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GUEST EDITORIAL

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The Gut Microbiome in Sickness and In Health*

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Hippocrates, who is considered as the father of medicine said, "All disease begins in the gut." In the absence of the modern microscope in his lifetime, one would wonder if he was thinking about the bacterial milieu in our gut when he wrote this quote.

According to the latest 2025 data from the Philippine Statistics Authority, six out of the top 10 causes of death are lifestyle related, namely: ischemic heart disease, neoplasms, cerebrovascular disease, diabetes mellitus, hypertensive disease, and chronic lower respiratory diseases.[1] According to studies, these chronic non-communicable diseases (NCDs), also commonly called lifestyle diseases, are determined by four behavioral risk factors such as tobacco use; unhealthy diets, including excess salt, sugar and fats; harmful use of alcohol; and insufficient physical activity.[2] Today, volumes of researches and publications, have associated ultra-processed foods as the main nutritional cause for the rise of these major health problems globally, including mental health issues.[3]

In 1989, Strachan proposed the *Hygiene Hypothesis* as the underlying cause of most allergic diseases, and in 2005, the *Microflora Hypothesis* was introduced, which extends the Hygiene Hypothesis by further emphasizing the role of microbes, originally considered as a mere commensal in our body. It is now known that there is a close microbial-immune cell interface cross talk between them, and is extensively implicated in relation to human health and development.[4] The human microbiota is estimated at 38 trillion (3.8×10^{13}) microbes per person, which is actually slightly higher in comparison with the human cells, estimated at about 30 trillion (3.0×10^{13}) per person. With about 70 to 80 percent of the immune cells being found in the human gut, much has been discovered on the intricate interplay between the intestinal microbiota and the intestinal epithelial layer, and its impact on the local mucosal immunity and the systemic immune system as well.

With the United States (US) having the largest number of immigrants in the world, research has shown that many of these immigrants develop metabolic diseases several years post immigration. Findings show that there is a fourfold obesity risk among them within 15 years post immigration. A multi-generational Asian American cohort, emigrating to the U.S. also showed a reduced gut microbial diversity and function. Among these microbes, the Genus *Prevotella*, whose enzymes help to degrade plant fibers, has been

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displaced and outnumbered by the Genus *Bacteroides*, so much so that the *Bacteroides:Prevotella* ratio showed an increase by factors of 10, correlating with the time on decades spent in the U.S.[5] This shift in the microbial population and diversity is attributed to the major shift in the diet, mostly to ultra-processed food that contains none or very minimal fibers, and high in sugar and saturated fat.

A review by Singh *et al* on the influence of diet on the gut microbiome showed how dietary intake, such as protein, fat, carbohydrates, polyphenols, and pre/probiotics can cause alterations in the gut bacteria. These alterations exert their biologic effects by changing the host metabolism, immune system production of pro- and anti- inflammatory metabolites, the effect of which are now closely linked with human disease conditions such as cardiovascular diseases, type 2 diabetes mellitus, obesity, metabolic syndrome and even autoimmune diseases.[6] For example, a comparison was made on the impact of dietary protein from plant sources (pea protein) versus high animal protein diet (meats, eggs and cheeses). The high plant protein diet revealed a predominance of *Bifidobacterium*, and *Lactobacillus*, with decreased *Bacteroides* and *Clostridium perfringens*, with an increased production of short chain fatty acids (SCFA). This metabolite is considered as a beneficial bacterial product, leading to an improved gut barrier, increased T-regulatory cell production and decrease inflammation. On the other hand, the high animal protein diet revealed the predominance of *Bacteroides*, *Alistipes*, *Bilophilia*, and *Ruminococcus*, which are classified as bile-tolerant anaerobes, with a decrease in *Bifidobacterium*. These predominant bacterial population are correlated with an increase in trimethylamine-N-oxide (TMAO) production, a proatherogenic compound that increases the risk of cardiovascular disease.[6] Bile tolerant anaerobes have also been implicated in the development of colorectal cancer.

Another dietary component that is considered as beneficial to human health are the non-digestible carbohydrates such as fibers and resistant starches, also known as prebiotics. These food components escape enzymatic degradation in the small intestine, and propelled down the large intestine, where they undergo fermentation through the help of the resident microbiota. Prebiotics is defined as the non-digestible dietary components that provides benefit to host health through selective stimulation of the growth and activity of certain microorganisms. Numerous studies on prebiotics and its effect on the gut microbiota, showed bacterial abundance and gene richness, with an abundance of *Lactobacilli* and *Bifidobacterium* and a decrease in *Clostridium* and *Enterococcus* species. The best sources of prebiotics are from soybeans, inulins, whole wheat and barley, rolled oats, non-digestible oligo-, fructo-, galacto- and arabino-oligosaccharides, mostly found in fruits and vegetables.[6]

The underlying mechanism in disease development through the influence of the microbiome is because of a dysbiotic state. Dysbiosis is defined as an imbalance in the microbiome population in the human body, bringing about harmful effects to the host, leading to inflammation and disease, with the gut microbiome playing a major role in causing dysbiosis. Several factors contribute to the development and maintenance of dysbiosis such as ongoing infection and inflammation, dietary type, use of antibiotics, hygienic practices, and genetics. Because of the microbial metabolites and toxins produced by dysbiosis, various disease conditions affecting not just the intestine, but distant organs as well like the brain, lung, liver, adipose tissue, and even systemic and metabolic conditions, such as mental health issues including sleep disorders, asthma, fatty liver, obesity, inflammatory bowel disease, diabetes, atherosclerosis and rheumatoid arthritis.[7]

Another review by Soldan, M et al on the effect of dietary types on gut microbiota composition and its relationship with the development of NCDs showed the difference between three popular diets. Firstly, the so-called Western diet, mainly consisting of processed foods, fats, red meat and salt, was shown to promote dysbiosis, with a higher ratio of *Firmicutes* vs *Bacteroidetes*, increase in TMAO levels, decreased SCFA production, which are all closely linked with obesity, diabetes, dyslipidemia, colorectal cancer and other chronic non-communicable diseases. Secondly, the plant-based diet, commonly consumed by vegetarians and vegans, showed a lower *Firmicute* to *Bacteroides* ratio, higher SCFA levels, a drop in TMAO levels, resulting to improved blood pressure levels, lipid profile, and improvement of rheumatoid arthritis symptoms. And lastly, the Mediterranean diet consisting of mostly plant-based food rich in fibers, with addition of extra-virgin olive oil, and polyunsaturated fatty acid, which showed a similar finding with the plant-based diet of a lower *Firmicute* to *Bacteroides* ratio, an increase in SCFA and a decrease TMAO, resulting to anti-inflammatory and cardioprotective, and anticancer effects. This comparison and many more scientific researches consistently showed the superiority of a plant-based and Mediterranean dietary habits in promoting gut health and preventing NCDs, as compared to the Westernized dietary pattern.[8]

The current evidences from scientific researches today, shows us that diet and nutrition plays a major role in the regulation or dysregulation of our immune system, through the intestinal microbiome, which in turn creates a significant impact on our health and wellbeing. The type of diet that many people eat today, particularly the westernized diet has been implicated in creating an imbalance, if not a significant shift, in the bacterial population in the gut, which is closely associated with ill-health. Being aware of this will help us in the management

of our patients, and that dietary intervention is a major key in the management of the of many chronic disease conditions, including allergy, cancer and autoimmune disorders. There is also a need for further research in the field of microbiome and dysbiosis, especially in its relation to the recently proposed epithelial barrier theory, which includes not only the microbiome but other environmental factors as well.

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