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Lifestyle May Affect the Onset of Some Symptoms in Perimenopausal Women

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Abstract

Perimenopause is the period before menopause and can last up to ten years. Cycles may become longer than usual or become shorter. Menstruation can be missed several times. The amount of menstrual bleeding may be weaker or more abundant. Abnormal bleeding can be a sign of a problem or illness. Perimenopause is a multi-year period of hormonal changes in which ovarian function is gradually extinguished. During the years of the reproductive period, oocytes are consumed, so after the age of 40, there are fewer quality oocytes. Their receptors change and thus hormone production changes - which can lead to several health problems related to the perimenopausal period.

Keywords: Perimenopause, Menopause, Transition, Women, Health

Introduction: Perimenopause is the phase prior to menopause [1]. For many women, this can begin as early as age 35. Perimenopause for some women is an easy transition with minimal symptoms. For other women, perimenopause is rife with adolescence-like symptoms that manifest as the adrenal glands, ovaries, and pituitary gland undergo transition. Women experience perimenopausal symptoms primarily in their 30s and 40s. Perimenopause is a normal phase of transition. It is marked by some of the same symptoms that occur during adolescence, another period of major hormonal transition. The hormonal environment in perimenopause (unlike in menopause) is tumultuous. Perimenopausal symptoms may be compounded by factors such as adrenal dysfunction, anovulatory cycles, and poor dietary habits.

Women

Women aged >40 years have the second highest proportion of unintended pregnancies, exceeding only girls 13–14 years old [2]. Although women still need effective contraception during perimenopause, issues including bone loss, menstrual irregularity, and vasomotor instability also need to be addressed. Oral contraceptives offer many benefits for healthy, nonsmoking perimenopausal women. They have been found to decrease the risk of postmenopausal hip fracture, regularize menses in women with dysfunctional uterine bleeding, and decrease vasomotor symptoms.

For perimenopausal women with cardiovascular risk factors, progestin-only methods may be preferred, including progestin-only pills, levonorgestrel (or copper) IUDs, contraceptive implants, and DMPA. Barrier methods or sterilization may also be appropriate for select women. Control of dysfunctional uterine bleeding can be obtained with injectable progestogens or the levonorgestrel IUD. Low-dose estrogen can be added to these methods if estrogen replacement is desired and appropriate.

Physiologically, menopause is the permanent cessation of menstruation as a consequence of the termination of ovarian follicular activity. Determining the exact onset of menopause in a woman using hormonal contraception can be tricky. Many clinicians measure the level of follicle-stimulating hormone (FSH) during the pill-free interval to diagnose menopause. However, because suppression of ovulation can vary from month to month, a single FSH value is unreliable. In addition, in women using COCs (combination oral contraceptives), FSH levels can be suppressed even on the seventh pill-free day. Given that most women do not become menopausal until after age 50, and considering the limited utility of FSH testing, one approach to managing this transition avoids FSH testing entirely. Women continue to use their COCs until age 50–52, at which time they can discontinue use or transition to hormone replacement therapy.

Transition

In the female reproductive phase, the pubertal girl starts with variable menses transitioning into regular monthly cycles. She will have normal GnRH, LH, FSH, AMH (anti-Müllerian hormone) and inhibin B levels, and between six and ten antral follicles with no vasomotor symptoms or urogenital atrophy [3]. In the late period of the reproductive phase, the woman will begin to see subtle

changes in the amount and length of the menstrual flow accompanied by lower hormone levels and there will be fewer antral follicles developing each month. No vasomotor symptoms or urogenital atrophy should be apparent during the late reproductive phase and pregnancy can occur with increased chances of birth defects that increase over time. This normally takes place between the age of 35 and 45 years but can be quite variable.

As a woman transitions into menopause, generally called perimenopause, the length of time between the first day of menses will be extended by at least 1 week (35-day cycles) and continue to increase over time to more than 60 days between cycles. Although less likely, some cycles can still produce ova and pregnancy can occur. This change will be accompanied by increasing levels of GnRH, LH and FSH, and continuing lower levels of AMH and inhibin B. In addition, vasomotor symptoms, sometimes called hot flashes, are likely to be experienced and are thought to be in response to spiking levels of P4. The time for this transition can vary from less than a year up to about 3 years. Finally, the woman will transition into the postmenopausal phase which will generally stabilize out to a constant state within 3–6 years. This time will be characterized by the highest GnRH and its responding gonadotropins (due to the nadir in negative feedback from steroids and inhibin) along with very low AMH and inhibin B. Vasomotor symptoms will peak early during this time and then eventually cease while increasing symptoms of urogenital atrophy reach their maximum for the remainder of the woman's life span.

Several cohort studies with a large number of subjects have been published so that comprehension and description of menopausal transition can be summarized as follows: (1) all stages have a vast variability in terms of duration and age of onset; (2) the decline of ovarian reserve starts 15 years before the complete cessation of menses (menopause) and is more pronounced after the age of 35; (3) clinically, one of the most important symptoms is the shortened follicular phase (and, consequently, the menstrual cycle length); and (4) the length of menopause is dependent on demographic characteristics of ethnicity, race, smoking, genetic background (family medical history), fat composition, and body mass index.

The menopausal transition starts physiologically when the inter-cycle FSH secretion increases and luteal P4 decreases. These events will decrease the follicular phase of the menstrual cycle. Consequently, older patients present with shorter menstrual cycle intervals. This observation occurs several years before the complete establishment of the post-climacteric stage (defined as 12 months after the last menstrual period). Furthermore, the anti-Müllerian hormone is a good marker of the ovarian reserve but not an accurate marker for ovarian menopausal transition as a predictive test for the start-day of menopause.

Menopause

Menopause is defined as permanent amenorrhea in a previously cycling woman [4]. Natural menopause is the permanent cessation of menstrual cycles caused by the exhaustion of the ovaries. Medical intervention that removes or terminates ovarian function also leads to menopause. If a premenopausal woman has a hysterectomy without oophorectomy, her ovaries may still produce hormonal cycles and she is considered premenopausal until ovarian cycles stop.

Perimenopause or climacteric, the period around menopause, begins with the onset of symptoms attributed to the menopausal transition. Common climacteric symptoms, in order of frequency, are vasomotor symptoms (hot flashes), mood disturbances, sleep disturbances, decreased libido, and vaginal dryness.

In addition to menopause, other changes affect women in the middle years. These include personal issues of sexuality and aging, the "empty nest" response generated by children becoming fledgling adults, aging parents who may be ill or disabled, and health problems of friends and spouses. These developmental life changes can provoke symptoms similar to those of menopause or aggravate ones that already exist. On the other hand, many women find "menopausal zest." Their children are out of the home, financial security may be reached, and there no longer is a fear of pregnancy.

Menopause signals the end of an era for many women [5]. It concludes their ability to reproduce, and some women find advancing age, altered roles, and these physiologic changes to be overwhelming events that may precipitate depression and anxiety. Menopause does not happen in isolation. Midlife is often experienced as a time of change and reflection. Change happens in many arenas: children are leaving or returning home, employment pressures intensify as career moves or decisions are required, elderly parents require more care or the death of a parent may have a major impact, and partners are retrenching or undergoing their own midlife crises. Women must negotiate all these changes in addition to menopause. Managing these stressful changes can be very challenging for many women as they make the transition into midlife.

As menopause approaches, more and more of the menstrual cycles become anovulatory. This period of time, usually 2 to 8 years before cessation of menstruation, is termed perimenopause. In perimenopause, the ovary begins to sputter, producing irregular and missed periods and an occasional hot flash. When menopause finally appears, viable ova are gone. Estrogen levels plummet by 90%, and estrone, produced in fat cells, replaces estradiol as the body's main form of estrogen. The major hormone produced by the ovaries during the reproductive years is estradiol; the estrogen found in postmenopausal women is estrone. Estradiol is much more biologically active than estrone. In addition, testosterone levels decrease with menopause.

Biomedical Approach

The biomedical approach conventionally treats health conditions as purely biological events explained by specific pathways [6]. Research on women, in particular, has been omitted and is sometimes assumed to be replicas of biological research on men found that having a menstrual cycle served as a confounding variable in medical research. Much of the menopausal research conducted from a biomedical perspective has treated menopause as a deficiency condition needing intervention. These definitions were not only transmitted from research perspectives but also influenced masses of women and physicians.

Biomedical approaches segment the menopausal experience into three stages: premenopause, perimenopause, and postmenopause. Premenopause is the time period after menarche with normal fertility function, which ends with the last menstrual cycle. The perimenopause phase occurs as the last menstrual periods are approaching and may bring symptoms like irregular menstrual cycles and hormonal fluctuations. Finally, postmenopause is confirmed when a woman reaches the 12-month mark after her last menstrual cycle. These stages have unique implications for each woman and are not as clearly defined as medical textbooks might suggest.

Perhaps one of the most problematic consequences of the biomedical approach is the acceptance of "fixing menopause" and the subsequent medicalization of menopause. Menopause management, along with the management of other chronic conditions, contributed to the expansion of the pharmaceutical industry, soaring prescription drug prices, and increased drug dispensing in high-income countries. The emergence of hormone replacement therapy is the result of a desire to remain youthful, feminine, and asymptomatic of menopause. While the clinical distinction may be clear to physicians for diagnosis, women may not understand their current menopausal stage.

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Ovarian Aging

Changes in ovarian function, dominated by the gradual decline of both oocyte quantity and quality, are major contributors to the reproductive aging process [7]. The latter becomes apparent both in increasing rates of infertility observed at an older age as well as increased aneuploidy rates, responsible for higher risk of miscarriage and trisomic births with increasing age.

The size of a woman's follicle and oocyte stock is already determined during the early stages of fetal development. At birth, this primordial follicle pool consists of around 1–2 million oocytes. Due to a continuous process of apoptosis, follicle numbers are reduced to approximately 300,000–400,000 at menarche. When follicle numbers fall below a critical threshold of a few thousand, the perimenopausal transition commences, which is characterized by overt cycle irregularity and altered cycle length. Finally, prolonged menstrual cycles proceed to cycle arrest, a milestone referred to as menopause, which coincides with a near absence of primordial follicles in the ovaries.

The normal process of ovarian aging varies considerably among women, with peak fertility in the mid to late 20s. The profound age-related decline in female fecundity, however, remains largely unnoticed until clinical signs of the perimenopausal transition are present. The loss of the capacity to create an ongoing pregnancy leading to a live birth is accompanied by an increase in early follicular follicle-stimulating hormone (FSH) levels, which cannot be easily recognized by an individual. The onset of the menopausal transition, expressed by lengthened cycles due to deficiency of antral follicles capable of growing into dominance, is usually a woman's first notification of advanced ovarian aging.

Despite the individual variation in the onset of menopause, a fixed time interval is believed to be present among the stages of reproductive aging. From natural population studies, an apparent variation in the age at last childbirth between age 31 and 50 years has been observed, with a distribution shape highly similar to the one for menopause. The presumed fixed time interval between menopause and natural sterility may prove of great clinical importance to provide information concerning a woman's fertility life span. Early menopause suggests an early loss of natural fertility resulting in infertility at a young age and vice versa.

One of the first hormonal indications of perimenopause is a rising FSH; this is secondary to decreasing production of Inhibin B by granulosa cells in antral follicles [8]. As ovarian function and antral follicle count declines, Inhibin B levels fall, allowing for rising levels of gonadotropins. Rising FSH drives increased recruitment of follicles, with a consequential increase in the rate of follicle loss during perimenopause.

In addition to Inhibin A and B, anti-Müllerian hormone (AMH) is a glycoprotein also produced by granulosa cells in preantral and small antral follicles. AMH inhibits the stimulatory actions of FSH follicle recruitment; as the number of antral follicles decreases with age, so too do AMH levels also decrease, reaching undetectable levels at menopause. As such, AMH has become increasingly popular as a measure of ovarian reserve and as an index for menopause.

Vasomotor Symptoms

Vasomotor symptoms are the second-most common symptom of perimenopause/menopause, with as many as 85% of perimenopausal women experiencing night sweats, hot flashes, and sleep disturbances secondary to vasomotor symptoms [8]. Also known as hot flushes or hot flashes, vasomotor symptoms (VMSs) are generally defined as episodes of intense heat and sweating, accompanied by flushing of the head, neck, chest, and/or upper back. The intensity, quality, and duration of hot flushes vary widely among patients from several minutes of extreme heat in the upper body and face to perspiration, chills, clamminess, anxiety, and palpitations.

Vasomotor symptoms are generally milder in early perimenopause and tend to worsen significantly throughout the late perimenopausal period. A recent study by Avis et al. found that the earlier VMS began in the pre/perimenopausal transition, the longer the total duration of symptoms, while women who were post-menopausal when vasomotor symptoms began had the shortest duration of vasomotor symptoms (median 3.4 years); on average, VMS lasted more than seven years for more than half of subjects and persisted for 4.5 years after their final menses. In addition, several studies have shown a correlation between vasomotor symptoms and cardiovascular disease as well as a greater degree of bone loss and increased bone turnover. Hot flashes generally stop within four to five years of onset; however, some women report a continuation of vasomotor symptoms for many years, and their impact on quality of life should not be underestimated.

Adrenal Dysfunction

The demands of work, family, children, aging parents, and society at large place undue stress on many women [1]. The result is a perpetual flight-or-fight cycle. The adrenal glands, which are designed to function only in times of danger, function constantly, releasing norepinephrine and epinephrine from the adrenal medulla and corticoids, mineral corticoids, and androgens from the adrenal cortex.

The mineral corticoids (primarily aldosterone) regulate the balance of minerals (sodium, potassium, and magnesium) in the cells. Stress triggers the release of aldosterone, which raises blood pressure by influencing cells to hold on to sodium and lose potassium. Long-term release of stress-level mineral corticoids can cause potassium deficiency, magnesium imbalance, chronic water retention, and high blood pressure. The resultant magnesium insufficiency, as noted by serum red blood cell magnesium levels, can affect many of the enzyme-driven metabolic pathways in the body.

In addition, the adrenal cortex makes all the sex hormones in small amounts and dehydroepiandrosterone (DHEA) in large amounts. DHEA is important in the growth and repair of protein tissues and is a precursor to androstenediol, testosterone, and estrogens. It is not a precursor to progesterone, aldosterone, pregnenolone, or cortisols. Alterations in the normal production of the hormones of the adrenal cortex can predispose women to multiple symptoms of perimenopause, including aggression and anger from too much testosterone; passivity, oversensitivity, mental confusion, and agitation from too much or too little estrogen; and depression from too little estrogen or progesterone.

Symptoms:

- Increasing vaginal dryness
- Decreased libido
- Acne
- Generalized fatigue
- Increasing blood pressure
- Endometriosis
- Uterine fibroids
- Symptoms of increased cortisol, which include papery (thin) skin, weight gain around the midsection, memory loss, blood sugar imbalances, and muscle wasting
- Mood swings
- Chronic fatigue
- Diabetes
- Menorrhagia and other menstrual irregularities
- Hot flashes
- Sleep disturbances
- Bladder problems
- Loss of bone mineral density

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HMB

Heavy menstrual bleeding (HMB) is excessive menstrual bleeding over several consecutive cycles that interferes with the woman's physical, emotional, social and material quality of life [9]. The old-fashioned measurement of total blood loss > 80 ml was shown to be inaccurate and clinically irrelevant (NICE), although generally, women's perception of menstrual bleeding is consistent with objective measurements of blood loss. The gold standard for measuring menstrual blood loss used to be an alkaline haematin test, which is not suitable for routine assessment. The trend was to develop simple low-cost self-assessment tools, which could be widely used, such as pictorial charts. Objective measurement might still have a place in menorrhagia management as some patients choose expectant management when their objective blood loss is shown to be within the normal range. Also, quantification is necessary for clinical trials of treatment.

HMB affects 3% of premenopausal women, with an even higher prevalence in perimenopausal women (40–51 years). About 30% of women will experience HMB at some point in their life.

Pelvic Ultrasound

A pelvic ultrasound can be used to evaluate the ovaries, uterus, and endometrial lining for abnormalities [10]. An evaluation of the ovaries can assist in the diagnosis of PCOS as many women with PCOS will have enlarged ovaries with multiple, small follicles. A pelvic ultrasound is also useful for evaluating an enlarged uterus for the presence of fibroids. Fibroids will appear as hypoechoic, solid masses seen within the borders of the uterus. Subserosal fibroids can be pedunculated and therefore can be seen outside the borders of the uterus. An endovaginal ultrasound can be used to evaluate the thickness of the endometrial stripe. The results need to be interpreted according to whether a patient is pre- or postmenopausal. An endovaginal ultrasound is a sensitive test for patients with postmenopausal bleeding regardless of whether they are using hormone replacement therapy (HRT). Therefore, postmenopausal patients with an endometrial stripe thicker than 4–5 mm should have a histological biopsy. Hormone replacement therapy can cause the proliferation of a patient's endometrium, rendering an endovaginal evaluation less specific. An endovaginal ultrasound is also useful in evaluating the endometrial stripe in premenopausal or perimenopausal patients. Whereas the normal endometrial stripe is thicker in the premenopausal patient than in the postmenopausal patient, the median thickness of an abnormal endometrium is similar for both. The endovaginal ultrasound examination is less likely to detect myomas and polyps.

At one time, hormone replacement therapy was prescribed extensively to decrease menopause symptoms because it was believed that this therapy reduced cardiovascular complications such as atherosclerosis or heart attacks as well [11]. HRT is no longer prescribed routinely as such therapy does not appear to reduce cardiac risk or prevent osteoporosis and may be associated with endometrial cancer, cerebrovascular accidents (strokes), and perhaps breast cancer.

HRT may be prescribed on a short-term basis (1 to 2 years) if a woman has symptoms so severe that they interfere with her life plans but women should not receive estrogen replacement therapy indefinitely because of the possible adverse effects.

Women who notice excessive vaginal dryness can be advised to use a lubricating jelly such as KY Jelly prior to sexual relations. Other possibilities are the application of estrogen cream or the insertion of a vaginal ring that dispenses low-dose estrogen. Low-dose estrogen or testosterone can also be prescribed to increase sexual libido. Practicing Kegel's exercises can help strengthen bladder support and reduce urinary incontinence.

Sexual Disorders

Sexual function is influenced by complicated and interactive biological and psychologic factors [12]. Thus, the diagnosis of sexual dysfunction is complicated because of the numerous diverse etiologies that must be considered. The differential diagnosis of sexual disorders is not widely understood by physicians. Because of the interaction between biological and psychologic factors, evaluation of many disorders of female sexual function by necessity involves close collaboration between practitioners in obstetrics and gynecology and those in psychiatry. The psychiatric clinician will focus on a careful sexual and psychiatric history, attempting to ascertain the specific nature of the psychological problem (e.g., affective disorder, marital discord, or transient stress) and whether it appears to be secondary to other psychiatric diseases. Evaluation by the gynecologist will be equally meticulous and will attempt to rule out diverse physical etiologies, including vulvovaginitis, normal hormonal changes associated with menopause or perimenopause, endometriosis, and other pathologic conditions.

The field of gynecology has shown an increasing awareness of the need to assess sexual function, and most gynecologists recognize the need to collaborate with psychiatrists in this assessment. It is indeed the rare psychiatrist or gynecologist who is capable of independent assessment and treatment of the full spectrum of female sexual disorders. The requisite knowledge base crosses subspecialty boundaries and is still evolving.

Conclusion

During perimenopause, mood swings can occur with hormonal changes. This can manifest as increased crying, excessive worry or anxiety, or a bad mood such as depression. Lifestyle factors can affect the severity of perimenopausal symptoms in some women, and small changes can help

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