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What is the best diagnostic approach to postmenopausal vaginal bleeding in women taking hormone replacement therapy?

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EVIDENCE-BASED ANSWER

Women on standard estrogen/progestin hormone replacement therapy (HRT) regimens frequently have irregular bleeding during the first 12 months of treatment. Therefore, those taking HRT should usually be evaluated after 1 year of treatment if bleeding continues. (Grade of recommendation: C, based on case series.) Evaluation of this bleeding should begin with a pelvic examination and Papanicolaou (Pap) test (if not done in the previous 12 months), then transvaginal ultrasound (TVUS), followed by endometrial biopsy or hysteroscopy, if indicated. (Grade: B, based on a systematic review of studies.)

EVIDENCE SUMMARY

Vaginal bleeding can be a sign of endometrial hyperplasia or cancer. Fifty-year-old perimenopausal women with an intact uterus have a 5% prevalence of hyperplasia1,[2] and a 2% to 3% risk of endometrial cancer in their lifetime.[2] HRT causes irregular bleeding for 8% to 60% of these women at 6 months and 4% to 30% at 12 months.[3,4] Roughly half of those bleeding at 6 months are no longer bleeding at a year.[3-5] Bleeding may be reduced by using lower-dose combinations, sequential hormones in perimenopausal women, and continuous regimens in women more than 3 years after menopause.[1,3,5]

Any woman taking HRT who has irregular bleeding after a year should have a Pap test, since cervical abnormalities are not uncommon.[6] Although HRT increases average endometrial thickness (at least initially),[6,7] TVUS showing an endometrial stripe of 5 mm or greater is more than 90% sensitive in detecting endometrial disease (cancer, complex hyperplasia, polyps).[7] Approximately 3% of endometrial stripes are unmeasurable by TVUS and should be treated as abnormal. TVUS also shows many structural abnormalities, including those outside of the endometrium. A negative TVUS using the 5-mm criterion is associated with a 0.6% to 1% chance of endometrial cancer.[6,7]

Abnormal sonograms or persistent unexpected bleeding after a normal sonogram requires further evaluation. Endometrial biopsy is a straightforward office procedure, and is as sensitive as dilatation and curretage.[4] It fails (eg, from cervical stenosis) or is nondiagnostic in 2% to 28% of attempts.[7] Hysteroscopy is also accurate but sometimes requires paracervical and general anesthesia. It also requires additional training and equipment.

Zero percent to 12% of attempts fail (failures are less common in patients taking HRT), and the false-negative rate is roughly 3%.[4]

■ RECOMMENDATIONS FROM OTHERS

The American Association of Clinical Endocrinologists states in its menopause management guideline: “Unexpected uterine bleeding or spotting during HRT is common and is managed by appropriate changes in therapy, not by discontinuation of HRT…. Nevertheless, monitoring of the endometrium by transvaginal ultrasound study or endometrial biopsy is indicated, especially in women who have an abnormal bleeding pattern.”[8]

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CLINICAL COMMENTARY

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I often recommend a fairly vigilant workup for women with irregular vaginal bleeding. Assuming that all patients initiated on HRT have already received a Pap-and-pelvic that was normal, I proceed directly to a TVUS in any patient with irregular bleeding after 6 months. Those with an endometrial lining that is 5 mm or greater require further evaluation with an endometrial biopsy. Finally, postmenopausal women with irregular vaginal bleeding who are taking raloxifene require similar but immediate evaluation, since this medicine causes no more irregular bleeding than placebo.

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