

# **The Silent but Deadly Impacts of Ovarian Ageing**

## Introduction

Aspiring and current healthcare professionals strive to provide the best possible care for every human being on the planet, regardless of extrinsic factors such as race, age or class. Yet, inequalities still exist. One prominent example is the gender inequality in healthcare, such as the fact that less research has been done on women's health compared to men's. We seem to understand how symptoms present on men but are unaware what it is on women. Maybe it's due to the assumptions made that they are all the same or the fact that this type of research is severely underfunded (Smith, 2023). Either way, women everyday suffer because of the ignorance of the country's healthcare. It's deplorable.

One problem that women face right now is ovarian ageing. This is the process where there is a decline in the quantity and quality of oocytes (Moghadam et al., 2021), which are the cells in the ovaries that undergo meiosis to form the ova. The reduction in the quality of oocytes accelerates during the ages of 35-40 for most women, marking the beginning of menopause which brings about its own symptoms such as reduced fertility and irregular menstrual cycles (Camaioni et al., 2022). There are also a small percentage of women who experience menopause below the age of 40 (Tesarik, Galán-Lázaro and Mendoza-Tesarik, 2021), leading to the condition premature ovarian insufficiency (POI). This goes to highlight the vast number of women that suffer from ovarian ageing.

Though the cause of ovarian ageing is unknown, there is an evolutionary theory as to why oocytes age faster. Female humans have a higher rate of aneuploidy, where an irregular number of chromosomes are formed during meiosis, which causes their ovaries to age faster as mentioned above. Due to this, they have evolved to ensure that excess ova made during ovulation was reduced to ensure the uterus only has enough it is capable of handling (Sirard, 2022). However, this is only a theory and is not a clear cut explanation as to why it is like this.

## Possible factors linked to ovarian ageing

Not much is known about ovarian ageing, but studies have suggested extra-ovarian and intra-ovarian factors both have an effect. An experiment was conducted on female rats where the ovaries of young rats were transplanted into older rats. Although it was hypothesised that the older

rats would experience the same ovarian activity as their younger counterparts, this was not the case as there was no change. This went on to prove that factors outside the ovaries influence ovarian ageing (Wang, Wang and Xiang, 2023).

Following this evidence, the changes in the hypothalamus-pituitary-ovary (HPO) axis is suggested to be one such extra-ovarian factor. This axis is controlled by negative feedback, where there is increased secretion of GnRH, a hormone which regulates the ovulation cycles (Cleveland clinic, 2022). This will lead to increased secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH). These hormones help in regulating the woman's menstrual cycle. An increased secretion of them will then lead to increased secretion of oestrogen, progestin and inhibin (Wang, Wang and Xiang, 2023). This is illustrated as such in the diagram (ibid) below.

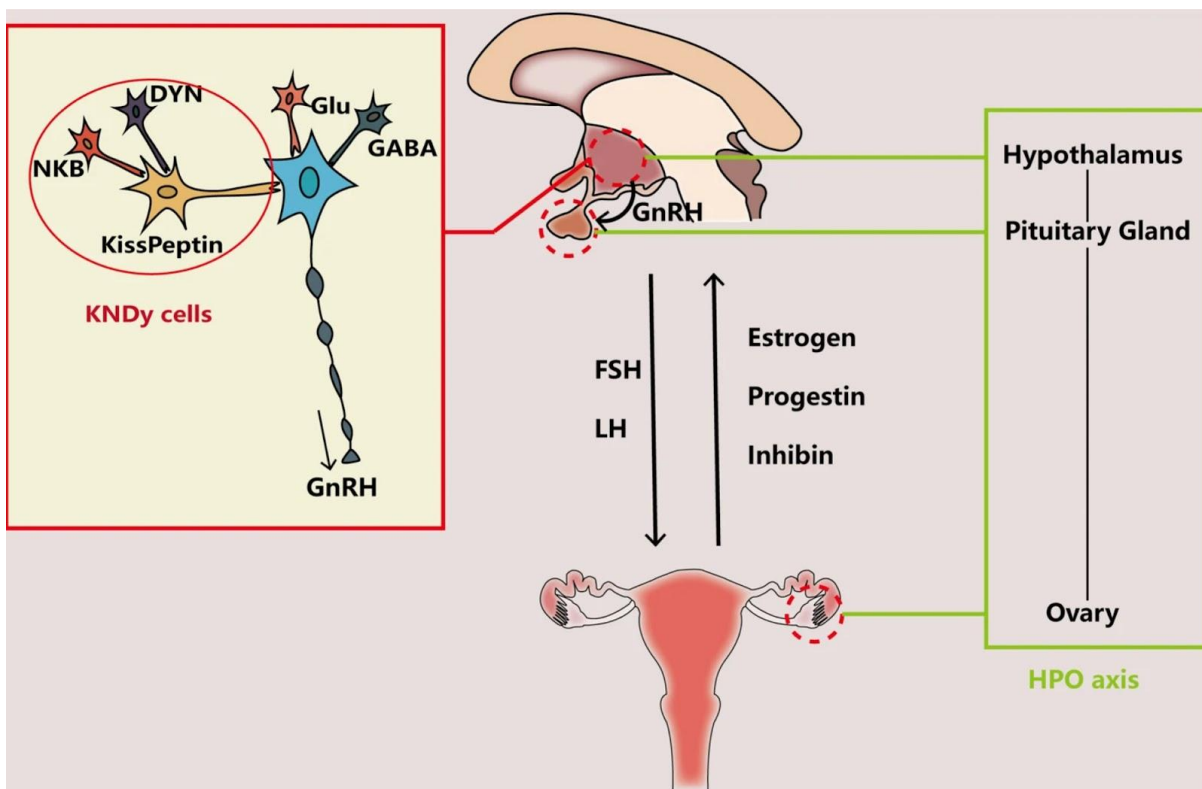


Figure 1. Diagram of the HPO axis

As women age, oestrogen levels naturally drop and the reason why, much like many issues surrounding ovarian ageing, are unknown. Because of this, it leads to a rise in the GnRH produced as the brain believes the signal is not being reached by the ovaries. Subsequently, this leads to a higher increase in FSH and LH hormones; this is why FSH levels are an indicator to how far along a woman's ovary has aged (Wang, Wang and Xiang, 2023). While some scientists make the association that an increase in GnRH will cause ovarian ageing, this is only a theory. The actual

mechanisms on how ovarian ageing occurs due to this is still not known (Park, Walsh and Berkowitz, 2021).

Intra-ovarian factors also contribute to ovarian ageing with shortening telomeres theorised to be one of them. Telomeres, which are DNA on the end of chromosomes that allows cells to be replicated continuously, are shortening every time the ovarian cycle starts again (Toupance et al., 2021). Telomerase is an enzyme which maintains the telomere length, but over time this enzyme gets damaged as its DNA gets eroded. The telomerase becomes inactive and will no longer maintain the telomere length (ibid). This means that the oocytes will soon be unable to replicate themselves leading to a reduction in the quantity of them. This contributes to ovarian ageing.

Other cytoplasmic and nuclear factors are examples of intra-ovarian factors suggested to have an impact on ovarian ageing. This includes the damage to the mitochondria in the oocytes.

Mitochondria are known to many as the ‘powerhouses’ of the cell, as they produce adenosine triphosphate (ATP) which is a high energy molecule that supplies energy throughout the body. When these mitochondria get damaged, they are unable to produce enough molecules of ATP to sustain cell division, so these oocytes die (Colella et al., 2021). This ultimately leads to a lower number of oocytes being produced as they are not replicating as often. Other factors such as aneuploidy or regular DNA damage due to harmful mutations could also be examples of intra-ovarian factors that cause ovarian ageing (Wang, Wang and Xiang, 2023). This will lead to less healthy oocytes being formed, leading to the ovaries ageing over time.

### Impact on woman’s health

As I spoke with Dr Fiona Sheppard, a GP with a background in women and sexual health, she explained to me the many different ways that ovarian ageing can impact a woman’s health. As mentioned above, this process leads to menopause. The symptoms of menopause are usually regarded as some of the major impacts by ovarian ageing on women’s health.

The most notable impact most women experience is that they have reduced fertility. Due to the decrease in oestrogen and progesterone, and an increase in FSH and LH, ovulation no longer occurs in a woman (Cleveland Clinic, 2021). Therefore, the pool of oocytes diminishes as these hormones are not working properly, leading to less follicles forming into ovarian cells. So, there is a lower chance that these oocytes will be capable of becoming egg cells that are then fertilised to form a zygote. Therefore, women have a harder time getting pregnant once they begin to experience

menopause. Even if a woman was able to get pregnant, which is rare as approximately 1% of women over 50 experience a natural conception (globmed, 2022), they would find it more difficult to maintain the pregnancy as they have a higher chance of miscarriages due to the body not being capable of supporting a pregnancy (Dr Fiona Sheppard, personal communication, July 2023).

Reduced oestrogen levels are another factor that can severely impact a woman's health as it causes many different ailments. For example, many women experience osteoporosis due to it; the hormone oestrogen plays a crucial role in maintaining bone health (Li and Wang, 2018) and without it, the bones become brittle. This is exemplified in the graph below.

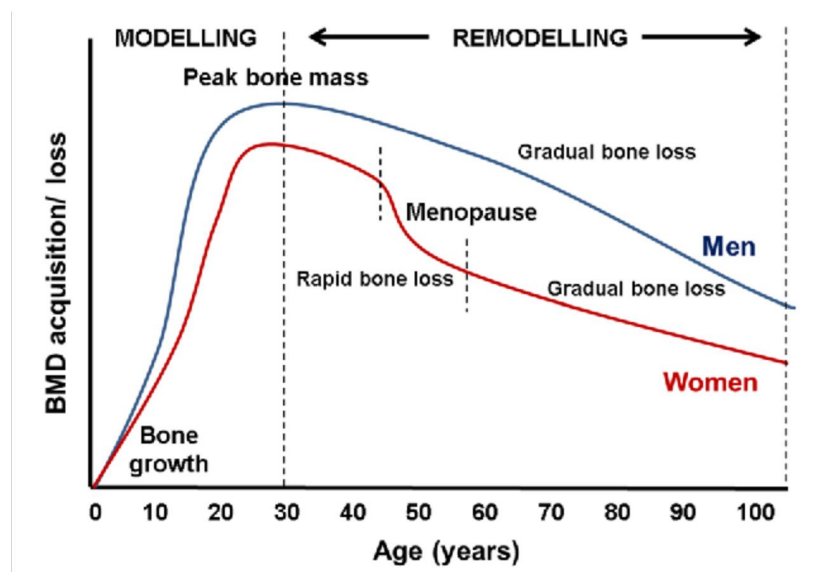


Figure 2. Changes in bone mass density over the years for men and women

As seen above (Cork Menopause Clinic, 2023), women experience a faster rate of loss in bone mass once they enter menopause. Compared to 25% of men, 50% of women are likely to experience a fracture due to bone atrophy (ibid). Oestrogen is also integral in maintaining good cardiovascular health. Therefore, as it decreases naturally for many women it makes them more susceptible to cardiovascular disease. Also, even though the mechanisms on why this occurs is still ambiguous, there is also a link between women in menopause being more likely to develop and suffer from endometrial cancer (Wu et al., 2019). However, many professionals attribute the reasons for this to deficiency in oestrogen levels as well (Scientific American, 2021). Other symptoms which are not mentioned as often as the others, like the lowered sex drive and vaginal dryness (Dr Fiona Sheppard, personal communication, July 2023), are also caused by a drop in oestrogen. Decreasing oestrogen levels is also one of the main factors that leads to weight gain for many women during menopause (Better Health Channel, 2022). This tends to develop into obesity which will put women

in a position where they will end up susceptible to more diseases such as type 2 diabetes, hypertension and strokes (Centers for Disease Control and Prevention, 2022).

Due to imbalances in the oestrogen and progesterone hormone, many symptoms arise such as moodiness and depression. As these decrease, serotonin (the neurotransmitter which makes one feel happy) also falls (Burch, 2021). From this, it is clear that women's mental health, as well as physical health, is severely impacted due to ovarian ageing. As I interviewed Dr Sheppard for this essay, she mentioned that there was more to the decline in mental health. Much of the mechanisms of ovarian ageing are still not known, which is clearly evident in this essay. Therefore, she mentions that many menopausal women feel isolated due to the lack of support from the medical community. One landmark study revealed that for around 33% of women, it had required multiple appointments with their GP before they were diagnosed with menopause (Murray, 2022). The fact that they couldn't have faith in the people meant to be helping them, even in times where they felt so lost and alone, is heartbreaking. This can clearly contribute to women's declining psychological health, which could then lead to other problems in the future.

### Possible treatments

Most treatments currently focus on treating the symptoms of ovarian ageing. One such example is hormone replacement therapy (HRT); this reassigns the sex hormones to the normal levels that were present before menopause (Armeni et al., 2021). This will decrease the risk of ovarian ageing problems, such as osteoporosis and cardiovascular disease, as more oestrogen will be produced once the original hormone levels have been restored. This will hopefully restore bone and cardiovascular health to what it was like before (ibid).

Yet, other treatments that actually tackle ovarian ageing are starting to show some promise. One treatment includes reactivating telomerase, which will then allow for it to maintain the telomere length and let more oocytes develop (Zhang et al., 2019). This will hopefully replenish the supply of oocytes and slow down ovarian ageing.

Other treatments include using stem cells to replenish oocyte supplies (Ali et al., 2022); this can also aid in slowing down ovarian ageing. It can also alleviate some of the symptoms caused by a low supply of oocytes, such as reduced fertility as there are now more oocytes which can form into healthy ova. These can then be fertilised by the sperm to form a zygote, then a foetus. Antioxidants,

such as Vitamin C, are another pharmacological method to slow down ovarian ageing as it helps ensure the mitochondria in the oocytes don't get damaged (Zhang et al., 2019). Mitochondria get damaged through oxidative stress, where oxygen atoms with an unpaired electron bind with the mitochondria. This ends up damaging the mitochondria, and makes it unable to carry out its function (Yan et al., 2022). With antioxidants, they react with the oxygen atoms so that they don't bind with and damage the mitochondria (Zhang et al., 2019). This leaves the mitochondria free to carry on making energy, which can be used to help the oocytes divide and produce more ovarian cells. This would replenish the oocyte supply and slow down ovarian ageing.

## Conclusion

In conclusion, ovarian ageing is clearly a very serious problem as it affects women in many different ways. The naturally reducing oestrogen levels that occur as a woman enters menopause is the main cause for many of the symptoms faced such as osteoporosis, cardiovascular disease and excessive weight gain (Wu et al., 2022). Women's psychological health is also impacted due to the imbalance in these sex hormones (Wang, Wang and Xiang, 2023). However, the exact mechanisms for ovarian ageing are not known and the ways to treat it are still ambiguous (ibid). This goes to emphasise just how vital and urgent more research in this topic is needed to benefit women everywhere in the world. It is time the world understands the deadly impacts of ovarian ageing and offers the support needed to ensure that women do not have to endure this suffering in silence.

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