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Hormonal changes and biomarkers in late reproductive age, menopausal transition and menopause

G.E. Hale, MD, PhD, Clinical Associated Lecture [a,*], H.G. Burger, MD, Director [b]

[a] *Department of Obstetrics and Gynaecology, Queen Elizabeth II Research Institute for Mothers and Infants, University of Sydney, NSW, Australia*
[b] *Department of Endocrinology, Prince Henry's Institute, Clayton, Victoria, Australia*

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This chapter describes current definitions of the climacteric, perimenopause, menopausal transition and menopause, and discusses the 2001 Stages of Reproductive Aging (STRAW) criteria in relation to more recently proposed categorization criteria for reproductive aging. Data from endocrine studies on women throughout the menopausal transition are discussed from earliest to most recent. The earlier studies focused on the changes in levels of steroid hormones and gonadotrophins, and established that follicle-stimulating hormone undergoes the first detectable change while menstrual cycles remain regular. Erratic and less predictable changes in steroid hormones follow, especially with the onset of irregular cycles. Later serum hormone studies on the inhibins and anti-Mullerian hormone established that diminishing ovarian follicle number contributes to the endocrine changes with advancing reproductive age. A classification system of cycle types incorporating all available endocrine data and their associated menstrual cycle patterns is proposed, and the application of biological markers as diagnostic tools for reproductive staging is discussed.

Definitions

A number of terms including 'climacteric', 'perimenopause', 'menopausal transition', 'postmenopause' and 'menopause' have been used to refer to the stages of reproductive aging surrounding the final menstrual period (FMP). The terms 'menopausal transition' and 'perimenopause' were

* Corresponding author. Tel.: +612 9351 2748; Fax: +618 9158 1755.
E-mail address: ghale@med.usyd.edu.au (G.E. Hale).

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recommended for use in place of the term 'climacteric' in 1996, with release of the definition by the World Health Organization (WHO). Although these two terms were initially used interchangeably, there is a slight difference in their definition according to the STRAW (Stages of Reproductive Aging) criteria, and the term 'menopausal transition' is now used in favour of both 'perimenopause' and 'climacteric' when referring to the stages of reproductive age in a scientific context.[1]

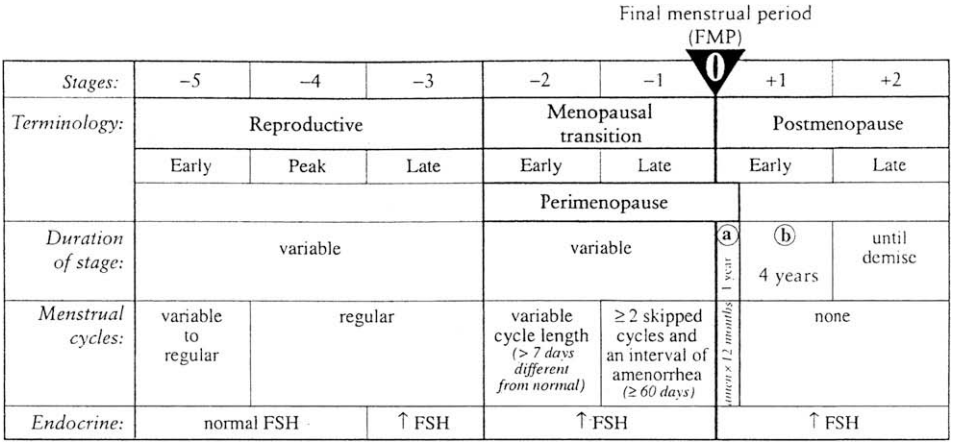
The menopausal transition or 'perimenopause' was first officially referred to by WHO in 1996 as 'that period of time immediately before menopause when the endocrinological, biological and clinical features of approaching menopause commence'.[2] Given that the 'endocrinological, biological and clinical features' referred to in the WHO definition remained undefined, many investigators proposed their own classification criteria to categorize study subjects for research purposes.[3–5] In the prospective Massachusetts' Women's Health Study (MWHS), a self-report of between 3 and 12 months of amenorrhoea was used for entry into the perimenopause.[3] Similar criteria were used for entry into the late perimenopause in the Seattle Midlife Women's Health Project.[4] A self-report of a change in menstrual flow, duration of menstrual flow or cycle length was used for entry into the early perimenopause, and new-onset variability in cycle length (two or more consecutive cycles that differ in length by at least 7 days) was used as entry into the mid-perimenopause.[4] In a major longitudinal study of the experiences of menopause, Burger et al and Dennerstein et al also used self-reported new-onset cycle irregularity as the marker of entry into the early perimenopause, and absence of menses for between 3 and 11 months for entry into the late perimenopause.[6,7]

The 5-year longitudinal MWHS (2570 women aged 45–55 years) produced important information on the mean length of time that women usually spend passing through the menopausal transition.[8] The authors reported a median age at inception of perimenopause of 47.5 years and a mean duration of the perimenopausal transition of approximately 4 years. The natural menopause occurred at a mean of 51.3 years, and a mean of 49.5 years if currently smoking.

The STRAW criteria

The first standardized classification guidelines for female reproductive aging were proposed in 2001 at the Stages of Reproductive Aging Workshop (STRAW).[1] These guidelines were proposed in order 'to develop a relevant and useful staging system, to revise the nomenclature and to identify gaps in knowledge that should be addressed by the research community' (Table 1). The stages were nominated using the FMP as a reference point, and were based on changes in the pattern of menstrual cycles levels of follicle-stimulating hormone (FSH). Subjective data such as changes in menstrual flow or vasomotor

Table 1
The Stages of Reproductive Aging (STRAW) criteria.



Soules MR et al. *J Womens Health Gender-Based Med* 2001; **10**: 843–848.[1]