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Endometrial Sampling

Introduction

The endometrium is sampled when pathology, particularly endometrial cancer, is suspected; this may be when the patient experiences a change in her normal pattern of menstrual bleeding or when bleeding is unexpected - eg, after the menopause.

When a patient presents with any of these symptoms the GP should undertake a full pelvic examination, including speculum examination of the cervix.

Guidelines in the UK advising when to refer urgently state:^[1]

If the patient is aged over 55 with:

- Unexplained bleeding more than 12 months after her last menstrual period, **refer** using urgent cancer referral.
- Unexplained discharge:
 - If it is new; **or**
 - If she has thrombocytosis; **or**
 - If she reports haematuria - consider direct access ultrasound to assess the endometrium.
- Visible haematuria and:
 - A low Hb; **or**
 - Thrombocytosis; **or**
 - Raised blood glucose - consider direct access ultrasound to assess the endometrium.

If the patient is aged under 55 with:

- Unexplained bleeding more than 12 months after her last menstrual period, **consider** referral using urgent cancer referral.

Risk factors for endometrial cancer^[2]

These include:

- Obesity:
 - 70-90% of women with endometrial cancer are obese.
 - Endometrial cancer has the greatest association with obesity of all cancers, with a relative risk of 6.25.^[3]
 - The majority of women are unaware of the link between obesity and endometrial cancer.^[4]
- Diabetes more than doubles the risk.^[5]
- Hypertension.
- Insulin resistance and hyperinsulinaemia.^[6]
- Sedentary lifestyle.
- Oestrogen-related:
 - Anovulatory cycles - eg, polycystic ovary syndrome.^[7]
 - Nulliparity.
 - Early menarche.
 - Late menopause.
 - Tamoxifen.
 - Unopposed oestrogen HRT.
- Family history of endometrial or colonic cancer.

Initial investigations

- Transvaginal ultrasound measurement of endometrial thickness has become a routine procedure and an initial investigation in most patients with abnormal uterine bleeding (see guidelines above).
- There is debate as to whether a cut-off of 5 mm or 4 mm endometrial thickness should be employed. 5 mm has become standard for the postmenopausal patient.^[8]
- In the pre-menopausal patient, the timing of the ultrasound should be as close to the end of the bleeding period as possible.^[9]
- If the endometrial thickness is above these values, polyps have been diagnosed or the patient is presenting with recurrent bleeding, endometrial disease has to be excluded by histological assessment.

- It should also be noted that advanced endometrial cancer has subsequently been diagnosed where the endometrium was measured at ≤ 5 mm, so high-risk patients should also have histological sampling.^[10]
- Outpatient aspiration curettage has superseded dilatation and curettage (see below), which was previously considered to be the gold standard for obtaining an endometrial biopsy.
- Hysteroscopy additionally allows visualisation of the uterine cavity and the opportunity for targeted biopsy and removal of endometrial polyps.

Endometrial biopsy

- Introduced in the 1930s, originally using a narrow metal cannula with side opening with serrated edges and syringe attached for suction as the instrument was removed.
- As the cannula was rotated during removal, a strip of endometrium was peeled off and sucked into the syringe. This caused significant cramping during removal.
- Subsequently, the Vabra® curette was introduced, which required a vacuum source and also caused significant cramping.
- Today the most widely used device is the disposable Pipelle® also known as Pipelle de Cornier®.
- Can now be performed without prior cervical dilatation and can be undertaken as an outpatient procedure or in general practice.^[11]
- Transcervical instillation of 5 mls 2% lidocaine can be used and has been shown to significantly reduce pain during endometrial sampling.^[12]

Clinical Editor's comments (October 2017)

Dr Hayley Willacy recently read a report of a pilot study for endometrial sampling in general practice^[13]. In the first year of the service 108 samples were taken by general practitioners. Initial management of these patients was exclusively in primary care in 97.2% (104/108) of cases; most patients were treated with the Mirena intrauterine system 73.1% (79/109) and there were no cases of hyperplasia or cancer. Most premenopausal patients with abnormal uterine bleeding could potentially be managed in general practice without referral to hospital if endometrial sampling was made available to appropriately trained and supported GPs. This report coming nearly 20 years after the reference cited above.

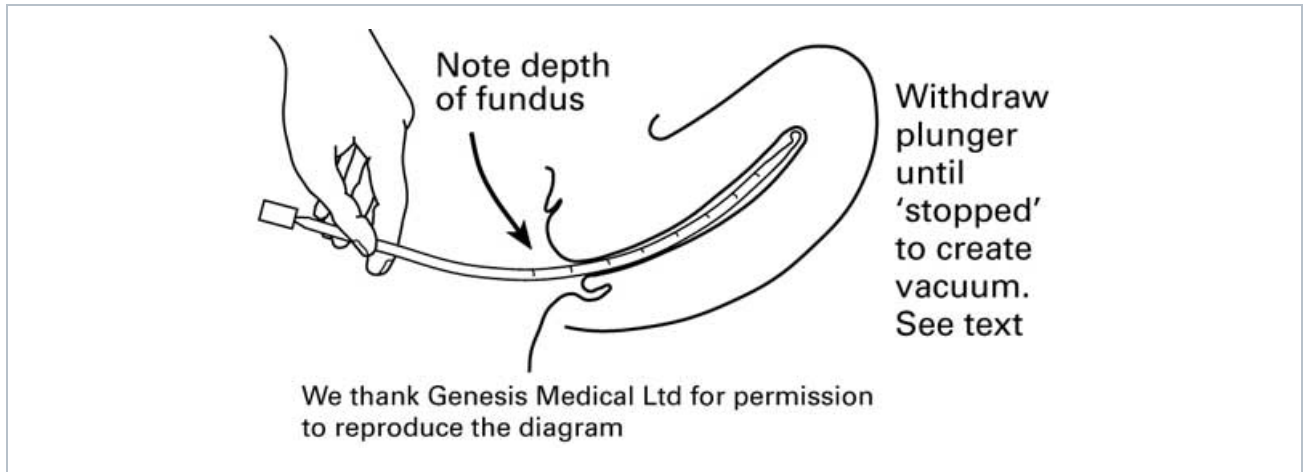
Pipelle® biopsy

- Pipelle® endometrial biopsy is a cost-effective and safe procedure that is well tolerated by patients.
- Pipelle® is a flexible polypropylene suction cannula with an outer diameter of 3.1 mm. For comparison, this is significantly narrower than the diameter of a Mirena® intrauterine system insertion tube, which is 4.4mm.^[14]
- There is less pain and a lower risk of perforation with the Pipelle® than with the Novak® curette.^[15]
- In addition, the Pipelle® is more portable than the Novak® curette and the Vabra® aspirator, both of which require external suction.
- A quantitative systematic review showed that, providing an adequate specimen is obtained, Pipelle® has a high positive predictive value. However, it also concluded that Pipelle® has a poor negative predictive value. Therefore if a woman is at high risk of endometrial carcinoma and her symptoms persist but her Pipelle® biopsy is normal, further evaluation is warranted.^[16]
- In postmenopausal women, the combined use of Pipelle® sampling and visualisation with either ultrasound or hysteroscopy, has a high detection rate for endometrial carcinoma.^[10]
- The Pipelle® is poor at detecting endometrial pathologies such as polyps and submucosal myomas.

Procedure

- A sexual history and screening for sexually transmitted infections should be considered
- Bimanual examination to assess the uterus.
- The cervix is then visualised.
- A tenaculum is applied to the anterior lip of the cervix and is used to provide gentle traction whilst a sound is inserted through the cervical os. This minimises the risk of perforation.
- Dilators may be required if there is difficulty in passing the sound.
- When the position and size of the uterine cavity have been assessed, the Pipelle® is inserted through the cervical os and advanced until gentle resistance is felt.

- The inner piston of the device is then withdrawn to create suction and the endometrial sample is obtained by moving the Pipelle® up and down within the uterine cavity by approximately 2-3 cm but not beyond the cervical os.



- This procedure should be repeated at least four times and the device rotated 360° to ensure adequate coverage of the area.
- The Pipelle® is then withdrawn from the cervical os and the endometrial sample expelled into a solution of formalin for transport to the laboratory.

Pipelle® endometrial sampling can also be combined with hysteroscopy.

Other devices include:

- The Gravlee Jet Washer®.
- The Mi-Mark® spiral sampler.
- The Gynoscann® surface stripper (based on the intrauterine contraceptive device (IUCD) insertion principle).
- The H Pipelle®.^[17]
- The Explora®.^[18]
- The Tao brush®.^[19]

Contra-indications

These include:

- Pregnancy.
- Acute vaginal or cervical infection.
- Pelvic inflammatory disease.
- Clotting disorders.

Risk of endocarditis is not a contra-indication and antibiotic prophylaxis is no longer recommended.^[20, 21]

Complications

These include:

- Prolonged bleeding.
- Infection.
- Uterine perforation and post-procedure pain.

Dilatation and curettage

This has been the traditional technique for obtaining samples of endometrium for pathological examination. However, 'blind' dilatation and curettage (D&C) has been shown to miss significant amounts of pathology, including:

- Endometrial polyps.
- Intrauterine mucous fibroids.
- Small areas of endometritis.
- Hyperplasia or cancer.
- Lost IUCDs.

Diagnostic curettage requires cervical dilatation to >8 mm and the use of a small sharp curette for systematic, thorough, gentle sampling of all parts of the uterine cavity, including the tubal ostial areas.

Fractional curettage uses endocervical curettage followed by endometrial curettage with two samples examined separately.

Endomyometrial resection biopsy

- 3-5 mm deep biopsy obtained with hystero-resectoscope loop.
- This is used to identify adenomyosis or to investigate deep lesions of the endometrium.
- It permanently removes a narrow strip of basal endometrium with underlying myometrium.
- This usually heals well.

Further reading & references

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