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Postmenopausal Bleeding Requires More Than Blind Biopsy

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PHILADELPHIA — Clinicians should regard postmenopausal bleeding as endometrial cancer "until proven otherwise" and recognize that blind biopsies alone are insufficient to rule out cancer, according to a presentation here at the North American Menopause Society (NAMS) 2017 Annual Meeting.

Steven R. Goldstein, MD, a professor of obstetrics and gynecology at New York University School of Medicine, New York City, gave the presentation October 12.

"We're talking about the [average] patient, basically on no hormone therapy, who has an episode of bleeding — and that's not uncommon — that mandates that it's cancer until proven otherwise," Dr Goldstein told *Medscape Medical News*. "If they're on hormones, it's a little bit different, and if they're on tamoxifen, it's a little bit different."

Cynthia A. Stuenkel, MD, a clinical professor of medicine in endocrinology and metabolism at the University of California San Diego School of Medicine, attended the talk and found it clinically valuable for non–obstetrician/gynecologists such as herself.

"A lot of people see postmenopausal women who are not gynecologists — nurse practitioners, physician assistants, family practice doctors, internists, and endocrinologists," Dr Stuenkel told *Medscape Medical News*. "It should be emphasized that postmenopausal bleeding is always a red flag."

An estimated 61,380 cases of endometrial cancer will be diagnosed in 2017 and 10,920 women will die of it, according to the American Cancer Society, and vaginal bleeding is the presenting sign in nearly all cases, Dr Goldstein said. The incidence of cancer in women with postmenopausal bleeding ranges from 1% to 14%, hovering around the 3% to 7% area, he said.

"The most common cause of postmenopausal bleeding is atrophy of the endometrium or of the vagina, not abnormal changes," Dr Goldstein said. "It's not always easy to tell if someone is menopausal if they're in that transition, but the guidelines are such that over 40, the chances of some kind of hyperplasia or cancer start to become significant enough that they should be evaluated."

New Standard of Care: Blind Biopsy Alone Is Inadequate

Guidelines from the American College of Obstetricians and Gynecologists (ACOG) recommend that any woman over age 40 years experiencing abnormal bleeding receive an endometrial evaluation. But ruling out cancer requires more than the blind biopsy that has been standard for years, Dr Goldstein said.

"The standard of care has changed," he told attendees. "Now the standard of care corroborates that a negative blind biopsy is not a stopping point. Clinicians can still begin with a blind biopsy, but unless it is malignant or complex atypical hyperplasia, the endometrial evaluation is not complete."

The bulk of Dr Goldstein's presentation focused on that new standard and the options clinicians have in completely excluding endometrial cancer.

"Blind endometrial biopsy has been the standard of care for probably close to 20 years, but we now recognize that if cancers occupy less than 50% of the surface area of the uterine cavity, a biopsy can be very much fraught with error," Dr Goldstein told *Medscape Medical News*. "That is a huge change in paradigm," he said. "One of the take-home messages is getting away from this over-reliance on blind biopsy as the first and last word in all these cases."

ACOG's practice bulletin on this topic dates to 2012, but awareness among practitioners remains inadequate, suggested Risa Kagan, MD, a clinical professor of obstetrics, gynecology, and reproductive sciences at University of California San Francisco and a practicing gynecologist with the Sutter East Bay Medical Foundation in Berkeley, California. Dr Kagan attended Dr Goldstein's talk.

"I think that this may be changing, but the message just hasn't caught on to the average practitioner or even to residents, either through reading or through CME [continuing medical education] or through educational programs, but it is happening slowly but surely," Dr Kagan told *Medscape Medical News*. "I think they need to hear the fact that if you have a negative biopsy, it may not be indicative of the fact that a patient doesn't have cancer."

Evaluation Ideally Begins With Ultrasonography

Ideally, the first step in the workup should be transvaginal ultrasonography, or sonomicroscopy, to examine the thickness of the endometrial lining, Dr Goldstein told attendees. A thin, distinct endometrial echo, or lining, no greater than 4 mm can effectively rule out malignancy.

Composite findings from multiple studies estimate the odds of endometrial cancer at 1 in 383 in those with 3-mm thickness, 1 in 339 at 4 mm, and 1 in 239 at 5 mm, Dr Goldstein said. He provided four principles for transvaginal ultrasonography:

- Use the highest-frequency transducer that still yields adequate penetration.
- Once the endometrial echo is well visualized, use as much magnification as feasible.
- Obtain multiple images in the long-axis plane, midline and to the right and left of the midline.
- Obtain measurements on a long-axis view of the thickest point.

However, "an important caveat is that not all uteri lend themselves to a meaningful evaluation of endometrial thickness," Dr Goldstein told *Medscape Medical News*. "There are sometimes technical reasons why you just can't see it well enough to rely on it, such as marked obesity, coexisting fibroids, adenomyosis, and an axial-accented uterus. These can inhibit the ability to see the endometrial thickness adequately enough to rely on it."

In addition, women who "rebleed" may need a follow-up evaluation, he said. For those women and women in whom the thickness line is not totally distinct, clinicians have two options. The first, and most common, is saline infusion sonohysterography.

Next Steps After Initial Ultrasonography

"Fluid is your friend" because it enhances sound transmission, Dr Goldstein told attendees.

"If I can't see well enough or if the line isn't thin like it's supposed to be, by putting in liquid, I can now see well enough, or if it's thick, I can see if the process is global or focal," Dr Goldstein told *Medscape Medical News*. "If the process is global, then a blind biopsy ought to be fine. If it's focal, meaning there's a polyp or there's a thick area in 20% or 30% of the uterine cavity, then we've already established a blind biopsy is not the way to go, and a biopsy would need to be done under direct vision with hysteroscopy."

The alternative to saline infusion sonohysterography, or the next step if the lining is thicker than 4 mm, is hysteroscopy. Previously, hysteroscopies have been logistically challenging for many practices because of time, patient discomfort, and the need to store and sterilize the equipment.

Today, however, a US Food and Drug Administration–approved disposable hysteroscope called *Endosee* (Cooper Surgical) eliminates the need for equipment storage space or resterilization. It provides a point-of-care option that can be done with the patient in stirrups just as previous Pipelle biopsies have been done, Dr Goldstein said.

"Until recently, saline sonograms were not easy to do for the everyday practitioner, and looking for focal lesions was not so simple," said Dr Kagan, who has consulted for Endosee's manufacturer. "It's a pretty remarkable instrument in that it's exactly the same size as the Pipelle we use for biopsies, and it's very simple, under direct visualization, to put in a little saline and see if you have a polyp or a fibroid, if you have a focal lesion vs a global thickening so you can biopsy right then and there."

New Standard Message Important for Non–Ob/Gyns Too

It's not only obstetrician/gynecologists, or even just physicians, who should be aware of the new standard of care regarding postmenopausal bleeding, Dr Kagan said.

"More and more family medicine clinicians are taking care of women because they're not necessarily coming to us unless they have a problem," Dr Kagan told *Medscape News*. Physician assistants and nurse practitioners in particular are "at the front line," Dr Kagan said, and, like all primary care clinicians, need education on the importance of not stopping at a blind biopsy for postmenopausal bleeding.

"Some non–ob/gyns do office biopsy, but many don't do hysteroscopy and saline sonograms," Dr Kagan said. "If a non–ob/gyn has a patient who is bleeding, the first thing they could do before just referring them is to get an ultrasound. Then, by the time they see the gynecologist, we have that initial ultrasound."

The presentation involved no external funding. Dr Goldstein consulted for or advised AbbVie Inc, Allergan, Pfizer Inc, and TherapeuticsMD. He consulted for Cook OBGYN and Cooper Surgical, which makes Endosee, and received an equipment loan for ultrasonography from Philips Ultrasound. Dr Kagan has received consulting fees from Cooper Surgical. Dr Stuenkel has disclosed no relevant financial relationships.

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