Editorial

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Recognizing the importance of ovarian aging research

The ovary is one of the first organs to functionally decline with age, leading to many deleterious consequences for health and well-being. A better understanding of ovarian aging through collaborative research and investments will play an important part in achieving healthy aging for all.

We often think of aging as a process that occurs in the later decades of our lives, but about half of the world's population experiences aging-related functional changes much earlier in adulthood as a result of declining ovarian function. Ovarian aging entails hormonal, tissue and cellular changes (including a reduction in oocyte quantity and quality) and also has systemic effects on other organs that lead to a cascade of negative health consequences, and ultimately a deleterious effect on well-being and on personal freedom[1]. Yet, ovarian aging has largely been overlooked as a target to promote healthy aging.

As a result of ovarian aging, persons affected are faced with changes to their bodies that often begin at 30 years of age. This is also the mean age at which the ability to have children declines and, for persons who want to bear children, infertility is a prevalent health concern. The chances of pregnancy complications also increase with age, and a parental age of 35 years or older may be considered a high-risk pregnancy[2]. The age of parenthood has risen in many countries[3], increasing the need for fertility treatments that are not routinely covered by health insurance — if they are financially supported and accessible at all. And working with a time window that is closing around the same time that many people are developing their careers, seeking greater financial stability and choosing partners severely restricts personal freedom.

Further, people with ovaries will experience menopause — commonly between the ages of 45 and 55, but possibly earlier for people with premature ovarian insufficiency, owing to genetic effects or cancer treatments[4]. The symptoms of menopause include hot flushes, difficulty sleeping, difficulty concentrating, mood changes and others. Those who are experiencing menopause often face difficulties in receiving confirmation of the cause of their symptoms and are insufficiently supported in social spaces, such as the workplace. A recent survey[5] has shown that most employers in the UK do not take steps to support their employees during menopause, and that menopause symptoms are a reason for reducing work or forgoing applications for promotion. Additionally, the risk for a number of chronic diseases (including osteoporosis and cardiovascular diseases) increases with menopause, suggesting that the menopausal transition initiates a cascade of negative health effects[6].

Medical research has led to an increase in lifespan, whereas the age of menopause has not changed much in recent years[7]. If the current trajectory continues, in the future, people affected by ovarian aging will live more of their adult lives after than before menopause. Yet, medical treatments in this area are sparse, if they are available at all. Although there are hormonal and nonhormonal interventions that can help to alleviate the symptoms of menopause[4], there are no therapeutic interventions that slow or reverse ovarian aging.

There are signs that research in the area of ovarian aging is gaining momentum. Dedicated and passionate work from academia, industry and nongovernmental organizations is emerging and holds promise for exciting future developments. Proof-of-principle research in animal models has demonstrated that intervening in ovarian aging to extend reproductive lifespan is feasible[8]. There is also promising evidence[9] that extending reproductive lifespan will have extensive benefits for human health, by delaying the cascade of negative health effects that occur owing to ovarian aging. It will also lead to societal benefits by increasing health-related equality.

However, many challenges remain. Currently, the mechanisms that drive ovarian aging are incompletely understood. Therapeutic targets such as ovarian fibrosis are emerging and show promise, but more candidate pathways for intervention are required to find the best possible therapeutic options. How established hallmarks of aging, such as senescence, affect ovarian aging needs extensive testing. Furthermore, finding ways of predicting and measuring ovarian functioning will be important to support clinical trials.

Research in this field will require interdisciplinary collaborations between aging and ovarian biologists. In June 2022, the first-of-its-kind 'Reproductive Aging Conference' in Palm Springs, co-organized by the Global Consortium for Reproductive Longevity and Equality, brought together aging researchers and reproductive biologists to discuss the mechanisms of ovarian aging and to promote interactions between these fields. In September 2022, the 'Science and Art of Reproductive Ageing' conference was held by the Bia-Echo Asia Centre for Reproductive Longevity and Equality in Singapore. Activity in this field is growing in academic research and also in the biotechnology sector, with companies such as Gameto, Oviva Therapeutics, GlycanAge and Conception, amongst others.

At *Nature Aging*, we look forward to more exciting research that aims at better understanding ovarian aging and how it affects healthspan more broadly. We believe that such research will ultimately contribute to a more equitable society. Going forward, we will continue to carefully think about how to support efforts and growth in this important field. We welcome submissions on ovarian aging research in cell systems, animal models and humans, and look forward to contributions and suggestions on how to feature the topic with opinion and review articles, and to raise awareness about important events and initiatives.

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