The Bleeding Pediatric Patient

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5/18/2012
Bleeding in Pediatric Patients

- Bruising and bleeding are commonly seen in children → usu 2/2 minor injury and trauma
- RULE OUT underlying inherited bleeding disorder OR non-accidental injury (NAI)
Bleeding History

- History is KEY: age, sex, clinical presentation, past history, and family history.
  - Bleeding into the skin and mucous membranes = d/o of platelets and blood vessels.
    - Purpuric disorders: present with petechiae and/or ecchymoses.
  - Bleeding into soft tissue, muscle, and joints.
    - Hemophilia or other coag disorders.
  - Not all bleeding episodes are suggestive of a disorder.
    - Epistaxis: rhinitis, trauma, superficial vessels.
    - Abnormal post-surgical bleeding: surgical trauma.
    - NAI
    - Medications: including herbal, asa, NSAID.
Key Questions in History

- Nosebleeds - at least 1-5/yr, lasting > 10 min.
  - Requiring packing and cauterization
- Bleeding at site of tooth extraction or dental work (> 3 hours of oozing, Need for packing)
- Heavy menstrual bleeding
  - h/o iron deficiency, passing clots the size of quarters, changes pad < q2h
- Heavy bleeding after childbirth
- Tendency to bruise easily at least weekly
- Prolonged bleeding (> 5 min) after trivial cuts
- Joint bleeding (knees, ankles, elbows, shoulder, hips)
- Bleeding into muscle
- GI bleeding
Primary vs Secondary Hemostasis

Mucocutaneous bleeding suggestive of defect in primary hemostasis: VWD

Deep-tissue bleeding suggestive of defect in secondary hemostasis: Hemophilia

VWD = von Willebrand disease.

Kouides, Peter A. Epidemiology and clinical characteristics of congenital and acquired bleeding disorders.
### Congenital Bleeding Disorders

#### Classification of Bleeding Disorders

<table>
<thead>
<tr>
<th>Type of Bleeding</th>
<th>Congenital Disorders</th>
<th>Acquired Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulopathic: usually abnormal PT and/or PTT</td>
<td>• Factor I, II, V, VII, VIII, IX, X, XI, or X III deficiency</td>
<td>• DIC</td>
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<td></td>
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<td>• Chronic liver disease</td>
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<td>• Vitamin K deficiency</td>
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<td></td>
<td></td>
<td>• Surreptitious warfarin use</td>
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<td></td>
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<td>• Coagulation factor Inhibitor</td>
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<tr>
<td>Thrombocytopenic: usually PC &lt;20K for spontaneous bleeding</td>
<td>• Wiskott-Aldrich Syndrome, Gray platelet syndrome, May-Hegglin</td>
<td>• ITP</td>
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<tr>
<td></td>
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<td>• Primary marrow disease</td>
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</tbody>
</table>
| Thrombocytopenic or VWF-related: can have prolonged closure time or abnormal platelet aggregation study if thrombocytopeny | • von Willebrand disease  
• Bernard-Soulier  
• Glanzmann’s  
• Storage pool deficiency | • Drug-induced platelet dysfunction-drugs “A”→”H”  
• Uremia  
• MDS  
• Acquired VWD 2° hypothyroidism, ciprofloxacin, inhibitor |
| Fibrinolytic: usually low fibrinogen and ELT and increased d-dimer | • Plasminogen activator inhibitor deficiency  
• α₂-antiplasmin deficiency | • Chronic liver disease  
• Vascular surgery |
What labs to obtain?

• Initial Labs:
  • CBC
  • PT/aPTT
    • Mixing studies
  • Fibrinogen level

• Additional Labs that can be ordered:
  • Antiphospholipid antibodies
  • Tests for fibrinolysis: D –Dimers
  • PFA-100
    • Measures platelet related primary hemostasis and has replaced the bleeding time.
Understanding the Cascade

The three pathways that makeup the classical blood coagulation pathway:

**Intrinsic**
- surface contact
- XII → XIIa
- XI → XIa
- IX → IXa
- X
- prothrombin
- thrombin (serine protease)
- fibrinogen → fibrin

**Extrinsic**
- TF:VIIa → tissue damage
- tissue damage

**Common**
- $X_\alpha$ → $X$
- $X$ → prothrombin
- thrombin (serine protease)
- fibrinogen → fibrin
- $X_{III}$ → stable fibrin clot

- XII → Hageman factor, a serine protease
- XI → Plasma thromboplastin, antecedent serine protease
- IX → Christmas factor, serine protease
- VII → Stable factor, serine protease
- XIII → Fibrin stabilising factor, a transglutaminase
- PL → Platelet membrane phospholipid
- Ca^{++} → Calcium ions
- TF → Tissue Factor

($\alpha$ = active form)
The Two Steps Involved in Forming a Clot
...and how a deficiency in a clotting protein can lead to bleeding

- **Step 1: Formation of platelet “plug”**
  - Exposed collagen + **VWF** + platelets
  - Deficiency of VWF leads to poor platelet plug formation = von Willebrand Disease

- **Step 2: Formation of fibrin clot over platelets**
  - Platelets + **cofactors V & VIII (IX)** + the remaining coagulation factors
  - Deficiency of factor VIII or IX leads to poor fibrin formation = Hemophilia (A,B)
Interpretation of Abnormal Coag Screen

<table>
<thead>
<tr>
<th>PT</th>
<th>APTT</th>
<th>TT</th>
<th>Possible abnormality/further investigation required</th>
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<tbody>
<tr>
<td>↑</td>
<td>N</td>
<td>N</td>
<td>• Factor VII deficiency</td>
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<td></td>
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<td></td>
<td>• Liver disease</td>
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<td></td>
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<td></td>
<td>• Vitamin K deficiency</td>
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<td></td>
<td></td>
<td></td>
<td><strong>Measurement of PT-based factors</strong></td>
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<tr>
<td>N</td>
<td>↑</td>
<td>N</td>
<td>• Deficiency of factor VIII (due to haemophilia A or VWD)</td>
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<td></td>
<td></td>
<td></td>
<td>factors IX, XI, XII or contact factors (intrinsic pathway)</td>
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<td><strong>Measurement of APTT-based factors and VW ‘screen’(FVIII:C, VWF:Ag, VWF:RCO, VWF:CB, PFA-100)</strong></td>
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<tr>
<td></td>
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<td>• Lupus anticoagulant or other coagulation factor inhibitor</td>
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<td>DRVVT, Exer, ACL, anti-β2GP1 antibodies</td>
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<td>N</td>
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<td>↑</td>
<td>• Hypofibrinogaenaemia</td>
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<td></td>
<td>• Dysfibrinogaenaemia</td>
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<td></td>
<td><strong>Reptilase time + other thrombin time corrections</strong></td>
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<td>↑</td>
<td>↑</td>
<td>N</td>
<td>• Deficiency of factor II, V, X (common pathway)</td>
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<td></td>
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<td>• Vitamin K deficiency</td>
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<td></td>
<td></td>
<td>• Liver disease</td>
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<td></td>
<td></td>
<td></td>
<td>• Massive transfusion</td>
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<td></td>
<td></td>
<td></td>
<td>• Oral anticoagulants</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• PT- and APTT-based factors, INR</td>
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<tr>
<td>N</td>
<td>↑</td>
<td>↑</td>
<td>• Heparin</td>
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<td></td>
<td><strong>Reptilase time and other thrombin time corrections</strong></td>
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<td>↑</td>
<td>• Disseminated intravascular coagulation</td>
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<td></td>
<td>• Large amount of heparin</td>
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<td></td>
<td>• Severe hypo- or asfibrinogaenaemia</td>
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<td></td>
<td><strong>D-dimers, Reptilase time and other thrombin time corrections</strong></td>
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<tr>
<td>N</td>
<td>N</td>
<td>N</td>
<td>All tests normal but history of bleeding – consider diagnoses in table 1</td>
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</tbody>
</table>
Hemostatic Disorders with Normal Labs

<table>
<thead>
<tr>
<th>Table I. Haemostatic disorders which may present with normal coagulation screen and full blood count.</th>
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<tbody>
<tr>
<td>Mild von Willebrand disease</td>
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<tr>
<td>Mild haemophilia A or B</td>
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<td>Mild factor XI or other single factor deficiency</td>
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<td>Factor XIII deficiency</td>
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<td>α-2 antiplasmin deficiency</td>
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<tr>
<td>Plasminogen activation inhibitor-1 deficiency</td>
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<tr>
<td>Glanzmann thrombasthenia</td>
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<tr>
<td>Platelet storage pool disease</td>
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<tr>
<td>Platelet release defect</td>
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<tr>
<td>Collagen disorders</td>
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<tr>
<td>Vitamin C deficiency</td>
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</tbody>
</table>
Management in the ED of Hemophilia

- Goal: elevate the circulating levels of the deficient clotting factor
  - Normal clotting factor levels in blood range from 50-150 IU/dL plasma (reported as 50-150%)
- ALWAYS start with ABC
- Multiple IV access lines
  - Ideally, supply the patient with specific clotting factor concentrates
  - FFP or cryoprecipitate should be used only if specific factor concentrates are not available.
    - Risk of volume overload
- Major Bleeds: iliopsoas, CNS/head, throat and neck, ophthalmic sites, GI
- Minor Bleeds: joints, muscle (minus the iliopsoas), renal or deep laceration
- Reserve diagnostic and laboratory testing until after factor levels have been raised.
- AVOID aspirin-containing compounds, IM shots, IA lines, arthrocentesis.
Replacement Therapies: FVIII deficiency

• Hemophilia A → goal of therapy is to achieve desired FVIII level (30-50% for minor/moderate bleeding, 80-100% for severe hemorrhage). 25 IU/kg vs 50 IU/kg followed by smaller dose.
• units of FVIII required = (BW) (% level desired)(0.5)
• Interventions
  • Purified FVIII concentrates
    • Plasma derived FVIII, recombinant FVIII
  • Intermediate purity FVIII (has some vWF)
    • Ie Humate
  • Cryoprecipitate contains FVIII, CWF
    • Dose 1 bag/6kg of BW
  • Desmopressin (must know to be a good responder and have had a DDAVP challenge)
Replacement Therapies: FIX deficiency

- Hemophilia B $\rightarrow$ achieve desired FIX level of 30-50% for minor bleeds or 80-100% for life threatening bleeds.
- Units of FIX required = (BW) (% level desired)
- Options:
  - Purified FIX concentrates
  - Recombinant FIX
  - FFP (contains FIX)
    - 15 ml/kg x1, check level
Complications in Treatment of Bleeding Disorders

- Development of an IgG neutralizing antibody (AKA inhibitor) to factor VIII replacement therapy.
  - Seen in 20-30% of pts with severe hemophilia A
- Inhibitors make tx with FVIII concentrates ineffective in achieving hemostasis.
- Inhibitors are less commonly seen in Hemophilia B and are extremely rare in vWD.
- Management of bleeding is based according to responder status and inhibitor titer.
  - Low responder/low titer (< 5 BU)
  - High responder/low titer (< 5BU)
  - High responder/high titer (>5BU)
- Administer bypassing agents (FEIBA or NovoSeven), ensure good venous access, replace red cell losses as needed, and involve with HTC/hematologist.
ED Management of vWD

- Goal is to increase plasma levels of vWF and FVIII
- Tx depends on baseline functional vWF and individual’s response to DDAVP therapy.
  - DDAVP, a synthetic vasopressin analogue, stimulates the release of vWF from endothelial cells to raise circulating concentrations of VWF and FVIII
- Desmopressin Responsive
  - Usually mild Type 1 and some type 2
  - Tx with desmopressin (alternative: antifibrinolytic)
- Desmopressive Unresponsive/Unknown
  - Type 1 with low vWF levels, Type 2b, Type3
    - FVIII/VWF concentrates (Humate P) or cryoprecipitate (less likely)
    - Alternative: antifibrinolytic amino acid, platelet concentrates.
Special Considerations in the ED

- The majority of pts who present to the ED will have a known diagnosis, but some may have a milder form of the disease where the diagnosis has been delayed or represent 25% of hemophilia cases that are a result of new spontaneous mutations and have no known family history.

- Must also rule out NAI
  - Family history of bleeding
  - CBC with peripheral blood smear
  - Screening coag labs: PT/PTT/fibrinogen
Typical Presentations of Bleeding Disorders

- Male infant learning to walk presents with painful swollen joint after a fall.
- Adolescent girl presenting with excessive menstrual bleeding, recurrent nosebleeds, and pallor.
- 5 yo child who is not ill, but presents with moderate mucocutaneous purpura along with a viral infection.
- Teen girl with easy bruising, pallor, and strong FHx of AI disorders
- 10 day old infant with bleeding from the umbilical stump or ICH
References

- UptoDate. Approach to the child with bleeding symptoms March 2012.