

Could excessive production of tyramine by the microbiota be a reason for essential hypertension?

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Microorganisms (bacteria, viruses, fungi, and parasites) are living creatures that cause diseases [1]. We, human beings, do not always become sick, although we live together with these living creatures. The number of microorganisms needs to be above the threshold value for infection in order for us to become sick. In other words, when the number of microorganisms is below the threshold value for infection, our immune system protects us from diseases by overcoming this condition [2]. The microorganisms do not always have to be exogenous to cause disease. The human body consists of 75 trillion eukaryotic cells [3] (Bianconi *et al.* recently reported that the total number of cells in the human body is 37 trillion) [4], and it also plays host the same order magnitude to prokaryotic cells as the number of human cells, with their total mass being about 0.2 kg [5]. Also, one should keep in mind that the primary source for the often-cited value of more than 100 trillion bacteria in the body dates back to the 1970s [6, 7]. The current estimated total number of bacteria in the 70 kg “reference man” was recently excellently summarized by Sender *et al.* [5].

Most of these bacteria cells constitute our microbiota, which is a new organ in humans comprised of microorganism that live in our intestines [8]. The rates of these mini living creatures should not be destroyed to be have a healthy microbiota. When the rates of these mini living creatures in our intestines change, we may be faced with a variety of diseases including obesity, psychological problems, cancer, and hypertension [9–11]. The reasons underlying the causes of hypertension are not generally fully known. However, in some cases, it is not known how hypertension comes into existence, and these cases of hypertension are referred to as essential hypertension [12]. Unfortunately, a considerable proportion of those having hypertension today are essential hypertension patients, and the principal cause of hypertension

is not known in these persons even though emerging evidence indicates that the gut microbiota has an essential role in hypertension development [13].

In this study, we assert that excessive production of tyramine resulting from microbiota dysbiosis could be responsible for essential hypertension as a possible etiopathogenesis [14, 15]. This may be explained by the tyrosine amino acid being transformed into tyramine through the aromatic-L-amino acid decarboxylase produced by the intestinal bacteria [15]. *Lactobacillus bulgaricus* (histamine, tyramine, and tryptamine), *Enterococcus faecalis* (tyramine), and *Lactobacillus plantarum* are histamine and tyramine producers [16]. In cases in which an excessive number of bacteria to able to produce aromatic-L-amino acid decarboxylase are produced in our intestines, tyramine accumulation will occur in the body. Additionally, this tyramine accumulation causes norepinephrine (NE) release from the adrenal medulla into the open above the limits of sympathetic release. The excessive release of epinephrine from adrenal medulla above the limits of sympathetic release may cause to the peripheral vasoconstriction, cardiac output increase and hypertensive crisis headache, throbbing, subdural hemorrhage, stroke, or myocardial infarction (MI) [17]. As mentioned above, when the normal rate microorganisms constituting the body’s microbiota change, there is an increase or decrease in the metabolic products they produce, such as tyramine. These products also cause several diseases (like hypertension). Moreover, while biogenic amines are naturally found in foodstuffs such as fish and fish products, they also occur in fermented foods such as cheese, wine, beer, and soudjouk as a result of decarboxylation of amino acids by several microorganisms [18].

For whatever reason, when the body’s microbiota changes, it needs to be reorganized, as changes in its condition can cause diseases. Wise use of the antibiotics in reorganizing the body’s microbiota is very important. It is surely beyond doubt that antibiotics should not be used excessively. Excessive use of antibiotics should be paid attention in all areas (in human beings, veterinary medicine, agriculture, animal husbandry, and textile and other). However, when the body microbiota

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deteriorates, it should not be forgotten that antibiotics are important weapons to eliminate the acute and advanced period diseases. What important for this is how to manage and bring under control the microbiota when the microorganisms of the body's microbiota deteriorate for any reason (such as to eliminate fevers depending on the bacteria). The principal duties of an infection diseases physician are probably the wise use of antibiotics and determination of how to form the body's microbiota as needed after antibiotic use. Maybe one day it will become a current issue to ensure the harmony of the body's microbiota by launching special microbiota solutions to the market for each tissue having a unique microbiota. Moreover, maybe one day it will also become a current issue to eliminate essential hypertension by reorganizing the intestinal microbiota by using broad spectrum antibiotics or even by transferring the intestinal microbiota from a healthy donor. We also anticipate that, maybe one day, when the underlying cause of essential hypertension turns out to be lying in microbiota, the currently used literature term "essential hypertension" may be replaced with "microbiota originated hypertension".

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