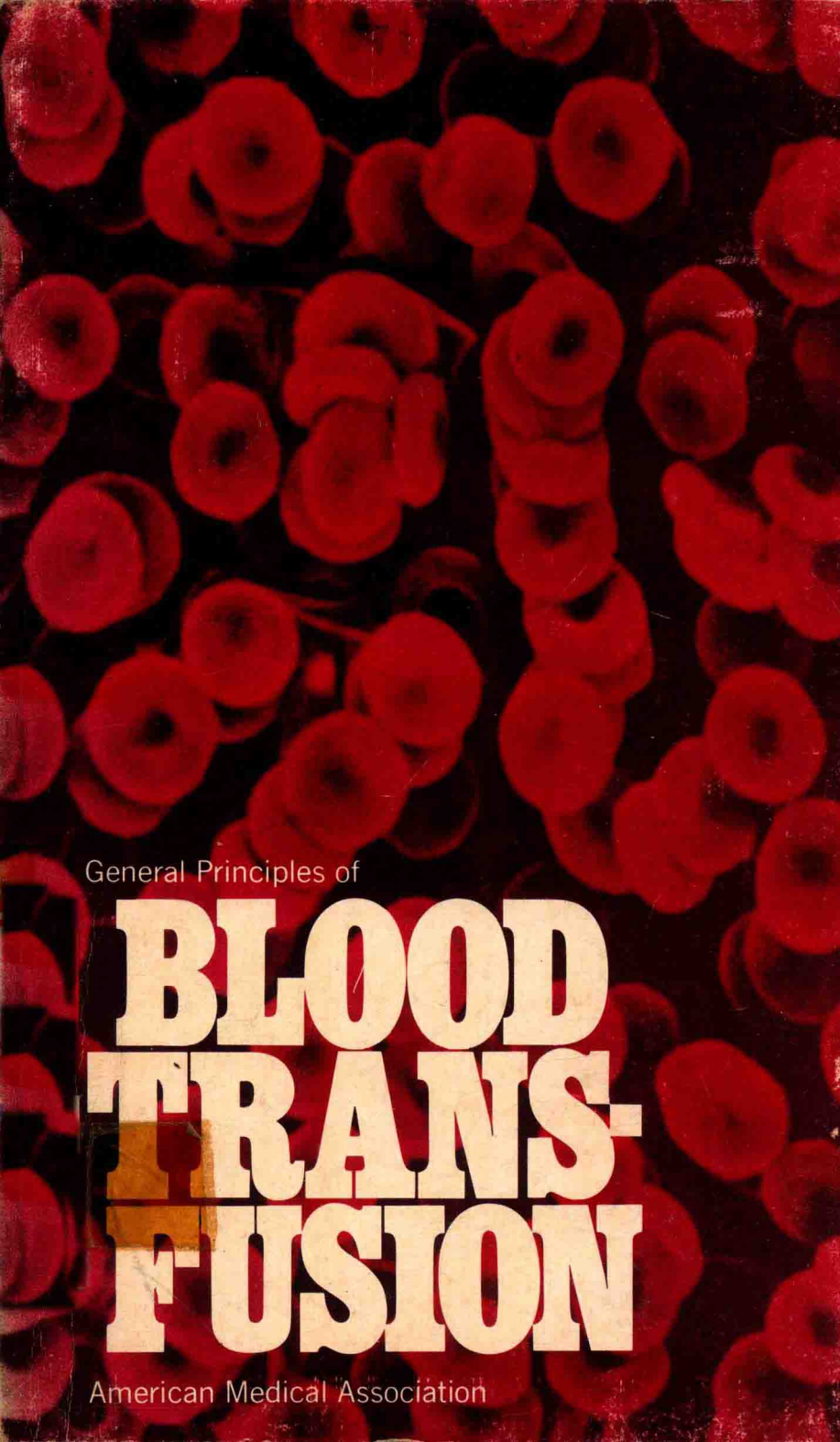
General Principles of
BLOOD TRANS-FUSION
American Medical Association

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BLOOD TRANS-FUSION

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Foreword

Blood, in one form or another, appears in the earliest pharmacopoeias. It was a favored remedy for lunacy and palsy and was freely prescribed for the rejuvenation of aging patrons. The direct transfusion of blood into the circulation had, however, to await the discovery that there was a circulation. As news of Harvey's work spread, it carried a wave of transfusion experiments in its wake. Some of the earliest of these, in which the blood of calves was infused into human subjects, was recorded in the Philosophical Proceedings of the Royal Society in 1667. Unhappily, the most notable proponent of the practice in France was persuaded to give a second transfusion to a patient three weeks after he had survived the first. The result, as the reader will surmise, was unfortunate; a law suit followed, and the issue of the affair was an edict prohibiting the practice.

Interest in the subject was revived briefly in the Nineteenth Century as it became generally recognized that human blood was the only proper blood for man. But the time was not yet ripe. It was, indeed, only at the turn of the century as a result of advances in sterile technics, in the control of the clotting process and, particularly, in the new knowledge of the factors that govern the compatibility of the blood of different persons, that the development of a rational technology for transfusion became possible. Even so, widespread recognition of the therapeutic power of the transfusion of blood has been delayed until the last few decades. Today, as we take note that some five million units of blood are administered to patients in this country in a single year, we should recall that it was not until 1937 that the first blood bank was established.

It is inevitable that new discoveries contributing to human welfare will not always be exploited with full understanding and good judgment. There will be examples of abuse which will arouse criticism that tends to bring some disrepute to the new practice. So it has been with the transfusion of blood which, as with any procedure that affects the integrity of the human body, is accompanied by some hazards. Year by year, however, the increasing power of medical science is progressively refining procedures toward maximizing the benefits and minimizing the risks. In this situation, the proper purpose of criticism of current inadequacies should be to emphasize the need for speeding up the incorporation into general medical practice of the fruits of contemporary experiment and experience.

For a number of years, the National Academy of Sciences-National Research Council has sustained a Subcommittee on Transfusion Prob-

lems to assist it in fulfilling its obligations to promote and interpret research in the interests of the National Blood Program. In 1961 the Subcommittee, recognizing the temporal gap between knowledge and practice, undertook responsibility for the compilation of a book that would bring to the practitioner a distillate of the best of informed opinion and experience in the field of transfusion.

Here is the outcome of this endeavor. It is the product of much consultation within a group of recognized authorities. It is authoritative and is offered as a guide and counsellor to the practicing physician —in no sense is it to be considered a definitive dictate. Hopefully, it will be helpful to him and will thereby contribute to the orderly and enlightened development of transfusion therapy by encouraging communication between medical science and medical practice.

R. Keith Cannan, Chairman
Division of Medical Sciences
National Academy of Sciences-
National Research Council
1963

Introduction

In 1961, the National Research Council's Division of Medical Sciences, after consulting with a number of authorities in the field, concluded that the general level of practice in the transfusion of blood and the use of blood products should be enhanced and that information was available from scientific research and from experience in large medical centers which, if compiled and widely distributed, would advance high standards in blood banking programs and transfusion services. Accordingly, *General Principles of Blood Transfusion* was published in 1963 as a concise, authoritative set of guidelines on the subject for the information of practicing physicians.

Funds for the support of the project and its preparation for publication were provided by the Office of the Surgeon General, Department of the Army, under Contract #DA-49-193-MD-2077 to an Editorial Board established by the Division of Medical Sciences, National Academy of Sciences- National Research Council.

The Division of Medical Sciences, recognizing a continuing need for authoritative, up-to-date guidelines on blood transfusion practice, invited the American Medical Association's Committee on Transfusion and Transplantation to undertake a revision of *General Principles of Blood Transfusion* and to effect a wide distribution of the revised edition about blood transfusion practice.

The purpose of this revised edition is to summarize the present status of clinical blood transfusion practice. It will be noted that the use of components is emphasized and the indiscriminate use of whole blood is discouraged. The patient should get what he needs and his circulation should not be burdened needlessly. Blood is a limited national resource, and each donation should be used to serve as many patients as possible.

It is not difficult to understand why so many of us have the whole blood habit when up to a decade ago whole blood and plasma were *all* that we would get from our blood banks. The advent of plastic containers with multiple satellite pouches has made it possible to split freshly donated units of blood into red cells, platelet concentrates, fresh frozen plasma and antihemophilic cryoprecipitate in a closed system without the hazard of bacterial contamination. Fortunately the densities of red cells, platelets, white cells and plasma differ sufficiently to make separation by centrifugation feasible.

Component transfusion therapy is better transfusion therapy.

Table of Contents

CHAPTER I

Responsibility of the Clinician in the Transfusion Service

The collection, processing and transfusion of blood and blood components are medical rather than administrative procedures. Therefore, the blood bank and transfusion service are the responsibility of a physician. In some instances the greatest technical knowledge and skill may be provided by a Ph.D. or other highly trained paramedical expert who may properly assume direct responsibility for the blood bank, provided the ultimate clinical judgment is that of a qualified physician.

The safest and best possible transfusion service is achieved when there is frequent consultation and communication between the physicians with clinical responsibility for the patient (intern, resident, attending physician) and the director of the transfusion service. The indications for the uses of the various blood components are relatively easy to master but in complex situations it may not be possible to make the wisest decision without taking full advantage of the special knowledge of *both* the clinician and the blood bank director. Consultation ordinarily should be initiated by the clinician.

In order to use blood and its components properly, the physician must know what is available and possible and must have knowledge about the properties of fresh and stored blood. He must also recognize that every transfusion of blood carries with it a *risk of hepatitis* and other disease entities in addition to the danger of incompatibility that may result in disaster for a particular patient. As with any drug with known side effects, the physician must weigh the potential danger against the expected benefit before ordering a blood transfusion. *A blood transfusion should never be ordered or given unless it is worth the risk.*

When a blood transfusion is considered essential, there is much that the physician can do to reduce the risk to the patient. One of the most valuable measures is the use of concentrated (packed) red cells rather than whole blood in almost all instances. The use of concentrated blood with an hematocrit of 60 to 80 percent reduces the incidence of circulatory overload[1] which is probably the most common cause of transfusion injury. Other advantages, incidental to the smaller volume of plasma given to the patient, are reduction of the amount

of sodium, potassium, citrate, and blood group antibodies infused and perhaps a decreased incidence of post-transfusion hepatitis.[2]

The following general measures are also recommended.

1. *Order blood or blood component* well in advance of planned transfusion and thus utilize the regular daytime technical staff rather than lesser skilled emergency or nighttime personnel. Allow time for the recognition of difficult antibody problems and the procurement of rare blood.
2. *Identify the presence of anemia* in advance of hospitalization for elective surgery and attempt to correct the anemia with appropriate hematinics before hospital admission. This simple precaution greatly reduces "unnecessary blood transfusion."
3. *Use as little blood as possible.* The incidence of hepatitis and other complications is increased in proportion to the number of units transfused. Although the incidence of "single unit" transfusion sometimes correlates with careless usage, there are times when it is more appropriate to transfuse one than two units.

The clinician's responsibility in relation to the transfusion service includes willingness to serve on the hospital transfusion committee, and active steps to encourage blood replacement by friends and relatives of the patient. Physicians should not expect unused blood to remain on reserve for a patient for more than 24 hours unless specific arrangements are made. Long periods on reserve result in blood wastage.

The clinician must have a willingness and ability to adapt to change and accept new information as it becomes available. This monograph is designed to provide a resume of knowledge and practice at the time of publication. The blood bank and/or transfusion service director should be the most available source of additional information and should be frequently consulted.

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CHAPTER II

Red Cell Concentrates and White Cells

The physician must be familiar with the concept of component therapy and the properties of fresh and stored blood in order to prescribe effectively for his patients. Only a minority of circumstances warrant the administration of whole blood.

The most important labile ingredients effectively obtained from fresh blood are the platelets and coagulation Factors V and VIII. Factor V deficiency is encountered as part of the multi-factor deficiency syndrome complicating severe hepatocellular disease and "consumption coagulopathy." Inherited Factor V deficiency (parahemophilia) is very rare. Fresh frozen plasma is the best way to raise Factor V levels. Factor VIII deficiency is most often found in classical hemophilia (hemophilia A) and, depending on the circumstances, is managed with fresh frozen plasma, cryoprecipitates or more potent Factor VIII concentrates. The needs of thrombocytopenic patients require the administration of platelet concentrates and not fresh whole blood. Red cell concentrates are used to supplement specific corrective measures for anemia as indicated.

Blood collected in either acid-citrate-dextrose solution or citrate-phosphate-dextrose solutions presently has a dating period of 21 days if stored continuously at 1 to 6°C within a 2°C range. During storage, lactic acid, potassium, inorganic phosphate and ammonia accumulate in the plasma (See Chapter V). These metabolic byproducts and the citrate ions may be deleterious when massive transfusions are given in the presence of hepatic, renal or cardiac disease. All of these potentially harmful properties developing during the storage of blood can be eliminated by simply removing most of the plasma. The residual packed red cells which are an enriched suspension of the donor's cells in the donor's plasma, more safely supplement the recipient's deficient oxygen-carrying capacity than does whole blood. The use of whole blood is "shotgun" therapy, wasting valuable components and endangering the patient with the unnecessary burdens of volume, acidosis, electrolytes, and antibodies.

Red Cell Concentrates (Packed Red Blood Cells)

Red cell concentrates are prepared to have a hematocrit value of 60 to 80%. The use of multiple plastic blood collection units has made

it possible to prepare red cell concentrates or enriched red cells as a routine inventory item. The shelf-life, requirements for crossmatching, and mode of administration are the same as for whole blood.

Whenever transfusion is indicated, the enriched red cell unit should be the first to be considered.[1] Most patients with anemia do not require transfusion. In iron, B12, and folic acid deficiency syndromes, specific therapy is the treatment of choice. If, however, there are acute signs and symptoms related to deficiency of oxygen carrying capacity, transfusion may be necessary. The rate of development of anemia and the level of the patient's activity will enter into the decision for transfusion. Chronic or slowly developing anemia is usually well tolerated. The sedentary patient does not require the same hemoglobin mass as a manual laborer. Transfusion therapy should not be ordered routinely. Each case must be evaluated individually by the physician. Arbitrary definitions such as "if the hemoglobin is less than 8.0 grams" or "the pulse rate is greater than 110" must not be used. The risks of transfusion are great enough to warrant delay of elective surgery until an iron deficient patient's hemoglobin level can be raised by specific therapy. If the decision is made to transfuse, then the enriched red cell unit should be the first choice. Even red cell concentrates may have to be given in small doses by slow drip, especially to patients with severe megaloblastic anemia, to avoid circulatory disaster.

General indications:

1. Anemia not responding to specific therapy.
2. Preoperative anemia not correctible by specific hematinics within the time available.
3. Patients with renal, hepatic or circulatory impairment and the elderly or debilitated.

Recent studies on the treatment of shock with buffered saline and red cell concentrates derived from frozen blood gave satisfactory results in severe battle casualties.[2] The use of red cell concentrates in pediatric transfusions is usually preferable. In the very young, volume overload is frequently overlooked.

Frozen-Thawed Red Cells

Frozen-thawed red cells are being prepared in a number of blood centers. Two techniques are being used; low glycerol, fast freezing (liquid nitrogen $-196^{\circ}C$); high glycerol, slow freezing ($-85^{\circ}C$).[3,4,5,6] Both techniques require the cryoprotective agent, glycerol, to be washed out of the thawed red blood cells. The washing process can be accomplished in a number of ways but improvements are needed and

are being sought for this portion of the technique. Red cells preserved by freezing can be stored for years and will become increasingly important clinically.

Frozen red cells of rare types can provide either autologous or homologus transfusion for patients whose surgery is scheduled months in advance. The process produces red cells of good quality which are free of irregular antibodies, white cells, plasma proteins, extracellular potassium and perhaps even hepatitis virus. This type of transfusion preparation is useful for patients who are scheduled for organ transplantation because the histocompatibility antigens are largely removed with the white cells. The chance of immunization to white cells or plasma proteins is minimized and patients already so immunized will not have adverse reactions to these antigens. Erythroblastosis requiring rare blood for transfusion therapy can be treated with the mother's red cells frozen in advance.

White Cell Poor Blood

The multitransfused patient frequently develops leuko-agglutinins which in subsequent transfusions may cause febrile reactions. Frozen red cells are ideal for these patients (see page 51). Continuous flow centrifugation is more efficient than repeated batch washing to remove the leukocytes and reduce the frequency of these reactions. In the absence of these methods, a nylon filter is effective in removing neutrophils from fresh heparinized blood.[7]

White Cell Transfusions

Occasional patients with life-threatening agranulocytosis may benefit from the transfusion of white cell concentrates prepared from 20 to 30 or more units of fresh blood. These concentrates, prepared from fresh whole blood or by leukopheresis, are not yet routinely available at many centers. Patients with chronic myelocytic leukemia, with white cell counts above 100,000/cu mm, have been used as leukocyte donors.[8] Possible hazards of transplantation and subsequent graft vs. host or host vs. graft reactions must be considered in such transfusions.

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CHAPTER III

Plasmapheresis

Plasmapheresis is the collection of blood from a donor, separation of the plasma and reinfusion of the red cells.[1]

An early use of plasmapheresis was to take advantage of unusual antibody levels for the preparation of blood typing sera. This was soon extended to donors who were artificially immunized to produce high levels of specific antibodies, e.g., antitetanus, antipertussis. Repeated plasmapheresis permitted preparation of potent immune globulins from these donors. Plasmapheresis has also been applied therapeutically to reduce abnormal levels of globulins (usually macroglobulins) in the management of hyperviscosity syndromes.

Plasmapheresis is being used to obtain large quantities of plasma for routine preparation of immune globulin, albumin, fibrinogen, fresh frozen plasma, and cryoprecipitate.

Plateletpheresis has been used primarily for preparation of the quantities of platelets needed to control thrombocytopenia. Leukopheresis for the preparation of leukocytes for transfusion is still in the experimental stage.

Though these procedures do not constitute blood banking in the traditional sense, knowledge of the management of plasmapheresis and the safeguards for participating blood donors is essential to the operation of many blood procurement centers today.[2]

The usual requirements for blood donors apply as well in the selection of donors for plasmapheresis but the plasma protein level and plasma protein distribution should also be monitored in donors subjected to repeated plasmapheresis. The informed consent of the donor should be obtained and he should be advised of the potential hazard resulting from inadvertent administration of any red cells other than his own.

Since a number of donors may be plasmapheresed at one time, *it is particularly important that the red cells be identified in a manner that will assure positively that the donor receives only his own red blood cells.* All personnel should be specially trained in those functions of the plasmapheresis program which they perform. A manual of standard operating procedures and methods must be available and a qualified physician must supervise.

If the donor is to participate in an extended program, it is important that red cell loss be kept at a minimum. Blood samples for laboratory tests should not exceed 30 ml of blood in a seven-day period. No more than 1000 ml of native plasma should be withdrawn from a donor within a seven-day period or more than 500 ml in a 48-hour period. A donor should be removed from a plasmapheresis program when there is a significant change in status from the initial examination. Restoration to the plasmapheresis program or intermittent donation of whole blood while in a plasmapheresis program is the decision of the physician in charge.

The real danger of a regular plasmapheresis donor being a carrier of hepatitis must be remembered.

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