Intestinal bacteria associated with nonalcoholic fatty liver disease

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Intestinal permeability and an overgrowth of bacteria in the small intestine are both associated with nonalcoholic fatty liver disease (NAFLD). These findings are revealed in a new study in the June issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD).

Previous studies have suggested that bacteria from the intestine might play a role in NAFLD, which is the hepatic component of the Metabolic Syndrome. NAFLD can worsen to nonalcoholic steatohepatitis, and some experts have wondered if liver exposure to bacteria from the gut could promote this progression.

Researchers, led by Antonio Grieco of Rome , investigated gut permeability in patients with NAFLD and compared the results to patients with untreated celiac disease, who are known to be prone to this condition, and to healthy volunteers.

Their study included 35 patients with biopsy-confirmed NAFLD, 27 with celiac disease and 24 healthy volunteers. The researchers checked the level of small intestinal bacterial overgrowth in each participant using glucose breath testing. They assessed intestinal permeability by looking at urinary excretion of Cr-EDTA. And they examined the integrity of tight junctions within the gut through duodenal biopsies.

"The main findings of this study are that both intestinal permeability and the prevalence of small intestinal bacterial overgrowth are increased in

patients with NAFLD and correlate with the severity of steatosis," the authors report. "Disruption of tight junction integrity may explain the increased permeability in these patients."

The authors hypothesize that small intestinal bacterial overgrowth and/or the associated increase in gut permeability may cause steatosis. This idea is supported by studies on mice, and by reports that probiotics can improve steatosis that is the result of a high fat diet.

Importantly, there was no association between either small intestinal bacterial overgrowth or intestinal permeability and steatohepatitis or fibrosis, which argues against a primary role for gut bacteria in the progression of NAFLD to more severe liver disease.

"In conclusion," the authors write, "we have demonstrated that NAFLD is associated with increased intestinal permeability and small intestinal bacterial overgrowth and that these factors are associated with the severity of hepatic steatosis." Further studies are needed to determine the exact causal relationship, and could lead to new therapies for NAFLD that address the microbiome of the gut.

An accompanying editorial by Elisabetta Bugianesi and Ester Vanni of the University of Turin applauds the new findings. "The authors were able to demonstrate both the presence of small intestinal bacterial overgrowth and of increased intestinal permeability in patients with NAFLD, providing the first demonstration of gut leakiness in NAFLD," they write.

"The study by Luca Miele and colleagues raises the possibility that gut microbiota and intestine permeability are important mediators of diet-induced metabolic disturbances in NAFLD," they conclude.

Lifestyle-focused therapy would be best for patients with NAFLD,

Bugianesi and Vanni suggest, but manipulating gut flora by antibiotics, prebiotics, and probiotics could help counteract the effect of unbalanced diets on metabolic diseases.

More information: Article: "Increased Intestinal Permeability and Tight Junction Alterations in Non-Alcoholic Fatty Liver Disease (NAFLD)." Miele, Luca; Valenza, Venanzio; La Torre, Giuseppe; Montalto, Massimo; Cammarota, Giovanni; Ricci, Riccardo; Masciana, Roberta; Forgione, Alessandra; Gabrieli, Maria; Perotti, Germano; Vecchio, Fabio; Rapaccini, Gian Ludovico; Gasbarrini, Giovanni; Day, Christopher; Grieco, Antonio. Hepatology; June 2009.

Editorial: "The Gut-Liver Axis in Nonalcoholic Fatty Liver Disease (NAFLD): Another Pathway to Insulin Resistance?" Bugianesi, Elisabetta; Vanni, Ester. Hepatology; June 2009.

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