**Today we will talk about Causes of thrombosis and and bleeding.**

**تم إعادة ترتيب المعلومات بطريقة تسهل الفهم.**

 **Causes of thrombosis:**

1- **Injury of blood vessels by any means**

-Mx: Intrinsic and extrinsic pathway are activated

**2- Infection of blood vessels of perivascular connective tissue:**

Mx: pathogens infect monocyte leading to

release of tissue factor 3 and subsequent activation of coagulation pathway.

3- **Slow of blood flow (Stasis)**

Ex.: After surgery and delivery

**4- Changes in blood composition:**

Ex.: Increased platelets number, increased fibrinogen concentration, or after surgery and delivery.

 **Causes of bleeding:**

The problem will be either in the blood vessel itself and the perivascular connective tissue or in the blood.

**1-Vascular defects or disorders.**

 **Could be in the blood vessel or perivascular connective tissue.**

 **Uncommo, Could be Genetic or acquired**

 **Characterized by bruising**

 **Bleeding is mild during childhood and become relatively severe in elderly**

 **Examples of acquired disorder:**

**1. Senile purpura :**

**-Most common**

**-Senile (old-aged), purpura (easily bruising**

**–ruptured- of blood vessels)**

In the old-aged people the blood vessels will become fragile so it is more compliant for rupture.

**2. Purpura associated with chronic infection especially viral**

**3. Deficiency of vitamin C (scurvy)**

**4. Steroid purpura (cortisol injection)**

**2-Blood defects: they are 4 :**

**1-Platelets number disorder:**

**2-Platelets function disorder**

**3-Coagulation factor abnormality**

4-Excess of fibrolytic system

**1. Platelets number disorder:**

**-Most common cause of bleeding , especially thrombocytopenia**

**-Rem.:** Platelets produces many factors PDGF, and they play a role in the integrity of blood vessels and angiogenesis, so the RBCs migrate from the blood vessels to the tissues.

**-THROMBOCYTOPENIA:** is the deficiency of the platelets, and it is accompanied by:

1-cutaneous skin purpura.

**Thrombocytopenic purpura**

2-mucosal hemorrhage.

3-Sometimes chronic bleeding especially after trauma.

**But how it causes Purpura and hemorrhage?!** Clot retraction needs 2 important factors Platelets and Ca+2, so when platelets count is low ,clot retraction is deficient and there is poor constriction or ruptured blood vessels. It's characterized by increased bruisability and multiple subcutaneous hemorrhages.

 The causes of THROMBOCYTOPENIA are:

1-**failure of platelets production** (most probably because of drugs, chemicals and chronic viral infections).

2-**Part of the general bone marrow failure** (like aplastic anemia or leukemia and megaloplastic anemia).

3-**Increase destruction of platelets**, in this case heparin concentration increases and Disseminated intravascular coagulopathy (increased coagulation-fibrinolysis cycle that will end by decreased platelets number) occurs.

4-**Abnormal distribution of platelets**, this is seen in "**Splenomegaly**", because the spleen enlarges in size and captures high percentage of platelets.

5-**Dilutional loss in massive transfusion of blood**

**2. Platelets function disorder (thrombocytopathia )**

**-3rd common cause of bleeding**

**-Maybe inherited or acquired**

**A) Inherited thrombasthenia:** results from deficiency in one or all of the following:

**1- in the released substances (ADP, Serotonin, granules especially electron dense granule).**

**2- in the adhesion factors**

**3- in the production of thromboxane or failure of aggregation.**

**4- of the coagulation factors from factor I to XII**

**and even factor XIII.**

**B)acquired thrombasthenia:** the most common example is aspirin ( and it is effect on the synthesis of TXA2)

- Can cause **thrombasthenic purpura:** here the function of platelets is abnormal while the platelets count is normal, also characterized by cutaneous skin purpura, mucosal hemorrhage.

**3. Coagulation factor abnormality (2nd most common)**

- Deficiency of Factor VIII (hemophilia A), Factor VIII (hemophilia B), vWF **are uncommon,** Deficiency of other factors **is rare.**

o **Haemophilia A :**

**- is the most common** inherited disorder

of blood coagulation factor deficiency **.**

**-** X-linked recessive trait **so the females are only carriers, and the males are affected.**

**- 33% of patients don't have family history.**

**-the incidence is 1/10,000.**

**-Hemophilia B has the same symptoms of hemophilia A, so sometimes we can't differentiate between haemophilia B and haemophilia B unless we use some tests.**

-Hemophilia A : **the problem is in factor**

**VIIIc,** so there is a coagulation defect.

o **Von willebrand disease:**

**-** The problem is in **factor VIII related antigen**

**-Somatic (Autosomal dominant)** disease (the problem is in the somatic chromosomes not in the sex chromosomes)

**-Factor VIIIc** is normal but it's rapidly destroyed in the absence of factor VIII related antigen.

**-There are Platelet adhesion and coagulation defects.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Hemphilia**  **A** | **Hemphilia**  **B** | **vWF** |
| **inheritance** | X-linked |  | AD |
| **Platelet**  **count** | Normal | Normal | Normal |
| **Bleeding**  **time** | Normal | Normal | prolonged |
| **Factor VIIIc** | low | Normal | low |
| **Factor**  **VIIIAg** | Normal | Normal | low |
| **aggregation** | Normal | Normal | impaired |

o Now we will talk about hereditary disorders of the other coagulation factors.  
- All these disorders are rare, in most inheritance is **autosomal**.

-there is **a good correlation** between the patient's symptoms and the severity of coagulation

factor deficiency.

-**factor XII** deficiency is not associated with abnormal bleeding

**4-mechanical stirring** : we take the blood into tube then we stir it using a glass rods then we stir it we remove the fibrin threads and this prevents Clotting.

Also in the Lab we use:

1. **Non-wettable surfaces**We take the blood into non-wettable surfaces, in this case we delay the formation of thrombokinase.
2. **Eliminators of Ca:**eg**.** CitrateandEDTA(Themostimportantone).

-**Factor XI** can be activated by platelets directly, therefore any deficiency in the factor XII and associated factors doesn't lead to severe or valuable bleeding, but **factor XI** deficiency produces mild symptoms.

**-Factor XIII** deficiency produces severe bleeding tendency because factor XIII stabilizes the fibrin threads to make them insoluble).

 Medications:

**1- Decomarol or warfarin(Coumadin):**

-it's very famous anticoagulant drug, it interacts to delay or prevent the synthesis of vitamin K- dependent coagulation factors, consequently affects the prothrombin and so prothrombinase **(delay the formation thrombokninase).**

**-acts slowly after 1-3 days, functions in vivo only and only in the liver** (because there is no vitamin K-dependent factors in vitro), plant source and DOA days.

**2- heparin:**

**-Acts rapidly, in vivo or vitro and is of animal origin and DOF hours .**

- Heparin is considered the "intrinsic pathway specialist" as it blocks the whole intrinsic pathway **(binds anti-thrombin 3)**

**3-hirudin:** is another anticoagulant drug, and is produced from the leeches, Chinese still use it in hypertensive patients; it prevents the action of thrombin.

4. Excess of fibrolytic system (excessive plasmin production).

ما حكى عنها اشي

بالنهاية بتمنى ترجعوا **لهاظ** الفيديو الي راح يساعدكم في فهم هذه المحاضرة.

<http://www.youtube.com/watch?v=fqgp7DpAmIg>

Done By: Ibrahim **(Shanti & Sabri)**

Good luck 