

## The education of the immune system

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*An important study has shown that exposure of children, early in their life, to bacteria in the environment is essential for the development of the immune system and also plays a significant role in the prevention of several autoimmune disorders such as type 1 diabetes, asthma and allergies.*

**Autoimmune disorders** are caused by dysfunction of the immune system: instead of limiting itself to defending the body against external aggression, as is usually the case, the immune system instead attacks the human body itself. This targeting error evidently has serious consequences and can lead to the development of a large number of diseases, including type 1 diabetes, inflammatory diseases of the intestine, lupus, asthma and even allergies.

The incidence of autoimmune disorders has strongly increased over the past decades and some scientists have put forward the hypothesis that this increase could be linked to the drastic decrease in the number of microbes present in our living environment.

According to this theory, called the “hygiene hypothesis”, the constant improvement in sanitary conditions decreases our exposure to different microbes in the environment and leads to a situation where our immune system is not in contact with sufficient microorganisms to allow it to properly learn its role in adequately distinguishing between what is dangerous (pathogens derived from the exterior) and what is not (the human body as such).

Related to this, it is interesting to note that children who grow up in an environment that is rich in microbes, such as a farm, are much less likely to develop asthma or allergies<sup>1</sup>. The factors responsible for this protection remain poorly understood but it seems likely that the intestinal microbiome, which is the community of bacteria present within the intestine, plays an important role since several studies have suggested that these bacteria are essential for the proper functioning of the immune system.

### HUMAN LABORATORY

To better understand this phenomenon, some scientists had the idea of studying microbial composition in the intestines of three populations who live very close to each other (Finland, Russian Karelia and Estonia), but who nonetheless exhibit very large differences in the incidence of autoimmune disorders.

Finland and the Russian republic of Karelia are literally connected from a geographic perspective, but the incidences of allergies and type 1 diabetes are up to six times higher in Finland. Estonia, for its part, is situated in the same region and has had, until very recently, an incidence of autoimmune disorders similar to Karelia, but industrialization and improvement in the quality of life has led to an increase in the incidences of these diseases, reaching levels similar to that seen in Finland.

### REDUCED TO SILENCE

To perform this study, the scientists obtained fecal samples every month for three years from over 200 children born in Espoo (Finland),



Petrozavodsk (Karelia) and Tartu (Estonia). The bacterial composition of these samples was analyzed by genetic sequencing and the general state of health for the children was assessed in parallel using a very detailed questionnaire.

The scientists initially observed that the bacterial composition of the microbiomes was very different depending on the location of birth: the intestinal flora of Finnish and Estonian children was dominated by *Bacteroidal* species whereas the flora from children of Russian Karelia was principally composed of *Bifidobacteria*<sup>2</sup>.

This difference certainly has serious consequences for the development of the immune system, since the researchers observed that the immune activity of individuals with a microbiome enriched in *Bacteroides* was abnormally feeble compared to that from an individual enriched in *Bifidobacteria*.

In other words, it seems that the sanitary conditions associated with the modern way of life favors the predominance of certain bacteria in Finnish and Estonian children (*Bacteroides*) and that these bacteria prevent the immune system from normal development. Inversely, the microbiome of the Karelian children is more representative of that which developed over the evolution of the human species and it consequently permits the optimal development of immunity.

These results remind us that, despite the generally positive effects of adopting a modern way of life, the improvement of sanitary conditions has also had a negative impact on the diversity of our intestinal flora.

This does not mean that we should return to the past, far from our sanitary present, but to take these observations into account to help us diminish, as much as possible, the negative effects of our sanitary lifestyle.

One of the most important things we can do is to limit, as much as possible, the use of antibiotics which have a devastating effect on our intestinal flora, particularly since they are often completely useless when the infection which prompts their use is caused by viruses (which are not affected by antibiotics).

The abundant consumption of foods derived from plants can also have a major impact on the composition of the intestinal flora since the presence of fibre and of alimentary polyphenols permits the establishment of a diversified microbiome, composed principally of beneficial bacteria.

<sup>(1)</sup> von Mutius, E and Vercelli D. Farm living: effects on childhood asthma and allergy. *Nat. Rev. Immunol.* 2010;10:861-868.

<sup>(2)</sup> Vatanen T et al. Variation in microbiome LPS immunogenicity contributes to autoimmunity in humans. *Cell* 2016;165:842-853.