

LIVER

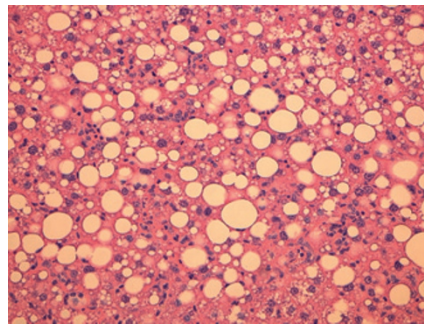
Dietary cholesterol and fat synergistically fuel the development of NASH in experimental models

Dietary cholesterol and fat interact synergistically in the development of NASH in experimental models, according to new data published in *Hepatology*. “The hepatic and metabolic effects induced by dietary fat and cholesterol together were more than twice as great as the sum of the separate effects of each dietary component alone,” adds author George Ioannou.

Ioannou and colleagues wanted to investigate the relative contributions of both dietary fat and cholesterol on the development of NASH, reasoning that “dietary cholesterol could be the spark that sets the fuel (that is, other major lipids) on fire: both the fuel and the spark would be necessary to get the fire going”.

In the study, mice were fed four different diets for 30 weeks: high cholesterol (1%); high fat (15%); high cholesterol, high fat (1% cholesterol, 15% fat); and control (4% fat, no cholesterol). Hepatic fat deposition and inflammation were then assessed.

Compared with controls, mice fed either the high-fat or high-cholesterol diet had increased fat deposition in the liver but little hepatic inflammation and no fibrosis—that is, ‘simple’ steatosis. By contrast, mice fed the high-fat, high-cholesterol combination diet had substantial hepatic steatosis,



Mouse liver section ($\times 200$ magnification) obtained after 30 weeks on a diet supplemented with fat (15%) and cholesterol (1%) and stained with haematoxylin and eosin (viewed with normal light). Courtesy of G. N. Ioannou.

perisinoidal fibrosis and inflammation (steatohepatitis), as well as markedly increased body mass and adipose tissue inflammation, and reduced plasma adiponectin levels. Moreover, this combination diet resulted in greater changes in liver parameters than either of the dietary components alone.

The authors conclude that an interaction between both dietary fat and cholesterol is needed for NASH to develop, and that neither factor alone is sufficient to cause NASH. “Moving forward we will investigate the molecular mechanisms by which cholesterol promotes NASH and the important cell types involved,” says Ioannou.

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Original article Savard, C. *et al.* Synergistic interaction of dietary cholesterol and dietary fat in inducing experimental steatohepatitis. *Hepatology* doi:10.1002/hep.25789