Title Perimenopause Changes Leading Up to the Transition

Background: Perimenopause, or the menopausal transition, encompasses the time of physiologic changes which mark the progression toward a woman's final menstrual period (FMP). Perimenopause lasts for a variable amount of time, with a median of 4 years. This phase begins with the onset of menstrual irregularities and continues until a woman reaches menopause, one year after her last menstrual period.[1] The changing hormone milieu manifests in varying symptoms that often present complex clinical management situations.[2] Up to 90% of women present to health care providers for advice on coping with perimenopausal symptoms.

Objective: Understanding the physiology of the menopause transition, the fluctuating and decline in ovarian function, the resultant systemic hormonal changes, and ultimately, symptoms will help providers and patients manage this transition.[2]

Methods: Review literature on perimenopause including the physiology of the menopause transition, the hormonal changes, mood changes, and evidence-based options for management of abnormal bleeding; the patterns of vasomotor symptoms across the menopause. ethnic differences in hot flash patterns from the Study of Women Across the Nation and evidence for hormonal and nonhormonal management options for hot flashes.

Results: The early stage of perimenopause is defined by occasional skipped cycles. The later stage is characterized by greater menstrual irregularity, with periods of amenorrhea over 60 days and finally up to 12 months.[1]Twelve or more months of amenorrhea defines the FMP and defines menopause. The top 10 perimenopausal symptoms include irregular menstruation and ovulation, loss of libido, hot flashes and night sweats[2], insomnia, increase in abdominal or 'belly fat,' changes in the breast size and shape, heart palpitations, brain fog with decreased concentration and memory, mood changes and fatigue. Abnormal bleeding may be controlled with oral contraceptives used cyclically or continuously, progestogen therapy including levonorgestrel intrauterine systems, and tranexamic acid used during the cycle. Structural abnormalities include polyps, leiomyomas, or the development of hyperplasia. Perimenopausal depression may respond to estrogen therapy or may need antidepressants, either used alone or in combination. [3,4] Memory and concentration changes are not dementia but may improve with adequate sleep, regular exercise, and a healthy diet.[4] Vasomotor symptoms may respond to hormone therapy but there are effective nonhormone options including SSRIs SSNRs, Gabapentin and the new neurokinin receptor NK3 inhibitors.

Conclusion: Perimenopausal women need guidance during this difficult time navigating the physical and emotional changes. Challenges include management of abnormal uterine bleeding, contraception options, management of moods and hot flashes understanding what is expected and what is abnormal, and when to intervene. The menopausal transition is the portal to the

second half of life for women but can be fraught with pitfalls to be avoided or managed through understanding the underlying physiology. [5]

References

1. Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. J Clin Endocrinol Metab 2012;97:1159-68.

2. Santoro N, Roeca C, Peters BA, Neal-Perry G. The Menopause Transition: Signs, Symptoms, and Management Options. J Clin Endocrinol Metab. 2021 Jan 1;106(1):1-15.

3. Pinkerton JV. Knowledge Gaps and Challenges in the Care for Menopausal Women. *OBG Manag*. 2022 June;34(6):21-26, 28-29

3. The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-794.

4. Maki PM, Kornstein SG, Joffe H, et al. Guidelines for the evaluation and treatment of perimenopausal depression: summary and recommendations. *Menopause*. 2018;25(10):1069-1085.

5. Santoro N, Roeca C, Peters BA, Neal-Perry G. The Menopause Transition: Signs, Symptoms, and Management Options. J Clin Endocrinol Metab. 2021 Jan 1;106(1):1-15.
6.