

## CLINICAL INQUIRIES

# What is the best way to diagnose menopause?

**Leila C. Kahwati, MD, MPH**

University of North Carolina at Chapel Hill

**Lori Haigler, MD**

Duke University/Southern Regional AHEC Family Practice Residency Program, Fayetteville, NC

**Stacy Rideout, MLIS**

East Carolina University, Greenville, NC

## EVIDENCE-BASED ANSWER

No single test for menopause is highly sensitive and specific. The best predictors that a woman will enter menopause within 4 years include age at least 50 years, amenorrhea for 3 to 11 months, and menstrual cycle irregularity within 12 months (strength of recommendation [SOR]: **B**; based on

multiple prospective cohort studies).

For diagnosing perimenopause, the level of follicle-stimulating hormone (FSH) is most useful for clinical situations in which the pretest probability, as based on history, is midrange (SOR: **B**, based on 1 systematic review and 2 cross-sectional studies).

## CLINICAL COMMENTARY

### Take an active approach, reassure patients they are experiencing a normal transition

Women usually come to our practice when they start experiencing perimenopausal symptoms and seek relief. After ruling out clinically similar conditions like diabetes or thyroid disease, we can take an active approach of patient education. We reassure patients that they are experiencing a normal hormonal transition that can take 6 to 7 years. It is important to emphasize any needed lifestyle changes in such areas as smoking, substance use, diet and exercise, weight management, bone loss prevention, and bladder control. We can discuss with our patients ways of alleviating

symptoms. In our practice, we do not frequently use hormonal lab tests (FSH, luteinizing hormone, estrogen), since they can be unreliable and do not usually affect our clinical approach. In addition to the perimenopausal syndrome, diagnosing the patient's condition as "menopause" only describes cessation of fertility. We encourage women to use safe methods of contraception until they experience 12 months of amenorrhea. Before that time, barrier methods (IUDs, condoms, etc) are options of choice, since oral contraceptives may mask perimenopausal symptoms and invalidate any hormonal measurements.

**Tsveti Markova, MD**

Wayne State University, Detroit, Michigan

### ■ Evidence summary

Since natural menopause is clinically defined as the final menstrual period, the best way to diagnose it is to retrospectively observe 12 consecutive months of amenorrhea. Several studies followed women longitudinally and found the characteristics that best predicted actual transition to menopause within 4 years were amenorrhea of between 3 and 12 months duration (sensitivity=0.16–0.32; specificity=0.98–1.0; positive likelihood ratio [LR+]=14.4–∞; negative likelihood ratio [LR–]=0.69–0.84), cycle irregularity within 12 months (sensi-

tivity=0.65–0.66; specificity=0.77–0.85; LR+ =2.84–4.17; LR– =0.42–0.84), and age ≥50 years (sensitivity=0.35; specificity=0.98; LR+ =15.4; LR– =0.66).<sup>1–3</sup> Change in the amount of flow is more sensitive but less specific (sensitivity=0.81; specificity=0.30; LR+ =1.15; LR– =0.65).<sup>3</sup> A woman's global perception of being perimenopausal can also be useful for "ruling-in" transition to menopause within the next several years (sensitivity=0.18; specificity=1; LR+ =∞; LR– =0.82).<sup>1,5</sup> No studies were identified that prospectively studied the usefulness of laboratory or radiologic findings

**TABLE**

**Symptoms and laboratory tests for diagnosing perimenopause**

SYMPTOM/LAB TEST	SENSITIVITY	SPECIFICITY	LR+	LR-
Elevated FSH* <sup>4,6,7</sup>	0.65–0.74	0.79–0.94	3.06–11.32	0.29–0.45
Inhibin (immunoreactive) <sup>4</sup>	0.07	0.96	1.90	0.97
Inhibin A <sup>4</sup>	0.61	0.54	1.31	0.73
Inhibin B <sup>4</sup>	0.46	0.78	2.05	0.70
Hot flashes <sup>1,4</sup>	0.22–0.59	0.83–0.91	2.12–4.06	0.54–0.87
Night sweats <sup>4</sup>	0.20–0.50	0.74–0.87	1.90	0.67–0.92
Vaginal dryness <sup>4</sup>	0.11–0.29	0.80–0.97	1.48–3.79	0.92
Self-perceived perimenopausal status <sup>1,4</sup>	0.77–0.95	0.39–0.64	1.53–2.13	0.10–0.36

LR+, likelihood ratio if the test is positive; LR-, likelihood ratio if the test is negative; FSH, follicle-stimulating hormone.

\*Two studies defined elevated FSH as  $\geq 20$  IU/L, one study defined elevated FSH as  $\geq 24$  IU/L.

among perimenopausal women for predicting transition to postmenopausal state.

Because the perimenopause marks the entry into the menopausal transition, whether a woman has entered perimenopause is often the more relevant diagnosis to be made. Factors often used to diagnose perimenopause include age, maternal age at menopause, vasomotor and vaginal symptoms, FSH level, and a patient's global perception of being perimenopausal. Other proposed methods include vaginal ultrasound to measure ovarian volume and number of antral follicles and assays for inhibins, but currently the test characteristics for these are inferior to less invasive and less costly methods.

Age alone can be a useful predictor for perimenopause; most women have either entered or completed the menopausal transition by age 50, and almost all by age 55.

The **TABLE** summarizes test characteristics for a variety of symptoms and lab assays to diagnose perimenopause. No one test is highly sensitive and specific. Typical symptoms of hot flashes, night sweats, and vaginal dryness are about as specific as laboratory tests, but are generally less sensi-

tive.<sup>1,4,6-7</sup> Self-perceived menopausal status is moderately to highly sensitive, but the range of specificity estimates are wide. The LR+ and LR- for FSH, which are of mid-high magnitude, would suggest it to be the best single diagnostic test.<sup>4,6,7</sup> However, because laboratory tests are usually ordered after some determination of pretest probability based on history and physical, FSH may be of less utility where the pretest probability for perimenopause is already high, such as the case of a 52-year-old woman seeking "confirmation" for perimenopausal symptoms. FSH levels are highly varied within individuals during perimenopause; and further variation due to body-mass index and ethnicity make defining diagnostic thresholds difficult.<sup>8</sup>

**Recommendations from others**

The American Academy of Family Physicians, American College of Physicians, and American College of Obstetricians and Gynecologists do not address the diagnosis of menopause in any recommendations.

The North American Menopause Society states that estradiol and FSH are of limited value in confirming perimenopause

**FAST TRACK**

**For diagnosing perimenopause, FSH level is most useful when the pretest probability is midrange**

## CLINICAL INQUIRIES

U.S. Postal Service  
STATEMENT OF OWNERSHIP, MANAGEMENT, AND CIRCULATION  
(Required by 39 U.S.C. 3685)

1. Publication title: **The Journal of Family Practice**
2. Publication No.: **0094-3509**
3. Filing date: **10/5/05**
4. Issue frequency: **Monthly**
5. No. of issues published annually: **12**
6. Annual subscription price: **\$144.00**
7. Complete mailing address of known office of publication:  
**Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712**
8. Complete mailing address of headquarters or general business office of publisher:  
**Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712.**  
Contact person: Mary Ellen Pollina. Telephone: 201-782-5728.
9. Full names and complete mailing addresses of publisher, editor, and managing editor:  
**Laura Dowden, Publisher, Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712; Charles F. Williams, Executive Editor, Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712; Paul Rieder, Managing Editor, Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712**
10. Owner (If owned by a corporation, its name and address must be stated and also immediately thereafter the names and addresses of Stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, the names and addresses of the individual owners must be given. If owned by a partnership or other unincorporated firm, its name and address, as well as that of each individual must be given. If the publication is published by a nonprofit organization, its name and address must be stated.): **Dowden Health Media, Inc, 110 Summit Avenue, Montvale, NJ 07645-1712.**
11. Known bondholders, mortgagees, and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages, or other securities: **None**
12. Tax status (For completion by nonprofit organizations authorized to mail at special rates.) The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes: **Has not changed during preceding 12 months.**
13. Publication name: **The Journal of Family Practice.**
14. Issue date for circulation data below: **October 2005**

	Average no. copies each issue during preceding 12 months	No. copies of single issue published nearest to filing date
15. Extent and Nature of Circulation		
a. Total No. Copies (Net Press Run)	98,007	98,692
b. Paid and/or Requested Circulation		
(1) Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. (Include advertiser's proof and exchange copies)	54,473	54,642
(2) Paid In-County Subscriptions Stated on Form 3541 (Include advertiser's proof and exchange copies)		
(3) Sales through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution		
(4) Other classes mailed through the USPS		
c. Total paid and/or requested circulation	54,473	54,642
d. Free Distribution by Mail	44,009	43,550
(1) Outside-county as stated on Form 3541		
(2) In-county as stated on Form 3541		
(3) Other classes mailed through the USPS		
e. Free Distribution Outside the Mail	25	0
f. Total Free Distribution	44,034	43,550
g. Total Distribution	97,507	98,192
h. Copies Not Distributed	500	500
i. Total	98,007	98,692
j. Percent Paid and/or Requested Circulation (15c/15g x 100)	55.6%	54.8%

16. This Statement of Ownership will be printed in the **November** issue of this publication.

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions and/or civil sanctions.

MaryEllen Pollina, Circulation Director 10/5/05

due to extreme monthly fluctuations. They say perimenopausal women are not protected from unplanned pregnancy until amenorrhea of at least 1 year's duration or consistently elevated FSH levels (>30 IU/L) are demonstrated. Confirmation of perimenopause relies on medical history and symptoms.

The American Association of Clinical Endocrinologists recommends a detailed history, exam, and measurement of FSH. The diagnosis of menopause is confirmed by FSH levels >40 IU/L; however, they note in perimenopause, FSH elevation is intermittent and not reliable for establishing the onset of menopause. ■

### REFERENCES

1. Dudley EC, Hopper JL, Taffe J, Guthrie JR, Burger HG, Dennerstein L. Using longitudinal data to define the perimenopause by menstrual cycle characteristics. *Climacteric* 1998; 1:18-25.
2. Brambilla DJ, McKinlay SM, Johannes CB. Defining the perimenopause for application in epidemiologic investigations. *Am J Epidemiol* 1994; 140:1091-1095.
3. Taylor SM, Kinney AM, Kline JK. Menopausal transition: predicting time to menopause for women 44 years or older from simple questions on menstrual variability. *Menopause* 2004; 11:40-48.
4. Bastian LA, Smith CM, Nanda K. Is this woman perimenopausal? *JAMA* 2003; 289:895-902.
5. Taffe J, Dennerstein L. Time to the final menstrual period. *Fertil Steril* 2002; 78:397-403.
6. Cooper GS, Baird DD, Darden FR. Measures of menopausal status in relation to demographic, reproductive, and behavioral characteristics in a population-based study of women aged 35-49 years. *Am J Epidemiol* 2001; 153:1159-1165.
7. Flaws JA, Langenberg P, Babus JK, Hirshfield AN, Sharara FI. Ovarian volume and antral follicle counts as indicators of menopausal status. *Menopause* 2001; 8:175-180.
8. Randolph JF Jr, Sowers M, Gold EB, et al. Reproductive hormones in the early menopausal transition: relationship to ethnicity, body size, and menopausal status. *J Clin Endocrinol Metab* 2003; 88:1516-1522.