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Haahtela, Tari

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Asthma as an example of non-communicable diseases – Let us simplify the chain of causality

Tari Haahtela
Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland

Clinically, asthma diagnosis is made by measuring lung function, recognizing the excess variation of airflow. What is the reason for variable airflow limitation? Something wrong in the smooth muscle? We know that already at the very early stages of asthma the airway wall expresses inflammatory changes: edema, disruption of epithelial cell junctions, swelling and thickening of basement membrane as well as influx of inflammatory cells, like eosinophils and neutrophils, into lamina propria.\(^1,2\) If the inflammatory process is severe enough and lasts long enough, the smooth muscle starts to restrict the damage by contracting. For that, a genetic disposition to increased bronchial responsiveness is also needed.

The questions do not stop here. What is causing the recurrent, long-term airway inflammation? Inflammation which seems to be inappropriate and excessive, not truly serving the host to cope with dangerous invaders. The obvious answer is lack of immune balance.\(^3\) The immune system does not make a proper distinction between danger and non-danger signals but keeps on pushing e.g. eosinophils to the epithelium. The biological role of eosinophils and their toxic proteins is to kill the potentially dangerous invader to the mucosa. But now the invader is lacking or is an innocent bystander like pollen.

What is then the reason of immune imbalance? We used to think allergy as hyper-responsiveness, i.e. too active immune response, but it may be the other way around. It might be caused by epithelial hyporesponsiveness to bioparticles, as a consequence of poor training by microbial exposure by commensals and saprophytes, especially in early childhood. During the birch pollen season, more transcripts showed modified expression levels in nasal epithelium in healthy compared to allergic students.\(^4\) Health is an active state.

Urban environment appears to lack elements, that are necessary for the proper development of tolerance against foreign proteins.\(^5\) In the Karelia Allergy Study,\(^6\) the skin and nasal microbiome of the Finnish and Russian youth were quite contrasting having a direct effect on immune responses (Ruokolainen, personal communication 2016).

Finally, what impoverish the human microbiome in the gut, skin and respiratory tract? The obvious answer is disconnection of man from natural contacts in the rapidly urbanizing world. Everything we eat, drink, touch and breathe modulates our microbiome and keeps immune processes alert.

The key issue in tolerance development might well be the diversity of microbial species in our microbiota, which in turn is dependent on the biodiversity of our living environment and lifestyle.\(^7,8\) Changes in life-style, e.g. increased use of processed food, lead to reduced human gut microbiota (dysbiosis), immune dysfunction (poor tolerance), inappropriate inflammatory responses and finally symptoms and disease. The clinical manifestation – what kind of a disease we get – is then largely dependent on our individual genetic architecture.

Loss of environmental biodiversity is one, if not the most dangerous global megatrend. The cross-talk of environmental metagenome and human genome (our first genome) is effected through the genome of human microbiota (microbiome, our second genome). This interplay determines health and disease. And not only in terms of asthma but also in many other non-communicable diseases, where low-grade inflammation and immune dysfunction play a role.

References