

Why Do Girls and Women have Abnormal Uterine Bleeding(AUB) ?

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AUB - A PUBLIC HEALTH CHALLENGE

WHO estimates that over 18 million Girls and Women are affected by abnormal uterine bleeding

10 – 62% of girls and women – underlying
Inherited Bleeding Disorder (IBD)

AUB affects 30% of women and at least 5% -10% of women of reproductive age will seek medical attention

8 -18% of women with IBDs – surgery for AUB

- Within a year of seeking medical attention, such a patient has up to a 50% probability of undergoing a surgical intervention
- **30% will have a hysterectomy < 60 yrs**
- 50% no definite pathology

OBJECTIVES

Define Normal and Heavy Menstrual Bleeding and Concerns (HMB) for Girls and Women

Discuss the " Clotting Cascade "

Common Inherited Bleeding Disorders causing Heavy Menstrual Bleeding

Review work up for HMB

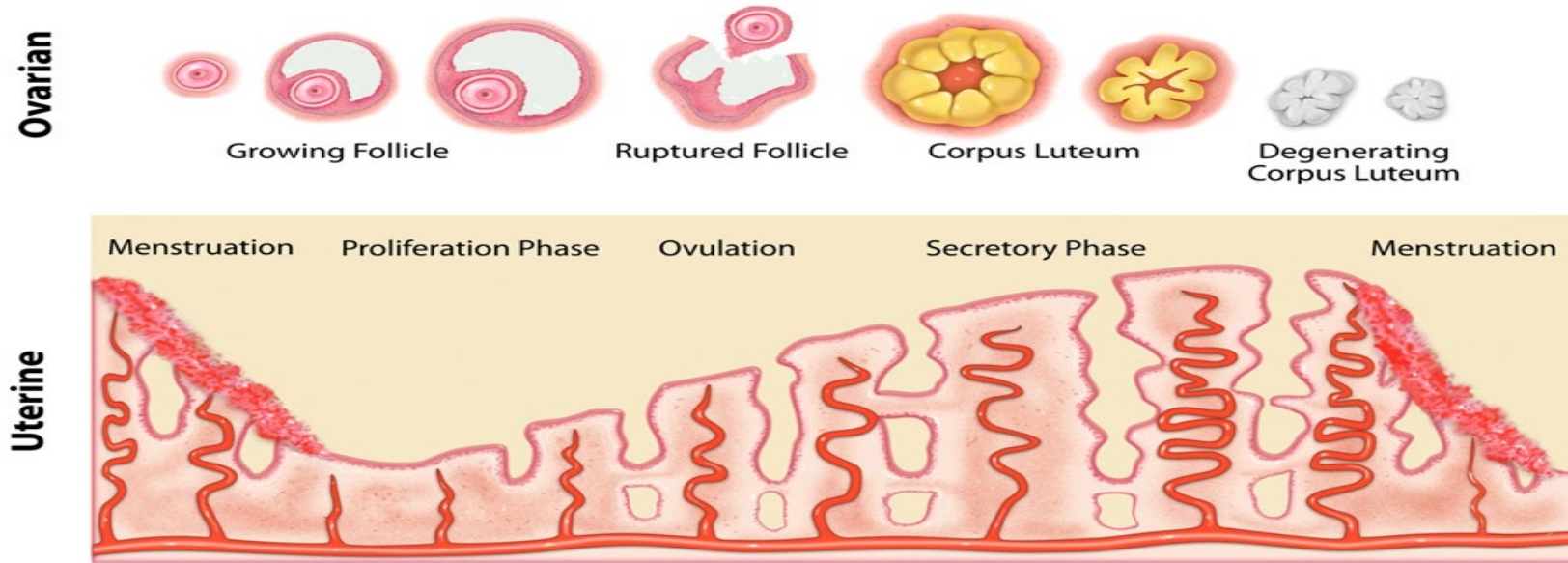
AND

Medical Management of HMB

Review Gaps in Current Guidelines

Where Do we Go From Here ?

Normal Menstrual Cycles in Adolescent Girls

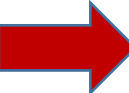
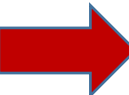
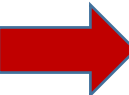
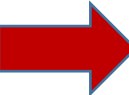


ACOG Definition of Heavy Menstrual Bleeding

Any of the following can be a sign of heavy menstrual bleeding:

- Bleeding that lasts more than 7 days.
- Bleeding that soaks through one or more tampons or pads every hour for several hours in a row.
- Needing to wear more than one pad at a time to control menstrual flow.
- Needing to change pads or tampons during the night.
- Menstrual flow with blood clots that are as big as a quarter or larger.

Normal limits for Menstrual Parameters

Menstrual characteristics	Description	Normal limits (5th-95th percentile)
 Frequency (days)	Frequent	< 24
	Normal	24-38
	infrequent	> 38
Variability(days)	absent	-
	regular	+/- 2 -20
  Duration of Flow (days)	irregular	> 20
	prolonged	> 7
	Normal	4.5-7
	shortened	< 4.5
 Monthly blood loss (mL)	heavy	> 80
	normal	5-80
	light	< 5

Issues Concerning Abnormal Uterine Bleeding

Provider

- Systematic evaluation not performed
- Lack of consensus re: testing
- Defining normal vs abnormal
- Lack of optimal Diagnostic approach



Patient/Family

- Bleeding Disorder / other Gyn diagnoses delayed
- Consequences of inaccurate/inadequate diagnosis
- Access to therapy and coverage
- Stigma, Fear, Isolation, absenteeism from school and work
- Quality of Life issues



Abnormal Uterine Bleeding

Hematologic ?
or
Hormonal ?

Heavy Menstrual Bleeding - Hematologic and Hormonal ?

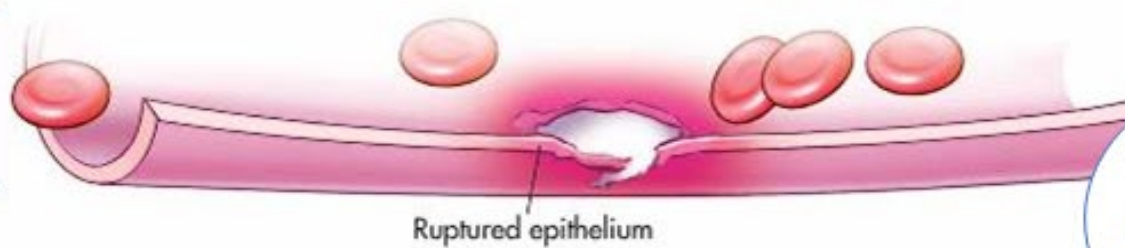
[My Movie 1-720p30.mov](#)

With permission from Drs Usha Reddy and Roshni Kulkarni

Hemostasis = Healing



Vessel injury



Ruptured epithelium

Collagen provides the anchor

Vessel spasm



Spasm

VWF is the tether

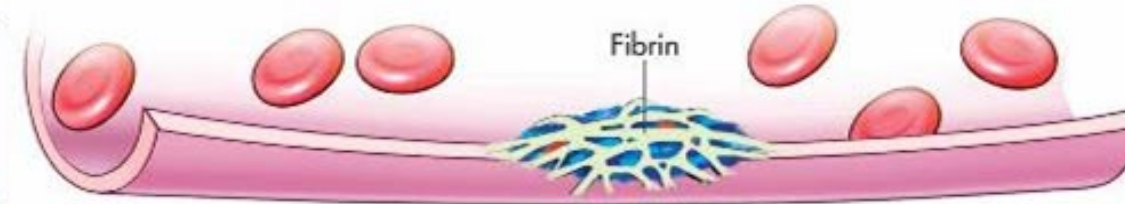
Platelets adhere to injury site and aggregate to form plug



Platelets

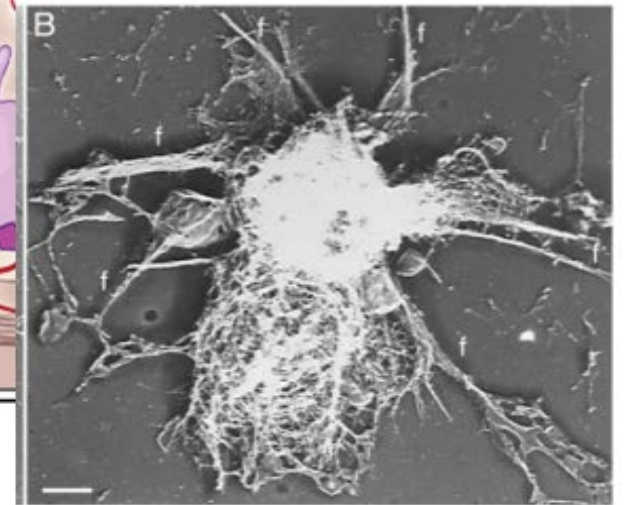
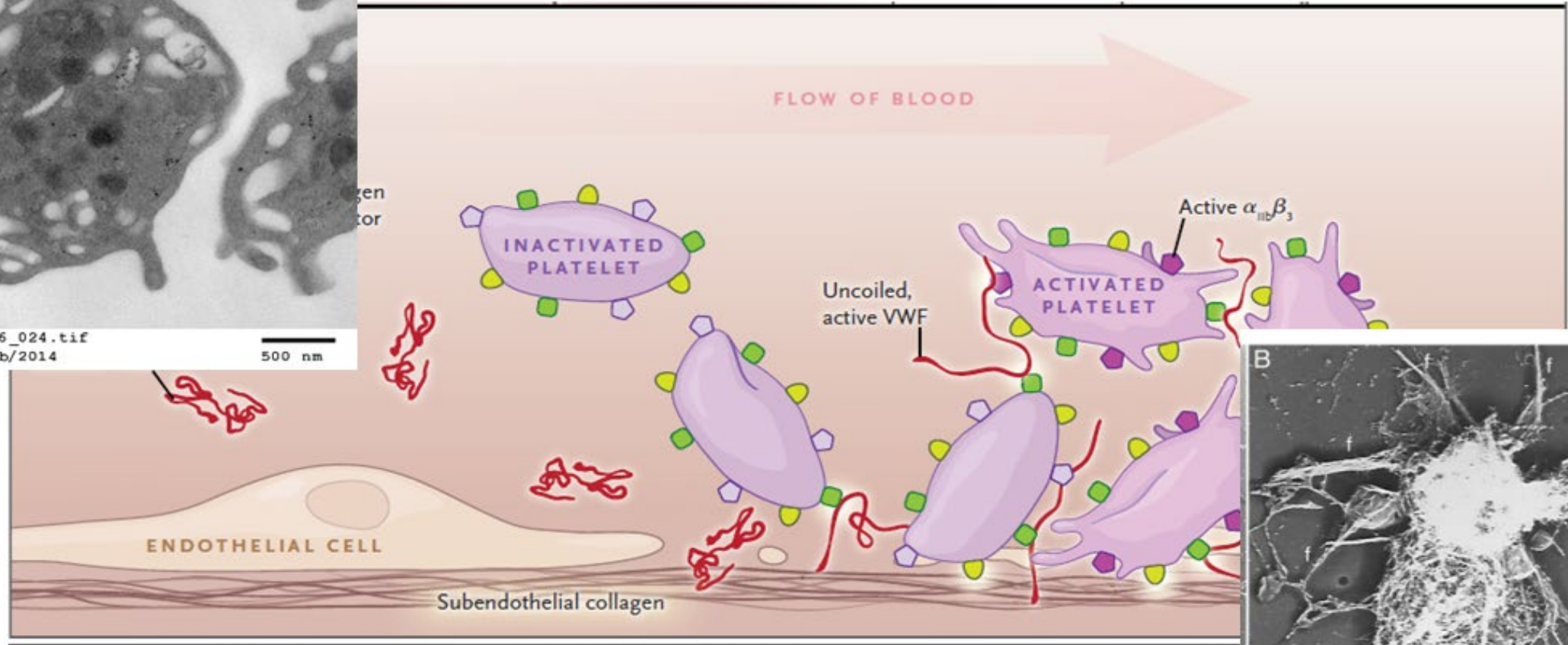
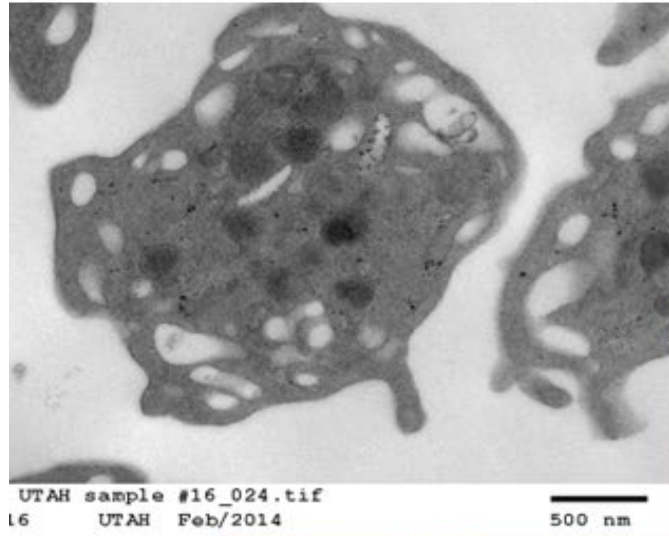
Platelets are the surface

Formation of insoluble fibrin strands and coagulation



Fibrin

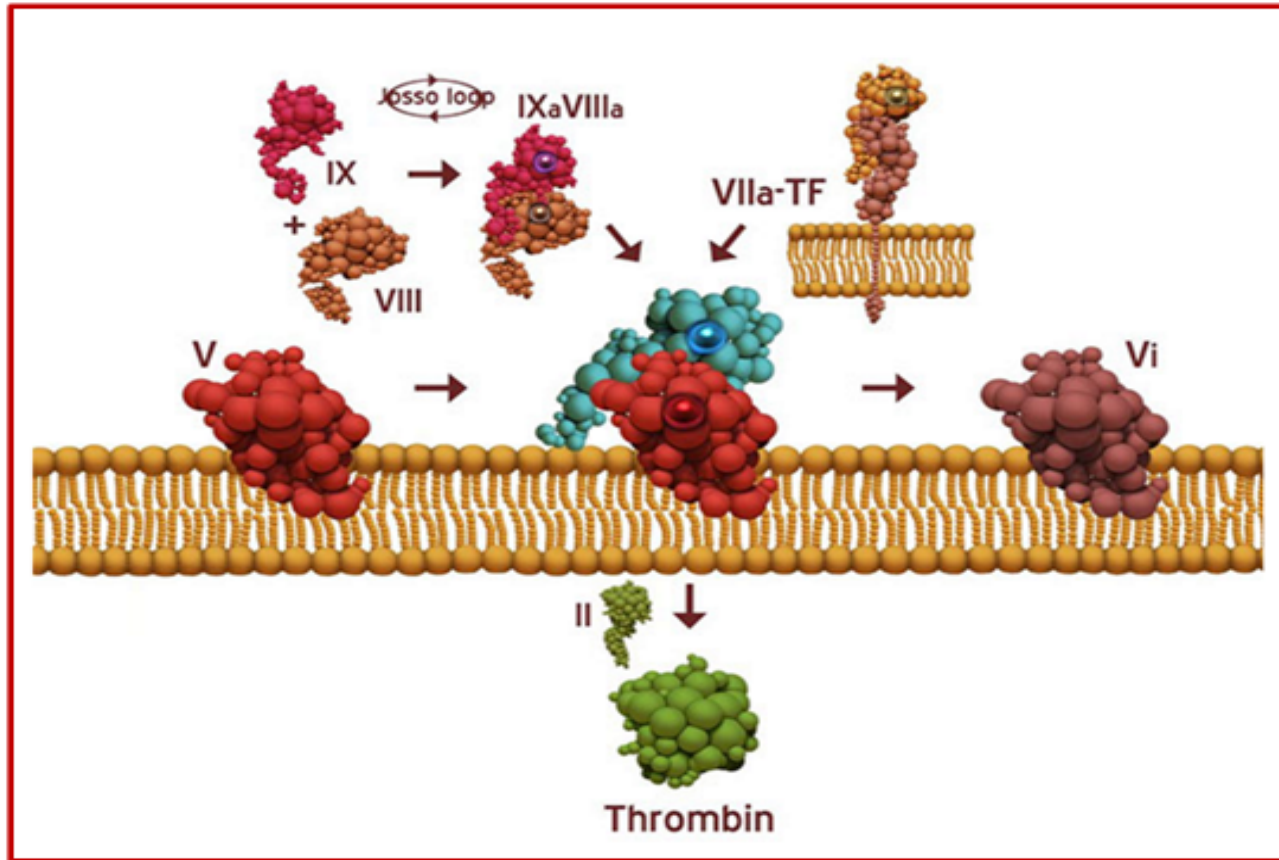
The Platelet Plug



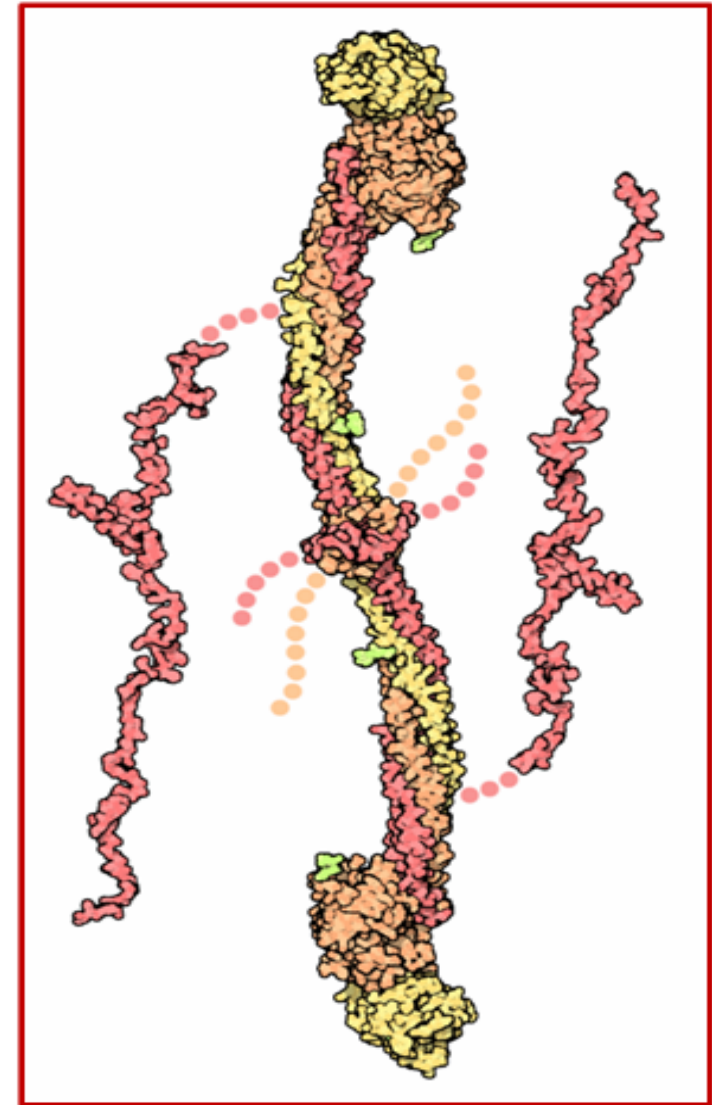
NEJM 2016;375:2067-80

Am J Physiol Cell Physiol 285: C797–C805, 2003.

The Fibrin Net



Multiple sites of feedback loops on the surface of the growing thrombus



Inherited Bleeding Disorders as a Cause of HMB

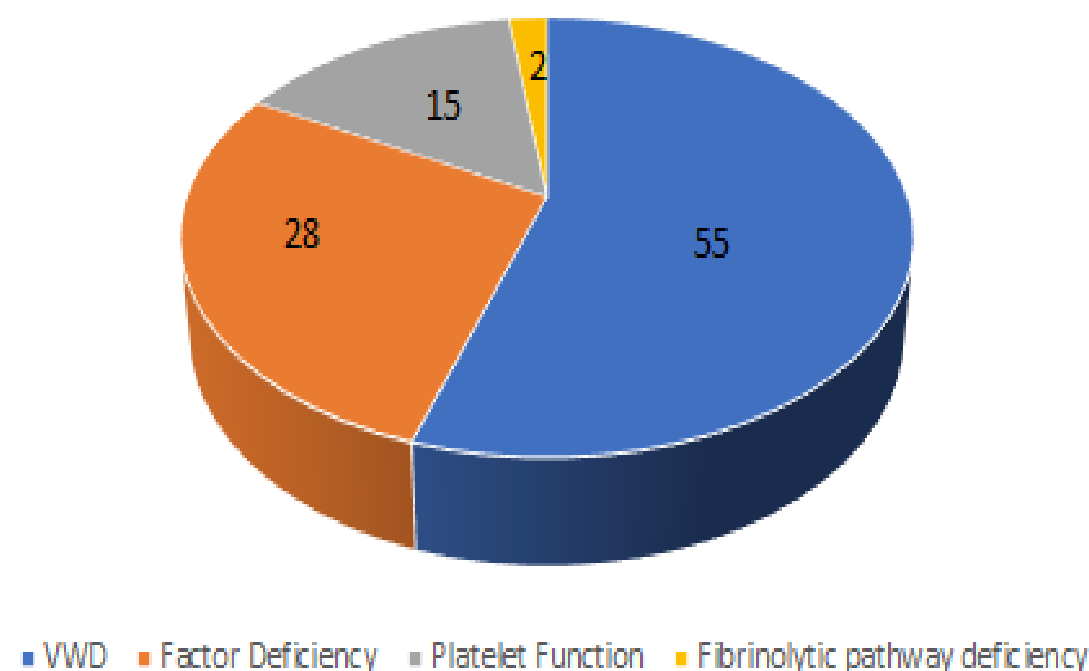
- von Willebrand disease (VWD)
- Quantitative and Qualitative Platelet Disorders
- Female hemophilia aka Hemophilia carriers
- Rare bleeding disorders (RBDs)
 - Fibrinogen (factor I), FII, V, VII, X, XI, XIII
 - Combined factor deficiencies
- Other disorders
 - Hereditary Hemorrhagic Telangiectasia
 - Ehlers Danlos Syndrome



Prevalence of Inherited Bleeding Disorders in Women and Teens with HMB

Von Willebrand disease	5-36%
Platelet dysfunction	2-44%
Low Factor VIII (hemophilia A carriers)	8%
Low platelets	13-20%

Frequency Distribution of Inherited Bleeding Disorders



1 Philipp CS, et al. 2005

3. Jayasinghe Y, et al. 2005 7. Mikhail S, et al. 2007

3.. Dilley A, et al. 2001 11. Philipp CS, et al. 2003

Inherited Bleeding disorders present with

Gynecological Bleeding

Heavy Menstrual Bleeding – menorrhagia
menometrorrhagia, pain during mid cycle

Use of OCPs to control HMB

Post partum Bleeding

Recurrent hemoperitoneum, bleeding
into ovarian cysts

Endometriosis

Miscarriages

Chronic iron deficiency anemia

Other Bleeding symptoms

Profuse bleeding from cuts/ wounds

Bleeding post dental extractions/
tonsillectomy

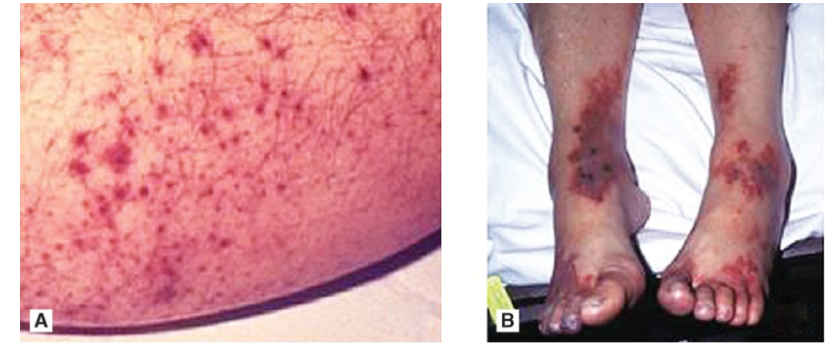
Musculoskeletal bleeding
asymptomatic joint bleeds

Intracranial bleeding with trauma

Known family h/o a bleeding disorder

Clinical Characteristics

- **Massive bruises** that migrate; Unexplained or extensive bruising, associated with soft tissue hematoma
- **Nose bleeds**, particularly lasting more than 30 minutes or causing anemia or admission to hospital;
- **Heavy menses**, since menarche; bleeding post child birth
- **Gum bleeding**;
- Blood in the urine and stool
- Bleeding following trauma/surgery(e.g., dental extraction, tonsillectomy, adenoidectomy).



Source: Bunn HF, Aster JC: Pathophysiology of Blood Disorders: www.accessmedicine.com
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Glanzmann Thrombasthenia and Bernard-Soulier Syndrome









Clinical Manifestations

GT: Excessive bleeding (often manifested as dental bleeding, epistaxis or menorrhagia).

Dental bleeding Epistaxis Menorrhagia

Causes of Heavy Menstrual Bleeding by Age

Courtesy AH James and FWGBD

Cause	Age 13-19	Age 20-34	Age 35-49	Age 50+
Adolescent anovulation				
Inherited Bleeding Disorder				
Local pathology				
New systemic disease				
Anticoagulant therapy				
Post-op complication				
Hypothyroidism				
Peri-menopausal anovulation				

Diagnostic Challenges

Diagnosis – difficult

More severe defects are easily diagnosed

Milder forms – do not come to attention

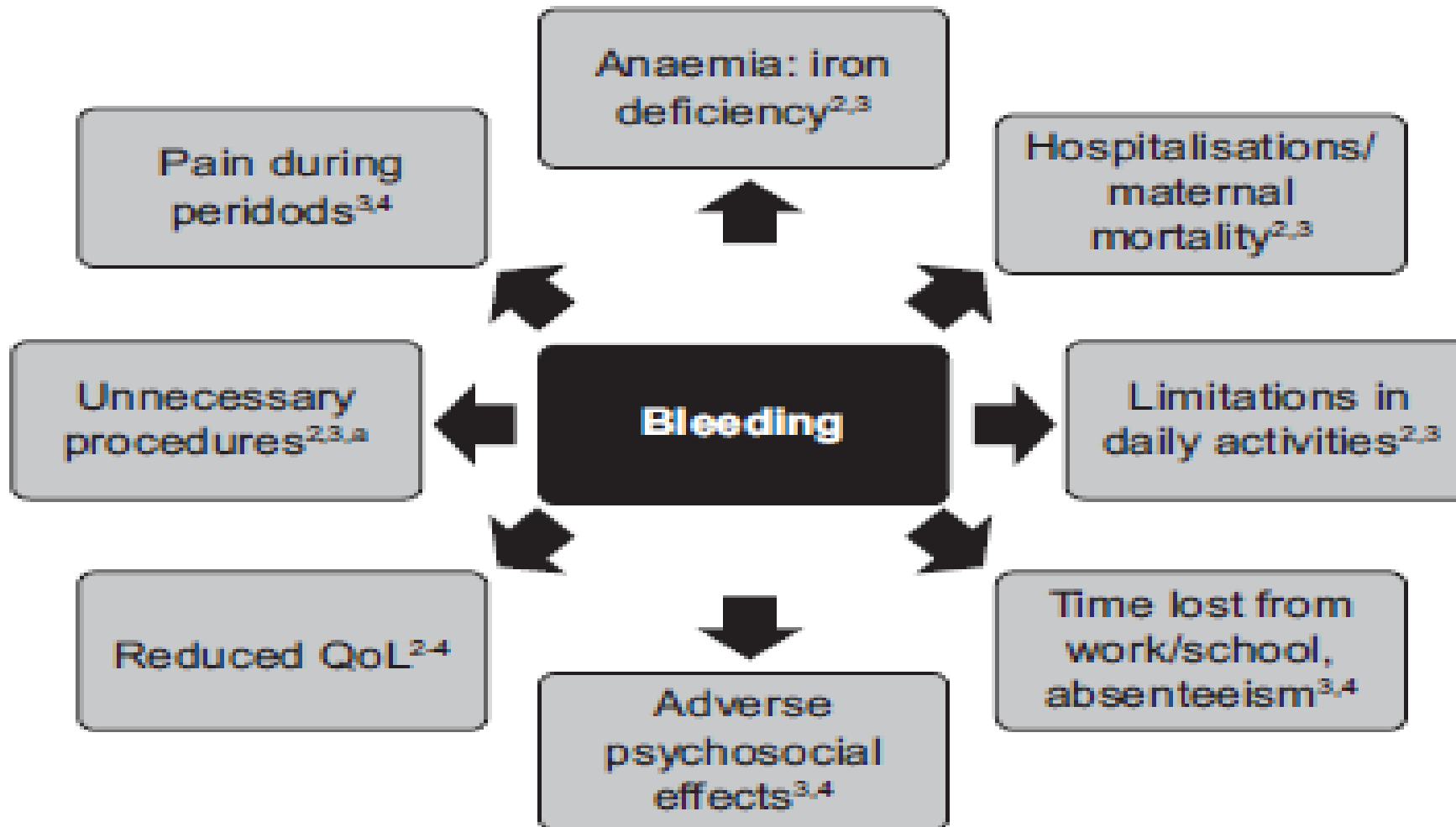
Milder forms – heterogeneous presentation — lack of precise laboratory testing

Determining if bleeding is abnormal – difficult to evaluate

Need to control for pre –analytical variables and time of testing

Molecular testing unavailable in most labs

Consequences of HMB



IRON DEFICIENCY ANEMIA

- Well known and under appreciated consequence of HMB
- Great concern in adolescents – increased dietary requirements , rapid growth, food fads, body image issues
- Iron deficiency (without anemia) occurs in 9- 16% of girls age 16- 19 yrs
- In a girl and woman with HMB and iron deficiency anemia- r/o an inherited bleeding disorder
- Iron studies: serum, iron, Total iron binding capacity, ferritin
- Treatment Options: oral iron, IV iron sucrose; Iron fortified diet

Diagnostic Workup

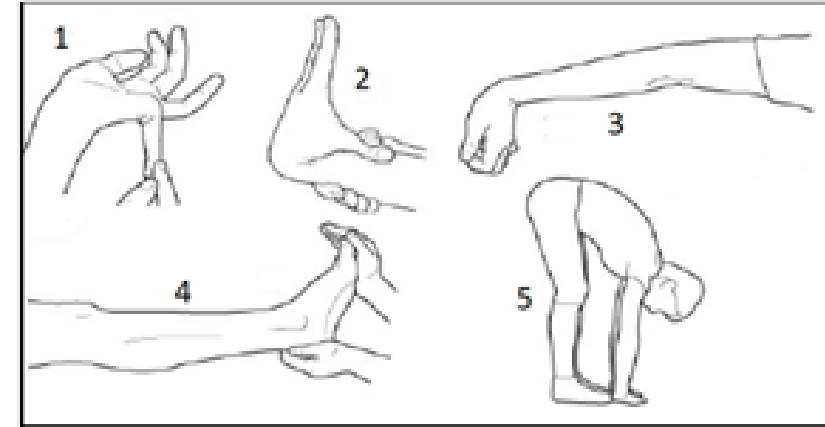
CBC , review of peripheral smear, assessment for hyperextensibility

PT/ aPTT, mixing studies, fibrinogen, thrombin time, reptilase time, factor activity and antigen levels

Von Willebrand panel, Blood Type

Platelet Function Tests; Electron microscopy

Molecular characterization



Score of 6/9 diagnostic of hyperextensibility¹

ISTH- BLEEDING ASSESSMENT TOOL (ISTH-BAT)

Insensitive to children, underestimation of bleeding ; insensitive to acq'd. bleeding disorders

Epistaxis
Cutaneous Bruising
Bleeding from minor wounds
Oral Cavity Bleeding
GI Bleeding
Haematuria
Dental Extractions
Surgery
Menorrhagia
Post-partum Haemorrhage
Muscle Haematomas
Haemarthrosis
CNS Bleeding
Other Bleeding Problems

MENORRHAGIA	POINTS
No	0
CONSULTATION ONLY	1
ANTIFIBRINOLYTICS OR OCP USE	2
CURETTAGE OR IRON THERAPY	3
BLOOD TRANSFUSION/ REPLACEMENT THERAPY or DDAVP / HYSTERECTOMY	4

Validated for
VWD, IPDs




ISTH- BAT : 100% sensitivity,
78% specificity for
BSS , GT




Male 0-3; > 4 abnormal; Female: 0-5; > 6- abnormal
Child < 2 – bleeding disorder less likely
Max score: 56 points

Bleeding Assessment

Pictorial Blood Loss Assessment Chart (PBAC) Menstrual chart and scoring system

Date of start Score
 day month year

Towel	1	2	3	4	5	6	7	8
								
								
								
Clots/flooding Clots: size								

Tampon	1	2	3	4	5	6	7	8
								
								
								
Clots/flooding Clots: size								

Scoring System

Towels

- 1 point for each lightly stained towel
- 5 points for each moderately soiled towel
- 20 points if the towel is completely saturated with blood

Tampons

- 1 point for each lightly stained tampon
- 5 points for each moderately soiled tampon
- 10 points if the tampon is completely saturated with blood

Clots

- 1 point for small clots
- 5 points for large clots

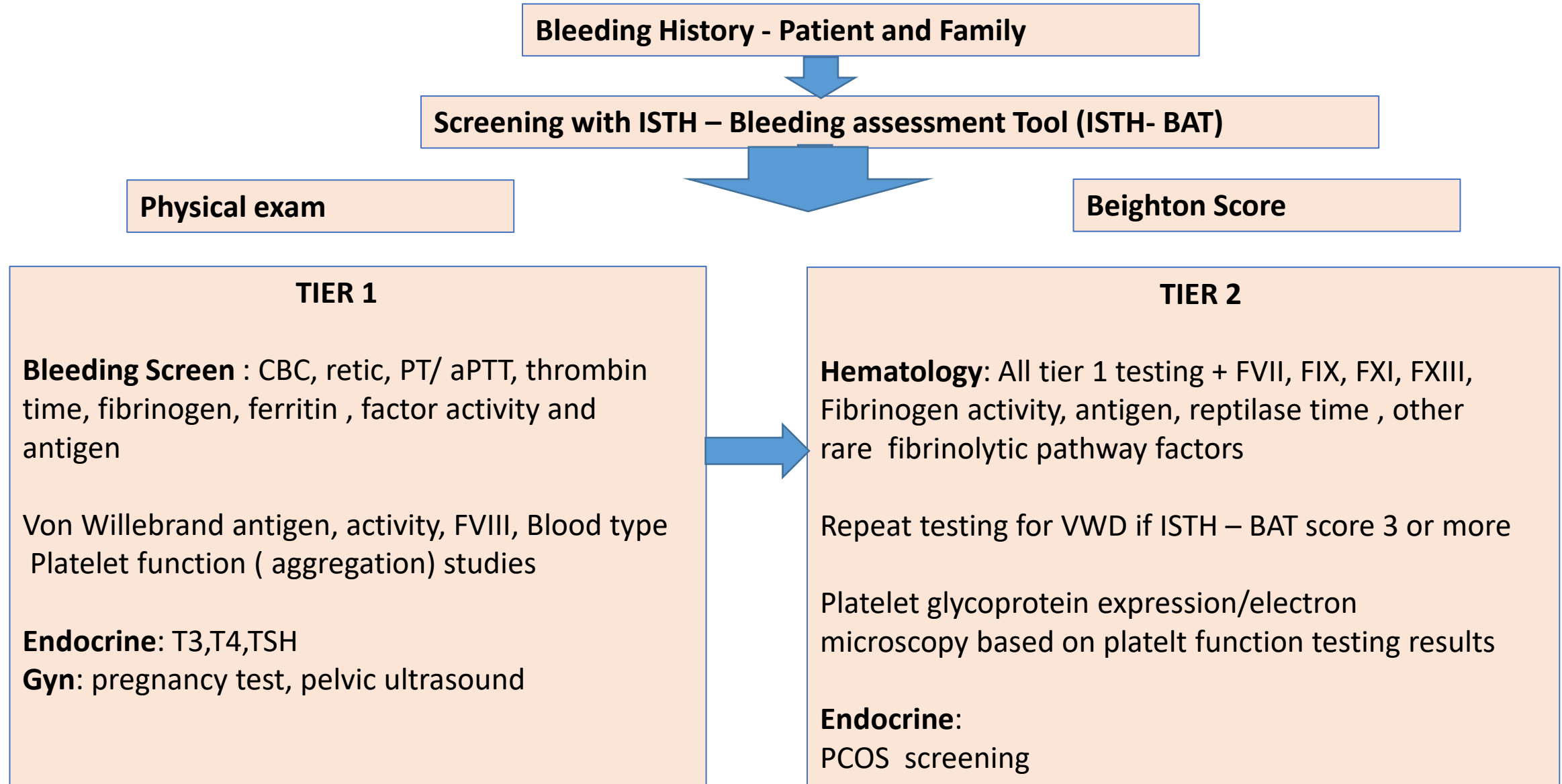
Source: U.K. Haemophilia Society, A Guide For Women Living with von Willebrand's

APP FOR WOMEN WITH BLEEDING DISORDERS TO TRACK MENSES

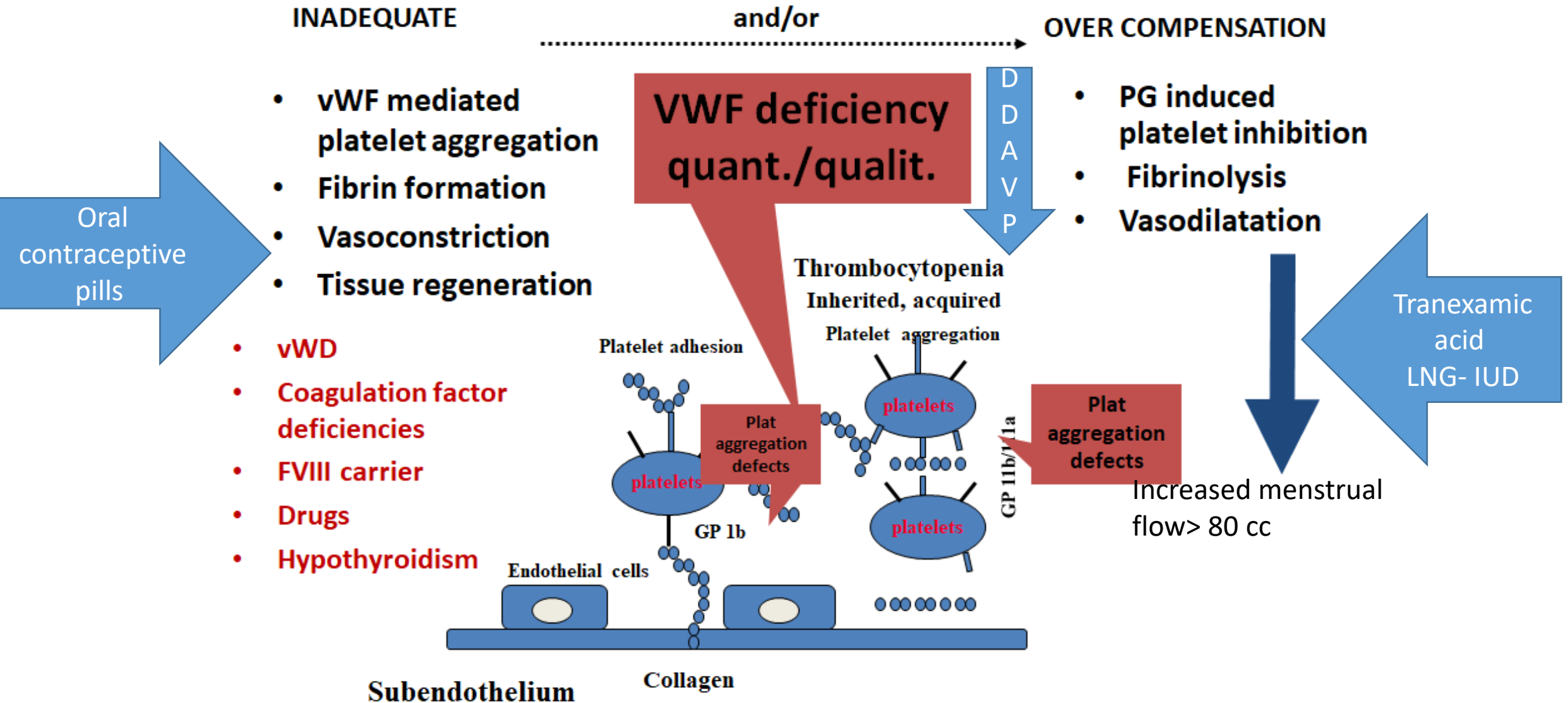
- Track Monthly Menstrual Cycle
- Log Symptoms
- Record Type of Treatment Used
- Period Reminder Alert
- Log Notes for Healthcare Provider
- Easily Share Information with your Provider
- Designed specifically for women with bleeding disorders



HIGH INDEX OF SUSPICION



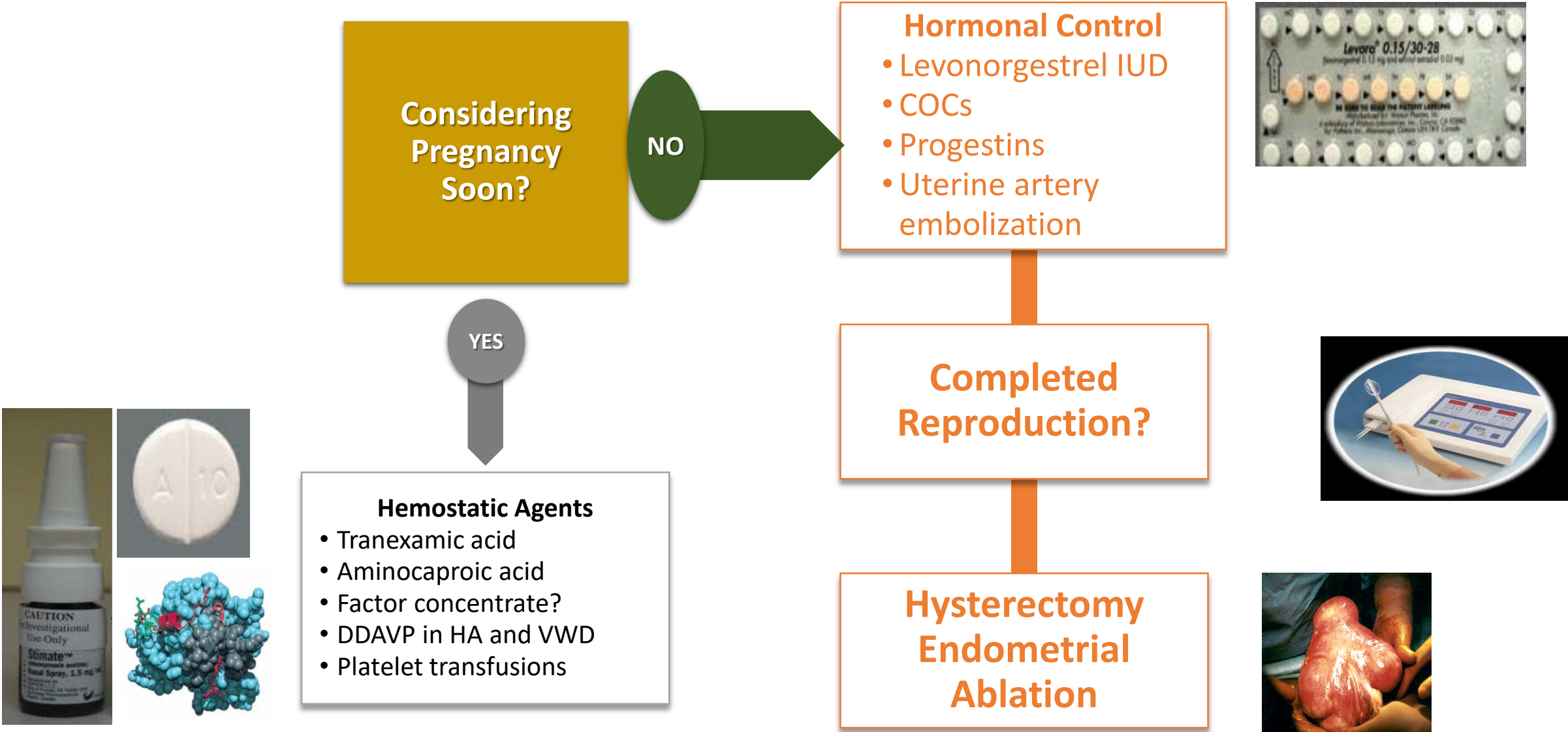
TREATMENT OPTIONS FOR HMB



Summary of Replacement Products

Deficiency	FFP	Platelet	Cryoppt	Plasma Concentrate	Prothrombin Complex (PCC)	Recombinant Factor
Factor VIII	Last choice					# 1 choice
Factor IX	Last choice					# 1 choice
Platelet Disorders		x				rVIIa, DDAVP/ IVIG
Fibrinogen (FI)	Last choice		# 2 choice	# 1 choice		# 1 choice
Prothrombin(FII)	# 2 choice				# 1 choice	
Factor V	x	x				
Factor VII	Last choice			x (not USA)	#2 choice	
Factor X	Last choice			# 1 choice	# 2 choice	
Factor XI	x			x (not in USA)		
Factor XIII	Last choice		# 2 choice	# 1 choice		# 1 choice

Best Options for AUB in women with a bleeding disorder ???



Labor and Delivery Management for Women with IBD

If second stage of labor prolonged : **NO FORCEPS/ VACUUM/ FETAL SCALP MONITORING**

*** C-SECTION – non –Bikini incision**

Cord blood sampling for factor level; For affected newborn - screening head USG

Close collaboration with HTC and obstetric team

Women with bleeding disorders at risk for post partum bleeding upto 6 weeks post partum ; **monitor hemoglobin pre-discharge and discuss delayed post partum hemorrhage**

Clot strengthening agents – tranexamic acid, amino caproic acid

Use of specific replacement factor concentrate

Labor and Delivery Management

Preconception genetic counseling consultation

Multi-disciplinary team: HTC , OB team, Lab, Genetics, SW

Measure clotting factor levels for mild hemophilia and carriers –
3rd trimester

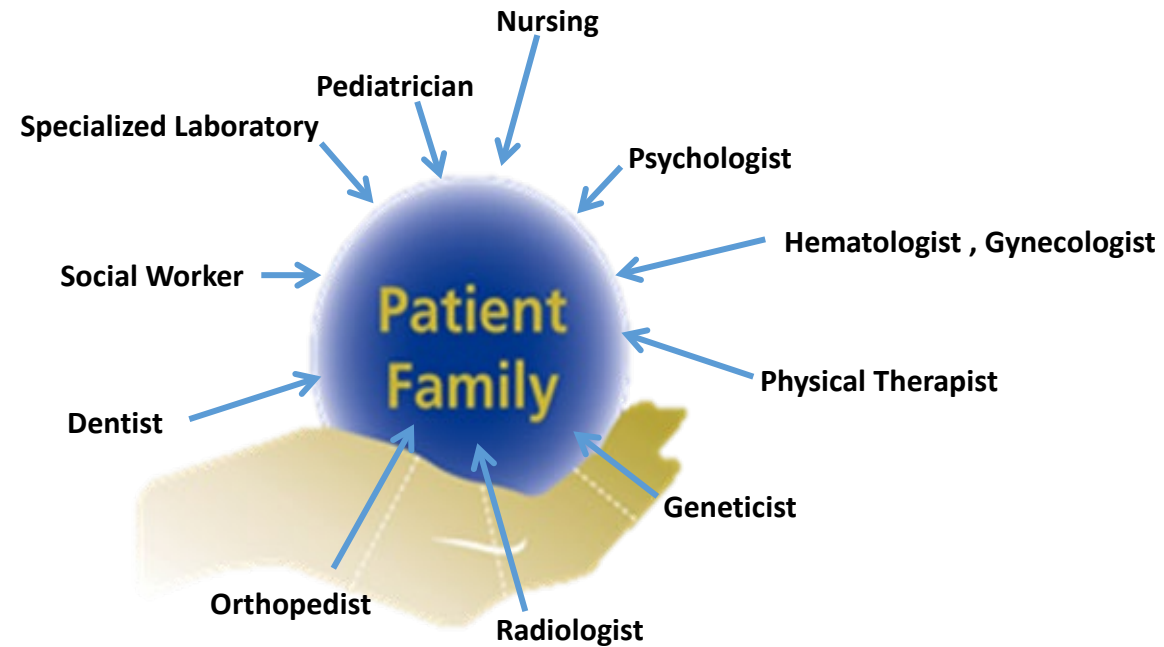
Epidural, regional anesthesia

Mode of delivery - safe for mother and child

Easy Vaginal delivery to be encouraged

Comprehensive Care

It Takes a dedicated TEAM



Hemophilia Treatment Centers (HTCs)



- The Hemophilia Program began in 1982 when the hemophilia community and the federal government devised a plan for the comprehensive care for treatment of persons with bleeding disorders under the auspices of the Maternal Child Health Bureau (MCHB). MCHB established criteria to qualify HTCs as Centers of Excellence. Currently, there are 130 Centers of Excellence (HTCs) nationally that are funded by the MCHB and the CDC.
- The HTCs comprehensive care model is recognized as specialized preventative care.
- Mortality decreased by 40% in patients using a comprehensive HTC.

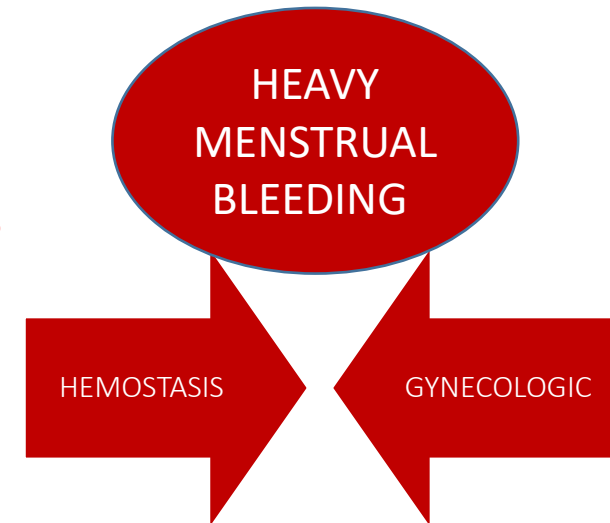
Comprehensive Care for Girls and Women at HTC

- Medical Home
- Diagnosis & Treatment Plans
- 24/7 Triage
- Home Treatment Goals
- **Prevention-focused**
- **Education-focused**
- Collaboration with:
 - Primary Care /Subspecialists
 - Schools/Daycare
 - Service Agencies
- Outcome Monitoring:
 - Data Collection
 - Identify emerging problems



Multidisciplinary Team:

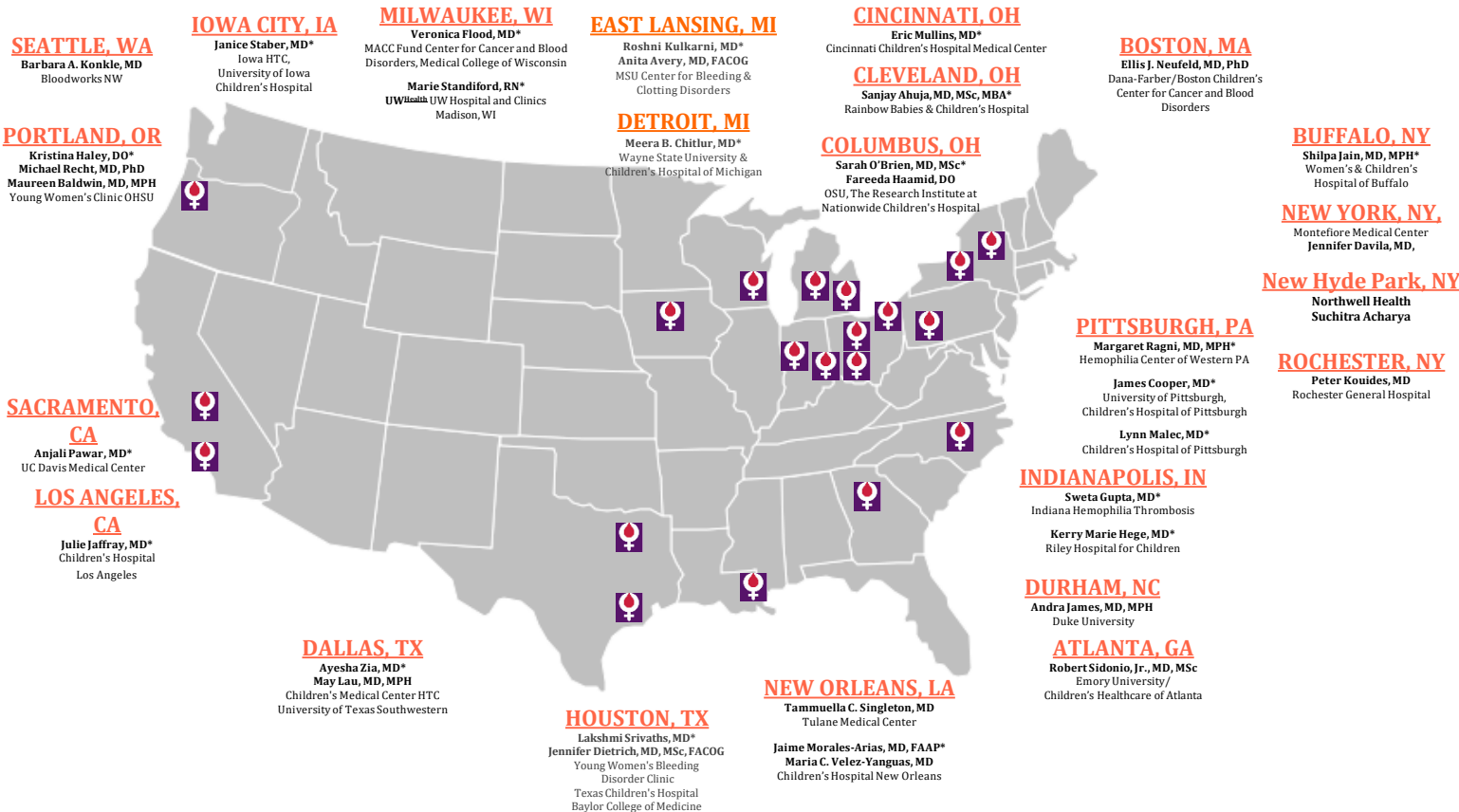
- **Hematologists**
 - Pediatric
 - Adult
- **Nurses/Nurse Practitioners**
- **Physical Therapist**
- **Social Worker**
- **Clinic for Girls and Women with Bleeding Disorders**
- **Other:**
 - Dental professionals
 - **Genetic counselors**
 - **Gynecologist/Obstetrician**
 - **Research coordinators**
 - Liver specialists
 - Nutritionists
 - Data managers
 - Pharmacy





FOUNDATION FOR
Women & Girls
with Blood Disorders

WGBD LAN Members and Clinic Locations



= WGBD LAN Clinic Location (*)



V4W

**HANDI, NHF's Information Resource
Center**



Do's and Don'ts for Females with Inherited Bleeding Disorders

Do's :

Bleeding symptoms – **GET TESTED**

Seek out a Hemophilia Treatment Center locally – www.hemophilia.org

Annual comprehensive visits - know your bleeds and treatment

- pre procedure treatment plan / dental
- up to date on vaccines –hep A, B
- IRON SUPPLEMENTS
- pre pregnancy counseling

DISCUSS MENSTRUAL HISTORY , Pain , discomfort , fear during menses

Self image and confidence – needs HELP

Marriage , sexuality, guilt

CONSULT HTC SOCIAL WORKER

Pregnancy: **Multi-disciplinary** team

Adequate supply : medications

Carry care plan letter to delivery room

Discuss **post partum bleeding** before discharge

Iron rich foods

Arrange **follow up appt.** with HTC and Gyn within 2 weeks

Healthy Life-style ; regular exercise ; iron rich diet ; Stay Positive

DON'Ts : Avoid **Aspirin** and ASA containing medications: Midol[®], Alka-Seltzer[®]

Avoid **Ibuprofen** containing medications e.g., Advil[®], Aleve[®]

Avoid **inebriation** from alcohol, illicit drugs

DO NOT DELAY seeking **medical care for major head trauma**

Heavy bleeding (menorrhagia) is one of the most common problems women report to their doctors.

It affects more than 10 million American women each year. This means that about one out of every five women has it.





- Menstrual hygiene and health - a call for dignity, rights and empowerment
- 28 May 2020 | Geneva

CURRENT GAPS AND WHERE DO WE GO FROM HERE ?

In adolescents with HMB when should we screen for bleeding disorder after menarche ?

When should a work - up be sent for those hospitalized for HMB ?

What is the optimal diagnostic panel ?

In adolescents with HMB on OCPs when to test for a bleeding disorder ?

Adolescents with HMB and bleeding disorder what are the first and second - line hormonal options ?

- Referral to Hematology even if initial coag tests are normal – screening if > 3 yrs after menarche, unknown FH, anemia, hospitalization
- Defer work up during hospitalization
- Time during period to test for VWD on OCPs
- For bleeding disorders – tranexamic acid – first line , others preferred OCPs as first line , adding TXA if no FH of thrombosis – deemed safe in clinical practice
- LNG-IUD be first line in non - acute HMB

In adolescent Girls and Women menstrual history should be a Vital Sign

Final Pearls ...

High Index of Suspicion to evaluate for an Inherited Bleeding Disorder - menstrual history as a vital sign

Stepwise approach to testing for hematologic, gynecologic, endocrine causes for HMB

Understand fallacies of coagulation testing

Repeat testing if high suspicion for inherited bleeding disorder

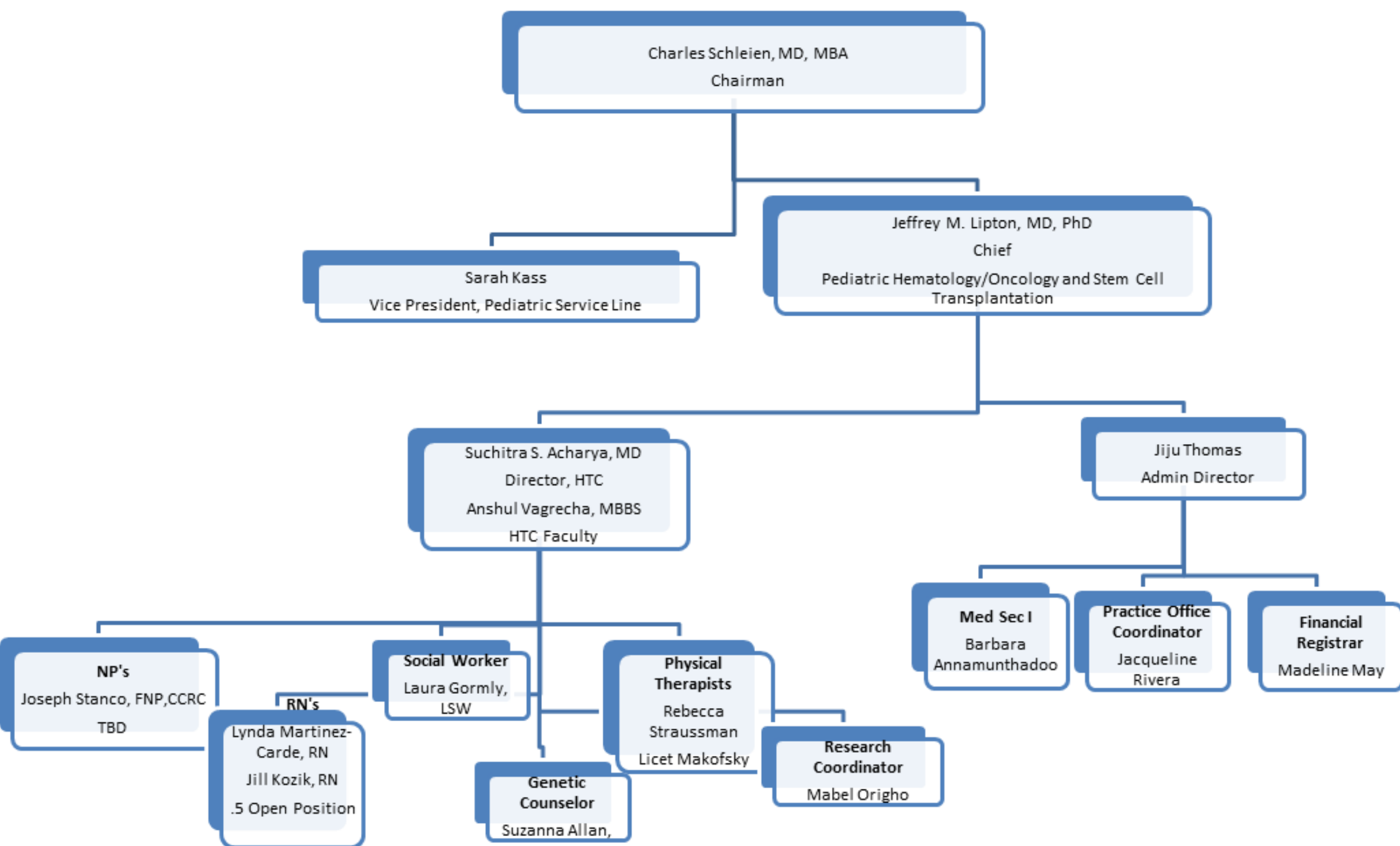
Monitor for iron deficiency anemia

Assess Quality of Life issues

Multi - disciplinary approach to HMB

More research to understand diagnostic approach , treatment modalities

Comprehensive Care at federally designated HTC's



New times demand new measures and new men (women);
The world advances, and in time outgrows
The laws that in our father's (mother's) day were best;
And, doubtless, after us, some purer scheme
Will be shaped out by wiser men (women) than we,
Made wiser by the steady growth of truth

James Russell Lowell

Thank you !

