HEMATOLOGY
&LYMPH SYSTEM

physiology sheet

Number	**9**
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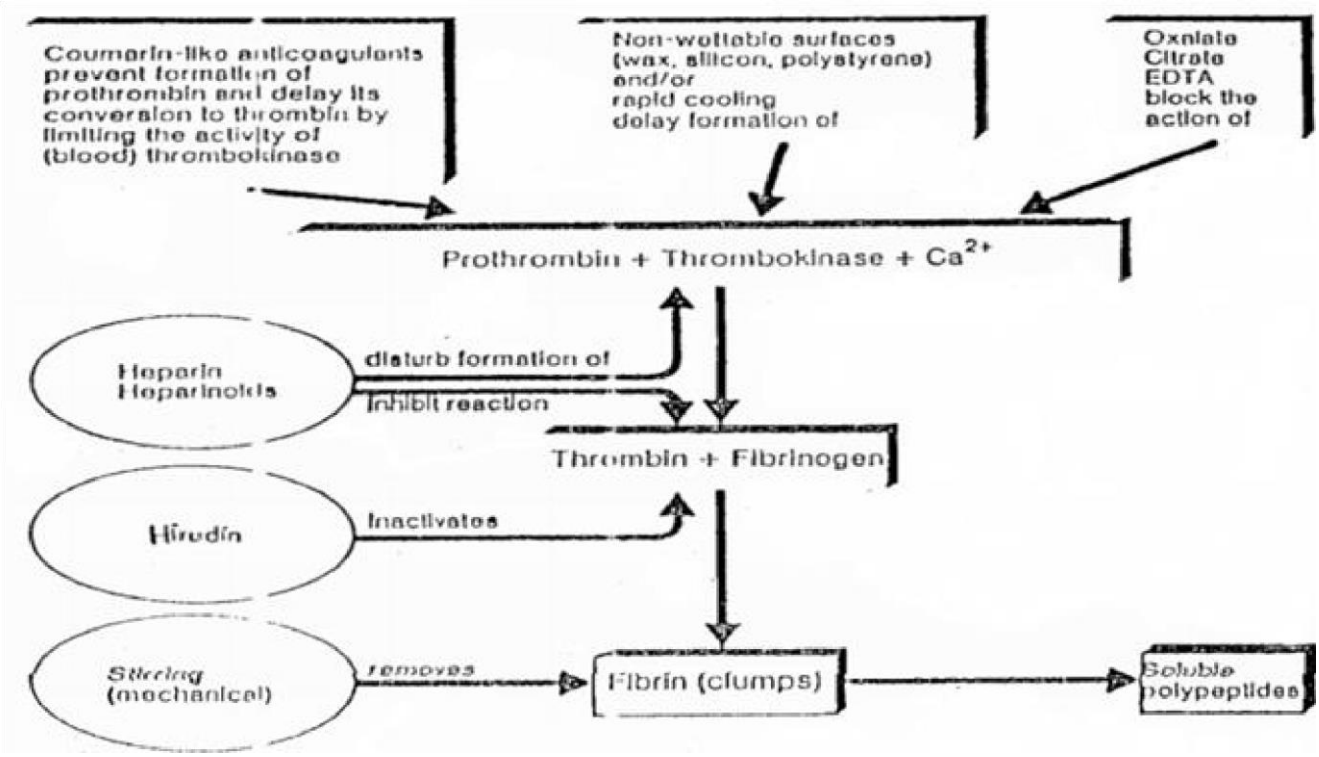
Anticoagulants

If we want to inhibit the coagulation, what can we do?

1) Inhibit thrombin **2)** Inhibit thrombokinase **3)** Decrease Ca++
4) Affect them all

There are chemicals or substances that inhibit the coagulation mechanism, these chemicals are known as *anticoagulants*, they are used in the labs for experiments also they are used in medicine (against diseases).



This figure shows exactly the action of *anti-coagulants*, they are divided into three categories (and others such Heparin):

1. **Coumarin-like** *anticoagulants:* (they are called in vivo Warfarinlike *anticoagulants*): they prevent the formation of Prothrombin and delay its conversion to Thrombin by limiting the activity of Thrombokinase.

2. **Non Wettable surfaces:** we put the blood in such surfaces (Tube covered by wax, silicon or polystyrene). Taken the blood nicely and smoothly in a tube covered by silicon or wax, by this way we inhibit the formation of Thrombokinase.
3. **Substances that capture the Ca++:** Oxalate, citrate, EDTA; they block the action of Ca++.

These are the three catabolic classes of *anticoagulants*, also we have:

HEPARIN; (very famous) produced by anti-thrombin three, it inactivates the whole intrinsic pathway; it can disturb the formation of Thrombokinase and it may inhibit the reaction between thrombin and fibrinogen.

HIRUDIN; this culture produced from the leech, (we don't think this method is still used), Pharaohs and Chinese used these leeches and put it on the vein or the blood vessel and this absorbs about 50ml of the blood, they use it to deal with patients who have **hypertension** but mainly they dry it and use it as fibers, these patients with hypertension are exposed to bleeding and in this way they use some of the blood in order to deal with the state of hypertension.

STIRRING; we remove the fibrin, so we prevent the coagulation.

We see here two main *anticoagulants*, **Warfirin** and **Heparin**:

Warfirin	Heparin
plant origin	animal source (origin); present in our body
acts slowly after one day sometimes	usually it acts rapidly
It acts for days	
It inhibit the formation of vitamin k dependent factors therefore	disturb the formation of thrombokinase and it may inhibit the reaction between thrombin and fibrinogen.
It is used in vivo only	in vivo and in vitro

Duration of action

Mechanism of action

It was one of the exam questions, but the doctor delete it

Blood Groups

There are **classic** blood groups and there are **minor** blood groups also there are Rh blood groups.

Blood groups named because of the presence of antigen, special antigens on the RBCs, there are A and B antigens, they are present on the surface of the cell and they make 4 blood groups (A,AB,O,B). (antigen = agglutinogens)

A

There are A antigens (agglutinogens) on the surface of the RBCs and in the plasma, there are antibodies; beta antibodies (agglutinin)

B

There are B antigens on the surface of the RBCs and in the plasma, there are alpha antibodies

AB

There are A and B antigens on the surface of the RBCs and in the plasma, there are no antibodies

O

There are no antigens on the surface of the RBCs and in the plasma, there are both antibodies; alpha and beta antibodies

That's mean when we donate blood type B to O; reaction will occur between antibodies and antigens. And A cannot accept from B; in blood group A there are antibodies against the antigens of the blood group B.

These antigens are present on the (1) surface of the RBCs as well as some other tissues such as (2) salivary glands, (3) pancreas, (4) kidney, (5) liver, (6) lungs, (7) testes, (8) semen and (9) amniotic fluid. These antigens are present from birth till death genetically but the antibodies production occur naturally from month 2 to 8; at the end of month 8 after birth the antibodies present inside the body of an individual, most probably they will be produced **because of the stimulation of the body by antigens from our food** especially the meat or bacteria, sometimes these antibodies don't occur at all and these individuals remain without them, unless these individuals are **exposed to a blood from another individual**, let us say in A no anti-bodies then A exposed to blood B so the antibodies stimulated, they occur.

The inheritance of the blood groups: Let us say we have A blood group (classic blood group), this is the phenotype, but we don't know the genotype. So what is the genotype? Either AO or AA, you remember the chromosomes one opposite the other; on one A and O on the opposite or on one A and A on the opposite, **DOMINANT** Or **RECESSIVE** similar BB Or BO, or AB two **DOMINANT** or OO always **RECESSIVE** "no antigens".

There are also minor blood groups, more than hundred blood antigen have been described, out of those, at least 15-25 have been identified, RBCs group systems exist in most racial groups. Which are: (MM, MN, NN, PP, Pp, Kell, Lewis, Kid, Lutheran, Duffy) and many others present in addition to the classical blood groups and in addition to Rh blood group, these are minor blood groups, they are sometimes important and they may cause problems; they stimulate the production of antibodies thus causing agglutination.

Also there are Rh blood groups, in 85% of white peoples there are Rh antigens (D antigens), in the others (the remaining 15%) there are no antigens, those who have Rh antigen (D antigen) we call them Rh positive and those they don't have it we call them Rh negative, but in both there are no antibodies.

There are at least three sets of the alternative antigen on the Rh system D or d (dominant or recessive), C or E. D is the strongest antigen and thus it is clinically

more important than the others, in the blood banks Rh grouping is performed with the anti-D serum

The importance of Rh groups, if blood donated from +ve to –ve, the –ve individual produces antibodies against Rh+ antigens, therefore, agglutination occurs.

From the past papers

A person with (A Rh-) blood can receive blood transfusion from which of the following?
1. A Rh+ **2.** B Rh+ **3.** AB Rh- **4.** O Rh- **5.** A Rh-

(a) 1 only (b) 4 only (c) 3 only **(d) 4 + 5** (e) 1 + 5

Just to have an idea, the table shows the distribution of blood groups by percents (and it's important to take a look and make an idea about them):

	A	B	AB	O	Rh+	Rh-
WHITES	41	10	4	45	85	15
BLACKS	28	20	5	47	90	10
CHINESE	28	23	13	36	99	1
INDIANS (IN UTAH)	3	0	0	97	100	0
JORDANIANS	39	14	8	39	97	3

Least common blood group in the region? **AB**

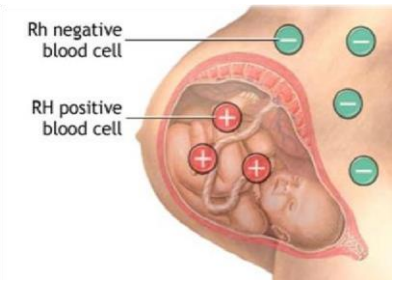
From the past papers

We must note the lowest and the highest, by the genetical presence of the gene; the lowest is **AB** in all people, whatever the race and the highest is **O**, and you see Rh distribution, low in white people (the lowest) but high in blacks, Chinese, Indians and others.

We said that if blood donated from +ve to –ve, then –ve produces antibodies antigens agglutination. **Hemolytic diseases** of the newborn will occur, for

example, we have –ve mother and this mother is pregnant, there are three conditions in which the mother may develop antibodies:

1. **Blood transfusion before marriage by blood from Rh person**; in this case either she will produce antibodies or she will have a sensitivity to produce antibodies. In this case, if she got married (the mother is negative) and the husband is positive and also the fetus is positive, the mother produces antibodies which will pass into fetus blood then antigens of the fetus with antibodies from the mother form agglutination.
2. **Leakage during pregnancy of small amount of fetal blood Rh+ into maternal circulation** (placental hemorrhage). So again Rh+ pass into maternal blood, the mother either develop antibodies or has the sensitivity to produce in the next time she becomes pregnant, so in the next time in any blood transfusion from Rh+ she will produce antibodies;
3. **During delivery, some blood squeezed back to maternal blood thus develop antibodies**.

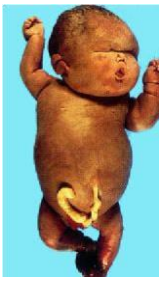


In these three cases the mother develop antibodies.

Mother is –ve, let us say that the phenotype is A, but sometime AA the fetus will be 100% positive, or AO; 50% either positive or negative. In this case if the father AA the probability of danger to the fetus is very high= 50:50. B similar to A and also C is the same (have same probability).!!

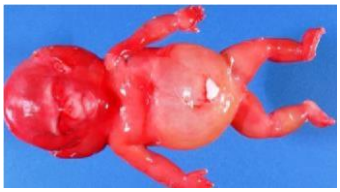
Now, what happens? In these conditions one of the following **hemolytic diseases** may occur:

1) Erythroblastosis fetalis: mild disease, a small amount of RBCs leaks into mother circulation, some mothers develop antibodies against D antigen. These antibodies pass into the fetal blood and cause mild hemolysis of the RBCs of the fetus. The baby can be rescued by giving him Rh- blood (does not have antibodies), but not from his mother, he is positive so why we transfuse negative blood? Because he has antibodies against Rh+. Why not from his mother? Because she has antibodies against Rh+.



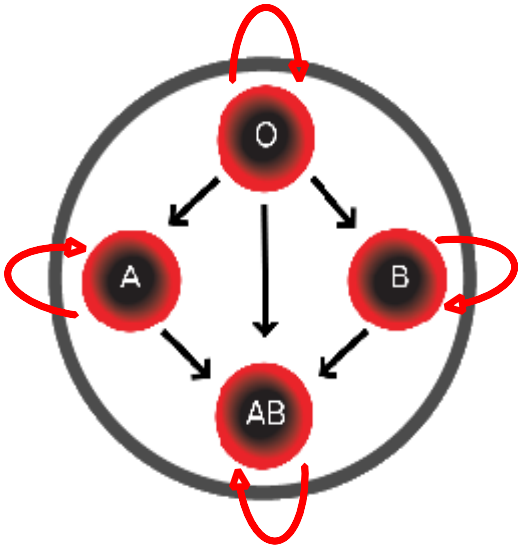
2) Icterus gravis neonatorum: moderate disease, the infant is born at term, is jaundice, or become so within 24 hours, there may be severe neurological lesions involving the basal ganglia in which the bile pigment deposited. These babies sometimes become mentally retarded.

3) Hydrops fetalis: severe disease; this means a lot of antibodies produced, these antibodies pass into the fetal blood. The hemolysis is severe, the infant may die in the uterus or may develop severe anemia, jaundice, and edema, dies within few hours.



Fortunately, the diseases can be prevented by giving an Rh- mother human gamma globulin against Rh+ erythrocytes within 72 hours after she has delivered her first Rh+ infant, in this case, we can inactivate these antigens. These antibodies bind to the antigenic sites on any Rh+ erythrocytes that might have entered the mother's blood during delivery and prevent them from inducing antibodies synthesis by the mother. The administered antibodies are eventually catabolized.

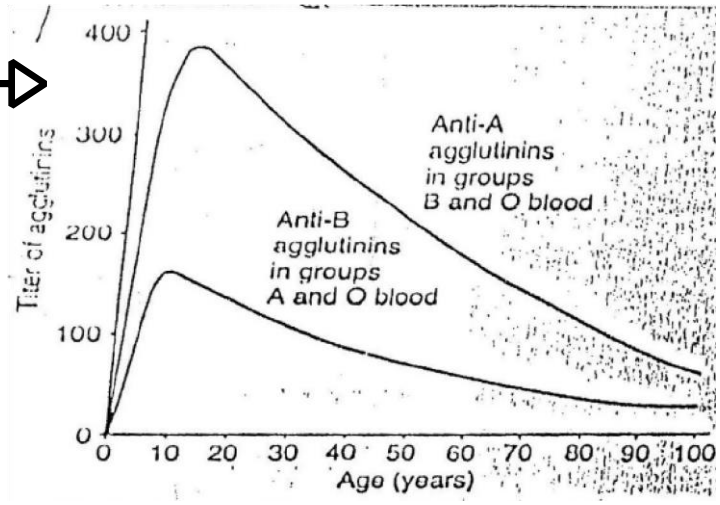
This is the compatible blood transfusion, you know about the blood transfusion (the donation of blood), there is general donor and there is general acceptor. So O donate blood to all blood groups "general donor", AB receives blood from all blood groups "general recipient". You remember when we say that O is the highest and AB is the lowest.



Do you think that O is always general donor And AB is always general recipient even if we donate 3-4 bags of blood? Is there any general rule? NO, maximally we can donate **2 bags** (one liter; one bag= 0.5L) otherwise problems will occur (agglutination), always there is agglutination! Whatever, from O to A; in O there are antibodies alpha and beta and in A there are A antigens so agglutination will occur (the antibodies from O diluted in A), only 1-2 bags then dilution occurs in the antibodies of the recipient, otherwise the agglutination will be much more and the liver will not tolerate, too much agglutination will occur.

So, up to 2 bags, maximally 3 (adventure; the patient may die and may not), otherwise, the antibodies cannot be diluted, in the recipient blood; 1 liter in 5 liters the antibodies will be diluted and the body, as well as, the liver can deal with it.

This figure shows the average titer of anti-A and Anti-B agglutinins in the blood of people in group A and group B at different ages. The doctor did not mention this slide in the lecture.



You may wonder if A B may also cause **hemolytic diseases** in the blood of the newborn, for example, woman with type O blood has natural antibodies to both A and B antigens, if her fetus is type A or B, this theoretically should cause a problem, fortunately that will not happen partly **because A and B antigens are not strongly expressed in the fetus erythrocytes** and partly **because of the natural antibodies such as IgM type which do not readily pass easily to the fetal blood (placenta)**; the fetal antibodies do not recognize easily the other antigens, therefore, there is no problem, and second the antibodies produced because of the A antigen and B antigen are of type IgM which cannot cross the fetal placenta.

"اللَّهُمَّ انْفَعْنَا بِمَا عَلَّمْتَنَا، وَعَلِّمْنَا مَا يَنْفَعُنَا، وَزِدْنَا عِلْمًا إِلَى عِلْمِنَا"