

## PREMATURE MENOPAUSE

Menopause occurs between the age of 40 and 60 in most women. The average age for menopause in Australia is approximately 51 years. However around 1-2% of women will be spontaneously menopausal before the age of 40 years.

### WHAT IS PREMATURE MENOPAUSE?

Menopause, which is literally defined as 'the last menstrual cycle' occurs between the age of 40 and 60. Often there is a clear 'family trend', and knowing when your mother experienced menopause will help you anticipate when it might occur for you. Many factors, mostly genetic, determine when natural menopause occurs.

If menopause occurs prior to the age of 40 it is deemed abnormal. The reason for this abnormality is that the ovaries stop producing the necessary hormonal support to stimulate endometrial growth, which causes the monthly bleeding. The technical term for this is 'Premature Ovarian Failure' (POF). This in itself is usually not a problem, except that you are unable to conceive naturally, as the ovary fails, it no longer produces eggs.

### WHAT MIGHT I NOTICE?

Periods can be quite variable in the lead up to early menopause. Some women with POF may never have had a period, or some notice their periods stop or become very irregular a few years after commencing puberty. Not every woman will have hot flushes either. Many women will have irregular periods before they finally stop.

### WHAT TESTS CAN BE CONDUCTED?

The diagnosis is confirmed via a blood test (finding elevated levels of FSH, >20U/L, usually over 40U/L), which is usually conducted by a reproductive endocrinologist. It is essential to repeat the FSH measurement to confirm the diagnosis.

If you are under the age of 30 your specialist can discuss with you the options of chromosomal analysis, bone mineral density, and an auto-antibody screen (e.g. thyroid, adrenal, ovarian, parietal cell auto-antibodies, ANA) as these are useful tests.

### IF I HAVE A FAMILY HISTORY, HOW CAN I TELL IF I AM AT RISK OF EARLY MENOPAUSE?

Anti-Mullerian hormone (AMH) can now be measured as a blood test and this gives us a rough estimation of your egg reserve. Blood AMH levels will fall years before your periods stop (or before FSH rises). Thus, an AMH measurement can be useful for women who want to know if they are at risk for early menopause, for example if you have a family history of menopause before 40 years.

## **WHAT CAUSES PREMATURE MENOPAUSE / OVARIAN FAILURE?**

Most cases of premature menopause remain 'unsolved', in other words there is no clear cause for the sudden cessation of menstruation and ovarian function.

Some conditions associated with premature ovarian failure (POF) are summarised below;

### **APPARENTLY HEALTHY WOMEN WITH POF:**

#### **Genetic causes**

- Fragile X syndrome is the most common genetically determined cause of premature ovarian failure in women who have no obvious signs of a genetic abnormality. This syndrome can now be detected by genetic testing. Young women who are diagnosed with fragile X syndrome are encouraged to consult a fertility specialist to consider their fertility options.
- Partial deletions of the X chromosome (parts of the chromosome are missing)

#### **Autoimmune causes**

- ovarian autoantibodies (your immune system attacks the ovaries)

#### **Mutations**

- Follicle Stimulating Hormone (FSH)
- Luteinising Hormone (LH) (very rare)

#### **Infections**

- Mumps: women may or may not have experienced pelvic pain during the infectious episode
- Tuberculosis: if it affects the genital tract it may destroy ovarian tissue to the extent of eliminating function

#### **Surgery**

- Aggressive surgery to remove ovarian cysts, especially endometriotic cysts reduces the 'life span' of the ovary sometimes to the point of causing premature failure.

### **WOMEN WITH A SIGNIFICANT MEDICAL HISTORY AND POF:**

#### **Genetic causes**

- Turner's syndrome
- Rare genetic syndromes (e.g. Swyer's syndrome, Perrault's syndrome, Blepharophimosis)

### **Ovarian antibodies associated with other autoimmune conditions**

- Addison's disease
- Diabetes mellitus
- Thyroid disease
- Myasthenia gravis
- Systemic Lupus Erythematosus (SLE)
- Rheumatoid arthritis

### **Infiltrative disease**

- Iron-overload (e.g. Thalassaemia major)
- Sarcoidosis of the ovary

### **Chemotherapy**

- Not all chemotherapy regimens will cause premature ovarian failure. Women treated at around puberty are the most at risk to develop POF secondary to treatment of a malignant condition with chemotherapy

### **Radiotherapy to the pelvis**

- Radiation of the pelvis with therapeutic doses to treat cervical, anal or vulval cancers will invariably lead to ovarian failure. In some women, surgical transposition of the ovaries is performed to lift the ovaries out of the radiation zone.

### **Enzyme deficiencies (rare)**

- Cholesterol demolase deficiency
- Galactosemia

## **TREATMENT OF PREMATURE OVARIAN FAILURE**

Treatment of Premature Ovarian Failure involves two distinct aspects: fertility and the hormone environment.

### **FERTILITY TREATMENT:**

There is unfortunately no treatment for premature ovarian failure. In some affected women, the ovarian function returns temporarily and some get pregnant (5 – 10%).

It is important for women to identify that they are at risk, such as through family or surgical history, and to be pro-active early on. Your reproductive endocrinologist can discuss the options with you.

The current recommendation by many IVF outlets of cryo-preservation of eggs is an option, however there is, as of yet not sufficient evidence to suggest that this is a 'sure thing' as many tend to believe.

### **HORMONAL TREATMENT:**

Estrogen, especially estradiol which is almost exclusively produced by the ovary, is an essential hormone not only for menstrual function, but also for the development and maintenance of almost every organ system in women.

If you suspect you are at risk of premature menopause, speak to your GP as referral to a reproductive endocrinologist is essential due to the far reaching effects of the loss of ovarian hormones, you do need specialist care. For example, if a young woman has not had any breast development, very low doses of oestrogen need to be initially given, and then slowly increased. If they are prescribed a contraceptive Pill, for example, the breasts usually remain small and misshapen.

### **More information**

Please see our website for more information about

- Fertility

### **Web links:**

- Jean Hailes Organisation <http://jeanhailes.org.au/health-a-z/menopause/premature-early-menopause/>