Inside Tract®

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The Brain-Gut-Microbiome Axis

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Gastrointestinal Society
Canadian Society of Intestinal Research

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ABOUT US

WHO WE ARE

The GI (Gastrointestinal) Society and the Canadian Society of Intestinal Research (CSIR) are registered Canadian charities committed to improving the lives of people with GI and liver conditions, supporting research, advocating for appropriate patient access to health care, and promoting gastrointestinal and liver health.

THE INSIDE TRACT®

The *Inside Tract®* newsletter is our primary tool for delivering up-to-date medical information, in lay terms, to the Canadian public in English and French. Subscribe now for a low annual fee of $20 on our website www.badgut.org or complete the mail-in form on page 23.

KEY TOPICS

We've been providing information to the public since 1976 and have a very wide range of free resources, articles, and tools online and in print on:

- Aging Digestive Tract
- Biologics & Biosimilars
- Celiac Disease
- *Clostridium difficile* Infection
- Colorectal Cancer
- Constipation
- Crohn's Disease
- Diverticular Disease
- Dysphagia
- Eosinophilic GI Disease
- Functional Dyspepsia
- Gastroparesis
- GERD (reflux & heartburn)
- Hemorrhoids
- Hepatitis B & C
- Hiatus Hernia
- Inflammatory Bowel Disease
- Intestinal Gas
- Irritable Bowel Syndrome
- Lactose Intolerance
- Medical Cannabis
- Non-Alcoholic Fatty Liver Disease
- Pancreatic Exocrine Insufficiency
- Pancreatitis
- Short Bowel Syndrome
- Ulcer Disease
- Ulcerative Colitis
- Ulcerative Proctitis

FREE PRINTED INFORMATION

Contact us today to request some specific free information, or check us out online and on our social media platforms for the latest digestive health news. Health care professionals can order these pamphlets in bulk online.

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President & CEO Report

Gail Attara, Gastrointestinal Society

This year we are very busy with BadGut® Lectures. We have added a new topic to our series, Medical Cannabis. These talks cover information on the potential benefits and risks of using cannabis medicinally to treat gastrointestinal diseases and disorders. Dr. Alan Low, a Vancouver-based pharmacist is presenting these talks. We had our first lecture on the topic in Vancouver, BC, with more than 350 attendees, on June 10. Our next Medical Cannabis lecture will be in Ottawa, ON, on July 30, with more to come.

Additionally, we have several lectures scheduled on our usual topics. We had a lecture on Crohn's Disease and Ulcerative Colitis in London, ON, on June 17, and have another lecture on that topic scheduled for August 12 in St. John's, NL; September 5 in Prince George, BC; and November 19 in Toronto, ON. Another lecture, this one on Irritable Bowel Syndrome, is scheduled for July 29 in Ottawa, ON. If you aren't able to make it, but are interested in the topic, we recorded the main presentation from our Vancouver lecture in April. You can view this at www.badgut.org/badgut-lecture-ibs/.

We'll be adding more lectures between now and this autumn. If you want to stay up to date with the schedule of our BadGut® Lectures, visit www.badgut.org/events/lectures or join our e-newsletter to get updates at www.badgut.org/email-sign-up/.

The Advisory Council on the Implementation of National Pharmacare released their Final Report, *A Prescription for Canada: Achieving Pharmacare for All*, on June 12. As the council pursued its dialogue with Canadians, in which the GI Society participated, it became clear that the issue is not whether Canada needs national pharmacare, it's how Canada should move forward to create it. This report is therefore about a plan for building national pharmacare.

It begins with an examination of the state of drug coverage in Canada, outlines its challenges, and describes necessary improvements. The report presents what national pharmacare might look like and lays out a detailed plan and timetable, including recommendations to government about how they should implement and finance national pharmacare. It concludes with a summary of what national pharmacare will mean for Canadians. I encourage you to search for the report online and see the changes in our future.

In Memory

Dr. Frank H. Anderson

1938-2019

We are saddened to announce the passing of Dr. Frank H. Anderson on April 1, 2019, just ten days short of his 81st birthday. Dr. Anderson dedicated his career to making the world a better place for individuals with digestive and liver diseases and disorders. In 1976, he co-founded the Canadian Society of Intestinal Research (at the time called the Northwestern Society of Intestinal Research) as a means to encourage more research on the taboo topic of gastrointestinal disease so that people wouldn't have to suffer or die as a result of their conditions. He was also the first chair of our Medical Advisory Council and co-founder of the Gastrointestinal Society in 2008. He mentored many students through the gastroenterology program at the University of British Columbia. He continued to serve as a member of the Medical Advisory Council and a Board Member until his retirement in 2014; for nearly 40 years he was a cornerstone of the work we do at CSIR and the GI Society.

"I say to patients, it's not my disease, it's your disease, and the more you know about it, the better you can deal with it."

~Dr. F. H. Anderson

Dr. Frank Anderson and Walter McNeish in 1978

Doris Raeside and Dr. Frank Anderson in 1976

"The vision I had for the Society in 1976 was a vehicle to be able to provide education to patients and education to the public and to raise funds for research in gastrointestinal diseases, and to provide a vehicle that was not doctor driven but which was patient and public driven."

~Dr. F. H. Anderson

Dr. Anderson wrote our first pamphlets on *Inflammatory Bowel Disease*, *Functional Bowel Disease* (now known as *Irritable Bowel Syndrome*), *Hepatitis*, *Intestinal Gas*, *Hiatus Hernia*, and *Ulcer Disease* in 1976. At that time, patient information such as this was basically unheard of, with most patients only learning about their disease through the scarce minutes they had at doctors' appointments. Throughout his life, he focused on empowering patients and helping them to better understand what it meant to be diagnosed with a digestive disease or disorder and was an early leader in study of the liver, back when what we now know as hepatitis C was called 'non-A, non-B hepatitis virus'.

Two of his patients have shared with us their stories of meeting Dr. Anderson, and how he changed their lives by listening and helping them understand their gastrointestinal conditions.

"Before being referred to Dr. Anderson, I can't recall just how many days of excruciating pain I endured, which led to many, many incidents of having to take a sick day. My GP learned about Dr. Anderson and made the referral and I never looked back. Dr. Anderson interviewed and examined me in his thoughtful and patient way and said "Well, it's like this: Do you know colicky babies? They suffer gastric pain when they eat something that doesn't agree with them and cry a lot as a result." Dr. Anderson told me that when my digestive tract sensed something it didn't like, it went into spasm, causing this terrible pain. He prescribed me a medication, which I took for a time and it was excellent at easing the spasms. I will be forever grateful to Dr. Anderson for his diagnosis and putting my mind at ease."

~M.McR.

"I first met Dr. Anderson when I was admitted to Vancouver General Hospital with a total intestinal obstruction. While the surgeon on duty was anxious to 'get inside to cut things out,' Dr. A. held the surgeons at bay. With time and his wisdom to most accurately and correctly assess the situation, he put me on a course of medication and followed me until his retirement. I'm ever so grateful for his wisdom to this day."

~A.H.

Dr. Anderson with his family and friends at the Inside Affair in 2017.

Dr. Anderson has contributed so much to the Society, as well as to the field of gastroenterology through his efforts in research and his unique approach to patient care.

During our Inside Affair in 2017, we honoured Dr. Anderson's achievements and contributions to the two charities he loved. Many of his former patients attended this event, some of whom had first met Dr. Anderson decades previously, and came to honour the physician who helped them gain control of their lives after developing a devastating gastrointestinal condition. We recorded Dr. Anderson for a video for that event, which you can watch at www.badgut.org/dr-frank-h-anderson. You can also make a donation to the Gastrointestinal Society in honour of Dr. Anderson at www.badgut.org/donate.

Support Group

Please call the Gastrointestinal Society office to check if the support group you are interested in attending is running for the month.

Inflammatory Bowel Disease (IBD)
7:00 pm, third Wednesday of each month
231-3665 Kingsway, Vancouver, BC

The Inside Affair

badgut.org

For more than 40 years we've been the Canadian leaders in providing trusted, evidence-based information on all areas of the gastrointestinal tract. The Gastrointestinal Society and the Canadian Society of Intestinal Research are committed to improving the lives of people with GI and liver conditions by supporting research, advocating for appropriate patient access to health care, and promoting gastrointestinal and liver health.

In 2019, we are hosting two Inside Affairs: one in Vancouver and one in Toronto. These networking events allow business, healthcare, and patient communities to come together to show support and generate essential new funds for the Gastrointestinal Society's charitable work.

Vancouver

Date **Tuesday, November 5**

Time **Reception 5:30PM** | Dinner 6:00PM

Location

Delta Hotels Conference Centre

4331 Dominion Street, Burnaby, BC

Featuring

Mitch Moneo, Assistant Deputy Minister, BC Pharmaceutical Services Division

Honouring

Dr. James Gray, gastroenterologist and long-standing chair of our medical advisory council

With music by Reid Jamieson

Toronto

Date **Monday, November 18**

Time **Reception 5:30PM** | Dinner 6:00PM

Location

Fermenting Cellar

28 Distillery Lane, Toronto, ON

Featuring

Dr. Brian O'Rourke, President & CEO, Canadian Agency for Drugs and Technologies in Health (CADTH)

With comic relief by Evan Carter

Tickets are $200 (includes a $100 tax receipt)

www.badgut.org/events **1-866-600-4875**

Top 3 Reasons to Get Cannabis from a Medical Source

If you have a gastrointestinal disease or disorder, and you've tried several treatment options without achieving the symptom relief you are looking for, you might be interested in trying medical cannabis. As we've mentioned before, the area of cannabis for medical purposes is complex. There is some evidence that it can help with symptoms such as abdominal pain, nausea, and reduced appetite, but not enough definition in the literature on dosage, long-term efficacy, safety, and other aspects. Now that recreational cannabis is legal in Canada, you might be tempted to go to a recreational shop and just purchase some to try and treat your condition. However, if you want to use cannabis medically, it is best to consult healthcare experts instead. Healthcare experts who are licensed practitioners, such as nurses, pharmacists, and physicians, must follow strict rules to provide accurate and evidence-based information to help you. Unregulated representatives may not have rules they must follow in providing information. Below, we've listed our top three reasons to talk to your doctor before trying medical cannabis.

Better Information

When you buy cannabis from recreational sources, you are just purchasing a product, and getting no medical information or guidance. The retail staff are not medical experts and it is their job to sell product, predominantly for a recreational purpose, not look out for your medical issues. This means you won't get the detailed, evidence-based information and advice you would get for the type of medications you pick up from a pharmacy. However, if you speak with your healthcare team, they can help figure out the best cannabis products for your unique medical situation. This can include assistance managing various factors, such as when and how to start treatment with cannabis, what type of cannabis, dosage, frequency, and method of administration are ideal for you, and whether there are any risks of interactions with cannabis and other medications you use. Your healthcare team can monitor your symptoms and ensure that cannabis is working for you, and make changes to the strain or dose as necessary, including any change in ratio of THC to CBD. You might even be able to stop taking other medications you had been taking and only your healthcare professional can assist with this deprescribing.

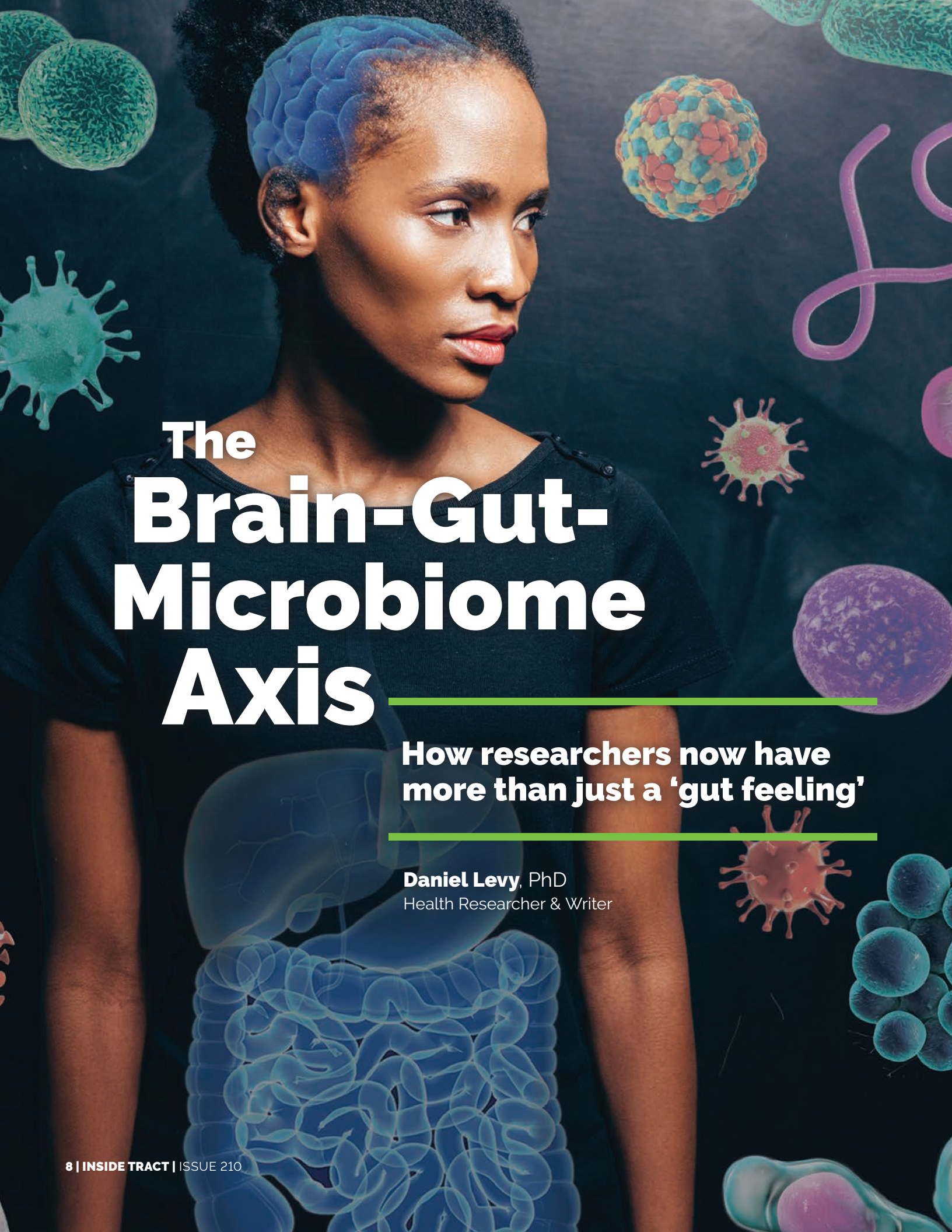
Access to Federally Licensed Producers

If your physician (or nurse practitioner, in certain provinces) decides that medical cannabis is a good choice for you, they will complete a Medical Document and submit it directly to a federally licensed producer. You can also transfer this document to other federally licensed producers. Purchasing through these channels ensures that you are getting good quality product, and that you know the amount of different compounds, such as cannabinoids (including THC and CBD) and terpenes, in each strain. Federally licensed producers have products which are better standardized and more reliable than other sources.

Increased Access

If your healthcare provider authorizes medical cannabis for you, then you can access it by buying directly from a federally licensed seller, but you can also register with Health Canada to produce your own cannabis for medical use. This allows you to grow a larger amount than is available to those who use cannabis recreationally, based on your recommended cannabis dosage. In addition, you are allowed to designate someone else to produce it for you. There are no limits on the amount of cannabis you can store in your home, as long as it is away from children, when you are using licensed medical cannabis. You can also carry more cannabis in public, with a limit of the lesser of 30-day treatment supply or 150 grams of dried equivalent (in addition to the 30 grams non-medicinal cannabis allowed).

Note: Not all physicians are supportive of medical cannabis, often due to the lack of clinical study and evidence. Since there is still a lot we don't know about proper medical use, some refuse to recommend it for their patients. In this case, if you are interested in cannabis, we recommend speaking with other members of your healthcare team, such as a pharmacist or nurse practitioner for advice. It might be that cannabis isn't a good idea for you. If this isn't the case, then you can consider contacting a physician who is comfortable prescribing cannabis, or seek out a Medical Cannabis Clinic online.



The Brain-Gut-Microbiome Axis

How researchers now have more than just a 'gut feeling'

Daniel Levy, PhD
Health Researcher & Writer

Biology is like a ball of string; as researchers unravel one aspect of the vast bundle that constitutes their field of work, they reach another tangle. To cope with this complexity – and as scientific understanding advances – scientists and physicians have become increasingly specialized within particular areas of research, which have themselves grown incredibly sophisticated. The result has been a huge leap forward in the ability of researchers to study specific aspects of biology, and of physicians to treat specialized conditions as never before. These scientific advances are influencing all areas of research and healthcare, from neuroscience and immunology, to endocrinology and gastroenterology.

Perhaps predictably, and fuelled by advances in 'big data' and genomic technologies, recent discoveries have reiterated that specialized areas of biology are, in fact, interconnected – they are knots made on the same ball of string. To build upon advances in individual fields of research, scientists and physicians must now adapt and learn to understand the ways in which their fields interact. One such area of study is the relationship between the brain and the gastrointestinal tract, and the communication that takes place between the two through the brain-gut axis.

The Brain and the Gut Do Not Exist in Isolation

Many aspects of the brain and the central nervous system are unique. The complex organization of neurons within our brains account for our very consciousness, our ability to perceive the world around us, to learn, and to form relationships.[1] The brain also enjoys a level of physical isolation from the rest of the body; a barrier separates the brain from circulating blood, providing protection for its delicate neurons.[2] External pathogens such as bacteria, and even the body's immune response against such pathogens, have limited access to the brain through this barrier. For many years, scientists had considered the brain to be completely isolated from the body's immune response – a view that is now changing. In reality, and in spite of its unique nature, the brain and the central nervous system serve many functions that require close communication with the rest of the body: from the conscious contraction of our muscles, to the unconscious beating of our hearts, and the regulation of our temperature.[3,4] One particular line of communication from the brain that researchers have been focusing on in recent years is that with the gut.

The gut contains neuronal connections with the brain and the central nervous system throughout its length, with perhaps the most interesting region of interaction being at the intestinal tract.[5] The intestines have their own specialized functions, including the absorption of nutrients from digested material within the small intestine, and extraction of water in the large intestine. From the point of view of the nervous system, many intestinal functions are controlled by the enteric nervous system – a collection of neurons that is able to function separately, at least to an extent, from the brain and the central nervous system, and so is sometimes referred to as the body's 'second brain'.[5,6] The very existence of an enteric nervous system, as well as the connections that exist with the brain, exemplify how gastroenterology and neuroscience cannot be considered truly distinct areas of study.

Microbiome

The human microbiome is a community of trillions of microbes – different species of bacteria, archaea, fungi, viruses, and protists – living in and on various areas of the body.

The Microbiome Resides Largely Within the Colon

Interest in the interactions that take place between the gut and the brain has grown with the discovery of the important role that intestinal communities of microbes play in human health. A healthy human gastrointestinal tract contains over 1 kg of microorganisms, corresponding to more than

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2 Daneman R, Prat A. The Blood–Brain Barrier. *Cold Spring Harb. Perspect. Biol*. 2015;7:a020412.
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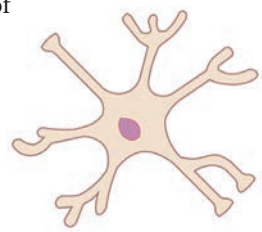
100 trillion in number – the most studied of which are bacteria.[7,8] To put this number in perspective, our guts contain significantly more bacteria (which are extremely small), than our bodies contain human cells. The vast majority of these microorganisms are present in the large intestine, and together constitute what is known as the human microbiome.[8] While the microbiome is flexible, changing with age and in response to factors such as diet, it can also be considered stable, in that healthy communities of different bacterial species become established – co-existing, and supporting both each other and their human host. In this way, the microbiome is dominated by 'friendly' species of bacteria which include *Firmicutes, Bacteroidetes, Actinobacteria*, and *Proteobacteria*.[9]

The presence of a healthy, balanced microbiome is not just important to our development, but also in the prevention of infection by pathogenic bacteria. By forming stable communities of healthy bacteria within a well-balanced microbiome, pathogenic bacteria have a much harder time becoming established within the gut, so the very presence of intestinal microbiota improves resistance of the gastrointestinal tract to harmful infection.[10] Interestingly, a much-publicized treatment to some harmful gastrointestinal infections involves ingesting a sample of microbiota from a healthy donor in order to effectively displace pathogenic bacteria with a healthy microbiome. Such treatment is known as a fecal transplant, although it has gained much publicity as a so-called 'poop pill'.[11]

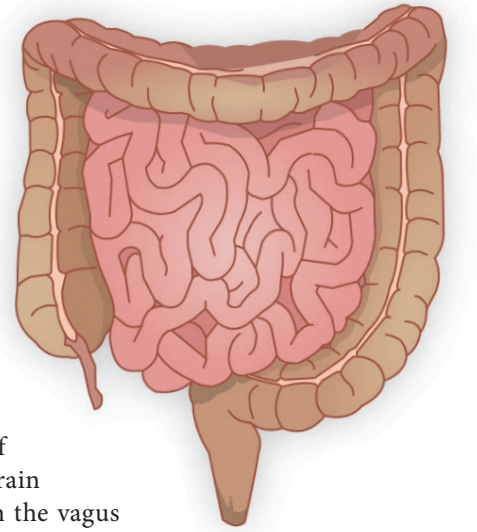
Multiple Paths, Multiple Directions

While the brain is largely isolated from microorganisms, the intestinal tract is the opposite. This has led researchers to develop their understanding of the interactions of the brain and the gut to incorporate the microbiota and establish the concept of the brain-gut-microbiome axis. As a result, a new appreciation of the interconnectivity of the microbiome and the brain has developed among researchers, with effects of the microbiome seen upon the brain and, conversely, effects of the brain and its activity seen upon the microbiome. This interconnectivity is achieved through multiple paths of communication.



Nervous Connections

Nervous connections allow our bodies to communicate information rapidly over long distances in the form of electrical impulses – acting like a form of biological broadband. The vagus nerve consists of two bundles of neurons that run on either side of the body, from the base of the brain to the abdomen; connections with the vagus nerve are made all over the body, including to the intestinal tract.[12] Stimulation of the vagus nerve can be achieved efficiently by signals derived from specialized cells of the gut, but scientists now know that this communication can also be triggered by signals from the bacteria of the microbiome.[8] Neurons of the brain use chemicals called neurotransmitters to communicate with each other, and these are affected by stimulation of the vagus nerve at the intestinal tract, and by the intestinal microbiota.[13-15] This means that bacteria of the microbiome are able to indirectly contribute to neuronal function within the brain.



Communication also occurs through the vagus nerve in the direction of the brain to the gut. Stimulation of the vagus nerve in this direction increases the integrity of the intestinal tract by encouraging cells which form the lining of the intestine to adhere to each other more tightly.[16] As the intestinal tract plays host to the bacteria of the microbiome, and any microorganisms that may be ingested with our food, intestinal integrity is important to avoid infections that may occur by breaching the intestinal wall.

The Circulatory System

As well as rapid neuronal connections, the brain-gut-microbiome axis also involves less direct methods of communication

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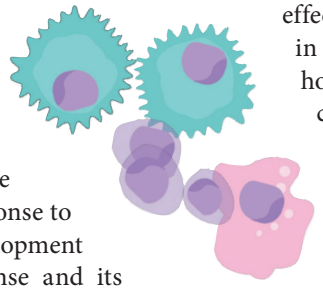
through the circulation of molecules in the blood. If neuronal communication can be described as biological broadband, communication via this circulatory system is perhaps more akin to a message in a bottle – but is by no means less important.

Hormones are molecules that specialize in using the circulatory system to communicate over long distances and are a major component of brain-gut-microbiome communication. A prime example of this is the regulation of stress hormones in the blood. Adrenocorticotropic hormone and corticosterone are mouse stress hormones which are partly regulated by a region of the brain called the hypothalamus, however, after a short period of stress, these hormones can become elevated in mice that lack a microbiome.[17] This elevated stress response can be brought back to normal by introducing these mice to even a single species of bacteria at an early age, which suggests that the gut microbiome not only affects the bodily response to stress, but also the very development of the hormonal stress response and its coordination within the brain. In developed mice, the introduction of stress has also been shown to work in the other direction, with just a short period of stress able to cause a measurable difference in the composition of bacteria within the microbiome.[18,19]



Bacteria of the microbiome, just like the cells of our own bodies, break down and build up molecules to survive, with many of these molecules sourced from the food that we eat. This process is known as metabolism, and many of the resulting metabolites proceed to circulate within the blood, where, like hormones, they can act as a method of long-distance communication.[20] Short-chain fatty acids are metabolites that intestinal bacteria can produce from dietary fibre, and are particularly interesting in brain-gut-microbiome communication as they may circulate in the blood or activate the vagus nerve directly.[13,21,22] Mice that lack a microbiome also have raised levels of an amino acid called tryptophan in their blood. In the context of the nervous system, tryptophan is a vital ingredient for the production of the important neurotransmitter, serotonin. By restricting the availability of tryptophan in the blood, intestinal microbiota can therefore affect neurotransmitter production and neuronal function in the brain.[23]

The Immune System

For the gut to host a healthy microbiome without an inappropriate or potentially damaging immune response, the intestinal tract has developed a specialized immunological environment.[24] The vagus nerve makes a contribution to this anti-inflammatory environment by promoting intestinal integrity, but also by actively dampening the activation of immune cells at the gut.[25] This anti-inflammatory effect of the vagus nerve is regulated, in part, by the aforementioned hormonal stress response that is coordinated at the hypothalamus of the brain, and that is also affected by the microbiota.[17,25] While it is important that the immune system at the intestinal tract remains active enough to respond appropriately to an infection, the importance of appropriate regulation of this response is best demonstrated by what happens when regulation goes wrong, such as in inflammatory bowel disease (IBD).

The effects of inflammation are not restricted to the gut, as immune cells and their inflammatory signals are highly adapted to circulating within the blood in order to bring about whole-body responses to infection. Researchers also know that excessive inflammation can have a particularly detrimental effect upon the delicate neurons of the brain. Even this relatively new area of study of neuroinflammation cannot be considered in isolation, as the microbiome plays an important role in 'training' the general immune response, but also in the development of specialized immune cells known as microglia that are found exclusively within the brain.[24,26]

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Role of the Gut and Microbiome Axis in Neurological Disease

As bacteria of the microbiome are in such close contact with the intestinal tract, it is unsurprising that changes in the microbiome are found in individuals with inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, as well as the functional bowel disorder, irritable bowel syndrome (IBS).[27-31] However, as we have discussed, the gut and the brain do not exist in isolation, and are, in fact, connected through multiple paths. Researchers now know that the microbiome can be perturbed not just in conditions of the bowel, but in a whole range of diseases and disorders, including those of the brain.[32]

Psychiatric Disorders

In spite of the nervous connections between the microbiome and the brain, it still seems staggering that experiments performed in mice indicate that the microbiome can affect our very behaviour. Specifically, mice lacking a microbiome display changes in how they behave that can be described as 'anxiety-like' and 'depression-like'.[33] Similar experiments have even shown that the microbiome affects the very development of the brain, with physical differences seen at the connections between neurons of mice that lack a microbiome.[34] Results such as these raise the interesting possibility that a subtle effect of the microbiome upon the development of the brain could affect an individual's behaviour and mental wellbeing over time. Scientists realize that using mice to investigate complex human mental illnesses has its limitations – a depressed mouse will only resemble a depressed human to a certain extent – but the change in both behaviour and neurodevelopment that stem from the microbiome are nevertheless striking.

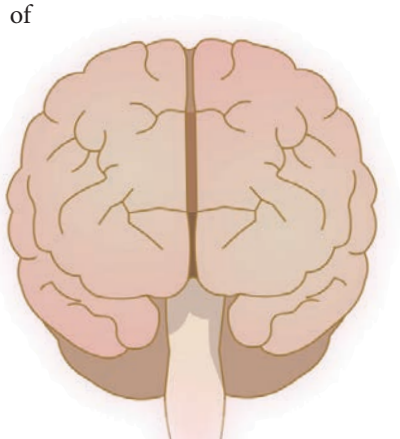
> *"The initial skepticism about reports suggesting a profound role of an intact gut microbiota in shaping brain neurochemistry and emotional behavior has given way to an unprecedented paradigm shift in the conceptualization of many psychiatric and neurological diseases."*[35]

Corresponding with results collected using mice, patients diagnosed with IBS or IBS-associated disorders (such as chronic pelvic pain or overactive bladder) also present with psychiatric problems such as depression more commonly than the wider population.[27,36] Gastrointestinal problems and a disrupted microbiome also occur in individuals with autism spectrum disorder, with gastrointestinal and autistic symptoms even appearing linked in severity.[37-39] These observations suggest that mental health and behaviour are linked to the gastrointestinal tract and the microbiome, not just by mouse experiments, but in humans also.

Neurodegenerative Disease

The brain-gut-microbiome axis is not only important in the development and function of the brain, but also in the death of neurons that occurs during neurodegenerative disease. Scientists have shown that patients with Parkinson's disease, and more recently Alzheimer's disease, also have an altered microbiome that signifies a link between neurodegenerative disease and the gastrointestinal tract.[40,41] To Parkinson's patients, involvement of the gastrointestinal tract in their condition will be of little surprise, as Parkinson's can present with well-documented gastrointestinal symptoms; however, recent evidence suggests that the gastrointestinal tract and the brain-gut-microbiome axis may be more important to the condition than previously thought.

Constipation is a common gastrointestinal symptom that presents at a very early stage of Parkinson's, often before the movement-related issues that define the condition.[42] Constipation occurs as a result of damage to the enteric nervous system of the intestinal tract; however, scientists have also found that the risk of developing Parkinson's can be estimated from the severity of constipation and the frequency of bowel movements.[43,44] Building upon this, in Parkinson's patients, physical signs of pathology can be found at the gastrointestinal tract up to 20 years prior to diagnosis



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of the disease.[45] Experiments in mice have even demonstrated that such pathology can spread from the intestinal tract to the brain through the vagus nerve.[46] There is also evidence of the active involvement of the microbiome in Parkinson's. In experiments performed using a mouse model of the disease, removal of the gut microbiome reduced movement-associated symptoms, while the introduction of gut microbes taken from human Parkinson's patients increased them.[41]

Together, these findings give credence to the idea that Parkinson's disease may actually originate in the gut, and spread to the brain through the brain-gut-microbiome axis. A hypothesis that aligns with the finding that in humans, severing the vagus nerve, and therefore one of the major channels of the brain-gut axis, reduces the risk of developing Parkinson's.[47]

The next issue of the *Inside Tract*® will include an in-depth look at the gastrointestinal symptoms of Parkinson's disease.

Future Perspectives and Treatments

The routes of communication that are part of the brain-gut-microbiome axis provide a mechanism by which diseases traditionally thought of as entirely neurological, or entirely gastrointestinal, may be related. Correspondingly, the numerous and wide-ranging conditions linked to a disrupted microbiome suggest that the microbiome and this communication axis might play an important role in promoting health, and potentially also in diagnosing and treating disease.

One approach toward utilizing the microbiome in healthcare is to supplement (probiotics), or provide nutrition to promote the growth of (prebiotics), healthy gastrointestinal bacteria as a method of preventing disease or alleviating symptoms in conditions such as irritable bowel syndrome.[8,9,21,27] Interest in this approach has built a global probiotics dietary supplements market that is expected to grow from $4.11 billion in 2016 to $6.95 billion by 2022 (USD).[48] However, in spite of this growth, there is currently little evidence regarding specific type, dosage, duration, and mode of delivery when it comes to treating individual conditions with probiotics, although we are consistently seeing more research in this area.

Fecal transplant may also play a role in future treatment of disease, not just for gastrointestinal conditions, but also for neurological and psychiatric ones. As an example, through a small clinical trial, researchers recently showed that transfer of healthy microbiota to individuals with autism spectrum disorder improved both gastrointestinal and behavioural symptoms.[49] In the brain to gut direction, the anti-inflammatory and pro-intestinal integrity effect of vagal nerve stimulation may have potential in the alleviation of intestinal inflammation in inflammatory bowel disease through the restoration of a healthy balance of bacteria in the microbiome.[8]

> *"The past decade has shown a potent hidden organ. This next decade will see widespread inclusion of this newly discovered organ into diagnostic consideration and in targeted manipulation for therapeutic intervention of many diseases"*[21]

We live in an exciting time for research with new discoveries providing more opportunities for interventions in the treatment and prevention of disease. The wide repertoire of interactions that exist simply between the brain, the gut, and the microbiome are just one example of the complex and interconnected nature of biology. To adapt, medical research is undergoing an exciting and unprecedented cultural shift toward collaboration between specialities that had previously been considered distinct. Perhaps there is no better example of this shift than in the study of the brain-gut-microbiome axis; however, the phenomenon is not limited to this area of study, with exciting new developments being made across the board, from the role of inflammation in psychiatric conditions, to the relationship between dental care and heart disease.[50,51]

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IBD versus IBS

What are the Key Differences?

We wanted to take some time to explain the differences between IBD and IBS. There are a lot of misconceptions about these two digestive conditions. Both affect the gut and often result in overlapping symptoms, such as abdominal pain and diarrhea, and the acronyms are very similar (which is often a point of confusion). However, that is where the similarities end.

Inflammatory bowel disease (IBD)

IBD is a term that primarily refers to two diseases of the intestines: **Crohn's disease** and **ulcerative colitis**. These both involve inflammation in the digestive tract, but where this inflammation occurs is different in the two diseases. Physicians can detect this inflammation in the gut through a colonoscopy.

Symptoms include:

- severe diarrhea
- abdominal pain
- rectal bleeding
- fever
- poor absorption of food and resulting complications, such as weight loss and nutrient deficiencies.

Treatment options:

- powerful medications that reduce inflammation, such as 5-aminosalicylic acid (5-ASA), corticosteroids, immunosuppressive agents, and biologics
- medications to help manage specific symptoms
- dietary changes and supplements to rest the bowel and/or improve any nutritional deficiencies
- some individuals might require surgery to remove part or all of the colon (colectomy) or small intestine (ileostomy) and a new surgical opening in the abdominal wall (ostomy) to collect stool

Irritable bowel syndrome (IBS)

IBS is a chronic, often debilitating, functional gastrointestinal disorder. In IBS, there is no physical evidence of disease apparent during a colonoscopy; instead, the problem occurs in how the gut functions and responds to stimuli such as eating and stress. A physician will typically diagnose IBS based on an individual's symptoms and medical history.

Symptoms include:

- abdominal pain
- bloating
- altered bowel behaviours, such as constipation and/or diarrhea, or alternating between the two

Treatment options:

- highly individualized management plans
- dietary changes, such as a low-FODMAP diet, reducing consumption of trigger foods, and increasing fibre
- medications targeted toward specific symptoms
- probiotics
- physiotherapy

To learn more about IBD and IBS, go to www.badgut.org or contact our office and ask for our *Inflammatory Bowel Disease* and *Irritable Bowel Syndrome* pamphlets.

Could Cannabis Offer a New Treatment Option for NAFLD?

Non-alcoholic fatty liver disease (NAFLD) is a condition in which fat accumulates in the cells of the liver (hepatocytes). It affects more than 20-30% of adults in North America and is becoming increasingly common. Many people with this condition have no symptoms and medical professionals might diagnose them as a part of an investigation into the cause of other abnormal lab tests or after they have had imaging of their abdomen for unrelated reasons. NAFLD is likely caused by metabolic factors, such as obesity, diabetes or pre-diabetes, high cholesterol, high blood pressure, sedentary lifestyle, and the use of certain medications.

While NAFLD is typically asymptomatic in its early stages, and might seem like a relatively harmless condition, it can lead to serious damage in the liver over time. The presence of fat in the liver can trigger inflammation, which can lead to scarring of the liver tissue, known as cirrhosis, at advanced stages. Once the liver develops cirrhosis, a number of other complications can occur, as the liver is unable to perform normal processes. These can include worsening fatigue, fluid accumulation in the abdomen (ascites), bleeding from veins in the esophagus or stomach (varices), and confusion (encephalopathy).

Typically, treatment for NAFLD focuses on dietary and lifestyle changes such as improved diet and increased exercise in order to lose weight and reverse the metabolic factors, such as high cholesterol and diabetes. There are no approved medications to treat NAFLD, and lifestyle modifications can be very difficult to maintain. With the need for more treatments – and the fact that NAFLD rates will likely increase over the coming years, as obesity and diabetes are becoming more prevalent – researchers are looking into pharmacological options.[1]

One particular area of interest is cannabis. Scientists suggest that our bodies naturally produce a family of neurotransmitters called endocannabinoids, which interact with specialized receptors located in the brain, muscles, fat, and digestive tract, called cannabinoid receptors. This array of interactions between the body's trigger substances and receptors is known as the endocannabinoid system. Cannabis contains similar molecules, cannabinoids, which include delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), that also interact with these receptors.

Researchers have found an inverse correlation between NAFLD and cannabis consumption, meaning that individuals who use (or previously used) a lot of cannabis are less likely to develop NAFLD than those who abstain, and those with the highest consumption rates were the least likely to develop NAFLD.[1,2,3] Studies have also found that cannabis use also correlates with lower rates of obesity and diabetes, two known risk factors for NAFLD, and posited that this might be the cause of the reduced risk of NAFLD in cannabis users.[3] However, the apparent benefit remained present when the researchers adjusted the data for body mass index, diabetes, and hypertension, which are known risk factors for NAFLD, as well as other variables such as education level, economic status, and use of alcohol, cocaine, heroin, and/or amphetamine, which could possibly affect the rate of NAFLD.[1] This correlation has not yet been proven as a cause and effect, which means that it has not been demonstrated that cannabis use will prevent or reduce the risk of obesity and diabetes, only that an association was found.

They suggest that cannabinoids might have a therapeutic benefit in NAFLD, possibly because of the way that they influence the endocannabinoid system. At this time, researchers are still unsure exactly how cannabis could reduce the rate of NAFLD and recommend further research into the precise methods. However, they suggest that including cannabinoids to the current NAFLD treatment plan could offer another method to reverse the fat build-up in the liver and prevent further complications.

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Five Gluten-Free Grains You Might Not Have Tried

Grains are nutritious, energy-dense staples for countries all around the world, and this includes gluten-free grains such as rice, corn, and sorghum. Many of us tend to eat the same grains all the time, and yet there are so many to choose from. This article will discuss five gluten-free grains you've probably never tried, including their nutrition potential and how to make them easier to digest. If you're tired of making quinoa and rice all the time, there are plenty of other options to choose from. If you want to experiment and try something new, it's time to challenge yourself to try one of these gluten-free grains today.

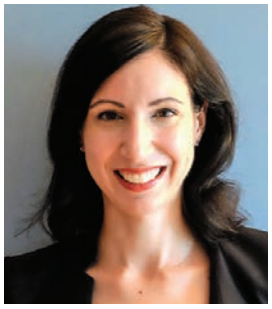
Nutrition

You can get plenty of nutrients from grains, including protein, fibre, healthy fats, antioxidants, vitamins (e.g., thiamin, riboflavin, niacin), and minerals (e.g., calcium, magnesium, zinc, iron). Can you get these nutrients elsewhere? Of course, but eating whole grains is an efficient, healthy, and affordable way to get a vast number of them, especially if you eat a predominantly plant-based diet. As with any food, variety is key. I encourage eating a variety of whole grains to maximize the type and amounts of nutrients you get on a regular basis. It could mean that you eat rolled oats and buckwheat one week, followed by quinoa and sorghum the next. It can be interesting and fun to try different types.

Digestion

Do you have trouble digesting grains? There are ways you can process grains to make them easier to digest and even more nutritious, such as soaking them overnight or fermenting them. I highly encourage trying these methods, as you may find that you have no trouble digesting grains after all. This explains why 100% sourdough wheat bread, which is a fermented food, is easier to digest than commercial wheat bread, which is not a fermented food.

Fermentation is the pre-digestion of food by bacteria and their enzymes. This food processing method breaks down compounds that are difficult to digest and can make nutrients more available for our bodies to absorb.[1] Grains naturally contain phytates, which bind to minerals like iron and calcium, reducing our body's ability to absorb them. Soaking grains helps activate enzymes like phytase, which will break down the bond between phytate and the mineral to which it's bound. This releases the mineral so that it is free to be absorbed by the intestine instead. Phytates are not all bad though, and science



Anne-Marie Stelluti, RD
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shows that if you are getting well-balanced nutrition, you are unlikely to become deficient in minerals simply from eating phytates. This only seems to be a problem if you are not eating enough food or are eating a nutrient-poor diet. Phytates have benefits, and although high quality human studies are needed to confirm these positive effects, they have been found to act as antioxidants, have anti-cancer effects, and prevent the calcification of tissue that can lead to heart disease.[2]

Blue Cornmeal

Blue cornmeal originally comes from Peru, but it is also produced in Mexico and the United States. What makes blue corn special is that it is rich in anthocyanins, which are healthy active plant chemicals with antioxidant activity.[3] Antioxidants are great in that they protect our cells from damage and may help prevent cancer. Blue and red fruits and vegetables like blueberries and beets also contain anthocyanins. One cup of blue cornmeal contains twelve grams of protein and ten grams of fibre. It also contains healthy fats, such as oleic acid, the same healthy fat found in olive and avocado oil. Have fun experimenting with blue corn, because the more antioxidants, the better!

Recipe Inspiration:

- blue polenta
- blue corn tortillas
- blue corn blueberry muffins

blue corn chips

Fonio (a.k.a. acha, 'hungry rice', podgi)

Fonio is an ancient grain from West Africa, predominantly grown in Mali, Senegal, Benin, and Guinea. It is often eaten as a porridge or as a steamed 'couscous'. It is a very small white or black grain that has a mild nutty flavour.[4] You can keep it simple and use fonio just as you would rice or quinoa. The Canadian Nutrient File and the USDA food database have not yet analyzed fonio at the time of writing this article. Third-party nutrient analysis from fonio supplier, Farafena Health, indicates fonio is gluten-free, approximately 7.5% protein, sugar-free, and a source of zinc and iron. It is also a good source of fibre.

Recipe Inspiration:

- fonio banana bread
- fonio porridge
- fonio tabbouleh

Job's Tears (a.k.a. coix seeds)

Job's tears look a lot like pearl barley, but they are not the same thing. This grain is grown in China, Malaysia, India, Pakistan, and Sri Lanka. It is considered a nutritious health

food in Asian countries but remains a mystery to many of us here in Canada. They come in a variety of colors: yellow, brown, white, and purple. Preliminary evidence shows that they may help lower cholesterol and blood sugar, which is likely due to their high fibre content.[5]

Recipe Inspiration:

- Job's tears salad
- Job's tears soup
- Job's tears stew

Sorghum (a.k.a. milo or broom corn)

Sorghum is a round red or white grain that comes from central Africa.[6] It is a staple in Sudan, where it can be used to make a fermented porridge, a non-alcoholic cereal beverage called kunu, and a paper-thin sourdough pancake called kissra, which is on my personal list of foods to try soon.[7] One cup of sorghum contains around twenty grams of protein and twelve grams of fibre.[8] You can also have some fun popping sorghum in a saucepan to make a tiny version of popcorn, which you can eat on its own or to add crunch to a salad or Buddha bowl.

Recipe Inspiration:

- kissra (thin sourdough pancake)
- sorghum popcorn
- sorghum risotto

injera (fermented Ethiopian flatbread)

Teff

Teff comes from Ethiopia and it is the smallest grain in the world. It can be ground into flour or fermented into a flavourful sourdough flatbread called injera. One cup of teff grain has about twenty grams of protein and ten grams of fibre.[9] It has a mild nutty taste and can be found in different colors: white, black, red, and brown. I have made injera several times and love it with a good spicy chickpea curry. Injera is only gluten-free if it is made with 100% teff flour. Many North American restaurants make it with a mix of flours (wheat, barley), so be sure to ask if you follow a gluten-free diet. If you haven't tried making injera yet, it's pretty easy to make, and you can refrigerate it for use during the week.

Recipe Inspiration:

- injera (fermented Ethiopian flatbread)
- teff porridge
- teff risotto

Conclusion

Whole, gluten-free grains are nutritious and versatile, and there are many to choose from. They can be made easier to digest through soaking and fermentation, food processing techniques that are used by many cultures around the world. If you have tried some or all of the gluten-free grains listed above, good for you! Other gluten-free grains you may not have tried are kaniwa, buckwheat, amaranth, forbidden rice, or Himalayan red rice. I challenge you to bring something other than a quinoa salad to your next social gathering.

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Photo (In order of appearance): Blue Corn © Deenida | Shutterstock, Fonio © Farafena, Coix Seeds © Subin Pumsom | Bigstockphoto, Sorghum © Vijaya narasimha | Pixabay, Teff © raptorcaptor | 123RF, and Injera © magicbones | 123RF.

Fonio Gluten Free Pancakes

Ingredients

¼ cup butter, melted
1 egg, tempered to room temperature
1 tbsp maple syrup (or alternative)
1¼ cup milk (or non-dairy alternative)
1 tsp vanilla extract
1¼ cup Farafena Fonio Flour
1 tbsp baking powder
½ tsp salt

Instructions

- In a mixing bowl, beat butter, egg, syrup, milk, and vanilla on medium speed for 1 minute. Allow to sit 3 minutes.
- In a medium bowl, sift together Fonio Flour, baking powder, and salt. Mix well.
- Add dry ingredients to wet ingredients.
- Mix just until incorporated. Do not over mix. The mixture will be thick (It's okay to have clumps).
- Heat a lightly oiled frying pan over medium heat or heat and grease a waffle iron.
- Pour ¼ cup of batter into pan.
- Cook 3-5 minutes or until bubbles form near center of pancake and edges are dry.
- Flip and cook additional 3-5 minutes.

Photo: © Farafena

About Farafena

Farafena was founded in Vancouver, BC by Oumar Barou Togola and Dylan Beechey. The company is committed to good food with purpose. Through social enterprise and direct trade, we invest in women farmers in Africa to grow and harvest the purest grains and fruits – so that we can bring delicious, nutrient-rich superfoods to your family, while building strong, healthy communities in Mali and Malawi.

Good Food. With Purpose.
From the rich soil of Africa, we share our nourishing, sustainable foods with the world, while transforming life for women farmers and their families. We believe in food that you can feel good about.

You can find Farafena Fonio Flour and Fonio Grain in grocery stores across Canada. Learn more about fonio and the work Farafena is doing at farafena.com.

Giveaway

Enter online to win Farafena products in July. Watch for our social media posts @gisociety!

Dr. Fasano to Speak on New Celiac Research in Vancouver

Dr. Fasano is the Director of the Center for Celiac Research and Treatment at MassGeneral Hospital for Children in Boston, Massachusetts.

Gut problems are universally painful and embarrassing – and are far more common than many of us might think. In fact, for celiac disease alone, research has established that approximately 1% of the population is affected. There are many intestinal conditions, each with their own name and symptoms: irritable bowel syndrome, ulcerative colitis, Crohn's disease, celiac disease, food allergies, etc. But in all cases, the diagnosis is devastating because it can mean years of pain, discomfort, curtailed enjoyment of life, and in a few cases, a shortened life. The treatments for many gut diseases and disorders are complicated and often involve trial and error, requiring patients to eliminate an assortment of foods from their diets and stress from their lives in an effort to keep the symptoms of cramping, diarrhea, constipation, and pain at bay.

However, for at least one of these illnesses, celiac disease, hope is on the horizon. We have known how celiac disease affects the body for a long time, but we have a better understanding of the process by which that happens, and a potential new way to treat the disease thanks to the research of Dr. Alessio Fasano.

Dr. Fasano is an Italian-trained medical doctor who is professor of pediatrics at Harvard Medical School and director of the Mucosal Immunology and Biology Research Center at MassGeneral Hospital for Children in Massachusetts. He trained at the University of Naples where celiac disease was one of the main scientific interests of the pediatrics department. In 2000, he and his team unlocked the mysteries of a potential way that celiac disease might occur when they discovered the protein zonulin.

Discovery of Zonulin

The discovery of zonulin was indirect, the way medical discoveries sometimes are. In the 1980s Dr. Fasano had been given the task of developing a vaccine against cholera, a devastating illness that attacks people when they are at their most vulnerable – often after a natural disaster when the water supply is polluted and untreated.

As it turned out, the vaccine that Dr. Fasano and his team created for cholera worked, but the residual diarrhea it produced, while less than what patients endured when they were

Kristin McCahon

Note: This article is an opinion piece; opinions reflected within do not necessarily represent those of our Medical Advisory Council. The information mentioned in this article is under-studied at this time.

suffering from untreated cholera, still remained at unacceptable levels. So the cholera vaccine efforts were abandoned.

What, Dr. Fasano wondered, was causing that residual diarrhea? As they looked into it further, his team discovered the protein zonulin, which he explains, "controls the opening of 'tight junctions' between cells lining the digestive tract."

The Relationship Between Zonulin, Celiac Disease, and Intestinal Permeability

Dr. Fasano determined that two major stimuli release zonulin in the body. The first is a bacterial infection (salmonella or cholera, as examples) in the small intestine, which prompts the body to eliminate the potentially very serious threat the bacteria poses. His research shows that when the gut detects a noxious substance, it releases zonulin, which, in turn, opens the tight cellular junctions that normally keep gut fluids separate from the rest of the body. The zonulin causes the small intestine to pull in large amounts of water from the rest of the body, which it uses to dilute the unwanted substance and then flush it out of the body as diarrhea. Once the poison or bacterium is gone, zonulin levels drop and the junctions close.

The other stimulus that Dr. Fasano found releases zonulin is gluten. When we eat gluten-containing products, zonulin production is triggered and, for a short period, the gut becomes permeable. Dr. Fasano has shown in the laboratory that material, including gluten, then flows from the intestine and into the bloodstream. In most people, the immune system will attack the gluten and get rid of it and we will be none the wiser. However, according to Dr. Fasano's research, people who have celiac disease, or who are sensitive to gluten, produce a lot more zonulin than the rest of the population. In their cases, their intestines become permeable for longer, which gives more time for substances, including gluten, to pass through to the bloodstream. To top it off, their immune systems are not working properly. When their bodies recognize the gluten enemy, they start to mount an immune response which attacks their own body.

The process of intestinal permeability is thought to

CAUTION

Leaky Gut versus Leaky Gut Syndrome

In the past, we've covered the topic of misinformation regarding leaky gut syndrome. Intestinal permeability, sometimes called 'leaky gut', can occur for several reasons, including damage or inflammation affecting the gut. These terms refer to what occurs when the barrier of the gut becomes compromised, allowing larger molecules to pass through the gut wall. However, be wary of those who try to sell 'leaky gut syndrome' as a catch-all cause of a wide variety of conditions, including all autoimmune conditions, metabolic conditions, cancers, mood disorders, fatigue, and many others, as there is little evidence for many of these. It is especially concerning if they offer expensive supplements or require that you buy their book in order to treat the condition, and they don't have a history of research or medical practice in the area. While leaky gut (intestinal permeability) might play a role in some conditions, there isn't a lot of evidence that it is related to many of the other conditions that proponents claim leaky gut syndrome causes.

contribute to inflammation throughout the body and even to the development of autoimmune disease. Consistent with the theory of leaky gut and autoimmune disease, excess zonulin production is found in a variety of autoimmune diseases.

Implications for Treatment

Although he is not keen on the catch-all term "leaky gut," Dr. Fasano suspects that "many illnesses link back to loss of barrier function in the gut."

Those who are concerned that they have leaky gut will be wondering if there is a test they can take to determine their own gut permeability. Unfortunately, there isn't one that is cheap, quick, and reliable for clinical purposes. While there is one that can be used for scientific purposes, it is fiddly, complex, and the results are difficult to interpret. Other tests are not particularly reliable.

So what can be done to modulate the release of zonulin, or counteract its effects?

There is, as yet, no single, approved drug that will do the job, though several are in various phases of trial. One is a zonulin inhibitor, AT1001, also called larazotide acetate, which has protected mice from colonic inflammation."

A number of factors exacerbate intestinal permeability. Check with your doctor, but some steps that might help control the symptoms include:

- reduce excessive sugar intake
- avoid excessive alcohol
- avoid stress
- be sparing in the use of non-steroidal anti-inflammatory drugs, such as ibuprofen
- support good gut bacterial health

Dr. Fasano adds that "if we know the cause of the breach of the intestinal barrier, then we can remove the cause… if [the patient has] gluten sensitivity or celiac disease, remove gluten... if a bacterial overgrowth … treat the bacterial overgrowth or [treat] with probiotics." If the problem is genetic, it is more complicated to treat.

On September 26, 2019, the biennial $250,000 Dr. Rogers Prize for Excellence in Complementary and Alternative Medicine will be presented in Vancouver and will feature Dr. Alessio Fasano as the keynote speaker. Dr. Fasano is the author of Gluten Freedom and is a renowned expert in intestinal permeability and autoimmune disorders. He will be discussing his discovery of zonulin and its role in leaky gut and celiac disease. Tickets to the award dinner will be available through drrogersprize.org.

Kristin McCahon, MA, is a freelance editor and writer. No part of this article is intended to be a substitute for professional medical advice.

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