Bleeding Disorders in Children:

Identification and primary care management

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Introduccion

- Bleeding symptomes like bruising and epistaxis are common in healthy children but occasionally may indicate an underlying congenital or acquired bleeding diathesis.
- Bleeding disorders can be inherited or acquired, and include:

1. platelet deficiencies and/or dysfunctions and von Willebrand disease,
2. coagulation factor deficiencies,
3. and disorders of fibrinolysis.

- The most common congenital coagulation disorders, following von Willebrand disease, are Hemophilia A and B.
- The rare bleeding disorders (RBDs) comprise inherited deficiencies of coagulation factors I,II,V,VII,X,XI and XIII and combined factor deficiencies (FV-FVIII, vitamin K-dependent factors).

History

Moderate and mild inherited hemostatic defects may not present with clinical bleeding until an older age, or until the child is exposed to a hemostatic challenge.

- Age
- Sex
- Past medical history
- Family history
- ***Bleeding manifestations***
- Physical Examination

Bleeding manifestations

- ✓ Mucocutaneous bleeding
- ✓ Bleeding into soft tissues, muscles and joints, or delayed surgical bleeding
- ✓ The onset and acuity of bleeding

The use of *standardized scores* to quantitate bleeding symptoms is recommended

SYMPTOMS (up to the time of diagnosis)	SCORE				
	0§	1§	2	3	4
Epistaxis	No/trivial	- > 5/year or - more than 10 minutes	Consultation only*	Packing or cauterization or antifibrinolytic	Blood transfusion or replacement therapy (use of hemostatic blood components and rFVIIa) or desmopressin
Cutaneous	No/trivial	For bruises 5 or more (> 1cm) in exposed areas	Consultation only*	Extensive	Spontaneous hematoma requiring blood transfusion
Bleeding from minor wounds	No/trivial	- > 5/year or - more than 10 minutes	Consultation only*	Surgical hemostasis	Blood transfusion, replacement therapy, or desmopressin
Oral cavity	No/trivial	Present	Consultation only*	Surgical hemostasis or antifibrinolytic	Blood transfusion, replacement therapy or desmopressin
GI bleeding	No/trivial	Present (not associated with ulcer, portal hypertension, hemorrhoids, angiodysplasia)	Consultation only*	Surgical hemostasis, antifibrinolytic	Blood transfusion, replacement therapy or desmopressin

Hematuria	No/trivial	Present (macroscopic)	Consultation only*	Surgical hemostasis, iron therapy	Blood transfusion, replacement therapy or desmopressin
Tooth extraction	No/trivial or none done	Reported in ≤25% of all procedures, no intervention**	Reported in >25% of all procedures, no intervention**	Resuturing or packing	Blood transfusion, replacement therapy or desmopressin
Surgery	No/trivial or none done	Reported in ≤25% of all procedures, no intervention**	Reported in >25% of all procedures, no intervention**	Surgical hemostasis or antifibrinolytic	Blood transfusion, replacement therapy or desmopressin
Menorrhagia	No/trivial	Consultation only* or - Changing pads more frequently than every 2 hours or - Clot and flooding or - PBAC score>100#	- Time off work/school > 2/year or - Requiring antifibrinolytics or hormonal or iron therapy	- Requiring combined treatment with antifibrinolytics and hormonal therapy or - Present since menarche and > 12 months	- Acute menorrhagia requiring hospital admission and emergency treatment or - Requiring blood transfusion, Replacement therapy, Desmopressin, or - Requiring dilatation & curretage or endometrial ablation or hysterectomy)
Post-partum hemorrhage	No/trivial or no deliveries	Consultation only* or - Use of syntocin or - Lochia > 6 weeks	- Iron therapy or - Antifibrinolytics	- Requiring blood transfusion, replacement therapy, desmopressin or - Requiring examination under anaesthesia and/or the use of uterin balloon/package to tamponade the uterus	- Any procedure requiring critical care or surgical intervention (e.g. hysterectomy, internal iliac artery legation, uterine artery embolization, uterine brace sutures)
Muscle hematomas	Never	Post trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring desmopressin or replacement therapy	Spontaneous or traumatic, requiring surgical intervention or blood transfusion

Hemarthrosis	Never	Post trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring desmopressin or replacement therapy	Spontaneous or traumatic, requiring surgical intervention or blood transfusion
CNS bleeding	Never	-	-	Subdural, any intervention	Intracerebral, any intervention
Other bleedings^	No/trivial	Present	Consultation only*	Surgical hemostasis, antifibrinolytics	Blood transfusion or replacement therapy or desmopressin

In addition to the guidance offered by the table, it is mandatory to refer to the text for more detailed instructions.

§ Distinction between 0 and 1 is of critical importance. Score 1 means that the symptom is judged as present in the patient's history by the interviewer but does not qualify for a score 2 or more

* Consultation only: the patient sought medical evaluation and was either referred to a specialist or offered detailed laboratory investigation

** Example: 1 extraction/surgery resulting in bleeding (100%): the score to be assigned is 2; 2 extractions/surgeries, 1 resulting in bleeding (50%): the score to be assigned is 2; 3 extractions/surgeries, 1 resulting in bleeding (33%): the score to be assigned is 2; 4 extractions/surgeries, 1 resulting in bleeding (25%): the score to be assigned is 1

If already available at the time of collection

^ Include: umbilical stump bleeding, cephalohematoma, cheek hematoma caused by sucking during breast/bottle feeding, conjunctival hemorrhage or excessive bleeding following circumcision or venipuncture. Their presence in infancy requires detailed investigation independently from the overall score

Laboratory Investigations

Initial tests to screen for bleeding disorders should include :

- ✓ CBC
- ✓ Peripheral Blood film
- ✓ PT
- ✓ PTT
- ✓ Fibrinogen/TT
- ✓ Von Willebrand antigen and activity - FVIII
- ✓ PFA

Others: Factor XIII activity

Platel function testing

Fibrinolysis inhibitors

Genetic testing

TABLE 2 Distinguishing Epidemiologic, Genetic, Clinical, and Laboratory Features of the Hemophilias and RBDs

HA and HB	RBDs
Together with VWD, account for >90% of all inherited bleeding disorders[17]	Account for 3% to 5% of all inherited coagulation disorders[19,20,25]
XR inheritance; therefore, majority of affected individuals are male	Autosomal inheritance, so both boys and girls affected; most are AR (except for FXI deficiency [AV] and dysfibrinogenemia [AD]); however, heterozygotes variably symptomatic, especially in FVII and FXI deficiencies
Family history of disease in brothers or in maternal male relatives; may be absent in up to one-third of patients[16]	Family history often lacking; most RBDs more prevalent where consanguinity is commonplace[21,22,27]
Clinical course predominated by soft tissue and musculoskeletal bleeding, especially in older children[16]; postcircumcision/post-heel stick and CNS bleeding most common bleeding events in newborns[16]	Clinical presentation variable within and among individual RBDs; mucocutaneous bleeding is most common symptom overall[20,22,25–27]; serious bleeding (eg, ICH) characteristic of FX and FXIII deficiencies in particular[22] but can occur in virtually any of the RBDs
Initial laboratory evaluation remarkable for isolated prolonged APTT that corrects in a mixing study	Both PT and APTT prolonged in most RBDs (see Fig 1); PT/APTT abnormalities correct in a mixing study; quantitative functional FXIII activity assay should be used to screen for FXIII deficiency, in which PT/APTT are normal[23]
Clinical severity correlates with coagulant activity[16]	Poor association between clinical severity and coagulant activity in FV and FVII deficiencies; no association between clinical severity and coagulant activity, both when undetectable or moderately reduced (<20%), in FXI deficiency[24]

AD, autosomal dominant; AV, autosomal variable penetrance; CNS, central nervous system; VWD, von Willebrand disease; XR, X-linked recessive.

Perinatal Management

- The general principles of the management of labour and delivery in women with rare bleeding disorders are similar to pregnancies at risk of hemophilia.
- Due to limited information available in the literature, *recommendations* are generally made based on evidence derived from case studies or opinions and experiences of respected authorities.
- A close and continuing collaboration between obtetrician, hematologist and pediatrician or neonatologist is essential for the management of pregnancy in women with bleeding disorders, ideally in a joint clinic especially for those with severe and rare disorders.

- A *detailed written plan* of management should be formulated during the third trimester of pregnancy and made available to all care givers.
- Delivery of a potentially affected neonate should ideally take place in a specialized center with advance planning to limit the risk of bleeding in both mother and child, and resources for *laboratory testing* and *clotting factor treatments* are readily available.

Recommendations

- ✓ The best mode of delivery remains debatable; the mortality and the morbidity of a planned caesarean section is comparable to a vaginal delivery.
- ✓ Avoid invasive intrapartum fetal monitoring techniques, prolonged labor, and traumatic instrumental deliveries (forceps- vacuum extraction).
- ✓ Obtain cord blood sample for assessement of neonatal coagulation status in neonates at risk of inherited bleeding disorder.
- ✓ Avoid intramuscular injection in neonates at risk until the coagulation status is known – give oral vitamin K and immunization through subcutaneous route.
- ✓ If delivery has been traumatic or if there are clinical signs suggestive of head bleeding, a cranial ultrasound should be performed.

Additional pediatric recommendations

- Hepatitis A and B vaccines.
- Routine preventive dental care.
- Parents should avoid giving children analgesics/antipyretics that may affect platelet function.
- Providers and parents may consult existing resources for guidance to physical activity and others aspects of care in children and adolescents with bleeding disorders.
- Genetic counseling and screening (especially for consanguinity).

Conclusions

Bleeding in a child can be a diagnostic challenge because of the wide range of possible causes.

Making a specific diagnosis is clinically important in order to provide appropriate therapy and to mitigate any risk for future bleeding.

Bleeding may be severe, even life-threatening ang given the congenital nature of these disorders, symptomes may begin during the neonatal period or early childhood.

Primary care and other nonhematologist pediatric providers must be familiar with the evaluation of these rare disordres.

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