



# Diet and Gut Microbiota, Don't Let Them Break Your Heart!

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## Abstract

As rising rates of obesity threaten to overwhelm healthcare services, physicians still lack effective therapies to halt the cardiovascular complications of this disease. The gut microbiota – a whole community of microorganisms that resides in our intestine – has recently emerged as major player in human health. Crucially, our gut microbes are shaped by our dietary habits, and in turn contribute to both health and disease. In obese patients, the gut microbiota is found to be profoundly altered, which is believed to promote disease complications including cardiovascular disorders. On the other hand, the preservation of a healthy gut microbiota has protective effects against obesity-related disorders. Consequently, understanding the relationship between diet, the gut microbiota, and our body could help scientists to develop new strategies for preventing cardiac diseases in obese patients.

*Keywords: obesity, gut microbiota, diet, cardiovascular disease, immune system.*

## Introduction

Although the world is still recovering from a viral pandemic, human society still has to face its greatest threat: obesity. Indeed, this disease - characterized by an excessive accumulation of body fat (BMI > 30) - has tripled in incidence worldwide since 1975, currently affecting about a fifth of the population. Even more worryingly, obesity rate is expected to increase further in the near future, with up to half of certain Western populations being affected by 2050.<sup>5</sup> Of note, obesity does not only represent a chronic disease affecting a patient's quality of life, but also a major risk factor for potentially fatal cardiovascular complications such as atherosclerosis (obstruction of blood vessels by fatty deposits), heart failure (inability of the heart to pump blood efficiently) or arrhythmia (abnormalities in heart pace). In fact, it is estimated that two thirds of obesity-related deaths are owed to cardiovascular disorders. Because of its epidemic rate of incidence and morbid consequences, obesity poses a major challenge to healthcare services. However, our methods have not evolved or adapted to deal with the overwhelming amount of

obese patients. It is thus urgent to improve our understanding of the disease to develop novel strategies to halt its complications.

Diet is a major lever in the progression of obesity. It is now evident that the quantity and the proportion of nutrients ingested daily influence body fat accumulation and disease development. However, another role of diet has emerged in the last decade: its impact on the gut microbiota. The gut microbiota is the community of microorganisms that resides within our intestines. Trillions of bacteria, fungi and viruses inhabit our digestive tract where they are directly exposed to our dietary choices. More importantly, these microorganisms are in close interaction with our body and support our vital functions. Consequently, the gut microbiota is a crucial player in human health whose actions are determined our dietary choices. In this article, we will discuss how understanding the role of diet and the gut microbiota in obesity could help us preventing cardiovascular diseases.

## The impact of diet on the gut microbiota

Although microorganisms are usually seen as vectors of disease, the fact that trillions of them reside within our bowels is not alarming at all. Indeed, our body actually appreciates the presence of these microbes since they help the digestion process while producing beneficial compounds such as vitamins.

On top of this, these microorganisms constitute a defensive barrier that guards us against intestinal infections. In return, the gut microbes enjoy the food that we ingest daily as well as the stable 37 degrees Celsius of our body. The peculiar relationship that we maintain with our gut microbiota is called mutualism: a biological interaction that benefits both parts.

However, this mutual relationship is solely granted as long as it stays reciprocal and can turn noxious if one part becomes unsatisfied. Our gut bacteria are exposed to our dietary habits in such a way that their survival directly depends on the nutrients we provide them. Certain diets support the development of healthy microbes, whereas others can deplete them or trigger aggressive behaviours. Consequently, our nutritional choices shape our microbiota, and in turn, the nature of the relationship we have with it. In the context of obesity, it has become evident that “Western” diets - rich in refined ingredients, fats and sugars and poor in plant-based products - are not only harmful to us humans, but also to our gut microbes. Indeed, this type of diet injures our gut microbiota by reducing microbial diversity, with the abnormal proliferation of certain species in favour of others. For instance, the microbiota of obese patients typically contains a higher abundance of bacteria belonging to the Firmicutes group, and fewer Bacteroidetes.<sup>2</sup> This could be because Western diets lack certain nutrients that are essential in supporting a healthy gut microbiota, like dietary fibre for instance that is mostly found in fruits, vegetables and wholegrain cereals. The absence of microbiota-friendly nutrients from our diet can affect our gut bacteria until compromising the mutual relationship that we normally maintain with them.

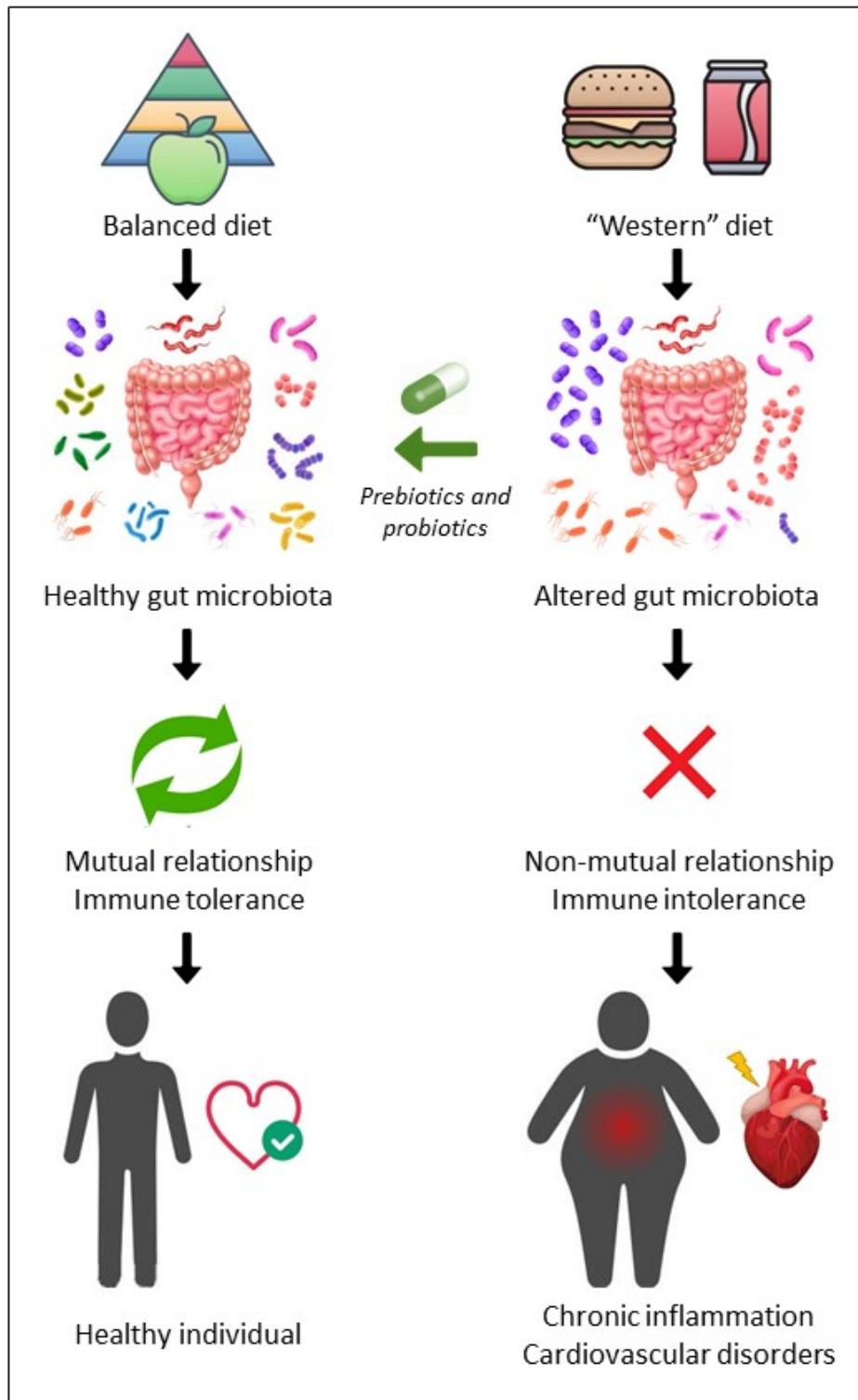


Figure 1: Effects of diet on the gut microbiota and cardiovascular health

## Our immune system controls the relationship we have with the gut microbiota

The immune system is the one in charge of interacting with organisms that are foreign to our body. It is incredibly efficient at dealing with harmful organisms such as infectious bacteria and viruses, but most importantly, it oversees the relationship we have with our gut microbes. Instead of fighting the beneficial bacteria hosted in our bowels, the immune system adopts a tolerant behaviour towards them in order to preserve a peaceful mutual relationship. These microorganisms are recognised by our immune system and allowed to interact closely with our body without being repelled and thereby support our body functions. However, the tolerant behaviour from our immune system is very strict and can be reversed when the gut microbiota experiences drastic changes, upon a Western diet for instance. Changes in the gut microbiota as seen in obese patients result in immune intolerance, which leads to the abnormal activation of the immune response and gut bacteria being repelled.<sup>3</sup> This may be due to the fact that an altered microbiota is not recognised as tolerable anymore by the gut immune system and treated like a harmful organism instead. The activation of immune defences triggers a process called inflammation. Inflammation is an extremely powerful biological weapon when fighting undesirable organisms during infections, but it can also be damaging for our own body if left out of control. Obese patients exhibit signs of gut inflammation and injury, that are believed to be owed to immune intolerance in response to an altered gut microbiota.<sup>9</sup> This abnormal inflammation of the gut can spread across the body over time, until reaching peripheral organs including the heart.

### From the gut to the heart, via the immune system

Inflammation appears to be involved in the multiple complications of obesity. Indeed, the immune system of obese patients appears to be more active in multiple organs including the liver, the brain, fatty tissues and the heart. This phenomenon is called chronic inflammation – a moderate but persistent activation of the immune response across the whole body. Chronic inflammation damages the affected organs over time and weakens their functions.

In the context of cardiovascular disorders, inflammation of the cardiac muscle modifies its structure and impairs its ability to contract, eventually reducing its efficiency in pumping blood that can lead to arrhythmia and heart failure.<sup>8</sup> Inflammation is also at the basis of atherosclerosis, a disease characterised by an excessive accumulation of fat into our arteries.<sup>4</sup> If left untreated, atherosclerosis may lead to infarcts and stroke events. Consequently, preventing chronic inflammation during obesity can protect against cardiovascular disorders, and this could be achieved by maintaining a healthy gut microbiota.

This is where my project stands: understanding the role of diet and microbiota in promoting chronic inflammation and cardiovascular disorders during obesity. Eventually, we aim at developing treatments that would restore the gut microbiota of obese patients and prevent

cardiovascular diseases.

## Microbiota treatment for preventing cardiovascular diseases in obesity

Due to its major role in supporting our health, the gut microbiota is a target of choice for future therapies, and especially for preventing the multiple complications of obesity. Moreover, the gut microbiota has the advantage of being easily reachable using specific nutrients or ingestible therapeutics. Ideally, a microbiota-targeted therapy would consist in regenerating an altered gut microbiota that would be tolerated by our immune system in order to re-establish mutual relationship.

Microbiota-targeted therapy can be achieved through the ingestion of prebiotics or probiotics. Prebiotics are nutrients that promote the growth of beneficial bacteria. An excellent example of prebiotic is dietary fibre that has the particularity of constituting an exclusive source of nutrients for our gut microbiota. Indeed, our body is not able to digest this nutrient, making it fully available for the gut bacteria. When feeding on it, bacteria release beneficial molecules called short-chain fatty acids that help to prevent chronic inflammation.<sup>6</sup> Probiotics on the other hand are literally made of live bacteria that can be consumed to directly re-colonise our gut microbiota with certain beneficial species. For instance, *Lactobacillus* or *Bifidobacterium* are two major probiotic species that have anti-inflammatory effects thanks to their ability to interact with our immune system.<sup>1</sup>

However, the precise nutrients and bacterial species that are key in regulating inflammation between the gut and the heart remain unclear. Moreover, we humans are incredibly diverse and each of us has a unique gut microbiota that will respond in a particular way to a given therapy, making these approaches complex to generalise between patients. Nonetheless, experimental models have shown very powerful effects of diverse prebiotics and probiotics in preventing cardiovascular disease in obesity.<sup>7</sup> Consequently, gut microbiota-targeted approaches may become powerful therapeutic strategies for fighting obesity in the future.

## Conclusion

The gut microbiota stands out as a major player in human health and may represent a promising target for halting obesity epidemic. The power of this microbial community resides in its mutual relationship with our body and in its ability to interact with our immune system. Future research will elucidate the precise parameters that rule these interactions, and how to take advantage of them to halt the cardiovascular complications of obesity.

## Acknowledgments

Many thanks to my supervisor and colleagues of the Centre of Research in Vascular Biology for their help and support over the course of this PhD project.

## Declaration of interest

Author has no conflict of interest to declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All ethical guidelines relating to the research and publication process were adhered to throughout this study.

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