

# Abstract

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## Insulin resistance and steatosis in humans.

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**BACKGROUND:** Insulin resistance is commonly found in a large number of adults-in particular, those with android obesity, the metabolic syndrome or type 2 diabetes. Strong adverse relationships between adipose tissue, liver and muscles in these patients result in lipotoxicity, with deposition of triglycerides (TG) within the liver and muscles together with insulin resistance. Such a situation is also seen in lipodystrophic patients with fat loss. Insulin signals in the liver through its tyrosine-kinase receptors to negatively control hepatic glucose production (HGP), replenish glycogen stores and synthesize **fatty acids (FA)**, leading to TG exported as VLDL.

**RESULTS AND DISCUSSION:** In liver insulin resistance, HGP is increased mainly by activation of the gluconeogenic pathway, resulting in increased fasting glycemia. Lipogenesis is also increased possibly due to direct activation of the SREBP-1 transcription factor and together with increased FA availability results in an increased production of VLDL-TG. An imbalance between the pathways of TG synthesis and oxidation or export results in 'metabolic' steatosis. **Increased cellular FA derivatives activate stress kinases, leading to phosphorylation of serine in insulin receptor substrate (IRS) proteins and, hence, insulin resistance.** A number of studies in normal subjects and patients have revealed a strong association between insulin resistance and metabolic steatosis. Moreover, when insulin resistance is decreased by weight loss in obese subjects or by treatment with insulin sensitizers such as thiazolidinediones, the levels of liver fat and insulin resistance vary accordingly.

**CONCLUSION:** An important question that remains unanswered concerns the relationship between steatosis and non-alcoholic steatohepatitis (NASH), and the potential roles of insulin resistance together with inflammation and oxidative stress in such a setting.

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