"Doctor, the flow won't stop!"

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UBC's 8th Annual Update in Office Gynecology and Women's Health, 2003

What is "normal"?

There is no universally accepted definition of what a "normal" menstrual cycle is like. Only 14% of women have the classic 28-day menstrual cycle, with 98% having a cycle length of 21 and 35 days.[1] In otherwise healthy patients, even greater cycle lengths may be normal. When the menstrual cycle is consistently less than 21 days, the frequency of bleeding may be sufficient to lead to iron deficiency anemia. The length of the menstrual cycle changes during reproductive life, and tends to be shorter in the perimenopausal years.[2]

The duration of menstrual flow is typically two to six days. Normal menstrual blood loss is defined as less than 80 mL,[1,2] which is the amount necessary to completely saturate one obstetrical sanitary pad.[3] Menstrual blood loss is too difficult to quantify. In one study of women undergoing hysterectomy for "intractable menorrhagia," the mean preoperative hemoglobin was 127,[4] suggesting a strong element of subjectivity in how much bleeding is "too much", or sufficient to impair quality of life.

In the patient who has iron deficiency anemia with no other apparent cause, the diagnosis of excess menstrual bleeding is relatively straightforward. In cases without anemia, it may useful to consider how the bleeding (on the heaviest day) is affecting the quality of life. For example, the patient should feel comfortable in changing a sanitary pad or tampon no more than every two hours, should be able to sleep through the night without having to change her protection, and should be able to continue all activities of daily living without fear of accidentally bleeding through her protection.

At least 80% of all women will experience at least one menstrual cycle which deviates from their normal pattern.[1] If the change is limited to one or a few cycles and not associated with excessive blood loss, there should be little cause for concern.

The extremes of reproductive life are the times when abnormal bleeding is most likely to manifest. Any post-

Barb's case

Barb, 47, presents in the emergency department with heavy vaginal bleeding lasting 21 days, a hemoglobin of 62, and a negative pregnancy test. Before this, she had a more or less regular menstrual cycle with periods occurring at 21- to 24-day intervals, which is less than the 28-day cycle she experienced in her 30s. Her periods have been longer and heavier, lasting up to 10 days. She has had iron deficiency anemia, with a hemoglobin of 105 recorded in the last year.

The current episode of bleeding began following 7 weeks of amenorrhea. She received medroxyprogesterone acetate, 10 mg daily, after 10 days of heavy bleeding. She used this for 1 week with no impact on the bleeding.

She has a body mass index of > 27, but is otherwise healthy. Physical exam was unremarkable, except for bleeding from the cervical os.

For more on Barb, go to page 109.

menopausal bleeding, defined as bleeding 12 months or more after the last spontaneous menstrual period, requires investigation. Post-menopausal bleeding is considered normal only if it clearly is the result of progestin withdrawal in patients using cyclical combine hormone replacement therapy.

Table 1
Laboratory investigations

Investigation	Comments
Blood count and RBC morphology	All patients with AVB
Group and screen, cross match	Where indicated by large blood loss
Pregnancy test	All women of child-bearing age
TSH and prolactin	All patients. Hypothyroidism is common, and a known cause of menorrhagia. Hyperprolactinemia is common, and a known cause of anovulation, which may lead to DUB
LH and FSH	Where anovulation of any cause is suspected
Testosterone and DHEAS	Where PCOS or other hyperandrogenic states are suspected
Ristocetin cofactor von Willebrand's factor antigen PTT and INR	Where blood dyscrasia is suspected on May be of particular value in an adolescent with patient with AVB

RBC: Red blood count
FSH: Follicle-stimulating hormone
PCOS: Polycystic ovary syndrome
TSH: Thyroid-stimulating hormone
PTT: Partial thromboplastin time
LH: Luteinizing hormone
DHEAS: Dehydroepiandrosterone sulfate
AVB: Abnormal vaginal bleeding
DUB: Dysfunctional uterine bleeding
INR: International normalized ratio

What are the patterns of AVB?

In evaluating the patient with abnormal vaginal bleeding (AVB), it is useful to consider the pattern of bleeding to guide the investigation and treatment.

Menorrhagia

In this case, the patient presents with regular, self-limited, cyclical bleeding which is heavier and/or longer than usual. Up to 80% of cases are idiopathic.[2,5] Isolated menorrhagia is rarely a symptom of endometrial malignancy even after age 40, but should be considered as a potential cause in this age group.[5] Once established, menorrhagia is a lifelong pattern of bleeding and resolves only with the cessation of periods at menopause.

Intermenstrual bleeding

With this type, the patient presents with cyclical menstrual bleeding, but also has bleeding at other times in the cycle. Light bleeding that reliably occurs for a few days in the premenstrual or post-menstrual phase of the cycle, or at the time of ovulation, is usually related to physiologic changes in estradiol and/or progesterone levels, and may be regarded as normal in patients at low

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Table 2
Risk factors for endometrial carcinoma

- Obesity, weight > 90 kg
- Hypertension
- Diabetes
- Personal or family history of colon or breast carcinoma
- Family history of endometrial carcinoma
- Tamoxifen use
- History of anovulatory cycles, particularly if due to polycystic ovarian syndrome
- Infertility
- Nulliparity
- Age > 40-45
- Premenopausal patient with abnormal bleeding and inhomogeneity of the endometrium or a focal lesion on ultrasound
- Premenopausal patient at otherwise low risk who fails to respond to therapy
- Highly irregular, "chaotic" pattern of bleeding
- Post-menopausal bleeding

risk of endometrial pathology. Intermenstrual bleeding with no specific relationship to the menstrual cycle may be associated with pathology, including malignancy, and should be investigated.

Metrorrhagia

Metrorrhagia, particularly in patients over age 40, should be considered a potential sign of genital tract malignancy until proven otherwise. Patients with metrorrhagia may or may not be ovulatory. The common clinical problem of anovulatory dysfunctional uterine bleeding (DUB), which may be associated with an increased risk of endometrial carcinoma, classically presents as metrorrhagia.[1,5] Anovulatory DUB is often limited to a single episode, but in some patients may be a recurrent pattern of bleeding.

How is it evaluated?

The management goals in abnormal AVB are:

1. To stop the current episode of bleeding, if unusually heavy or protracted.
2. To establish the cause of the bleeding, specifically ruling out underlying malignancy and complications of early pregnancy.

Cont'd on page 108 ⟶

Table 3
Treatment options for AVB

Medication	Comments
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Useful in long-term management of menorrhagia. Associated with 20-50% reduction in blood flow. Must be taken just prior to or at the start of menses, and regularly, for the duration of flow, to be effective. No one NSAID appears to be superior.
Tranexamic acid 500-1000 mg tid (Cyklopron)	Extensive use in Europe and North America. Main indication is long-term management of idiopathic menorrhagia, but may be a useful to treat menorrhagia due to fibroids and as an adjunct in stopping an acute dysfunctional uterine bleeding (DUB). Associated with 40% reduction in blood flow. Is used at the onset of, and throughout menses. Minimal side-effect profile.
Danazol (Cyclomen) 100-200 mg daily	Indicated in long-term management of menorrhagia. Up to 90% of patients experience amenorrhea or oligomenorrhea. 30% of patients experience unacceptable side-effects; hirsutism is rare at this low dose.
Cyclical oral progestins (Medroxyprogesterone acetate 5-10 mg daily, Micronized progesterone 100-200 mg daily)	Not effective in management of menorrhagia. May be useful in reducing blood loss at the onset of an episode of an anovulatory DUB, but not after the first few days. Indicated in the long-term management of anovulatory DUB, where it is given for 12-14 days of the cycle.
Injectable progestins (Depo Medroxyprogesterone acetate 150 mg every 3 months)	May be of use for all types of abnormal vaginal bleeding. Induces amenorrhea in 80% of patients after 1 year of use. Abnormal bleeding persists or is increased in up to 50% of patients in first 6 months, limiting its acceptability to most patients.
Levonorgestrel intrauterine system (Mirena®)	Only current indication in Canada is as a contraceptive. Highly effective treatment for menorrhagia. May have a role in management of DUB.
Intravenous conjugated estrogens 25 mg IV every 4 hours up to 24 hours	Indicated in emergency situation where the endometrium may be denuded as a result of prolonged bleeding. Requires in-patient setting for administration.
Gonadotrophin-releasing hormone (GnRH) analogues	Limited role as a temporizing measure for up to 6 months. Bone loss a concern with chronic use.

3. To correct the underlying cause of bleeding, if possible.
4. To initiate long-term therapy if there is no correctable cause.

What about the history and physical exam?

Cervical cytology to rule out invasive cervical carcinoma should be considered in all patients with AVB. This

Barb's followup

Barb presents with a history of menorrhagia, with superimposed acute bleeding, classically seen with anovulation. In her case, progestin therapy would not be expected to have been helpful, as it was started 10 days into the dysfunctional uterine bleeding, when one would expect the endometrium to require estrogenic support.

A dilation and curettage was performed in this case as a tissue diagnosis was necessary because of risk factors for endometrial carcinoma, and the likelihood that it would be of some temporary therapeutic value pending full investigation. She was started on an oral contraceptive pill (OCP) post op and instructed to continue for 21 days.

Pathology showed fragments of benign, disorganized proliferative endometrium. Outpatient investigations did not reveal abnormalities to suggest other causes of the acute bleed, or to explain the menorrhagia.

This patient was felt to be a suitable candidate for OCPs, tranexamic acid, danazol, or a levonorgestrel intrauterine system for long-term management of the menorrhagia. She opted to use tranexamic acid and has had a marked and sustained reduction in the menstrual cycle.

examination should not be deferred because of bleeding at the time of the examination, as most cytology labs are able to interpret the smear under the circumstances. Colposcopy is strongly indicated in patients with abnormal cytology.

Intermenstrual or irregular bleeding patterns may be a sign of endocervicitis; swabs for chlamydia and gonorrhea are helpful in such cases.

Polyps are a common cause of AVB, and most can easily and safely be removed in the office setting by grasping the polyp with ring forceps and making several complete turns with the instrument until the stalk severs.

What are the useful lab exams?

Useful investigations for AVB are summarized in Table 1. Measurement of estradiol and progesterone are not helpful for most patients with AVB. Ultrasound may be used to confirm the clinical suspicion of a mass lesion of the pelvis, such as a fibroid uterus or ovarian cyst. Measurement of the thickness of the endometrial echo is of no value whatsoever in the premenopausal patient and should not be used to guide further investigation.[5,6] However, ultrasound of the endometrial echo does have

a limited role in the premenopausal patient as the presence of a focal abnormality, inhomogeneity, or displacement of the endometrial echo is highly suggestive of a lesion requiring further investigation.

Sampling of the endometrium is indicated in all patients at increased risk of endometrial neoplasia (Table 2).[1,2,5] Office endometrial biopsy should be the initial diagnostic procedure of choice due to its convenience, accuracy, availability, safety, and low cost.[6] Dilation and curettage (D&C), with or without hysteroscopy, is a highly acceptable alternative that may be associated with a higher diagnostic yield[1,5,6] and should be strongly considered in patients with a negative office endometrial biopsy and ongoing AVB.

Cervical biopsy and endocervical curettage are simple and safe office procedures, which are of value in cases where bleeding may be cervical in origin.

How is it managed?

Treat the underlying cause of bleeding, if possible. Idiopathic menorrhagia, ovulatory DUB, and to a lesser degree, anovulatory DUB, present particular management challenges which may not respond well to medical therapy. Long-term medical therapy, often at the time of menopause, is necessary in many patients with AVB if there is no correctable underlying factor.

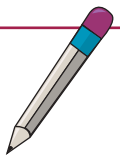
Medical therapy

Combined oral contraceptives (OCPs) should be considered as first-line therapy in the management of all abnormal vaginal bleeding of uterine origin, except in patients with contraindications (Table 3).[2,5,7] When used for menorrhagia, blood loss is reduced by about 50%.[1] OCPs are also highly effective for physiologic intermenstrual bleeding that is sufficiently troubling to the patient to warrant therapy. They offer excellent cycle control in the management of DUB, and are the only potentially effective medical therapy in patients with ovulatory DUB. Monophasic OCPs with 30 to 50 mcg ethinyl estradiol appear to be more effective than other formulations.[5]

In the case of an acute DUB where there has been protracted or extremely heavy bleeding, then endometrium is almost completely denuded and there is a need for estrogenic stimulation to stop the bleeding episode. In patients who are suitable for management in the outpatient setting, an OCP used bid or tid for seven days may be a good alternative to intravenous estrogen. It is important that the patient then continue to take the OCP, once daily, for 21 days after bleeding has stopped. Premature cessation of OCP use in this setting will precipitate a withdrawal bleed within a matter of days, which most patients and many physicians will identify as treatment failure.

Other medical treatment options have specific indications in the management of AVB of uterine origin. D&C is predominantly a diagnostic investigation. It may be used to stop an episode of bleeding, particularly if medical therapy has failed, but does not have any therapeutic effect beyond that cycle.[1,5]

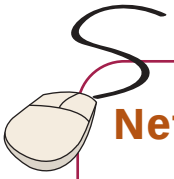
Take-home message



When you evaluate a patient with AVB, it is useful to consider the pattern of bleeding to guide the investigation and treatment.

The management goals in abnormal AVB are:

1. To stop the current episode of bleeding, if unusually heavy or protracted.
2. To establish the cause of the bleeding, specifically ruling out underlying malignancy and complications of early pregnancy.
3. To correct the underlying cause of bleeding, if possible.
4. To initiate long-term therapy if there is no correctable cause.



Net Readings

1. Society of Obstetrics and Gynecologists of Canada
   www.sogc.org
2. American College of Obstetrics and Gynecologists
   www.acog.com

AVB continues to be the leading indication for hysterectomy worldwide,[1,5] but there are less radical surgical options that may be appropriate for many of these patients.

Endometrial polyps and small submucous fibroids (to 4-cm diameter) may be hysteroscopically resected.

Endometrial ablation, by any technique, may be offered to the patients who have completed childbearing and have an endometrial cavity of normal size and shape with no lesions present.[1,5] Long-term results tend to be best the closer a patient is to menopause at the time of the procedure, with fewer requiring reoperation at a later date.

Myomectomy is an invasive option for women who wish to preserve the uterus. This procedure is technically more difficult and is associated with a greater potential for blood transfusion than is hysterectomy. Percutaneous embolization of the uterine arteries, which has limited availability in Canada, appears to be a satisfactory minimally invasive procedure for patients with fibroids that have enlarged the uterus to no more than a 20-week size. Laparoscopic electromyolysis of fibroids up to 4 cm in size has been described, but is not widely available. CME

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