

Testing menopausal hormone levels: Is it necessary?

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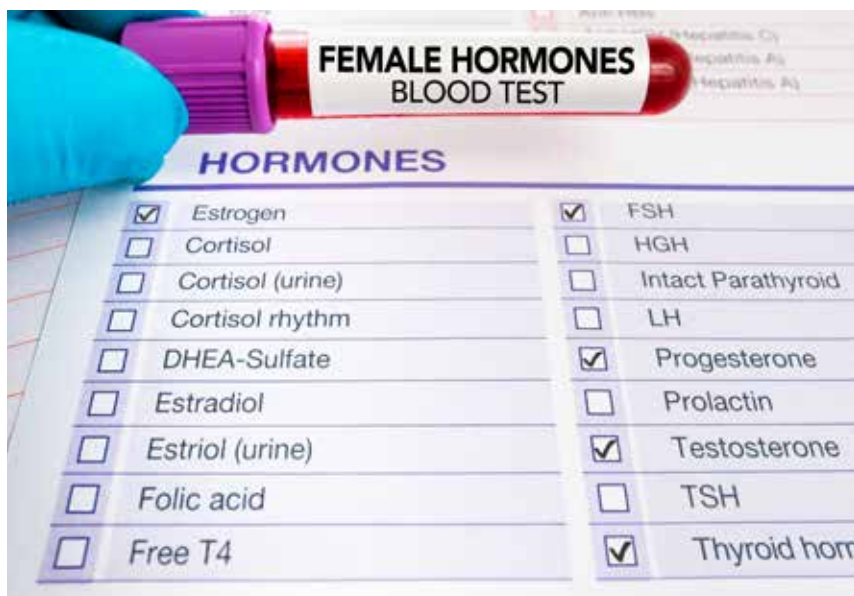
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Natural menopause is the end of ovulation and often determined retrospectively by 12 consecutive months of amenorrhea. The average age of menopause in North America is 52 years, but it can range from age 40 to 60 years.¹ Perimenopause begins with menstrual cycle irregularities or other menopausal symptoms and extends through the 12 consecutive months of amenorrhea that define menopause.¹ Perimenopause on average lasts 4 years, during which time significant hormonal changes

can cause bothersome symptoms including vasomotor symptoms (VMS). Menopausal hormone therapy (MHT) is considered the gold standard for treating moderate-to-severe VMS, but the results of the Women's Health Initiative (WHI) have had long lasting negative effects on its perceived safety. Compounded bioidentical hormone therapy is marketed as a safer alternative to MHT manufactured by a commercial pharmaceutical company with individualized dosing based on hormonal lab values. As well, at-home hormone testing kits

are widely marketed by independent companies for women to purchase online. These kits may collect blood, saliva, or urine, and the price ranges from \$99 to \$399. The various companies advertise that they have the "ultimate test for hormone replacement therapy monitoring" or "measuring and tracking a woman's estradiol level is crucial to evaluate her need for hormone replacement therapy." The use of compounded bioidentical hormone therapy and availability of commercial online hormone testing kits has resulted in conflicting messages about the necessity and usefulness of hormone testing that may cause confusion for both healthcare providers and patients. Although monitoring lab values is recommended for some hormonal therapies, it is not indicated to define menopause or to make decisions about treatment of menopause symptoms. This article reviews the standardized reproductive staging system, its utility and limitations in guiding clinical decisions, and provides three cases to illustrate common scenarios in which nurse practitioners can use skilled history taking and listening to provide individualized care without unnecessary hormone tests.



The stages of reproductive aging workshop

In 2001, scientists from multiple disciplines and countries convened and developed the Stages of Reproductive Aging Workshop (STRAW), a system to characterize ovarian aging from the reproductive years through menopause for consistency in research and reporting and to be used as a clinical tool to guide decisions regarding contraception and fertility.²

Due to limitations of STRAW and an improved understanding of ovarian aging, it was updated to STRAW+10 in 2011.² A continuum of seven stages of reproductive aging include five before and two after the final menstrual period. The tool uses menstrual cycle bleeding patterns, follicle-stimulating hormone (FSH), antral follicle count, anti-Mullerian hormone (AMH), and inhibin B levels, and VMS to characterize these stages.¹ Menstrual cycle characteristics provide the principal criteria with quantitative biomarkers (ie, FSH, AMH, inhibin B, antral follicle count) providing supportive criteria. VMS are considered a descriptive characteristic rather than criteria. An executive summary of STRAW+10 notes that because biomarker assays lack standardization and are expensive and/or invasive, they should only be used as necessary and should not be interpreted as required for a diagnosis of perimenopause or menopause.² Furthermore, it is noted that although most women progressively move through the menopause transition and early postmenopause stages, some women may not, and the variability of FSH levels in these stages make it difficult to determine perimenopause or menopause by a single lab value. Although STRAW+10 can be generalized to most women,

it cannot be applied to women with a history of primary ovarian insufficiency, hysterectomy or endometrial ablation, polycystic ovary syndrome, or women with chronic illness and/or undergoing chemotherapy.²

Changes in the menstrual cycle (variable length and intervals of amenorrhea of ≥ 60 days), VMS, variable FSH levels and low AMH, inhibin B, and antral follicle count define the menopause transition in STRAW+10.¹ Menopause is determined retrospectively by 12 consecutive months of amenorrhea in women age 40 years and older, but this criteria does not apply to women younger than 40 years.¹

Although STRAW+10 is useful for classifying ovarian staging in research and may help guide clinical decisions, limitations have been acknowledged including a lack of highly sensitive standardized assays and the need for more research to better characterize staging.² Included in future goals is to expand the research so that it can be generalized to the women for whom the current criteria do not apply.²

Case 1

JL is 50 years old and presents to her nurse practitioner with concerns about hot flashes, night sweats, difficulty sleeping, and weight gain. Her menses have spaced out over the last year, and her last menstrual period was 4 months ago. JL has a history of tubal ligation and is not concerned about pregnancy. She tells the nurse practitioner that she took an at-home hormone test 2 months ago that showed both her FSH and estrogen levels were elevated. She is confused by the results but assumes she is transitioning to menopause and is requesting bloodwork to assess her current hormone levels. She would also like to know

when she can consider hormone therapy to manage her symptoms.

Based on JL's age, symptoms, and amenorrhea for 4 months, the nurse practitioner explains that she is very likely in perimenopause. As women age, the hypothalamic-pituitary-ovarian axis becomes less sensitive to estrogen, ovulation no longer occurs on a regular basis, the follicular phase is shortened, and initially estradiol and progesterone levels may be intermittently elevated in the luteal phase.¹ Irregular menstrual cycles may be one of the first symptoms of perimenopause with other common symptoms of VMS, difficulty sleeping, mood changes, weight gain, vulvovaginal dryness, and/or arthralgia.

An FSH and/or estradiol lab value can only give the healthcare provider and patient a snapshot of what was happening in that moment. Because of the variability of the hormones in perimenopause, daily sampling during a woman's cycle would be needed but not feasible.³ Furthermore, it may be the individual's reaction to the fluctuation in hormone levels and not a specific value that causes symptoms.³

The US Food and Drug Administration has approved MHT for four indications: moderate-to-severe VMS; prevention of osteoporosis in postmenopausal women; treatment of hypoestrogenism caused by hypogonadism, bilateral oophorectomy, or primary ovarian insufficiency; and treatment of moderate-to-severe vulvovaginal symptoms.⁴ The North American Menopause Society (NAMS) published a 2022 position statement on the risks and benefits of MHT. Included in the statement is the recommendation for shared decision making regarding hormone therapy. There is no recommendation for hormone testing.⁴ Based on the patient's per-

imenopausal symptoms, and if no contraindications exist, if JL desires, the nurse practitioner can provide a prescription for MHT at this visit.

Case 2

KS is 48 years old and uncertain if she is in menopause. She has a progestin-releasing intrauterine device (IUD) approved as effective for up to 8 years and has been amenorrheic since it was placed 6 years earlier. KS states that although she tends to “run hot,” it is worsening and she is embarrassed when she breaks out in a sweat at work. She has not experienced mood changes but she does have trouble staying asleep, often waking up at 3 am and unable to fall back asleep. KS also has noticed recent weight gain and difficulty concentrating. She is hesitant to have the IUD removed. Although she does not desire any more pregnancies, she is wondering if the IUD is necessary and how she will know when she is in menopause.

Despite a decline in fertility with age, women not using hormonal contraception may continue to ovulate irregularly through the menopause transition. Determining menopause by 12 months of amenorrhea is not applicable to women who are amenorrheic due to the use of hormonal contraception.

The Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and NAMS recommend that women using hormonal contraception can continue their method if there are no contraindications until they are in their mid-50s and therefore statistically likely to be menopausal.^{1,5,6}

Based on the patient's age and vasomotor symptoms along with other menopausal symptoms, she is likely in her menopause transition. KS likes not having periods and wants

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to continue the IUD to prevent any chance of pregnancy. Menopausal estrogen therapy can be initiated with the progestin-releasing IUD providing uterine protection. If she desires to have another progestin-releasing IUD placed in 2 years, she could choose one that is effective for at least 5 years that will take her to her mid-50s. No hormone lab testing is needed now or if she waits until her mid-50s to discontinue contraception.

Case 3

SK is 55 years old and has been in menopause for 1 year. She started MHT 6 months previously for severe VMS. Initially her VMS along with her insomnia were improved with .05 mg estradiol patch and 100 mg micronized progesterone orally, but now she states her hot flashes have come back with a “vengeance.” SK asks the nurse practitioner to check her hormones so that her dosing can be adjusted for better symptom relief.

Therapeutic drug monitoring is necessary for drugs that have a narrow therapeutic index, nonlinear pharmacokinetics, not metabolized via first pass through the liver, renally eliminated as the active drug, and drugs with clearly defined

therapeutic and toxic ranges based on serum concentrations in population-based pharmacokinetic studies.⁷ Thyroxine used for treatment of hypothyroidism and gonadotropins used in fertility therapy are examples of hormones that require measurements to guide individualized drug therapy. Typical doses of all commercially available MHT achieve concentrations within what is considered a normal range. Dosing needs may vary due to an individual's amount and type of receptors in target tissues.⁷ Therefore, dosing is based on an individual's resolution of bothersome symptoms.⁷ NAMS' 2022 position statement on hormone therapy includes the recommendation for individualized adjustments of hormone dose for symptom relief. Periodic assessment of the need for ongoing use of hormone therapy should be individualized to the patient's preference and their individual risk/benefit profile.⁴ There is no recommendation for hormone testing. SK's estradiol patch can be increased to either .075 mg or .1 mg, and a follow-up should be scheduled to discuss her response. The 100 mg progesterone orally will continue to offer uterine protection

for any of the menopausal estrogen doses and therefore does not need to be adjusted.

Looking to the future

In 2019, NAMS held a workshop to evaluate existing data to establish normal postmenopausal estradiol ranges. The workshop committee concluded that standardized gas chromatography or liquid chromatography/mass spectrometry/mass spectrometry assays certified by the CDC HoSt [Laboratory/Manufacturer Hormone Standardization] program with a sensitivity to at least 2 pg/mL can provide more sensitivity than immunoassays.⁸ Standardized estrogen levels may be beneficial in interpreting research and understanding the role of estrogen and its effects on medical concerns such as breast cancer risk prediction models, fracture risk, or cardiovascular risk.⁸ This is currently a goal of the committee that has not yet been accomplished.

Furthermore, testing AMH may be a future option for menopause prediction and diagnosis. Follicles in the ovaries express AMH, and its measurement reflects the size of the growing follicle pool referred to as the functional ovarian reserve.⁹ More commonly used in reproductive medicine, its benefits as a marker include its exclusive secretion by the ovarian follicles and a constant pattern throughout the menstrual cycle.⁹ Research on AMH levels as a prediction for age of menopause and diagnosis is promising, but due to the variability of levels among women, there are not enough data to recommend it at this time.⁹

Implications for practice

For most patients, a thorough history is all that is necessary to determine perimenopause and menopause

status. Measuring hormone levels is not necessary to assess this status, to validate symptoms, or prior to starting or adjusting MHT. We do not typically measure hormone levels to assess puberty status. Our approach to other conditions that have hormonal components such as postpartum depression or premenstrual syndrome is not to order hormonal testing but to use a thorough history to validate symptoms and provide individualized treatment.

Nevertheless, conflicting information regarding menopause is plentiful and patients want answers and to feel heard and validated. We may not be able to offer specific answers for patients about when their menopause will occur or how much longer they will have bothersome symptoms. We can explain what happens in the process, listen to each patient's particular concerns, and discuss options for management of symptoms for shared decision making. We will see patients who request hormone level tests. We can provide evidence-based information on the limitations of such testing and the importance of individualized treatment based on the patient's health, symptoms, and response to therapy, not lab values. ■

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