EDITORIAL

Stomachs: does the size matter? Aspects of intestinal satiety, gastric satiety, hunger and gluttony

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Many surgeons and most laypeople think that there is a strict correlation between the size of the stomach and the size of the meals. The term ''stomach reduction'' became a synonym for weight loss surgeries, as if by reducing the stomach, all meals would automatically be small.

However, there is no strict correlation between the size of this organ and the size of meals. Some morbidly obese patients have previously undergone total gastrectomy! If a simple stomach reduction treated obesity, the absence of a stomach should cause impressive weight loss; however, this principle is not always true. On the other hand, some patients, despite having normal-sized stomachs, feel very satisfied with three spoonfuls of food. How can these phenomena be explained?

The stomach is a pouch with a hole. The rate of emptying is even more important than the size of the pouch itself. In addition, a variety of different and complex mechanisms are involved in the initiation and termination of a meal.

The rate of gastric emptying to the bowel is very important. It defines the amount of nutrients that may, through absorption, enter the blood stream, thereby altering the blood composition and threatening the homeostasis. A fast and intense nutrient absorption rapidly changes the blood composition (i.e., with elevations in sugars and lipids) and demands a quick and efficient metabolic answer.

Some refined and pre-digested elements of the modern diet are free of fiber and completely ready for a fast absorption. These elements have been called high-glycemic index foods, ever since Jenkins (1) defined the concept of the glycemic index in 1980.

In the stomach, food is mixed with acidic gastric secretions and proteolytic enzymes. Most microbes ingested with food are killed by acid; therefore, any contamination risk is minimized. Large pieces of food are broken down, and the osmolarity of the content is adjusted. The food and drink that present the right osmolarity will leave the stomach sooner, thereby explaining why one can drink a liter of sweet iced tea more easily and quickly than a liter of pure water. Additionally, the stomach adds the R factor and intrinsic factor to allow vitamin B12 to be absorbed in the ileum.

Once these steps are complete, the stomach sends the chyme (i.e., the food mixed with digestive secretions) to the small bowel, where it is immediately admixed with the biliopancreatic juices that lead to near-complete digestion (mammals cannot digest fiber without the bacterial help of fermentation, which occurs in the colon).

In the duodenum, the absorption of small particles is initiated promptly, and the chyme keeps moving downwards as the absorption process occurs. Endogenous glucose production is not interrupted at this stage (i.e., the pancreatic α-cells do not suspend glucagon production). Hypoglycemia may kill an animal in minutes, so the proximal bowel does not have the ''authority'' to give such an extreme order, but it can produce a less powerful one (i.e., the proximal gut secretes glucose-dependent insulinotropic polypeptide, an insulinotropic agent that cannot suppress glucagon and the endogenous production of glucose (2-4)). At this point, satiety is not supposed to occur. For quite obvious reasons, the proximal gut is not the point at which food should trigger intense satiety or initiate the suspension of glucagon production.

Nonetheless, when the distal portion of the small bowel receives nutrients (meaning that a significant meal was effectively consumed), the neuroendocrine L cells in the mucosa produce hormones like glucagon-like peptide 1 (GLP-1), oxyntomodulin and polypeptide YY (PYY), which are typical postprandial hormones (5-7). These hormones promote the transition from the fasting state to a postprandial state. In the fasting state, there is hunger, high levels of glucagon, endogenous glucose production, and lipolysis. In the typical postprandial state, an intense production of insulin, blood clearance of glucose and lipids, lipogenesis, and a diminution in the gastric emptying and satiety progressively appear. They are opposite metabolic states.

GLP-1 inhibition of gastric emptying indeed outweighs its insulinotropic effects (8). In other words, the distal intestine stops the gastric emptying at a certain point (e.g., when stimulated by nutrients). Therefore, the intestine defines the functional size of the stomach.

If we suddenly eat progressively more and more refined food, absorption becomes easier and more intense in the proximal gut, thereby reducing the distal stimulation.

As a consequence, there may be deficiencies in the production of distal gut hormones, like GLP-1 and PYY (which happens in obese and type 2 diabetic patients (9,10)), and much food may pass through stomach, regardless of its size. If we do not have the proper stimulation of the distal gut, a simple reduction of the stomach may not work. Indeed, some post-surgical patients left with 30-mL stomach pouches can still eat enough to remain obese or at least to regain most of the lost weight after post-operative adaptation.

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After the distal intestine is busy with digestion and absorption, it secretes the distal gut hormones, which impede further gastric emptying. The typical hunger is suppressed in the brain, where there are receptors for gut hormones. Elevated GLP-1 and insulin suppress the production of ghrelin (a hormone that provokes hunger and the behavior aimed at seeking food (11)).

Surprisingly, even then, superior animals (including humans) do not stop eating. At this stage, the stomach is not emptying well anymore, yet the animal continues eating until the stomach is very full. GLP-1 facilitates this storage process because it provokes a relaxation of the gastric fundus, therefore allowing the stomach to receive more food (12). At this point, an animal would not actively look for food (i.e., the foraging behavior); however, if there is space in the stomach and food available, the animal continues eating. The ''intestinal satiety'' has already been initiated, the typical hunger is gone, but ''the gastric satiety'' does not appear until the stomach is completely full.

It is not hunger that motivates the animal at this point, but gluttony. The distinction between *intestinal* and *gastric* satiety was just created as an important didactic division for general understanding.

Gluttony is not a sin. It is a wonderful instinct, developed over millions of years, for times of scarcity. A wild dog that finds food today is not certain he will find it again tomorrow. Creating reserves may cause some fullness today, but it may save his life in the near future.

In summary, there are two different phases of alimentation. Initially, there is hunger: the stomach empties easily (and its size does not much matter at this point), and the intestine is receptive. Later, the intestine is loaded, and the distal gut hormones are produced to trigger a metabolic response. Gastric emptying is dramatically reduced, and GLP-1 relaxes the gastric fundus to allow further eating. Thus, the hunger is gone, but there is gluttony. With gluttony, the animal keeps on eating until there the stomach is physically full, and the gas at the gastric fundus is progressively expelled by eructation.

Therefore, after the intestinal satiety phase, it is normal to continue eating, so an animal can take along what the bowel cannot process immediately. The animal eats until the stomach is full. This gastric satiety phase complements the intestinal satiety phase. It is common to hear from patients: ''Doctor, I keep on eating even when I am not hungry anymore! I think it is anxiety!''

Most obese patients present with an attenuated and delayed intestinal satiety because they have a diminished secretion of distal gut hormones after meals. Therefore, the stopping point in gastric emptying is also delayed and the central satiety signals are jeopardized.

In this extreme scenario, impeding someone from eating by simply tying the digestive tract with bands, narrowing anastomoses or reducing stomachs will create either a lean but unhappy patient if he or she really cannot eat or a patient who is still fat if he or she can continue to eat.

So, does the size of the stomach matter at all? Yes, it matters. The development of this storage chamber that allows you to ''overeat'' to create storage if the next meal fails is very adequate during times of scarcity. If food scarcity is suddenly substituted by food abundance and the next meal is always there, overeating may occur with every meal. To proportionally reduce this organ adapts the individual to abundance. The evolutionary data strongly support the idea that mechanisms of food storage are found in those individuals exposed to scarcity (e.g., a camel stocks water, a frog does not).

In the current western world, there is abundance: the food is refined, pre-digested and quickly absorbed in the upper bowel (i.e., high glycemic index foods are prevalent). In these circumstances, the intestinal satiety may come too late, and the gastric emptying is not properly diminished in time. In this case, the size of the stomach (although over-sized for the times of abundance) will not matter greatly, and it will be perfectly possible for someone with a minimal stomach, or even none, to be very fat.

Mechanical restriction and malabsorption were always the two pillars of classic bariatric surgery. However, it is now clear that neither of these factors is responsible for the most beneficial effects of this type of surgery (13). Instead, they are a primary source of post-operative problems (14).

To reach ''the two satieties'' at the optimal time and in the absence of mechanical restriction and malabsorption is a physiological method of approaching the epidemics of obesity and diabetes.

In recent years, the majority of researchers in the field recognize that the most effective models of classic bariatric surgery work because of the hormonal changes they provoke (13). As such, they started calling this surgical specialty ''Bariatric and Metabolic Surgery.'' Nonetheless, the procedures are the same, and they still contain restrictive and malabsorptive elements because they have been designed to include them.

New procedures, mainly developed in Brazil (15-20), were specifically designed to selectively cause the hormonal and metabolic corrections. By abolishing mechanical restriction (21) (through the means of minimal stomachs with narrow anastomoses or bands) and also avoiding excluded digestive segments and malabsorption, we may reach the ''Pure Metabolic Surgery.'' It will be an evolution.

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