Let’s Talk Period: Women and Bleeding Disorders

Paula James MD, FRCPC
18th Australian & New Zealand Conference on Haemophilia and Rare Bleeding Disorders
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Clinical and Molecular Hemostasis Research Group
## Disclosures for Paula James

<table>
<thead>
<tr>
<th>Potential conflict</th>
<th>Disclosure - if potential conflict of interest exists</th>
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<tbody>
<tr>
<td>Direct financial interest in a company</td>
<td>N/A</td>
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</table>
1. Menorrhagia

2. Bleeding Disorders that Affect Women

3. Approach to Diagnosis and Management

4. Iron Deficiency

5. Let’s Talk Period Project
1. Why is menorrhagia a problem?

**The Past**
- 160 menstrual cycles
- late menarche
- high parity
- extended breastfeeding
- early menopause

**The Present**
- 450 menstrual cycles
- early menarche
- low parity
- short breastfeeding
- late menopause
Menorrhagia

- 30% females report at some point
- 10 – 15% have objective menorrhagia
- 5 – 10% seek medical attention

Causes of Menorrhagia

- Organic cause of menorrhagia: ~50%
- Subnormal vWF: ~15%
- plt or fibrinolytic disorder: ~10%
- Undiagnosed: ~25%

Kouides, PA. Hemophilia 2002; 8:330-338
Incidence of Menorrhagia

Kadir et al. Hemophilia 1998; 4:836-41
Definition of Menorrhagia (Heavy Menstrual Bleeding)

>80 mls menstrual blood loss
Clinical Correlates of > 80 mls MBL

- soaking through pad in 1 hour
- soaking pj’s
- clots > 1 inch
- low ferritin

Warner ACOG 2004
Impact of Menorrhagia

- work and school absenteeism
- cause of 2/3 hysterectomy in women of reproductive age
- iron deficiency anemia
- negative impact on QoL

*Kadir 1998, Kouides 2000*
2. Bleeding Disorders that Affect Women

- Von Willebrand Disease
- Hemophilia Carrier
- Platelet Function Disorder
- Factor Deficiency – Factor XI
- (Collagen Vascular Diseases)
Von Willebrand Disease

- most common inherited bleeding disorder
- excessive bleeding skin, mucous membranes
- joint and muscle bleeds in severe cases
- inherited ♀=♂, ♀ diagnosed 3:1
Von Willebrand Factor

- essential for blood clotting
- sticks platelets down to sites of vascular injury
- carries and protects FVIII
- missing/dysfunctional in VWD
I wonder what Queen Victoria’s periods were like?
Hemophilia Carriers

- historically considered asymptomatic
- 30% have low FVIII/FIX levels
- ~50% have abnormal bleeding, even when FVIII/FIX levels are normal

James et al, Haemophilia 2016
Platelet Function Disorders and Other Factor Deficiencies

• less common

• same symptoms
  – heavy periods
  – nosebleeds
  – easy bruising

• common treatment strategies
Collagen Vascular Disorders

- mucocutaneous bleeding
  - collagen/VWF/platelets

- musculoskeletal bleeding
  - soft tissue fragility

- Ehlers-Danlos Syndrome (EDS)

- can occur alone or in combination with other bleeding disorders

- clinical diagnosis (confirmed with biopsy or genetic testing)
CVD are Common in WBD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases $n = 55$</th>
<th>Control $n = 50$</th>
<th>Odds Ratio (95% CI)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic joint hypermobility $^a$</td>
<td>13 (24%)</td>
<td>1 (2%)</td>
<td>15.2 (1.9–120.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypermobility $^b$</td>
<td>16 (32%)</td>
<td>22 (40%)</td>
<td>1.4 (0.64–3.2)</td>
<td>0.4</td>
</tr>
<tr>
<td>Arthralgia $^c$</td>
<td>21 (38%)</td>
<td>1 (2%)</td>
<td>30.3 (3.9–236)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>History of collagen disorder</td>
<td>10 (18%)</td>
<td>1 (2%)</td>
<td>10.9 (1.2–88.5)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Alternate SJH criteria $^d$</td>
<td>15/27</td>
<td>6/43</td>
<td>4.0 (1.4–11.5)</td>
<td>&lt; 0.05</td>
</tr>
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</table>

$^a$ is 2 major Brighton criteria where:
$^b$ Beighton score $\geq 4$.
$^c$ Arthralgia in $\geq 4$ joints simultaneously $>3$ months.
$^d$ 1 major Brighton criteria + 2 minor criteria OR 4 minor criteria.

Jackson et al, Haemophilia 2013
3. Approach to Diagnosis

• Bleeding and other symptoms

• Family history

• Laboratory studies
Bleeding Symptoms

• **Mucocutaneous bleeding**
  • heavy periods
  • nosebleeds
  • bruising
  • excessive bleeding from cuts
  • GI, bowel bleeding
  • mouth/post-dental procedure
  • post-operative
  • post-partum

• **Musculoskeletal bleeding**
  • joint/muscle bleeds
Assessing Bleeding Symptoms

- bleeding in women is normal
  - how to distinguish between normal and abnormal?

- Bleeding Assessment Tools (BATs) standardize
  - PBAC score
  - expert administered
  - Self-BAT
Screening for EDS

Table 1. The Brighton revised diagnostic criteria for benign joint hypermobility syndrome (BJHS).

Major criteria:
- A Beighton score of 4/9 or greater (either currently or historically).
- Arthralgia for longer than 3 months in four or more joints.

Minor criteria:
- A Beighton score of 1, 2 or 3/9 (0, 1, 2 or 3 if age >50).
- Arthralgia (>3 months) in one to three joints or back pain (>3 months), spondylosis, spondylolysis/spondylolisthesis.
- Dislocation/subluxation in more than one joint, or in one joint on more than one occasion.
- Soft tissue rheumatism, at least 3 lesions (e.g. epicondylitis, tenosynovitis, bursitis).
- Marfanoid habitus (tall, slim, span/height ratio >1.03, upper: lower segment ratio less than 0.89, arachnodactyly (positive Steinberg/wrist signs).
- Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring.
- Eye signs: drooping eyelids or myopia or antimongoloid slant.
- Varicose veins or hernia or uterine/rectal prolapse.

The BJHS is diagnosed in the presence of two major criteria, or one major and two minor criteria, or four minor criteria. Adapted from Grahame and Hakim [6].

Jackson et al, Haemophilia 2013
### Other Gynecologic Issues

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>WBD (n=102)</th>
<th>Normal (n=88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menorrhagia</td>
<td>95%</td>
<td>61%</td>
</tr>
<tr>
<td>Ovarian Cyst</td>
<td>52%</td>
<td>22%</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>30%</td>
<td>13%</td>
</tr>
<tr>
<td>Fibroids</td>
<td>32%</td>
<td>17%</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>Polyps</td>
<td>8%</td>
<td>1%</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>26%</td>
<td>9%</td>
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*Kirtava Haemophilia 2003*
Family History

- Inherited bleeding disorders can be:
  - autosomal dominant (from one parent)
    - Type 1, 2A, 2B and 2M VWD, platelet function disorders
  - autosomal recessive (from both parents)
    - Type 2N and 3 VWD, Factor Deficiencies
  - sex linked (on the X chromosome)
    - Hemophilia A and B

positive family history isn’t always present
Lab Tests

- specialized blood work required

- VWF and FVIII affected by:
  - stress (crying, fainting)
  - exercise
  - pregnancy
  - medications (birth control pill)
  - age

- Platelet function testing affected by
  - medications
Why diagnose?

- Quality of life
  - up to 15 years from onset of bleeding symptoms to diagnosis

- Symptoms are treatable

- Prevent bleeding
Management

- Individualized
- Medical – 1st line
  - Hormonal
    - combined hormonal contraceptive
    - depot medroxyprogesterone
    - levonorgestrel IUD (Mirena®)
  - Non-hormonal
    - Tranexamic acid (Cyklokapron®)
- Surgical – if no preservation of fertility
  - endometrial ablation
  - hysterectomy

Demers et al. SOGC Clinical Practice Guidelines 2005; 163:707-718
Desmopressin

- causes release of stored VWF (FVIII)
- injection, nasal spray
- fluid restriction
- works for many patients
  - poor response
    - severe Type 1s
    - some Type 2s (2B)
    - Type 3s
- response is short lived
Factor Replacement

- factor concentrates
  - VWF/FVIII - Biostate
- required in rare cases to manage menorrhagia, mucocutaneous bleeds
- women with severe bleeding disorders may need regular MSK prophylaxis
4. Iron Deficiency

- WBD are often iron deficient
- **NOT NORMAL!**
- tired, affects sleep, poor concentration
Iron Deficiency

- ferritin – best test
- result of excessive bleeding
- iron deficiency $\Rightarrow$ anemia (low Hgb)
- ?symptomatic even if not anemic
Prevent Iron Deficiency
• red meat
• prevent bleeding

Treat Iron Deficiency
• dietary sources alone are not enough
• oral iron supplements/IV iron
• manage bleeding
5. Let’s Talk Period Project
Prevalence of Inherited Bleeding Disorders

• estimated by WFH ~ 1 in 1,000
  – 35,000 affected Canadians

• ~4,000 diagnosed
  – ~31,000 undiagnosed
  – ?majority are women
Barriers to Diagnosis

• lack of understanding of normal vs. abnormal bleeding

• lab tests are challenging and not widely available

• lack of resources and tools

• discomfort in discussing heavy menstrual bleeding
1 in 1000 Canadians has a bleeding disorder but most don’t know it

Could you be one of them?

Are You Concerned
You May Have Abnormal Bleeding?

TAKE THE TEST NOW
DO YOU EXPERIENCE THE FOLLOWING WITH YOUR PERIODS?

- Having to change protection more than every hour
- Iron deficiency anemia
- Frequently soaking the sheets
- Periods consistently lasting longer than 7 days

ABOUT THE DOCTOR
DR. PAULA JAMES
ABOUT LET'S TALK PERIOD

Let's Talk Period aims to increase awareness of the signs and symptoms of bleeding disorders. As many as 35,000 Canadians may be suffering from a bleeding disorder, but many of these may not understand if their bleeding is normal or abnormal and therefore do not seek help. Through her internationally recognized research program at Queen's University, Dr. James, Hematologist at Kingston General Hospital, and her team have developed a self-administered bleeding assessment tool (Self-BAT) that will help inform people about their bleeding and guide them toward the help they need.

ABOUT THE DOCTOR
DR. PAULA JAMES

A graduate of the University of Saskatchewan (MD, 1996), Dr. James joined the Queen's University faculty as an Assistant Professor in the Department of Medicine in 2004. She was promoted to Associate Professor in 2008 and full Professor in 2015. She holds cross-appointments to the Department of Pathology and Molecular Medicine and Pediatrics at Queen's University.
VON WILLEBRAND DISEASE IN THE MEDIA

Von Willebrand Disease (VWD) is the most common bleeding disorder and occurs in ~1 in 1000 individuals.

THE BIGGEST LEARNINGS FROM THE SELF-BAT

The secret is out! The Self-BAT is making its way around the world - both physically and online. Thanks to Let's Talk Period's high school outreach program, our social media outreach efforts, and talks delivered by Dr. Paula James, the ... Read More
1 in 1000 Canadians has a bleeding disorder but most don't know it

Could you be one of them?

Are You Concerned
You May Have Abnormal Bleeding?

TAKE THE TEST NOW
The Self-BAT (self-administered bleeding assessment tool) is a scientifically validated scoring tool developed by Dr. Paula James targeted at individuals who are concerned about bleeding. Taking this test will help you better understand whether current, or previous, bleeding episodes are normal or abnormal.

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1. This Self-Administered Bleeding Assessment Tool ("Self-BAT") is for informational and research purposes only and does not constitute medical advice, nor is the result of the Self-BAT a substitute for professional medical advice, diagnosis or treatment. You should seek the advice of your physician or other qualified, licensed healthcare practitioner if you have any medical questions or concerns based on the result of the Self-BAT and you should never disregard professional medical advice or delay in seeking treatment or advice based on the result of this Self-BAT.

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Julie Grabell, 2025 Etherington Hall, Queen’s University, Kingston, Ontario, Canada K7L 3N6 (613 533 6329)
Have you ever had a nosebleed?

- No
- Yes, but trivial (less than 5 per year or less than 10 minutes in length)
- More than 5 per year or more than 10 minutes in length
- Spoke to doctor about nosebleeds but did not need medical treatment
- Had packing/cauterization of nose or needed oral medication
- Had blood transfusion or I.V. medication as a result of a nose bleed
Your bleeding score is normal

If you are still concerned about your bleeding you may want to speak with your physician

Click here to see your score
Your bleeding score is abnormal

Your bleeding score is abnormal (25). The normal range for your age and gender is (0-5). You could have a bleeding disorder which you may want to discuss with your physician.

Click here to see your score
Website

• launch May 2016

• 17,167 page views, 112 countries

• 2,463 Self-BAT
  – 1,429 (58%) abnormal bleeding scores
1 in 1000 Canadians has a bleeding disorder but most don't know it

Could you be one of them?

Are You Concerned
You May Have Abnormal Bleeding?

Learn More
Facebook Activity

- launch September 19, 2016
- followers = 883
- reach = 159,104
Let's Talk Period
Women's Health Clinic
We aim to increase awareness around the signs and symptoms of bleeding disorders.
letstalkperiod.ca/self-bat/
Queen's University, Kingston, Ontario
Followed by harpelllori, kathfahl, mymissingfactor + 3 more
High School Outreach

THE LET’S TALK PERIOD HIGH SCHOOL PROGRAM IS UNDERWAY!

Hemorrhaging disorders are still not common knowledge even though they affect a large number of people—both men and women. This is the reason behind our new high school outreach program. We recently visited a grade 11 class at local high school to offer an engaging and dynamic presentation on bleeding disorders in order to raise awareness about them.

Our program is designed to educate students about genetic and inherited bleeding disorders. In just one class period our researchers cover everything from hemophilia to VWD and also provide them with the tools to find more resources. We even invite students to participate in a microscope activity for a little hands-on learning. “The microscope activity seemed to be the most popular”, notes Julie Erdell (CCHR Clinical Research Assistant to Dr. Paula Jaenisch) who administered our first presentation.
really good and informative.
I want to do lab research when I'm older.
Local Impact of Let’s Talk Period

- 8 referrals for + Self-BAT scores
  - 1 Type 1 VWD
  - 2 still being investigated
  - 3 iron therapy (1 oral, 2 IV)
  - 3 WBD Clinic F/U to see Gyne
Accurate diagnosis of women with bleeding disorders is critically important in order to ensure proper management.

Let’s Talk Period!
- because your health is important.
Acknowledgements

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Clinical and Molecular Hemostasis Research Group