

## Microbiota in the Onset of Heart Diseases the Role of Trimethylamine N-oxide (TMAO)

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In general: The gut microbiome is considered as a virtual organ and significantly extend the metabolic capacity of the host.

1. Combining microbial phenotyping, metabolic profiling and clinical application will drive our understanding of the metabolic language of mammalian-microbial communication therapies for a range of acute and chronic pathologies.
2. This gives rise to a new paradigm for developing new therapies for a range of acute and chronic pathologies.

**Human microbiota systems differ from place to place in the body. Diet influences microbiome composition:** Long-term diet is associated with the development of specific enterotypes - for instance diets high in animal protein and fat with high levels of *Bacteroides* and low levels of *Prevotella* - diets high in carbohydrates but low in animal protein and fat with higher levels of *Prevotella* but lower levels of *Bacteroides*.

Research published in a *Heart Journal* [1], has indicated that poor gut microbiome may be a potential risk factor for cardiovascular diseases.

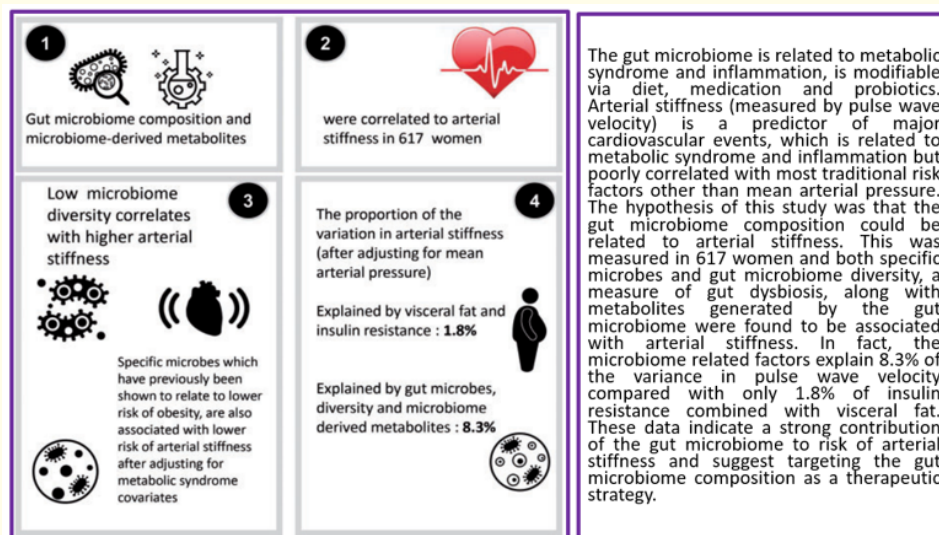


Figure 1: Gut heart research scheme [1].

Many diseases may result from dysregulated gut microbiome

Diabetes Obesity, Metabolic syndrome, Stress/anxiety, Heart disease, Allergic disorders, IBD, Cancer, migraine, Fibromyalgia, Alzheimer’s, Parkinson’s and much more neurodegenerative diseases.

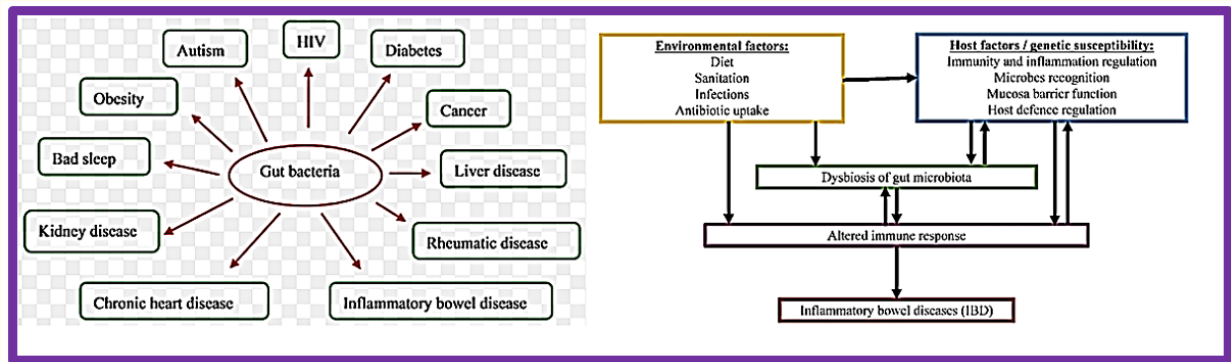


Figure 2: Origen of many diseases is in the gut bacteria’s [2].

Our partners, the various gut microbes, in their unique pathways [3], the microbiome that is a present in our body in the blood, in the brain for example, is a partner in the food digestion. The blend of the various cell lines may change due to many variants, like different foods consumed by the human [4]. This digestion process produces by harming microbes toxins and another harming agent. One of the is the trimethylamine N oxide (TMAO), that may cause heart-damaging effects. No doubt, this is only one example of the harming effects of some microbial cell lines that proliferate in our body. Nowadays, the way to avoid some damage is by consuming a suitable diet. In this composition we describe the effects to cardiovascular morbidity and even to death.

Discussion

In recent years interest has focused on gut microbiota-host interaction. This because accumulating evidence has revealed that intestinal microbiota plays a crucial role in human health and disease, Some examples are cerebral irregularities and neurodegeneration, blood sepsis, cardiovascular diseases. It was reported [5-7] that changes in the composition of gut microbiota associated with the disease, known as dysbiosis, have been linked to many neurological diseases. The gastrointestinal tract is home to several hundred trillion bacteria that are collectively referred to as the gut microbiome [8,9]. Scientific evidence reveals that the gut microbiome is associated with the pathogenesis of both intestinal and extra-intestinal disorders, other examples are obesity [10] and other related metabolic diseases, inflammatory bowel disease, and non-alcoholic steatohepatitis, among others [11-13]. Modern techniques expanded our knowledge of the microbial world. A new era is dawning with the investigations of the gut microbiome as a “multifunctional organ”. Cardiovascular diseases [14] (CVDs) are included in this association [15].

Gut microbiome composition is a modifiable factor influenced by dietary fiber intake. Fiber intake is part of the current recommendations for a healthy diet in the 2016 Task Force recommendation.

The gut microbiome contributes to human health and is being currently thoroughly investigated as a diagnostic and therapeutic target for CVDs. in this review we discuss the evidence for the relationship between our biological nemesis and CVDs. This to intensify an understanding of the latest view of the role of the microbial fauna in CVDs.

**Gut microbial involvement in cardiovascular disease pathogenesis**

It is increasingly recognized that gut microbes represent a filter of our most significant exposure: what we eat. The microbial metabolites are sometimes toxic [16].

Meanwhile, gut microbe-derived metabolites that are biologically active such as trimethylamine *N*-oxide (TMAO) are now recognized as contributors to atherogenesis (Figure 3).

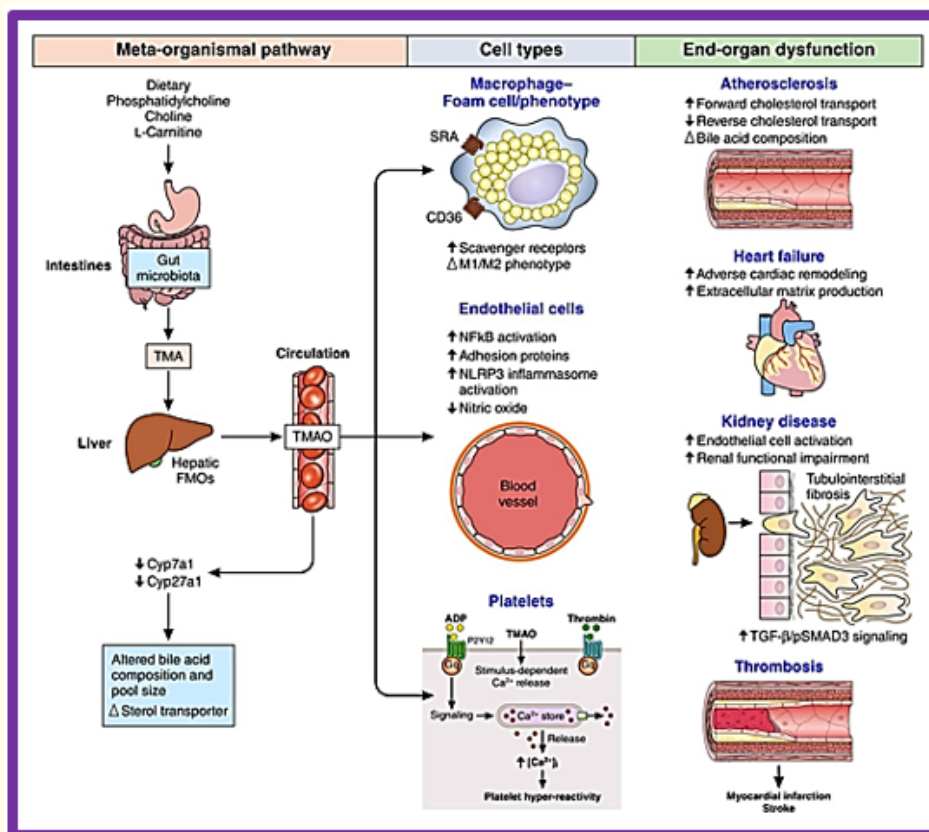


Figure 3: The gut microbiome. Its role in cardiovascular diseases [17].

Using untargeted metabolomics as a discovery platform, researchers identified trimethylamine *N*-oxide (TMAO) as a strong predictor of coronary artery disease risk. Research through animal studies revealed the causal link of TMAO to atherogenesis [5,18,19]. Mechanistic studies show a crucial factor for gut microbes in TMAO generation from trimethylamine-containing nutrients examples are phosphatidylcholine, choline [3] and *L*-carnitine in both mice and humans. TMAO levels increase 4 to 8 hours after are largely normalized within 24 hours in the setting of preserved renal clearance. Consistent with the effects of dietary exposure affecting microbial function, vegetarians and vegans (without *L*-carnitine dietary intake) produce less TMAO compared with omnivorous subjects, with correspondingly distinct microbiota composition. It is also confirmed a mechanistic role for both gut microbes and trimethylamine/TMAO generation in atherogenesis, tissue cholesterol balance, and thrombosis risks [20].

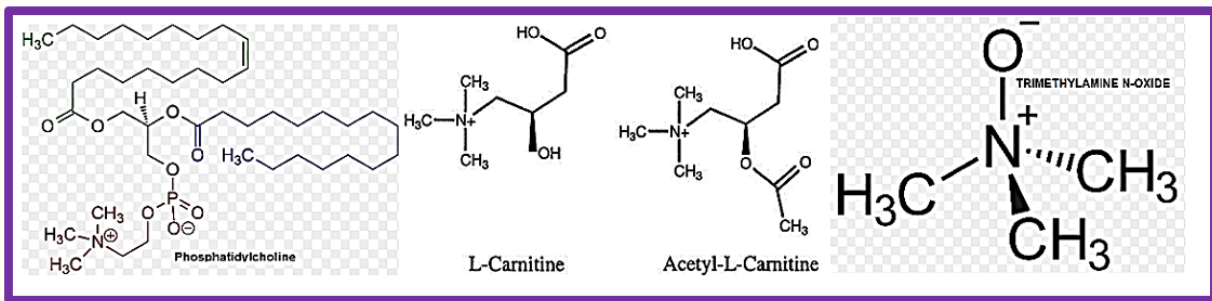


Figure 4: TMAO and its nutritional origin [15].

## Conclusions

The trimethylamine/TMAO pathway may represent only one of many microbe-dependent pathways that will ultimately be linked to cardiovascular disease pathogenesis, proven to be an important diagnostic and therapeutic target for cardiovascular diseases. It is important to note that these studies also help us better understand how nutrition is linked to host health and disease susceptibility, requiring a global examination and view of nutrition, microbe community composition and function, and host genetics. It is not only conceivable but probable that multiple distinct microbial pathways contribute to and protect against cardiovascular and other metabolic disorders. Once revealed, novel diagnostic, therapeutic, and preventive strategies that leverage their identification may become part of our arsenal for halting and reversing cardiovascular diseases [17].

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