BLOOD TRANSFUSION REACTIONS: THEIR ETIOLOGY, PREVENTION AND TREATMENT *

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There is no doubt but what blood transfusions have been responsible for the saving of many lives. Occasional untoward reactions occur but these are far outweighed by the beneficial results obtained from the judicious use of this valuable therapeutic agent. The causes of these untoward reactions are myriad and it is necessary that those responsible for blood transfusions be familiar with their etiology, prevention and treatment. The most common transfusion reactions are caused by incompatible blood, poor storage of blood, the inadequate care and cleaning of equipment, and improper transfusion technic. Urticarial and other allergic reactions are encountered.

Errors in the Grouping (Typing) of Blood

Even in the best of laboratories an occasional mistake will be made in the typing or grouping of blood. If human blood grouping sera of high titer are used by well-trained personnel these mistakes are infrequent.

The Lansteiner Groups and Subgroups.—The grouping of blood into four main groups is a standard procedure; according to Lansteiner or International classification, these are groups O, A, B, and AB. Group A may be further divided into the principal subgroups A₁ and A₂. Other common terms used are “strong titer” A for A₁, and “weak titer” A for A₂. If typing sera of low titer or potency are used there will be frequent errors. A₂ will be typed as Group O, and A₂B will be typed as B. Dire reactions can occur when these mistakes are made. The blood sera of most donors are not of high enough titer to avoid these mistakes. Enough good commercial high titer typing is available in sufficient quantities that it is indeed inexcusable to use ordinary anti-A and anti-B sera in any laboratory. High titer sera are produced by the injection of blood group specific substances into human donors (1). The sera used at the University of Kansas Medical Center are of a

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high titer, the anti-B sera having a titer of 1:512 and the anti-A sera a titer of 1:1,024.

**Group O, Universal Donor.**—Every attempt is made not to use universal or O Group blood except for Group O recipients. In emergencies, however, Group O blood is given without hesitation to recipients of any group. Occasionally an individual is encountered in which the anti-A agglutinins are of such a high titer that he should be classed as a “dangerous universal donor.” Reactions can occur when Group O blood is given to other groups (2). It has been recommended that only Group O blood with an isoagglutinin titer of 200 units or less be used as universal donor blood (4). The average laboratory cannot stand the burden of determining the titer of Group O blood. Witebsky and his associates (3, 4) and Wiener and his associates (5) have recommended the addition of purified blood group substances A and B to Group O blood to neutralize the anti-A and anti-B isoagglutinins that might be present. These substances are now commercially available and are kept on hand in our blood bank to be used whenever the occasion arises. A critical review of the use of A and B specific substances has been published by Tisdall, Garland and Wiener (6). These investigators stated that the addition of group-specific substances A and B is a safe and reliable method for preparing all Group O blood for use as universal donor blood.

**The Rh Typing of Blood.**—Within the last few years it has become necessary to do Rh typing of blood to avoid transfusion reactions in Rh negative recipients (7). This is a blood group entirely separate and distinct from the four main groups of the Lanstheimer classification. Weiner (8, 9, 10) stated that there are at least eight Rh blood types which would indeed make the routine typing of blood a most complicated procedure. Of these types, Rh_0 is by far the most antigenic and therefore the most important clinically. For the solving of most clinical problems it is sufficient to make tests with anti-Rh_0 serum (85 per cent) positive. All recipients should be Rh typed and only in a dire emergency should Rh positive blood be given to an Rh negative individual, and then only after a careful history has been obtained as to pregnancies and previous transfusions. It is an excellent policy to have more than one “batch” of typing sera on hand and the negative Rh bloods should be checked to be sure of the Rh blood group.

**The Care and Cleaning of Transfusion Equipment**

The care and cleaning of technical equipment used in obtaining, storing and administering blood is of the utmost importance. Many sudden and severe elevations in temperature are caused by improperly cleaned apparatus. These reactions are caused by the presence of pyrogens. With the usual hospital personnel available at the present time, adequate cleaning of apparatus is almost an impossibility. Even with the
best of trained personnel the cleaning of transfusion equipment is a most difficult procedure. It is indeed discouraging to cut open the rubber tubing of the most carefully cleaned equipment and find dried blood clinging to the inner surfaces. The problem has largely been solved by the use of pyrogen-free solutions, glassware, and plastic tubing, all of which can be used once and then discarded, never to be used again. This probably is the least expensive and most satisfactory method of dealing with the pyrogen problem.

**The Storage and Refrigeration of Blood**

If blood is not to be used immediately, a poor quality of blood will result unless a well-regulated refrigerator is available. Fibrin will precipitate to such a degree that the blood cannot flow through any available type of filter. Fibrin is precipitated but little if the temperature is never lower than 42° F. Blood maintained at this temperature will flow through almost any commercial filter if it has been well citrated and mixed when obtained from the donor. Whether or not blood containing precipitated fibrin will cause a reaction is problematical but it definitely is not desirable. Hemolyzed stored blood should not be used as reactions may occur.

**The Rate of Flow of Blood**

The technic of the actual administration of blood is still an important procedure. Marked variation in opinion exists as to the correct rate of administration of blood (11). In many instances the blood can be given at almost any desired rate. However, the rate should be varied according to the physical state of the patient and the desirability of increasing the circulating blood volume slowly or rapidly. Most recipients will tolerate the administration of 15 cc. per minute. When a tremendous loss of blood has occurred, 500 cc. of blood can be given in most instances as rapidly as possible. It should be remembered that the too rapid injection of blood, particularly in patients with cardiac disease, is probably still one of the most dangerous complications and has been responsible for a number of fatalities. Treatment in these cases should consist of phlebotomy, administration of oxygen and of those drugs desired to improve the cardiac state, such as morphine and aminophylline.

**The Recognition and Treatment of Transfusion Reactions**

Untoward reactions of varying degrees of severity during or following blood transfusions will occur in spite of all the precautions taken during the collection, storage, and care and cleaning of transfusion equipment.

**Febrile Reactions.**—Reactions of this type are usually due to the presence of pyrogens. These are substances probably of bacterial
origin which when injected intravenously with any type of solution result in febrile reactions. The occurrence of chills and fever following intravenous injections is a disturbing complication. Pyrogen-free solutions, glassware, and tubing have eliminated most of these reactions. The rise in temperature following transfusions may be accompanied by mild symptoms or actual chills and is usually of only a few hours’ duration. The treatment consists in applying heat and the administration of sedatives to decrease the apprehension of the patient.

Allergic Reactions.—These may be manifested by urticaria angioneurotic edema, difficult breathing, asthmatic rales, involuntary excretion of urine or feces, or even anaphylactoid shock of sufficient severity to produce death of the recipient (11). Weiner (12) stated that probably many of the so-called cases of allergic shock following transfusions are really instances of “speed shock,” and he quoted the experiments of Hirschfeld, Hyman, and Wanger (13) who showed that in dog experiments the rapid intravenous injections of fluid gave rise within forty to sixty seconds to cardiac failure, a sharp drop in blood pressure, and respiratory distress. Patients with the simpler types of allergic reactions respond to epinephrine or the newer antihistamine drugs or both. The application of heat and administration of sedatives and oxygen are necessary if dyspnea or cyanosis is severe.

Hemolytic Reactions.—Hemolytic transfusion reactions are of two principal types, (1) those due to incompatibility between the donor and recipient bloods, and (2) those caused by nonspecific agents. Other conditions that may cause hemolytic reactions are Landsteiner’s irregular iso-agglutinins, normal cold agglutinins, pathologic cold agglutinins, and on rare occasions blood from a “dangerous” universal donor with high serum titer. Incompatible blood causes the most severe hemolytic reactions. It is indeed tragic that errors of typing still occur in modern laboratories. Strumia (14) gave an excellent account of the clinical signs of such a reaction. These signs are noticed during or very shortly after the transfusion. They commonly consist of a chill, followed by nausea, vomiting, pain in the lumbar region, a sense of constriction in the chest and fever. Abdominal cramps, pain over the gallbladder and an urge to defecate have been noted. Transient hemoglobinemia with passage of scanty, reddish-brown urine is followed within five hours by hyperbilirubinemia, and shortly after by jaundice, usually reaching a peak within twenty-four hours. The oliguria may improve and the patient rapidly recover, but more often azotemia follows. This may lead to uremia and death or after a period of several days the flow of urine increases and recovery may ensue. Treatment consists in combating shock, stimulating renal function and increasing the urinary output (11). Alkalization by the intravenous administration of 5 per cent solution of sodium bicarbonate may be of benefit. Fluids should be given orally and intravenously with the aim of obtaining a daily intake of 3,000 to 4,000 cc. a day. An alkaline urine
should be maintained. Hesse and Filstov (15) originally recommended retransfusion with compatible blood, this resulting in counteracting a depressor substance causing renal vasospasm.

**Conclusions**

Blood transfusions are undoubtedly one of the most valuable lifesaving agents in modern medicine. Occasional untoward reactions may occur and all individuals responsible for the administration of blood should be familiar with their etiology, prevention and treatment.

**References**


The Section on Anesthesiology of The American Medical Association will hold its meetings in conjunction with the Scientific Assembly of The American Medical Association from June 8 to June 10, at Atlantic City, N. J.

It is important that all anesthesiologists planning to attend register in the Section on Anesthesiology for this meeting.