

Up to date guidance

Abnormal uterine bleeding

Dr Ho San Ni
Specialist in O&G



Introduction

- The normal menstrual cycle lasts 28 ± 7 days, the flow lasts 4 ± 2 days, and the average blood loss is 40 ± 20 ml
- **Abnormal uterine bleeding** (AUB) is defined as changes in frequency of menses, duration of flow or amount of blood loss.
- **Menorrhagia** (hypermenorrhoea) is defined as heavy cyclical menstrual bleeding occurring over several consecutive cycles during the reproductive years.
- Objectively menorrhagia is defined as blood loss of more than 80 ml per cycle, the 90th percentile in a study of 476 Gothenberg women published by Hallberg *et al.* in 1966.
- Monthly blood loss in excess of 60 ml may result in iron deficiency anemia and may affect the quality of life.

OVERVIEW

- Modern management of abnormal uterine bleeding
- Medical management
- Surgical management and fibroid management
- Recommendation
- Common presentations of abnormal uterine bleeding

Diagnostic approach to abnormal uterine bleeding

- History
- It is important to distinguish anovulatory AUB, which is more likely to lead to endometrial hyperplasia, from ovulatory AUB.
- Women presenting with ovulatory AUB will likely have heavy cyclical menstrual blood loss over several consecutive cycles without any intermenstrual or postcoital bleeding.
- They may have dysmenorrhea associated with passing of clots. Premenstrual symptoms also suggest ovulatory cycles.
- The history should include symptoms suggestive of other pathology, such as irregular bleeding, postcoital bleeding, and pelvic pain.
- Polyps or submucous fibroids are present in 25 to 50 percent of women who present with irregular bleeding

Diagnostic approach to abnormal uterine bleeding

- **DIAGNOSIS**
- A thorough abdominal and pelvic examination is essential.
- Cervical cytology should be obtained if indicated.
- A complete blood count (CBC \pm ferritin) is needed to determine degree of anemia.
- Other investigations to be considered include:
 - Thyrotropin stimulating hormone, when other symptoms of thyroid dysfunction are present;
 - Prolactin; day 21 to 23 progesterone to verify ovulatory status;
 - follicular stimulating hormone and luteinizing hormone to verify menopausal status or support a diagnosis of polycystic ovarian disease;
 - a coagulation profile when menorrhagia is present at puberty or if there is a clinical suspicion for a coagulopathy.

Diagnostic approach to abnormal uterine bleeding

- **ASSESSMENT OF THE ENDOMETRIUM**
- Endometrial assessment is performed to diagnose malignancy or pre-malignant conditions
- Sampling of the endometrium should be considered in all women:
 - >40 years with abnormal bleeding;
 - in women who are at higher risk of endometrial cancer, including:
 - nulliparity with a history of infertility;
 - new onset of heavy,
 - irregular bleeding; obesity (≥ 90 kg);
 - polycystic ovaries; a family history of endometrial and colonic cancer; and on tamoxifen therapy.
 - a woman who has no improvement in her bleeding pattern following a course of therapy of three months.

Diagnostic approach to abnormal uterine bleeding

- **TECHNIQUES FOR ENDOMETRIAL SAMPLING**
- Office endometrial biopsy results in adequate samples 87 to 97 percent of the time and detects 67 to 96 percent of endometrial carcinomas.
- Although the choice of sampling device may affect accuracy, no existing method will sample the entire endometrium.
- Hysteroscopically-directed sampling detects a higher percentage of abnormalities when compared directly with dilatation and curettage (D&C) as a diagnostic procedure.
- Even if the uterine cavity appears normal at hysteroscopy, the endometrium should be sampled since hysteroscopy alone is not sufficient to exclude endometrial neoplasia and carcinoma.

Diagnostic approach to abnormal uterine bleeding

- **DILATATION AND CURETTAGE**
- In 10 to 25 percent of women D&C alone does not uncover endometrial pathology.
- D&C was associated with uterine perforation in 0.6 to 1.3 percent of cases and hemorrhage in 0.4 percent of cases.
- D&C is a blind procedure with significant sampling errors; it also requires anesthesia which carries a risk of complications.
- It should be reserved for those situations where office biopsy or directed hysteroscopic biopsy are not available or feasible.

Diagnostic approach to abnormal uterine bleeding

- **ULTRASOUND EXAMINATION OF THE ENDOMETRIUM**

- Transvaginal sonography (TVS) assesses endometrial thickness and detects polyps and myomata with a sensitivity of 80 percent and specificity of 69 percent.
- Although there is evidence that endometrial thickness may be indicative of pathology in the postmenopausal woman, such evidence is lacking for the woman in her reproductive years.
- Meta-analysis of 35 studies showed that in menopausal women, endometrial thickness of five mm at ultrasound has a sensitivity of 92 percent for detecting endometrial disease and 96 percent for detecting cancer.

- **SALINE SONOHYSTEROGRAPHY**

- The introduction of five to 15 m of saline into the uterine cavity using a saline primed catheter or a pediatric feeding tube may improve the diagnosis of intrauterine masses during TVS



Treatment of abnormal uterine bleeding

- **MEDICAL MANAGEMENT**
- Age, desire to preserve fertility, coexisting medical conditions, and patient preference are essential considerations.
- For each of the suggested methods, the patient should be aware of the risks and contraindications to allow informed choice.
- The degree of patient satisfaction may be influenced by efficacy, expectations, cost, inconvenience, and side effects.

Treatment of abnormal uterine bleeding

- **NON-STEROIDAL ANTI-INFLAMMATORY DRUGS**
- Endometrial prostaglandins are elevated in women with heavy menstrual bleeding.
- Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase and reduce endometrial prostaglandin levels.
- In a review of randomized controlled trials, NSAIDs taken with menses decrease menstrual blood loss by 20 to 50 percent.
- NSAIDs improve dysmenorrhea in up to 70 percent of patients.
- Therapy should start at the first day of menses and be continued for five days or until cessation of menstruation. (I A)

Treatment of abnormal uterine bleeding

- **ANTIFIBRINOLYTIC AGENTS**

- Tranexamic acid (cyclokapron), a synthetic derivative of the amino acid lysine, exerts an antifibrinolytic effect through reversible blockade on plasminogen.
- The drug has no effect on blood coagulation parameters or dysmenorrhea.
- One third of women experience side effects, including nausea and leg cramps.
- Tranexamic acid one g every six hours for the first four days of the cycle reduces menstrual blood loss by up to 40 percent, based on 10 randomized placebo-controlled trials. (I A)

Treatment of abnormal uterine bleeding

- **PROGESTINS**

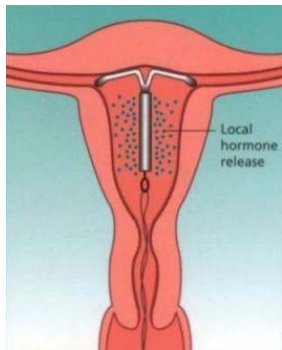
- Randomized controlled trials have shown cyclic progestins to be ineffective in controlling regular heavy menstrual bleeding compared to NSAIDs and tranexamic acid.
- Progestins may be useful for women with irregular cycles and with anovulatory cycles when given for 12 to 14 days of each month.
- Medroxyprogesterone acetate given for contraception induces amenorrhea within the first year in 80 percent of women, although as many as 50 percent experience irregular bleeding.

Treatment of abnormal uterine bleeding

- **COMBINED ORAL CONTRACEPTIVE PILL**
- The reduction of menstrual blood loss with the combined oral contraceptive pill (OC) is probably the result of induced endometrial atrophy.
- A randomized controlled trial of women taking an OC containing 30 μ g ethinyl estradiol showed a 43 percent reduction in menstrual blood loss compared to baseline.
- 47 Two longitudinal case control studies have found that users were less likely to experience heavy menstrual bleeding or anemia.
- Additional advantages of OCs include contraception and reduction of dysmenorrhea

Treatment of abnormal uterine bleeding

- **PROGESTIN INTRAUTERINE SYSTEM**
- Progesterone impregnated intrauterine devices (IUDs) have been reported to reduce menstrual bleeding.
- The newest levonorgestrel intrauterine system (LNG-IUS) is a T-shaped IUD which releases a steady amount of levonorgestrel ($20 \mu\text{g}/24 \text{ hrs}$) from a steroid reservoir around the vertical stems of the device.



**Mirena**[®]
Levonorgestrel

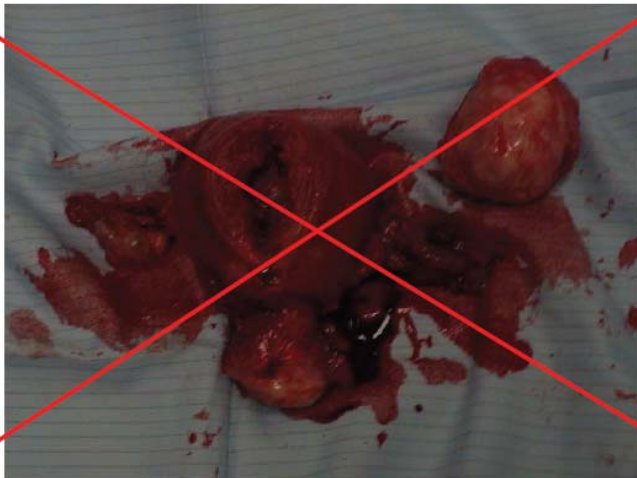
Treatment of abnormal uterine bleeding

- **GNRH AGONISTS**

- GnRH agonists induce a reversible hypoestrogenic state, reducing total uterine volume by 40 to 60 percent.
- Myomas and uterine volume expand to pretreatment levels within months of cessation of therapy.
- GnRH agonists are effective in reducing menstrual blood loss in perimenopausal women, but are limited by their side effects, including hot flashes and reduction of bone density.

Surgical treatment and fibroid management

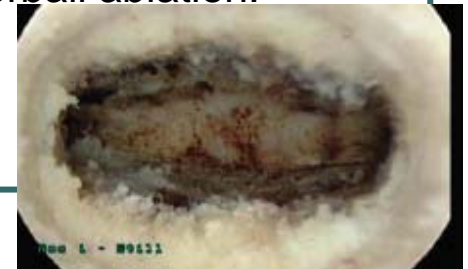
- Routine hysterectomy



- **HYSTERECTOMY**
- The risks of major surgery must be weighed against alternatives.
- Hysterectomy is a permanent solution for the treatment of menorrhagia and abnormal uterine bleeding, and is associated with high levels of patient satisfaction in properly selected patients.
- For the woman who has completed her childbearing, reviewed the alternatives, and has tried conservative therapy without acceptable results, hysterectomy is often the best choice.

Surgical treatment and fibroid management

- **Endometrial destruction can be performed by several surgical techniques.**
- Hysteroscopic endometrial ablation with photocoagulation, rollerball, electrocoagulation or loop resection, have shown satisfaction rates of approximately 85 percent..
- Patients undergoing surgery after age 40 years appear to have a better outcome.
- There is no clear evidence that the presence of fibroids or dysmenorrhea prior to endometrial ablation surgery reduces the rates of success. Preoperative medical treatment does not appear to improve long-term outcome but does improve ease of surgery and short-term amenorrhea rates
- Reoperation rate at five years may be up to 40 percent with rollerball ablation.



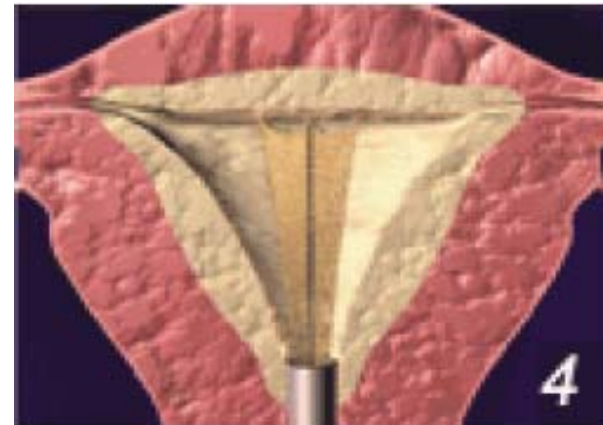
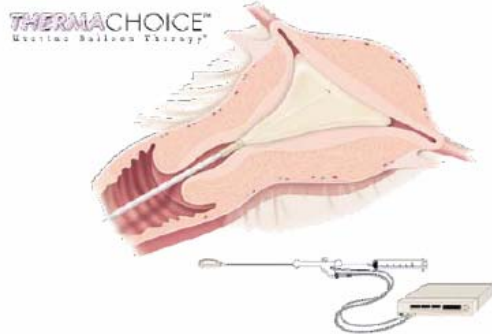
Surgical treatment and fibroid management



- Global endometrial ablation, recently reviewed by Vilos, was introduced in the 1990s as an easier, safe, and equally effective alternative to hysteroscopic ablation.
- Several different devices, some of which are still undergoing feasibility studies or clinical trials, have been introduced, including: hot water intrauterine balloons, intrauterine free saline solution, an electrocoagulating balloon, a 3-D bipolar electrocoagulation probe, a microwave device, a diode fibre laser, and several different cryoprobes.
- These devices require less operator skill than for hysteroscopic endometrial ablation and no irrigant or distending solutions.
- All utilize either heat or cold to destroy the endometrium. Although all devices are promising and have produced impressive preliminary results, the long-term efficacy, complication rates, and cost effectiveness have not been established.

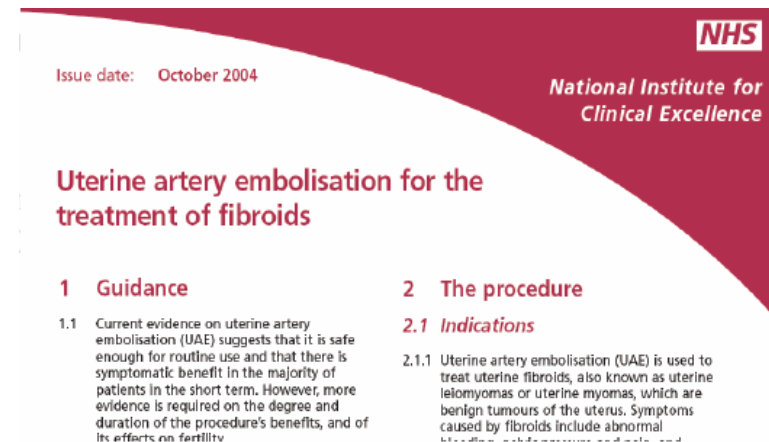
Surgical treatment and fibroid management

- Since all procedures are performed without hysteroscopic visualization (except hydrothermablation), it would be prudent to perform hysteroscopy prior to and following the treatment to ensure that only the endometrial cavity has been treated.
- False passages and partial or complete uterine perforations occur at a frequency of 0.8 to 1.5 percent and may result in adjacent organ injury.



Fibroids management

- Medical
 - TXA, MFA, Progestogens, GnRH-a
- Radiological
 - Uterine artery embolisation
- Surgical
 - Endometrial ablation
 - Sound length < 12 cm
 - Regular cavity (no distorting SMFs)
 - Myomectomy
 - Hysteroscopic +/- endometrial ablation
 - Laparoscopic
 - Open
 - Hysterectomy



Recommendation

- 1. Women with irregular menstrual bleeding should be investigated for endometrial polyps and/or submucous fibroids.(II-2 B)
- 2. Women presenting with menorrhagia should have a current cervical cytology and a complete blood count. Further investigations are individualized. It is useful to delineate if the bleeding results from ovulatory or anovulatory causes, both in terms of tailoring the investigations and in choosing a treatment. (III B)
- 3. Clinicians should perform endometrial sampling based on the methods available to them. An office endometrial biopsy should be obtained if possible in all women presenting with abnormal uterine bleeding over 40 years of age or weighing more than or equal to 90 kg. (II B)
- 4. Hysteroscopically-directed biopsy is indicated for women with persistent erratic menstrual bleeding, failed medical therapy or transvaginal saline sonography suggestive of focal intrauterine pathology such as polyps or myomas. Women with persistent symptoms but negative tests should be reevaluated. (II B)

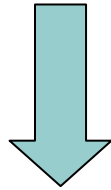
Recommendation

- 5. Progestogens given in the luteal phase of the ovulatory menstrual cycles are not effective in reducing regular heavy menstrual bleeding . (I A)
- 6. While dilatation and curettage (D&C) may have a diagnostic role, it is not effective therapy for women with heavy menstrual bleeding. (II B)
- 7. The endometrium can be destroyed by several different techniques but reoperation rate at five years may be up to 40 percent with rollerball ablation. This should be reserved for the woman who has finished her childbearing and is aware of the risk of recurrent bleeding. (I A)

Example : Old vs new approaches: uterine polyp

- Inpatient :

- Abnormal uterine bleeding



- Hysteroscopy/ D&C under GA

- Office

- Abnormal uterine bleeding



- Pelvic Ultrasound



- Outpatient hysteroscopic polypectomy

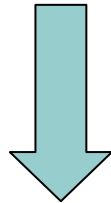
Example : Old vs new approaches: submucous fibroid

- **Inpatient**

- Abnormal uterine bleeding



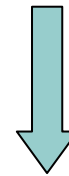
- Hysteroscopy/ D&C under GA



- Reschedule for hysteroscopic resection under GA or hysterectomy

- **Office**

- Abnormal uterine bleeding



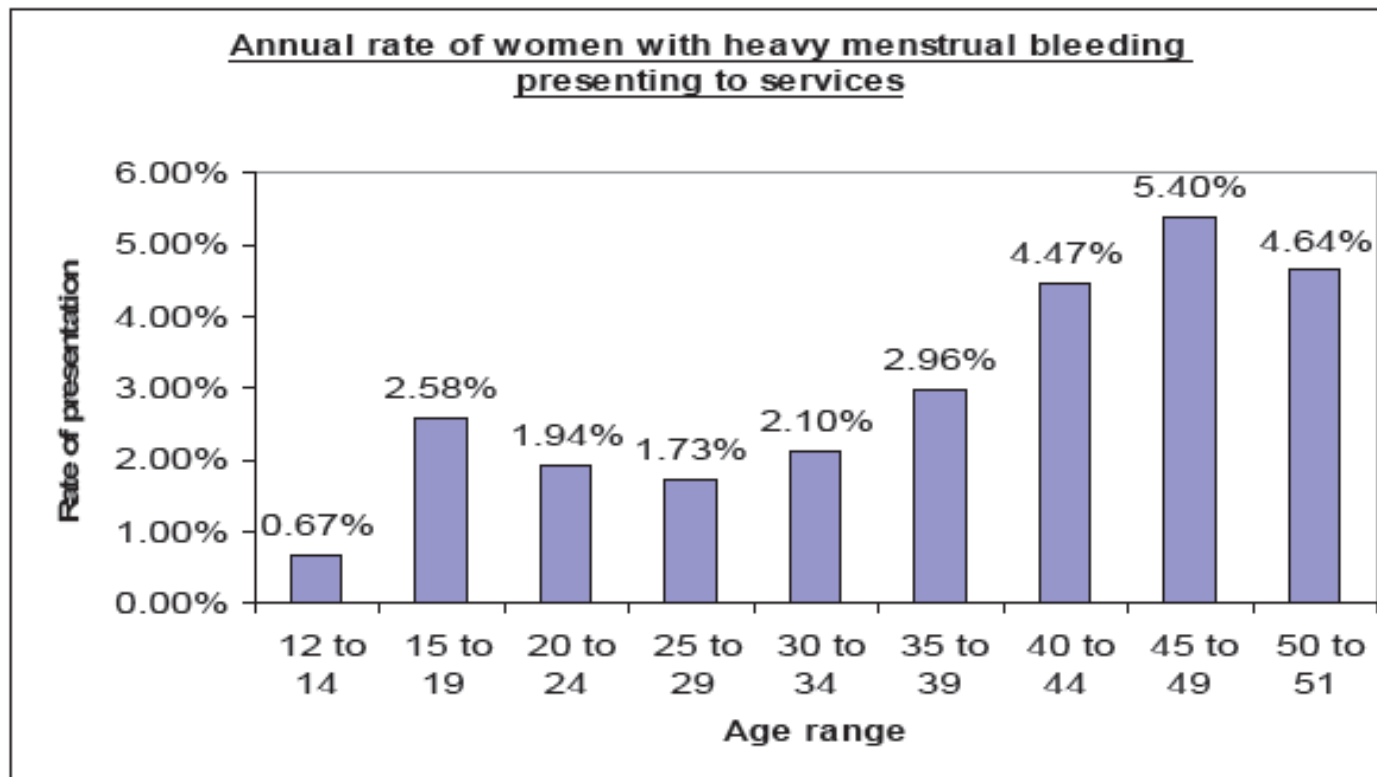
- Pelvic ultrasound



- Outpatient hysteroscopic resection of fibroid or scheduling for GA procedure (hysteroscopic resection or hysterectomy)

Incidence and prevalence of menorrhagia

- Affects approximately 880,000 women in England



Likely cause of heavy menstrual bleeding

Common

Dysfunctional Uterine Bleeding

- Ovular
- Anovular (endometrial hyperplasia)

Fibroids

- Submucous
- Intramural

Less common

Gynaecological disease

- Endometriosis
- Adenomyosis
- Diffuse myometrial hypertrophy
- Pelvic inflammatory disease
- Intrauterine polyps

Pregnancy related

- Retained products of conception

Iatrogenic

- Intrauterine contraceptive devices
- Exogenous sex hormones
- Anticoagulants

Rare

Gynaecological cancer

- Uterus
- Ovary (theca and granulosa cell tumours)

Endocrine

- Thyroid dysfunction

Haematological

- von Willebrand's disease
- Idiopathic thrombocytopenia

Common presentations:

- **Heavy regular periods + fibroids**

- In the presence of fibroids pharmacological treatment more likely to fail – earlier referral to secondary care for

- Myomectomy

- Hysteroscopic

- Open

- Radiological (uterine artery embolisation)

- Hysterectomy

- Laparoscopic / vaginal

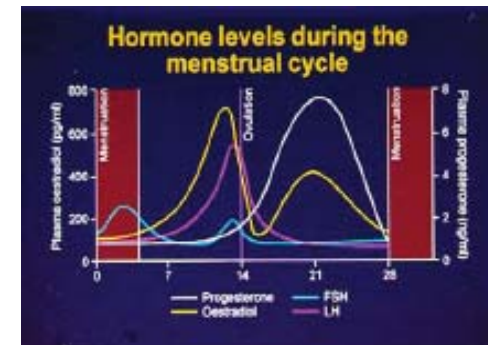
- Open



Take Home message = Fibroids are common; symptoms more resistant to standard pharmacological treatment and endometrial ablation

Common presentations:

- Heavy irregular periods
- Likely diagnosis
 - Dysfunctional uterine bleeding
 - Anovulation
 - Endometrial hyperplasia
- Treatment
 - First line
 - Hormonal
 - OCP
 - Mirena
 - Cyclical systemic progestins
 - Second- line therapy
 - Endometrial ablation
 - Hysterectomy



Takee Home message = Erratic menstruation requires hormonal or surgical management; further endometrial assessment (biopsy +/- hysteroscopy) is required if >40 years or obese

Common presentations:

- **Heavy periods in Teenagers / Young**
- Likely diagnosis
 - “Dysfunctional uterine bleeding”
 - Anovulation
 - But consider Heamatological problem
 - Von Willebrand’s disease
 - Platelet disorder
- First –line therapy
 - Hormonal
 - OCP
 - Cyclical systemic progestins
- Second line therapy
 - Heamatologist / Desmopressin Endometrial ablation (Octim nasal spray)
 - ~~Endometrial ablation~~
 - ~~Hysterectomy~~

Takee Home message = Consider clotting disorders in young women
(bleeding history)

Common presentations:

- **Inter-menstruation bleeding :**

- Likely diagnosis

- Endometrium

- Physiological (hormonal)
- Dysfunctional uterine bleeding
- Endometrial instability -? Progestogen insufficiency
- Endometrial polyp

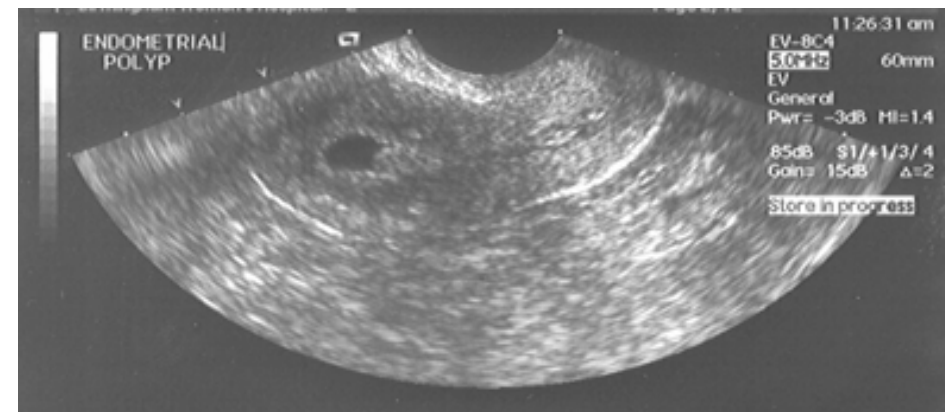
- Cervix

- Cervical cancer rare (especially in women with normal cervical smear history)
- Cervical polyp

- Lower genital tract infection

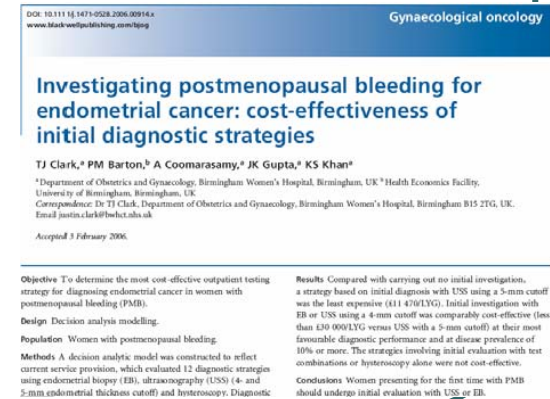
- Treatment

- Reassurance
- COC
- Cervical cautery



Postmenopausal bleeding

- Likely diagnosis :
 - 5-15 % = endometrial cancer / pre-cancer (atypical endometrial hyperplasia)
 - 85-95% = benign pathology
 - Atrophic changes to lower genital tract
 - Endometrial polyp
- Investigation
 - Pelvic examination
 - Pelvic ultrasound (endometrial thickness)
 - Outpatient endometrial biopsy +/- outpatient hysteroscopy
- Management
 - Reassurance
 - Benign pathology
 - Outpatient hysteroscopy clinic – hysteroscopic polypectomy . Myomectomy
 - Local / systemic oestrogen
 - Malignant pathology
 - Oncology (hysterectomy, radiotherapy/ chemotherapy)



Take Home message = Arrang urgent referral via “PMB” for rapid pelvic ultrasound

HRT related bleeding

- Likely diagnosis

- Absorption – compliance / mal-absorption
- Cervical / endometrial / Ovarian pathology
 - Common
 - Endogenous ovarian activity (“peri-menopause”)
 - Endometrial pathology
 - Hyperplasia, polyps, unstable atrophic endometrium

- Investigation

- Pelvic examination
- Pelvic ultrasound
- Outpatient endometrial biopsy +/- outpatient hysteroscopy

- Management

- Pathology
 - Polypectomy, systemic / local progestins (Merina for hyperplasia)
- No pathology
 - Review need for HRT
 - Change HRT preparation: sequential – sequential; sequential – continuous combined or ERT + Mirena

Take Home message = Exclude gynaecological pathology (pelvic exam + pelvic ultrasound and review the need for and type of HRT

When is referral to secondary care warranted ?

- Symptoms refractory to medical treatment
- Post-menopausal bleeding
- Abnormal clinical examination
 - Abnormal cervix
 - Significant tenderness
 - Pelvic mass not thought to be fibroids
 - Significant fibroid uterus (palpable abdominally)
- Abnormal ultrasound scan
 - Endometrial thickness > 5 mm in PMB
- Lower threshold for referral if
 - Risk factors for endometrial hyperplasia
 - Irregular periods, obesity, family history, > 40 years
 - Substantial impact on health related quality of life
 - Associated iron deficiency anaemia

*Thank you for your
attention*

Any Question ?