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Menopause e-Consult®

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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. Cheryl C. Kinney, MD, FACOG, the editor of *Menopause e-Consult*, encourages your suggestions for future topics. The opinions expressed in the commentaries are those of the authors and are not necessarily endorsed by NAMS or by Dr. Kinney.

Question

A 62-year-old postmenopausal woman is anticipating the birth of her first grandchild in 2 months. She has requested that multiple vaccines, including the measles, mumps, and rubella (MMR) vaccine; the diphtheria, tetanus, and acellular pertussis (Tdap) vaccine; Shingrex (recombinant zoster vaccine for shingles); and an influenza vaccine be given at her annual gynecologic exam. How many vaccines can be given during one office visit? If live vaccines are not administered during the same visit, how far apart should the vaccines be separated?

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Commentary by

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This woman is being seen by her gynecologist, who may not be her primary care provider. As with many women, this may be the only doctor she sees in a given year. Even if her gynecologist does not immunize personally, the National Vaccine Advisory Committee in 2014 stated, "All providers who care for adult patients are responsible for assessing immunization needs at every clinical encounter . . . [those] who do not vaccinate [should] refer adult patients to providers who administer vaccines."[1] Thus, the question of vaccination should be discussed in this visit.

1. The MMR vaccine is very important for primary protection. Generally, adults born before 1957 were exposed to the diseases and do not need ongoing immunization. In unusual circumstances, a patient could have titers drawn for antibody levels to confirm immunity and safely be reimmunized if titers are not readily available.
2. Tdap is an important vaccine, and all adults are recommended to be boosted when they are next due for a tetanus shot. The pertussis component will protect the patient from whooping cough. Because this is important for newborns, pregnant women are advised to be immunized or reimmunized in each pregnancy between 27 and 36 weeks of gestation. By increasing mom's immunity, the newborn will have increased protection in those first few months while receiving primary immunization beginning at 2 months old.
3. Shingrix is a new nonlive glycoprotein subunit two-dose vaccine for shingles. Both the US Centers for Disease Control and Prevention[2] and the Canadian National Advisory Committee on Immun-

ization[3] recommend this vaccine for everyone aged older than 50 years. It is presumed that this woman had primary varicella infection when younger, and the current guidelines do not recommend testing for titers before immunization. Because it is not a live virus vaccine, this woman's pregnant daughter or her grandchild would not be at any risk for viral exposure.

4. The influenza vaccine is recommended for all adults. Pregnant women and children aged younger than 5 years have increased risk, so it is well advised to immunize them as well as those around them. For patients aged older than 65 years, a high-dose influenza vaccine is the product of choice because it has been shown to decrease the risk of hospitalization from influenza. Although the various vaccines have slight differences, any influenza vaccine is a benefit to decrease the risk of serious complications from the disease.

In general, both live virus and inactivated viral vaccines can be administered at the same time in separate sites. Multiple live virus vaccines can be given at the same visit. (MMR, for example. is a multiviral vaccine.) However, once a live virus vaccine is given, there is generally a 4-week interval before giving another live virus vaccine.

In this scenario, I would immunize with all the vaccines needed, and importantly, book the patient back for her second Shingrix vaccine due in approximately 8 weeks or longer. Patients often miss the second or third doses in a multidose schedule, and it is important to try to finish the vaccination protocol as planned.

Should she delay, whenever she does return to the clinic, one would finish the vaccination even if it is now late according to the product monograph. Generally, we only restart a vaccine sequence from the beginning in a patient who is significantly immunocompromised, such as a bone marrow transplant patient.

References

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Disclosure: Dr. Brown reports Speaker and Teaching: Merck, Pfizer, Valneva, and Amgen.

Case

A 44-year-old woman presents to the clinic and reports that she has been having severe hot flashes and a diminished sex drive since undergoing endometrial ablation at age 36 for abnormal uterine bleeding. The hot flashes interfere with her daytime chores and cause nighttime awakenings. She had been using testosterone pellets, prescribed elsewhere 10 months ago, for a period of 3 months with minimal relief. She also reports associated thinning of hair, vaginal discharge, and vaginal dryness but denies any vaginal bleeding or spotting. She reports dyspareunia as well and uses a nonspecific vaginal lubricant during intercourse.

Her past medical history is uneventful. She has had a benign breast lump removed and cholecystectomy in the past. She has hypertension and diabetes on her maternal and paternal sides. She is obese but normotensive, and her physical exam is otherwise unremarkable.

Given the history of endometrial ablation, it would be difficult to rule out hyperplasia without hysteroscopy-guided endometrial sampling. How and when would you determine the "start" or age of menopause, since she became amenorrheic after ablation and started having menopause symptoms at about the same time? This question becomes crucial, especially 8 to 10 years from presumed menopause, when offering these women hormone therapy (HT) versus nonhormone options.

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Commentary by

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This case illustrates several excellent teaching points:

1. Not all women with hot flashes and amenorrhea are postmenopausal.
2. Not all dyspareunia is vulvovaginal atrophy (VVA) or the genitourinary syndrome of menopause. Conditions such as lichen sclerosis, lichen planus, vaginal intraepithelial neoplasia, infection, and vaginismus have to be considered.
3. Testosterone pellets are *not* FDA approved for use in women. Systemic testosterone is aromatized to estradiol, and unopposed estrogen increases the risk for endometrial hyperplasia and cancer.
4. Women who have had endometrial ablation may have amenorrhea for several years before actual menopause or the last ovulation.
5. The Study of Women' Health Across the Nation (SWAN) has taught us that vasomotor symptoms (VMS) can start in perimenopause long before the final menstrual period, and VMS can last a long time.

I would start off by *not* presuming that this women became menopausal at the time her VMS started at age 36. In fact, women at early onset of perimenopause tend to have the longest duration of perimenopause, which averages 8.57 years in the youngest age-at-onset quartile.[1] Thus, in women with endometrial ablations and amenorrhea, I usually obtain yearly follicle-stimulating hormone (FSH) and estradiol levels in order to "date" the onset of menopause, because we know that there are critical windows that affect the risk-benefit equation of HT.

Furthermore, in SWAN, we learned that women who were premenopausal or early perimenopausal when they first reported frequent VMS had the longest total duration of symptoms (median, 11.8 y) and postmenopausal persistence in contrast with women who were postmenopausal at the onset of VMS who had the shortest duration of VMS duration.[2] In addition, black women, who reported the longest duration of VMS and additional factors related to longer duration of VMS, were a younger age (such as in this case), had a lower educational level, had greater perceived stress levels, and had high levels of depression and anxiety, highlighting the need to assess for mental health issues in women suffering with VMS.

We are told that this woman's physical exam, save for obesity, is unremarkable. If she doesn't have VVA or lichen sclerosis or other vulvovaginal abnormalities, it is possible she

is still premenopausal or has received enough systemic testosterone that aromatized to estradiol to treat her atrophy.

I would first obtain FSH, estradiol, free testosterone, and DHEA levels. If indeed she is still premenopausal or perimenopausal, I would prescribe continuous contraceptive doses of hormones with a drospirenone-based therapy for the hair thinning. It is important to note that endometrial ablation is not a contraceptive therapy.

If she is menopausal, I would offer her HT. If mood and hair thinning were major concerns and/or her androgens are elevated, I would offer oral therapy unless there is a risk for venous thromboembolism.

We know that standard estrogen-progesterone therapy is not always ideal because of adverse events such as uterine bleeding and breast tenderness. Given her history of endometrial ablation, I would favor a so-called "designer estrogen" such as Duavee, a combination of 0.45 mg oral estrogen with 20 mg bazedoxifene.[3]

I would not cycle her or separate the estrogen and progesterone/progestin component. If she preferred a nonoral option or she was at a higher risk for thrombosis or had elevated triglycerides, a combination estrogen-progestin patch (weekly ClimaraPro 0.045 mg estradiol plus 0.015 mg levonorgestrel or twice weekly Combipatch 0.05 mg estradiol with norethindrone acetate 0.14 mg or 0.25 mg) could be used. Oral HT will elevate sex-binding globulin hormone levels, thus lowering free testosterone levels, which will likely help her skin and hair.

As far as the reduced libido, I would assess for secondary causes versus primary hypoactive sexual desire disorder (HSDD) before considering the pros and cons of prescribing flibanserin.[4] I would first treat her symptoms of vaginal dryness with vaginal dehydro-epiandrosterone (DHEA).

Since the seminal publication of Labrie and colleagues in 2009,[5] I have prescribed compounded vaginal DHEA until it became commercially available in 2016 in the form of Intrarosa (prasterone) 0.05%. Because there are no aromatase enzymes in the endometrium, vaginal DHEA will not stimulate the endometrium in women as higher doses of vaginal estrogen could.

Given her obesity, her endometrial ablation, and her prior unregulated, unapproved testosterone pellets, avoiding extra estrogenic stimulation to her endometrium is very important, especially given assessing post-menopause bleeding, if it occurs, will be more challenging given the scarring from the endometrial ablation.

I also would provide her with easy-to-read information on menopause, perimenopause, female sexual function, and other common midlife concerns and monitor her blood pressure, weight, and symptom response within 3 months.

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How and when do you determine the "start" or age of menopause in women who have had endometrial ablation or are amenorrheic with or without menopause symptoms? Visit our Member Forum to discuss the November *Menopause e-Consult*.

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