What is Happening to Our Livers?

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Welcome to Issue 122 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 research news that our team of doctors, scientists, and experts are most excited about—without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

A Liver Mystery Solved (thank you, dolphins)

The countdown is on until Simon & Schuster's March 25th release of *The Longevity Nutrient*. This book tracks our 20-year scientific journey - starting with an unexpected discovery of C15:0's health benefits while helping dolphins - which has culminated in a movement to improve global health. And dare we say, humanity?

In this series of *Science Says!*, we provide a behind-the-scenes science peek relevant to each of the book's chapters - from surprising dolphin discoveries to longevity molecule must-haves, from how essential fatty acids are discovered to the many ways C15:0 works, from how a newly found nutritional deficiency accelerates aging to how fixing and optimizing our C15:0 levels can slow aging to help us live healthier, longer.

This week, let's talk about how dolphins revealed an underlying cause of impaired liver function - now present in 1 in 3 people globally.

What's all the hub-bub about liver health these days?

Back in 1980, the Mayo Clinic reported the first 20 cases of people with abnormal fat in their livers, some of whom progressed to having inflammation and scarring (aka liver cirrhosis) - without a history of consuming excessive alcohol. They called this condition nonalcoholic steatohepatitis (NASH), where "steato" means "fat" and "hepatitis" means "inflamed liver".

Fast forward to today, and more than 1 in 3 people globally have the precursor to NASH, called metabolic dysfunction-associated steatotic liver disease (MASLD). This alarming rise has made MASLD one of the leading causes of liver cancer and liver transplants throughout the world. Yikes.

How is abnormal liver function detected?

During the early stages, most people don't know that their liver function is heading downward. That is why these changes are most often detected during routine health and blood checkups, where doctors find that a person has abnormally high liver enzymes, including:

- ALT (alanine aminotransferase)
- AST (aspartate aminotransferase)
- GGT (gamma-glutamyl transferase)

When declining liver function has advanced, a person might be tired and have pain in their upper right belly.

What is causing our liver health to decline?

There have been a lot of hypotheses to explain why so many of us have less than optimal liver health. These include the following known or possible risk factors:

- Obesity
- Dietary sugars
- Ultraprocessed foods
- Trans-fats and saturated fats

Interestingly, back in 2012, we discovered that some older dolphins were developing the same fatty changes in their livers... which were not due to any of the bullets above. Instead, it was due to too-low dietary C15:0.

Our studies have continued, alongside leaders in liver health for the past 10 years, which have led to the following conclusions:

- **Fragile cells.** Nutritional C15:0 deficiencies cause Cellular Fragility Syndrome, which makes our cells fragile, including our red blood cells.
- **Too much iron in the tissue.** Fragile red blood cells are engulfed by cells in the liver, called Kupffer cells. When there are too many fragile red blood cells, the Kupffer cells become overloaded with too much free iron. This iron can spill over into our blood, heart, pancreas, and brain.
- **Hello, ferroptosis.** Fragile cells throughout the body increase systemic lipid peroxidation, and when paired with excess iron, this results in ferroptosis. Ferroptosis is a new form of cell death that accelerates aging and impairs our red blood cell, liver, heart, and gut health.
- **Less-than-optimal liver health.** A leading hypothesis is that nutritional C15:0 deficiencies are causing the global rise we are seeing in impaired liver function.

So, give me some good news.

You got it. The good news is that daily C15:0 supplementation has been clinically proven to raise C15:0 levels and treat nutritional C15:0 deficiencies. By doing so, Robinson et al. showed that C15:0 supplementation improves both red blood cell health and liver function within 12 weeks. This means that, just like dolphins, some of us have low C15:0 levels that can affect our liver function... and restoring those C15:0 levels can help restore our long-term liver health.

The fascinating story and scientific sleuthing behind these discoveries - along with helpful dietary and weight loss tips on how to keep our livers healthy - are provided in *The Longevity Nutrient*.

Next up, how C15:0 helps to support our heart and metabolic health.

Next week, we'll talk about how C15:0 helps our hearts and metabolism - from mechanism of action to clinical trials.

In the meantime, have a wonderful week, everyone!

Dive deeper into the science

READ THESE STUDIES

- Ludwig et al. Nonalcoholic Steatohepatitis: Mayo Clinic Experiences with a Hitherto Unnamed Disease.
- Amini-Salehi et al. Global prevalence of fatty liver.
- Venn-Watson et al. Hemochromatosis and fatty liver disease: building evidence for insulin resistance in bottlenose dolphins.
- Venn-Watson et al. C15:0 top predictor of healthier dolphins.
- Venn-Watson S. The Cellular Stability Hypothesis: Evidence of Ferroptosis and Accelerated Aging-Associated Diseases as Newly Identified Nutritional Pentadecanoic Acid (C15:0) Deficiency Syndrome. Metabolites. 2024; 14(7):355.
- Dixon et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death.
- Robinson et al. C15:0 Supplementation in Young Adults at Risk for Metabolic Syndrome: A Randomized Controlled Trial.
- Chooi et al. Effect of An Asian-Adapted Mediterranean Diet and Pentadecanoic Acid: The TANGO Randomized Controlled Trial.
- Nerd out on all the C15:0 science at DiscoverC15.com