Is this bleeding normal?
Evaluating a child with a suspected bleeding disorder

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Disclosures

FINANCIAL DISCLOSURE

Grants/Research Support:

Diagnostic Services Manitoba
Children’s Hospital Research Institute of Manitoba

Speaker bureau/Honoraria: None

Consulting fees: None
Objectives

After this session participants will:

1. Have an approach to evaluating a child who presents with bleeding

2. Be familiar with common bleeding disorders in children as well as other common causes of bleeding

3. Recognize presentations of bleeding in children requiring urgent referral to a hematologist
What do you need to form a blood clot?

1. A normal blood vessel
2. Platelets:
   - Normal number
   - Normal function
3. Coagulation factors:
   - I to XIII
Referral to Pediatric Hematology

“Dear Pediatric Hematologist:

Please see this seven year old boy with recurrent epistaxis for investigation of a bleeding disorder.”

1. Does this child have a bleeding disorder?
2. What kind of investigation does he need?
Evaluation of the bleeding patient

- Presentation
- Acute onset or chronic/recurrent?
- Family history
- Bleeding assessment score
- Laboratory investigation
Tip #1: Most children with epistaxis do not have a bleeding disorder

- 30% of children < 5 years and 56% of children aged 6 - 10 years have had at least one nosebleed.
- Why so common?
  - Anatomy

- Local causes
  - Trauma: nose-picking*; foreign bodies
  - Mucosal irritation: dry air*; allergic rhinitis; inhaled irritants, URIs or other local infection
  - Anatomic abnormalities, deviated septum, benign tumors

- Systemic causes

(UpToDate 2016)
Bleeding assessment tools (BAT)

- Standardized questionnaires that can help quantify clinical bleeding symptoms/signs
  - Consist of a series of questions and a scoring system
  - BATs have been created for different purposes and with different scoring systems; several have been validated
- BATs can be:
  - Age specific: adults or children
  - Disease specific: VWD, platelet function disorders
  - Symptom specific: epistaxis and menorrhagia

ISTH-BAT can be used for all ages, all symptoms. It has been evaluated in >1000 adults and >300 children to develop normal ranges.
### ISTH-BAT scoring sheet

<table>
<thead>
<tr>
<th>SYMPTOMS (up to the time of diagnosis)</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0°</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>No/trivial</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>No/trivial</td>
</tr>
<tr>
<td>Bleeding from minor wounds</td>
<td>No/trivial</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>No/trivial</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>No/trivial</td>
</tr>
</tbody>
</table>

14 categories: hematuria, tooth extraction, surgery, menorrhagia, postpartum hemorrhage, muscle hematoma, hemarthrosis, CNS bleeding, other.

(www.isth.org/resource/resmgr/ssc/isth-ssc_bleeding_assessment.pdf)
Value of BATs

<table>
<thead>
<tr>
<th>ISTH-BAT cut-off scores:</th>
<th>Utility of ISTH-BAT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ≥4 for men</td>
<td>• Sensitivity 97%</td>
</tr>
<tr>
<td>• ≥6 for women</td>
<td>• Specificity 50%</td>
</tr>
<tr>
<td>• ≥3 for children</td>
<td>• NPV 99%</td>
</tr>
</tbody>
</table>

Tip #2:
A validated BAT score does not provide a diagnosis, but it can help to identify which patients do not need further investigation.
Approach to the bleeding child

Primary hemostatic defects

- Normal
  - Coagulation screen
    - PTT, PT
  - Normal
    - Vasculitis
    - Non-accidental trauma
    - 1° hemostatic dysfunction
      - VWF studies
      - Platelet function studies

- Decreased
  - Acute, isolated
  - Acute, with other cytopenias
  - Chronic
    - Mixing study with normal plasma
      - Correction
        - Clotting factor studies
          - Single deficiency
          - Multiple deficiencies
      - No correction
        - Inhibitor studies

Thrombocytopenia

- CBC with platelet count
- History and physical exam
  - Standardized questionnaire or score

Secondary hemostatic defects
Child with bleeding symptoms

Medical history: age, sex, past medical history, use of medications
Bleeding history: standardized bleeding questionnaire
Family bleeding history: standardized bleeding questionnaire, ethnicity
Physical examination: hemodynamic status, pattern of bleeding, other findings

Initial laboratory tests: CBC, PT/INR, aPTT

Normal platelet count, PT/INR, aPTT

- Consider nonhemostatic causes:
  - Vasculitis
  - Nonaccidental trauma

If hemostatic causes are suspected proceed with investigations:
- Mild factor deficiencies
- FXIII deficiency (urea dot lysis, quantitative assay)
- Dysfibrinogenemia (thrombin time, specific assay)
- VWD (VWF:Ag, VWF:RCo, FVIII)
- Platelet function disorders (platelet aggregometry)
- Fibrinolytic defects (α2-AP, PAI-1)

Platelet count <100 × 10^9/l

- Peripheral blood film (i/o pseudothrombocytopenia)

New onset:
- Isolated
- With other cytopenias
- With coagulopathy

Chronic:
- Isolated
- With other cytopenias
- With platelet function abnormalities
- With congenital anomalies
- With immunodeficiency

Abnormal PT/INR and/or aPTT

- Correction
- Clotting factor assays (based on PT/INR/aPTT results)

Abnormal PT/INR and aPTT

- FX deficiency
- FV deficiency
- FII deficiency
- Fibrinogen deficiency/dysfunction
- Combined factor deficiencies
- Vitamin K deficiency
- Oral VKA excess
- Liver disease

Abnormal aPTT

- FXII deficiency
- FXI deficiency
- FIX deficiency
- FVIII deficiency
- Severe VWD

Abnormal PT/INR

- Normal PT/INR
- Normal aPTT
- Oral VKA

What laboratory tests should I order?

Most algorithms are based on basic testing followed by specialized testing:

1. CBC with platelet count
2. PT/INR, PTT
3. Specialized testing (requires consultation with a Hematologist or Hematopathologist)

It depends where you practice:

- Recent changes to DSM guidelines have removed the PTT from general requests except for UFH monitoring or as part of evaluation for DIC
- Other laboratory services still provide PTT testing
- PTTs can always be requested via Hematopathologist
Why the PTT is a poor test for bleeding

- **Inappropriately sensitive:**
  - Lupus anticoagulants
  - Clotting factor deficiencies that do not cause bleeding (FXII)

- **Inadequately sensitive:**
  - Mild clotting factor deficiencies

- **Not built to measure:**
  - Von Willebrand Disease
  - Factor XIII deficiency
  - Some fibrinogen abnormalities
  - Fibrinolytic defects
  - Platelet disorders

What the PTT is good for:

- Severe clotting factor deficiencies
- Multiple clotting factor deficiencies
- Unfractionationed heparin monitoring
Tip #3: Laboratory screening tests may not help you

- The exception is the CBC
- Critically ill children often have abnormalities if they have sepsis or consumptive coagulopathy
- Other children:
  - Rarely have abnormalities of PTs unless they have Vitamin K deficiency
  - Abnormal PTTs are more likely to be caused by infection-associated LA than a factor deficiency
  - More common bleeding disorders require specialized testing
Referral to Pediatric Hematology

“Dear Pediatric Hematologist:

Please see this 5 year old girl, previously well, with sudden onset of bruising, a petechial rash and epistaxis. She previously had an adenoidectomy without bleeding complications.”

1. Does this child have a bleeding disorder?
2. What kind of investigation does she need?
<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC x 10^9/L</td>
<td>11.2</td>
<td>5.0-15</td>
</tr>
<tr>
<td>HGB (g/L)</td>
<td>115</td>
<td>115-125</td>
</tr>
<tr>
<td>HCT</td>
<td>0.34</td>
<td>0.34-0.4</td>
</tr>
<tr>
<td>RBC x 10^{12}/L</td>
<td>3.9</td>
<td>3.9-5.4</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>79.8</td>
<td>75-87</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>27.2</td>
<td>24-34</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.1</td>
<td>11.4-14.4</td>
</tr>
<tr>
<td>Retic. x 10^9/L</td>
<td>65</td>
<td>25-75</td>
</tr>
<tr>
<td>Platelets x 10^9/L</td>
<td>4</td>
<td>150-400</td>
</tr>
<tr>
<td>Blood film</td>
<td>Lymphocytosis Occ. Large platelets</td>
<td></td>
</tr>
</tbody>
</table>
Thrombocytopenia in a child

Thrombocytopenia

- blood smear
- platelet clumping
- Pseudothrombocytopenia
  - Evaluation for pancytopenia or for anemia/thrombocytopenia
    - Congenital or acquired bone marrow failure
    - Autoimmune cytopenias
    - Sepsis/DIC HUS

- multiple cytopenias
  - Microangiopathic changes
    - Consumptive Coagulopathy
    - Microangiopathic changes
  - Macro-thrombocytopenia
    - Autoimmune cytopenias

- Microthrombocytes
  - Macrocytosis and PMN hypersegmentation
    - Vit B12 or Folate deficiency
    - Vit B12 or Folate deficiency
  - MYH9 related disorders
    - Gray platelet syndrome
    - Bernard Soulier Syndrome

- Congenital bone marrow failure syndromes: Fanconi Anemia, TAR
  - Evaluation for Wiskott Aldrich syndrome
    - Evaluation for Wiskott Aldrich syndrome
    - Bone marrow evaluation

- Congenital anomalies
  - Medications, toxins
    - Splenomegaly

- Congenital anomalies
  - Splenomegaly
  - Chronic Infection
  - Portal hypertension

Thrombocytopenia in a child
Primary ITP in children

- Incidence: 4/100,000 children
- Mean age: 5.7 years
- Seasonal variation
- More common in boys than girls
- Previously healthy children
  - >60% have a history of antecedent infectious illness or immunization in the preceding 4 weeks
- Typical abrupt onset of bleeding
- Isolated severe thrombocytopenia
  - >75% have platelet counts <20 x 10^9/L

(ICISI Registry: Lancet 2001; J Peds 2003; PBC 2006)
The special case of thrombocytopenia in a neonate

Thrombocytopenia

Well neonate

NAIT

Maternal illness

Preeclampsia/HE LLP

Congenital thrombocytopenia

Ill neonate

Perinatal asphyxia

Sepsis/ NEC

Thrombosis

Hemolytic disease of the newborn

Drug-induced
Tip #4: Thrombocytopenia has many causes in children

- Acute onset of isolated thrombocytopenia in otherwise well children is most likely to be ITP
- Thrombocytopenia associated with other cytopenias raises concerns for bone marrow disorders
- Persistent thrombocytopenia raises the possibility of congenital causes; look for signs of associated anomalies
Referral to Pediatric Hematology

“Dear Pediatric Hematologist:

Please see this 3 month old boy who has developed extensive bruising and swelling at site of venipuncture. No family history of a bleeding diathesis.”

1. Does this child have a bleeding disorder?
2. What kind of investigation does he need?
<table>
<thead>
<tr>
<th>Test</th>
<th>Patient</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC x $10^9$/L</td>
<td>12.8</td>
<td>5.0-15</td>
</tr>
<tr>
<td>RBC x $10^{12}$/L</td>
<td>3.8</td>
<td>2.7-4.9</td>
</tr>
<tr>
<td>HCT (L/L)</td>
<td>0.34</td>
<td>0.28-0.44</td>
</tr>
<tr>
<td>HGB (g/L)</td>
<td>120</td>
<td>90-140</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>85</td>
<td>74-115</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.5</td>
<td>11.4-14.4</td>
</tr>
<tr>
<td>Retic. x $10^9$/L</td>
<td>65</td>
<td>25-75</td>
</tr>
<tr>
<td>Platelets x $10^9$/L</td>
<td>320</td>
<td>150-400</td>
</tr>
<tr>
<td>Blood film</td>
<td>Typical for age</td>
<td></td>
</tr>
<tr>
<td>PT (sec)/ INR</td>
<td>12/ 1.1</td>
<td>10-12.5/0.9-1.1</td>
</tr>
<tr>
<td>PTT (sec)</td>
<td>87</td>
<td>26-38</td>
</tr>
</tbody>
</table>

Factor VIII 1% (50-150)
Factor IX 62% (50-150)
What does hemophilia look like in young children?
Tip #5: Hemophilia in young boys looks different

- An unusual bruising pattern or soft tissue bleeding
  - Always be alert to the possibility of non-accidental trauma
- Joint bleeds are rare in children before they are walking
- There is not always a family history:
  - 30% of cases are the result of new mutations

An aPTT is helpful if the question is hemophilia
When to consider referral to Pediatric Hematology

1. Thrombocytopenia (platelet count <100 x 10⁹/L), particularly if accompanied by additional cytopenias

2. A severe or unusual pattern of bleeding in a young child*

3. A child with bleeding symptoms and a significant family history of bleeding [with or without a diagnosis]; sooner if surgery is planned*

4. Menorrhagia in adolescent girls, severe enough to cause iron-deficiency anemia or impact ADL *

* Likely to have a positive BAT score
Take Home Messages

1. Most mucocutaneous bleeding in children is not the result of a hemostatic disorder.
2. A careful history and a BAT may be more helpful than laboratory screening tests (except CBC) in determining the need specialized testing.
3. Remember that your pediatric hematologist cannot always give you a definitive diagnosis for mucocutaneous bleeding.
4. Be alert to severe bleeding conditions that require urgent attention.
ISTH Bleeding Assessment Tool:

Questions?
sisraels@cancercare.mb.ca
Frequent epistaxis in a child is more likely to be a sign of a bleeding disorder if any of the following are true, except:

A. He has seasonal allergies.
B. He previously had nasal cautery to manage the epistaxis.
C. His brother also has epistaxis.
D. He has a positive history for bleeding at sites other than the nose.

Question:
Frequent epistaxis in a child is more likely to be a sign of a bleeding disorder if any of the following are true, except:

A. He has seasonal allergies.
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