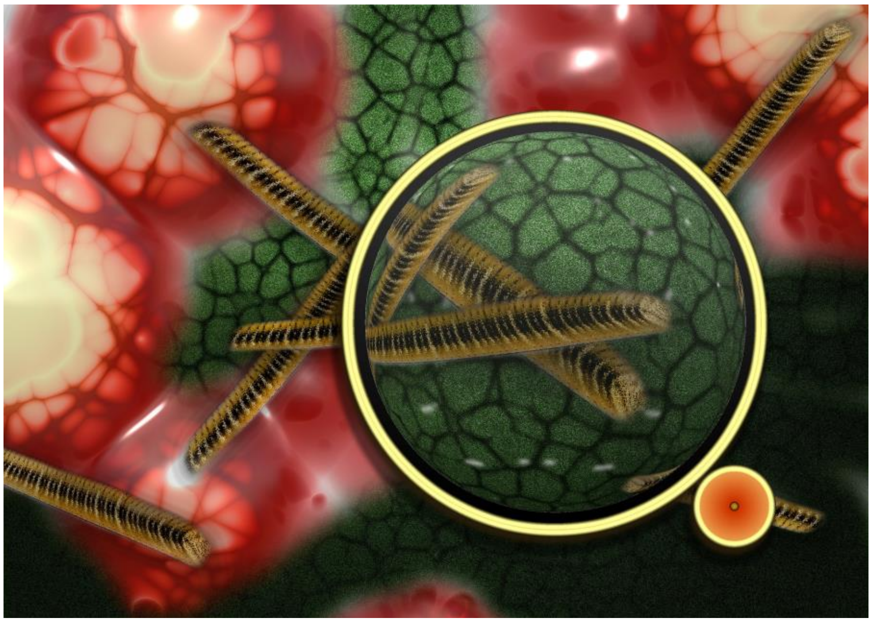
Restoring Balance and Harmony to the Gut Microbiome



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Introduction

Bacteria have a long-held reputation as a health threat. Television ads ask parents to “protect” their children with disinfectants. Travel-sized antibacterial gel is sold alongside candy at checkout aisles in pharmacies and gas stations. Even body wash was once marketed as antibacterial. However, not all bacteria are harmful. In the past decade, a growing movement is reexamining the role that bacteria plays in our health and researchers are finding ways to preserve and nurture the huge ecosystem of bacteria that is crucial for human health in the gut.

In 2008, a scientific collaboration called The Human Microbiome Project undertook the task of studying the genomes of the microbes that live in humans. The project took advantage of the latest computer analytics and gene sequencing technology to begin cataloguing the hundreds of bacterial strains living on and inside the human body. As a result, a flood of research was opened into the function of the gut microbiota –- the community of bacteria living in the intestines.

It turns out gut microbes affect far more than digestion. Dysbiosis, or an imbalance in a person's gut microbiome, may harm the heart, the immune system and even a person's mental health. As science continues to track how different bacteria strains influence the body, more doctors and members of the healthcare community are starting to treat dysbiosis through probiotic foods that contain helpful bacteria and prebiotic foods that feed the helpful microbes in the intestines.

Discovering the gut microbiome

The sheer size of the gut microbiota is staggering. There are 10 times the number of bacterial cells living in the human body as there are human cells, and 100 times the number of bacterial genes to sequence in a person's microbiome than genes in a human genome. Most of those microbes live in the gut.

The Human Microbiome Project has greatly expanded the understanding of the role of these gut bacteria in overall human health. Additionally, it has overturned long-held beliefs about the influence the gut has on the rest of the body. People are truly living in a symbiotic relationship with the bacteria they carry in their gut. The gut microbiota feeds on the food that humans eat and, in turn, the gut bacteria protect and nourish the body.

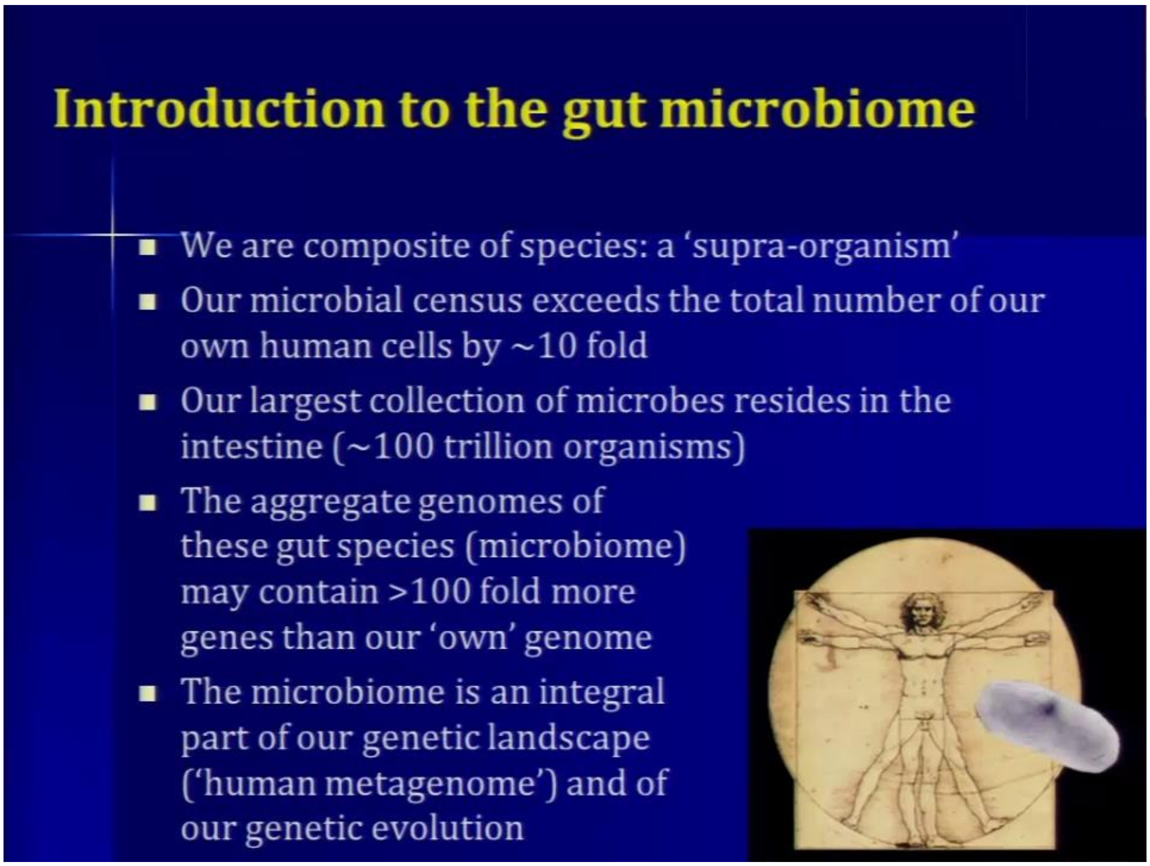

Figure 1

What good bacteria can do

An individual's gut microbiome begins to develop at birth. Infants pick up bacteria from the birth canal, from surfaces the baby touches in the hospital and even from breastmilk. In the first few years of life, infants continually acquire bacteria, which will help the infant digest food and ward off disease. In fact, 70 percent of the immune system is found in the gut. In addition to the immune system, it is understood that gut bacteria help break down plant materials during digestion and create short chain fatty acids that are crucial to the body's metabolism. Gut bacteria help to prevent inflammation, help the body rid itself of harmful toxins, help metabolize xenobiotics and even help create some essential vitamins.

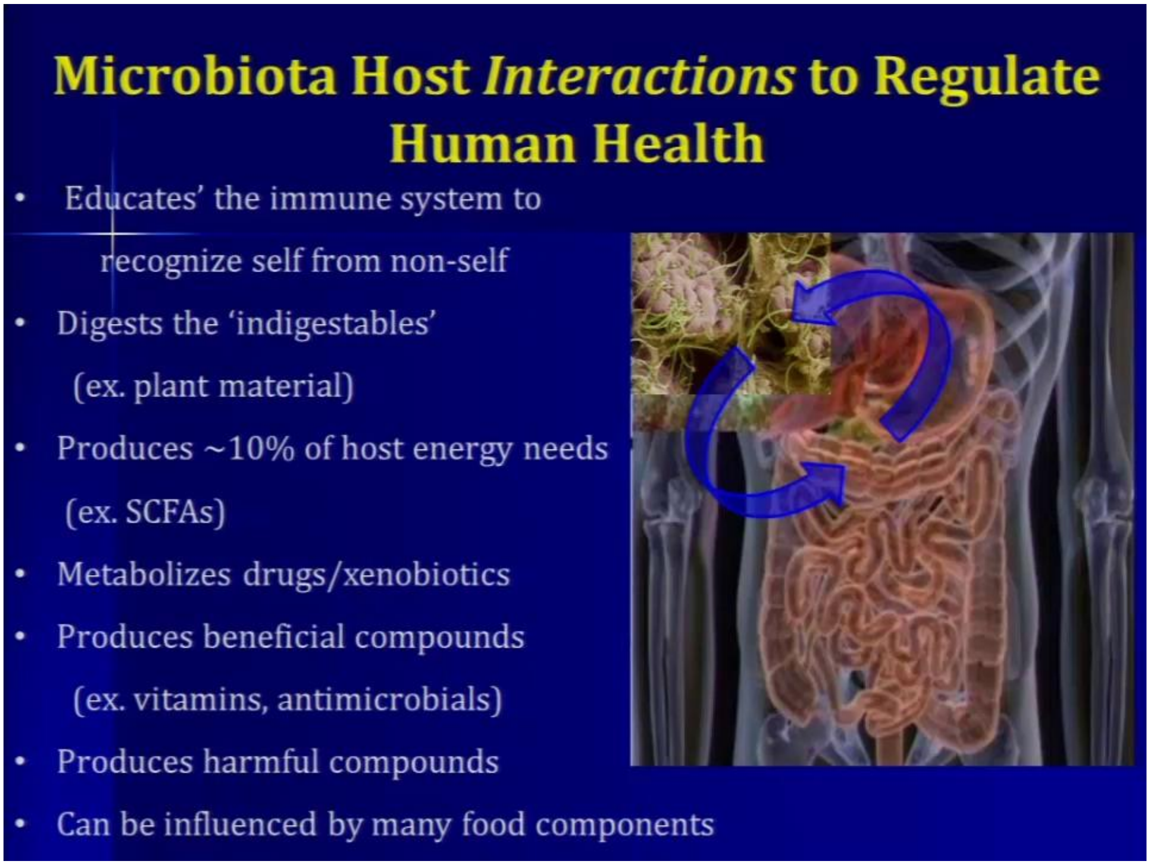

Figure 2

Diet, hygiene, and an individual’s stress level can all impact which bacteria strains thrive. Infections and exposure to antibiotics can also have a lasting effect on an individual's microbiota.

When the balance of bacterial strains in the gut is altered significantly, it is possible that the gut microbiome can become harmful to its human host and instead of symbiosis, dysbiosis occurs. Examples of diseases influenced by dysbiosis include allergies, asthma, eczema, and inflammatory diseases in the gut.

Research into dysbiosis has been greatly advanced by metabolomics. In metabolomics, scientists can screen for metabolites – the substances produced when gut microbes metabolize food – and match that metabolic activity to the strains of responsible bacteria. Metabolomics can then identify and stratify the bacteria present in an individual's gut.

Healthy bacteria, healthy gut

Researching the metabolomics of gut microbes can also help to identify bacterial function. For example, some bacteria eat, biotransform, and activate compounds that are essential for our everyday physiological function. An individual may eat food with histidine, glutamate, and dietary fiber which are then bioactivated by gut bacteria in a way that helps to maintain gut integrity. Scientists are just beginning to realize how critical gut integrity is for normal immune function and the prevention of systemic inflammation. In irritable bowel syndrome (IBS), which is quite common, doctors now know that gut bacteria are dysregulated and that dysbiosis not only exists, but that it will impact the brain.

The biofilm in the colon, for example, can greatly affect the immune system. The colon is a long tube with several layers – the lumen, the outer layer, the inner mucus layer and the lamina propria. The lamina propria is where the final, outer coating of bacteria lies and it has a very powerful impact on the immune system. A very healthy immune system with good gut integrity and a secretory IGA will have gut homeostasis without a lot of inflammation. However, a person with microbial dysbiosis will experience a breakdown in that healthy barrier between the stool and the colon, which can result in increased inflammation.

A person with a healthy microflora in the colon will have enough good bacteria to outcompete pathogens. Some bacteria will even kill the pathogenic invading bacteria. Yet, a person who takes a round of antibiotics, for example, may eventually end up depleting these good gut bacteria and leave an opportunity for the small number of pathogens that flow through the gut every day to take hold. *Clostridium difficile* (*C. difficile*), vancomycin-resistant enterococci (VRE), toxins, salmonella, and shigella can all disrupt gut integrity and lead to systemic inflammation and endotoxemia.

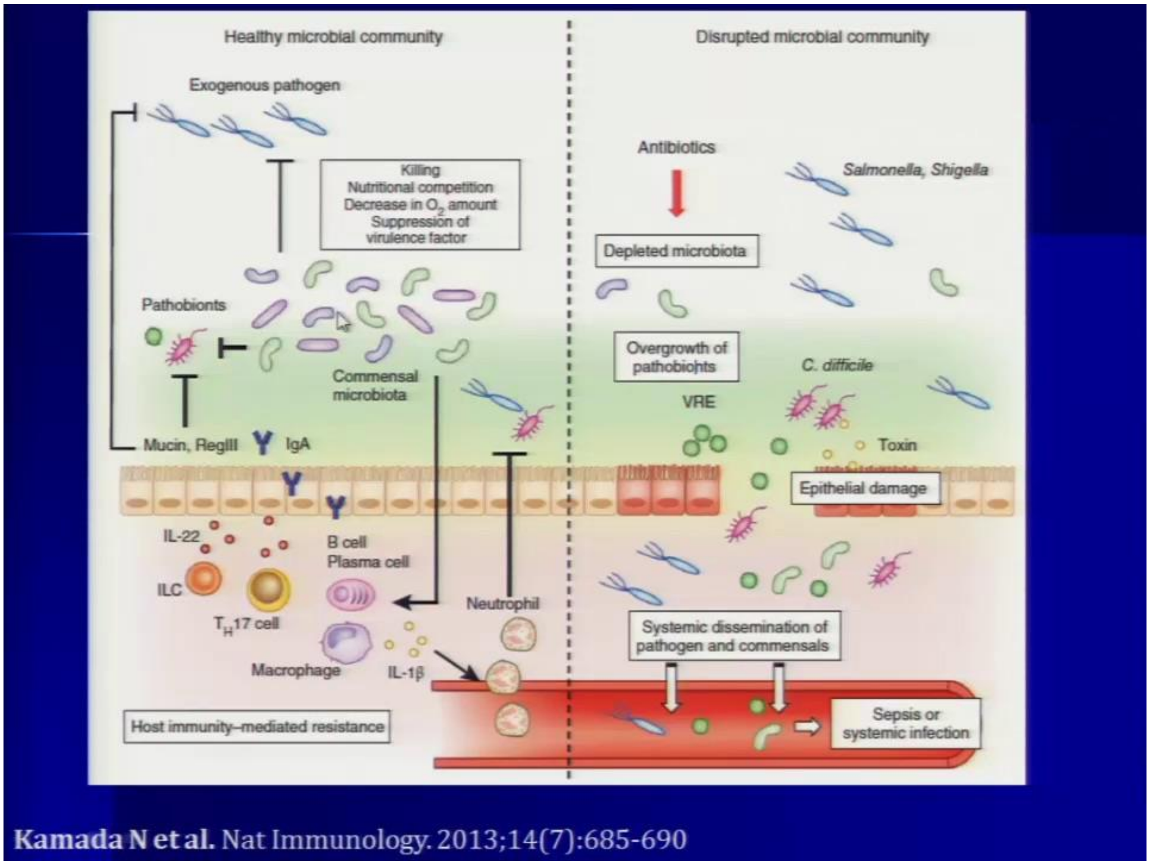

Figure 3

Dysbiosis and disease

When the gut becomes compromised through dysbiosis, the whole body may feel the effects. Scientists are only now beginning to discover and catalog the systemic damage caused by dysbiosis and to understand the mechanisms behind this damage.

For example, seminal experiments conducted by Dr. Martin Blaser at New York University found that administering antibiotics to animals increased their fat mass, but not their lean muscle mass. Meat producers in the U.S. had long noticed the correlation between weight gain and antibiotics confirmed in Blaser's experiments. A mechanistic explanation for how these gut bacteria can make people fat comes down to inflammation: antibiotics can lead to dysbiosis, which leads to inflammation. Inflammation can reduce insulin resistance and cause fat cells to store more fat molecules. Inflammation also decreases gut hormones that are protective against obesity, and decreases butyrate production.

Gastrointestinal issues associated with dysbiosis include gallstones, colorectal cancer, IBS, inflammatory bowel disease (IBD), gastric cancer and recurrent *C. difficile* infections. Other systemic health problems that may be linked to dysbiosis include anxiety and depression, hepatic encephalopathy, lymphoma, arthritis, asthma, autism, multiple sclerosis, chronic fatigue, diabetes, fatty liver disease and cardiovascular problems.

Exactly how dysbiosis contributes to these conditions may sometimes depend on an individual's diet. For instance, the connection between dysbiosis and accelerated atherosclerosis is likely connected to a Western diet. A diet rich in eggs and red meat will load the body with phosphatidyl choline and carnitine, which will then be metabolized to TMA, or trimethyl amine. The liver will then oxidize the TMA to TMAO, which will block the transport of cholesterol from your coronary arteries back to the liver. At this point, the cholesterol simply remains in the coronary arteries, thereby accelerating atherosclerosis.

In the case of obesity, how the gut microflora process carbohydrates may come into play in a phenomenon known as the carbohydrate salvage pathway. About 10 percent of the energy needs of an average person are sourced from the re-salvaging of undigested plant carbohydrates by the colon and by colon bacteria. Indigestible plant carbohydrates are first broken down by good gut bacteria and then salvaged through the removal of short chain fatty acids. The short chain fatty acids feed the colon, from which point any leftovers are directed to the liver where they are then converted into glucose and fat to be stored as additional energy. Recent studies have shown that different gut bacteria have different levels of efficiency with this process, and the gut microflora in those with obesity is predominantly firmicutes, which are phylum of bacteria, and very efficient fat-forming organisms.

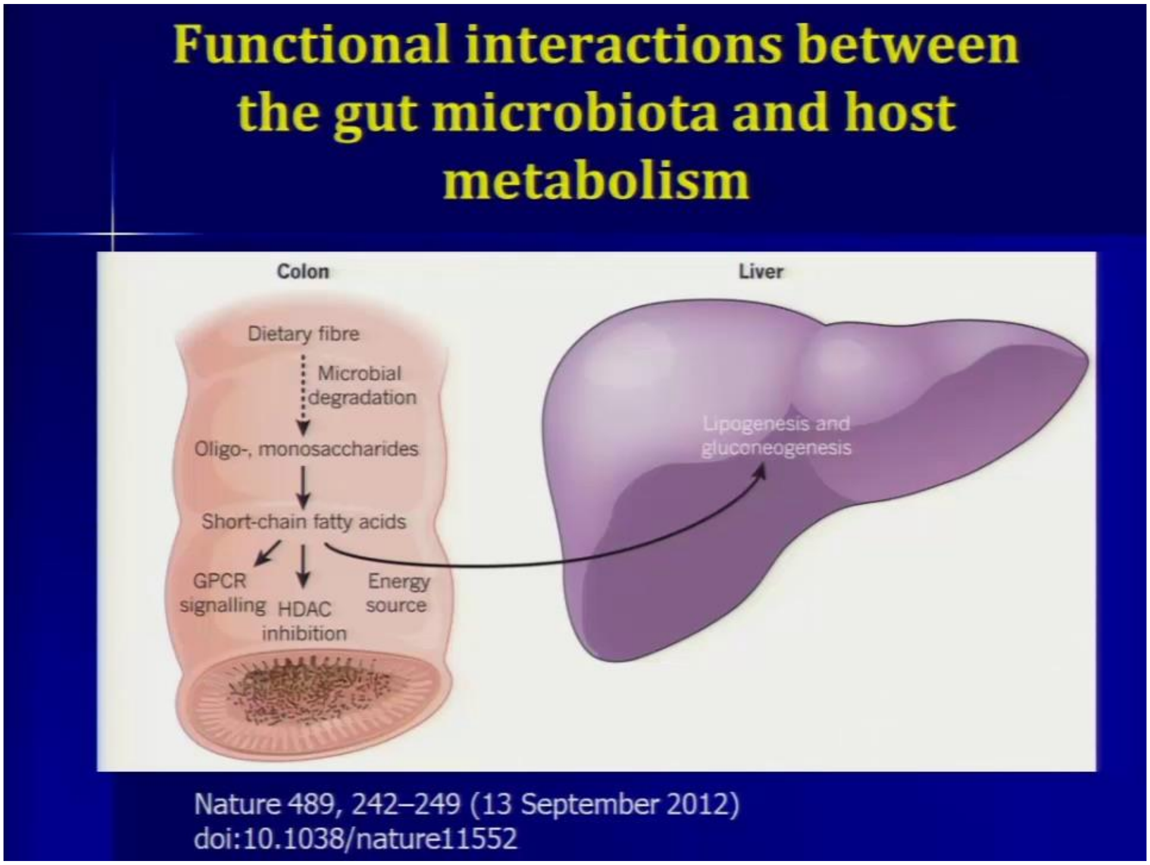

Figure 4

What disrupts the gut microbiome?

Many factors that influence gut microbes are outside of the control of an individual. People have little choice over whether they were born by cesarean, whether they badly need antibiotics, or which foods they ate as a toddler. However, many other factors that have been shown to cause dysbiosis can be altered by an individual.

Some medications seem to be especially risky for inducing dysbiosis. For example, about half of the patients with irritable bowel syndrome have a condition called small bowel overgrowth and the first line of treatment for IBS, among many general practitioners, is an antibiotic called rifaximin. There is evidence that rifaximin is useful for some immune-related disorders, such as Crohn's Disease, because it alters immunity. However, for non-immune related IBS, there is the risk that the medication could cause some permanent, unintended effects on the gut bacteria.

The proportion of macronutrients and micronutrients in an individual’s diet may also affect the microbiome. For example, a high protein diet may overproduce hydrogen sulfide, which is very toxic to the body because it can destroy the epithelium and make it leaky. High protein diets may work well in the short term, but in the long term there are some definitely dangerous after effects, including the possibility of an increased cancer risk. On the other hand, fiber in the diet will be broken down by gut bacteria and result in more short chain fatty acids that can protect against cancer. A diet high in saturated fat can induce primary bile acids, and those bile acids can be both neoplastic and contribute to dysbiosis, thereby making the body more inclined towards obesity.

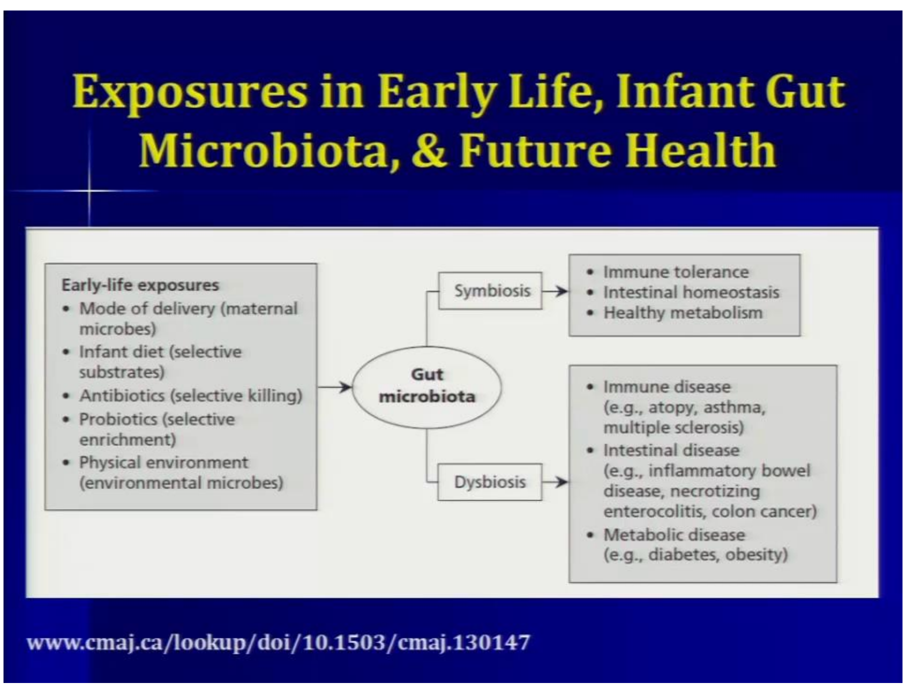

Figure 5

Drinking alcohol habitually and in excess may also be a cause of dysbiosis. Alcohol can alter gut permeability and cause endotoxemia, which is one of the leading causes of liver disease. In fact, animal studies have shown that taking probiotics can mitigate the dysbiosis effects of alcohol.

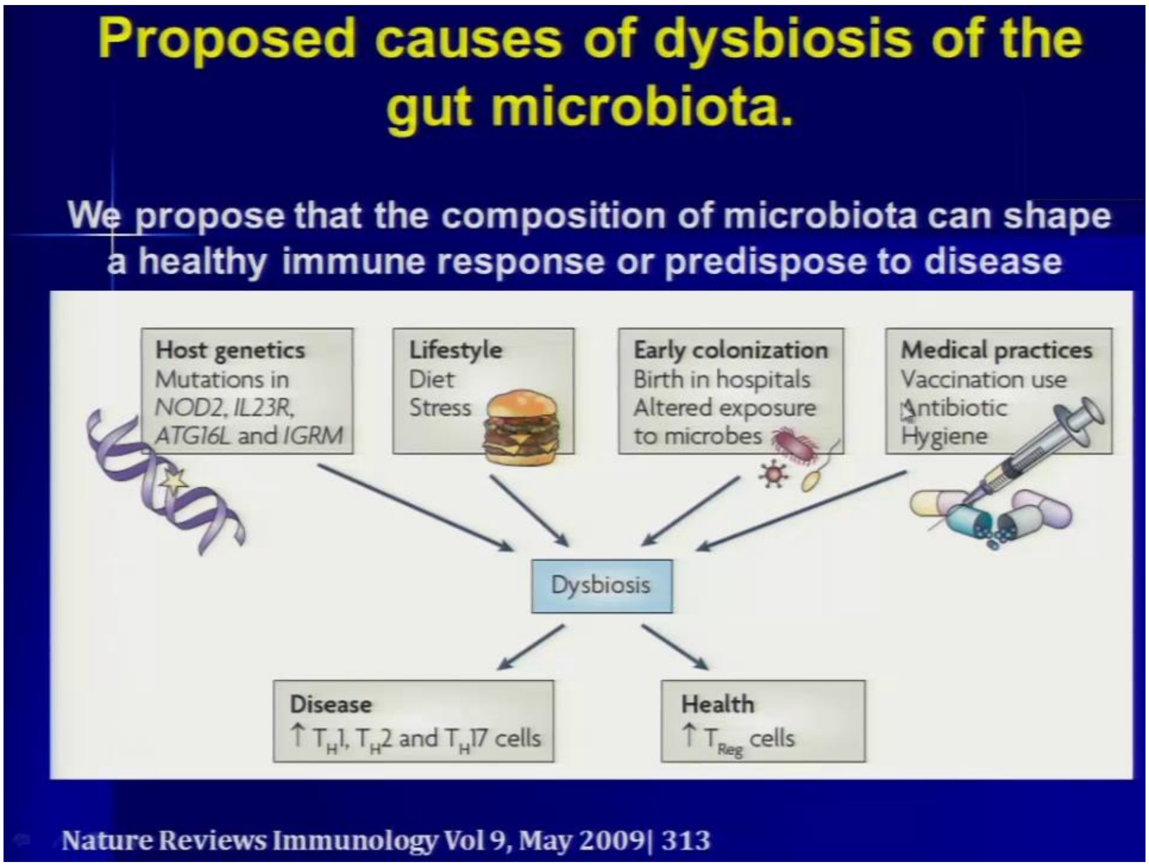

Figure 6

The metabolomic approach to treatment

For clinicians, the real crux of metabolomics is how to best use information to treat dysbiosis. Even in these early years of microbiome research, it is now possible to do some diagnostics and try therapeutic approaches for some patients. Commercial functional medicine laboratories can confirm whether an individual has a normal amount of beneficial bacteria or whether they have pathogenic bacteria. If a problem is found, rounds of probiotics can be recommended as a treatment to inhibit the growth of the bad bacteria, foster growth of the beneficial bacteria and alter the immunity and inflammatory conditions of an individual, all at the same time. If an individual has a pathogenic bacteria or small bowel overgrowth, another treatment route would be to prescribe antimicrobials. Antimicrobial herbs, for example, may represent a kinder, gentler approach to treating dysbiosis.

Take, for example, an anecdotal case study of a person who had been suffering with IBS for four years. Like many people with IBS, this woman had come to a sort of equilibrium with her symptoms by severely restricting her diet. She limited her diet to non-starchy vegetables, proteins and a little bit of fats. Yet, she only experienced moderate relief. Clinicians are well aware that IBS is a tricky diagnosis. About 50 to 78 percent of people who have IBS may actually be suffering from an undiagnosed issue such as food sensitivity, dysbiosis, parasites, a fungus, stress, or even neurotransmitter imbalances. This woman was prescribed an antimicrobial regimen commonly used to treat small bowel overgrowth, which included a combination of herbs, berberine, oil of oregano and black walnut. Within three weeks, her symptoms subsided and she was able to eat a variety of foods again. Treating dysbiosis can have a profound effect on a person's quality of life.

In another case, a middle aged man found relief from symptoms that, at first, seemed to have nothing to do with dysbiosis. This man had a long history of depression, and a more recent gastrointestinal issue that required the removal of most of his colon. Years before the colon surgery, the man had started to treat his depression with psychotherapy and various medications. In addition to depression, he also long suffered from chronic fatigue. However, once his colon was removed, his depression symptoms eased to the point where he could go off medication.

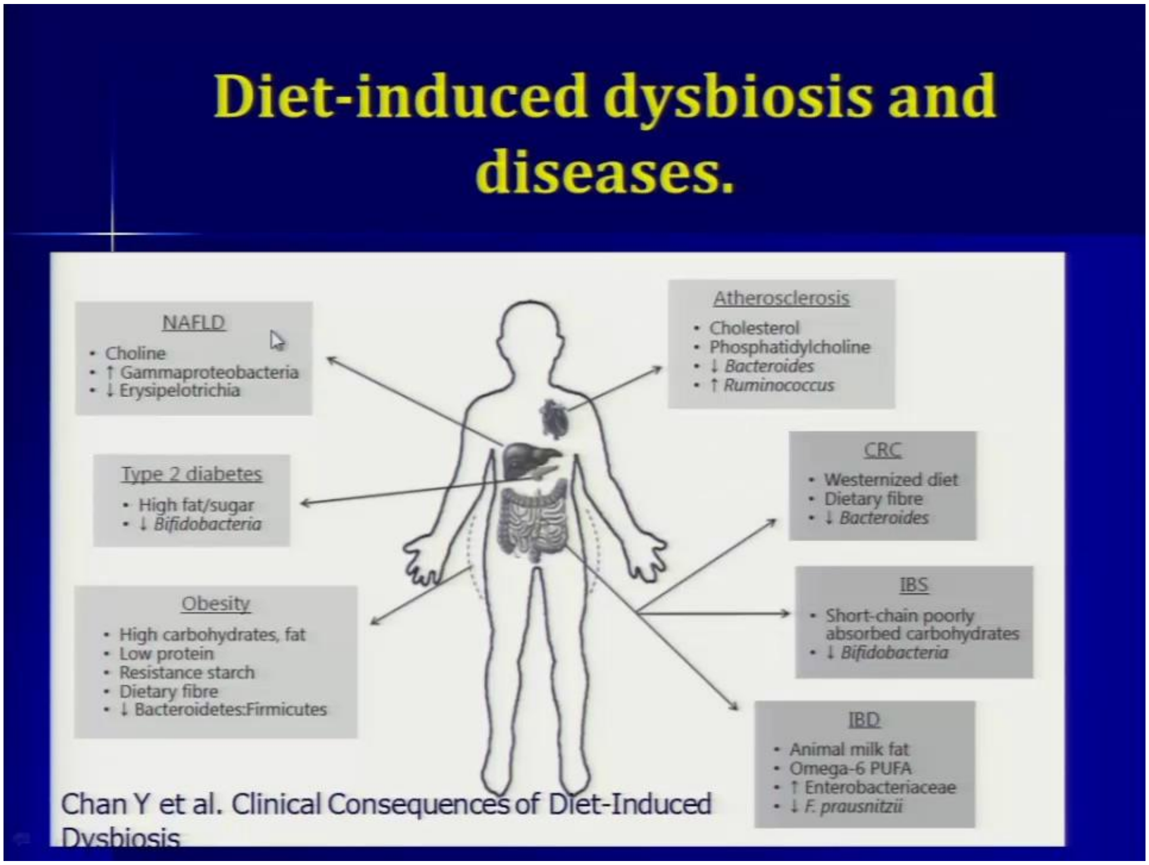

Figure 7

How to heal the gut microbiome

Early research has demonstrated that it is possible to change the make-up of the gut's microbiota by selectively eating food that nourishes certain strains and by eating selective healthy strains of bacteria.

According to a 2011 paper published in the journal *Science*, changes in a person's microbiome composition were detectable within 24 hours of starting a controlled diet. Researchers in the experiment gave participants either a high fat and low fiber diet, or a low fat and high fiber diet. This simple diet change resulted in small changes in the volunteer's gut microbiome nearly overnight. However, the study also found that long-term diet habits, and not short term changes, were more strongly associated with enterotypes. Specific diets known to alter the microbiome include a low FODMAP diet, the GAPS diet, the so-called paleo and ketogenic diets.

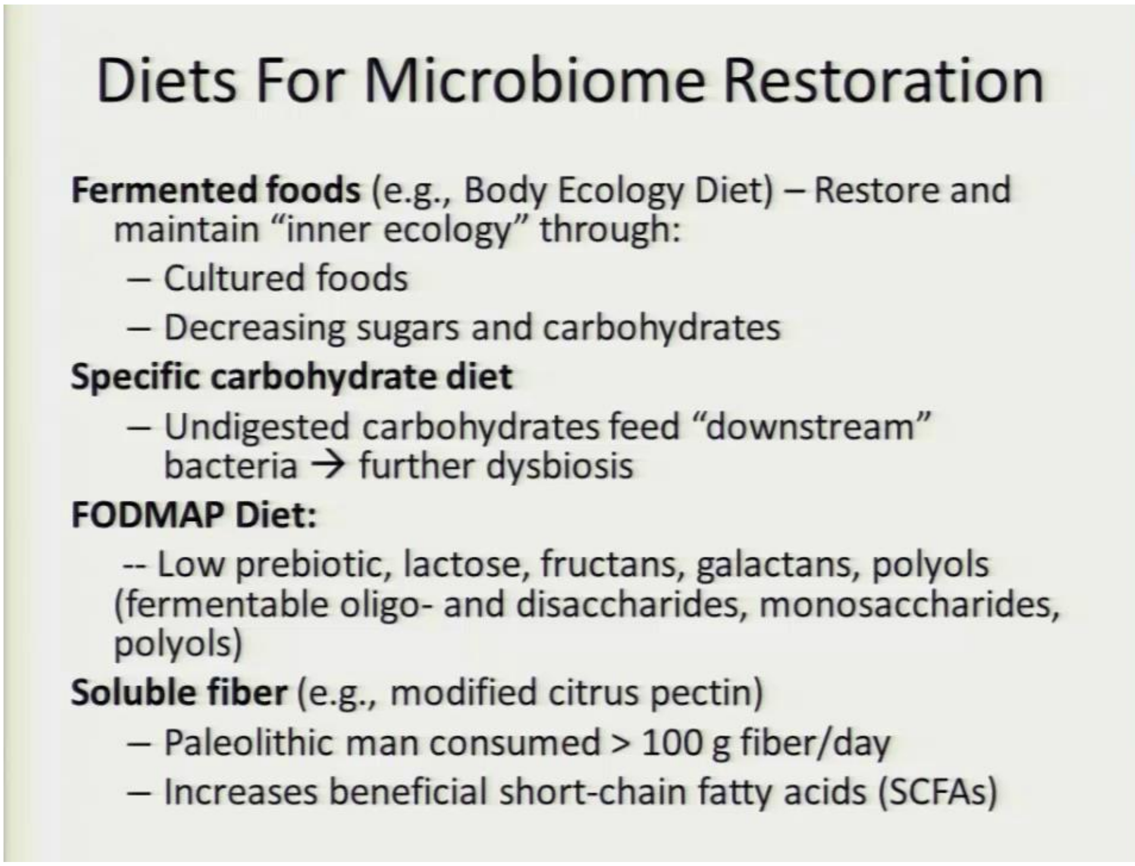

Figure 8

Old fashioned food storage and the gut

As the public learns more about the power of the gut microbiome, the popularity of probiotic supplements has also grown. Probiotics have been defined as microorganisms that convey a specific health benefit. They are typically identified at the level of the strain, such as lactobacillus acidophilus, and can be quite genetically different from each other. Common probiotic supplements include lactobacilli and bifidobacteria. The lactobacilli are more prevalent in the small intestine, while bifidobacteria are more prevalent in the large intestine. Some healthcare providers are turning to probiotic supplements for specific health issues; this includes using certain strains of bifidus for IBS. Additionally, some probiotics are now being recommended to restore colonies in the gut following an infection, such as 50 billion to 100 billion colony-forming units for a period of three or four weeks in a mixed strain probiotic supplement. Others recommend probiotics for health maintenance, on the order of 2 billion to 15 billion colony-forming units. As research into the microbiome continues, it is likely that clinicians will identify more strains of probiotics that can treat specific conditions such as IBS or eosinophilic esophagitis.

Figure 9: Traditional preservation techniques create probiotic foods

Probiotics play an important role in modulating the immune system and inflammation in the body. Probiotics are also crucial to the production of the B complex vitamins and the vitamin K that we use in our bodies. They help to detoxify arsenic, lead, and mercury from the body. Probiotics can shorten the duration of the cold and flu as well as assist in the digestion of lactose in dairy. Research has shown that probiotic strains move in and out of the gut within a few weeks. This means that to keep up a healthy microbiome, an individual should aim to eat probiotic foods several times a week.

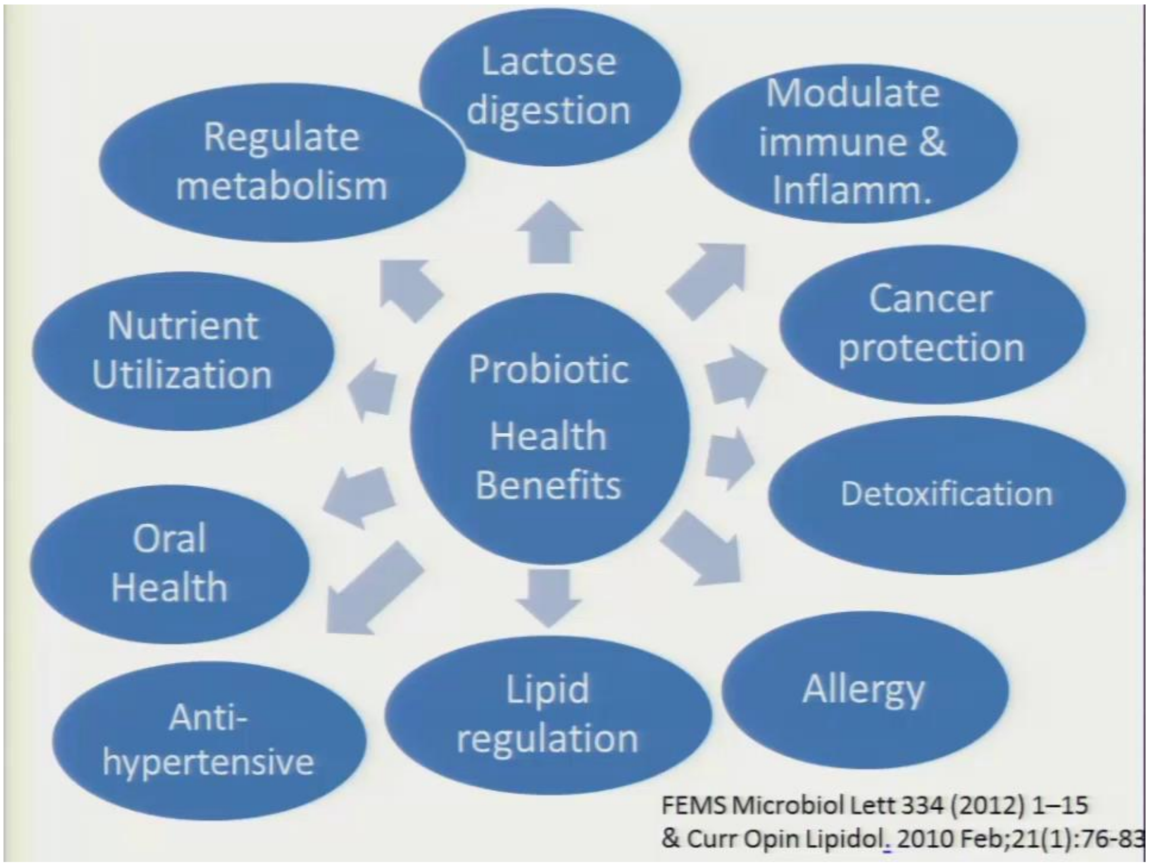

Figure 10

Probiotics do not exist solely in the form of supplements. In fact, until the advent of refrigeration, foods were regularly preserved through the fermentation process, thereby making them probiotic foods. These aged, fermented and pickled dishes span the globe; from the Hawaiian dish poi to sauerkraut, to kimchi, to aged meats or fermented dairy like yogurt or kefir. Miso, for example, has over 50 different types of bacteria in it. Even black tea has fermented leaves and healthy probiotics.

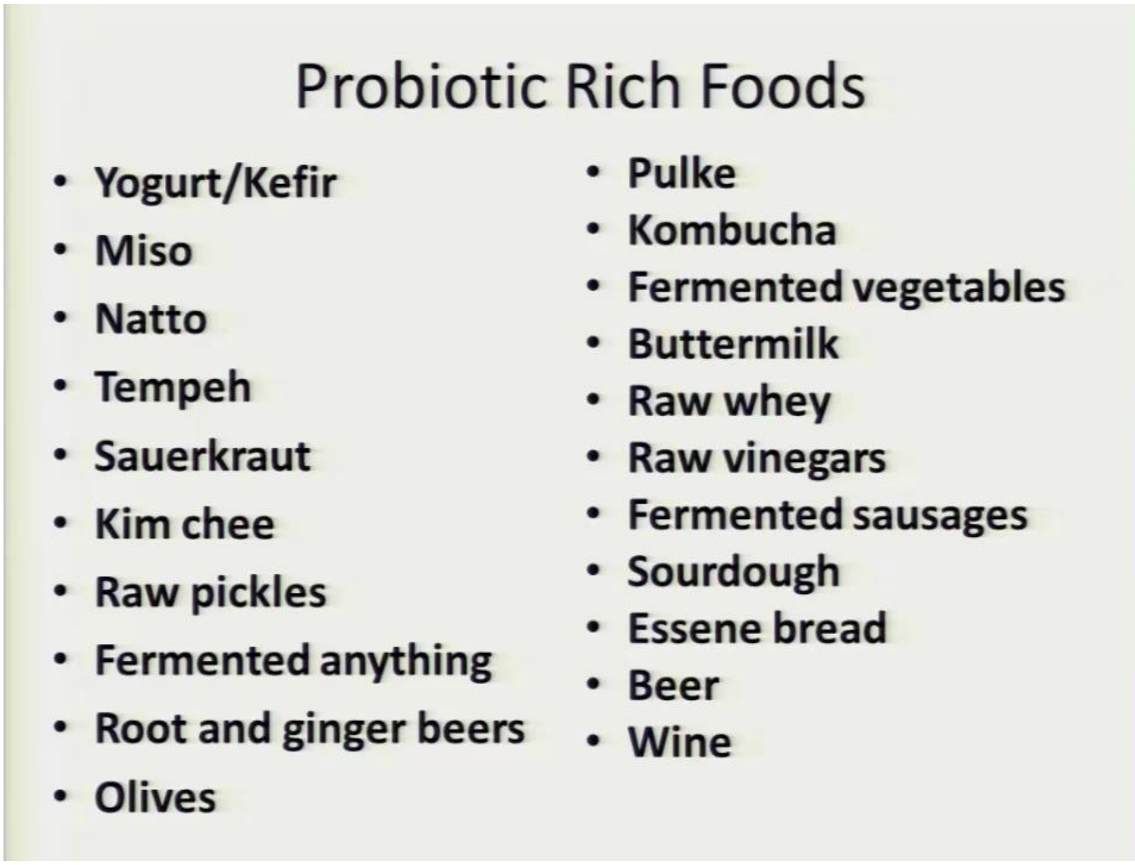

Figure 11

These foods were traditionally eaten for the sake of convenience and flavor, but for those who are concerned about getting enough probiotics in their diet, probiotic-rich foods can be made right at home. Easy recipes include pickles, where cucumbers are covered in a seasoned, salt water brine and left to sin in a sealed jar for several days before refrigerating. Kefir is another simple recipe: simply add dry kefir culture to warm milk, stir, and leave the solution sealed in a container at room temperature for 24 hours before refrigerating.

Prebiotics and their important role

When cultivating a healthy gut microbiome, it is important to also consider eating prebiotic foods. Prebiotic foods are primarily the plants that feed probiotic bacteria in the gut. Prebiotics help keep the gut microflora system balanced and they discourage the growth of clostridia and other pathogenic organisms. Most prebiotic foods have a low glycemic index, so they help regulate blood sugar levels. Some prebiotics may also lower ammonia levels in people who have liver illnesses such as cirrhosis.

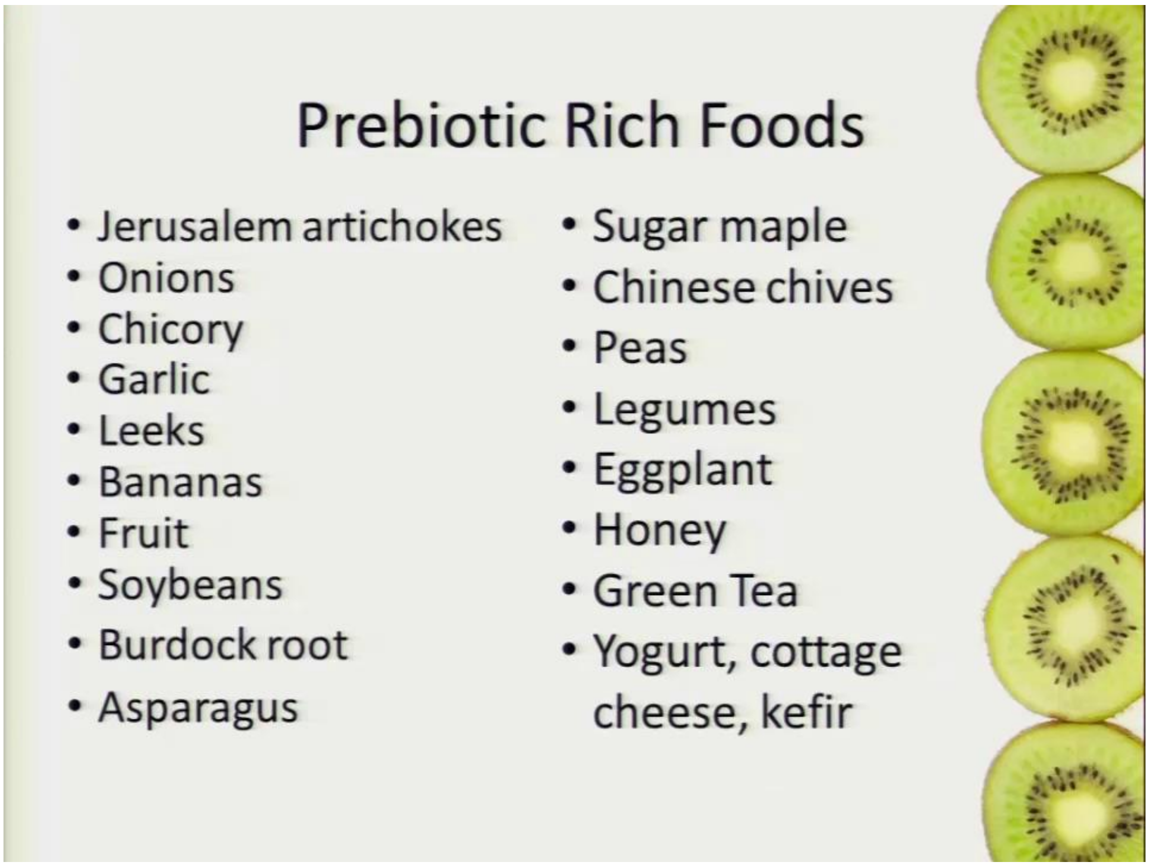

Figure 12

Beets, garlic, onions, and peas are all examples of prebiotic foods that provide starches for probiotic bacteria to digest. When individuals eat these foods, some of the starches go undigested into the gut, where they are taken up by probiotic bacteria such as bifidobacteria. The prebiotic fibers create short chain fatty acids to make butyric acid, which is used to maintain and renew every cell in the colon.

Artichokes, asparagus and ginger are also prebiotic foods that resist acid in the stomach. These foods aren't completely digested, but are partially fermented by intestinal bacteria.

In general, foods with plenty of polyphenols are also considered to be prebiotic. Polyphenols are often found in seasonings and fruits. Green tea, red wine, apples, and chocolate all have prebiotic polyphenols.

Conclusion

In truth, each person is not just an individual human but a walking ecosystem of human and microflora. Any attempts to keep a person healthy will require that they also create and culture a healthy gut microbe population. A balanced gut microbiome will deliver much needed nutrients and improve the immune system of an individual. However, there are a variety of common events that can disrupt this balance and cause dysbiosis.

Alcohol, antibiotics, extreme diets, lifestyle, and even hygiene can all play a role in dysbiosis. Early research shows that changing the macronutrients in a person's diet can influence the number of strains found in the gut within 24 hours. Fortunately, more practitioners are investigating ways to restore microbiome balance with probiotics. Several probiotic bacteria strains have been identified to help recolonize a person's gut, or even maintain a healthy microbial balance.

Prebiotics are another aspect to maintaining a healthy gut microbiome. Just as the food a person eats nourishes their body, it also nourishes the three-and-a-half to four pounds of microbes that live in their gut.

While more research into individual probiotics and prebiotic supplements is needed, there are plenty of traditional foods that can help restore a healthy microbiome. Probiotic-rich foods include sauerkraut, kimchi, kefir, yogurt and pickles. Prebiotic foods include teas, many fruits, many seasonings and even chocolate.

Biography

Gerard E. Mullin, MD, is an internationally recognized expert in integrative gastroenterology and nutrition, with more than 20 years of clinical experience. He is an associate editor of several nutrition and integrative medicine journals and is board-certified in internal medicine, gastroenterology, integrative medicine, functional medicine and nutrition. In 2009, Dr. Mullin was named by the American Dietetic Association as honorary member of the year. He earned the Grace A. Goldsmith award presented by the American College of Nutrition in 2011. Dr. Mullin is currently an associate professor of medicine at the Johns Hopkins Hospital in Baltimore, Maryland.

Liz Lipski, PhD, is a faculty member at the Institute for Functional Medicine (IFM) and is a special adviser to the National Association of Nutrition Professionals and the Autism Hope Alliance. Lipski is the author of several books, including "Digestive Wellness." She is board certified in clinical nutrition, holistic nutrition, and in functional medicine. Lipski offers webinar-based mentoring programs and advanced nutrition forums for clinicians through her company, Innovative Healing Inc. She is a professor of clinical nutrition and the director of Academic Development, Nutrition & Integrative Health at Maryland University of Integrative Health (MUIH).