ERN-EuroBloodNet Topic on Focus on Inherited Platelet Function Disorders (IPFD)

webinar

HEALTH PROFESSIONALS

Pediatric-specific aspects and transition of care in inherited platelet function disorders

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Disclosure for conflict of interest

Conference fees	Novonordisk, Sobi, Roche, Octapharma, CSL,

Pediatric-specific aspects and transition of care in inherited platelet function disorders (IFPD)

- Diagnoses
- Treatment
- Transition

Diagnostic Approach : pediatric specificity

- **Severe forms**
  - Early diagnosis
  - Tailored management
  - Specialized follow-up
- **Mild forms**
  - When should IFPD be suspected?
  - What are the diagnostic challenges?
  - What are the clinical implications during childhood?

Standardized Bleeding Questionnaires

Bleeding history

- Frequency of bleeding episodes
- Bleeding sites

Pediatric-specific features

- umbilical stump bleeding
- cephalohematoma,
- post-circumcision bleeding,
- venipuncture bleeding,
- conjunctival hemorrhage,
- macroscopic hematuria

Menstrual bleeding (adolescents)

ISTH/SSC Bleeding Assessment Tool

Pediatric Bleeding Questionnaire

> 2

Pictorial Blood Loss Assessment Chart (PBAC)
>100

Pediatric Bleeding Questionnaire (PBQ) / IFPD

Table 1 Bleeding score according to sex, age group and diagnosis in children with an inherited platelet function disorder ($n = 23$)

	Number of patients	Age (years), median (range)*	Bleeding score, median (range)*
Sex			
Male	11	12.2 (6.5–18.0)	8.0 (3–19)
Female	12	9.9 (0.6–17.8)	10.5 (1–20)
Age group (years)			
<6	1	0.6	8
6–9	10	8.8 (6.5–9.5)	9.0 (1–20)
10–14	8	12.8 (10.3–14.2)	13.0 (2–19)
15–18	4	17.3 (16.4–18.0)	7.5 (3–16)
Diagnosis			
Glanzmann thrombasthenia	4	7.6 (0.6–10.3)	8, 10, 13, 14
Dense granule deficiency	7	12.7 (7.1–14.1)	7.0 (2–15)
Hermansky–Pudlak syndrome	2	11.8, 16.8	4, 6
MYH9-related macrothrombocytopenia	3	9.2 (7.3–18)	1, 3, 12
Noonan syndrome	2	9.5, 14.2	17, 8
Ehlers–Danlos syndrome	2	8.9, 9.2	7, 20
Undefined platelet function disorder	3	16.4 (12.2–17.8)	9, 16, 19
Total	23	10.3 (0.6–18.0)	8.0 (1–20)

*For categories in which there are four or fewer patients, all values of bleeding score are shown.

Biss, Toronto Canada JTH 2010

- pediatric-specific symptoms (35%)
- early manifestations
- usefulness for stratification of bleeding severity
- prediction surgical risk assessment ?

ISTH BAT/ IFPD in Children

Pediatric	ISTH-BAT median (IQR)		
	All	Female	Males
IPFD	8 (6.5-14)	8 (8-13)	8 (4-11)
IT	1 (0-3)	1.5 (0-4.2)	1 (0-2.5)
VWD-1	3 (1-6)	6 (0-12.5)	3 (1-5)
HC	0 (0-1)	0 (0-1)	0 (0-0)

Validation of the ISTH/SSC bleeding assessment tool for inherited platelet disorders Gresele, JTH, 2019

Bleeding phenotype in children with Glanzmann thrombasthenia

ISTH- BAT score according to bleeding symptoms in cases and controls.

	Cases Median (Interquartile Range)	Control Median (Interquartile Range)	p-value
Epistaxis	3 (2-4)	2 (1-2)	0.001*Significant
Cutaneous/Wounds	2 (1-2)	1 (0-1)	0.004* Significant
Oral/Gums	2 (1-2)	2 (0-2)	1.00
GIT	1 (1-4)	0	
Tooth	4 (1-4)	0	
Surgery	4 (2-4)	0	
Menorrhagia	1 (1-1)	1	0.536
Hematoma	2 (1-2)	0	
Hemarthrosis	1 (0)	0	
CNS bleed	2 (0-1)	0	
Others (circumcision/ cephalohematoma/ umbilical stump)	4 (1-4)	0	

Utility of the ISTH bleeding assessment tool (BAT) in diagnosis of Glanzmann Thrombasthenia patients Nazish Saqlain 2022

Heavy Menstrual Bleeding in Adolescents

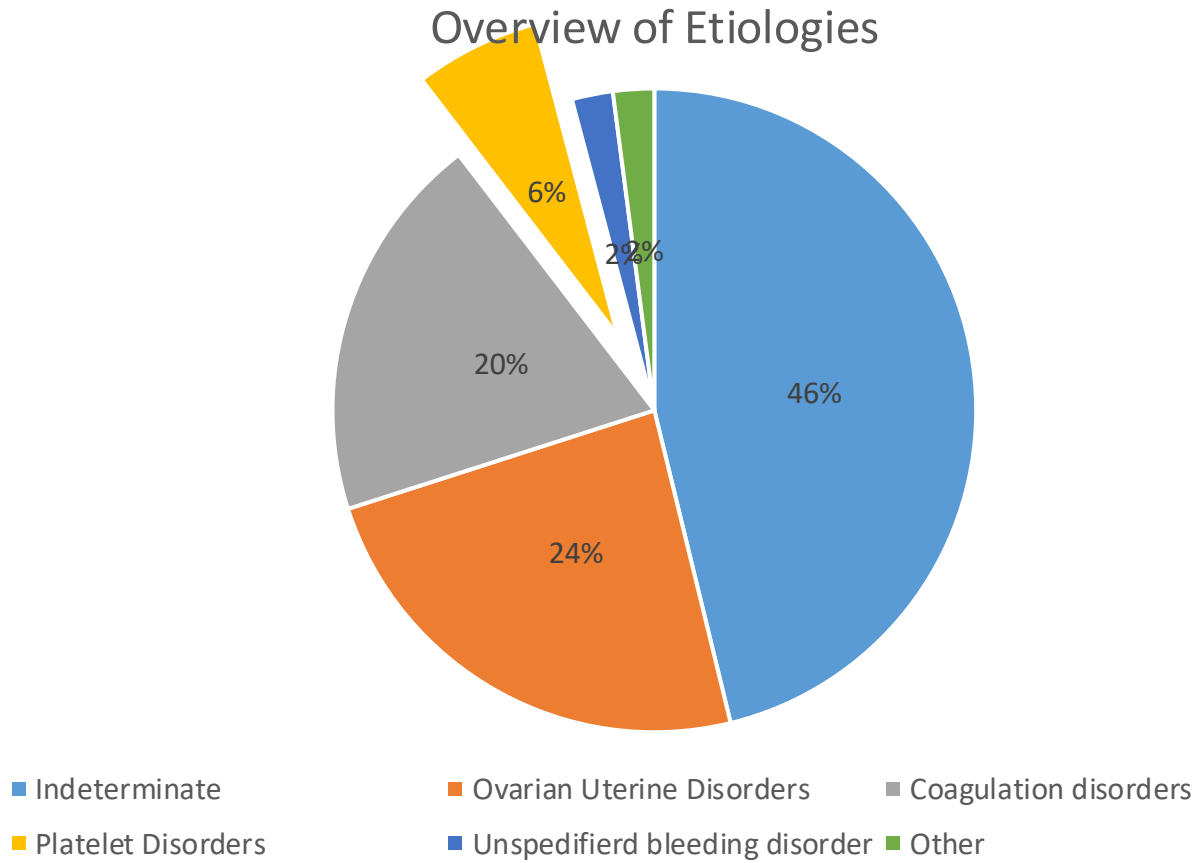
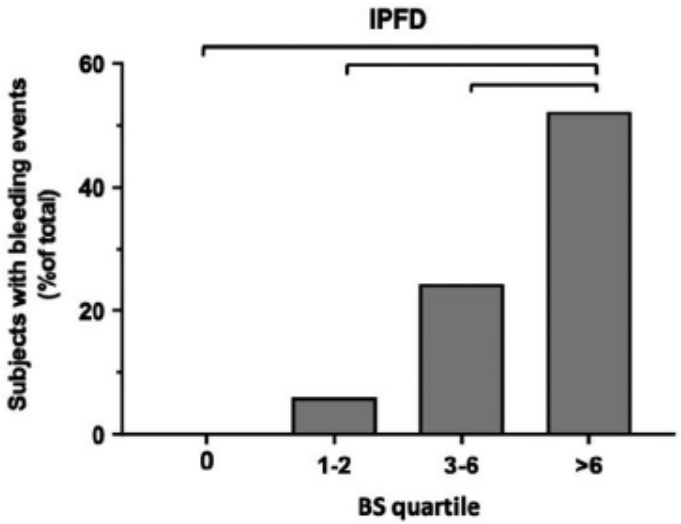


Table 6 Etiologies of platelet abnormalities

Platelet Abnormalities	n	MLE	LCredL	UCredL
Platelet Function Disorder	53	37.9	30	46
Inherited Thrombocytopenia	24	17.1	11.4	23.8
Platelet Qualitative Disorder	19	13.6	8.43	19.7
ITP	12	8.57	4.54	13.7
Platelet Quantitative Disorder	7	5	2.05	9.16
Dysfunctional Platelet Aggregation	6	4.29	1.6	8.19
Multiple Platelet Secretion Defects	4	2.86	0.79	6.18
Unspecified Thrombocytopenia	4	2.86	0.79	6.18
Other Immune Thrombocytopenia	2	1.43	0.175	3.94
Multiple Platelet Aggregation Defects	1	0.714	0.0182	2.62
Platelet Secretion Defects	1	0.714	0.0182	2.62
Aggregation Secretion Defects	7	5	2.05	9.16

Systematic review and meta-analysis of the etiology of heavy menstrual bleeding in 2,770 adolescent females *Erin M Hall 2024*

Bleeding score/IFPD : Follow up



N=174 (39 child) - Follow up 2 y

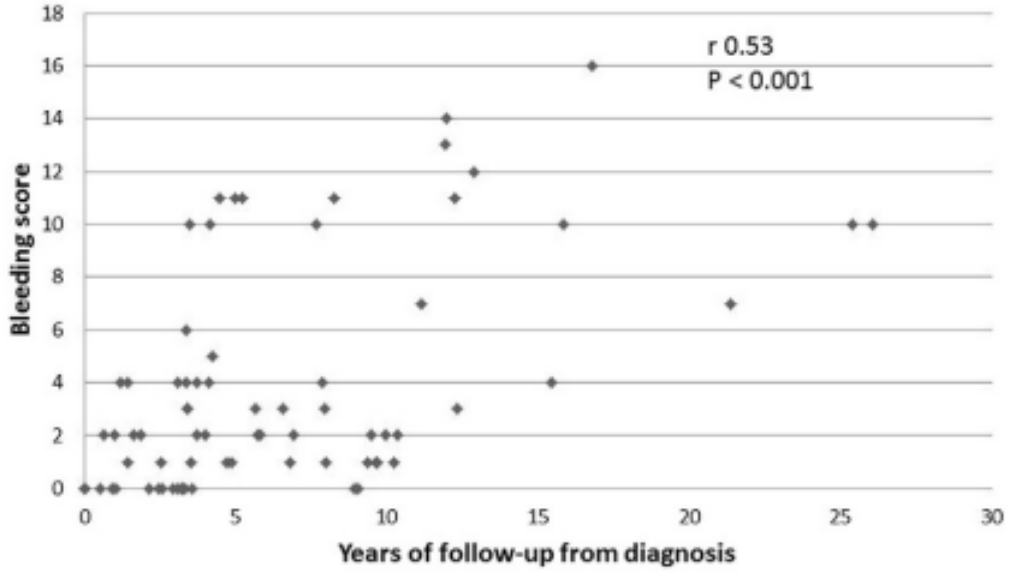


Fig. 2. Correlation between the PBQ bleeding score and years of follow-up assessed by Spearman's nonparametric correlation.

Quantitation of bleeding symptoms in a national registry of patients with inherited platelet disorders Gili Kenet 2016

Gresele, BAT-VAL Study Investigators**, JTH, 2021**,

High bleeding score at diagnosis may predict future bleeding risk

PBQ - ISTH BAT in Children

OK to assess bleeding severity in children with patients with platelet disorders

Healthy children = cutaneous bruising and epistaxis

Few hemostatic challenges : as surgery, dental extractions, menses and childbirth

Platelet disorders in children: A diagnostic approach 2011 Sara J . Israels

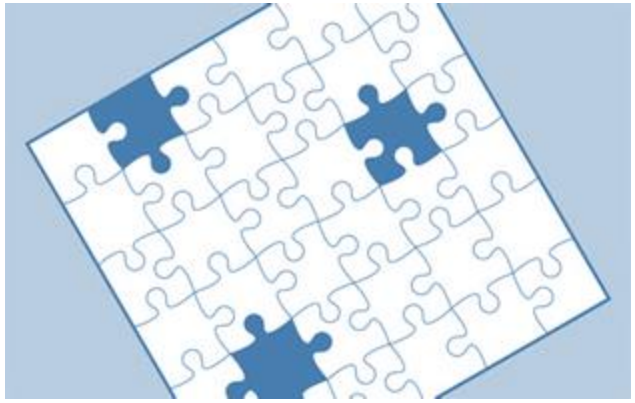
Bleeding Score is necessary but not always sufficient

Event characteristics

- Early onset ?
- Spontaneous or trauma related bleeding ?

Family History

- Other affected family members ?
- Consanguinity ?



Glanzmann Thrombasthenia - pediatric

	France 2025	Egypt 2025	Southern India 2019	Pakistan 2016
Children	N=37	N=87	N= 48	N=163 (0-35y)
Median Age of Diagnosis	0,48 y	3 y	2,75 y	7 y 52,7% = First bleeding <1y
Consanguinity	61% (all cohort, adult + children)	55,2%	67%	65%

Laila M Sherief, 2025

Irem Iqbal,2016

Smitha Kongalappa 2019

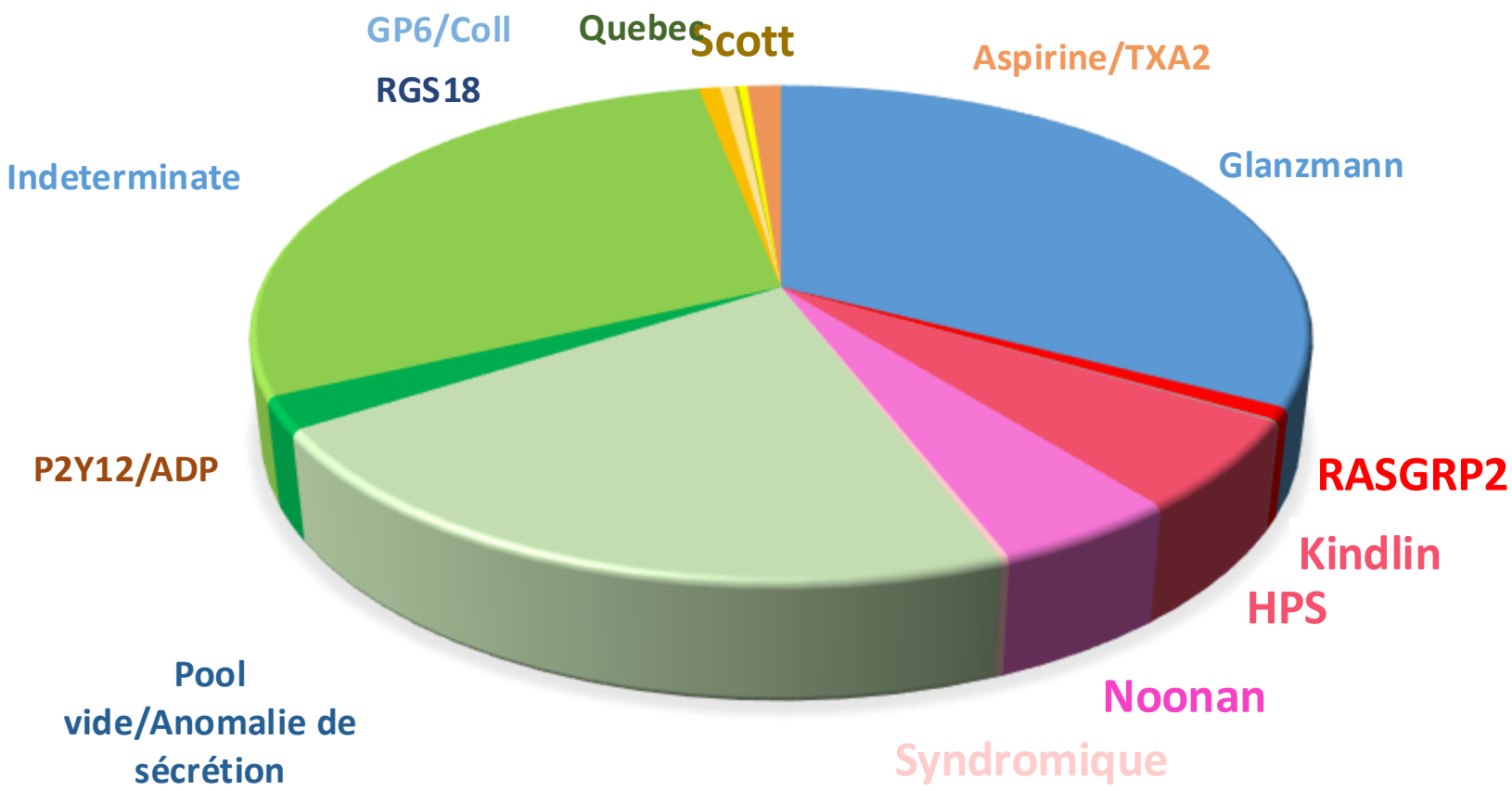
Extra haematological manifestations / IFPD

- Albinism – Nystagmus (Hermansky Pudlak)
- Congenital heart disease (Noonan syndrome)

- Immunodeficiency (Kindlin 3)

- Facial dysmorphy, psychomotor delay (Syndromic disorder with complex karyotype = Thrombopenia +/- IFPD)

Extra haematological syndrome and IFPD



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IFPD + extra hematological symptom

≈ 10%

Which biological investigations should be performed in children?

- Limitation :
  - difficult venous access
  - blood volume / repeat blood sampling
  - local test availability / constraints in specimen transport
  - Pediatric reference range

- Aim :
  - Diagnose quickly severe IFPD (Glanzmann and Glanzmann like)
  - Diagnose step by step mild IFPD

Which Biological Tests to Perform in Pediatric ?

	Severe IFPD	Mild IFPD
PT, aPTT, fibrinogen, von Willebrand factor	First-line	First-line
Complete blood count, including Platelet count Platelet morphology : platelet volum + Platelet granular appearance	First-line	First-line
Platelet Aggregometry (Light transmission aggregometry (LTA))	+/-	+
Flow cytometry analysis (baseline +/- platelet activation)	+	+
Evaluation of platelet granules		+
Genetic analyses (Next-generation sequencing (NGS)	+	+ If Abnormal biology

Part 2 : Pediatric-specific aspects : Treatment

Preventive treatment

- **Dental hygiene**
  - Gingival bleeding, dental caries, periodontal disease = impair quality of life
  - Oral health education improve oral hygiene status
  - First tooth loss

K Salem 2013 Hemophilia

Nayera H K El Sherif 2024 Expert Rev Hematol

- **Vaccination**
  - According national guidelines
  - preferentially subcutaneously for severe IFPD

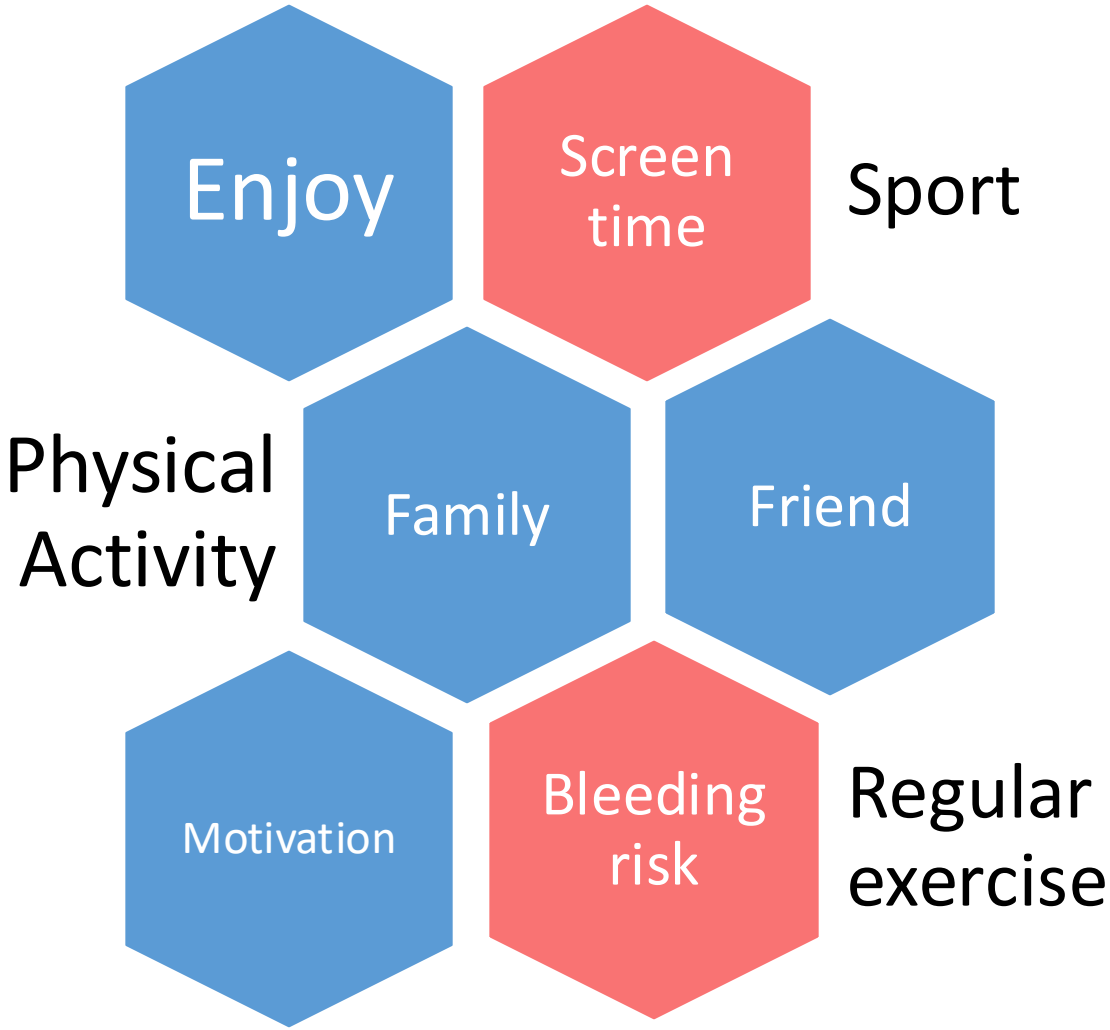
Preventive treatment

- **Physical Activity**
  - ✓physical fitness
  - ✓cardiometabolic health
  - ✓bone health
  - ✓cognitive outcomes
  - ✓mental health
  - ✓reduced body fat

- **sedentary behaviour and inactivity**
  - ✓Obesity
  - ✓Cardiometabolic complications
  - ✓Cardiovascular disease
  - ✓Diabetes
  - ✓reduced sleep duration
  - ✓adverse mental health

World Health Organization

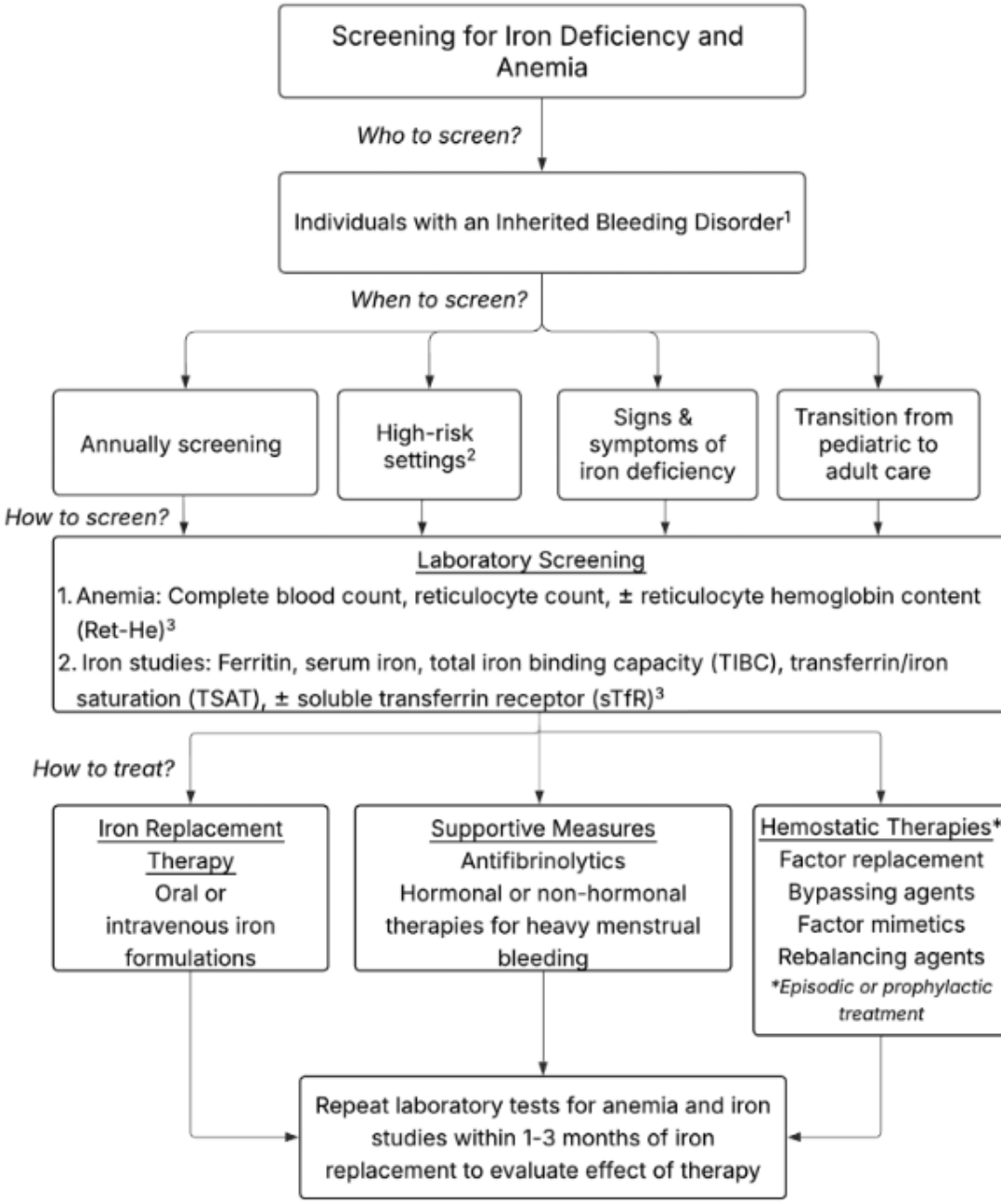
Promote Physical Activity



Iron Deficiency +/- Anemia

- 79% of Children with Glanzmann Thrombasthenia and Bernard Soulier Syndrome
- Heavy Menstrual Bleeding : 80% of women and girls with inherited bleeding disorders

- Optimized dietary intake of iron
- 3 mg/kg elemental iron once daily in children
- 65 mg elemental iron with ferrous sulfate once daily in adolescents
- IV Iron supplementation



Lee A, Haemophilia 2022
Glaivy Batsuli Haemophilia 2026

Bleeding management

- Tranexamic Acid :
  > 1 year
  20–25 mg/kg/day fractionated into 2–4 doses

- Desmopressin (Granule Defect)
  > 2 years
  risk of hyponatremia
  difficulties in fluid restriction in young children (20 ml/kg/d)

Bleeding management

- Transfusion of Platelet Concentrates :
  Antibody antiHLA
  Antibody antiHPA

- rFVIIa

GTR Pediatric Treatment and Outcomes D'oiron 2019

Saultier, Haemophilia 2024

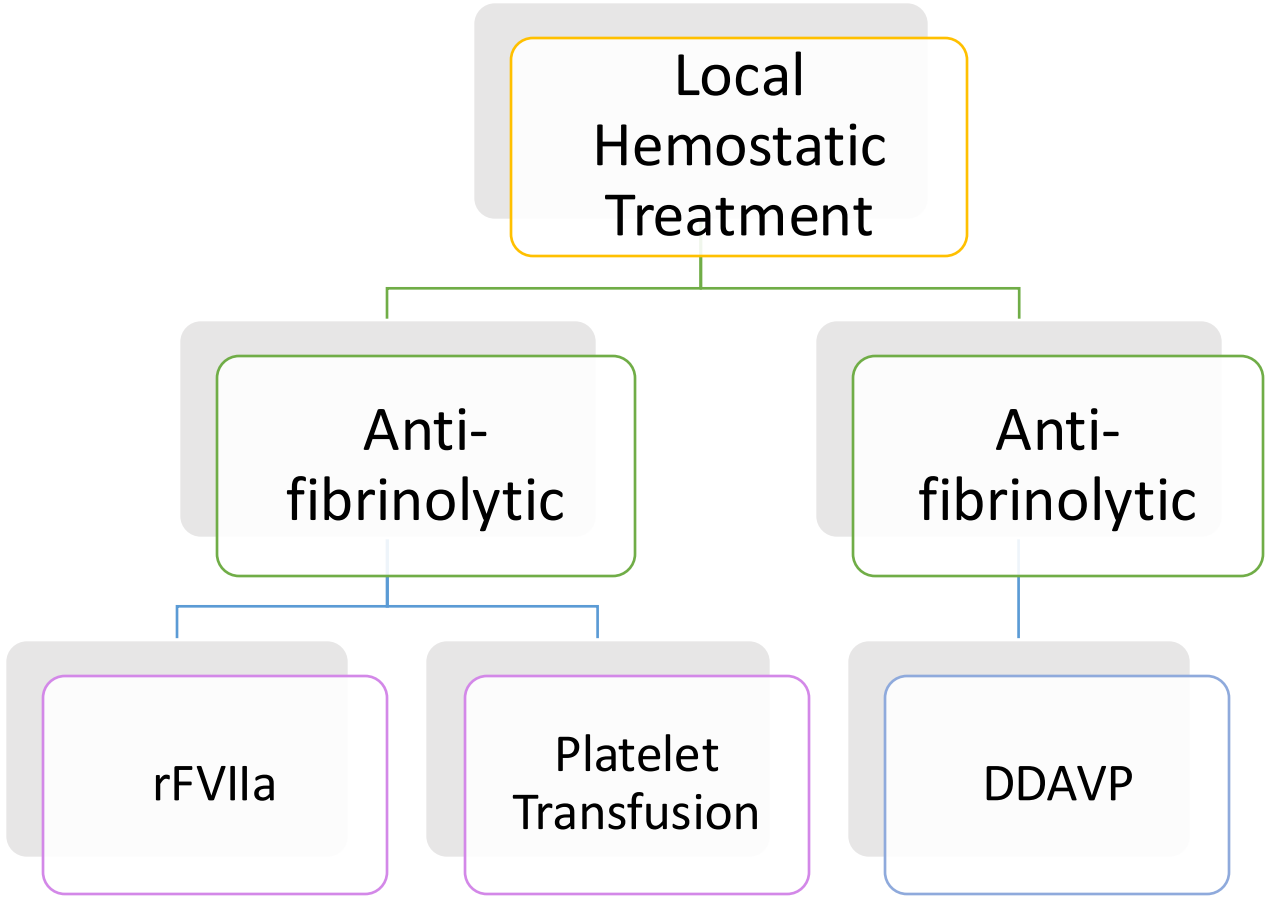
- Allogeneic Hematopoietic Stem Cell Transplantation
  Severe Glanzmann
  Immunodeficency

Ramzi M 2016

Surgery management

Severe IFPD

Mild IFPD



High Risk Bleeding Surgery

Mild Risk Bleeding Surgery

Patient and family therapeutic education

- Understanding the disease, treatment and complications
- Knowing the care pathway/Carry an identification card
- Recognising bleeding risk situations
- Appreciating the value of follow-up
- Actively participating in treatment decisions
- Intregate disease into child’s everyday and family life
- Recognize its impact on siblings….

Part 3 : Transition from childhood to adult care

Transition

- Adolescence
  - vulnerable period
  - increased risk of treatment non-adherence
  - loss to follow-up
- Transition from paediatric to adult care to ensure
  - long-term safety
  - continuity of care
  - patient autonomy
- Transition should be
  - structured
  - gradual
  - individualized


Self-care / self-management
•Understanding the disease and treatment
•Self-management skills
•Healthy lifestyle behaviors
Managing daily life constraints
Living with a chronic disease
Integration into daily life
Stress management
Taking control of adult life
Decision-making
Life planning
Education and career planning
Self-confidence
Development of self-esteem
Coping with others' perceptions

Transition

When?

- Ideally initiated between 12 and 14 years of age
- Adapted to the adolescent's maturity and readiness

Who?

- Adolescent and family, followed progressively by independent consultations
- Particular attention to heavy menstrual bleeding in adolescent girls

Where?

- dedicated space

With whom?

- Multidisciplinary team (pediatric hematology, adult hematology, specialized nurses, psychology)
- Therapeutic education program

Summary

- Severe *IFPDs* = pediatric diagnoses
- Diagnosis IFPDs :
  - careful clinical assessment,
  - age-adapted interpretation of bleeding symptoms
- Laboratory tests :
  - child’s age
  - stepwise laboratory investigations
- Preventive care :
  - oral health,
  - physical activity,
  - iron deficiency ,
  - therapeutic education
- Transition to adult care should be early, structured, gradual, and individualized

THANK YOU

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