

BRINGING HEALTH THROUGH GUT: IMPORTANCE OF NUTRITION A woskshop fos dietitians

ROME March 9th, 2018

"Gut health is for everyone. In both health and disease, the microbiome plays a key role. Evidence supports that diet plays an important role in supporting gut health. Getting people invested in gut health can shape outcomes in both wellness and disease."

Andrea Hazdy, RD (Calgazy, Canada)

TODAY I LEARNED ABOUT ...

...the important interactions between the molecules in food and the gut microbiota ...the real impact that diet has on the gut microbiota

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...myths and realities about probiotics ...the importance of functional foods for a good microbiota



BRINGING HEALTH THROUGH GUT: Impostance of Nutrition

A person's overall health is increasingly recognised to be closely linked to the microbiota. Science is pointing to the importance of building and maintaining a healthy microbiota in order to help prevent a range of diseases, from allergies to metabolic disorders, as well as gastrointestinal symptoms. There is a clear need for healthcare professionals, including dietitians working on the front line, to have more information on the subject, so they can provide the appropriate advice and support during their consultations. In fulfilling its mission of bringing health through food to as many people as possible, Danone organized a workshop designed for dietitians, which took place in Rome on 9 March 2018. It brought together 86 dietitians and nutritionists from 10 European countries. In addition to translating the current science on gut microbiota, health and the role of nutrition into clinical applications for everyday practice, it also enabled those attending to gain the insight necessary for them to take their full place as "ambassadors of gut health".



Dr. Gianluca laniro, gastroenterologist and expert on gut health for numerous scientific institutions. *e.mail: gianluca.ianiro@hotmail.it twitter: @gianluca1aniro*

"When micsobiota capacity fos sesilience is exceeded, eubiosis is lost and we move on to a state of imbalance called dysbiosis." "I like to see it as an interplaying team". It's in these terms that Dr. Gianluca laniro, gastroenterologist and scientific expert on gut health for a range of scientific institutions, describes our relationship with the various microbes that comprise the gut's microbiota. The microbiota is composed mainly of bacteria, but it also contains viruses and fungi. It is a community in constant interaction with the constituents of the intestinal tract: the epithelial cells, the immune cells (particularly numerous within the gut) and the mucus layer.

But what makes the gut's microbiota so special ? The first time one takes them on board, the quantitative data on the gut's microbiota can seem vertiginous: together amounting to between one and two kilograms, it comprises over 10 000 different species of monocellular organisms; individually, they number in the trillions. Dr.Ianiro continues: *"All in all, the gut's microbiota contains more than three million genes, when the human genome numbers only 22 000".* This is why some researchers, in addition to considering it as an organ – able to digest certain foods and produce molecules like vitamins - describe the microbiota as "our other genome".

A WIN-WIN RELATIONSHIP

Beyond these figures, the importance of the gut's microbiota lies in the functions it performs for us. First, it acts as a barrier to potentially pathogenic microorganisms entering the intestinal tract. Second, it helps us to mature and train our immune system and to develop an appropriate tolerance towards one's own body, towards food and towards friendly microbes. The microbiota also helps our intestinal cells harvest energy from food : it produces short-chain fatty acids (SCFAs, *i.e.* butyrate, acetate, and propionate) from fibers, that would otherwise pass through the intestinal tract undigested. In addition to feeding our gut cells, these compounds contribute a range of positive effects on the whole organism (transit, immune function, appetite regulation, mucosal functioning, *etc.*). The gut microbiota also participates in the production of some

FROM EUBIOSIS TO DYSBIOSIS

A state of eubiosis is one in which we live in harmony with the bacteria and other microorganisms that we host in our gut. When the microbiota is put under excessive pressure by our lifestyle, notably our diet, this eubiosis is jeopardized and can lead to a state of dysbiosis. Such a state is characterized by a loss in bacterial diversity as well as a change in the balance between bacterial species in favor of the harmful at the expense of those that are beneficial; it translates into a disruption of the mutually beneficial relationships between the host and the microbiota, and can lead to diseases.



Patrick Veiga, Head of the *"Microbes & Foods for Health"* Science team in the Innovation, Science & Nutrition Department of Danone Nutricia Research.

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"We have moved from a 'health of the gut' paradigm to a 'health through gut' paradigm." vitamins such as vitamin K. The microbiota is increasingly perceived, moreover, "as a potent bioactivator of dietary compounds", notes Patrick Veiga, Head of the "Microbes & Foods for Health" Science team in the Innovation, Science & Nutrition Department of Danone Nutricia Research. He likes to illustrate this feature with the example of a family of compounds found in cruciferous vegetables: "Under the action of the microbiota, these molecules otherwise inactive are transformed into active compounds known to protect cells against carcinogens", he explains.

SHAPING OUR MICROBIOTA ACROSS LIFE-STAGES

The composition of the gut's microbiota – characterized by the total number of microbes, their diversity in terms of species and the relative abundance of each one – is dependent on a range of factors. Among them, the person's age is the first that Dr. laniro cites: the colonization of the intestinal tract starts at birth. The microbiota gains in diversity throughout infanthood, as Bifidobacteria species preponderate during the milk feeding period and new species appear with the introduction of solid foods. It reaches maturity at about 3 years of age. The child's microbiota is also shaped by the mode of its birth (vaginal or caesarean), whether or not it is breastfed, and its exposure to microbes in the course of its infancy. During adulthood, *"microbiota can experience disruption in response to events such as psychological stress or the use of antibiotics"*, Dr. laniro explains. As for the elderly, their microbiota is substantially different to that of younger adults: diversity, in particular, diminishes during ageing.

DIET, A POTENT INFLUENCE ON THE MICROBIOTA

The composition of the microbiota is determined largely by our environment and our lifestyle: for example, whether one lives in an industrialized or an agrarian society, the extent of one's exposure to tobacco or stress, the quality and duration of one's sleep, the level of physical activity, as well, of course, as the nature of one's diet. Dr. Sculati, Medical Doctor and Specialist in Clinical Nutrition, has absolutely no doubt that diet acts as a potent modulator of the gut's microbiota. As one of many examples, he refers to the fact that the Japanese, thanks to enzymes that their microbiota has acquired or has activated, tend to be much more able than Westerners to digest seaweeds.

OUR MICROBIOTA IS HIGHLY CHALLENGED

From the days of the active hunter-gatherers in the Paleolithic era, modes of life have changed considerably to the sedentary and hygienist one that prevails nowadays. The so-called Western diet, high in fats and sugars yet low in fibers, is particularly challenging for our microbiota. It tends, indeed, to lead to a state of dysbiosis, characterised by a decline in the microbiota beneficial bacteria and a loss in diversity (see box). Notably, the low quantity of fiber in our diet has been shown to cause a decrease in the microbiota's production of SCFAs, compounds that are essential to human health. As Patrick Veiga points out, *"less fiber in our diet means less food for the gut microbiota"*. When fibers are lacking, bacteria from the microbiota are thought to feed on the mucus layer as an alternative source of energy, contributing to an increase in the permeability of the intestinal barrier, *i.e.*, the *"leaky gut"* phenomenon.



Michele Sculati, Medical Surgeon and Specialist in Food Science. *e.mail: michele@sculati.it*

"It is cleasly impostant to include in one's diet foods that contain psebiotic substances, nutrients which ase necessary to keep the micsobiota healthy."

GUT HEALTH AND BEYOND

Many gastrointestinal disorders have been associated with microbiota dysbiosis, for example diarrheas or inflammatory bowel diseases (IBD). But beyond the gut, dysbiosis has also been associated with a range of diseases affecting other organs. In particular, it has been linked to type 2 diabetes, obesity, insulin-resistance, metabolic syndrome, and liver disease. It is not clear yet to what extent dysbiosis is a cause or a consequence of metabolic diseases. That said, human trials and the use of animal models tend to show that improving the microbiota leads to an improvement in health parameters such as glucose tolerance, fat mass and the biomarkers of inflammation. As Dr. Sculati explains, the most widely shared hypothesis to explain how dysbiosis might contribute to metabolic disorders points to the role of lipopolysaccharides (LPS). What are they ? *"LPS are endotoxins which originate in the outer cell membrane of Gramnegative bacteria; they are thought to cross the gut barrier and to initiate inflammation-related processes elsewhere in the body"*. Emphasizing further the systemic influence of gut microbiota, dysbiosis has also been linked with immune system and inflammatory diseases such as asthma.

SHAPING A HEALTHY MICROBIOTA THROUGH ONE'S DIET

Fecal microbiota transplants have received a lot of attention lately, as it seems to be possible to transfer a healthier microbiota along with their measurable health benefits. Nevertheless, *"it clearly raises a question of acceptability"*, Patrick Veiga comments, wondering with a touch of humor if we really are intended to become *"Homo coprophagus*¹". In his view, fecal microbiota transplants, once their safety has been established, may prove to be useful for treating certain severe medical conditions but, so far as the wider population is concerned, improved microbiota should be sought first through a change in diet.

Fibers, the sine qua non for a healthy microbiota

Though human cells cannot digest fibers, the microbiota certainly can and fibers can be categorized as prebiotics, "a substrate that is selectively utilized by host microorganisms conferring a health benefit"². Inulin-type fibers known as fructo-oligosaccharides (FOS) are present in many vegetables: onions, garlic, leeks, asparagus, cruciferous vegetables but also chicory and dandelion. Accordingly, Dr. Sculati underlines that to maintain a healthy microbiota, "these vegetables should be eaten several times a week, in significant portions". He gives a few tips to maximize their potential: "The stalks of broccoli or asparagus should be eaten as much as possible; also roots such as chicory roots or Jerusalem artichokes should be gradually introduced in our diets. The microbiota has to be progressively exposed to prebiotics, otherwise abdominal bloating and distention could be experienced."

¹ *i.e.* literally, a species who eats faeces

² According to the <u>International Scientific Association for Probiotics and Prebiotics</u> (ISAPP) definition

When ous diet is fibes depsived, bactesia ase thought to feed on the mucus layes instead (mice sesults)

Credit : <u>Desai *et al.*</u> <u>Cell. 2016 Nov 17;</u> <u>167(5):1339-1353</u>



ature mucus layer: intact barrier function

Fiber-free (FF) diet



Microbiota eroded layer:barrier dysfunction Fiber-degrading
 microbiota

Mucus-degrading microbiota

Muceal pathogen

RESTRICTIVE DIETS: Neves fos too long

Following a dietetic prescription or through independent choice, low FODMAP* or gluten-free diets are often tried by patients who are experiencing symptoms of lower gastrointestinal problems such as pain or bloating. Yet these diets are low in fiber and as such, may have deleterious effects on the gut's microbiota. Indeed, they have been associated with an increase in pro-inflammatory bacteria and in a reduction of the SCFA butyrate producing bacteria such as Akkermansia muciniphila. For this reason, these diets should not be followed for too long.

*Fermentable Oligo-, Di-, Mono-saccharides And Polyols



Lorenzo Morelli, Professor of Food Microbiology and Director of DISTAS- UCSC Piacenza Cremona.

"Probiotics carry out a protective action against pathogenic bacteria and intestinal visuses. Other effects are under investigation and concern their ability to reduce allergies as well as levels of anxiety and stress."

Resistant stasch

Although food starch is mostly digested, a small part termed "resistant starch" is not. Pulses are rich in resistant starch, and, together with another fiber named galacto-oligosaccharides (GOS), are a thorough source of prebiotics. In order to limit unpleasant meteorism provoked by pulses, "we should train our microbiota with a progressive and regular intake", Dr. Sculati points out; "and regular consumption of fermented milk has been shown to reduce the gastrointestinal symptoms of a flatulogenic diet³", he continues. Pasta, especially from durum wheat, is another source of resistant starch; interestingly, resistant starch content decreases with cooking time – a further reason for eating one's pasta *al dente*, as highlighted by Dr. Sculati.

Fermented foods

Eating fermented foods is another way to maintain a healthy microbiota. Fermentation is a natural process which has a long history as a means of lengthening food conservation. The living ferments inhibit the development of alteration microorganisms. In a sense, the same thing occurs in the gut as the ingested ferments promote a healthy microbiota. This idea, explains Lorenzo Morelli, Chair Professor of Food Microbiology, was first put forward over a century ago by Elie Metchnikoff (see Box), who believed that micro-organisms found in fermented milk could suppress "putrefactive" colonic bacteria and improve general health. In line with this view, Isaac Carasso, the founder of Danone, launched the first yogurts in 1919 to help Spanish children suffering from intestinal infections, "showing that taking care of the gut by consuming fermented foods containing live bacteria is a concern embedded in Danone's DNA since its origin", Patrick Veiga continues. Since then, the beneficial effects that can be expected from fermented foods such as yogurts has been confirmed. Notably, the role of yogurt's ferments in helping lactose digestion has been convincingly demonstrated, and validated as such by the acceptance of a claim on the subject by the European Food Safety Agency (EFSA), highlights Professor Morelli. Among fermented products, "yogurt is the only one that is standardized in terms of the bacteria species present⁷⁴, Dr. Sculati adds.

Probiotics

Fermented foods have inspired the development of living cultures of bacteria known today as probiotics. These are defined as *"live microorganisms that, when administered in adequate amounts, confer a health benefit on the host*"⁵. A wide range of probiotics are available on the market. So far, Professor Morelli reports, *"some probiotics have been recognized as being useful in preventing or managing four types of gut disorders, namely pediatric antibiotic associated diarrheas,* Clostridium difficile *infections, necrotizing enterocolitis in preterm neonates, and abdominal pain*". These conclusions are based on Cochrane reviews, *"the most rigorous standard for reviewing the level of evidence on health matters*". The European Society For Primary Care Gastroenterology (ESPCG) has also recently released an updated international consensus⁶ about the use of probiotics in the management *(continued on page 7)*

- ⁵ Definition by <u>FAO/WHO</u> (2001) updated by <u>ISAPP</u> (2014)
- ⁶ Hungin et al. Aliment Pharmacol Ther. 2018 Feb 20. doi: 10.1111/apt.14539

THE FATHER OF PROBIOTICS

Elie Metchnikoff (1845-1916), awarded the Nobel Prize for his discovery of phagocytose – the process by which some immune cells engulf and destroy harmful bodies such as bacteria – is often thought to as *"the father of probiotics"*. Over a century ago, he put forward the hypothesis that health could be improved through enhancing the



intestinal bacteria with host-friendly bacteria found in fermented milk.

³Le Nevé *et al.* Effects of flatulogenic diets combined with a fermented milk product on subjective and objective markers of flatulence in patients and healthy subjects. Clinical trial n°NCT02936713. Poster Session at the Gut Microbiota for Health World Summit 2018.

⁴ Lactobacillus delbrueckii subsp. bulgaricus and Streptococcus thermophilus



Andrea Hardy, registered dietitian from Calgary, Canada, specialized in gut health & gastrointestinal diseases. *e.mail: andrea@ignitenutrition.ca twitter: @AndreaHardyRD facebook: @IgniteNutritionInc*

"Dictitians play an integral sole in connecting the public to credible nutrition information."

USING PROBIOTICS IN THE MANAGEMENT OF LOWER GI SYMPTOMS IN YOUR PRACTICE: What the science currently supports

Grade of evidence	Symptoms/indications	Meaning for physicians
High	 Overall symptoms and abdominal pain in IBS Prevention or reduction of diarrhoea in patients receiving antibiotics and <i>H. pylori</i> eradication therapy 	Probiotics with supportive evidence for benefit should be tried
Moderate	 Bowel movements and bloating/distension in IBS 	Probiotics with supportive evidence for benefit could be tried
Low	- Overall symptoms in IBS-D - Flatus in IBS - Constipation in IBS	Probiotics with supportive evidence for benefit could be considered
Very low	- Overall symptoms in IBS-C - Diarrhoea in IBS	Currently no evidence to support use of probiotics

IBS, irritable bowel syndrome; IBS-C, constipation-predominant IBS; IBS-D, diarrhoea-predominant IBS. Source : Hungin *et al.* 2018⁶

KEY POINTS ABOUT PROBIOTICS TO KEEP IN MIND:

• Effects are **strain specific.** Make sure the strain you may recommend has demonstrated efficacy.

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- Select from among the products whose **content is as high as the one used in the trials which demonstrated an effect.**
- Patients will not all respond in the same way.

CLINICAL CASE : WHAT CAN YOU DO IN YOUR EVERYDAY PRACTICE TO IMPROVE YOUR PATIENTS' HEALTH AND MICROBIOTA?

Try this clinical case, presented during the workshop by Andrea Hardy

PATIENT : 32 year old women. C-section for birth of her second child. She has a 4 year old daughter and a 9 month old infant at home.

SYMPTOMS DESCRIBED : constipation, abdominal bloating, distension, feeling of incomplete evacuation.

CURRENT DIET: recently cut out gluten, dairy and soy because her youngest has colic. She skips breakfast as she is busy with the kids, eats lunch with her daughter – gluten free toast, fruit, rice cakes and peanut butter, *"veggie pizza"*, pasta with tomato sauce, *etc.* and has a balancer supper with family. 1. What factors could potentially influence her microbiome ?

2. What might be your suggestions to improve her gut health?

Answess brought up dusing the woskshop :

- 1. What factors could potentially influence her microbiome ?
- Lot of dietary changes introduced in a short time
- Low dietary variety and restrictive diet likely inadequate intake
 Stressful period
- Lot of processed foods and not enough vegetables/fibers
- Inadequate fluid intake especially as she breastfeeds
- Antibiotics post c-section
- Pelvic floor, diastasis recti?

2. What might be your suggestions to improve her gut health ?

The underlying symptom (*i.e.*, constipation) needs to be taken care of as a priority. Solutions include increasing intake of fluid, fiber, and fermented foods containing probiotics for symptom management and gut health. Make sure to give lots of practical examples in each category and keep in mind that a busy mother will appreciate practical suggestions (*e.g., "Include breakfast each day, for instance with a fermented food such as yogurt or with granola for resistant starches and fibers"*). Then, focus should be on foods that have been avoided. Discuss whether the infant colic is better/worse/the same since starting the restrictive diet and discuss the risks of following a restrictive diet and the benefits of liberalizing.



Zelda Wilson, registered dietitian working at Danone Health Affairs.

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"As a company, we want to make sure that the information that goes out is correct and up-to-date. We do everything to make sure that the right messages are sent out to the public."

TRANSLATING EVIDENCE INTO PRACTICE

syndrome (IBS) symptoms as abdominal pain, bloating or distension.

Given the frantic rhythm of scientific publications on the gut, microbiota and health – every day, at least two papers with the key word "probiotic" are entered into Pubmed, Professor Morelli informs us –, it requires a lot of work to keep up-to-date with the evidence and understand how best to put it to practical use. In prevention as well as in disease, maintaining or rebuilding a healthy microbiota in her patients is at the very heart of Andrea Hardy's approach as a registered dietitian in Calgary, Canada, specialist in gut health & gastrointestinal diseases. "I always consider food as a front line treatment, she underlines, with a focus on foods high in fibers and containing living ferments". Regarding the use of probiotics in clinical practice, "this should be guided by consensus statements at the international level", she insists, as the extent of evidence varies by strain and dose as well as by the intended outcome (see Box page 6). Andrea Hardy also shared her conviction that any dietary intervention should be framed in what she calls a 'bigger picture'. In particular, patients' barriers to change should be addressed through dialogue, to engage them and create personal investment in nutrition changes. Developing general healthy habits in their daily routine beside the intervention might also be helpful.

of lower gastrointestinal symptoms. Notably, it concludes that there exists a moderate to high degree of evidence regarding the effects of some probiotics in relieving irritable bowel

HEALTH THROUGH GUT FOR EVERYONE

This workshop session gave visibility to the huge amount of science on the gut microbiota and generated a lively confrontation on the theme. All scientific evidence concurs on the proposition that dietary patterns have a fundamental influence on the balance of the gut microbiota, which in turn contributes to overall health and well-being. Along with the support of healthcare professionals, regular dialogue and discussion among experts, will help to underline the importance of a good diet to maintain the correct balance of our gut. What should be the next steps ? A need was expressed for healthcare professionals to be issued with clinical guidelines at the EU level for probiotics use; for the general public, it was felt that a particularly useful contribution would come from the development and dissemination of handouts to increase awareness about gut health and nutrition. Getting all the people – patients and the general population, dietitians and gastroenterologists – invested in gut health can shape positive outcomes in both wellbeing and disease. Dietitians have important work to do in translating the evidence into usable, practical interventions. So join the movement!

SYMBIOTIC PARTNERSHIPS TO MAKE SCIENCE AND EVIDENCE BASED FACTS ACCESSIBLE TO THE PUBLIC How Danone supposts advocacy on gut health?

- Since 2012, Danone has been supporting the **Gut Microbiota For Health** (<u>GMFH</u>)⁷ initiative from the European Society for Neurogastroenterology and Motility (ESNM). GMFH's mission, *"increase recognition of the links between gut microbiota and human health and to spread knowledge and interest in this field"*, is implemented through tangible actions: namely an annual event (Gut Microbiota





for Health Summit) and a digital public information service and ecosystem. Since its launch, GMFH has produce more than 1000 pieces of content in a range of formats (written posts, infographics, videos, interviews, *etc.*).

- Inside-Ology⁸, a comic book narrated by the great immunologist Elie Metchnikoff himself, was developed with the support of Danone conjointly by the European Paediatric Association and the Union of National European Societies and Associations (EPA-UNEPSA). "This is another example of our company's dedication to transmitting scientific knowledge and communicating important messages to the public", explains Zelda Wilson, a registered dietitian working at Danone Health Affairs.

⁷ http://www.gutmicrobiotaforhealth.com/fr/accueil/ ⁸ http://inside-ology.com/

LIVE FEEDBACK FROM THE WORKSHOP



Andrea Hardy RD @AndreaHardyRD . 9 mars Great presentations today - tell me: what is the ONE thing you're going to change about pratice after today's talks on #guthealth @GMFHx @ Danone #guthealthrd

77 %

of the attendees declared they will make change in their practice or research after the workshop. And you ? What learnings will you turn into daily practice ?

"More practical examples for my patients on the importance of fermented foods and probiotics"

"Consider fiber consumption"

"Focus in improving gut health in all my clients"

"I will explain to my patients the importance of gut microbiota"



Nutrition is a fundamental asset to build and maintain on a daily basis a good microbiota for a lifespan health.

Probiotics represent the new frontier to contribute to health and wellbeing through gut.

Fermented milks with probiotics, together with a prebiotic rich diet, are our best daily alies to stay healthy.

It is crucial to disseminate credible information regarding the existing and coming knowledge about microbiota role.



"HEALTH THROUGH **GUT IS FOR EVERYONE**" Join the movement!

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