

THE HISTORY OF BLOOD TRANSFUSION

G. W. G. BIRD

Director, Regional Blood Transfusion Service, Birmingham

It is sufficiently knowne that mans body is joined of four kinds of humours or complexions: to wit, of BLOOD, Cholera, Melancholia, and Phlegma; but amongst these is the Bloud one the best, partly, for that it is the matter of the vitall spirits wherein life itself hath its being. . . if the same be taken away, then death doth ensue.

WIRTZUNG (1617)

THE SPRING OF LIFE

THE concept of blood as the source of life itself probably preceded civilization. God, making a covenant with Noah, said 'flesh with the life thereof, which is the blood thereof' (Gen. 9).

Death from battle wounds led primitive man to believe that blood had magical powers. It was the vehicle of life, and through blood came man's physical and mental attributes. Its health-giving properties were acclaimed by the ancient Egyptians who took baths in the blood of their victims. In ancient Rome spectators used to rush into the arena to drink the blood of dying gladiators.

BIRTH OF THE IDEA

The value of blood transfusion in saving life is now well known. Its evolution from small and uncertain beginnings to its present status is of much interest.

The earliest 'transfusion' of blood from one person to another seems to have been given by mouth. A draught of blood, obtained from three boys, who were bled to death for the purpose, was given to Pope Innocent VIII in 1492.

Possibly the first recorded suggestion for a real transfusion was that of Libavius in 1615 (Keynes, 1922), who wrote:—

Let there be present a robust healthy youth full of lively blood Let there come one exhausted in strength, weak, enervated, scarcely breathing. Let the master of the art have little tubes that can be adapted one to the other; then let him open an artery of the healthy one, insert the tube and secure it. Next let him incise the artery of the patient and put into it the feminine tube. Now let him adapt the two tubes to each other and the arterial blood of the healthy one, warm and full of spirit, will leap into the sick one, and immediately will bring him to the fountain of life, and will drive away all langour.

This suggestion is of interest because William Harvey first propounded his theory of the circulation in 1616, a theory which was not generally known until it was published twelve years later. It would perhaps be wise not to credit any suggestions made before the discovery of the circulation.

Francisco Folli, a physician of Florence, in a book published in 1680, stated that transfusion of blood should be able to cure diseases and rejuvenate the aged. He visualized twenty young men as donors, so that every day fresh blood could be given to the patient. He conceived an apparatus consisting of a funnel connected to a gold or silver cannula by means of a tube which consisted of a length of a goat's artery. There is however no firm evidence that he put his ideas into practice.

TRANSFUSION OF ANIMAL BLOOD TO HUMAN PATIENTS

In England, Sir Christopher Wren, the celebrated architect and astronomer, who pioneered intravenous injections, was aware of the beneficial potentiality of blood transfusion. He left it to his friend, Richard Lower, actually to put his ideas into practice. Lower successfully transfused a dog by connecting the donor's carotid artery to the recipient's jugular vein with a silver tube. However, the first transfusion to a human being appears to have been given by Jean Denys of Montpellier, Physician to Louis XIV of France. A translation (Keynes, 1922) of Denys' account published in 1667, reads as follows:—

I attributed all these changes to the great evacuations of blood the Physicians had been oblig'd to make for saving his life, and I perswaded myself that the little they had left him

was extremely incrustated by the ardour of the fever Accordingly my conjecture was confirmed by our opening one of his Veins, for we beheld a blood so black and thick issue forth, that it could hardly form itself into a thread to fall into the porringer. We took about three ounces at five of the Clock in the morning and at the same time we brought a Lamb whose Carotis Artery we had prepar'd, out of which we immitted into the young man's Vein, about three times as much of its Arterial blood as he had immitted into the Dish, and then having stopt the orifice of the Vein with a little bolster, as is usual in other phlebotomies, we caus'd him to lie down on his bed expecting the event; and as I askt him now and then how he found himself, he told me that during the operation he had felt a very great heat along his Arm, and since perceived himself much eased of a pain in his side, which he had gotten the evening before by falling down a pair of staires of ten steps; about ten of the clock he was minded to rise and being I observed him cheerful enough, I did not oppose it; and for the rest of the day he spent it with much more liveliness than ordinary, eat his Meals very well, and shewed a clear and smiling countenance. He grows fat visibly, and in brief is a subject of amazement to all those that know him, and dwell with him.

Denys also claimed to have cured by transfusion a patient suffering from 'an inveterate Phrenzy'. This case is of special interest because he chose to transfuse the blood of a calf in order to transfer placid bovine characteristics to the patient. Denys actually recorded what must be the first description of the symptoms of an incompatible transfusion:—

. . . the Patient must have received more than one whole pound. As this second Transfusion was larger, so were the effects of it quicker and more considerable. As soon as the blood began to enter into his veins he felt the like heat along his Arm and under his Arm-pits which he had felt before. His pulse rose presently, and soon after we observed a plentiful sweat all over his face. His pulse varied extremely at this instant, and he complained of great pain in his Kidneys, and that he was not well in his stomach, and that he was ready to choak unless they give him his liberty.

Presently the pipe was taken out that conveyed the blood into his Veins, and whilst we were closing the wound he vomitted store of bacon and Fat he had eaten half an hour before. He found himself urged to urine, and asked to go to stooll. He was soon made to lie down and after two good hours strainings to void divers liquors, which disturbed his stomach he fell asleep about 10 a clock and slept all the night without wakening until next morning, was Thursday, about 8 a clock. When he awakened, he showed a calmness, and a great presence of mind, in expressing all the pains and a general lassitude he felt in all his limbs. He made a great glass full of Urine, of a colour as black, as if it had been mixed with the soot of Chimneys.

The patient survived these unfortunate sequelae and indeed appeared to have derived some benefit from the transfusion.

Preliminary animal experiments were shortly afterwards carried out in England. Samuel Pepys, the celebrated diarist, records on 14 Nov., 1666, the following description of what he had witnessed:—

Here (at the Pope's Head) Dr. Croone told me that, at the meeting at Gresham College to-night . . . there was a pretty experiment of the blood of one dogg let out, till he died, into the body of another on one side, while all his own run out on the other side. The first died upon the place, and the other very well, and likely to do well. This did give occasion to make pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but, as Dr. Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body.

On 16 Nov., 1666 Pepys records:—

This noon I met Mr. Hooke, and he tells me the dog which was filled with another dog's blood, at the College the other day, is very well, and like to be so as ever, and doubts not is being found of great use to men—and so do Dr. Whistler, who dined with us at the tavern.

In November, 1667, Pepys writes about a blood transfusion to a human subject:—

Among the rest they discourse of a man that is little frantic, that hath been a kind of minister, Dr. Wilkins saying that he hath read for him in his church, that is poor, and a debauched man, that the College have hired for 20s, to have some of the blood of a sheep let into his body; and it is to be done on Saturday next. They purpose to let in about twelve ounces; which they compute is what will be let in in a minute's time by a watch. They differ in the opinion they have of the effects of it; some think it may have a good effect upon him as a frantic man by cooling his blood, otherwise that it will not have any effect at all. But the man is a healthy man, and by this means will be able to give an account what alteration, if any, he do find in himself, and so may be useful.

On 29 November he writes:—

I was pleased to see the person who had his blood taken out. He speaks well, and did this day give the society, a relation thereof in Latin, saying that he find himself much better since, and as a new man, but he is cracked a little in his head, though he speaks very reasonably, and very well. He had but 20s for his suffering it, and is to have the same again tried upon him; the first sound man that ever had it tried on him in England, and but one that we hear of in France, which was a porter hired by the virtuousos.

An interesting indication for transfusion which was considered during the early years was the settling of marital discord by reciprocal transfusion of husband and wife.

After these pioneer efforts blood transfusion to human beings became more frequent. Animal blood was used and many disasters resulted. It was by no means generally popular since many believed that unfortunate late results, such as the development of horns by those who had received sheep's blood, might occur. Transfusion fell into disrepute and was actually forbidden by law in France after Denys' fourth patient died. Denys was tried for manslaughter and acquitted.

The idea seems to have been revived about 100 years later when transfusion was used for hydrophobia, fever, cancer of the oesophagus, and impaired nutrition.

TRANSFUSION OF HUMAN BLOOD TO HUMAN PATIENTS

In 1818, James Blundell, physiologist, physician, and obstetrician, restimulated the interest of the medical profession in blood transfusion and actually carried out the first transfusion of human blood to human patients. Haemorrhage after childbirth was so alarmingly fatal that he decided to replace the lost blood by transfusion. He devised an apparatus known as Blundell's impellor, which was fixed to the chair on which the recipient was made to sit. His first four attempts at transfusion in patients with post-partum haemorrhage were unsuccessful, but the lives of the next three were saved. Blundell's work provided considerable impetus to progress in this field. The main technical difficulties, however, were clumping and breakdown of transfused blood cells, infection, and clotting of the blood in the apparatus.

In 1857, Higginson introduced a rubber syringe with ball valves to transfer blood into the veins of the patient. This modification materially aided the introduction of blood with some force, which was necessary whenever the patient's veins were collapsed. 'Mr. Higginson's Transfusion Instrument' (Higginson's syringe) was dangerous and not particularly successful. It was later relegated to the less laudable function of giving enemas.

THE PROBLEM OF CLOTTING

In 1835, Bischoff overcame the problem of coagulation by using defibrinated blood. The need for an anticoagulant solution which would simplify the transfusion of blood was always in the minds of earlier workers. Among the different

substances investigated were ammonia, sodium phosphate, various oxalates, hirudin, and peptone. Although these substances prevented clotting they produced such toxic symptoms that each was quickly abandoned. Kimpton and Brown (1915) used, with some success, apparatus lined with paraffin wax. A significant advance however was the discovery of sodium citrate as a safe and effective anticoagulant by Hustin (1914), Agote (1915), and Lewisohn (1915). Even today sodium citrate is the fundamental component of anticoagulant solutions used in blood transfusion.

BLOOD GROUPS

Landois (1875) showed that the red blood-corpuscles of one animal were agglutinated or haemolysed by the serum of another. This was undoubtedly one of the major reasons for the reactions earlier workers had observed during the transfusion of animal blood to human recipients.

At the beginning of the present century, Karl Landsteiner (1900, 1901) discovered human blood groups and really laid the foundation of successful blood transfusion. He showed that the blood of one human being may be incompatible with that of another. He did this by simply making suspensions of his own red cells and those of five members of his staff and adding each suspension to each person's serum. It was immediately clear that there were three different blood groups which he named O, A, and B. The fourth group, AB, was discovered a year later by Landsteiner's pupils, von de Castello and Sturli. The term O was used by Landsteiner to mean 'null' or zero, because group O cells lack the A and B characters.

Today there are fourteen major blood group systems in man, and several minor ones. Nevertheless, the ABO blood group system is still the most important in blood transfusion.

In 1940 Landsteiner (with Wiener) discovered the Rhesus blood group system which ranks next in importance to the ABO system from the blood transfusion point of view. This system however is of prime importance in paediatrics because Rhesus blood group incompatibility between mother and child is the commonest cause of haemolytic disease of the newborn.

BLOOD TRANSFUSION IN WAR

It seems that blood transfusion, by the direct method, was first used in the field during the Franco-Prussian War (1870). Although the citrate method was discovered in 1914 just before the start of the First World War, it was not until

1917 that citrate was used in our military hospitals in France. It was introduced to Casualty Clearing Stations by Robertson, a Canadian. Early in 1918, Ward, a Captain in the R.A.M.C., urged the use of citrated plasma instead of whole blood in oligæmic shock.

The first organized blood transfusion service in the field was created during the Spanish Civil War (1937-9). However, it was during the Second World War (1939-45) that the first large scale blood transfusion service was organized in Britain and in the various theatres of war in which the British fought. The development of the blood transfusion services was rated as one of the three greatest medical advances of the Second World War, the other two being the bringing of the surgeon to the battlefield and the discovery of penicillin.

THE VOLUNTARY BLOOD TRANSFUSION SERVICE

The first voluntary blood transfusion service was founded in London in 1921 by the British Red Cross Society. Percy Lane Oliver, Honorary Secretary of the Camberwell division of the County of London Branch, prepared a list of volunteers. By the end of 1925 the scope of the service had increased so much that the headquarters of the British Red Cross was approached to take over the organisation. It is interesting to note that in 1921 there were four donors on the panel and that the Service received one call. Ten years later there were 1304 donors on the panel and the Service received 2442 calls.

The National Blood Transfusion Service (England and Wales) was formed in 1946 out of Centres administered by the Army, the Emergency Medical Service, and the Medical Research Council. The number of registered blood donors in England and Wales is now over a million.

BLOOD BANKS

Storage of citrated blood was practised in a small way by Rous and Turner in the United States of America as far back as 1916, and Robertson (1918) used stored citrated blood in the battlefield with excellent results. In fact, Robertson added glucose to the citrate solution, thereby greatly increasing the storage period from the then accepted 7 days to 21 days.

Storage on a larger scale was exploited by the Spaniards during the Spanish Civil War, and by the Russians, who stored cadaver blood (*see below*). The term 'blood bank' originated in the United States. The blood bank was originally intended to operate on the deposit and withdrawal

system, so that an organization could not withdraw blood if its account was, to use a seemingly inappropriate expression, 'in the red'!

TRANSFUSION APPARATUS

A detailed account of transfusion apparatus throughout the ages would be too long for inclusion in this account. The evolution of transfusion apparatus from the early days of direct transfusion, through Blundell's impellor, the Kimpton-Brown paraffin-coated bottle, and open conical flasks containing anticoagulant solution, to closed systems in glass bottles will be found in various publications, the most informative being the book by Kilduffe and DeBailey (1942). At the present time the glass bottle is being replaced by the plastic bag, developed by Walter in 1952.

CADAVER BLOOD

The idea of using cadaver blood for transfusion was that of the Russian, Vladimir Shamov (1928). His experiments on dogs showed that transfusion of cadaver blood was harmless and effective.

Yudin (1930), a Soviet surgeon, was the first to use the procedure in man. The patient was a man who had attempted suicide by cutting the veins of his wrist. Transfusion of cadaver blood at the Sklifosovsky Institute saved his life.

Cadaver blood is still used in Russia; it must be collected within six hours of death. After sudden death 'without long agony' blood does not clot for 20-30 minutes after collection. It then clots but becomes liquid again in about 90 minutes. No anticoagulant solution is therefore necessary.

The Sklifosovsky Institute has a special operation theatre open twenty-four hours a day for bleeding corpses. Victims of myocardial infarction, hypertensive heart disease, alcohol intoxication(!), electric shock, and severe (non-penetrating) head or brain injuries are bled. Victims of motor or other accidents involving crushing of tissues are unsuitable because of the danger of infection.

About 3 litres of blood are obtained, mixed with a glucose-phosphate stabilizer and antibiotics, and stored in the refrigerator until necropsy and all relevant laboratory tests are carried out.

Whereas the use of cadaver blood does not appeal to many, it is fair to say that the work of Shamov and Yudin opened up an epoch of cadaveric tissue transplantation which has been extended to corneal and organ transplantation.

COMPONENT THERAPY

Today, blood transfusion does not necessarily mean the giving of whole blood. Indeed, it is

more economical and efficacious to give, whenever indicated, the appropriate component. The first blood component to be used was, of course, plasma (see above). The use of red-cell concentrates ('packed cells') was a logical sequel. Fractionation of blood was first carried out in 1940 by Cohn, who prepared serum albumin (Cohn, Leutscher, Oncley, Armstrong, and Davis, 1940). Gamma-globulin, fibrinogen, anti-haemophilic globulin and other coagulation factors were later prepared in purified form. The preparation of platelet concentrates was made comparatively easy with the introduction of plastic equipment.

PLASMAPHORESIS

Although plasmaphoresis has only recently become popular, the idea first occurred to Abel about sixty years ago (Abel, Rowntree, and Turner, 1914). Abel's method differs from that in current use in only one respect: he added Locke's solution to the red cells before returning them to the donor.

CONCLUSION

The last twenty-five years have seen great advances in blood transfusion. The subject is comprehensively treated by Mollison (1967).

Happily, the voluntary blood donor system has survived in Britain. The transfusion services are now highly developed so that the supply of blood is largely taken for granted. Clinicians should remember, however, that blood is a gift from altruistic members of the public which should not be misused or wasted.

REFERENCES

- ABEL, J. J., ROWNTREE, L. G., and TURNER, B. B. (1914), 'Plasma Removal with Return of Corpuscles (Plasmaphoresis)', *J. Pharmac. exp. Ther.*, **5**, 625.
- AGOTE, L. (1915), 'Nuevo Procedimiento para la Transfusion del Sangre', *An. Inst. modelo Clin. med. B. Aires*, Nos. 1 and 3.
- BISCHOFF, T. L. W. (1835), 'Beiträge zur Lehre von den Blute und der Transfusion desselben', *Arch. Anat. Physiol.*, p. 347.
- BLUNDELL, J. (1818), 'Experiments on the Transfusion of Blood by the Syringe', *Med. chir. Trans.*, **10**, 269.
- COHN, E. J., LEUTSCHER, J. A., jun., ONCLEY, J. L., ARMSTRONG, S. H., jun., and DAVIS, B. D. (1940), 'Preparation and Properties of Serum and Plasma Proteins. III. Size and Charge of Proteins separating on Equilibration across Membranes with Ethanol-water Mixtures of Controlled pH Ionic Strength and Temperature', *J. Am. chem. Soc.*, **62**, 3396.
- HIGGINSON, A. (1857), 'Report of Seven Cases of Transfusion of Blood with a Description of the Instrument invented by the Author', *Lpool med. chir. J.*, **1**, 102.
- HUSTIN, A. (1914), 'Note sur une Nouvelle Methode de Transfusion', *Bull. Séanc. Soc. Sci. méd. nat. Brux.*, No. 4.
- KEYNES, G. (1922), *Blood Transfusion*. London: Henry Frowde and Hodder & Stoughton.
- KILDUFFE, R. A., and DEBAKEY, M. (1942), *The Blood Bank and the Technique and Therapeutics of Transfusion*. St. Louis: Mosby.
- KIMPTON, A. R., and BROWN, J. H. (1915), 'Technique of Transfusion by Means of Glass Tubes', *Boston med. surg. J.*, **173**, 425.
- LANDOIS, L. (1875), *Die Transfusion des Blutes*. Leipzig: Vogel.
- LANDSTEINER, K. (1900), 'Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe', *Zentbl. Bakt. ParasitKde.*, **27**, 357.
- (1901), 'Ueber Agglutinationserscheinung normalen menschlichen Blutes', *Wien. klin. Wschr.*, **14**, 1132.
- and WIENER, A. S. (1940), 'An Agglutinable Factor in Human Blood recognised by Immune Sera for Rhesus Blood', *Proc. Soc. exp. Biol. Med.*, **43**, 223.
- LEWISOHN, R. (1915), 'Blood Transfusion by the Citrate Method', *Surgery Gynec. Obstet.*, **21**, 37.
- MOLLISON, P. L. (1967), *Blood Transfusion in Clinical Medicine*. Oxford: Blackwell.
- PETROV, B. (1962), *Rakt Daan*, **1**, No. 2, p. 11.
- RIDDELL, V. H. (1939), *Blood Transfusion*. London: Milford.
- ROBERTSON, O. H. (1918), 'Transfusion with Preserved Red Cells', *Br. med. J.*, **1**, 691.
- ROUS, P., and TURNER, J. R. (1916), 'The Preservation of Living Red Cells in Vitro', *J. exp. Med.*, **23**, 219.
- SHAMOV, V. (1928), cited by PETROV (1962).
- WALTER, C. W. (1952), 'New Methods of Blood Collection', *Am. J. Pharm.*, **124**, 148.
- WARD, G. R. (1918), 'Transfusion of Plasma', *Br. med. J.*, **1**, 301.
- WIRTZUNG (1617), *General Practice of Physicke*. London. Quoted by RIDDELL (1939).
- YUDIN, S. (1930), cited by PETROV (1962).