ABNORMAL VAGINAL BLEEDING IN PRE- AND PERI-MENOPAUSAL WOMEN
A diagnostic guide for General Practitioners and Gynaecologists

This guide was developed to assist general practitioners and gynaecologists in assessing pre- and peri-menopausal women with abnormal vaginal bleeding, to maximise diagnostic accuracy for endometrial cancer. This is a general guide to appropriate practice to be followed subject to the clinician's judgement in each individual case, and is based on the best available evidence and expert consensus (February 2011). The Commonwealth does not accept any legal liability or responsibility for any loss or damages incurred by the reliance on, or interpretation of, information contained in this guide.

RISK FACTORS
Risk factors for endometrial cancer include:
- History of chronic anovulation
- Exposure to unopposed oestrogen
- Polycystic ovary syndrome (PCOS) associated with chronic anovulation
- Exposure to tamoxifen
- Strong family history of endometrial or colon cancer (Lynch syndrome)
- Nulliparity
- Obesity (often with diabetes and hypertension)

NB ‘Natural’ hormones
- There is no evidence of sufficient quality around the safety and efficacy of natural or bio-identical hormones. However, many of these preparations contain oestrogen and are likely to carry the same risks as other types of HRT. Bio-identical hormones come in the form of lozenges, troches or creams.

History
- A medical history of the woman should be taken including the menstrual history, the nature of the current bleeding problems, the patient’s quality of life with respect to the current problem and any other related symptoms.
- Heavy bleeding and irregular bleeding patterns should be investigated. Over 80mls of blood loss is considered to be heavy menstrual bleeding. Blood loss could be calculated by measuring the blood loss after 90 minutes. A pelvic examination should be performed on days 4–7 of the menstrual cycle during which the TVUS is performed. Most accurate results are achieved if performed on days 4–7 of the cycle, when menses have ceased.

Blood and Other Tests
- A full blood count should be undertaken.
- A thyroid function test should only be undertaken if there are indicators for thyroid disorder. Testing for coagulation diseases such as von Willebrand disease is recommended for those with indications. Hormone testing of women who have heavy menstrual bleeding is not recommended.

Transvaginal Ultrasound (TVUS)
- TVUS is an initial screening tool for identifying high and low risk; it is not a diagnostic tool.
- TVUS should be performed by an experienced examiner using high quality ultrasound equipment and a standardised measurement technique.
- TVUS is best performed in the first half of the menstrual cycle.
- When a TVUS is ordered, GPs should request that the report includes the endometrial thickness. The GP should also indicate on the request form the menopausal status of the patient (eg. pre, peri or post).

Endometrial Biopsy
- Invasive procedures should be undertaken (when possible) by the relevant specialist (gynaecologist, gynaecological oncologist).
- If insufficient material is obtained for a histological diagnosis, no further investigation is required in the absence of ongoing bleeding unless the woman has an endometrial thickness over 12mm for pre-menopausal women and 5mm for peri-menopausal women.
- Adequate samples from biopsies are more likely to be obtained if performed simultaneously with a hysterectomy.

DIAGNOSTIC HYSTEROSCOPY
- Diagnostic hysteroscopy is a highly specific, accurate, safe and clinically useful tool for detecting intrauterine abnormalities and to direct treatment at the specific pathology while avoiding needless surgery.
- A thick endometrium can obscure a complete view of the uterine cavity, so to achieve optimal visualisation diagnostic hysteroscopy should be performed in the follicular phase of the cycle.

DEFINITIONS
Abnormal vaginal bleeding: an increase in frequency, duration or volume of blood loss.
Conservative treatment: the use of hormone therapy or non-hormonal pharmacological therapy to reduce heavy bleeding, and control irregular bleeding. More aggressive treatment options include the surgical options of endometrial ablation or hysterectomy.
Pre-menopause: is characterised by continuation of regular menstrual cycles without any changes in the symptoms of menstruation transition or hormonal variability.
Peri-menopause: about or around the menopause. The average length of this stage is 5 years. Cyclic irregularities increase as women enter this stage with prolonged ovulatory and anovulatory cycles. Levels of follicle stimulating hormone and oestradiol oscillate frequently with decreasing luteal function.

ENDOMETRIAL THICKNESS IN PERI-MENOPAUSAL WOMEN
- Interpretation of endometrial thickness in the peri-menopausal woman is dependent on the time of the menstrual cycle during which the ultrasound is performed. Most accurate results are achieved if performed on days 4–7 of the cycle, when menses have ceased.

www.canceraustralia.gov.au
**VAGINAL BLEEDING IN POST-MENOPAUSAL WOMEN**

**A diagnostic guide for General Practitioners and Gynaecologists**

This guide was developed to assist general practitioners and gynaecologists in assessing post-menopausal women with vaginal bleeding, to maximise diagnostic accuracy for endometrial cancer. This is a general guide to appropriate practice to be followed subject to the clinicians’ judgement in each individual case, and is based on the best available evidence and expert consensus (February 2011). The Commonwealth does not accept any legal liability or responsibility for any loss or damages incurred by the reliance on, or interpretation of, information contained in this guide.

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**DEFINITIONS**

- **Post-menopausal bleeding:** spontaneous vaginal bleeding that occurs more than one year after the last episode of bleeding.

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**INVESTIGATIONS**

**Pelvic Exam**

- All women presenting with post-menopausal bleeding should have a pelvic examination. The speculum examination should include the cervix and vagina, and inspection of the vulva.

**Ultrasounds**

- Ultrasonography of endometrial thickness alone, using best quality studies cannot be used to accurately rule out endometrial hyperplasia or carcinoma.

**Transvaginal Ultrasound (TVUS)**

- TVUS is an initial screening tool for detecting intrauterine abnormalities.

**Hysteroscopy and D&C**

- Adequate samples from biopsies are likely to carry the same risks as other diagnostic procedures.

**ENDOMETRIAL BIOPSY**

- Invasive procedures should be undertaken (when possible) by the relevant specialist (gynaecologist, gynaecological oncologist).

- If a patient has post-menopausal bleeding and an endometrial thickness of greater than 4mm, an endometrial biopsy should be undertaken with an endometrial sampling device.

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**RISK FACTORS**

Risk factors for endometrial cancer include:

- History of chronic anovulation
- Exposure to unopposed oestrogen
- Polycystic ovary syndrome (PCOS) associated with chronic anovulation
- Exposure to tamoxifen
- Strong family history of endometrial or colon cancer (Lynch syndrome)
- Nulliparity
- Obesity (often with diabetes and hypertension)
- Endometrial thickness > 8 mm

**NB Natural hormones**

- There is no evidence of sufficient quality around the safety and efficacy of natural or bio-identical hormones. However, many of these preparations contain oestrogen and are likely to carry the same risks as other types of HRT. Bio-identical hormones come in the form of lozenges, troches or creams.

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**PRACTICE POINTS**

**Tamoxifen**

- Endometrial biopsy should be used to assess women on tamoxifen experiencing vaginal bleeding, as TVUS has been shown to be neither sensitive nor specific for neoplasia in these women.

**HRT**

- Vaginal bleeding or spotting may be an expected side effect of HRT, thus routine evaluations of the endometrium are not essential in the first 6 months. However, if bleeding persists after the initial 6 months, evaluation should be undertaken. Bleeding outside of the time of progestin withdrawal is deemed atypical for women using cyclic progestins, and requires investigation.

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**DEFINITIONS**

- **Pre-menopausal bleeding:** any vaginal bleeding that occurs more than one year after the last episode of bleeding.

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**HISTORY**

- All vaginal bleeding should be investigated.
- Dark, blood stained or ‘unusual for the woman’ discharge is a possible symptom of endometrial cancer. However, clear or yellow vaginal discharge is usually not indicative of a malignant aetiology.
- Review the patient’s history, especially with regard to risk factors, pattern of bleeding, the relationship between bleeding and the use of HRT.

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**RISK FACTORS**

- History of chronic anovulation
- Exposure to unopposed oestrogen
- Polycystic ovary syndrome (PCOS) associated with chronic anovulation
- Exposure to tamoxifen
- Strong family history of endometrial or colon cancer (Lynch syndrome)
- Nulliparity
- Obesity (often with diabetes and hypertension)
- Endometrial thickness > 8 mm

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**DEFINITIONS**

- **Pre-menopausal bleeding:** any vaginal bleeding that occurs more than one year after the last episode of bleeding.

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**GP**

- Full blood count (where indicated)
- Exclude cervical pathology: pap smear +/- chlamydia test
- Request transvaginal ultrasound (TVUS)
- Report to include endometrial thickness
- Endometrial thickness ≤ 4 mm
- Endometrial thickness > 4 mm or focal lesions
- GP surveillance* and reassessment with endometrial biopsy if persistent bleeding

**GP Surveillance**

- Women on Tamoxifen
- All other women with post-menopausal bleeding

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**REFER TO GYNAECOLOGIST**

- Refer to gynaecologist (consider transvaginal ultrasound (TVUS) prior to referral to assess for presence of polyps)
- Report to include endometrial thickness
- Endometrial thickness ≤ 4 mm
- Endometrial thickness > 4 mm or focal lesions
- GP surveillance* and reassessment with endometrial biopsy if persistent bleeding

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**REFER TO GYNAECOLOGICAL ONCOLOGIST**

- Refer to gynaecologist for endometrial biopsy (with or without hysteroscopy). Appointment should ideally be within 6 weeks of referral

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**PRACTICE POINTS**

- Endometrial biopsy should be used to assess women on tamoxifen experiencing vaginal bleeding, as TVUS has been shown to be neither sensitive nor specific for neoplasia in these women.

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**Definitive Management**

- All vaginal bleeding should be investigated.