## Ovaries Age Faster Than The Rest Of The Body. **Experts Are Racing To** Figure Out Why.

The latest in longevity research is woefully underfunded yet incredibly promising for human health. By Currie Engel Photographed by Jarren Vink



Despite the fact that half of the population has ovaries, this organ is still a bit of an enigma in the scientific and medical world. And this has broad-sweeping implications for female health and longevity. "We've thought of women as baby-making machines and not really considered how our ovaries are supportive of our broader health, beyond the capacity to make a child," says Daisy Robinton, PhD, cofounder and CEO of Oviva Therapeutics, a biotech start-up focused on our opportunities, and our vibrancy."

It's a strange but little-known fact that you actually made your appearance on this

mysteries of the human ovary that doesn't have a ready explanation.)

planet as an egg in your grandmother's uterus. Yep. A female fetus (your mom, in this scenario)

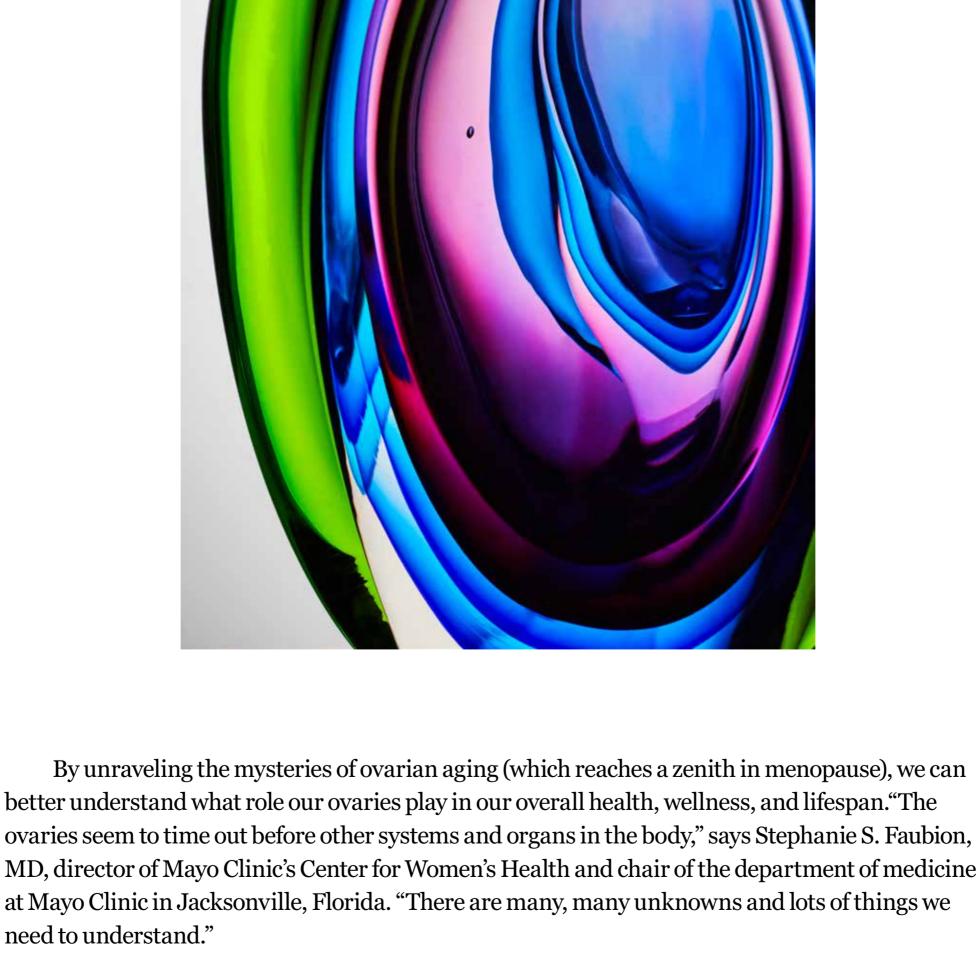
develops ovaries, with all the immature eggs she will ever have, by 20 weeks gestation. So, your

X chromosome has likely existed for decades before you were even conceived. (One of the many

improving ovarian function and extending female health span. "It really impacts our quality of life, In recent years, the scientific community has finally started to recognize that the ovaries aren't just an essential part of human reproduction but are also the hidden key to health and longevity in women. Scientists have only recently recognized the myriad ways in which ovarian aging, which eventually leads to menopause, impacts the entire body. So, that's why finding answers to big questions such as why the ovaries age faster than any other organ in our bodies and developing therapeutics to address the physical and hormonal changes involved—may be the

key to helping women live longer, better lives. "Ovaries are the architects of healthy female bodies," says Jennifer Garrison, PhD, an assistant professor at the Buck Institute for Research on Aging, and cofounder and executive director of ProductiveHealth.org. But no one—except a small group of experts in the ovarian aging research space—is truly paying attention to that fact. When Garrison first began to recognize the unrealized potential of the ovaries, she says she went through what she has jokingly dubbed the "four stages of grief." First, she was embarrassed that, as an informed scientist, she knew so little

about one of her own organs. But that embarrassment quickly turned to shock, followed by "abject anger and rage," she says. "I was like, 'Wait a second. If we were talking about male bodies, this would not even be a question. It would have been solved a long time ago. We would know how all of this works." Garrison's fourth and final stage of grief had her rolling up her sleeves and diving in. "Fixing this data gap is now my life's work, and I don't think there is anything more important that I could be doing with my time and energy," she says. "It definitely motivated me to change the direction of research in my lab and the entire course of my professional career."



responsible for the production and secretion of at least two essential hormones, progesterone and estrogen, and they house immature eggs called oocytes. They have three layers: an outer layer, a middle layer of connective tissue and follicles, and an inner layer with blood and lymphatic vessels, per the Cleveland Clinic. The ovaries also shrink with age. At birth, female babies have around 1 to 2 million oocytes, and roughly 1,000 immature eggs are lost each month after the first period. In their late 30s, most women have about 25,000 oocytes remaining. When the total egg count gets to around 1,000, the ovaries usually stop functioning normally, signaling the approach of menopause.

A Brief Biology Breakdown

Here's what scientists do know: The ovaries are oblong glands each about the size of a kiwi. They're

"Ovaries are the architects of healthy female bodies," says Jennifer Garrison, PhD. But no one—except a small

five species of whales, but no other mammals). Or why some women are born with fewer eggs-and lose them faster-than others. Garrison suspects ovaries produce other hormones that have yet to be identified as well. There are also a "huge number" of interactions likely occurring between the brain and the ovaries throughout a woman's life, Garrison says, but "we don't know all the words in that chemical conversation that's happening, and we certainly don't understand very much about how it changes with age." Some effects from that ovary-brain connection are clearer than others, especially during menopause. But the scientific world is only starting to look into how the connection impacts things like normal organ function, learning, memory, mood, and behavior. The Menopause Effect

Experts still don't have basic answers as to why human ovaries age two times faster than the

rest of their body. Or why humans go through menopause in the first place (a process we share with

women who hit menopause later, per research. What's more, removing the ovaries surgically before 50 (with no hormone therapy) may be "associated with increased mortality," according to another study. The average American woman will reach menopause at age 52, but onset age can range from about 45 to 58, per the Office on Women's Health in the U.S. Department of Health and Human Services. The average life expectancy for women is 80.2 years, per the CDC, which means women spend about a third of their life in this post-menopausal phase. So, while women live longer, on average, than men, they often do so in worse health. And experts look at ovarian aging as a big factor in the onset of chronic conditions, aches, and pains that so many women begin to suffer

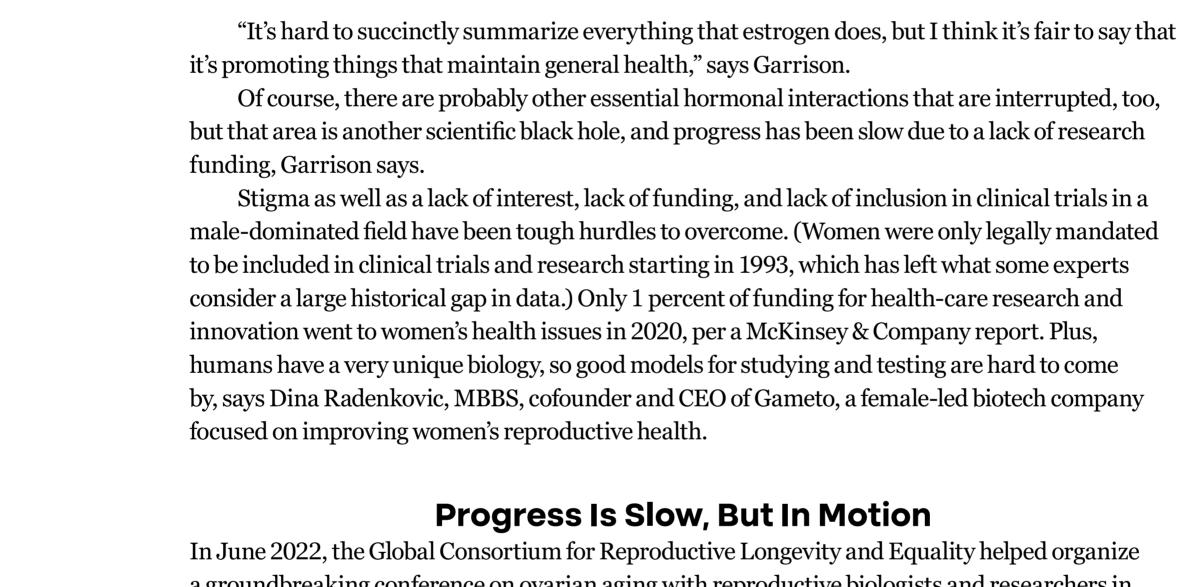
around the time they hit menopause.

Menopause affects women's health and well-being on both micro and macro levels. Women who

hit menopause before 45 are at increased risk of cardiovascular problems and dying earlier than

everywhere, Garrison explains, so, as estrogen levels begin to fluctuate during perimenopause, then drop after menopause, the impacts can be far-reaching. For starters, women's cholesterol panels look worse and they tend to gain weight, which increases the risk of developing diabetes and cardiovascular disease, says Dr. Faubion. But decreasing estrogen also directly impacts bone, cardiovascular, and brain health. Women's sleep worsens. They experience brain fog and cognitive

A big factor in these health hits? Low estrogen. The female body has estrogen receptors almost



therapeutics.

decline.



of research. Lack of grant funding created a "real and insurmountable barrier" that made the work

"It's been exponential since we started, and there are now hundreds—literally, hundreds of

people—who consider this a primary research question and are doing active science in the space.

It's really exciting," she says. Interest in all things menopause and hormone health has hit the

"almost impossible," Garrison says. Now, that's starting to shift.

mainstream, too, which helps visibility and funding efforts.



lifespan) will be very different from those that help a 40-year-old woman, Garrison explains.

the rate of follicle loss, a woman heading into perimenopause might be more concerned with

While a younger woman thinking about family planning may look for therapeutics that slow down

Therapies that can support a

20-year-old's ovarian health (and thus

support a healthier lifespan) will be

very different from those that help a

40-year-old woman, Garrison explains.

preserving follicle quality or maintaining the ovaries' endocrine functions. "It's not going to be like

For starters, hormone therapy (formerly hormone replacement therapy, or HRT) can make

we just find one cure," she says. "It's going to be lots of different things, and so that's why we need

a big difference for some women in addressing the health impacts linked to low estrogen during

perimenopause and menopause. From pesky symptom relief to essential bone-health support,

this army of scientists and clinicians working on this problem."

also not going to have good treatments."

the additional estrogen and progesterone can help immensely. The treatment was growing in popularity through the 1990s until a 2002 study suggested it elevated all kinds of health risks, including breast cancer. This jump-started a two-decade-long aversion to hormone therapy. Flash forward to 2024, and doctors have a better understanding of its benefits and the study's shortcomings. Specifically, there have been dozens of other studies showing hormone therapy is safe, Garrison says. Experts tell women to have a conversation with their doctors to see if it might be an effective treatment based on their health history. At Gameto, the lack of testing models that mimic human ovaries actually pushed Dr. Radenkovic and her team to develop what she calls "ovaries in a dish," which used stem cells to

recreate the organ in a lab. "Many animals that we use for research do not exhibit the same method

of ovarian aging as we do," Dr. Radenkovic says. "If you do not have a good model to test it, you're

In April, engineers at the University of Michigan also announced they'd successfully completed a cellular atlas of the human ovary as part of the Human Cell Atlas project, which involves mapping all the cells in the human body and their "molecular characteristics and where they are located." The study says that this breakthrough could help restore hormone production and fertility in ovaries one day. Over at Oviva Therapeutics, Robinton and her team are developing their own anti-Müllerian hormone (or AMH), which regulates how fast the ovaries lose eggs. AMH suppresses the eggs, preventing them from leaving the ovarian reserve, with fewer eggs being released, Robinton says. So, instead of losing about 1,000 eggs each month, with elevated AMH levels you might lose only 800 or 500 from your ovarian reserve. "We don't want to take it [egg loss] to zero because then you just go into menopause, but I think it's fair to say that we could expect some moderate decrease that saves our eggs over a greater period of time, extending the runway to menopause without impacting cycling," Robinton explains.

These petri dish-derived ovarian models can now be used to test out and, hopefully, answer

use that word anymore because it's kind of been co-opted," she says. Instead, Garrison uses the term health span, because it better captures what these scientists are trying to figure out: how women can be as healthy as possible for as long as possible.

some of those big questions about ovarian aging, without any risk to real women.

**Focusing On Quality Over Quantity** These efforts to better understand female longevity and ovarian aging are very different from the male-dominated world of biohacking, which seems obsessed with reversing the aging process and trying to live in the body of an 18-year-old until you're 120. Robinton, Garrison, and Dr. Radenkovic are focused on ensuring a woman's natural lifespan is filled with healthy years not "optimization." The male-dominated longevity space often seems wholly focused on optimal personal performance, versus trying to make quality of life better and society healthier as a whole, Robinton says. "I don't think trying to live to be 800 is a good way for us to spend our research dollars right now," says Garrison. In fact, she doesn't even like the word longevity. It makes her cringe. "I don't



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