Bleeding Disorders

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Content

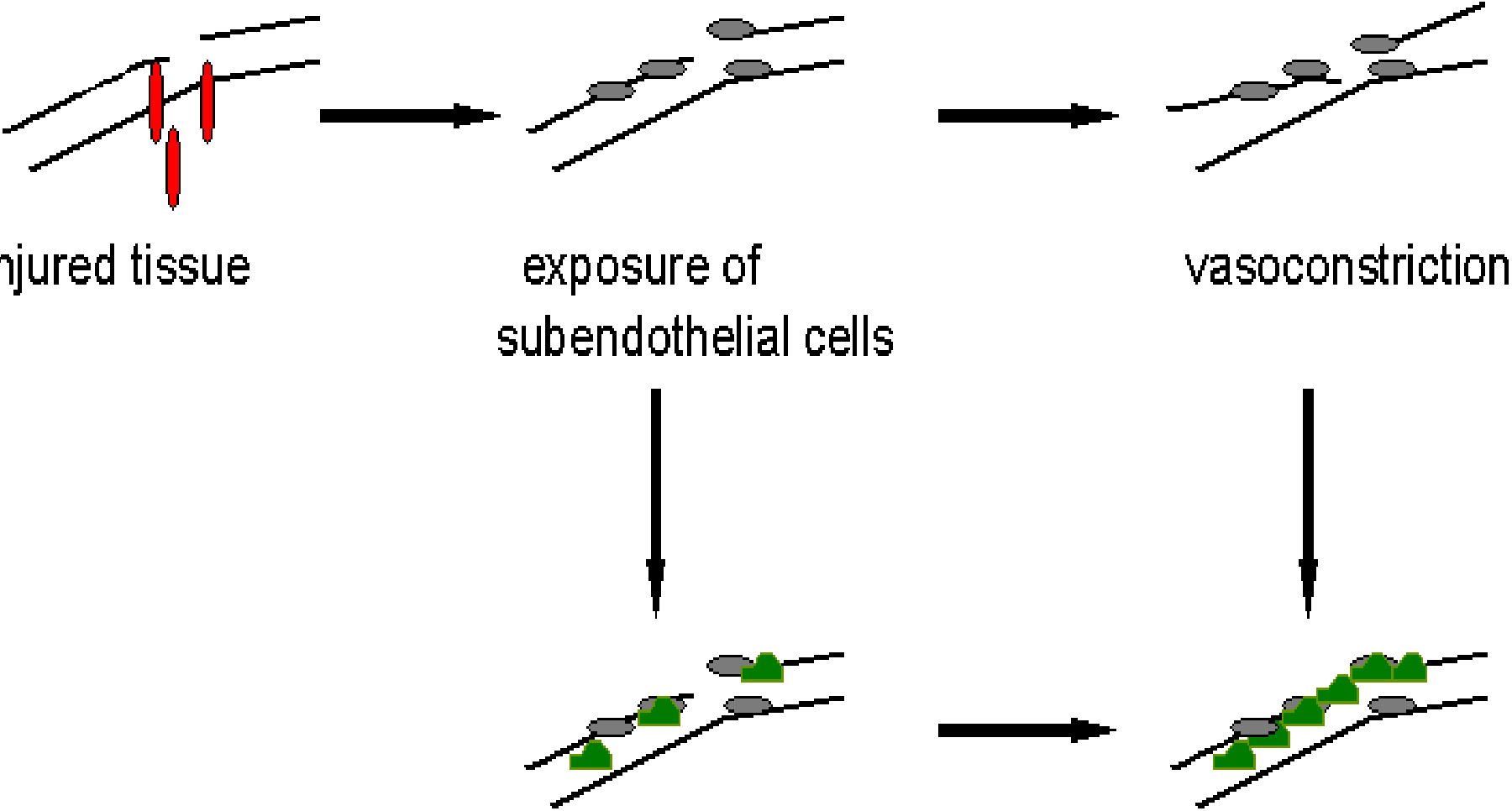
- Physiology of Hemostasis
- Etiology of bleeding disorder
- Evaluation of bleeding disorders

Primary hemostasis:

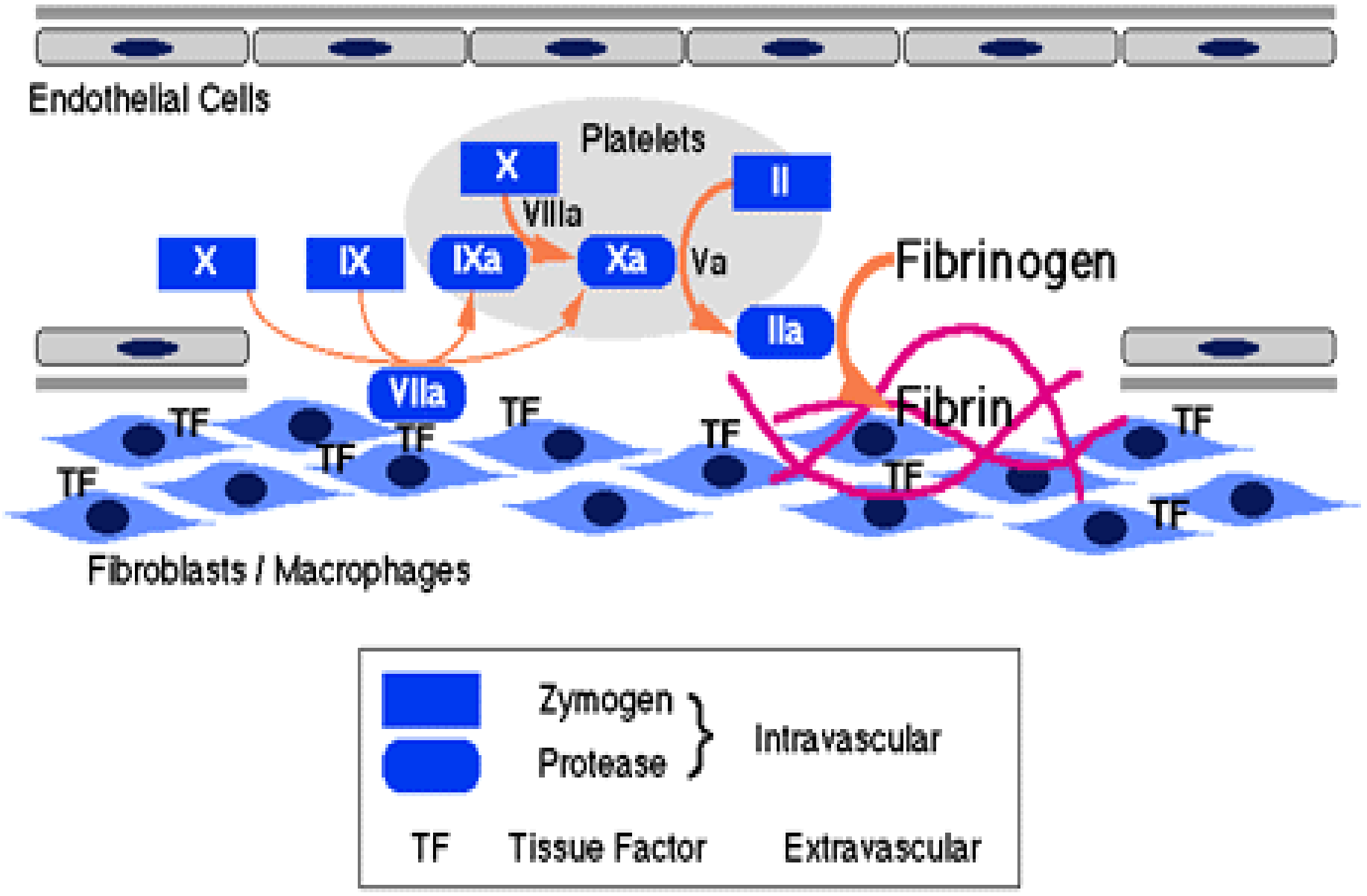
- Vascular phase : vasoconstriction, immediately
- Platelet phase : adhesion & aggregation, several seconds

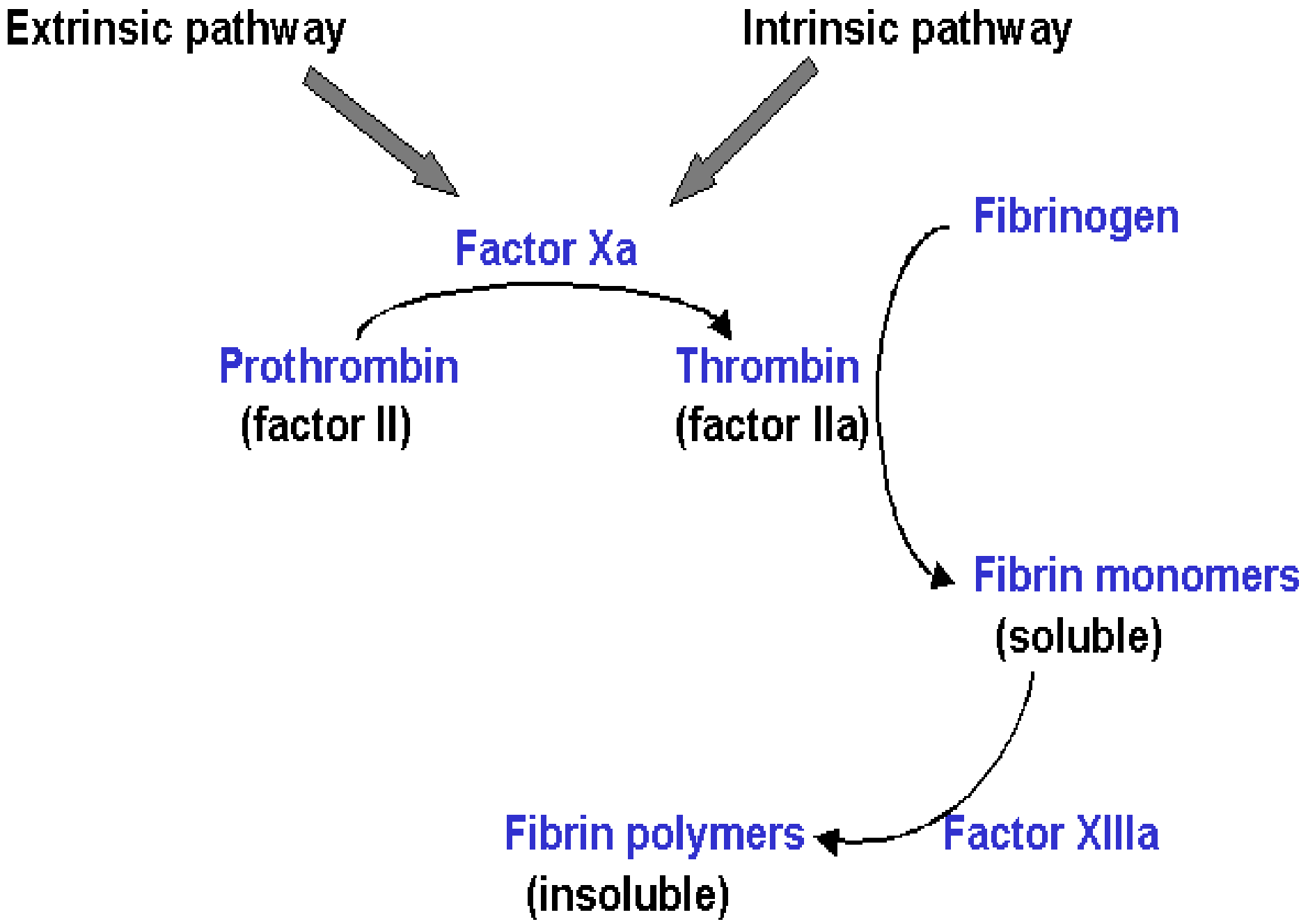
Secondary hemostasis:

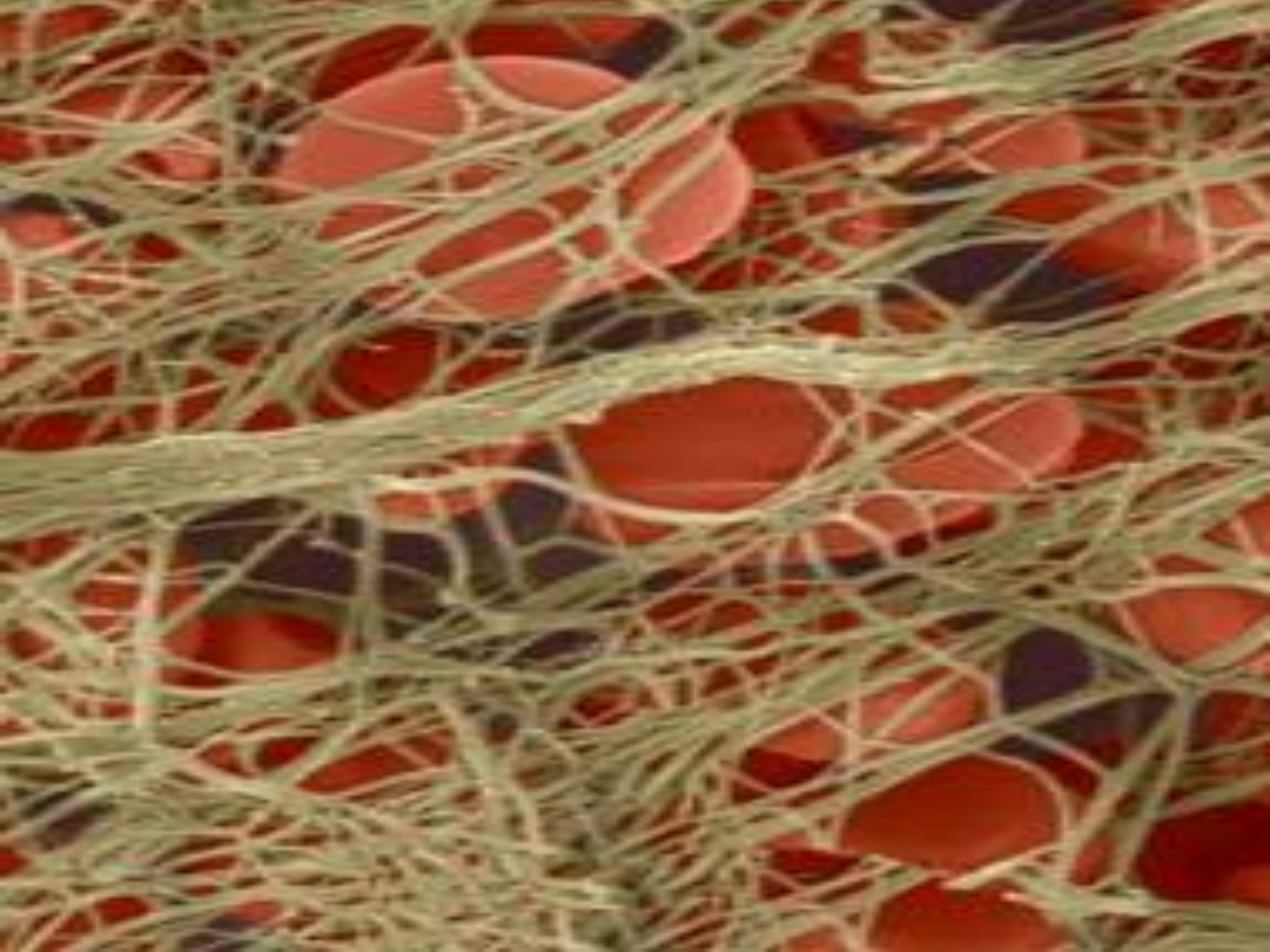
- Coagulation phase : later, contains extrinsic & intrinsic
- Metabolic (fibrinolytic) phase: release antithrombotic t


njured tissue
exposure of
subendothelial cells
vasoconstriction
platelets adhere to
exposed cells
platelets aggregate
and form a “plug”
blood
subendothelial cells
platelets

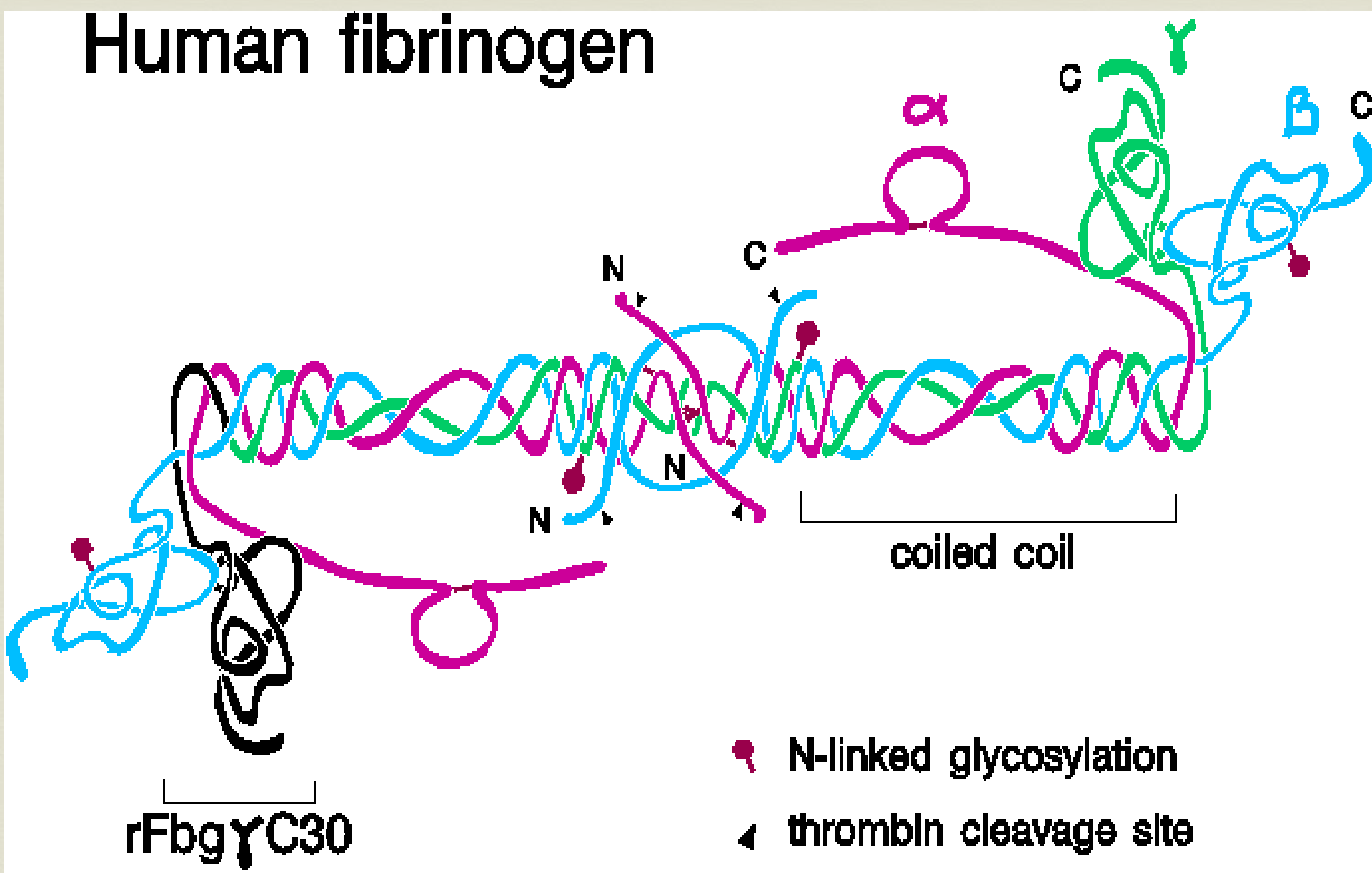
Initiation of Coagulation *In Vivo*




Extrinsic pathway
Intrinsic pathway
Factor Xa
Fibrinogen
Prothrombin
(factor II)
Thrombin
(factor IIa)
Fibrin monomers
(soluble)
Fibrin polymers
(insoluble)
Factor XIIIa

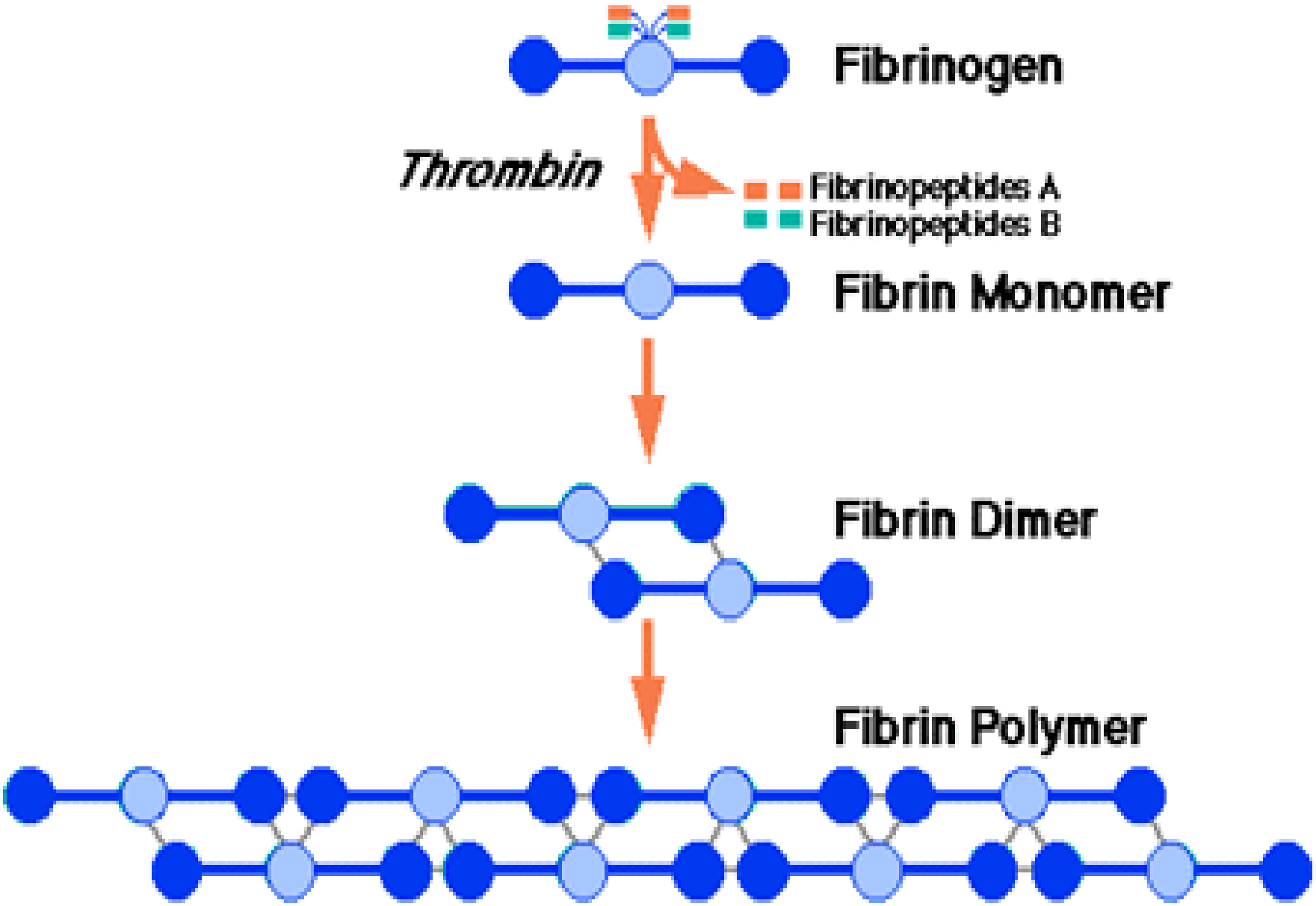


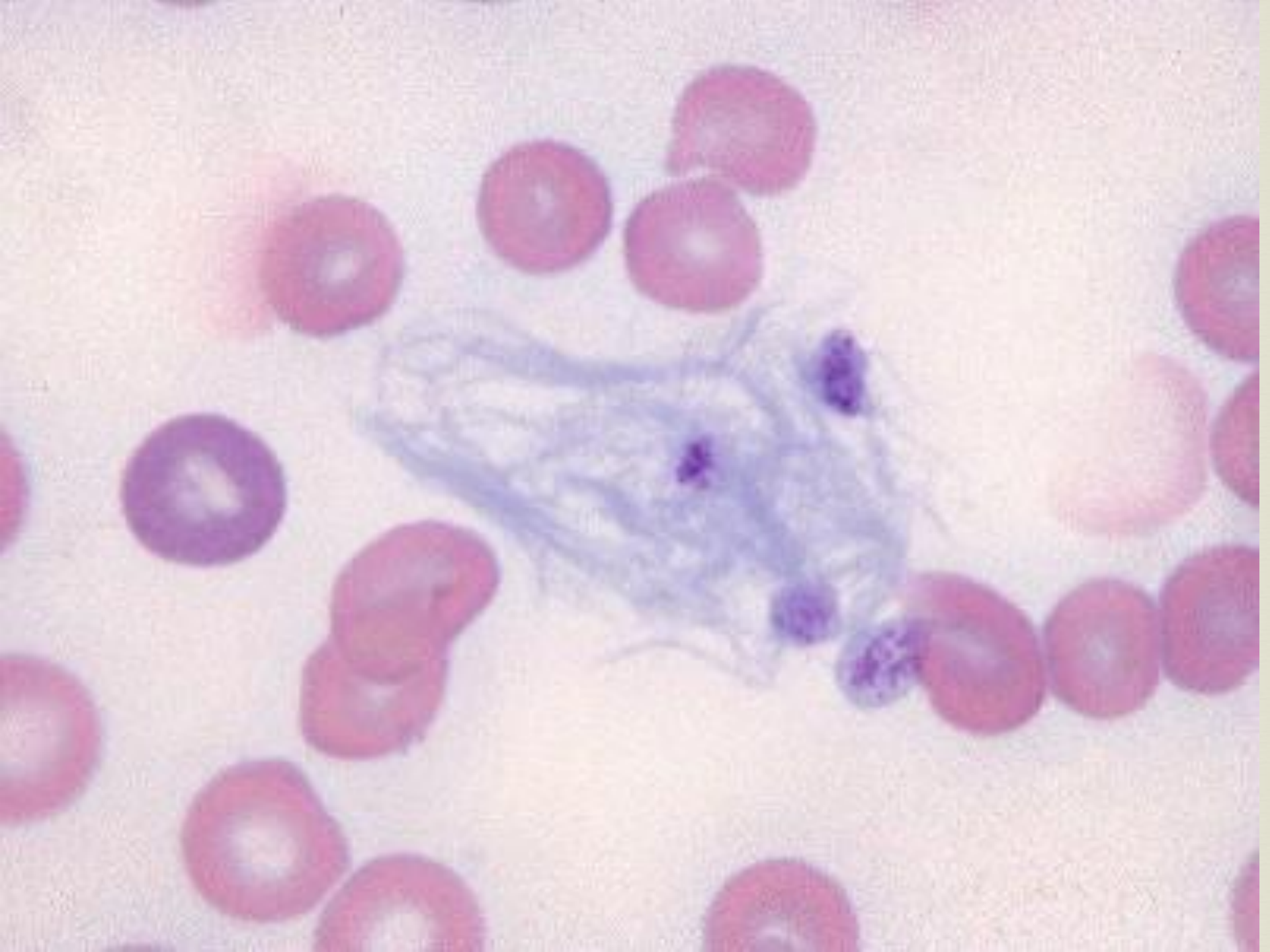
Human fibrinogen

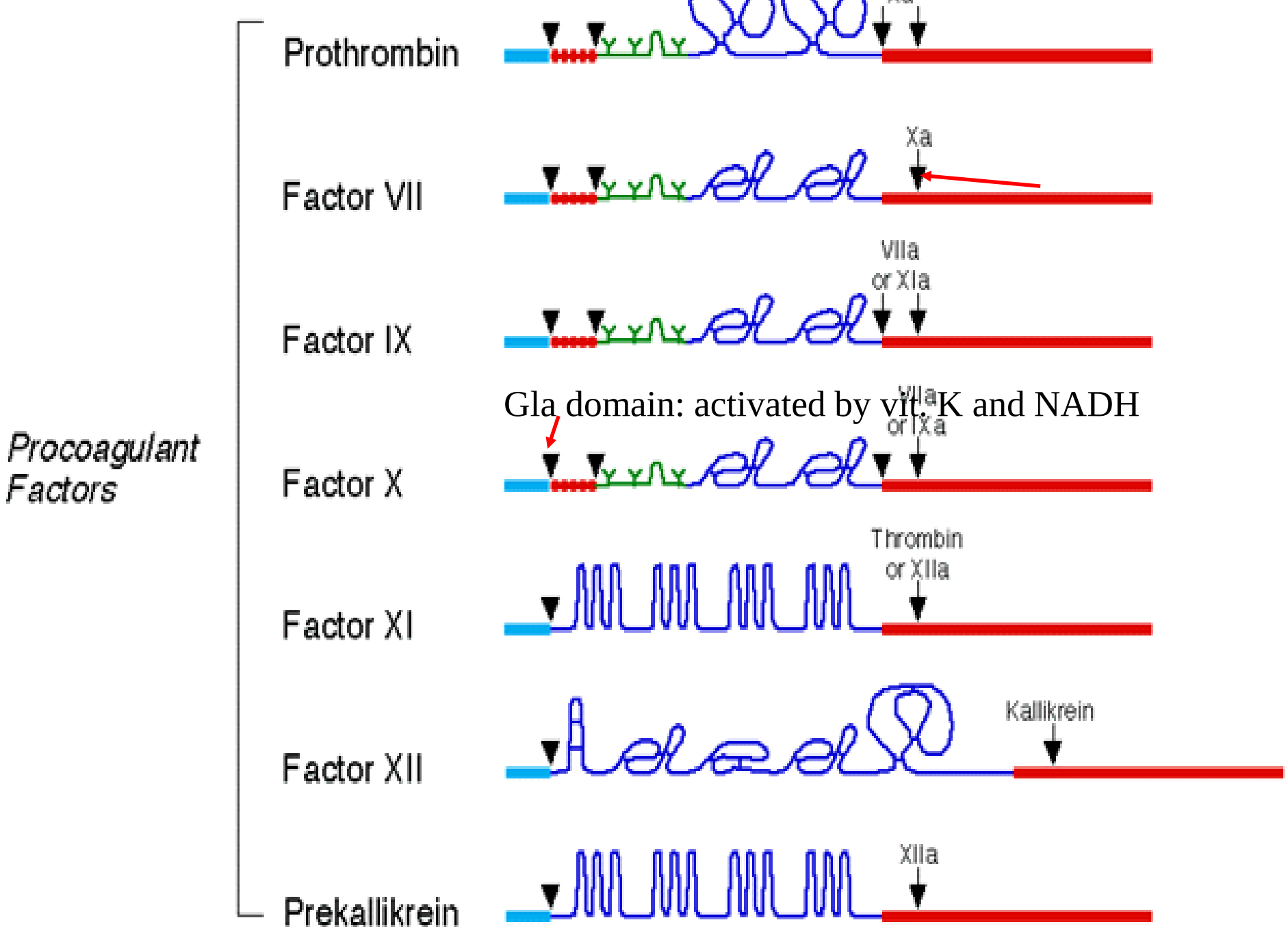


(H. Cote, adapted from R. F. Doolittle)

Fibrin Polymerization



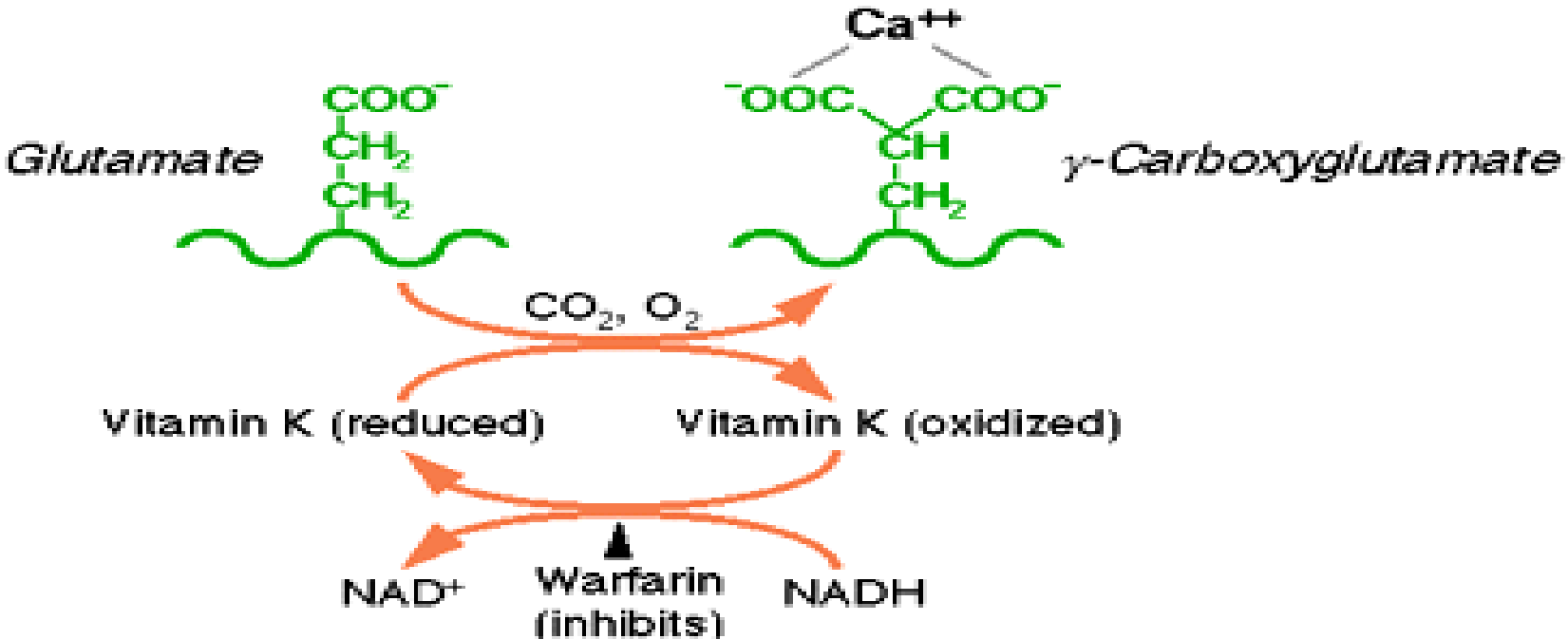



Procoagulant Factors
Prothrombin
Factor VII
Xa
Factor IX
VIIa or XIa
Gla domain: activated by vit. K and NADH
Factor X
VIIa or IXa
Factor XI
Thrombin or XIIa
Factor XII
Kallikrein
Prekallikrein
XIIa

γ-Carboxylation of Prothrombin (Factor II)

Fig. 7

Role of Vitamin K in Biosynthesis of Factors II, VII, IX, and X



Etiology of bleeding disorders:

- 1. Vascular
- Plat. Defect
- 3. Disorders of coagulation

Etiology of bleeding disorders:

1. vascular wall alteration : infection, chemical, allergy

2. Disorder of platelet function :

1- Genetic defects

(Bernard-Soulier disease: GP-Ib /IX dysfunction with VWF)

2-Aquired:

- *Autoimmune disease.*
- *Drugs: Aspirin, NSAIDs, broad-spectrum antibiotics (Ampicillin, Penicillin, Gentamycin, Vancomycin)*

Etiology of bleeding disorders

Thrombotic Thrombocytopenia purpuras (TTP) :

1. primary
2. secondary : Chemicals, ex: mitomycin C
   Physical agent (radiation)
   Systemic disease (leukemia)

Character:

1.1.Thrombocytopenia 2. Micro-angiopathic hemolytic anemia(MAHA) 3. Fever 4. renal impairment 5. Neurological symptoms.

2. Considered to be an emergency

3.TTT : plasma exchange and glucocortisone application

Etiology of bleeding disorders

Disorders of coagulation factors:

1. Inherited : Hemophilia A
   Christmas disease
   von Willebrand Disease
2. Acquired : Liver disease
   Vitamin K deficiency
   Anticoagulation drugs (heparin, coumarin)
   Abs

Evaluation of bleeding disorders

- 1. Take history
- 2. Physical examination
- 3. Screening clinical laboratory tests
- 4. Observation of excessive bleeding following a surgical procedure

History

- Bleeding problems in relatives
- Bleeding problems following operations and tooth extractions, trauma
- Use of drugs for prevention of coagulation or pain
- Spontaneous bleeding from nose mouth etc..

Screening laboratory tests

- 1. Platelet count 150- 400X 10^9/l
- 2. BT (Bleeding Time) 2-5 min
- 3. PT (Prothrombin Time) 10-13 sec.
- 4. aPTT (active Partial Thrombopastin Time) 28-36 sec
- 5. TT (Thrombin Time)

Platelet count

- Normal (140,000 to 400,000/mm3)
- Thrombocytopenia : < 140,000/mm3
- Clinical bleeding problem : <50,000/mm3
- Spontaneous bleeding with life thearten bleeding <20,000/mm3

B.T (Ivy method)

- Test platelet & vascular phase
- Normal if adequate number of platelets of good quality present intact vascular walls
- Normal Ivy's (2 to 5 minutes)

PT (Prothrombin Time)

- Activated by tissue thromboplastin
- Tests extrinsic (factor VII) and common (I,II,V,X) pathways
- Normal (10-13.5sec)
- International normalized ratio= INR : 0.9
-

Activated PTT (aPTT)

- Activated by contact activator (kaolin)
- Tests intrinsic and common pathway
- Normal (28-36 sec)
- Heparin therapy-a PTT is prolonged : 50-65 sec

TT (Thrombin Time)

- Activated by thrombin
- Tests ability to form initial clot from fibrinogen
- Normal (11 to 13 seconds)

condition	Platelet count	BT	PTT	PT	TT
1. Aspirin therapy		+			-
2. Coumarin therapy	-	-		++	-
3. Heparin therapy	+	+	++	-	-
4. Liver disease	+	+	++	++	++
5. leukemia	+	+	-	-	-
6. Long term antibiotic	-	-	++	++	++
7. Vascular wall defect	-	+	-	-	-
8. thrombocytopenia	++	++	-	-	-
9. hemophilia	-	-	++	-	-
10. fibrinogenolysis	-	-	+	+	++

-: normal, +: may be abnormal, ++: abnormal

Patient at low risk

- Patient with no history of bleeding disorders, normal
  examinations, no medications associated with bleeding
  disorders and normal bleeding parameters
- Patients with nons pecific history of excessive bleeding
  with normal bleeding parameters (PT, PTT, BT,
  platelet count, are within normal time)

Patient at moderate risk

- Patients in chronic oral anticoagulant therapy
- Patients on chronic aspirin therapy

Patient at high risk

- Patients with known bleeding disorders
  - Thrombocytopenia
  - Thrombocytopathy
  - Clotting factor defects
- Patient without known bleeding disorders found to
  - have abnormal , platelet count, BT, PT, PTT

Thrombocytopenia

- Disease in number of circulation platelets
- Idiopathic thrombocytopenia, secondary thrombocytopenia
- TTT : is none indicated unless

  platelets<20000/mm3, or excessive bleeding

von Willebrand Disease

- Type I : 70%-80%, partial loss on quantity
- Type II : poor on quality
- Type III : severe loss on quantity, inactive to DDAVP

Hemophilia

- Sex-linked recessive trait,
- Prolong aPTT, normal BT,PT
- Hemophilia A (factor VIII deficiency)
- Hemophilia B or Christmas disease (factor IX deficiency)
- Severity of disorder :
- severe<1%,
- moderate 1-5%,
- mild 6-30%


THANK YOU