Inherited and acquired Bleeding Disorders in Pregnancy

2025

Assistant prof

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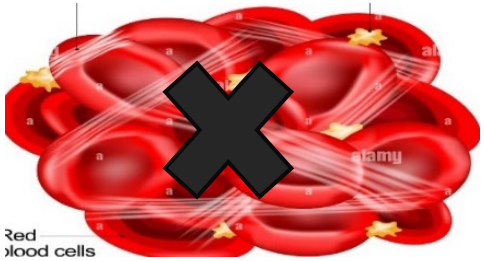


Effects of pregnancy on the clotting system

Increase↑clotting factors factor

- VIII
- VII
- X
- XI
- Fibrinogen(from 200 to 600 mg/dl
- von Willebrand Factors

Effects of pregnancy on the clotting system

Reduction↓ of coagulation inhibitors

1. Proteins S
2. Antithrombin
3. fibrinolysis inhibition

Pregnancy is a hypercoagulable state

This has two main effects:

 # It helps reduce the risk of excessive bleeding during delivery.

 # but it also increases the risk of blood clots, like deep vein thrombosis or pulmonary embolism."

Bleeding disorders during pregnancy

Inherited

1. Coagulation disorders
2. Platelet disorders
3. Vascular abnormalities

Acquired

1. Thrombocytopenia
2. Disseminated intravascular coagulation
3. Acquired coagulation disorders
4. Marrow disorders

Coagulation disorders

1. Congenital coagulopathies(Inherited)

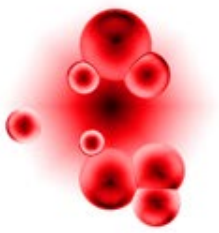
1. Hemophilia A (factor VIII (8) deficiency)
2. Hemophilia B (factor IX (9) deficiency)

- both are X-linked recessive disorders

3.Von willebrand's disease (mostly Autosomal dominant)

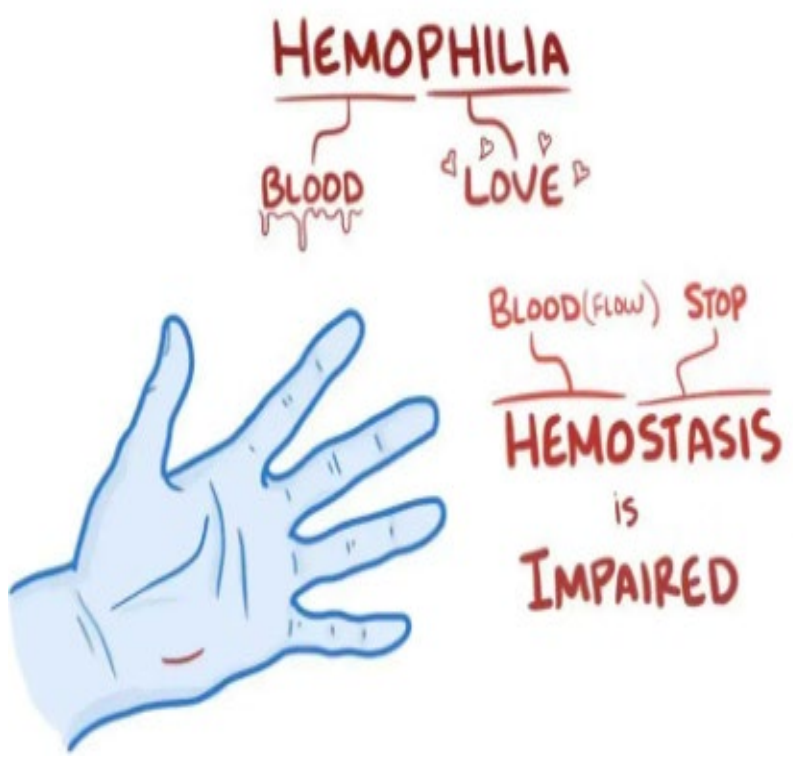
2. Acquired coagulopathies:

1. Pregnancy induced hypertension
2. Placental Abruption
3. Retained dead fetus
4. Amniotic fluid embolus
5. Liver disease
6. Anticoagulants: Aspirin and Heparin



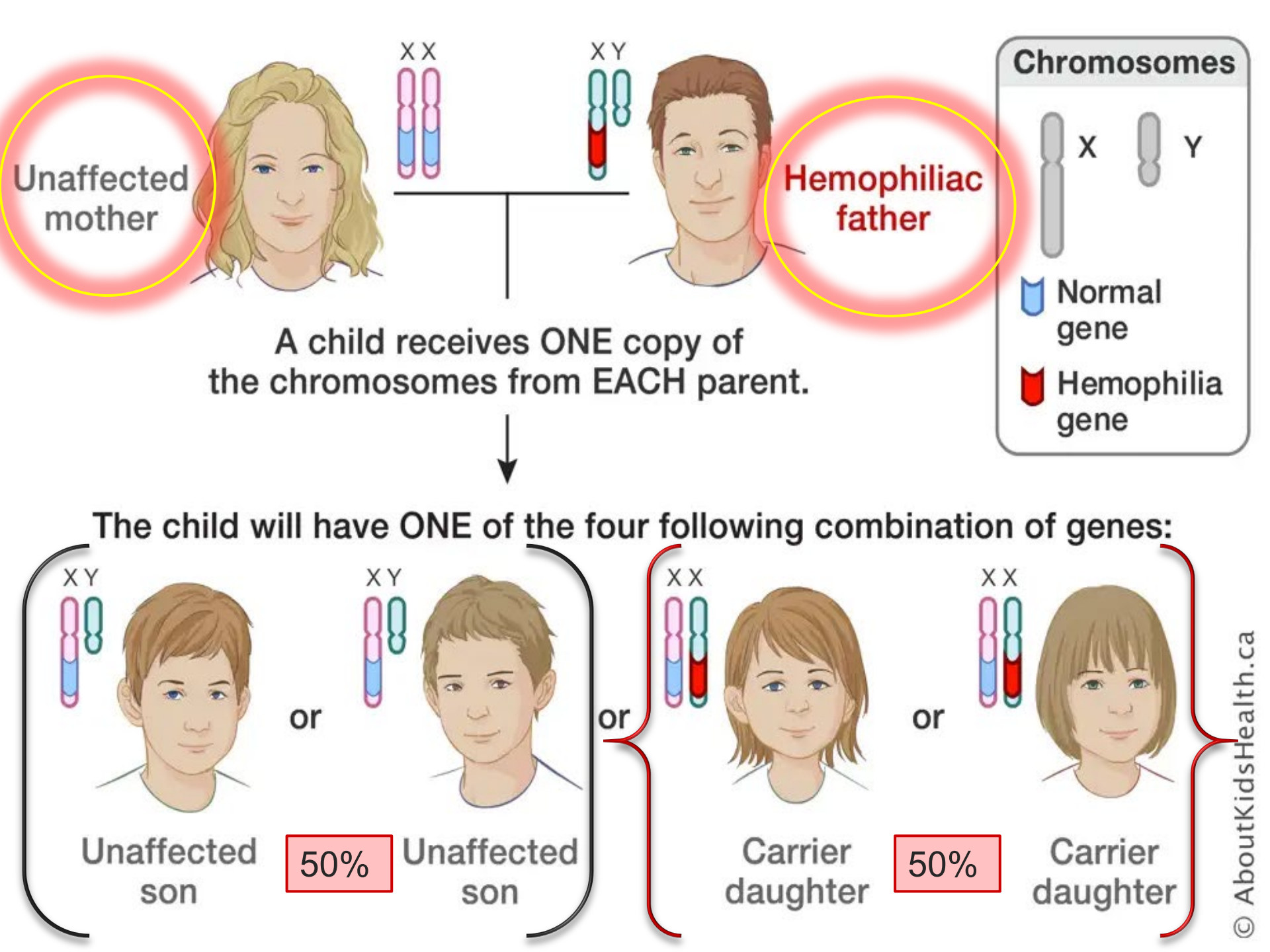
Hemophilia


MOST COMMON SYMPTOMS OF HEMOPHILIA
Nosebleeds
Mouth bleeds
Heavy bleeding from minor injuries
Easy bruising
Joint pain and swelling
Muscle bleeds
Coughing or vomiting blood
Blood in stool or urine
Heavy menstrual bleeding
Bleeding in the brain


HEMOPHILIA
BLOOD
LOVE
BLOOD(FLOW) STOP
HEMOSTASIS
IS
IMPAIRED

HEMOPHILIA

- Hemophilia A and B are **X-linked recessive disorders**
- The genes for factor 8 and Factor 9 are located on the X-chromosome.


Unaffected mother
XX
XY
Hemophiliac father
Chromosomes
X
Y
Normal gene
Hemophilia gene
A child receives ONE copy of the chromosomes from EACH parent.
The child will have ONE of the four following combination of genes:
XY
or
XY
Unaffected son
50%
Unaffected son
or
XX
or
XX
Carrier daughter
50%
Carrier daughter
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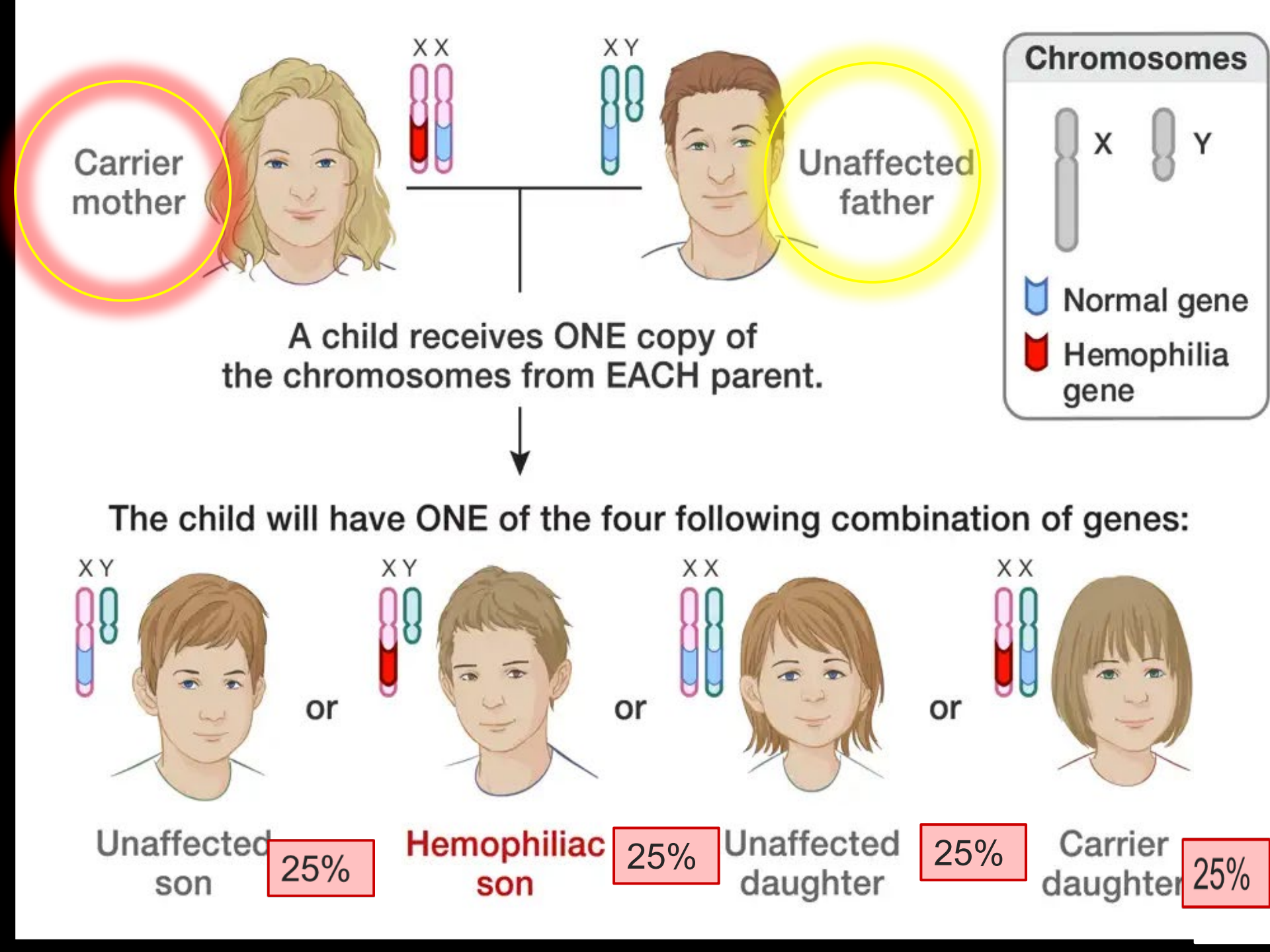
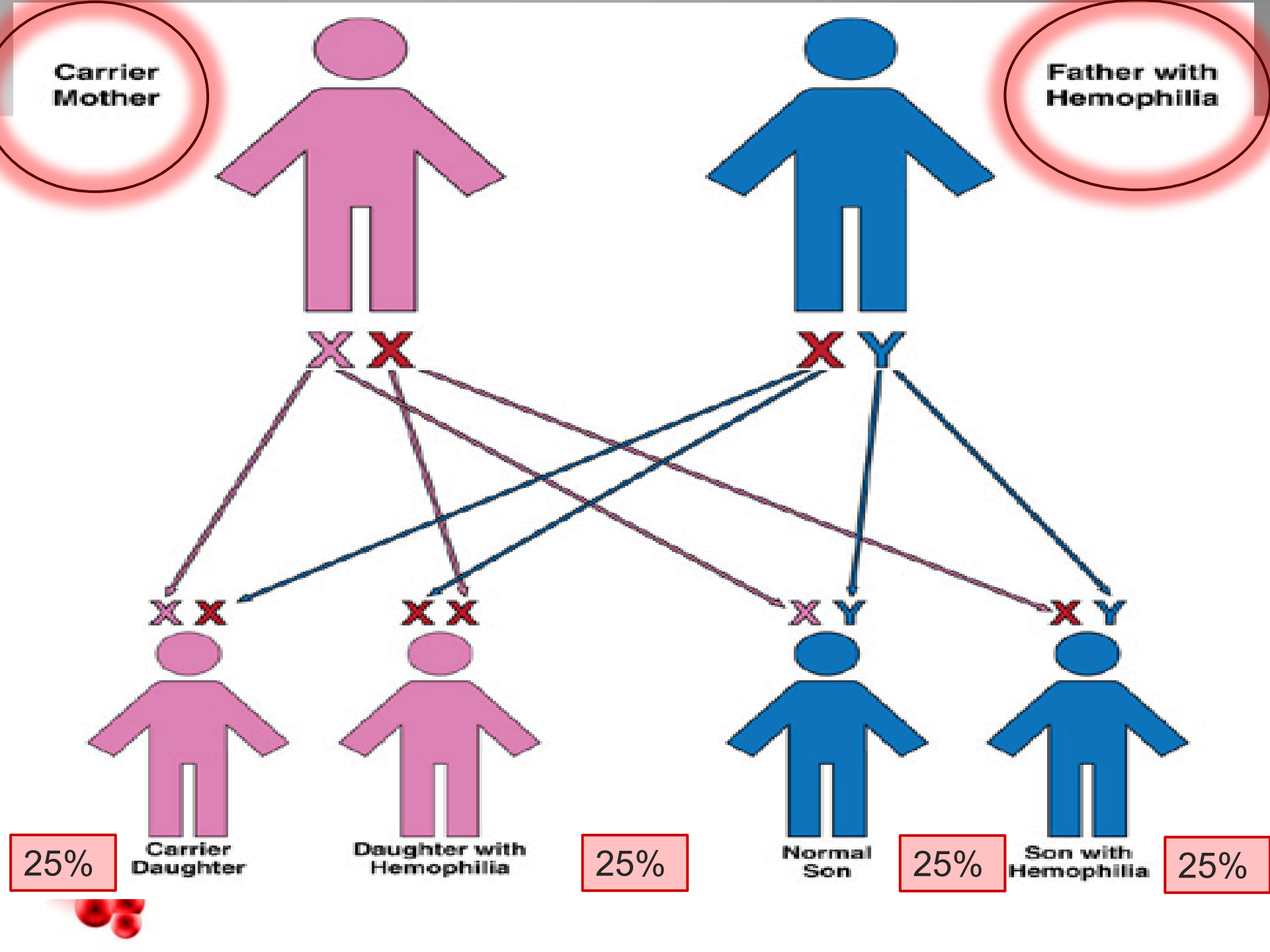

Carrier mother
X X
X Y
Unaffected father
Chromosomes
X
Y
Normal gene
Hemophilia gene
A child receives ONE copy of the chromosomes from EACH parent.
The child will have ONE of the four following combination of genes:
X Y
or
X Y
or
X X
or
X X
Unaffected son
25%
Hemophiliac son
25%
Unaffected daughter
25%
Carrier daughter
25%


Carrier Mother
Father with Hemophilia
X X
X Y
X X
X X
X Y
X Y
Carrier Daughter
Daughter with Hemophilia
Normal Son
Son with Hemophilia
25%
25%
25%
25%

Case senario

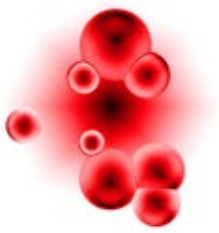
"swsan is 30-year-old woman presented with her husband to the outpatient clinic seeking help to achieve pregnancy. The couple are relatives and have a strong family history of hemophilia. They are concerned about the risk of having a child affected by hemophilia.

What is the investigations need to be sent ?

Answer

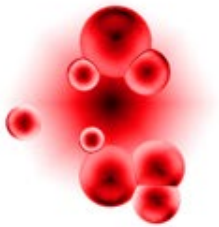
Send both partner

- Genetic Testing for Hemophilia A and B
- Coagulation factor activity (Factor VIII or IX levels)



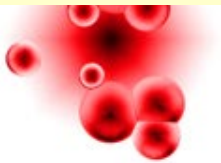
By investigation swsan was hemophilia carriers

Q/what is your advice prior to get pregnancy??

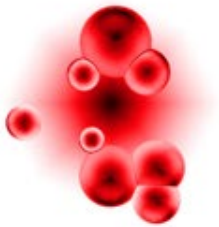


Pre-pregnancy counseling of hemophilia carriers of

1. weight optimization
2. correction of any iron deficiency
3. preimplantation genetic diagnosis in ICSI cycle only



she comes 3 month later with pregnancy test positive what is Q/what is your Antenatal management ??



NOTE :during pregnancy

#hemophilia A carriers= increase Factor 8 levels

#hemophilia B carriers=Factor 9 levels do not rise

Carriers of hemophilia are typically healthy because they usually have enough clotting factor (around 50% of normal levels) . Some carriers might have:Heavy menstrual ,Easy bruising, Prolonged bleeding after surgeries or injuries depending on their actual clotting factor levels.

Antenatal management of Hemophilia carriers

1. **multidisciplinary team of** specialists(hematologist, obstetrician and anesthetist)
2. **Test clotting factor (FVIII or FIX) level**

- at booking
- before any antenatal procedure
- in third trimester (28-34)

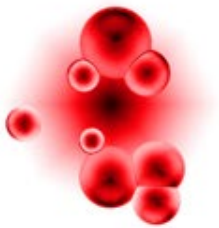
3. **free fetal DNA analysis** at 9 weeks of gestation: for fetal sex determination

4. **PND (prenatal diagnosis) with chorionic villous sampling** at 11–14 weeks of gestation. If free fetal DNA analysis show the fetus if male

5. **External cephalic version should be avoided**

during ANC she comes with LOW clotting factor (8 or 9) level

Q/how can you replace the clotting factor (FVIII or FIX) level ??



Replacement

Hemophilia A

- **recombinant factor VIII (8) concentrates :** increase in coagulation factor for 6 hrs.
- **cryoprecipitate**
- **Desmopressin (DDAVP):** it is a synthetic analogue of antidiuretic hormone, given IV or intranasally during (labor due to risk of uterine contractions)

Desmopressin (DDAVP):

- **Used for Hemophilia A** and **von Willebrand disease (type 1)** for its ability to increase the levels of **factor VIII** and **von Willebrand factor (vWF)** by releasing stored factors from the endothelial cells.
- Desmopressin is generally avoided in women with **preeclampsia** or **fluid retention disorders**, as it can exacerbate these conditions.
- **Fluid intake should be restricted to 1 liter for 24 hours following DDAVP administration**

Replacement

Hemophilia B

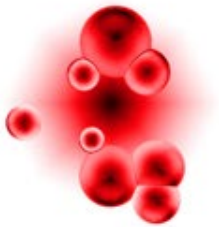
1.factor IX concentrates

2.fresh frozen plasma.

don’t use Desmopressin it not affected

she start labor

Q/what is your management ??



carriers management during delivery

1)avoid:

- ✓fetal scalp electrode (FSE)
- ✓ventouse delivery
- ✓midcavity forceps
- ✓fetal blood sampling

2)Regional block don only if:

- ✓the coagulation screen should be normal
- ✓factor level is above 50 IU/dL.

3)active management of the third stage of labor.

4)Tranexamic acid could be considered and /or DDAVP to increase factor VIII

5)Tranexamic acid should be continued postpartum until lochia is minimal

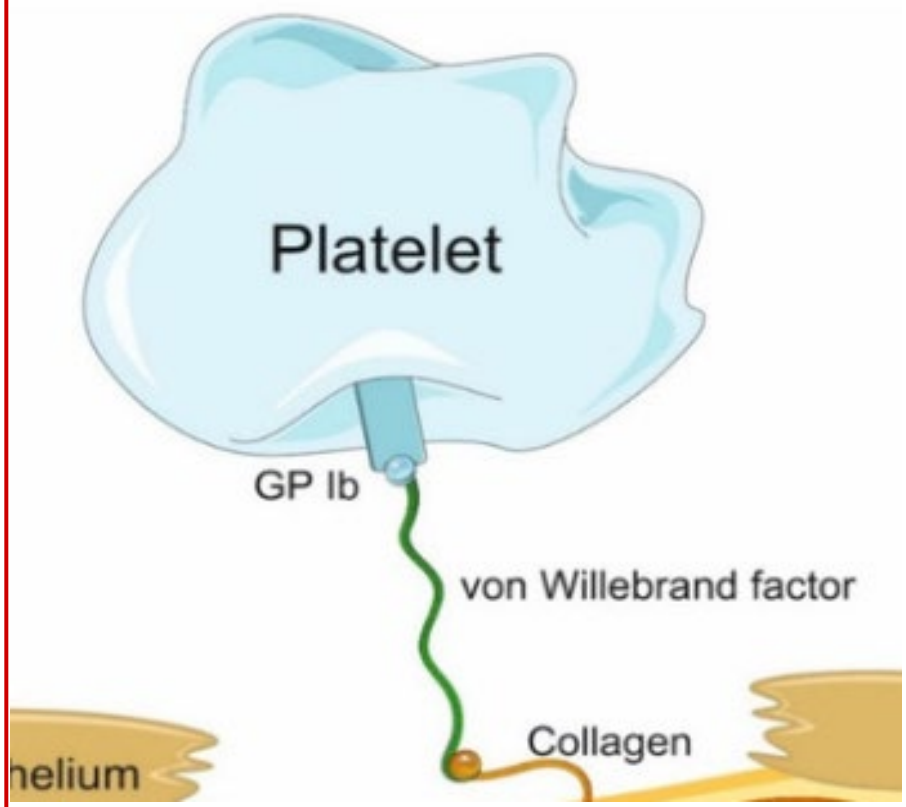
6)Newborn:

- all male newborns sent for urgent cord blood factor(8 or 9)level (according to type of hemophilia) ; if low the neonate receive a dose of (recombinant factor 8 or 9) to minimize the risk of intracranial hemorrhage.
- I M injections should be avoided until hemophilia status is known. So, Vitamin K can be orally.

Von willebrand disease (VWD):

VWF is a plasma protein that has two main functions:

1. **stabilization of factor VIII**
2. **adherence of platelets to injured vessel walls**



Von willebrand disease (VWD):

- most common inherited bleeding disorder
- both sexes are affected
- In pregnancy vWF and factor VIII levels increased so it difficult to confirm the diagnosis in pregnancy

There are 3 types of VWD

Type 1 (is the most common)

- Autosomal dominance
- mildest form
- decrease in numbers of vWF
- improve during pregnancy as the vWF levels increase up to the normal range.

There are 3 types of VWD

Type 2

Autosomal dominance or recessive

the defect in function of vWF

do not improve during pregnancy.

Type 3:

Autosomal recessive

absence of vWF

is the most severe but rare

do not improve during pregnancy.

Case senario

“farah is 20-year-old woman presented to the outpatient clinic she has bleeding disorder diagnosed as von Willebrand disease ,What is the management antenatally and intra partum and post partum ?

Antenatally

1)multidisciplinary team of specialists(hematologist, obstetrician and anesthetist)

2)in each trimester and before any intervention send to :

1)Von Willebrand screen

2)platelet count

3)levels of factor VIII (8)

3)Replacement :corrected according to the loss

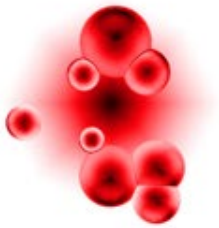
- ✓ Platelet transfusions:if platelet low
- ✓ vWF factor replacement:if vWF low
- ✓ Recombinant factor VIII (8): if factor 8 low

4)Avoid external cephalic version

Labor management

1)Labor in specialist tertiary hospital have hematological department provide investigation and treatment

2)The mode of delivery guided by obstetric indications.

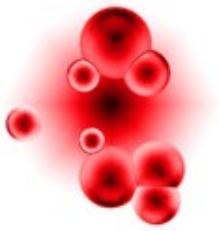


3)avoid

1. fetal scalp monitoring
2. fetal blood sampling
3. ventouse delivery
4. midcavity forceps
5. Intramuscular injections

4)Anesthesia:

- Regional anesthesia used for type 1 only
- **In patients where an epidural catheter has been placed,** catheter removed immediately after delivery**, due to** risk of epidural hematoma.



5)Measure the level of vWF

- ❑if vWF is > 40 IU /dl Vaginal delivery is considered safe
- ❑If C/S is necessary, the level must be >50 IU/ dl.
- ❑If vWF low use :
- ✓(desmopressin)
- ✓ vWF concentrates

Postpartum

1)Monitor the

Von Willebrand screen

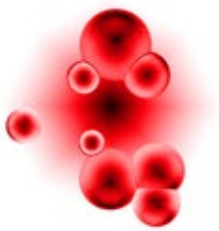
platelet count

factor VIII (8) levels should be >50IU/dL

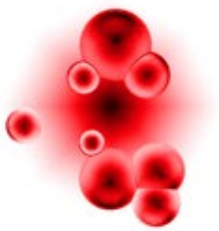
Replacement given if needed for

- 3days post vaginal delivery
- 5days following caesarean section.

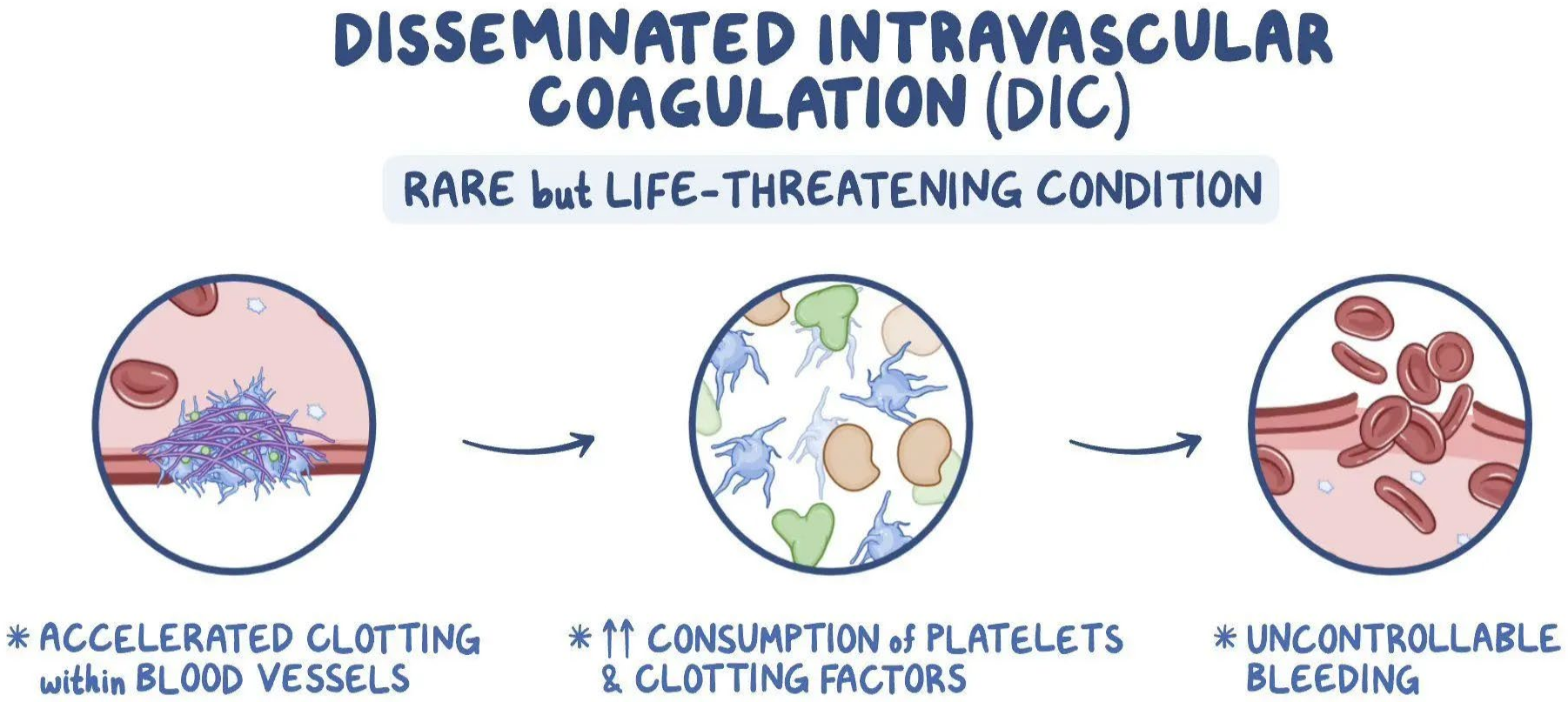
2) tranexamic acid for the postpartum period for 7–14 days.



Disseminated intravascular coagulation (DIC)



it is **never primary**, but **always secondary***

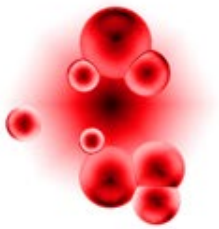


- Disseminated Intravascular Coagulation (DIC) is a complex syndrome characterized by abnormal activation of the coagulation and fibrinolysis pathways, leading to:

1. **Excessive Clot Formation:** Formation of small clots in small to medium-sized blood vessels, causing ischemia and organ damage.
2. **Excessive Bleeding:** Due to the consumption of platelets and clotting factors, along with increased fibrinolytic activity leading to clot breakdown

Box 39.5: Complications and Trigger Factors for DIC

Endothelial Injury	Release of Thromboplastin	Release of Phospholipids
♦ Pre-eclampsia, eclampsia, HELLP syndrome	♦ Amniotic fluid embolism	♦ Fetomaternal bleed
♦ Septicemia	♦ Dead fetus syndrome	♦ Incompatible blood transfusion
• Septic abortion	♦ Abruptio placentae	♦ Hemolysis
• Chorioamnionitis	♦ Hydatidiform mole	♦ Septicemia
• Pyelonephritis	♦ Cesarean section	
♦ Hypovolemia	♦ Intra-amniotic hypertonic saline	
	♦ Shock	



CNS

- **Infarcts Cerebral**
- **edema**

Abnormal bleeding

Hemoptysis, hemothorax

GI bleeding

Oozing of blood from surgical wounds or IV lines

Hematuria

Petechiae, purpura, echymoses

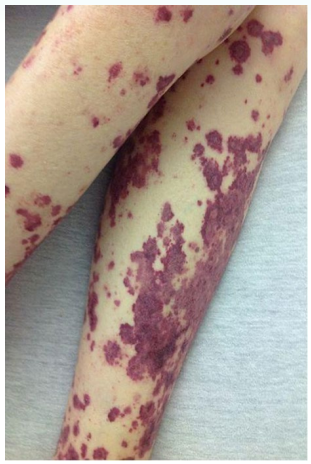
Organ failure

ARDS

Acute renal failure

Thrombosis

Deep vein thrombosis



Management of patient with DIC

Investigations

1. **Fibrinogen level :** **(Decreased) less than 175 mg/dl**
2. **platelet count :(decrease because of depletion) less than 150X10^9 /L**
3. **Both PT and aPTT are prolonged** (due to the widespread consumption of clotting factors)
4. **Thrombin time(TT) (prolong) (**measures the time it takes for thrombin to convert fibrinogen into fibrin)
5. **(D-dimer) : (increase) More than 0.05 µg/ml**

1.Maternal resuscitation:

A.Replacement of blood and clotting factors by given:

1) **Fresh blood.**
2) **FFP**: provides

- ✓ **factors V**
- ✓ **VIII**
- ✓ **some antithrombin IIIa**
- ✓ **fibrinogen.**

3. **Cryoprecipitate** :(high fibrinogen content)
4. **platelets** added After initial resuscitation

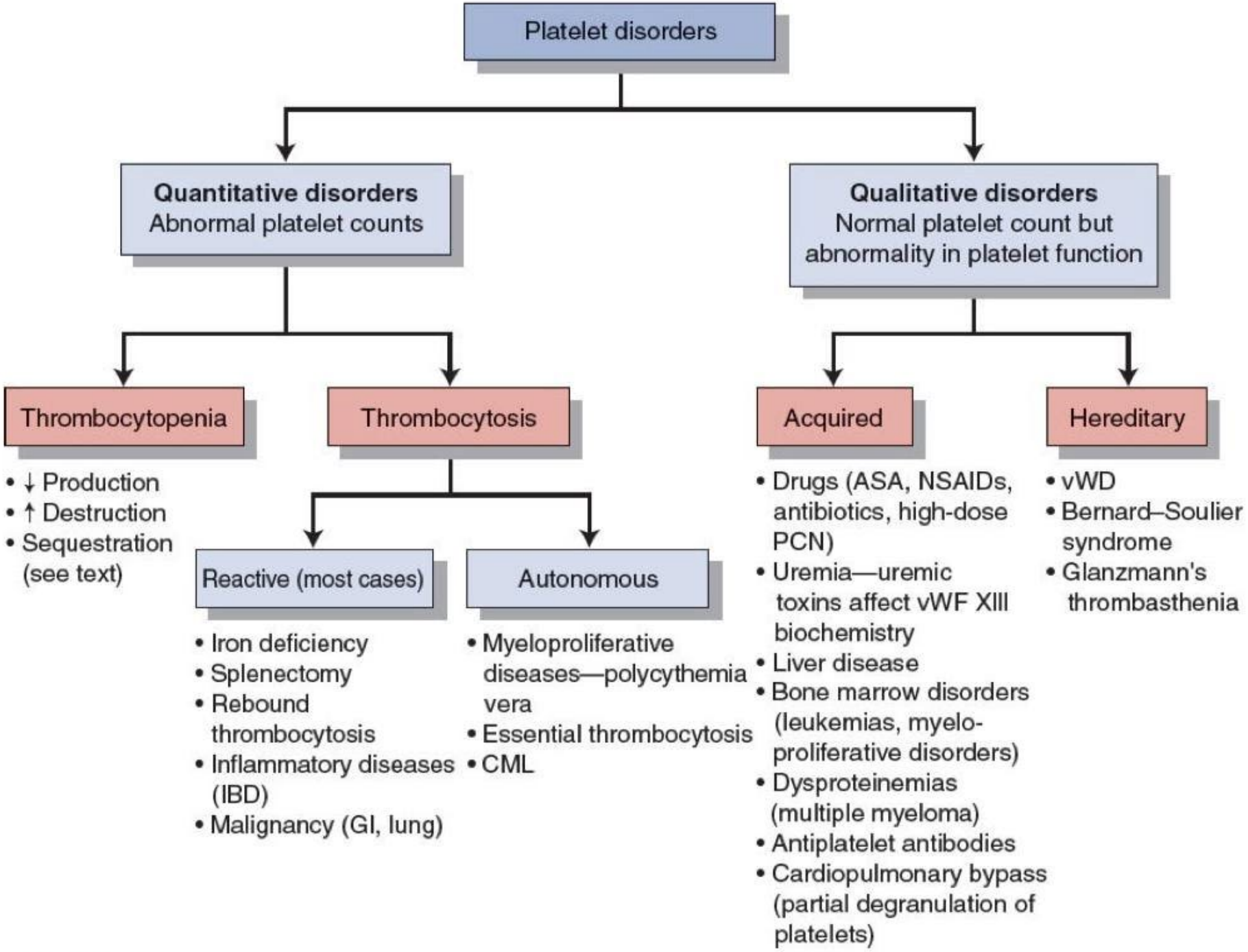
B) fluid replacement to limit damage to the endothelium and allow rapid clearance of fibrin-platelet clumps

C) Intensive monitoring repeated checks:

- ✓ Hemoglobin
- ✓ platelets

D)Treat the cause

1)Pre-eclampsia/HELLP syndrome
2)Placental abruption
3)Peri partum Hypovolemic shock (placenta previa/accreta) (Postpartum hemorrhage)
4)Amniotic fluid embolism
5)Prolonged intrauterine fetal death
6)Septic abortion
7)Incompatible blood transfusion
8)Trophoblastic disease.
9)Acute fatty liver of pregnancy


Platelet disorders
Quantitative disorders
Abnormal platelet counts
Qualitative disorders
Normal platelet count but abnormality in platelet function
Thrombocytopenia
Thrombocytosis
Acquired
Hereditary
• ↓ Production
• ↑ Destruction
• Sequestration (see text)
Reactive (most cases)
Autonomous
• Iron deficiency
• Splenectomy
• Rebound thrombocytosis
• Inflammatory diseases (IBD)
• Malignancy (GI, lung)
• Myeloproliferative diseases—polycythemia vera
• Essential thrombocytosis
• CML
• Drugs (ASA, NSAIDs, antibiotics, high-dose PCN)
• Uremia—uremic toxins affect vWF XIII biochemistry
• Liver disease
• Bone marrow disorders (leukemias, myelo-proliferative disorders)
• Dysproteinemias (multiple myeloma)
• Antiplatelet antibodies
• Cardiopulmonary bypass (partial degranulation of platelets)
• vWD
• Bernard–Soulier syndrome
• Glanzmann's thrombasthenia

FIGURE

Thrombocytopenia

- **defined** as a platelet count <150×10^9 /L.
- Thrombocytopenia classification:

- Mild: >80 × 10^9 /L
- Moderate: 50 -80 × 10^9 /L
- Severe: <50 ×10^9 /L

causes of thrombocytopenia in pregnancy

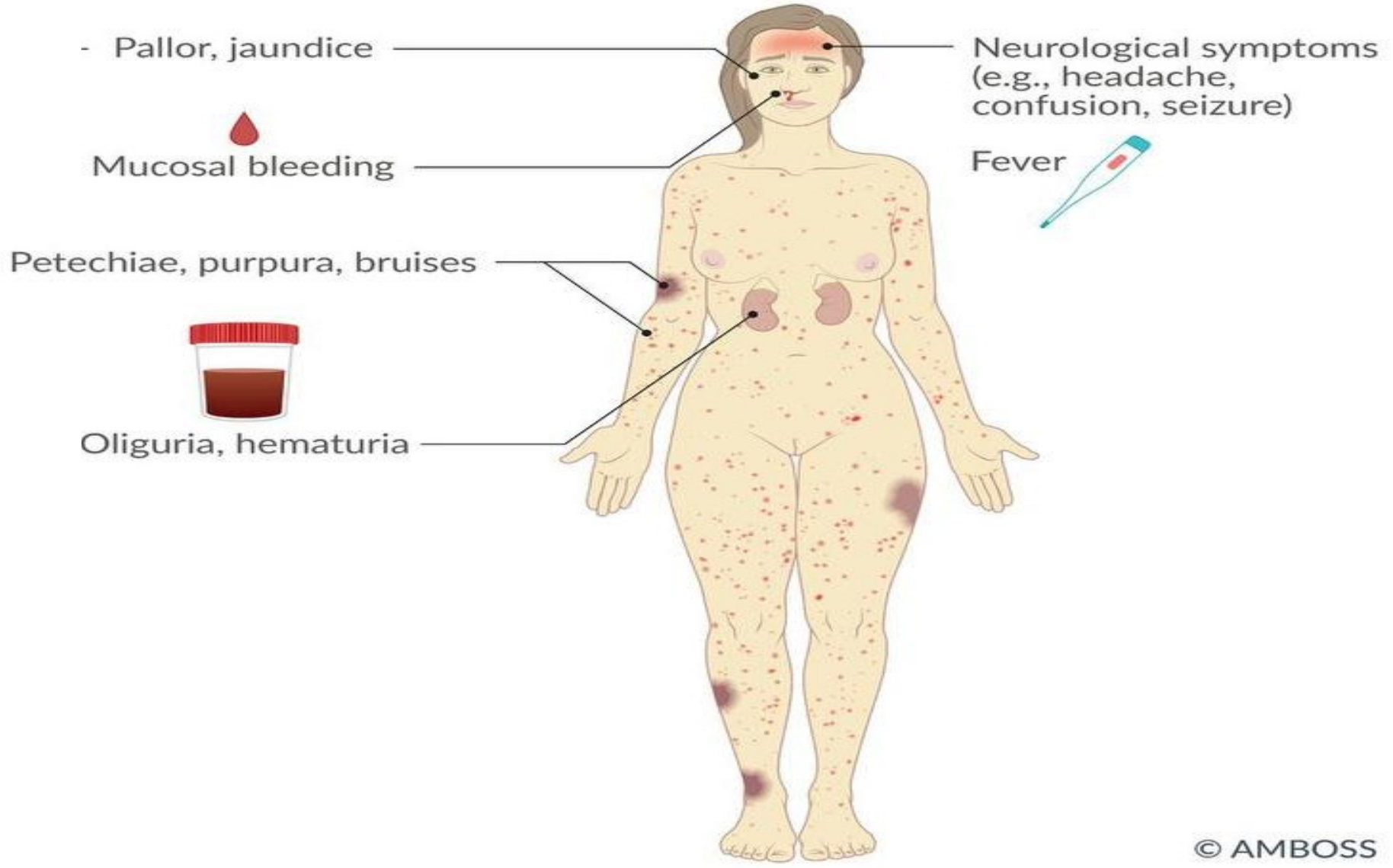
- **Idiopathic**
- **Increased destruction**

1. HELLP syndrome.
2. Thrombotic thrombocytopenic purpura
3. Auto immune thrombocytopenic purpura(ITP)
4. Anti phospholipid antibody syndrome
5. SLE
6. DIC
7. Hypersplenism

Decreased production

1. Sepsis
2. HIV infection
3. Malignant marrow infiltration

Thrombotic thrombocytopenic purpura (TTP)



Full history including:

1. **Bleeding history**: (eg menorrhagia, bleeding after tooth extraction/ surgery, easy bruising).
2. **Constitutional symptoms** (fever, weight loss, night sweats) e.g. in SLE , HIV
3. **(pre-eclampsia symptoms):**Headaches, visual problems, swelling
4. **drug history** (including herbal medicines, NSAID and heparin).
5. **Recent transfusions** to exclude post-transfusion purpura.
6. **Family history.**

Full examination

1. Signs of bleeding tendency e.g. petechiae, mucosal bleeding, purpura.
2. Lymphadenopathy
3. Hepatomegaly
4. splenomegaly
5. Features of autoimmune disease.
6. Signs of infection.
7. Signs of pre-eclampsia: oedema, hyperflexia, hypertension

Investigations of thrombocytopenia

1. **Repeat CBC:**
   - confirm thrombocytopenia
   - exclude anemia or leucopenia.
2. **Blood film**: to exclude pseudo-thrombocytopenia (platelet clumps)
3. **Coagulation screen :**aPTT/PT / fibrinogen/D-dimer levels
4. **HIV, hepatitis B and hepatitis C screening**
5. **Renal and liver function tests**
6. **TSH: for** Hypothyroidism
7. **Antiphospholipid antibodies:**(anti-cardiolipin ,lupus anticoagulant , B2-glycoprotein)
8. **antinuclear antibody: to exclude SLE**

- aim platelets >50 x10^9 /L prior to labor
- aim platelets >80 x10^9/L prior to regional anesthesia
- platelet count less than 20×10^9 /L can lead to spontaneous bleeding during pregnancy

- 5-10% chance of fetal thrombocytopenia
- A cord blood platelet count in all babies should be determined and close monitoring for 2–5 days.

Autoimmune thrombocytopenia

- Immune (idiopathic) thrombocytopenic purpura (ITP): autoantibodies are produced against platelet surface antigens, leading to platelet destruction.

1) if platelet count is < $20x10^9$ /L , treatment with:

- ✓ corticosteroids
- ✓ intravenous immunoglobulin (Ig)G.

2) Platelet transfusion is indicated when there is clinically significant bleeding (as a temporary measure)

Thank you

Good luck