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PRESERVED BLOOD—AN ANALYSIS OF ITS USE REPORT FROM THE MERSEYSIDE WAR BLOOD BANK

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In reporting this analysis of the first 1,500 bottles of preserved blood distributed by the Merseyside War Blood Bank an attempt has been made to discover the conditions under which preserved blood is a satisfactory substitute for fresh blood, and the extent to which its convenience of administration and potentially unlimited supply outweigh any possible shortcomings in therapeutic action. A preliminary brief account of the working and technique of the Merseyside War Blood Bank is included.

Blood Bank

The blood taken is preserved in 3.8% sodium citrate solution, one part to nine parts of blood. This solution was chosen in preference to others because it was felt that in providing a service of blood for all purposes, both medical and surgical, the highest concentration of blood compared with the amount of diluent should be used. The unit adopted is one of 450 c.cm.—405 c.cm. of blood and 45 c.cm. of anticoagulant solution. This is a smaller unit than normal, but the withdrawal of only 405 c.cm. from the donors, who are mostly unselected, is less likely to cause distress. Group O (IV) and Group A (II) donors are used regularly, the O (IV) blood being intended for recipients of Groups O (IV) and B (III), while the A (II) blood is for patients of Groups A (II) and AB (I). In actual practice, however, the emergency demands and the difficulties, real and imagined, of grouping patients have resulted in the use of four or five Group O (IV) donors to every Group A (II) donor.

The blood is stored in refrigerators in four main and numerous subsidiary depots in the area over which the service is maintained. Transport between depots is undertaken in cold insulated boxes, each of which holds two bottles of blood.

From the date of declaration of war the whole of the transfusion needs of the area has been supplied by stored blood. The use of this blood rose sharply from the first week of the war until it reached an average consumption of approximately fifty bottles per week, which has been steadily maintained, and it is already evident from comparison with the pre-war figures that the ready availability of stored blood and the standardization of the technique of transfusion have increased the frequency of blood transfusion practically twofold. This doubling of the transfusion rate may be taken to indicate that the blood bank system has repaired a real deficiency inherent in the older personal donor system, and that the number of patients now receiving blood transfusions is nearer the number that should receive this form of treatment than was formerly the case. This is particularly evident in the smaller and outlying hospitals; in the larger municipal

and voluntary hospitals the increase in the transfusion rate is not so striking. In some of these larger institutions, where there are resident medical officers with considerable experience of transfusions, it has now been found convenient to reintroduce to a limited extent the personal donor system for those types of case in which transfusion with absolutely fresh blood appears to be either essential or at least likely to be greatly superior to the use of preserved blood. These points are brought out later in our discussion of the reported results of the transfusions performed.

Donors are bled twice weekly, the numbers used on each occasion being such as to maintain the amount in the bank and its depots at a more or less constant level, determined in terms of an arbitrarily chosen multiple of the daily requirements for civil use. At the time over which this review was made the supply was ten times the daily requirements, but with the likelihood of air raids this figure has been considerably increased.

Method of Taking and Delivering Blood

After an extensive trial of various types of apparatus that of Boland, Craig, and Jacobs (1939), modified slightly to suit local conditions of equipment and personnel, was adopted. These modifications are not in any way claimed to be "improvements," and in our opinion the basic principles incorporated in the above authors' apparatus are the most satisfactory yet devised and possess the added advantage of cheapness and simplicity. In a transfusion service which caters for a large number of both skilled and unskilled transfusers this apparatus, which involves no removal of stoppers, no introduction of additional units, and no transference of the contents to other vessels, maintains a standard of asepsis high enough to make it acceptable to the most exacting surgeon. The internal filter of glass shot is one of its most important features: by its use the clogging of needles and filters with clot or coagulum is avoided, and because of it the storage bottle need never be opened, and thereby exposed to the dangers of infection, from the time it is sterilized before being filled with blood until it is returned to the centre for washing and resterilization after the transfusion is completed. The method of use is indicated in Figs. 1 and 2; its simplicity allows a considerable number of transfusions to be given simultaneously by one person in times of emergency.

The difficulties of administration of blood to patients with collapsed veins have been overcome by the use of the "vein-seeker" (Edwards, 1939)—Fig. 3—and this instrument is supplied with each delivery apparatus in our transfusion service.

The following analysis of the use of 1,500 bottles of preserved blood is based on the medical reports sent in by the surgeons who performed the transfusions during the period September, 1939, to May, 1940.

FIG. 1.—Method of taking blood for preservation.

FIG. 2.—Method of delivering preserved blood.

Wastage of Blood

The question of how much blood is wasted by using the bank system is an important one. Out of the first 1,500 bottles supplied 136 were unused, giving a total discard rate of

FIG. 3.—The vein-seeker.

9.07 %. When owing to the outbreak of war the bank was organized on a large scale, with numerous secondary depots, a certain amount of wastage was inevitable during the instruction period. Time, however, has largely overcome this, but it appears that a constant wastage factor of about 7% will occur.

Wastage is due to two factors: (a) haemolysis, and (b) accidents in the preparation of blood for transfusion. The wastage from haemolysis, which includes that due to the blood getting too old, can be overcome by ensuring that subsidiary depots return all unused blood on its fourteenth day to the main banks in the larger hospitals. Here much larger quantities of blood are used, and it has a greater chance of being administered before the degree of haemolysis becomes too great. In any case, blood that has reached the limit of twenty-one days is now condemned, whatever its apparent condition. The main causes of accidental wastage were found to be overheating of the blood and the failure to return immediately to the refrigerator blood removed for a transfusion but not used. A few bottles have also been unnecessarily discarded by clinicians who have interpreted the turbidity of the plasma and the white scum of lipoids as evidence of bacteriological infection. Accidental switching off and other breakdowns in refrigerators have also caused the loss of a few bottles. Out of 136 bottles discarded, 64 were condemned because of haemolysis, 43 because of age (though not necessarily severely haemolysed), and 4 because of the presence of large clots; 25 were accidentally wasted.

1,364 bottles of the original 1,500 taken were thus used—709 (over 50%) within a week of collection, and 956 (practically 70%) within the first ten days; the average age of the blood for the whole series was seven days.

Reactions

The reactions due to the administration of blood may be divided into three grades (Riddell, 1939): Grade 1, in which there is a slight rise of temperature a short while afterwards

to less than 100° F. with no constitutional effects; Grade 2, in which a similar or greater rise is associated with a feeling of coldness but no actual rigor; and Grade 3, in which there is a definite rigor.

In order to compare the results in these three grades a series of 100 consecutive transfusions with absolutely fresh citrated blood performed at the Liverpool Royal Infirmary was compared with a similar series of transfusions with stored blood performed in the same hospital. The two groups were comparable, as approximately the same number of cases had been transfused for haemorrhage, medical anaemias, and sepsis. Two series were examined at other hospitals—Mill Road Infirmary and Walton Hospital (Liverpool Corporation) respectively—and are included in the same table for comparison.

	Fresh Citrated Blood	Preserved Blood			
	Royal Infirmary	Royal Infirmary	Mill Road	Walton	
No reactions	37%	53%	66%	57%	
Reaction difficult to determine (blood given during or immediately after operation) ..	15%	14%	25%	25%	
Reactions :					
Grade 1	15%	9%	—	—	
Grade 2	25%	19%	5%	6%	
Grade 3	8%	5%	4%	12%	

While too much importance should not be attached to these figures, it would at least appear that the incidence of all three grades of reaction is probably no greater with preserved blood than with fresh blood. Since, obviously, changes occur in preserved blood which should affect its constitution detrimentally, results such as these, if substantiated by further investigations with larger numbers of cases, must be attributed on the one hand to the removal of some reaction-producing substance during storage or to the improved chemical constitution of the transfused blood, or, on the other hand, to the elimination of reaction-producing conditions by the more efficient manipulation by transfusers familiar with the simplified technique of stored blood administration.

The various causes of reactions have been well reviewed by Riddell (1939), and it merely remains for us to emphasize the importance of absolutely correct grouping, the complete cleanliness of all apparatus used, and the elimination of all pyrogen factors in diluting solutions. The most potent single cause of reactions appears to be the introduction of some foreign protein. Riddell is a strong supporter of the foreign protein theory, and draws attention to the similarity between these reactions and serum shock and to the fact that reactions are commoner in recipients sensitized by previous transfusions or exhibiting an allergic taint. In this connexion the experience of other workers is of interest. Lewisohn and Rosenthal (1933) reported that they had reduced their reaction rate to 1.5% by maintaining scrupulous cleanliness in all apparatus used. They also satisfied themselves that the sodium citrate used as anticoagulant was never in itself a cause of reactions. Riddell (1939), giving his figures for his last 100 transfusions with fresh blood, noted rigors in 11%; and Fell (1938) analysing 500 cases, found reports of rigors in 4.8%. Kordenat and Smithies (1925) maintain that nearly all transfusions are associated with some rise in temperature, even though this may be symptomless, and Riddell expresses a similar opinion. These figures all relate to transfusions with fresh blood. With preserved blood, reactions have been noted as follows:

Author	No.	Grades 1 and 2	Grade 3
Biddle and Langley (1939) ..	150	10%	5%
Leedham-Green (1939) ..	60	16.6%	combined
Hamilton-Paterson (1939) ..	46	13%	6%
Elliot, Macfarlane, and Vaughan (1939) ..	50	8%	8%
Cameron and Ferguson (1939)	1,000	4.6%	2.8%

As the criteria for minor grades of reaction vary considerably, while those for Grade 3 are more or less constant, further consideration may profitably be confined to these. In our series, out of 1,364 bottles administered by numerous surgeons in a variety of hospitals, 69 (5%) gave rise to a

Grade 3 reaction or severe rigor. Further analysis shows considerable differences in the rigor rate amongst the different conditions for which transfusions were administered.

Indication	Total	No. of Grade 3 Reactions	Percentage
Acute post-haemorrhagic anaemia ..	509	29	5.7
Chronic secondary anaemia ..	316	11	3.5
Post-operative shock ..	177	6	3.4
Other diseases of haemopoietic system ..	128	6	4.7
Acute septic conditions ..	163	13	8.0
Chronic septic conditions ..	45	3	6.7
Multiple injuries and shock ..	14	0	—
Jaundice ..	12	1	8.3
	1,364	69	5.0

Grade 3 reactions are undoubtedly increased by the age of the blood, and it would appear that preserved blood over ten days old is better not administered. If it was economically possible the age limit should be cut down even more, but the advantage of having a considerable amount of blood ready for immediate administration must be balanced against this. No serious or permanent ill effect following the rigor has been observed in any one of these 69 cases. Riddell (1939) draws attention to the danger of cardiac failure in such cases, and this must be borne in mind.

Four cases of incompatibility of group have occurred, and the transfusion was stopped immediately on the onset of symptoms. Subsequent investigation proved that in each case the recipient's blood had been wrongly typed. In no instance has a wrongly grouped bottle been supplied—a very happy state of affairs which has been ensured by retesting the blood group, both by cells and serum, of each bottle collected. Numerous mistakes have been found in the preliminary mass groupings, and more than once it has been suspected that a donor has utilized someone else's group card.

Urinary Complications

Five cases developed a considerable degree of haemoglobinuria. Three of these patients were children suffering from anaemia associated with unresolved pneumonia, influenza meningitis, and meningococcal meningitis, respectively. All the transfusions given were with blood over three weeks old, and there would almost certainly be an associated toxic nephritis. The two other cases—one an ulcerative colitis—received blood two days old; and the other—an ectopic pregnancy—received blood three weeks old and had an auto-transfusion at the time of operation.

No case of anuria occurred in this series, although one is reported in the series of 100 cases of transfusion with fresh citrated blood. The use of 3.8% sodium citrate solution, which entails the simultaneous administration of 55 grains of alkali with the blood, will effect a moderate degree of alkalization of the urine, and, provided a grossly haemolysed blood is not given, the safety factor is considerable.

Jaundice; Urticaria; Transmitted Disease

Seven cases of jaundice occurred. These were as follows:

Disease	Age of Blood
Menorrhagia	14 days (2 bottles)
Intestinal obstruction	25 ..
Carcinoma of colon	14 .. (2 bottles)
Marasmus (child)	46 ..
Meningococcal meningitis (child) ..	33 ..
"	10 ..
Cancerum oris (child)	34 ..

Undoubtedly these patients received blood in which, although the supernatant plasma was clear, there was gross haemolysis of the red cells. The leucocyte layer over the red cells becomes "organized" into a dense layer, which in some bottles prevents the diffusion of the haemoglobin from the red cell layer to the plasma. This complication, although not serious, is undesirable, and it demonstrates one of the objections to the use of aged preserved blood.

A giant urticarial reaction is reported in one case associated with secondary haemorrhage from a wound, and this appears to have been a true allergic reaction. It responded to calcium and adrenaline.

No case of transmitted disease has been reported in this series. So far as is known no infected bottle of blood has been supplied. It was found impracticable to test every bottle bacteriologically, and we have relied instead on a high standard of aseptic technique. Every bottle that is returned unused because of condemnation for some reason or other is examined bacteriologically, and no definitely infected bottle has yet been found. This agrees with the observation of Biddle and Langley (1939) that infection is extremely rare.

Deaths

There were five deaths during transfusion of preserved blood. They occurred in one case each of agranulocytosis, ruptured liver in a child, placenta praevia, ectopic pregnancy, and haematemesis. All these patients were moribund before transfusion, and it is doubtful whether the blood or its administration played any part in the fatal outcome.

Of the patients 71 died soon enough after the transfusion—i.e., within approximately twelve hours—to justify consideration as to whether the transfusion was the cause of death. These cases are grouped in the following table:

Indication	No. of Deaths
Acute post-haemorrhagic anaemia	19
Post-operative shock	18
Other diseases of the haemopoietic system	4
Acute septic conditions	19
Multiple injuries and shock	7
Burns	1
Prematurity	1
Marasmus	2

In only one of these cases did a rigor occur during or immediately after the transfusion; this was in a child with streptococcal septicaemia. The patients who died from acute haemorrhage, post-operative shock, and multiple injuries may be eliminated as unlikely to have been affected adversely by transfusions *per se*. The four cases of blood disease consisted of melaena neonatorum in two children, myeloid leukaemia and a superimposed ischio-rectal abscess in one adult, and pernicious anaemia in an adult *in extremis*. The 19 cases of acute sepsis were:

Disease	No.
Pneumonia (children)	2
Mastoid and lateral sinus thrombosis (children)	2
Streptococcal septicaemia (children)	2
(1 severe rigor)	
General peritonitis: appendix (child)	1
Puerperal pyrexia	4
Perivesical abscess	1
Empyema (children)	2
Meningococcal meningitis (children)	2
Carcinoma oris (child)	1
Influenzal meningitis (child)	1
Umbilical sepsis (child)	1

Presumably most of these showed some degree of anaemia, but one is tempted to conclude that transfusion was resorted to in many of these cases as a counsel of desperation. The majority certainly appear to have been suffering from disease of severe character, and it is doubtful whether any real benefit from transfusion could reasonably have been expected.

Results of Administration

Transfusions were given for a great variety of clinical conditions, which for convenience have been divided into eight broad classes.

Indication	Satisfactory	No Clinical Benefit	Total
Acute post-haemorrhagic anaemia	463 (91%)	46 (9%)	509
Chronic secondary anaemia	292 (92%)	24 (8%)	316
Post-operative shock and/or haemorrhage	160 (89%)	17 (11%)	177
Other diseases of haemopoietic system	109 (85%)	19 (15%)	128
Acute septic conditions	111 (68%)	52 (32%)	163
Chronic septic conditions	43 (96%)	2 (4%)	45
Multiple injuries and shock	5 (36%)	9 (64%)	14
Jaundice	11 (92%)	1 (8%)	12
Totals	1,194 (87.5%)	170 (12.5%)	1,364

The term "satisfactory" is a wide one, and represents the opinion of the transfuser: it may be taken to mean

that the result was as good as could be expected, judged by the condition of the patient both before and after transfusion. For instance, 68% of the group of acute septic conditions are tabulated as having a satisfactory result, yet this result in many cases would be very fleeting and no more than would be expected with any transfusion in such a condition. Thus it is seen that 87.5% of all transfusions were considered to be of benefit to the patient and 12.5% were regarded as having produced no evidence of improvement.

The Therapeutic Action of Preserved Blood

The assessment of the value of a transfusion by means of a blood count is in most cases of very little value. The administration into the blood stream of extra fluid associated with fresh plasma proteins so alters the blood volume that comparative erythrocyte and haemoglobin estimations are unreliable, and in a number of cases the second count may be lower than the first by reason of absorption of fluid from the tissues. In massive transfusions—for example, in haematemesis—the giving of three to five bottles is seen to produce a substantial rise in haemoglobin, which is comparable to that obtained from transfusions with fresh citrated blood. Some doubt has, however, been cast upon the erythropoietic action of preserved blood, and the general opinion among the physicians whose cases have been transfused is that preserved blood is not as efficient as fresh citrated blood. Nevertheless, the administration of stored blood does tide patients over the acute stage of their disease until the more rational treatment of the bone-marrow deficiency by iron or liver extract therapy can be instituted.

As a life-saving measure in cases of acute haemorrhage there is no doubt whatsoever that preserved blood is as efficacious as fresh blood, while its convenience in administration and its immediate availability in large quantities are advantages which cannot be overestimated. Out of 509 transfusions given for acute haemorrhage 463 (91%) were considered to be satisfactory and only 46 (9%) resulted in no obvious benefit.

For chronic secondary anaemia and as a preparation for operation equally satisfactory results are obtained. Out of 316 transfusions given for secondary anaemia 292 (92%) were considered satisfactory and 24 (8%) unsatisfactory.

For post-operative shock and haemorrhage preserved blood has again proved its value. In such cases, however, unless a severe loss of blood has taken place, it is probable that the plasma elements of the blood produce the major therapeutic effect. The reduced blood volume occasioned by shock is increased by the administration of the plasma proteins, which raise and maintain the osmotic pressure and so draw fluid back into the circulation from the tissues. In such cases it is probable that the administration of plasma, plasma saline, or reconstituted dried plasma will produce a similar effect. The advantage of having the blood at hand in such cases far outweighs any possible arguments against its therapeutic value as compared with fresh citrated blood. It is probable also that stored blood of considerable age is as efficacious as newly preserved blood, as the plasma proteins undergo little change with storage. In 177 cases of post-operative shock and haemorrhage, 160 cases (89%) were satisfactorily transfused and 17 cases (11%) derived no benefit.

Transfusion in the Anaemias

Study of the dyshaemopoietic anaemias has shown that the rational treatment of most of them is by iron or liver extract therapy, and that blood transfusion is only of value in the acute phases or in those in which an aplastic tendency is manifested. It is the considered opinion of many

clinicians that fresh blood gives a more pronounced immediate result and is more prolonged in its effect, and thus if stored blood is to be used it should be the freshest available. Aged erythrocytes and those in which the fragility has been increased have only a short effective span of life and can therefore have little lasting value. It should, however, not be forgotten that probably the most important feature of any blood transfusion in all, and especially the chronic, anaemias is the provision of an immediately available store of organic iron (or possibly even of haemoglobin) for utilization by the marrow. Cases of leukaemia are rarely benefited by any form of blood transfusion, and preserved blood appears to have only a very temporary effect and to be less valuable than fresh blood in cases of the haemolytic anaemias, agranulocytosis, and the haemorrhagic diseases—for example, purpura haemorrhagica. These defects of stored as compared with fresh blood are probably associated with the rapid destruction of platelets and leucocytes during storage (Kolmer, 1939).

The administration of blood to cases of acute anaemia associated with sepsis has never been a very satisfactory procedure, and is associated with a raised reaction rate. The increase of haemoglobin is only temporary, and the administration of blood appears to be of value more for its complement and antibody factors than for its erythrocyte content. As the complement value of preserved blood falls rapidly in the first forty-eight hours it would seem that in these cases also the administration of fresh blood is preferable to preserved blood. Out of 163 transfusions administered in cases of acute sepsis, 52 (32%) were unsatisfactory and 111 (68%) were considered satisfactory; but it must be remembered that this satisfactory result was merely to a degree commensurate with the condition of the patient.

Transfusion in Various Conditions

In multiple injuries and shock blood transfusions have been shown to be of great value (Cannon *et al.*, 1917), again most probably because of the plasma elements producing an increase in blood volume. Saxton (1937) showed that in the Spanish Civil War the mortality rate in cases of severe injury was lowered by transfusions of stored blood from an estimated rate of 90% to 60%. Here again the advantage of having the blood on hand and ready for immediate administration outweighs any other objection, and in military engagements, where facilities for taking fresh blood in large quantities become almost impossible, preserved blood or plasma will find its greatest field of usefulness (Edwards, Kay, and Davie, 1940). In this series the number of such cases is small and no definite conclusions can be drawn. The place of plasma transfusion in these cases is receiving attention at the present time not only in our service but all over the world.

In jaundice the prothrombin content of the blood is lowered, and on the investigation of Rhoads and Panzer (1939), who showed that the prothrombin value of preserved blood falls rapidly, it would appear important that fresh blood be used. The administration of vitamin K and bile salts has, however, been shown to increase this content of the patient's blood, and unless an anaemic factor is present the administration of blood appears to be now unnecessary. Preserved blood was, however, administered with benefit in 11 out of 12 cases of obstructive jaundice, but as vitamin K and bile salts were also given no conclusions can be drawn.

In children acute haemorrhage and post-operative shock respond to preserved blood as in adults, but cases of sepsis and blood diseases, particularly those of the new-

born—conditions which make up the major indications for transfusion in children—appear to respond poorly to stored blood.

One of the most satisfying aspects of the use of preserved blood has been the reports of its use in those places where formerly there was often a very considerable delay before blood could be given. This has been particularly so in cases operated on in nursing homes and for maternity patients on the district. The administration of blood to patients in their own homes has now become a recognized procedure, and, provided the practitioner familiarizes himself with the apparatus, is as easy as in the hospital ward.

Conclusion

Our investigations appear to indicate that the response to the administration of preserved blood is clinically satisfactory in cases of acute haemorrhage with or without shock and in chronic secondary anaemia. In these groups the ready availability of stored blood in bulk marks a true advance over the individual donor system. For certain other diseases of the haemopoietic system, however, and for cases of anaemia associated with sepsis, the administration of fresh blood is to be preferred, and in our opinion the organization of a blood bank should be elastic enough in its regulations to make available freshly drawn blood for selected cases even when large stocks of older blood are awaiting distribution.

Summary

An account is given of the organization of the Merseyside War Blood Bank and of the technique adopted for the collection, storage, and administration of preserved blood.

A wastage of 9% of the blood collected is reported. The causes for this are investigated and the means of reducing it discussed.

The reaction incidence (rigors) is found to be 5% over the whole series, and this is examined in relation to the various clinical states for which transfusions were administered and also compared with the reaction incidence in transfusions of fresh blood. Similar analyses are made of other complications of transfusion—for example, haemoglobinuria, anuria, jaundice, urticaria, etc.

The incidence of most complications is found to increase with the age of the preserved blood, and it is recommended that stored blood should if possible be administered before it is ten days old.

The therapeutic value of administration of preserved blood is considered for the whole of the 1,364 transfusions reported and the differences of the results are examined in relation to a number of clinical subdivisions of the cases—for example, acute post-haemorrhagic anaemia, chronic secondary anaemia, post-operative shock with or without haemorrhage, acute and chronic septic states, anaemias of infancy and childhood, etc.

Our grateful thanks are due to the honorary and resident staffs of all the hospitals supplied by the Merseyside War Blood Bank for forwarding medical reports and records and for reporting all complications and difficulties that have arisen during the administration of preserved blood. Without their willing co-operation this analysis would not have been possible. Mr. Douglas J. Kidd has very kindly drawn the illustrations.

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