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## INTRODUCTION

The microbiome is a term used to describe the microorganisms which live inside the human body, especially in the digestive tract, in health and disease. The human body contains 10 times more microbial cells than human cells. The total collection of microbial cells makes up less than 3% of body weight and about 3 pounds.

The human immune system is heavily influenced by the microbiome. Scientists are looking at connections between the microbiome and autoimmune diseases like diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, fibromyalgia, and possibly some cancers. Organisms in the digestive tract can also play a role in obesity, depression, schizophrenia, and bipolar disorder.

The Human Microbiome Project was launched by the United States National Institutes of Health in 2008. The ultimate goal of the project is to identify the relationship between the human microbiome and health and disease. The project is also sequencing the genes of the organisms within the human body. This is a big task as the number of genes involved could be 100 times the number of genes in human DNA.

The nature of the microbiome has profound effects upon health. A healthy microbiome makes for a healthy person. People with health problems of different types often manifest abnormalities in their gut flora. They often show lack of diversity of intestinal microorganisms, presence or overgrowth of pathogens, or unbalanced populations of gut microbes.

This newsletter provides an update on some of the key findings related to the Human Microbiome Project.

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# **BACTERIAL FLORA**

The lower part of the digestive tract is filled with bacteria. More than 90% of the bacterial population is composed of two classes of organisms, Firmicutes and Bacteroidetes.

Bacteroidetes are efficient at breaking down complex carbohydrates and plant fibers. They are not as efficient at extracting calories from food as Firmicutes. Firmicutes thrive on sugars and fats.

Firmicutes contains a large number of species associated with disease



and inflammation. Firmicutes bacteria are very efficient at extracting calories fom food. Those who are overweight or diabetic tend to have a gut bacteria dominated by this family.

Firmicutes not only increase the energy harvest from the gut, but they also alter genes affecting how calories are utilized in the body. A major component of the outer membrane of some bacteria in this family is a substance called LPS (or lipopolysaccharide).

# LPS

LPS stands for lipopolysaccharide. That big word simply means that the molecule is a combination of a fat and a sugar. LPS is a biological terrorist. It lights up the inflammatory pathways in the body.

LPS provides structural integrity for bacteria. It also protects them from being digested. LPS is a toxin which comes from within bacteria, hence it is called an "endotoxin". LPS is used in the laboratory to rapidly create an inflammatory state. All that is needed is to introduce LPS to the blood stream.

LPS elicits a strong reaction from the immune systems of animals. Humans are much more sensitive to LPS than most animals. Mice can tolerate an exposure a thousand times greater than what will induce shock in a human being.

The interaction of LPS with animal



immune systems results in the release of powerful inflammatory substances. Endotoxin has been implicated in the development of obesity and insulin resistance due to the induction of inflamma-

tation. LPS also increases intestinal permeability contributing to what has been called "leaky gut".

Portions of LPS are also very similar or identical to cell surface molecules of human beings. The ability of bacteria to produce substances on their surface similar to host tissues is called molecular mimicry and is associated with the development of autoimmune conditions like multiple sclerosis and rheumatoid arthrtis. Molecular mimicry is a defense mechanism utilized by pathogens to redirect the lethal activity of the immune system to the host organism rather than toward the invading pathogen.

Bacteria containing LPS inhabit the digestive tract of everyone. It is normally prevented from entering the blood stream by a structure called the "tight junction" in the lining of the intestine. The integrity of the tight junction can be breached by a number of factors including toxins, gluten intolerance, or vitamin D deficiency. These factors create a "leaky gut" leading to all manner of inflammatory problems.

Injections of LPS into laboratory animals leads to accumulation of beta-amyloid in the brain tissue. This is a marker for Alzheimer's. Studies have shown that Alzheimer's victims have 3 times higher LPS levels in their blood than normal healthy controls. Elevated levels of LPS have also been associated with ALS (Lou Gehrig's disease and Parkinson's disease.

LPS generates free radical production in the mitochondria when energy is produced in brain and nerve cells. This suggests a role for antioxidants such as polyphenols in reducing the neurological damage which can be induced by elevated levels of LPS in the blood. The ultimate protection against LPS is to restore a healthy gut which does not allow LPS into the bloodstream.

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# FAT AND THIN

More than 1 in 3 American adults are obese (36%). Almost 1 in 5 children and adolescents (17%) are also suffer with obesity. Scientists are increasingly looking at the bacteria in the gut as contributors to the problem of obesity.

Researchers have transfered the bacteria from lean mice into obese mice and the obese mice become lean. Conversely, when the bacteria in the digestive tract of obese mice are transplanted into thin mice they become obese.

Animal studies are supported by the evidence of bypass surgery. The surgery changes the bacteria in the digestive tract which may partially explain the success of the surgery.

Children in rural Africa are rarely obese. A classic study was published in 2010 comparing the bacteria in the digestive tract of African children compared to European children. The African children had far more bacteria from the Bacteroidetes family and far fewer from the Firmicutes family than did European children.

Some of the bacteria in the gut of African children were efficient at breaking down plant fiber. These bacteria were completely lacking in European children. The researchers concluded that the bacteria in the gut of the African children allowed them "to maximize energy intake from fibers while also protecting them from inflammations and noninfectious colonic diseases."

The bacteria in the gut of African children did not allow them to extract calories as efficiently as the bacteria in the guts of European children.

There were also dramatic differences in short chain fatty acids produced n the digestive tract by the different bacteria in Europeans and Africans. The most prominent fatty acid in Europeans was propionic acid while in Africans acetic and butyric acids predominated. Propionic acid is produced by less friendly bacteria and can contribute to problems. Butyric acid is a key nutrient for the cells that line the colon.

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# Propionic Acid

Propionic acid derives its name from Greek two words: protos (first) and pion (fat). It is the smallest acid that exhibits the properties of a fat thus the "first fat". Propionic acid is a very small molecule which be-





haves in many ways like alcohol, for example, it can easily bypass the blood brain barrier.

S o d i u m propionate, a substance similar to propionic

acid, is widely used to protect bread, dairy products, and animal feed from molds.

Propionic acid is also a byproduct of the activity of certain bacteria as they feed in the human digestive tract. Bacteria with the ability to produce propionic acid are called Propionibacteria. One of these bacteria is the principal cause of acne.

Children with autism are often observed to be populated with specific species of Propionibacteria. Exposure to propionic acid can come from fermentation of carbohydrate in the digestive tract or by consumption of foods which contain it.

A rare genetic disorder exists called propionic acidemia. In this disorder propionic acid alters gene expression and causes neurologic damage. Many short chain fatty acids are produced in the digestive tract by bacteria. Researchers have focused on this one because it seems to have the most effects that relate to autism.

## DERRICK MACFABE

The research of Derrick Mac-Fabe and his associates is considered among the 50 greatest research projects ever to have been conducted in Canada. MacFabe's research suggests that propionic acid may be a contributor to the development of autistic behavior.

Bacteria which produce propionic acid have been isolated from autistic children. Propionic acid can enter the brain and alter cell to cell communication in a number of ways.

MacFabe introduced a tiny quantity of propionic acid into the brain of rats resulting in behavior characteristic of autism including hyperactivity, object fixation, social impairment, and repetitive behavior. Rats started running around in circles and walking in reverse. When two animals were placed in a cage together they ignored each other. The rats would learn a maze, but they could not unlearn it. The rats also preferred to spend time with objects and even had favorite objects.

Propionic acid was also found to lead to oxidative stress and reduction of the antioxidant glutathione in the brain. The likelihood of tic and seizure activity was also increased. Propionic acid also profoundly altered the fatty acid composition of the brain.

Propanol, an alcohol almost identical to propionic acid, had none of these behaviroal effects. The behaviors also disappeared as the propionic acid was metabolized.

Focus on the bacteria in the gut grew out of the observation that children with autism frequently suffer with severe digestive disturbances. They also can become very rigid in their dietary preferences eating large quantities of sugar, wheat products, or dairy items which can favor the growth of bacteria which produce propionic acid.

Another factor which suggests that gut bacteria may play a role in autism is *sudden improvement* which has been noted in some children when carbohydrates are restricted or when they are given antibiotics.

The researchers are looking at other fatty acids produced by bacteria. They are also extending research to look at the long term developmental effects when young animals are exposed to elevated propionic acid levels. Excess of this substance during the crucial developmental period may contribute to lifetime abnormalities such as are seen with autistic children.

Gut bacteria can be altered by many factors. Antibiotics can completely alter the bacteria in the digestive tract. Being born by C-section and lack of breast feeding can also have profound effects upon gut bacteria.

The interaction of bacteria in the gut is very complex and we are only beginning to understand the relationships between different organisms.

Increased gut permeability may also play a role in the behavioral disturbances we have been discussing. Deficiency of vitamin D or intolerance to food constituents like gluten can increase gut permeability leading to increased absorption of bacterial toxins into the bloodstream.

The introduction of genetically modified foods seems to parallel the increased incidence of autism. Residues of the herbicide glyphosate found in genetically modified crops have been shown to alter intestinal bacteria. One of these changes is an increase in the numbers of bacteria associated with botulism. This has become a problem among food producers in Germany.

Sodium propionate has recently been approved for use as a preservative on meats and poultry.

MacFabe suggests that the problem could be too much of a good thing. Too much learning becomes obsession and too much vigilance becomes anxiety.

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## BUILDING A HEALTHY MICROBIOME

The health of the microbiome can be improved in almost everyone by making a few simple lifestyle choices. Firstly, add fermented foods like yogurt, kimchi, tempeh, and sauerkraut to the diet.

Secondly, reduce the intake of refined sugars and carbohydrates, while increasing the intake of complex plant carbohydrates with their natural fibers. Healthy fats as found in avocado, nuts and olives will also promote beneficial bacteria. Avoid junk fats.

Thirdly, supplement the diet with sources of polyphenols and fla-

vonoids. These powerful antioxidants found in tea have been shown to positively promote diversity of microbes in the digestive tract while suppressing pathogens. Polyphenols also reduce the inflammatory activity in the gut.

Fourthly, increase the intake of prebiotics or food beneficial bacteria can feed upon. This includes garlic, onions, leeks, Jerusalem artichoke and many other fiber rich foods. The mucilage in Aloe vera is such a potent prebiotic that researchers have suggested adding it to a variety of food products. Healthy fiber intake also promotes a normal transit time which prevents the overgrowth of bacteria in the colon which can lead to toxin accumulation.

Fifthly, drink pure water. The chlorine and fluorine in many drinking water supplies is sufficient to kill off beneficial gut bacteria.

Finally, periodic fasting or caloric restriction has been shown to promote beneficial bacteria associated with an increased lifespan. Undereating also prevents overgrowth of bacterial populations in the gut due to reduced material to feed upon.

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