

The gut microbiota appears to play a role in a number of diseases. «Gut profiling» and «gut cocktails» may become standard diagnostic tests and treatments in everyday clinical practice

Personalised medicine targeting the gut microbiota?

The recent national report on personalised medicine (1) devotes little space to microbiomics, that is, studies of the normal microbiota and its genes, owing to a limited existing knowledge base. It is implied, however, that the field will acquire clinical significance. What form might this take?

The gut microbiota varies greatly and has significant metabolic activity. The bacteria constitute a manipulable organ and therefore represent a potential therapeutic target. As more and more diseases are linked to disturbances of the gut microbiota, many of us will find ourselves faced with the option of gut microbiota-directed diagnostics or therapy.

Cross-sectional studies have revealed differences between diseased and healthy individuals in the composition of their gut microbiota, for example in type 2 diabetes (2). Whether it is single bacteria or the entire intestinal environment that plays a role, or whether the observed changes are secondary to disease, is unclear. The studies show, however, that the gut microbiota profile in itself has potential as a diagnostic tool and may become clinically relevant.

A better understanding of the relation between gut microbiota and disease will enable the use of personalised therapy. Trimethylamine-*N*-oxide (TMAO), a product of bacterial metabolism of choline and carnitine (in eggs and meat), is directly involved in atherosclerosis, and is moreover a marker for cardiovascular events (3). We have recently shown that plasma levels of this oxide are also related to survival in patients with heart failure (4). Identification of specific environment-gut microbiota interactions such as these could lead to novel therapeutic recommendations and lifestyle advice, based on either the gut microbiota profile or bacteria-related metabolites.

The efficacy and toxicity of drugs is affected by the gut microbiota. Digoxin, for example, is inactivated in 10 % of us by the bacterium *Eggerthella lenta*, while adverse effects of cytostatics can be reduced by bacterial enzymes (5). Pharmacomicrobiomics may therefore become part of personalised medicine.

The condition for which most progress has been made in this regard is *Clostridium difficile* colitis, in which faecal transplantation for recurrent disease can be regarded as established (6). A Dutch group recently showed that faecal transplantation also improved insulin sensitivity in metabolic syndrome (7). Such data give rise to hopes that targeted treatment of the gut microbiota can provide health benefits also for conditions outside the intestines.

In Norway, there has been research into the relation between intestinal bacteria and health for some time (8). The gut microbiota has become a major field of research internationally, driven by new genetic methods that allow culture-independent analyses of the microbiota, and by publicly funded projects in Europe (MetaHIT) and the USA (the Human Microbiome Project). In addition, pioneering work in germ-free mice has directly linked the composition of the gut microbiota to factors such as obesity and behaviour (9, 10).

There are many challenges remaining before terms like «gut microbiota medicine» or «gut microbiota disease» can become part of clinical practice. The gut microbiota is affected by many known and unknown confounding factors, including diet and age. It is important that methods are standardised, as the conditions used can greatly affect the results obtained. In Norway, optimal methods have been established to only a limited degree, and the lack of facilities for research on germ-free animal models is a particular challenge.

Who will claim ownership of this new organ? Gastroenterologists will be in a unique position, with endoscopic access to diagnosis and treatment, but it is difficult to envisage the development of a modern gut microbiota medicine without microbiologists and infectious disease specialists. In order to conduct high quality studies of conditions such as obesity, diabetes and rheumatic diseases, to name but a few, interdisciplinary collaboration will be required. The first national microbiota conference, held in 2014, was a step in that direction, as was the foundation of a Norwegian Microbiota Society.

It is important not to get carried away. A thorough understanding of the gut microbiota in different diseases is needed, and clinical trials will be required before implementation in clinical practice. The risk of transmission of infectious diseases and a more theoretical risk of transmission of a deleterious microbiota must be monitored and weighed up against presumed health benefits. We know little about whether probiotics, for example, have positive effects in the long term, such that one can usefully refrain from such treatment given that the benefits are not proven. All in all, there is still legitimate cause for optimism. By means of high-quality scientific studies of the gut microbiota, we can achieve better understanding of disease, diagnosis and treatment in a personalised manner.

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