Hemostasis Update

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Director, The Hemophilia Center @ OHSU
Disclosures

• I receive grant funding from the American Thrombosis & Hemostasis Network/Hemostasis & Thrombosis Research Society

• I will talk about some off-label use of medications
Objectives

- Describe the structure and services of The Hemophilia Center @ OHSU
- Review recently updated hemophilia nomenclature
- List treatment options for individuals with hemophilia
- Review recently updated VWD guidelines
- Identify and characterize bleeding disorders in people with the potential to menstruate
Injury!
Hemostasis - How it can not work...

- Collagen problems - ? platelet sticky problems? constriction?
- Von Willebrand protein - deficiency - absence - mild-mod
  - dysfunction - collagen binding - VIII binding ↓
  - platelet binding ↑
  - platelet binding ↓

- Platelets - granules
  - dense granule
  - hemarsky Pseud
  - Bernard Soulier Syndrome
  - Glanzmann Thrombasthenia

- Factor deficiency - VIII, IX, VII, X, XIII, VIII+, V, II

- Fibrinolysis - too much
Background on Bleeding Disorders

Symptoms:

• Nosebleeds
  • Can be frequent and prolonged (20+ minutes)
  • Can interrupt school/work

• Oral bleeding
  • Recurrent gum bleeding can decrease desire to perform oral health
  • Minor dental procedures can become a life-threatening event

• Heavy menstrual bleeding & bleeding with pregnancy & childbirth
  • Can result in severe symptomatic anemia requiring transfusion
  • Often goes undetected and undertreated
  • Can be the first and only sign of a bleeding disorder
Background on Bleeding Disorders

Symptoms Continued:
• Muscle bleeding
  • Can inhibit function/movement
  • Can cause nerve injury, compartment syndrome, myositis ossificans (bone tissue forms inside a muscle), pseudotumor, infection
• Joint bleeding
  • Can inhibit function/movement
  • Can cause long-term joint damage/arthropathy that may require joint replacement
• Intracranial bleeding
  • rarely spontaneous – higher risk in severe bleeding disorder, extremes of age
  • Trauma-induced – treat the bleeding disorder and then look for blood
## Treatments

<table>
<thead>
<tr>
<th>Before Bleeding Happens</th>
<th>While Bleeding is happening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stay active – keep muscles and joints strong</td>
<td>First Aid measures – pressure, RICE</td>
</tr>
<tr>
<td>Brush your teeth &amp; go to the dentist regularly</td>
<td>Hemophilia: factor med +/- Antifibrinolytic</td>
</tr>
<tr>
<td>Wear a helmet and a seat belt</td>
<td>VWD: DDAVP or VWF concentrate +/- Antifibrinolytic</td>
</tr>
<tr>
<td>Avoid contact sports</td>
<td>Platelet Disorder: DDAVP or rFVII or platelet transfusion +/- antifibrinolytic</td>
</tr>
<tr>
<td>Take prophylactic medicine as prescribed (factor, hormones, anti-fibrinolytic, etc)</td>
<td>Other meds used: other factor products (VII, XIII)</td>
</tr>
<tr>
<td>HMB: oral hormones, implants, IUD</td>
<td>HMB: estrogen + progesterone or progesterone only +/- antifibrinolytic</td>
</tr>
</tbody>
</table>

*Factor medications are given intravenously. Because they are expensive, not all hospitals have factor on formulary. We encourage patients to keep at least one dose of their medicine on hand in case of emergency.*
Hemophilia Treatment Center

• A specialized health care center that brings together a team of doctors, nurses, and other health professionals experienced in treating patients with bleeding disorders.

• 1993-1995 CDC study of mortality of 2950 patients with hemophilia A and B: 236 people died (8%); people who received care at a HTC were 30% less likely to die than those who didn’t.

• 1993-1966 CDC study of bleeding events requiring hospitalization in 2650 patients with hemophilia A and B found that people receiving care at an HTC were 50% less likely to experience a bleeding event requiring hospitalization.

The Hemophilia Center @ OHSU

• An inter-disciplinary team caring for patients of ALL ages with bleeding and clotting disorders.
  • We are a life-span program

• Catchment area: Oregon, SW Washington, Northern California, sometimes Idaho, sometimes Alaska
  • We are the only HTC in the state of Oregon.
  • The next closest HTC is in Seattle or Spokane depending on where you are and how you drive.
The Hemophilia Center @ OHSU

Administrative Team
- PAS
- Managed Care expert
- Clinic Manager
- Administrative Coordinator
- Program Administrator

Research Team
- Research Coordinators
- Research RN
- Data Analyst
- Associate Director & Regional Coordinator

Clinical Team
- RNs
- MA
- Genetic Counselor
- Physical Therapists
- Nurse Practitioner
- Social Worker
- Pediatric hematologists
- Adult hematologists
- Education Specialist

340b pharmacy team
- Pharmacists
- Pharmacy technician
- Managed Care expert
- Program Manager
- Billing expert
- Compliance expert
The Hemophilia Center @ OHSU

• Partners
  • Pediatric Dentistry Residency
  • Adult Pain Clinic
  • Center for Women’s Health
  • Pediatric Hematology/Oncology and Adult Hematology
  • NICH
  • Interventional Radiology
  • LEND program
  • Molecular & Medical Genetics
  • Maternal Fetal Medicine
  • Hereditary Hemorrhagic Telangiectasia Center

• Clinics:
  • Comprehensive clinic
  • Acute/urgent visits
  • Spots, Dots, & Clots and Reproductive Hematology
  • Vascular Interventions Program
The Hemophilia Center @ OHSU

525 patients with diagnosed bleeding disorders seen January 2021-November 2021.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th># of patients seen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia A</td>
<td>269</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td>59</td>
</tr>
<tr>
<td>Von Willebrand Disease</td>
<td>146</td>
</tr>
<tr>
<td>Other factor deficiencies</td>
<td>34</td>
</tr>
<tr>
<td>Other bleeding disorders</td>
<td>37</td>
</tr>
</tbody>
</table>

**does not include new consults, uncertain diagnoses, thromboses**
The Hemophilia Center @ OHSU

Age Breakdown - 2021

- 85+ (13.58%)
- 65-84 (15.76%)
- 50-54 (25.43%)
- 45-64 (20.07%)
- 30-44 (11.99%)
- 20-29 (7.09%)
- 15-19 (5.76%)
- 0-4 (11.99%)

Age Groups:
- 0-4
- 5-14
- 15-19
- 20-29
- 30-44
- 45-64
- 65-84
- 85+
Hemophilia nomenclature

- Normal factor VIII levels are ~50-100%

<table>
<thead>
<tr>
<th>Factor VIII level</th>
<th>Severity classification</th>
<th>Bleeding Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1%</td>
<td>Severe</td>
<td>Spontaneous bleeding into joints and muscles, bleeding with trauma/surgery, mucocutaneous bleeding</td>
</tr>
<tr>
<td>1-5%</td>
<td>Moderate</td>
<td>Bleeding with trauma/surgery, rare spontaneous bleeding, mucocutaneous bleeding</td>
</tr>
<tr>
<td>6-40%</td>
<td>Mild</td>
<td>Bleeding with trauma/surgery, mucocutaneous bleeding</td>
</tr>
<tr>
<td>&gt;40% + gene + bleeding</td>
<td>Symptomatic carrier</td>
<td>Bleeding with trauma/surgery, mucocutaneous bleeding</td>
</tr>
<tr>
<td>&gt;40% + gene, no symptoms</td>
<td>Carrier</td>
<td>none</td>
</tr>
</tbody>
</table>

Factor VIII treatment in general

- **Plasma-derived**
  - Pooled human plasma
  - Contains VWF in addition to FVIII

- **Recombinant**
  - 3 cell lines: CHO, BHK, and HEK
  - Full length vs B-domain deleted
  - 1st (animal and/or human plasma-derived proteins in cell culture medium and final formulation) vs 2nd (animal and/or human plasma-derived proteins in cell culture medium) vs 3rd generation (no animal or human plasma-derived proteins) vs 4th generation (made in HEK cells)
  - Extended half-life (Fc, PEG)

Factor VIII treatment in general

• Inhibitor treatment
  • Treating bleeding: recombinant factor VIIa or FEIBA
  • Preventing bleeding: rFVIIa or FEIBA
  • Treating the inhibitor: immune tolerance induction

• Emicizumab
  • Bispecific antibody for activated factor IX and for factor X
  • Given subcutaneously to prevent bleeding
    • Weekly, q 2 weeks, q 4 weeks
  • For patients with and without inhibitors
Factor IX treatments in general

- Plasma derived
  - Pooled human plasma
- Recombinant
  - CHO lines
  - Extended half life with Fc, Alb, PEG fusion
Non-factor options on the horizon

• Concizumab: monoclonal antibody against TFPI
  • Daily subcutaneous injections
  • Trials complicated by thrombotic events
  • Open trial for patients with Hem A and Hem B with inhibitors

• Fitusiran: antisense oligonucleotide against anti-thrombin
  • Monthly subcutaneous injection
  • Trials also complicated by thrombotic events
  • Open trial for patients with Hem A and Hem B with inhibitors
Gene therapy

• Most gene therapy products use an AAV vector with hepatic tropism
• FVIII – B domain deleted
• FIX – Padua variant
• Challenges:
  • AAV antibodies
  • Liver toxicity
  • Sustained expression
  • Need for immune suppression
  • Integration into host genome?
• Anticipate FDA application for gene therapy in the next 6 months?
Gene therapy

<table>
<thead>
<tr>
<th>Product</th>
<th>Vector</th>
<th>Promotor-transgene</th>
<th>Clinical trial status</th>
<th>Trials identifier</th>
<th>Study population</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMT-180</td>
<td>AAV5</td>
<td>BDD-FVIII</td>
<td>Pre-clinical development n/a</td>
<td>n/a</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1% PTPs ≥150 exposure days, excluding those with antibodies reactive with AAVhu37 capsid</td>
<td>UniQure Biopharma</td>
</tr>
<tr>
<td>BAY259023</td>
<td>AAVhu37</td>
<td>BDD-FVIII</td>
<td>Phase I/II, recruiting</td>
<td>NCT03588299</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1% PTPs ≥150 exposure days, excluding those with large deletions (multiple exons) and nonsense mutations of the F8 gene and HIV</td>
<td>Bayer/Ultragenyx</td>
</tr>
<tr>
<td>GO-8</td>
<td>AAV2/8</td>
<td>HLP-FVIII-V3</td>
<td>Phase I, recruiting</td>
<td>NCT03004044</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1% active high titer FVIII inhibitors (&gt;5 BU), excluding those with known co-existing thrombophilia gene and HIV</td>
<td>University College, London</td>
</tr>
<tr>
<td>Lenti-FVIII (Auto CD34 + PBSC)</td>
<td>Lentiviral vector Peightlet (MUT6)</td>
<td>BDD-FVIII</td>
<td>Phase I, recruiting</td>
<td>NCT03818763</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1% active high titer FVIII inhibitors (&gt;5 BU), excluding those with known co-existing thrombophilia gene and HIV</td>
<td>Medical College Wisconsin</td>
</tr>
<tr>
<td>SB-525</td>
<td>AAV2/6</td>
<td>BDD-FVIII</td>
<td>Phase II, recruiting, Phase III lead-in, recruiting</td>
<td>NCT03061201, NCT03587116, NCT04370054</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1%, PTPs ≥150 exposure days and on FVIII prophylaxis, excluding those with (SB-525 capsid) neutralizing antibodies Prior Hemophilia A Patients of the lead-in study (NCT03587116)</td>
<td>Pfizer</td>
</tr>
<tr>
<td>SPK-8011</td>
<td>AAV-UK03</td>
<td>BDD-FVIII</td>
<td>Phase I/II, recruiting, Long-term follow-up, enrolling Phase III lead-in, recruiting</td>
<td>NCT03003533, NCT03443250, NCT034876301</td>
<td>Male, ≥18-years-old, FVIII activity ≤2%, PTPs ≥150 exposure days, excluding those with anti-AAV-Spark 200 Previously dosed on a SPK-8011 study Male, ≥18-years-old, FVIII activity ≤2% PTPs, excluding those with anti-AAV-Spark 200 neutralizing titers &gt;1:1 and HIV</td>
<td>Spark Therapeutics</td>
</tr>
<tr>
<td>TAK-754</td>
<td>AAV8</td>
<td>BDD-FVIII</td>
<td>Phase I, active, not recruiting</td>
<td>NCT03370172</td>
<td>Male, ≥18-75-years-old, FVIII activity &lt;1%, PTPs &gt;150 exposure days, excluding those with AAV8 neutralizing titers &gt;1:5 and HIV</td>
<td>Takeda</td>
</tr>
<tr>
<td>Vallocoagene</td>
<td>AAV5</td>
<td>BDD-FVIII</td>
<td>Phase I/II, active, not recruiting Phase III, active, not recruiting Phase III, not yet recruiting</td>
<td>NCT02576795, NCT03370913, NCT04323098</td>
<td>Male, ≥18-years-old, FVIII activity &lt;1% PTPs ≥150 exposure days, excluding those with detectable pre-existing antibodies to the AAV5 Capsid and HIV same population as above Addition of prophylactic steroids</td>
<td>BioMarin</td>
</tr>
</tbody>
</table>

Gene therapy

<table>
<thead>
<tr>
<th>Product</th>
<th>Vector</th>
<th>Promotor-transgene</th>
<th>Clinical trial status</th>
<th>Trials identifier</th>
<th>Study population</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIG-001</td>
<td>Encapsulated cell therapy</td>
<td>BDD-FVIII</td>
<td>Phase I, recruiting</td>
<td>NCT04541628</td>
<td>≥18-years-old, FVIII activity &lt;1%, PTPs ≥150 exposure days</td>
<td>Sigilon Therapeutics</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPK-9001</td>
<td>AAV-Spark 100</td>
<td>hFIXco R338L, Padua</td>
<td>Phase II, completed</td>
<td>NCT02484092, NCT03587116, NCT0307980</td>
<td>Male, ≥18-years-old, FIX activity ≥2%, PTPs ≥50 exposure days, excluding those with anti-AAV-Spark 100 neutralizing titers ≥20 defined titer Male, ≥18-64-years-old, FIX activity ≥2% and on FIX prophylaxis, excluding those with anti-AAV-Spark 100 neutralizing titers ≥1:1 Previously dosed on a SPK 9001 study</td>
<td>Pfizer</td>
</tr>
<tr>
<td>scAAV2/8-LP1-hFIXco</td>
<td>scAAV2/8</td>
<td>LP1-hFIXco</td>
<td>Phase I, active, not recruiting</td>
<td>NCT00979238</td>
<td>Male, ≥18-years-old, FIX activity &lt;1%, PTPs ≥50 exposure days, excluding those with detectable antibodies reactive with AAV8</td>
<td>St. Jude Children's Research Hospital</td>
</tr>
<tr>
<td>FLT-180a</td>
<td>AAV-S3</td>
<td>hFIXco R338L, Padua</td>
<td>Phase I, recruiting</td>
<td>NCT03669444, NCT03641703</td>
<td>Male, ≥18-years-old, FIX activity ≥2%, PTPs ≥150 exposure days, excluding those with AAV neutralizing antibodies and HIV Previously dosed on a FLT180a study</td>
<td>University College, London Freeline Therapeutics</td>
</tr>
<tr>
<td>TAK-748</td>
<td>AAV8</td>
<td>hFIXco R338L, Padua</td>
<td>Phase I/II, suspended</td>
<td>NCT04394286</td>
<td>Male, ≥18-75-years-old, FIX activity ≥2%, PTPs ≥50 exposure days, excluding those with anti-AAV8 neutralizing titers ≥1:5</td>
<td>Takeda</td>
</tr>
<tr>
<td>Etranacogene Dezaparovec (AMT-061)</td>
<td>AAV5</td>
<td>LP1-hFIXco R338L, Padua</td>
<td>Phase II, active, not recruiting</td>
<td>NCT03489291, NCT036569891</td>
<td>Male, ≥18-years-old, FIX activity ≥2%, PTPs &gt;20 exposure days Male, ≥18-years-old, FIX activity ≥2%, PTPs ≥150 exposure days</td>
<td>UniQure Biopharma</td>
</tr>
<tr>
<td>SB-FIX</td>
<td>AAV2/6</td>
<td>ZNF mediated gene-editing three components of SB-FIX (ZFN1, ZFN2, and FIX cDNA Donor)</td>
<td>Phase I, active, not recruiting</td>
<td>NCT02695160</td>
<td>Male, ≥18-years-old, FIX activity &lt;1%, excluding those with HIV</td>
<td>Sangamo Therapeutics</td>
</tr>
</tbody>
</table>

2021 VWD guidelines

• ASH, ISTH, NHF, and WFH consensus guidelines on diagnosis and management of VWD

• A few highlights will be presented here – there are also one page summary documents available:

### Table 1. Classification of VWD: major types and subtypes

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Quantitative decrease in VWF with preserved ratios between VWF/Ag, VWF/Act, and FVIII; normal multimer distribution</td>
</tr>
<tr>
<td>1C</td>
<td>Quantitative decrease in VWF with preserved ratios between VWF/Ag, VWF/Act, and FVIII; increased VWF/pp compared with VWF/Ag</td>
</tr>
<tr>
<td>2A</td>
<td>Decreased platelet-dependent VWF activity with loss of high-molecular-weight multimers</td>
</tr>
<tr>
<td>2M</td>
<td>Decreased platelet-dependent VWF activity with preserved multimer pattern</td>
</tr>
<tr>
<td>2N</td>
<td>Decreased binding of FVIII</td>
</tr>
<tr>
<td>2B</td>
<td>Increased binding to GPIbα, often leading to thrombocytopenia</td>
</tr>
<tr>
<td>3</td>
<td>Absence or near absence of VWF</td>
</tr>
<tr>
<td>Platelet-type VWD</td>
<td>Functional defect of platelet GPIbα, leading to excessive binding of platelets and VWF and subsequent thrombocytopenia and loss of high-molecular-weight multimers</td>
</tr>
<tr>
<td>Acquired von Willebrand syndrome</td>
<td>Decreased VWF and particularly loss of high-molecular-weight multimers as a result of either shearing from mechanical forces (e.g., aortic stenosis resulting in Heyde syndrome), adsorption on tumors (e.g., Waldenström macroglobulinemia or Wilms' tumors), or autoimmune inhibitor formation</td>
</tr>
</tbody>
</table>

Act, activity; Ag, antigen; GPIbα, glycoprotein Ibα; pp, propeptide.
2021 VWD guidelines on diagnosis

• Panel suggests using the newer assays of VWF activity that evaluate platelet binding (e.g. VWF:GPIbM, VWF:GPIbR) over the VWF:RCo assay
• Use a VWF level of <0.3 regardless of bleeding and <0.5 if + bleeding (ABO specific ranges are not needed)
• For people who have historical type 1 VWD but now have normal levels, reconsider the diagnosis but don’t necessarily remove it
• For type 2B, use genetic testing over the RIPA test

2021 VWD guidelines on diagnosis

VWD diagnosis

• Multi-site study looking at “onsite” vs “off-site” VWD testing including 251 females

• <40% of people were ultimately diagnosed with VWD

• ~40% referred had normal hemostatic testing

2021 VWD guidelines on management

• For patients with VWD and severe and frequent bleeds, long-term prophylaxis is suggested.

• DDAVP challenges should be done for those who will likely respond (note Stimate is still not available) (could maybe skip it for adults if levels >0.30).

• DDAVP contraindications: active CV disease, seizure disorders, type 1C and surgery, type 2B, pre-eclampsia.

• For surgeries: get FVIII and VWF levels >0.5 for at least 3 days.

2021 VWD guidelines on management

- For minor surgery, get levels over 0.5 AND use TXA
- Type 1 VWD with VWF >0.3 and mild bleeding phenotype, just give TXA for minor mucosal procedures
- Use TXA or oral hormonal pill for heavy menstrual bleeding rather than DDAVP
- For women with VWD and who are pregnant and need an epidural, get levels 0.5-1.5
- Give women TXA during post-partum period
Other VWD thoughts

• It’s important to consider the pre-test probability
• Combining your bleeding history with your labs is critical
• When the levels are not so low but the patient is really a bleeder, consider testing for platelet disorders
• Continuity of care is critical for patients with VWD – bleeding phenotype is an important factor in treatment considerations
The potential to menstruate + a bleeding disorder: fast facts

Up to 30% of women report heavy menstrual bleeding at some point during their life. For every 20 individuals with the potential to menstruate you see:

- 6 will report heavy menstrual bleeding at some point in their life
- Up to 1-2 may have an underlying bleeding disorder

15-30% of those with HMB may have an underlying bleeding disorder

<table>
<thead>
<tr>
<th>Age Group</th>
<th>US Residents</th>
<th>US Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19 yrs</td>
<td>16.0%</td>
<td>10,308,633</td>
</tr>
<tr>
<td>20-24 yrs</td>
<td>34.3%</td>
<td>21,929,275</td>
</tr>
<tr>
<td>25-29 yrs</td>
<td>34.1%</td>
<td>22,672,694</td>
</tr>
<tr>
<td>30-39 yrs</td>
<td>35.6%</td>
<td>21,929,275</td>
</tr>
<tr>
<td>40-44 yrs</td>
<td>15.6%</td>
<td>10,015,484</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>64,325,356</td>
</tr>
</tbody>
</table>

64,325,356 individuals with the potential to menstruate

The potential to menstruate + a bleeding disorder: fast facts

• Up to 65% of adolescent patients with HMB have iron deficiency or iron deficiency anemia.

• Individuals with the potential to menstruate experience delays in bleeding disorder diagnosis (11.6 +/- 16.4 years vs 7.7 +/- 16.6 years for those without the potential to menstruate)

• In a review of 75 patients with von Willebrand Disease, 25% of women received a blood transfusion before being diagnosed with VWD

• Only 4 out of 10 women with HMB will seek care for their HMB.

Sexism in hematology

- In a 2017 survey of >10,000 men and women, 56% said they would rather be bullied than talk about periods.
- <10% of pediatricians and family medicine physicians document a full menstrual history during well adolescent visits.
- Individuals with XX chromosomes “should” make up 30% of the patients we see with hemophilia, but they make up only 3.5% of the population.
- VWD is at least 10x more common than Hemophilia A and B combined but there are at least 15,000 fewer publications in PubMed.
Sexism in hematology

Differences between men and women with autosomal dominant bleeding disorders including 1092 participants, 60.9% women

- "to make a better comparison between men and women, sex-specific bleeding was excluded from bleeding scores." (excluded HMB, PPH, circumcision)

- For participants presenting with bleeding:
  - Half of all men were diagnosed within 2 years (0.8-3.2 years) after 1st bleeding episode
  - Women were diagnosed 14 years (10.4-17.6 years) after 1st bleeding episode

- "Remarkably, the diagnostic delay was longer in women with bleeding disorders than in men, independent of the type of bleeding disorder and severity of bleeding phenotype. This is probably because women may have less traumatic bleeding episodes at an early childhood than men. Men may present more often with spontaneous or traumatic bleeding at a younger age, and since these bleedings are not physiologic, they may be investigated early to diagnose or to rule out an underlying bleeding disorder."

There is hope!

- 1990: females comprised 13% of HTC patients
- 2010: females comprised 31% of HTC patients

- Map of clinics with heme/gyn focus across the US.
- The number of adult patients with the potential to menstruate and a diagnosed bleeding disorder seen at our center tripled when we dedicated staff to this population (2009: 43 patients. 2019: 141 patients).

https://www.fwgbd.org/clinics

What can you do?

• Include a menstrual history –for all your patients who could be having periods!
  • How often are you having bleeding? (more than once per month = too often)
  • How many days does it last? (more than 7 = too long)
  • Do you have to change your pad/tampon more often than every 2 hours (yes = too heavy)
  • Do you have to wake up in the middle of the night to change products (yes = too heavy)
  • Do you have leaking/soaking of blood onto your clothes on a regular basis (yes = too heavy)
What can you do?

• When a patient tells you that their periods are heavy, believe them.
• Not everyone with heavy periods needs a bleeding disorder work up but they may need an intervention to decrease iron deficiency and improve quality of life.
• Counsel the patients that you take care of with bleeding disorders that their children may be at risk for heavy periods, depending on the disease.
• Befriend a gynecologist to help make sure the patients get good therapy.
• Or, connect them to our combined heme/gyn clinics at OHSU.
• Identify and treat iron deficiency.
Side note...

Iron deficiency: bleeding disorders

- From the Registry for Bleeding Disorders Surveillance (9173 males with hemophilia):

<table>
<thead>
<tr>
<th>Iron deficiency anemia</th>
<th>Age Group</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less than 20</td>
<td>20–44</td>
<td>45–64</td>
<td>65+ years</td>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>252</td>
<td>133</td>
<td>127</td>
<td>42</td>
<td>554</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>5.3%</td>
<td>4.6%</td>
<td>10.6%</td>
<td>12.0%</td>
<td>6.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- In 196 adolescents patients who presented with heavy periods, 43% of whom had a bleeding disorder, 119 (61%) were iron deficient

Questions/Comments/Thoughts

"Anemia"