Hematology

PHYSIOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number: 8

Subject: Haemostatic defects and Blood groups

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By the Name of Allah the Compassionate the Merciful

❖ In this sheet we are going to discuss :

1) The Haemostatic defects which means bleeding disorders.
2) The blood groups.

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1) Haemostatic defects are associated with one of these disorders:

a) Vascular defect (in the blood vessels themselves).
b) Platelets number defect (platelets deficiency). >>> **the most common !**
c) Platelets function defect.
d) Coagulation defect . >>> **the 2nd most common !**
e) Excessive fibrolytic system.

- *Vascular Defects :*

➢ The problem (or defect) is either in the blood vessel itself, or in the perivascular connective tissue around it.

➢ Could be inherited/Acquired :

- Inherited: Appears mild at childhood, becomes moderate, sever in adulthood and old age.
- Acquired: examples :

I. Senile Purpura (purpura of old age); in the old age the vessels will rupture easily.
II. Purpura associated with Infections specially chronic infections.
III. Purpura because the Vit. C deficiency ((Scurvy Disease)).
IV. Steroid Therapy Purpura.

➢ Characterized by**: Easily Bruised vessels [Purpura]**, and Spontaneous Bleeding.

➢ Usually not severe if the problem is only in the blood vessel.

- *Platelets Number Defect (Thrombocytopenia)*

- As we said the most common cause of haemostatic defects is the **Thrombocytopenia**
- Platelets are important for maintaining the normal integrity of the blood vessel so there is purpura bcz of the thrombocytopenia.
- The main causes of thrombocytopenia:
  i. Failure of platelets production >>>due to leukemia, B12 deficiency.
  ii. General Bone Marrow Failure.
  iii. Increased destruction of platelets
  iv. Abnormal Distribution of Platelets (Splenomegaly: enlargement of spleen thus it captures a lot of platelets)
  v. Dilutional Loss (Massive Blood Transfusions) <<< the percentage of the plasma higher than the HTC then consequently affect the platelets number.

- **Thrombocytopenic Purpura:**

Occurs bcz of low platelet count then there is clot retraction deficiency { clot retraction needs platelets and calcium to occur } ,
these blood vessels **cannot vasoconstrict** and they are easily rapture characterized easily bruising, and **multiple** subcutaneous hemorrhage .

- *Platelets' Function Defect { Thrombocytoasthenia } :*

- Characterized by: Skin Purpura, Mucosal Hemorrhage, Prolonged BT.
- Inherited/Acquired;
  - Inherited:
    characterized by either the deficiency in the granules number, or in the contents of these granules.
  - Acquired:
    Aspirin Therapy (which delays the production of Tx-A2) is the most common cause.
- **Thrombasthenic Purpura**:
  purpura bcz of the Thrombocytoasthenia ,,,,
  normal platelet count, but abnormal function of circulating platelets.

- *Coagulation Defect*

- 2nd most common cause of bleeding.
- There is disorder in the coagulation factors.
- Haemophilia A (deficiency of factor VIII {8}), Haemophilia B (a deficiency of factor IX {9}) , von Willebrand Diseases are uncommon, but the others are rare!

- **Haemophilia A:**

- The most common inherited coagulation defect among the uncommon.
- Incidence 1:10000.
- Factor8-c is deficient but no problem in the Factor8-related Ag so that will lead to only coagulation defect. { 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 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 Ag, and this results in rapid destruction of Factor8-c that leads to platelets adhesion and coagulation defect . { see the figure below }

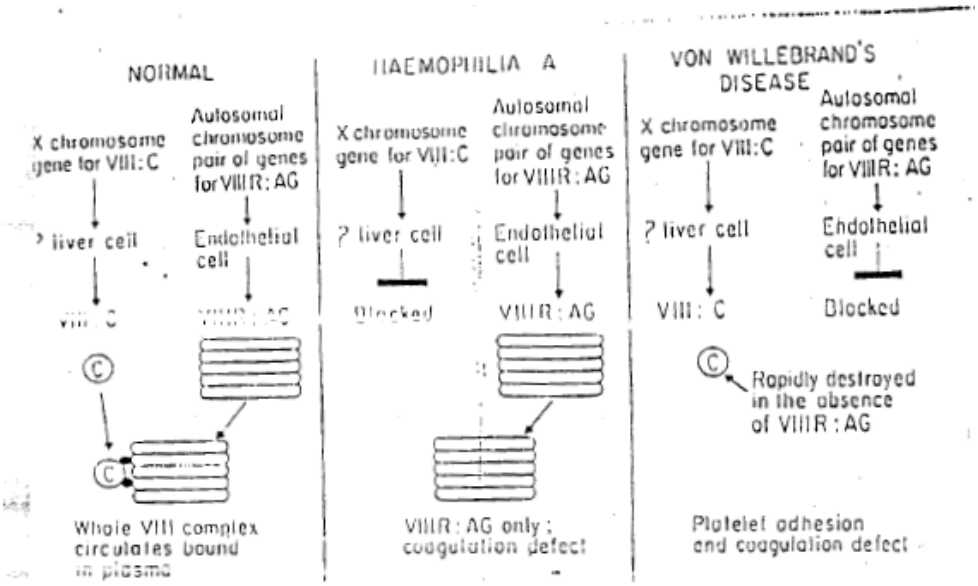

Fig. 13.2 The synthesis of factor VIII in normal individuals, in haemophilia A and in von Willebrand's disease.

- **Haemophilia B:**
  - Similar symptoms to 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 Ag: for Aggregation
  - Factor8 (vWF): for Adhesion
  - Factor8-c: for Clotting

In this table we can compare between these three defects !!

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

- **Hereditary disordered other coagulation factors :**
  - They are rare.
  - In most, inheritance is somatic; however, some are X-linked.
  - There's usually a correlation between the patient' symptoms and the severity of the disease.
  - Factor12 deficiency is not associated with abnormal bleeding.(hemophilia C)
  - Factor11 is activated directly by platelets, and if deficient produces mild symptoms.
  - Factor13 is important in stabilizing the fibrin threads; along with Thrombin and Ca. Factor13 deficiency produces severe bleeding.

- *Excessive Fibrolytic System*

➢ Fibrinolysis is a physiological response, but excessive fibrinolysis is pathological.

- Ca is usually eliminated by EDTA or oxalate to decrease its effect on thrombosis.

➢ Anticoagulants prevent the coagulation :P , they are clinically used also used in the labs .

➢ generally they're classified into 3 (Famous) classes:

a) Coumadin -like anticoagulants (Warfarin):

- Decrease the production of prothrombin and delay the conversion to the thrombin by limiting the activity of the (blood) Thrombokinase .
- Plant origin.
- Act slowly but for long time.
- Inhibit the production of vit.K so vit.K dependent factors will be affected
- Used only in vivo.

b) Non Wettable surfaces:

- Tube covered by wax , polystyrene or silicon
- Rapid cooling.
- Delay the formation of thrombokinase.

c) Others : **EDTA , Oxalate , citrate** , ,,

- They eliminate the **calcium**, so they block the action of thrombokinase as well as the formation of thrombus.

➢ **Heparin:**

- is very important anticoagulant which can inhibit the whole intrinsic pathway , it can disturb the formation of thrombokinase as well as inhibit the reaction between the thrombin and fibrinogen.
- Animal origin.
- Act immediately within hours.
- In vivo and vitro.

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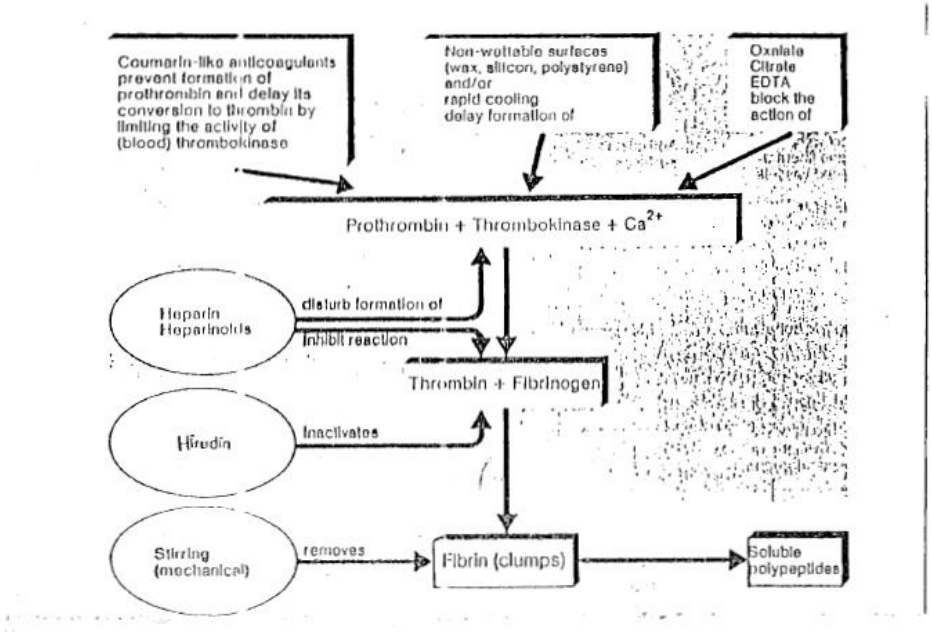
➢ There is a substance called **Hirudin**:

- A chemical taken from leech { العلق} .
- Inactivate the reaction between thrombin and fibrinogen.

- *Old Egyptians and Chinese used these leeches on patients with high blood pressure (until now some people do).*

➢ **Stirring**: (mechanically to remove the thrombus.)

- 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.



2) Blood Groups :

➢ There are classic blood groups , Rh blood groups and minor blood groups

➢ Classic blood groups are A, B, AB, O, these are named bcz of the antigens *(or agglutinogens)* present on the surface of RBCs. In the plasma there are Abs {called agglutinins} .
see the table .

	Group A	Group B	Group AB	Group O
Red blood cell type	A	B	AB	O
Antibodies in Plasma	Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens in Red Blood Cell	A antigen	B antigen	A and B antigens	None

- Agglutination occurs between antigen and antibody but the aggregation in the platelets.

- These antigens are found on the surface of RBCs also in the Salivary glands, Pancreas, Kidneys, Liver, Lungs, Testes, Semen, Amniotic fluid.
- Antibodies in the plasma usually don't present in the newborn babies but they increase in concentration after 6 to 8 month, after that antibodies will occur naturally maybe under the effect of antigen of food in meat or special type of bacteria, sometimes they don't occur at all but that is rare .
  { they increase gradually within 6 month reach the higher concentration between 8 and 10 years . } (maximum at 10 years of age)

- The antigens are determined genetically and continue throughout the life without changes.

- on the surface , there are genetically determined glycoprotein or glycolipids that act as blood groups antigen , appear early in fetal life and remain unchanged throughout the life , more than hundreds of antigen present in surface of RBC beside the classical but only 15 of them have been identified. The most important antigen in minor blood group are : MM,MN, NN, PP, Pp, KELL, LEWIS, LUTHERAN ..etc (capital is dominant , small is Recessive).
- There are many blood systems two of major important (ABO and Rh- blood group).

- The inheritance of the blood groups :
  - ABO system : see the table >>>

Phenotypes (Blood Group)	Genotypes
O	ii
A	I^AI^A or I^Ai
B	I^BI^B or I^Bi
AB	I^AI^B

- **Rh blood group**: by accident they found on RBC the Rh antigen or they call it D antigen.
  - In Europeans, 85% of individuals' RBC have the D antigens but no antibodies in their plasma: these are called Rh or D positive.
  - The remaining 15%: neither antigen or antibody is present, these are called rh or D-negative.
  - When the blood is transfused from a D+ person to a D- patient, the D- blood will start making antibodies against D antigens.
  - There are at least three sets of alternative antigens in the Rh group system:
    D or d, C or c and E or e and D is the most dominant antigen therefore most important clinically and it's the set that is considered in physiology :P .
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- **Racial distribution of blood groups:**
  - From table in slide this is the distribution of blood group in America: White A 41%, B 10%, AB 4%, O 45%, Rh-positive 85%, Rh-negative 15% .
  - the Rh is positive 90% in black ,99% in Chinese , 100% in Indian , 97% in Jordanian { close to the Third World countries }
  - The table from 1943 :O , to show us that there is no significant changes in compare to new studies !

Wish you all best of luck ^^
sorry for any mistake !
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,,, Revised by Omar Saffar