage in COVID-19: Evaluating the Evidence

Krishna Sriram and Paul A. Insel *Clinic Pharmacol Ther* April 22, 2020

<https://ascpt.onlinelibrary.wiley.com/doi/abs/10.1002/cpt.1863>

The COVID-19: Role of Ambulatory Surgery Facilities in this Global Pandemic

Niraja Rajan and Girish P. Joshi *Anesth Anal* April 1, 2020

<https://pubmed.ncbi.nlm.nih.gov/32243288/>

Why is COVID-19 so Mild in Children?

Petter Brodin (Editorial) *Acta Pædiarica* March 25, 2020

<https://onlinelibrary.wiley.com/doi/full/10.1111/apa.15271>

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