

Information for  
women with  
Premature Ovarian  
Insufficiency

Patient version based  
on the ESHRE Guideline on  
management of women  
with Premature Ovarian  
Insufficiency

Version 2016

# Introduction

## This booklet is for you if:

- You have been diagnosed with premature ovarian insufficiency (POI).

This booklet is intended for patients, but may also be useful for their family members and caregivers.

If you have been diagnosed with premature ovarian insufficiency as a result of treatment for cancer or benign disease, or you are about to undergo treatment that could result in POI, please find more appropriate information in the ESHRE booklet “Information for women with IATROGENIC Premature Ovarian Insufficiency”

## This booklet aims to:

- increase awareness of premature ovarian insufficiency
- encourage women with POI to attend their healthcare provider.
- provide women with POI with tools to discuss their options with their healthcare provider.

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This booklet and the information presented are entirely based on the ESHRE Guideline on the management of women with Premature Ovarian Insufficiency. All the information and recommendations in the guideline are based on the best available evidence from research. When there is insufficient evidence from research, a group of experts have formulated recommendations based on their clinical expertise.

We have added the following symbols to explain the strength of the recommendations

	Strong recommendation based on research evidence
	Recommendation based on considered opinion of the guideline development group

More information is available at the last pages of this booklet. The entire guideline is available on the website of ESHRE ([www.eshre.eu/guidelines](http://www.eshre.eu/guidelines))

# What is Premature Ovarian Insufficiency (POI)?

Premature Ovarian Insufficiency or “POI” was first described in 1942 and since then has been described with different names and definitions. Other names often used for premature ovarian insufficiency are primary ovarian insufficiency, premature ovarian failure, gonadal dysgenesis, premature menopause, early menopause and hypergonadotropic hypogonadism.

POI is a condition where the ovaries stop functioning properly before the age of 40. The ovaries stop releasing eggs and stop producing hormones (estrogen, progesterone, testosterone).

The diagnosis of POI is made by evaluating the frequency of periods (over at least 4 months), and by measuring the hormone levels in the blood (2 measurements at least 4 weeks apart both showing elevated levels of Follicle Stimulating Hormone [FSH]).

## What causes POI?

POI can be iatrogenic, which means it has been caused by a previous medical treatment, for example, chemotherapy, radiotherapy or surgery for cancer or benign disease<sup>1</sup>.

POI may also be spontaneous (non-iatrogenic), and in this case, your doctor will perform several test to search for an underlying cause.

### **Genetic and chromosomal causes**

POI can be caused by a defect in your chromosomes or genes. This is the genetic information you received from your parents and which you pass on to your children. Examples of the most frequent chromosomal/genetic causes are Turner Syndrome and Fragile-X syndrome respectively.

To check whether you have a chromosomal or genetic defect causing POI, chromosomal analysis and Fragile-X testing are recommended (blood test).

**Chromosomal analysis and Fragile-X-premutation testing is recommended in women with POI.**



*If a genetic or chromosomal cause for POI is found, this may have implications for your family members. Your doctor should discuss this with you before testing and provide you with information on how to inform your relatives.*

### **Autoimmune diseases**

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<sup>1</sup> More information on iatrogenic POI is available in the ESHRE booklet “Information for women with IATROGENIC Premature Ovarian Insufficiency”

Antibodies are produced by our body to fight intruders, for instance a virus or bacteria. In autoimmune diseases, antibodies are produced that attack your own body: these are known as autoantibodies. Certain autoantibodies are more common in women with POI, for example, against the thyroid gland which lies in the base of the neck. These can be associated with an under- or over-active thyroid gland (thyroid antibodies). It is not understood how, or indeed if, these autoantibodies are involved in the cause of POI. Rarely, autoantibodies are found that are directed against the adrenal glands, which lie adjacent to the kidneys, (adrenal antibodies). The presence of adrenal antibodies is associated with a process of inflammation in the ovaries that results in the destruction of eggs. Your doctor may perform a blood test to search for these antibodies.

**Autoantibody testing (adrenal and thyroid antibodies) is recommended in women with POI, especially if an autoimmune problem is suspected.**



*If autoantibodies are detected, your doctor may perform additional tests to check whether your adrenal glands or thyroid gland are functioning normally, and if needed refer you to an endocrinologist.*

### **Other causes of POI**

Some studies have shown that diabetes mellitus type I may be more common in women with POI. As type I diabetes is usually diagnosed in childhood, it is not necessary to screen all women with POI for diabetes.

Case reports have linked POI to a previous infection (of, for instance, mumps). However, this has not been shown in larger studies, and therefore women with POI do not need to be screened for (previous) infections.

### **Idiopathic or unexplained POI**

In the majority of women with POI, none of the performed tests are positive and hence the cause of POI is unknown. These women are diagnosed with idiopathic or unexplained POI.

## What are the symptoms of POI?

Women with POI will often stop menstruating (called amenorrhea), or they will have less frequent periods (called oligomenorrhea). Some women with POI caused by a genetic or chromosomal abnormality will never start menstruating (termed primary amenorrhoea).

You may also experience a range of symptoms resulting from a reduction in estrogen, or you may not have any symptoms.

Possible symptoms caused by low estrogen are hot flushes, night sweats, vaginal dryness, pain during sexual intercourse, sleep disturbances, mood changes, poor concentration, stiffness, low libido, dry eyes, change in urinary frequency, and lack of energy. ✓

## 5 Tips to manage your symptoms

①

Keep a healthy lifestyle, including

- A balanced diet and a healthy weight
- Regular (weight-bearing) exercise
- Limited alcohol



*Although the evidence is limited, a healthy lifestyle is believed to have a beneficial effect on general health and on the impact of POI on your body.*

*Particularly, a healthy lifestyle can reduce the impact of POI on bone and heart health, and therefore it is recommended that you try to be healthy.*

②

Stop smoking ✓

*There are no studies showing that stopping smoking has a beneficial effect on the symptoms of POI. However, quitting smoking will benefit your general health and may have positive effects on POI.*

③

Get an annual appointment with your doctor ✓

*Cardiovascular risk should be assessed in women diagnosed with POI, at least blood pressure, weight and smoking status. Women with POI using HRT should have a clinical review annually.*

④

Comply with your therapy ✓

*Unless you have a history of breast cancer, HRT is safe and helpful to relieve symptoms and prevent problems with heart disease, or bone health later in life. Compliance with treatment is essential.*

⑤

Discuss any symptoms you experience with your doctor. S/he can inform you of treatment options, or advice on how to deal with these symptoms. Never hesitate to mention questions or concerns ✓

*If you feel the diagnosis of POI has a major impact on your well being, your doctor can offer you psychological support. Similarly, treatments are available for the impact of POI on your sex life.*

# What are the effects of POI on my health?

Being diagnosed with POI may be a life changing experience and **you may feel overwhelmed and lost.**

POI can have an impact on different parts of your body.

## 1. Infertility

As POI is a condition where the ovaries stop functioning properly before the age of 40, the chance of conceiving naturally is significantly reduced.

If you have POI, you may have difficulties getting pregnant naturally. However, there may be a small chance of spontaneous pregnancy, so your doctor should discuss the need for contraception with you.



Currently there are no treatments or procedures that can increase your chances of getting pregnant.



Oocyte (egg-cell) donation could be an option to get pregnant.



If you consider oocyte donation from your sister you should be aware that this carries a higher risk of an insufficient number of eggs maturing in your sister's ovaries during treatment leading to cancellation of the cycle.



If you get pregnant through oocyte donation, you may be at increased risk for complications during pregnancy. To prevent these complications, your doctor may perform some additional test before pregnancy, and monitor you more closely during pregnancy.



## 2. Sex life

You may experience vaginal dryness, reduced libido, and pain during intercourse due to POI. These symptoms could have significant impact on your sex life.



The combination of infertility, menopausal symptoms, and lack of energy may result in a significant impact on your sex life and the relationship with your partner.

Your doctor should discuss the impact on your sex life with you, and can recommend the use of hormone replacement therapy, estrogen creams, testosterone or lubricants.



It may also be helpful to discuss your feelings and concerns with your partner.

### 3. Bone, heart and brain

Hormones, especially estrogen, are important for the normal functioning of a (young) woman's body. Reduced estrogen levels do not only result in menopausal symptoms, but can also affect the health of your bones, heart and brain.

POI is associated with reduced bone mineral density; you may be at increased risk of bone fractures later in life.



POI is associated with an increased risk of developing heart disease.



POI may have an impact on your memory.



A healthy lifestyle (e.g. exercise, cessation of smoking, maintaining a healthy weight) can reduce the impact of POI on your bones, heart and brain.



Your doctor will monitor the health of your bones (if needed by performing a DEXA scan) and your heart (by checking your blood pressure). S/he will also prescribe hormone replacement therapy (HRT), if this is not contra-indicated for you (see also next section).

# What are my options for treatment?

POI cannot be cured, but treatment can alleviate your symptoms and reduce the long term effects on your health.

## 1 HORMONE REPLACEMENT THERAPY (HRT)

*In women with POI, the ovaries will stop producing hormones (estrogen, progesterone, testosterone), which are needed for a healthy body. HRT aims to restore the levels of these hormones in your body to a similar level as women of the same age without POI.*

**Hormone replacement therapy is indicated for the treatment of symptoms of low estrogen in women with POI.** 

**HRT may have a role in the prevention of heart disease, and it may protect your bones** 

*Studies have shown that HRT improves the typical symptoms of POI (hot flushes, night sweats). In women with POI, HRT is safe; studies have shown that HRT in women with POI does not increase the risk of breast cancer.*

**Patient preference for route and method of administration of each component of HRT must be considered when prescribing, as should contraceptive needs.** 

**The combined oral contraceptive pill may be appropriate for some women but effects on the bones are less favourable.** 

*Your doctor should discuss the different HRT options with you to help you decide which one would be the most appropriate for you.*

**Your underlying condition and general health will have a significant impact on whether or not you can receive HRT and which regimen is best for you. Also, your doctor may perform some tests before prescribing HRT. The recommended treatment is as follows:**

<b>Migraine</b>	Not contraindicated – estrogen patches preferred	
<b>Hypertension</b>	Not contraindicated – estrogen patches preferred	
<b>History of prior venous thromboembolism (VTE) or thrombophilic disorder</b>	Not contraindicated – referral to a haematologist recommended before starting HRT – estrogen patches preferred	
<b>Obesity or overweight</b>	Not contraindicated– estrogen patches preferred	
<b>Fibroids</b>	Not contraindicated	

## 2

### ANDROGEN THERAPY (testosterone)

*Androgen therapy has been proposed as a treatment for the effects of POI on your sex life, bones and memory, but studies are limited and the long-term side-effects of androgen treatment are unknown*

Androgen treatment is only supported by limited data, and the long-term health effects are not clear yet.



If androgen therapy is commenced, treatment effect should be evaluated after 3-6 months and should possibly be limited to 24 months.



## 3

### LOCAL TREATMENTS (vaginal estrogen cream/pessaries, lubricants)

*Some women with POI experience significant sexual problems, either uncomfortable or painful intercourse from vaginal dryness (genito-urinary symptoms), or sexual changes such as altered libido and arousal.*

*HRT may improve these symptoms, although there are no good studies of women with POI.*

Local estrogens are effective in treatment of genito-urinary symptoms



You may experience genito-urinary symptoms despite seemingly adequate systemic hormone replacement therapy (HRT). Vaginal estrogens may be given in addition to systemic HRT.



Lubricants are useful for treatment of vaginal discomfort and painful sex due to vaginal dryness whether or not HRT is being used.



## 4

### COMPLEMENTARY TREATMENTS

*Several alternative and complementary treatments have been advocated to reduce symptoms of low estrogen, including phyto-estrogens (soy and red clover), black cohosh, evening primrose oil, dong quai, panax ginseng, wild yam and vitamin E.*

*For some of these treatments, studies have shown a small reduction in symptoms. However, these studies are small and of low scientific quality. In addition, they do not provide information on whether the treatment is safe.*

For most alternative and complementary treatments, evidence on efficacy is limited and data on safety are lacking.



## Where can I find more information or support?

More detailed information on each of the topics in this booklet can be found in the clinicians' edition of the guideline on the ESHRE website ([www.eshre.eu/guidelines](http://www.eshre.eu/guidelines)).

For more detailed information or support, you can contact your doctor or a patient organisation.

In some European countries, there are patient organisations specifically for women with Premature Ovarian Insufficiency, while in other countries, these patients could find information and support through national patient organisations for infertility.

**The Daisy Network** is a support group for women suffering with Premature Ovarian Insufficiency (POI). They are a registered charity in the UK but have members from all over the world. Their aim is to provide support, information and a friendly network of people for their members. You can find more information at their website <https://www.daisynetwork.org.uk/>

For contact details of national patient organisations for infertility, you can ask your doctor, or contact **Fertility Europe** ([www.fertilityeurope.eu](http://www.fertilityeurope.eu))

## About this booklet

This booklet aims to involve patients in healthcare improvement, either by learning about the current standard of care, or by enabling patients to make informed decisions on their health, supported by the best available evidence.

## How this booklet was developed

This booklet was written by Dr Nathalie Vermeulen (methodological expert), and revised by the Daisy Network (patient group) and Dr Lisa Webber (gynecologist and chair of the Guideline Development Group). All the information provided is based on the recommendations in the ESHRE guideline: management of women with Premature Ovarian Insufficiency (POI).

## Who developed the ESHRE guideline?

The ESHRE guideline: management of women with Premature Ovarian Insufficiency (POI), was developed by a multidisciplinary guideline development group including gynaecologists and endocrinologists, but also experts in bone health, cardiology, psychology and neurology, a literature methodology expert and a patient representative.

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# Dictionary

**Assisted reproductive technology (ART):** The name for treatments that enable people to conceive by means other than sexual intercourse. Assisted reproduction techniques include **intra-uterine insemination (IUI)**, **in vitro fertilisation (IVF)**, **intracytoplasmic sperm injection (ICSI)**, donor insemination and egg donation.

**Controlled ovarian stimulation (COS):** For ART: pharmacologic treatment in which women are stimulated to induce the development of multiple ovarian follicles to obtain multiple oocytes at follicular aspiration.

**Dysmenorrhea:** Severe pain in the lower abdomen or back, sometimes together with nausea, depression and headache, directly before and/or during **menstruation**.

**Dyspareunia:** Recurrent or persistent genital pain directly before, during or shortly after coitus (sexual intercourse).

**Embryo:** A fertilised egg.

**Estrogen/Oestrogen:** A female sex **hormone** produced by developing eggs in the ovaries, which stimulates the development of female sex characteristics.

**Hormone:** A molecule that is produced by one tissue and carried in the bloodstream to another tissue to cause a biological effect.

**In vitro fertilization (IVF):** A technique by which eggs are collected from a woman and fertilised with a man's sperm outside the body. Usually one or two resulting embryos are then transferred to the womb. If one of them attaches successfully, it results in a pregnancy.

**Infertility:** the state of being not fertile and unable to become pregnant. Clinical definition of infertility: A disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

**Intra-uterine insemination (IUI):** A technique to place sperm into a woman's womb through the cervix

**Intracytoplasmic sperm injection (ICSI):** A variation of **IVF** in which a single sperm is injected into an egg.

**Medically assisted reproduction (MAR):** Reproduction brought about through ovulation induction, **controlled ovarian stimulation**, ovulation triggering, ART procedures, and intrauterine, intracervical, and intravaginal insemination with semen of husband/partner or donor.

**Menstruation:** The monthly period or bloody discharge from the uterus; it consists of blood and **endometrium** sloughed from the uterine lining.

**Ovary:** a paired organ in the pelvis of women containing the eggs and the site of female sex hormone production.

**Progesterone:** A **hormone** produced by the **ovary**, but only if ovulation has occurred (after the egg is released). Its action is to prepare the **endometrium** for implantation of the embryo.

## Disclaimer

*The European Society of Human Reproduction and Embryology (ESHRE) developed the current information booklet for patients based on the clinical practice guideline. The aim of clinical practice guidelines is to aid healthcare professionals in everyday clinical decision about appropriate and effective care of their patients.*

*This booklet is in no way intended to replace, dictate or fully define evaluation and treatment by a qualified physician. It is intended solely as an aid for patients seeking general information on issues in reproductive medicine.*

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