

## <u>How Intermittent Fasting Could Prevent</u> <u>Heart Disease</u>

<u>Intermittent fasting</u>, which consists of going without food for 16 hours up to 24 hours — longer than that is usually "prolonged fasting" — could be one of the most potent anti-aging measure around, as potent or more so than exercise. One of its main mechanisms of action is through increasing <u>autophagy</u>, the cellular self-cleaning process that rids cells of junk organelles and macromolecules. Intermittent fasting could prevent heart disease through the same mechanism.

## Autophagy declines with age

Aging is the number one correlate of increased risk for coronary heart disease (atherosclerosis), and aging also correlates strongly with a decline in natural levels of autophagy.

Dysfunction of the arterial walls plays a key role in coronary heart disease. This dysfunction is related to declining autophagy.

Researchers decided to test the idea that declining autophagy is important to arterial dysfunction. They used human volunteers, mice, and cell culture in a three-pronged experiment.  $(\underline{1})$ 

They showed that blood flow in the forearm in response to infusions of acetylcholine was only about half in healthy older humans, age 61 to 71, compared to that in healthy young people, age 20 to 31. The lower blood flow was shown to be due to lower production of nitric oxide, which mediates vasodilation.

Levels of autophagy in older people, as shown by protein markers, were about *half* those in younger people. The correlation between autophagy markers and forearm blood flow was high at 0.61.

The mouse segment of the experiment studied markers of autophagy in old and young mice. In the old mice, the markers showed about half the level of

autophagy as in the young mice. Their arterial function was also much worse.

## Trehalose restores autophagy in old mice

Then, they gave the old mice trehalose, a sugar which <u>promotes autophagy</u>, similarly to resveratrol or curcumin.

Trehalose completely restored autophagy levels in old mice to those seen in young mice, and restored arterial function to the same degree. Graphs below from the paper:



Autophagy is impaired in the vasculature of old mice and restored by trehalose supplementation  $\Box$  A, key autophagy mediator beclin 1 in aorta of young and old control (YC and OC) and young and old trehalose supplemented (YTre and OTre) mice. B, p62, a marker of undegraded autophagy substrates. C and D, WIPI-1 and LC3-II, markers/indexes of macroautophagy. E, LAMP-2a, critical mediator of chaperone-mediated autophagy. Data expressed relative to GAPDH and normalized to YC mean value. Representative Western blot images below. Values are means  $\pm$  SEM (n= 5–7 per group). \*P < 0.05 vs. YC.

Human cell cultures treated with trehalose responded with a restoration of nitric oxide production.

The scientists stated:

The present findings suggest that autophagy is reduced in arteries of older mice and humans and contributes to impaired vascular endothelial function, a clinically important expression of arterial ageing. Importantly, our parallel findings in mice and humans indicate that autophagy protects vascular endothelial function with ageing by reducing oxidative stress and inflammation and increasing NO bioavailability. These results provide a basis for translational research aimed at enhancing autophagy to reverse arterial ageing and reduce the risk of age-associated CVD in humans.

Declining autophagy is linked to increased oxidative stress, inflammation, and mitochondrial dysfunction, all of these being main physiological processes that accompany aging. In fact, they just *are* aging.

Unfortunately, trehalose appears to be highly metabolized in the gut when humans ingest it, so using trehalose to enhance autophagy is probably out of the question. Trehalose has also been linked to Clostridium dificile infections.

## Intermittent fasting could prevent heart disease by improving arterial health

Increasing autophagy will lower these other markers of oxidative stress and inflammation, resulting in improved arterial health. As inflammation has been strongly implicated in coronary artery disease, increasing autophagy will lower inflammation and help prevent atherosclerosis.

Intermittent fasting strongly increases autophagy during the fasting window, so it has great potential in the prevention of coronary heart disease.

Other interventions already mentioned, curcumin, resveratrol, nicotinamide, etc. (you can see all of these on <u>my supplements page</u>) also increase autophagy — they have been called calorie restriction mimetics — and therefore have the same potential. <u>Trehalose</u> works in mice, though human data is lacking, and it's cheap.

PS: <u>Check out my Supplements Buying Guide for Men.</u>