(2) During storage at 4°C, the red cells show a progressive decrease in content of adenosine triphosphate and 2,3-BPG, while with decreased activity of the Na^+–K^+ pump, the cells gradually lose K^+ to the surrounding plasma and gain Na^+ from it. The concentration of K^+ in the plasma may reach values as high as 30 mmol L^{-1} after storage of blood for 4 weeks. The pH of the plasma also decreases with time of storage and its concentration of ammonia rises. These changes can make stored blood dangerous for transfusion in certain patients, e.g. those with renal or hepatic failure. The decline in Na^+–K^+ pump activity makes some red cells spherocytic, with loss of deformability. These effects may be irreversible and after transfusion the abnormal red cells are destroyed very rapidly by macrophages in the spleen and elsewhere. Other constituents of blood do not withstand prolonged storage. Granulocytes begin to lose their phagocytic capacity within 6 h of collection and they are functionally inert after 24 h. Platelets lose their haemostatic effect (p. 310) within 48 h at 4°C, while the labile coagulation factors, V and VIII (p. 314), also rapidly deteriorate in chilled blood.

(2) Before donated blood is made available for issue from a blood-bank, the ABO and rhesus groups of the cells are determined and commonly the serum is screened for atypical antibodies. Serological tests are also done for syphilis, hepatitis and human immunodeficiency virus (HIV). Before transfusion, the ABO and rhesus groups of the patient's red cells are determined, the serum is checked for unexpected antibodies and red cells from the donor are tested against the patient's serum by **cross-matching** tests (compatibility tests). These cross-matching tests are essential for checking that there has been no error in ABO grouping of donor and recipient, and for ensuring that the recipient's serum does not contain naturally occurring or immune antibodies active against the donor's cells.

Transfusion of whole blood is sometimes necessary but, over recent years, the use of cell-separator machines and large-scale production of plasma constituents have made it increasingly possible to transfuse specific components of blood which the patient lacks. Thus **red-cell concentrates**, often resuspended in a small volume of electrolyte solution, are used to restore the haemoglobin concentration in an anaemic patient in whom the plasma volume may already be expanded. **Platelet concentrates** are of use in patients with severe thrombocytopenia (p. 317). A variety of plasma fractions is also available to supply coagulation factors, e.g. **cryoprecipitate**, which is rich in factor VIII and fibrinogen, and for expanding plasma volume, e.g. **stable plasma protein solution**. A useful source of antibodies against common viruses is **pooled normal immunoglobulin** and various specific immunoglobulins are also available, e.g. anti-D and antibodies against tetanus, hepatitis B and diphtheria.

However much care is taken in cross-matching and administering blood, transfusion carries definite risks of unpleasant or even fatal complications. Major red-cell incompatibility can lead to lethal intravascular haemolysis or delayed extravascular breakdown of donor cells. Transfusion of blood contaminated with bacteria can cause profound shock with hyperpyrexia, while allergic reactions to transfused white cells, platelets and plasma proteins can also be severe. Circulatory overload, air embolism and changes in plasma electrolyte concentrations (e.g. hyperkalaemia) may occur and there may be direct transmission of disease, e.g. HIV and cytomegalovirus infections, hepatitis and malaria.

13.9 Blood transfusions and the ABO system of blood groups

Early attempts to restore heavy loss of blood by transfusion of blood from another person were frequently disastrous. The transfused cells aggregated together in clumps which were sufficiently large to block minor blood vessels. This clumping is known as *agglutination*. Following the agglutination reaction, the red cell membranes broke down and hemoglobin was liberated into the plasma (this is known as *hemolysis*). The liberated hemoglobin was converted to bilirubin by the liver and this resulted in jaundice (yellowish skin coloration). In addition, the high plasma levels of bilirubin adversely affected urine production by the kidney. When such clinical signs follow the transfusion of blood the transfused blood is said to be *incompatible* with that of the recipient. Death frequently occurred as a result of the transfusion of incompatible blood.

(2)

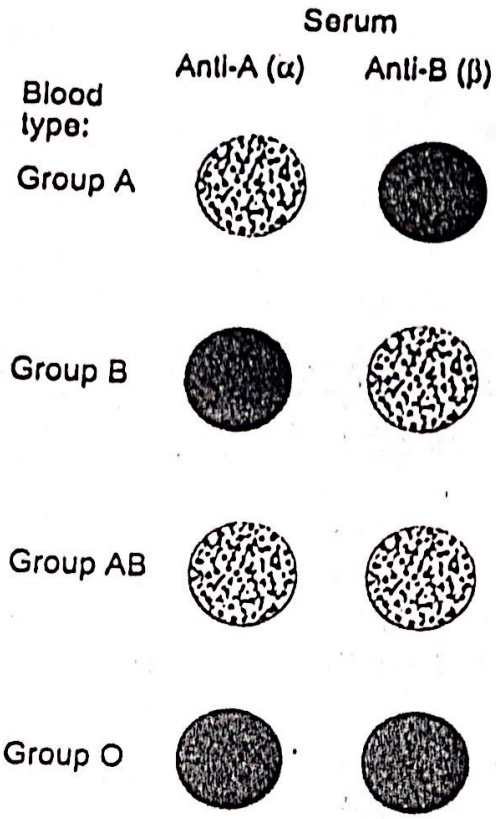


Fig. 13.12 The agglutination reaction of incompatible blood types. Drops of anti-A and anti-B serum are placed in shallow wells on a porcelain plate as shown in the figure. A drop of the test sample of blood is added to each well and mixed. If the blood is compatible, the mixed blood sample appears uniform but, if the blood is incompatible with the serum, it aggregates and precipitates as shown.

(3) What is the basis of this incompatibility and why is some blood compatible while other blood is not? It is now known that agglutination results from an antibody–antigen interaction. Normal human plasma (and the corresponding serum) may contain antibodies that cause red cells to stick together in large clumps (i.e. to agglutinate; Fig. 13.12). The antibodies that cause the reaction are known as *agglutinins*. Unlike most other antibodies, the agglutinins have not arisen as a result of a specific antibody reaction. They occur naturally and are inherited by mendelian laws. Clearly, if red cells agglutinate in response to a particular kind of plasma or serum, they must possess the corresponding antigen, which is known as an *agglutinogen*.

(41)

To account for the known cross-reactivity of blood from different people, Landsteiner proposed that two kinds of agglutinogen are present on human red cells. These agglutinogens are called A and B and they may be present separately, together, or be completely absent, so giving rise to four groups: A, B, AB and O (Table 13.5). In addition, human plasma may contain antibodies to one or both agglutinogens. The plasma antibodies are known as anti-A and anti-B or as agglutinins α and β. Where the blood contains red cells with a particular agglutinogen, the corresponding agglutinin is absent from the plasma. Thus people with agglutinogen A on their red cells do not have anti-A in their plasma as they do not agglutinate their own blood. Nevertheless, this group of people do have anti-B in their plasma. Conversely, group B have agglutinogen B on their red cells but anti-A in their plasma. Group AB have both agglutinogens A and B on their red cells but no agglutinins in their plasma and group O have neither agglutinogen but both anti-A and anti-B agglutinins. Table 13.5 gives the relationships between the different groups and their approximate frequency of occurrence in the general population of the United Kingdom and United Sates.

(5) The rhesus blood group system

In 1940 Landsteiner and Wiener found that the serum of rabbits that had been immunized against the blood of rhesus monkeys could agglutinate human blood. Using this antibody they identified two groups in the general population. Those whose blood could be agglutinated by this serum, now known as rhesus (or Rh) positive (about 85 per cent of the population), and those whose blood could not be agglutinated—Rh-negative. Rh-positive persons have a specific antigen on their red cells known as the D-antigen (also known as the rhesus factor).

Since the D-antigen is inherited like the AB agglutinogens, anti-Rh antibody can occur in the serum of Rh-negative mothers who have had Rh-positive children. During pregnancy a Rh-negative mother may form anti-Rh antibodies in response to the leakage of fetal red cells into her circulation. This immunization of the mother by the baby's red cells may occur at any time during pregnancy but is most likely to occur when the placenta is separating from the wall of the uterus while the mother is giving birth. For this reason anti-Rh antibodies generally arise

(6)

after the first or second pregnancy. The anti-Rh antibodies are IgG antibodies of about 150 kDa and are sufficiently small to pass across the placenta into the fetal circulation. If this happens, they may cause a severe agglutination reaction. The resulting disorder is known as hemolytic disease of the newborn and, in the absence of suitable preventative measures, it occurs about 1 in every 160 births. As indicated above, this problem usually arises during a woman's second or third pregnancy. About half of the affected babies will require a partial replacement of their blood by transfusion. This problem can be avoided by injecting Rhesus negative mothers with anti-D immunoglobulin immediately after delivery. This neutralizes any Rhesus positive fetal red cells that may be present in the maternal circulation.

Although hemolytic disease can occur as a result of an anti-A antibody in the blood of group O mothers, ABO blood group incompatibility generally causes no problems during pregnancy. This reflects the fact that the plasma agglutinins are IgM antibodies of high molecular weight (about 900 kDa) and proteins of this size do not readily cross the placenta.

7

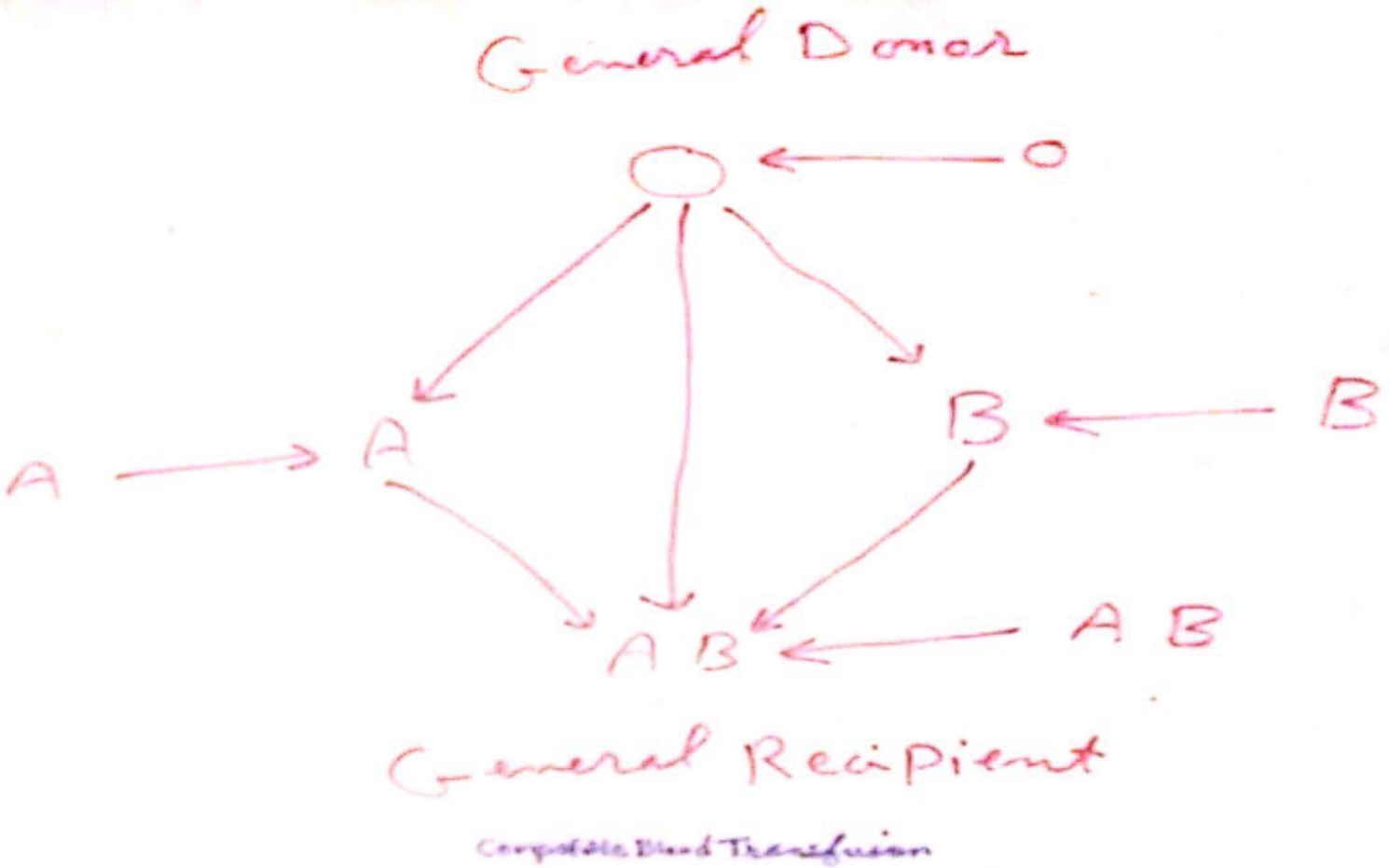
Other blood group types

The blood group antigens (agglutinogens) are found on the surface of the red cell membrane and many kinds of antigen have been discovered in addition to the fundamental ABO system. For example, soon after the original description of the ABO system of blood groups it was discovered that group A could be further subdivided into two groups: A_1 and A_2. Other blood groups such as the M, N, P, and Lewis groups are also known. Nevertheless, the A_1 and A_2 subdivisions and other blood groups are not generally of significance in blood transfusion.

(8)

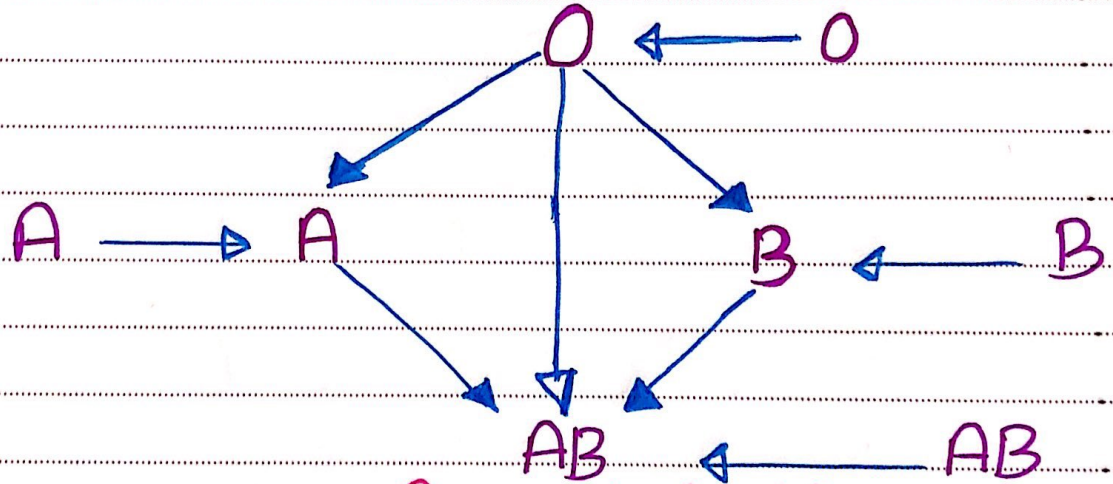
Blood must be cross-matched for safe transfusions

To prevent the problems of blood group incompatibility, blood for transfusion is *cross-matched* to that of the recipient. In this process, serum from the recipient is tested against the donor's cells. If there is no reaction to the cross-match test, the transfusion will be safe. Note that *this test screens for all serum agglutinins and not just those of the ABO system.* Although correct matching of blood groups of both donor and recipient is preferable, in emergencies group O blood can be transfused into people of other groups because group O red cells have neither A nor B antigens. For this reason a group O person is sometimes called a *universal donor.* As the plasma of group AB has neither anti-A nor anti-B antibodies other blood groups can be transfused into a group AB patient. Such a patient is known as a *universal recipient.* The plasma agglutinins present in the blood of a donor do not generally cause adverse reactions because they become diluted in the recipient's circulation.



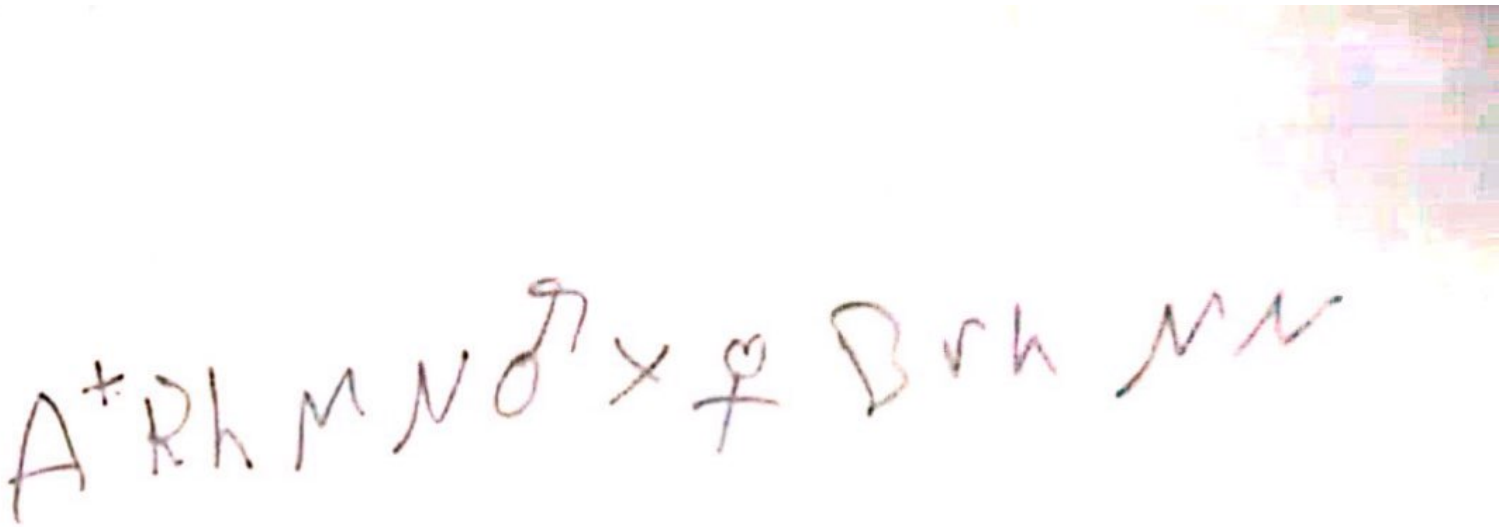
Compatible Blood Transfusion

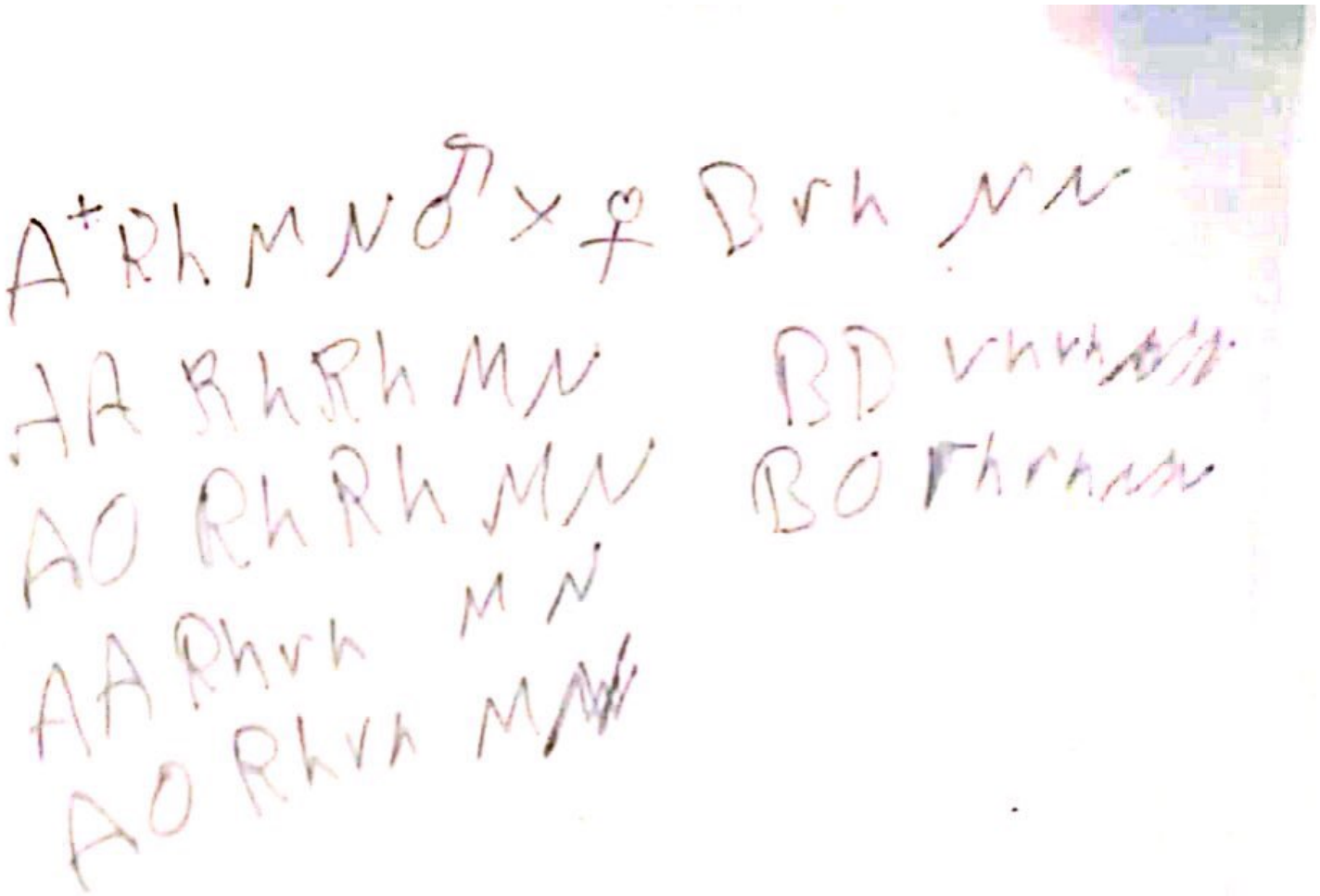
General Donor



General Recipient

* Compatable Blood Transfusion.





♂ X ♀

A^+ Rh MN B rh NN

AA Rh Rh MN
AO Rh Rh MN
AA Rh rh MN
AO Rh rh MN

BD rh rh NN
BO rh rh NN