HEMATOLOGY
&LYMPH SYSTEM

physiology sheet

Number	8
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In this sheet I'm going to write every word the doctor said, but excuse me because some of the words weren't clear to me so I expressed the concepts in my way. I also added some slides from 2013's handout, which I think is the same as ours. Anyway, I hope it will be enough for you.

Any extra information will be written in italic.

Corrector's note: this sheet is even easier than the previous one. Mid material ends here. You're doing a great job ^_^.

P.s: any sarcastic note is mine too, sorry in advance XD.

Previously, on Physiology with Professor K: *(omg lol)*

Prof. K briefly revised the factors which cause normal fluidity of the blood:

1. Heparin
2. Clotting factors which circulate as proenzymes in the blood, or removal of some factors by the liver. *Maintaining the normal amount of clotting factors is done either by being inactive unless needed, or by removal of the active form from the circulation by the liver.*
3. Minor clotting
4. Protein S and protein C
5. Normal fibrinolytic system

Fibrinolytic system:

It means production of plasmin to lyse clots in the blood vessel, **how?**

1. Activated factor XII potentiate the action of plasminogen activators.
2. Plasminogen activators in turn cause the conversion of plasminogen to plasmin.
3. Plasmin causes proteolysis of fibrinogen, fibrin, factor V and factor VIII.

This will result in fibrin degradation products which function to inhibit the polymerization of fibrin and platelet aggregation, I.e. clot dissolution.

Plasminogen activators:

promote the conversion of plasminogen (inactive form) to plasmin (active form).

They are either endogenous or exogenous:

- **Endogenous**, such as: **tissue plasminogen activators (TPA)**, *can be produced commercially by genetic engineering. Given by injection to dissolve a clot hence its name " life injection".* Also, **contact phase of coagulation**, the exposure of the blood to the medium.
- **Exogenous,** such as: **streptokinase**, *produced normally by certain types of bacteria,* and enzyme **Urokinase** that is present in plasma and activate the plasminogen activators.

All of this will lead to production of plasmin from plasminogen and α_2-anti plasmin which inhibits fibrin.{ figure1 last page}

Clot retraction time:

Assume we have a sample of untreated blood (blood with no anti-coagulants) which is left in the lab. We will notice that a clot was formed. The untreated blood will shrink either partially or completely, and extrude the entrapped fluid inside as a *serum*. The time needed for this is called "clot retraction time", and it's used in diagnosis of hemorrhagic indices such as **Purpura**, in which the clot retraction time is greatly increased. In severe cases, there is no retraction of the blood clot, even after 24 hours!

Two factors which play a vital role in clot retraction:

a. Platelets
b. Calcium

Clot retraction measures the normal platelet count and the normal calcium present in blood.

10 min.

Thrombosis:

- Sometimes, an unwanted clot (thrombus) is formed in the blood vessel. This condition is called thrombosis (duh -_-). The thrombus does not dissolve, it remains.
- This clot sometimes -by the effect of blood flow- is removed from its attachment site and moved throughout the circulation, this condition is called embolism, and the circulating clot is called embolus. It is not always a blood clot; it could be an air bubble, fat, a piece of a broken bone, or might be debris of an injured tissue.
- This embolus will continue circulating in the blood vessels until it faces a narrow or a small blood vessel and lodges there, thus obstructing that vessel. This will cause problems such as tissue ischemia. This happens usually in blood vessels supplying heart or lungs.

****Make sure you know that an embolus in arteries is much more dangerous than in veins, and specially in arteries supplying vital organs such as Heart (*leads to heart infarction)* and Brain (*leads to stroke).***

General causes of thrombus:

1. Injury to a blood vessel by a trauma, this will activate intrinsic and extrinsic pathways which start a coagulation cascade, which in turn will lead to formation of a thrombus.
2. Infection, this induces platelet adhesion to the inner endothelium cells of the blood vessel, which leads to ATP release and platelet aggregation.
3. Changes in blood composition such as *high fibrinogen* which causes the platelets to stick to the inner surface of the blood vessel and aggregate forming a clot.

Professor K said that point 2 and 3 occur during delivery or after a major surgery; since both sleep for a long time and sometimes they cannot move. Doctors' advise the patients to walk after a major surgery, otherwise they will need anti-coagulants.

Arteriosclerosis and Atherosclerosis:

Arteriosclerosis: It is a condition where a blood vessel loses its elasticity and flexibility, either because of a disease or aging, and it is the most common underlying cause of heart attacks.

Atherosclerosis: The accumulation of fat in the inner surface of the blood vessel resulting in its narrowing, this will lead to formation of a blood clot or a circulating thrombus (embolus).

Hemostatic Defects:

- **Causes of hemostatic defects:**
    1. Vascular disorder.
    2. Platelets *count* abnormality.
    3. Platelets *function* abnormality.
    4. Coagulation factors abnormality.
    5. Excessive fibrinolytic system.

Which one is the most common cause?

> *First is platelets count abnormality, then comes coagulation factors abnormality, platelets function abnormality comes last.*

- **Vascular disorder:**

The problem here is either in the blood vessel itself or the connective tissue around it, this disorder is either genetic or acquired.

- **Genetic**: usually appears mild during childhood and then becomes more numerous (more vessels affected) during adulthood. It is characterized by microvascular swelling with minor bleeding.
- **Acquired (latent)**: examples:
    1. Senile purpura: easily bruised blood vessels because of advancing age. That doesn't necessarily mean in occurs in all elderlies; because it depends on genetics and nutrition too. It appears more in poor population.
    2. Purpura associated with infection which causes toxic damage to

the epithelium.

3. Scurvy: vitamin C deficiency, it causes purpura.
4. Steroid purpura: a result of prolonged steroid therapy such as cortisol.

❖ **Platelets number disorder:**

Such as thrombocytopenia: low platelets count characterized by continues skin bruising (purpura) *now we finally know what a purpura is!!* Platelets maintain the integrity of the blood vessel and when there is a low count of platelets this will affect their integrity.

Causes of thrombocytopenia:

- Failure of platelets production due to some drugs, chemicals, or viral infections.
- Bone marrow failure due to Leukemia, Aplastic anemia, and megaloblastic anemia.
- Increased destruction of platelets because of high concentration of heparin, or a condition called *disseminated intravascular coagulation*.
- Splenomegaly: enlarged spleen which captures a lot of platelets.
- Loss of platelets by massive blood transfusion.

Thrombocytopenic purpura: It is a purpura due to low platelets count, when platelets' count is low, clot retraction is deficient, so there is poor repair of the injured blood vessels. This leads to higher susceptibility to bruising and multiple subcutaneous hemorrhages.

Clot retraction is very important because when the clot shrinks it releases the entrapped platelets and fibrin. This helps the injured blood vessel to repair the damage.

Thrombocytopathia: Platelet function abnormality. It means that there is a problem in the function of the platelets.

It's either:

Genetic: problem in the related substances or deficiency in vWf or deficiency in glycoprotein-1 on the platelet or failure in thromboxane synthesis.

- **Acquired:** Aspirin therapy; very high doses of aspirin (unlike the dose used to prevent heart attacks)

Thrombasthenic purpura; easily bruising due to problem in the platelets function. Purpura can happen also when the count of the platelet is normal but the function is abnormal or vice versa.

❖ **Coagulation factors disorder:**

An Inherited deficiency of a coagulation factor, such as Hemophilia A (deficiency of factor VIII "8"), Hemophilia B (a deficiency of factor IX "9"), von Willebrand's Diseases all are uncommon, but the other factors disorders are rare!

- **Hemophilia A**:

  - The most common inherited coagulation defect among the uncommon.
  - Incidence 1:10000.
  - Factor8-c is deficient, but Factor8-related Antigen is intact. That will lead to coagulation defect only. {see the figure below}
  - Sex-linked (still 30-35% of patients don't have a family history)
  - Appears in Males. Females are only carrier (a female cannot be diseased; 2 abnormal genes (Homozygosity): Fatal).

- **Von Willebrand's disease**:

  - Inheritance is autosomal {somatic}

- No problem in the X chromosome of the factor 8 c, but there is a problem in the Factor8-related Antigen, and this results in rapid destruction of Factor8-c which leads to platelets adhesion and coagulation defect. {figure2 }

- **Hemophilia B**:
  - Similar symptoms to Hemophilia A, but less common.
  - Factor9 is deficient.
  - Sex-linked.

Clinical features of Patients with these defects:

Severely affected infants may suffer from profuse post-circumcision hemorrhage. Prolonged bleeding occurs after dental extraction. Operative and post traumatic hemorrhage are life threatening in both severely and mildly affected patients.

Remember that:

- Factor8-related Antigen: for Aggregation
- Factor8 (vWF): for Adhesion
- Factor8-c: for Clotting.

The Doctor compared between them, study the table below.

Table 13.2 Main clinical and laboratory findings in haemophilia A, factor IX deficiency (haemophilia B, Christmas disease) and von Willebrand's disease.

	Haemophilia A	Factor IX deficiency	Von Willebrand's disease
Inheritance	Sex-linked		Dominant
Platelet count	Normal	Normal	Normal
Bleeding time	Normal	Normal	Prolonged
Factor VIII:C	Low	Normal	Low
Factor VIII:AG	Normal	Normal	Low
aggregation	Normal	Normal	Impaired

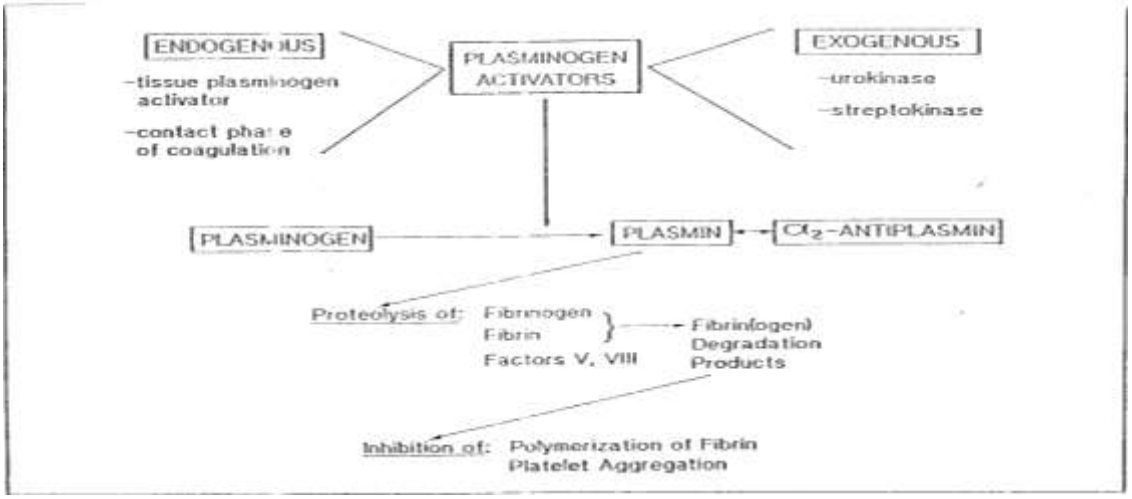

figure 1

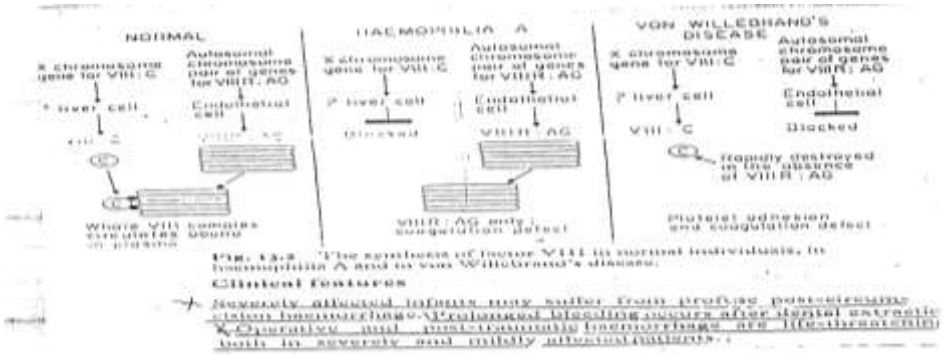

figure 2

That was my first sheet, I tried my best to make it clear and easy. I'll accept any feedback, forgive me for any mistakes. Good luck on Saturday.

The End.