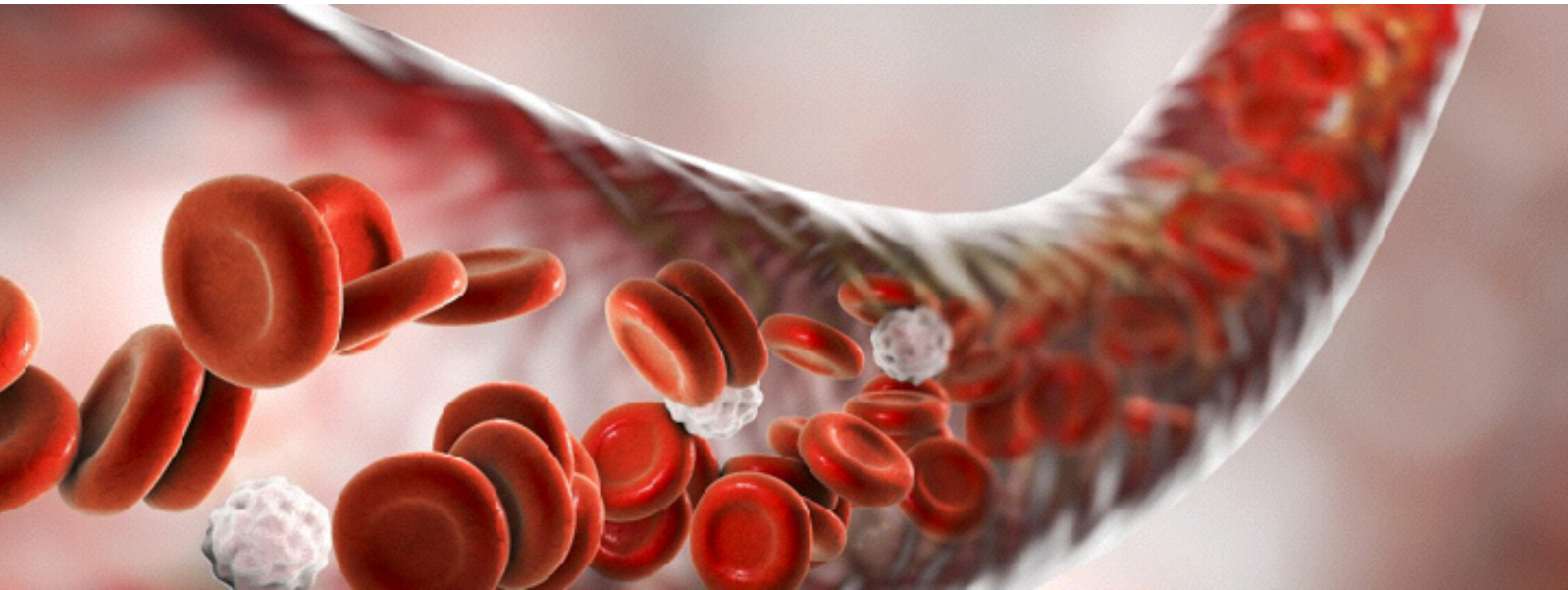




# ***Bleeding Disorder for Medical Student***



**MAKE IT  
EASY**

**Apichat Photi-A, MD.**

*Division of Hematology & Oncology, Department of Pediatrics  
Phramongkutklao Hospital*



# Outlines



Basic Hemostasis

Case discussion

Conclusion

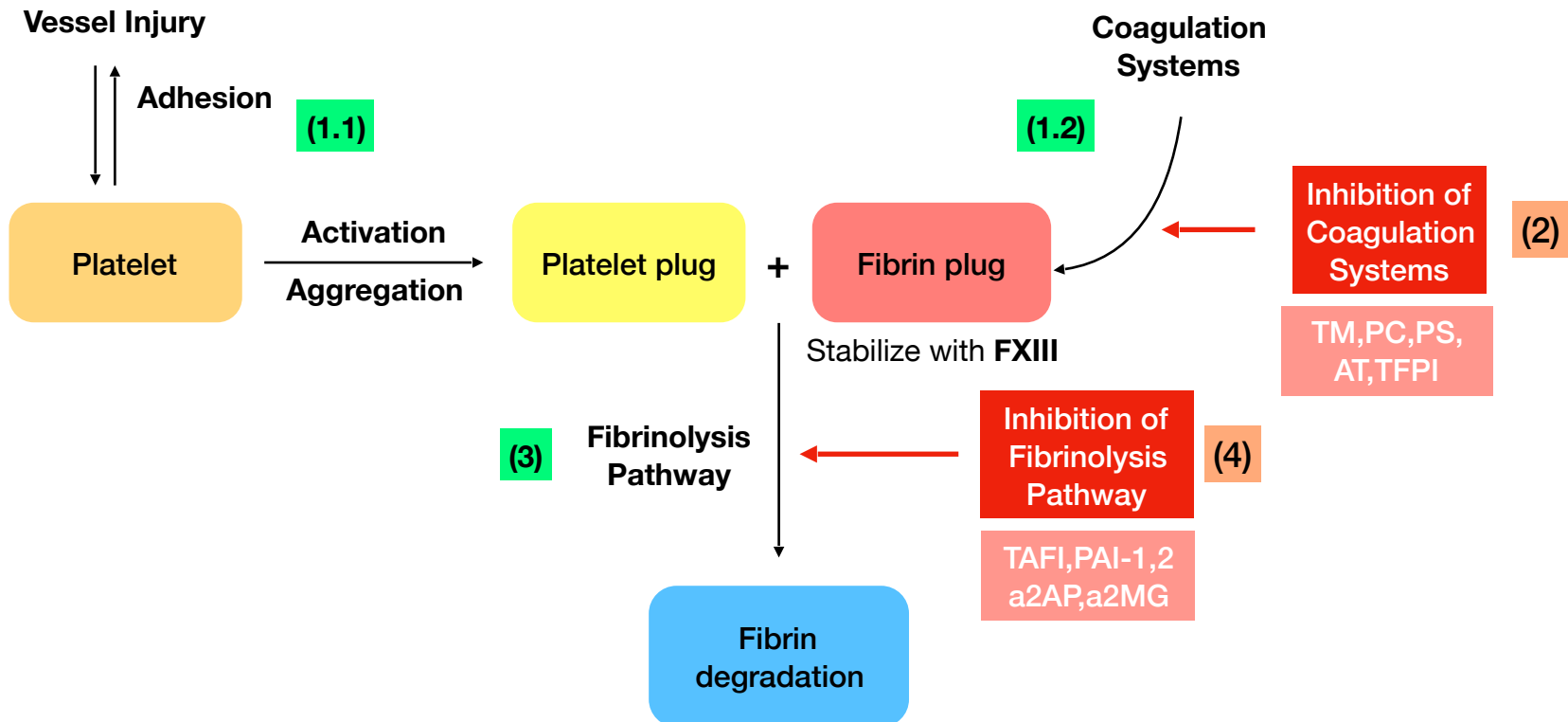


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# Normal Hemostasis





# Case #01



**Case :** A 3 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable

## Physical examination

Multiple scattered **bruises** over the extremities and trunk.

Petechiae were seen on these areas and face. No splenomegaly and lymphadenopathy.

Complete neurological examinations were normal





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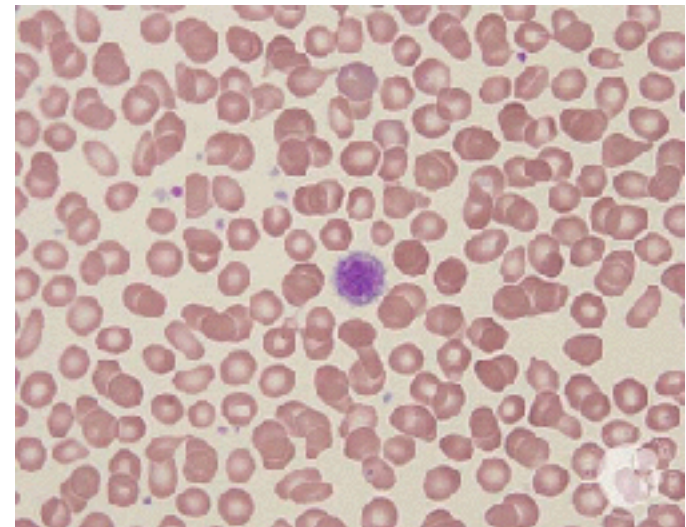
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Complete neurological examinations were normal

Investigations			
Hb	10 g/dl	WBC	5,300
Hct	29%	PMN	44
MCV	65 fl	Lymph	39
MCH	29.6 pg	Mono	14
MCHC	35.9 g/dl	Plt	348,000
RDW	17%	MPV	13.2 fl





# Case #02



**Case :** A 8 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable

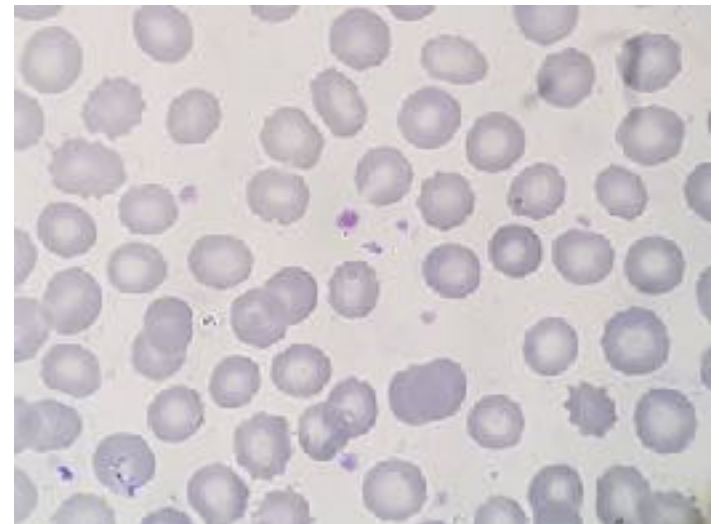
## Physical examination

Multiple scattered **bruises** over the extremities and trunk.

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Complete neurological examinations were normal

Investigations			
Hb	12.6 g/dl	WBC	9,200
Hct	38%	PMN	54
MCV	83 fl	Lymph	44
MCH	23.6 pg	Mono	2
MCHC	33.1 g/dl	Plt	176,000
RDW	14%	MPV	12.2 fl





# Case #03



**Case :** A 4 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable

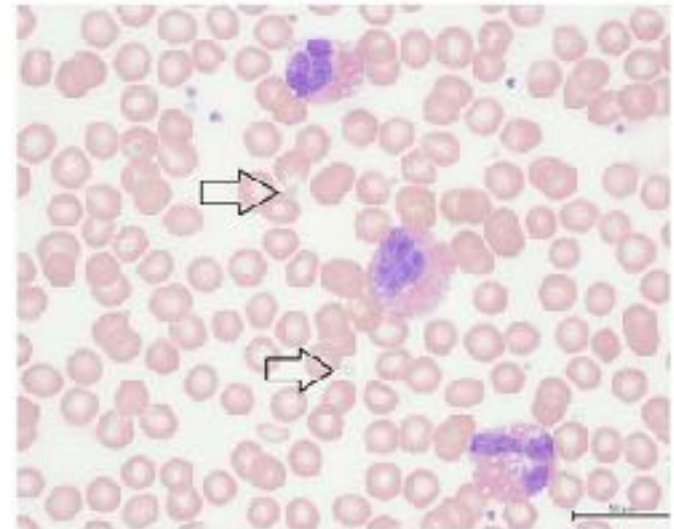
## Physical examination

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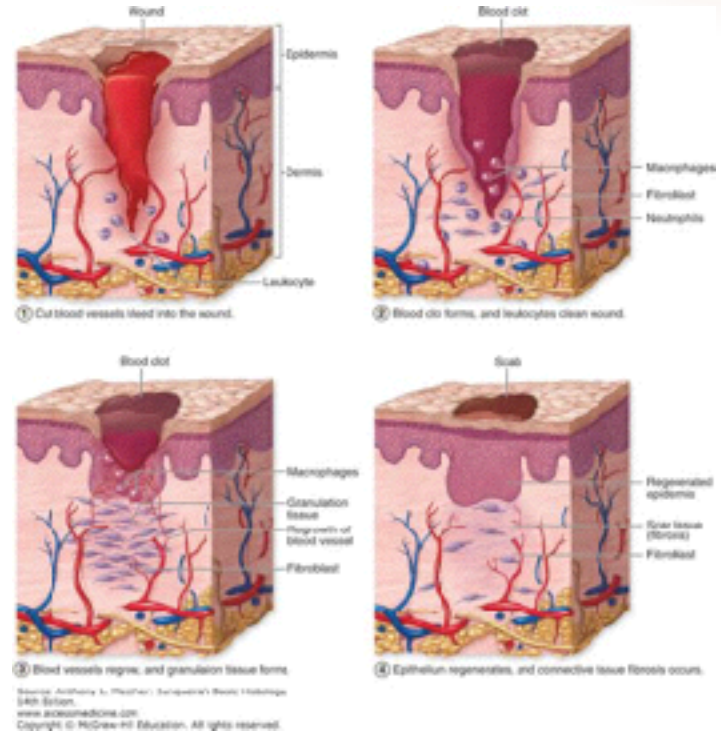
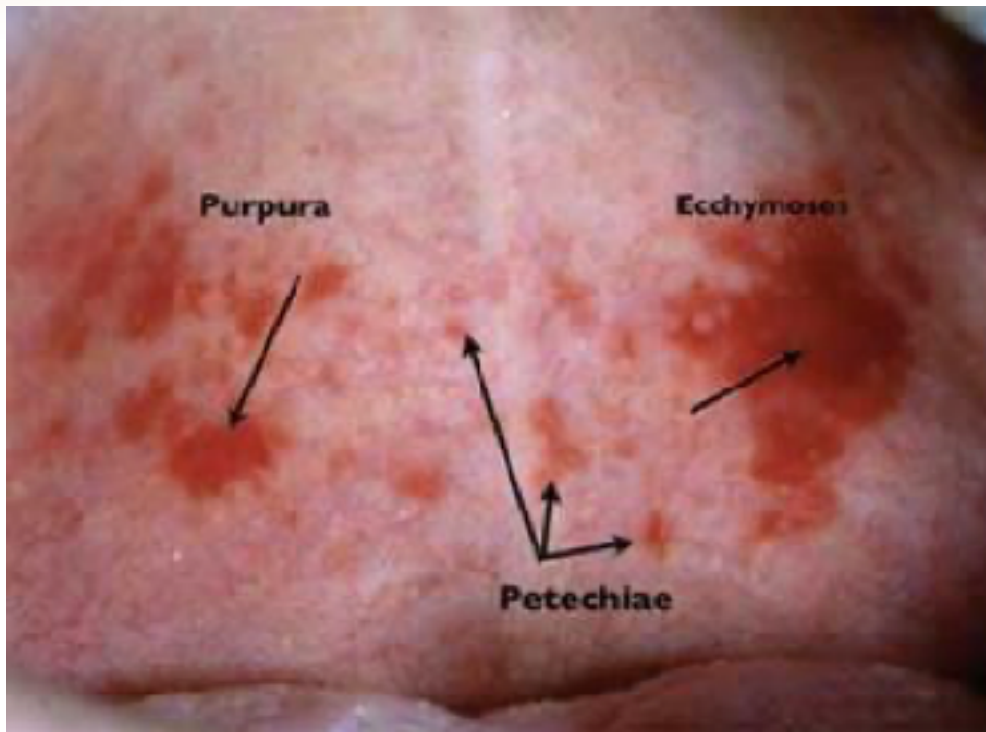
Complete neurological examinations were normal

Investigations			
Hb	11.6 g/dl	WBC	10,660
Hct	33%	PMN	34
MCV	93 fl	Lymph	40
MCH	23.6 pg	Eosin	22
MCHC	34.1 g/dl	Plt	108,000
RDW	12%	MPV	11.2 fl





# Skin Lesions



**Petechiae** : Red/purple dots that represent bleeding from capillaries

**Ecchymosis** : Occur deeper in the dermal layers

**Purpura** : Petechiae that have coalesced and become bigger





# *Hemostatic Disorder*



	Primary Hemostatic Disorder	Secondary Hemostatic Disorder
<b>Prototypic disorders</b>	thrombocytopenia platelet function defect von Willebrand disease	hemophilia
<b>Bleeding</b>	immediate	delayed
<b>Petechiae</b>	yes	no
<b>Hemarthrosis</b>	no	yes
<b>Intramuscular Hematoma</b>	uncommon	common
<b>Epistaxis</b>	common	uncommon
<b>Menorrhagia</b>	common	uncommon



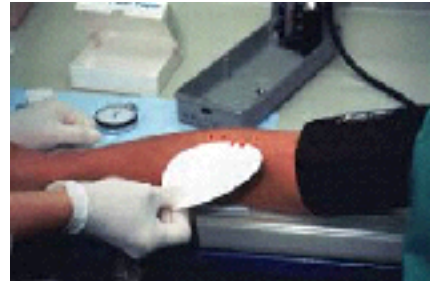
# Lab in Hemostasis



CBC+PBS

Platelet number and morphology

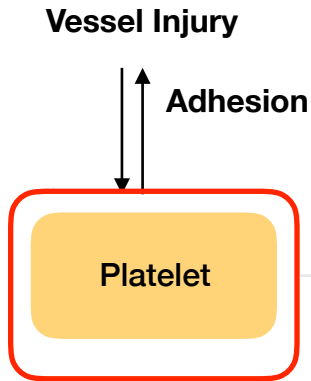
Bleeding time



Normal < 9 mins

Inhibition of Coagulation Systems

(3)



(1)

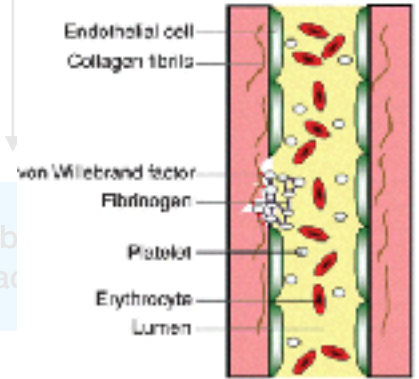
PFA-100

Membrane closure time response to ADP and Epinephrine

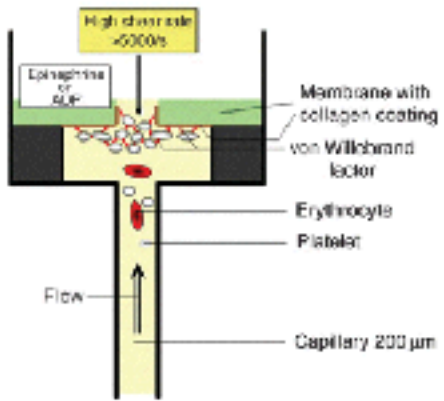
Required... Hct 25-50  
Plt > 50k

Fibrin plug

In vivo haemostasis



PFA-100<sup>®</sup>

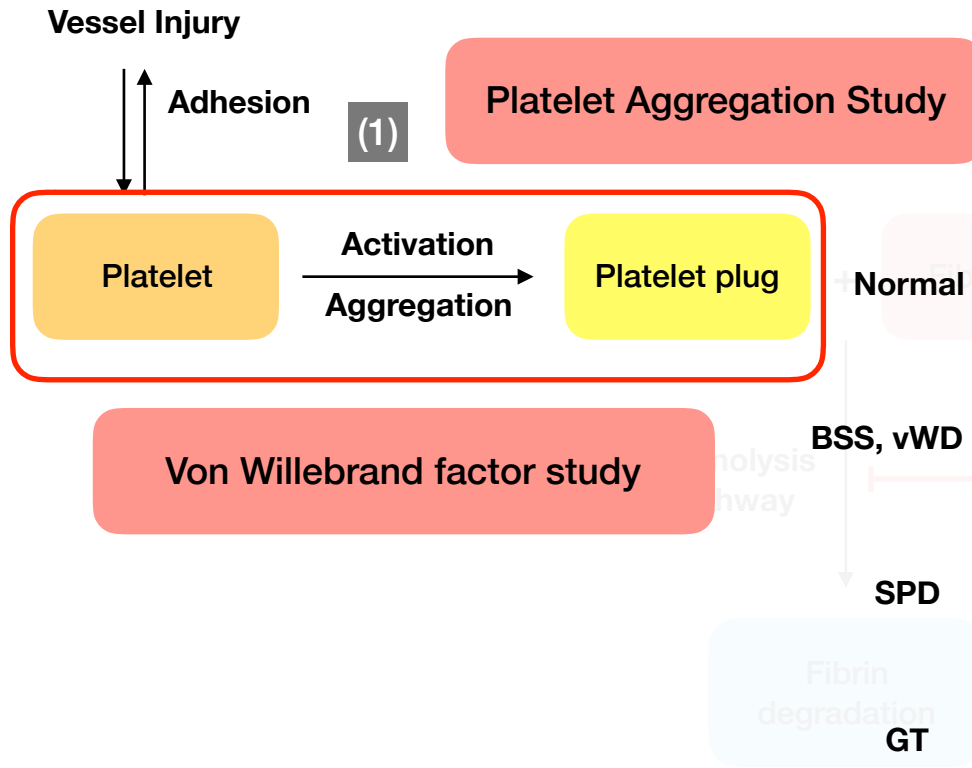




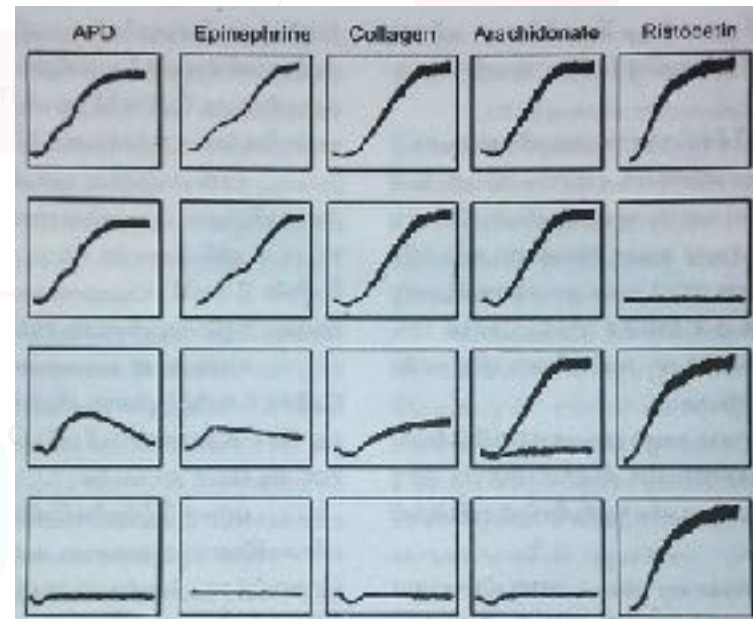
# Lab in Hemostasis



## Platelet Aggregation Study



Need to control the affect factor  
 Detect : Adhesion - Activation - Aggregation

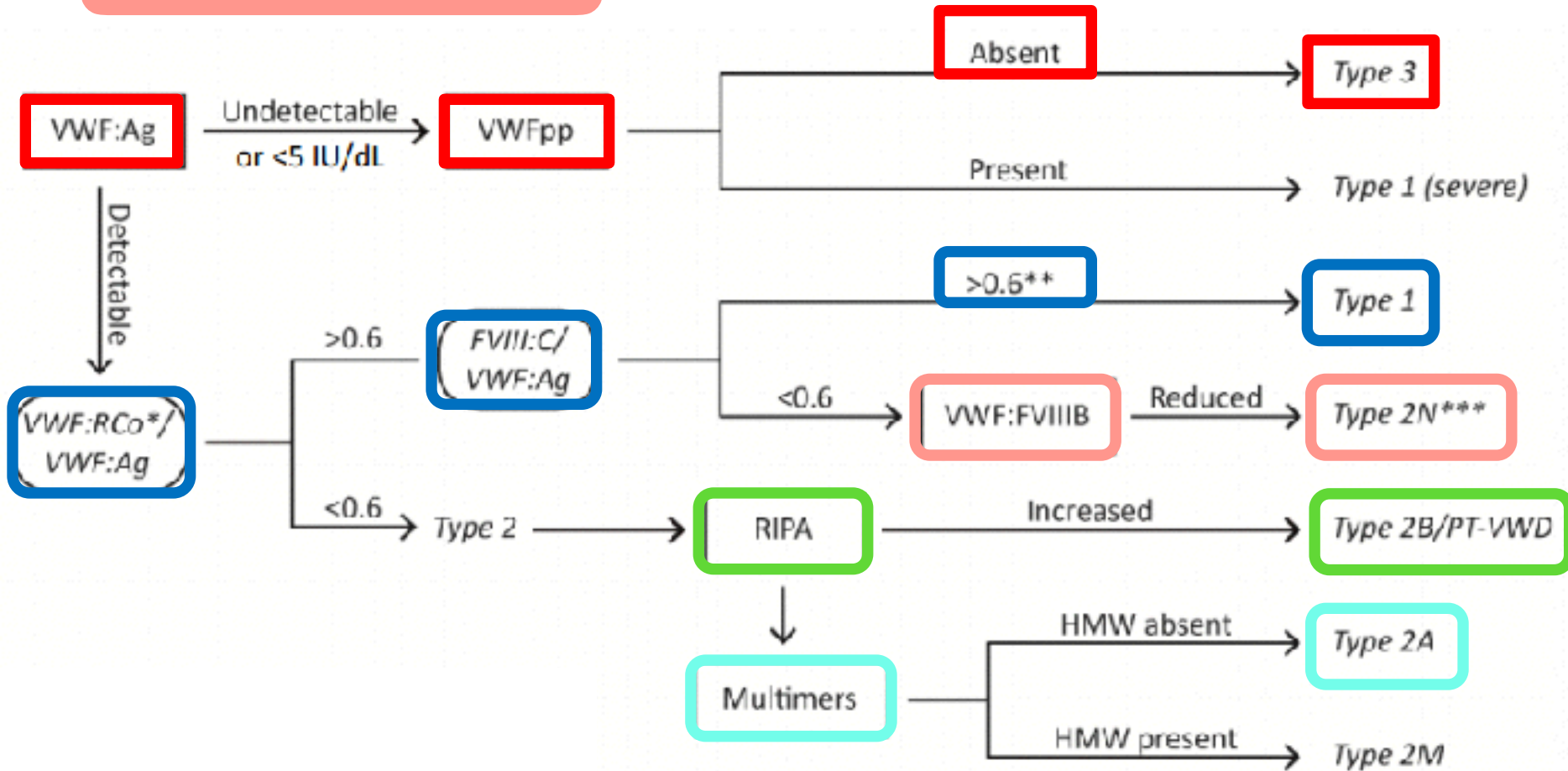




# Lab in Hemostasis



## Von Willebrand factor study





# Case #01



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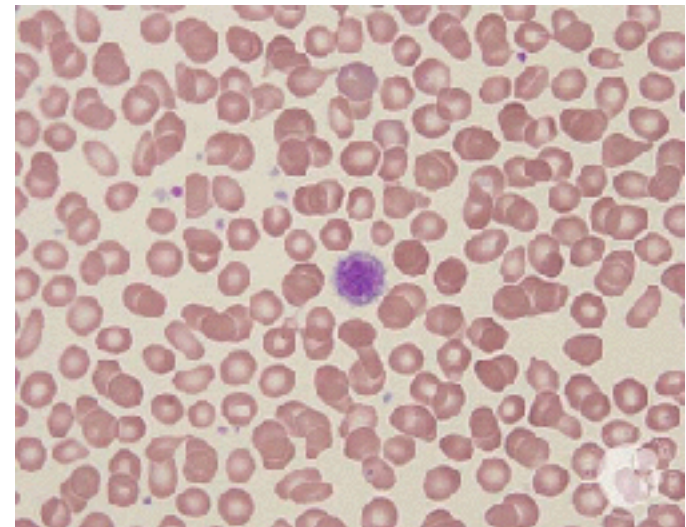
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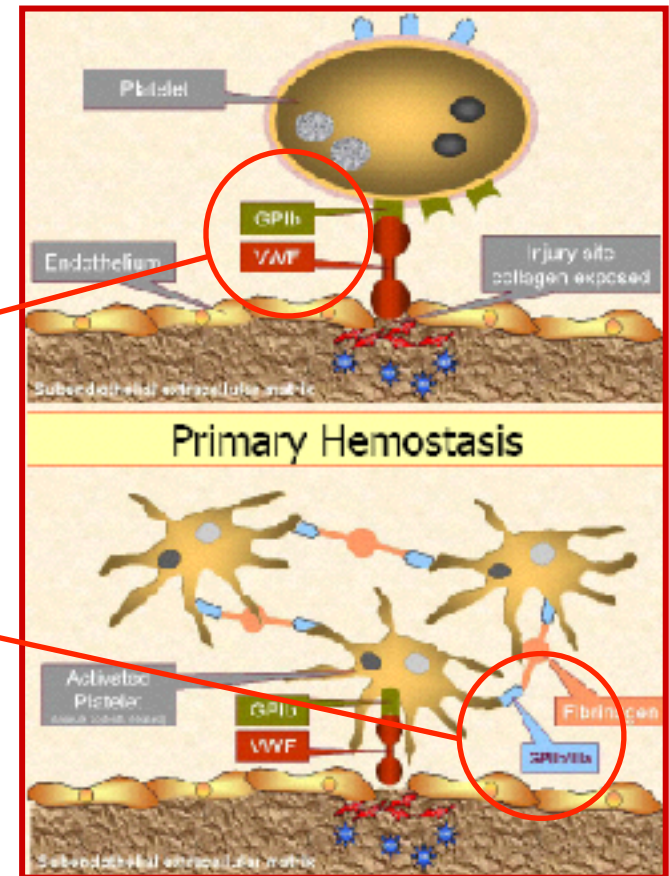
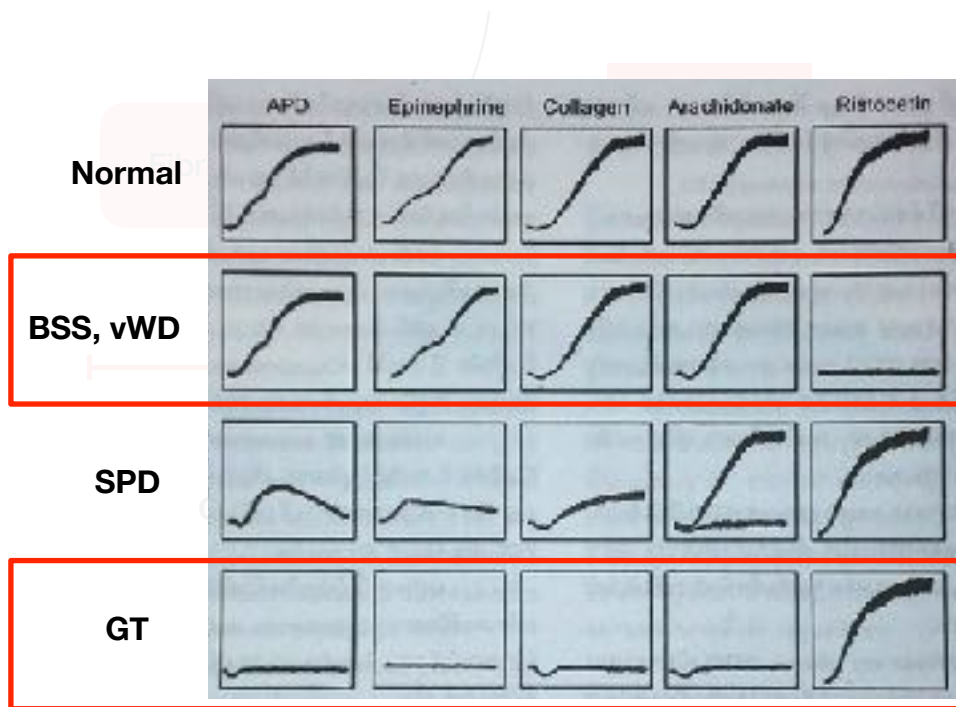




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# ***Bernard-Soulier Syndrome***



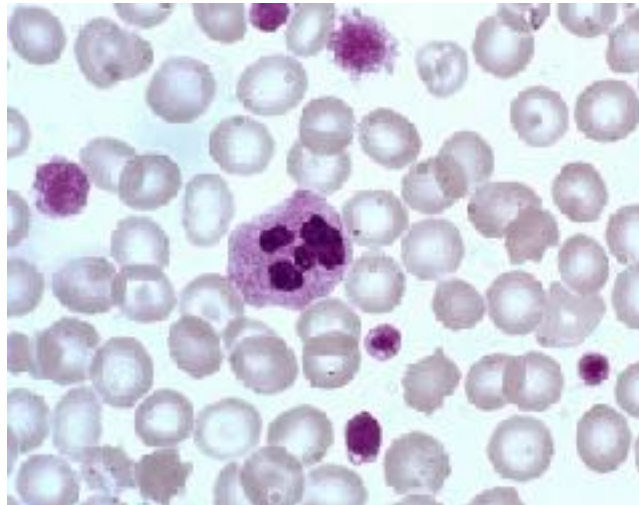
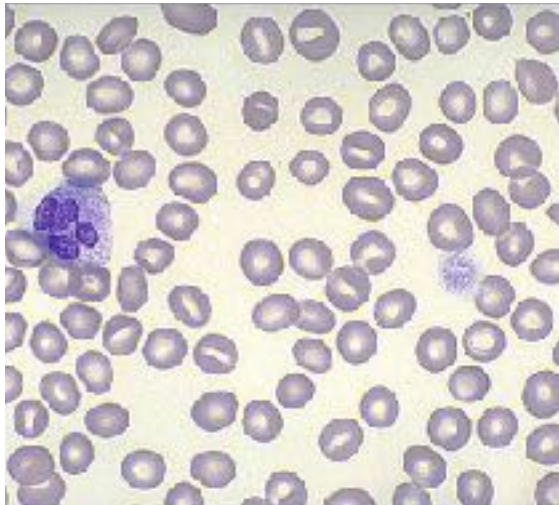
Autosomal recessive inheritance (consanguinity frequent)

Deficiency or abnormality of **GPIba**, **GPIb $\beta$** , **GPIX** (platelet adhesion)

**Prolonged bleeding time**

Normal platelet aggregation in response to ADP, epinephrine, and collagen

Abnormal or absent agglutination in response to ristocetin





# Glanzmann Thrombasthenia



Autosomal recessive inheritance (high rate consanguinity)

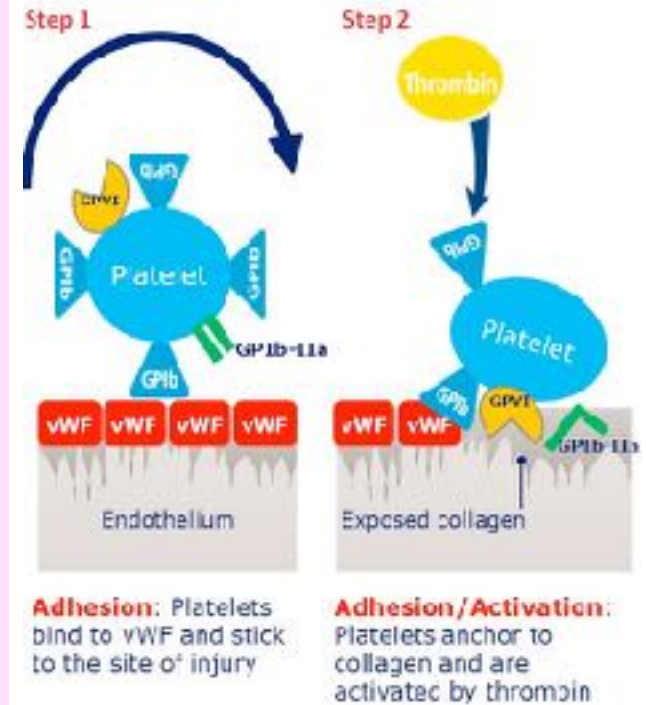
Severe mucocutaneous bleeding starting in infancy

Deficiency or abnormality of **GPIIb/IIIa (platelet  $\alpha$ IIb $\beta$ 3 integrin)**

Normal platelet count and morphology and ristocetin-induced platelet agglutination

**Absent platelet aggregation in response to ADP, epinephrine, collagen**

Treatment: local pressures, DDAVP, fibrinolytic inhibitors, platelet transfusion, FVIIa



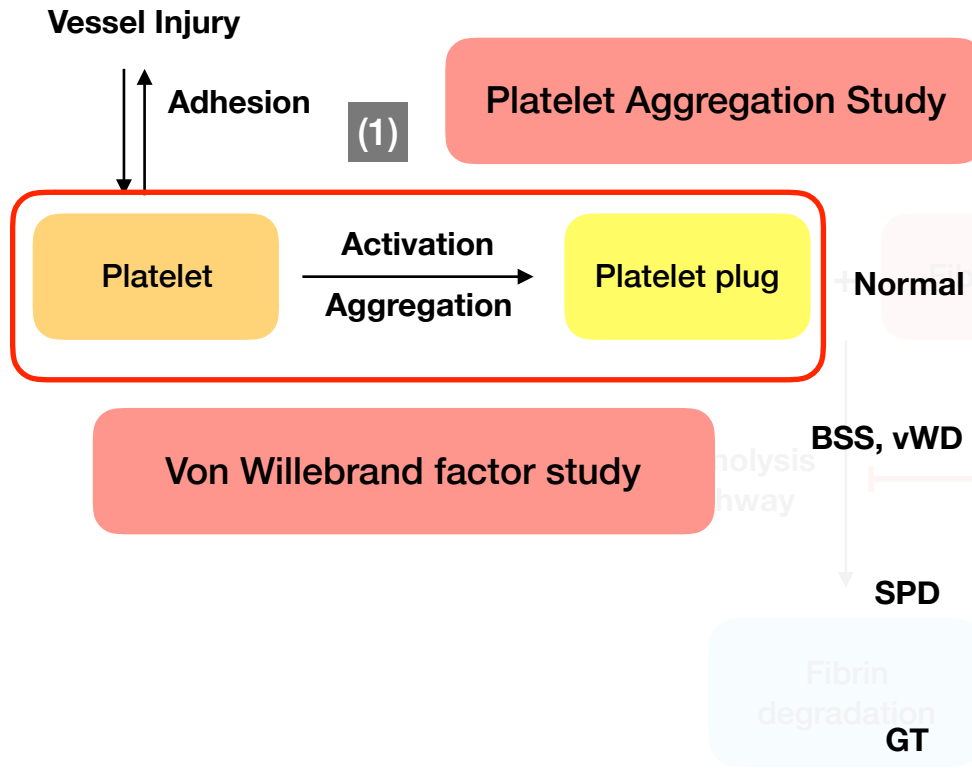




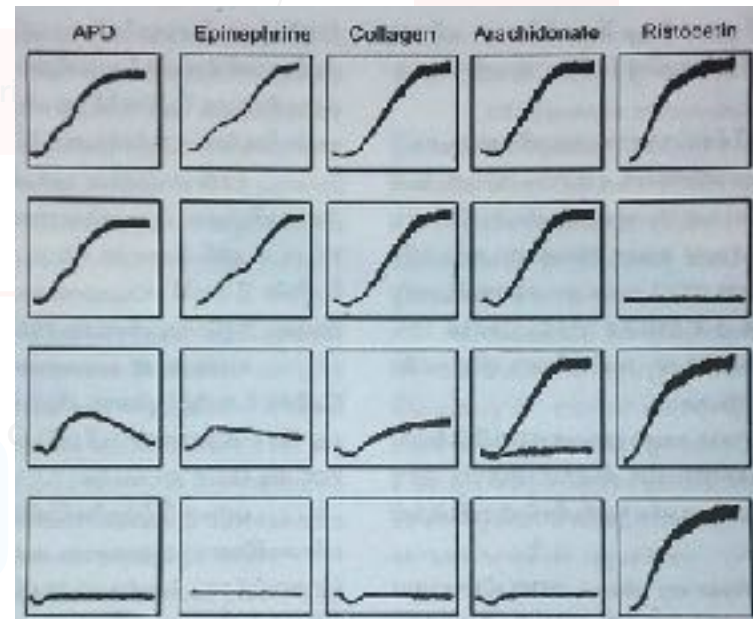
# Lab in Hemostasis



## Platelet Aggregation Study



Need to control the affect factor  
 Detect : Adhesion - Activation - Aggregation





# Case #02



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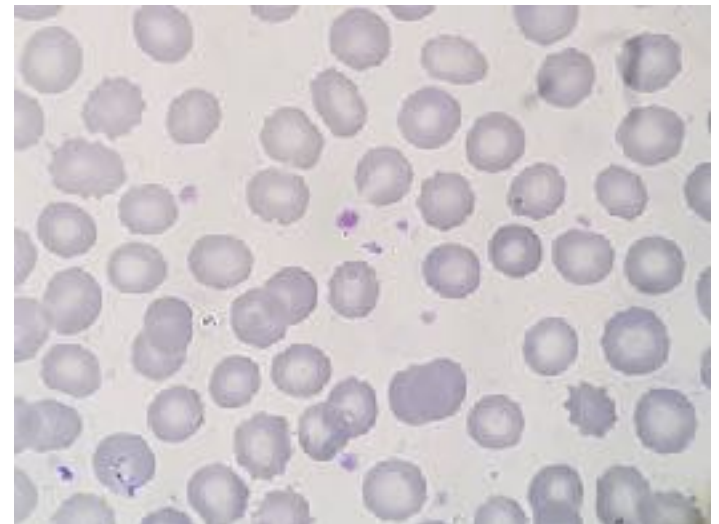
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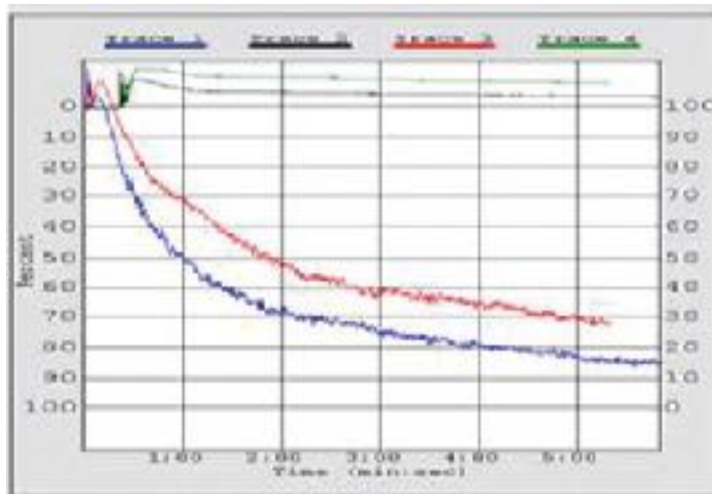




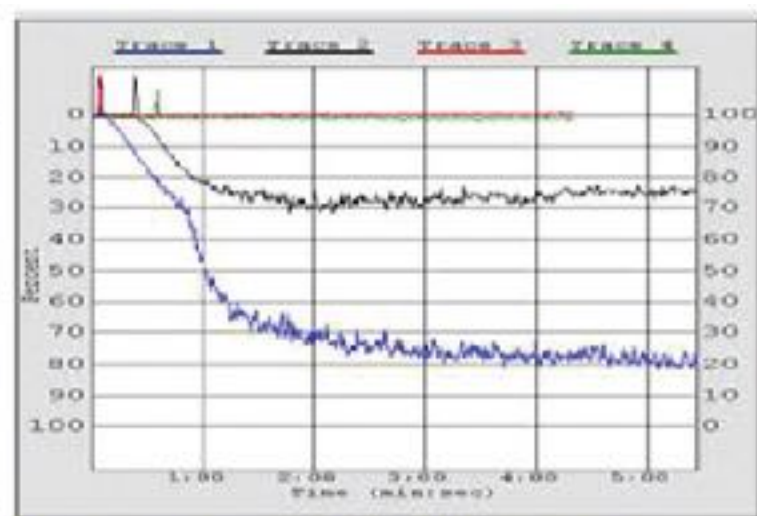
# Case #02



**Case :** A 8 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable



**Control: ADP (10 $\mu$ m/l) – 86%**  
**Test: ADP (10 $\mu$ m/l) – 0%**  
**Control: ADP(2.5 $\mu$ m/l) – 74%**  
**Test: ADP (2.5 $\mu$ m/l) – 0%**



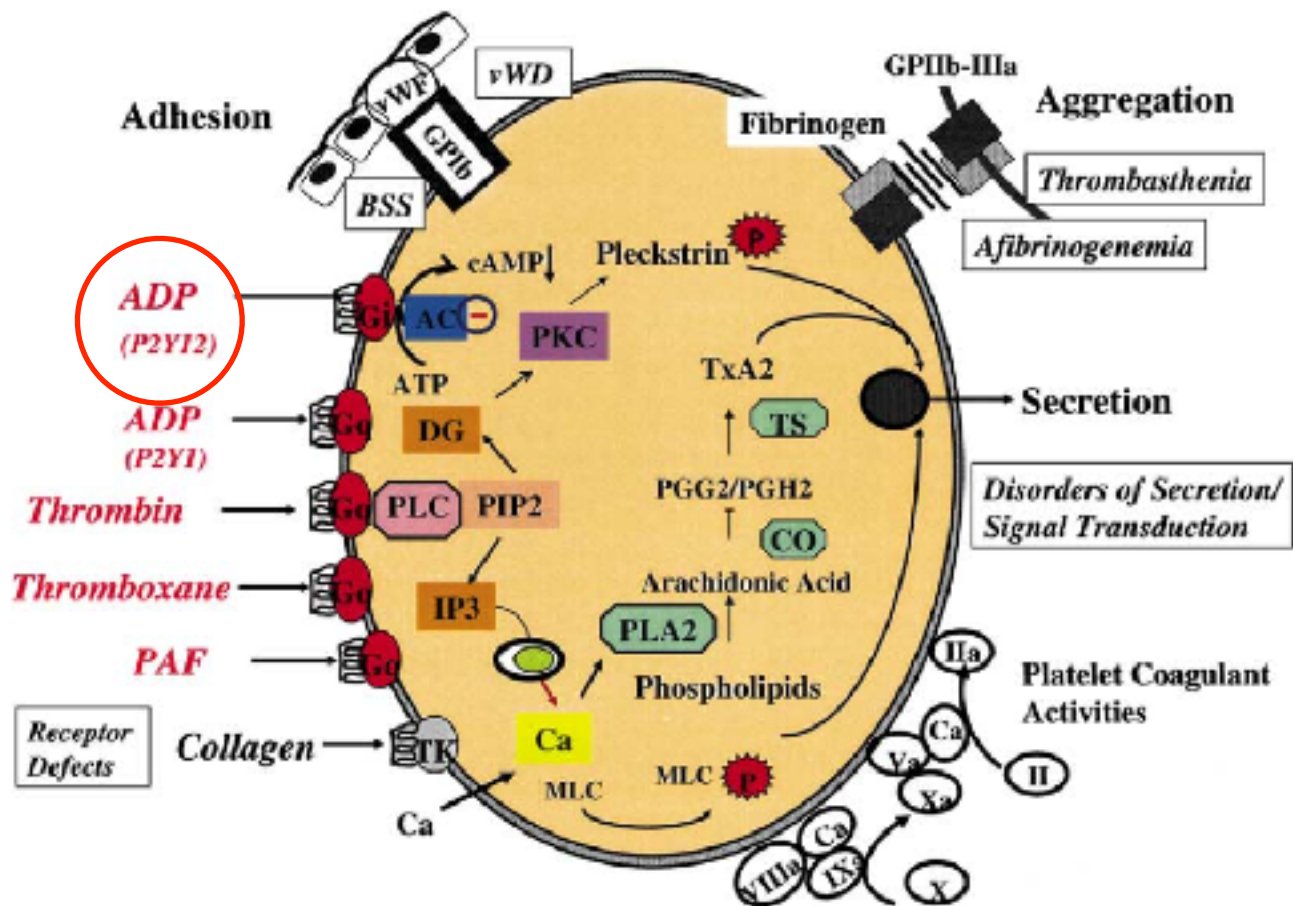
**Control: Ristocetin(1.25mg/ml) – 81%**  
**Test: Ristocetin (1.25mg/ml) – 32%**  
**Control: Ristocetin (0.25mg/ml) – 1%**  
**Test: Ristocetin (0.25mg/ml) – 0%**



# Case #02

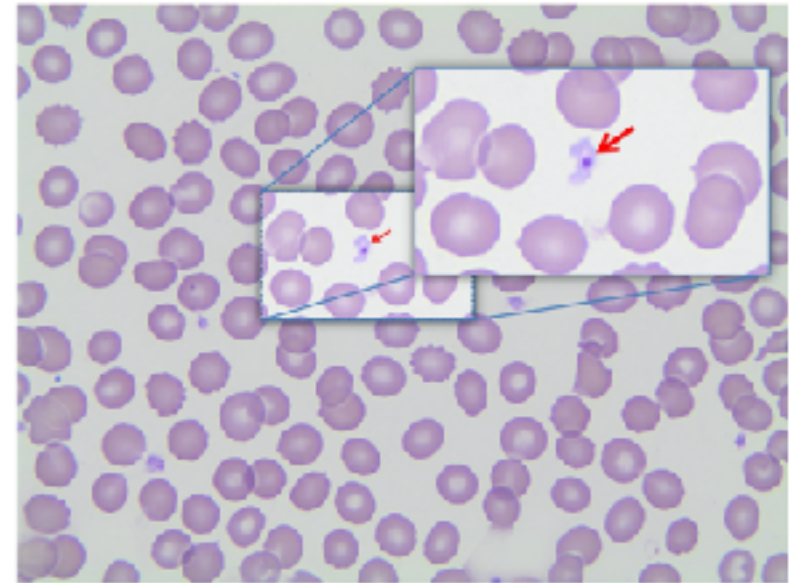
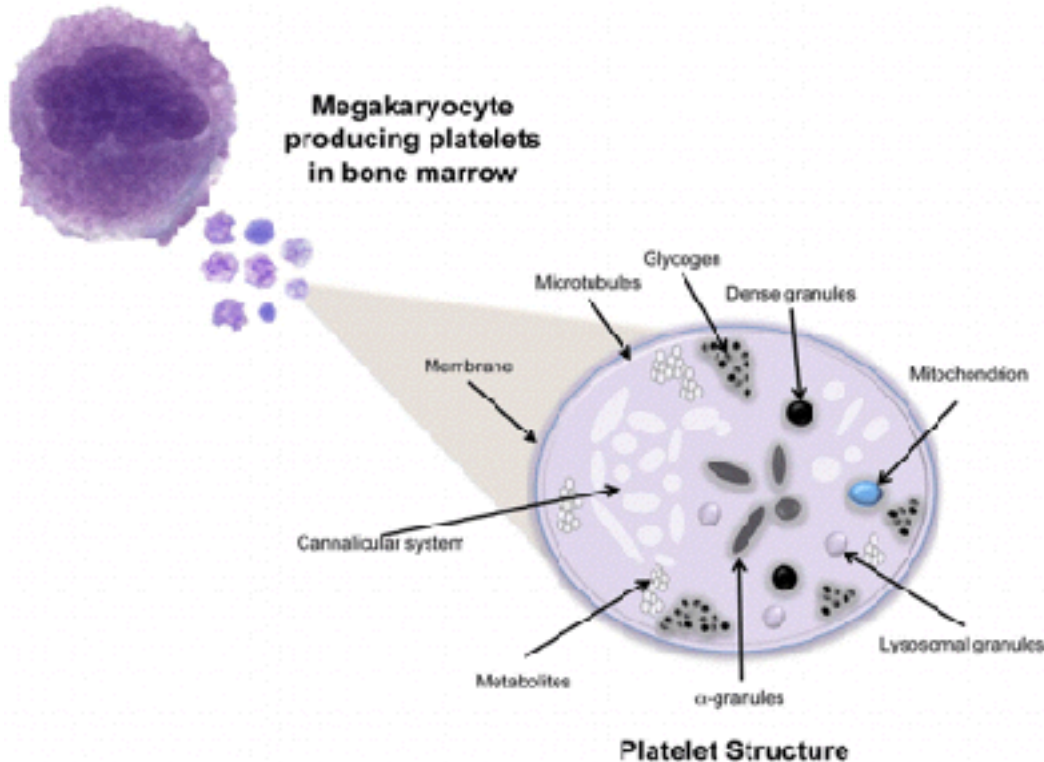


**Case :** A 8 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable





# Storage Pool deficiency



**Jacobsen/Paris-Trousseau Syndrome**

Partial deletion of chromosome 11q23

Defects in secondary aggregation or granules

Bleeding is usually mild to moderate but can be exacerbated by aspirin



# Case #03



**Case :** A 4 years old boy was noted to have bruises over his extremities off and on. He presented with several episodes of epistaxis. Other history was unremarkable

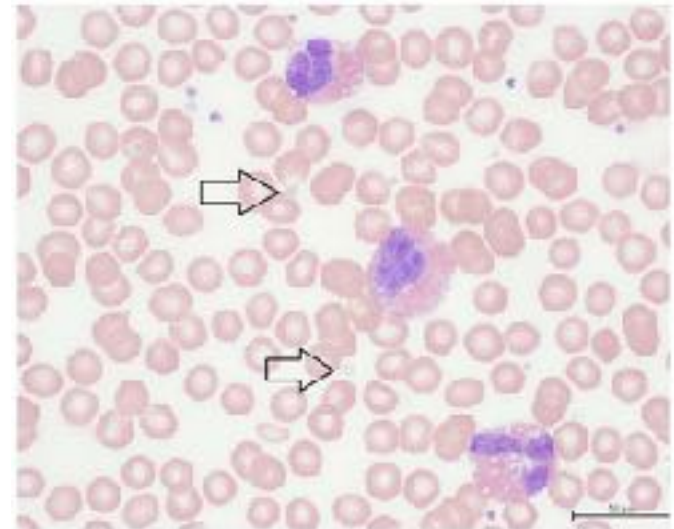
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Complete neurological examinations were normal

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Hb	11.6 g/dl	WBC	10,660
Hct	33%	PMN	34
MCV	93 fl	Lymph	40
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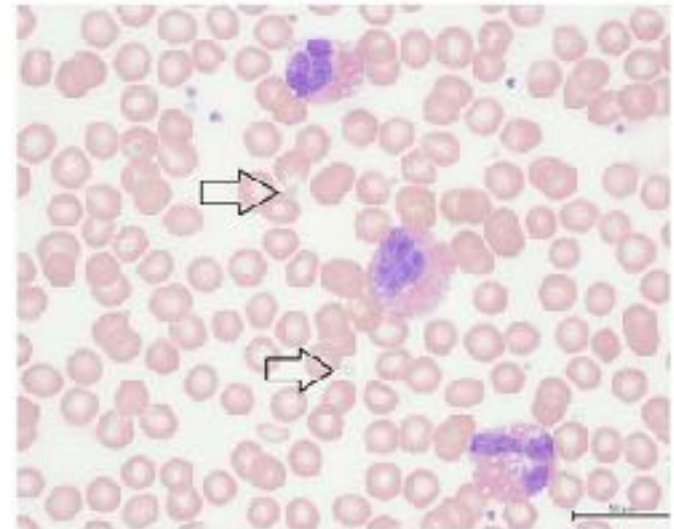
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MCHC	34.1 g/dl	Plt	108,000
RDW	12%	MPV	11.2 fl





# Acquired Platelet Dysfunction with Eosinophilia (APDE)



Acquired

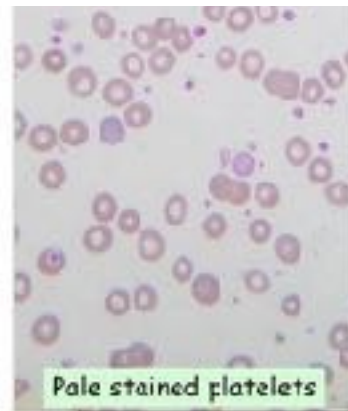
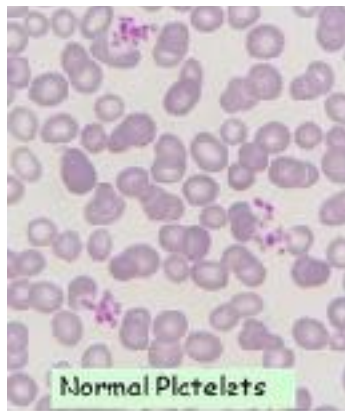
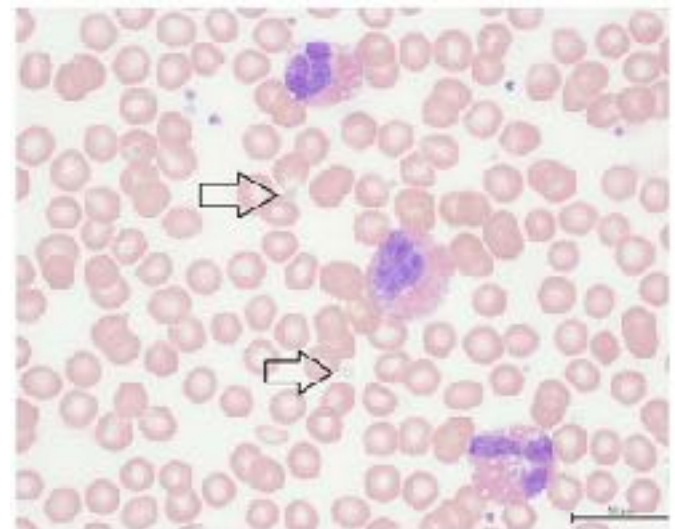
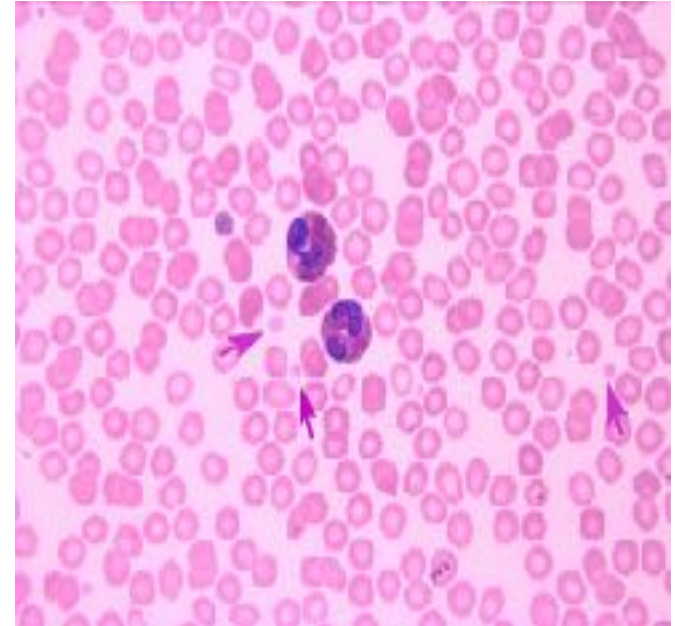
Normal Platelet count with eosinophilia

Absent platelet aggregation in response to **ADP, epinephrine, collagen**

Normal ristocetin-induced platelet agglutination

Treatment: **local pressures, platelet transfusion**

Resolve in 6-12 mo.







# Lab in Hemostasis

CBC+PBS

Platelet number and morphology

Bleeding time



Normal < 9 mins

Systems

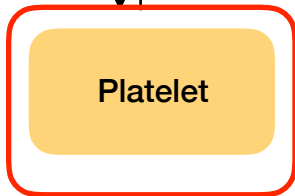
Inhibition of Coagulation Systems

(3)

Vessel Injury

Adhesion

(1)



Activation  
Aggregation

Platelet plug

PFA-100

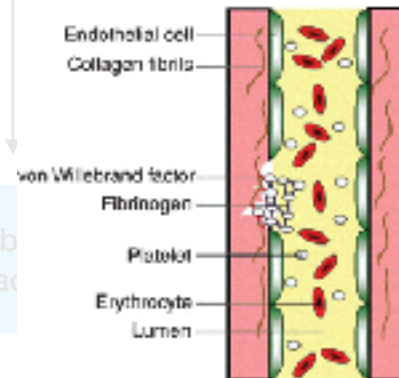
Membrane closure time response to ADP and Epinephrine

Required... Hct 25-50  
Plt > 50k

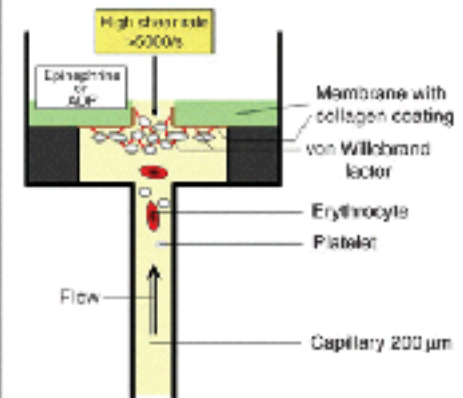
+

Fibrin plug

In vivo haemostasis

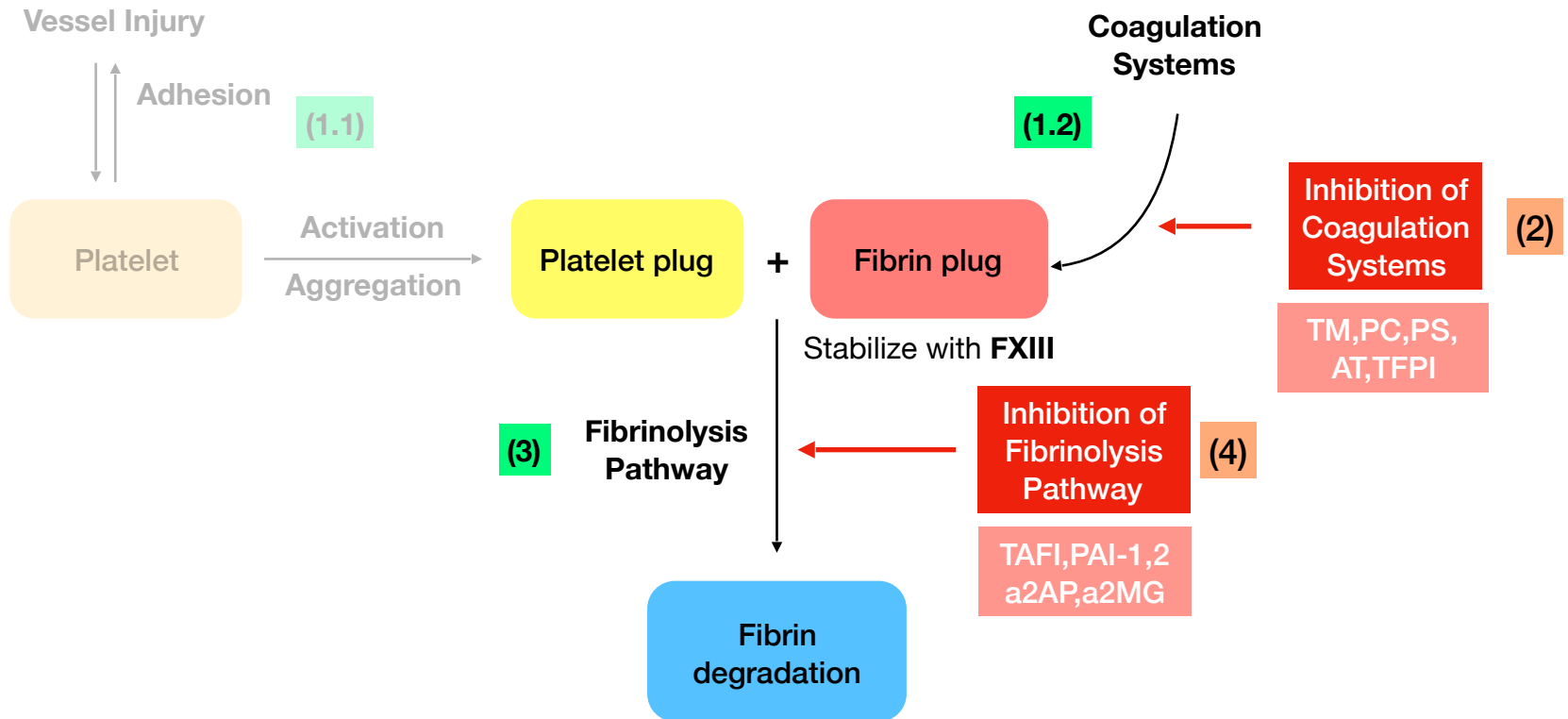


PFA-100®



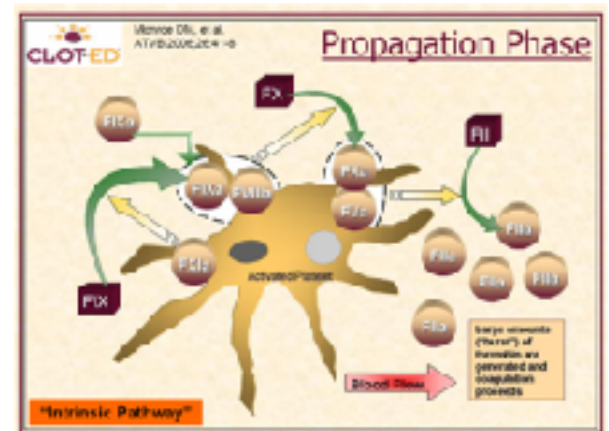
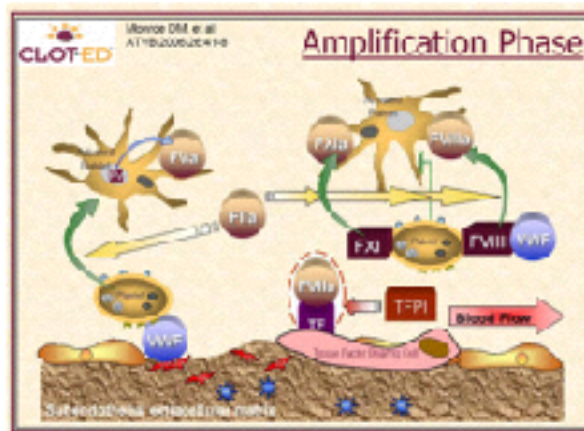
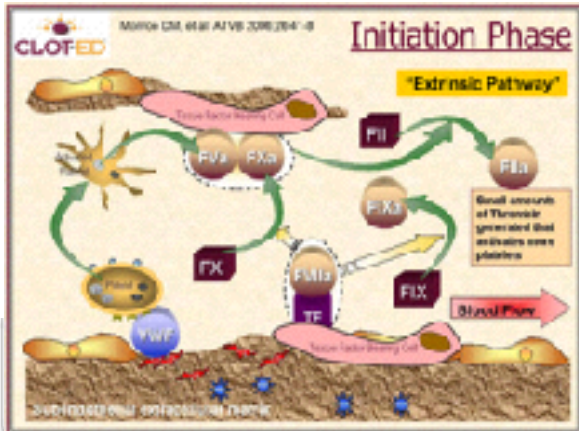
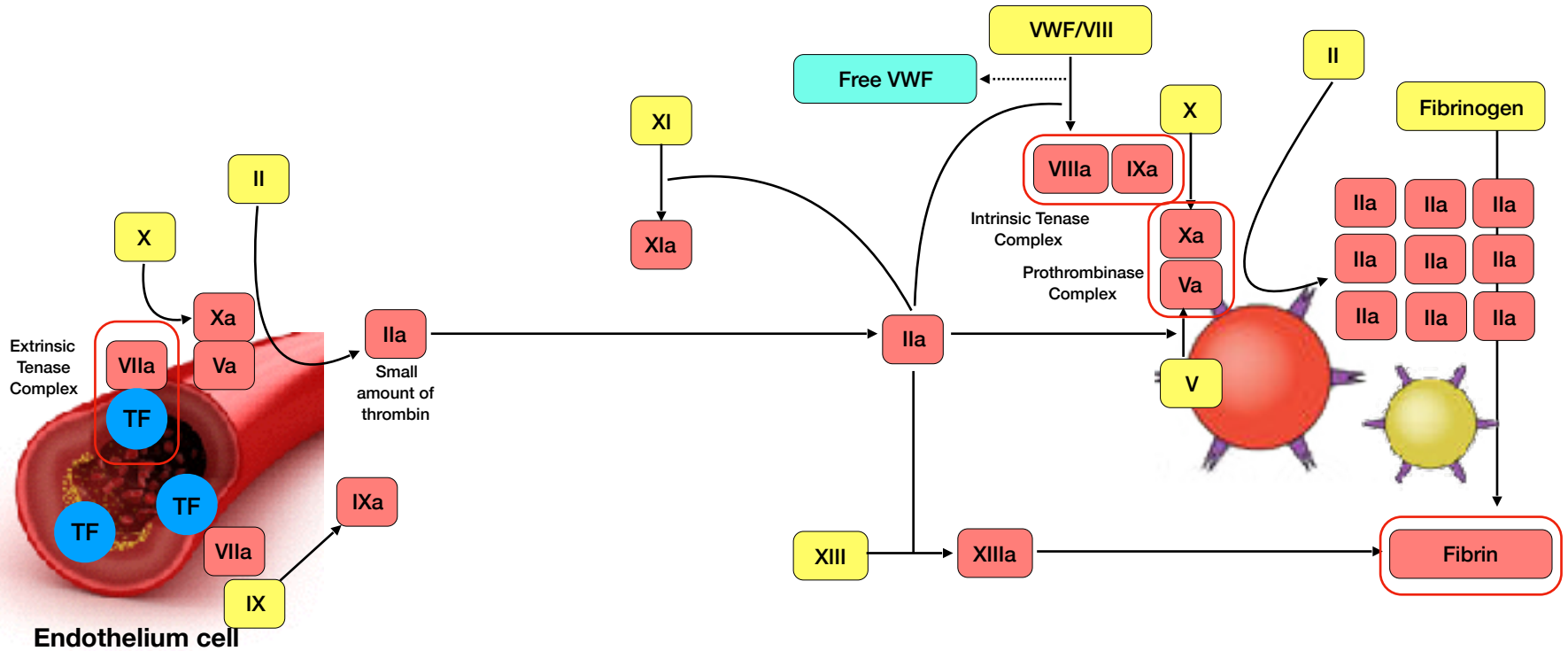


# Lab in Hemostasis





# Cell-based Model of Coagulation





# Case #04



**Case :** A 2-year-old boy who had fallen from upstairs. Then he developed drowsiness, and soft tissue swelling at right frontal area.

Past history : There was only circumcision without complications.

Family history : Negative for bleeding disorder

## Physical examination

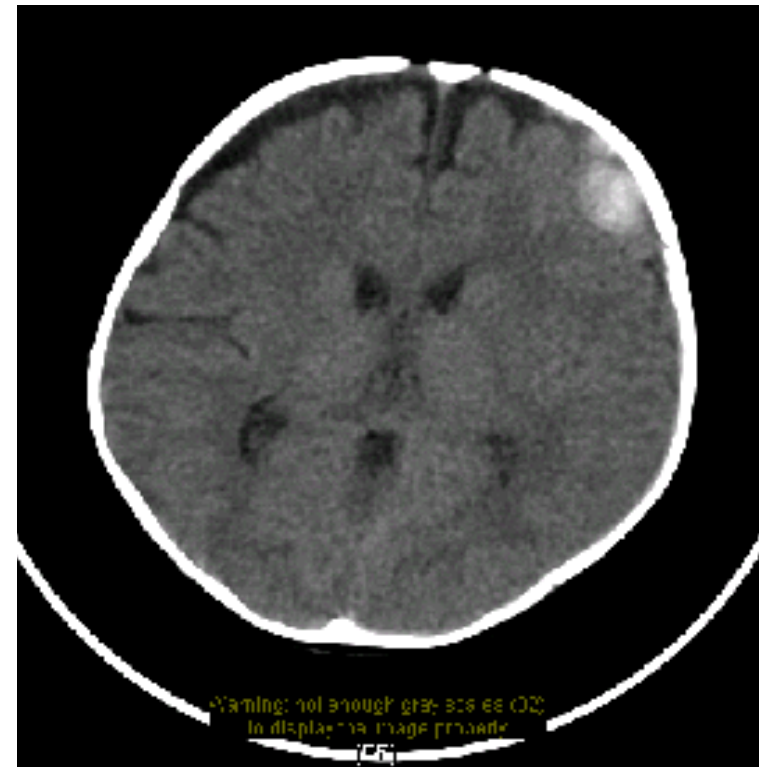
V/S : WNL

HEENT :swollen at right frontal and face area

Extremities : No bruises over extremities

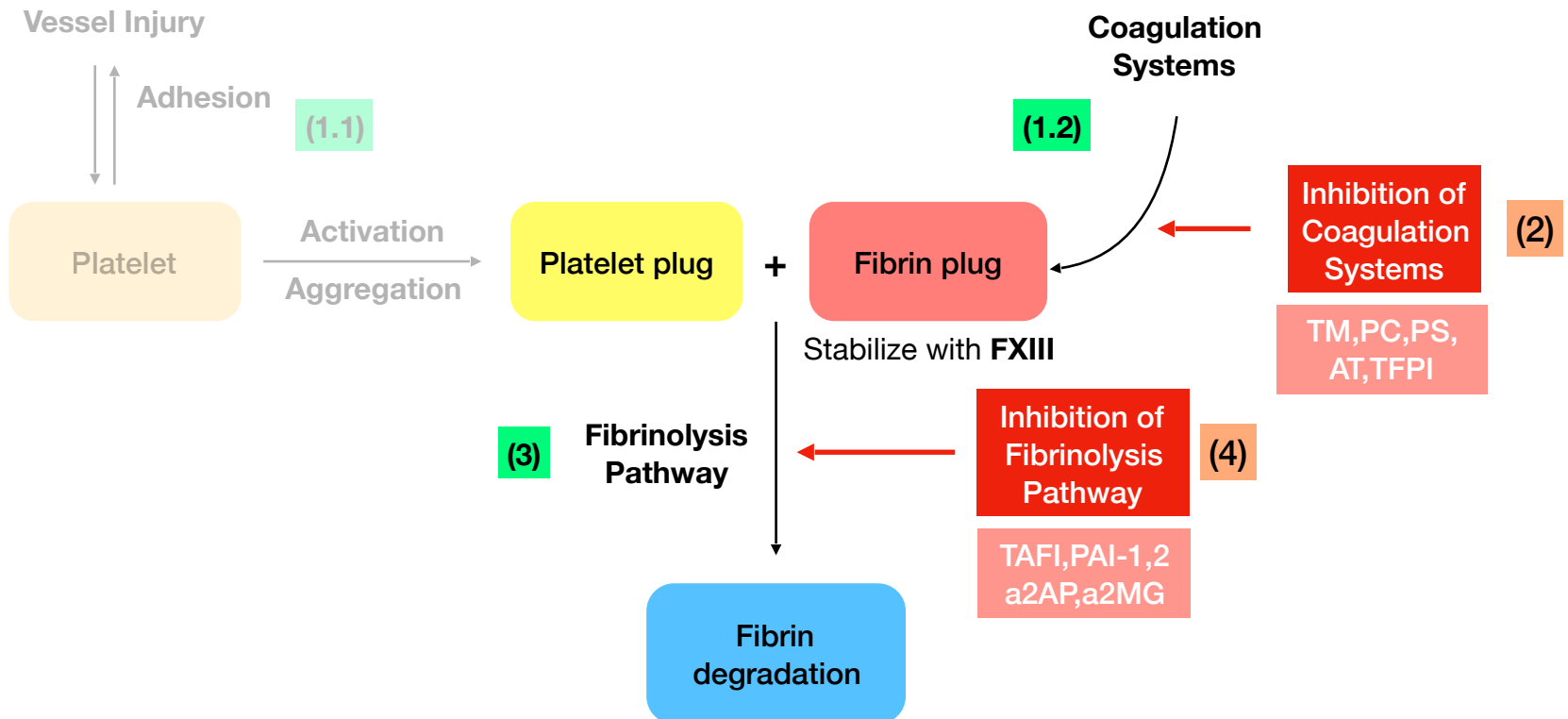
Neurological examination : Drowsiness

Sensory & motor : WNL





# Lab in Hemostasis





# Case #04



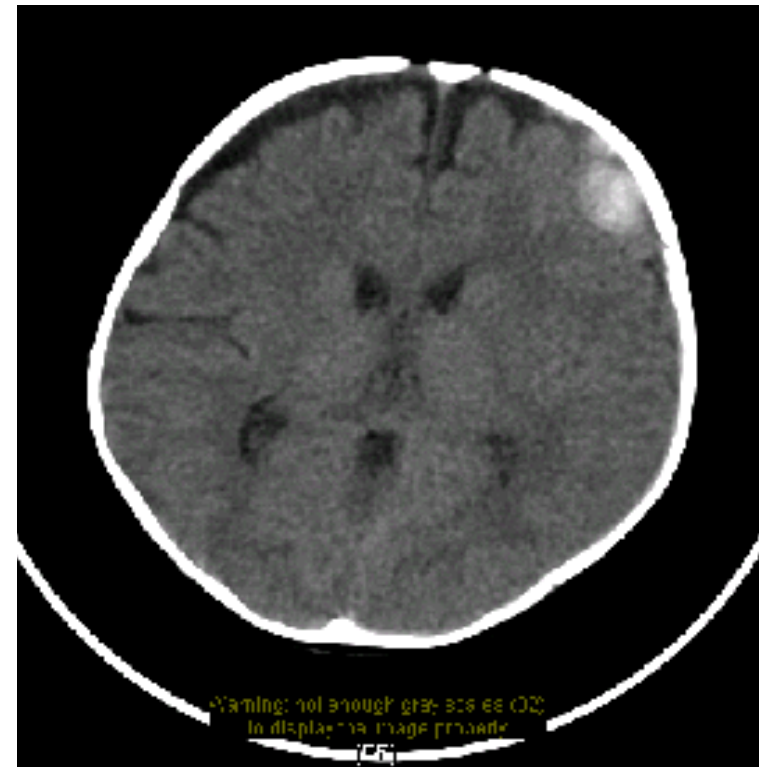
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Hct	37%	PMN	36
MCV	83 fl	Lymph	62
MCH	24.6 pg	Eosin	2
MCHC	35.1 g/dl	Plt	360,000
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# Case #04



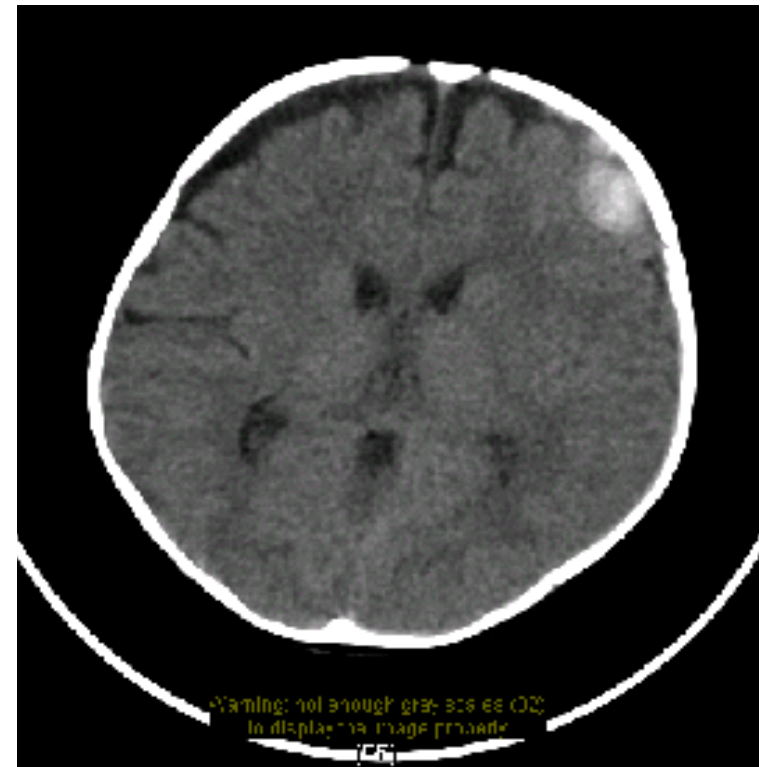
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MCV	83 fl	Lymph	62
MCH	24.6 pg	Eosin	2
MCHC	35.1 g/dl	Plt	360,000
RDW	13%	MPV	9.4 fl
aPTT	40 sec	(25-35 sec)	
PT	12 sec	(12-15 sec)	
TT	11 sec	(10-20 sec)	





# Case #04



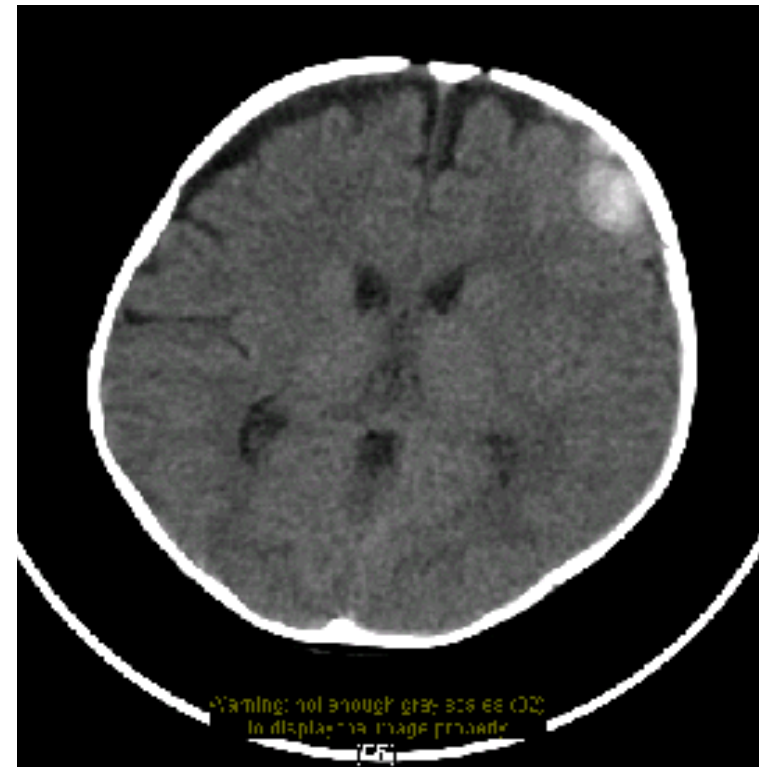
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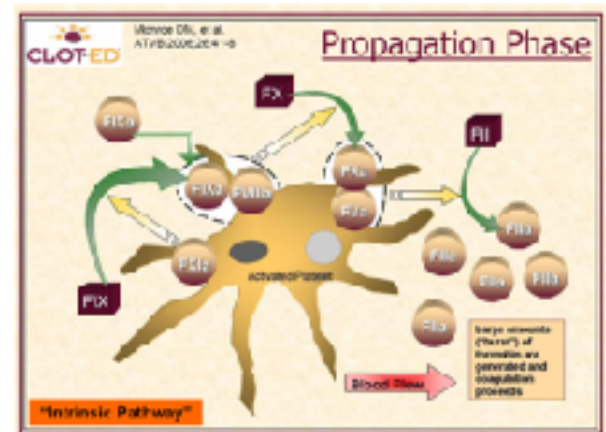
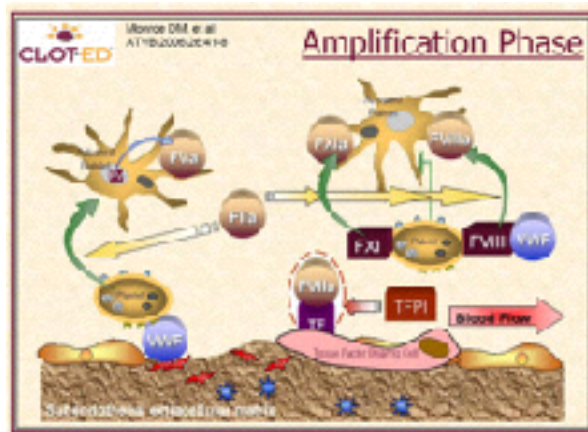
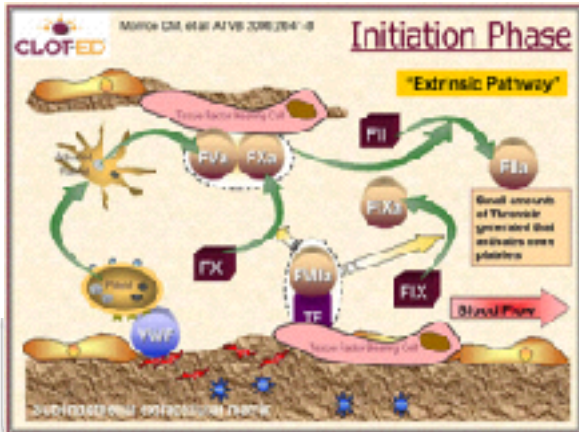
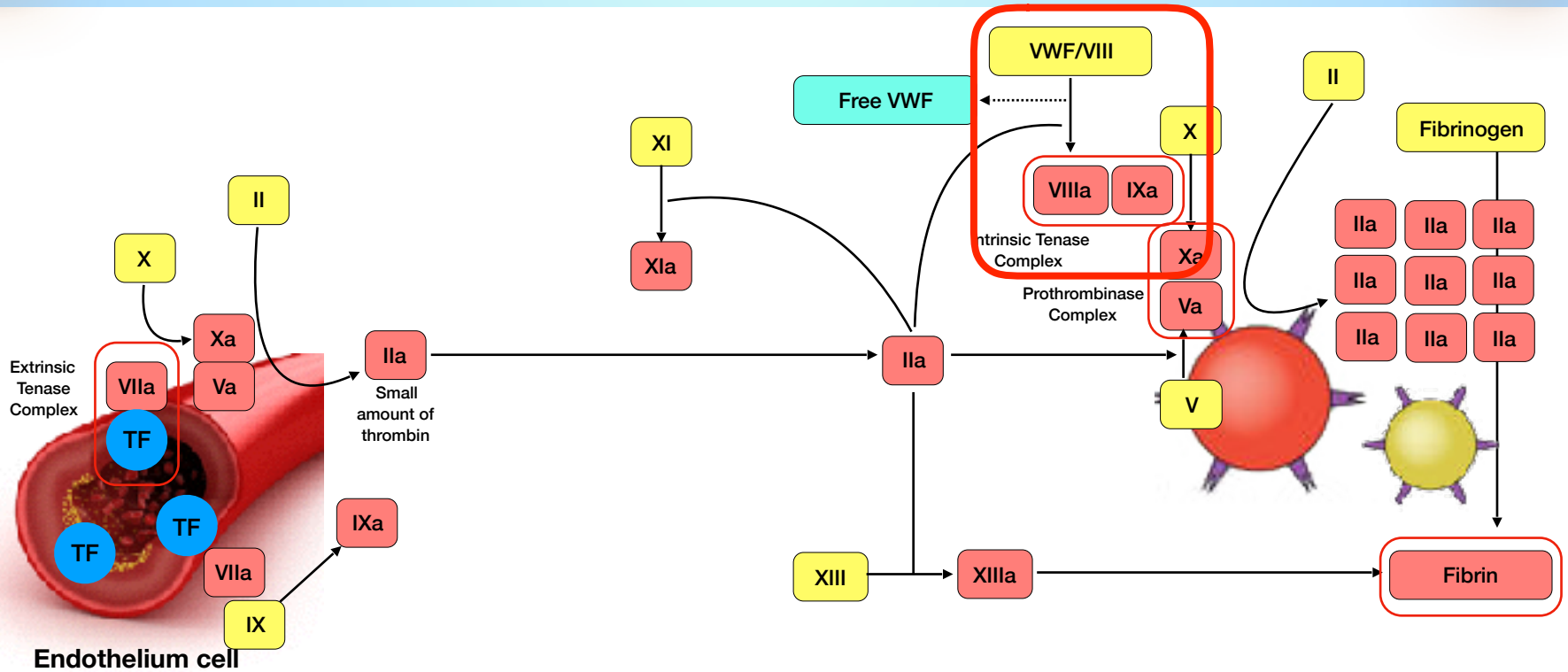
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MCHC	35.1 g/dl	Plt	360,000
RDW	13%	MPV	9.4 fl
aPTT	40 sec	Bl.gr	A+
PT	12 sec	<b>FVIII level</b>	<b>12%</b>
TT	11 sec	vWF	95%







# Cell-based Model of Coagulation





# Hemophilia

## Severe Haemophilia

- < 1% factor level
- Spontaneous bleeding
- May bleed 1-2 times per week
- Characterized by joint involvement (haemarthrosis)

## Moderate Haemophilia

- 1% to 5% factor level
- Can bleed with slight injury
- May bleed 1 time per month
- May have joint involvement

## Mild Haemophilia

- > 5% -30% factor level
- Can bleed with severe injury, surgery, invasive procedure
- May never have a bleeding
- Rarely has joint involvement



Normal Blood Vessel



Bleeding starts



HEMOPHILIA  
Incomplete Fibrin clot  
Continued bleeding



Completed Fibrin clot



# Hemophilia



Normal  
Blood Vessel



Bleeding starts



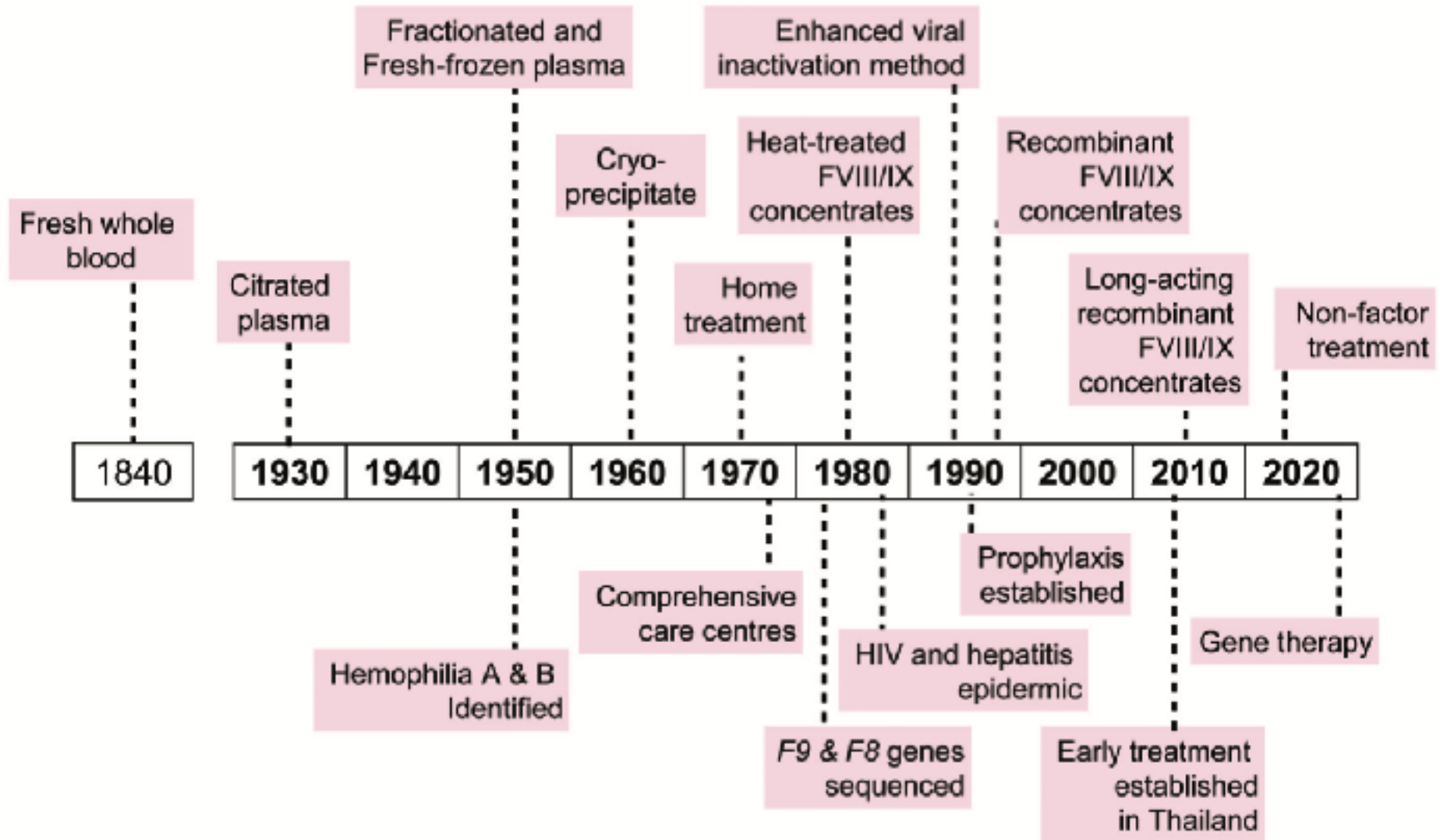
**HEMOPHILIA**  
Incomplete Fibrin clot  
Continued bleeding



Completed  
Fibrin clot



# Hemophilia





# Case #05



**Case** : An 8-year-old boy who presented with drowsiness and high fever since last 4 days.

Past history: No underlying disease

## Physical examination

Vital signs : T 39 C ,Tachycardia

Lung &CVS: WNL

Abdomen : hepatomegaly

Ext. : generalized petichiae

NS : Drowsiness

Sensory & motor : WNL





# Case #05

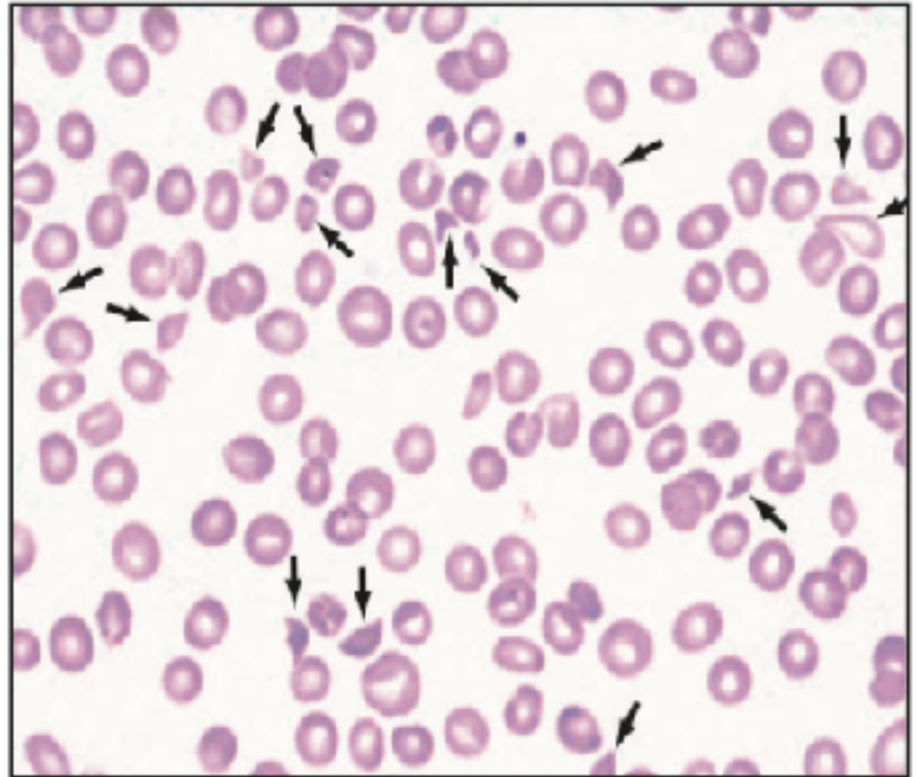


**Case :** An 8-year-old boy who presented with drowsiness and high fever since last 4 days.

Past history: No underlying disease

## Investigations

Hb	8.5 g/dl	WBC	25,900
Hct	25%	PMN	80
MCV	86 fl	Lymph	18
MCH	28.9 pg	Eosin	2
MCHC	35.9 g/dl	Plt	30,000
RDW	14.5%	MPV	10.2 fl
aPTT	40 sec	(25-35 sec)	
PT	20 sec	(12-15 sec)	
TT	20 sec	(10-20 sec)	





# Differential Diagnosis



Component	Vit.K def.	Liver disease	DIC
RBC Morphology	Normal	Target cell	Fragmented cells, burr cells, schistocyte
PTT	Prolonged	Prolonged	Prolonged
PT	Prolonged	Prolonged	Prolonged
D-dimer	Normal	Normal	Markedly increased
Platelets	Normal	Normal	Reduced
Factors decreased	II, VII, IX, X	I, II, V, VII, IX, X	VIII



# Clinical Manifestation







# Take Home Message



**Primary and secondary hemostasis : what's the different**

## **Isolated thrombocytopenia**

- approach by platelet size and others systemic disease

## **Isolated APTT prolong**

- Acquired Hemophilia
- Hemophilia
- Von Willebrand disease

## **DIC : “consumptive coagulopathy”**

Low platelets counts, high FDP, D-dimer

Low fibrinogen

PT, PTT prolong



# Question?



ทีมแพทย์ประจำบ้าน.

หมอใบ

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