Since a long time paediatricians and gastroenterologists have been intrigued by the evolution of lactose intolerance in relation to age.

In infants, lactose ingestion induces diarrhoea that may threaten life. In children, this consumption leads to a discomfort sensation and the child learns to identify the responsible sources of that and banish them of his diet. However, in the course of teenage and moreover in adult age, it is usual and surprising to record that persons who consume again milk products do not suffer from discomfort despite the lack of β-galactosidase activity, which is confirmed by intestinal biopsy.

Numerous factors probably participate to this phenomenon. The chronic consumption of lactose seems to induce, in adults, a metabolic adaptation of the intestinal flora, this leading to a functional complementation with the host. This attractive hypothesis does not allow us to understand why this new equilibrium does occur so late in the developmental stage since fermentation is in breast-fed infant an important physiological phenomenon (35% to 55% of the ingested lactose). The mode of ingestion of lactose is an important feature. In the intolerant adult, the troubles may be important or weak according to the load of lactose consumed alone or during a meal.

Particularly, the nature of the lactose-containing product seems to affect its tolerance. A study supported by the Scientific Mission of Syndifrais confirmed this. Even though the production of breath hydrogen (a quantitative indicator of lactose fermentation in intolerant subjects) slightly increases when milk is consumed, it doesn’t vary after consumption of the same load of lactose in yoghurt containing at least 10^8 live bacteria per millilitre.

The yoghurt may represent a "self-digestible" source of lactose but only in the case where bacteria are alive and are present in a sufficient amount. These results arise other questions (are bacteria responsible for the differences observed between milk and yoghurt, and by which mechanism ?) at which new studies, supported by Syndifrais, will propose answers for the first time.

To a next letter, and ... Happy New Year
Lactose intolerance and importance of live flora consumption

In subjects who lack the ability to digest lactose, milk consumption may result in development of digestive discomfort symptoms. The enhanced production of breath hydrogen reflects this lactose maldigestion, which is improved by yoghurt consumption. Numerous studies aimed to explain the specific effect of yoghurt compared to milk and the beneficial effect seems to be linked to the presence of yoghurt lactic acid bacteria. A well-designed study examined whether long-term consumption of milk fermented with Lactobacillus GG could reduce gastrointestinal and respiratory infections in children attending in day care centres. These children are at high risk of respiratory and gastrointestinal infections (2).

This randomised, double blind, placebo controlled clinical study was carried out in 18 municipal day care centres in Finland. The intervention lasted seven months over the winter and 571 healthy children aged 1-6 years were recruited, half of them received the fermented milk, the others received the same milk but without probiotic. Nevertheless the effects of the probiotic are modest, the authors conclude that the consumption of Lactobacillus GG reduced respiratory infections and their severity among children in day care units.

Preventing respiratory infections by probiotics

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Preventing E. coli infection with B. lactis

Researchers from a university of New Zealand demonstrate that dietary supplementation with Bifidobacterium lactis HN019 can reduce the severity of enterohemolytic E. coli 015:H17* in mice (3). Compared to control mice, mice that received orally the probiotic before and after oral challenge with the pathogen show lower cumulative morbidity rates following infection and decreased E. coli translocation in blood, liver or spleen. In the probiotic group, these effects were accompanied by higher phagocytic capacities of blood leukocytes and peritoneal macrophages, and enhanced intestinal IgA antibody titers against E. coli.

The authors suggest that reduction of infection severity may be associated with enhanced immune protection conferred by the probiotic.

Preventive effect of yoghurts

A randomised clinical trial tested the effect of yoghurt consumption on the human salivary microbiota. It shows that 8 weeks consumption of yoghurt can decrease the number of salivary streptococci like lactobacilli (4). This Italian team from "La Sapienza" University of Rome, University of Cagliari and University of Verona used a convicing study.

Lactobacillus lactis

Bacteriocins are bacterial proteolytic enzymes or peptides that are usually active against bacterial species. Many bacteriocins produced by different species of the genus Lactobacillus have been described (5, 6).

Lactobacillus delbrueckii, which is a natural inhabitant of the intestine, can be used as a suitable starter for the production of fermented milk. It is shown that Lactobacillus delbrueckii subsp. lactis produces a bacteriocin named U0004 controlled by two promoters (1).
Beneficial effect of yoghurt on human oral bacteria

A randomised clinical trial of the effect of yoghurt consumption on the human salivary microflora shows that 8 weeks consumption of yoghurt can decrease the numbers of salivary streptococci and lactobacilli (4). This Italian team from “La Sapienza” University of Roma also shows that the yoghurt bacteria are unable to colonize the mouth. As the food clearance from the mouth is rapid and the time contact between yoghurt bacteria and oral bacteria is short, the authors attributed the observed effect to a residual antimicrobial activity contained in the yoghurt. They suggest the possible use of yoghurt as caries-preventing food.

Lactobacillus lactis produces a bacteriocin

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Probiotics benefits on intestinal barrier function

Aberrant immune responses to indigenous microflora have been implicated in inflammatory bowel diseases (8, 9). For example the interleukin-10 knockout mice, which is predisposed to develop enterocolitis in the presence of an enteric bacterial flora, remains disease-free when maintained under germ-free conditions. This mice model is used to determine the effect of probiotic consumption on the gastrointestinal microflora, tumour development and colitis. A team from the University of Cork in Ireland showed in a placebo-controlled trial that the consumption of Lactobacillus salivarius by IL10-deficient mice induced a reduction of faecal coliforms and enterococci as well as a reduction of mucosal inflammation and colonic adenocarcinoma development (10). This study assessed the ability of Lactobacillus salivarius in modulating enterocolitis in IL10-deficient mice model and gave an in vivo evidence for the use of this probiotic as biotherapeutic agent in the treatment of inflammatory bowel disease.

Preventing infections by probiotics

Probiotics enhance intestinal barrier function

Clinical evidence supported the theory that pathogenesis of Crohn’s disease occurs as a result of an aggressive immune response to the resident microflora of the gastrointestinal tract. This is also supported by results showing that the intake of a supplement of probiotic bacteria may be effective on the treatment of this disease.

As this inflammatory bowel disease is accompanied by an abnormal immune response and an abnormal intestinal permeability to intestinal luminal contents (like bacterial products and dietary antigens) we can ask the question if the benefits provided by a probiotic had a direct effect on barrier function or if it is a result of down regulation of the inflammation process.

A team from the Universities of Alberta, Canada and of L’Aquilia, Italy tried to answer to this question (11).

They used the probiotic mixture VSL#3® and as model the interleukin (IL)-10 gene-deficient mice which develop a patchy, chronic colitis that is similar to human Crohn disease.

Compared to normal mice, IL10 gene-deficient mice spontaneously secreted higher amounts of proinflammatory cytokines (TNFα and IFNγ) from both the ileum and the colon.

The treatment with VSL#3® compound resulted in a substantial increase in the total load of non-pathogenic bacteria in the colon in both groups of mice in conjunction with the reduction in mucosal levels of proinflammatory cytokines, TNFα and IFNγ. This observation indicates that the intestine is able to discriminate and define selective responses to different strains of non-pathogenic bacteria.
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In addition, VSL#3 treatment reduced colonic permeability in both IL10 gene-deficient mice and control mice leading to the normalization of colonic physiologic function and barrier integrity as suggested by the measurement of mannitol fluxes and spontaneous transepithelial potential difference.

This result suggests that the type and quantity of bacterial species present in the colon modulate intestinal permeability.

Although this reduction may have occurred as a result of a reduction in proinflammatory cytokine release, in vitro studies show that epithelial barrier function can be modulated by exposure to proteinaceous soluble factor secreted by the probiotic mixture.

Another mechanism by which probiotic bacteria could protect epithelium is by receptor competition.

In vitro results showed that resistance to Salmonella could be increased by exposure to a proteinaceous factor secreted by the probiotic mixture VSL#3.

In conclusion, this study showed that probiotic mixture VSL#3 treatment of both normal mice and IL-10 gene-deficient mice resulted in a direct enhancement of epithelial barrier function.

This beneficial effect is a probably a result of a combination of :

1) an immunomodulatory effect of the probiotic mixture on cells of the immune system,
2) the ability of the probiotic mixture to inhibit the attachment of pathogenic bacteria,
3) the secretion of a factor (or factors) by the probiotic mixture that enhances barrier integrity.

Probiotics enhance intestinal barrier function

VSL#3 est une préparation contenant un mélange Lyophilisé de : B. longum, B. infantis, B. breve, L. acidophilus, L. casei, L. bulgaricus, L. plantarum et S. thermophilus.


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1. Probiotics enhance intestinal barrier function

Probiotics benefits on intestinal barrier function

Probiotics enhance intestinal barrier function

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Probiotics benefits on intestinal barrier function
**Enhancing cellular immunity in elderly**

In a trial conducted with 27 volunteers (60-94 years), Gill et al. from the Milk & Health Research Centre of New Zealand (12) showed that the daily consumption of milk containing *Lactobacillus rhamnosus* HN001 or *Bifidobacterium lactis* HNO19 during 3 weeks increases Natural Killer activity cells. This increase was significantly correlated with age, subjects older than 70 years experiencing greater improvements than those under 70 years. This activity persisted only as long as supplementation with probiotics could represent a mean of enhancing the activity of NK and polymorphonuclear cells in the elderly.

**Immune cellular immunity enhancement in mice**

In a trial conducted in mice, Gill & Rutherfurd (14) show that *L. rhamnosus* HN001 delivered orally as a viable probiotic supplement in a milk-based substrate is able to enhance phagocytic capacity. At similar doses of that of live bacteria, heat-killed preparations also enhanced phagocytic responses. In contrast to the results obtained with cellular phagocytosis, this study indicated that live, but not heat-killed *L. rhamnosus* HN001 enhanced gut mucosal antibody responses to orally administered cholera toxin vaccine. This result suggests that persistence of probiotic microorganisms in the gut may be a prerequisite to enhancement of the mucosal immune system. Interestingly, while a dose of 10⁷/day of probiotic was shown sufficient to enhance phagocytic capacity of blood leukocytes, a minimum daily dose of 10⁸ was found necessary to enhance the phagocytic capacity of peritoneal cells. The conclusion of this study is that *L. rhamnosus* HN001 exhibits dose-dependent effects on the phagocytic defence system of mice, and suggests that while the innate cellular immune system is responsive to killed forms of probiotic; live forms may only stimulate specific gut mucosal immunity.
The data base LAB-DOC organised by SYNDIFRAIS, brought together the bibliographic references of the international scientific publications accompanied by the authors’ summaries.


Your suggestions and comments will draw all our attention. Please send them to: SYNDIFRAIS

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