NATIONAL RESEARCH COUNCIL

DIVISION OF MEDICAL SCIENCES

THE BLOOD PLASMA PROGRAM

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INTRODUCTION

The modern history of blood transfusion began with the twentieth century. Light began to break upon a basic difficulty with the discovery in the middle of the century past of substances in blood that caused incompatibility between bloods of different species of animals. These were found to be sharply specific and on account of the effects produced were called hemolysins. Despite these findings blood from animals continued to be transfused into human subjects and untoward effects charged to disease of the patient. Technical difficulties, particularly those due to blood coagulation, combined to keep transfusion from general use.

About 1880 the advantages of physiological salt solution won recognition, bringing about the practical abandonment of blood transfusion. Toward the end of the century, however, the application of asepsis to surgery and discovery of means to prevent coagulation spurred anew hopes for successful blood transfusion. The high claims that had been made for physiological salt solution as a blood substitute were recognized as fallacious.

The epochal announcement in 1901 by Landsteiner[1] of the discovery of the isoagglutinins of the human blood and the consequent recognition of blood grouping, brought a safety to the operation of blood transfusion that had never before been present.

The first decade of the present century was a period of intensive research the world over on methods of direct blood transfusion. Notable

in this country was the work of Carrell and Crile. The result was the perfection of methods that required skill beyond that of the ordinary practitioner of surgery. Surgical ingenuity was then directed toward methods of semidirect transfusion that would have wider use. The earlier discovery of the use of paraffine on glassware and rubber tubing was a great help in this connection.

The next great advance was the employment of sodium citrate and glucose in 1914 and of sodium citrate alone in 1915 to prevent the coagulation of drawn blood. By these advances in knowledge and technique, indirect transfusion was made simple, safe and practical. The use of citrated blood was standard practice in the first World War.

BLOOD GROUPING

Beyond the discovery of the incompatibility of bloods of different animal species, the biochemistry of human blood applicable to the problems of blood transfusion had made little progress to the close of the past century. There was still no explanation for the serious or fatal reactions following transfusion of human blood, that had caused the practical abandonment of the procedure. In 1900, however, Landsteiner[1] announced the discovery that the serum of one normal human being can agglutinate or hemolyse the bloods of certain other individuals. In the following year[2] he extended his observations and upon the basis of his findings of substances in the red blood cells which he called <u>agglutinogens</u> and of substances in the serum which he called <u>agglutinins</u> which together reacted to cause agglutination of the red blood cells, he made a classification of bloods into three groups, which was soon there-

after increased to four. As the interaction of the substances involved took place in bloods all from human subjects these substances were called isoagglutins and isoagglutinogens.

On the basis of the agglutinogen content of the red blood cells the groups were named O, A, B and AB, a grouping accepted by the Health Committee of the League of Nations as the International Nomenclature.

The existence of the four blood groups depends upon the presence or absence in the red blood corpuscles of the isoagglutinogens A and B and in the serum of the isoagglutinins alpha and beta (or anti-A and anti-B).

Table I shows the classification and composition of the Landsteiner blood groups.

TABLE I

International Nomenclature	Red Cells (Isoagglutinogens)	Serum (Isoagglutinins)
O	--	Alpha and beta
A	A	Beta
B	B	Alpha
AB	AB	-- --

The practical method of determining an individual's blood group is by testing a suspension of his red cells with sera known to belong to groups A and B. If the red cells are agglutinated by neither serum, the specimen is of the O group. If agglutination takes place with the A serum, the specimen is of the B group; while if agglutination takes place with the B serum, the specimen is of the A group. If agglutination

takes place with both sera, the specimen is of the AB group. This is shown in Table II.

TABLE II

Cell suspension of group	A serum (Agglutinin beta)	B serum (Agglutinin alpha)
O	—	—
A	—	+
B	+	—
AB	+	+

+ signifies agglutination
— signifies absence of agglutination

The incompatibility between the blood groups, occurring in blood transfusion are brought about by the action of the agglutinins of the serum of the recipient upon the agglutinogens of the donor's red cells. Theoretically upon this basis, individuals of the O group, with red blood cells containing no agglutinogen, can be regarded as "universal donors." Similarly individuals of the group AB, with blood serum devoid of agglutinins, can be regarded as "universal recipients." Practical objections to unqualified acceptance of these rules are discussed later.

Landsteiner, in the second paper quoted,[2] records his realization of the practical significance in blood transfusion of blood grouping. In 1907, Hektoen[3] repeated and emphasized the suggestion that the blood groups be made the basis for the selection of donors in blood transfusion. Practical application of this knowledge of blood grouping was

reported by Schultz[4] in Germany in 1901 and by Ottenberg[5] in this country in 1911. These early observations and the experience of the first World War led to universal acceptance of this basis for the selection of blood donors.

With blood grouping thus well established and the procedures involved in blood transfusion standardized, there still occurred instances of blood incompatibility, more or less, apparently within the groups. The more serious of the reactions were usually found to have been caused by mistakes somewhere in the chain of procedure and the incompatibility really an inter-group occurrence.

There still remained cases in which the incompatibility lay certainly within the group lines. The biochemistry of the blood was under constant study and a subdivision of groups A and AB was suggested by von Dungern and Hirszfeld[6] as early as 1911.

The basis for these subdivisions was the discovery that the agglutinogen A was not a single substance, but exhibited two differing properties in relation to serum agglutinins, bringing the subclassification into agglutinogens, A and A2, by Landsteiner and Levine[7] in 1930.

There are thus two varieties of A blood, depending upon whether the A agglutinogen is A or A2, and two kinds of AB blood, depending upon the class of the A agglutinogen content. It thus follows that bloods of group A are subdivided into subgroups A. and A2, and of group AB into subgroups A.P and A2B.

In more recent research into blood physiology Landsteiner and Levine[8] identified tw additional agglutinogens M and N, found singly

or in combination in bloods of all of the four groups and unrelated to agglutinogens A and B. Still more recently they reported[9] the discovery of agglutinogen P. In 1940 Landsteiner and Wiener[10] added an agglutinogen, designated the Rh factor, which is present in approximately 85 per cent of human subjects irrespective of their group.

By means of the agglutinogens noted above, scores of distinct types of blood can be identified within the original four groups. This research is continuing apace bringing an ever growing realization of the individuality of human blood.

It should be understood that in blood incompatibility hemolysins are correspondingly specific with agglutinins. Especially in dealing with fresh serum a hemolytic raction should be rated the equivalent of that of agglutination to any extent that it may replace it.

BLOOD DONORS

There are two types of blood incompatibility in blood transfusion, (1) in which the recipient's serum agglutinates or hemolyzes the donor's red cells, and (2) in which the donor's serum agglutinates the recipient's cells, while the recipient's serum does not agglutinate the donor's cells. The former reaction can well produce serious results, while the second is usually harmless. The practical importance of the second type of incompatibility appears in the use of O blood as a universal donor. Blood of this type with a high titer of agglutinins may cause an agglutination of the recipient's red cells. However, both the Army and the Navy have demonstrated that the use of known group O blood may be resorted to without the development of reactions

of sufficient severity to argue against the practice. This procedure has the approval of the National Research Council, provided cross-matching is done prior to transfusion.

The popularization of blood transfusion brought about the establishment by hospitals and surgical groups of "donor registers" of individuals who, for a consideration, were willing to give a measure of their blood for transfusion. These prospective donors were examined as to their general health, in regard to certain communicable diseases and to the quality of their blood. Their eligibility being thus established, their blood was tested for type and their names placed on the appropriate group register.

The recipient's blood must be typed so that a donor from the proper register can be obtained. As an added precaution the two bloods must be "cross-matched," that is, a cell suspension of the donor must be tested with the serum of the recipient, and vice versa. This is an additional check upon the typing and also the presence or absence of irregular isoagglutinins. These irregular isoagglutinins are the causes of the occasional instances of intragroup incompatibility. Practically, patients who have had no previous transfusion are scarcely affected by the irregular isoagglutinins. Repeated transfusions, however, may bring about a condition of isoimmunization in the serum and reactions result. These reactions are manifested in vitro by slight degrees of agglutination of the red cells and by chills and fever in the patient.

The factor Rh is reported to be the most commonly observed cause of intragroup incompatibility[11] though occasional instances with the other recognized irregular isoagglutinins are encountered.

Isoimmunization of Rh negative persons (the 15 per cent with no Rh factor in their blood cells) to Rh positive blood may be induced by multiple transfusions, or by pregnancy when an Rh negative woman bears an Rh positive fetus from an Rh positive father. Reactions to the transfusion of Rh positive blood in persons thus sensitized are apt to be severe, even fatal, especially in women sensitized by pregnancy; for successful transfusion, an Rh negative donor of compatible blood group must be selected. Rh negative women after isoimmunization, induced by either transfusion or pregnancy, tend to form anti-Rh agglutinins increasingly during the gestation of an Rh positive fetus, and these agglutinins cause in the infant a profound hemolytic anemia, known as erythroblastosis fetalis. In the treatment of infants so affected, Rh negative blood should be selected for transfusion because antibodies absorbed from the mother persist for a time in the infant, continuing to destroy Rh positive red cells.

It should be routine practice when cross matching shows the donor's cells to be agglutinated to any extent whatever by the patient's plasma, that other donors be tried until one with wholly compatible blood is found.

The donor must be reexamined before the transfusion, for acute disease. Chronic infections such as syphilis and malaria will already have been eliminated.

It has been made the practice in the Army and the Navy to type the blood of recruits and to stamp the type symbol on the individual's identification disc. This information is useful in the selection of donors when whole blood transfusion becomes necessary.

STORED BLOOD

In the basic studies upon the preservation of whole blood reported by Rous and Turner[12] in 1916, there occurred the suggestion that stored blood might be used for blood transfusion. These studies disclosed that definite proportions of sodium citrate and dextrose added to whole blood preserved the functional role of the red cells for about four weeks. Subsequent studies have modified the procedure of these workers only in the proportions of the agents employed.

The response to the publication of a method of whole blood preservation was the more immediate on account of its great need incident to the existing state of war. In the British service the field employment of the indirect method of transfusion with citrated blood had made little headway and there was a sentiment that the inconveniences of determining blood types, including the loss of time, outweighted the dangers of blood incompatibilities.[13] A stimulation was given to the use of transfusion when in June 1918 Robertson[14] reported that, following the technique of Rous and Turner, he had performed transfusion with stored blood upon twenty patients at a British casualty clearing station in the previous year. He employed blood of group O only, as universal donors and encountered no serious effects.

In March 1918, a committee representing the laboratory and surgical services of the United States Army adopted transfusion with citrated blood as the method for combatting shock and hemorrhage in the hospitals of the American Expeditionary Forces.[15] The reasons for the choice were simplicity of equipment and technique, convenience to donor and recipient, and the excellent results obtained.

The method thus adopted was in general use to the end of the war. There developed serious objections, mainly those relating to the time consumed in obtaining suitable donors and of obtaining the requisite amounts of blood. It was evident that the method was not well adapted for the emergency treatment of numbers of patients. For the time being, the use of stored blood seemed the method of choice.

During the period of peace that ensued between the two World Wars, the indirect transfusion of citrated blood answered the purposes of the military services satisfactorily and there was little or no necessity for the use of stored blood in their hospitals. In large civil hospitals, however, where blood donors were not so conveniently at hand for emergencies, blood banks were widely employed. Fantus[16] has described in detail the establishment and operation of the blood bank of the Cook County Hospital, one of the first in the country. Soutter[17] relates the history of the blood bank of the Massachusetts General Hospital and describes the practical system now in use. De Gowin[18] has recently summarized the accepted practices in the storage, transportation and administration of whole blood. He finds the Rous-Turner blood-dextrose-citrate mixture as modified by himself and his associates satisfactory to inhibit hemolysis during refrigeration to permit 30 days of storge. For use to supply plasma proteins and functioning erythrocytes by transfusion, the 30 day limit is found satisfactory with a low incident of reactions. Transportation of this blood mixture by automobile upwards of 700 miles and by airplane of 3500 miles has been found possible. Length of distance of transportation is limited only by the ability to keep the blood

containers refrigerated with cracked ice. He found that it was unnecessary to warm the refrigerated blood before using it for transfusion.

PROBLEM CONFRONTING THE SERVICES

The realization that the methods of blood transfusion in practice in World War I were quite inadequate and that methods based upon the employment of stored whole blood had insuperable difficulties of application upon a mass scale posed an urgent problem to the Government medical services with the outbreak of war in Europe in 1939. In the following year when our Allied friends were suffering reverses and our own entrance into the conflict could be visualized, the problem became increasingly acute.

The search for suitable blood substitutes that must be undertaken was not, however, to be made in an entirely untilled field. It was already clear that blood serum and plasma were the basic materials from which the acceptable blood substitute was to come. In January 1918, following their brilliant work on the preservation of whole blood, Rous and Wilson[19] reported the successful treatment of experimentally induced hemorrhage in animals by the injection of plasma. Accepting the basic conception that the replacement of red blood cells was not necessary even in severe hemorrhage, they demonstrated that the restoration of blood volume with plasma was the essential factor in bringing about a return of normal blood pressure.

The earliest recorded suggestion of the use of plasma for human transfusion came in a letter dated March 3, 1918, from Captain Gordon R. Ward, R.A.M.C., to the editor of the British Medical Journal.[20]

The letter shows such clear understanding of the value of plasma transfusion that it is well to quote the more pertinent phrases:

"Apparently one of the chief troubles is the question whether or not recipient's plasma will haemolyze the corpuscles of the donor. Surely this difficulty might be avoided by not transfusing the corpuscles at all, but only citrated plasma, which would be easy to keep and easy to give. There is abundant clinical and experimental evidence that it is not the corpuscles that are wanted, but the ideal fluid for keeping blood pressure at the proper level*******. A man dying from haemorrhage is not dying from lack of haemoglobin****, but from draining away of fluid, resulting in devitalization and low blood pressure."

The letter ended with a recommendation that a trial of this plasma method be made, controlled by an equal number of transfusions with whole blood and an equal number with a gum acacia solution. There is no record of any such trial or of particular interest in the suggested method for nearly a score of years.

Following studies upon surgical shock produced experimentally in dogs, Mann[21] reported that parenteral injections of homologous serum gave results in treatment fully as good as any other available method, if not better. He thought that homologous serum might be found a valuable agent in the treatment of shock under conditions where it was available and whole blood was not. In 1918, Hartman[52] reported good results in the treatment of 22 cases of influenza with human plasma.

Studies with far-reaching potentialities were begun in 1927 by Strumia and his associates.[22] They began the employment of human serum intravenously in the treatment of severe infections. Later plasma

was substituted for the serum on account of the greater simplicity of its separation and because the yield from a similar quantity of blood was greater. Up to this time there was no certain recognition of practical differences between the effects of serum and plasma. It was shown, however, by these studies that, while severe reactions could result from the intravenous injection of homologous serum, no reactions resulted from the injection of even heterogeneous plasma. Serum, it should be understood, is the supernatant fluid that separates upon the clotting of the blood. Plasma on the other hand is the fluid that is obtained when an anticoagulant is added and the blood centrifuged.

Experimental studies on serum and plasma continued and occasional reports of their therapeutic use began to appear. Elliott[23] in 1936, in reporting an improved method of indirect transfusion, suggested that typing and cross-matching were unnecessary if serum or plasma was used in the treatment of surgical, obstetrical or traumatic shock. He considered the essential in these conditions to be the maintenance of the serum proteins at a safe level and further, the red cells being of little or no importance in treatment of the conditions named, there was no advantage in transfusing them. Fantus[16] in 1937 advocated the utilization of the blood hemolyzed in storage by the recovery of the serum. This he suggested would be valuable for transfusion in cases of shock with little or no hemorrhage. He further stated that in extensive burns in which shock and loss of blood serum were the causes of the circulatory depression, intravenous injection of blood serum was a more rational procedure than that of whole blood. Notable work in corroborating the therapeutic value of serum and plasma and of

extending their proven usefulness was done during the following two years by Mahoney,[24] Elkinton,[25] and McClure,[26] working separately.

In 1939, Tatum, Elliott and Nesset[27] recommended plasma as "an ideal substitute for whole blood in the emergency treatment of shock and hemorrhage from war wounds" and outlined a technique for its collection and elaboration. By the use of the "sealed vacuum transfusion set," the blood was collected, centrifuged, and the plasma separated by a closed system that prevented contamination. In this paper the statement that "Plasma can be used without typing or cross-agglutinating" was reported to be supported by the experience of 191 such transfusions without reaction.

STUDIES ON PLASMA

By the time that war burst upon Europe in 1939, it was quite well established that in blood serum and plasma lay the best prospects for the agent to be used in the mass blood transfusions that could be foreseen.

By this time it was recognized that there was practically no difference in the therapeutic value of plasma and serum. They differed in biochemical content in the fact that fibrinogen was removed from the serum in the process of clotting. There were reported cases of reactions from the transfusion of serum, which were lacking from plasma. Neither was a complete substitute for blood in certain conditions. An advantage of plasma over serum was that its yield from a given quantity of blood exceeded by approximately 15 per cent that of serum.

The special problem then lay in determining the best form in which plasma could be put down at any place where its use was indicated. Experience had already shown that liquid plasma could be kept for months and still be safe and efficient and that frozen plasma would keep for indefinite periods. Dried serum and plasma had been known in experimental work since the beginning of the century. In 1909, Shackell[28] described a process for the desiccation of biological substances in the frozen state which has been much followed since that time. With the increasing interest in plasma for transfusion much study has been put upon improving methods of drying. Mudd and Flosdorf developed the "Cryochem" process in 1938[49] and the"Desivac" process in 1940.[50] In 1940, Hill and Pfeiffer described their Atovac process[51] for drying plasma. Other procedures evolved are those of Hartman,[29] Thalhimer,[30] Edwards, Kay and Davie,[31] and Harper, Essex and Osterberg.[32] These studies upon small quantities of material laid the foundation for the mass methods that were to be employed.

At about the same time in March 1940, the Army and the Navy selected each a representative of its medical service to concentrate upon the study of blood substitutes for military use. These officers working respectively at the Army Medical Center and The National Navy Medical Center soon developed a close cooperation in their work. Early studies were centered upon the problem of obtaining blood and upon perfecting a form in which the plasma or serum content could best serve the needs of the services. The definite advantages of plasma over serum, noted above, centered the study upon this agent. Employing the "closed system" of collecting plasma as advocated by Elliott, these

co-workers began the collection of liquid plasma for therapeutic use in September 1940. Within a few months they had demonstrated the practicability of furnishing liquid plasma to any part of the country. They instituted the Army - Navy Blood Donor Center in August 1940 and during the following year secured blood from 1510 donors.

With the obvious advantages of dried plasma in mind, and the methods and equipment devised by Shackell and his followers as landmarks, they devised a set of equipment based upon that used in the commercial drying of milk. In the furtherance of their work they made personal visits of investigation to a dozen or more hospitals and commercial laboratories to inspect the methods and equipment used in the preparation of blood substitutes.

Published accounts[33,34] of these early studies on plasma for the military services show the vision and practical talents of these officers. Kendrick[35] in October 1940 proposed the Army use of plasma transfusions in field service as far forward as the battalion aid station.

One of the achievements of these service officers, Kendrick and Newhouser, with Veldee of the Public Health Service, was the development of the transfusion set with its container that is in use in the military services.

ROLE OF NATIONAL RESEARCH COUNCIL

The spring of 1940 with its reverses to Allied arms in Europe brought a sense of national danger to this country. In May of that year the President proclaimed a stste of national emergency. With a

realization of the extreme gravity of the situation, the Surgeons General of the Army and Navy called upon the National Research Council for its help in the many medical problems that were presenting themselves in the prospect of the rapid expansion of the armed service that was inevitably to take place. In compliance with this request Dr. Lewis H. Weed, Chairman of the Division of Medical Sciences, appointed a number of committees to serve during the emergency in an advisory capacity. To a Subcommittee on Blood Substitutes was assigned the task of advising the military service upon a number of unresolved problems in this important field. On the list of this Subcommittee were names that have been associated in the literature with American blood substitute studies, including representatives of the Army, Navy and Public Health Service. The first meeting of the subcommittee was held early in May 1940 though its membership had not yet been fully made up. Periodic meetings have been held since that time. The studies of the subcommittee and its decisions are reported in a mimeographed Bulletin on Blood Substitutes and in special reports. At the time the subcommittee was assembled, the relative merits of serum and plasma were undergoing study and the choice between them awaiting decision. A tentative approval of the use of plasma, liquid or dried, was made early to the military services and later a definite recommendation of dried plasma was made for use by the military medical services.

Certain differences between plasma and serum are evident. When blood is allowed to clot fibrinogen and prothrombin are completely lost. These are retained, in part at least, in the preparation of

dried plasma. While these proteins do not contribute to the treatment of shock, they may serve a useful purpose in certain other conditions. Furthermore, freshly prepared serum may, at times, prove toxic although this toxicity disappears on standing for two or three days. These considerations and the fact that the "reaction" rate in studies carried out by the National Research Council with the administration of plasma was slightly lower than that found when serum was employed, were factors that favored the recommendation of dried plasma. In addition, it was found that the facilities that were in operation and those being prepared were for the production of dried plasma, and it was realized that the utilization of these facilities would expedite the production of the much needed blood substitute for the armed forces.

An early concern that the Subcommittee shared with the supply officers of the government services was the ability of existing pharmaceutical laboratories to obtain equipment and to perfect procedures for the processing of blood to dried plasma. This entailed much correspondence and much personal inspection. The first contract for 15,000 units was given to a firm already equipped for limited production. Other firms interested in participating in the program called upon the Subcommittees and upon the Army and Navy for help to obtain materials for centrifuges and drying machinery. The Subcommittee became the agency for determining when a pharmaceutical plant was considered equipped to process blood and for making recommendations of such firms to the Army and Navy. A certain number of laboratories received such recommendation. Later a general recommendation was made that plasma might be contracted for with any

firm whose methods were found acceptable to the United States Public Health standards.

In the early stage of the blood substitute program, with highly favorable reports coming in on the use of albumin, there was a feeling by all concerned that this might be found ultimately the agent of choice and that the pharmaceutical industry should not be committed too unreservedly to the production of plasma. During this time a considerable quota of blood was diverted to the production of albumin.

In the performance of the first contract for dried plasma the processing laboratory developed a dispensing set and package which, upon trial, proved to be unsatisfactory. The government service members of the Subcommittee, Kendrick, Newhouser and Veldee, had been making a study of a dispensing equipment with its containers and they were appointed a technical subcommittee on this project. They took into consideration plans developed by Strumia and submitted their report to the Subcommittee on May 23, 1941, with a demonstration of the proposed dispensing set. The complete package that had been evolved was approved and was recommended for adoption by the government medical services.

Previous to this an important item for settlement was the size of the unit of plasma and its container. Through force of circumstances, the unit of normal human serum had been fixed at 250 cc. One pint of blood normally yields about 250 cc. of plasma and, as a pint is the unit of blood transfusion, it was but natural that the plasma yield of a pint of blood should be fixed as the plasma unit. In approving the general specifications, the Subcommittee approved the 250 cc. unit of

plasma and the 400 cc. bottle in which it should be dried.

Specifications for dried plasma drawn up by Dr. Veldee of the Public Health Service and approved by the Subcommittee were sent to the Surgeon General of the Army on May 7, 1941. They are as follow:

(a) Moisture content less than one per cent.

(b) Hemoglobin content not over 25 mgs. per 100 cc.

(c) Sterility standards as found acceptable to the National Institute of Health.

(d) The product to be soluble within 10 minutes when made to the original volume.

(e) The redissolved material should have no more turbidity than the product from which it is made.

(f) The final dispensing unit, probably a flame sealed container, awaiting decision.

In the early operation of bleeding centers, there was no uniformity in the number of bleedings that were pooled for processing. Pools of considerable size were occasionally found to be contaminated and thus unusable. The point being raised by the American Red Cross, the Subcommittee voted in May 1941 that the pools be made up of not less than eight nor more than twelve individual bleedings. Later, following recommendations of processing firms, pools of 25 bleedings were authorized and were generally employed. However, pools of 50 bleedings, with individual sterility tests have been used.

At a meeting in March 1941, the attention of the American Red Cross was directed to the urgent need of a full-time field director of the blood procurement program and a recommendation was made for the appointment of such an officer who should be responsible to the Subcommittee on Blood Substitutes for the operation of the program.

Dr. G. Canby Robinson was selected for director of the program and Dr. Earl S. Taylor as technical director.

In February 1943, the Subcommittee issued a brief summary of its activities over the previous two years, as follows:

(1) Study of the relative merits of various types of preparations of human plasma and serum and final recommendation of dried plasma to the armed forces.

(2) Development of packaging and dispensing equipment for dried plasma which was recommended to and adopted by the armed forces.

(3) Recommendation of 0.1 per cent citric acid as a diluent for dried plasma has recently been made to the armed forces.

(4) Improvements in the methods of drying of plasma, the study of effects of these methods upon the product obtained and the development of equipment for drying plasma adapted for use by hospitals as well as by large manufacturing firms have been sponsored by the committee.

(5) Recommendation to the Red Cross of professional personnel to be responsible for the control of blood procurement centers.

(6) Recommendation of technique to be employed in procurement of blood and the standardization of equipment which is now being used throughout the country by the Red Cross.

(7) The preparation of a concentrated solution of human albumin which is stable over a wide range of conditions, which consumes little space in packaged form and which can be given with great facility and without diluent. This was prepared to meet certain specific requirements of the armed forces, particularly the Navy. This product has

been recommended to the armed forces and is now being prepared in considerable amounts for their use.

(8) The possible use of globulin by-products of human albumin production for the control of measles, mumps and other diseases is being studied and offers hope of widespread practical application in the armed forces.

(9) The use of human fibrinogen and thrombin, also by-products of albumin production, is being studied in relation to the local treatment of burns.

(10) Recommendations concerning the grouping of blood have been made to the Red Cross and the armed forces.

(11) Recommendations have been made to the Surgeons General for the establishment of a "section on shock and transfusion."

(12) The study of possible blood substitutes of other than human origin is in progress. These studies include bovine albumin, gelatin, pectin, aldebionic acid, glutamyl polypeptide, etc.

(13) The committee is holding conferences to consider progress made in these studies and offers facilities for the extension of such studies to various groups of workers.

(14) Preparation of Manuals on Blood Transfusion and Blood Plasma for the office of Civilian Defense.

This condensed report gives something of an idea of the extended scope of the studies that this Subcommittee has set for its members. The list of topics covered shows that, in addition to its well-recognized problems in bio-chemistry, there have been also those involving inventive ingenuity, administration and supervision that have

been no less exacting.

From its inception the Subcommittee has been the clearing house for all studies of blood substitutes being made in the country. The decision having been definitely made that dried plasma and human serum albumin were the present agents of choice and the facilities of the country geared to their production, investigation is turned upon the other numerous agents that have been proposed. In this connection special mention is due the work of Dr. Edwin J. Cohn of Harvard Medical School and his coworkers in the fractionation of the plasma proteins of the blood. Beginning with the production of a stable liquid serum albumin, they have isolated fibrinogen, fibrin foam, thrombin, isohemagglutin globulin and measles immune globulin. These by-products are used as hemostatic agents in brain surgery, as grouping serum in blood transfusion and in the immunization and treatment of measles.

Working in close cooperation with the Subcommittee in the practical problems of blood processing and plasma packaging and distribution were Brigadier General Charles C. Hillman and Rear Admiral Charles S. Stephenson, who represented respectively the medical services of the Army and the Navy.

RED CROSS DONOR PROGRAM

The beginning of the vast enterprise that the Red Cross Donor Program has become was the inauguration in New York in August 1940 of the Blood for Britain project. Its purpose was to send whole blood to England for treatment of victims of German bombing raids. By January 1941, about 17,000 pints of blood had been sent abroad, at which time the English gave notice that they could thereafter supply their own needs.

Soon after the New York bleeding center was opened, similar work was begun at the Army Medical Center and at the Naval Medical Center in Washington. These two were shortly consolidated at the Navy Center. There liquid plasma was being prepared for the use of the military services and experimentation carried out on the production of dried plasma.

In February 1941, the Surgeons General of the Army and Navy requested the American Red Cross and the National Research Council to undertake jointly the procurement from voluntary donors of a supply of blood for processing for use by the armed services. An urgent request was made to the Red Cross for 15,000 units of blood for early processing.

The agreement which set forth the responsibilities assumed by each of the agencies was signed by the Chairman of the American Red Cross, the Honorable Norman H. Davis, and by the Chairman of the Division of Medical Sciences of the National Research Council, Dr. Lewis H. Weed.

Upon accepting this responsibility, the Red Cross took over control of the donor center operating in New York, which thus became the nucleus around which were assembled the dozens of blood donor centers of today. In May 1941, the military demand had been raised to 224,000 units to be delivered by July 1, 1942.

There was gradually built up a set of agreements and undertakings, some contractual, between a group of agencies, under which the nation-wide program would be carried out. They are as follows:

The American Red Cross undertook to collect for the military services blood to be contributed by the civilian population.

The United States Army and the United States Navy, to receive through its agencies the contributed blood and to contract for its

processing by the pharmaceutical industry into blood substitutes.

The Blood Substitutes Subcommittee of the National Research Council, to bear the responsibility of advising the armed forces regarding all phases of the problem of blood substitutes.

The National Institute of Health, to be responsible for the setting up and the enforcement of regulations to insure the safety of blood substitutes.

The Red Cross began immediately to expand the number of its donor centers. The first request from the government services for 15,000 units was met by centers in New York, Philadelphia, Baltimore, Buffalo and Rochester. By January 1, 1942, the number of centers had been increased to eleven, a number expanded to thirty-five in January 1944. This expansion has about reached its limit, due to circumstances of geographical locations, density of population and more especially to difficulties of assembling competent staffs.

The demands thus far made upon the Red Cross for plasma is set forth in the following table of requests from the Army and Navy.

TABLE III

Requests for Plasma

Feb. 1941		15,000 units
May 1941	additional	209,000 "
Dec. 1941 - June 30, 1942	additional	165,000 "
July 1, 1942 - June 30, 1943		900,000 "
Jan. 1, 1943 - Dec. 31, 1943		4,000,000 "
Jan. 1, 1944 - Dec. 31, 1944		5,000,000 "

The completion of the first project of 15,000 units convinced the Red Cross authorities of the feasibility of a greatly expanded

program, the expansion to be of necessity a gradual process. A factor was the slow development of laboratory capacity for processing the blood.

The success that has since been achieved shows what an appeal this program has for the American public. Reports of the almost incredible effects of plasma upon wounded service men brought to the people a realization of the priceless contribution each could make toward the saving of precious life.

Publicity was the urgent, early need of the blood donor service, publicity to aid in getting the donor centers started and to keep up the uniform flow of donors. To a project of such popular appeal there was the readiest response by all publicity agencies. The press and the radio were the main channels of information. The direction of these publicity campaigns requires intelligence and discrimination, particularly in the timing of news releases.

There was need for heavy recruitment of donors to inaugurate each new center and the continuing need to maintain the flow of donors in relation to the capacity of the center. The publicity service, necessarily a part of each donor center, receives the accounts of new events and of important happenings pertinent to the donor campaign, makes timely issue of them to the press and radio and brings them to public attention by every dignified means. Much of its material may be furnished from the national headquarters of the organization where a central agency has been set up for the collecting and disseminating of material calculated to spur the enthusiasm of prospective blood donors. It is well recognized that this publicity campaign must be

kept up week in and week out without abatement as long as the national emergency need for plasma shall last.

Even with the highly efficient publicity effort that has been, and is still being, employed, there has been necessary a vast deal of active personal solicitation of donors. Solicitation of individuals is entirely uneconomical, but personal contacts with fraternal groups, church organizations, unions, office, store and factory groups are productive of good results. At such meetings volunteers are signed up for definite times. A donor once obtained is likely to repeat his donation.

The following table, a recent production report issued by the headquarters of the American Red Cross, gives a comprehensive idea of the immense volume of blood that the American people have given for the care of its service wounded.

TABLE IV
PRODUCTION REPORT FROM BLOOD DONOR CENTERS
July 1, 1944

Maximum Weekly Production	Center	Feb.'41 through Dec.'43	Jan.1,'44 through Jan.29,'44	Jan. 31 through July 1,'44	Total to Date
1750	Atlanta	55,780	6,373	36,722	98,875
	" *	8,512	- -	- -	8,512*
2500	Baltimore	165,053	12,550	68,484	246,087
5500	Boston	362,984	25,734	124,203	512,921
4000	Brooklyn	182,182	13,639	84,161	279,982
2500	Buffalo	189,160	11,940	52,575	253,675
5000	Chicago	325,523	24,966	115,403	465,892
2500	Cincinnati	172,530	11,578	50,738	234,846
4000	Cleveland	223,037	17,874	84,678	325,589
2750	Columbus	110,148	11,304	57,916	179,368
2000	Dallas	- -	6,488	43,263	49,751
1750	Denver*	63,489	8,101	35,080	106,670
5000	Detroit	329,389	22,737	109,826	461,952
1500	Fort Worth	- -	2,510	31,099	33,609
1500	Harrisburg	72,450	7,058	35,590	115,098
2500	Hartford	124,835	11,571	53,015	189,421
2000	Indianapolis	162,180	10,178	47,282	219,640
2750	Kansas City	101,195	10,083	56,084	167,362
9000	Los Angeles	403,638	35,884	191,322	630,844
2000	Louisville	51,335	7,914	41,865	101,114
3000	Milwaukee	163,193	11,932	62,278	237,403
2250	Minneapolis	84,731	9,112	46,737	140,580
2000	New Orleans	8,622	7,662	49,450	65,734
	" " *	27,551	- -	- -	27,551*
9000	New York	517,727	37,591	200,476	755,794
5500	Philadelphia	325,651	24,236	122,114	472,001
4000	Pittsburgh	268,104	17,885	94,633	380,622
2500	Portland	88,932	9,763	52,449	151,114
	" *	7,293	- -	- -	7,293*
1500	Rochester	178,465	11,566	42,359	232,390
1500	San Antonio	1,223	4,245	37,338	42,806
	" " *	22,879	- -	- -	22,879*
2000	San Diego	24,325	6,593	39,401	70,319
4250	San Francisco	226,453	14,400	86,954	327,807
1750	Oakland	54,371	5,494	34,117	93,982
1500	Schenectady	70,150	7,332	38,859	116,341
3500	St. Louis	219,054	14,034	71,151	304,239
1750	St. Paul	61,539	6,842	37,641	106,022
3500	Washington	148,838	14,170	74,830	237,838
500	" *	49,830	1,506	11,059	62,395
	TOTAL				
10,500	BLEEDINGS	5,652,351	462,845	2,421,152	8,536,348
2,250	LIQUID PLASMA*	179,554	9,607	46,139	235,300
	DRIED PLASMA &				
08,250	SERUM ALBUMIN	5,472,797	453,238	2,375,013	8,301,048

* - This mark indicates blood processed into liquid plasma.

DONOR CENTERS

The premises to accommodate a blood donor center must be central and convenient to the community that it serves. A considerable floor space is needed, subdivided to meet the needs of the service. As all of the centers are housed in buildings already existing, there is no uniformity of arrangement. To each is assigned an administrative director whose great duty is the recruitment of donors and a medical director who supervises the technical operation of the center.

According to the population served by a center and the experience in recruitment of donors, a weekly quota is set for each. These quotas vary from 1200 to 8500, the average being somewhat less than 3000. The average center is manned by 30 to 40 graduate nurses and by sufficient paid and volunteer personnel to care for the necessary records and for the packing and shipping of the collected blood.

Taylor[36] gives one of the earliest accounts of the Red Cross program and the operation of a center. Bleeding is done either in cubicles or in a large room fitted with the requisite number of tables. The average center has facilities for the simultaneous bleeding of twenty to thirty donors.

The operation of the blood donor center is governed by Minimum Requirements: Filtered Normal Blood Serum, prepared and issued by the National Institute of Health, revised to February 29, 1944. Within these regulations there is opportunity for variation in details, and individual centers have issued their own governing rules.

The requirement that the drawing of blood shall conform to accepted standards of aseptic surgery is met by the use of a relatively closed

system apparatus. A technique of bleeding followed at most of the donor centers and performed by graduate nurses under the supervision of qualified physicians is as follows:

Preparation of Site of Venepuncture: (a) The donor is placed in a recumbent position on a padded table. (b) The arm is bared to the shoulder and examined for the most suitable site for venepuncture. A blood-pressure cuff, folded to one-half its width, is applied to serve as a tourniquet. (c) An area 4" x 4" is mechanically scrubbed with 50 per cent solution of green soap followed by alcohol (70 per cent by weight). Iodine (2 per cent aqueous solution U.S.P.) is then applied. After being allowed to dry this is removed with an alcohol sponge. (d) If venepuncture is not to be performed immediately, the arm is to be covered with a gauze square saturated with alcohol. (e) Before the venesection the pressure in the cuff is raised to 40-60 millimeters of mercury.

Sterilization: Gauze wipes, novocain, syringes, and hypodermic needles are sterilized by autoclave. The efficiency of the autoclave is checked monthly. This is done by determining its ability to kill a known resistant strain of a spore-bearing organism.

Novocain: Diaphragm-stopped bottles for multiple withdrawal of novocain are not permitted. The novocain for each day's use is set up at the beginning of the day by one nurse under as nearly aseptic conditions as possible.

Hypodermic Needles: An individual hypodermic needle is used for each donor. They are dispensed from individual containers (test tubes) or from containers that insure simple dispensing without danger of

contamination from the air or from the hands of the operator.

Venesection: The actual venesection is accomplished by a non-touch technique. No manual palpation is done after the arm is prepared. With difficult veins, palpation may be done after the needle is inserted, above or below the site of venepuncture. If a needle penetrates the skin and is withdrawn, the entire bleeding set is discarded and another used for a second attempt. No more than two venepunctures are attempted.

Labeling: The bleeding set is tagged while the venesection is is progress. The serology tube is also labeled at this time. The names on both are checked with the donor. The serology sample is taken at the conclusion of the venesection by the nurse who has overseen it.

Clamping of Set: The small spring clamp is placed over the two steel inserts in such a manner that the rubber tubing is securely clamped at the base of the steel inserts. One-eighth of an inch of the tubing should extend above the edge of the steel insert so that there is no danger of the insert cutting through the tubing. Both inlet tube and breather tube are cut flush with the edge of the stopper.

The Tourniquet: At no time should the tourniquet be released (except when there is a flow of blood into the bottle) without first applying the clamp to seal off completely the inlet tubing.

Potential Contamination: The designation "P.C." will be placed on the bleeding tag if (a) any mechanical defect appears in the bleeding set during or after venesection; (b) if there is any question of a break in technique on the part of the operator at any time during the procedure; (c) if any defect in the air-tight closure of the completed

bleeding is noted during refrigeration or packing of bottles for transportation.

Volume: Every effort is made to secure a full bleeding of 500 cc. of blood. No bottle is to be considered a bleeding unless it is filled to the 300 cc. level.

Treatment of Site of Venepuncture: After the withdrawal of the needle, the arm is not flexed at the elbow. Pressure by a sponge over the site of venepuncture is applied manually by the donor, or nurse, with the arm in a vertical or elevated position. Suitable instructions are given the donor as to the aftercare of the puncture site.

The bottles of collected blood are packed and after a period of cooling are shipped by express to the designated processing plant, where upon arrival they become the property of a joint Army and Navy authority.

A really serious obstacle to the expansion of the Red Cross Blood Donor Program has been the difficulty of obtaining a sufficient number of competent medical men for the technical supervision of the bleeding service. This has been met by the assignment of medical officers of the government services to the work and by intensive training of graduate nurses, upon whom has devolved everything except the broad supervision of the bleeding of donors.

MOBILE UNITS

A substantial proportion of the blood collected by the donor centers is obtained through the employment of so-called mobile units. Each center has one or more such units, which are operated to a wide

radius from the central plant. The equipment and supplies carried on a one-ton delivery truck is the same as for the fixed establishment except that folding beds, tables and chairs are used and portable refrigerators are carried.

The personnel and the procedure is, to the extent possible, the same as for the fixed group. The unit operates wherever an appropriate assemblage of donors can be found, in recreation rooms of factories and department stores, in church parlors, women's clubs, community centers, or in local hospital wards. A unit of this type is equipped to take care of about 200 donors. Experience has shown that loss of blood from breakage, hemolysis and contamination is no greater than in the operation of the fixed stations.

CARE OF BLOOD

There is much to be done with the donated blood from the time it is drawn into the standard bottle until the drying process is begun.[37] Some donor centers are as much as 500 miles from the processing plants that serve them. The dangers to the product during this period are those due to breakage, hemolysis and contamination. The precautions for the avoidance of loss of blood from these causes are covered in regulations on minimum requirements, published by the National Institute of Health.

The bottles containing donor blood are packed within the hour of bleeding into refrigerating containers that will maintain a temperature of 6 - 10° Centigrade. These containers are shipped by express to the designated processing laboratory within 24 hours. Care in

packing and in handling during transportation will reduce breakage to a minimum. In practice there is very little breakage during this stage. The maintenance of refrigeration is one of the most important factors in limiting loss from hemolysis and bacterial contamination.

The blood is centrifuged in the bottles in which drawn. The supernatant plasma is drawn off through a closed system and pooled in lots of not less than eight blood donations. Many more may be pooled, but losses are minimized by small pools. There will be some hemoglobin present in the pooled plasma, but this may not exceed 25 mgm. per 100 cc. of plasma. This determination is made by a colorimetric comparison with a standard of hemoglobin solutions. Taylor reports loss of 0.569 per cent of blood from this cause.

Tests for sterility are made on the liquid plasma, either from individual bottles or from the pool. Regulations prescribe the proportion of plasma that must be taken for the test and the medium (fluid thioglycollate) that must be used. Losses from bacterial contamination ran as high as 2.26 per cent in the early part of the Red Cross program, but this figure has been greatly reduced. To losses from these causes must be added those due to a strongly positive serologic test which is made upon each donation of blood.

Maintenance of sterility is provided by the addition of a preservative. This is added to the pooled plasma after the sample for the sterility test has been taken.

The laboratory processes by which the plasma is dried and packaged for the military use is beyond the scope of this paper.

SELECTION AND PROTECTION OF DONORS

It is obvious that there must be some selection exercised in the acceptance of blood donors. Both for the welfare of the proposed donor and for the protection of the processed product, unsuitable volunteers for blood donation must be weeded out. The regulations prescribed by the National Institute of Health specify only that the person to serve as a source of normal human serum must be free from disease transmissible by blood transfusion, particularly malaria, other protozoal diseases and syphilis, and free from acute respiratory disease as far as can be determined by the donor's personal history and by such physical and clinical examinations as may appear necessary on the day set for the withdrawal of blood.

Under this broad directive, individual centers have published specific rules formulated by the American Red Cross Donor Service, for the acceptance or rejection of proposed donors. The substance of such a set of rules is as follows:[38]

(1) Age: Donors 21 to 60 years of age are accepted; donors who have attained their 60th birthday cannot be accepted. Minors 18 to 20 inclusive can be accepted only with written permission from a parent or legal guardian. Married minors who are economically independent and living apart from their parents may be accepted without permission of parent or legal guardian; but if possible, written permission of the mate should be obtained.

No one under 18 will be accepted as a donor whether in the military or in civilian life. Minors belonging to the armed services of the United States and Allied Nations and members of the Merchant Marine

may be accepted without written parental permission.

(2) Sex: Both male and female donors are taken.

(3) Race: Members of all races are accepted.

(4) Temperature: A donor is not acceptable if the temperature by mouth exceeds 99.5° F.

(5) Hemoglobin: Hemoglobin is determined according to the stated modification of the Phillips-Van Slyke copper sulphate specific gravity method. The critical level of acceptance is determined by using specific gravity of 1052 which corresponds to 12.3 grams of hemoglobin. The same standard is to be used for both male and female donors.

(6) Blood Pressure: A donor is not acceptable unless his systolic pressure is between 100 and 200 mm. of mercury. Diastolic pressure is to be checked by the physician when over 100 and any check reading of 110 will disqualify the donor. The diastolic is read in the second phase. The intervening group, 100 to 110, is to be approved only at the discretion of the physician in attendance.

(7) Pulse: The pulse rate is recorded. Particular note is made of irregularity as well as decided bradycardia and tachycardia. The significance of these variations from the normal are judged by the physician in attendance.

(8) History: The history is taken by a registered nurse employed by the center or by a qualified physician. The questions asked are as follows:

(a) When did you last donate blood? The donor may give every eight to ten weeks but not more than five times in any twelve month period. However, any donor may be accepted after an eight week period provided five donations

in twelve months are not exceeded. With accurate means of hemoglobin determination there is no evidence to warrant any change from the eight week period between donations.

(b) Have you had any illness within the last month? Particular note is taken of presence or expected occurrence of upper respiratory infections. Due to variability in severity and duration of these infections, no hard and fast rules can be made. The judgment of the physician in attendance must be used.

Donors with chronic sinusitus and hay fever are acceptable if they are not in an acute stage and are otherwise in good health. A history of a septic sore throat within three months should call for the decision of the physician in charge.

(c) Have you had any chronic or serious illness? A history of malaria within a period of fifteen years, of clinical pulmonary tuberculosis, of diabetes, or of undulant fever within five years is a positive disqualification. The judgment of the physician in charge governs in cases of extra-pulmonary tuberculosis.

(d) Have you ever had shortness of breath? Swelling of the feet? A persistent cough? Pain in the chest? Have you ever had any form of heart trouble? Any evidence of cardiovascular disease, elicited either by history or by physical findings, disqualifies the prospective donor.

(e) Do you have fainting spells? Do you have convulsions? An affirmative answer calls for further inquiry by the physician in charge who should here, as in all cases referred to him, question the donor as to whether he is under the care of a physician, and for what cause. Recent use of the sulfonamides should be brought out and evaluated.

(f) Have you had jaundice within the past six months? An affirmative answer is arbitrarily disqualifying. A history of jaundice in the immediate family calls for the judgment of the physician in charge, in regard to closeness of contact and of the nature of the jaundice.

(9) Pregnancy: No donors are accepted who are pregnant or who have been delivered within the past nine months. No donors will be accepted who have miscarried within the preceding six months.

(10) Weight: Donors, male or female, must weigh at least 110 pounds. There are no exceptions to this rule and special consideration is given to history and physical findings of donors, male or female, at this minimum weight.

(11) Regulations regarding nourishment before venesection are as follows:

(a) Donors should be instructed to eat a substantial meal three to five hours before donating. They should be instructed not to deviate to any marked degree from their normal eating habits.

(b) Light nourishment (no fats) is permitted in the interim before coming to the donor station.

(c) Only those donors who have had a heavy meal (especially fatty foods) within two hours of coming to the station, should be subjected to postponement.

(12) Special problems concerning requirements: All cases of doubt regarding the suitability for venesection are resolved by rejection. Applicants who, though meeting minimum requirements, appear "poor risks" to the physician in charge, are rejected.

Some other problems that have arisen have been ruled upon by the various government agencies concerned.

(a) Donors are refused who have had treatment for rabies within five years.

(b) Donors who have had virus infections, such as dengue, yellow fever, or virus pneumonia, are not acceptable until six months have elapsed. Cases of common cold and the virus exanthemata should have individual rulings.

(c) Subjects of immunization shots should be passed upon by the physician in charge. They will ordinarily be found acceptable.

(d) Donors offering satisfactory proof of a cured syphilis may be accepted.

(e) Donors should not be accepted who must return to work with heavy machinery within eight hours. Delayed reactions may cause accidents.

(f) Members of the Air Forces who participate in flights are not accepted. The same applies to plane crews of commercial airlines.

The blood donor program in this country has been carried out without a fatality and without a case of serious accident or complication directly attributable to the donation of the pint of blood. Untoward incidents may be classed as local and general.

The local complications affecting mainly the region of the venepuncture are (a) blood extravasation locally; (b) cellulitis; (c) venous thrombosis; (d) contusions and lacerations incident to syncope; and (e) burns, dermatitis and allergic manifestations, mainly due to agents used in sterilization. The occurrence of these minor complications are extremely rare. Complications of a general nature are (a) syncope, actual or threatened; (b) hysteria.

The experience with syncope among blood donors in the American Red Cross program is discussed by Taylor.[36] It is the main anxiety concerning donors wherever blood donations are made. A rather uniform rate of 3.5 per cent of donors throughout the country are affected to some extent, about half losing consciousness momentarily. Occasional cases experience convulsions, incontinence, cyanosis and tetany. Whiteby[40] reports a syncope rate of 2.8 per cent among British donors and cites the occurrence of serious syncope coming on one to six hours after bleeding.

Attacks take place before, during and after the bleeding. The causes are mainly psychical, but certain physical conditions are contributory as hunger, fatigue, dehydration and low blood pressure. At all of the American donor centers records are kept of all cases of actual and threatened syncope, with a view of determining the cause and as to whether the donor could be accepted or continued as such.

All bleeding teams, whether working at a center or with a mobile unit, are equipped with the materials and appliances to treat syncope cases with sedatives and stimulants; to administer also intravenous saline solutions if necessary. At the donor centers special rooms are set aside, equipped like small hospital wards, where these cases may be treated and cared for until they are ready to travel without danger or anxiety.

Neither in the American nor British donor services has there been a case of more than passing seriousness. The personnel of the donor centers are alert for the onset of symptoms and are thus able to prevent a multitude of contusions, abrasions and lacerations that are concomitants of syncopal attacks. It is expected that much advantage will accrue to the subjects of these attacks from the study that is being made of them at the donor centers.

BRITISH AND CANADIAN PROGRAMS

The threat of war in 1938 brought the British Ministry of Health to a realization that the peace-time provisions for blood for transfusion were totally inadequate for a national emergency. Proger[39] describes the development of a program undertaken by the Medical Research Council to meet the needs primarily of civil hospitals. This began with the establishment of four Blood Supply Depots in London, and this was extended by the creation of emergency blood stores in most of the large cities. During this early period and until after the beginning of war in 1939, stored whole blood was used exclusively. Then with air attack possible anywhere in the country a regional

organization was established with nine Regional Blood Transfusion Offices, and early in 1940 drying equipment was installed. A panel of blood donors was begun which, at the end of 1942, had reached a total of 800,000.

The program of the Army Blood Transfusion Service, paralleling that of the Ministry of Health and cooperating with it, is described by Whiteby.[40] It had its beginning in the organization of a technical staff drawn from the laboratories of the Royal College of Surgeons and the Middlesex Hospital shortly before the onset of war in 1939. An agreement was entered into providing for the establishment of a blood processing center in the west of England whenever it was needed. The service was in operation when war did start, at which time 5000 donors had been obtained. The static war situation through the winter and spring gave opportunity for great expansion of the donor service and for research work upon the handling and processing of the blood. During the French and Norwegian campaigns of 1940, supplies of stored blood and transfusion equipment were sent by an air service to transfusion units that had been organized earlier for service with the troops.

The functions of the Army Transfusion Service went far beyond the collection and processing of blood. It was a procurement agency for the equipment and supplies of the service and it was charged with the recruitment, equipping and training of special transfusion units for service overseas and for training of all ranks of the Royal Army Medical Corps in transfusion technique.

The recruitment of donors is carried on by the Donor Registration and Publicity Department which also serve the program of the Ministry of Health. It carries on periodical publicity campaigns and local recruiting drives in preparation for projected visits of collecting units. The registered donors are grouped into donor centers of which about nine hundred have been organized.

The British practice is to bring the bleeding service to the donors. For this purpose the service has fifteen fully equipped mobile teams that make periodic visits upon the donor centers. Each team consists of a medical officer, four nurses, two drivers and one orderly. The personnel and equipment are carried in a truck, furnished with a refrigerator, and a passenger car. The equipment will transform a suitable room into a small hospital ward in a half-hour and furnish refreshments for donors. These teams average 70 to 90 pints of blood daily. From each donor 440 cc. of blood is drawn into a bottle, devised by the Medical Research Council, which contains 100 cc. of 3 per cent sodium citrate to which has been added 20 cc. of 10 per cent dextrose. The blood is kept refrigerated in this bottle until processed or used as drawn.

The process here described indicates that this blood is to be processed to plasma. This is at variance with the generally expressed preference of the British authorities for the use of serum. As late as the summer of 1941, blood serum was the agent of choice on account of the greater ease of filtration. It was being used in the liquid form and its employment was accompanied by the use of a quantity of whole blood. It was estimated that at this time whole blood was used

for home casualties at the rate of one unit to two of serum. At that time serum and plasma were being dried only for export to the forces fighting abroad. Twenty-five per cent of British war casualties were being given plasma or whole blood transfusions. The average requirement was two and one-half pints per casualty.

Later reports indicate that the greater part of the blood being obtained is processed to form plasma, dried for use overseas, or fluid for home use. The proximity of the sources of blood to the theatres of its use had brought about considerable use of whole blood, and later the use of liquid serum and plasma. Though dried plasma is now the agent most generally employed, there is still considerable use being made of whole blood and liquid serum and plasma. Blood donations to the Army to December 1943 were about 400,000. Reports on accidents and complications involving donors indicate similar conditions as in the United States.

Statistics on the issue of blood substitutes by the Army up to December 1943 indicate that 5.4 per cent was whole blood used in France and Norway and for civilian casualties, 60 per cent was dried plasma largely sent to the Near East, North Africa and India, and 34.6 per cent of liquid plasma largely used for the home forces, but shipped in considerable quantity to overseas forces.

Reports on use by field forces indicate that ordinarily about 10 per cent of casualties requiring hospitalization were given transfusion though on certain occasions the rate reached 25 per cent. The average amount of fluid transfused was approximately three pints in all of the war theatres. There was a considerable use of whole blood in field

services, usually to supplement the plasma supply. This whole blood was obtained in substantial quantities from base troops in North Africa and the Near East.

The needs of the Royal Navy for material for transfusion were met up to 1942 by donor registers from its own personnel. Later additional needs were met by the Ministry of Health and still later by its own laboratories.[48]

The Canadian project for the supply of a blood substitute for military use was inaugurated in the Department of Physiology and Physiological Hygiene of the University of Toronto in the later months of 1939.[41] Cooperation was soon obtained from the National Research Council of Canada and the Canadian Red Cross Society. As in the United States, the recruitment of donors was taken over by the Red Cross Society. The processing of blood is done in the laboratories of the University. The first output was serum concentrated to one-third volume by the Thalhimer method. At the end of a year apparatus was secured for producing dried serum.

The Red Cross program has brought about the establishment of bleeding "clinics" in various cities of the country, and the fixing of a quota of 8000 donations a week. The selection of donors and the technique of bleeding is not materially different from our own methods. At the end of the first year the rate of donations had reached 3500 a week.

From the Province of Ontario all donations are sent in as whole blood, while from the rest of Canada it is sent as serum.

In the early months of the project the sera were pooled according to the blood groups. Later the sera were pooled in the same proportion as the various types occur in the population as follows: O, 40 per cent; A, 41 per cent; B, 10 per cent; and AB, 3 per cent. It was later decided that pooling by proportion of type was unnecessary if sufficiently large pools were used.

The Department of National Defense has first call upon the dried serum made available. After its demands are met, the remainder is available to the Department of Pensions and National Health.

All serum is issued through the Department of National Defense, which provides the transfusion set and prescribes a technique of administration.

The choice of serum by the Canadian authorities and probably by those of Britain is explained by Best as follows:[42]

"In England the Medical Research Council prefers dried serum. We do not hold any brief for serum or against plasma. We believe that they are practically identical, but it was important to make a decision and then get on with it."

TECHNIQUE OF PLASMA TRANSFUSION

This subject leads naturally to a detailed description of the Standard Army and Navy Package of Normal Human Plasma, Dried,[33,34] references to which have been made above.

The materials and equipment are snugly contained in a tape-sealed waterproof fiberboard box. The contents consist of two 400 cc. bottles and the intravenous equipment in sealed metal cans. One bottle

contains the dried plasma obtained from 300 cc. of citrated plasma and is sealed under 29 inches of vacuum. This bottle is provided with a cloth tape for suspending it in an inverted position while the plasma is being injected. The other bottle contains 300 cc. of sterile pyrogen-free distilled water sealed without vacuum. The intravenous equipment consists of an airway assembly and an intravenous set. The airway assembly consists of nine inches of rubber tubing with a needle attached on it for insertion into the rubber stopper and a cotton filter on the other end. The intravenous set is made up of forty-eight inches of rubber tubing which contains a glass cloth filter for filtering the plasma as it is administered. At one end of the tube is an intravenous needle and at the other end a short needle which connects the set to the plasma bottle. The bottle containing the distilled water is sealed in one metal can which is filled with dry nitrogen. The bottle containing the dried plasma along with the intravenous needle, clamp and double-ended needle used for adding the distilled water to the plasma is placed in the second can which is sealed under 25 inches of vacuum. The fiberboard box has on one end the label of the processing firm and on the other the label of the Red Cross.

The instructions for the preparation and use of the material in the package, lithographed upon the can containing the plasma, are as follows:

1. Open metal cans with attached keys.

2. Remove plasma and water bottles. Cleanse stoppers with alcohol.

3. Remove double-ended needle from envelope and remove glass tube from one end of needle.

4. With water bottle in upright position insert uncovered end of double-ended needle through stopper into the water bottle.

5. Remove glass tube covering airway needle and insert needle of airway assembly through rubber stopper into the water bottle.

6. Elevate free end of airway assembly to prevent water from wetting cotton filter in airway. Caution: If cotton is airway filter becomes wet, remove it.

7. Remove glass tube from other end of double-ended needle. Invert water bottle and insert needle through stopper into plasma bottle.

8. Allow water to be drawn into plasma bottle. Caution: If vacuum in plasma bottle is lost, remove stoppers and pour into plasma bottle. Replace stopper on plasma bottle and continue immediately.

9. After water is added, double-ended needle is removed from the water bottle first (to maintain sterility of water bottle so it can be used later as blood transfusion container). Needle is then removed from plasma bottle.

10. Gently agitate plasma bottle until plasma is completely dissolved.

11. Remove covering from short needle attached to the intravenous set and insert through stopper of plasma bottle.

12. Withdraw needle of airway assembly from water bottle and insert through stopper into plasma bottle.

13. Invert plasma bottle and suspend it for administration.

14. Fix glass end of the airway assembly with the suspension tape above the inverted plasma bottle.

15. Remove covering from observation tube and intravenous needle.

16. Attach intravenous needle to tube and remove glass tube from needle.

17. Allow plasma to fill rubber tubing.

18. Cleanse skin and insert needle in vein. If patient is to receive additional plasma, restore second bottle as outlined. Pull out needle from first bottle and insert in second bottle while pinching intravenous tube to prevent it from filling with air. Elevate end of airway and fix it in place with suspension tape. Plasma should be used within three hours after restoration.

It is obvious that these instructions are not intended to be read and followed preparatory to transfusion. All personnel to whom the plasma package is entrusted have a more or less competent knowledge of its use. In the officers' schools of the Army and Navy, the technique of blood and plasma transfusion has an important place. From there, the instruction is carried down to the smallest medical unit. The Army and the Navy have produced film strips for use in this instruction, and there has been manufactured a demonstration package identical in every way with the Army - Navy package, except that the plasma is replaced by dried glucose. Appropriate instructions support the films and thus the necessary information is made available to all military elements. This instruction covers the procedure that can be taken to prevent infection of the patient during the process of transfusion.

THE LARGER PACKAGE

As early as May 1941, Kendrick (Bulletin Blood Substitutes, page 46) stated that individuals who required a plasma transfusion should have at

least two units of plasma, and argued from this that it would be an economy in every way if the plasma unit could include double the amount of original plasma.

This observation in regard to the initial dosage of plasma has been verified by experience of the armed services and in civil hospitals. The economy of a larger unit was recognized early, and studies started on the problem by the same technical subcommittee that had produced the package in current use.

The idea of using a concentrated plasma, as suggested above, was not pursued. Instead there was developed a larger package of the dried plasma.[43] The basic difficulty in making the change involved changes in equipment and machinery in the processing laboratories and the breaking down of routine procedures that were in operation. However, in November 1942, a start was made in production of a package to contain approximately 500 cc. of plasma. It had been reasoned that if 300 cc. of citrated plasma could be dried in a 400 cc. bottle, it might be possible to dry 600 cc. in a 750 cc. bottle. Trial showed that this was quite feasible with a relative saving in the drying time. Serious difficulties arose in the procurement of the larger tin cans and in the satisfactory production of the larger bottle, but these were overcome.

It was found that the two 750 cc. bottles of plasma and distilled water in their containers could be packaged in a box only two inches longer than the original standard package. This is an important logistic saving, involving car and shipping space. Thus eighteen of the larger packages fit into the same space as twenty-four small

packages and contain as much plasma as 36 of the smaller size. The saving in rubber tubing, needles and cans is equally impressive.

The result is a package carrying double the amount of plasma with a great relative reduction in the size of the package. With this package the ordinary initial dosage of plasma that experience has found necessary is readily at hand for one transfusion. Production of the large package is well under way and it promises to become the standard basic plasma unit.

CLINICAL EVALUATION

Numerous statements from high authority in the military medical services repeat the low mortality rates of our wounded in the current war. A report of the Surgeon General of the Army, covering two years of war, gives a death rate of 3.7 per cent of our wounded soldiers compared with a rate of 6.1 per cent in the previous world war. This reduced mortality rate is credited to better surgical methods at more advanced stations, plasma transfusions, sulfonamide drugs and air evacuation. There will be no general agreement as to the distribution of credit among the four factors. But plasma transfusion, spectacular in its application and in its effects, is accumulating a multitude of witnesses to its efficiency.

Whether the traumatism under treatment is a gunshot wound, a burn or hemorrhage, the basic condition for which the transfusion of a blood substitute is given is shock. Within this limitation the use of transfusion in traumatism of different type and degree will vary widely.

Shock has been broadly classified as "neurogenic" or primary and "hematogenic" or secondary. An essential difference lies in whether or not there has been a loss of effective circulating blood volume. There is no such loss in the neurogenic type. It is characterized by acute and temporary circulatory failure following trauma, fear, emotional stress and surgical procedures. There has been produced a discrepancy between the circulating blood volume and the volume capacity of the vascular bed. Treatment is directed toward overcoming vasodilatation by the administration of vasoconstrictor drugs and by posture. Prompt treatment prevents peripheral circulatory failure, a serious complication.

In hematogenous or secondary shock there is a loss of effective blood volume. The physiological effects are progressive and of a more complex nature than in the neurologic type. Shock of this nature results from all kinds of tissue injuries due to missile wounds, compound fractures, burns, bacterial toxins and prolonged surgical procedures.

The loss of blood volume is made up, not alone of blood lost from the body, but of fluids lost into tissues adjacent to the trauma. There is no general acceptance of the mechanism that initiates this loss of fluid into the tissue and that produces the resultant vicious cycle. It begins, however, with damage to the capillary epithelium at the site of the injury. When this occurs, blood plasma with a small proportion of blood cells passes into the extravascular tissues in the vicinity of the trauma. The fluid thus lost from the blood stream causes a decrease in the quantity of blood being returned to the heart and a corresponding decrease in cardiac output. In order to compensate

for this loss of fluid volume from leakage at the site of injury, there is produced a generalized reflex vasoconstriction. The constriction thus put upon arterioles and capillaries, increasing peripheral resistance, maintains the effective blood flow through the heart and brain at the expense of the spleen, liver, and the peripheral vascular system generally. With the continued loss of plasma locally and the retention of the red cells in the blood stream, a hemoconcentration is seen in burn shock and in toxic shock. The associated conditions of vasoconstriction and low arterial pressure result in a relatively sluggish peripheral circulation. This condition is augmented by exposure to cold. This in turn brings about a degree of anoxia of the peripheral tissues. Increasing anoxia causes increased permeability of the capillary epithelium and increased loss of plasma into the tissues. The vicious cycle thus established becomes increasingly difficult to overcome until a stage arrives when the process is recognized as irreversible and death ensues. Before the end, cardiac decompensation takes place manifested by generalized vasodilatation and a fall in blood pressure. At this stage there is such a disparity between the effective blood volume and the volume capacity of the vascular system that an effective peripheral resistance cannot be maintained. Kendrick quotes a definition of shock as "the clinical condition characterized by progressive reduction in circulatory blood volume due to increased capillary permeability" and adds "with a continuously increasing tissue anoxia."

It thus becomes clear that the reduction in blood volume is the conspicuous variation from normal physiology in the failure of

peripheral resistance in hemotogenic shock. It follows then that the restoration of that volume as early as possible to prevent the effects of tissue anoxia is the first essential in treatment.

It is axiomatic that the treatment of shock begins with its prevention. The first item in the scheme of prevention is to recognize that shock is impending. It is generally regarded that with an injured person the pulse rate and the systolic blood pressure are the best indices of his condition.

Cannon,[44] emphasizing the importance of the recognition of impending shock, quotes an English experience indicating that a pulse rate of 120 with a systolic pressure of 80 calls for transfusion. The Shock Committee of the National Research Council places reliance upon the general appearance of the patient, the cold ashen skin, the restlessness and thirst, together with a falling arterial pressure and decreasing pulse volume with increase in rate. Work is being done upon methods for the quick determination of relative erythrocyte volume and of total plasma volume with a view to their field use.

PLASMA IN WAR WOUNDS

The use of plasma in the treatment of battle wounds has been life-saving in thousands of cases in the war now in progress. One of its greatest accomplishments is the changing of hopelessly non-transportable cases to condition to support transportation. These cases are thus brought to hospital treatment and care otherwise unobtainable. To be most effective in this role, it should be available, as it is, as far forward in Army medical installations as the aid station.

Its use is routine in the clearing station and in advanced hospitals.

The shock in these cases is usually of the hematogenic type calling for the immediate use of plasma. From all sources comes the warning of the importance of the time element and of the adequacy of dosage. There is general agreement of the need of at least two units of plasma for the initial treatment and often twice this amount is needed. Rapid administration is emphasized until the blood pressure is approximately normal; then the administration becomes more gradual. Continual watchfulness against a relapse into shock must be maintained. Frequently, plasma administration has been continued without interruption during, and following, essential surgery. As a part of the preparation of patients for evacuation farther to the rear, plasma is often given shortly before the trip and in severe cases may be continued at a slow drip during the progress of the trip. This measure has been found necessary in many cases of abdominal injury and in fractures of the femur.

A warning has been sounded to field surgeons that the intravenous administration of glucose and saline solutions is not an adequate substitute for plasma; it should not be used where plasma is available.

PLASMA IN BURNS

The war has brought to the medical personnel serving the Navy, the Air Forces and the mechanized units of the Army an unprecedented experience in the handling and treatment of burns. Especially is this true of the Navy. Roddis[45] in summarizing Navy experience in this field says, "the most important single advance in the treatment of

burns is the use of blood plasma." As in traumatic shock, large quantities of blood plasma are lost into the tissues, and the restoration of plasma with its proteins becomes an urgent matter. Plasma loss in burns is high in relation to the area involved. The quantity of plasma transfused must be adequate and must be given early for maximum results. Where burns involve from one-sixth to one-third of the body surface, 1000 to 5000 cc. of normal plasma may be required in the first twenty-four to forty-eight hours. The earlier the transfusions are given after the occurrence of the burn, the better are the clinical results and the less total plasma needed. Distinctly less prompt benefits are seen when transfusions are delayed to over eight hours. If transfusion is long delayed, irremediable changes take place in the kidneys, liver and other organs.

If laboratory facilities are available, a check should be kept upon the red cell count, hæmoglobin index and serum protein content, to judge how well blood concentration is being brought back to normal levels. When laboratory facilities are not at hand, the relief of tissue oedema is a useful check on the amount of plasma to be given as also are the readings of blood pressure.

Ogilvie[46] discusses the British Army experience in the Near East during the year from March 1942 to March 1943. He stresses the numerical importance of burns, both of accidental and battle origin. They averaged 4.5 per cent of all casualties, those incurred in battle averaging greater severity than the accidental. Mortality rate of all burns reaching hospital was 2.2 per cent; that of battle burns, 6.6 per cent. In addition many battle burns were fatal upon the field.

Of battle burns, forty per cent were of serious character, with all layers of skin, and with more than ten per cent of the body area, involved. Intercurrent injury was a factor in the high death rate of these cases.

It was emphasized that treatment of shock must have precedence over local treatment. Plasma is given as early, and as rapidly, as possible. The first three pints are given at the rate of a pint every five minutes. It must be repeated every two to four hours, as indicated by the readings of blood pressure and hemoglobin. Ogilvie stresses the need of vigilance over the blood pressure and warns of a low pulse pressure. He says, "you can resuscitate a man once, but very rarely twice." Eight to twelve pints were often found necessary in the first forty-eight hours of treatment of severe burns, with as much as thirty pints used in five days.

Experience in this theatre was that severe burn cases stood evacuation less well than any other class of casualties except abdominal wounds. It was recommended that if evacuation was imperative, they should be given a running drip of plasma during the trip.

PLASMA IN HEMORRHAGE

In a hemorrhagic emergency, plasma, while inferior to whole blood, is usually more available and will meet the need for blood volume which is the immediate danger. The loss of erythrocytes and of oxygen carrying function can be met at a later time by transfusion of whole blood.

OTHER USES OF PLASMA

Much experimental study is being made of therapeutic uses of plasma, the more important to the military services being its application to the treatment of infections and to the healing of wounds. Judgment on these uses must be held in abeyance.

Plasma has definite use in the hypoproteinemic states, but these are conditions that have little interest to the military services and will not be discussed.

ALBUMIN

The Bulletin, issued by the Subcommittee on Blood Substitutes of the National Research Council, states (page 712) as follows:

The Subcommittee "has thus far recommended only two products to the armed forces, both derived from blood collected by the American Red Cross, both of which are being produced in ever-increasing amounts and are being delivered to our fighting services."

The first was dry plasma and the second was albumin, concerning which the Bulletin continues: "Albumin prepared by a chemical fractionization of the plasma into component parts which have different physiological and therapeutic functions. Of these, albumin, which represents over half the solids of plasma, performs approximately 80 per cent of the work of maintaining the blood in its normal state of balance with the tissues. Although it performs the same function, whether in blood, in plasma, or when separated, albumin is so stable that it can be concentrated many fold and dispensed as a stable solution of small bulk, ready for immediate emergency use."

The processing of serum albumin paralleled the production of dried plasma, but in a lesser amount. Over 300,000 units of human albumin have been produced, of which about 60,000 units have gone to the Army, the remainder to the Navy. The army has distributed albumin in limited quantities to all theatres of operations and to the general hospitals in this country. The Navy has given it a more general distribution to its hospitals and ships.

The Navy Medical School has evolved a Standard Army-Navy Package of albumin.[47] It consists of a double-ended glass container holding 100 cc. of a 25 per cent solution of albumin. It is furnished with a small rubber stopper at each end, with airway, intravenous equipment and suspension tape.

The lithographed instructions on the Standard Army and Navy Package of Normal Serum Albumin (Human) Concentrated are as follows:[53]

1. Open metal can with attached key.

2. Remove air filter needle, intravenous set, and intravenous needle.

3. Remove albumin container.

4. Apply alcohol or iodine to both rubber stoppers.

5. Hold container in the upright position, insert air filter needle through top rubber stopper.

6. Insert short needle of the intravenous set through the rubber stopper at the opposite end.

7. Attach intravenous needle to observation tube.

8. Allow tubing to fill with albumin solution.

9. Insert needle into vein. Venipuncture may be difficult in

shock. If necessary cut down on vein.

10. Suspend container approximately three feet above patient.

11. Except in severe shock, the rate of administration should not exceed 5 cc. per minute.

Precaution: in the presence of dehydration, albumin must be given with or followed by additional fluids.

While plasma is preferable to albumin in conditions where either is applicable and both available, albumin has some special indications and some limitations. Being given in small volume, it does not supply volume to the blood. If given to a dehydrated patient, it must be accompanied or followed soon by parenteral administration of an adequate amount of fluid. An absolute contra-indication is the presence of cardiac decompensation where a sharp increase of blood volume could produce grave danger. A positive indication for its use in preference to plasma is the presence of intracranial pressure.

On account of the small size of the albumin unit, it has great potential usefulness. The logistic advantages are great. However, it is having very limited use by the Army in the field, though experience may prove that it has greater application than has so far been demonstrated. In this connection the studies that are in progress upon the use of bovine serum albumin may possibly have useful results.

WHOLE BLOOD

Neither serum nor plasma nor any blood protein is, by itself, a perfect substitute for whole blood. Each of these and of other proposed blood substitutes has its certain advantages and likewise its

limitations that make it especially useful in some conditions and unsatisfactory in others. There are functions that plasma and blood proteins perform equally as well as whole blood, while there are others in which they are vitally lacking. Similarly, erythrocytes, separated and suspended in an appropriate medium, perform but partially the role of whole blood.

For the present then and perhaps indefinitely, there is an unquestionable need for whole blood. Wherever there is need to increase the oxygen distribution by the blood to the body tissues, there will be need of transfusion of whole blood. This may be due to severe hemorrhage, to hemolysis, or to failure of erythropoieses. A definite indication for whole blood is the treatment of carbon monoxide poisoning as is also the presence of a hemorrhagic diathesis.

Notation has been made under the chapter devoted to the British program of the considerable use of whole blood, both initially and as a supplement to serum or plasma. Reports indicate that whole blood forms the staple supply for transfusion in the Russian army service. The proximity of the fighting lines to the civilian population with the cold climate may be the explanation of their use of whole blood; whereas, it may be due to lack of facilities for processing it to serum or to plasma.

However, unpublished reports from our medical officers in the field tell of the need of whole blood and of a considerable employment of it. The indications are that plasma meets the emergency need in combating shock in a satisfactory manner, but that whole blood is more generally beneficial. It has been found of more value than plasma in

the resuscitation of certain types of casualties. It is being found the agency of choice where patients with severe hemorrhage are to undergo surgical procedures. Furthermore the statement is made that practically all of the more severely wounded require a certain amount of whole blood.

The need for whole blood is being met in certain of our combat areas by the establishment in every hospital in the rear areas of either a blood bank or a roster of donors or both. The blood is obtained from troops serving the base units or from civilians. Needless to say this service is operated only in fixed hospitals, or mobile hospitals up through field hospitals.

There has been put in operation in the European Theatre of Operation a plan for a service of whole blood transfusion, the details of which are briefed as follows:

"The blood is to be drawn in England, citrated, bottled and refrigerated. It will be then transported under refrigeration (planes, trucks, etc.) to the combat area and distributed for use as far forward as the field hospital. The plan includes the use of teams to draw the blood and to administer it."

There is nothing in this reported employment of whole blood that indicates that plasma is inefficient. The most that can be said is that field experience indicates that there is need of supplementary whole blood. A certainty in the matter is that the emergency need for blood transfusion could only be met in adequate quantity by the use of a dried product such as plasma or serum, however helpful the supplementary whole blood is proving.

This paper is closed with the thought that, while the plasma program is certainly serving our emergency with high credit, the complete blood substitute is yet to be found.

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