

Your arteries may be suffering insulin resistance, too

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In people with insulin resistance or full-blown diabetes, an inability to keep blood sugar levels under control isn't the only problem by far. A new report in the May issue of *Cell Metabolism* shows that our arteries suffer the effects of insulin resistance, too, just for entirely different reasons.

"We think about insulin resistance in liver, muscle, and fat, but insulin also works on vascular cells," said Christian Rask-Madsen of the Joslin Diabetes Center in Boston.

And what insulin does in our arteries sends a signal that helps prevent the buildup of fatty plaques that can cause arteries to harden, new research in mice shows.

Earlier studies showed that in the context of systemic insulin resistance, blood vessels become resistant, too. Doctors also knew that insulin resistance and the high insulin levels to which it leads are independent risk factors for vascular disease. But it wasn't clear if arteries become diseased because they can't respond to insulin or because they get exposed to too much of it.

Now comes evidence in favor of the former explanation. Rask-Madsen along with George King and their colleagues find that mice prone to atherosclerosis fare much worse when the linings of their arteries can't respond to insulin. The animals' insulin-resistant arteries develop plaques that are twice the size of those on normal arteries.



Insulin-resistant blood vessels don't open up as well, and levels of a protein known as VCAM-1 go up in them, too.

VCAM-1 belongs to a family of adhesion molecules, Rask-Madsen explained. "It sits on the endothelium and binds white blood cells." Those cells can enter the artery wall, where they start taking up cholesterol, and an early plaque is born.

"The results provide definitive evidence that loss of insulin signaling in the <u>endothelium</u>, in the absence of competing systemic risk factors, accelerates atherosclerosis," the researchers conclude.

The findings should come as good news to those on <u>insulin therapy</u>, since they suggest the hormone itself should not cause harm to arteries, as some had feared. "If anything, it should be beneficial in preventing atherosclerosis," Rask-Madsen said.

The results also suggest drugs specifically designed to treat insulin resistance in the vasculature might prevent cardiovascular complications in people with <u>insulin resistance</u> or type 2 diabetes, the researchers say.

While the researchers emphasize that it will remain critical to keep blood sugar in check with more traditional therapies, new treatments aimed at blood vessels could mean big gains for those with diabetes. After all, atherosclerosis is responsible for many of diabetes' worst complications—heart disease, stroke, and leg amputations among them.

"Atherosclerosis is the main reason for shorter life spans in diabetes patients," Rask-Madsen said.

More information: Rask-Madsen et al.: "Loss of Insulin Signaling in Vascular Endothelial Cells Accelerates Atherosclerosis in Apolipoprotein E Null Mice." Publishing in Cell Metabolism 11,



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