

Liver injury in NASH leads to a leaky gut

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Non-alcoholic steatohepatitis (NASH), the more severe form of non-alcoholic fatty liver disease (NAFLD) that can progress to liver fibrosis and cirrhosis, is associated with leakiness of the intestinal wall, which in turn may worsen liver disease, according to research¹ published in *Cellular and Molecular Gastroenterology and Hepatology*, the new basic science journal of the American Gastroenterological Association.

"Our study strengthens the clinical association between intestinal permeability and NASH, although we were unable to identify a mechanism," said lead study author Jay Luther, MD, from Massachusetts General Hospital. "We are hopeful that our findings add enthusiasm to the investigative efforts examining the liver-gut axis," added senior authors Suraj J. Patel, MD, PhD, and Raymond Chung, MD.

Researchers performed a meta-analysis of literature examining [patients](#) with NASH, and then tested their hypothesis using an animal model, which enabled them to eliminate possible confounders of the clinical data, such as antibiotic exposure and medical comorbidities. They show NASH patients are more likely to have increased intestinal permeability compared to healthy controls. In animal studies, they found evidence for liver injury preceding increases in [intestinal permeability](#); suggesting that bacteria and bacterial products from the gut move into the bloodstream, which in turn worsens the [liver disease](#).

These data suggest that communication between the intestine and liver, the so-called gut-liver axis, plays a role in NASH development. As evidence continues to mount supporting the notion of gut-liver cross-

talk, further research is needed to decipher the mechanism by which this cross-talk occurs. It is likely that the findings of such research will have significant clinical implications for NASH patients.

"Hepatologists are currently ill-equipped at identifying the patients who are most likely to develop NASH. This is a pressing clinical challenge, as these patients are at greater risk for liver-related adverse events," said Rebecca G. Wells, MD, associate editor of Cellular and Molecular Gastroenterology and Hepatology. "This well-designed study enhances our understanding of the pathophysiology of NASH, which is critical to help identify high-risk NAFLD patients and therapeutic targets."

Fatty liver disease, in particular NASH, is increasing in the U.S. and the rest of the world, and has reached epidemic status. It is highly associated with obesity and diabetes, and is one of the reasons for concern over the increasing rates of both problems in the U.S. NASH can lead to [cirrhosis](#) and to hepatocellular carcinoma (liver cancer), so understanding its development is becoming more and more important.

More information: — 1 Luther, Jay, et al., Hepatic Injury in Nonalcoholic Steatohepatitis Contributes to Altered Intestinal Permeability, Cellular and Molecular Gastroenterology and Hepatology 2015: 1(2); Pages 222-232.e2, www.cmghjournal.org/article/S200035-1/abstract

— www.cmghjournal.org/article/S200041-7/fulltext

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