Nutrition and Fresh Dairy Products

SYNDIFRAIS' Scientific and Pratical Newsletter

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Intestinal microbiota

Yoghurts • Fermented milks • Living bacterial cultures • Microbiota • Nutrition • Health

Obesity and IBD: the role of the gut microbiota

The bacteria located in the gut have many functions essential to our health (see previous issue).

However, the microbiota also appears to be involved in certain diseases. There are differences in microbiota composition between obese and normal-weight individuals, as well as between people suffering from chronic Inflammatory Bowel Disease (IBD) and healthy subjects. While the origin of the observed differences is not yet known, they are strongly suspected to have a negative effect on these illnesses.

The ability to directly affect the intestinal microbiota therefore represents a significant step towards the prevention and treatment of certain illnesses which appear to be associated with microbial imbalances. In particular, some bacteria which are already commonly found in yogurt and fermented milk may have a beneficial effect.

CONTENTS

Key Points

- **The intestinal microbiota is involved in certain illnesses, such as IBD and obesity.**
- **Altering the microbiota to prevent or even treat these illnesses is a promising line of research.**
- **Yogurt and fermented milk, which contain living bacteria, may have a preventive or therapeutic effect.**

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The intestinal microbiota: a new factor in health

Chronic Inflammatory Bowel Disease

Under conditions which are not yet well-known, the immune system can be excessively stimulated by the microbiota, leading to chronic Inflammatory Bowel Disease (IBD). The microbiota is involved, but it is not the sole cause for this illness.

A different microbiota from healthy individuals

It has recently been discovered that the microbiota of patients suffering from IBD, as well as patients in remission, is significantly different from that of healthy individuals (called **dysbiosis***)[1].

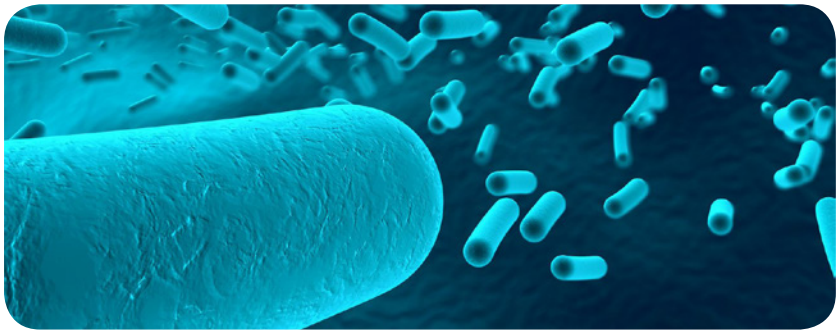
The ratio between the bacterial phyla *Firmicutes* and *Bacteroidetes* appears to be the main marker of these imbalances (table 1). The microbiota of persons suffering from IBD presents a significant deficit in the *Firmicutes* phylum both in number of species and in proportion. The very small quantity of one of the most representative *Firmicutes* species - the bacterium *Faecalibacterium prausnitzii* - may be largely responsible for this deficit.

Nevertheless, these differences are not systematic enough to allow the definition of a "good" or "bad" bacterial profile for this illness. The origin of these imbalances also remains unknown: **the state of dysbiosis may be the origin of the illness or simply a marker of the pathological state.**

An increased risk of inflammation

Though there is no one type of microbiota which is systematically detected, the imbalances which are normally observed point to increased inflammation with:

- a reduction of bacteria with protective anti-inflammatory function which are normally dominant in healthy individuals. In particular, the bacterium *F. prausnitzii* might have significant anti-inflammatory properties[2]. In addition, for patients for whom surgery has proved necessary, the risk of early relapse is inversely proportional to their *F. prausnitzii* levels.
- an increase in pro-inflammatory bacteria with pathogenic potential of the type *Escherichia coli*[3].



Focus on IBD

- IBD includes Crohn's disease (CD) and ulcerative colitis (UC).
- These are characterized by inflammation of the lining of the digestive tract, most frequently in the intestine for CD, and in the rectum and colon for UC.
- They alternate between inflammatory eruptions, which cause diarrhea, stomach pain, weight loss and fever, and periods of remission.
- They are most frequently diagnosed in patients between 20 and 30 years old, but may develop at any age.
- The prevalence rate of IBD reaching up to 396/100,000 persons worldwide.

GLOSSARY:

* **Dysbiosis:** Significant differences in the composition of the intestinal microbiota for a sick individual compared to a healthy individual.

Key point

- The microbiota imbalances that have been observed indicate an increased risk of inflammation.

IN PRACTICE:

- During a flare-up, **recommend a low-fiber diet in order to limit digestive symptoms**.
- During periods of remission, **recommend a varied and balanced diet to avoid deficiencies.**

➜ Refer the patient to a gastroenterologist or dietician.

Obesity

Obesity is linked to complex interactions between genetic and environmental factors such as diet and lifestyle. But the microbiota may be an additional factor.

A different microbiota from healthy individuals

The *Firmicutes/Bacteroidetes* ratio also appears to be the main marker for microbial imbalances in obese individuals, characterized by a decrease in *Bacteroidetes*[5] (table 1). Weight loss caused by a low-calorie diet can allow the patient to return to a bacterial profile resembling that of thinner individuals[5].

Nevertheless, research on the composition of the intestinal microbiota of obese individuals has produced conflicting results. **It does not permit the definition of a single type of intestinal microbiota associated with obesity.**

In addition, the observed dysbiosis does not allow us to say whether this microbiota is partly responsible for obesity or whether it is simply evidence of dietary changes or of the state of obesity.

Could the microbiota play a role in weight gain?

The microbiota could be involved in our energy metabolism: intestinal bacteria may provide energy to the body which has been recovered from food by-products[6].

Might there therefore be a type of microbiota which leads to an increased ability to extract energy from food? For animals, during a high-fat diet, the microbiota of obese mice seems to be slightly more efficient in recovering energy than that of thin mice[7]. Nevertheless, it is essential to consider the interaction between the diet and the intestine and microbiota: **attributing a decisive role in the development of body fat to the microbiota on its own is not feasible.**

We now know that a combination of environmental and genetic factors contributes to the creation of an individual's specific microbiota, which may or may not favor the development of obesity.

Microbial markers that predict obesity?

Recent studies suggest that individuals with little bacterial diversity (in number of genes) are at greater risk of developing complications associated with obesity[8,9]. These results have yet to be confirmed, but they may indicate a new tool for diagnosing obesity.

Population	Adult of normal weight (20-50 years)	Obese adult (20-50 years)	Adult suffering from IBD (20-50 years)
***Firmicutes/Bacteroidetes* ratio**	10/1	100/1	1/1 à 3/1

Table 1 - The *Firmicutes-Bacteroidetes* balance, the main bacterial marker.

Focus on obesity

- Around 10% of men and 14% of women in the world are obese[4].

Key points

A combination of environmental and genetic factors contributes to:

- the creation of an individual's specific microbiota,
- which may or may not favor the development of obesity.

PERSPECTIVES

The confirmation of these observations would open lines of research on:

- the causes of these illnesses,
- diagnostic tools,
- new therapeutic factors.

Bacterial components involved in low-grade inflammation

Obesity is characterized by a combination of metabolic issues whose development is associated with **chronic low-grade inflammation*** [10] (figure 1). More and more evidence suggests that the microbiota might be involved in this low-grade inflammation.

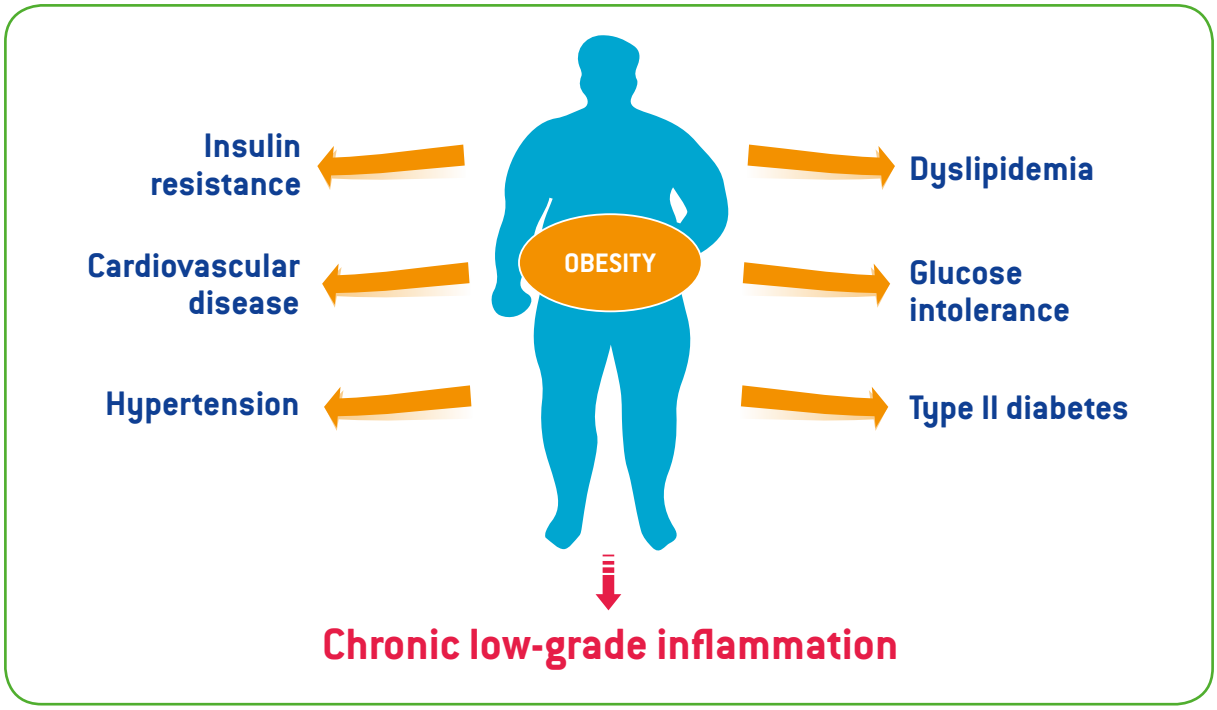


Figure 1 - Obesity and its illnesses are associated with chronic low-grade inflammation.

Excess lipids may affect intestinal permeability

A high-fat diet may affect intestinal permeability and enable the entry of bacterial compounds into the bloodstream [11]. In animals, **Lipopolysaccharide**** (LPS) – molecules from the cell walls of gram-negative bacteria –, appear to pass more easily into the bloodstream. While in healthy mice, plasmatic LPS levels are very low, they are nearly doubled for mice fed a high-fat diet [12].

However, a high-fat diet also changes the composition of the intestinal microbiota, characterized by a drastic reduction in the number of *Bifidobacteria* (gram-positive bacteria). Surprisingly, the number of *Bifidobacteria* is directly associated with the blood LPS level:

- the less *Bifidobacteria* in the microbiota, the higher the blood LPS level [12].

Many mechanisms of action have been suggested, such as an increase in the formation of chylomicrons (molecular complexes which allow bacterial molecules to pass into the bloodstream) or a decrease in the activity of the enzyme responsible for splitting LPS in the intestine (figure 2).

GLOSSARY:

* **Chronic low-grade inflammation** in obese individuals corresponds to a moderate but lasting increase in inflammatory markers in the blood.

** **Lipopolysaccharides (LPS):** Bacterial components continually produced in the intestinal lumen following lysis of gram-negative bacteria.

And favor the development of low-grade inflammation

Once LPS is in the bloodstream, it can stimulate the synthesis and secretion of pro-inflammatory cytokines in peripheral tissue, also favoring the development of chronic low-grade inflammation.

LPS may also be involved in the development of type 2 diabetes associated with obesity: type-2 diabetic patients also present with significantly higher plasma LPS levels compared to healthy individualss [13].

Key point

- Excess lipids may be involved in the development of low-grade inflammation.

IN PRACTICE:

Recommend a balanced diet and avoid excessive fat.

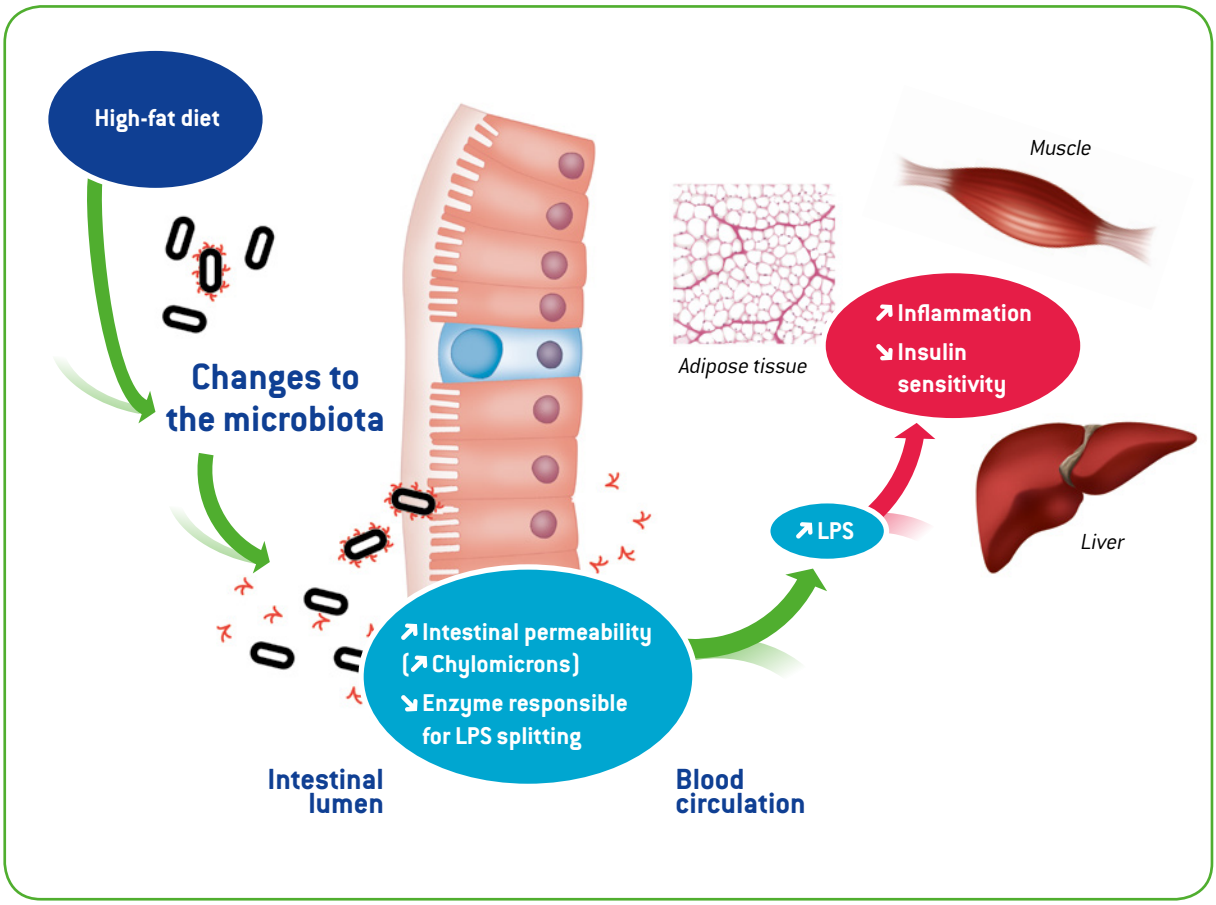


Figure 2 - The consumption of a high-fat diet may contribute to the development of low-grade inflammation (adapted from Cani & Delzenne 2011 [14]).

Bacteria in Fresh Dairy Products: a therapeutic and preventive role

Modulation of the microbiota presents new possibilities for treatment. There is growing scientific evidence demonstrating or suggesting the beneficial effects of certain bacteria which are already commonly found in yogurt and fermented milk (*Streptococcus thermophilus, Lactobacillus bulgaricus* and others – mainly strains of *Lactobacillus* and *Bifidobacteria*).

Preventive and curative effects on IBD

Clinical trials demonstrate uneven effectiveness of probiotics on IBD, but certain promising strains may be used in treatment of the illness in the future.

Recent examples include a synbiotic (combining *Bifidobacterium* and a prebiotic) which has enabled a reduction in the intensity and severity of CD symptoms [15], while a significant reduction in bleeding was achieved for UC with a combination of probiotic species [16].

Research on the effects of probiotics on UC demonstrate greater rates of remission (around 10 %) for patients taking a probiotic (isolated species of bacteria or bacterial cocktails, whether or not they are combined with a prebiotic) [17]. These patients also present a lower relapse rate, of around 10 % [17].

Key points

Certain probiotic strains reduce:

- the intensity of symptoms,
- the risk of relapse.

IN PRACTICE:

Though further research is required for routine prescription, there are no contraindications to recommending dairy products for individuals suffering from IBD.

Body fat reduction and reduction of the risk of developing obesity

More and more studies are demonstrating that yogurt and fermented milk may be beneficial for weight management and the reduction of the risk of becoming obese.

▶ Significant reduction of body fat

Yogurt consumption appears to facilitate the reduction of body fat while preserving lean body mass, especially for obese or overweight individuals on a low-calorie diet [18] (three servings of non-fat yogurt per day). Yogurt consumption also appears to effectively suppress hunger during a diet.

Some lactic cultures may also be especially beneficial. In particular, daily consumption of fermented milk containing a strain of *Lactobacillus* (*L. gasseri* SBT2055) significantly reduces body fat, especially abdominal fat, in obese individuals [19,20].

▶ Reduction of the risk of developing obesity

Many studies have suggested that certain probiotics have a beneficial effect on obesity prevention. Two recent intervention studies have demonstrated significant results.

- A combination of probiotics during pregnancy **significantly reduces the risk of developing abdominal obesity after birth** [21].
- Newborns with a high number of bifidobacteria in their intestinal microbiota (from birth to 12 months) are **less likely to develop obesity at 7 years of age** [22].

Key points

Yogurt and fermented milk may be beneficial for the reduction of:

- body fat,
- the risk of developing obesity.

IN PRACTICE:

- Yogurt and fermented milk may be recommended as part of a low-calorie diet for obese or overweight patients.

Summary

Key points

- **The microbiota of obese individuals and those suffering from IBD are in a state of dysbiosis.**
- **Over the course of the illness, these microbial imbalances may increase the risk of complications.**
- **Modulation of the intestinal microbiota constitutes a promising line of research for the prevention and treatment of certain illnesses associated with dysbiosis.**
  - ➡ **In particular, certain bacteria which are already commonly found in yogurt and fermented milk may have a therapeutic or preventive effect.**

IN PRACTICE

Prevention

- A varied and balanced diet.
- Avoid excess fat.
- Regular consumption of Fresh Dairy Products.

Therapy

- **For individuals suffering from IBD:**
  - ➡ Limit fiber consumption during flare-ups.
  - ➡ A highly varied and balanced diet during periods of remission.
  - ➡ No contraindication to recommending yogurt and fermented milk.
- **For overweight or obese individuals:**
  - ➡ Add yogurt and fermented milk to low-calorie diets.

Figure 3 - The major role of yogurt and fermented milk in prevention and therapy.

Warning!

- In some farm animals, certain probiotics, **which are different from those used for human consumption**, stimulate immunity and lead to better resistance to illness, which enables the animal to grow at a normal rate.
- Lactic cultures used in the milk fermentation process have never been implicated in weight gain by any scientific study.

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