The FIGO classification of causes of abnormal uterine bleeding in the reproductive years

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At this juncture, clinical management, education for medical providers, and the design and interpretation of clinical trials have been hampered by the absence of a consensus system for nomenclature for the description of symptoms as well as classification of causes or potential causes of abnormal uterine bleeding (AUB). To address this issue, the Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) has designed the PALM-COEIN (Polyp, Adenomyosis, Leiomyoma, Malignancy and Hyperplasia, Coagulopathy, Ovulatory Disorders, Endometrial Disorders, Iatrogenic Causes, and Not Classified) classification system for causes of AUB in the reproductive years. (Fertil Steril® 2011;■:■–■. ©2011 by American Society for Reproductive Medicine.)

Key Words: Menstrual disorders, menorrhagia, heavy uterine bleeding, classification

The investigation and management of abnormal uterine bleeding (AUB) for nongravid women in their reproductive years has been hampered both by confusing and inconsistently applied nomenclature and the lack of standardized methods for investigation and categorization of the various potential causes (1, 2). These deficiencies impede the ability of investigators to study homogenous populations of patients experiencing AUB, and make it difficult to compare studies performed by different investigators or research groups. The Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) oncology staging systems are practical, universally accepted, and aid clinicians and investigators in the guidance of research, treatment, and prognostication of gynecologic cancers (3). This summary report describes the new PALM-COEIN Classification for Causes of Abnormal Bleeding developed by the FIGO Menstrual Disorders Group (FMDG) (4) (Fig. 1). The system was developed with contributions from an international group of both clinical and nonclinical investigators from 17 countries on six continents. A system for symptom nomenclature developed by the FMDG was described elsewhere in other publications that recommended standardized nomenclatures as well as abandonment of the terms menorrhagia, metrorrhagia, and dysfunctional uterine bleeding (5).

ACUTE, CHRONIC, AND INTERMENSTRUAL AUB

Chronic AUB is defined as bleeding from the uterine corpus that is abnormal in volume, regularity, and/or timing that has been present for the majority of the last 6 months. Acute AUB is distinguished as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient severity to require immediate intervention to prevent further blood loss (6, 7). Acute AUB may present in the context of existing chronic AUB or might occur without such a background history.

Intermenstrual bleeding (IMB) is defined as that which occurs between clearly defined cyclic and predictable menses and includes both randomly occurring episodes as well as those that manifest predictably at the same time in each cycle. This designation is designed to replace the word "metrorrhagia," which was one of the terms that the group recommended should be abandoned.

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FIGO CLASSIFICATION SYSTEM

The classification system is stratified into nine basic categories that are arranged according to the acronym PALM-COEIN [*pahm-koin*]: Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory Disorders, Endometrium, Iatrogenic, and Not Classified (4). In general, the components of the PALM group are discrete (structural) entities that are measurable visually, by use of imaging techniques, and/or by use of histopathology while the COEIN group is related to entities that are not defined by imaging or histopathology (nonstructural). The categories were designed to facilitate the current or subsequent development of subclassification systems.

The system was constructed recognizing that any patient could have one or a spectrum of entities that could cause or contribute to the complaint of AUB and that definable entities such as adenomyosis, leiomyomas, and endocervical or endometrial polyps may frequently be asymptomatic and, therefore, not a contributor to the presenting symptoms.

Polyps (AUB-P)

Polyps are categorized as being either present or absent as defined by one or a combination of ultrasound (including saline infusion sonography) and hysteroscopic imaging with or without histopathology. Although there is no current distinction regarding the size or number of polyps, it is probably important to exclude polypoid-appearing endometrium from this category, for such an appearance may well be a variant of normal.

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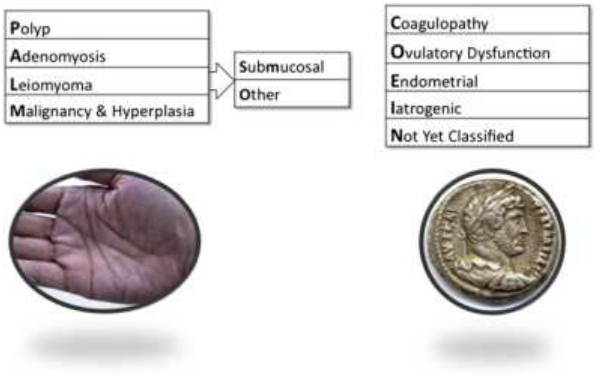
FIGURE 1

Basic classification system. The basic system comprises four categories that are defined by visually objective structural criteria (PALM: Polyp, Adenomyosis, Leiomyoma, and Malignancy or hyperplasia); four (COEI) that are unrelated to structural anomalies; and one (N) reserved for entities that are not yet classified. The leiomyoma category (L) is subdivided into those patients who have at least one submucosal myoma (Lsm) and those with myomas that do not impact the endometrial cavity (Lo). (Reproduced with permission granted by FIGO from Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders, FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age, Int J Gynaecol Obstet 2011;113:3–13.)



Munro. FIGO classification system for causes of AUB. Fertil Steril 2011.

The P category allows for the future development of a subclassification for clinical or investigative use that could include a combination of variables including polyp dimensions, location, number, morphology, and histology.

Adenomyosis (AUB-A)

The relationship of adenomyosis to the genesis of AUB is unclear (8). Whereas the criteria for diagnosing adenomyosis have traditionally been based on histopathologic evaluation of the depth of "endometrial" tissue beneath the endometrial–myometrial interface from hysterectomy specimens, the histopathologic criteria vary substantially (9), and the requirement to diagnose adenomyosis in this fashion has limited value in a clinical classification system. Consequently, and because there exist diagnostic criteria based on both sonography (10) and magnetic resonance imaging (MRI) (11, 12), in this system adenomyosis is diagnosed by uterine imaging (4).

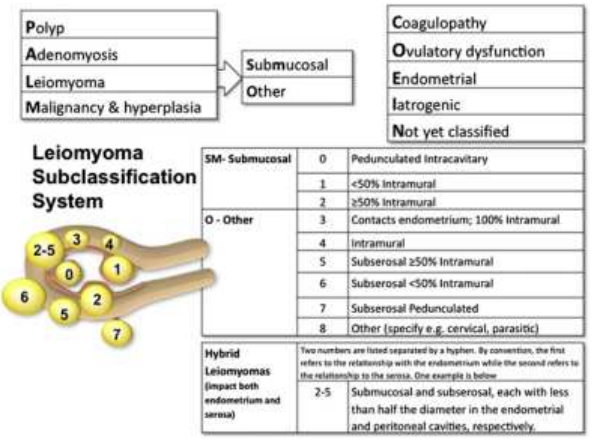
Recognizing the limited access of women to MRI in the world community, it is proposed that sonographic criteria for adenomyosis comprise the minimum requirements for assigning the diagnosis (13) (Supplemental Fig. 1, available online). As with polyps and leiomyomas, adenomyosis is a disorder that could benefit in due course from its own subclassification system (14), including standardization of methods of both imaging and histopathologic diagnosis.

Leiomyomas (AUB-L)

Most leiomyomas (fibroids) are asymptomatic, and frequently their presence is not the cause of the complaint of AUB. This, in combination with the prevalence of leiomyomas, caused the FMDG to create primary, secondary, and tertiary classification systems that are illustrated in Figure 2 (15).

FIGURE 2

Classification system, including tertiary leiomyoma subsystem. The system that includes the tertiary classification of leiomyomas categorizes the submucosal (sm) group according to the Wamsteker system (15) and adds categorizations for the intramural, subserosal, and transmural lesions. Intracavitary lesions are attached to the endometrium by a narrow stalk and are classified as type 0; types 1 and 2 require that a portion of the lesion is intramural, but with type 1 being 50% or less and type 2 more than 50%. The type 3 lesions are completely extracavitary but abut the endometrium. Type 4 lesions are intramural leiomyomas that are entirely within the myometrium, with no extension to the endometrial surface or to the serosa. Subserosal (types 5–7) myomas represent the mirror image of the submucosal myomas, with type 5 being more than 50% intramural; type 6 is 50% or less intramural, and type 7 is attached to the serosa by a stalk. Classification of lesions that are transmural will be categorized by their relationship to both the endometrial and serosal surfaces. The endometrial relationship would be noted first, and the serosal relationship would be second (e.g., 2–3). An additional category, type 8, is reserved for myomas that do not relate to the myometrium at all and would include cervical lesions, those that exist in the round or broad ligaments without direct attachment to the uterus, and other so-called "parasitic" lesions. (Reproduced with permission from Munro MG, Abnormal uterine bleeding, Cambridge, UK: Cambridge University Press, 2010.)



Munro. FIGO classification system for causes of AUB. Fertil Steril 2011.

The primary classification system reflects only the presence or absence of one or more leiomyomas, as determined by sonographic examination, regardless of the location, number, and size. In the secondary system, the clinician is required to distinguish myomas that involve the endometrial cavity (submucosal or SM) from others (O), because SM lesions are those that most likely contribute to the genesis of AUB.

The root of the tertiary classification system is a design for subendometrial or submucosal leiomyomas originally submitted by Wamsteker et al. (16) that was subsequently adopted by the European Society for Human Reproduction and Embryology (ESHRE). The PALM-COEIN system adds categorization of intramural and subserosal myomas as well as a category that includes lesions ("parasitic") that appear to be detached from the uterus (4). When a myoma abuts or distorts both the endometrium and serosa, it is categorized first by the submucosal classification, then by the subserosal location, with these two numbers separated by a hyphen (4).

Considered but not yet included are the size, number, and location of the tumors longitudinally in the uterus (e.g., the fundus, lower segment, or cervix).

Malignancy and Premalignant Conditions (AUB-M)

Although relatively uncommon in reproductive-aged women, atypical hyperplasia and malignancy are important potential causes of or findings associated with AUB. This diagnosis must be considered in any woman in the reproductive years and especially where there may be predisposing factors such as obesity or a history of chronic anovulation. Consequently, when an investigation of a women in her reproductive years with AUB identifies a premalignant hyperplastic or malignant process, it would be classified as AUB-M (4) and then subclassified by the appropriate World Health Organization (WHO) or FIGO system (17, 18).

Coagulopathy (Systemic Disorders of Hemostasis) (AUB-C)

The term *coagulopathy* is used to encompass the spectrum of systemic disorders of hemostasis that may cause AUB. High-quality evidence demonstrates that about 13% of women with heavy menstrual bleeding (HMB) have biochemically detectable systemic disorders of hemostasis, most often von Willebrand disease (19). Approximately 90% of patients with these abnormalities are included in a group that can be identified by a structured history (20) (Table 1). However, it is not clear how often these abnormalities cause or contribute to the genesis of AUB, and how often they are asymptomatic or minimally symptomatic biochemical abnormalities.

Ovulatory Disorders (AUB-O)

Ovulatory dysfunction can contribute to the genesis of AUB, generally manifesting in some combination of unpredictable timing of bleeding and a variable amount of flow, which in some cases results in HMB (21). Some of these manifestations relate to the absence of predictable, cyclic production of progesterone, but in the later reproductive years they may be a consequence of "luteal out-of-phase" (LOOP) events (21).

Although most ovulatory disorders elude a defined etiology, many can be traced to endocrinopathies (e.g., polycystic ovarian

TABLE 1

Structured history to screen for coagulopathies (AUB-C) also known as disorders of systemic hemostasis.

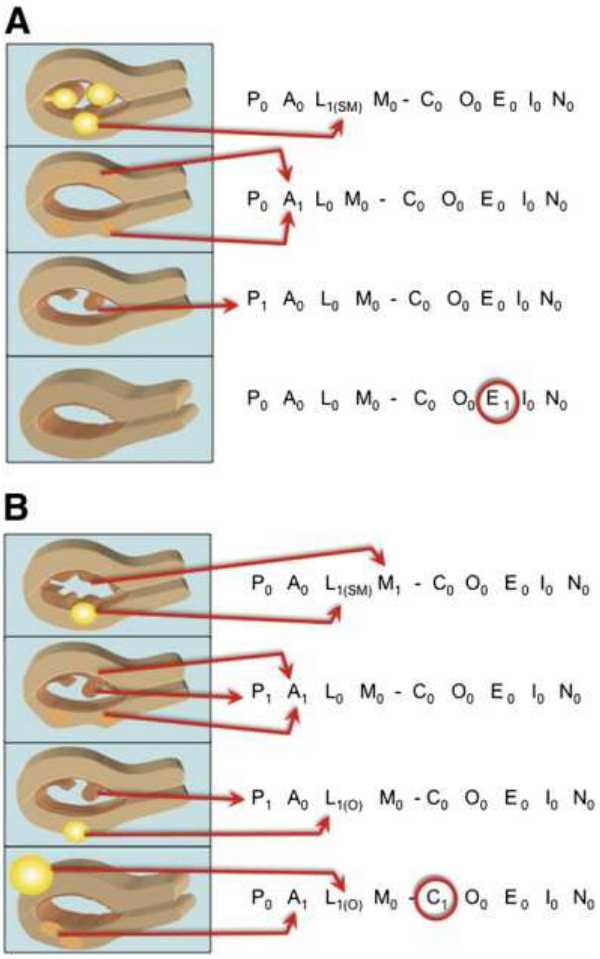
1. Heavy menstrual bleeding since menarche
2. One of the following:
   - Postpartum hemorrhage
   - Surgical related bleeding
   - Bleeding associated with dental work
3. Two or more of the following symptoms:
   - Bruising 1–2 times/month
   - Epistaxis 1–2 times/month
   - Frequent gum bleeding
   - Family history of bleeding symptoms

Note: Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding should be by a structured history: A positive screen comprises any of the following: heavy bleeding since menarche, one item from list 2, or two or more items from list 3. Patients with a positive screen should be considered for further evaluation, including a consultation with a hematologist and/or testing for von Willebrand factor and ristocetin cofactor. Modified from Kouides et al. (27).

Munro. FIGO classification system for causes of AUB. Fertil Steril 2011.

FIGURE 3

(**A**) Notation for each case, the presence or absence of each criterion is noted, using 0 if absent, 1 if present, and "?" if not yet assessed. Each of these cases have one abnormality identified, from the top: at least one submucosal leiomyoma (L_{SM}); adenomyosis, in this instance both focal and diffuse (A); endometrial polyps (P); and an absence of any abnormality leaving endometrial causes (E) as a diagnosis of exclusion. (**B**) Each of these cases has more than one positive category. In the top panel, there is a submucosal leiomyoma (L_{SM}), as well as atypical endometrial hyperplasia (M) diagnosed by endometrial sampling. The second case is found to have both endometrial polyps (P) and adenomyosis (A). The next case is characterized by both a subserosal leiomyoma (L_O) and endometrial polyps (P); and the bottom case has a subserosal leiomyoma (L_O) as well as a coagulopathy determined by a positive screening test and subsequent biochemical confirmation of von Willebrand disease. (Reproduced with permission granted by FIGO from Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders, FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age, Int J Gynaecol Obstet 2011;113:3–13.)



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syndrome, hypothyroidism, hyperprolactinemia, mental stress, obesity, anorexia, weight loss, or extreme exercise such as that associated with elite athletic training). In some instances, the disorder may be iatrogenic, caused by gonadal steroids or drugs that impact dopamine metabolism such as phenothiazines and tricyclic antidepressants.

Endometrial Causes (AUB-E)

When AUB occurs in the context of predictable and cyclic menses, suggestive of normal ovulation, and absent other definable causes, the mechanism is likely a primary disorder residing in the endometrium (4, 22). If the symptom is HMB, there may exist a primary disorder of mechanisms regulating *local* endometrial "hemostasis" itself, secondary to deficiencies in local production of vasoconstrictors such as endothelin-1 and prostaglandin F2α, and/or accelerated lysis of endometrial clot because of excessive production of plasminogen activator (23) and increased local production of substances that promote vasodilation such as prostaglandin E2 and prostacyclin (I_2) (24, 25).

There may be other primary endometrial disorders that do not manifest in HMB per se, but may, for example, cause IMB, such as endometrial inflammation or infection, abnormalities in the local inflammatory response, or aberrations in endometrial vasculogenesis. At the present time, there are no available specific tests for these disorders, so the diagnosis of AUB-E should be determined by exclusion of other identifiable abnormalities in women of reproductive years who appear to have normal ovulatory function.

Iatrogenic (AUB-I)

There are a number of mechanisms by which medical interventions or devices may cause or contribute to AUB (AUB-I). Unscheduled endometrial bleeding that occurs during the use of exogenous gonadal steroid therapy is termed "breakthrough bleeding" (BTB), the major component of the AUB-I classification (4). Included in this category are the women using the levonorgestrel-releasing intrauterine system (LNG-IUS), who frequently experience BTB in the first 6 months of therapy (26).

When AUB is thought to be secondary to anticoagulants such as warfarin or heparin, or systemic agents that contribute to disorders of ovulation such as those that interfere with dopamine metabolism, it is categorized as AUB-C or AUB-O, respectively (4).

Not Classified (AUB-N)

There exist a number of entities that may or may not contribute to or cause AUB in a given woman for they have been either poorly defined, inadequately examined, and/or are extremely rare. Examples in this category might include arteriovenous malformations and myometrial hypertrophy. Furthermore, there may exist other disorders, not yet identified, that would be defined only by biochemical or molecular biological assays. Collectively, these entities (or future entities) have been placed in a category termed N for Not Classified. As further evidence becomes available, they may be allocated a separate category, or may be placed into one or the existing categories in the system (4).

NOTATION

After appropriate investigation, an individual may be found to have one or multiple potential causes of or contributors to their complaint of AUB. Consequently, the system has been designed to allow categorization and notation in a fashion that allows for this circumstance (4).

The formal approach follows the example of the WHO TNM (tumor, node, metastasis) staging of malignant tumors, with each component addressed for all patients. Examples are provided in Figure 3. Recognizing that, in clinical practice, the full notation might be considered to be cumbersome, an abbreviation option has been developed.

GUIDELINES FOR INVESTIGATION

Women with AUB may have none, one, or multiple identifiable factors that may contribute to the genesis of the abnormal bleeding (4). There may also be pathology, such as a subserosal leiomyoma, that is present but is thought not to be a contributor to AUB. Consequently, the investigation of the woman with AUB must be undertaken in as diligent and comprehensive a fashion as is practicable, given the clinical situation and the available resources (4). This suggested approach for investigation is demonstrated in Supplemental Figure 2 (available online); the suggested approach for evaluation of the uterus is provided in Supplemental Figure 3 (available online).

CONCLUSION

It is anticipated that this system of classification should facilitate multi-institutional investigation into the epidemiology, etiology, and treatment of women with acute and chronic AUB (4). The system should also foster meta-analysis of clinical trials that are appropriately designed and reported. It is also recognized that the system will require periodic modification and occasional substantial revision, depending on advances in knowledge and technology, and increasing availability of investigative options across geographic regions.

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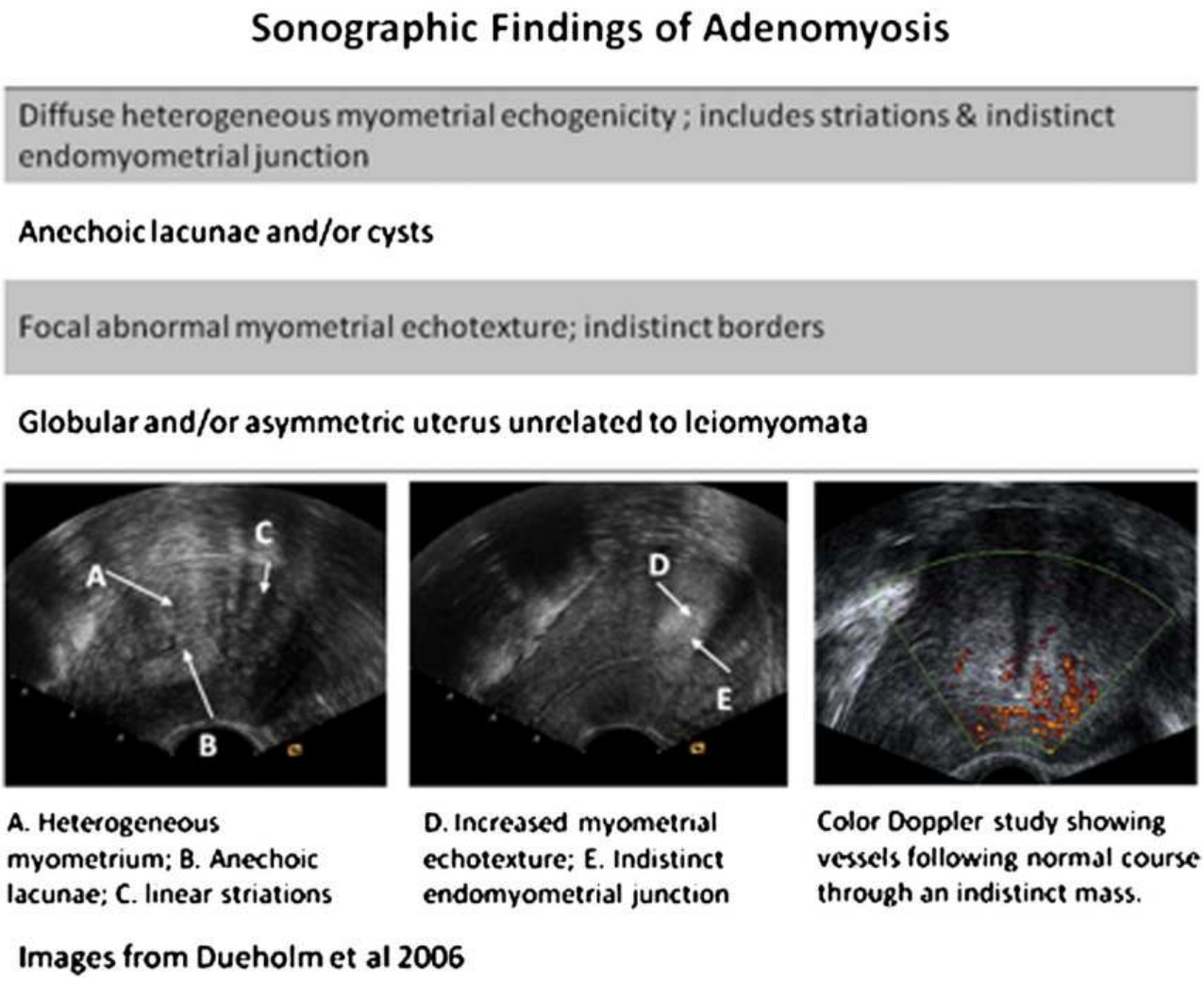
SUPPLEMENTAL FIGURE 1

Adenomyosis detection by transvaginal ultrasound. The criteria for diagnosis based on transvaginal ultrasound of adenomyosis are shown. When the uterus is larger than 300 to 400 mL, the accuracy of vaginal sonography diminishes. Indistinct borders characterize focal lesions or adenomyomas, and if color Doppler is available, blood vessels course through the mass. Leiomyomas tend to have a more distinct margin, and distort the surrounding myometrium; if color Doppler is used, vessels tend to cluster around the mass. (Images reproduced with permission from Dueholm M, Transvaginal ultrasound for diagnosis of adenomyosis: a review, Best Pract Res Clin Obstet Gynaecol 2006;20:569–82, and Dueholm M, Lundorf E, Hansen ES, Sorensen JS, Ledertoug S, Olesen F, Magnetic resonance imaging and transvaginal ultrasonography for the diagnosis of adenomyosis, Fertil Steril 2001;76:588–94.)



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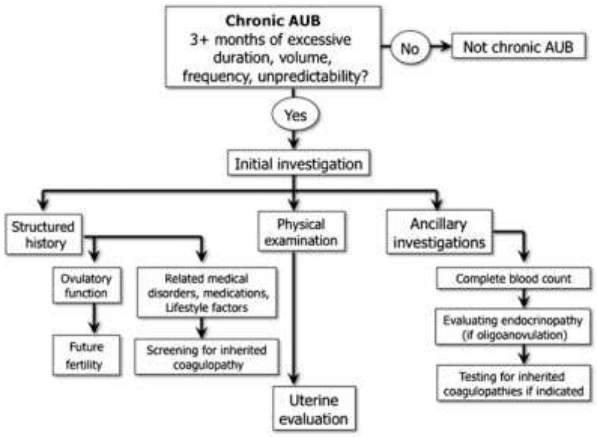
SUPPLEMENTAL FIGURE 2

Initial evaluation. The initial assessment requires that the patient have a majority of the previous 6 months characterized by one or a combination of unpredictability, excessive duration, abnormal volume, or abnormal frequency of menses. Patients should undergo a structured history designed to determine ovulatory function, potential related medical disorders, medications, and lifestyle factors that might contribute to abnormal uterine bleeding. For those with heavy menstrual bleeding, the structured history should include the questions from Table 1. Understanding the future fertility desires of the patient will help frame the discussion of therapy after appropriate investigation. Ancillary investigations should include hemoglobin and/or hematocrit, appropriate tests for features that could contribute to an ovulatory disorder (thyroid function, prolactin, serum androgens), and, if the structured history based on Table 1 is positive for coagulopathy, either referral to a hematologist or measurement of appropriate tests for von Willebrand disease. (Reproduced with permission from Munro MG, Abnormal uterine bleeding, Cambridge, UK: Cambridge University Press, 2010.)



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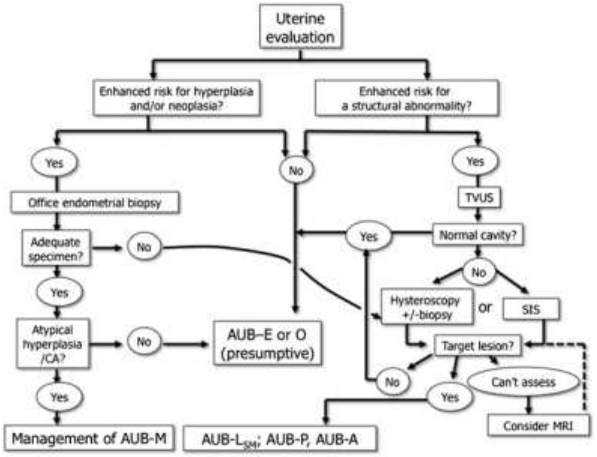
SUPPLEMENTAL FIGURE 3

Uterine evaluation. The uterine evaluation is in part guided by the history and other elements of the clinical situation such as patient age, presence of an apparent chronic ovulatory disorder, or the presence of other risk factors for endometrial hyperplasia or malignancy. For those at increased risk, endometrial sampling is probably warranted. If the risk of a structural anomaly is present, particularly if previous medical therapy has been unsuccessful, evaluation of the uterus should include imaging, at least with a "screening" transvaginal ultrasound examination. Unless the ultrasound image suggests a normal endometrial cavity, it will be necessary to use one or a combination of hysteroscopy and saline infusion sonography to determine whether target lesions are present. Such an approach is also usually desirable if endometrial sampling has not provided an adequate specimen. Uncommonly, these measures are inconclusive, or, in the instance of girls and women who have never had sexual intercourse, are not feasible outside of an anesthetized environment. In these instances, magnetic resonance imaging may be of value, if available. (Reproduced with permission from Munro MG, Abnormal uterine bleeding, Cambridge, UK: Cambridge University Press, 2010.)



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