

# Premature Ovarian Insufficiency

## What is Premature Ovarian Insufficiency (POI)?

Menopause usually occurs in women between 45 and 55 years. The average age of the menopause is 51 years. When menopause occurs under the age of 45, it is called early menopause. Menopause in women under 40 years is termed Premature Ovarian Insufficiency (POI).

Premature ovarian insufficiency, also referred to as premature menopause or premature ovarian failure, occurs when the ovaries stop working properly. The ovaries are unable to produce normal amounts of the hormones oestrogen and progesterone and they may stop producing eggs. This causes periods to become irregular or to stop completely, as well as symptoms of menopause.

## How common is POI?

POI occurs in approximately 1 in 100 women under the age of 40 and 1 in 1,000 women under 30.

## What are the causes of POI?

In many cases, the cause of POI is unknown. However, several known causes include:

### **Autoimmune disease**

Autoimmune disease, where the body's immune system attacks its own tissues, can lead to POI. Damage to the ovaries can result in POI. POI is associated with autoimmune diseases including Type 1 Diabetes, Hypothyroidism (under active thyroid gland) and Addisons Disease (under active adrenal gland).

### **Genetic conditions**

Abnormalities in the female sex chromosome (X chromosome). The most common of these is Turners syndrome, where one the X chromosomes is missing. Genetic causes are more common in women with a family history of POI, if POI is diagnosed at an early age, or in those who have never started having periods.

### **Cancer treatment**

Radiotherapy and chemotherapy can damage the ovaries, leading to POI. The risk depends on the site of radiotherapy, the type of chemotherapy used, and the age at which treatment is given.

### **Surgery**

Bilateral oophorectomy (removal of the both ovaries) inevitably leads to POI. Additionally, hysterectomy (removal of the womb) can cause an earlier onset of menopause, even if the ovaries are not removed.

## How is POI diagnosed?

If your periods stop or become irregular for at least 4-6 months, it may indicate POI. A blood test measuring levels of follicle-stimulating hormone (FSH) is used to aid diagnosis. Elevated FSH levels (over 30 iu/l) strongly suggest menopause. This test should be repeated 4-6 weeks later to confirm the diagnosis, as FSH levels can fluctuate during the menstrual cycle.

If you have had both of your ovaries removed, no tests are needed to confirm POI.

## What is follicle stimulating hormone (FSH)?

FSH is released by the pituitary gland at the base of the brain and stimulates the growth of follicles in the ovaries before the release of an egg from one follicle at ovulation. As the follicles grow, they produce increasing amounts of oestradiol, which feeds back to the pituitary gland to reduce FSH release. When the egg follicles become depleted over time and do not respond to stimulation, the pituitary gland compensates by producing more FSH, resulting in elevated levels. For women still having periods, FSH is measured on days 2-5 of the cycle; it can be measured at any time for women not having periods.

## Additional investigations for POI

- **Luteinising hormone (LH) Test:** A blood test. Elevated LH levels may indicate POI.
- **Antibody screening:** A blood test to check for thyroid and adrenal antibodies as POI is associated with autoimmune diseases.
- **Genetic testing:** Chromosome tests may be offered if POI is diagnosed before age 35 to check for genetic causes.
- **Bone density scan (also known as a DEXA Scan):** To assess the risk of osteoporosis. This scan may need to be repeated every 3-5 years. Low levels of oestrogen increases the risk of developing osteoporosis.
- **Pelvic ultrasound scan:** To exclude other causes for your symptoms.

## What are the symptoms of POI?

Women with POI may notice that their periods become irregular or stop altogether. Other symptoms are those experienced by any woman going through the menopause transition, most commonly hot flushes, night sweats, difficulty sleeping, low mood or anxiety, reduced libido (sex drive), memory or concentration problems, vaginal dryness, and discomfort during intercourse.

## What are the long-term effects of POI?

### Osteoporosis

Oestrogen is needed to keep bone strong and healthy. A lack of oestrogen leads to reduced bone density and weaker bones, increasing the risk of osteoporosis, where bones are more prone to fracture with little or no trauma. A DEXA scan at initial diagnosis, repeated every 3-5 years helps to monitor bone density

### **Heart disease**

Oestrogen is important for the cardiovascular system (the heart and blood vessels). It helps to keep blood vessels healthy. Lack of oestrogen in POI leads to an increased risk of hypertension (raised blood pressure), angina, heart attacks and stroke. In addition, 'good' cholesterol (HDL cholesterol) may reduce and 'bad' cholesterol (LDL cholesterol) may increase.

### **Other effects**

POI may also affect cognitive function and increase the risk of dementia as well as having an impact on a woman's psychological and physical health and quality of life.

## **Hormone Replacement Therapy (HRT)**

HRT is not only the most effective treatment for menopausal symptoms, it also reduces the risk of osteoporosis and heart disease. It may also lower the risk of dementia in women with POI. HRT does not increase breast cancer risk when taken before the natural menopause age (51 years). Even when continued beyond

this, the risk of breast cancer with HRT is less than the increased risk associated with drinking 2 units of alcohol per day or being overweight (BMI over 25) or obese (BMI over 30).

## **Testosterone: An essential hormone for women**

Testosterone is a sex hormone, considered a 'male hormone' but women also produce testosterone. Testosterone is made by the ovaries and the adrenal glands, which are small glands located near the kidneys). Testosterone levels tend to be lower in women with POI.

### **Symptoms of testosterone deficiency**

Symptoms of testosterone deficiency in women include:

- Lack of energy
- Low mood
- Poor concentration
- Low sex drive (lack of libido)

### **When is testosterone replacement considered?**

Testosterone may be considered for women with POI who continue to experience symptoms while taking Hormone Replacement Therapy (HRT), particularly if they suffer from lack of libido and fatigue.

### **Forms of testosterone replacement**

Testosterone replacement comes in the form of a gel or a cream applied to the skin. Although testosterone is not licensed for use in women in the UK, it is often prescribed 'off-licence' by menopause experts as it is effective and safe.

### **Available Testosterone Gels**

- **Tostran**
- **Testogel**
- **Testim**

These gels are licensed in the UK for use as male HRT and can be prescribed to women at a much lower dose. **Androfeme** is a testosterone cream licensed in Australia for women and is generally available in the UK on a private prescription.

### **Monitoring testosterone levels**

A blood test before starting testosterone and another test three months after are recommended to ensure the prescribed amount does not take blood levels above the normal range for women.

### **Side effects**

At the correct dose, side effects such as acne, excess hair growth,

male pattern baldness, enlargement of the clitoris, and deepening of the voice are rare.

### **Optimising your health**

Understanding and addressing testosterone deficiency can significantly improve the quality of life for women with POI. If you are experiencing symptoms, consult with a menopause expert to discuss whether testosterone replacement therapy is suitable for you.

### **Lifestyle factors**

Maintaining a healthy lifestyle is important for everyone, especially for women with POI, to prevent cardiovascular disease and osteoporosis. Implementing the following lifestyle changes can significantly reduce the risk of the long-term effects of POI:

- **Stopping smoking:** Quitting smoking is essential to reduce the risk of cardiovascular diseases and other health complications.
- **Eating a healthy balanced diet:** A diet rich in nutrients supports overall health and well-being.
- **Maintaining a healthy weight:** Keeping a healthy weight can help manage symptoms and reduce health risks.
- **Limiting alcohol:** Reducing alcohol intake helps maintain bone health and prevent other health issues.
- **Regular exercise:**



- **Aerobic exercise:** Engaging in regular aerobic exercise supports cardiovascular health
- **Weight-bearing exercise:** Weight-bearing exercises strengthen bones and help prevent osteoporosis.
- **Strength exercise:** Strength exercise helps to build and maintain muscle mass, which increases metabolic rate
- **Adequate calcium and vitamin D:** Consuming a diet rich in calcium helps maintain healthy bones. Vitamin D is essential for bone health and is produced by the skin when exposed to sunlight. Since sunlight exposure is limited during the winter months in the UK, Vitamin D supplements are recommended.

### How does POI affect fertility?

Unlike menopause in older women, the ovaries in women with POI may not completely fail. Ovarian function can fluctuate over time, occasionally resulting in a period, ovulation (release of an egg), or even pregnancy, sometimes many years after the diagnosis. Consequently, around 5-10% of women with POI can become pregnant.

### The combined contraceptive pill and POI

Some young women prefer to take the combined oral contraceptive pill (COC) rather HRT to manage symptoms of POI.

The COC pill is a simple method of hormone replacement and may be seen as more socially acceptable within a peer COC pill contains both oestrogen and progesterone, helping to alleviate menopause symptoms while also providing effective contraception. However, it is thought to be less effective than HRT for cardiovascular and osteoporosis protection.

When contraception is needed, an alternative to the COC pill is the Mirena coil which releases a progestogen (levonorgestrel) in the uterus. The Mirena provides contraception and can also provide the progestogen component of HRT when used alongside oestrogen HRT in the form of a patch, gel, spray, or tablet.

### **What support is available for women with POI?**

Support is available for women with POI through various resources, including the Daisy Network. The Daisy Network is a charity dedicated to providing information and support to women with POI. You can find more information and support at The Daisy Network.

For more information and personalised advice, contact our menopause clinic.