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1. Ultrasound guidance has been used for intrauterine procedures such as chorionic villus sampling, embryo transfer, and difficult intrauterine surgery. Sonohysterogram has been recommended for assistance with biopsies of intrauterine lesions (Obstet Gynecol 2009;113:881–7; see also video courtesy of Moschos). Is there a role for ultrasound-directed office endometrial biopsy of focal or asymmetrical lesions?

Response from Dr. Goldstein:

In the past, performing an endometrial biopsy when a saline infusion sonohysterography demonstrated a global lesion (thus allowing for appropriate use of endometrial sampling) often resulted in inadequate samples. There now exist “sonobiopsy catheters” that give an adequate specimen even when the blind endometrial sampling is performed directly after saline infusion sonohysterography. The problem with ultrasound visualization during a biopsy is that it would need to utilize transabdominal ultrasound since there is virtually no room for the vaginal probe, the biopsy instrument, and the speculum all concurrently. We did some initial research with an Israeli product that had a specially designed speculum and articulating arm that allowed intrauterine manipulation while visualizing with the vaginal probe (Timor-Tritsch I, Goldstein SR, Masch R. TUAGS [transvaginal ultrasound assisted gynecological surgery]: a new technique to improve uterine surgery. Ultrasound Med Biol 2003;29:S52). However, this never came to market and is not commercially available. Thus, being able to see exactly where the biopsy is occurring with ultrasound guidance is appealing but “not yet ready for prime time.” Perhaps developments in the future will allow for this to happen.
2. Does a sonohysterogram affect the diagnostic accuracy of office endometrial biopsy if the biopsy is done immediately after the sonohysterogram?

Response from Dr. Goldstein:

As mentioned in the answer to number 1 above, it has been my experience that performing a blind endometrial biopsy directly after saline infusion sonohysterogram usually results in mostly saline coming back in spite of numerous passes with a suction piston biopsy. At least one commercially available product allows for “sonobiopsy” and has yielded adequate tissue specimen. However, this would still be done blindly.

3. Is an endometrial biopsy unnecessary prior to hormonal treatment of postmenopausal bleeding attributed to endometrial atrophy (endometrial thickness less than 4 mm)?

Response from Dr. Goldstein:

There is little that will be added by a blind endometrial biopsy in patients who have postmenopausal staining and a thin distinct endometrial thickness ≤ 4 mm. As referenced in the article, if one does perform endometrial sampling on such patients, the majority of the time it is impossible to obtain tissue. And, if tissue is obtained, it is often insufficient for histologic diagnosis.
4. In today’s legal climate, is there no substantial medical liability risk in following an asymptomatic postmenopausal patient with an incidental finding of a thickened endometrium without a biopsy? How frequently should she be re-evaluated if she remains asymptomatic? Is there a threshold endometrial thickness in an asymptomatic postmenopausal woman where endometrial biopsy would be prudent?

Response from Dr. Goldstein:

It is very interesting that the question asks about today’s legal climate. I would shift the “burden of proof” back on to the questioner. There has never been any validation whatsoever about a thick echo discovered incidentally being “abnormal.” As outlined in my article, the whole purpose of transvaginal ultrasound in patients with bleeding was to identify those who lack tissue and can avoid any type of diagnostic intervention. However, the rank and file clinicians and many academic physicians as well have unfortunately chosen to turn this around and assume that a thick echo is pathologic and has to be evaluated. This has always been a source of continued wonder to me. It appears that 10–17 percent of asymptomatic postmenopausal women, if interrogated with ultrasound, will have a thick endometrial echo. Most of these are old asymptomatic polyps whose risk of malignancy is approximately 1/1000. Some of these will be old leiomyoma or adhesions or simply thick-appearing central uterine echoes that do not represent any pathologic process. Thus, if there are concerns about the medical–legal climate, one should recognize that without any justification for endometrial sampling in such nonbleeding patients, should complications arise (such as perforations, anesthesia accidents, etc.)—in my mind—there is in fact liability associated with the intervention.

However, having said all that, if patients are at high risk for endometrial disease (diabetes, polycystic ovary syndrome, marked obesity, etc.) and have a thick endometrial echo, then on a case-by-case basis a decision to want to evaluate such patients represents good clinical judgment. However, having some sort of numerical “cut off” above which one thinks that endometrial sampling should be performed is in my opinion inappropriate. Additionally, I do not think these patients need to be followed up. I do not believe there is any number at which
endometrial biopsy is necessary. It is crucial that such patients understand that if there is any bleeding per vaginam, they must report this quickly and evaluation should be carried out thoroughly and promptly.

5. Does the presence of fluid in the uterine lumen on vaginal ultrasound of a woman with postmenopausal bleeding change the algorithm for evaluation of abnormal uterine bleeding? Does it change your recommendations for evaluation of the asymptomatic postmenopausal woman with a thickened endometrium?

Response from Dr. Goldstein:

Endometrial fluid collections are an extremely interesting topic. In 1994 I published a paper entitled “Postmenopausal endometrial fluid collections revisited: look at the doughnut rather than the hole” (Obstet Gynecol 1994;83:738–40). Endometrial fluid is a natural occurring sonohysterogram. It gives you excellent visualization of the endometrium. If the tissue surrounding the fluid is thin, this proves endometrial atrophy. One needs to consider the possibility of endocervical disease causing cervical stenosis and a build up of fluid (usually transudate) behind it. At a recent international meeting, Dr. Elizabeth Epstein reported on a handful of endocervical carcinomas causing cervical stenosis. Some have argued that the fluid might represent blood that cannot escape because of cervical stenosis. Thus, if the tissue surrounding the fluid is seen to be thick, heterogeneous, or containing a polyp, then I believe endometrial evaluation is in fact necessary because admittedly such patients may have blood but the cervical stenosis may not have allowed that to be expressed vaginally. So in summary, endometrial fluid collections allow excellent visualization of the endometrium, keeping in mind that the endocervix may need to be evaluated.
6. Are there methods, such as multiple passes or rotation of the device, for office endometrial biopsy with a Pipelle that will increase the sampling area of the endometrium? Is the sampling area operator-dependent?

Response from Dr. Goldstein:

I am not familiar with any well-performed studies that deal with the number of passes or rotation of the suction piston biopsy instrument (remembering the Pipelle is simply one brand of those). I think that the sampling error is less operator-dependent and more dependent on the amount of surface area that the pathologic process involved. I would refer the reader to an article by Guido et al (Pipelle endometrial sampling sensitivity in the detection of endometrial cancer. J Reprod Med 1995;40:553-5). Guido sampled 65 patients with known carcinoma in the operating room with Pipelle biopsy prior to the hysterectomy. They missed 11/65 cancers but all of those occupied less than 50% of the surface area of the endometrium. Of 11 cancers in polyps they missed 5. This caused Guido to conclude that “Pipelle is excellent for detecting global processes in the endometrium.” I think that patients, and unfortunately too many physicians, believe that a “biopsy” taken from the uterus is representative of the entire uterine cavity. This may be true in normal cycles and even in infertility patients. Unfortunately, serious pathologies like complex atypical hyperplasia and cancers are often not global. In such cases a small piece of tissue obtained with Pipelle biopsy may not necessarily be reflective of the endometrial cavity. This underscores one of the problems with biopsy as the first step in triage. When it is positive it is extremely significant. When it is negative it may not prove anything. Unfortunately, this technique of blind suction piston biopsy has gained widespread acceptance with extremely little validation.
7. Is there cost-effectiveness evidence that sonohysterography, rather than office hysteroscopy and directed biopsy, should be done upon discovery of a thickened endometrium in a woman with postmenopausal bleeding?

Response from Dr. Goldstein:

I am not aware of cost-effectiveness evidence relative to office hysteroscopy and directed biopsy versus sonohysterography. Keep in mind that there is a difference between “cost” and “charges.” Certainly those accomplished in office hysteroscopy can and should continue to evaluate such patients with that modality. It is my opinion and experience that saline infusion sonohysterography is easier to perform, has greater patient comfort, is less operator dependent, and start up equipment is much cheaper (if you already have an ultrasound machine). Certainly, sonohysterography shows a focal lesion such as a polyp or focal thickening. Then, in my hands, such patients go to ambulatory surgery for an operative hysteroscopy with anesthesia and definitive therapy.