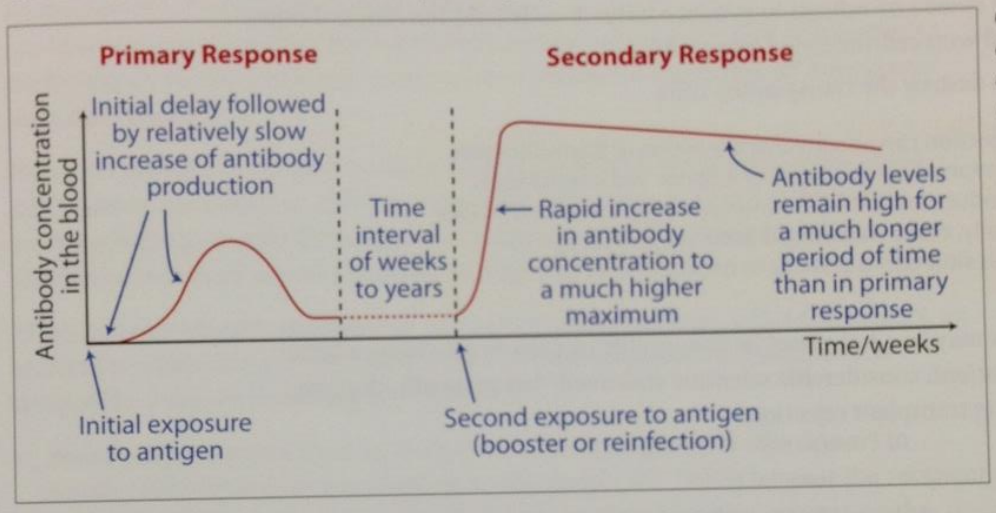
- Modified **toxins** produced by the pathogen – With some pathogens it is their toxins that can produce the immune response. The toxins must be modified and made harmless but not changed so much they do not produce an immune response.
- Isolated **antigens** separated from the pathogen itself – For some pathogens the antigens can be made by genetic engineering.

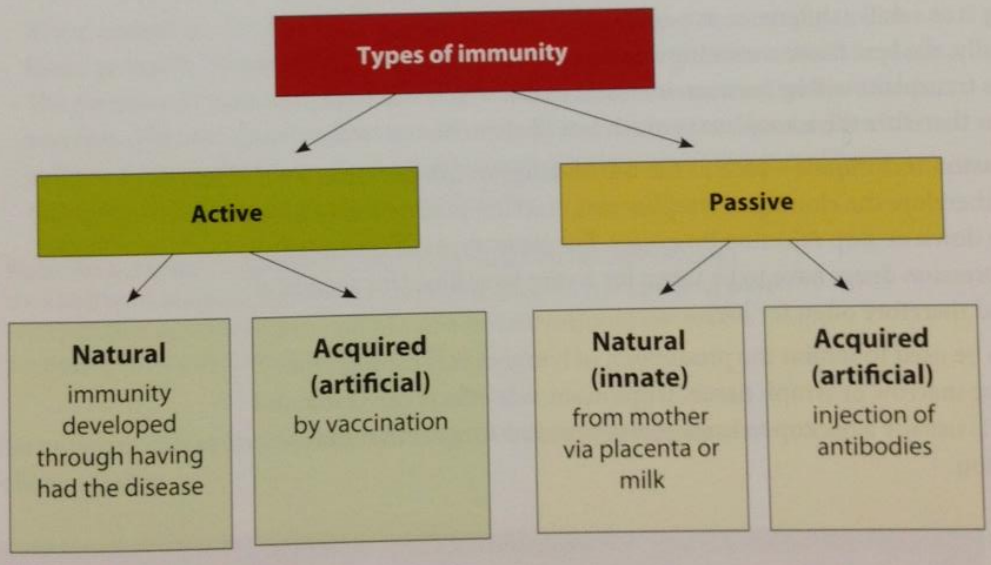
Sometimes vaccinations require subsequent **booster** injections. These produce a secondary immune response, similar to the response produced when catching a particular disease for a second time.

The characteristics of active immunity are highlighted in the following diagram.



Changes in the concentration of antibodies during active immunity

The different types of immunity can be summarised in the following flow diagram.



Transplanting tissue

As discussed in the previous section, the body will produce an immune response to the presence of any non-self antigens. Normally this response occurs as a consequence of infection. However, transplanted organs, for example, kidneys, or tissue (such as skin grafts), will also produce an immune response as the transplanted organs/tissue will contain non-self antigens if they come from someone else. Exceptions are if the tissue

is transplanted within the same person, as can happen with skin grafts or if tissues/organs are transplanted between identical twins (identical twins are genetically identical therefore they have identical antigens).

Transplant rejection – However, most organ transplants do not take place between identical twins, therefore the risk of transplant rejection exists. Transplant rejection is the main reason for many organ transplants failing.

The process of rejection involves the following steps:

- **T-lymphocytes** are stimulated (sensitised) by the non-self antigens present in the transplanted tissue.
- These T-cells are cloned by mitosis to produce **killer T-cells** (and the range of other T-cells associated with cell-mediated immunity).
- The killer-T cells destroy the transplanted cells.

Note: Transplant rejection can also involve the action of B-lymphocytes and antibodies. For example, if the blood of a donor and a recipient is different this can produce an immune response involving antibodies (see next section). Normally, tissue matching is accurate so rejection by B-lymphocytes in this situation is unlikely to occur.

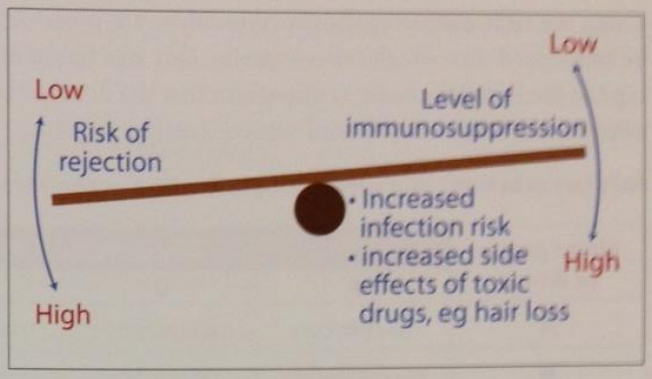
As organ transplants may be a last resort in saving a life or even in providing a better quality of life for a patient, considerable scientific endeavour has gone into devising strategies for reducing transplant rejection.

These include:

- **tissue typing** – This is the term that describes the process of matching the donor and recipient cell-surface markers (antigens) so that there is as good a match as possible, ie there is as small a difference as possible between the self and non-self antigens. Generally, the best tissue matching will take place between close relatives. The best possible transplant will be between identical twins, which will have identical antigens therefore the transplant is much less likely to be rejected.
- **immunosuppression techniques** – such as the use of **drugs to inhibit DNA replication** and therefore the cloning of lymphocytes (and the production of killer T-cells) will slow down or stop rejection processes. For many types of transplant, the immunosuppression drugs have to be taken for a very long time (for the life of the transplant and therefore often for life).
- **X-rays** – can also be used to inhibit the production of lymphocytes through the irradiation of bone marrow or lymph tissue. Unpleasant side effects can result and the use of X-rays is usually a backup to immunosuppressant drugs rather than a first course of action.

Immunosuppression (whether by drugs or X-rays) will **compromise the recipient's immune system**. This makes the individual susceptible to infection, as immunosuppression depresses the immune system in general (not just its response to the antigens involved in the transplanted tissue). A number of additional strategies are used to help support the transplant patient against subsequent infections including anti-viral drugs, anti-bacterial mouth rinses and the use of monoclonal antibodies to help target and reduce the effect of the T-cells involved in rejection.

Nonetheless, there is a delicate balance between reducing the risks of rejection and restricting the side-effects that are linked to the use of immunosuppressant technologies.



The delicate balancing act between risk of transplant rejection and use of immunosuppressant agents

Blood transfusion

Erythrocytes (red blood cells) also have **antigens** (markers) on their cell-surface membrane. The blood of any one individual will not have antibodies that correspond to the antigens on his/her red blood cells as this would trigger an immune reaction. As with other B-lymphocytes that correspond with self-antigens, the lymphocytes responsible for these blood antibodies are switched off during very early development.

However, the type of antigens on the erythrocytes of different people varies. In the **ABO** system there are four different types of blood group (A, B, AB and O) and everyone belongs to one of these groups. This is an example of **polymorphism** – a situation where there are several distinct categories or forms.

When giving a **blood transfusion** to an individual (for example, following surgery, an accident or when treating some illnesses), it is important that the transfusion is compatible. Take the following two examples:

- Blood **can** be donated from an individual with blood **group A** (**the donor**) to another individual with blood **group A (the recipient)**. This is because the recipient has no antibodies (no anti-a antibodies) that correspond to the antigens on the donor's erythrocytes.
- Blood **cannot** be donated from a donor with blood **group A** to a recipient with blood **group B**. This is because the recipient has anti-a antibodies in his/her plasma. The presence of both antigen A and anti-a antibodies causes an antigen-antibody reaction. The anti-a antibodies cause the blood, containing red blood cells with antigen A, to **agglutinate** or clump. This agglutination could block capillary networks and lead to organ failure and death.

Note: An individual with blood group B will have anti-a antibodies as they had no A antigens in early development; therefore, A antigens were not identified as self antigens and the lymphocytes responsible for producing antibody-a were not 'switched off'.

The antigens and antibodies of the ABO blood group system are shown in the following table.

Blood group	Antigens on erythrocytes	Antibodies in plasma
A	A	anti-b
B	B	anti-a
AB	both A and B	neither anti-a nor anti-b
O	neither A nor B	both anti-a and anti-b

Using the information in the previous table, it is possible to work out which blood can be transfused into which other types(s). Donated blood does not have to be the same type as the recipient but it is important that the donated blood type does not lead to an antigen-antibody reaction and subsequent agglutination.

Safe (no reaction) and unsafe (agglutination occurs) transfusion combinations

Blood group of donor	Blood group of recipient			
	A	B	AB	O
A	no reaction	agglutination	no reaction	agglutination
B	agglutination	no reaction	no reaction	agglutination
AB	agglutination	agglutination	no reaction	agglutination
O	no reaction	no reaction	no reaction	no reaction

As blood of group O does not have either A or B antigens, blood of group O can be transfused into any of the four blood groups. Consequently, blood group O is referred to as the **universal donor**. Blood group AB lacks both anti-a and anti-b antibodies, therefore this is referred to as the **universal recipient**, as people with blood group AB can receive blood from any group.

Note: A key point when working out transfusion compatibility is that donated blood is mainly red blood cells and that the amount of donated plasma is insignificant. The table above indicates that blood group A can be donated to a recipient with blood group AB. This is only because none, or a very insignificant number of, anti-b antibodies in blood group A will be transfused into the recipient with blood group AB.

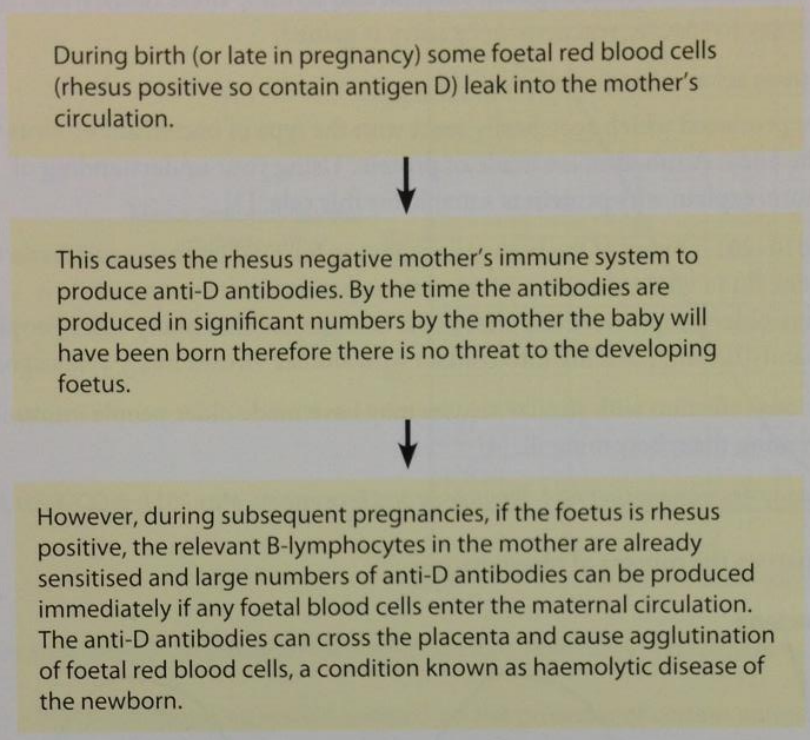
Why do we have an ABO system? It is thought that the different antigens (groups) evolved as a consequence of mutations. Currently, none of the blood groups appears to give individuals a selective advantage (ie the mutations are neutral). However, it is possible that in our evolutionary past some of the mutations gave selective advantage against specific diseases – this would explain why the different groups have persisted through time. The ABO is only one of a number of many blood group systems in humans, although it is the most important in clinical practice. Another very important blood group system is the **rhesus system**.

The rhesus system – This system is based on the presence or absence of an antigen (the rhesus antigen or antigen D) on the cell-surface membranes of the red blood cells. Around 85 % of the population have this antigen and are described as **rhesus positive** (Rh^+). **Rhesus negative** (Rh^-) individuals do not have the antigen. Unlike the antibodies for the ABO system, antibodies against the antigen D marker, (anti-D antibodies) do not occur naturally in the plasma. An individual who is rhesus positive will not produce anti-D antibodies (relevant B-lymphocytes are 'switched off' when the rhesus positive marker is recognised as self during development).

Rhesus negative individuals do not normally have the antibodies either, **but** can produce anti-D antibodies if their blood becomes contaminated with blood containing antigen D as can happen in the following situations:

- Blood transfusion between a rhesus positive donor and a rhesus negative recipient. In reality, this is unlikely to occur with modern blood matching techniques.

- When a **rhesus negative mother** has a **rhesus positive baby**. The typical sequence of events is explained in the following flow diagram.



Foetal death, or serious illness, due to haemolytic disease of the newborn seldom occurs today as rhesus negative mothers are treated during pregnancy (around 30 weeks) by being given an injection of anti-D antibodies. These attach to any antigen D-containing foetal red blood cells fragments that may pass across the placenta and enter the mother's circulation before the mother's B-lymphocytes are stimulated to produce anti-D antibodies. Following birth, if the baby proves to be rhesus positive, another injection of anti-D antibodies is given within 72 hours.

However, if medical screening and intervention is bypassed and the condition does occur, the baby can be treated by blood transfusion.