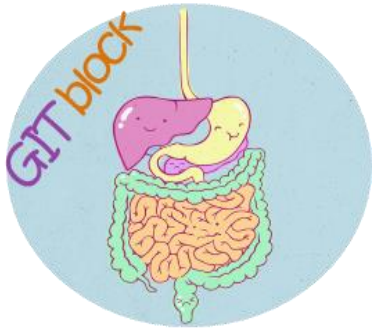





# L12 approach to bleeding disorders

These team work only contain the important info noted by the doctors

**Color coding**

- important
- Extra info
- Notes from lecturer

دعاء قبل المذاكرة :

(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل )

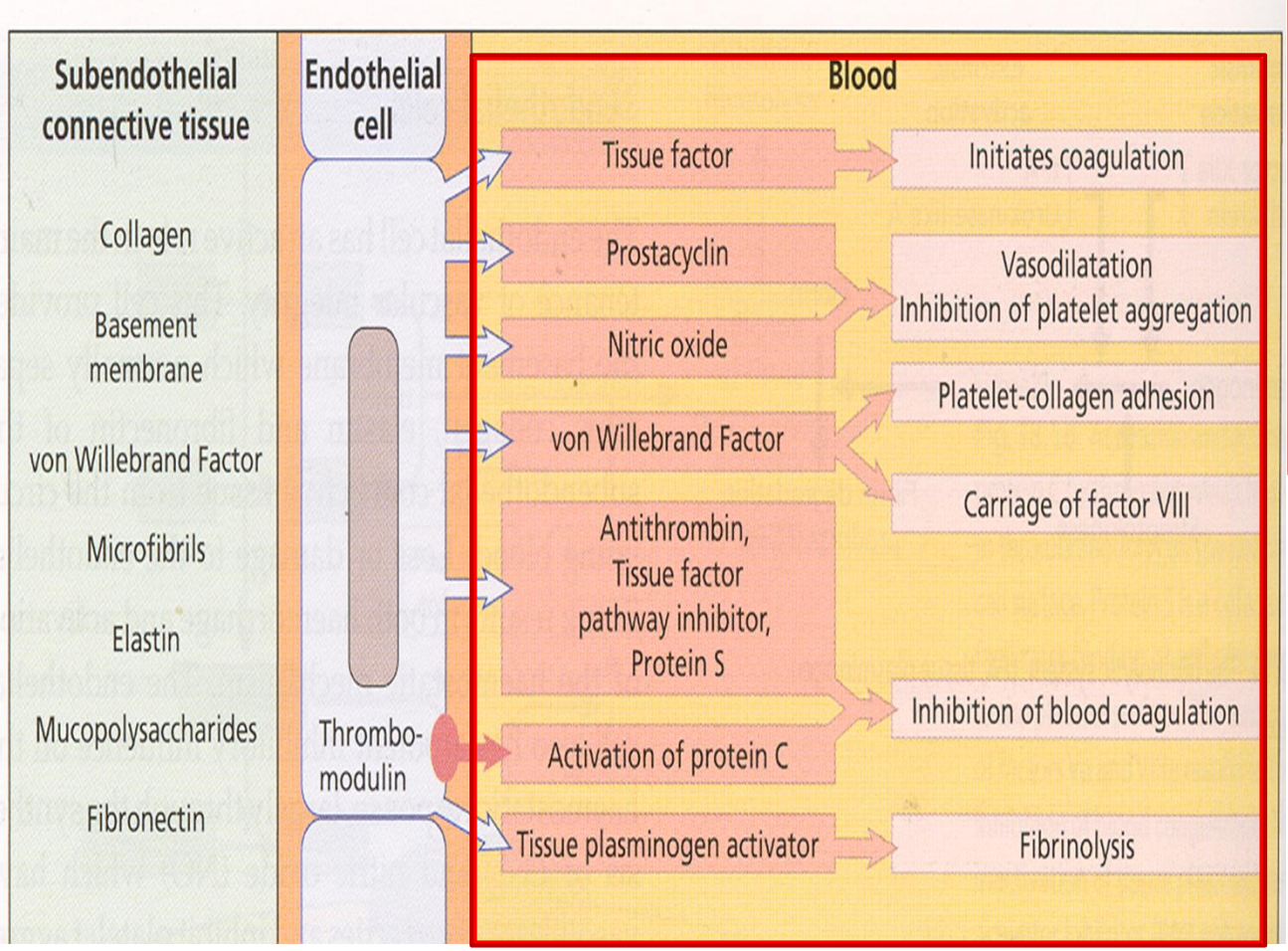
DON’T FORGET to check our editing file : haematology edit

Please don’t hesitate to contact us on:Haematology434@gmail.com

| | Male | Female |
|---|---|---|
| Hemoglobin(g/dL) | 13.5-17.5 | 11.5-15.5 |
| Hematocrit (PCV) (%) | 40-52 | 36-48 |
| Red Cell Count ($\times 10^{12}$) | 4.5-6.5 | 3.9-5.6 |
| Mean Cell Volume (MCV) (fL) | 80-95 | |
| Mean Cell Hemoglobin (MCH) (pg) | 30-35 | |
| MCHC % | 31 - 37 | |
| Platelet count | 140-450x$10^3$/L | |
| NORMAL PLATELET SIZE MPV | 7.2-11.1 fl | |
| NORMAL PLATELET DIAMETER | 1-2.5 µ | |
| WBC | 4000-11,000 /L | |
| Segmented (neutrophils) | 1.8-7.8 | |
| Eos | 0-0.45 | |
| Baso | 0-0.20 | |
| Lymphs | 1.0-4.8 | |
| Monos | 0-0.80 | |

A Good Doctor Knows normal CBC

# Fibrin and thrombin and subendothilial cell role:




Fibrinogen → fibrin monomer + peptides a & b

Fibrin manomers ⇆ aggregation

Fibrin aggregation ⇄ fibrin( s ) (polymerization)

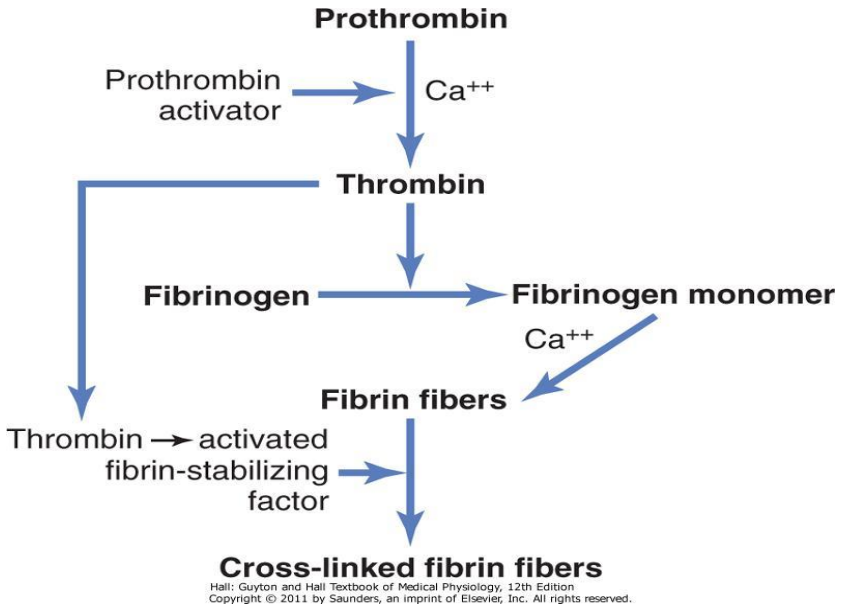
Fibrin (s) → fibrin ( I ) ( cross linked)

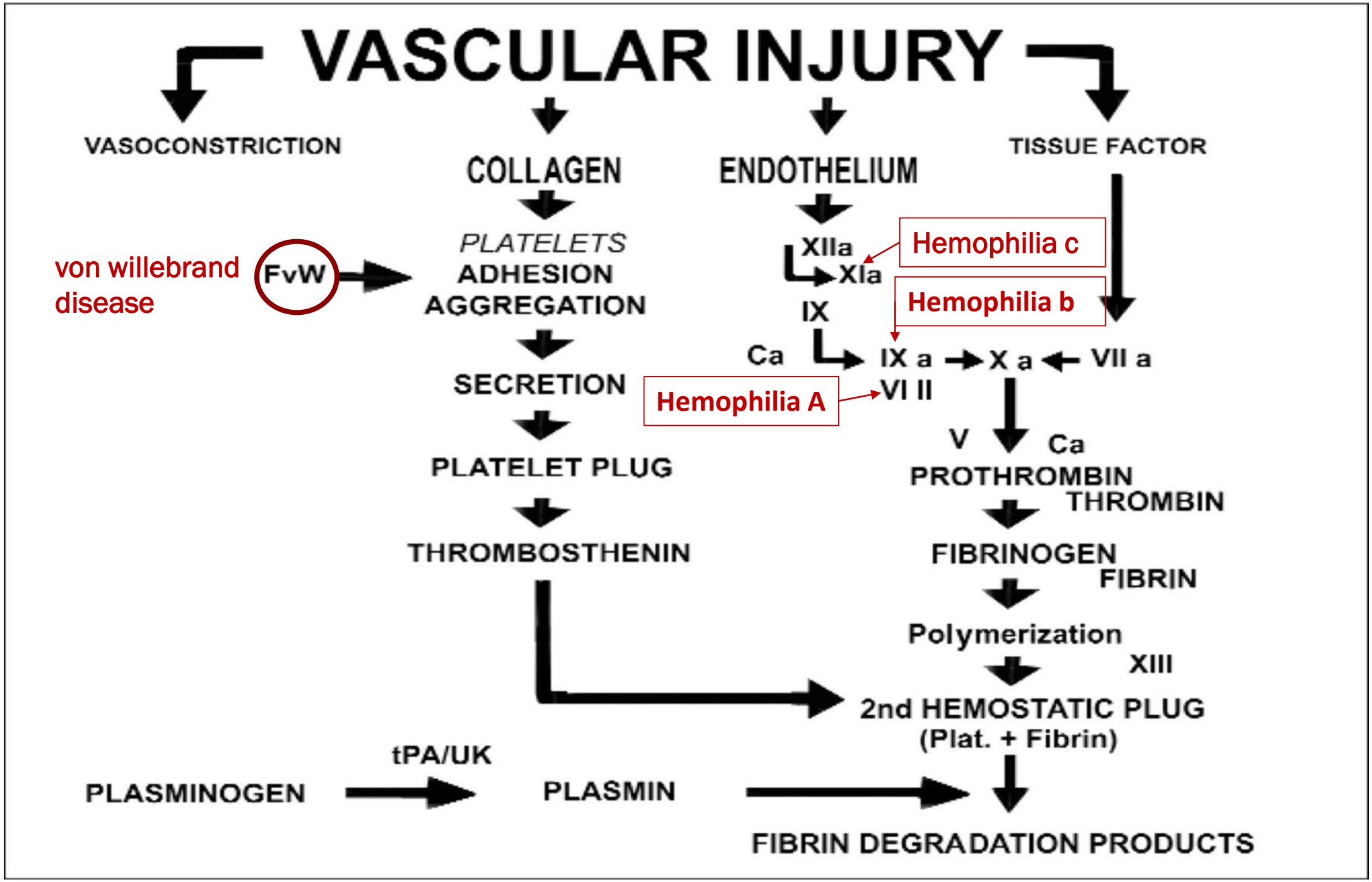
XIII

Factor 13 is important to strength the plague

Fibrin ( s ) = soluble in 5m urea

Fibrin ( I ) = insoluble in 5m urea




VASCULAR INJURY
VASOCONSTRICTION
COLLAGEN
ENDOTHELIUM
TISSUE FACTOR
PLATELETS
ADHESION
AGGREGATION
FvW
von willebrand disease
XIIa
XIa
Hemophilia c
IX
Hemophilia b
Ca
IX a
X a
VII a
VI II
Hemophilia A
SECRETION
PLATELET PLUG
V
Ca
PROTHROMBIN
THROMBIN
THROMBOSTHENIN
FIBRINOGEN
FIBRIN
Polymerization
XIII
2nd HEMOSTATIC PLUG
(Plat. + Fibrin)
tPA/UK
PLASMINOGEN
PLASMIN
FIBRIN DEGRADATION PRODUCTS

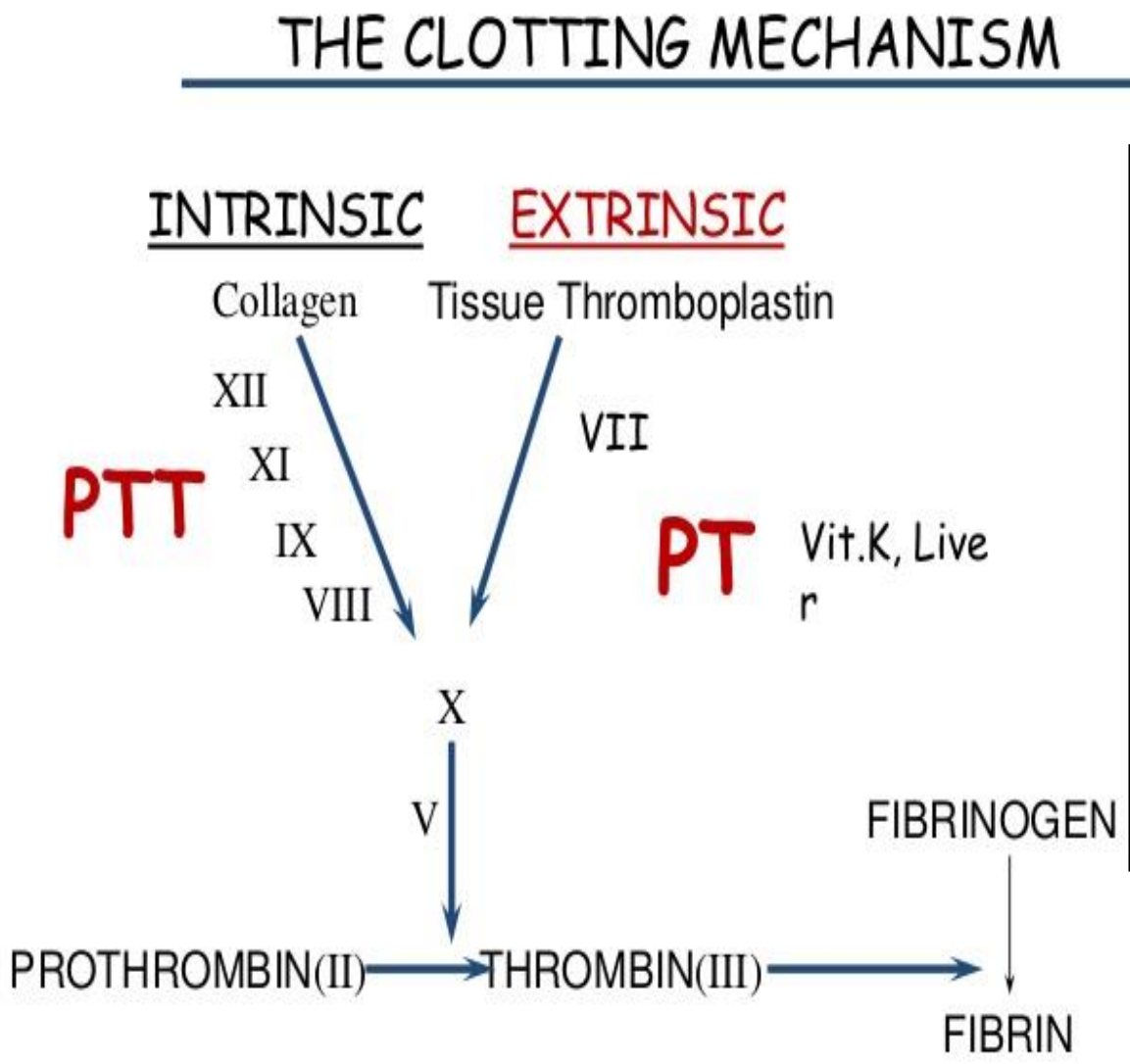
# Bleeding disorders:

Bleeding disorders are a group of disorders that share the inability to form a proper blood clot.

| Disorder | Pathophysiology/ deficiency | Inheritance |
|---|---|---|
| Haemophilia A | VIII | X linked recessive |
| Haemophilia B | IX | X linked recessive |
| Haemophilia C | XI | Autosomal dominant or recessive |
| VW disease | VW factor | Autosomal dominant or recessive |
| Factor X deficiency | Factor X | Autosomal recessive |
| Factor V deficiency | V | Autosomal recessive |
| Factor VII deficiency | VII | Autosomal recessive |
| Prothombin deficiency | II | Autosomal recessive |
| Afibrinogenemia/ dysfibrinogenemia | I | Autosomal dominant |

VW factor – Von Willebrand factor

# PTT and PT:



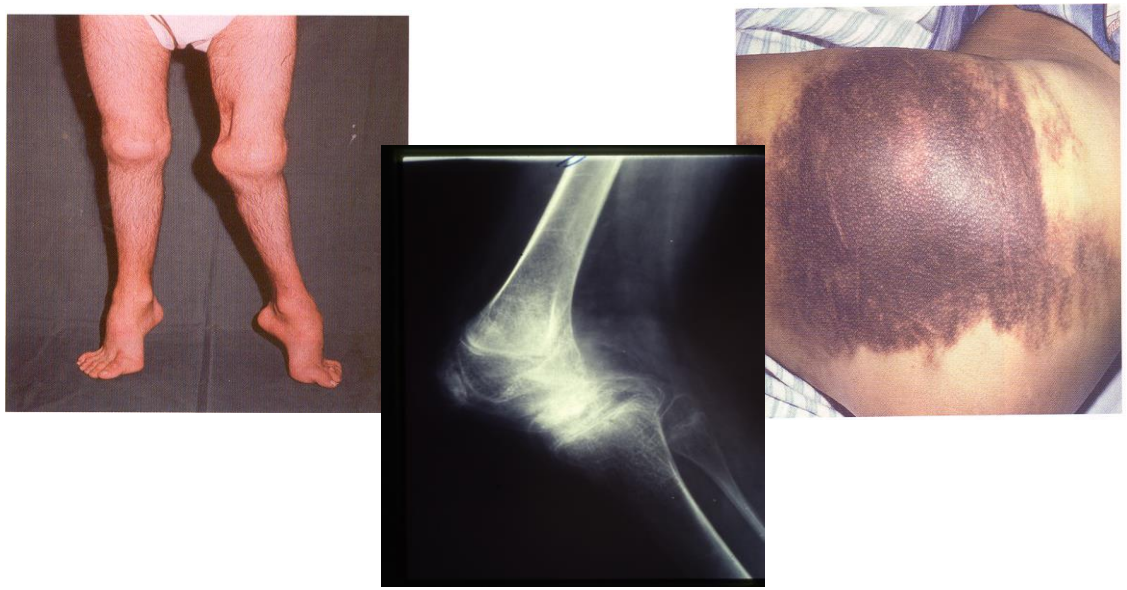

- Partial thromboplastin time( APTT) TO Measure intrinsic pathway if it prolong the defect will be in factors above 10 (12 ,11,9,8)
- Prothrombin time (PT) Measure extrinxic pathway if it is prolong defect in factor 7
- If both are prolong then the defect is in the common pathway

# Correlation of coagulation factor activity and disease severity in hemophilia A or hemophilia B

| Coagulation factor activity (percentage of normal) | Clinical manifestations |
|---|---|
| <1 | • Severe disease<br>• Frequent spontaneous bleeding episodes from early life<br>• Joint deformity and crippling if not adequately treated (disability ) |
| 1 – 5 | • Moderate disease<br>• Post-traumatic bleeding<br>• occasional spontaneous episodes |
| 5 – 20 | • Mild disease<br>• Post-traumatic bleeding |

## Symptoms:

- Join bleeding (deep bleeding ) musculoskeletal bleeding "hemoarthrosis“
- Deep tissue bleeding
- Muscle wasting
- Bruising
- Shortage of joint space



# The Abnormalities in Von Willebrand Disease

## Features:

- Abnormal bleeding time "important feature"
- Prolonged APTT & normal PT "Because it could have factor VIII deficiency"
- Deficiency of Factor VIII Clotting activity
- Deficiency of Von Willebrand Factor (Ristocetin Co-factors)
- Low Von Willebrand Antigen
- Abnormal Platelet Aggregations

## Diagnosis of Hemophilia A & Von-Willebrand's

| Haemophilia A | VW Disease |
|---|---|
| Bleeding time normal | Bleeding time abnormal |
| PT normal | PT normal |
| PTT abnormal | PTT abnormal |
| Factor VIII C "decreased" | Factor VIII C "decreased" |
| VW : normal | VW "decreased" *confirm the disease |
| Platelets aggregation normal | Platelets aggregation abnormal |

# Classification of Von Willebrand disease

Type 1. Partial quantitative of vWF.

Type 2. Qualitative "function" deficiency of vWF.

2A. Decrease platelet dependent function associated with absent high molecular weight multimers of vWF.

2B. variants with increased affinity for platelet Glyloprotein- 1b.

2M. As 2A but high molecular weight multimers of vWF present.

2N. Variants with decreased affinity for factor VIII.

Type 3. virtually complete deficiency of vWF.

## Secondary classification of type 2 VWD

| Subtype | Platelet-associated function | Factor VIII binding capacity | High MW VWF multimers |
|---|---|---|---|
| 2A | Decreased | Normal | Absent |
| 2B | Increased affinity for GPb | Normal | Usually reduced / absent |
| 2M | Decreased | Normal | Normal or ultra Large |
| 2N | Normal | Reduced | Normal |

GPb : glycoprotein Ib. MW : molecular weight. VWD : von willebrand disease. VWF, von willebrand factor.

# Level of Factor VIII Desirable 15 mins. After the First Transfusion (IU/DL)

This slide is not important just read it

## Lesion

| | |
|---|---|
| **Early haemarthroses**<br>**Minor external bleeds** | **20-30%** |
| **Dental Extractions**<br>**Severe Haemarthroses**<br>**Internal Hemorrhage** | **50-100%** |
| **Major surgery**<br>**Serious accidents** | **70-100%** |

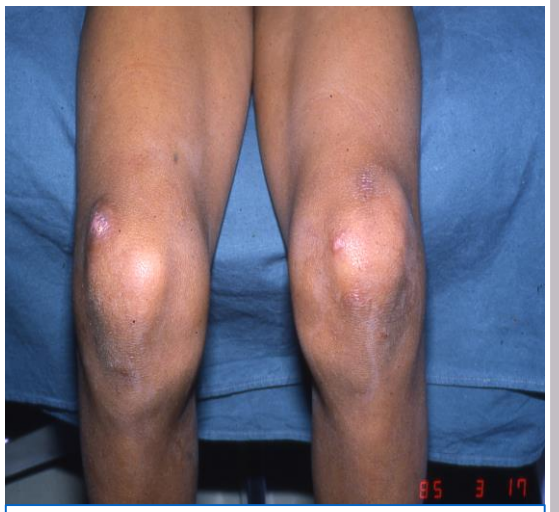
## Formula for calculating the dose of factor

(Body Weight Kgs x Desired % rise of VIII)/2 = dose of factor VIII units every 8hrs/12hrs

# FACTOR XIII DEFICIENCY "important in stabilizing the fibrin"

**Features:**

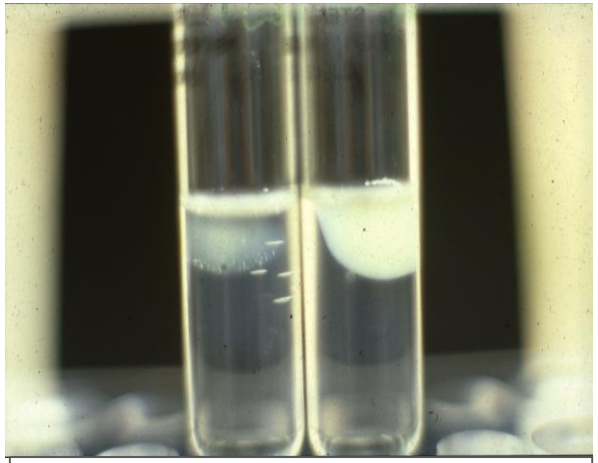
- Bruising with minor injury
- Hematoma after trauma
- Bleeding (secondary bleeding)
- Abnormal healing of wounds with excessive scar formation (keloid formation "thickening in the healed wounds") "important feature"



Abnormal healing of wounds

# LABORATORY DIAGNOSIS OF FACTOR XIII DEFICIENCY

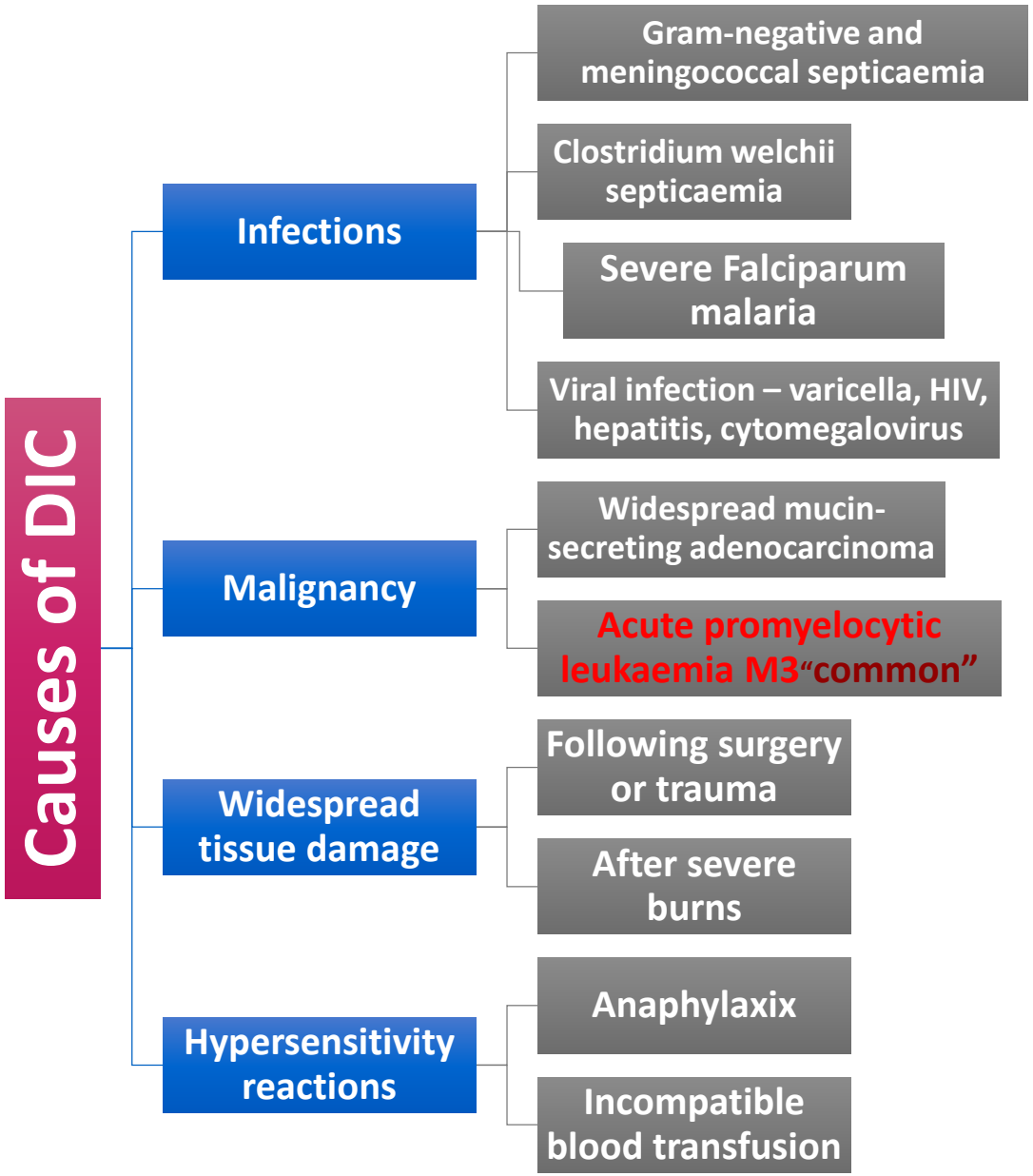
- Normal PT & Normal APTT
- Normal Bleeding time & Normal Platelet aggregation
- Normal fibrinogen level
- Abnormal clot stability with five molar urea "the dissolvement of plasma when you put it with 5 molar urea" "important"
- Low Factor XIII level

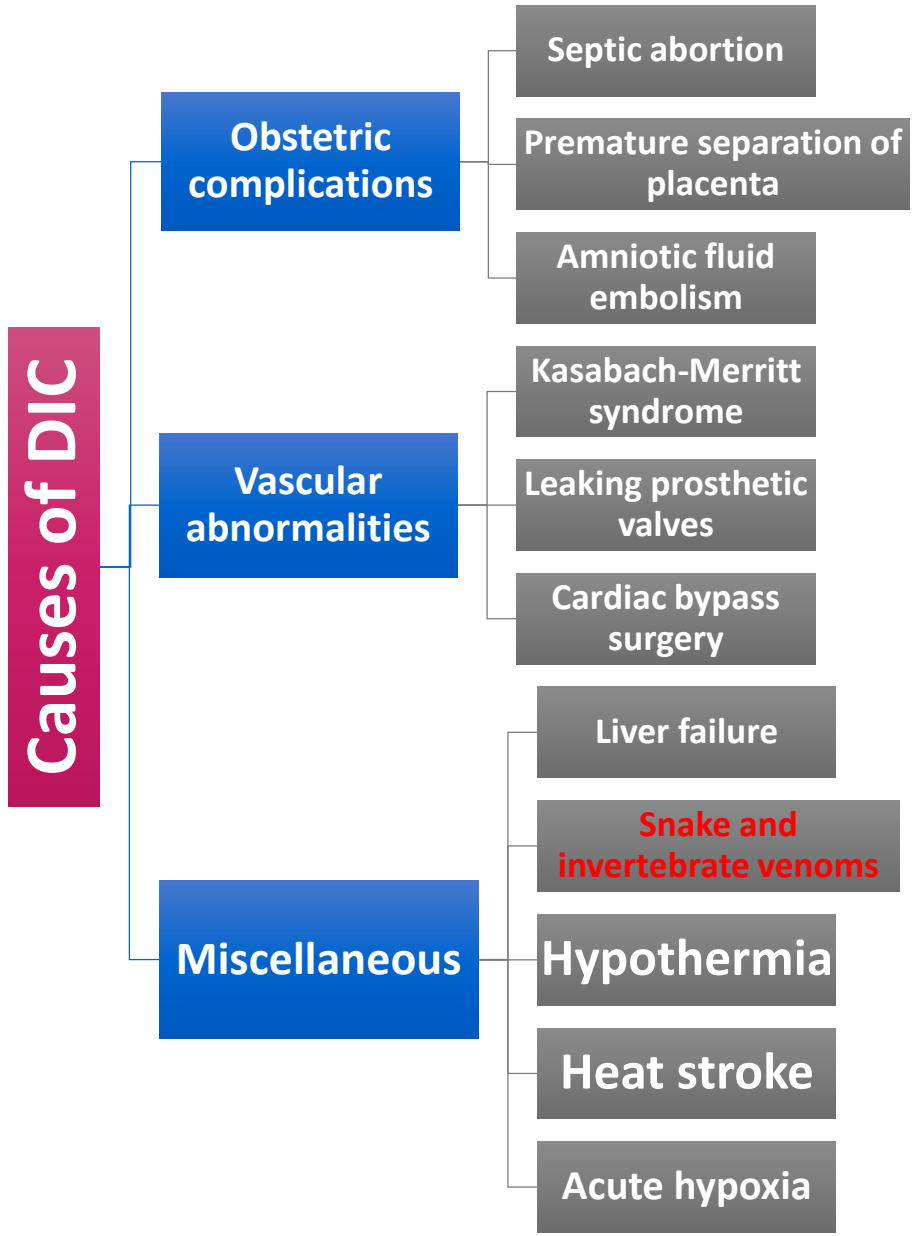


five molar urea test

# DISSEMINATED INTRAVASCULAR COAGULATION

## 'CONSUMPTION COAGULATIONPATHY','DEFIBRINATION SYNDROME'




ACQUIRED BLEEDING DISORDERS

# Pathogenesis of DIC

Abnormal substances stimulus (either interred the body or was from the body tissues like in malignancies)

Endothelial damage

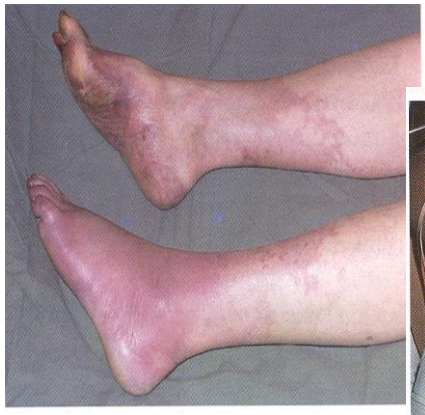
Un control generalized platelet aggregation

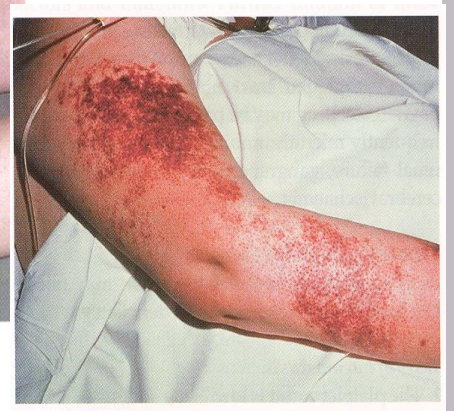
Wide spread activation of coagulation

Micro-thrombi in the circulation and multi-thrombi + decrease clot factors & platelet in blood circulation + FDPs

DIC and other acquired bleeding disorders:

- Sever wide spread activation of coagulation leading to
- sever purpra
- In sever cases we might find gangrenous necrosis of lower limbs
- Eye bleeding





# Laboratory aspects of haematological coagulation

## Tests are :

**Prothrombin time PT** Normal 10-14 sec

- test extrinsic & common pathways

**Activated partial thromboplastin time APTT** Normal 30-40 sec

- test intrinsic & common pathways

**Thrombin time TT** Normal 10-12 sec

## A - screening tests:

## B- Other tests :

- Plasma fibrinogen
- Caogulation factors ASSAYS
- Plasmia fibrin / fibrinogen degradation

It can be measured either automatic or manual

# Screening Tests of Hemostasis

| Screening tests | Defects |
|---|---|
| B.T. Prolonged | Platelets (↓ or dysfunction) + Von Willebrand's disease |
| APTT prolonged<br>Normal : 30-40 sec | Factors: XII, XI, VIII, IX, X, V, II, I instintric + common<br>e.g : Liver disease /DIC / Massive transfusion/anticoagulants/Heparin |
| P.T. Prolonged<br>Normal 10-14 sec | Factors: VII, X, V, II, I extintric and normal<br>e.g : Liver disease /DIC / Massive transfusion<br>may be in : anticoagulants/Heparin |
| T.T. Prolonged<br>Normal :10-12 | Fibrinogen (Factor I) high FDPS<br>e.g :Heparin /DIC –but Grossly- |
| Reptilase time prolonged | Fibrinogen (factor I) high FDPS. Not effected by Heparin therapy |
| FDPS high | ▪ D.I.C. most important<br>▪ Snake Bite<br>▪ Thrombolytic therapy<br>▪ Dysfibrinogenemia |
| Platelet Count Low | Thrombocytopenia<br>e.g :Heparin /Liver disease /DIC / Massive transfusion |
| Platelet Count Normal | Platelet dysfunction |

## Q1 Abnormal vwf disease will cause :

A. Abnormal bleeding time
B. Abnormal healing of wounds
C. ristocetin rection
D. cofactor high

## Q2 Prolong Partial thromboplastin time means :

A. defect is in the common pathway
B. defect in factor 9
C. defect in factor 7

## Q3 Causes of disseminated intravascular coagulation:

A. Gram-positive septicemia
B. Acute promyelocytic leukemia
C. SLE

## Q4 Vwf in hemophilia a will be :

A. Normal
B. high
C. low

## Q5 Hemophilia b is deficiency in :

A. factor 8
B. vwf
C. factor 9

1- A
2-B
3-B
4-A
5-C

1) A patient was diagnosed with factor xiii deficiency what are the Laboratory test they done to come up with diagnosis ?:

- PT , APTT , Normal Bleeding time , Normal Platelet aggregation ,and fibrinogen level **are all normal**
- **Abnormal clot stability with five molar urea ( most important )**
- **Low Factor XIII level**

2) DIC what does it stand for and what is it called other than that and name 3 of it's causes

**D**isseminated **I**ntravascular **C**oagulation

- CONSUMPTION COAGULATIONPATHY
- DEFIBRINATION SYNDROME

**Causes**

Snake and invertebrate venoms,
Infections e.g (Gram-negative and meningococcal septicaemia)
Malignancy e.g (Acute promyelocytic leukaemia AML M3)

3)Main classification of vw disease :

- Partial quantitative deficency of vwf
- Qualitaive deficency in vwf
- Virtually complete deficency in vwf

4) Fibrin Degeneration Porducts (FDPS)is high in:

- D.I.C. most important
- Snake Bite
- Thrombolytic therapy
- Dysfibrinogenemia

# Thank you for checking our work

Now you can check a lecture out :D


Done by :

Shaima Alduaiji

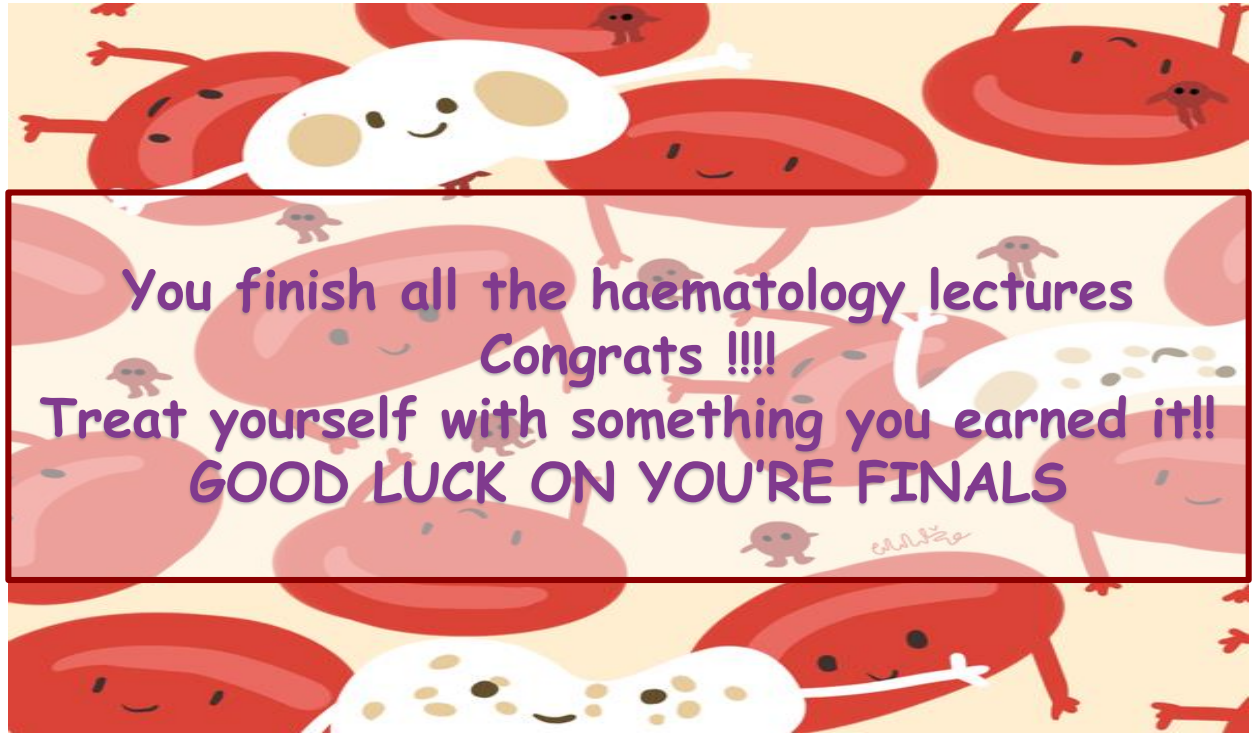
Lamyaa Althawadi

Hadeel B.Alsulami

Reviewed by:

Hadeel B.Alsulami

Abdullah M. Albasha


دعاء بعد المذاكرة :

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت، فرده لي عند حاجتي اليه أنك على كل شيء قدير، وحسبنا الله ونعم الوكيل)