Matters of the Heart

A publication by Academy of Cardiovascular Sciences
(International Academy of Cardiovascular Sciences – India Section)

Volume 2; No.2 **July 2018**

There is an urgency to extend initiatives for cardiovascular health protection, such as increasing awareness for improved life style, nutritious and healthy food, and promote health wellness programmes to combat heart diseases. *Matters of the Heart* is designed to provide public health education in these areas.

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GUT-HEART AXIS

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"All diseases begin in the gut."
Hippocrates (460 – 370 BC.)

If you give the same diet to two different persons, one person sometimes acquires more weight than the other one. Do you have any idea why this happens?

Researchers have come out with certain clues to this. The answer may be gut microbiota or the gut bacteria. Those people having higher Firmicutes population in their gut gain more weight with the same diet than those people with the abundance of Bacteroides species. Such "obese microbiome" has an increased capacity to harvest energy from the diet. So in short whether you will

become obese or not will depend upon the relative abundance of the two dominant bacterial divisions, the Bacteroidetes and the Firmicutes.

Interestingly, to support this hypothesis it is also found that the Obese "trait" is transmissible: colonization of germ-free mice with an 'obese microbiota' results in a significantly greater increase in total body fat than colonization with a 'lean microbiota', with the same diet.

In the last few years research has brought out the relation between the gut microbiota and several diseases including heart disease, hypertension, diabetes and obesity. We will discuss in here briefly how gut bacteria predisposes us to heart diseases.

What is human gut microbiome?

A healthy adult harbors ~100 trillion bacteria in gut alone. This is 10 times the number of cells in the human body. While humans possess 23,000 genes, the gut microbiome has 150 times more. It is found that 1000 –1500 bacterial species colonize the human gut. It is reasonable to view microbiome as an "organ" which weighs about 1 kg – 2 kg although it is without a distinct structure. The microbiome is constantly making compounds, some of which gets absorbed and are biologically active. So it can be considered as an endocrine organ, producing biologically active entities that diffuses in the bloodstream and act at distant sites.

The gut microbiome is acquired from the environment; it is not genetically acquired. The gut is sterile in the womb. The fetus acquires different microbia during caesarean section and during vaginal delivery. Then the fetus starts acquiring different types of microbiome which depends on the diet and the exposed environment.

Human gut microbiome is dominated by 4 large groups of bacteria or phyla: Bacteroidetes, Firmicutes, Actinobacteria and Proteobacteria.

What decides the pattern of your gut microbiome?

The specific patterns of gut microbia are called 'enterotypes'. The unwelcome change in the gut microbiome is called 'dysbiosis'. One of the most important factor which results in the gut microbial pattern is your long-term diet. For example diets high in animal protein and fat -high levels of Bacteroides and low levels of Prevotella. On the contrary, diets high in carbohydrates but low in animal protein and fat will have low levels of Bacteroides and high levels of Prevotella.

Another example of the diet – gut microbial interaction is that Japanese harbor organisms that produce enzyme that aids in seaweed digestion.

How does gut microbiota benefit the host?

The gut microbiome has many functions. One of the functions is a protective function - it is by pathogen displacement,

nutrient and receptor competition and production of antimicrobial factors. It secretes some of the vitamins. One of the most important functions of gut microbiome is metabolic as it aids in digestion of food components. For example, gut bacteria is involved in the break down of sugars – glycans by glycoside hydrolase (glycans or complex sugars cannot be cleaved by any human enzymes).

How do we study the gut microbiome?

It is not easy to study gut microbiome as there are millions of bacteria and thousands of species; also there are fungi and viruses which can pose difficulties. The traditional method is culture – but it is tedious and time consuming. Bacterial genomic sequencing is the next method. 16S analysis and metagenomic sequencing are the methods which is gaining popularity.

Association of gut microbia and heart diseases

There are many recent studies which reveal association of gut microbia with heart disease, especially heart failure. In a study comparing patients who had heart attacks and those who did not have, it was found that in patients who had heart attacks, the proportion of phylum Bacteroidetes was lower and Firmicutes was higher. Also high blood pressure, obesity and diabetes mellitus are found to have associations with specific gut microbial patterns and researchers have

found certain links in the pathogenesis of these diseases with bacterial interactions.

The gut microbia produce many substances which enter the blood stream and can get involved in several pathobiological processes. One of the molecules identified is TMAO or (trimethylamine oxide). The precursor of TMAO is L-Carnitine or Choline which is present in food substances like red meat. If you have high intake of red meat, TMAO production is increased and this is implicated in the pathogenesis of heart diseases.

Gut microbia is also implicated in the pathogenesis of heart failure. In heart failure, there is reduction in pumping of the heart and thus reduction in intestinal blood flow and low oxygen delivery. This predispose to the growth of pathogenic types of anaerobic bacteria (which does not require oxygen for their growth) in the intestine. These bacteria produce several harmful substances including TMAO and endotoxin (lipopolysaccharides- LPS) which predisposes or leads to worsening of heart failure. These discoveries have lead to the concept of "Heart-Gut axis" or "Heart – gut hypothesis" of heart failure.

Can we manipulate the gut microbiome and treat diseases?

Yes; there are some studies in this aspect which gives us some hope. Manipulations can be done in many ways. We can alter

the diet and change the type of microbia. We can target the chemicals produced by the gut microbia or we can directly alter the microbial flora by giving probiotics.

If we reduce red meat in the diet, we reduce intake of choline and lecithin and thereby reduce TMAO with all positive effects in heart disease. For example, changing to a Mediterranean diet has been shown to reduce markers of heart failure. Another method is to give non-absorbable antibiotics to kill specific microbiota and thus alter the microbial pattern.

Use of probiotics is another method of changing the gut microbial pattern. Probiotics are live beneficial bacteria (Bifido bacteria, Lacto bacilli, Streptococci and non-pathogenic strains of E. coli) that can be ingested to create an appropriate intestinal microbial balance. There are studies using *Saccharomyces boulardii* in patients with heart failure which revealed benefits.

The last and a very interesting method which is gaining popularity in many gastrointestinal diseases is fecal transplantation. Fecal transplantation from lean volunteers was found to benefit by weight reduction and also reduction in risk factor levels of heart failure.

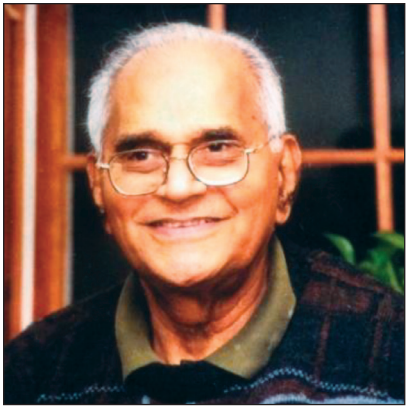
Future

Millions of years of co–evolution have created diverse ecosystems of gut microbiota which contribute to the maintenance of human metabolic homeostasis. We are slowly

discovering the various ways how these co-habitants work in health and disease. So we are not alone – we are with our gut microbia who control our systems remotely. Understanding and probably manipulating them may hold the future for health and disease.

Epilogue: A popular saying is "The way to a man's heart is through his stomach." We may add: "Presumably, the results also apply to women!"

MY EXPERIENCE OF A HEART DISEASE



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I am 70years old. It is 1995 and I am visiting my children in Boston. One day in June, I feel a sort of dull pain in my chest. I did not think much of it but casually mentioned it next morning to my daughter. She took me the same day to the private Community hospital where she worked. I have a stress test but am unable to complete it since my heart rate went up very high. I repeat the stress test the next day with the same results. The cardiologist changes my medicine from Atenolol to Nadolol.

A few days later I feel a tingle in my left ring and middle fingers and later over my left shoulder. My kids gather together. An unspoken thought looms in everyone's mind.

I have no medical insurance. My son had just started his fellowship in Boston University Hospital. He spoke to Dr Gary Balady, a cardiologist and Head of the Department of Medicine. He gives him my history and adds “My Dad does not have medical insurance”.

“That’s OK”, Dr. Balady tells him. “I am on call for the Emergency room today. Just ask him to come to the ER.” Dr. Balady added.

I go to the ER where they do some preliminary testing and I am admitted to the hospital. The next day, I undergo cardiac catheterization under the supervision of Dr Balady. “He has a 70 % block in his left main”, he tells my children. I did not know then that the left main was the worst place to have a block. Left main meant the left main branch of the coronary artery which supply blood to the heart. A Cardiothoracic surgeon comes to see me and they schedule me for bypass surgery.

All aspects of the procedure including the possible complications are explained to me and I sign a consent. A priest visits me in my room and offers to pray for me. I politely decline his offer and tell him that my wife has already done that. I have my surgery the next day. I leave my room in the ward at 12:00 noon and I am admitted after surgery to the cardio thoracic ICU at 7:00 PM. Dr Lazar, the surgeon, visits me that evening and tells me that everything went fine. Three bypasses were done using a vein in my leg and an artery in my chest wall.

The day after surgery I walk a short distance. I have no appetite. I have no interest in listening to music or watching television. I am discharged after I attend a class on "What to do at home after discharge".

I bid farewell to my roommate Mr. Harrison, a World War 2 veteran. He promises to send me a copy of the leaflet that the US troops dropped over Japan before bombing Hiroshima and Nagasaki. He keeps his word and I still have that pamphlet as a precious possession. My appetite returns and I take regular walks inside the house.

On the 6th day after my surgery I have a follow up appointment with Dr.Balady who assures me that everything is fine. He tells me that the exercises I have to do in the cardiac rehabilitation center are as important as the surgery itself. I take the subway to Boston three times a week. I exercise on the treadmill and various other equipments. A technician supervises me while I exercise on the treadmill, gradually increasing the intensity of the exercises. This goes on for about three months. Dr Balady drops in from time to time to check on my progress.

Finally, when my rehab is over, he tells me that I have the heart of a 30 years old youngster!

I hold his hands and thank him. Tears blur my vision and I am unable to express my gratitude. "Call me if you have any problems and visit me whenever you feel it is necessary", Dr Balady says.

I am told that the American medical system has many flaws. However, no patient is turned away from the Emergency Room regardless of their ability to pays or their legal status in the country.

Thanks to Dr.Balady and Dr. Lazar, twenty three years later at 93 years of age, I am physically active and spend an hour or two every day doing yard work.

CONQUERING AFIB: MY ORDEAL WITH ATRIAL FIBRILLATION

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To me, heart is the most important organ in the body. This assumption is not based on any scientific or statistical facts but rather based on my biased experience of how I went through an annoying heart condition called Atrial Fibrillation (AFib or AF).

AFib is a condition where you experience quivering or irregular heartbeat (arrhythmia) that can eventually lead to blood clots, stroke, heart failure and other heart-related complications. Normally, our heart contracts and relaxes to a regular beat and at a fixed rate. In AFib, the upper chambers of the heart (the atria) beat irregularly instead of beating effectively

to move blood into the ventricles. There are two aspects to AFib: one, the rate (heart beat exceeds more than normal), second, the rhythm, the regular rhythmic beating (lub-dub, lub-dub) is disturbed and becomes chaotic. However, it should not be confused with palpitation, which most individuals with a normal functioning heart face without any discernible risk or abnormalities.

In a normal heart, the stimulus for every signal of heart beat initiates from a place called the sinoatrial/sinus node. However, in AFib, the signals are generated not only from the sinus node but also from other parts of atria (the upper chambers of the heart). A web search will tell you that the symptoms of AFib are rapid and irregular heartbeat, fluttering in the chest, dizziness, general fatigue, shortness of breath and anxiety, fatigue when exercising, chest pain, sweating, or pressure in the heart. The good news is that AFib is not a killer. However, if left untreated, it increases your risk for stroke/heart attack or heart failure. Let me share with you my experiences how I dealt with AFib.

My encounter with AFib dates to over a decade ago while I was pursuing my doctoral degree in India. I experienced few episodes of AFib that generally lasted few hours and resolved on its own. I felt some discomfort but was not enough to affect my daily activities. Moreover, when I later went to the physician my ECG was found to be normal as it was recorded after the episode had happened, and therefore the condition

remained undiagnosed. Recounting the psychological and emotional stress that I went through after the diagnosis at a later point, I consider myself fortunate not to have been diagnosed when it first happened, as it would have affected my studies. It was five or six years after of my first AFib episode that my condition was diagnosed during my post-doctoral training in the United States. I think I was lucky to have obtained the best heart care possible for the condition.

I remember it was a day after the Halloween (a traditionally Christian festival celebrated in the US and Europe, that marks the end of harvest season and beginning of winter; now mostly celebrated as a day of costumes, parties, jack-o-lantern, and sweet treats for kids and adults) in October that I had a severe episode of Afib that lasted through the night. Unable to sleep, I went to the emergency room accompanied by a friend. The nurses checked my ECG and immediately moved me into a monitoring room. Soon after that, one of the doctors explained to me about what my condition was. It was the first time that I heard the term AFib; afterwards it became most common in my vocabulary. I was given medications, mostly beta-blockers (or beta-adrenergic blocking agents that block the effect of hormone epinephrine that induces your hear beat, as a result your heart beats more slowly and with less force reducing blood pressure) and calcium channel blocker (or calcium antagonists prevents calcium from entering cells of the heart and blood vessel walls, resulting in lower blood pressure, also relaxing blood vessels by affecting the

muscle cells in the arterial walls) for heart rate and rhythm control, and monitored for next hour or so. Afterwards, the doctor recommended immediate “cardioversion” to restore the regular rhythm. In simple language, cardioversion is a procedure in which electrical shock waves are given to the heart stopping the irregular beats momentarily to restart it again with new and regular beats, something akin to what most people of are familiar to from TV shows and movies, the physician takes two electrode plates and zaps your heart with the intent to restore heartbeat. This procedure is carried out after you are anesthetized. Following cardioversion, I was put under rate and rhythm maintaining medications along with blood thinner to reduce risk of blood clot and stroke associated with AFib. I was then discharged in the morning with referral to a cardiologist and a whole set of materials for understanding AFib.

On a funny side, I also learnt a new term called “Holiday heart”. Apparently, alcohol induces AFib and during holidays like Halloween people tend to have arrhythmias due to binge drinking. Doctors in the emergency suggested that mine could be a holiday heart. Next day, I went to the cardiologist and whole week I was busy with various testsranging from stress echocardiography to MRI. Finally, after a battery of tests my cardiologist was unable to find any problems in my heart. Such condition in medical terminology is called “lone AFib” that occurs without any heart abnormalities. Surprisingly, it is quite rare at my age although quite common with older

members of the population. I was asked to continue with the medication for maintaining heart rate and rhythm along with the blood thinner. Blood tests and regular checkups continued for the next three to four weeks to measure the level of medication in the blood and to standardize doses to maintain normal heart rhythm. Besides, I was also fitted with a "Holter monitor" at home for a couple of days, where I had to wear a small ECG monitor continuously on my chest. Then, I was given another monitor to score occurrence of small episodes that might have escaped surveillance. It was a long month of incessant testing and monitoring.

By then, I had read almost everything about AFib and was equipped with a vast amount of knowledge on the subject. The overall idea of the treatment was to keep my heart rhythm and rate under control with medication and keep risk for blood clot at the minimum with blood thinners. Unfortunately, this strategy did not last long and I had three to four emergency visits in two years and had to be electrically cardioverted three times. Finally, my cardiologist suggested a treatment; a surgical procedure called "Catheter Ablation" and referred me to a cardiac surgeon. Catheter ablation is keyhole surgical procedure where electrodes (catheters) are inserted into the heart and errant regions in the heart other than sinus node from where abnormal stimuli are originated are killed off. This involves inducing AFib with certain drug to observe cells with abnormal source of conduction and ablating them with high-energy radiofrequency from the electrode. I was bit nervous in

the beginning but felt positive after reading a lot about it and hearing from the surgeon himself. My new cardiac surgeon was quite reassuring and very helpful. He explained to me the intricate details about the procedure, risk factors and success rates and so on to make me more comfortable about it.

My surgery was scheduled three weeks after my visit to the surgeon's office. This was my first experience of any kind of surgery and it involved a team of specialist that include anesthesiologist, cardiac surgeon, physician for pre- and post-operative care, pharmacist, and a group of helpful nurses and support staff, all of whom were introduced to me before the surgery. I was given anesthesia around 9 AM after which I had no recollection of what happened. I woke up in the recovery room retching (apparently side effect of anesthesia) at around 1 PM with a group of nurses around me. It was quite painful as it put pressure on my fresh surgical wounds. I was then shifted to critical care unit for the rest of the night with continuous monitoring of my heart with periodic visits of nurses and doctors. I highly appreciate and will always remember the professionalism of nurses and how they took care of me. Moreover, I am forever thankful for the excellent care provided to me by the University of Wisconsin (UW)-hospital and staff. Later in the night my surgeon visited me and explained to me what he did in my heart. He had ablated more than 120 spots in the atria and marked a circle around pulmonary artery to prevent future recurrence. Recurrence after such surgery is the biggest challenge in AFib treatment

and it is not uncommon as well. Fortunately, eight years on and so far, my AFib has not recurred. My hope and prayer is that my AFib has been conquered.

Lastly, I would like to point out a few issues that are associated with AFib. This can be divided into three parts: its symptoms, side effects of medication, and psychological and emotional stress. When I was going through AFib episodes, I generally felt a sense of uneasiness in the heart in addition to light headedness quite regularly and sometimes as if fainting was imminent. Difficulty in breathing, chest pain and discomfort were other annoying symptoms. Besides, I become restless and anxious and may be a small part of this anxiety remains with me even to this day. The most damaging of all however was the psychological stress associated with it. I had two anxiety attacks that needed emergency visits but these were not actually AFib. I felt that counseling or making patients understand about the condition to reduce the anxiety should be a key component of treatments for AFib or related conditions. Another aspect of this treatment is the side effects of the medications. A pounding heart, extreme night sweats, palpitation, anxiety, insomnia and frequent waking from sleep, neuropathy are some of the symptoms I had as a consequence of rhythm control medications. My cardiologist had to prescribe me other drugs due to multitude of side effects I suffered from. The second drug worked fine with me but was detrimental for the liver. Therefore, doctors had to monitor my liver function for at least three months to make

sure that the dosage I was taking was not affecting my liver. The heart rate controlling drugs were milder and they were also medications commonly used to control blood pressure. Also, included to the regimen was a blood thinner. Although, it reduces the risk of stroke or heart attack by reducing blood clots, I had to be careful as cuts or wound or even simple bleeding from the gums due to dental problems may lead to excessive bleeding.

With advancement in medical science several improved medications and modified drugs from the pre-existing ones have come in the market, in addition to improved surgical methods. I believe the methods for treatment of AFib will continue to evolve. With the current scientific research in the field, I look forward to future development of a potential molecular intervention based on RNA/protein therapeutics or stem cell based regenerative therapeutics for Afib or similar arrhythmias. Lastly but not the least, I know from firsthand experience that it is hard to keep calm when you have such a heart condition but at least we have to try to stay composed reminding ourselves that “AFib is not a killer”.

Shhhh! No loud noise please!

Surya Ramachandran

If you always thought that bad cholesterol, lack of exercise and unhealthy food habits are the only reasons for heart disease, you are wrong. Loud noises too are bad for the heart!

We worry about air pollution and smog in metropolitan cities, but are we concerned about the high decibel sounds the yanking horns produce? We have always linked noise to hearing problems. According to a new study by the National Institute for Occupational Safety and Health (NIOSH), millions of people are exposed to excessive noise in the workplace which not only affects their hearing but also their blood pressure and cholesterol levels in blood.

Several manifestations of cardiovascular disease, including hypertension (chronically elevated blood pressure),

arteriosclerosis (abnormal thickening or hardening of the arterial walls), and ischemic or coronary heart disease (CHD) have been linked to exposure to loud noise.

In this new study, researchers analyzed data which was sourced from the publicly available 2014 National Health Interview Survey conducted by the National Centre for Health Statistics (NCHS) in non-institutionalized US civilian populations to monitor the health of the nation. The survey was aimed to understand how many among the people exposed to excessive noise in the workplace, have hearing-related conditions and how many people have a heart condition.

The outcomes of interest in this study were hearing difficulty, hypertension, elevated cholesterol, and CHD or stroke. Hearing difficulty was assessed based on the question "Is your hearing excellent, good, a little troubled hearing, moderate trouble, a lot of trouble, or are you deaf? [without the use of hearing aids or other assistive devices]" Answers of "a little troubled hearing," "moderate trouble," and "a lot of trouble" were grouped together as "Yes" (has difficulty) and answers of "excellent" or "good hearing" were grouped together as "No" (does not have difficulty). Those who reported excellent hearing in one ear and deafness in the other were excluded from the analysis as this kind of hearing impairment is unlikely to be caused by occupational exposures. Those who reported being deaf in both ears were also excluded as this is unlikely to have been caused predominately by occupational noise, and because bilateral deafness would prevent the worker

from having any potential cardiovascular effects from noise. Workers who reported having any level of hearing difficulty were asked about the main cause. Workers who reported that their hearing difficulty was either present at birth due to the mother having an infectious disease or a genetic defect or present after birth due to an infectious disease or from a brain tumor, were excluded from the analysis as these causes are definitive and verifiable. The reference industry assigned for the industry analyses of hearing difficulty was Finance and Insurance, as it had the lowest prevalence of noise exposure.

Of the 22,906 current workers, 49% were male; 62% were white. The industries with the highest prevalence of self-reported occupational noise exposure were Mining (61%), Construction (51%), Manufacturing (47%), Utilities (43%), and Transportation and Warehousing (40%). Workers in Mining, Utilities, and Manufacturing had significantly higher risks of hearing difficulty than workers in Finance and Insurance, with 150%, 90%, and 72% higher risks, respectively. Healthcare and Social Assistance workers had a significantly higher risk of hypertension. Public Administration workers had a significantly higher risk of elevated cholesterol. Workers in Arts, Entertainment, and Recreation industry had a significantly higher risk for CHD or stroke. The highest prevalence of noise in an occupation was Production (55 %), Construction and Extraction (54 %) industries and those associated with Installation, Maintenance, and Repair (54 %).

The study reports that 25% of the people had been exposed to excessive noise levels in the workplace during their work. Fourteen percent of current workers were exposed to excessive noise at work during the past 12 months. Twelve percent of the workers had reported hearing–related problems while 24% had hypertension. Twenty eight percent of the workers had high blood levels of cholesterol. Among those who had hearing-related issues, 58% had acquired these problems during the time when they were working in conditions of dangerous levels of noise at their workplace. Many individuals who reported high blood pressure or hypertension also reported noise exposure. Fourteen out of 24% of the workers with hypertension, and 9 out of 28% of those with high cholesterol, had developed these conditions in noisy workplaces. The study showed that a significant percentage of the workers had hearing-related issues. They also had hypertension and high blood cholesterol which can all be attributed to exposure to excessive noise levels at work.

The pathway from noise exposure to diseases of cardiovascular has been suggested to be through both autonomic nervous system and endocrine system via a stress response that elevates many of the key biological risk factors for cardiovascular disease such as blood pressure and blood lipids (*ie*, cholesterol). Loud noises induce stress responses and activate the sympathetic "fight or flight" nervous system response. This causes a spike in stress hormones, which can eventually lead to vascular damage. Noise also seems to be a

driving factor in oxidative stress and metabolic abnormalities, which could contribute to other chronic diseases such as diabetes. For people who already have risk factors for cardiovascular disease, living in a noisy environment could accelerate issues like atherosclerosis.

It is a fact that no one can develop tolerance to noise. In fact, an individual's cardiovascular system seems to become more sensitive to noise and more easily damaged over time. Chronic exposure to anything over 60 decibels (the level of a typical conversation in an office) has the potential to do harm to the cardiovascular system. A telephone ring produces about 80 decibels, a jack hammer about 100db, and an airplane on takeoff produces about 120db.

The association among occupational noise exposure, hypertension, elevated cholesterol, CHD or stroke is alarming. But the good news is that, reducing noise exposure may also reduce the risk for developing these conditions. Hence shut the noise down in your work place!

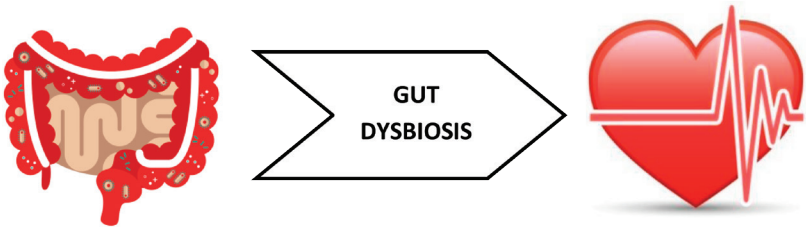
References

Münzel T, Schmidt F, Steven S, Herzog J, A Daiber, Sørensen M. Environmental noise and the cardiovascular system. *Journal of the American College of Cardiology* 2018; 71: 688-97.

Kerns E, Masterson EA, Themann CL, Calvert GM. Cardiovascular conditions, hearing difficulty, and occupational noise exposure within US industries and occupations. *American Journal of Internal Medicine* 2018 https://doi.org/10.1002/ajim.22833

GUT MICROBES AND HEART DISEASES

Madhu Khullar and Satish K Raut



We have known for decades that there is a strong link between the foods we eat and our risk of developing heart diseases. Still we do not know why certain foods reduce the risk of heart disease and others do not. Recent studies suggest that there may be a link among our diet, bacteria present in our gut (gut microbiota) and heart diseases.

The human body is inhabited by a large number of bacteria, viruses, and unicellular organisms. The human gut harbours nearly 100 trillion microbial cells, which live in harmony with their hosts. Gut bacteria have been shown to help us digest our food, strengthen our immune system against various infections and help us fight many diseases including cancer and heart diseases. An imbalance between good and harmful gut microbes, called dysbiosis, can result in a diseased condition. For example, changes in prevalence of different types of gut bacteria have been found to be linked with diseases such as

cancer, obesity, asthma, type 2 diabetes, arthritis and heart disease.

Recent research suggests that when certain bacteria are present in excess numbers, they produce harmful compounds which can cause 'clogging of the arteries' result in heart disease. For example, a comparison of bacteria present in stool samples from patients with heart disease and healthy subjects showed that stool samples from patients had increased number of bacteria such as Enterobacteriaceae and Streptococcus spp which cause inflammation and a fewer number of bacteria (fermentative) which help in reducing inflammation. It has been suggested that some of the harmful bacteria produce metabolites which promote hardening of arteries. The reasons for and mechanisms, which increase these bacteria are not well understood. A change in blood supply to intestinal wall due to a variety of reasons such as infection or injury can cause a leaky gut. This 'leaky gut' allows translocation of endotoxins, microbial components, and microbial metabolites produced by gram positive bacteria to systemic circulation. This process can further activate cytokines and generate systemic inflammation and contribute to progression of heart failure.

It has been observed that gut bacteria may interact with certain foods, producing metabolites that have harmful effects on the heart. For example, some bacteria such as Acinetobacter may convert foods rich in lecithin, phosphatidylcholine, and

L-carnitine into harmful compounds such as trimethylamine N-oxide (TMAO). TMAO alters cholesterol metabolism in various organs such as intestines, liver, and in arterial wall. In presence of TMAO, there is increased deposition of cholesterol in the cells of the arterial wall. TMAO has been found to cause hardening of arteries by increasing deposition of cholesterol in the arterial wall. High TMAO levels, therefore, increase risk of heart disease. High concentration of L-carnitine is found in red meat, some of the energy drinks, and some dietary supplements; whereas lecithin is found in soy and eggs in processed foods. It is also sold as a dietary supplement. Consumption of such foods can increase the risk for heart diseases. Increased TMAO levels also can increase the risk for kidney diseases and heart failure.

The type of food that we eat also influences the type of bacteria in the gut. For example, the guts of people eating diet rich in meat have more of bacteria which make TMAO in comparison to those who have a vegetarian diet, suggesting that vegetarian diet is better for heart health.

Can changing gut bacteria composition prevent heart disease?

Lower consumption of foods such as red meat, egg yolks and high-fat dairy products may be beneficial to the heart as this can result in a gut bacterial population which reduces TMAO generation. Further, consumption of foods such as olive oil and grape seed oil which contain a natural substance

DMB (3,3-dimethyl-1-butanol) reduces TMAO levels and is considered to decrease atherosclerosis (fat deposition in arterial wall). Search is also on for drugs which can inhibit TMAO production by bacteria and thus decrease risk for heart disease. Prebiotics and probiotics are also being suggested as a therapy to reduce atherosclerosis. For example, consumption of non-fat foods fermented with Lactobacilli may be effectively used for prevention of heart disease. Probiotic bacteria reduce blood cholesterol by increasing metabolism and excretion of cholesterol, thereby inhibiting intestinal cholesterol absorption and reducing blood levels of bad cholesterol.

Although scientific evidence linking heart health to gut bacteria is yet scanty, available preclinical and clinical evidences support the theory that gut microbes and their metabolites have the potential to be novel therapeutic and preventive targets for heart diseases.

References:

Wilson Tang W.H., Kitai T, Hazen S L. Gut microbiota in cardiovascular health and disease. *Circulation Research* 2017; 7:120.

Wang Z, Roberts AB, Buffa JA, *et al.* Non-lethal inhibition of gut microbial trimethylamine production for the treatment of atherosclerosis. *Cell* 2015; 163:1585- 1595.

Sobol C V. How microbiome impact on the cardiovascular system. *Journal of Clinical Trials in Cardiology* 2014; 1:1-4.

Gina Kolata. Eggs, too, may provoke bacteria to raise heart risk. The New York Times. Retrieved April 25, 2013.

Hazen Stanley. New Research On Red Meat And Heart Disease. The Diane Rehm Show (Transcript). WAMU 88.5 American University Radio. Retrieved 10 April 2013.

Mitsuoka T. Intestinal flora and human health. *Asia Pacific J Clin Nutr* 1996; 5: 2-9.

O'Mahony, S M, Clarke G, Borre Y E, Dinan T G and Cryan J F. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behav Brain Res* 2015; 277: 32–48.

Durgan, D J, Ganesh B P, Cope JL, *et al.* Role of the gut microbiome in obstructive sleep apnea-induced hypertension. *Hypertension* 2016; 67: 469–474.

Yang T, Santisteban, M M, Rodriguez V, *et al.* Gut dysbiosis is linked to hypertension. *Hypertension* 2015; 65: 1331–1340.

SORE THROAT: 'STREP' TO AN INFECTED HEART

Nimmy Francis

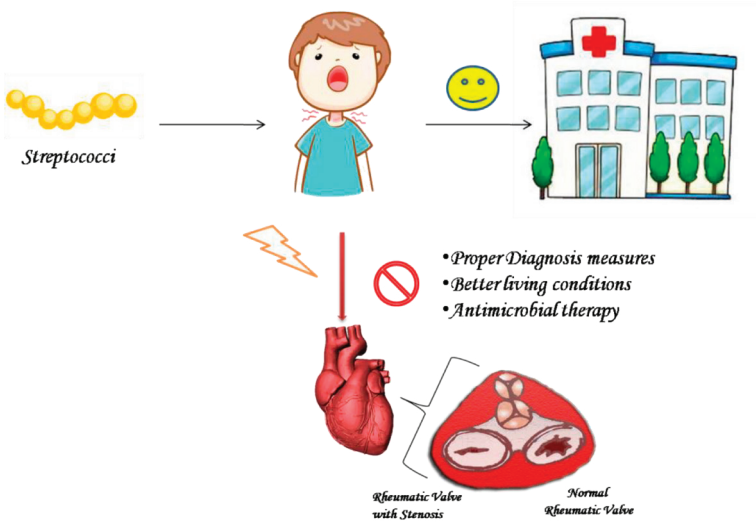
Deep in the chest cavity, cuddled up occasionally within protective tissue, your heart usually stays sterile. But bacteria and viruses in the blood can occasionally invade deeper causing infections and inflammation. At times, the infection and resulting inflammation caused by these microorganisms are troublesome.

Sore Throat to Rheumatoid Heart Disease

With frequent rainy seasons and quick shift in tropical climates, we are well aware of itching and painful sore throats. Though sore throats can be general, throat pain associated with Group A Streptococcus (GAS) infection contributes to 30% of the sore throat causes. Streptococcal infections of throat (strep throat) are common in children aged 5 to 15 years than in youth and adults. Strep throats are mild in symptoms and much preventable with current antimicrobial therapies. Still, increased self-medication and antibiotic therapy can be more worrisome as this leads to the emergence of antibiotic resistant pathogens with higher survival chance within the host.

We generally neglect such throat pains, by self-medications with analgesics and antibiotics to alleviate pain and get temporary comfort. Do we have to worry about such

occasional irritations in the throat? Answer is yes! A little negligence in throat pain can cost as much as your heart. Every infection finds its way to systemic organs through blood. The scenario is not much different here. Streptococci, Streptococcus pyogenes find its way from throat through lymph to reach skin, joints, heart and brain can result in severe fever, joint pains and chorea (jerky involuntary movements). Acute rheumatic fever (ARF) marks an autoimmune response to repeated infections of Group A Streptococcus. It typically occurs two to three weeks after a throat infection. Antibodies produced against bacterial carbohydrates recognize other host carbohydrates and causes molecular mimicry between streptococcal surface M protein and several heart proteins (cardiac myosin, tropomyosin, keratin, laminin, and vimentin). One such interaction between VCAMI, the valvular



endothelial surface protein triggers cell mediated immunity and triggers infiltration of immune response cells leading to tissue damage and lesion formation in heart valves. Valve damage and remodelling includes valvular thickening, valve immobility and closure of valves at later stages, leading to valvular closure (stenosis) and/ or leak (regurgitation). Such long-term damages to cardiac valves from a single severe episode or from multiple recurrent episodes of the illness, is known as Rheumatic Heart Disease (RHD).

Worldwide, approximately 500,000 new cases of acute rheumatic fever occur every year with at least 15 million people bearing rheumatic heart disease. Research interest in ARF and RHD has declined as improved housing conditions and better environment have brought great reduction in the incidence of ARF and RHD in most western and developed countries. However, developing countries such as India require more research focus in this regard as situation is alarming here. We are threatened with a prevalence rate of 2.2 or RHD cases per1000 person. In 2013, India reported >8000,000 cases of RHD whereas in the US it was only <5,000 cases. Hence this disease is still the commonest preventable cardiac disease in children and young adults with public health significance. In India, incidence of GAS sore throat is more common among 5-15 years age group. A recent survey across various tertiary care hospitals reported 5%–26% of all cardiac admissions were of RHD patients. In Orissa number and proportion of RF/RHD did not decline significantly over

a 20-year period. Epidemiological surveys on RF/RHD have been conducted in selected population groups in India. It was found that the prevalence of RHD increased to 2.2 per 1000 in an average and females were more prone RHD as compared to males. ICMR Jai Vigyan Mission report identified that all the RHD children were not enrolled in the hospital-based registries indicating considerable under-reporting in RF/RHD registries. In India GAS prevalence ranged from 0.1% (Jammu) to 11.3% (Vellore) in sore throat cases and 0.5% (Chandigarh) to 12.5% (Vellore) among those who did not have sore throat (carriage). GAS prevalence in impetigo cases (studied only at Chandigarh and Vellore) was 2.7% in Chandigarh and 27.3% in Vellore. The genetically close relatives of GAS, i.e., Group C Streptococcus (GCS) and Group G Streptococcus (GGS) were also found to be common in throat swabs particularly in Vellore and Mumbai centers. The bottom line is that the burden of RF/RHD continues to be high in India, hence, RHD should be detected early and secondary prophylaxis needs to be implemented. Typing almost 567 cultures from different regions in India identified 98 different strains circulating in different states urges the need of safe vaccine prophylaxis.

Though antibiotic therapy with penicillin and its derivatives (benzathine penicillin) are used as first line of treatment, it may not be sufficient to eradicate the disease from endemic areas with high prevalence risk. This scenario pushes our research towards vaccines to prevent GAS infections. The crux of the matter is concerns like widespread Streptococcus pyogenes

strains, cross reactivity between the proteins of host and pathogens, and lack of animal model for developing effective vaccines. The general strategy for vaccine developments include vaccine based on cell surface proteins, vaccine based on secreted proteins and vaccines based on Streptococcal carbohydrates. M protein based Streptlncor, and J14 peptide has been shown to be protective in animal models. Many other vaccines are under study which are based on C5a peptidase (SCPA), Streptococcal hemoprotein receptor (Shr) Shr ,heme binding proteins like HtsA and SiaA , *S. pyogenes* cell envelope protein (SpyCEP) etc. Streptococcus protective antigen (Spa) Spa peptide fragment of Spa18 was incorporated in the recent 30 valent M protein based vaccine and has been found to be a better option in animal studies. Other than these, toxoid against one of the eleven pyrogenic toxins is found to elicit effective immune response in the studies conducted. Jai Vigyan Mode project of ICMR on rheumatic and rheumatoid heart disease report states the lack of effective vaccine against streptococcal diseases though a number of candidate vaccines are in development phase which may develop in another two

or three decades. Hence preventing rheumatic fever and rheumatic heart disease at its later stage is a myth and reality favours primordial prevention.

When your child screams out because of throat pain, take him to a hospital. Stay away from home medications and remember – Today it is just a sore throat; it may change the child's heart tomorrow.

References:

Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. *Lancet* 2005; 366: 155–68.

Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. *Lancet* 2012; 379:953–964.

Mariana M, et al. Prevention of acute rheumatic fever and rheumatic heart disease. *Circulation* 2014; 130.: e35-e37.

Jonathan R, et al. Acute rheumatic fever and rheumatic heart disease. *Nature Reviews Disease Primers* 2016; 2: 15084.

Jai Vigyan Mission Mode Project- Community Control Of Rheumatic Fever/ Rheumatic Heart Disease In India Comprehensive Project Report [2000-2010]; Published on Nov 2016.

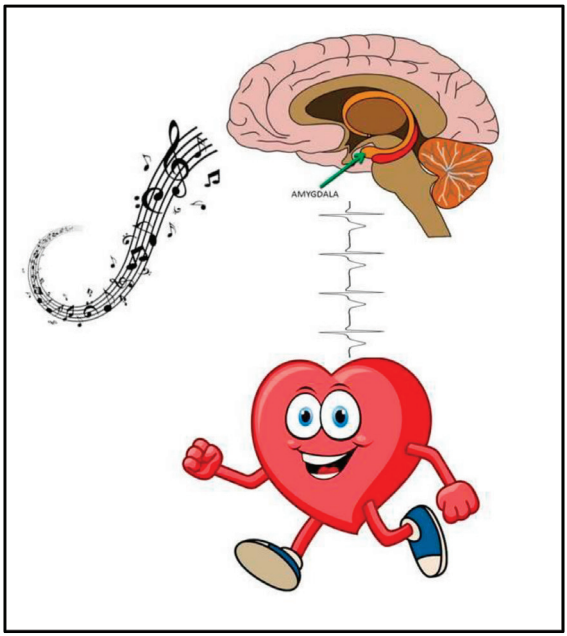
Tandon, Rajendra. Preventing Rheumatic Fever: M-Protein Based Vaccine. *Indian Heart Journal* 66.1 2014; 64–67.

Gandhi, Geethanjali Devadoss, *et al*. Towards Developing a Vaccine for Rheumatic Heart Disease. *Global Cardiology Science & Practice* 2017.1 2017; e201704. PMC. Web. 29 June 2018.

Jayanta Saha. Primary Prevention of Rheumatic Fever in India: The Reality. *EC Cardiology* 3.2 2017; 38-40.

THE HEART-BRAIN CONNECTION

Sumi S



Psychological or emotional stress comes with a wealth of disease conditions. It is known that excessive stress causes high blood pressure, ulcers and irritable bowel syndrome. The link between stress and heart disease has also been long known. Chronic emotional stress carries a very significant risk for cardiovascular disease that is on par with other risk factors for heart disease, such as smoking, hypertension, and diabetes. Exactly how an emotion developed in the brain can directly influence the heart was a mystery.

Investigators from Massachusetts General Hospital and Icahn School of Medicine at Mount Sinai answers this question in the January 2017 issue of The Lancet. They studied imaging and medical records data from 293 individuals who had PET/CT brain mapping. Using a radiopharmaceutical called fluorodeoxyglucose they measured both the activity of areas within the brain and areas of inflammation within arteries. The selected individuals never had any active cancer or cardiovascular disease. Patients were followed up for approximately 4 years. Twenty two participants had a cardiovascular event, such as stroke or heart attack during the follow-up period.

Dr. Tawakol, an Associate professor of Medicine at Massachusetts General Hospital and Harvard Medical School with the assistance of his team was able to show an association between cardiac event and activity in a specific part of the brain, the amygdala, a region involved in emotional processing. Amygdala is a region of the brain that is responsible for detecting fear and preparing for emergency events. They showed for the first time in humans that resting metabolic activity within the amygdala is significantly associated with the risk for developing cardiovascular disease. Even after adjusting for other cardiovascular risk factors and atherosclerosis, the association was very significant. They found that the link between amygdalar activity and cardiovascular diseases was mediated by arterial inflammation which was caused by increased bone-marrow activity.

They also showed that activity in the amygdala could predict the timing of the heart diseases. Higher levels of activity were related with the occurrence of cardiac events sooner in time.

Their findings suggest that reduced stress could help in improved psychological well-being as well as maintenance of enhanced arterial wellness, which in turn could protect from heart attacks and strokes.

Reference:

Tawakol A, Ishai A, Takx RA, Figueroa AL, Ali A, Kaiser Y, Truong QA, Solomon CJ, Calcagno C, Mani V, Tang CY. Relation between resting amygdalar activity and cardiovascular events: a longitudinal and cohort study. *The Lancet* 2017; 389: 834-45.

CHOCOLATES ARE GOOD FOR THE HEART

Ciji Varghese

Almost all of us have craving for chocolates. Chocolate has become one of the most popular food types and flavors across the world. In fact, we could coin it as a portable food for both energy and enthusiasm.

Among the different categories of chocolates, dark chocolate is loaded with nutrients that can positively influence our health. There is an abundant concentration of cocoa in dark chocolate. This cocoa bean is rich in plant nutrients called flavonoids which are powerful antioxidants.

Cocoa specifically contains a large amount of dietary flavanols such as epicatechin, catechin and procyanidins (naturally active plant nutrients). These antioxidants help the body's cells to resist damage caused by free radicals formed in the biological system.

According to a recent study, consuming dark chocolate offers greater beneficial influence for the maintenance of cardiovascular health. Flavanols influence vascular health by lowering blood pressure, improving blood flow to brain and heart as well as making the blood platelets (tiny white cells in blood) less sticky and able to clot. Consumption of diets rich in flavonoids is also associated with a reduced risk for cardiovascular diseases. The intake of flavanols can improve

endothelial (cells lining inner wall of blood vessels) function, whereby the endothelial cells release substances that control vessel wall relaxation and contraction as well as enzymes that control blood clotting, immune function and platelet adhesion. The study also indicates that regular consumption of a flavanol-containing chocolate bar with added plant sterols as a part of a low-fat diet can significantly lower blood cholesterol levels. The recommended dose of dark chocolate is approximately 30g to 60g/day for humans.

The more the chocolates are processed, the more flavanols are lost. Best choices are dark chocolates over milk chocolates. We should therefore be careful in choosing the right quality before consumption. Along with a healthy and balanced diet, these types of functional foods in moderate amounts would be helpful in the dietary management of risk for cardiovascular diseases.

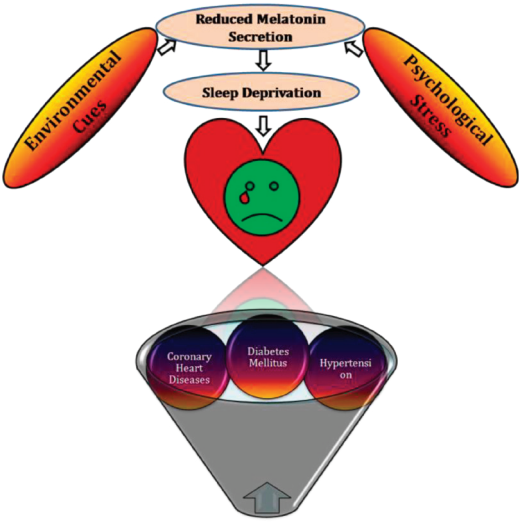
References:

Kord-Varkaneh H, Ghaedi E, Nazary-Vanani A, Mohammadi H, Shab-Bidar S. Does cocoa/dark chocolate supplementation have favorable effect on body weight, body mass index and waist circumference? A systematic review, meta-analysis and dose-response of randomized clinical trials. *Critical Reviews in Food Science and Nutrition*. 2018 Apr 12:1-4.

Allen R R, Carson L A, Kwik-Uribe C, Evans E M and Erdman J W Jr. Daily consumption of a dark chocolate containing flavanols and added sterol esters affects cardiovascular risk factors in a normotensive population with elevated cholesterol. *The Journal of Nutrition* 2008; 138:725-731.

LET YOUR HEART SLEEP

Sudheesh A P



Science is a systematic way of logical thinking and reasoning to find evidences based on facts and actual data to prove speculations or discard myths. A notion associated with cardiovascular diseases (CVD) is its association with certain age group of patients. Many people consider that cardiovascular disease arises after reaching middle age, and hence less care is given to the body during adolescence.

Most of the time, cardiovascular and other associated diseases appear without a prior warning. Certain life styles stress our body and diseases such as obesity, type 2 diabetes,

and hypertension are quite common even during adolescence and sometimes even in early childhood. Although, a family history could leave us with a higher risk for CVD, a healthier life style could help us tackle many of them even before they develop. Maintaining an active life with healthy eating habits, to maintain an appropriate body weight and metabolic parameters such as blood sugar and cholesterol levels can help prevent serious health problems.

Our body with its various organ systems works 24 hours a day for 7 days a week throughout the year. An entire days' tension is released by the body to rejuvenate and start fresh the next day by a good night's sleep; often this is neglected. Sleep performs a range of vital bodily functions, which include replacement of damaged tissues, flushing out toxins, additive stimulation of sympathetic nervous system, prevention of an increased heart rate and vasoconstriction. Sleep deprivation also results in auxillary complications such as coronary heart diseases affecting the normal functioning of heart. As per the report of an online survey conducted by Curofy, a medical application exclusively for the doctors, it was found that one in every five patients in India suffers from a sleeping disorder; but they hardly ever notice it. A major proportion of the working population consumes sleeping pills daily. Another group comprising educated youthoften demand sleeping pills. These pills have several side effects including drowsiness, changes in appetite, dizziness, respiratory depression and even impaired learning abilities. Sleep deprivation is often

due to the work schedule at nights and also because of the time people spent on social media or electronic gadgets.

Table 1: Time required for sleep per age group

Category	Age group	Hours of Sleep needed
Newborns	0-3 Months	14-17 hours
Infants	4-11 months	11-14 hours
Preschoolers	3-5 years old	10-13 hours
School age children	6-13 years old	09-11 hours
Teenagers	14-17 years old	08-11 hours
Younger adults and adults	Young & Adults	07-09 hours
Older adults	Older Adults	07-08 hours

The new guidelines of The National Sleep Foundation (NSF) recommend specific hours of sleep required at each stage of an individual's growth (Table. 1). A good way to keep the heart young and healthy is to get enough sleep and by keeping stress away from the bedroom, trying to develop a positive attitude, developing a habit of eating healthy food along with regular, moderate exercises. Good-quality sleep at night reduces the burden of your heart, as blood pressure and heart rate go down at night. Lack of proper sleep makes the heart rate go up even in the night, constantly putting the heart at an elevated stress. Studies also suggest that lack of sleep can increase the chances for insulin resistance, which in turn is a risk factor for type II diabetes. Importantly, reduced sleep

makes the body synthesise an increased amount of C-reactive protein or CRP, which is otherwise released only during stress and inflammation.

References:

Covassin N & Singh P. Sleep duration and cardiovascular disease risk: epidemiologic and experimental evidence. *Sleep Medicine Clinics* 2016, 11: 81-89.

Yuan R, Wang J, Guo L L. The Effect of Sleep Deprivation on Coronary Heart Disease. *Chinese Medical Sciences Journal* 2016, 31: 247-253.

Hirshkowitz M, Whiton K, Albert S M, Alessi C, Bruni O, Don Carlos L, et.al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health: Journal of the National Sleep Foundation* 2015; 1:40-43.

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