We're In The Midst of A Metabolic Storm

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Welcome to Issue 178 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and CISO 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 Deeper Metabolic Meaning Behind Recent Changes in Disease Names

Over the last few years, teams of leading experts in endocrinology, cardiology, gastroenterology, reproduction, hematology, and more have been meeting throughout the world to define or redefine names of diseases. Together, these efforts are communicating that we're in the midst of a global metabolic storm. The latest example? Last month's publication in *The Lancet*, announcing the change name from polycystic ovary syndrome (PCOS) to polyendocrine metabolic ovarian syndrome (PMOS). This week, we dive into three recently named or renamed diseases that, combined, are telling a much bigger story.

Got it. So, what's up with PCOS changing to PMOS?

Let's start with defining PCOS (polycystic ovary syndrome), which affects 1 in 8 women. Wang et al. reported that PCOS has been on the rise among adolescents and young adults, with an estimated 50% increase in incidence since the 1990s. Worse yet, according to the World Health Organization, it is estimated that 70% of women with PCOS don't know they have it.

Simplified, PCOS has been diagnosed based on the presence of:

- Infrequent or irregular ovulation
- Hyperandrogenism (excess levels of androgen hormones)
- Polycystic ovaries or elevated anti-Mullerian hormone (AMH) (for adults)

Tons of research, however, have revealed that PCOS: 1) is not just limited to the ovaries, 2) doesn't always involve increasing pathological cysts, and 3) often involves metabolic, reproductive, psychological, and dermatological components - many of which are linked to insulin resistance. Due to the high prevalence of women with PCOS and the low rate of accurate diagnoses, a multi-year consensus process was completed to change the name of PCOS to ***polyendocrine metabolic ovarian syndrome (PMOS).***

The goal is to help more patients and physicians understand that the underpinning of PMOS is dysregulated metabolism (most often including insulin resistance) that has many (aka, poly) effects throughout the body, including the ovaries.

Why NAFLD, a liver disease, changed to MASLD. Similar story, different organ.

In 1980, Mayo Clinic reported the first 30 cases of a newly recognized disease involving excess fat in the liver with inflammation and fibrosis (aka cirrhosis) absent of alcohol as an inciting cause. Ludwig et al. named this disease ***nonalcoholic steatohepatitis, or NASH.*** The precursor to NASH, involving excess fat in the liver without cirrhosis, was named nonalcoholic fatty liver disease, or NAFLD.

Similar to PCOS, there were concerns from the medical community that NASH and NAFLD focused on the wrong things, distracted the diagnosis and understanding of the underlying causes of this new disease. Specifically, dysregulated metabolism was impacting not just the liver, but the whole body - especially the heart. This wasn't about a disease not caused by alcohol - it was a new metabolic disease impacting the liver and more.

So, many groups of experts met over many years. Which resulted in a 2023 consensus statement published in the journal, *Hepatology*, changing the name from NAFLD to ***MASLD (metabolic dysfunction-associated steatotic liver disease)*** and NASH to ***MASH (metabolic dysfunction-associated steatohepatitis).*** Importantly, MASLD and MASH have been increasing at an alarming rate. Younossi et al. estimate that 38% of people globally, including up to 14% of children, have MASLD. By 2040, they estimate that more than **55% of adults will have MASLD.** We care about this because MASLD is becoming a leading cause of liver transplants, liver cancer, and cardiovascular disease.

And then there's metabolic hyperferritinemia.

During 2023, the same year that NAFLD was renamed MASLD, there was another consensus statement published in *Nature Reviews* on the updated definition and classification of a new disease - named ***metabolic hyperferritinemia.*** In their paper, Valenti et al. provide detailed criteria to diagnose this disease involving iron overload in the tissues and dysfunctional metabolism. Here are the diagnostic criteria for metabolic hyperferritinemia:

Serum concentration of ferritin > 300 ng/ml in men and > 200 ng/ml in women

AND

Evidence of fatty liver

OR type 2 diabetes and/or obesity

OR two or more features of altered metabolism associated with insulin resistance, including:

- Overweight
- Increased triglycerides (> 150 mg/dl)
- Low HDL cholesterol (< 45 mg/dl in men and < 55 mg/dl in women)
- Increased fasting levels of glucose (> 100 mg/dl)
- Arterial hypertension (> 130/85 mmgHg or use of anti-hypertensive agents)
- Evidence of fasting hyperinsulinemia or insulin resistance (such as a HOMA-IR index > 2.7)

Soon after this consensus paper was published, Geneluckzee et al. showed that among 8,408 people in a general population, 13% met the criteria high ferritin (aka hyperferritinemia). Of these, 81% met the criteria of metabolic hyperferritinemia. That's about 1 in 10 people. Similar to PMOS and MASLD, these cases are on the rise.

The power of awareness

The take home point from these three consensus statements above? It's not despair. Instead, they convey tremendous progress. More than ever, experts and patients from around the world are crossing disciplines and working together to define a changing landscape of health, which is a must-do in order to improve it. The more we understand the common ground of something's-up-with-our-metabolic-health, the better we are at identifying people with these conditions, and the more likely we are to find upstream risk and protective factors that may help address all three conditions to keep us healthy.

Be a metabolic health advocate - for yourself and your family.

Let's use these consensus statements above to provide a few pro-tips for the next time you or a family member get a routine checkup.

1. Well, start by getting routine checkups.
2. Get a full CBC and chemistry blood panel, including a metabolic panel (including glucose, HbA1c, lipids, and HOMA-IR), liver panel (ALT, AST, and GGT), red blood cell panel (including hemoglobin, hematocrit, and red blood cell distribution width - RDW), and iron indices (including ferritin and transferrin saturation).
3. See where you're at with regard to body weight, body composition, and blood pressure.

If you have signs of dysfunctional metabolism, work with your doctor to address it. Including leveraging the robust studies supporting the positive effects of diet and exercise. Together, we can downsize this metabolic storm at the earliest stages and get global health back on track. Here's to progress. Have a great week, everyone!

Dive deeper into the science

READ THESE STUDIES AT
DISCOVERCIS.COM/RESOURCES

- Teede et al. Polyendocrine metabolic ovarian syndrome, the new name for polycystic ovary syndrome: a multistep global consensus process.
- Wang et al. Evolving global trends in PCOS burden: a three-decade analysis (1990-2021) with projections to 2036 among adolescents and young adults.
- World Health Organization. Polycystic ovary syndrome.
- Ludwig et al. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease.
- Rinella et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature.
- Younossi et al. Epidemiology of metabolic dysfunction-associated steatotic liver disease.
- Valenti et al. Consensus Statement on the definition and classification and metabolic hyperferritinemia.

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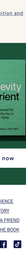

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