The Bleeding Pediatric Patient

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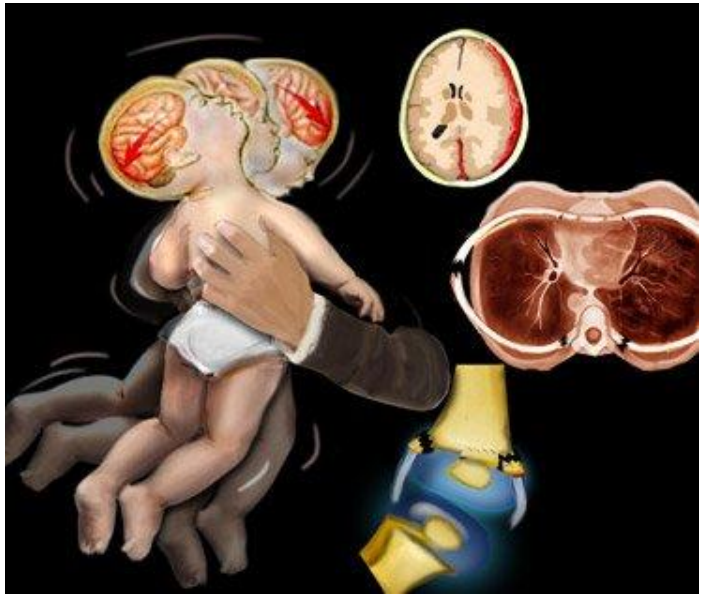
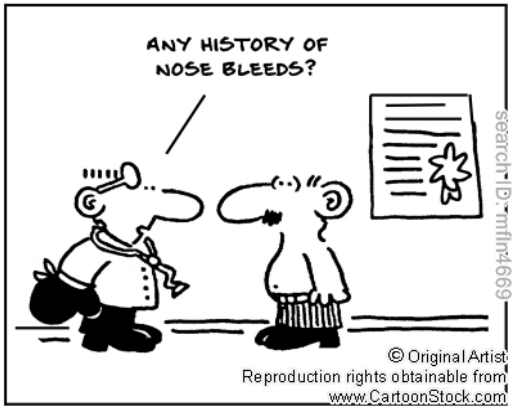
Bleeding in Pediatric Patients

- 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 ves
    - Abnormal post-surgical bleeding→ surgica
    - NAI
    - Medications: including herbal, asa, NSAID

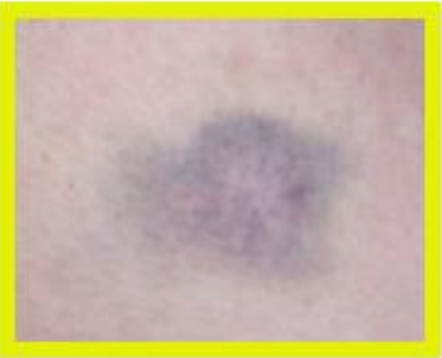


Key Questions in History

- 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
- Bleeding after surgery requiring

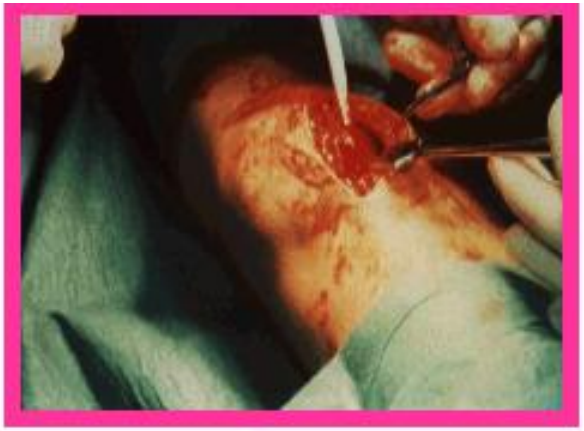
- Joint bleeding (knees, ankles, elbows, shoulder, hips)
- Bleeding into muscle
- GI bleeding

Primary vs Secondary Hemostasis

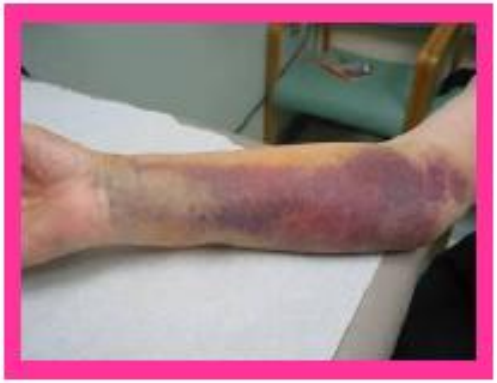


Mucocutaneous bleeding suggestive of defect in primary hemostasis: VWD

VWD=von Willebrand disease.



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



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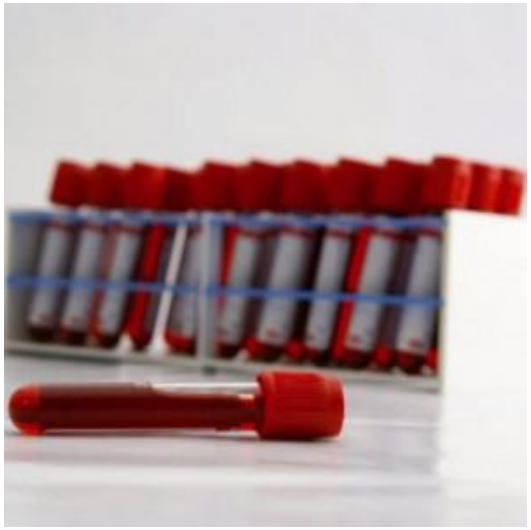
Congenital Bleeding Disorders

Classification of Bleeding Disorders

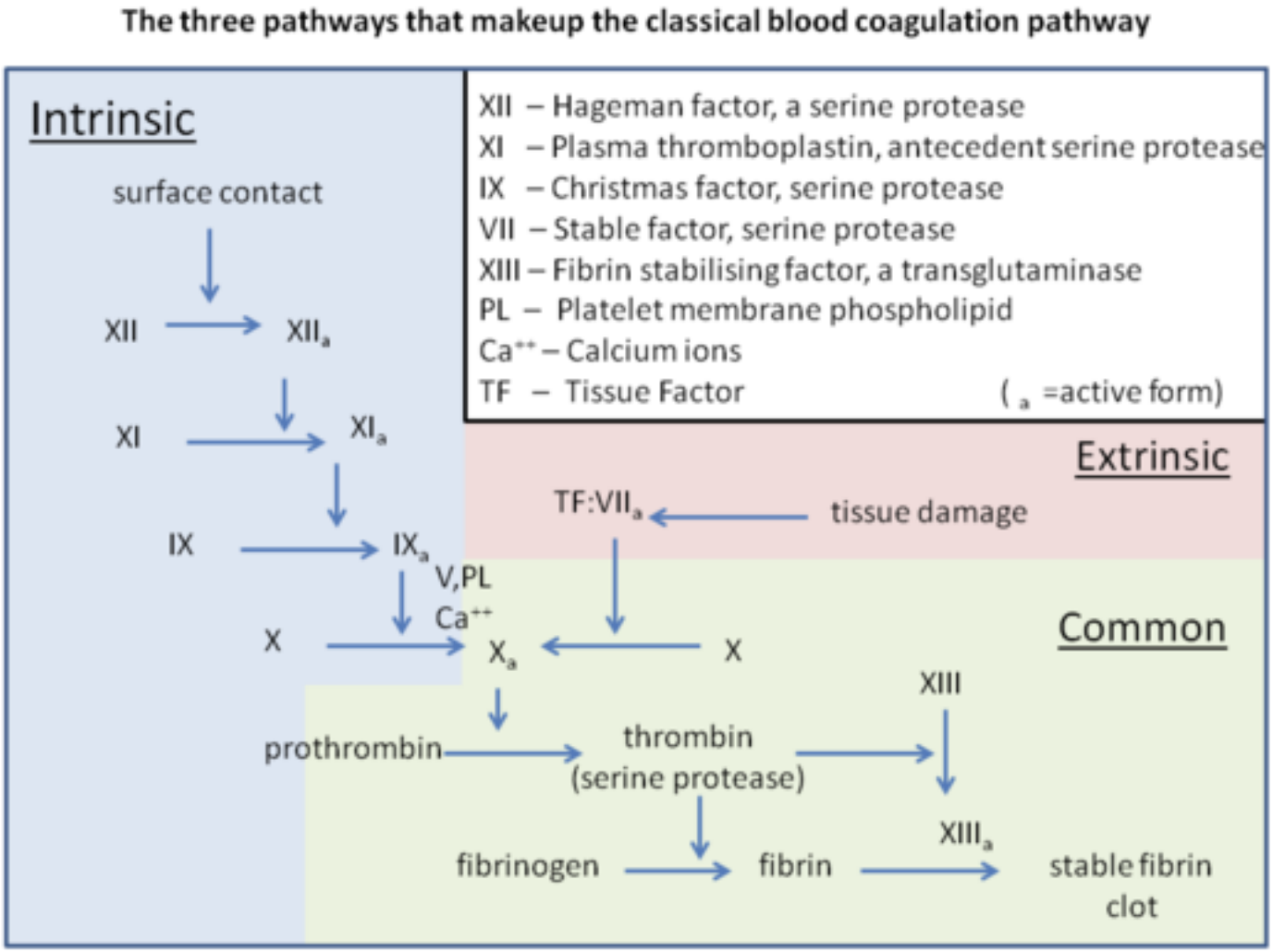
Type of Bleeding	Congenital Disorders	Acquired Disorders
Coagulopathic: usually abnormal PT and/or PTT	• Factor I, II, V,VII, VIII, IX, X, XI, or XIIII deficiency	• DIC • Chronic liver disease • Vitamin K deficiency • Surreptitious warfarin use • Coagulation factor Inhibitor
Thrombocytopenic: usually PC <20K for spontaneous bleeding	• Wiskott-Aldrich Syndrome, Gray platelet syndrome, May-Hegglin	• ITP • Primary marrow disease
Thrombocytopathic or VWF-related: can have prolonged closure time or abnormal platelet aggregation study if thrombocytopathy	• 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 • α_2-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
    - Meausures platelet related primary hemostasis and has replaced the bleeding time.

Understanding the Cascade



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)

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Interpretation of Abnormal Coag Screen

PT	APTT	TT	Possible abnormality/*further investigation required*
↑	N	N	• Factor VII deficiency • Liver disease • Vitamin K deficiency *Measurement of PT-based factors*
N	↑	N	• Deficiency of factor VIII (due to haemophilia A or VWD) factors IX, XI, XII or contact factors (intrinsic pathway) *Measurement of APTT-based factors and VW 'screen'(FVIII:C, VWF:Ag, VWF:RCo, VWF:CB, PFA-100)* • Lupus anticoagulant or other coagulation factor inhibitor *DRVVT, Exner, ACL, anti-β2GP1 antibodies*
N	N	↑	• Hypofibrinogenaemia • Dysfibrinogenaemia *Reptilase time + other thrombin time corrections*
↑	↑	N	• Deficiency of factor II, V, X (common pathway) • Vitamin K deficiency • Liver disease • Massive transfusion • Oral anticoagulants • *PT- and APTT-based factors, INR*
N	↑	↑	• Heparin *Reptilase time and other thrombin time corrections*
↑	↑	↑	• Disseminated intravascular coagulation • Large amount of heparin • Severe hypo- or afibrinogenaemia *D-dimers, Reptilase time and other thrombin time corrections*
N	N	N	All tests normal but history of bleeding – consider diagnoses in table 1

Hemostatic Disorders with Normal Labs

Table I. Haemostatic disorders which may present with normal coagulation screen and full blood count.

Mild von Willebrand disease
Mild haemophilia A or B
Mild factor XI or other single factor deficiency
Factor XIII deficiency
α-2 antiplasmin deficiency
Plasminogen activation inhibitor-1 deficiency
Glanzmann thrombasthenia
Platelet storage pool disease
Platelet release defect
Collagen disorders
Vitamin C deficiency

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 facot 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→ 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 hemostatis.
- 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

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

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- Singleton, T, et al. Emergency Department Care for Patients with Hemophilia and vWD. *The Journal of Emergency Medicine.* 2010; 39:158-165.
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