

Menstrual Patterns Best Indicator of Aging Path

BY JENNIE SMITH

FROM MENOPAUSE

Changes to the menstrual cycle remain the most important clinical indicators of women's reproductive aging, according to new standardized staging criteria.

The changes identified by the most recent Stages of Reproductive Aging Workshop are now defined in 10 stages, whereas the 2001 STRAW criteria had 7. The new criteria, STRAW-10, offer more detail on the characteristics of flow and cycle length at each stage, along with corresponding endocrine changes. The arti-



With STRAW-10, most women can use the changes in their menstrual pattern to find how close they are to menopause.

DR. GASS

cle was published in *Menopause*, *Climacteric*, *Fertility and Sterility*, and the *Journal of Clinical Endocrinology and Metabolism*.

The late reproductive stage is now subdivided into two stages, -3b and -3a, instead of only stage -3 as before (*Menopause* 2012 Feb. 16 [doi:10.1097/gme0b013c31824d8f40]). In stage -3b, flow remains regular, whereas in stage -3a there are subtle changes in flow and length of cycle.

The postmenopausal stage +1, identified in the earlier STRAW criteria, also has been subdivided into three lettered stages, with the endocrine changes and duration of each stage described.

Unlike the previous STRAW criteria, the menstrual changes identified in STRAW-10 are relevant to any healthy woman, regardless of ethnicity, age, body mass index, or lifestyle, the researchers said, noting that although factors such as smoking status and BMI may affect the timing of menopause, the

bleeding patterns remain reliable indicators of the reproductive stage.

"Despite the availability of blood tests and sonograms, the menstrual cycle remains the single best way to estimate where a woman is along the reproductive path," said Dr. Margery Gass, a STRAW-10 coauthor, executive director of the North American Menopause Society (NAMS), and editor of *Menopause*.

"According to STRAW-10, most women (and their clinicians) can use the changes in their menstrual pattern to determine how close they are to menopause: late reproductive phase (subtle changes in cycle length and blood flow), early menopause transition (menstrual period 7 or more days early or late), and late menopause transition (the occurrence of more than 60 days between cycles)," Dr. Gass said in an interview.

STRAW-10 incorporates three biomarkers, anti-Müllerian hormone (AMH), inhibin B, and antral follicle count, which were not mentioned in the original STRAW criteria, along with follicle-stimulating hormone (FSH), which was included in the original criteria.

In developing the new criteria, an international group of 41 researchers, led by epidemiologist Siobán D. Harlow, Ph.D., of the University of Michigan, Ann Arbor, evaluated data from cohort studies of midlife women with the aim to incorporate the scientific findings of the past decade on ovarian aging and its endocrine and clinical indicators.

Although much has been learned since 2001 with regard to biomarkers, Dr. Harlow and colleagues said that the biomarker criteria outlined in STRAW-10 must still be considered "supportive," in part because more research is needed and because of the invasiveness and expense of testing.

Dr. Gass said that checking hormone levels is not necessary "except in women who have undergone endometrial ablation or hysterectomy, or who have unusual health circumstances."

Women for whom the STRAW-10 criteria do not apply include those with poly-

cystic ovarian syndrome or hypothalamic amenorrhea. Women with chronic illnesses such as HIV-AIDS, or those undergoing certain types of cancer treatments, also are difficult to assess under STRAW-10, as cycles and hormone levels can change in response to medication.

The new criteria do not use age to determine reproductive staging, but women younger than 40 years who have premature ovarian insufficiency or premature ovarian failure do not fit well under STRAW-10, the researchers noted, as their course of reproductive aging is more variable.

STRAW-10 meetings were funded by the National Institutes of Health, the De-

partment of Health and Human Services through the National Institute on Aging (NIA) and the Office of Research on Women's Health, NAMS, the American Society for Reproductive Medicine (ASRM), the International Menopause Society in Cape Town, South Africa, and the Endocrine Society.

Dr. Gass receives support from NAMS. Dr. Harlow disclosed ties with the NIA, NAMS, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Other coauthors disclosed ties with the Endocrine Society, ASRM, the NIA, NAMS, and various pharmaceutical companies. ■

STRAW-10 Will Spur More Research

VIEW ON THE NEWS

The main changes [in STRAW-10] have to do with the late reproductive stage and the early postmenopausal stage, which has been subdivided to give more detail, and in turn help understand the physiologic changes which occur at these times. In particular, the late reproductive stage has been subdivided so the measurement of the anti-Müllerian hormone (AMH) and follicle count can be used as a measure of decreased fertility, but the menstrual bleeding is still regular and unchanged. Inhibin B also may be low.

The next stage adds a change in menstrual pattern, usually shorter cycles, and also some variability in FSH levels early in the cycle (days 2-5). Unfortunately, there is no standardization for the AMH assay, so a quantitative measurement is not available.

The bottom line is that these definitions will be helpful mostly for research, but will give us only some guidance to counsel patients about their fertility.

In terms of the late reproductive stages, there now are three subdivi-

sions based on stabilization of key hormones at this time (FSH and estradiol). Perimenopause also is better defined and the addition of symptoms with a description of bleeding patterns will be helpful both to researchers and clinicians. This will lead to more research and understanding of the key physiologic events that lead to reproductive decline and menopausal changes. There also is a description of what happens to reproduction with various dysfunctions, such as chemotherapy and in polycystic ovarian syndrome, which can be helpful both clinically and particularly in research.

DR. MICHELLE WARREN is professor of medicine and obstetrics and gynecology at Columbia University Medical Center, New York, and medical director of the Center for Menopause, Hormonal Disorders, and Women's Health at Columbia. She commented in an interview regarding the STRAW-10 findings. She disclosed ties with Pfizer, Yoplait, and Ascend Therapeutics.

Packaging Error Spurs Nationwide Recall of Generic OC

BY ELIZABETH MEHCATIE

Seven lots of oral contraceptives containing norgestimate and ethinyl estradiol have been recalled nationwide because of a packaging error that could result in suboptimal protection against pregnancy, according to an announcement Feb. 27 by the Food and Drug Administration.

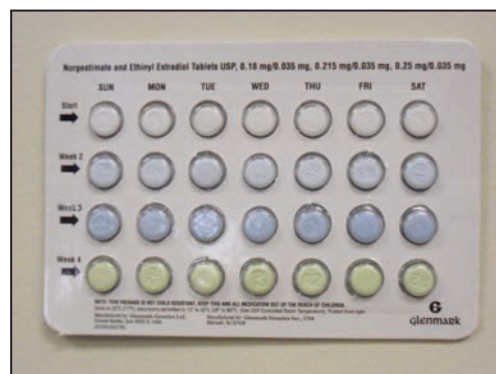
A statement on the agency's MedWatch site said that as a result of the packaging error in these lots, "the daily regimen for these oral contraceptives may be incorrect and could

leave women without adequate contraception, and at risk for unintended pregnancy." The FDA advised that women who have been "exposed to" the affected packaging should start using a nonhormonal form of contraception immediately and those who have the product should return it to the pharmacy and contact their physician.

The affected OCs, manufactured by Glenmark Generics, were distributed to

wholesalers and retail pharmacies nationwide between Sept. 21, 2011, and Dec. 30, 2011, and contain the following doses of

norgestimate and ethinyl estradiol: 0.18 mg/0.035 mg, 0.215 mg/0.035 mg, and 0.25 mg/0.035 mg.



In the recalled lots, blisters rotated 180 degrees in the card reverse tablet orientation.

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The packaging error that prompted the recall is described as select blisters that are rotated 180 degrees within the card, which reverses the weekly tablet orientation and makes the lot number and expiration date visible on the outer pouch only, according to the FDA.

A statement issued by Glenmark said the following lot numbers are affect-

ed: 04110101, 04110106, and 04110107, with the expiration date of 7/31/2013; 04110114, 04110124, and 04110129, with the expiration date of 8/31/2013; and 04110134, with the expiration date of 9/30/2013. ■

Adverse events that may be related to the use of these products should be reported to Glenmark Generics, 888-721-7115 (8 a.m. to 5 p.m. ET Monday through Friday), or to the FDA's MedWatch Program anytime by faxing 800-332-1078 or visiting www.fda.gov/medwatch/report.htm.