TRANSFUSIONS OF BLOOD AND PLASMA

THOMAS H. SELDON, M.D., JOHN S. LUNDY, M.D.,
AND R. CHARLES ADAMS, M.D.

Rochester, Minn.

In 1616 to 1628 William Harvey (1) discovered and announced the theory of the circulation of the blood. This was the first important contribution which made possible the technic and practice of the transfusion of blood as we know it today. One must consider the history of blood transfusions prior to this date as not being similar to the procedures as we know them today, because without the knowledge of the circulation of the blood, it would seem impractical to conceive of blood being administered by the intravenous route.

Harvey’s discovery was therefore the direct factor that stimulated many investigators to study the results of adding various fluids to the circulation. Many names are mentioned during the next few years; however, the one most generally recognized is that of Sir Christopher Wren (2), who in 1656, injected ale, wine and opium into the veins of dogs. Richard Lower (3) apparently was the first man to accomplish successfully the direct transfusion of blood from one animal to another. He connected the jugular veins of two dogs but found that the blood clotted because it flowed so slowly. However, when the carotid artery of the donor dog was connected with the jugular vein of the recipient dog, the transfusion was more successful than when it was from vein to vein. At this early stage was experienced one of the difficulties that one still tries to avoid today, that is, the clotting of the blood during its transference from donor to recipient. In November, 1667, for a monetary consideration, Arthur Coga allowed Lower to transfuse blood from a lamb into his veins. In June of the same year, Denis, Louis XIV’s personal physician, also transfused lamb’s blood into a youth. On a later occasion one of Denis’ fifteen patients unfortunately died and he was tried for murder but eventually exonerated. However, the procedure was prohibited and throughout Europe interest was lost quickly.

Relatively little was done with this procedure for 150 years. In 1818 Blundell (4–9) revived the interest of investigators. He was much impressed with the lack of adequate and suitable treatment in cases of puerperal hemorrhage. His treatment by transfusions of blood was apparently successful in several cases in which under ordinary circumstances the patients might have died. To this day severe hemorrhage is one of the most important causes for the transfusion of blood into human beings.

*From the Section on Anesthesia, Mayo Clinic, Rochester, Minn.

22
In Blundell's time the coagulation of blood was still one of the great difficulties. However, defibrination of blood overcame this difficulty. Larsen (10), in 1847, performed one of the earliest transfusions of defibrinated blood; this was another advance in the technic of successful transfusion of blood. Cohnheim (11), in 1882, stated that "the serum of one species is a direct poison for the corpuscles of another." The most important single discovery relative to blood transfusions was that of Landsteiner (12, 13). In 1900 he discovered three of the four groupings, dividing them according to their agglutinating reactions. In 1902 the fourth group was added by his co-workers, DeCastello and Sturli (14). Jansky (15) in 1907 worked out their reciprocal agglutinating reactions. Moss (16) independently corroborated Jansky's work but unfortunately groups 1 and 4 were transposed, resulting in much confusion. In 1914 Hustin (17, 18, 19) of Brussels advocated a solution of sodium citrate and glucose as a preservative agent. Agote (20) of Buenos Aires used sodium citrate alone in the same year. Lewisohn (21) and Weil (22) independently worked out the technic and standardization of the dosage of sodium citrate in 1915.

PERSONNEL

The transfusion of whole citrated blood or plasma is directly under the supervision of the Section on Anesthesia at the Mayo Clinic. The physicians of the Section on Anesthesia (23) are responsible for the withdrawal of the blood from donors and the transfusions of the blood. The processing of blood plasma and the eventual administration of the plasma also come under the same supervision.

WITHDRAWAL OF BLOOD

Whole citrated blood is collected into suitable containers in which there is 75 cc. of 2.5 per cent solution of sodium citrate for each 500 cc. of blood to be withdrawn from the donor. No special apparatus, for example, suction machines for creating vacuums in bottles or bottles already containing a vacuum, is used for the withdrawal and storage of blood to be used in transfusion of whole blood. Before the actual withdrawing of blood is begun, both arms of the donor are examined to find the veins most readily accessible and easy to puncture with a large needle. The donor's arm is cleansed, painted with one of the accepted antiseptic solutions and suitably draped. A rubber tourniquet is applied reasonably close to the point of entrance of the needle. Procaine hydrochloride in 1 per cent solution is injected into the skin and around the vessel wall to make the entrance of the needle painless. Following the insertion of a No. 15 Lewisohn needle, the blood is allowed to flow into the bottle containing the sodium citrate. All precautions are taken to have as sterile a surgical technic as possible.

If the blood is to be used immediately, it is not placed in the refrigerator. However, if the citrated blood is to be stored, the bottle is suitably
sealed and kept in a refrigerator at 10 C. Although we usually take the chill off refrigerated blood before administration (24), this is not absolutely necessary (25). There are certain special preservative agents that may be used to delay hemolysis, thus allowing the storage of blood for thirty or more days. It has been shown that there is minimal hemolysis for the first five days when the blood is mixed with sodium citrate, and as we do not plan to keep blood in the refrigerator longer than five to seven days before use, we find it unnecessary to have the extra amounts of fluids that are needed for the special preservative agents. Therefore, 75 cc. of 2.5 per cent solution of sodium citrate usually is adequate to prevent the coagulation of 500 cc. of blood. While blood is being collected, gentle agitation of the container by a manual rotary motion should be carried out. When the bottle has been sealed suitably, vigorous shaking for a few seconds will mix the blood and the sodium citrate thoroughly. We have found this to be advantageous, as it is very rare that small clots are seen in the citrated blood.

For the withdrawal of whole blood to be processed into plasma we use an entirely closed system, thus cutting to a minimum the possibility of contamination of the final product, blood plasma. These vacuum bottles are purchased from a commercial firm. We find it a convenient, practical and safe method of handling and processing the blood and plasma. The plasma is frozen and stored in a special refrigerator unit in which the temperature is maintained at −20 C. Care is exercised to melt the frozen plasma in a water bath at 37 C. This permits relatively quick thawing, and one does not obtain the thick clots of fibrinogen that are seen frequently when thawing is carried out either too rapidly or too slowly. When plasma is being administered either intravenously or into one of the bone marrow spaces, it always is passed through a filter.

**Administration**

Our blood transfusions are administered by the physician personnel. About 90 per cent of all transfusions are administered by the Section on Anesthesia; the rest, which are usually emergency treatment, are administered by the medical or surgical residents. Whole citrated blood is administered by the indirect method. We usually employ blood of the same group as that of the patient; however, in emergencies, blood of group 0 is transfused into any patient if his blood group has not been determined or if the emergency does not allow sufficient time to call a donor of the same group and to withdraw the blood from the donor.

The rate of administration can be observed and controlled by the rapidity of the drops visible in the glass dropper which is part of the intravenous apparatus. Ordinarily a No. 18 gauge Lewisohn intravenous needle is used for giving blood to patients. Five hundred cubic centimeters of whole citrated blood is administered usually in thirty to forty-five minutes; this time may be increased or decreased as the particular need of the patient demands. In the operating room a No. 15 gauge
Lewisohn needle is used. If an emergency arises whereby a large quantity of blood must be administered relatively rapidly in the operating room while an operation is in progress, the blood may be given at the rate of 500 cc. of blood every three to five minutes through the No. 15 gauge Lewisohn needle. If a smaller gauge needle has been used and the blood must be administered more quickly than the smaller gauge needle will allow it to pass through by the gravity method, then an apparatus devised by Adams (26) is employed. By this apparatus, a positive pressure is created within the bottle containing the blood. The increased pressure within the bottle will force the blood through smaller needles, according to the pressure created within the bottle. This apparatus is particularly useful when blood must be transfused into small children, and relatively small needles are used to deliver the blood within a vein.

In transfusing blood into adults, usually one has no great difficulty in finding a vein into which the blood may be administered. In the ante-cubital fossa one has a choice of several veins. The cephalic vein at the wrist or the dorsal metacarpal veins on the dorsum of the hand usually can be found. In the lower extremity usually the great saphenous vein can be identified anterior to the medial malleolus or one of its tributaries on the dorsum of the foot. If these veins are not easily visible, the extremity can be hung over the side of the bed and gravity will help to fill them with blood. If they are still difficult to see or find, hot compresses applied from the tips of the digits to above the elbow or knee will greatly facilitate the filling of these vessels with blood (27). If this method is used, a tourniquet should be applied cephalad to the compress before its final removal, thus keeping the extra blood in the extremity. As an added benefit, a warm antiseptic solution should be used in preference to a cold one, as a cold one will tend to stimulate a reflex contraction of the already dilated and filled vascular system in the extremity. A second tourniquet should be applied as closely as possible to the point of entrance of the intravenous needle. This allows a stretching of the vein when pulled on by the physician; the tourniquet acts as a counterextension, helping to get the vein into as straight a line as possible, facilitating the venipuncture. Before attempting to insert the needle into any vein, one should always be sure that one can see or feel the vein. This is important. Indiscriminate exploring with the needle, in the hope of hitting a vein, usually is inexcusable. In transfusing blood into small children, if the possibility of entering one of the aforementioned veins is poor, we use a vein of the scalp or one of the external jugular veins.

Tocantins and O'Neill (28), and these authors and Price (29), have reintroduced the practical and useful method of administering fluids, plasma and whole citrated blood parenterally into certain spaces of the bone marrow. In transfusing blood into adults, it is easy to insert a needle into the space of the sternal bone marrow and we have used this route frequently to good advantage. In transfusing blood into small children, it is equally easy to insert a needle into the space of the bone marrow of the tibia near the upper end of the shaft; this route has been
very valuable in specific instances. One must take care not to injure the epiphysis.

The youngest child on whom we have used the tibial administration of blood was nine months of age. This child was exceedingly fat, dehydrated and very ill. It was impossible to get a vein sufficiently well defined to enable one to insert a needle into it. Intratibial administration of 5 per cent solution of glucose in physiologic saline solution, 5 per cent solution of glucose in distilled water, and blood for three days sufficiently supported the child and improved his condition that his peripheral vascular system became distended; easily recognized veins could be used for the administration of fluids and blood for the rest of his stay in the hospital.

The age of the youngest infant on whom venipuncture has been performed at the Clinic was two hours. In extreme cases, in transfusing blood into very young children, one can insert a needle into the superior sagittal sinus through the anterior fontanelle and administer blood in this manner. In the past two years it has not been found necessary to cut down on a vein for the intravenous administration of fluids, blood or plasma to an adult or a child, as it has been possible to insert a needle into a vein, into the superior sagittal sinus through a fontanelle or into certain spaces of the bone marrow. We wish to avoid venesection whenever possible, in order to preserve the veins for any future use.

**Amount of Blood or Plasma Administered**

The amount of blood or plasma administered depends to a certain extent on the reason for the transfusion of whole citrated blood or plasma and on the size of the patient. Whether one wishes to have repeated, small transfusions or less frequent, large transfusions also depends on the patient’s condition, and so forth. However, for single blood transfusions into infants, 5 to 10 cc. of blood per pound of body weight usually is all the infant can receive safely. If too great an amount is administered, the cardiovascular system may be embarrassed, the venous pressure increased too greatly and the patient may become dyspneic, cyanotic, flushed, and occasionally in apparent distress.

For adults frequently a standard dose of 500 cc. of citrated blood is ordered and no adequate follow-up check of the number of erythrocytes and the concentration of hemoglobin is done. Thus, otherwise than by clinical means, one does not know whether the patient has received an adequate amount of blood to obtain the desired results or whether more blood should be administered. Sibley and Lundy (30) showed that if bleeding and reactions occurred after transfusion in the general run of cases, the value for hemoglobin increased to an amount about equal to that added by the transfusion, only to decrease at the end of the eighth day to 65 per cent of the amount added by the transfusion. If reactions occurred after transfusion, but bleeding did not occur, the total hemoglobin increased to more than the amount added by transfusion until the
Transfusions of Blood and Plasma

Eighth day, at which time it decreased to 89 per cent of the amount added by transfusion. If neither reaction nor bleeding occurred, the total hemoglobin increased progressively until the tenth day, at which time it was 40 per cent greater than the amount added by transfusion. Also, the increase of total hemoglobin of the group of patients who did not have any reactions was 50 per cent more than the increase shown on the tenth day by the patients who had reactions.

When a transfusion is ordered it is only fair to the patient that the results of the administration of the blood should be checked by laboratory tests and clinical observations of the patients. In cases of severe shock in which blood or plasma is being used and it is impossible to obtain blood samples from the patient, frequently one has to rely on clinical observation only to evaluate the need for further blood or plasma.

Several months ago a child, aged four years, was brought in very severely burned; about 75 per cent of the body was involved with first or second degree burns. Shock was well advanced on the child’s arrival at the hospital. It was impossible to withdraw any blood from the vascular system, although we were able to get needles into veins for the administration of plasma, blood and 5 per cent solution of glucose in physiologic saline solution or distilled water.

The amount of fluids or plasma intravenously administered to combat shock depended very largely on clinical observation. We might have calculated how many cubic centimeters of plasma ordinarily should be used according to the system outlined in the publication of the Bureau of Medicine and Surgery, Navy Department, April, 1942 (31), but we based our quantities of fluids on clinical observations only. In spite of the hopeless outlook, this child has now recovered almost completely; he is still in the hospital undergoing plastic surgical care; he has received in all thirty-five transfusions during his convalescent period, ordered as the clinical and laboratory findings indicated that such treatment was needed.

In certain surgical cases in which shock is impending or in which the patient has had severe hemorrhage on the operating table, very large amounts of blood are sometimes needed quickly. Recently in a case of pneumonectomy, 7,500 cc. of blood was required for a severe, almost uncontrollable, hemorrhagic oozing over the exposed pleural surfaces, as the lung was being removed. Clinical observation of the patient played an important part in gauging the total amount of blood needed in this particular case. About three hours elapsed from the beginning of bleeding till the 7,500 cc. of blood was entirely administered. Whether several small repeated transfusions of blood or plasma or large massive transfusions are administered, a sufficient amount should be given to assure that the desired results are obtained.

Recently a patient was in the hospital for unexplained bleeding in the gastrointestinal tract. For about four weeks this patient had almost daily transfusions of blood or plasma; sometimes the amounts ordered were 250 cc., while at other times very large amounts were ordered.
Once a slow drip of 2,250 cc. was given over a period of twenty-four hours. At all times an attempt was made to keep this patient's general condition as good as possible. If 250 cc. of blood was expected to be sufficient, that amount was ordered. However, when the patient bled profusely, larger amounts of blood accordingly would be given.

For a number of years a patient suffering from hemophilia has been reporting to the Clinic at regular intervals. The patient can tell his general condition reasonably accurately; laboratory findings almost invariably coincide with the expressed feeling of his general condition. Repeated transfusions have carried this patient along for a number of years.

**Indications**

There are as many tables of indications and contraindications to the transfusion of blood as there are investigators. Briefly, the indications may be classified as follows:

1. *To Increase the Blood Volume.*—This is especially important in cases of shock. It is granted that there are many causes of shock, for example, severe hemorrhage, severe trauma and so on. However, it is generally agreed that there is an appreciable decrease of the blood volume in shock and this usually can be combated adequately by some solution of sufficient colloidal osmotic pressure to remain within the vascular system a reasonable length of time. It is agreed that physiologic solution of sodium chloride, with or without glucose, or some other fluids are excellent first aid measures until such time as 6 per cent solution of acacia, whole citrated blood or plasma can be procured.

For well developed shock it is preferable to use one of the latter therapeutic agents. Occasionally 6 per cent solution of acacia in physiologic solution of sodium chloride is used at the clinic; it does not necessarily take the place of either whole citrated blood or plasma. In a severe hemorrhage there is nothing as beneficial as whole blood itself. In dealing with shock one always should give enough of the therapeutic agent to get desired results. Standard doses cannot be used for everyone, or all conditions.

2. *To Increase the Oxygen Carrying Power of the Blood.*—Frequently this is a necessity in cases of very severe hemorrhage; in cases of acute or chronic anemias blood transfusions are beneficial. Often certain debilitating diseases accompany these acute or chronic forms of anemia or the disease may be the cause of the anemia. In either instance the blood transfusion is usually beneficial. In certain cases in which the hemopoietic power of the patient is decreased, the transfusion of blood supplies an additional number of erythrocytes to allow a resting period for the blood-forming organs, and thus the hemopoietic system can recover some of its former ability to produce blood cells.

3. *To Increase Concentration of Protein.*—The plasma proteins play an important part in the fluid balance between the extracellular and intravascular fluids. This depends on the colloidal osmotic pressure of the
plasma proteins. Besides edema, healing of wounds and gastrointestinal motility may depend to a certain extent on the protein level. The transfusion of whole blood, plasma or serum may correct these conditions. This has been observed in the clinic. Certain forms of edema have been relieved by the intravenous administration of plasma. In a case in which gastroenterostomy had been performed, gastric retention and vomiting suddenly developed ten days after operation. Laboratory tests demonstrated a condition of low serum proteins; it was felt advisable to transfuse concentrated plasma into the patient on two occasions; his retention and vomiting cleared and he left the hospital shortly thereafter.

4. To Increase Coagulability of the Blood.—In certain conditions of blood dyscrasias, hemorrhage and so on, the transfusion of blood is a valuable adjunct in the treatment. In certain cases of gastrointestinal hemorrhages, bleeding esophageal varices, and so forth, the patient seems unable to produce blood that will form a clot and attempt to stop bleeding. Transfusions of whole citrated blood, sometimes in large amounts and given slowly, are of extreme benefit. In certain cases in which dicumarol has been administered, the coagulation time is greatly lengthened and oozing from wound surfaces or into tissues is produced. A quick remedy for this effect of an otherwise valuable therapeutic measure is one or more transfusions of fresh citrated blood.

5. To Increase the Immunity of Patients in Certain Conditions.—Although there is probably no direct stimulus of immunity in the recipient, nevertheless, transfusions frequently appear to have a valuable therapeutic effect in infections and in sepsis. This may be due in large part to a generalized improvement of the condition of the patient; however, certain normal antibodies may be transferred from the donor. Seventy years ago Leisrink (32) said that “transfusion is indicated in all those pathologic conditions where the blood, in quantity or quality, is so altered that it is unfit to fulfill its physiologic duties.” This statement still holds true today.

**Contraindications**

The contraindications to blood transfusions fortunately are relatively few. It might be said that if a transfusion is especially indicated, it should be performed with extra caution, in spite of the possible presence of a condition which otherwise would be a contraindication to a transfusion. However, acute pulmonary edema, cardiac decompensation and massive pulmonary embolism are said to be absolute contraindications. Especial care must be exercised in cases in which there have been previous severe reactions following blood transfusions. This is also true in cases of severe renal damage.

**Untoward Effects of Transfusion**

Frequently it is difficult to say whether a given transfusion is the cause of an untoward effect or whether this untoward reaction is a conse-
quence of the patient's illness or a surgical operation. Briefly a few of the more commonly observed reactions are outlined.

1. **Reactions Due to Defects of Technic.**—Use of sodium citrate has now become sufficiently widespread that to blame this agent when it has been prepared by a reputable pharmaceutic firm seems unfair at times. However, we feel that poorly distilled water and improperly cleansed apparatus used in the performance of the withdrawal, storage and administration of blood are the cause of many of the untoward reactions. These reactions are characterized by the development of chills and a rise of temperature. This may occur within a few minutes after the completion of the transfusion or it may be delayed for an hour or two. The temperature may rise slightly or on occasion go as high as 105°F. Usually the temperature returns to normal within a few hours. The application of heat, administration of a sedative and, on occasion, epinephrine usually are sufficient for these reactions.

2. **Hemolytic Reactions.**—These may be due to several causes, for instance, incompatibility, minor hemagglutinins and certain pathologic conditions. The reaction following the administration of incompatible blood usually makes its appearance very early during the administration of the blood. These reactions may take a very severe form, ending in the death of the patient. Severe pain in the back and chest, dyspnea, cyanosis, sweating and shock are some of the manifestations. Hemoglobinuria usually appears; jaundice may occur but anuria does not follow necessarily. The reactions which sometimes follow repeated transfusions from Rh positive donors to Rh negative recipients in whom anti Rh agglutinins develop come under this category (33). Sedatives, heat, the alkalinization of the patient, forcing fluids to a degree, and the maintenance of the general condition of the patient are accepted methods of treatment.

3. **Allergic and Anaphylactic Reactions.**—The allergic reactions are characterized by urticaria, angioneurotic edema, dyspnea, asthmatic rales, involuntary movements of the bowel and excretion of urine. An anaphylactic shock may occur which is sometimes immediately fatal. Usually epinephrine injected subcutaneously is sufficient to offset the symptoms of the reaction. We had one patient who invariably on receiving blood had an urticarial rash. It was controlled in subsequent transfusions by addition of 1 cc. of 1 : 2,600 solution of epinephrine directly into the pint of blood to be transfused. These allergic reactions can occur from blood withdrawn from a donor who has recently ingested some food to which the recipient is allergic. This was shown dramatically in a case of a small child who was allergic to onions and whose father before serving as donor had had a recent meal including some onions. The child had widespread urticarial rash. Three-tenths of a cubic centimeter of 1 : 2,600 solution of epinephrine was administered subcutaneously, with dramatic relief of the symptoms.

4. **Transmission of Infectious Diseases.**—Syphilis and malaria are two diseases which can be transmitted by the transfusion of blood. Influenza,
measles, smallpox and septicemia have been reported as being transmitted. In any of these diseases the patient perhaps would have been much better if he never had received the blood, unless the transfusion was a dire emergency therapeutic measure. The treatment for any of these, of course, will necessitate the care for any of the particular diseases.

Recently we drew blood from a professional donor in whom chickenpox developed about three days after the withdrawal of the blood. The patient did not receive any untoward effect from this blood transfusion. We were not able to elicit that this patient had had chickenpox previously nor did chickenpox develop subsequent to the blood transfusion.

**Conclusions**

The final therapeutic value of the transfusion of blood or plasma depends on rational consideration of its need and on the proper withdrawal, storage and introduction into the recipient of the blood or plasma, with no untoward results to the patient.

**References**

15. Jansky, Jan: Haematologické, studie u psychotiků (Études hématoLOGiques, dans les malades mentales), Sborn. klin. 8: 85-139, 1907.
20. Agote, L.: Personal communication to Dr. Lundy.

---

ELECTION OF OFFICERS

The following officers of the American Society of Anesthetists, Inc., were elected at the December 3rd meeting to serve from January 1, 1944 to and including December 31, 1944: President: E. A. Rovenstine, M.D., New York, N. Y.; President-Elect, Ralph M. Waters, M.D., Madison, Wis.; 1st Vice President: Leo V. Hand, M.D., Boston, Mass.; 2nd Vice President: Hugh O. Brown, M.D., Chicago, Ill.; 3rd Vice President: Kenneth M. Heard, M.D., Toronto, Ont.; Secretary: McKinnie L. Phelps, M.D., New York, N. Y.; Assistant Secretary: John G. Dunlop, M.D., Los Angeles, Calif.; Treasurer: Virginia Appar, M.D., New York, N. Y.; Assistant Treasurer: Elisha D. Embree, M.D. (Lt. Col., M.C., A.U.S., Lincoln, Neb.).

The following members were elected to serve on the Board of Directors from January 1, 1944 to and including December 31, 1946: Maximillian C. Fishman, M.D., New York, N. Y.; Robert B. Hammond, M.D., White Plains, N. Y.; Frederick P. Haugen, M.D., Philadelphia, Pa.; Max L. Sulkow, M.D., Bronx, N. Y.; Paul M. Wood, M.D., New York, N. Y.; Harold C. Kelley, M.D., Yonkers, N. Y. Those members of the Board of Directors serving through 1944 and 1945 have been announced previously.