FOOD, STRUCTURE, BACTERIA AND HEALTH

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There's a revolution happening in health. Bacteria—long maligned as the arch nemeses of human health and wellbeing, to be destroyed at all costs—are now being recast in a different light.

While there is little doubt that bacterial infections are a bad thing—after all, most deaths prior to the introduction of antibiotics in the 1930s resulted from bacterial infections—there is now a growing appreciation that extensive and complex bacterial communities, when confined within specific ecological niches of a mammalian host (like the large bowel of humans or the rumen of a cow), can be of great benefit to their host.

Over the past 10 years, and as an important (though unanticipated) legacy of the Human Genome Project, new DNA sequencing techniques have allowed the identification of bacterial species in complex microbial mixtures, without the need to be able to culture the individual species. We already knew that the bacteria of the human gut were helpful to our nutrition: extracting residual energy from components of food that are not digested in the small intestine and making certain micronutrients, such as vitamin K, B group vitamins, folate and the building blocks of proteins, amino acids.

Recent research, however, in both animal and human models has associated changes in the bacterial populations of the gut—the gut microbiota—to a wide range of diseases, not only those of the gut, such as colorectal cancer, irritable bowel syndrome and inflammatory bowel diseases, but also others where the target organ is remote from the microbial repository, such as obesity, diabetes, cardiovascular disease, autism, Parkinson's disease and even depression.

Now, I'm not suggesting that the gut microbiota is the only factor affecting these diseases, but the evidence is now suggesting that it may be a significant contributor to the aetiology, maintenance or progression of a number of chronic diseases. Importantly, microbiota provide a previously unrecognised additional target for either disease prevention, or pharmaceutical or dietary intervention for such diseases—and this is what's getting the health sector very excited.


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So, how can we manipulate our gut microbiota for better health and to reduce our long-term risk of chronic diseases? It turns out that one of the factors affecting our gut microbiota is the food we eat. In particular, it is those components of our diets that are not digested in the small intestine that provide the nutrients to feed our hungry microbiota, all 100 trillion of them in each of us. In the absence of this dietary contribution, the gut microbes rely on the slim pickings found in secretions and cellular material, and mucus sloughed from the epithelial cells lining the gut.

So, through this lens, we can see that our modern Western diets—with their abundance of highly digestible, energy-dense, foods that are high in sugars and saturated fats—are probably overfeeding our bodies and underfeeding our gut microbiota, providing a two-lane expressway to longer-term ill-health.

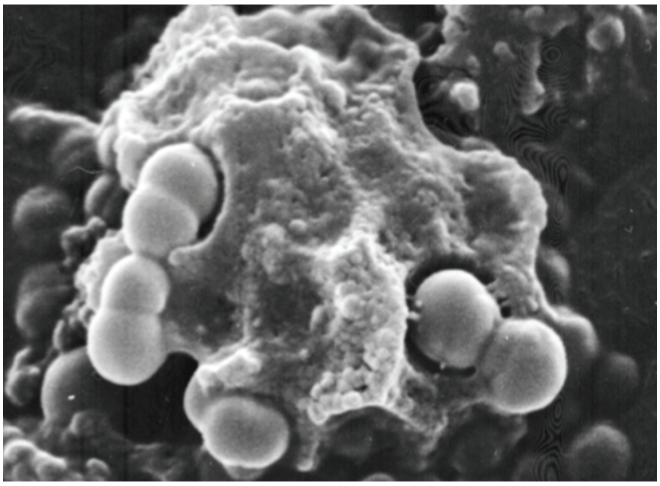
What appears to have been lost from our modern diets, compared to those of the past, is dietary fibre. Fibre is a complex mixture of food components that evade digestion in the small intestine and pass through to the large bowel. Most dietary fibre comprises the cell wall material from plants, but indigestible components of animal origin, including glycans from milk and cartilaginous components from meat, can also be considered as fibre.

Grains are a particularly rich source of fibre, and this is where structure first kicks in. In grains, most of the fibre is associated with the outer parts of the grain, with the inner parts—the endosperm—being filled with starch, which will provide the energy source for the fledgling plant on germination. The fibrous outer part plays at least two critical roles. Firstly, it protects the embryo from the harsh environmental conditions that often occur between seed formation and germination; and secondly, when rain comes, it absorbs moisture, swells and maintains the moist environment for the germinating plant, seeing it through its 'valley of death' period between its growth phases relying on energy from the seed endosperm, until the root system and first leaves take over the job.

From a baker's perspective, these fibrous components are a nuisance. They negatively affect dough properties and can lead to a mottled appearance, a rough mouthfeel and sometimes a heavy finish to the final baked product. Advances in grain processing, involving the crushing of grains between steel rollers to release the starchy flour within (rather than ripping and tearing the grains apart between rotating stones), have made it easier to separate out the seedcoat materials from the flour, resulting in a reduced fibre content in modern flours, compared to those of yesteryear.

Interestingly, many of those properties of fibre that serve the plant so well as it negotiates the path from germination to growing plant are also helpful to our digestive systems. The structural properties that allow components of fibre to absorb water and swell also work well for our gastrointestinal systems. When consumed with adequate water, a diet rich in fibre increases the volume of stool and its water content, diluting toxic food components that have also been adventitiously co-ingested, while also softening the stool, increasing the rate of transit of waste products through the colon and improving regularity. But even in the small intestine, where fibre is not digested, it increases the viscosity of the digesta, slowing the digestion of food and leading to a slower, more even uptake of nutrients and energy from a meal over time. This also has benefits for maintaining our general metabolic health.

But from the gut microbes' perspective, while they enjoy the enriched environment provided by the roughage components of fibre, cellulose, hemicelluloses and lignins that are so abundant in wheat bran, for example, they are far more interested in other, less well recognised components of fibre—the fermentable carbohydrates. These include components like fructooligosaccharides (inulin), pectins, beta-glucans and arabinoxylans, but a major contributor to gut microbiota nutrition is another different component called resistant starch.



Bacteria digesting a starch granule

Not all starches are equal. Depending on its chemical structure and/or physical presentation in the diet, starch can be more or less readily digested by the enzymes of the host's small intestine. Most flours commonly used in Western cooking are highly digestible, so how can starches differ in digestibility?

The first way is the physical presentation of the starch. Wholegrain flours and kibbled grains retain a proportion of their starch within grain fragments that have survived the milling process. A proportion of the starch retained within these fragments can't be accessed physically during small intestinal transport, so it transfers to the colon where that sub-population of the gut microbiota that are able to ferment starch get their opportunity to have a go.

Secondly, the starch in flours can occur in two different structural forms. Starch is a polymer of glucose molecules. One of its structural forms is amylopectin, a large, highly branched polymer. The other is a much shorter, linear polymer (amylose). These pack differently in the starch granule. The amylopectin assumes a diffuse type of conformation that is quite open and accessible to the enzymes that break down starch (amylases). The amylose, however, forms more closely packed aggregates within the granule, which are less water- and enzyme-accessible, so this form of starch is digested more slowly, increasing its chance of making its way to the colon and feeding the hungry microbiota.

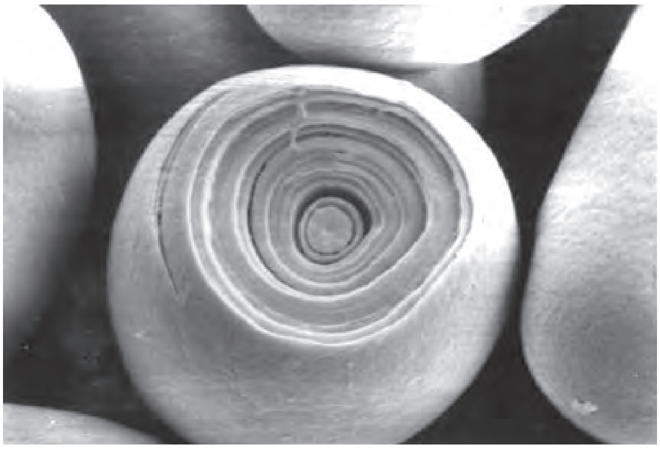
The ratio of amylose to amylopectin in grains is controlled genetically. The CSIRO has developed new varieties of barley and wheat that contain elevated levels of the amylose form of starch. Dietary intervention studies in animals using these grains have confirmed an associated increase in the level of resistant starch, an improved ability to feed the gut microbiota and follow-on physiological benefits in markers of gut health in the host. Cooking and cooling of starch causes it to undergo further structural changes through a process called retrogradation, which also increases the resistant starch content of these products, while chemical modification of starches can also increase their resistance to small intestinal digestion.

Once in the colon, consortia of bacteria band together to take advantage of this new food source. Some bacteria produce enzymes that the host is unable to make, facilitating the breakdown of these small intestine–resistant long sugar polymers into shorter polymers (oligosaccharides), or simple sugars. Other bacteria are then able to ferment these sugars into different chemical products that are of use to yet other bacteria within the community, or to the host.

So, this new food source provides a selective advantage and growth benefit to those sub-groups of the more than 1000 bacterial species that make up the gut microbiota that can use them, and a disadvantage to others that cannot, thereby reshaping the structure of the gut microbial community. Key products resulting from bacterial action on these fermentable carbohydrates are food acids, but particularly short-chain fatty acids: primarily acetate, propionate and butyrate.

These acids reduce the pH of the colonic digesta, which provides a selective advantage to some of the well-known healthy bacteria, such as lactic acid bacteria and *Bifidobacteria*, while producing a more challenging environment for some of the less-healthy ones, like certain members of the *Clostridia*. But these acids are also of significant benefit to the host. Butyrate, for example, is the preferred energy source for the cells that line the colon, promoting the health and integrity of this important barrier between the microbiota of the gut and the host tissues.

But short-chain fatty acids are also bioactive messengers in their own right, and have also been



Starch ultrastructure

implicated in reducing the risk of bowel cancer, improving gastrointestinal mobility, reducing inflammation and allergy, modulating satiety and may even be candidate mediators of cognitive health via the gut-brain axis.

But we have a conundrum. These fibre components that are so important for the health of the human gut microbiota are carbohydrates. And in our body form–obsessed, calorically oversupplied society, carbohydrates are the widely vilified scourges of the supermarket shelves. Key messages around eating for weight control energetically promote low-carbohydrate diets, so how do we reconcile any of this, because both gut health and obesity are huge problems nationally?

The first thing to note is that 'low carbohydrate' does not mean 'no carbohydrate'. So, it is more about ensuring carbohydrate quality within a target carbohydrate envelope, particularly ensuring that fibre intakes are at least 30 grams per day where a significant proportion of that fibre, perhaps as much as two-thirds, is in the form of fermentable carbohydrates like resistant starch. Clearly grains, pulses, fruit and vegetables will provide important components of the equation, but even within the fermentable carbohydrate sources, careful selections need to be made depending on an individual's health status.

For example, some of the fermentable carbohydrates are actually FODMAPs, so people with disorders such as irritable bowel syndrome may need to be more careful than others in their fibre source selections. These are early but exciting days in understanding how best to optimise our gut microbiota for health, but the complexities outlined above highlight the need for greater public awareness about the potential impact of dietary choices on multiple aspects of health.

Trevor Lockett will be speaking at the 17th International Biotechnology Symposium (IBS2016).