

# Management of Postmenopausal Bleeding

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**Abstract:** *Postmenopausal bleeding is a common patient complaint that is encountered by all physicians and other clinicians of gynecologic care. The clinician faces the possibility that there exists an underlying malignancy, while knowing that, in most instances, the bleeding comes from a benign source. In years past, the gold standard of clinical investigation was the institution-based dilation and curettage (D&C), but there now exists a number of office-based methods for the evaluation of women with this complaint. The postmenopausal use of gonadal steroids for the treatment of menopausal symptoms (HRT) is often associated with endometrial bleeding. Although the number of women using these agents decreased in the first decade of the 21st century, reevaluation of the literature and the release of new studies have collectively suggested that such therapy may provide benefit in at least selected instances*

**Keywords:** postmenopausal bleeding, benign, malignant, pathologies, management

## 1. Introduction

Interestingly, there is a paucity of guidelines worldwide. However, most importantly, any bleeding postmenopause necessitates further evaluation and referral. Postmenopausal bleeding (PMB) accounts for five per cent of office gynaecology presentations (1). Its definition is self-explanatory, as any bleeding from the genital tract occurring in the postmenopausal period, arising after 12 months of amenorrhoea in a women of menopausal age.<sup>2</sup> Generally, four to 11 per cent of postmenopausal women will experience bleeding (1). The chance of this occurring reduces as time since menopause increases (1).

## 2. Material and Methods

The investigation and management is relatively straightforward but still there is a paucity of guidelines worldwide. However, most importantly, any bleeding postmenopause necessitates further evaluation and referral. This is a systematic review of postmenopausal bleeding, a reevaluation of the literature and of new studies.

## 3. Results

### Aetiology

While the most common cause for PMB is atrophy, the diagnostic algorithm for PMB is designed to detect cancer, particularly endometrial cancer. Vaginal, endometrial and urogenital atrophy is par for the course with postmenopausal hypoestrogenism.<sup>1</sup> Atrophy accounts for 60–80 per cent of all causes of PMB, while endometrial hyperplasia and cancer each account for ten per cent of cases (1,3). The remaining causes are attributed to endometrial or cervical polyps (two to 12 per cent); exogenous oestrogen (15–25 per cent); cervical cancer (one per cent) and factors such as vaginal trauma, anticoagulants and bleeding from non-gynaecological sites (1,3). Table 1 for a summary of these causes.

## 4. History and Examination

Like any other presentation in gynaecology, and more broadly medicine, the evaluation of PMB starts with a thorough history and physical examination. This will usually

be first encountered with a presentation to a patient's general practitioner; however, presentations to emergency departments also occur. Salient history surrounding the bleeding includes: when it started, duration, pattern, amount, frequency and any associated trauma.<sup>1</sup> Changes in bladder or bowel function and associated factors such as pain and weight loss are also important to ascertain.<sup>1</sup> It is imperative to determine the use of hormone replacement therapy (HRT), the type of HRT (continuous, cyclical, oestrogen and progesterone or oestrogen only), duration of use and whether the patient has had a hysterectomy. It cannot be highlighted too strongly that any woman who is on HRT and has a uterus requires progesterone for endometrial protection. Details of the patient's past gynaecological, obstetric, medical, surgical, medication and family history are also essential (1). In particular, and often forgotten, is a thorough list of all over-the-counter medications, especially phytoestrogens (1,3). Phytoestrogens in brief are plant derivatives from, for example, soy, alfalfa and red clovers, that have an oestrogenic effect.<sup>4</sup> They are often taken to relieve vasomotor symptoms of menopause as an alternative to traditional HRT preparations (4). Tamoxifen, a medication used to reduce the risk of breast cancer recurrence in patients who have had breast cancer, is also worth a mention. Tamoxifen has been associated with changes to the endometrium including polyps, hyperplasia and cancer (1,3,5). Thus it is important to establish a patient's personal history of breast cancer and treatments undertaken, as well as a family history of this disease and other cancers such as colon and endometrial (1). In terms of physical examination, this should begin with general appearance and establishing body mass index, as obesity is a well-recognised risk factor for the development of endometrial cancer (1,3). An abdominal examination should focus on palpation for discernible masses. A systematic pelvic examination may yield the cause of the PMB.<sup>1</sup> Examination should include a detailed inspection of the vulva and vagina, particularly looking for atrophy, suspicious lesions, trauma and a foreign body (1). A speculum examination should be performed in order to evaluate the cervix for polyps and cancer. It is imperative a pap smear is taken at this time. A bimanual examination to evaluate uterine size, mobility and the adnexae as well as a rectal examination completes the assessment of the pelvis (3),

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### Investigations

The investigation of PMB is relatively straightforward, involving a pelvic ultrasound and tissue biopsy. Depending on the findings of physical examination, this biopsy may be from the vulva, vagina or cervix, but most commonly the evaluation needs to include an endometrial biopsy (1,3). Women should be referred to a gynaecologist for ongoing investigation of PMB (3)

### Transvaginal ultrasound

The majority of women referred to outpatient gynaecological services have had pelvic ultrasound in order to evaluate the endometrial thickness and assess for pelvic pathology. Transvaginal ultrasound (TVUS) is considered an acceptable initial investigation in women with PMB. In this group of women, as distinct from women with an incidental finding of thickened endometrium or fluid without bleeding, an endometrial thickness of 4–5mm typically correlates with low risk for endometrial disease (7). As the endometrial thickness increases to 20mm so too does the risk of endometrial cancer. It is important to remember that there is no accepted agreement on the cut-off for normal endometrial thickness and, thus, any women with risk factors and symptoms require endometrial sampling. There have been many studies looking at the sensitivity and specificity of TVUS in detecting endometrial cancer in women with PMB. This varies depending on the endometrial thickness used. For example, a sensitivity and specificity of 96 and 53 per cent respectively for an endometrial thickness of 4mm and 96 and 61 per cent respectively for endometrial thickness of 5mm (7). It was the consensus of the UpToDate article that an endometrial thickness less than 5mm on TVUS usually excluded endometrial cancer, however solitary use of ultrasound is not recommended in the exclusion of cancer (7).

### Endometrial biopsy

An endometrial biopsy is considered the gold standard for evaluation of PMB (3,7). Endometrial biopsy can be obtained with an endometrial pipelle in the outpatient setting, or by hysteroscopy and curettage (with or without dilatation) in either the outpatient or inpatient setting. Overall, the endometrial pipelle has been shown to adequately sample the endometrium. It is considered the more sensitive device in identifying hyperplasia or cancer compared to other sampling devices (7). The sensitivity of the pipelle endometrial sampling in the detection of endometrial hyperplasia and cancer was 99.6 and 81 per cent, respectively, in postmenopausal women (7). It is important to remember pipelle sampling of the endometrium may miss pathology, as often less than 50 per cent of the endometrium is sampled, thus it is most useful with greater than 50 per cent of the endometrium is involved with disease (7). Potential complications of endometrial pipelle biopsy include uterine perforation and infection. Patients should be counselled regarding the possibility of insufficient or non-diagnostic sampling, which may necessitate further investigation. Hysteroscopy and curettage is typically saved for cases where office sampling was insufficient or not possible owing to patient discomfort or cervical stenosis (3). The advantage to hysteroscopy is it provides the ability to see the entire endometrial cavity and is particularly useful in detecting and removing focal lesions such as polyps (7).

Again, this can be performed on an outpatient basis, avoiding the complications of general anaesthesia; however, appropriate patient selection is essential. Risks involved in this procedure include infection, bleeding, uterine perforation and, again, insufficient sampling.

### Cervical cytology

A diagnostic Pap smear in any women presenting with PMB should also be undertaken. This can help provide a differential between an endocervical and endometrial cause of PMB.

### Management

After a thorough evaluation for PMB and arrival at a diagnosis, the question arises as to what to do next. For women with cervical or endometrial cancer, prompt referral to the gynaecological oncology service is imperative for definitive management (3). A gynaecologist in conjunction with the patient's general practitioner typically manages other causes. Causes such as cervical or endometrial polyps may have already been managed and removed in the work up of PMB. As long as benign histopathology is confirmed, no further investigation or treatment is required. In such situations, patient education is paramount, as patients should be informed that any further episodes of PMB require re-evaluation.

### Atrophy

A diagnosis of vulvovaginal or urogenital atrophy is not cause for treatment of atrophy may be recommended in the context of vulvovaginal surgery or in cases of pelvic organ prolapse and urinary incontinence (8). Aside from vaginal bleeding or spotting, symptoms of atrophy typically include vaginal dryness, burning, pruritis and dyspareunia (8). An approach to management of vulvovaginal atrophy includes vaginal moisturisers and lubricants, as well as topical vaginal oestrogens (8). Generally, topical vaginal oestrogen is more successful than vaginal moisturisers and lubricants. Topical vaginal oestrogen is the treatment of choice over systemic HRT for women where atrophy is the predominant symptom. There are many preparations of commercially available vaginal moisturisers and lubricants. These are designed for regular use, typically a few times per week, not just at the time of sexual intercourse (8).

### Endometrial hyperplasia

Endometrial hyperplasia is defined as proliferation of endometrial glands and consequentially an increased gland to stroma ratio (9). Endometrial hyperplasia can be subclassified into simple or complex with or without atypia (9). The importance of endometrial hyperplasia is each subcategory has a corresponding risk of progression to endometrial cancer for simple or complex hyperplasia with or without atypia the risks are one, three, eight and 29 per cent, respectively (9). An overview to the management of endometrial hyperplasia in postmenopausal women can be summarised into treatment with progestins or hysterectomy. The decision of treatment modality is usually based upon the presence of atypia, as this increases the risk of progression to endometrial cancer (10)

## 5. Conclusion

The treatment of post-menopausal bleeding will depend on what's causing it. There are well-developed and evidence-based strategies on how best to investigate women with PMB. These strategies, formulated in several guidelines, are discussed and critically appraised.

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**Table 1:** Origin of PMB incidence

Atrophy	60–80%
Exogenous oestrogen	15–25%
Polyps (endometrial/cervical)	2–12%
Endometrial hyperplasia	10%
Endometrial cancer	10%
Cervical cancer	<1%