Clot retraction and fibrinolysis

- Clot retraction is the shrinkage of the blood clot which occurs hours afterwards.
- This shrinkage causes the clot to contract and express (release) the fluid known as serum.
- It is brought about by contraction of platelets due to the presence of the contractile protein **thrombosthenin**.

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Clot retraction and fibrinolysis cont'd

- In the presence of Ca^{2+} and ATP, thrombosthenin functions like the actino-myosin complex of muscles.
- The thrombosthenin attaches to the fibrin fibers and as they contract, the size of the blood clot reduces.

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Clot retraction and fibrinolysis cont'd

- Fibrinolysis or clot dissolution is necessary whether to remove occasional intravascular clots formed

-in response to endothelial damage or during healing of a normal vascular damage.

- It is brought about by **plasminogen** or **profibrinolysin**, which when activated becomes plasmin or fibrinolysin.
- **Plasmin** is a proteolytic enzyme, & its primary role is to digest the fibrin fibers, as well as fibrinogen, prothrombin, Factor V, Factor XII and Factor VIII.

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Clot retraction and fibrinolysis cont'd

- When a blood clot is formed, a large amount of plasminogen is trapped in the clot together with other proteins.
- However, its activation requires tissue plasminogen activator (t-PA)

  - released from damaged endothelium and injured tissue a day or two following the tissue damage.

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Clot retraction and fibrinolysis cont'd

- Small amount of plasmin is formed in blood all the time but its activity is held in check

- by yet another factor known as $alpha_2$-antiplasmin, which binds with plasmin and inhibits it.

- The most important function of the plasmin system is to remove the millions of minute clots from the tiny peripheral vessels,

- which would otherwise become occluded.

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Blood coagulation tests

1. Bleeding time: when the tip of the finger or the lobe of the ear is pierced, bleeding commences immediately and lasts for 1 to 6 minutes.

- This time is the bleeding time.

- The time will vary with the depth of the cut and blood supply to the area, but is increased notably when platelets are lacking.

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Blood coagulation tests cont'd

2. Clotting time: when blood is collected in a chemically clean glass test tube and

- then tipped back and forth every 30 seconds, there comes a time when the blood can no longer move with each stroke.

- The time taken for this to occur is the clotting time, and is normally 6 to 10 minutes.

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Blood coagulation tests cont'd

3. Prothrombin time: in this method, blood is drawn directly into oxalated tube to prevent activation of prothrombin.

- Then a large excess of Ca^{2+} and tissue factor is suddenly mixed with the oxalated blood.

- The Ca^{2+} will nullify the effects of the oxalate and the tissue factor activates the prothrombin-to thrombin reaction by means of the extrinsic pathway.

- The time now required for coagulation to take place is known as the prothrombin time. This is ~ 12 s.

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Introductory Immunology and Blood Groups

Antigens

- Antigens are substances, usually protein in nature, which when introduced into the body stimulate production of specific antibodies.
- They are recognized as 'foreign elements' by the body's immune system, so the primary purpose of the antibody is to neutralize and/or destroy the antigen.
- RBCs contain many different antigens on their cell surfaces which have been used to classify individuals of a species into blood group types.

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Antigens cont'd

- Some blood group antigens also occur on WBCs, platelets, spermatozoa and various tissue cells such as the skin.
- In human beings, most blood group antigens are glycoprotein in nature,

- the **carbohydrate moiety** being responsible for the **antigenetic specificity.**

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Introductory Immunology and Blood Groups cont'd

Antibodies

- Antibodies react with specific antigens both *in vivo* and *in vitro*.
- In the case of blood group antigens, this antigen-antibody reaction causes

- clumping together of RBCs, a process known as agglutination.

- Such antibodies are known as **agglutinins**.

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Antibodies cont'd

- Other types of antibodies react with specific antigens to cause damage of the RBC membranes, leading to hemolysis.
- Such antibodies are therefore called **hemolysins**.
- In humans, the two most common types of blood group systems are the **A-B-O system** and the **Rhesus blood group system**.

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The A-B-O Blood Group System

- In **the A-B-O blood group system**, the two blood group antigens, type A and type B occur on the RBC surfaces.
- These antigens are also called agglutinogens because they cause agglutination of RBCs when they react with specific antibodies.

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A-B-O blood group system cont'd

- Concerning the blood groups, when the antigen is present on the RBC membranes,

- the corresponding agglutinins cannot be present in the plasma.

- This is because a severe agglutination reaction, not compatible with life, would occur leading to death.

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A-B-O blood group system cont'd

- Also when the antibodies are present in the plasma, the antigens cannot be present on the RBC surface.
- This principle, first discovered by an Austrian called Landsteiner, is known as Landsteiner's law

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The A-B-O Blood Group System cont'd

Genotype	Blood type	Agglutinogens	Agglutinins
OO	O	none	Anti-A and Anti-B
OA or AA	A	A	Anti-B
OB or BB	B	B	Anti-A
AB	AB	A and B	none

- When the RBCs have neither A nor B agglutinogens, the blood type is O and the serum contains both anti-A and Anti-B agglutinins.
- This group can donate blood to any of the other groups without risk of antigen-antibody reactions and is the universal donor.

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The A-B-O Blood Group System cont'd

- When the RBCs have the A agglutinogens on their membranes, anti-B agglutinins will be present in the plasma.
- When the RBCs have the B agglutinogens, anti-A agglutinins accumulate in the plasma.

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The A-B-O Blood Group System cont'd

- When the RBCs have both A and B agglutininogens, the plasma will be devoid of either anti-A or anti-B agglutinins.
- This group can receive blood from any of the other groups.
- This is because it has no agglutinins in the plasma to react with the agglutiongens on the RBC membranes.
- Therefore the AB type is the universal recipient.

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The A-B-O Blood Group System cont'd

Blood typing: is the determination of the blood group of a potential donor and the recipient before transfusion.

- This is done using commercial sera known as anti-A and anti-B.
- A small sample of diluted blood is mixed with either anti-A or anti-B serum on a white tile.
- After 5-8 mins., the mixture is observed under the microscope for signs of agglutination.

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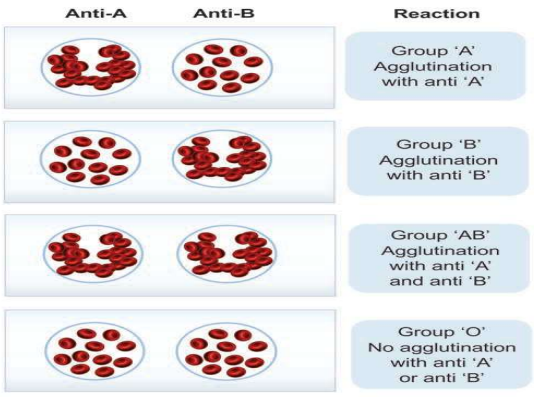

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The Rhesus Blood Group System

- **The Rhesus blood group system** is made up of six Rhesus (Rh) factors: C, D, E, and c, d, and e.
- However, only the D factor is important because of its strong antigenic characteristics.
- Persons with the D factor are designated Rh positive (Rh+) and those without are negative (Rh-).
- When a Rh+ person donated blood to a Rh- recipient, anti-Rh agglutinins will develop slowly, reaching the maximum in 2-4 months.

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The Rhesus Blood Group System cont'd

- Repeated transfusion of Rh+ blood to the same recipient will cause accumulation of the anti-Rh agglutinins.
- This eventually leads to severe transfusion reactions consisting of agglutination and hemolysis.
- The Rh blood grouping systems differs from the A-B-O system in that spontaneous agglutination never occurs in first transfusion as in A-B-O.

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The Rhesus Blood Group System cont'd

- This is because the Rh agglutinins are not present in the plasma.
- Rh agglutinins only develop over time, following massive exposure to the Rh agglutinogens.
- The exposure usually occurs through transfusion or a mother carrying a foetus who has the antigen.

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The Rhesus Blood Group System cont'd

- In the latter case, a condition is known as **erythroblastosis foetalis.**
- The condition is characterized by agglutination and phagocytosis in the foetus or newborn, leading to severe hemolytic crisis.
- In this case, the mother is Rh- and the father Rh+.

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Erythroblastosis foetalis cont'd

- The baby inherits the Rh+ antigen from the father and

- the mother develops Rh+ agglutinins from exposure to the baby's Rh antigen.

- The mother's agglutinins will diffuse through the placenta into the fetus to cause agglutination.

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Erythroblastosis foetalis cont'd

Incidence of the disease

- A Rh-negative mother having her first Rh-positive child usually does not develop sufficient anti-Rh agglutinins to cause any harm.

- However, about 3 per cent of second Rh-positive babies exhibit some signs of erythroblastosis fetalis;

- about 10 per cent of third babies exhibit the disease; and

- the incidence rises progressively with subsequent pregnancies.

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Tissue and Organ Transplantation

Organ and Tissue Transplantation: antigens found on tissue cells are responsible for tissue graft rejection

- following transplantation of organs such as the skin, the kidneys, the liver, the heart, the bone marrow, etc.

- Rejection is minimal with **autografts** from another part of the same person, and **isografts** from one identical co-twin to another.

- Tissue and organ transplantation is important in reconstruction surgery.

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Tissue and Organ Transplantation cont'd

Grafts rejection can be minimized by:

(i) performing tissue typing:

- Antigens responsible for tissue graft rejection are known as histocompatibility antigens or human leucocyte antigens (HLA).

- They are located on the surfaces of various tissue cells, and WBCs.

- Those located on WBCs are easy to access and are used in routine tissue typing.

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Tissue and Organ Transplantation cont'd

(II) Prevention of graft rejection by suppressing the immune System

- If the immune system were completely suppressed, graft rejection would not occur.
- Because the T cells are mainly the portion of the immune system important for killing grafted cells,

- their suppression is much more important than suppression of plasma antibodies.

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Tissue and Organ Transplantation cont'd

- Some of the therapeutic agents that have been used for this purpose include the following:

1. ***Glucocorticoid hormones*** *isolated from adrenal cortex (or drugs with glucocorticoid-like activity)*,

- which suppress the growth of all lymphoid tissue and, therefore, decrease formation of antibodies and T cells.

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Therapeutic agents cont'd

2. ***Various drugs that have a toxic effect on the lymphoid system*** and, therefore, block formation of antibodies and T cells, especially the drug *azathioprine*.

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Therapeutic agents cont'd

3. ***Cyclosporine***, which has a specific inhibitory effect on the formation of helper T cells and, therefore blocks the T-cell rejection reaction.

- This has proved to be one of the most valuable of all the drugs because it does not depress some other portions of the immune system.

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