

Middle-Aged Men Are Most Vulnerable to Faster Aging Due to “Forever Chemicals”

Some PFAS, or “forever chemicals,” have been implicated in human cancers, obesity, infertility and hormonal imbalances.

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PFAS or ‘forever chemicals’ have wide-ranging toxic effects. Now, researchers have found that two non-legacy PFAS, namely perfluorononanoic acid (PFNA) and perfluorooctanesulfonamide (PFOSA), appear to speed up biological aging in middle-aged men, but not women. These results suggest that newer PFAS are not necessarily risk-free and should be considered for stricter regulation.

Per- and polyfluoroalkyl substances (PFAS) — “forever chemicals” in common parlance — are a class of thousands of synthetic chemicals often used in non-stick coatings, water-resistant fabrics, fire-fighting foams, food packages, cleaning products, and plastics. They contain exceptionally strong molecular bonds, which makes them hard to break down. PFAS pollution is increasingly detectable in water, soil, and tissues of organisms, and some have been implicated in human cancers, obesity, infertility, and hormonal imbalances.

A handful of “legacy” PFAS, like perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorohexane sulfonate (PFHS), have already been targeted for elimination worldwide under the 2001 Stockholm Convention on Persistent Organic Pollutants. But new PFAS have hit the market since, for example for use in emerging applications like AI data centers.

“Here we show that specific forever chemicals, namely perfluorononanoic acid (PFNA) and perfluorooctanesulfonamide (PFOSA), appear to accelerate biological aging, with middle-aged men being the most vulnerable group,” said Dr Xiangwei Li, a professor at Shanghai Jiao Tong University School of Medicine in China and the corresponding author of a new study in [Frontiers in Aging](#).

“These findings suggest that some newer PFAS alternatives are not necessarily low-risk replacements and warrant serious attention regarding their environmental impact.”

Li and colleagues used public data on a nationally representative, randomly chosen group of 326 older women and men enrolled in 1999 and 2000 through the U.S. National Health and Nutrition

Examination Survey. Each had donated a blood sample, in which NHANES staff measured the concentration of 11 PFAS. The DNA “methylome” — an epigenetic marker regulating gene expression — had also been measured in the blood cells. Each participant filled in a questionnaire reporting demographic and socioeconomic variables as well as lifestyle factors.

Li and colleagues fed these DNA methylome data into the algorithm for 12 older and recently developed “epigenetic clocks” to estimate each participant’s biological age. Previous NHANES studies have shown that higher PFAS concentrations in the blood tend to be associated with faster biological aging, possibly through increased inflammation.

Speeding up the clock

Li and colleagues here showed that PFNA and PFOSA were each present in the blood of 95% of participants. Importantly, higher concentrations of PFNA and PFOSA were strong predictors of faster epigenetic aging in men between 50 and 64 years of age, but not in women.

PFNA and PFOSA were invented in the 1950s and 1960s and today are commonly used in consumer and industrial products for their water-, grease-, and stain-repellent properties and ability to withstand heat and corrosion. They have been shown to be persistent and bioaccumulative with toxic effects on health.

Other PFAS found in at least 85% of the participants were 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid (EPAH), 2-(N-methyl-perfluorooctane sulfonamido) acetic acid (MPAH), PFOS, PFOA, and PFHS.

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PFAS concentrations overall did not differ between women and men or across age classes, nor was there any association between the concentrations of EPAH, MPAH, PFHS, PFOA, or PFOS and biological age.

The authors concluded that the effects of forever chemicals on epigenetic and biological aging depend on the compound, and that regulations should look beyond legacy PFAS alone to also cover PFNA and PFOSA.

Midlife crisis

But why would the effects of PFNA and PFOSA be strongest in middle-aged men?

“Midlife is a sensitive biological window where the body becomes more susceptible to age-related stressors, which may explain why this group responds more strongly to chemical exposure,” explained Dr Ya-Qian Xu from Shanghai Jiao Tong University School of Medicine, the first author of the study.

Li added: “We suspect that men may be at higher risk because the aging markers we analyzed are heavily influenced by lifestyle factors such as smoking, which can compound the damaging effects of these pollutants.”

France recently banned the use of all PFAS in clothing and cosmetics, while the EU is considering a similar ban for specific uses.

“Meanwhile, to reduce risk, individuals can try to limit their consumption of packaged foods and avoid microwaving fast-food containers. Looking ahead, we are actively modeling how PFAS interacts with other common pollutants, as we need to understand the cumulative health risks of these chemical mixtures,” said Li.

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