

# HKCOG Guidelines

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## Guideline on investigations of premenopausal women with abnormal uterine bleeding

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### 1 INTRODUCTION

Abnormal uterine bleeding (AUB) is a common problem in gynaecological practice and represents a major proportion of outpatient attendance. In a postal survey in the United Kingdom, AUB and its subgroup, heavy menstrual bleeding affected 15% to 25% of women aged 18 to 54 (1). In Hong Kong, the prevalence of AUB is not available but the following reference can provide some information. According to the 2014 HKCOG Territory Wide Audit, the numbers of hospital admissions with the diagnosis of 'Menorrhagia' and 'Dysfunctional uterine bleeding (DUB)' were 4,080 and 3,806 respectively (2). There were 6455 diagnostic hysteroscopies and 3075 hysteroscopic procedures (2). Of all operative hysteroscopic procedures, the numbers of polypectomy and myomectomy were 2468 (80%) and 380 (12%) respectively (2). While many patients with AUB might not require admission, the volume of work in the above report may reflect to some extent the scope of the problem locally.

As the patterns of investigation are diversified, a guideline on AUB was considered necessary. Premenopausal women will be targeted in this

guideline. Postmenopausal bleeding is caused by a different disease spectrum and will not be included in this guideline.

### 2 DEFINITIONS AND INITIAL INVESTIGATIONS FOR AUB

FIGO classified AUB in reproductive years into chronic and acute nongestational AUB (3). Chronic nongestational AUB is defined as bleeding from the uterine corpus that is abnormal in frequency, duration, regularity, and/or volume (Table 1), and has been present for the majority of the preceding 6 months. Acute AUB is defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to minimize or prevent further blood loss. Menorrhagia is heavy cyclical menstrual blood loss over several consecutive cycles without any intermenstrual or postcoital bleeding (i.e. without cycle disturbance). NICE defines heavy menstrual bleeding as excessive menstrual loss which interferes with a woman's physical, social, emotional and/ or material quality of life (4). Intermenstrual bleeding, pre and postmenstrual spotting, perimenopausal bleeding can be referred as dysfunctional uterine bleeding after exclusion of organic causes.

**Table 1. FIGO AUB symptoms**

Frequency	- Absent (no bleeding) = amenorrhoea - Infrequent (>38 days) - Normal ( $\geq 24$ to $\leq 38$ days) - Frequent (<24 days)
Duration	- Normal ( $\leq 8$ days) - Prolonged (>8 days)
Regularity	- Normal or regular (shortest to longest cycle variation $\leq 7$ to 9 days*) - Irregular (shortest to longest cycle variation $\geq 8$ to 10 days)
Flow volume (patient determined)	- Light - Normal - Heavy

\* The normal range (shortest to longest) varies with age: 18-25 y of age,  $\leq 9d$ ; 26-41 y,  $\leq 7d$ ; and for 42-45 y,  $\leq 9 d$ .

Obtaining a good menstrual history is mandatory to guide the clinician in making the correct diagnosis and help to understand the impact on a woman's quality of life (Appendix 1). On general examination, any pallor or thyroid gland enlargement should be noted. If there are features suggestive of thyroid dysfunction or coagulopathy from history or physical examination, a thyroid function test or coagulopathy screening can be ordered accordingly. History suggestive of coagulopathy includes heavy menstrual bleeding since menarche, a family history of coagulopathy, easy bruising, gum bleeding and epistaxis. Routine thyroid function test or coagulopathy screening however is not recommended in all patients with menorrhagia. A speculum examination and bimanual examination could elucidate causes for abnormal bleeding such as cervical polyp, cervical carcinoma, uterine fibroids, adenomyosis and ovarian tumours etc (Appendix 1). The following investigations can be arranged depending on the clinical situation: (1) complete blood count to look for any anaemia (2) pregnancy test (3) ultrasound scan especially if physical examination suggests a pelvic mass (4) endometrial assessment (5) cervical smear if due and (6) Chlamydia screening in cases of post-coital bleeding or intermenstrual bleeding.

### 3 ENDOMETRIAL ASSESSMENT

Essentially there are five methods of endometrial assessment namely, ultrasound scan, MRI, endometrial biopsy or aspirate, hysteroscopy and dilatation and curettage (D&C) under various modes of anaesthesia.

#### 3.1 Ultrasound scan

Ultrasound scan, particularly the transvaginal route, is used to assess endometrial thickness, endometrial and myometrial consistency and abnormalities of endometrial lining like submucosal fibroid or polyp etc. Most of the studies however were on the endometrial thickness of postmenopausal women. According to Smith Bindman et al (5), the average endometrial thickness for normal postmenopausal women was 4 mm, those with endometrial polyp 10 mm, those with endometrial hyperplasia 14 mm and endometrial carcinoma 20 mm. However, the prediction of

endometrial pathology based on ultrasound scan in premenopausal women is not as reliable because of the great overlap between normal range and those with endometrial pathology.

The NICE guideline (4) had recommended that in patients with examination suggestive of fibroid, a pelvic ultrasound should be performed. Depending on the size of the uterus, a transvaginal ultrasonography or transabdominal ultrasonography could be performed. Transvaginal ultrasonography produces better image quality. This is achieved because of its higher frequency which allows greater image resolution at the expense of decreased depth of penetration. In patients whom physical examination is not possible or unsatisfactory, or symptoms persist despite medical treatment, an ultrasound should also be arranged. Pelvic ultrasound can be of use in detecting gross endometrial or myometrial pathology such as fibroids and adenomyosis. However, pelvic ultrasonography does not replace an endometrial biopsy.

In cases where vaginal access is difficult or impossible, such as in adolescents and virginal girls, trans-rectal ultrasonography should be offered. It had been shown to provide better image quality when compared with the trans-abdominal route without causing significant patients' discomfort (6).

Saline infusion sonohysterography (SIS) involves the instillation of 5-15 ml of normal saline into the uterine cavity and may allow better detection of endometrial polyp and submucosal fibroid. A meta-analysis in 2017 concluded that 2D SIS is highly sensitive for endometrial polyps and submucosal uterine fibroids with a pooled sensitivity of 93% and 94% and specificity of 81% and 81% respectively (7). SIS can be considered in cases where further evaluation of endometrial lesion is required.

#### 3.2 MRI

MRI was shown to be more sensitive than transvaginal ultrasound in the identification of fibroids, especially for the growth of submucosal fibroid into the uterine cavity (8). MRI is slightly more sensitive than transvaginal ultrasound in diagnosing adenomyosis (sensitivity 77% versus

72%) (9, 10). However, the chance of identifying important additional findings from MRI over ultrasound has to be weighed balance against the waiting time and its cost. It should not be the routine for all cases of AUB. In cases where vaginal access is difficult or impossible, or when there is difficulty in differentiation between fibroid and adenomyosis, there is a role for MRI.

### 3.3 Endometrial biopsy

The main purpose of obtaining an endometrial biopsy or endometrial aspirate is to exclude endometrial pathology like hyperplasia, disordered endometrium or malignancies. Most endometrial biopsies can be performed in outpatient or office clinics and have the advantage of being simple, quick, safe, convenient and avoiding the need for anaesthesia. Furthermore, the device is disposable and is much less costly than a conventional dilatation and curettage (D&C).

Pipelle is the most common outpatient endometrial assessment device used in the United Kingdom and Hong Kong. Other devices includes Novak (a silastic cannula with a beveled lateral opening), Tis-u-Trap (a plastic curette with suction), Vabra aspirator (a cannula connected to a vacuum pump), Endorette (a plastic cannula with multiple openings), Tao Brush (a sheath brush device), Cytospat (a polypropylene cannula with a rhomboid head), Accurette (a quadrilateral shaped curette with four cutting edges), Explora (a plastic curette with Randall-type cutting edge) and Z-sampler (flexible polypropylene device). A meta-analysis including 60 articles found that Pipelle perform as well as D&C and as well as or better than other endometrial sampling devices in terms of sampling adequacy and sensitivity. Pipelle seems to be better in terms of pain/ discomfort and costs (11). The sample adequacy rate was consistently high for Pipelle, mostly >85%, compared to 98% for D&C (11). The specimen adequacy rate and concordance rate to histology on hysterectomy were similar to D&C. Pipelle biopsy is reliable in excluding endometrial carcinoma. Previous studies had shown that Pipelle detected 98% of

endometrial carcinomas (12).

A study has shown that the Vabra device can sample more endometrium (42%) compared with Pipelle (4%) (13). However, other studies did not find a better specimen adequacy rate of Vabra device over Pipelle (14, 15).

Endometrial cancer is thought to be uncommon in women under the age of 40 and this was also the local experience (16). The Hong Kong Cancer Registry report in 2017 showed that out of a total of 1076 new cases of cancer of corpus, only 47 cases (4.4%) occurred in women under 40 (16). Though endometrial cancer is uncommon in women aged <40, its number is increasing. In 2017, the age specific incidence for endometrial carcinoma in various age group were: 4 per 100,000 for women at 30, 9 per 100,000 for women at 35, and 18 per 100,000 at 40. The incidence rose sharply to 66 per 100,000 for women at 50, and 64 per 100,000 when women reached 55 and peaked at 50-54 (16). In 2007, the figures were 2 per 100,000 for women at 30, and 6 per 100,000 for women at 35.

At what age should the gynaecologist perform endometrial biopsy? It had been suggested that routine endometrial biopsy is not necessary for AUB in women <40 years old. However, in view of the increasing incidence of endometrial cancers among younger women, an endometrial assessment is warranted for women <40 years old presenting with AUB and other high risk features (Table 2). Instead of choosing arbitrarily an age at which endometrial biopsy should or should not be done, the woman's risk of having endometrial carcinoma should be assessed. Women at high risk of endometrial cancer would need endometrial biopsy regardless of age. Therefore, HKCOG recommends endometrial biopsy in all women with AUB at or above the age of 40, and in women with risk factor for endometrial carcinoma irrespective of age. Those patients with persistent symptoms or having failed medical treatment should have endometrial biopsy as well.

**Table 2. Risk factors for endometrial cancer**

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| <ul style="list-style-type: none"> <li>a. Obesity</li> <li>b. Polycystic ovarian syndrome</li> <li>c. Lynch syndrome</li> <li>d. Family history of gynaecological and gastrointestinal malignancy</li> <li>e. Unopposed oestrogen therapy</li> <li>f. Tamoxifen therapy</li> <li>g. Persistent or long standing AUB</li> <li>h. Not responding to medical treatment</li> </ul> |
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### 3.4 Hysteroscopy

Hysteroscopy allows direct visualization of the whole endometrial cavity, lower segment and cervical canal. Hysteroscopy can detect small polyp or submucosal fibroid and provide an opportunity for endometrial biopsy without the need of general anaesthesia. The NICE guideline recommends outpatient hysteroscopy for women with uterine cavity abnormalities or when endometrial pathology is suspected because it is more accurate than pelvic ultrasound (4). A study in Hong Kong showed that out-patient hysteroscopy was successful in 92% of patients (17). Prospective studies had shown that diagnostic hysteroscopy had significantly better diagnostic performance compared to saline infusion sonohysterography (SIS) and transvaginal ultrasound (TVS) (18). The sensitivity and specificity for any uterine abnormality for SIS and TVS were 92% versus 89% and 60% versus 56% respectively. The sensitivity and specificity for diagnostic hysteroscopy were 97% and 92% respectively (18). The patients' acceptability was high and the failure rate was low; the latter was mainly due to pain during the procedure, distorted uterine cavity, and tight cervical os especially in postmenopausal and nulliparous patients. The last problem can partially be overcome by hysteroscope of smaller diameter (minihysteroscopy). A "no touch" approach with vaginoscopy had been shown to be quicker, less painful, and more successful than standard hysteroscopy and can be considered for outpatient hysteroscopy (19).

A randomized controlled trial (20) comparing transvaginal ultrasound, outpatient hysteroscopy and endometrial biopsy with inpatient hysteroscopy and curettage showed that a

combination of transvaginal scan, Pipelle endometrial biopsy and outpatient hysteroscopy had similar efficacy to inpatient hysteroscopy and curettage for the investigation of AUB. Transvaginal scan and endometrial biopsy can therefore be considered as the first line investigation followed by outpatient hysteroscopy.

Some authors suggested that a normal cavity on hysteroscopy will obviate the need for an endometrial biopsy. However normal findings at hysteroscopy are not conclusive of absence of premalignant or malignant lesion and do not eliminate the need for endometrial sampling as they are not substitute for benign findings on histological examination (21).

### 3.5 D&C

D&C and endometrial histology so obtained were considered as the 'gold standard' in the management of AUB previously. However, multiple studies had shown that D&C is not superior to an endometrial assessment with Pipelle, or other outpatient endometrial assessment devices, while D&C requires general anaesthesia. D&C only should no longer be the gold standard in assessing endometrial pathology. D&C with concurrent hysteroscopy may be useful in women whom intrauterine lesions is suspected as it allows direct visual assessment of the endometrial cavity. For patients where outpatient hysteroscopy or endometrial biopsy is not possible, in-patient hysteroscopy and D&C under general anaesthesia should be offered. D&C does not have therapeutic value in AUB except in stopping heavy menstrual bleeding temporarily.

## 4 SUMMARY OF RECOMMENDATIONS

- 4.1 The chance of endometrial carcinoma in women below the age of 40 is low. However, an endometrial assessment is warranted if there are risk factors for endometrial carcinoma or if symptoms are persistent / long standing or symptoms fail to respond to medical treatment.
- 4.2 Pelvic ultrasound (preferably transvaginal ultrasound) and endometrial sampling with Pipelle are the preferred first line methods of assessing AUB. Hysteroscopy is indicated if uterine cavity abnormality is suspected.
- 4.3 Out-patient hysteroscopy is safe and reliable and should be the preferred setting for diagnostic hysteroscopy.
- 4.4 Routine first line D&C should be discouraged. D&C should be reserved for women requiring general anaesthesia for other indications.

The recommendations are also summarized in the appended flow-chart (Appendix 2).

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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.

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**History**

Menstrual history:

- Frequency
- Regularity
- Duration
- Amount
- Presence of intermenstrual or post-coital bleeding

Associated symptoms:

- Dysmenorrhea
- Dyspareunia
- Chronic pelvic pain
- Pressure symptoms
- Abnormal vaginal discharge

Presence of systemic disorders:

- Recent weight gain / weight loss
- Obesity
- PCOS
- Endocrine disorders: thyroid, pituitary, adrenal
- Bleeding tendencies
- Drug: Tamoxifen, unopposed estrogen, anti-coagulants, anti-platelets, anti-psychotics (first generation and risperidone), herbal medicines

Sexual and reproductive history:

- Contraception and risk of pregnancy
- Risk of sexually transmitted disease
- Desire for future pregnancy
- Up-to-date cervical smear

Family history:

- Coagulopathy
- Malignancy (especially endometrial, ovarian, colorectal, urological)
- Venous thromboembolism

Impact on women:

- Presence of anaemic symptoms
- Impact on quality of life

**Physical examination:**

General examination:

- BMI
- Pallor
- Signs of thyroid disease, Cushing's, hyperandrogenism
- Signs of bleeding tendencies: bruising, petechiae

Abdominal examination:

Presence of abdominal / pelvic mass

Speculum and bimanual examination:

- Look for anatomical causes (e.g polyp, fibroid)
- Uterine size
- Adnexal mass

<b>Screening tool for coagulopathies by a structured history:</b>
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A positive screening result comprises any of the following:
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1. Heavy menstrual bleeding since menarche
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2. One of the following:
A. Postpartum haemorrhage
B. Surgical related bleeding
C. Bleeding associated with dental work

3. Two or more of the following symptoms:
A. Bruising 1-2 times per month
B. Epistaxis 1-2 times per month
C. Frequent gum bleeding
D. Family history of bleeding symptoms

Patient with a positive screening result should be considered for further evaluation including haematologist consultation
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**Clinical Evaluation of Abnormal Uterine Bleeding for Premenopausal Women**

