Team Medicine

2#

Bleeding disorders

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■ Slides ■ Doctors notes ■ Additional

431 Teams

Bleeding disorders

Normal Hemostasis

- A **protective mechanism** that has evolved to maintain physiological Hemostasis.
- Blood coagulation is complex and finely balanced system of activating & inhibitory feed-back or feed-forward pathways with integration & coordination of its five major components i.e.,
  1. Blood Vessels
  2. Blood Platelets.
  3. Coagulation factors
  4. Coagulation inhibitors
  5. Fibrinolytic system

  (links with immune system)

Blood Vessels

First line of defense in haemostasis. Vascular endothelium synthesizes & releases a variety of factors and also has receptors for large no. of molecules.

Endothelium is usually activated by trauma, or stimulated by thrombin, cytokines or shear stress

- Leucocyte & Platelet adhesion
- Inflammation
- Phagocytosis
- Vascular Permeability

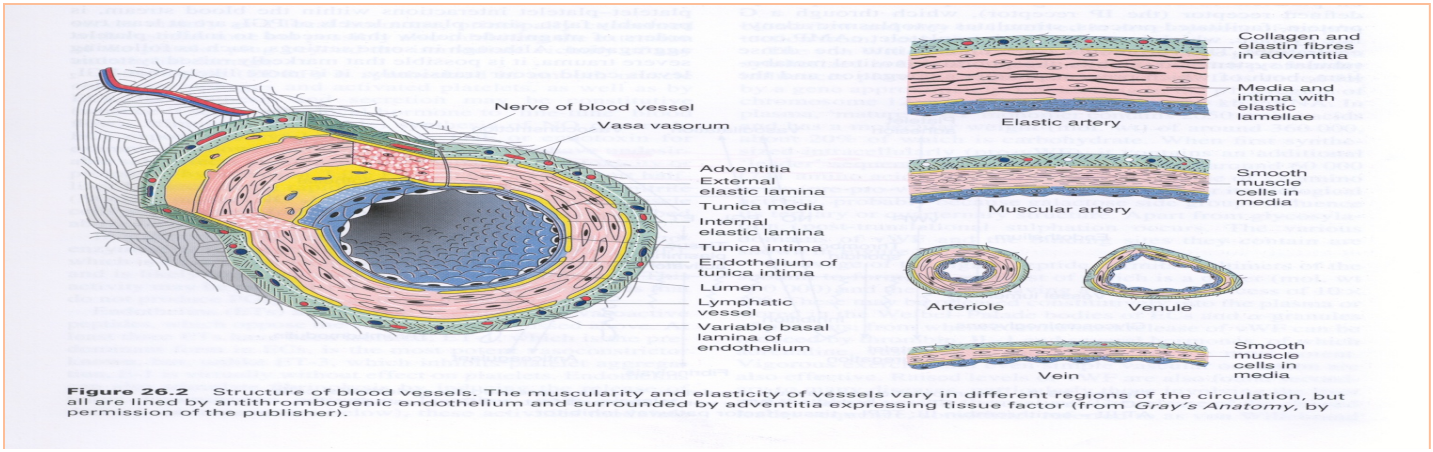


Figure 26.2 Structure of blood vessels. The muscularity and elasticity of vessels vary in different regions of the circulation, but all are lined by antithrombogenic endothelium and surrounded by adventitia expressing tissue factor (from *Gray's Anatomy*, by permission of the publisher).

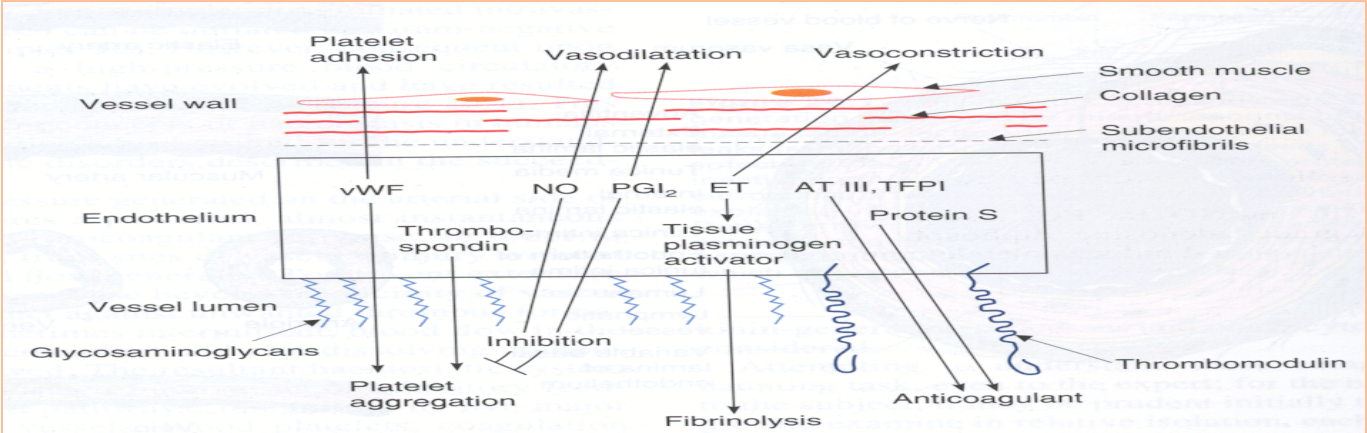


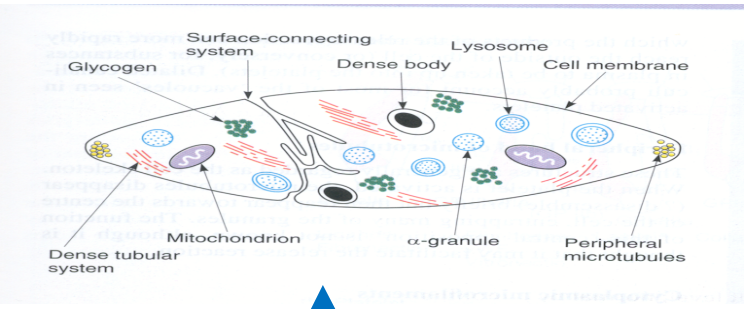
Figure 26.3 Haemostatic and vasculoregulatory factors expressed by endothelial cells. NO = nitrous oxide; ET = endothelin; vWF = von Willebrand factor; PG = prostaglandin; AT III = antithrombin III; TFPI = tissue factor pathway inhibitor.

- Most of the heparin that we are using comes from Chinese pigs
- Heparin stick to the endothelium by charge , so the charge is on the endothelium
- Endothelium is responsible to repel the protein
- Subendothelium is highly charged but with the opposite ,so when you injure endothelium you will expose yourself to the opposite charge which will attract the protein in
- Endothelial cell will produce Vwf :Von Willebrand factor " essential protein allows platelet to attract to the injury not to activate the platelet"

Platelets

Platelets **are fragments** of the cytoplasm of megakaryocytes formed in the bone marrow and are non-nucleated.

Many substances can induce platelet aggregation e.g., ADP, TXA2, adrenaline, 5HT, vasopressin and platelet activating factor. This helps in **forming a platelet plug at the site of injury & stop bleeding.**



- They have connected tubules to increase surface area when platelet gets activated it looks like star "the connected tubule flip to the other way"

- platelets are not cells →they are fragments "very active" of megakaryocytes
- life span of platelet :-5-7 days "disturb very quickly and the moment you shake them little bit they get activated "
- platelets are full of granules (α granules (or called δ granule)) → which play a major role on attracting coagulation (coagulation is not allowed to happen in circulation but happens at the site of injury)

Calcium	?
Pyrophosphate	?
Alpha-granules	
PF4	Heparinoid neutralization
Beta-thromboglobulin	? Chemotaxis
Thrombospondin	? Aggregation
PDGF	Mitogenesis, vessel repair
vWF	Adhesion, aggregation
Fibrinogen	Aggregation, coagulation
Factor V	? Prothrombinase activity
Fibronectin	Fibroblast and platelet adhesion
PAI-1	Inhibition of fibrinolysis
α_2-antiplasmin	Inhibition of fibrinolysis

They are in the plasma but also store in the platelet

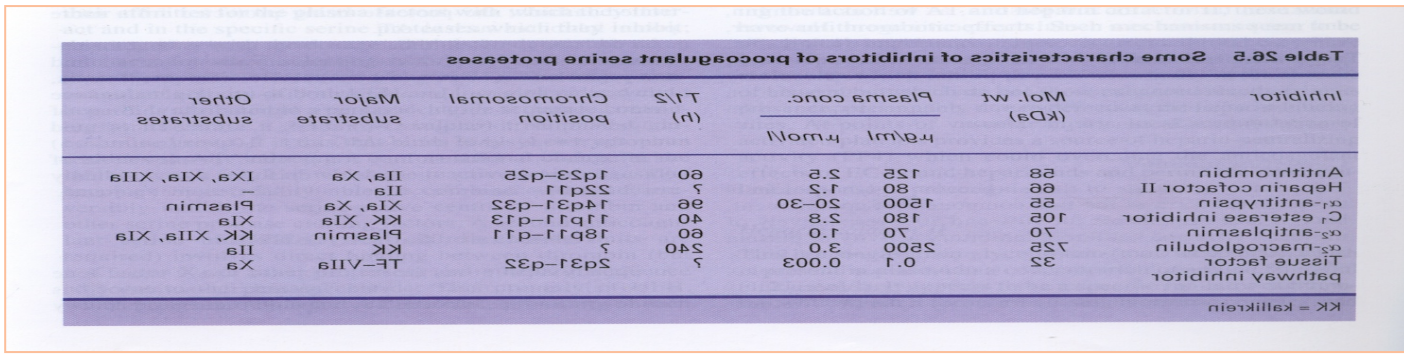
Coagulation Factors

Table 26.4 Some characteristics of clotting factors in man

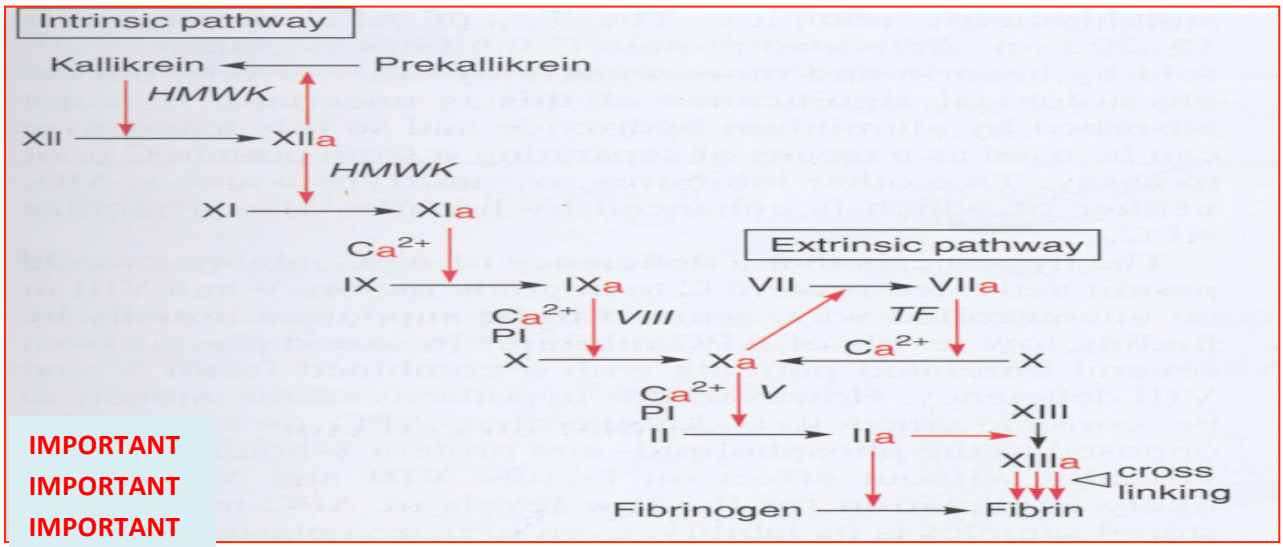
Traditional name	*Preferred nomenclature*	*Mol. wt*	*Plasma conc. (μg/ml)*	*Half-life (h)*	*Gene size; location**	*Product†*
Fibrinogen	Factor I	340 000	2–4 × 10^3	90	50kb; C4q26–q28	3026
Aα-chain		56 000				
Bβ-chain		52 000				
γ-chain		46 000				
Prothrombin	Factor II	72 000	120	65	24 kb; 11p11	579
Tissue factor	Factor III	45 000	0	–	12.6 kb; 1p21	263
Calcium	Factor IV	40	100	–	–	–
Proaccelerin	Factor V	330 000	10	15	6.8 kb; 1q21–25	2224
Proconvertin	Factor VII	48 000	1	5	12.8 kb; 13q34	406
Antihaemophilic factor	Factor VIII	360 000	0.05	10	190 kb; Xq28	2332
Christmas factor	Factor IX	57 500	4	25	35 kb; Xq26	415
Stuart–Prower factor	Factor X	55 000	12	40	25 kb; 13q34	445
Plasma thromboplastin antecedent	Factor XI	160 000	6	45	25 kb; 4q35	1214
Hageman factor	Factor XII	85 000	40	50	13.5 kb; 5q33	536
Fibrin stabilizing factor	Factor XIII	320 000	20	200	a 160 kb; 6 p ter; b 28 kb; 1q31	a = 731 b = 641
Fletcher factor	Prekallikrein	90 000	40	35	?	619
Fitzgerald factor‡	High mol. wt Kininogen	120 000	70	150	27 kb; C3q26	626

* Chromosome number and band location.
† Number of amino acids.
‡ Also known as Williams, Flaujeac or Reid factors.

Naturally Occurring Anticoagulants in Blood



Traditional Coag. Pathway



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- The coagulation intrinsic &extrinsic pathways have been invented to monitor warfarin and heparin.extrinsic pathway which we really need to initiate the clot
- Extrinsic pathway measures warfarin , intrinsic pathway measures heparin
- TF:-tissue factor.
- X→Xa (a:-activated).
- Factor VIII is a cofactor , so you don't need it much "who are the patent who defiant factor VIII? Hemophilia A
- In intrinsic pathway you need kallikrein or HMWK (High-molecular-weight kininogen)
- Why patients with hemophilia A bleed (you can live your daily life with just the extrinsic pathway) → we need factor VIII to sustain the propagation of the cascade
- Thromboplastin is the strongest ever clotting insult that you can give to the circulation. You need just a micromole and the whole system will clot.

Problems with traditional coagulation pathway

- No explanation why FVIII or FIX deficiency causes clinically severe bleeding , since the extrinsic pathway ought to bypass the need for FVIII and FIX.
- No explanation for less severe bleeding in FXI deficiency
- No explanation for absent bleeding in FXII deficiency
- No explanation for the lag phase followed by explosively rapid thrombin generation observed experimentally

- Christmas disease — also called hemophilia B or factor IX hemophilia (Christmas was the patient name)
- New concept of blood coagulation :- crossover between the intrinsic and extrinsic pathway which happen in the surface of the platelets (not in the plasma)
- Platelet surface has phospholipids
- All clotting should appear at the surface of the cell membrane and cannot appear in the plasma

New Concept of Blood Coagulation

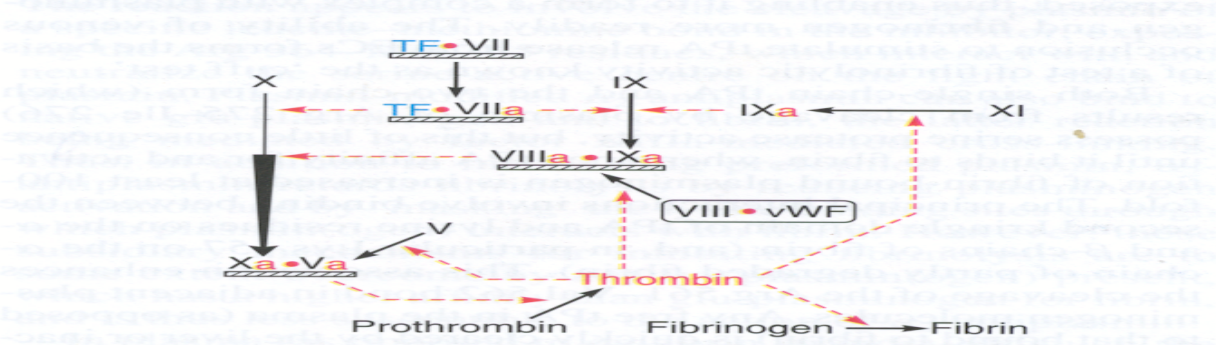

Figure 26.12 Thrombin generation network initiated by TF–VIIa. Symbols as in Figure 26–1. The activator complexes Xa–Va and IXa–VIII, assemble on the surface of an activated platelet. Factor VIII bound to vWF is inactive. Direct activation of X by TF–VIIa allows a small amount of thrombin to be generated, which feeds back to activate the cofactors V and VIII, leading to an explosive burst of further thrombin generation.

Approach to a Patient with Bleeding Tendency

History

-Type of Bleeding

Mucosal & Skin

Joint & Muscles

-Past Surgical History

- Family History
- If +ve family history, pattern of inheritance
- Drugs

-Examination

- Skin & oral mucosa
- Joints
- Associated abnormalities

-Investigations

- Prothrombin time
- Partial thomboplastin time
- Platelet count
- Bleeding time
- Thrombin time

- Patient who have low platelet will have epistaxis whereas hemophilia patient their joint is destroyed.
- Coagulation factors is a major source in preventing bleeding in high stress areas (joints(e.g. knee)) while platelets are a major source in preventing bleeding in low stress areas (e.g. mouth , nose)
- prothrombin time: - when you standardize it-> it will become international normalized ratio (INR)
- Bleeding time: - Bleeding time is a crude test of hemostasis (the arrest or stopping of bleeding). It indicates how well platelets interact with blood vessel walls to form blood clots.-> can be used for low platelets. Cannot be used for hemophilia
- Thrombin time :- measures the clotting factors on the common pathway->suppose you have a patient with prolonged INR with normal thrombin time where do you think the problem ?->factor V & factor VII .patient with growing APTT with normal thrombin time where is the problem? Intrinsic pathway->factors XII,XI,IX and VIII

First-line tests in a case of Bleeding tendency

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pattern of abnormalities obtained using the

Table 16.3 First-line tests used in investigating acute haemostatic failure

	Test				Condition
	PT	APTT	TT	Platelet count	
1.	N	N	N	N	Disorder of platelet function. Factor XIII deficiency. Disorder of vascular haemostasis. Normal haemostasis
2.	Long	N	N	N	Factor VII deficiency. Early oral anticoagulation
3.	N	Long	N	N	Factors VIII:C, IX, XI, XII, prekallikrein, HMWK deficiency. von Willebrand's disease. Circulating anticoagulant
4.	Long	Long	N	N	Vitamin K deficiency. Oral anticoagulants. Factors V, VII, X and II deficiency
5.	Long	Long	Long	N	Heparin. Liver disease. Fibrinogen deficiency. Hyperfibrinolysis
6.	N	N	N	Low	Thrombocytopenia
7.	Long	Long	N	Low	Massive transfusion. Liver disease
8.	Long	Long	Long	Low	DIC. Acute liver disease

N, Normal.

and V

- Warfarin affects clotting factors (II, VII, IX,X)
- Why in early Oral anticoagulation , PT looks prolong and TT is normal ? because VII has the shortest half-life "PT long" ,IX is normal "TT is normal"
- Factor VII is the shortest living factor (2 hours only)
- subendothelium is highly charged it cannot attract the simple coagulation factors→ needs vWF which will attract the platelets and in the surface of the platelets the coagulation factors will stick around
- vWF is essential in making a link between platelets and coagulation cascade
- vWF protect factor VIII
- Commonest coagulation defect is von willebrand disease

Inherited Platelet disorders

Thrombocythopathy	*Molecular abnormality*	*Functional abnormality*
Defect of adhesion		
Bernard–Soulier syndrome	*GPIb, GPV, GPIX↓	F V:VWF binding to platelets ↓ Platelet adhesion to microfibrils ↓
von Willebrand platelet syndrome	*GPIb↑	V:VWF binding to platelets ↑ Plasmatic FV:VWF level ↓ Platelet adhesion to subendothelium ↓ (?)
Defect of reactivity to collagen	*GPIa↓	Platelet adhesion to collagen ↓
Defect of activation		
Abnormality in intracellular Ca^{++} fluxes	?	Defect in enzymatic reactions and metabolic events responsible for activation. Platelet release and aggregation ↓
Abnormality in prostaglandin pathway	Cyclooxygenase or thromboxane synthetase deficiency	Platelet release and aggregation ↓
Defect of reactivity to ADP	Receptors number ↓	Defect in activation and aggregation to ADP''
Defective response to epinephrine	Decrease in platelet alpha$_2$–adrenergic receptors	Defective activation induced by epinephrine
Montreal platelet syndrome	Decrease of calpain	Spontaneous aggreation by increased exposure of binding sites for adhesive proteins ?
Defect of secretion of adhesive proteins		
Grey platelet syndrome	α-granule content and typical α-granules number ↓	Release of adhesive proteins ↓ Adhesion (?) and aggregation ↓
Defect of secretion of dense granules		
δ-storage pool disease	Dense bodies number ↓ and function ↓	Release of ADP ↓ Aggregation ↓
Defect of aggregation		
Glanzmann disease	*GPIIb and GPIIIa ↓	Fibrinogen binding ↓ Aggregation ↓
Variant thrombasthenia	Abnormal *GPIIb–GPIIIa complex	idem
Defect of procoagulant activity		
Platelet factor 3 deficiency	Abnormality in phospholipids involved in binding of factors Va and Xa	Defect of activation in situ of plasmatic factors

Inherited Thrombocytopenias

- May-Hegglin thrombocytopenia. :- have large platelets
- Thrombocytopenia with absent radii (TAR).
- Wiskott-Aldrich syndrome.
- Epstein's Syndrome.

- Treatment of platelet defect is to transfuse platelet except in von willebrand disease we use cryoprecipitate
- patient who don't want to receive any blood product → (DDAVP) desmopressin is an alternative for them→ increase vWF
- desmopressin can cause hyponatremia

Treatment of platelet disorders

- - Avoid antiplatelet drugs & trauma
- - Local measures
- - DDAVP infusion
- - Platelet transfusion (HLA compatible)

- - Recombinant activated factor VII
- - Bone marrow transplantation (rarely required)

Inherited Bleeding disorders

Focus on the top

Disorder	Screening tests				Specific assays* (u/dl)
	PT	PTTK	TCT	BT	
Haemophilia A	N	↑	N	N	Factor VIII <50 vWF:Ag N Ricof N
von Willebrand's disease	N	↑ or N	N	↑ or N	Factor VIII <50 vWF:Ag <50 or N Ricof <50 or N
Haemophilia B	N	↑	N	N	Factor IX <50
Factor XI deficiency	N	↑	N	N	Factor XI <35
Factor X deficiency	↑	↑	N	N	Factor X <50
Factor V deficiency	↑	↑	N	N or ↑	Factor V <50
Factor VII	↑	N	N	N	Factor VII <50
Factor II	↑	↑	N	N	Factor II <50
Afibrinogenaemia	↑	↑	↑	↑	Fibrinogen undetectable
Dysifibrinogenaemia	↑	↑	↑	↑	Fibrinogen N or ↓
Factor XIII deficiency	N	N	N	N	Fibrin solubility ↑ Factor XIII <5%
Factor V plus VIII deficiency	↑	↑	N	N	Factor V <50 Factor VIII <50
Hyperplasminaemia	N	N	N	N	Euglobulin clot lysis time short (α_2-antiplasmin absent)

PT = prothrombin Time; PTTK = activated partial thromboplastin time; TCT = thrombin clotting time; BT = bleeding time; ↑ = increased, ↓ = decreased; N = normal.
* Factor VIII (formerly VIII:c); vWF:Ag, von Willebrand factor antigen (formerly VIIIR: Ag); Ricof, ristocetin cofactor.

Hemophilia – A

- *X-Linked recessive disorder*
- *Males are affected and females are carriers.*
- *Deficiency of FVIII* due to gene mutations or deletions

  Severe (< 1%)

  Moderate (1-5%)

  Mild (5-40%)

Clinical Features

- Severe spontaneous recurrent bleeding
- Usually muscle & joints
- Internal organ bleeds also occur
- Recurrent bleeds lead to joint & muscle damage.
- Family history or new mutation

Severity of Hemophilia

Severity of Hemophilia		
Severity	**Factor VIII or IX level**	**Clinical Presentation**
Severe	<1%	Spontaneous hemarthrosis & muscle hematomas
Moderate	2 – 5 %	Mild trauma or surgery cause hematomas
Mild	5 - 50 %	Major injury or surgery result in excess bleeding

22

Findings on investigation Hematology

Hematology

- CBC → normal
- clotting studies :-
- PT normal
- Bleeding time N
- APTT
- VIII:C
- vWF: Ag normal

patient with very severe hemophilia and the gene is completely deleted from him and you are trying your best you give him all the plasma product and the Recombinant → antibodies development because he will see protein that he haven't seen it in his life

Diagnostic imaging

- Joint X-ray → 2nry osteoarthritic changes
- U/S , CT in loin pain (psoas bleeds, renal capsule bleeds, retroperitonial bleeds)

Treatment of Hemophilia

1) Factor concentrates for acute bleed

Sources of FVIII conc.:

a) Donated human blood (plasma)
b) Recombinant DNA technology (transforming non-human, mammalian cell lines to express human FVIII)
c) Cloning of the normal FVIII gene and production of synthetic FVIII

Dosage guidelines

Dosage is for your own

*Based on the pt's body weight
Rule of thumb:-
*FVIII levels will be increased 2% for every 1 unit/kg infused, thus 50 units/kg IV bolus will rise FVIII to 100%
*FIX levels will be increased 1% for every 1 unit/kg infused, thus 50 units/kg IV bolus will rise FIX to 50%

Example of dosage calculation for Hemophilia A

- Patient:14 y/o boy with a knee bleed
- Weight: 55 kg
- Goal: raise factor VIII level to 50% of normal
- Calculate: 25 units x 55kg= 1375 units
  Or 50 x 55/2 = 1375 units

2) DDAVP (synthetic vasopressin)

-Used either IV or intra-nasaly to Rx pt with mild hemophilia A with the FVIII levels>10% -The drug releases FVIII stored in the endothelial cells, it can double or triple the body's plasma level of FVIII.
-Not all pts respond to DDAVP
-Dose (0.3 microgram/kg) it can be repeated 6-8 hourly
-Response to the second dose is less due to tachyphylaxis

3) Gene Therapy

It involves taking normal clotting factor genes and placing them into the body of a person with hemophilia, with the hope that patients' body will begin to make clotting factors on its own. However this approach is still investigational and not yet applicable clinically .

Complications:

Contamination with viruses

Factor concentrates, like many blood products, are made from pooled plasma. It can take up to 30,000 donations of blood to make one batch of factor concentrate and blood products have always been susceptible to contamination by viruses. (Hep A, B, C, HIV and others)

Development of inhibitors

- 10-20% have IgG antibodies to FVIII (mostly in severe cases) in pt Rx w/F concentrate
- High doses of FVIII may not produce a rise in the plasma level of FVIII
- How do we deal with pts who develop inhibitors ?
- Purified procine FVIII may not cross-react with pts antibodies.
- Prothrombin complex (Feiba, autoplex)
- Recombinant F VIIa also "bypass" FVIII
- Immunosuppression/immunoabsorption .

Indication of factor VII :- anyone who develop inhibitors against factor VIII

Clinical management of bleeding

As soon as bleeding is suspected treatment should be given according to its severity

*Minor bleeding: (e.g laceration,dental extraction,early joint or muscle bleeding) the FVIII level should be raised to 30-50%

*Moderate bleeding: (e.g major joint or muscle bleeds) FVIII raised to at least 50-70%

*Severe bleeding: (e.g CNS, GI bleed, postoperative, major trauma) FVIII raised to 80- 120% for 7-10 days . And 100% preoperatively and maintained above 50% until healing

Acquired hemophilia

- Due to the development of an inhibitor (antibody) against factor VIII in a previously normal individual.

- It is rare, and affects both males and females.
- It is sometimes associated with cancer, auto- immune conditions and pregnancy but most cases arise spontaneously
- Severe and often life threatening
- Treatment includes factor raVIIa, prothrombin complex, immunosuppression and rituximab (anti CD20 antibody)

Surgery in hemophiliacs

Minor surgery

- DDAVP with Tranexamic acid may suffice (mild haemophilia). Need to check response before hand
- Raise FVIII level 50-70%

Intermediate & major surgery

- FVIII raised to 80- 120% for 7-10 days and 100% preoperatively and maintained above 50% until healing .
- Twelve hourly boluses or continuous infusion

von Willebrand's disease (vWD)

vWD-investigations:

Ristocetin Induced Platelet Agglutination
VIII:C
vWF:Ag
vWF multimeric analysis

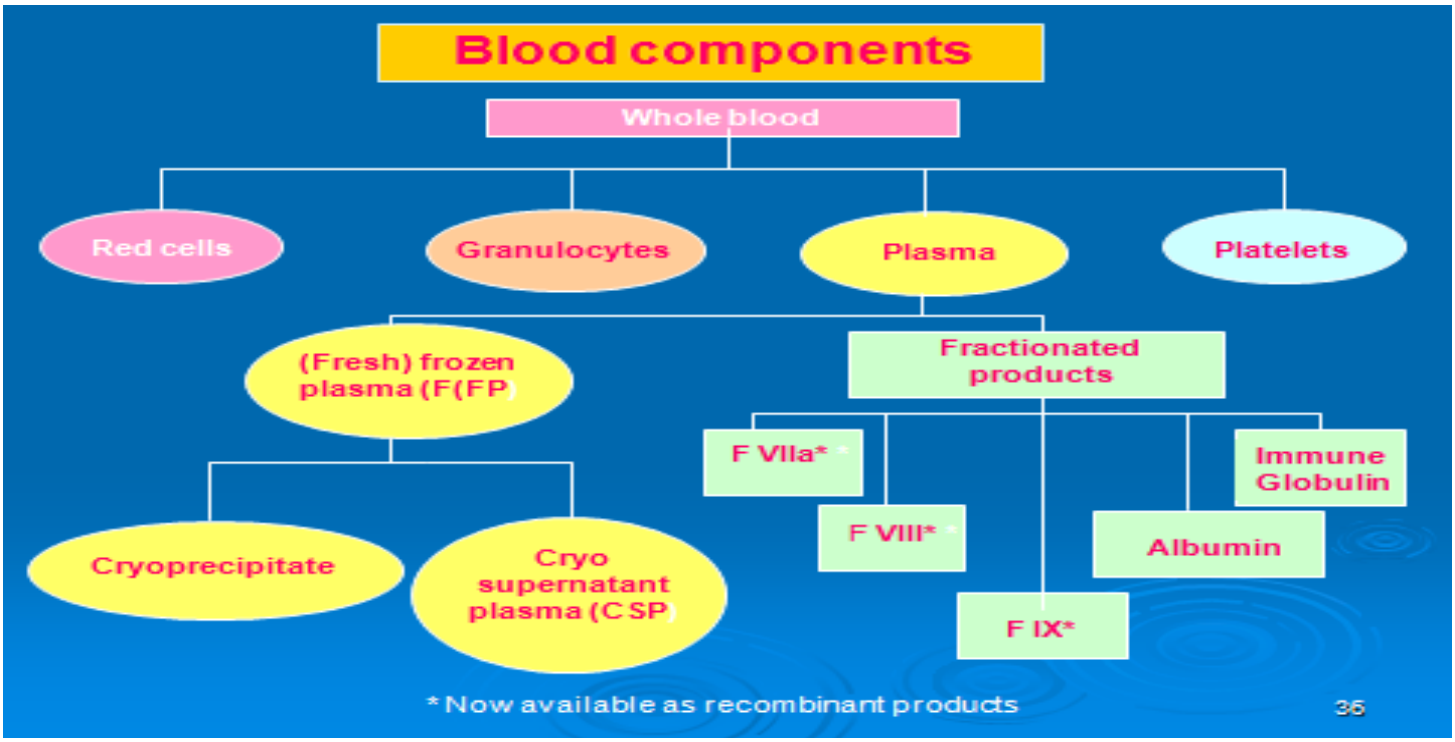
Type :

1 - Partial deficiency of vWF
2A - Absence of large and interm. multimers
2B - Absence of large multimers
2M- multimers normal, pl. function ↓
2N - ↓ affinity for FVIII
3 - severe deficiency of vWF

Treatment of bleeding and surgery in vWD

- DDAVP for minor bleeding and surgery in type 1 & type 2A

- Intermediate purity FVIII (8Y, Hemate P)
- If above measures fail
    - Cryoprecipitate
    - Platelet transfusion
- Purified vW factor is available but needs to be given along with FVIII



Blood components

1. Red blood cells: leukocyte reduced by filtration (LRF)
2. Autologous blood
3. Platelets: (LRF)
4. Platelets, apheresis (LRF)
5. Fresh frozen plasma (FFP)
6. Plasma, apheresis
7. Cryosupernatant plasma (CSP)
8. Cryoprecipitate (Cryo)
9. Serum albumin
10. IV immune globulin (IVIG)
11. Rh immune globulin (Anti-D)
12. Other immune globulins
13. Factor VIII, Factor VII, Factor IX

14. Factor XIII
15. Fibrinogen
16. Zoster immune globulin

Fresh Frozen Plasma

- single donor, infection risks
- ABO typing recommended
- should be used within 2 hours of thawing
- unit contains all factors and activity of a similar volume of plasma (250 ml) ~ 8% plasma volume

Cryoprecipitate

- pooled
- factors VIII, I, XIII, vWF, Fibrinogen
- each unit provides 80 - 100 units of factor VIII

After the slide of cryoprecipitate the doctor said the rest is for your own reading

Summary

Normal Hemostasis:

A protective mechanism that has evolved to maintain physiological Hemostasis.

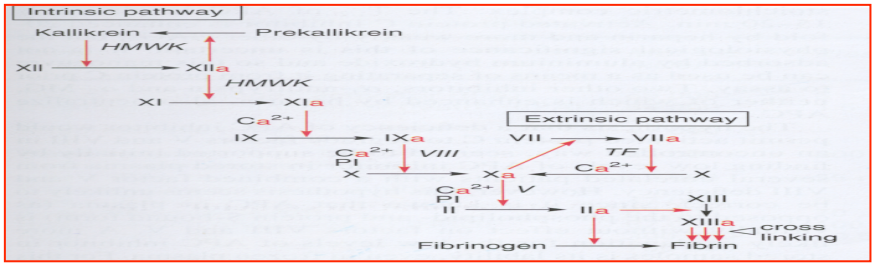
Major components of blood coagulation:

1- Blood Vessels. 2- Blood platelets. 3- Coagulation factors.

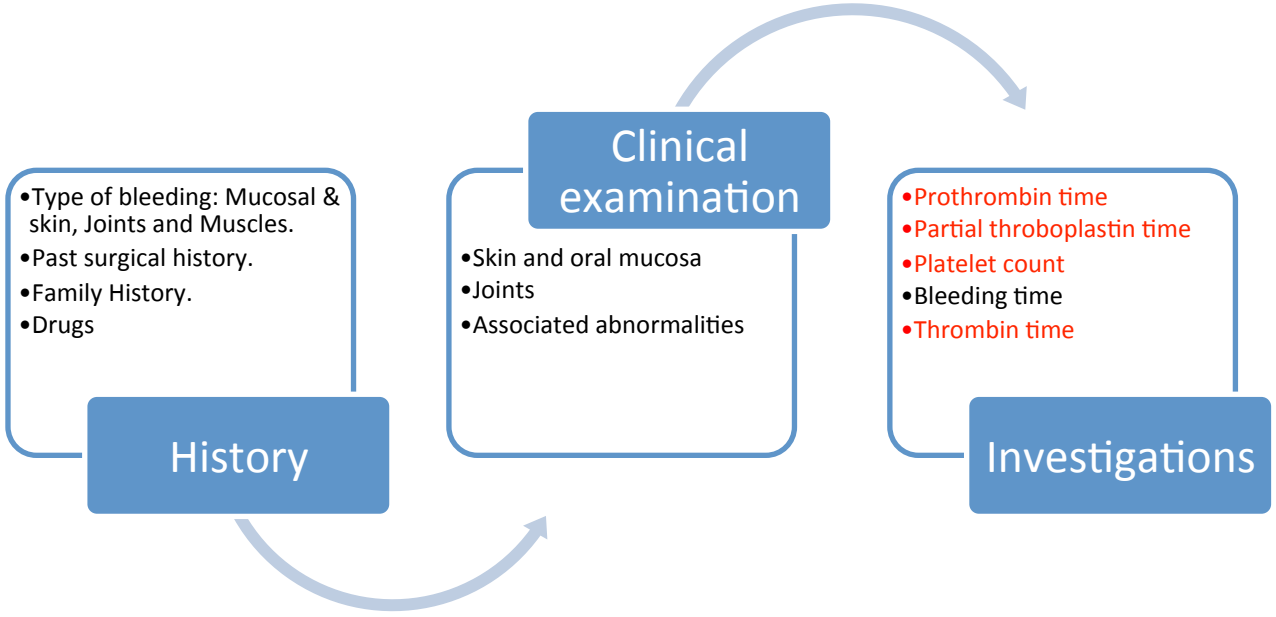
4- Coagulation inhibitors. 5- Fibrinolytic system.

Platelets: are fragments of the cytoplasm of megakaryocytes formed in the bone marrow and are non-nucleated. Activation of the platelets helps in forming a platelet plug at the site of injury & stop bleeding.

Traditional coagulation pathway: (IMPORTANT)



Approach to a patient with bleeding tendency:



Inherited bleeding disorders:

- Haemophilia A
- Von-Willebrand's disease
- Haemophilia B

Haemophilia A:

X-Linked recessive disorder, deficiency of FVIII, males are affected & females are carriers.

Severity of Hemophilia		
Severity	Factor VIII or IX level	Clinical Presentation
Severe	<1%	Spontaneous hemarthrosis & muscle hematomas
Moderate	2 – 5 %	Mild trauma or surgery cause hematomas
Mild	5 - 50 %	Major injury or surgery result in excess bleeding

22

Diagnosis: Prolonged PTT, Low FVIII and normal levels of vWF.

Treatment: factor concentrate for acute bleed, DDAVP, gene thrapy.

Acquired haemophilia:

due to the development of antibody against FVIII in previously normal person.

Von-Willebrand's disease:

Autosomal dominant, deficiency of FVIII-related antigen.

Types: Type 1 - Partial deficiency of vWF

2A- Absence of large and interm. multimers
2B- Absence of large multimers
2M- multimers normal, pl. function ↓
2N- ↓ affinity for FVIII
3- severe deficiency of vWF

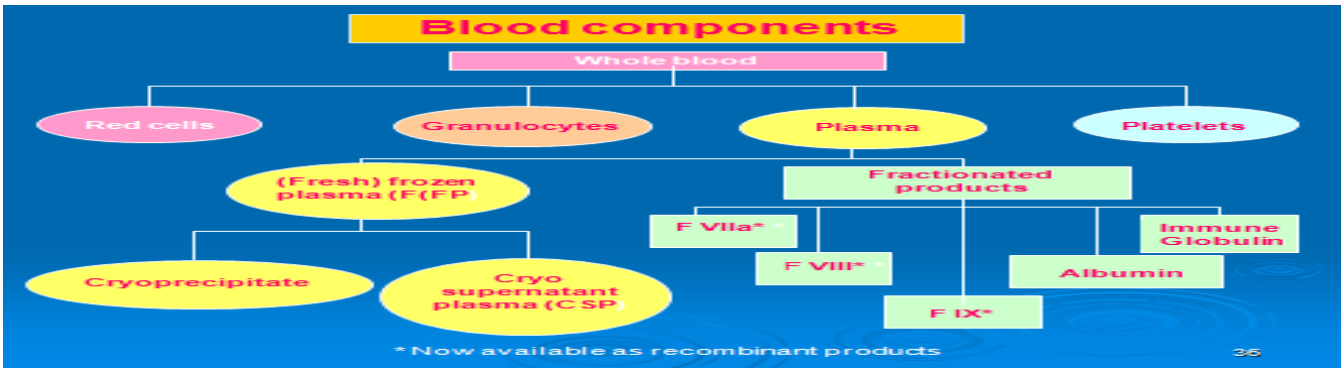
Diagnosis:

- Ristocetin induced platelet agglutination.
- FVIII
- vWF

- vWF multimeric analysis.

Treatment: DDAVP for minor bleeding and surgery in type 1 & 2A, Intermediate purity FVIII. If fail: cryoprecipitate, platelet transfusion.

Blood components:



Questions

(308 PreTest): A 25-year-old woman complains of persistent bleeding for 5 days after a dental extraction. She has noticed easy bruisability since childhood, and was given a blood transfusion at age 17 because of prolonged bleeding after an apparently minor cut. She denies ecchymoses or bleeding into joints. Her father has noticed similar symptoms but has not sought medical care.

Physical examination is normal except for mild oozing from the dental site. She does not have splenomegaly or enlarged lymph nodes. Her CBC is normal, with a platelet count of 230,000. Her prothrombin time is normal but the partial thromboplastin time is mildly prolonged. The bleeding time is 12 minutes (normal 3-9 minutes). What is most appropriate way to control her bleeding?

a. Factor VIII concentrate
b. Fresh frozen plasma
c. Desmopressin (DDAVP)
d. Whole blood transfusion
e. Single donor platelets

(15 First Aid Q&A Step2): A 32-year-old woman presents to the emer- gency department with edema and pain of the right lower extremity that began

after a 6-hour car ride. A Doppler ultrasound was completed in which a deep vein thrombosis (DVT) was noted. The patient has no prior history of DVT or pulmonary emboli. The patient has been taking oral contraceptive pills for the past 2 years and is currently compliant with her med- ication. Her family history is significant for a maternal grandmother, mother, and sister with recurrent DVT. Her temperature is 36.2°C (97.2°F), blood pressure is 112/78 mm Hg, heart rate is 86/min, and respiratory rate is 14/ min. There is no clinical evidence indicating a pulmonary embolism. Which of the following is the most likely cause of her DVT?

(A) Antithrombin deficiency
(B) Coagulation factor V gene mutation (C) Protein C excess
(D) Protein S deficiency
(E) Prothrombin gene mutation

(51 First Aid Q&A Step2): A 7-year-old boy presents to his pediatrician be- cause of increased gingival bleeding after brush- ing his teeth. The patient's mother denies a his- tory of easy bruising or prolonged bleeding. The boy also reports an episode of prolonged and painful knee swelling after a fall in which he hit his knee. The patient's family history is significant for a maternal grandfather who died of a massive hemorrhage after a minor surgical procedure. On examination there are no ecchymoses or pete- chiae. His conjunctivae are pink and a full physi- cal examination is noncontributory. His activated partial thromboplastin time is 63 sec, prothrom- bin time is 12 sec, bleeding time is 4 min, and coagulation time is prolonged. Which of the fol- lowing additional laboratory results is most likely to be seen in this patient?

(A) Decreased factor VIII concentrations
(B) Decreased platelet concentrations
(C) Decreased WBC count
(D) Increased factor V concentrations
(E) Increased hemoglobin

(53 First Aid Q&A Step2): Which of the laboratory findings in the table below are characteristic of von Willebrand's dis- ease? PT refers to prothrombin time and aPTT refers to activated partial thromboplastin time.

(A) A

(B) B

(C) C

(D) D

(E) E

Choice	Bleeding Time (min)	PT (sec)	aPTT (sec)	Platelet Count (/mm³)	Factor IX	Factor VIII
A	3	13	32	202,000	abnormal	normal
B	10	15	42	140,000	abnormal	normal
C	4	12	45	230,000	normal	abnormal
D	10	13	27	58,000	normal	normal
E	9	12	35	143,000	normal	abnormal

C

B

A

E