

# Premature Ovarian Failure (POF)

## Definition:

Premature Ovarian Failure (POF), also known as early or premature menopause, is defined as the loss of normal functioning of the ovaries before the age of 40<sup>(1,2)</sup>. Menopause – the stage in a woman’s life in which there is permanent cessation of menstruation and a significant change in hormone levels – typically occurs between 45–55 years of age. Where menopause occurs early, as seen in POF, infertility is a common result<sup>(5)</sup>.

## Epidemiology:

POF typically affects 1 in 100 women under the age of 40 years<sup>(3)</sup>. It can also occur in women under the age of 30, but incidence is lower – at approximately 1 in 1000 women<sup>(3)</sup>. A woman is at higher risk of developing POF if there is a positive family history.

## Causes:

Although the exact mechanism of POF is not understood, many possible causes have been identified<sup>(1,4,5)</sup>. Women that are known to have chromosomal abnormalities, as seen in Turner’s syndrome or fragile X syndrome, are more likely to present with POF. Similarly, those with auto-immune diseases, such as Systemic Lupus Erythematosus (SLE) or Rheumatoid Arthritis (RA), can also present with POF. Deficiencies or defects in certain enzymes, as seen in Galactosemia and Haemochromatosis, have been linked to POF. Iatrogenic causes include chemotherapy and/or radiotherapy, as well as surgery on the reproductive organs (e.g. ovariectomy). Rare causes include viral infections.

## Clinical Features:

The presenting signs and symptoms of women with POF are very similar to that of menopause<sup>(4,5,6)</sup>. Commonly, women present to their doctor due to the cessation of their menstrual periods and/or infertility. Some may also present with associated disruption of sleep, hot flushes, mood swings and night sweats. Other symptoms include vaginal dryness, painful sexual intercourse and low sex drive.

## Investigations:

Undertaking a full clinical history is very important. This will help ensure that other causes for the loss of menstruation, such as pregnancy and pituitary pathologies,

are excluded. Similarly, it helps reveal the possible cause of POF, if the diagnosis is indeed made. Many women that present to their doctor with symptoms of POF have found that their symptoms are instead attributed to stress or significant life events, so it is important to fully investigate symptomatic women to rule out POF.

After a detailed history from the patient, a physical examination is undertaken. However, often, very few signs are found on examination.

Several biochemical tests should then be undertaken<sup>(5)</sup>. To rule out the chance of pregnancy, hCG levels are measured, especially in women of childbearing age. Follicle Stimulating Hormone (FSH), Luteinising Hormone (LH) and Oestradiol are also measured in aid of confirming or refuting the diagnosis of POF, in adjunct to the clinical presentation. Levels of FSH above 30iu/l (international units per litre of blood) taken on 2 separate occasions, at least 4 weeks apart, is deemed highly indicative of POF<sup>(4,6)</sup>. LH and oestradiol levels are usually low in POF, and so can help in confirming the diagnosis.

Other tests that are carried out include looking for auto-antibodies and karyotyping, which again, help to identify the cause of POF.

### Complications:

POF, like menopause itself, involves a significant change in ovarian function, involving lack of ovulation and significant changes in hormonal environment. Women with POF will find it very difficult to conceive, and so infertility is often a serious and life changing complication<sup>(4,5)</sup>. As such, anxiety and depression can result<sup>(5)</sup>, particularly in those who develop POF before having children. Osteoporosis is also an important complication to bear in mind<sup>(1,4,5)</sup>, and should thus be considered when formulating the management for the patient. Oestrogen, amongst other functions, is involved in maintaining strong and healthy bones, thus with a sudden drop in oestrogen levels, as with POF, the bones become brittle and are at a higher risk of fractures.

### Management:

POF cannot be reversed, but management involves replacing the hormones no longer being produced by the ovaries, through Hormone Replacement Therapy (HRT)<sup>(5)</sup>. Oestrogen is given to prevent osteoporosis, in addition to relieving other symptoms associated with oestrogen deficiency, like hot flushes, and also improve cardiovascular health. However, unless the patient has had a hysterectomy, oestrogen **must** be given with progesterone to prevent the risk of developing endometrial cancer. HRT can be given through many means including oral tablets, patches and vaginal pessaries<sup>(7)</sup>; the choice of which method depends on the patient and their clinical presentation.

Calcium and Vitamin D supplements are advised to patients in helping to prevent osteoporosis, in addition to encouraging regular exercise, a healthy diet and stopping smoking (if appropriate)<sup>(5)</sup>.

Infertility is a common and significant complication, and unfortunately no treatment is able to restore fertility. A very small number of women may conceive spontaneously, but majority of women, if wishing to have children, need to be advised on alternative forms of conception (like IVF) or consider adoption<sup>(5)</sup>.

Support and counselling are very useful in enabling the patient to come to terms with her diagnosis<sup>(1,4)</sup>. As such, advising her on local groups, wherein other women also have POF, can also be invaluable for supporting her through the management.

# References

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