

Just the Berries



Who needs an endometrial biopsy?

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Endometrial biopsy is a way to sample the endometrium that can be done as an office procedure. It is an important diagnostic tool in evaluating abnormal uterine bleeding. It is used to exclude diseases, such as endometrial cancer and its precursors, especially atypical endometrial hyperplasia. Endometrial biopsy is also used in evaluating infertile patients to diagnose luteal phase defects. This article, however, focuses on the role of endometrial biopsy in determining causes of abnormal uterine bleeding.

Endometrial biopsy versus dilation and curettage

The criterion standard for sampling the endometrium used to be dilation and curettage (D&C) under general anesthetic. It is now recognized, however, that D&C is really just another blind technique that often samples less than half the endometrium.¹

Endometrial biopsy has replaced D&C as the first-line diagnostic test for evaluating abnormal bleeding. The two tests have been shown to have similar accuracy; several studies comparing endometrial biopsy and D&C samples have found excellent agreement, from 83% to 90% of samples²⁻⁵ (level III evidence). Endometrial biopsy has several advantages over D&C. It is safer because there is no need for general anesthetic or cervical dilation, and there is markedly less risk of hemorrhage, infection, and perforation.⁶ Endometrial biopsy is also more convenient and saves time for both physicians and patients.

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Just the Berries has been available on the Internet for several years. You can find it at www.theberries.ns.ca. Visit the site and browse the Archives and the Berries of the Week. We are always looking for articles on topics of interest to family physicians. If you are interested in contributing an article, contact us through the site. Articles should be short (350 to 1200 words), must be referenced, and must include levels of evidence and the resources searched for the data. All articles will be peer reviewed before publication.

Risk factors for endometrial cancer

Most endometrial cancers are related to chronic unopposed endogenous or exogenous estrogen. Prolonged exposure to unopposed estrogen occurs in obese patients and those with polycystic ovary syndrome or chronic anovulation. Unopposed exogenous estrogen is a serious risk factor, so postmenopausal women with a uterus should not be taking estrogen without appropriate progesterone. Other women at increased risk of endometrial cancer include those with a relatively long period of exposure to estrogen, such as women with early menarche and late menopause, and nulliparous women. The pattern of abnormal bleeding is also important because women with irregular menstrual cycles are at higher risk of endometrial cancer than women with regular cycles.⁷

Age is also an important risk factor for endometrial cancer; peak age for endometrial cancer is 60 years.⁸ Most physicians agree that women 40 years and older are at increased risk. Other risk factors include diabetes and hypertension. Women with diabetes have a 2.8-fold increased risk of endometrial cancer.^{9,10}

In two studies,^{9,10} hypertension was not an independent risk factor when adjusted for body weight. Women using tamoxifen as adjuvant therapy for breast cancer are also at increased risk of endometrial cancer¹¹; risk is highest in women who have used tamoxifen for more than 2 years.

Indications for endometrial biopsy

Postmenopausal bleeding. Any woman with postmenopausal bleeding

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who is not receiving hormone replacement therapy (HRT) requires endometrial sampling. About 7% of such bleeding is caused by malignancy,¹² so postmenopausal bleeding should be considered to be from endometrial cancer until proven otherwise.

Most women taking cyclic combined HRT experience regular withdrawal bleeding. They should be counseled about this beforehand and reassured that it is normal. Patients with irregular bleeding, not associated with progesterone withdrawal, should be considered to have abnormal patterns of bleeding and should undergo endometrial sampling.^{6,8}

In women taking continuous combined HRT, the endometrium often becomes atrophic, and these women become amenorrheic; 75% of these women develop amenorrhea after 6 months.¹³ If bleeding continues beyond 6 months, it should be considered abnormal, and endometrial sampling should be considered.⁶ The Society of Obstetricians and Gynaecologists of Canada recommends endometrial biopsy for patients who continue to experience bleeding after the first 6 months of treatment with continuous combined HRT.⁸

Perimenopausal bleeding. During the perimenopausal years, waxing and waning ovarian function affects menstrual cycles. Women often have cycles that vary in length and fluctuating amounts and duration of flow. Anticipated changes in menstrual cycles sometimes make it difficult to determine whether patients are experiencing abnormal uterine bleeding.

Perimenopausal women with abnormal bleeding are at increased risk of endometrial cancer secondary to their age and anovulatory cycles. All women with abnormal uterine bleeding in the perimenopausal period require endometrial sampling.^{9,14} The most worrisome patterns are persistently increased menstrual flow, decreased menstrual interval, and intermenstrual bleeding.¹⁴

Premenopausal bleeding. Indications for endometrial biopsy in premenopausal women with abnormal bleeding are not straightforward. Adolescents generally do not require sampling because their abnormal bleeding is often due to anovulation secondary to an immature hypothalamic-pituitary-ovarian axis or, less commonly, to an underlying inherited coagulopathy. After adolescence, endometrial cancer should be considered in the differential diagnosis of abnormal bleeding because up to 10% of women with endometrial cancer are diagnosed before age 45.¹⁰

Risk factors for endometrial cancer should be considered when determining whether endometrial biopsy is needed for premenopausal women. Women

younger than 40 with no risk factors have minimal risk of endometrial cancer.⁷ For these women, it might be appropriate to initiate hormone treatment after an endocrine workup and sample the endometrium only if there is no response to treatment. On the other hand, women with one or more risk factors are at increased risk of endometrial cancer and probably should be sampled. The most important risk factor in premenopausal women is irregular menstrual cycles, which are associated with a 14% risk of abnormal results of endometrial biopsy (including both benign and malignant lesions).⁷ Hence, endometrial biopsy should be considered for almost all women with irregular cycles.

Tamoxifen. Because of the estrogenlike effects of tamoxifen on the endometrial lining, patients taking tamoxifen who experience abnormal vaginal bleeding should have an endometrial biopsy.⁸

Abnormal Pap smear cytology. In postmenopausal women, presence of any endometrial cells on Pap smear is an indication for endometrial sampling.^{6,9} In all women, presence of atypical endometrial cells on Pap smear warrants endometrial biopsy. Patients with malignant endometrial cells on Pap smear are at serious risk of endometrial cancer, often high-grade malignancy.¹⁵

Follow up. Women who have been treated for endometrial hyperplasia with hormone therapy require a follow-up endometrial biopsy in 3 to 6 months to ensure the hyperplasia has regressed.

Screening with endometrial biopsy. Currently, there is no reason to screen women with no abnormal bleeding. Asymptomatic women are at low risk of endometrial cancer,¹⁶ and endometrial biopsy has poor accuracy for identifying well differentiated, low-volume, minimally invasive tumours, which makes it a poor screening test.¹⁷

Accuracy

The accuracy of endometrial biopsy to detect endometrial disease, especially endometrial cancer, is extremely good. Studies comparing endometrial biopsy samples with specimens taken during hysterectomy indicate that endometrial biopsy has a sensitivity ranging from 83% to 96% for detection of endometrial cancer.^{18,21}

Indications for D&C

Although endometrial biopsy has replaced D&C as the first-line test for abnormal bleeding, there are still

circumstances where D&C is indicated. If an endometrial biopsy cannot be done, if the sample is insufficient, or if patients' bleeding persists after negative biopsy results, further investigation is needed.

When a biopsy cannot be performed or a sample is insufficient, patients should be triaged according to risk of endometrial cancer to determine the next appropriate step. If patients are at high risk of endometrial cancer, they require D&C. If they are at relatively low risk or at increased risk of being adversely affected by anesthetics, a transvaginal ultrasound examination could be used to guide further management. If the ultrasound examination demonstrates an endometrial thickness of ≤ 4 mm, then the risk of having serious endometrial disease is low, and further investigation is probably not required, other than close follow up.^{8,22} If the thickness is > 4 mm, patients probably require D&C.^{8,23}

If the results of an endometrial biopsy are negative and patients continue to have abnormal bleeding, studies show that there is a 10% to 11% risk that a lesion has been overlooked.^{8,24} Such patients need to be reevaluated. Options for further evaluation include repeating endometrial biopsy, transvaginal ultrasound examination, or hysteroscopy and D&C.

Conclusion

Endometrial biopsy is an important diagnostic tool in investigating abnormal uterine bleeding. It has replaced D&C as the first-line diagnostic test because it has similar accuracy, yet is safer, quicker, and more convenient. Primary care physicians and gynecologists should be aware of the risk factors for endometrial cancer so that they know which women require endometrial biopsy. All postmenopausal women with uterine bleeding who are not taking HRT require endometrial sampling. All women taking HRT with unexpected uterine bleeding need endometrial biopsy. All perimenopausal women with abnormal bleeding should be sampled. Premenopausal women with irregular cycles or with one or more other risk factors for endometrial cancer should have endometrial biopsy. When endometrial biopsy cannot be performed or produces insufficient tissue, or patients have persistent bleeding after negative biopsy results, transvaginal ultrasound can help guide decisions about who to sample with D&C and who to monitor with close follow up. ❖

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