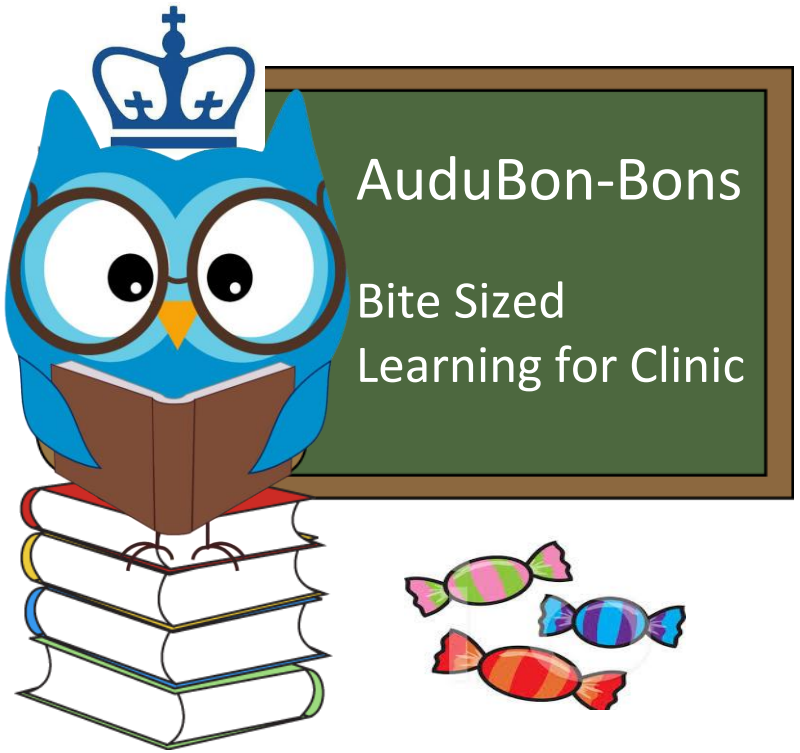
INHERITED BLEEDING DISORDERS IN PREGNANCY

Week 62



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Reading Assignment:

Lagrew D. (2015). *Obstetric hemorrhage task force: Inherited coagulation disorders in pregnancy.* The California Maternal Quality Care Collaborative (CMQCC). Stanford University, Palo Alto, CA.

LEARNING OBJECTIVES 

- Review when a patient should be evaluated for a coagulation disorder
- Discuss inherited coagulation disorders that may complicate pregnancy
- Understand basic management of inherited bleeding disorders in pregnancy

CASE VIGNETTE

- Ms. HM is a 23 yo G0 woman who presents for her annual GYN exam. She mentions to you that she is planning to get pregnant in the next year.

FOCUSED HISTORY

What aspects of this patient's history are most important?

- **PMH:** Anemia since time of starting menses at age 12
- **PSH:** None
- **PObH:** Nulliparous
- **PGynH:** **Heavy menses lasting 7 days, 1 history of admission as a teenager for blood transfusion after menses at age 14,** denies STIs, abnl pap
- **Social:** Denies T/E/D
- **Allergies:** NKDA
- **Meds:** Prenatal multivitamins, iron
- **FHx:** **Mother with history of PPH during patient's birth**
  "Heavy periods run in family"

PERTINENT PHYSICAL EXAM

VS: Height 162, Weight: 60 kg, BMI: 22.9, HR: 90, BP: 105/78, RR: 18

- **Gen:** NAD
- **HEENT:** Normal gums
- **Pulm:** CTAB
- **Cardio:** RRR, no murmurs, rubs, or gallops
- **Abd:** Soft, non-tender
- **Pelvic:** Normal external genitalia, normal cervix, physiologic discharge
- **Ext:** WWP

NORMAL EXAM

DIFFERENTIAL DIAGNOSIS

Given the patient's significant personal and family bleeding history, she should be screened for inherited coagulation disorders. What are some of the most common ones?

- von Willebrand Disease (vWD)
- Hemophilia A (Factor VIII deficiency)
- Hemophilia B (Factor IX deficiency)
- Hemophilia C (Factor XI deficiency)
- Other: congenital factor XIII deficiency (extremely rare, AR)

WHAT'S YOUR WORK-UP?

Screening tests to evaluate suspected coagulopathies:

- **vWF:** Ristocetin Co-factor, vWF antigen, and FVIII activity
- **Hemophilia A:** measurement of Factor VIII activity
- **Hemophilia B:** measurement of Factor IX activity
- **Hemophilia C:** measurement of Factor XI activity

Other tests for patients with bleeding disorders:

- CBC
- aPTT
- PT
- INR
- Fibrinogen level

von Willebrand Disease (vWD)

- **Most common** hereditary coagulation disorder
- Caused by missing or defective von Willebrand factor (vWF), a plasma protein that binds to factor VIII to help stabilize platelets during clotting process

- **3 types:**
  - **Type 1:** AD. 60-80% of patients. Reduced levels of vWF (quantitative defect)
    - Mostly normal lives, with some bleeding following surgery (dental extractions), noticeable heavy bruising, or HMB
  - **Type 2:** AD. 20-30%. Dysfunctional vWF (qualitative defect)
    - Tendency to bleed varies between individuals
  - **Type 3:** AR. Very rare, most severe. Absent or undetectable levels of vWF
    - Severe mucosal bleeding, no detectable vWF antigen, low factor VIII, + family history

- **Pregnancy implications:**
  - Antepartum hemorrhage is uncommon
  - **PPH risk of 20-40%**

Hemophilia A (Factor VIII deficiency)

- Caused by mutation of VIII gene leading to Factor VIII deficiency
- Most common of hemophilias
- X-linked recessive males are affected, females are carriers or rarely display mild phenotype

Hemophilia B (Factor IX deficiency)

- Caused by mutation of IX gene leading to Factor IX deficiency
- Rare
- X-linked recessive

Pregnancy implication:

Besides risk of genetic inheritance of fetus, carriers of hemophilia are at risk of PPH if they have reduced coagulation factor levels at term.

Hemophilia C (Factor XI deficiency)

- Extremely rare (<1/100,000) but more common in Ashkenazi Jews (8% incidence)
- Can be AR or AD inheritance
- Extremely variable bleeding patterns **20% risk of PPH**

- Risk stratified in obstetrics by %XI level
  - **>40% XI level**
    - manage as routine, generally fine for neuraxial anesthesia
  - **<40% XI level**
    - consider prophylactic administration of antifibrinolytic agents to decrease PPH
    - Administration of factor XI prior to neuraxial anesthesia
  - **<20% with prior bleeding history**
    - consider factor XI replacement in labor continued for 24-48 hrs PP

MY PATIENT IS PREGNANT! WHAT'S NEXT?

- Referral to hematologist for co-management of bleeding disorders
  - Most coagulation disorders require testing of coagulation factor levels between 28-34 weeks for intrapartum planning
- Referral to genetics for testing/ evaluation of fetus/ newborn
- MFM and anesthesia consultation
  - Especially important to consider risks of neuraxial anesthesia
- Develop intrapartum AND postpartum management plan with recommended delivery at tertiary care center due to blood bank availability

CMQCC
California Maternal
Quality Care Collaborative

https://www.cmqcc.org/resource/ob-hem-inherited-coagulation-disorders-pregnancy

COAGULATION FACTORS IN PREGNANCY

Coagulation factor	Change from non-pregnant state
Antithrombin III	No change
Plasma fibrinogen (factor I)	↑
Factor II	No change
Factor V	No change
Factor VII	↑
Factor VIII	↑
Factor IX	No change
Factor X	↑
Free protein S	↓
Plasminogen activator inhibitor 1	↑
Plasminogen activator inhibitor 2	↑
Protein C	No change
von Willebrand factor	↑

https://www.cambridge.org/core/books/maternal-critical-care/physiological-changes-of-pregnancy/06AAE1CF94F4A096194A0C60495AD81D.

INTRAPARTUM MANAGEMENT

- **vWF:**
  - Desmopressin acetate (DDAVP) for mild forms
  - vWF and VIII factor replacement for severe forms
  - TXA for prevention of PPH at delivery
- **Hemophilia A/B:**
  - Concentrates of factor VIII (for Hemophilia A) or clotting factor XI (for B)
  - Consider DDAVP adjunctive therapy
- **Hemophilia C:**
  - FPP
  - TXA post-partum
- **Hemophilia carrier status is NOT a contraindication to vaginal delivery**
  - Elective section may be considered to reduce risk of ICH on individual basis
  - FSE, vacuum and forceps deliveries are contraindicated

SOCIAL DETERMINANTS OF HEALTH

Impact of a genetic bleeding disorder on **psychological wellbeing** and **reproductive choices**

Being a carrier of hemophilia can result in feelings of **guilt and self-blame** (especially for those with male offspring as males express more severe disease) and **difficulty in discussing carrier status** with a partner

1 in 4 women with IBDs reported that their condition either severely **impacted their decision** to have children or **prevented them from having children** due to reasons such as social stigma, barrier to changing IBD treatment, early hysterectomy to control IBD symptoms, and cost of genetic testing/preimplantation diagnosis

Greater impact to reproductive choices seen in those who experienced a delay to diagnosis, often women without a family history, highlighting the **need for clinical awareness**

Proactive engagement from healthcare, including education and counselling by experienced health care workers, support networks for women with bleeding disorders, and improved prenatal support is needed to improve the experience of women with IBDs

Epic .phrase

BBonBleedingDisCounseling

Description: Preconception/prenatal counseling

Patient with ***[bleeding disorder] counseled on risk for obstetric hemorrhage. The need for multidisciplinary care for planning and coordination of antepartum and intrapartum care was discussed including hematology, anesthesiology, and perinatal consults. Referrals for each were made. In addition, referral for genetic consult regarding possible testing and evaluation of the fetus and newborn was made. Management plans will be made well in advance of the anticipated date of birth so specific medications and blood components are available at the time of delivery and given in consultation with a hematologist.

CODING AND BILLING

- **O99.119** Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, unspecified trimester
- **D68.0** von Willebrand disease
- **D68.9** Coagulation defect, unspecified

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- Noone D, Skouw-Rasmussen N, Lavin M, van Galen KPM, Kadir RA. Barriers and challenges faced by women with congenital bleeding disorders in Europe: Results of a patient survey conducted by the European Haemophilia Consortium. *Haemophilia*. 2019;25(3):468-474. doi:10.1111/hae.13722