Case 6
A 58-year-old woman with postmenopausal bleeding

Luisa Riglinski is 58-year-old cook at a local secondary school. She thinks her last menstrual period was about 6–7 years ago. Two months ago she had a few days of vaginal bleeding which was like the end of period and since then she has continued to spot most days. This is dark red or brown and she has taken to wearing panty liners. She has no pain or any associated symptoms. Initially she thought that her periods had restarted but a friend told her that she should see her GP. She has no pain or any other symptoms. She has never been on hormone replacement therapy (HRT).

What are the most likely causes of her bleeding?
- Endometrial cancer
- Atrophic vaginitis
- Local cervical lesion
- Cervical cancer
- Iatrogenic
- Chlamydia infection

What further questions would help to establish the diagnosis?

History of bleeding
Postmenopausal bleeding (PMB) is defined as bleeding more than 12 months since a woman’s last normal menstrual period so you need to establish when this was. You should ask about the amount and duration of bleeding and any associated symptoms. Try to clarify the site of bleeding to confirm that it is vaginal and not rectal or in her urine. Some women may find this very difficult to define.

Smear history
You need to check if she has attended for cervical screening and the result of her last smear test.

Drug history
Iatrogenic causes are important so you need to take a drug history. HRT is a common cause of PMB and if she is taking HRT, you need to ask about unscheduled bleeds; bleeding not at the time of the withdrawal bleed for women in taking a cyclical preparation or bleeding on continuous combined preparations. Check if she has had any problems with compliance, absorption (e.g. gastrointestinal upset) or metabolism (see Case 8).

Women currently or previously on tamoxifen are at increased risk of endometrial polyps, endometrial cancer and endometrial sarcoma although vaginal bleeding is a common side-effect.

Sexual history
Although Chlamydia infection is less common in older women, you should not ignore this as a possible cause. You do not need to take a full sexual history but you should ask if she has changed her sexual partner in the last 12 months.

KEY POINT
Women who continue to have periods after the age of 55 years also need to be investigated as for PMB.

Mrs Riglinski tells you that she has never been on HRT or tamoxifen (Box 6.1). She has no history of breast cancer. She had regular smears with normal results until the age of 55 but she declined the last invitation to attend. She did not want to be a ‘difficult patient’ but she found the examination to be too uncomfortable. Her husband is 68 years old and has been in a nursing home for the last year following a stroke. He had another stroke 2 months ago and she is worried that the stress of this event has
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caused her to bleed. She has not been sexually active since.

What would you look for on examination to aid your diagnosis?

Abdominal examination

There are unlikely to be any findings that will aid your diagnosis. Endometrial cancer usually presents with early stage disease which is confined to the uterus. It is rare for endometrial cancer to present at an advanced stage when there may be an omental cake (from tumour infiltration), peritoneal disease, liver enlargement or ascites.

Genital examination

It is important to look for local causes for bleeding including examination of the vulva. It is essential to perform a speculum examination to inspect the vagina and cervix. The finding of a clinical cervical cancer will prompt you to make an urgent referral. A bimanual examination may not be revealing. The uterus is small in postmenopausal women. Uterine enlargement may be incidental (e.g. caused by old calcified fibroids) and the uterus is not usually enlarged with a very early stage endometrial cancer. Less common are ovarian cysts, fibrothecomas, which produce oestrogen which causes endometrial hyperplasia and possible cancer. These ovarian tumours are benign and have the consistency of a fibroid on palpation. They are firm, well defined and mobile. However, it may be difficult to palpate the adnexa in postmenopausal women who find vaginal examinations uncomfortable. Obesity will also make pelvic examination difficult and you may not be able to feel the uterus clearly.

On examination, her vulva is normal and she has mild atrophic changes of her vagina and her cervix. She has some laxity of the vaginal walls but no significant prolapse. She has a small anteverted mobile uterus. You are unable to feel any adnexal masses.

Now review the possible causes of postmenopausal bleeding

• Endometrial cancer. You cannot exclude endometrial cancer from the history and examination and you need to consider further investigations.
• Atrophic vaginitis. You have found atrophic changes but you still need to exclude other pathology before you can attribute her symptoms to this. This can be treated by topical (intravaginal cream or pessary) oestrogens.
• Local cervical lesion. You have excluded local lesions such as a cervical polyp on your examination. Remember that ‘ectopy’ is related to high oestrogen levels and you should be suspicious of such a finding in a postmenopausal patient.
• Cervical cancer. Although she did not attend for her last smear, she has a previous negative screen history and you have not found a clinical cancer. As you have to perform a speculum examination, you should ask her if

Box 6.1 Tamoxifen

Tamoxifen is a non-steroidal oestrogen antagonist which is used widely as adjuvant treatment for women who have oestrogen receptor positive breast carcinoma. It reduces the risk of recurrence particularly during the first 5 years of treatment, decreases the overall progression of the disease and prevents disease in the contralateral breast. Long-term tamoxifen use is controversial because of its oestrogenic effects on the endometrium. Although it acts as an anti-oestrogen on breast cancer cells, it has a mild oestrogenic effect on the endometrium, bone and cardiovascular system.

Long-term use is associated with proliferative endometrium and a spectrum of benign and malignant changes of the endometrium have been reported including hyperplasia, polyps and carcinoma. The incidence of endometrial carcinoma in the postmenopausal women taking tamoxifen is significantly higher than women not on tamoxifen. Overall, the benefits of tamoxifen against breast cancer recurrence are greater than the risks of developing endometrial cancer.

EB is appropriate as the first line of investigation but you need to remember that a negative result is not conclusive. This will require further investigation by hysteroscopy. TV US appearances can be misleading as tamoxifen can give a sonotranslucent effect on both the endometrial stroma and myometrium. This results in false positive reports in cases of cystic atrophy which appears as thickened cystic endometrium on scan. Histology will confirm multiple cystic spaces lined by atrophic epithelium.

Hysteroscopy is the investigation of choice for women with PMB and a history of tamoxifen usage. It allows direct inspection of the endometrium and full-thickness biopsies using a resectoscope can be taken at the same procedure.
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you can take a smear to keep her screening up to date (not to diagnose cancer).

- *Iatrogenic.* She has not taken any medication that may cause vaginal bleeding.
- *Chlamydia infection.* You do not need to pursue this as she has not been sexually active in the last year.
- *Stress (as suggested by Mrs Riglinski).* Although some woman may relate bleeding to a stressful event, this does not cause PMB.

**What further investigations must you now consider?**

Women with PMB can be investigated effectively as outpatients.

**Transvaginal ultrasound scanning**

Transvaginal ultrasound (TV US) is an accurate method of excluding endometrial cancer. TV US identifies those women who need further investigation by endometrial biopsy (EB) on the basis of the scan findings. Findings that require further investigation by EB:

- Women with an endometrial thickness >4–5 mm (the exact cut-off will depend on local protocols)
- An irregular endometrial outline
- Fluid in the uterine cavity

Fifty percent of postmenopausal women scanned for the investigation of PMB will have a thin regular endometrium and can be reassured at this first visit that no further investigation is required. The negative predictive value is almost 100% in excluding endometrial cancer. This reduces the need for further intervention and allows you to provide reassurance for those women with a normal result.

**What do you do next?**

As her endometrial thickness is >4 mm, she requires further investigation. It is often not possible to clearly delineate normal atrophic postmenopausal ovaries. The aim of the scan is to look at the endometrial thickness and outline, although the sonographer may comment on other pelvic structures.

1 *Endometrial biopsy.* There are a number of different devices for obtaining an outpatient EB. If the scan finding represents a polyp, it is unlikely to be removed by EB.

**Figure 6.1** Transvaginal ultrasound scan result for Mrs Riglinski.

2 *Hysteroscopy.* Hysteroscopy is often used to investigate PMB as it allows direct inspection of the endometrium. It can detect intrauterine abnormalities and is a sensitive means of identifying polyps and submucous macroscopic findings. It can be used in the outpatient setting using a paracervical block for anaesthetic. Outpatient hysteroscopy is highly acceptable to women. Alternatively, it can be performed under general anaesthetic.

Mrs Riglinski agrees to have an outpatient hysteroscopy with a paracervical block. At hysteroscopy, the cervical canal is normal, the uterine cavity is smooth and regular with a fundal polyp. Both uterine coruna are seen. The polyp is removed using biopsy forceps and sent for histology (Fig. 6.2).

**KEY POINT**

You need to identify the tubal cornuae to confirm that the hysterocope is in the uterine cavity.

The report from the pathology laboratory confirms a simple endometrial polyp with no evidence of hyperplasia or malignancy.

**What further management is required?**

Mrs Riglinski does not require any further treatment. Polyp formation after the menopause can be related to tamoxifen or oestrogens. As she is not on HRT this may be related to obesity because of peripheral conversion of androgens (androstenidione) in subcutaneous fat to oestrogens. Polyps may recur but there is no need for follow-
You should advise Mrs Riglinski to contact her GP if she has further PMB occurring 6 months after her investigations for polyp removal. Remember to warn Mrs Riglinski that it is normal to have some spotting or discharge following the removal of the polyp.

What would have been the management if she was found to have an endometrial cancer?

Women with endometrial cancer confined to the uterus are usually curable by surgery and most women present with early stage disease. The treatment of choice is total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH/BSO) with peritoneal washings taken on opening the abdominal cavity for staging cytology.

When there is deep myometrial invasion or grade 3 disease, the prognosis with standard surgery alone is poorer because of the risk of spread to pelvic lymph nodes and recurrence. Endometrial cancer is radiosensitive and cure can still be achieved in early stage disease. Radiotherapy may also be given following surgery for women considered at increased risk of recurrent disease. Adjuvant radiotherapy is given to treat the pelvis by external beam with a caesium insertion to the vaginal vault and/or chemotherapy.

Women with endometrial cancer are often elderly with other medical problems and preoperative assessment for fitness for an anaesthetic and surgery is essential.

### CASE REVIEW

Postmenopausal bleeding is defined as bleeding more than 12 months since a woman’s last normal period. However, women who continue to menstruate after the age of 55 years, who have unscheduled bleeds on cyclical HRT or continue to bleed more than 6 months after starting continuous combined HRT also need to be investigated.

Transvaginal ultrasound scan should be the first line investigation as it allows good views of the pelvis and the endometrium. Transabdominal scanning may be used for the few women who cannot tolerate the intravaginal probe. Women with an endometrium measuring 5 mm or greater are at increased risk of endometrial cancer and require an endometrial biopsy. This can be performed at the same visit using an endometrial sampler. However, if the specimen is inadequate for histology, cancer has not been excluded and a hysteroscopy and biopsy are required to obtain an adequate biopsy or confirm the absence of endometrial pathology. Hysteroscopy should also be performed if an endometrial polyp is suspected on TV US.

Women with a history of taking tamoxifen, especially for longer than 5 years, are at increased risk of endometrial polyps, cancer and sarcoma. However, the effects on the endometrium and myometrium mean that TV US is not reliable and a hysteroscopy and full-thickness biopsy are essential to exclude cancer. Women who are asymptomatic on tamoxifen do not need to be investigated or screened for endometrial cancer.

Once endometrial cancer has been excluded, any local causes can be treated. Often reassurance is all that is required. Following investigation, women should be referred for further investigation if they continue to experience PMB after 6 months.
Key Points

- Women with PMB need to be investigated to exclude endometrial cancer
- About 8–10% of women with PMB will have endometrial cancer
- A further 1–2% will have a malignancy at another site, e.g. cervix, vulva, bladder or anus
- Visual inspection of the cervix is essential to identify cervical cancer
- TV US is an accurate method of excluding endometrial cancer and provides rapid reassurance to women with a thin and regular endometrium

- Women with a endometrial thickness >5 mm or an irregular contour require further investigation by endometrial biopsy +/- hysteroscopy
- Women with unscheduled bleeds on HRT need to be investigated
- Women on continuous combined HRT may initially have irregular bleeding but need to be investigated if this continues beyond 6 months
- The benefits of tamoxifen in breast cancer treatment outweigh the risks but any abnormal vaginal bleeding while on tamoxifen requires full investigation

Further reading