

## Perils of the Perimenopause

While most women have heard of the term "*Menopause*", the term "*Perimenopause*" is less well known and even less well understood. Perimenopause is the stage from the beginning of menopausal changes to the post-menopause, the time following the last period. Post-menopause is usually defined as more than 12 months with no periods in someone with intact ovaries, or immediately following surgery if the ovaries have been removed. The perimenopause can be a stage of changing periods and early menopausal symptoms, changes which can often vary from month to month causing confusion and unpredictable inconveniences.

## PERILS OF THE PERIMENOPAUSE!

To best understand what happens during the perimenopause stage and the changes leading up to the menopause, it is important to understand the normal *menstrual cycle*. For ovaries to function, a complex interaction occurs between the *pituitary gland* (at the base of the brain), egg cells within the ovaries responding to chemical stimulation, and the release of hormones from the ovaries.

### **Follicular phase**

The first day of a period is called Day 1 of the menstrual cycle. In the few days leading up to Day 1, if pregnancy has not occurred, estrogen and progesterone levels fall and this fall leads to a shedding of the lining of the womb – *menstruation*. The fall in estrogen and *inhibin* (a hormone which has been researched only fairly recently), also allows a rise in *follicle stimulating hormone (FSH)*, which is produced from the pituitary gland, since high levels of estrogen and inhibin suppress FSH production through a feedback mechanism. FSH then stimulates development of egg cells in the ovary and by days 5–7, usually one egg cell in particular continues to respond. Developing egg cells are surrounded by fluid and are known as *follicles*. The 'dominant' follicle produces large amounts of estrogen and inhibin, resulting in a fall in FSH.

Other effects of estrogen at this stage include stimulation of the lining of the womb to become thickened, ready to receive a fertilised egg.

### **Ovulatory phase**

At about days 12 to 14, high estrogen levels stimulate release of *luteinising hormone*

(LH) from the pituitary gland. The surge in LH causes the egg to be released from the follicle (*ovulation*).

### **Luteal phase**

During days 14–28, the area of the ovary that has released the egg, the *corpus luteum*, produces progesterone. Progesterone further prepares the womb lining for accepting a fertilised egg. If the egg is not fertilised, the corpus luteum ‘collapses’ and the levels of estrogen and progesterone fall. Without these hormones to support the lining, the womb then sheds its lining and menstruation begins again. Also, with a low estrogen level, FSH rises and a new cycle begins.

## **Why menstrual cycles change**

The maximum number of egg cells (*oocytes*) within the ovaries is present before we are born; at around the fifth month of gestation there are thought to be around 7 million, and these decline to 1–2 million by birth. From birth onwards there is a gradual reduction, with around 400,000 remaining by the time of puberty, thereafter a gradual decline by the age of 40 years and then a rapid decline up to the menopause. Leading up to the menopause during the perimenopause, the follicles remaining are not only fewer in number but also of poorer quality and less able to respond to the stimulation by FSH. Occasionally, cycles occur where follicles have not developed fully and less estrogen is produced. Low levels of estrogen lead to menopausal symptoms, a rise in FSH, and a failure to trigger the LH surge leading to absence of egg release (*ovulation*). With no *ovulation*, progesterone production is also reduced, leading to irregular shedding of the lining of the womb and hence irregular periods. In the early stages, the ovaries fluctuate in how well they work, so that cycles may be normal some months and abnormal in others. Gradually the number of abnormal cycles increases so that eventually, no follicles develop, estrogen and progesterone production becomes very low, the lining of the womb is not stimulated at all, periods stop and FSH levels remain high. Finally, the menopause, the last period, occurs and is confirmed by having 12 months without periods. Following this, there may occasionally be episodes where the ovaries again produce a later burst of hormones, the womb lining is stimulated and subsequent bleeding may occur, but this is unusual and any bleeding occurring more than 12 months after a period should be reported and investigated. Generally, estrogen and progesterone levels after the menopause remain steady and low, unlike levels during the perimenopause. During the perimenopause, the ovaries are still working and producing hormones but are not producing the correct balance of hormones. In the early stages, the levels of FSH, LH, estrogen and progesterone fluctuate markedly and symptoms and period patterns may change from month to month.

## **Period problems**

Often the changing and falling progesterone level, which regulates the lining of the womb (the *endometrium*), causes erratic, heavy or prolonged periods before any other menopausal symptoms are noticed. Many women experience periods which can be unpredictable and so heavy that the flow can be difficult to control, often flooding through sanitary wear and clothing. Women often put up with this inconvenience for some time before seeking help but since very effective treatments are available, help should be sought sooner rather than later. With this change in period pattern, your doctor will usually arrange investigations such as an examination and possibly referral for a sample to be taken from the lining of the womb or a pelvic scan. These

investigations are to exclude causes other than the hormonal changes of the perimenopause. Hormone levels can fluctuate for several years before eventually becoming so low that the endometrium stays thin and does not bleed and so periods can be troublesome for a number of years before they stop, but can also vary in that some months may be normal, often giving a false sense of security! Once it is established that the cause is hormonal imbalance, treatments can be considered.

## Treatments

If the main problem is heavy periods which are not too frequent, the tablet Tranexamic acid can be used; this is taken during the period and simply leads to less fragility of the blood vessels within the womb lining, and hence less bleeding. If the heavy periods are also prolonged and/or frequent, some form of the hormone progestogen can be given. This can be given in tablet form or in the form of Mirena; a small plastic device which is inserted into the womb, and gradually releases progestogen into the womb lining, making the lining thin and reducing bleeding. Insertion is a simple procedure and usually takes place in a clinic without problems. Mirena has the added benefit of providing effective contraception, which is still required in the perimenopause, right until 2 years after the menopause in women who become menopausal under the age of 50, and for 1 year after the menopause in women becoming menopausal after the age of 50.

Other treatments for period problems include various forms of heat treatment aiming to destroy most of the womb lining (known as endometrial ablation), leading to reduced bleeding and are usually carried out as day-case procedures.

For some women, a hysterectomy (surgical removal of the womb) may be needed but is carried out less often in recent years than was required in the past, due to the introduction of simpler, effective treatments.

## Other problems of the perimenopause

The fluctuating and gradually falling level of estrogen taking place during the perimenopause, can lead to early signs of the symptoms more often associated with the menopause such as hot flushes, night sweats, mood changes, disturbed sleep, joint aches and change in weight and distribution of fat; more fat tends to be deposited around the waist rather than the hips leading to a change to the "apple" shape rather than "pear" shape. Symptoms affecting the vagina and bladder such as vaginal dryness, irritation and itch, discomfort during sex, passing urine often and at night and discomfort when passing urine, are thought to be later symptoms of the menopause, but some women may notice them in the perimenopause. Symptoms may be initially mild and, because periods are still present, are often not recognised as being hormone related. Further confusion may arise because, as with period problems changing from month to month due to fluctuating ovarian function and hence fluctuating progesterone production, estrogen production may also fluctuate and so these estrogen deficiency symptoms may also vary.

It is important that these early changes are recognised and that discussions take place so that women understand what is happening.

Management of the estrogen deficiency symptoms of the perimenopause should start with review of diet and lifestyle; the early changes should alert us to put in place whatever changes are needed, such as improving diet, losing weight, increasing exercise, stopping smoking and reducing alcohol and caffeine, to reduce not only early

symptoms but also long term effects of estrogen deficiency such as osteoporosis and cardiovascular disease.

Specific treatments such as Hormone Replacement Therapy should be considered and would aim to "top up" the declining estrogen levels, while providing progestogen for protection of the womb lining.

Often, the effects of the changing hormone levels of the perimenopause can be challenging to treat since each month can be different but effective treatments are available and when the changes are troublesome, information and advice should be sought.