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This clinical e-newsletter from The North American Menopause Society (NAMS) presents questions and cases commonly seen in a menopause specialist's practice. Recognized experts in the field provide their opinions and practical advice. Gloria Bachmann, MD, the Editor of *Menopause e-Consult*, encourages your suggestions for future topics. Note that the opinions expressed in the commentaries are those of the authors and are not necessarily endorsed by NAMS or Dr. Bachmann.

Case:

Your 68-year-old patient wants to continue using estrogen. Will insurance classify this as high-risk medication requiring a trial of alternatives such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), gabapentin, or progesterone before continued authorization?

Management issues by:

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Estrogens in women aged older than 65 years

If you have a patient aged older than 65 years on hormone therapy (HT), you have or will be receiving notification from her insurance company stating that "this drug falls under Beers Criteria for Potentially Inappropriate Medication Use in Older Adults and/or the 2013 Healthcare Effectiveness Data and Information Set (HEDIS) of high-risk medications in the elderly due to carcinogenetic effects and the risk of deep vein thrombosis, pulmonary embolism, stroke, and myocardial infarction." Beers Criteria also classifies testosterone and methyltestosterone as potentially inappropriate because of cardiac problems. The notice requests that you weigh risk versus benefit in your patient and assess whether an alternative therapy could be used.

HEDIS and Beers Criteria

HEDIS is a registered trademark of the National Committee for Quality Assurance and mostly uses Beers Criteria and their list of medications.[1] They define older adults as 65 years of age or older. Beers Criteria is generated by a US consensus panel of experts and is updated annually. For estrogens, these criteria are largely based on Women's Health Initiative (WHI) and WHI follow-up studies.

Beers Criteria lists oral and transdermal estrogens and estrogen/progestogens as potentially inappropriate because of carcinogenic potential (in the breast and endometrium), the lack of cardioprotective effects, and the lack of cognitive protection in older women. Beers Criteria describes the use of topical intravaginal estrogen cream at a low dose as acceptable for the prevention of urinary tract infections and the management of dyspareunia and other vaginal symptoms. At doses less than 25 µg twice weekly, Beers Criteria finds that evidence exists for safety of use in women with breast cancer.

Extended estrogen use

Many women currently on HT wish to remain on it beyond age 65 for several reasons,

including persistent vasomotor symptoms, dyspareunia caused by vulvovaginal atrophy, and treatment for osteopenia and osteoporosis. Many women just plain feel better on HT and comment on improvement cognitively and sexually and on how youthful they feel and look. It is now recognized that the length of time of the menopause transition (and therefore of symptoms) is nearly 12 years in many women, not 3 to 4 years as previously thought. In a study of older menopausal women, with a mean age of 67 years and mean time since menopause of 19 years, 11.8% still reported clinically significant hot flashes.[2,3]

When the WHI was initiated, the average woman in the study was aged approximately 63 years. Since then, there have been several subgroup analyses and other studies that have shown that benefits and risks of HT may depend on many factors, such as dose, age at initiation, length of duration of therapy, form (oral vs transdermal), the use of progestogens, family history (such as the risk of breast cancer), and more. Individualization of therapies has long been advocated by numerous articles and professional organizations. The NAMS 2012 position statement on HT states that "provided that the woman is well aware of the potential benefits and risks and has clinical supervision, extending [estrogen and progestin therapy] with the lowest effective dose is acceptable under some circumstances, including 1) for the woman who has determined that the benefits of menopause symptom relief outweigh the risks, notably after failing an attempt to stop (estrogen and progestin therapy) and 2) for the woman at high risk of fracture for whom alternative therapies are not appropriate or cause unacceptable adverse effects."[4] A 2014 practice bulletin from the American College of Obstetricians and Gynecologists (ACOG) on the management of menopausal symptoms states that "the decision to continue HT should be individualized and be based on a woman's symptoms and the risk-benefit ratio, regardless of age. Because some women aged 65 years and older may continue to need systemic HT for the management of vasomotor symptoms, ACOG recommends against routine discontinuation of systemic estrogen at age 65. As with younger women, use of HT and estrogen therapy should be individualized based on each woman's risk-benefit ratio and clinical presentation."[5]

Age 65 and beyond

We have many patients who initiated HT within 10 years of menopause and who wish to stay on HT at age 65 years and beyond. This milestone can be another opportunity to discuss with our patients the benefits, risks, and alternatives to HT. There is a lot of new thinking about extended HT. An excellent recent article by Andrew Kaunitz, MD, on when a menopausal woman should discontinue HT[6] takes the reader through the different options for managing the patient who wishes to stay on extended HT. Kaunitz's approach is very similar to mine: to use transdermal estradiol in the lowest possible dose, as low as a .025 mg patch (or equivalent gel/cream) or even a .014 mg patch—and for women with an intact uterus, to use progesterone in the lowest possible dose and as infrequently as possible. We often use 200 mg of micronized progesterone for 14 nights every 3 months with transdermal estrogen patch doses of .025 mg or higher. For the .014 mg dose, we use that same amount of micronized progesterone every 12 months. We frequently do an endometrial assessment (sonohysterogram and/or endometrial biopsy) in patients with an intact uterus for abnormal uterine bleeding or when progesterone is not possible or who use progesterone less often than noted above. We don't use extended HT in women at high risk for endometrial carcinoma or with a family history of breast cancer. Because of potential cardiovascular risks, we don't use oral estrogen in women aged older than 60 years.

Discussion with the patient regarding risks

It is important to keep in mind and discuss with the patient that the data regarding the risks of HT are mostly from the WHI and WHI follow-up studies. The incidence of breast cancer and mortality from breast cancer increased after 3 to 5 years of estrogen and progestin therapy,

and the risk of stroke remained elevated throughout use of this combination. However, in the WHI, the higher-dose Premarin combined with medroxyprogesterone acetate was used, a higher and different dose than we would typically use in a 65-year-old woman today. The risk of breast cancer and stroke in many women might be different and lower with the use of lower doses of transdermal estrogens and lower doses and longer cycles of micronized progesterone. Also, keep in mind that there was no increased risk of breast cancer observed in the estrogen-only arm of the WHI, and this has continued after more than 7 years of follow-up.[7] It is also very important to know that newer analyses and interpretations of WHI data are showing potential decreases in cardiovascular as well as overall mortality, especially for estrogen-only users.[8,9] The use of minimal long-term cyclic progesterone in HT users may eventually show this same effect.

What are the options?

Some patients will be interested in continuing HT at age 65 even after there is a discussion of the issues. Some will go off and stay off, and some will want to go back on. Some will consider the alternatives. For many of our patients, vasomotor symptoms will be less severe than in early menopause, and some of the alternative therapies may be more effective at this age than when they were younger. Low-dose SSRI or SNRI therapies may be effective. Venlafaxine at 37.5 mg has been reported as useful for vasomotor symptoms but may cause a decrease in libido. A new low dose of paroxetine (7.5 mg) has recently been approved by FDA for the relief of moderate to severe vasomotor symptoms. This low dose is effective without evidence of decreased libido as an adverse event. Note that SSRIs are also on Beer's Criteria as potentially contraindicated in the older patient. However, at these low doses, I believe that an insurance denial could easily be challenged.

Some patients also use gabapentin at doses as high as 300 mg 3 times a day. Fatigue may be an adverse event. Progesterone at 300 mg at bedtime has also been suggested. The data on breast safety for daily progesterone is limited. Some women with mild to moderate hot flashes at this time of life may find some herbal therapies helpful. We often recommend black cohosh in this situation. As with most herbs, the integrity of the product is important. We recommend Remifemin to our patients.

Estrogen in women aged older than 65 years: discussion and documentation

The age of 65 is another ideal landmark for discussion with the patient about menopausal therapies, especially estrogen. There are many situations in which low-dose estrogen or estrogen and progesterone therapies can be medically justified and not considered high risk in women aged older than 65 years. Documentation in the electronic medical record of such a discussion with the patient and justification for continued estrogen use is the current quality-assurance expectation.

Disclosure: Dr. Hess reports: Speakers bureau: Noven, Shionogi.

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Question:

Why does weight gain occur around the time of menopause, and how can women counteract it?

Commentary by:

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Weight gain from midlife through the menopause transition is common, but it does not need to be inevitable; there are measures one can take to counteract the problem. In the United States, 66% of women aged 40 to 59 years and more than 73% of women aged 60 years or older are overweight, as defined by a body mass index (BMI) greater than 25 kg/m^2. Forty percent of those age groups are obese, as defined by a BMI at or above 30 kg/m^2. However, it should be noted that the BMI is an imperfect indicator of a person's health. People at the low end of normal BMI or who are underweight can also face health problems. The elderly can even have some protection in being overweight when the fat layer serves as an energy source in combating chronic disease. The more important issue appears to be the distribution of accumulated fat. The change in the hormone status at menopause is associated with an increase in body fat and in particular an increase in abdominal fat that is related to several adverse health problems. The effects on weight gain with hormone therapy is unresolved, but some studies have indicated that it may reduce overall fat mass.[1]

As people age, the tendency is to become more sedentary and to maintain the same caloric intake. In addition, lean muscle decreases, and fat deposits increase. For women, muscle is the largest reservoir of estrogen receptors in the body. As estrogen declines, muscle volume and function decline. Lean muscle is a prime caloric burner and does so less effectively as this lean muscle is lost. The distribution of fat tends to be abdominal or central in this scenario. This type of fat is metabolically active and is related to numerous health issues including type 2 diabetes mellitus, cardiovascular disease, and some cancers, such as breast cancer. It may also adversely affect overall quality of life and sexual health. Sleep deprivation, which can be caused by vasomotor symptoms (night sweats), can also be related to weight gain, possibly because of fatigue and reduced activity, as well as to an increase in hunger and food intake. Sleep restriction has also been associated with carbohydrate intolerance and increased cortisol levels, which may increase the risk for diabetes and memory deficits, similar to that seen in aging.[2]

The real key to counteract this unwanted weight gain around the time of menopause is to get back to the basics of a healthy diet and regular exercise. Numerous studies have shown that physical activity is the single most important factor that prevents or attenuates age-related weight gain and preserves muscle mass. Studies have shown that aerobic or endurance exercise can counter unwanted weight gain in postmenopausal women. A lifestyle intervention program with premenopausal women aged 44 to 50 years showed better weight maintenance compared with controls over 5 years using a low-fat dietary and physical activity program.[3,4] Along with cardio exercise, the balanced exercise program would also include resistance and strength training. This can help flexibility and balance and help preserve and build lean muscle. Also, an added perk of weight loss is a possible reduction of bothersome vasomotor symptoms.

The other important component is the food we consume. This is not the format to discuss the long list of diets that are currently promoted to the general public. Suffice it to say that the general consensus is to eat a diet rich in plant-based sources and to reduce saturated fat food sources. It has also been shown that postmenopausal women who made use of food journals, who ate out less, and who ate at regular intervals were more successful with their weight loss and weight maintenance goals.[5] One additional important point is that there may be racial or ethnic differences in how women perceive body image.[6] It's been shown that women's perception of what constitutes overweight and obesity may vary from established norms. This could have a direct effect on one's behavior and motivation to pursue a weight loss program.

Weight gain is all too common for midlife and older women. This is related to several factors, but the most severe are an increasingly sedentary lifestyle and a diet that is calorie dense and low in plant-based foods. As lean muscle decreases and fat deposits increase with aging, it is the central or abdominal fat deposits that are of concern because of their relationship to numerous health problems. The good news is that one can take steps to counteract this trend by choosing healthy lifestyle options that become *permanent* changes:

1. Move more (eg, brisk walking for a least 2-3 hours per week)
2. Eat less (eat wisely)
3. Seek support from family and friends[1]

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What are your clinical challenges with weight gain? Post on our Member Forum (www.menopause.org/member-login?ReturnUrl=%2fforum) to discuss this and the rest of the papers from April *Menopause e-Consult*.

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