A Brief Report on Academic Expert-Adjunct faculty Interaction series: Lecture II

(Enhancing professional skills)

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Name of the presenter:

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Title of the presentation:

GUT Microbiome: The Pharmacy in Your Gut

Program Organized by:

Dept. of Pharmacy Practice & Pharmacy Education Unit
JSS College of Pharmacy, Ooty JSS College of Pharmacy, Ooty

Adjunct faculty bring value to academic institutions by sharing their expertise with students. Students gain additional knowledge along with experiential learning by participating in projects and activities connecting the curriculum to practice. With an objective of enhancing professional skills Department of Pharmacy Practice in association with Pharmacy Education Unit, JSS College of Pharmacy, Ooty has planned to conduct Academic Expert-Adjunct faculty Interaction series

Dr Asha Hegde is presently working as Unit Head, DR TMA Pai Rotary Hospital, Karnataka and he is also identified as an Adjunct Faculty of JSS Academy of Higher Education & Research, Mysuru. She is Professor & Head of Dept. of Paediatrics at Melaka Manipal Medical College, Manipal Campus.

Dr Asha Hegde started her presentation with the basic introduction to Gut and Gut microbes as approximately 100 trillion micro-organisms (most of them bacteria, but also viruses, fungi, and protozoa) exist in the human gastrointestinal tract—the microbiome is now best thought of as a virtual organ of the body. Gut microbes are key to many aspects of human health including immune, metabolic and neuro behavioural traits. The human genome consists of about 23 000 genes, whereas the microbiome encodes over three million genes producing thousands of metabolites, which replace many of the functions of the host, consequently influencing the host's fitness, phenotype, and health. Although there is a heritable component to gut microbiota, environmental factors related to diet, drugs, and anthropometric measures are larger determinants of microbiota composition.

Microbiome refers to the collective genomes of the micro-organisms in a particular environment, and microbiota is the community of micro-organisms themselves. Microbiota diversity—a measure of how many different species and, how evenly distributed they are in the community. Dysbiosis -Lower diversity is considered a marker of dysbiosis (microbial imbalance) in the gut and has been found in autoimmune diseases and obesity and cardiometabolic conditions, as well as in elderly people. Further, she also described about the various/ common organisms present in stomach/duodenum; colon; jejunum and ileum. She further explained about the impacting factors on gut microbiome such as: Diet, Pharmaceuticals, Stress (excercies, metabolic, psychological), Infant feeding method, Birthing process, Lifecycle stages and Geography.

How do we quantify?: The composition of gut microbiota is commonly quantified using DNA based methods, such as next generation sequencing of 16S ribosomal RNA genes or whole genome shotgun sequencing, which also allow inference of microbiota functions. Metabolic products of the microbiota are now measurable in stool and serum using metabolomic methods.

What does the gut microbiota do?: The gut microbiota provides essential capacities for the fermentation of non-digestible substrates like dietary fibres and endogenous intestinal mucus. This fermentation supports the growth of

specialist microbes that produce short chain fatty acids (SCFAs) and gases. The major SCFAs produced are acetate, propionate, and butyrate.

Infant Gut Microbiome: The first 1000 days of life, the time between conception and the child's first 2 years, is deemed a critical window in life where noxious environmental exposures can have adverse intergenerational effects Interestingly, the first 1000 days is also a crucial window for the gut microbiome assembly, whereby perturbation to this process also carries health consequences later in life. It has been proposed that the trajectory of gut microbiota of the offspring might be established before birth and that maternal nutrition and microbiota composition influences colonization.

Clinical Implications: Diet is a key extrinsic factor that impacts the gut microbiome, particularly during the dynamic colonization process that occurs in the first several years of life. An imbalance in the complex gut ecosystem referred to as a dysbiosis can have short- and long-term effects on immune system development and impart life-long health complications on an individual in intestine and extra intestine. Gut microbial diversity seems to be a generally good indicator of a "healthy gut. Lower bacterial diversity has been reproducibly observed in people with inflammatory bowel disease, psoriatic arthritis, type 1 diabetes, atopic eczema, coeliac disease, obesity, type 2 diabetes, and arterial stiffness, than in healthy controls. New research suggests effects of microbiome on the central nervous system. The "gutbrain- microbiome axis" may have a significant role on brain development and the pathogenesis of neuropsychiatric disorders. Autism spectrum disorder, which is often associated with constipation, has been connected to gut dysbiosis in the form of an increased Firmicutes/Bacteroidetes ratio and high levels of facultative anaerobes Escherichia/Shigella and the fungal genus Candida. It is suggested that leaky gut contributes to the pathogenesis of autism by increasing systemic metabolites that alter the neuroimmune and neuroendocrine systems, thus affecting the brain and neurodevelopment

Probiotics and Prebiotics: Probiotics are live bacteria and yeasts that, when administrated in a viable form and in adequate amounts, are beneficial to human health. They are usually added to yoghurts or taken as food supplements.
Prebiotics are defined as a substrate that is selectively used by host micro-organisms conferring a health benefit. Although all compounds considered prebiotics are microbiota accessible carbohydrates or fermentable dietary fibre, the reverse is not true. The prebiotic concept is an area of current debate. Synbiotics contain a mixture of prebiotics and probiotics. Most national authorities define dietary fibre as edible carbohydrate polymers with three or more monomeric units that are resistant to the endogenous digestive enzymes and thus are neither hydrolysed nor absorbed in the small intestine. A subset of dietary fibre sources is fermentable, which means that they serve as growth substrates for microbes in the distal bowel. Some non-digestible carbohydrates have been referred to as "prebiotics," which are defined as food components or ingredients that are not digestible by the human body but specifically or selectively nourish beneficial colonic micro-organisms. The prebiotic concept has been criticised for being poorly defined and unnecessarily narrow, and some scientists prefer the term "microbiota accessible carbohydrates," which are essentially equivalent to fermentable dietary fibre in that they become available as growth substrates for gut microbes that possess the necessary enzymatic capacity to use them.

Pharmacomicrobiomics (effects of food and drugs on the gut microbiota): Specific foods and dietary patterns can all influence the abundance of different types of bacteria in the gut, which in turn can affect health. The interaction between gut microbes and commonly used non-antibiotic drugs is complex and bidirectional. Gut microbiome composition can be influenced by drugs, but, vice versa, the gut microbiome can also influence an individual's response to a drug by enzymatically transforming the drug's structure and altering its bioavailability, bioactivity or toxicity (pharmacomicrobiomics). The gut microbiome can also indirectly impact an individual's response to immunotherapy in cancer treatment.

High-intensity sweeteners are commonly used as sugar alternatives, being many times sweeter than sugar with minimal calories. Despite being "generally recognised as safe" by regulatory agencies, some animal studies have shown that these sugar substitutes may have negative effects on the gut microbiota. Sucralose, aspartame, and saccharin have been shown to disrupt the balance and diversity of gut microbiota. Rats given sucralose for 12 weeks had significantly higher proportions of Bacteroides, Clostridia, and total aerobic bacteria in their guts and a significantly higher faecal pH than those without sucralose. Mice given sucralose for six months had an increase in the expression in the gut of bacterial pro-inflammatory genes and disrupted faecal metabolites

Antibiotics clearly have an effect on gut microbes, and low doses are routinely given to livestock to increase their growth and weight. A large proportion of antibiotic use in many countries is for agriculture—particularly intensive farming of poultry and beef. Several observational human studies as well as many rodent studies have pointed to an obesogenic effect of antibiotics in humans even in tiny doses found in food. But humans have very variable responses to antibiotics, and intervention studies have not shown consistent metabolic consequences.

Microbiota transplantation: The functional role of the gut microbiome in humans has been shown using faecal microbiota transplantation. This procedure is effective in cases of severe drug refractory Clostridium difficile infection and is now routinely used for this purpose around the world. For other pathologies, faecal transplants are not yet clinical practice but have been explored. For example, transplanting faeces from a lean healthy donor (allogeneic) to recipients with metabolic syndrome resulted in better insulin sensitivity, accompanied by altered microbiota composition, than using autologous faeces.

Covid 19 alters gut microbiome: To date, a growing number of studies have investigated the role of the gut microbiota and SARS-CoV-2. A recent shotgun metagenomics sequencing from a small cohort of 15 COVID-19 patients revealed significant gut microbiota dysbiosis in patients versus controls. The authors observed an increase in the abundance of pathogenic bacteria and decreased beneficial microbes, which persisted even after resolving respiratory symptoms and negative throat swabs.

What we know?.

- Probiotic supplementation has several beneficial effects on human health
- The microbes in our gut influence and human energy metabolism
- Diet and medication have a strong influence on gut microbiota composition
- Microbiota composition influences response to chemotherapy and immunotherapy
- Microbiome composition defines glucose response to foods and can be used to personalise diet
- Dietary fibre intake influences gut microbiota composition and is related to better health

What we don't know?

- Are natural probiotics in food better than probiotic supplements? Should we take them preventively?
- Can microbes influence food choices and appetite?
- Do low dose antibiotics in food affect human health?
- What is the effect of pesticides in food on the gut microbiome? Is organic food better for the gut microbiota?
- Should all new drugs and food chemicals be tested on the gut microbiota?

Dr Asha concluded here presentation with the statement that; we are entering an era where we can increasingly modify health through food and measure the effects through our microbes or metabolites. Fibre is a key nutrient for a healthy microbiome and has been overlooked while debates have raged about sugar and fat. The adverse effects on the microbiome of drugs and processed food ingredients can no longer be ignored. Given the current gaps in knowledge, we need clinical evidence that can be translated into clinical practice, ideally through randomised controlled studies that use consistent matrices of prebiotics or probiotics or faecal microbiota transplantation to assess changes in gut microbiota composition and in health outcomes.

Key Messages of the presentation:

- Gut microbiota influences many areas of human health from innate immunity to appetite and energy metabolism
- Targeting the gut microbiome, with probiotics or dietary fibre, benefits human health and could potentially reduce obesity
- Drugs, food ingredients, antibiotics, and pesticides could all have adverse effects on the gut microbiota
- Microbiota should be considered a key aspect in nutrition; the medical community should adapt their education and public health messages
- Fibre consumption is associated with beneficial effects in several contexts

There was a question-and-answer session where staff and students clarified their doubts related to gut microbiome. Dr KP Arun delivered the welcome address and the importance of the academic expert interaction series, and even delivered the vote of thanks. A total of 89 participants were present in the session.

Report submitted by: DR S Ponnusankar, Professor & Head, Dept. of Pharmacy Practice