

## WEIGHT (FATT!!!) LOSS

There is One Essential Prerequisite.

Do you see a bit of a belly bulge? That is the warning sign; it is your first footprint along the path to destruction. The sequential stepping stones along that perilous pathway are:

- belly bulge,
- hyperinsulinism,
- rising triglycerides,
- dysinsulinism,
- tubby tummy,
- falling HDL cholesterol,
- insulin resistance,
- rising blood pressure,
- rising blood sugar,
- full-blown Metabolic Syndrome, ultimately expressed as ...
- Type 2 Diabetes and/or cardiovascular disease.

Not a pretty picture!

If you and your patients want to reverse course, you need to look back at square one, that “pinch an inch” over the belt line. What went wrong? There are hundreds of research studies blaming a high sugar diet. The literature is equally replete with research implicating a high-fat diet. The most patho-physiologically sound research points to cortisol stress, plus dietary intake of polyunsaturated oils. Yet, there is one even more fundamental cause predisposing to an expanding waistline – a force so powerful it will sabotage even the most sensible weight-loss diet. An unhealthy intestinal microbiota will relentlessly push you down the road to rotundity.

### Microbiota-Driven Weight Gain

You and your patients must fully appreciate the far-reaching effects of the microbiota on metabolism. Gut microbes, for better or for worse, exert powerful control over all metabolic processes. These wee beasties have direct communication lines over which they influence the assimilation and destination of macronutrients. (1-6) They operate via ...

- The Microbiota-Gut-Adipose Axis
- The Microbiota-Gut-Liver Axis
- The Microbiota-Gut-Pancreas Axis
- The Microbiota-Gut-Muscle Axis
- The Microbiota-Gut-Hypothalamus Axis.

Obesity is associated with altered gut microbiota and impaired gut barrier function. The metabolic effects of deranged gut-adipose-liver axis cross-talk cause release of pro-inflammatory cytokines into the portal circulation, leading to the development of insulin resistance, and ultimately Metabolically-Associated Fatty Liver Disease, all the while directing macronutrients

into abdominal adipose storage. Unless a healthy microbiota is restored with select prebiotic + probiotic (= synbiotic) supplementation, a calorie-restrictive diet may be futile. (7)

The interrelationship between gut microbiota, the brain, and skeletal muscle plays a key role in energy homeostasis, particularly the directing of macronutrients into either cellular energetics or fat storage. Microbiota metabolites are intestinally absorbed and carried to the brain, where they bind to specific receptors. This microbiota-brain axis is a two-way communication line, as the CNS feeds back to the intestinal system, affecting intestinal transport, secretion, and permeability of the digestive system. In turn, the GI tract collects information about food absorption, sending signals to the brain through the vagus nerve as well as the blood, stimulating secretion of brain-gut peptides, and thus exerts control over feeding behavior.

Skeletal muscle also has receptors for microbiota metabolites, which influence its energy metabolism. This is another example of cross-talk in that the muscles also communicate with the gut system. Release of skeletal muscle myokines causes the secretion of intestinal hormones, and these hormones signal the brain as yet another mechanism to control food intake and macronutrient utilization. (8)

The link between the gut microbiota and the development of obesity and associated disorders such as insulin resistance, Type 2 diabetes, and fatty liver disease is a loss of, or an excess of, inter-organ communication. The key disruptor of inter-organ communication is metabolic endotoxemia (an increase in plasma lipopolysaccharide (LPS). LPS is one of the triggering factors leading to the development of metabolic inflammation and insulin resistance. Gut microbes contribute to the onset of low-grade inflammation via mechanisms associated with gut barrier dysfunction. The gut lining includes enteroendocrine cells that communicate with the brain, with the liver, and with adipose tissue. The key to maintaining proper communication along these axes is minimizing the production of gut endotoxins with specific synbiotic supplementation. (1)

Studies show a direct link between abnormal gut microbiota and excessive gut permeability, low-grade inflammation, and insulin resistance. The breakdown in gut barrier function particularly results in obesity in individuals for whom even extraordinary calorie-restrictive diets yield mostly frustration in terms of weight loss and lipid control. Dietary sugars and carbohydrates are very easily converted to triglycerides. Dietary polyunsaturated fatty acids also increase systemic pro-inflammatory free fatty acids and their derivatives in these patients by increasing plasma LPS.

The most direct way to control obesity and the consequences of Metabolic Syndrome in these patients is to reduce LPS production in the gut by synbiotic supplementation. Synbiotics reinforce the gut barrier, promote gut hormones that control appetite, promote glucose homeostasis, decrease systemic inflammation and obesity, and counteract hepatic steatosis and hepatic insulin resistance. (9)

Restoration of an anti-obesity microbiota cannot be achieved with any random assortment of pre- and probiotics. Certain prebiotics are far more effective than others. A typical probiotic

supplement is likely to yield as many weight-gain-promoting critters as weight-loss-inducers. Specificity is key to the essential metabolic balancing.

A high formation of Short-Chain Fatty Acids (SCFA) from select prebiotics stimulates PPAR- $\gamma$ , which increases GLUT-4 and insulin sensitivity. The decreased insulin resistance explains the benefits on weight loss, diabetes, and triglycerides associated with prebiotic supplementation. Do all types of dietary fiber that give rise to high amounts of SCFA have an effect on weight gain? Different fibers yield different formations of SCFA. For example, propionic acid has been shown to increase satiety, while butyric acid has anti-inflammatory effects through NF-kappa-B, which in turn influences parameters associated with the Metabolic Syndrome.

Evidence suggests that the systemic inflammation observed in obesity does not result from the accumulation of fat, but causes it. Studies show that adding the prebiotic inulin to the diet of obese women increases the count of bacteria that reduce systemic inflammation. The intervention works best on patients who, at the outset, already harbor microbiota associated with a low-inflammatory status. Those without healthy microbiota do not benefit as much from prebiotics until after the microbiome is fully established with long-term synbiotic supplementation. (10)

In one study, microbes were transplanted from lean donors to patients recently diagnosed with Metabolic Syndrome. The recipients saw improvements in insulin sensitivity and the enrichment of their microbiota. However, 6 months after the bacterial transplant, the patients had relapsed, with metabolic improvements fading and the precursors to Type 2 diabetes returning. The researcher emphasized that the long-term key to success here was not transplanting microbes but fostering an ideal environment for healthy microbe development through prebiotic supplementation. (7)

Recent epidemiological studies show that eating “fast food” items such as potato chips increases the likelihood of obesity (--- No surprise!). There are also demonstrations that the immune system plays a critical role in this process. In both human and mouse models, consuming a Westernized “fast food” diet increases CD4+ T helper Th-17-biased immunity, with changes in microbial communities causing abdominal obesity in humans.

Surprising benefits on the obesity-generating effects of “fast food” are found with probiotic *L. reuteri* supplementation. In fact, *L. reuteri* therapy alone is sufficient to change the pro-inflammatory immune cell profile and prevent abdominal fat pathology as well as age-associated weight gain in mice, and does so regardless of their baseline diet. In other words, the effect of *L. reuteri* is so powerful that the development of obesity is inhibited to some degree even when the “fast food” diet is maintained. (11)

It is interesting that while synbiotic supplementation is the most direct and powerful way to favorably influence the communication line of the gut with the brain, the liver, adipose tissue, muscle tissue, and the pancreas, one particular bacterial species actually disrupts this communication line. That species is the ever-popular *Lactobacillus acidophilus*. Yes, the most common of all probiotic supplements makes your patients fat, sick, and old. *Lactobacillus acidophilus* distorts the communication line between the gut and adipose tissue, increasing the

obesity-generating messenger CB2. Indeed, not just abdominal weight gain but all pathologies associated with insulin resistance can be exacerbated by *L. acidophilus*. (12)

In studies on obese mice and on mice bred to be diabetic, certain species of bacteria are identified exclusively in obese and diabetic mice. There are also certain strains of bacteria identified exclusively in lean mice that are not found at all in obese and diabetic mice. The most significant findings of these studies is that even in mice genetically bred to be obese or diabetic, the gut microbiota can be altered with synbiotics so as to control the obesity and the diabetes by improvements in adipose tissue metabolism. (13)

Human studies show that there are at least 100 species that differ between a control diet and a synbiotic-supplemented diet. This response to prebiotic supplementation is huge. Of the more than 100 species that are altered by prebiotics, 8 of the species are shown to increase more than tenfold, and 8 of the species are decreased by more than tenfold. These studies permit identification of bacteria that are promoted using a synbiotic approach. Other studies show that synbiotic supplementation decreases the ratio of Firmicutes to Bacteroidetes, the ratio that is elevated in obesity. (14)

Obviously, random probiotic supplementation is not the answer to weight loss. There is no way to supplement with 100 different species of probiotics, most of which are obscure and some of which have not even yet been identified. Only specific synbiotic blends will achieve a major impact on gut barrier function and reduce the production of endotoxins that cause obesity, high triglycerides and cholesterol, high blood pressure, cardiovascular disease, and diabetes.

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