

# Clinicians' FORUM

From time to time, the editors of *Menopause Management* field interesting clinical questions and dilemmas. In this forum, our Editorial Advisory Board members, experts in a range of fields related to midlife women's health, tell readers how they handle these situations.

## Participants

Margery L.S. Gass, MD  
Professor, Clinical Obstetrics & Gynecology  
University of Cincinnati College of Medicine  
Cincinnati, OH

Bruce Kessel, MD  
The Queen's Medical Center  
Queen Emma Outpatient Center  
Honolulu, HI

Robert L. Reid, MD  
Professor of Ob/Gyn and Head, Division of  
Reproductive Endocrinology and Infertility  
Queen's University,  
Kingston, Ontario, Canada

Michelle P. Warren, MD  
Professor of Medicine and Ob/Gyn  
Wyeth Professor of Women's Health  
Columbia University, College of Physicians  
and Surgeons  
Medical Director, Center for Menopause,  
Hormone Disorders  
Columbia University Medical Center  
New York, NY

**Questions:** How have you changed your clinical practice since publication of data from the Women's Health Initiative (WHI)?

**Do you have any limits for prescribing hormones for vasomotor symptoms?**

**Under what circumstances would**

**you consider prescribing hormones long-term (ie, 5 years or longer)?**

**Do you think there should be a patient age limit when it comes to prescribing hormones?**

## Answers:

Results from the WHI hormone therapy (HT) trials nudged forward what had been a slowly changing menopause paradigm. The popular paradigm of the 1980s and 1990s held that menopause was an endocrine deficiency state<sup>1</sup> associated with a number of health problems, such as osteoporosis, cardiovascular disease, cognitive decline, macular degeneration, urinary incontinence and moodiness, to name a few. Before the publication of the Heart and Estrogen/progestin Replacement Study (HERS) data, it had been proposed that secondary prevention of cardiovascular disease was an even stronger indication for HT than was primary prevention.<sup>2,3</sup> Similarly, research demonstrated that HT would be effective in older women who already had osteopenia (for example, a study by Recker et al,<sup>4</sup> in which the mean age of participants was 73 years, approximately 10 years older than the participants in the WHI). The trend was toward initiating HT in older women for prevention of osteoporosis, heart disease and dementia.

Prior to WHI, I observed the recommendations published by groups such as Health Plan Employer Data and Information Sets (HEDIS). The benchmark was to discuss HT with every menopausal woman who had no contraindication to therapy. At that time in my practice, I reviewed the potential benefits and the potential risks of HT with my patients. I discovered shortly after completing my residency that lower doses were often sufficient, and generated fewer complaints of breast tenderness, bleeding and bloating.

Post-WHI, I no longer consider it mandatory to discuss HT with all menopausal women. I query women regarding their



Margery L.S. Gass, MD

menopausal symptoms. If women desire help with their symptoms, I discuss HT as one of several options. For women who choose to use HT, I prefer to start with a low dose and titrate upward as needed, simply because lower doses are presumed safer, create fewer side effects and produce less of a drop in systemic

*The WHI has allowed me to stop saying “potential” risks and benefits. I now inform my patients that specific benefits and risks have been identified and that the risks are small, especially in the 50- to 55-year-old age group.*

– Margery L.S. Gass, MD

hormone levels upon discontinuation. For women with severe symptoms who desire immediate relief, estrogen doses equivalent to conjugated equine estrogens 0.625 mg may be more effective and appropriate. I think women should know prior to starting hormones that their menopausal symptoms may recur upon discontinuing HT.<sup>5</sup>

The WHI has allowed me to stop saying “potential” risks and benefits. I now inform my patients that specific benefits and risks have been identified and that the risks are small, especially in the 50- to 55-year-old age group. I advise women not to take HT indefinitely. There are a few women in my practice who, despite being informed of the risks of HT (including increased absolute risk with aging), feel adamant about continuing it because they feel better using HT. Most of them have tried doing without it. In these circumstances the patient is generally using a low dose, and we revisit the issue each year.

Use of moisturizers, lubricants, and vaginal estrogen has increased in my practice as a result of the WHI and the availability of new vaginal estrogen products.

My practice has evolved since the WHI, and I tell patients that it will continue to evolve. As medical science progresses, we will have even more data to inform our decision-making.

– Margery L.S. Gass, MD

#### References

1. American Association of Clinical Endocrinologists. AACE medical guidelines for clinical practice for management of menopause. *Endocrine Pract* 1999;5:355-66.
2. Sullivan JM, Vander Zwaag R, Hughes JP, et al. Estrogen replacement and coronary artery disease. *Arch Intern Med* 1990;150:2557-62.
3. Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA* 1998;280:605-13.
4. Recker RR, Davies M, Dowd RM, et al. The effect of low-dose estrogen and progesterone therapy with calcium and vitamin D on bone in elderly women. *Ann Intern Med* 1999; 130:897-904.
5. Ockene J, Barad DH, Cochrane BB, et al. Symptom experience after discontinuing use of estrogen plus progestin. *JAMA* 2005;294:183-93.

At a very fundamental level, my clinical practice has not changed following the publication of the results of the WHI HT trial.<sup>1,2</sup> Prior to the WHI, women presenting at menopause for a consultation were assessed for vasomotor symptoms and quality of life. The consult was further used as an opportunity to address lifestyle factors and risk for cardiovascular disease, breast cancer and osteoporosis. Appropriate health maintenance testing was ordered. The risks and benefits of HT were discussed based on the knowledge available at that time. Shared decision-making based on symptoms and risk factors then resulted in decisions for lifestyle changes, HT or alternatives to HT.

In this sense, the way in which I conduct a menopause consult has not changed; the basic concepts, as addressed above, still hold true. What has changed is that the discussion of risks and benefits is now evidence-based, assuming



Bruce Kessel, MD

the patient is characteristic of a participant in the WHI trial. Prior to the publication of HERS and the WHI, an asymptomatic, healthy postmenopausal woman would have been counseled regarding the possible preventive health benefits of HT with regard to cardiovascular disease and dementia; whereas, post-

*For many decades, the driving force behind a woman's decision to use HT has been moderate to severe vasomotor symptoms. This has not changed post-WHI.*

– Bruce Kessel, MD

HERS and WHI, the same woman will be counseled that these preventive health benefits have not been demonstrated. Special attention should be placed on offering appropriate counseling to women with a uterus (WHI estrogen-plus-progestin arm) versus women who have had a hysterectomy (WHI estrogen-only arm).<sup>3</sup>

For many decades, the driving force behind a woman's decision to use HT has been moderate to severe vasomotor symptoms.<sup>3</sup> This has not changed post-WHI. Despite active research into nonhormonal management of severe vasomotor symptoms, such treatment has not been found to have the same efficacy as HT.<sup>4</sup> A symptomatic woman who is deriving a significant quality-of-life benefit from HT is a candidate without regard to age. Long-term use of HT is appropriate as long as there is a continuing, significant quality-of-life benefit, particularly in women in whom symptoms have returned after discontinuation of HT.<sup>5</sup>

Further research is needed in a number of areas, particularly the risks and benefits of initiating HT in younger symptomatic women, and identifying safe nonhormonal therapies with excellent efficacy for management of vasomotor symptoms.

– Bruce Kessel, MD

## References

1. Rossouw JE, Anderson GL, Prentice RL, et al. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33.
2. Anderson GL, Limacher M, Assaf AR, et al. Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701-12.
3. The North American Menopause Society. Treatment of menopause-associated vasomotor symptoms: position statement of The North American Menopause Society. *Menopause* 2004;11:11-13.
4. Kessel B, Kronenberg F. The role of complementary and alternative medicine in the management of menopausal symptoms. *Endocrinol Metab Clin N Am* 2004;33:717-39.
5. The North American Menopause Society. Recommendations for estrogen and progestogen use in peri- and postmenopausal women: October 2004 position statement of The North American Menopause Society. *Menopause* 2004;11:589-600.

Since publication of the first data from the WHI, I have spent more time carefully evaluating the literature in order to be prepared to provide a balanced view on the benefits and risks of HT to women and their family physicians—many of whom have been confused by scary media stories. On behalf of the Association of Professors of Obstetrics and Gynaecology of Canada and the Society of Obstetricians and Gynaecologists of Canada (SOGC), I have been working with a group of colleagues (ob/gyns and senior health reporters) in Canada to develop an e-learning site for journalists covering medical stories. The site, among other things, is intended to help reporters understand how to better communicate benefits and risks, and to put these into context. The Web site will be launched at the Annual Clinical Meeting of the SOGC in June in Vancouver.

In particular, I find that women who have become prematurely menopausal due to chemotherapy or surgery are very wary of longer-term HT, which may be integral to the prevention of premature cardiovascular disease

(continued on page 30)



Robert L. Reid, MD

## Clinicians' Forum

(continued from page 28)

and osteoporosis. More detailed counseling is often necessary to enable them to appreciate the potential for reductions in cancer (breast, uterus and ovary) and the safety and benefits of HT—at least until the natural age of

*Post-WHI I no longer emphasize cardioprotection as a possible long-term benefit of HT (although I remain open to the possibility that early initiation may be beneficial), and I suggest that HT is useful for bone protection only as long as it is indicated for control of menopausal symptomatology.*

— Robert L. Reid, MD

menopause. The North American Menopause Society (NAMS) 2004 guidelines on HT<sup>1</sup> are a good counseling resource. Another excellent discussion of the impact of early suppression of ovarian function and HT on lifetime cancer risk appears in an article examining ovarian suppression as a novel means of contraception.<sup>2</sup>

Prior to publication of the WHI results, most Canadian ob/gyns counseled symptomatic postmenopausal women about the potential cardiovascular benefits of long-term HT as part of an overall discussion of benefits and risks. Relatively few women were started on HT solely to prevent cardiovascular disease, or in the later menopausal years. Post-WHI I no longer emphasize cardioprotection as a possible long-term benefit of HT (although I remain open to the possibility that early initiation may be beneficial), and I suggest that HT is useful for bone protection only as long as it is indicated for control of menopausal symptomatology. Rather, I recommend lifestyle

changes and alternative medical therapies for cardioprotection and protection of bone mass.

I have no limits for duration of therapy, although I do suggest that women should try to gradually reduce the dosage of hormones they take. Given the apparent small increase in the lifetime risk of breast cancer with cumulative exposure to ovarian hormones, I believe it is prudent to reduce hormone exposure to the minimum necessary to maintain quality of life. When systemic estrogen is no longer required for vasomotor symptoms, and topical intravaginal estrogen will suffice to maintain urogenital health, I believe that systemic HT should be stopped and alternatives for cardioprotection and bone protection should be considered.

I have found that if I prescribe a dosage form that offers half of the dose that I believe the woman requires, she will reduce the dosage over time. (For example, if I anticipate that a newly menopausal woman requires 0.625 mg of conjugated equine estrogens, I will prescribe 0.3 mg and tell her to use one or two tablets as required.) In my experience, this results in the fastest reduction in hormone requirements and allows the woman to feel in control of her hormone dosing.

I am prepared to discuss risks and benefits and to allow any woman to decide to continue HT as long as needed, if she feels she requires it to maintain or improve her quality of life.

I believe that current research indicates we should be cautious about starting HT in older women with potential pre-existing cardiovascular disease unless symptom severity and patient understanding of potential risks dictate otherwise. However, I do not see any reason to stop HT in a woman who has safely used hormones into her later menopausal years, and where attempts to stop HT have, in her opinion, lead to deterioration in quality of life.

— Robert L. Reid, MD

## References

1. The North American Menopause Society. Recommendations for estrogen and progestogen use in peri- and postmenopausal women: October 2004 position statement of The North American Menopause Society. *Menopause* 2004;11:589-600.
2. Spicer DV, Pike MC. Future possibilities in the prevention of breast cancer: luteinizing hormone-releasing hormone agonists. *Breast Cancer Res* 2000;2:264-7.

*I do have patients on long-term HT. They are usually patients who cannot tolerate any other therapy for osteoporosis, or who have unusual symptoms such as severe mood problems or memory issues.*

– Michelle P. Warren, MD

I do not give HT to patients with a history of breast cancer unless there are extreme circumstances, or to patients with a history of venous thromboembolism and stroke or heart disease. I use low doses and minimal or vaginal progesterone, particularly in these patients. I do not give hormones to patients with bleeding or with endometrial hyperplasia.



Michelle P. Warren, MD

I do have patients on long-term HT. They are usually patients who cannot tolerate any other therapy for osteoporosis, or who have unusual symptoms such as severe mood problems or memory issues. These are unusual cases, and since I individualize therapy I do not have an age limit for which I take women off therapy; however, since the WHI I have many fewer patients over age 60 who are on HT.

– Michelle P. Warren, MD

I have changed my practice since the WHI in that I do not recommend long-term HT for prevention of heart disease. I also tell patients that an ideal time span for taking HT is 2 to 5 years. I now prescribe lower HT doses and find I have many fewer reports of side effects.

## Exercise and Menopause: Positive Health Effects

(continued from page 25)

21. Stoll BA. Timing of weight gain in relation to breast cancer risk. *Ann Oncol* 1995;6:245-48.
22. Kotsopoulos J, Olopado OI, Ghadirian P, et al. Changes in body weight and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res* 2005;7:R833-43.
23. Ng EH, Gao F, Ji CY, et al. Risk factors for breast carcinoma in Singaporean Chinese women: the role of central obesity. *Cancer* 1997;80:725-31.
24. Byyny RL, Speroff L. *Clinical guide for the care of older women: primary and preventive care*, 2nd ed. Baltimore: Lippincott Williams & Wilkins, 1996.
25. Harris TB, Launer LJ, Madans J, et al. Cohort study of effect of being overweight and change in weight on risk of coronary heart disease in old age. *BMJ* 1997;314:1791.
26. Mosca L, Appel LJ, Benjamin EJ, et al. Summary of the American Heart Association's evidence-based guidelines for cardiovascular disease prevention in women. *Arterioscler Thromb Vasc Biol* 2004;24:394-96.
27. Van Pelt RE, Jankowski CM, Gozansky WS, et al. Lower-body adiposity and metabolic protection in postmenopausal women. *J Endocrinol Metab* 2005;90:4573-78.
28. Wing RR, Mathews KA, Kuller LH, et al. Weight gain at the time of menopause. *Arch Intern Med* 1991;151:97-102.
29. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of obesity and risk of coronary heart disease in women. *N Engl J Med* 1990;322:882-89.
30. Legato MI. Gender-specific aspects of obesity. *Int J Fertil Womens Med* 1997;42:184-97.
31. RJ Petrella, CN Lattanzio, A Demeray, et al. Can adoption of regular exercise later in life prevent metabolic risk for cardiovascular disease? *Diabetes Care* 2005; 28:694-701.
32. Manson JE, Rimm EB, Stampfer MJ, et al. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991;338:774-78.
33. Frisch RE, Wyshak, Albright TE, et al. Lower prevalence of diabetes in female former college athletes compared with nonathletes. *Diabetes* 1986;35:1101-05.
34. Anderson JB, Metz JA. Contributions of dietary calcium and physical activity to primary prevention of osteoporosis in females. *J Am Coll Nutr* 1993;12:378-83.
35. Khan H, McKay HA, Haapasalo H, et al. Does childhood and adolescence provide a unique opportunity for exercise to strengthen the skeleton? *J Sci Med Sport* 2000; 3:150-64.
36. Dook JE, James C, Henderson NK, et al. Exercise and bone mineral density in mature female athletes. *Med Sci Sports Exerc* 1997;29:291-296.
37. Taaffe DR, Robinson TL, Snow CM, et al. High-impact exercise promotes bone gain in well-trained female athletes. *J Bone Miner Res* 1997;12:255-60.
38. Cavanaugh DJ, Cann CE. Brisk walking does not stop bone loss in postmenopausal women. *Bone* 1988;9:201-04.
39. Nelson ME, Fiatarone MA, Morganti CM, et al. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. *JAMA* 1994;272:1909-14.
40. Martin P, Notelovitz M. Effects of aerobic training on bone mineral density of postmenopausal women. *J Bone Miner Res* 1993;8:931-36.
41. Barrett-Connor E, Kritiz-Silverstein D. Does hyperinsulinemia preserve bone? *Diabetes Care* 1996;19:1388-92.
42. Parra-Cabrera S, Hernandez-Avila M, Tamayo-y-Orozco J, et al. Exercise and reproductive factors as predictors of bone density among osteoporotic women in Mexico City. *Calcif Tissue Int* 1996;59:89-94.
43. Heuser I. Depression, endocrinologically a syndrome of premature aging? *Maturitas* 2002;41(Suppl 1):S19-S23.
44. Avis NE, Brambilla D, McKinlay SM, et al. A longitudinal analysis of the association between menopause and depression. Results from the Massachusetts Women's Health Study. *Ann Epidemiol* 1994;4:214-220.
45. Wassertheil-Smolter S, Shumaker S, Ockene J, et al. Depression and cardiovascular sequelae in postmenopausal women: the Women's Health Initiative. *Arch Intern Med* 2004;164:289-98.
46. Coelho R, Silva C, Maia A, et al. Bone mineral density and depression: a community study in women. *J Psychosomatic Res* 1999;46:29-35.
47. Colt EWD, Wardlaw SL, Frantz AG. The effect of running on plasma beta-endorphin. *Life Sci* 1981;28:1637-40.
48. Bravo G, Gauthier P, Roy PM, et al. Impact of a 12-month exercise program on the physical and psychological health of osteopenic women. *J Am Geriatr Soc* 1996; 44:756-62.
49. Yusuf HR, Croft JB, Giles WH, et al. Leisure-time physical activity among older adults, United States. *Arch Intern Med* 1996;156:1321-26.