

# Dysfunctional Uterine Bleeding

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## ABSTRACT

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**Background:** One in five women bleed so heavily during their periods that they have to put their normal lives on hold just to deal with the heavy blood flow! Heavy menstrual bleeding (HMB) has an adverse effect on the quality of life of many women. Dysfunctional uterine bleeding (DUB) is defined as abnormal uterine bleeding in the absence of organic disease.

**Keywords:** Dysfunctional uterine bleeding (DUB), Heavy menstrual bleeding (HMB)

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## INTRODUCTION

One in five women bleed so heavily during their periods that they have to put their normal lives on hold just to deal with the heavy blood flow! Heavy menstrual bleeding (HMB) has an adverse effect on the quality of life of many women. It is not a problem associated with significant mortality. In order for women to be treated successfully, it is essential that the underlying problem be understood by both the patient and the healthcare professional. Till last decade, hysterectomy was offered as the first line treatment; however matters have changed with alternative effective treatments.

- Dysfunctional uterine bleeding (DUB) is defined as abnormal uterine bleeding in the absence of organic disease. (Pitkin J. 2007 May)
- The diagnosis of DUB can only be made once all other causes for abnormal, or heavy, uterine bleeding have been excluded. The pathophysiology is largely unknown.
- It usually presents as heavy menstrual bleeding (HMB). HMB is defined as excessive menstrual blood loss which interferes with the woman's physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms.

As Clinicians, we may see DUB commoner in adolescents, and women in late 40's. DUB affects more than 30% of women and account for a significant reason for gynecological referral. It was estimated that in 5 years of referral; more than 60% of women will

have undergone hysterectomy making it the commonest major gynecological operation. In fact. British Medical Journal May 2007 writes that "one in 20 of women aged 30- 49 consults her GP each year with menorrhagia". Menorrhagia is derived from Greek and literally means to burst forth monthly (mene, the moon and rhegnymi, to burst Forth). Concerns about the invasiveness of hysterectomy have led to development of minimal access approaches including endometrial resection and ablation. With the development of minimal access techniques it is possible to destroy the endometrium in situ; in short a day care operation. Literature mentions at least 1 in 5 women who undergo these procedures will require further surgery at a later stage. Effective medical therapies still stands a place in the management of DUB.

## CAUSE

The precise cause of DUB is thought to lie at the level of the endometrium itself. Homeostasis during menstruation is achieved by vasoconstriction, until the bleeding is finally checked by repair of the endometrial vessels in the first 7 days of the cycle. A number of factors are thought to be involved in the local control of menstrual blood loss and abnormalities in the prostaglandin and fibrinolytic systems in the endometrium have led to rational medical approach to the treatment of heavy bleeding in these women.

## Framework for analysis

Of the several frameworks for analyzing the consultation, two methods are known; 'biological model' where

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physical processes are measured and compared with a 'normal' reference. Another approach is a psychosocial model where the woman's psychological disturbance and social impairment are the focus. In reality, most clinicians use a combination of the two models.

The history should aim at defining the nature of bleeding, potential pathology, and identifying patient's ideas, concerns, issues, expectations, and needs.

Questions about medical history should include the following:

- Signs and symptoms of hypovolemia,
- Diabetes mellitus,
- Hypertension,
- Hypothyroidism,
- Hyperthyroidism,
- Liver disease,
- Medication usage, including exogenous hormones, anticoagulants, aspirin, anticonvulsants and antibiotics,
- Alternative and complementary medicine modalities, such as herbs and supplements.

Research guidelines do not recommend measurement of menstrual blood loss by any method, rather by woman herself.

Physical examination of the woman by observation, abdominal palpation, visualization of the cervix and bimanual (internal) examination has the purpose of detecting underlying pathology to inform treatment and the need for investigations. The examination should look for the following:

- Trauma to the vaginal walls or cervix
- Retained foreign body
- Cervical or vaginal laceration
- Bleeding from the cervical os.

Approximately 90% of DUB results from anovulation, and 10% occur with ovulatory cycles.

### Description for bleeding pattern

Dysfunctional bleeding from the uterus can be described as follows:

1. Menorrhagia - Prolonged (>7 d) or excessive (>80 mL daily) uterine bleeding occurring at regular intervals.
2. Metrorrhagia - Uterine bleeding occurring at irregular and more frequent than normal intervals.

3. Menometrorrhagia - Prolonged or excessive uterine bleeding occurring at irregular and more frequent than normal intervals.
4. Intermenstrual bleeding (spotting) - Uterine bleeding of variable amounts occurring between regular menstrual periods.
5. Polymenorrhea - Uterine bleeding occurring at regular intervals of less than 21 days.
6. Oligomenorrhea - Uterine bleeding occurring at intervals of 35 days to 6 months.
7. Amenorrhea - No uterine bleeding for 6 months or longer.

The major categories of DUB include the following:

- Estrogen breakthrough bleeding
- Estrogen withdrawal bleeding
- Progestin breakthrough bleeding

Workup for DUB calls for several studies to ensure hemodynamic stability.

1. A full blood count test should be carried out on all women with HMB. This should be done in parallel with any HMB treatment offered.
2. Testing for coagulation disorders (for example, von Willebrand disease) should be considered in women who have had HMB since menarche and have personal or family history suggesting a coagulation disorder.
3. Thyroid function tests are not routinely recommended, but worth considering in selected cases.
4. Our next modality of investigation for identification of structural abnormality is Ultrasound. This imaging modality is of immense value if done by TVS, endovaginally. The information to be sought are cavity echo of the uterus, myometrial echoes, if suspicion of adenomyosis I endometrial thickness I adnexal pathology assessment.
5. Saline infusion sonography may be used as second line for establishing cavity assessment.
6. Hysteroscopy should be used as a diagnostic tool only when ultrasound results are inconclusive, for example. to determine the exact location of a fibroid or the exact nature of the abnormality.
7. If appropriate, a biopsy should be taken to exclude endometrial cancer or atypical hyperplasia. Indications for a biopsy include, for example, persistent intermenstrual bleeding, and in women

aged 45 and over treatment failure or ineffective treatment.

8. Dilatation and curettage alone should not be used as a diagnostic tool.

The guidelines place a high value on the need for education and information provision for women with HMB. A woman with HMB should be given the opportunity to review and agree any treatment decision. She should have adequate time and support from healthcare professionals in the decision-making process.

## TREATMENT

### Objectives

- To control bleeding
- Prevent recurrence
- Preserve the opportunity for future child bearing if patient desires

Pharmaceutical treatment should be considered where no structural or histological abnormality is present, or for fibroids less than 3 cm in diameter which are causing no distortion of the uterine cavity. The healthcare professional should determine whether hormonal contraception is acceptable to the woman before recommending treatment (for example, she may wish to conceive). The scientific basis for the hormonal treatment is on the anovulatory status of the woman. The bleeding arises from abnormalities of the hypothalamic-pituitary-ovarian endometrial axis. This results in anovulatory (generally) irregular cycles, which are particularly common at the time of menarche and around the perimenopause. The failure of the ovulation and progesterone induced luteal phase transformation of the endometrium results in bleeding that is often heavy, less clearly defined and irregular.

Antifibrinolytic agents, such as tranexamic acid, provide a rational and effective treatment reducing the MBL by 50%. It is also effective for intra-uterine contraceptive induced dysfunctional uterine bleeding. The incidence of adverse effects is related to the dose of drug prescribed. A third of women experience gastrointestinal side effects following treatment with a dose of 3 - 6 g daily. The dose related side effects may be minimized after the first 3 days of menses ceased, or limiting to the same period of medication. There is no evidence to prove thromboembolic diseases or rise in the incidence of embolic phenomenon. Thus it

remains as safe early first line therapy for reducing the bleeding.

Anti prostaglandins: NSAIDS remain popular choice for the treatment of HMB. Their main mechanism of action is to decrease endometrial PG (prostaglandin) concentrations. The NSAID most often used is mefenamic acid; reducing blood loss upto 56%. The beneficial effect also includes relief from dysmenorrhoea, headache, nausea, that persists for months. Systemic progestogens such as Norethidrone, and Medroxyprogesterone acetate offer a logical approach to the treatment of anovulatory DUB.

Intra uterine progestogens: MIRENA, the device delivers 20mcg of levonorgestrel to the endometrium every 24 hour in a sustained release formulation that can last up to 5 - 7 years. The main side effect is irregular breakthrough bleeding and spotting particularly within the first few months after insertion of the system. These events must be discussed with patient prior to insertion of the system. Combined Pill reduces MBL by endometrial suppression (50%). Nevertheless, the pill is limited by the risks of thrombosis in elderly aged women. At a dose of 3-4 pills daily in divided doses, it may be used in acute bleeding DUB.

### Guidelines

1. NSAIDS are used in management of reduction of MBL, mefenamic acid 500 mg every 6 hours and continued till bleeding ceases or even justified in the first 3 days of the menstrual cycle. The NSAIDS can be monotherapy or combination with other pills. It is most effective in ovulatory DUB.
2. Inhibitors of fibrinolysis have a procoagulant activity, indicated in ovulatory DUB. Epsilon-aminocaproic acid (EACA), tranexamic acid and para aminomethylbenzoic acid are used. It is preferred to combine these with pills or progestogens for better efficacy.
3. Ergot derivatives, as methyergometrine should not be advocated for lack of efficacy and limited by serious side effects.
4. Progestogens or synthetic progestins are of significant value in anovulatory DUB in reduction of MBL. The regime of oral norethidrone 5 mg twice daily/ oral Medroxyprogesterone acetate 30 mg in divided doses/oral or vaginal micronised progesterone in doses of 300 mg daily are used. The protocol is either last ten days of the menstrual cycle or day 5 to day 26 of the menstrual cycle.

5. A seven year intrauterine device, MIRENA which releases levonorgestrel reduced MBL by 83% in 3 months and by 97% in 12 months. The latest guidelines of the NICE, UK recommends this system as first of the order for hormonal management of DUB.
6. Danazol at doses of 400 mg daily did reduce the MBL; however the serious androgenic side effects limited its use in DUB.
7. Gonadotrophin releasing agonists by creating medical menopause is of value as last resort especially in those preferring to choose child bearing later.
8. Oral synthetic progestin 's is of significance in reduction in acute bleeding DUB
9. Ongoing use of NSAIDS and or tranexamic acid is recommended for as long they are found to be beneficial by the woman.
10. Use of NSAIDs and/or tranexamic acid should be stopped if it does not improve symptoms within three menstrual cycles.
11. When a first pharmaceutical treatment has proved ineffective, a second pharmaceutical treatment can be considered rather than immediate referral to surgery.

### Surgical Options

The surgical options include dilation, curettage/ endometrial ablation/ hysterectomy. The surgical management is reserved for those patients who are unresponsive, hemodynamically unstable, and excessive bleeding must be stopped within short span of time. Curettage will reduce the acute blood loss and may resume at the next cycle unless medical therapy is initiated. Endometrial ablation is reserved for those women desiring for preserving the uterus, failed medical therapy, no future fertility, normal cervical cytology and endometrial histology or even other pelvic disease. The technique involves destruction of endometrium by laser, / roller electrocautery, / ball end electrode.

#### *Thermal balloon technique*

Thermal balloon ablation of the endometrium involves inserting a balloon tipped catheter in to the uterine cavity inflating the balloon so it conforms to the shape of the cavity and then heating the fluid within it to 85 C. There are currently two devices available, The thermachoice and cavaterm system.

The other systems are

1. Endometrial laser intra uterine thermotherapy
2. Intra uterine surgery using co axial electrode
3. Hydrothermal ablation of the endometrium
4. Cryo ablation of the endometrium
5. Photodynamic endometrial ablation
6. Radio frequency induced thermal endometrial ablation
7. Microwave endometrial ablation

Rates of success defined as amenorrhea or lesser flow cycles or normal menstrual flow varies between 80% to 95%. Hysterectomy is a definite surgery and treatment too, and has rates of patient satisfaction. It is appropriate for associated pelvic pathology, say myoma or prolapse. Women offered hysterectomy should be informed about the increased risk of serious complications (such as intraoperative haemorrhage or damage to other abdominal organs) associated with hysterectomy when uterine fibroids are present. Women should be informed about the risk of possible loss of ovarian function and its consequences, even if their ovaries are retained during hysterectomy. Individual assessment is essential when deciding the route of hysterectomy. The following factors need to be taken into account:

- presence of other gynaecological conditions or disease
- uterine size / presence and size of uterine fibroids
- mobility and descent of the uterus
- history of previous surgery

### Key points

- Management of DUB should be individualized and a plan of management to be developed for the control of excessive uterine bleeding in the specific patient.
- Mefenamic acid and tranexamic acid combination have been shown to reduce the bleeding by 50%, with fewer side effects; forming the first line agents for the treatment of DUB.
- The pill reduces bleeding by 50%, provides good cycle control and effective contraception.
- The Levonorgestrel intrauterine system reduces menstrual blood loss by over 80% and may offer acceptable alternative to other medical treatment and surgery.
- Thermachoice balloon device is most studied, and reported.

- Most of the techniques use disposable probes, increasing the costs which need research.
- Women can choose the therapy medical or surgery.
- Hysterectomy should be considered only when other options have failed, are contraindicated, or are declined by the woman.
- Women offered hysterectomy should have a full discussion of the implication of the surgery before a decision is made. The discussion should include: sexual feelings, fertility impact, bladder function, need for further treatment, treatment complications, the woman's expectations, alternative surgery and psychological impact.

## END NOTE

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