

Male fruit flies' decline in fertility with age is not only driven by changes in sperm

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Infertility is one of the most striking effects of aging. The impact of aging on females' fertility is more severe and much better understood, but it also affects males. Male reproductive aging is less researched, but

of those studies that do address it, most focus on sperm. However, ejaculate contains more than just sperm. Proteins in the seminal fluid are important for fertility, and in many animals, they have a dramatic effect on female physiology and behavior. Little is currently known about the impact of male aging on these proteins, and whether any changes contribute to poorer ejaculates in older males.

To resolve these questions, researchers at the University of Oxford's Department of Zoology conducted experiments in a model organism, the fruit fly, *Drosophila melanogaster*. This species typically lives for less than five weeks, which means that researchers can very rapidly measure the impact of age on male fertility, and their [sperm](#) and seminal fluid proteins. This species is also highly amenable to genetic studies, which allowed the researchers to genetically manipulate [male lifespan](#), to see how this impacted the decline in fertility with age.

Published this week in *PNAS* are their results which show that both sperm and [seminal fluid protein](#) quality and quantity decline with male age, making distinct contributions to declining reproductive performance in older males. However, the relative impacts on sperm and seminal fluid often differ, leading to mismatches between ejaculate components. Despite these differences, experimental extension of male lifespan improved overall ejaculate performance in later life, suggesting that such interventions can delay both male reproductive aging and death.

Lead author Dr Irem Sepil, from the University of Oxford's Department of Zoology, says: 'These results highlight that the decline in fertility with male age is not exclusively driven by changes in sperm. The quality and quantity of the seminal [fluid](#) proteins also change as males age, and these patterns can differ from the changes seen in sperm, but still impact male reproductive function. However, a manipulation aimed at increasing lifespan also slows down age-related reproductive decline. This means that it is possible that drugs and treatments aimed at

promoting healthy aging could be co-opted to slow down male reproductive aging.'

Going forward, the researchers want to look into the health of offspring. In humans, children of old fathers are more at risk of certain medical disorders, but the mechanisms driving these changes remain unclear. Also, whilst a lifespan-extending [genetic manipulation](#) helped fertility in older [males](#), it is not clear whether less invasive treatments, which might be used in human medicine, would work similarly. There is ongoing research to understand how we can increase the healthspan of individuals. The aim is not to live longer but to age healthily, slowing down the onset of age-related diseases such as cancer, Alzheimer's and arthritis.

It is important to note that the work described here was on a species of fly. While aging mechanisms are often similar across animals, to understand whether the patterns are commonly shared, they will need to be examined in other species.

More information: Irem Sepil et al. Male reproductive aging arises via multifaceted mating-dependent sperm and seminal proteome declines, but is postponable in *Drosophila*, *Proceedings of the National Academy of Sciences* (2020). [DOI: 10.1073/pnas.2009053117](https://doi.org/10.1073/pnas.2009053117)

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