Premature Ovarian Insufficiency (Premature Menopause)

2025

What is Premature Ovarian Insufficiency (POI)?

Premature Ovarian Insufficiency is when someone under 40 years of age does not have an adequate supply of ovarian hormone in their body. It is a serious medical condition that demands medical attention. You should have a full supply of sex hormones throughout your reproductive life but especially if you are under 40. If you are unfortunate enough to have abnormally low levels of estrogen and an elevated level of FSH (Follicle Stimulating Hormone), it can have potentially life limiting consequences – you need hormone supplementation if at all possible.

How common is POI?

POI is seen in 1 in 1000 (0.1%) of females under 30, it is more common between 30 and 40 years of age with 1 in 100 people affected (1%).

What are the causes of POI?

1. **Idiopathic POI** - 70% of people with POI will never know why this is happening to them (idiopathic means we haven't identified the cause yet). There may be as yet unidentified genetic links as POI can run in families.

2. Known **Genetic causes of POI**- POI can also be linked to known genetic conditions such as Turner's syndrome, Fragile X Syndrome and Down's syndrome.

What is Turner's syndrome?

This is a chromosome abnormality that affects about 1 in 2500 people wherein your X chromosome is either partially or totally missing. Genes located on that chromosome may be lost. Expression is variable so some people with Turner's syndrome feel and look quite well. Some patients may have learning delays or might be of short stature. Turner's syndrome can be associated with a webbed neck, abnormal bones in the hand or a high palate. Turner's syndrome can also be linked to serious medical problems such as kidney and liver disease, diabetes, cerebrovascular disease and people with Turner's syndrome should always be evaluated and reviewed by a multidisciplinary clinic to keep on top of risks. See https://www.youtube.com/watch?v=fA4jmD4OR-g

What is Fragile X syndrome?

Fragile X syndrome is another rare genetic condition which results from a mutation on a gene called the "fragile X-mental retardation-1 gene" (FMR1), which is located on the X chromosome. When you have Fragile X syndrome, the damaged gene segment cannot make the protein "FMRP", which is essential for normal brain cell connections and learning delay can occur. It is the most common form of inherited learning disability and can cause a list of other physical, intellectual and behavioural problems.

Some people carry the Fragile X gene mutation but have no symptoms or signs themselves, others can have a variety of health issues including FXPOI. That is **Fragile X associated Premature Ovarian Insufficiency.** About 25% of females who carry FX permutation will experience FXPOI and we sometimes diagnose FX carrier status in the POI clinic.

What is Down syndrome?

Also known as Trisomy 21, it is when a person is born with a third 21st chromosome instead of the usual two. It can be associated with developmental delays and intellectual disability. Trisomy 21 can be partial or full so there can be a lot of variation in the impact of the extra 21st chromosome. It is hard to predict whether or not you will develop POI if you have Down's syndrome but hormone screening should be part of your normal medical assessments.

3. Enzyme deficiencies – disorders like galactosaemia (where you are born missing the enzyme "galactose-1-phospahte uridyl-transferase") or 17- alpha- hydroxylase deficiency, are quite rare but can be linked to POI.

4. Iatrogenic Premature Ovarian Insufficiency (POI) - Many medical interventions can result in early or premature menopause/ POI. Iatrogenic POI means POI having been caused by medical treatments. Radiotherapy to the abdomen, pelvis or spine can affect ovarian function and fertility. Chemo and radio therapy for cancers (or Hodgkin's lymphoma) are associated with the highest incidence of Iatrogenic POI. Gynaecological cancers (esp. uterine, cervical and ovarian), BRCA mutation, severe endometriosis, PMDD and some blood disorders that may be managed by removing your ovaries (oophorectomy) will result in POI. Even when they leave you with one or both ovaries, e.g. after a hysterectomy you might still develop earlier menopause symptoms as a result of the impact of the surgery on blood flow in the pelvis.

5. Autoimmune diseases and infections - Conditions such as Hashimotos disease of the thyroid gland, Rheumatoid Arthritis, SLE, Myasthenia gravis, etc. can all be linked to POI.

POI Diagnosis and Assessment

- If you have POI, you are at increased risk of reduced fertility, osteoporosis, cardio vascular disease and cognitive impairment among other things.
- **POI is diagnosed when someone under 40 years of age who has skipped more than 4 months without a period and has abnormal Follicle Hormone levels.** Your GP will arrange two separate sets of blood tests at 4 - 6 week intervals. If they show that you have follicle stimulating hormone (FSH) levels of greater than 30 IU/L in both of those tests, that suggests you have POI.
- **People may skip periods for various reasons.** Some contraceptives will intentionally shut off periods, people who have lost weight rapidly sometimes stop getting periods for a time, PolyCystic Ovarian Syndrome (PCOS), certain non- contraceptive medications, various hormonal disorders, some diseases of the reproductive system and many other things can stop periods so you need to have a conversation and full consultation with your doctor as well as FSH blood tests before being referred to a POI clinic.

Other Tests for people with POI

Full blood tests will usually be done by your GP before your visit to the POI clinic (often to out rule some of those other conditions mentioned above). We may repeat them in the POI clinic. You may be offered genetic testing too. You might also be advised to have a DEXA X-ray of the bones to rule out Osteoporosis and an Ultrasound Scan of your pelvis. Ovarian follicle reserve may be assessed by measuring blood levels of AMH (Anti-Müllerian Hormone) and if you are struggling to conceive, you can be referred to the Fertility Services.

Treatment of POI

There are excellent guidelines available for the management of POI. The European Society of Human Reproduction and Embryology (ESHRE) offers up to date advice. They recommend that people with POI should be encouraged to use some form of replacement sex hormones (HRT or one of the estrogen containing contraceptive products) and be reassured that the usual perceived "risks" from HRT do not always apply to them.

HRT and some contraceptives contain estrogen and progestagen. HRT might be "better" for POI but it really depends on the person and their own medical needs and risk factors as to which of these you might be offered.

Combined Hormonal Contraception for POI

Combined Hormonal Contraceptives (CHCs) are available in one of the many contraceptive tablets or the ring or the patch that are made up of both estrogen and progestagen. They are contraceptives, but they also replace low levels of ovarian hormone. CHC's are more potent than HRT and there are more restrictions about who may use them. If you are quite overweight, if you smoke, if you experience migraines associated with neurological phenomenon, etc. it may not be safe for you to be on any CHC. In this case, you will be offered HRT.

Hormone Replacement Therapy for POI

HRT hormones contain estrogen and progestogens that are more like the "natural" estrogen molecule that the ovaries make and so for patients who want as close to natural hormone replacement as possible, HRT is preferable. The milder, more natural hormones of HRT have less known medical risks linked to them and are less likely to cause serious side effects. People who are not allowed to use CHC can usually use HRT. There is no contraceptive protection from HRT though and this needs to be discussed as about 10 - 15% of people with POI can conceive spontaneously.

Testosterone for POI

Some POI patients notice a significant reduction in their sex drive (libido) and / or difficulties with sexual arousal and orgasm. This is known as HSDD or **hypoactive sexual desire disorder**. This may not be improved by the addition of estrogen +/- progestagen and in this situation an androgen (male hormone) should be offered. Testosterone replacement therapy may be needed to supplement what a typical ovary would be producing and restore libido and sexual enjoyment.

Vaginal Estrogen for POI

As the number of blood vessels that bring estrogen from the blood stream to the pelvis are reduced in POI, as in natural menopause, additional estrogen delivered directly into the vagina is often needed alongside either HRT or the CHC.

Fertility and POI

There are many levels of fertility support available for people who want to conceive and it is important to discuss this issue with your doctor BEFORE you have a surgery or start treatments that might affect your fertility.

Support for people with POI

Getting a diagnosis of POI can be quite a shock. Depression and low self-esteem are often associated with a diagnosis of POI and ideally all people with POI (like all people with any medical condition) should have access to counselling and peer support. In Ireland, it can be challenging to access free one to one counselling in general. Therapists with specific training in POI are also in short supply. As an alternative, online resources can be helpful. One of the most well-known and well respected POI support organisations is the Daisy Network in the UK - see www.daisynetwork.org/.