Responses of body to vascular injury:

1. Vasoconstriction of blood vessels to reduce blood flow
   A) myogenic stimuli under effect of injury
   B) Chemical substances such as endothelin from the injured endothelial cells, serotonin from platelets, thrombaxane due to aggregation and adrenaline.

2. Platelet plug formation, if there is injury collagen will be released, platelets will adhere then they will rupture and release substances so that phospholipids or platelet factor 3 is formed, forming a clot and closing the injury.

3. Formation of fibrin threads.

- During formation of platelet plug: thromboplastin is formed \(\rightarrow\) activate factor 3+12 and initiate clotting mechanism.

- Almost all clotting factors are produced by liver so usually any disease affecting liver will affect coagulation factors.

- Factors 2,7,9,10 need Vitamin K for their synthesis “vitamin k dependent factors”

Coagulation mechanism has 3 pathways: intrinsic, extrinsic and common pathway

- Intrinsic and extrinsic pathways activate factor 10
• Intrinsic is initiated when plug is exposed to foreign surface. “contact phase “
  a) Factor 12 activation: high molecular weight kininogen +kalikrein are involved.
  b) Activated factor 12 activates factor 11
  c) Activated factor 11 in presence of Calcium activates factor 9
  d) Tenase complex (activated factor 9 +calcium +phospholipid +factor 8) activates factor 10.

• Extrinsic pathway initiated during injury, pathway in slides.

• Fibrin threads first produced under effect of thrombin is soluble and not stable, factor 13 stabiles it which is activated by thrombin and calcium to become insoluble.

• platelets can directly activate factor 11 without factor 12 or kininogen so people with deficiency of these 3 factors (kinonigen +12+kalikrein ) doesn’t have bleeding where as people with factor 11 deficiency have problems .

• If we eliminate Calcium blood doesn’t clot because it is needed in every step except first 2 steps of intrinsic pathway.

• In vivo mainly extrinsic pathway plays the major role although tissue thromboplastin is not present but monocytes +endothelial cells produce tissue thromboplastin in infection.
Intrinsic pathway is slow and weak (6 minutes) and all components are present in blood while extrinsic is fast and powerful (16 seconds).

- Thrombin actions: activation of factors 8,5,13, platelets and proteins C &S.

- Calcium activate granules in platelets and activates actin and myosin fibrins...

Factors causing normal fluidity of blood

1. Heparin in plasma produced by basophiles and mast cells.
2. Thrombin and fibrin present in blood in an inactive form (prothrombin +fibrinogen), these factors are removed during circulation by liver.

- Minor clottings are present in everyone; these can dissolve and end as fibrin or fibrinogen degradation products that function as anticoagulant factors.
- Endothelial cells, platelets and other blood cells are negatively charged and so repel each other so they don’t stick to inner surface of blood vessels so clotting is not initiated.
• Anticoagulation factors including tissue factor pathway inhibitor +ant thrombin 3 +protein S&C and thrombomodulin move from endothelium to interact with elements from coagulation pathway.
• Tissue factor pathway inhibitors inactivates (tissue activated factor 7 and calcium) complex.
• Antithrombin 3 inactivates factor10 +thrombin
• Thrombomodulin bind with protein C & S to inactivate factor 8+5 And also bind with thrombin to eliminate it from circulation.
• Alpha-2 macroglobulin and alpha-1 antitrypsin contributes to antithrombin effect of plasma.
• Fibrinolytic system works if these don’t function properly.

Fibrinolytic System

• Plasminogen →b-globulin proenzyme in blood and tissue fluid made by liver , eosinophils and intravascular endothelial cells
• Plasminogen is activated by intrinsic and extrinsic pathwas
• Trauma , exercise emotional stress will cause the release of it
• Activated factor 12 als potentiates plasminogen action so it have 2 function 1) coagulation 2) fibrinolytic system .......Also produces bradykinnin that increase vascular permeability and act as vasodilator.

Activators of plasmenogen :1)endogenous tissue plasminogen activator and contact phase of coagulation

2)exogenous urokinase and streptokinase
• Urokinase and streptokinase are given to patients to dissolve clottings in seconds ...they are called life injection.

• Clot retraction measures the ability of blood clot to retract. Normally after 2 hours there is partial retraction and after 24 hours there is complete retraction.

• Platelets and calcium play major role in retraction.

• If we remove platelets, blood or plasma will still coagulate because of clotting factors but is deficient as platelets are not present.

➢ Thrombus is unwanted clot in blood vessels, this clot may dissolve or it may be removed under effect of blood pressure and circulate ....this is called embolus. Embolus may be a clot bubble of air piece of fat or debris. This may block arteries supplying brain, heart and lungs.

➢ Arteriosclerosis and atherosclerosis are main conditions underlying most heart attacks.

➢ Arteriosclerosis :losing of flexibility of blood vessels in old people

➢ Atherosclerosis :lipid on inner surface of blood vessels so they lose flexibility

➢ After major patients are advised to move to increase blood flow and if they can’t they need to take heparin.
Classification of haemostatic defects:

- Defects in blood vessels, platelets number, platelets function, in coagulation factors or excessive fibrolytic system activity.
- Platelet deficiency is most common.
- 2\textsuperscript{nd} is clotting factor problems.
- Vascular abnormalities may be either from the blood vessel itself or perivascular C.T around them.
- Vascular disorder characterized by easy bruising and spontaneous bleeding from blood vessels.
- Usually disorders are not sever in childhood and may become sever in adults.
- They maybe inherited or acquired.
- Acquired such as 1) senile purpura 2) purpura assosiated with infection 3) scurvy purpura associated with vit. C deficiency 4) (slowed)?? purpura associated with medication or cortisone.

- Purpura is easy bruising and rupture of blood vessels.

- Deficiency in number of platelets is thrombocytopenia so factors are deficient and so the blood vessels integrity is affected and RBC’s leave circulation into tissues \(\rightarrow\) bleeding \(\rightarrow\) spontaneous skin purpura and mucosal hemorrhage and prolong bleeding after trauma.
Causes of thrombocytopenia

1. Failure of platelet production which is seen in leukemia and sometimes in B12 deficiency or from drugs affecting Bone Marrow.
2. Chemicals, viral infection or part of B.M failure in aplastic anemia or megaloblastic anemia.
3. Increased destruction which will increase heparin conc. In blood because of basophiles destruction and disseminated intravascular coagulation.

- In this coagulation there is continuous destruction of platelets so more utilizing of coagulation factor causing thrombosis.....They say that this maybe due to infection or antibodies.
- these patients are usually given heparin

4. Abnormal distribution of platelets in spleenomegaly, diminished loss and massive blood transfusion to bleeding patients.

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