A BLOOD TRANSFUSION SERVICE DANGERS AND SAFEGUARDS *

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

Rochester, Minn.

THE last five years have seen the establishment of many centers for the withdrawal and storage of blood, processing of plasma and administration of blood and plasma. Each center has its own individual problems and difficulties. However, there are certain more or less common problems and dangers that seem to go with such a service. To draw attention to some of these problems and to show how the Mayo Clinic has attempted to solve them is the purpose of this paper.

LABORATORY WORK

In the Mayo Clinic all laboratory work that is necessary for the patient and the donor is carried out in the Division of Clinical Pathology. This work is done by especially trained technicians under the supervision of physician personnel. The system has worked out to advantage because the people who are primarily interested in the administration of blood are thus relieved of this work and their time is not devoted to exacting laboratory procedures in which a mistake could be disastrous to a patient.

DONORS

For several years 90 per cent or more of our supply of whole citrated blood was obtained from professional donors. Our list of professional donors was adequate for our needs. However, the need of our armed services for young adults has depleted our supply of donors. Because of this an effort has been made to get friends and relatives of patients either to donate the blood for the transfusion or else to replace blood already used from our refrigerator supply. Many organizations request two donors for each pint of blood or unit of plasma used. On the other hand, our practice has been an even trade; that is, one donor per 500 cc. of blood or unit of plasma administered. If there are a greater number of suitable donors than are required for the patient or to repay the bank, then the difference is credited to the patient's account. Also, past-due clinic accounts can be paid by regular donations of blood. It has been our experience that many people will

* From the Section on Anesthesiology, Mayo Clinic, Rochester, Minnesota.

gladly donate blood, who are unable otherwise to look after a financial payment.

Our professional donors have periodic physical examinations and serologic tests. This group of donors then is carefully supervised. Friends and relatives of patients who are eager to help may themselves not be entirely well. Although they are not given as complete a physical examination as the professional donors, nevertheless we determine their hemoglobin, blood grouping, serologic reaction and a brief history of past illnesses. A donor's concentration of hemoglobin must be at least 80 per cent, his blood pressure must be within reasonable limits and he must have a negative reaction for syphilis. As late as 1943, Frye and his associates (1) showed that of 603 hospitals, 6.5 per cent did not test blood donors for syphilis before their blood was used. Donors who have had or may have had malaria are not used.

Usually our donors present themselves after having eaten a normal diet. Donors for those patients who are allergic to certain foods or other things are requested to report on a fasting stomach and must not be allergic to the same things to which the patient is allergic. If a donor has severe seasonal "hay fever," we exclude him during the period of this active sensitivity.

An impression has been gained that hunger or fatigue plays a role as a contributing factor in fainting. If these two factors are combined (for example, working all night plus no breakfast), the donor frequently feels faint after his blood has been drawn. We try to avoid this combination, asking the donor to report at another time or sending him out for a breakfast. In a mild syncopal attack, breathing through a sponge moistened with aromatic spirit of ammonia, swallowing 2 fluidrams (7.4 cc.) of aromatic spirit of ammonia in a glass of water and lowering the head usually are adequate. However, in a certain few cases in which the cardiovascular system presents no contraindication it is necessary to administer 25 mg. of ephedrine intravenously. The ingestion of food and coffee following donations has a double role: it is both physiologically and psychologically beneficial.

Recently a female donor experienced an attack of tetany during the withdrawal of blood. The donor did not appear unduly nervous when she was on the table. However, her breathing was more rapid and deep than usual. When about 200 cc. of blood had been withdrawn, she exhibited typical spasms of the hands and feet and a positive Chvostek's sign. It is felt that the attack was not wholly dependent on the amount of blood withdrawn but was largely due to the hyperventilation. Treatment consisted in the administration of inhalations of 5 per cent carbon dioxide and 95 per cent oxygen. No other untoward effect was noted and the donor quickly recovered.

All our professional donors are tested for the presence or absence of the Rh factor. All obstetric patients and certain patients who are receiving repeated transfusions are also tested for the presence or

absence of the Rh factor. At all times Rh-negative group O (zero) blood is available in the refrigerator for emergency transfusions. Rh-negative donors of all blood groupings are available on short notice.

In this service we do not hesitate to use group O blood as a universal donor blood. Aubert, Boorman, Dodd and Loutit (2) demonstrated intravascular agglutination and hemolysis in certain cases in which patients belonged to group A and received group O blood. This was felt to be due to the high titer of anti-A agglutinins present in the serum of the group O blood. Recently a patient belonging to group A received blood from a group O donor. The patient did have a severe hemolytic reaction. Grouping and cross matchings of this patient and donor were checked and found compatible. Whether, if the purified group specific substances A and B of Witebsky and his associates (3) had been added to this particular donor's blood, they would have prevented the hemolytic reaction is not known. Nevertheless the donor's anti-A agglutinin titer was found to be 1:512. Although no appreciable ill effect had been found on seventeen previous transfusions of this donor's blood, the blood of this donor and all other group O donors having a high anti-A titer is now used only for group O recipients (4).

WITHDRAWAL OF BLOOD

In any transfusion service mistaken identity of donors must be avoided. This mistake is particularly easy in a busy service. Each donor is provided with an identifying card. His blood grouping is on this card and, if he is a non-professional donor, the name of the recipient or the name of the patient who is to receive financial credit for the donation is also shown. One nurse is responsible for the filling out of the labels for the collecting bottle from these data. Before the donor leaves the withdrawing room, a second interested person, either the nurse or the physician officiating at the withdrawal of blood, checks the donor's card and the labels on the bottle. The card and the labels must check for name and grouping.

As a tourniquet on the donor's arm we use a sphygmomanometer cuff. Usually the cuff is inflated to a point halfway between the systolic and diastolic pressure. However, occasionally blood flows from the needle more readily if a pressure is maintained in the cuff just slightly less than the diastolic pressure. This blood pressure cuff serves two further uses: to check the blood pressure before phlebotomy and, if the donor feels faint, to check the blood pressure before the donor leaves the table. If either reading is markedly off normal range, appropriate treatment may be instituted. It is well for all donors to rest for a period after donating blood; however, professional donors who have given blood repeatedly feel that this is a waste of their time and immediately walk away.

Nervous donors, donors who are giving blood for the first time, obese donors and donors whose veins apparently have an abundance of

valves not infrequently experience difficulty in donating a full 500 cc. of blood. Fasting and fatigued donors have been discussed. Nervous donors and donors who are giving blood for the first time, especially if they are chilly or cold, frequently have very poorly defined veins. If hot packs are applied to their arms, or even if these donors wash their arms to above their elbows under comfortably hot water for several minutes, the results are well worth the effort. Their arms become hyperemic and the veins stand out very well. In an exceptionally fat arm sometimes it is difficult to identify a vein. If a blood pressure cuff as a tourniquet is applied and inflated as previously described and the arm is allowed to hang downward for several minutes, the veins become engorged and easily identified.

Under no circumstances is it justified to probe around in an arm with a needle, blindly hunting for a vein. Trauma to a vein with a resulting hematoma, or possibly the accidental entrance of a bacterial skin contaminant, may result in cellulitis. Granted that the cellulitis may be only mild and transient, nevertheless these accidental happenings should be avoided.

In spite of heat applied or arms hanging down, the veins may be very small. To facilitate the free flow of blood in these cases the needle should be inserted against the direct flow of blood.

We have found it helpful to have the donor contract and relax his hand periodically while holding a piece of sponge rubber in his palm. A hard object like a bandage roll does not seem to give the freedom of squeezing that sponge rubber does. Furthermore, the sponge rubber has the advantage that, if a female donor has long fingernails, she may bury the nails into the rubber instead of her own skin. In order to establish a suitable rhythm of contraction and relaxation of the hand one may have the donor audibly count to four at the rate of one count per second during a hand squeeze and relax the hand for the same count. Furthermore, the counting distracts the donor's mind from the actual withdrawal of his own blood.

A snug pressure dressing should be placed on the arm following withdrawal. However, one should be sure that the dressing is not above the puncture wound; else a tourniquet-like effect will be produced and a hematoma result. An unpleasant looking black and blue discoloration is no advertisement for further withdrawals from this donor or possible future donations from his friends and relatives.

A little food and coffee are usually appreciated by the donors. They are medically sound and psychologically pleasant for the donor.

The optimal and minimal times for donors to have periodic withdrawals have not been agreed on. At the Mayo Clinic a research project is being planned to determine this time if possible, and also whether or not some preparation of iron improves the donor's condition and enables him to regenerate and replace more readily the original count of red blood cells and hemoglobin.

CONTAINERS AND STORAGE

At the Mayo Clinic we are running a series of transfusions, using both the system of collecting blood by gravity in open flasks and the closed system in commercial vacuum bottles. We are endeavoring to find out the relative transfusion reaction rate of the two systems. No data have been prepared for publication as yet. In both systems there is adequate sodium citrate for the preservation of 500 cc. of whole blood; yet the dose per 500 cc. is far less than the toxic dose as far as the patient is concerned. Solution of sodium citrate is toxic only in excessive doses. On more than one occasion it has been necessary to transfuse patients undergoing operation with very large amounts of whole citrated blood. Enough blood to contain 10 Gm. or more sodium citrate has been administered intravenously over two to three hour periods with no apparent ill effects to the patient. It is admitted that sodium citrate is not the ideal preservative. There are other preservatives for keeping blood longer but for ordinary short periods sodium citrate appears as good as any other.

When either the closed vacuum or the gravity system of collecting blood is used, it is well to moisten the inside of the container thoroughly with sodium citrate. If this is done, the fresh uncitrated blood does not come in contact with a surface of glass that may tend to injure the cells, predisposing toward rupture of cells and causing enough hemolysis to color the supernatant plasma during storage. A small amount of free hemoglobin does not harm a patient but the full benefit of the transfusion is not obtained. The blood bottle is shaken gently throughout withdrawal. At completion of withdrawal of the blood the bottle is given a thorough shaking before being placed in the refrigerator.

Well-constructed commercial refrigerators the temperature of which approximates 5 C. seem to be adequate for storage. With the frequent opening and closing of its doors it is impossible to keep an even, cool temperature within the refrigerator; however, once the blood is chilled, the small variations of temperature due to opening and closing the door do not seem to have any appreciable effect on the good preservation of the blood.

DeGowin and his associates (5) have shown that cold refrigerated blood can be administered without untoward effect on the patient. However, at the clinic we have found on occasions when we wanted blood to run very rapidly that cold blood running into one of the extremities produced a marked chilling of the particular venous area and a constriction of the vein, thus making it almost impossible to get blood to run in more rapidly than a slow drip. Heat in the form of hot water bottles or hot packs applied to the chilled area helps somewhat but added help in the form of the Lundy-Rogers roller or the Adams pressure arrangement is usually necessary (6, 7). It has been reported that certain bloods preserved with sodium citrate have within themselves a pressor substance producing vasoconstriction; in that case one

of the mechanical aids is essential. Where there is a large surgical service and an emergency blood transfusion may be required quickly, it is our practice to keep a bottle of group O blood constantly warmed for immediate use. This is done by placing a bottle of group O blood in a warming bath, maintained at 35 C., the first thing in the morning. Toward the end of the day we endeavor to use this blood rather than chill it again. However, if we do not use it, we place it in the refrigerator to be used the following day. In slow administration of blood certain other mechanical warmers may be used if thought advisable (8).

Before a bottle of whole citrated blood is placed in the warming bath it is well shaken, because if the cells are too tightly packed they have a tendency to clump together when warmed. This seems to be obviated by shaking the cells thoroughly in the plasma before placing the bottle in the warming bath.

RECIPIENTS

Our transfusions are administered entirely by the indirect method. As in identifying the donor, we also make very certain that we are identifying the correct patient to receive the particular bottle of blood. Not only are there identifying cards on the patient's door but the patient is asked: "What is your name?" Further interrogation, such as "Where is your home?" and so forth, may be necessary. On occasion we have had two patients in the same semiprivate room with the same surname, both of whom were to receive a transfusion. If the patient is too ill to answer intelligently, then a floor nurse must identify him.

The proper introduction of the needle into the recipient's vein is at times as important and as difficult a step as one will encounter. This particular procedure alone accounts for the greatest number of unsuccessful transfusions or poorly executed technic of the whole transfusion.

The selection of the vein to be used depends somewhat on the age of the patient, his position in bed, his physical condition and his cooperativeness. Usually the veins in the antecubital fossa, the dorsum of the hand and the radial border of the wrist, the internal saphenous vein in the ankle and the veins in the dorsum of the foot, and among small children the veins of the scalp, allow one ample selections of sites of entrance of needles.

It is our practice to use as large a needle as is possible to place in the vein in the operating room. This usually is a 15 gage Lewisohn needle. However, for ordinary transfusions or other parenteral therapy an 18 gage Lewisohn needle is inserted if possible. In administering a transfusion to an infant, we occasionally have to use a 23 gage needle if the infant's veins are small.

If veins are collapsed, difficult to find and so on, heat applied in the same manner as to a donor may be of value. If hot compresses are

applied, we find it expedient to place our tourniquet on the arm before the compresses are removed. Warm antiseptic solutions do not tend to produce vasoconstriction as does a cold alcoholic antiseptic solution.

Infants' veins are frequently difficult to identify at the best of times. It is well to get the infant into as convenient a position on the bed or table as possible for the operator. For the person doing the transfusion to be cramped for room, to be "off balance" or to have poor light is similar to getting a couple of strikes on a batter.

Adults about to undergo transfusion are frequently apprehensive. Infants are often difficult to handle. In both cases a sedative is of value. It is a practice in the clinic, when a transfusion is to be given to a child, to arrange that a sedative (¾ to 1½ grains [0.05 to 0.1 Gm.] of pentobarbital sodium or ¾ to 1½ grains [0.05 to 0.1 Gm.] of seconal sodium) be given every three-fourths hour until the child is asleep. Certain children require large doses of sedatives to get desired results; also, certain illnesses, for example, chronic nephrosis with generalized edema, seem to predispose the child to the need for larger doses than one would expect normally. In several cases children were still awake after administration of 4½ grains (0.29 Gm.) of either pentobarbital sodium or seconal sodium. We do not require that such sound sedation of adults as of children be produced. Splinting of arms or legs of both infants and adults facilitates the keeping in place of needles for long periods.

In those cases in which veins are impossible to identify, blood and other parenterally administered fluids may be injected into the marrow of a bone. In adults and older children the sternum is readily accessible; in children less than three years of age the tibia or fibula is more readily used. Our procedures for using this method have recently been described in another article (9).

The total dose of blood and the rate of administration depend on several factors. For practical purposes it may be accepted that an addition of 500 cc. of blood will correspond to a 10 per cent rise in concentration of hemoglobin; also, that an addition of 500 cc. of blood will add 500,000 erythrocytes per cubic millimeter of blood. This is to be given to an average adult weighing 150 pounds (68.0 Kg.). Weight for weight, infants and children need corresponding sized doses. It should be emphasized that this is not an absolute rule, as larger amounts may be needed in certain cases. If very large amounts are needed, it should be remembered that the body has a very well-regulated compensatory mechanism to maintain the volume of plasma at a fairly constant level under various conditions. Boycott and Oakley (10) demonstrated this in 1934.

There exists considerable variation in opinion regarding the correct rate of administration of blood. Of necessity the rate varies according to the physical condition of the patient and the necessity or desirability of getting the blood into the patient slowly or very rapidly. It is felt

at the clinic that in most cases a rate of administration of 15 cc. per minute is optimal. However, if necessary, we do not hesitate to introduce 500 cc. of blood in less than five minutes. On the other hand, for patients having definite myocardial damage it may be very desirable to administer blood at the rate of 1 cc. per minute. In certain cases of chronic bleeding, for example, gastric or duodenal ulcers, in which it is undesirable to raise the blood pressure, a slow continuous administration at the rate of 1 cc. per minute may be carried on for hours.

It must be remembered that a child should receive a transfusion at a rate comparable to that of transfusion of an adult. If we administer 500 cc. of blood in thirty minutes to an adult weighing 150 pounds (68.0 Kg.), then administration of 50 cc. to a child weighing 15 pounds (6.8 Kg.) should take approximately thirty minutes. Many physicians are prone to give a child a transfusion quickly to get it completed. It is not uncommon to see a crying, cyanotic, dyspneic child if the blood is administered too rapidly.

REACTIONS

Reactions during or following the administration of blood cannot be entirely prevented. In spite of all the usual precautions of laboratory technic, sterilizing of apparatus and so on, in a certain number of transfusions there are reactions of varying degrees of severity.

For long enough, advocates of the direct method of blood transfusion have condemned the use of sodium citrate. It is felt that this is unjustified in most respects, because the solutions of sodium citrate now available are uniformly highly purified and properly prepared. It is also felt that in those cases in which citrate may be blamed it would be more proper to blame the inadequate citration of the blood during the collection and storage. For all practical purposes sodium citrate is adequate for short periods of storage.

Unclean apparatus, resulting in the presence of pyrogens, accounts for many of the sudden and occasionally severe rises of temperature. Usually the temperature returns to its previous level within a few hours. The chilling accompanying these elevations of temperature varies from mild discomfort to actual rigors.

Treatment of these patients consists in application of heat and administration of 0.25 to 0.5 cc. of 1:2,600 solution of epinephrine hydrochloride, if thought necessary, and of a sedative. Intravenous administration of 1 to 2 grains (0.065 to 0.13 Gm.) of codeine sulfate gives the patient a feeling of warmth and converts the apprehensive patient to one enjoying comparative ease of mind.

Allergic reactions manifest themselves by urticaria, angioneurotic edema, difficult breathing, asthmatic râles, involuntary excretion of urine or feces or even an anaphylactic shock sufficiently severe to produce death. The explanation of the mechanism of all these reactions is not entirely satisfactory. Wiener and his associates (11) have sug-

gested that immune isoprecipitins, like isohemolysins, can be produced by repeated transfusions of homologous blood. Other cases in which the reaction is due to ingestion by the donor of food to which the recipient is susceptible are met with. The application of heat and administration of 0.25 to 0.5 cc. of 1:2,600 solution of epinephrine hydrochloride and of a sedative are accepted treatment. Occasionally, if dyspnea or cyanosis is severe, inhalations of oxygen may be necessary. Before blood is administered subsequently, the cause of previous reactions must be thoroughly investigated.

Hemolytic reactions may be caused by several conditions, for example, gross incompatibility, minor hemagglutinins such as Landsteiner's irregular iso-agglutinins, normal cold agglutinins, pathologic cold agglutinins, the rouleaux formation and occasionally blood from a universal donor whose serum titer is very high. Incompatibility with the Rh factor is important if the patient is in the Rh-negative classification and produces anti-Rh agglutinins.

The variety of therapeutic measures used to treat a hemolytic reaction shows the variability of opinions concerning the cause of the condition. It must be admitted that some patients receiving incompatible blood will live, while others will die in spite of any measures used. If uremia appears following a hemolytic reaction, the prognosis is much more serious than if uremia is not present. The ultimate outcome depends to a large degree on the amount of blood injected, the ability of the kidneys to handle the insult and the general condition of the patient. Patients receiving 250 cc. or less of incompatible blood have better chances of recovery than those receiving more than 250 cc.

The main purpose in treating these patients is to combat shock, stimulate renal function and increase the flow of urine. The patient should be alkalinized by intravenous administration of 5 per cent solution of sodium bicarbonate. Ten grains (0.65 Gm.) of sodium bicarbonate four times daily taken orally subsequent to the intravenous injection usually is sufficient to keep urine alkaline. Alkalosis of these patients must not be permitted. Sufficient fluids should be given orally and intravenously to get a daily average intake of 3,000 to 4,000 cc. for an adult. Plain water by mouth or glucose in distilled water administered intravenously may be used.

The retransfusion of compatible blood as treatment was originally suggested by Hesse and Filatov (12–14). These workers demonstrated that this is sound treatment. Experimentally and clinically they showed that in hemolytic reactions a depressor substance acts directly on the walls of blood vessels causing renal vasospasm. They further showed clinically and experimentally that immedate transfusion counteracts this effect.

The transmission of a disease to a recipient from the donor is particularly unfortunate. Reference is especially made to syphilis and malaria. It is well not to use donors who have a history of malaria or who once lived in areas infested with malaria. This is a point to

remember because so many returning military personnel have been exposed to such conditions.

A cardiovascular accident, such as cardiac failure producing pulmonary edema, depends to a great degree on the original cardiac condition, plus the speed of administration and the amount of blood transfused. Prophylaxis is the best treatment; however, when such a complication occurs, withdrawal of an amount of blood equal to that administered is usually beneficial. Inhalation of oxygen and administration of 1/150 grain (0.00043 Gm.) of atropine, 1/6 grain (0.01 Gm.) of morphine and occasionally 7½ grains (0.49 Gm.) of aminophylline may be necessary. Very rarely embolism or thrombosis may occur.

CONCLUSIONS

Crile (15) said in 1909: "Judiciously employed, transfusion will surely prove a valuable, often life-saving, resource; injudiciously employed, it will surely become discredited." We all agree that the results obtained from the judicious employment of this therapeutic procedure have far outweighed the occasional untoward reaction which is encountered.

REFERENCES

1. Frye, W. W.; Keller, A. E., and Kampmeier, R. H.: The Hospital and the Syphilis Problem in Prospective Blood Donors, J. A. M. A. 121: 182–186 (Jan. 16) 1943.
2. Aubert, E. F.; Boorman, Kathleen, E.; Dodd, Barbara E., and Loutit, J. F.: The Universal Donor with High Titre Iso-agglutinins; the Effect of Anti-A Iso-agglutinins on Recipients of Group A, Brit. M. J. 1: 659–664 (May 30) 1942.
3. Witebsky, Ernest; Klendshoj, N. C., and Swanson, Paul: Preparation and Transfusion of Safe Universal Blood, J. A. M. A. 116: 2654–2656 (June 14) 1941.
4. Klendshoj, N. C., and Witebsky, Ernest: Transfusion of O Blood: Conditioned by the Addition of Blood Group Specific Substances; Further Clinical Investigations, J. A. M. A. 128: 1091–1093 (Aug. 11) 1945.
5. DeGowin, E. L.; Hardin, R. C., and Swanson, L. W.: Studies on Preserved Human Blood. IV. Transfusion of Cold Blood Into Man, J. A. M. A. 114: 859–861 (Mar. 9) 1940.
6. Lundy, J. S., and Rogers, D. A.: A Hand-roller for the Rapid, Intravenous Administration of Urgently Needed Blood or Solutions, Proc. Staff Meet., Mayo Clin. 13: 726–727 (Nov. 16) 1938.
7. Adams, R. C.: Intravenous Anesthesia, New York, Paul B. Hoeber, Inc., 1944, 663 pp.
8. Seldon, T. H.: A Device for Warming Cold Refrigerated Blood, Proc. Staff Meet., Mayo Clin. 16: 52–53 (Jan. 22) 1941.
9. Seldon, T. H.: General Supportive Measures in Course of Anesthesia. Therapeutic Agents and Apparatus, S. Clin. North America (Aug.) 1945, pp. 743–774.
10. Boycott, A. E., and Oakley, C. L.: The Adjustment of the Blood Volume after Transfusion, J. Path. & Bact. 38: 91–97 (Jan.) 1934.
11. Wiener, A. S.; Oremland, B. H.; Hyman, M. A., and Samwick, A. A.: Transfusion Reactions; Experiences with More Than Three Thousand Blood Transfusions, Am. J. Clin. Path. 11: 102–121 (Feb.) 1941.
12. Hesse, E., and Filatov, A.: Experimental Investigations Regarding the Question of Haemolysis in Blood Transfusions, Internat. Abstr. Surg. 56: 241–242, 1933.
13. Hesse, E., and Filatov, A.: Die klinische Bestätigung der Möglichkeit der Behandlung des hämolytischen Schocks bei der Bluttransfusion nach unserer Methode, Zentralbl. f. Chir. 60: 851–854 (Apr. 15) 1933.
14. Hesse, E., and Filatov, A.: Experimentelle Untersuchungen über das Wesen des hämolytischen Shocks bei der Bluttransfusion und die therapeutische Beeinflussung desselben. I. Die Nierenfunktionsstörungen im akuten Experiment, Ztschr. f. d. ges. exper. Med. 86: 211–230, 1933.
15. Crile, G. W.: Hemorrhage and Transfusion; an Experimental and Clinical Research, New York, D. Appleton and Company, 1909, 560 pp.