Rapid Resource

Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence | FOUNDATION FOR Women & Girls with Blood Disorders

Anticoagulation Use in Menstruating People

Prior to Initiating Anticoagulation

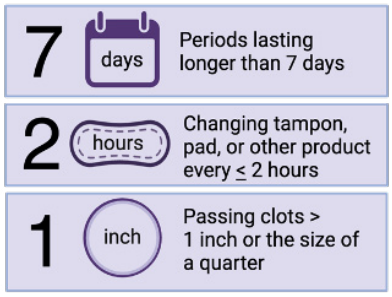
Get to know the patient

Take a Baseline Menstrual History
Ask the patient:
- Do you have a history of heavy or irregular periods?
- How often are you changing your protection?
- Are you experiencing painful periods?
- What are you using to prevent pregnancy?

Screen for medications that increase the risk of bleeding (ex. Aspirin, NSAIDs)
- Counsel on risks and deprescribe Aspirin and NSAIDs when appropriate

Share trusted resources:
https://www.betteryouknow.org/

Discuss Heavy Menstrual Bleeding



OR Excessive menstrual blood loss that interferes with **physical, emotional, social & material quality of life**

Holding anticoagulation during heavy menstrual periods can increase the risk for recurrent VTE

Screen for Anemia and Iron Deficiency

Important labs (with normal ranges)
- Ferritin (50-150 ng/mL)
- Hemoglobin (12-15 mg/dL)

Patients can be iron deficient without being anemic!

Monitor for symptoms & consider testing if new or worsening: Fatigue, inability to concentrate, headaches, easy bruising, hair loss, restless legs

If **ferritin < 50 ng/mL**, the patient is iron deficient. Start oral or IV iron supplementation

Quality of Life Matters!

HMB can significantly impact **physical, emotional, social & material quality of life**

- Patients may feel isolated and suffer in silence
- Studies show only **4 in 10** effected seek care due to[1]:
  - Lack of awareness that heavy menstrual bleeding is NOT normal
  - Perceived discriminations
  - Stigmas surrounding menstruation
- **2 of 3** women who start anticoagulation for acute VTE experience some degree of AUB[2], and this has been directly correlated to a negative impact on their Quality of Life

The Impact of Antithrombotics on Heavy Menstrual Bleeding

Incidence of CRNMB or MB[3]
*Many cases of AUB are underestimates

Medication	OR	Incidence
Warfarin	Ref.	4.5 - 9.6%
Rivaroxaban	2.1	9.5%
Edoxaban	1.26	9.0%
Apixaban	1.18	5.4%
Dabigatran	0.59	5.9%

- Actual incidence of bleeding events is likely higher due to underreporting & lack of awareness
- People with uterine fibroids on anticoagulation have reported greater reductions in Hemoglobin and are at higher risk for bleeding events
- By age 50, 90% of Black people with a uterus have fibroids which can result in heavy bleeding[4]

What about antiplatelets?[5]

9-12% of patients on aspirin 100mg reported an increase in flow duration
&
13-20% reported an increase in flow intensity

Key Touch Points and Referrals For Your Patients

Anticoagulation Clinics	Screen for changes in menstrual flow. Discuss impact on QOL
Primary Care Providers and Antithrombotic Prescribers	Take a complete menstrual history and incorporate in management decisions of antithrombotic medications
OBGYN	Engage in shared decision making around contraception, prenatal planning, pregnancy, breastfeeding and treatments for menopause
Hematology	Participate as needed in the management of complex antithrombotic therapy management
Interventional Radiology	Participate as needed for procedural interventions to manage AUB (ex. Uterine artery embolization)

This content was developed in partnership with Foundation for Women & Girls with Blood Disorders.

Created: 04/25 **Next Review:** 06/25

Anticoagulation Use in Menstruating People

AUB Management and Treatment Options

	Administration	Effectiveness for HMB[6,7]	Contraception Efficacy[8]	VTE Risk
Hormonal Options:				
Levonorgestrel IUD (Mirena®, Skyla®, Liletta®)	Set it and forget it!	• Reduction in MBL by estimated 96% at 1 year • Amenorrhea in up to 50% at 1 year	99.7%	No increased risk
Etonogestrel implant (Nexplanon®)	Set it and forget it! Subdermal arm	• Amenorrhea in 22% • May result in irregular bleeding	99.9%	No increased risk
Progesterone pill	Must take at the same time daily for effective pregnancy prevention (drospirenone may be more flexible)	• Significantly reduces MBL • Amenorrhea in up to 20%	91-94% in typical use, up to 99% when used as directed	No increased risk
Depot medroxypro-gesterone acetate IM (Depo Provera®)	Administration q3 months by healthcare provider	• Significantly reduces MBL • Amenorrhea in up to 50%	96%	• No evidence of increased risk when used with AC • Discontinue 3 months prior to stopping AC
Combined Hormonal Contraceptives	Oral, patch, or vaginal ring	• Reduction in MBL by estimated 50% • Can induce amenorrhea when used continuously	93%	• No evidence of increased risk when used with AC • Discontinue 4 weeks prior to stopping AC
Non-Hormonal Options:				
Antifibrinolytic Tranexamic acid	2 tabs TID while bleeding	Reduction in blood loss by estimated 50%	N/A	No increased risk
Change anticoagulant	Switch to agents with lower HMB risk: apixaban or dabigatran (dabigatran has the lowest risk of HMB) *Don't forget to discuss/ensure agent is affordable at time of prescribing			
Procedures:				
For patients who have completed childbearing: • **Uterine artery embolization (UAE):** Post-UAE pregnancies have been reported, but risks are unknown • **Endometrial ablation:** Highly effective contraception required due to risk of fatal placental complications • **Hysterectomy**				

Don't Forget!

- Continue to reevaluate menstrual bleeding control, QOL, cost of treatment at each visit
- Iron supplementation may be necessary with or without anemia
- Holding anticoagulant during a period may increase risk for recurrent VTE
- It is important to identify the cause of the AUB and the etiology can help tailor your treatment plan

This content was developed in partnership with Foundation for Women & Girls with Blood Disorders.

Created: 04/25 **Next Review:** 06/25

Rapid Resource | Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence | FOUNDATION FOR Women & Girls with Blood Disorders + Includes people who have or had the ability to menstruate

Anticoagulation Use in Menstruating People

Contraception Counseling

Preventing unplanned pregnancy is critical for patients on AC

- Risk of first and recurrent VTE are increased in pregnancy
- Other conditions requiring AC, such as mechanical valves, are associated with higher risks in pregnancy
- Oral anticoagulants are teratrogenic (warfarin) or have limited safety data (DOACs) in pregnancy

All forms of contraception can be considered in patients on therapeutic AC

- Long-acting reversible contraceptive methods (IUD, etonogestrel implant) are highly effective and decrease menstrual blood loss (although bleeding may be unpredictable)
- Traditional progestin-only pills are extremely time-sensitive, but newer formulations (i.e. drospirenone) are more reliable and less time sensitive

Access to reproductive health services vary by location. AC clinics are an important source of information on local resources, access & alternatives.

Preconception Planning & Counseling

Preconception counseling is critical for patients desiring pregnancy and should include:

Patients on chronic AC *(discuss periodically)*

- AC options in pregnancy: Low molecular weight heparin [LMWH] preferred over unfractionated heparin (UFH)
- When to transition from current drug to LMWH (e.g. either upon D/C of contraception or after 1st positive pregnancy test)

Patients with VTE <u>not</u> on chronic AC *(discuss at least once before discharge)*

- When to start prophylactic AC (first positive pregnancy test vs confirmation of intrauterine pregnancy on ultrasound)
- Need for AC through 6 weeks postpartum

All Patients

- Additional planning around delivery: when to discontinue AC; when to resume AC
- AC options during lactation: LMWH or warfarin

Peri- & Post-Menopause

Vaginal bleeding in peri- & post-menopause

- Be aware that vaginal bleeding can become heavier, more irregular leading up to menopause
- Acute changes in vaginal bleeding and/or post menopausal bleeding requires referral to OBGYN to exclude malignancy or other non-hematologic causes

Estrogen supplementation for menopausal symptoms

- Topical vaginal estrogen does not increase thrombotic risk and can be safely used in patients with VTE history
- Transdermal estrogen has a lower thrombotic risk than oral estrogen. Either agent can be used in patients on anticoagulation
- In patients with a history of VTE not on anticoagulation, oral estrogen is avoided and transdermal estrogen may be considered

Bottom Line

Do	Take a menstrual history. Take a multidisciplinary approach including gynecology, vascular surgery etc. Treat iron deficiency. Start or continue contraception at diagnosis.
Don't	Don't stop CHCs in patients on anticoagulation. Don't withold HRT (specifically vaginal or transdermal estrogen) in anticoagulated patients or low to moderate risk of recurrence.
Consider	Consider dose reduced extended prophylaxis in patients who qualify (*not proven to decrease menstrual losses). Consider QOL based approach to menstruation.
Caution	Caution holding anticoagulation for menstruation/menstrual bleeding (5-fold increased risk of VTE). Counsel patients on not holding AC without discussion.

Think about PADS at every visit:

Periods are heavier or more painful than before starting anticoagulation
Are they replacing pads or tampons more frequently
Did they recently stop hormonal therapy (CHCs or HRT)
Send labs and consider supportive therapies or consults when appropriate

Abbreviations: AC, anticoagulation; AUB, abnormal uterine bleeding; CHC; combined hormonal contraceptive; CRNMB, clinically relevant non-major bleeding; HRT, hormone replacement therapy; IUD, intrauterine device; MB, major bleeding; MBL, menstrual blood loss; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio; QOL, quality of life; TID, three times daily; VTE, venous thromboembolism

References: 1. Edlung M, Magnusson C, von Shoultz B. Quality of life – A Swedish survey of 2200 Women. London: The Royal Society of Medicine Press Limited, London. 1994:36-7. 2. de Jong CMM, et al. Incidence and impact of anticoagulation-associated abnormal menstrual bleeding in women after venous thromboembolism. Blood. 2022;140(16):1764-73. 3. Godin R, MarcouxV, Tagalakis V. Abnormal uterine bleeding in women receiving direct oral anticoagulants for the treatment of venous thromboembolism. Vascul Pharmacol. 2017;93-95:1-5. 4. Baird DD, et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol. 2003;188(1):100-7. 5. Boonyawat K, et al. Heavy menstrual bleeding in women on anticoagulant treatment for venous thromboembolism: Comparison of high- and low-dose rivaroxaban with aspirin. Res Pract Thromb Haemost. 2021;5:308-13. 6. Maybin JA, Critchley HOD. Medical management of heavy menstrual bleeding. Womens Health (Lond). 2016;12(1):27-34. 7. The American College of Obstetricians and Gynecologists Committee on Clinical Consensus. General approaches to medical management of menstrual suppression. Obstet Gynecol. 2022;140(3):528-541. 8. The American College of Obstetricians and Gynecologists: https://www.acog.org/womens-health/infographics/effectiveness-of-birth-control-methods

Lead: Bethany Samuelson Bannow, MD, MCR **Faculty:** Tara Lech, PharmD, CACP; Jori May, MD; Jennifer Morgan, PharmD, CACP
Reviewer: Marissa Egipciaco, PharmD, MSCP and Foundation for Women & Girls with Blood Disorders Board of Directors
Rapid Resources Editorial Board Representative: Bishoy Ragheb, PharmD, BCACP, CACP

This content was developed in partnership with Foundation for Women & Girls with Blood Disorders.

Created: 04/25 **Next Review:** 06/25