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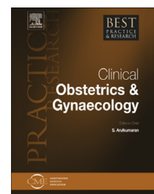

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# Abnormal Uterine Bleeding including coagulopathies and other menstrual disorders

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A B S T R A C T

Abnormal Uterine Bleeding (AUB) is a frequent cause of visits to the emergency department and a major reason for concern among adolescents and their families. The most common cause of AUB, in otherwise healthy adolescents, is ovulatory dysfunction, although 5–36% of adolescents who present with heavy menstrual bleeding, have an underlying bleeding disorder (BD). The most common form of BDs is von Willebrand Disease, reflecting 13% of adolescents with AUB. Management of AUB depends on the underlying etiology, the bleeding severity, as well as the need for hospitalization. Treatment of adolescents with an underlying coagulopathy depends on the severity of the BD, while therapeutic interventions are summarized in supportive measures, hormonal treatments (e.g. Combined Oral Contraceptives), non-hormonal treatments (e.g. tranexamic acid and desmopressin), surgical options (e.g. dilatation & curettage) and treatment options in specific conditions.

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## Introduction

Abnormal Uterine Bleeding (AUB) includes several symptoms during adolescence, such as heavy menstrual bleeding and intermenstrual bleeding, as well as coexisting heavy and prolonged menstrual

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bleeding [1]. It is a frequent cause of visits to the emergency department among adolescents, affecting up to 14% of women during their reproductive years [2,3]. In 2011, the International Federation of Gynecology and Obstetrics (FIGO) Menstrual Disorders Working Group proposed a new classification system for the diagnosis of AUB in reproductive age nulligravid women. Specifically, FIGO suggested the term PALM-COEIN, which stands for the following causes of AUB: Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not otherwise classified [1].

Almost 95% of otherwise healthy adolescents presenting with AUB are diagnosed with ovulatory dysfunction-anovulation, due to immaturity of Hypothalamic-Pituitary-Ovarian (HPO) axis [4]. Despite high frequency of anovulation during adolescence, other underlying pathologies, such as BD (e.g. von Willebrand Disease), pathologies of the reproductive tract (e.g. polyps), trauma, pregnancy, medication, as well as other endocrine disorders (e.g. hypothyroidism) affecting ovulation, should be taken into consideration, before establishing the diagnosis [5]. An inherited, acquired, or iatrogenic systemic disorder of hemostasis, also known as coagulopathy, seems to be a more frequent cause of AUB than generally recognized, particularly in perimenarcheal girls. In particular, 10.7% of women with menorrhagia were found to be affected by coagulopathies, in a case-control study by the US Centers for Disease Control and Prevention (CDC) [6].

## Evaluation of Abnormal Uterine Bleeding (AUB)

Several diagnoses need to be considered for the evaluation of adolescents with AUB. Careful examination of each patient is mandatory in order to establish the proper diagnosis. Pregnancy related complications require immediate exclusion, due to their high morbidity and mortality rates [7], and physicians should be alert, about the fact that they can present with any pattern of menstrual disorders. Ectopic pregnancy is one of the most serious and life-threatening conditions among pregnancy related complications. As mentioned above, the incidence rates of coagulopathies frequency is significantly greater in adolescents than the general population, posing a challenging and imperative diagnosis for clinicians. BDs are usually associated with menorrhagia [8,9], while the same pattern may be seen in adolescents receiving medication, such as anticoagulants. A variety of different medications, including glucocorticoids and tamoxifen can predispose to AUB [10], while pelvic inflammatory disease (PID), especially when caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, can be expressed with AUB, but most of the time is accompanied by lower abdominal pain [7]. Other conditions, such as fibroids, dysplasia or cancer, are rarely seen in adolescence, but should always be considered during the differential diagnosis of AUB. An underlying pathology must always be suspected, in cases of need for hospitalization and if hemoglobin is less than 10 g/dL [9].

Anovulation is the most common cause of AUB during adolescence. Increased age at menarche is correlated with prolonged ovulatory dysfunction [11]. Cycle length, bleeding length in days and number of pads or tampons used over a 24-h period should always be recorded in a menstrual calendar. Normal blood loss must not exceed 80 mL, which is equivalent to three soaked pads or six full regular-absorbency tampons per day for 3 or more days [12]. History of bleeding episodes and clots or leaking during menstruation, especially at night, is commonly linked with a BD and should always be reported [9,12]. Adolescent's past medical history and family history is very important, while clinical examination should never be omitted. Vital signs, as well as any signs like tachycardia, hypotension or orthostatic changes should be recorded and treated accordingly. Physical examination should be focused on the genitourinary system (discharge/inflammation, trauma, etc.), while in sexually active girls, the clinician must clarify that the bleeding comes in fact from the vagina/cervix, no foreign body (e.g. a retained tampon) is present and cervix has a normal appearance. PID should always be suspected in cases of tenderness or pain at the cervix, the adnexa or the uterus during bimanual gynecological palpation. In non-sexually active adolescents, recto-abdominal palpation should be carefully considered.

Three initial laboratory investigations may significantly aid the diagnosis; urine pregnancy test and/or quantitative serum β-HCG, a complete blood cell count and a pelvic ultrasound scan. Prothrombin time, partial thromboplastin time, bleeding time, platelet aggregation and von Willebrand panel, must be measured prior to initiating coagulation factor levels/activity (depending on family history and

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