Abnormal menstrual bleeding in young women

When to investigate

MIKHAILA K. LAZANYI MB BS(Hons), MPHTM, FRANZCOG, IFEPAG
SONIA R. GROVER MB BS, FRANZCOG, MD, FFPMANZCA

Irregular menstrual cycles and bleeding among adolescent girls are common and developmentally normal but can be difficult to distinguish from abnormal bleeding. An understanding of normal physiological processes in this younger age group, along with careful history taking and assessment, can help avoid unnecessary investigations and alleviate anxiety.

Abnormal uterine bleeding is common in adolescent girls and often reflects anovulatory cycles related to an immature hypothalamic-pituitary-ovarian (HPO) axis. The aetiology of and approach to management to abnormal menstrual bleeding is different from that of older women. This article discusses the approach to investigating and managing abnormal menstrual bleeding in young women.

The HPO axis

When the HPO axis first switches on, with resultant breast development, the cycle control processes are still immature. Thus, anovulatory cycles occur, which are associated with disorganised menstrual bleeding. Defining normal, and therefore abnormal, bleeding in the adolescent population is thus challenging. Irregular cycles and ovulatory dysfunction are a normal component of pubertal transition, and the rate of physiological maturation of the HPO axis varies among adolescent girls.[1]

When is irregular menses abnormal?

Defining irregular menses during adolescence is challenging because of a lack of high-quality normative data. During the second year after menarche, 50% of menstrual cycles range between 21 and 45 days, increasing to 80% at two years, and 95% at three years postmenarche.[1-4] By comparison, a menstrual cycle of 21 to 35 days is considered normal in a typical adult woman. Age at menarche and time since menarche are important predictors of menstrual cycle length and regularity. Menstrual cycles are more likely to become regular earlier, that is if menarche occurs before 12 years of age compared with at 15 years of age.[1,5] Factors such as stress, changing exercise levels and changes in body weight influence the HPO axis and are common causes for irregular periods in adolescence.

According to the *International Evidence-based Guideline for the Assessment and Management of Polycystic Ovarian Syndrome (PCOS) 2023*, irregular menstrual cycles are defined as occurring less than 21 days or more than 45 days between one and three years after menarche.[6] After this time, the definition of irregular cycles is less than 21 days, or more than 35 days, or any one cycle more than 90 days. However, based on this normative data, about 50% of adolescents will experience irregular menses in the second year after menarche and 20% at two years, which, from a statistical definition, cannot be considered 'abnormal.' It is therefore the authors' opinion that investigating irregular menses alone may not be necessary until three or more years after menarche, unless the cycle remains over 45 days. It is important to consider factors such as level of physical activity, body weight and stress levels, in addition to the cycle pattern, as all these factors contribute to the menstrual cycle pattern. Most irregularities will naturally improve with time.

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Dr Lazanyi is a Consultant Obstetrician and Gynaecologist at Joan Kirner Women's and Children's Hospital and Royal Children's Hospital, Melbourne.
Professor Grover is Director of the Department of Paediatric and Adolescent Gynaecology at Royal Children's Hospital, Melbourne; Head of Plenty Gynaecology unit at Mercy Women's Hospital, Melbourne; and Honorary Professor at The University of Melbourne, Melbourne, Vic.
SERIES EDITOR: Clinical Associate Professor Deborah Bateson MA(Oxon), MSc(LSHTM), MB BS, Professor of Practice, The University of Sydney, Sydney, NSW.

Irregular menses and potential polycystic ovarian syndrome

Diagnosing polycystic ovarian syndrome (PCOS) is difficult and controversial in adolescents, given that irregular cycles and other features of PCOS, such as mild acne and multicystic morphology of the ovaries on ultrasound, are a part of normal puberty.[1,6,7] The diagnostic definitions for PCOS were initially derived for adult women and those trying to conceive, and do not take into account the normal and relatively immature physiological processes in adolescents. The International PCOS guidelines suggest that 'the value and optimal timing of assessment and diagnosis of PCOS [in adolescents] should be discussed with the patient, taking into account diagnostic challenges at this life stage'.[1]

A pelvic ultrasound within the first eight years of menarche should not be performed in the work up for PCOS.[1,6,7] Androgen studies, if performed, should include measurement of free testosterone level, free androgen index or bioavailable testosterone.[7] Androgen studies are useful in adolescent girls presenting with symptoms of severe hyperandrogenism, including virilisation, clitoromegaly and voice changes, and when an androgen-producing tumour needs to be considered. If a tumour is considered, investigations should also include androstenedione and dihydrotestosterone levels.

Differential diagnoses of irregular menses or hyperandrogenism include hypothyroidism, hyperprolactinemia, Cushing's disease, glucocorticoid resistance and androgen-secreting ovarian or adrenal tumours. A thorough history and examination should consider these uncommon causes. If suspected, appropriate testing to exclude pathology should occur.

Any adolescent with features of PCOS should be considered 'at risk' for PCOS, independent of a diagnosis. They should be regularly re-evaluated and receive lifestyle optimisation information and treatment for symptoms.[6,7] It is recommended that menstrual irregularity that has persisted to beyond three years after menarche (in the absence of other explanations such as stress, weight change and exercise levels) be investigated, as 95% of cycles should be ovulatory by this time. Irregular menses should also be reviewed eight years after menarche if multicystic morphology of the ovaries is present on ultrasound.[7] Important lifestyle interventions include screening for mental health conditions, optimising body mass index (BMI) and improving lifestyle measures such as nutrition, reducing sedentary behaviours and increasing physical activity.[6,7] Symptomatic treatment may include combined hormonal contraceptives (CHCs), metformin, antiandrogens, or a combination of these.[1,6,7] Discussing preventative health measures with adolescents, including the use of contraception, is important given that Australian data show young women who have been labelled as having PCOS may presume they have reduced fertility, and not use contraception, resulting in unplanned pregnancies.[8]

Any adolescent with features of PCOS [polycystic ovarian syndrome] should be considered 'at risk' for PCOS, independent of a diagnosis

When is heavy menstrual bleeding considered abnormal?

Heavy menstrual bleeding (HMB) is defined as excessive menstrual blood loss that interferes with a woman's quality of life. Clinically, this often equates to prolonged (seven days or more) or heavy bleeding (flooding onto bed sheets, changing pads or tampons more often than two-hourly, developing iron deficiency anaemia), or both. HMB occurs in up to 40% of adolescents and is most commonly due to irregular anovulatory cycles postmenarche.[9-13] Other causes include pregnancy, infection, medications, weight changes and mild bleeding disorders (MBDs). Compared with adult women, structural causes are an uncommon cause of HMB in adolescents.

About 1% of the general population has a bleeding disorder; however, 10 to 20% of adolescent girls and about 10% of adult women presenting with HMB have an MBD.[10,14-16] Of adolescents with a known bleeding disorder, 70% report HMB.[14,17] Although there is no exact definition for MBDs and a wide variation in phenotypes exists, they are distinct from rare severe bleeding disorders that may cause life-threatening bleeding if untreated.[18]

The International society of Thrombosis and Haemostasis (ISTH) created a standardised bleeding assessment tool (BAT) for use in children and adults (ISTH-BAT).[19] The aim is to improve diagnostic accuracy and avoid unnecessary testing, and has been shown to have a high negative predictive value in adults.[20] Self-administered BATs, such as that found on the Let's Talk Period website (https://letstalkperiod.ca/self-bat/eng/) are web-based validated BATs comparable to the ISTH-BAT in assessing the likely signs of a bleeding disorder.[21] They can be completed by young people during or before an appointment; however, given that self-BATs have a low positive predictive value, abnormal result should be followed up with appropriate diagnostic testing.[20] The following personal or family history also warrants diagnostic testing:[14,22,23]

- duration of menses of seven days or more and 'flooding' or changing tampon or pad less than two-hourly
- a history of anaemia (secondary to heavy menstrual bleeding)
- a family history of bleeding disorders
- a history of excessive bleeding after tooth extraction or surgery.

Testing should include screening for von Willebrand disease, platelet function disorders and thrombocytopenias. Testing should not be undertaking when NSAIDs have been used within seven days of the test because of the impact on platelet function, or when the patient is particularly stressed about the potential for false normalisation of von Willebrand screening results. Less commonly, factor deficiency studies may be required.

When is amenorrhoea considered abnormal?

Primary amenorrhoea is defined by the absence of menses by the age of 15 years, or if no menses occurs within three years of thelarche. Causes of primary amenorrhoea should be investigated, although they are beyond the scope of this article.

Secondary amenorrhoea is an absence of menses for more than three months in someone who previously had regular menstrual cycles, or six months in those with irregular menses. In young women, secondary amenorrhoea is commonly related to functional hypothalamic causes, such as significant weight loss, excessive exercise or high levels of stress. In those with disordered eating, losing 10 to 15% of normal body weight may lead to amenorrhoea.[24-26] The cluster of moderately high exercise and calorie restriction for the purposes of being 'really healthy and fit' can lead to amenorrhoea, and may be labelled as an 'eating disorder not otherwise specified'.

Important predictors associated with the resumption of menses after an eating disorder include BMI, age and menarche status before the onset of the eating disorder, and BMI when menses stopped during the eating disorder itself.[27] The delay between a return to a healthy BMI and resumption of menses is often 12 to 18 months. An earlier resumption of menses occurs more frequently in those with a low- or normal-range BMI before the eating disorder, postmenarchal status and older age at onset, greater change in BMI at diagnosis and recovery, and shorter duration of the eating disorder.[27-29] A target body weight for menses to resume in adolescents is difficult to predict given that height and weight increase during the developmental period in which an eating disorder is occurring.[30] Reaching and maintaining a healthy BMI of at least 18 to 20 kg/m^2 is favourable for resuming menses, alongside optimising body weight and normalising healthy eating patterns.

CHCs do not improve bone mineral density in those with an eating disorder who are amenorrhoeic as long as eating patterns are unstable, calorie intake is restricted and weight recovery has not occurred.[24,30-33] Management of the eating disorder with an expectant approach to the return of menses without the use of CHCs is appropriate. However, CHCs are recommended for those in this group who are sexually active and require reliable contraception despite amenorrhoea, as ovulation can occur, albeit unpredictably, with the subsequent risk of pregnancy. Further management of eating disorders from a gynaecological perspective is beyond the scope of this article; however, useful links can be found in the Box.

An approach to history taking

History taking is paramount in any adolescent presenting with irregular menstrual bleeding. General history in this group includes a medical and surgical history, current and past medication use and family history, including the mother's age of menarche, menstrual concerns, maternal postpartum haemorrhage, coagulation disorders, hormone-sensitive cancers and blood clots. Performing a HEADSSS psychosocial assessment and history taking, ideally in the presence and absence of a caregiver, are recommended for all adolescents. Important components of the patient's menstrual history include age of menarche, cycle regularity, length of a cycle, duration of menses and associated symptoms, including the presence of heavy bleeding, pain and luteal phase symptoms. The length of cycle in the context of time since menarche is important. Previous sexual activity, sexually transmitted infection screening, risk of infections and use of contraception should be discussed.

Patients' general appearance should be observed, including ethnicity, BMI and vital signs, and an abdominal examination performed for masses, tenderness and guarding. Speculum and bimanual examinations are rarely required unless pregnancy-related bleeding is suspected. Depending on this initial history, further questioning for irregular menstrual presentations are presented in the Table.

USEFUL RESOURCES ON MANAGING ADOLESCENT PATIENTS

Royal Children's Hospital Clinical Practice Guideline on heavy menstrual bleeding in adolescents:
https://www.rch.org.au/clinicalguide/guideline_index/Adolescent_Gynaecology_Menorrhagia/

Royal Children's Hospital Clinical Practice Guideline on engaging with and assessing the adolescent patient:
https://www.rch.org.au/clinicalguide/guideline_index/Engaging_with_and_assessing_the_adolescent_patient

American College of Obstetricians and Gynecologists Screening and Management of Bleeding Disorders in Adolescents With Heavy Menstrual Bleeding:
https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2019/09/screening-and-management-of-bleeding-disorders-in-adolescents-with-heavy-menstrual-bleeding

American College of Obstetricians and Gynecologists Gynaecologic Care for Adolescents and Young Women With Eating Disorders:
https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/06/gynecologic-care-for-adolescents-and-young-women-with-eating-disorders

Faculty of Sexual and Reproductive Healthcare FSRH CEU Statement: Contraception for Women with Eating Disorders (May 2021):
https://www.fsrh.org/standards-and-guidance/documents/fsrh-ceu-statement-contraception-for-women-with-eating/

Managing a young person with abnormal menstrual bleeding

Optimal management depends on the presenting symptoms, its impact on quality of life and patient preference. The risks and benefits of any treatment should be discussed in detail, including with family members, if available.

TABLE. ASSESSMENT OF ADOLESCENTS WITH IRREGULAR MENSTRUAL PRESENTATIONS AFTER INITIAL HISTORY

Assessment	Presentation	
	Irregular bleeding	Heavy menstrual bleeding
When to investigate	• ≥3 years post menarche and cycle <21 or >35 days • <3 years if cycle >45 days	• Duration of period >7 days or more and changing pads or tampons >2-hourly • Soaking bed sheets overnight • Bleeding causing lifestyle disturbance • Personal history of anaemia • Personal history of excessive bleeding after tooth extraction or other surgery • Family history of bleeding disorder*
Additional history	• Check for hyperandrogenic symptoms, including severe acne, hirsutism, alopecia and virilisation • Consider BMI, ethnicity and family history of premature ovarian insufficiency • Ask about symptoms of thyroid dysfunction, including heat intolerance and weight changes • Check for symptoms of hyperprolactinaemia, including headache and visual disturbance	Ask the patient to perform a self-BAT questionnaire[21]
Additional examination	• If hirsutism is present, determine the modified Ferriman Gallwey score[1] • If alopecia is present, determine the extent using the Ludwig visual score[1]	• Check for the presence of bruising, epistaxis, bleeding and petechiae • Ask about a family history of bleeding problems
Additional investigations	• FSH, LH, oestradiol, TSH, prolactin and bhCG levels† • If hyperandrogenic symptoms are present, consider androgen studies after discussion with the patient and their carer‡	• FBE, iron studies, bhCG and TSH levels, aPTT and PT† • If abnormal ISTH-BAT score, perform von Willebrand screen and platelet function assay (PFA-100)§ • Pelvic ultrasound is rarely required given structural causes are uncommon

Abbreviations: aPTT = activated partial thromboplastin time; bhCG = beta human chorionic gonadotrophin; BAT = bleeding assessment too; BMI = body mass index; FBE = full blood examination; FSH = follicle-stimulating hormone; ISTH = International Society of Thrombosis and Haemostasis; LH = luteinising hormone; PT = prothrombin time; TSH = thyroid-stimulating hormone.
* No clinical variables have been found to discriminate girls and young women with or without a bleeding disorder.
† Refer to a haematologist if initial laboratory testing is not definitive but a high clinical suspicion remains.
‡ Androgen studies include free testosterone, androstenedione, dihydrotestosterone (DHEAS) and free androgen index.
§ Von Willebrand screening includes VWF antigen, VWF ristocetin cofactor activity, factor VIII level and VWF collagen binding assay.

Nonhormonal and hormonal medications remain the mainstays of standard management of abnormal menstrual bleeding. Expectant management may be a reasonable option for those who are not bothered by their symptoms, for those in whom irregular cycles or HMB is perimenarchal and in those wanting to avoid medical therapy. Nonhormonal approaches to managing HMB are often acceptable for younger adolescents and their parents. Follow up in a reasonable timeframe, for example three months, is recommended. Medical management for patients who are iron deficient, with iron tablets or, if very ferritin deficient and symptomatic or unresponsive to oral therapy, iron infusion is recommended. Surgical management is rarely required.

When to refer

Abnormal menstrual bleeding in young women that interferes with daily activities warrants discussion and possible investigation and management. If this bleeding continues despite management in the general practice setting, referral to a gynaecologist with experience in adolescents and young people is warranted. Patients with recurrent iron deficiency or in whom secondary causes of abnormal menstrual bleeding are identified should also be referred to a gynaecologist.

Conclusion

Menstrual irregularities in girls and young women are common and often reflect normal physiological processes. Aetiology and management are different from those of older women and, therefore, require adequate education and awareness of the overlap of normal irregular menses in younger people, and abnormal menses in older women, to avoid unnecessary inves-tigation or management.

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

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