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Malnutrition in children mars gut microbiome

Nutritional interventions fail to restore intestinal microbiota.

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Severely malnourished children, like those being treated here at Dhakar Hospital in Bangladesh, have a less diverse mix of gut microbes.

The mix of microbes in people's gut gets established early on in childhood and plays a large part in keeping kids healthy. But starvation disrupts the development of a healthy microbiome, according to a study comparing the gut microbiota of healthy and severely malnourished children from the same slum area of Dhaka, in Bangladesh, in the crucial two years after birth. This disruption persisted even after the malnutrition was treated with high-nutrient foods. The results suggest the mix of gut microbiota, which is known to contribute to immune function and nutrient extraction, could play a significant role in the pathology of malnutrition.

Age correlation

To determine the composition of normal microbiota and how they develop, a team of researchers from the United States and Bangladesh, led by Jeffrey Gordon of Washington University in St Louis, Missouri, took monthly faecal samples from 12 healthy children from the slum over the first two years of life. Using DNA sequencing to distinguish the different bacteria present (the microbiome), the team compared the diversity and proportions of different species in the samples, and found that the relative abundances of 24 species in particular strongly correlated with the child's age when the sample was taken. Gordon and his colleagues found that the proportions of the 24 species changed as the children grew older, and that particular microbial compositions correlated with age across all the children. The team tested their model on 38 healthy, well-nourished children from the same area, and found that it accurately predicted these children's ages.

When the researchers analysed the gut microbiota of starving children from the same part of Dhaka, however, they found that the microbial composition did not correspond to the children's actual age. Instead, it was that expected in a younger child. The discrepancy was greatest in the most severely malnourished children. Moreover, although the microbiota temporarily 'matured' after feeding treatment had improved the children's weight and nutritional status, it soon returned to a 'young for age' status. More extensive analysis of the microbiomes of the malnourished children showed that they were less diverse and that many species were less abundant than in healthy children of similar age.

The well-nourished children had a resilient microbiome: although its composition changed, for example, during diarrhoeal infections, it returned to the normal state within a month or so.

The study is published on *Nature*'s website today[1].

Essential partners

The team correlated age with 24 species, which offered an additional means of classifying malnutrition and evaluating how effective feeding therapies are at influencing the gut microbiota, according to Gordon. The technique could potentially be used as a biomarker to define and improve children's health, says Dennis Lang, a microbiologist involved in global health at the Fogarty International Center of the US National Institutes of Health in Bethesda, Maryland, who was not involved in the study.

The algorithm the group used to distinguish the species is the first that can help gauge the degree of development of this microbial community, says biochemist Sandrine Claus at the University of Reading, UK. "In the future, we can imagine applying this to other diseases where early microbial development may be involved, such as autism," says Claus.

Gordon's group plans to study how the altered proportions of their 24 species may actually cause malnutrition, or they could just be indicators correlated with microbiome health.

"We want to know the functional consequences of immaturity, and whether it can be repaired with food or with microbes," says Gordon.

Although the nutrient-rich diets used in child-health clinics have significantly reduced deaths, malnutrition still leaves long-term marks on children's health. Lower IQ and immune dysfunction, for example, can persist even after the child's nutritional status and weight improve.

An immature microbiome may contribute to these problems. A previous paper[2] from Gordon and his colleagues reported that differences in the intestinal microbial mix could contribute to kwashiorkor, a disease caused primarily by protein deficiency, in children in Malawi.

"We haven't yet satisfactorily addressed these issues," says Gordon. The current work, he says, "raises the spectre that healthy growth and development shouldn't be judged just based on our human cells, but also on the important roles of our microbial partners."

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References

1. Subramanian, S. *et al*. *Nature* http://dx.doi.org/10.1038/nature13421 (2014).
2. Smith, M. I. *et al*. *Science* **339**, 548–554 (2013).