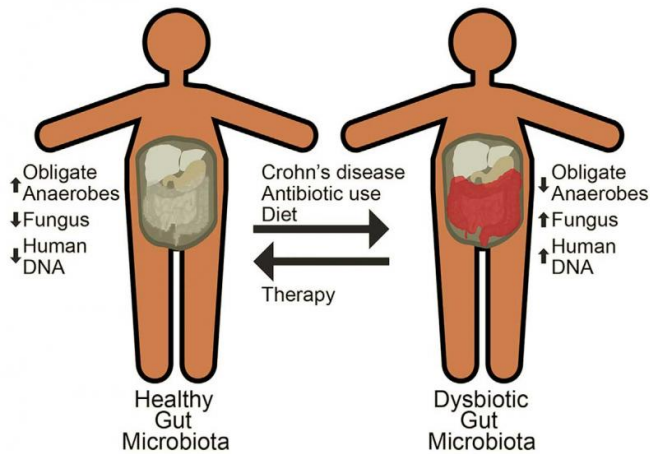


Crohn's disease treatments don't fully restore healthy gut microbes in children

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By examining pediatric Crohn's disease patients, Lewis et al. show that dysbiosis independently associated with antibiotics, inflammation, and diet and decreases with reduced intestinal inflammation. Credit: Lewis and Chen et al./*Cell Host & Microbe* 2015

A gut microbe analysis of children receiving treatment for Crohn's disease reveals that diet-based and anti-inflammatory therapies alter different components of the microbial community without fully restoring the normal balance of gut bacteria and fungi. The surprising findings, published October 14 in *Cell Host & Microbe*, could lead to new strategies for the diagnosis and treatment of inflammatory bowel disease.

"We show that microbes in the gut respond to treatment of inflammatory bowel disease in a much more complex way than has been previously appreciated," says co-principal investigator Gary Wu of the University of Pennsylvania. "The results of our study provide information that could be used to track or predict disease, as well as new diet-based therapeutic strategies."

Early Crohn's disease onset can cause problems

such as stunted growth, weakened bones, and delayed puberty. Patients are often treated with antibiotics, an anti-inflammatory drug called anti-TNF, or a highly restrictive diet that may involve tube feeding. However, no special diet has been proven effective for preventing or treating Crohn's disease, and the lack of knowledge about what causes the disease and how currently available treatments work has limited the development of improved therapeutic options for patients.

To address this need, Wu and co-principal investigators James Lewis and Frederic Bushman of the University of Pennsylvania and their collaborators led an international study of 90 children with Crohn's disease who were being treated with a formula-based diet or anti-TNF therapy and compared them to 26 healthy control children. Using shotgun metagenomic sequencing to analyze fecal samples, they found that antibiotics, anti-TNF, and formula-based diet therapy had different effects on the abundance of distinct types of gut microbes.

None of these treatments fully restored the normal balance of gut microbes. The recent use of antibiotics, which are direct toxins to bacteria, was associated with highly disturbed bacterial communities and an abundance of fungi in the gut. Meanwhile, the formula-based diet reduced inflammation and rapidly decreased fungal abundance, but shifted the composition of gut bacteria further from the normal balance. Although anti-TNF therapy nudged the microbial community closer to the healthy state, patients who benefited from this therapy did not show a decrease in fungal abundance and largely retained an abnormal composition of gut bacteria.

"These data are a step to trying to identify ways to manipulate the gut microbiome to provide favorable outcomes to patients with Crohn's disease," says first author James Lewis of the University of Pennsylvania. "We observed that upon initiation of

a therapeutic formula-based diet, the gut microbiota look even less similar to that of a healthy child, suggesting that one does not have to necessarily give back the healthy microbiota to have a therapeutic effect. It is possible that the effect of the formula diet is through mechanisms other than altering the microbial community."

Although more research is needed, the findings could pave the way for new ways to diagnose and treat inflammatory bowel disease. For example, patients who responded to treatment showed different changes in the composition of gut microbes compared to non-responders, suggesting that assessments of the gut microbe community could be used to predict responses to therapy.

In future studies, the researchers will analyze the metabolites produced by gut microbes to further examine the mechanisms underlying Crohn's disease. Some of these metabolites may be altered by the dietary therapy and could potentially be used as novel therapies.

The researchers will also continue to study how formula-based diets work. "We hope to use this information to develop diets that are less restrictive but equally effective, or medications that mimic the mechanisms of the formula-based diets," Lewis says. "We also hope to study other diets that are popular among patients with Crohn's disease in the coming years."

More information: *Cell Host & Microbe*, Lewis and Chen et al.: "Inflammation, Antibiotics, and Diet as Environmental Stressors of the Gut Microbiome in Pediatric Crohn's Disease"

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