ABNORMAL UTERINE BLEEDING

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Overview

Abnormal uterine bleeding is a broad term that indicates a change in frequency of menses, duration of flow or amount of blood loss.[1] Pregnancy should always be ruled out in a woman of childbearing age.

Diagnostic Considerations

Definitions

Dysfunctional Uterine Bleeding: Diagnosis of exclusion when there is no pelvic pathology or underlying medical cause[1]
Menorrhagia: Heavy bleeding over several consecutive cycles during reproductive years with > 80 ml blood loss per cycle[1]
Metrorrhagia: Uterine bleeding at irregular intervals, particularly in between expected menstrual periods
Menometrorrhagia: prolonged or excessive bleeding which occurs irregularly and more frequently
Normal menses: [1]

Frequency: 28 days +/- 7 days
Flow duration: 4 days +/- 2days
Average blood loss: 40 ml +/- 20 ml

History

- Bleeding history: pattern, timing, frequency, amount
- Ovulatory vs Anovulatory bleeding (see Table 1)
- If postcoital or intermenstrual history → r/o local causes such as cervical infection, polyps, dysplasia/cancer
- Medication history: bleeding can be caused by medications including anticoagulants, ASA, antipsychotics (phenothiazines), antidepressants (SSRI/TCA), tamoxifen, herbal supplements (ginseng/ginkgo/soy), corticosteroids, hormone replacement therapy, thyroxine and contraception (OCP, IUD, Norplant, Depoprovera)

Table 1: Characteristics of Anovulatory vs Ovulatory Bleeding[2]

Anovulatory	Ovulatory
Irregular bleeding	Cyclical bleeding
Minimal pain	Premenstrual symptoms
Often heavy	Midcycle pain
Higher risk for endometrial hyperplasia, adenocarcinoma	Dysmenorrhea
More common in obese women and extremes of reproductive age [3]	

Adapted from Bordman et al. [2]

Physical Examination

- Weight, BMI
- Thyroid exam
- Abdominal exam to look for stigmata of liver disease
- Dermatologic exam (acne, hirsutism, jaundice acanthosis nigricans)
- Pelvic exam: uterine enlargement, adnexal mass, cervical changes, cervical motion tenderness

Investigations

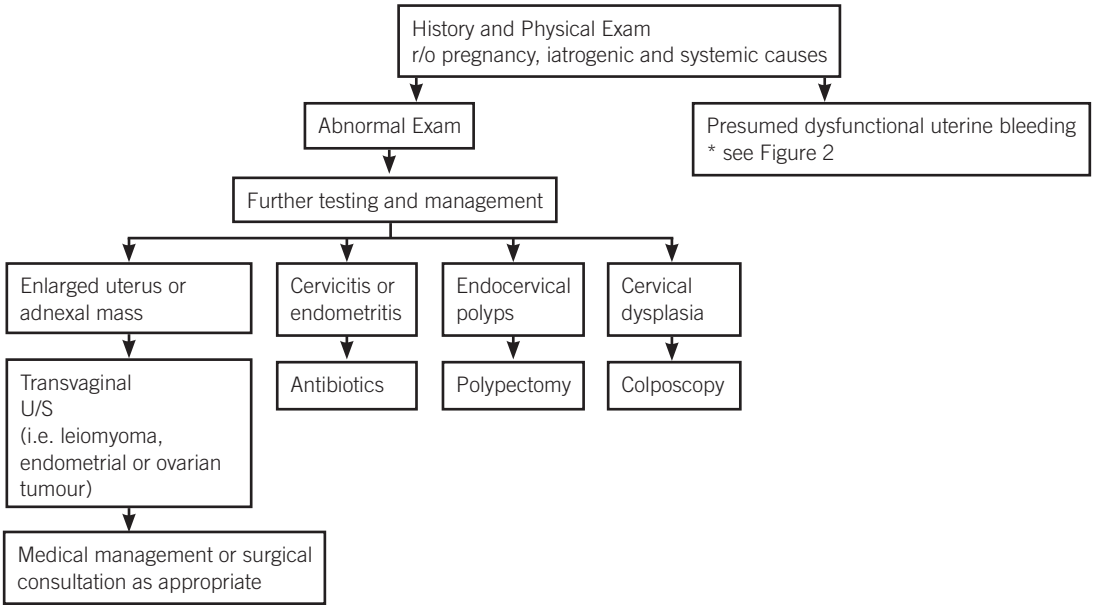
- CBC, ferritin – r/o anemia
- Pap +/- STI swabs to r/o infection, cervical dysplasia
- Transvaginal U/S (day 4-5 of cycle[3]) to r/o abn on pelvic exam or if has ongoing bleeding
- Endometrial sampling should be considered if patient has risk factors for developing endometrial carcinoma (see Figure 2)
- D&C alone is not an ideal investigation as there can be sampling errors, it requires anesthesia, and there is a risk of perforation or hemorrhage. It is generally reserved for cases where office biopsy or directed hysteroscopic biopsy are not available or feasible.
- Saline sonohysterography: may improve the diagnosis of an intrauterine mass or endometrial abnormality during TVUS
- Further investigations should be considered if clinical suspicion is high (See Table 2: Investigations for systemic causes of Abnormal Uterine Bleeding)

Table 2. Systemic causes of abnormal uterine bleeding and appropriate investigations

Systemic causes	Investigation
Thyroid dysfunction	Sensitive TSH
Polycystic ovary syndrome	Free testosterone, DHEAS, LH:FSH>3:1, TVUS
Coagulopathies, leukemia, thrombocytopenia	CBC, INR, PTT, Bleeding time
Pituitary adenoma or hyperprolactinoma	Fasting prolactin
Hypothalamic suppression (stress, weight loss, excessive exercise, eating disorder)	Measure weight/BMI
Hepatic disease	LFTs, INR
Renal disease	Creatinine
Adrenal hyperplasia	DHEAS, free testosterone
Cushing's disease	24 hour urine free cortisol, overnight dexamethasone suppression test
Tumours-gynecological, hormonally active	Testosterone, estradiol, DHEA, AFP, hCG, LDH
Late onset Congenital Adrenal Hyperplasia	17 alpha-hydroxy-progesterone

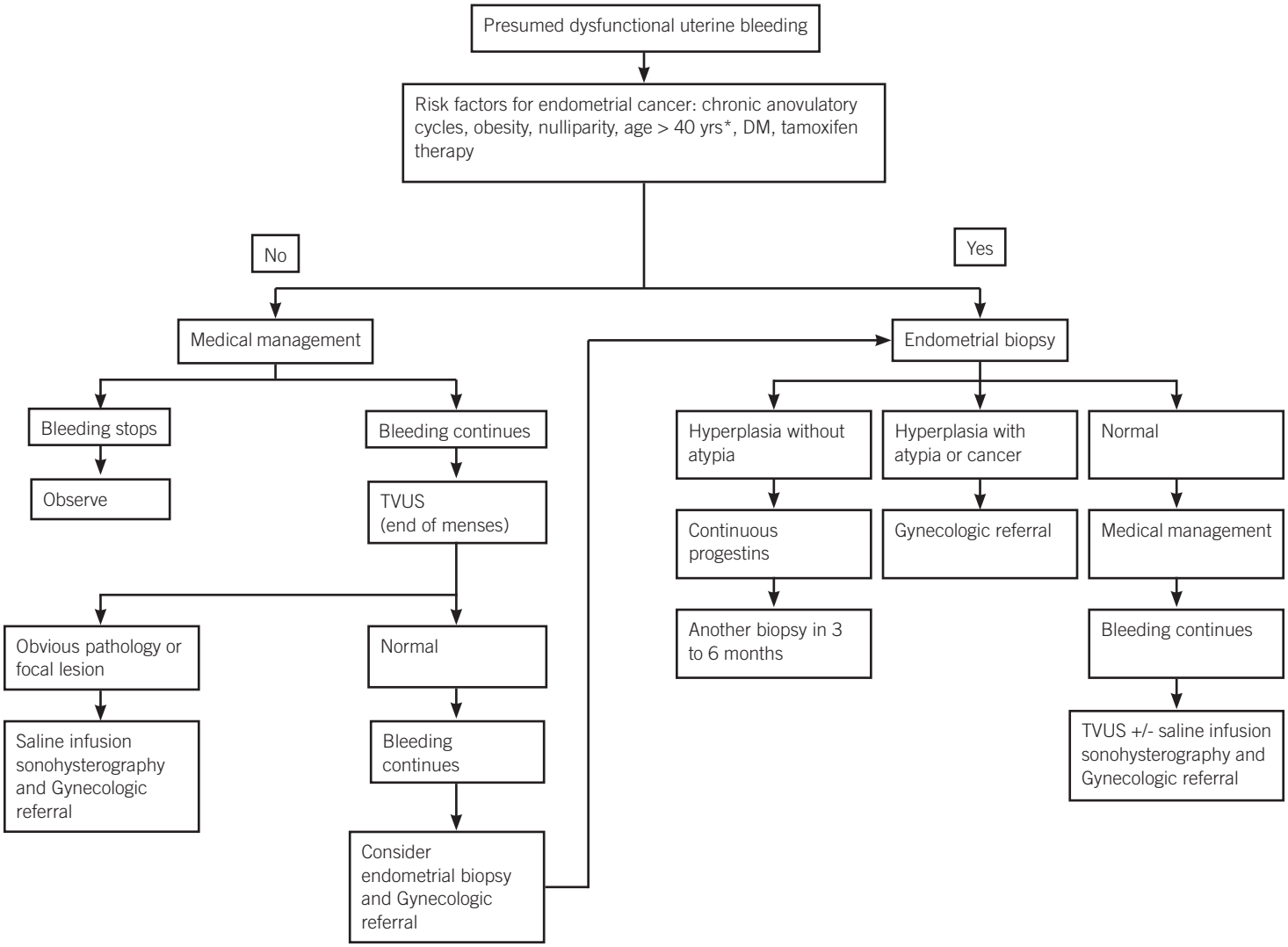
Used with permission from Bordman et al. [2]

Figure 1: Evaluation of Abnormal Uterine Bleeding in premenopausal women



Adapted from Albers et al. [4]

Figure 2: Evaluation of dysfunctional uterine bleeding in premenopausal women



* SOGC states 40 years of age[1], while ACOG states 35 years of age[4]

Adapted from Albers et al.[4]

Management

When selecting a treatment, patient preference, desire to preserve fertility, age, cost and coexisting medical conditions must be considered. Medical treatments for ovulatory abnormal uterine bleeding include NSAIDs, antifibrinolytics, levonorgestrel IUS (LNG-IUS) and combined oral contraceptive pills (COCP).

Medical treatments for anovulatory abnormal uterine bleeding can be treated pharmacologically with cyclic progestin, COCPs and LNG-IUS. Androgens and GNRH agonists are second line treatments that may be prescribed after consultation with a gynecologist.

Medical treatments

Medication	Indication	Dose	Side-effects	Contraindications
Danazol (Cyclomen®)	• Fibroids • Endometriosis • Abnormal uterine bleeding • Chronic pelvic pain	• Fibroids 100 - 200mg OD • Endometriosis 200 - 800mg OD (divided BID) • Dys uterine bleeding 200 mg OD	Menopausal symptoms, lipid changes, liver disease, muscle cramps, break through bleeding, need barrier contraception	Undiagnosed vaginal bleeding, genital neoplasia, impaired hepatic/renal/ cardiac function, pregnancy, attempt at pregnancy, lactation, porphyria, active thrombosis or thromboembolic disease
Estrogen (IV)	• Acute severe menorrhagia due to anovulation	• 25mg IV q6hr up to 4 doses	Headache, nausea, increased risk of stroke, PE, DVT	Venous thrombosis or thrombophilia
GnRH agonists	• Fibroids • Endometriosis • Chronic pelvic pain	• Leupride acetate (Lupron®) 3.75mg/ month or 11.25mg/3 months IM • Naferelin (Synarel®) 200ug 1-2 spray intranasal bid • Goserelin (Zoladex®) 3.6mg sc monthly or 10.8mg sc q3 months)	Menopausal symptoms 80-90% (hot flashes, vaginal dryness etc.) irregular bleeding, need barrier contraception, possible bone density loss if used > 6 months without add-back HT	Pregnancy, breast feeding, undiagnosed vaginal bleeding
Non-steroidal anti-inflammatory drugs (NSAIDs)	• Dysfunctional uterine bleeding • Endometriosis • Adenomyosis • Dysmenorrhea • Chronic pelvic pain	• Mefenamic acid (Ponstan®) 500 mg then 250mg q6h prn • Naproxen: (Naprosyn® 250 bid-qid • Anaprox® 275-500 bid) • Ibuprofen (Advil®, Motrin®) 400 mg q4-6h	Nausea, GI upset, diarrhea, dizziness, headache, rashes, GI bleed	Acute peptic ulcers or hx of ulcers, active IBD, hypersensitivity to NSAIDs, caution in patients with asthma, nasal polyps, renal ds, liver ds, CHF, HTN, pregnancy
Combined oral contraceptive pill	• Dysfunctional uterine bleeding • Endometriosis • Fibroids • Adenomyosis	• Use monocyclic compound cyclically 21d on/7d off or continuously every day without stopping	Breakthrough bleeding, bloating, nausea, headache, breast tenderness, weight gain	Hx/active thromboembolic disorder, cerebrovascular disorder, CAD, DVT, acute liver disease, breast cancer, migraine with aura, diabetes with renal, vascular or neuro complications, undiagnosed abnormal vaginal bleeding, pregnancy, uncontrolled HTN, smoker >35 years old
Oral progestins	• Anovulation • PCOS	• Provera 5-10mg OD x 5-10 or Prometrium 200 – 400mg po to induce bleeding for anovulation or starting on day 16 for dys uterine bleeding	Abnormal uterine bleeding, breast tenderness, fluid retention, acne, nausea, headaches, depression	Undiagnosed vaginal bleeding/ breast disease (including cancer), pregnancy, severe liver disease, depression, Prometrium®: peanut allergy
Injectable Medroxy-progesterone (Depo-Provera®)	• Fibroids • Dysfunctional uterine bleeding • Endometriosis	• 150mg IM q3 months Tip: May ↓ interval if ++ breakthrough bleeding	Bloating, weight gain, depression, irregular bleeding, amenorrhea, ↓ BMD with long term use	Same as above for oral progestins and possible decreased bone mineral density
Intrauterine Levonorgestrel releasing system (Mirena® IUS)	• Dysfunctional uterine bleeding • Endometriosis • Adenomyosis Fibroids	• 20ug/d	Breakthrough bleeding, amenorrhea, perforation, expulsion, pain, rarely progesterone side-effects from systemic absorption	Pregnancy, undiagnosed uterine bleeding, uterine abnormalities that distort cavity, uterine/cervical malignancy, acute liver ds, immunodeficiency, leukemias
Tranexamic acid (Cyclokapron)	• Endometriosis • Adenomyosis • Dys Uterine Bleeding • Fibroid	• 500mg-1500mg q 6-8 h PRN Maximum daily dose: 6gm	GI (nausea, vomiting, diarrhea, dyspepsia), occasional disturbance of colour vision	History, risk or active thromboembolic disease (DVT, PE) Acquired colour vision disturbance

Surgical options

- Endometrial destruction: hysteroscopic endometrial ablation or global endometrial ablation
- Uterine artery embolization and myomectomy are treatments available for the management of fibroids
- Decision to proceed with hysterectomy depends on the underlying diagnosis; it is a permanent cure for menorrhagia, but the risk of surgery must be weighed against the risks of other treatments

When to Refer

- No improvement in bleeding despite medical management
- Unable to do endometrial biopsy when indicated
- Obvious pathology or focal lesion/Abnormal results of endometrial biopsy

Bottom Line

Dysfunctional uterine bleeding is a diagnosis of exclusion and pregnancy, systemic, anatomic and iatrogenic causes for abnormal uterine bleeding must be ruled out. Thorough history, physical exam and investigations must be completed as clinically indicated. Endometrial biopsy should be considered in all patients with risk factors for endometrial carcinoma. There are several medical and surgical options for the treatment and management of DUB.

Patient Resources

Uptodate
AAFP

1. Vilos GA, Lefebvre G, Graves GR. Guidelines for the management of abnormal uterine bleeding. J Obstet Gynecol Can 2001;23(8):704-9.
2. Bordman R, Telner D, Jackson B, Little D. An Approach to the diagnosis and management of benign uterine conditions in primary care. Toronto, Ont: Centre for Effective Practice, Ontario College of Family Physicians; 2005.
3. Telner D, Jakubovicz D. Approach to diagnosis and management of abnormal uterine bleeding. Can Fam Physician 2007;53:58-64.
4. Albers JR, Hull SK, Wesley RM. Abnormal Uterine Bleeding. Am Fam Physician 2004;69(8):1915-26.

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm