leave the task of destroying bacteria to the human body, which in the performance of its normal functions kills enormous numbers every day.

REFERENCES

- Adkins, E. W. O., and Davies, D. V. (1940). *Quart. J. exp. Physiol.*, **30**, 147.
 Allen, A. L. (1935). *S. Afr. J. med. Sci.*, **1**, 31.
 Bauer, W., Short, C. L., and Bennett, G. A. (1933). *J. exp. Med.*, **57**, 419.
 ———, Ropes, M. W., and Waine, H. (1940). *Physiol. Rev.*, **20**, 272.
 Colebrook, L. (1939). *Proc. roy. Soc. Med.*, **33**, 72.
 Drinker, C. K., and Field, M. E. (1933). *Lymph and Lymphatic Tissue*, London.
 Field, M. E., Drinker, C. K., and White, J. C. (1932). *J. exp. Med.*, **56**, 363.
 ———, Schaffer, M. F., Enders, J. F., and Drinker, C. K. (1937). *Ibid.*, **65**, 468.
 Finucci, V. (1935). *Pathologica*, **27**, 518.
 Florey, H. (1927). *Brit. J. exp. Path.*, **8**, 479.
 Halley, C. R. L., Chesney, A. M., and Dresel, I. (1927). *Johns Hopk. Hosp. Bull.*, **41**, 191.
 Issaef, (1893). *Z. Hyg. Infektr.*, **16**, 287.
 Lewis, J. H. (1921). *J. Amer. med. Ass.*, **76**, 1342.
 McMaster, P. D. (1937). *J. exp. Med.*, **65**, 347.
 Menkin, V. (1929). *Arch. Path.*, **8**, 263.
 ——— (1931). *J. exp. Med.*, **53**, 647.
 Noetzel, W. (1906). *Beitr. klin. Chir.*, **51**, 740.
 Pawlowsky, A. D. (1900). *Z. Hyg. Infektr.*, **33**, 261.
 ——— (1909). *Ibid.*, **62**, 433.
 Schimmelbusch, C. (1894). *Dtsch. med. Wschr.*, **20**, 575.
 Schulz, R. Z., Warren, M. F., and Drinker, C. K. (1938). *J. exp. Med.*, **68**, 251.
 Trueta, J. (1939a). *The Treatment of War Wounds and Fractures*, London.
 ——— (1939b). *Proc. roy. Soc. Med.*, **33**, 65.
 Wells, H. G., and Johnstone, O. P. (1907). *J. infect. Dis.*, **4**, 582.
 White, J. C., Field, M. E., and Drinker, C. K. (1933). *Amer. J. Physiol.*, **103**, 34.

TRANSFUSION OF FRESH AND STORED BLOOD*

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The object of the present investigation was to obtain information on: (1) the relative therapeutic value in cases of acute and non-acute haemorrhage of transfusions with fresh and stored blood; (2) the relative incidence and character of reactions following the use of fresh blood and stored blood.

Clinical Material used in the Investigation

Many clinicians in the hospitals in the four depot areas collaborated in this investigation by referring cases requiring blood transfusions to the clinical observers attached to the four depots. The general treatment, which was under the direction of the physician or surgeon in charge of the case, was not confined to blood transfusion. This meant that, in many instances, in addition to the transfusion of test material the patient was given saline, glucose saline, or iron and other therapy, which rather confused the picture. For our purpose cases have been divided into three groups:

- (i) Acute haemorrhage (considerable blood loss within twenty-four hours of administration).
- (ii) Non-acute haemorrhage (simple blood loss at least twenty-four hours before the transfusion or repeated haemorrhages over a long period).

* Preliminary report on their relative values made for the Blood Transfusion Research Subcommittee and the Committee on Traumatic Shock of the Medical Research Council.

(iii) Miscellaneous—which includes cases of haemorrhage complicated by gross sepsis, obscure anaemias, and patients subsequently found to have some complicating condition, such as leukaemia or malignant disease. Whether a patient were given fresh or stored blood depended on a number of factors. In a few cases the physician or surgeon in charge was insistent that fresh blood should be used. In some instances, analysed in detail, patients were given a transfusion of fresh blood followed after an interval by stored blood, or vice versa.

To obtain uniformity in the presentation of essential facts the clinical observers were asked to furnish particulars concerning each case transfused. The important points in the analysis of the information are presented in the tables which follow.

All blood used was obtained from the four depots. Two parts of blood were added to one part of diluent, consisting of 3% glucose in 0.85% sodium chloride and 1.05% sodium citrate. *Fresh blood* we defined as blood that had been stored for less than twenty-four hours; *stored blood* as blood that had been kept from ten to fourteen days. Blood was given by the Medical Research Council apparatus, except in a few instances when hospitals preferred to use their own.

Method of Examination

A. Clinical.—The difficulty of obtaining an objective measure of improvement or lack of improvement in a series of cases seen by different observers was appreciated from the outset. Improvements in pulse and blood pressure are a valuable indication in patients with shock and acute haemorrhage, but are less important with non-acute haemorrhage. An attempt has been made to assess various factors such as improvement in colour and general well-being and mental attitude under the term "general improvement."

B. Pathological: Red Cells and Haemoglobin.—A rise in the number of red cells and the haemoglobin level might be expected to offer a measure of satisfactory haematological response. Red cell counts and haemoglobin estimations were therefore made whenever possible. In the accompanying tables an increase in haemoglobin has been expressed not as an absolute figure but in relation to the amount of blood given. The observed gain has been divided by the number of bottles administered; the figures shown therefore represent the gain per bottle, each bottle containing 360 c.cm. of whole blood—approximately two-thirds of a pint. Haemoglobin was always estimated by Haldane's method. Before accepting the results it is important to realize there are possible difficulties in their interpretation.

Errors of the Method: 1. Colorimetric Error.—Any colorimetric method of estimation is open to error. In practice in one laboratory it has been found that technicians practised in using the Haldane standard will usually estimate any sample of blood within 2% of one another. It was felt that such sources of error were equally present in all cases. Therefore if a significant rise in haemoglobin was found in one group of cases and not in another it might be accepted as an indication of greater improvement in the former. Since haemoglobin usually runs parallel with the red cell counts and haematocrit readings in the type of cases under consideration the two latter have not been tabulated, though they were noted in making the analysis.

2. Normal Daily Variation.—Several observers have shown that in a normal person the haemoglobin may vary by as much as 8% in twenty-four hours: small individual variations are therefore probably without significance.

3. Blood-volume Changes.—In a patient with acute haemorrhage rapid changes in blood volume take place. There is no satisfactory method of estimating blood volume, especially in patients who are acutely ill. The influence of such changes on the circulating haemoglobin cannot therefore be estimated. An apparent fall in haemoglobin immediately following transfusion may be due only to blood dilution or to a persistence of bleeding. In acute cases haemoglobin estimations were therefore felt to be of little value between case and case, but probably were of some significance where two large groups, one receiving fresh blood and the other stored blood, were compared.

4. Raised Plasma Bilirubin.—Following the use of stored blood there may be a rise of plasma bilirubin in the first twenty-four

hours. This in some cases may be high enough to make accurate estimation of the haemoglobin difficult.

What Constitutes a Reaction?

What can be considered a reaction following a transfusion is a matter of dispute. Since many of the acute cases studied might have been expected to have a rise of temperature, irrespective of whether they had had a transfusion or not, such a rise cannot necessarily be considered significant. In the miscellaneous cases fever was often present before the transfusion was given. A rise in temperature has therefore not been included among reactions but has been analysed separately. Severe headache, rigors, vomiting, sudden pain in the head, back, or loins, jaundice, haemoglobinuria, and urticaria during or immediately following transfusion have been taken as an indication of an untoward reaction, even though of a temporary nature. It has been generally accepted in this country that blood should be warmed to approximately body temperature before administration, and that reactions are more frequent when blood is given cold. We sometimes brought the blood to body temperature by standing it in water at 40° C. for fifteen to twenty minutes before administration, it reaching a patient at a temperature of 31° C. In other instances the blood was given without warming, and reached the patient between 8° and 15° C., depending upon how long it had been standing at room temperature after removal from the ice-box. The incidence of reactions in cases receiving warmed and those receiving cold blood has been analysed in an attempt to determine whether the temperature of the blood is important.

The distribution of the 153 cases to which this study relates is given in Table I: 58 were given fresh blood and 95 stored blood.

TABLE I.—*Number of Cases Transfused by Different Means*

Type of Case	Fresh Blood			Stored Blood		
	Warm	Cold	Total	Warm	Cold	Total
Acute haemorrhage	17	3	20	20	12	32
Non-acute haemorrhage	16	6	22	20	14	34
Miscellaneous	7	5	12	10	10	20
Miscellaneous included for reaction only	3	1	4	6	3	9
Total	43	15	58	56	39	95

Clinical Improvement Shown

The degree of improvement is analysed in detail in Table II. There appears to be no significant difference in this respect between the three groups of cases given fresh and stored blood. For instance, general improvement was reported in 90% of the 20 cases of acute haemorrhage given fresh blood and in 81% of the 32 given stored blood. In the non-acute haemorrhage cases it was reported in 77% of 22 patients given fresh blood and in 71% of the 34 given stored blood—again a negligible difference. In the group of miscellaneous cases a larger proportion showing general improvement lay in the

stored blood group, but the numbers involved in the fresh blood group are so small that no stress can be laid upon this difference. Finally, adding the three type groups together shows that 104, or three-quarters of the total 140 cases, showed a general improvement in condition after transfusion, with an equal relative frequency in the fresh and stored blood groups (74% and 76%). Similarly, there is no significant difference between the numbers reporting subjective improvement (44% of patients given fresh blood and 36% of patients given stored blood).

Blood-pressure and Pulse-rate Changes

These are variable, both with fresh and with stored blood; but, considering the smallness of the group, the frequency of the different changes is observed with remarkable equality. In the patients with acute haemorrhage given fresh blood the blood pressure fell by 10 or more mm. Hg in 10%, rose by that amount in 60%, and showed no material change in 30%. In the similar cases given stored blood it fell also in 10%, rose in 58%, and showed no change in 32%. In the cases of non-acute haemorrhage the corresponding figures are: for fresh blood, 19% fell, 33% rose, and 48% remained stationary; and for stored blood, 19% fell, 31% rose, and 50% remained stationary. (Only 7 observations are available for the 12 patients in the miscellaneous group given fresh blood, so comparison here is useless.) The pulse changes are less uniform, though in each group a fall was rather more often observed with stored blood. The differences are, however, not great: of the 51 patients transfused with fresh blood the rate fell in 31%, rose in 16%, and showed no material change in 53%; of the 85 patients given stored blood it fell in 43%, rose in 12%, and showed no change in 45%. The differences are clearly very small and might easily be due to chance. (It may be noted that these totals include, both for the fresh and the stored blood groups, nearly exactly the same proportions of patients in the three type classifications—acute, non-acute, and miscellaneous—so that for broad comparative purposes their addition is justified.)

Haemoglobin Changes

For the purposes of comparison readings were taken at approximately twenty-four hours, forty-eight hours, and on the fifth to seventh day after transfusion (Table III). The numbers available are very small, and with both fresh and stored blood the degree of change observed varies widely from case to case, as would be expected. Conclusions can therefore be only tentatively drawn. It is clear that at each of the three points of time stored blood often gave quite as good a result in this respect as fresh blood. On the other hand, in both the acute and the chronic haemorrhage groups rather more patients gave a relatively poor response after stored blood than after fresh blood. For instance, if a rise of 6% or more per bottle administered be taken arbitrarily as a "good" response we get the following results. Of non-acute haemorrhage cases given fresh blood 50% (5 out of 10) gave a good response at twenty-four hours, 90% (9 out of 10) at forty-eight hours, and 92% (11 out of 12) at five to seven

TABLE II.—*Effects of Fresh and Stored Blood. Clinical Improvement*

Type of Case and Type of Blood Given	Total Cases	Average Amount of Blood Given, in Bottles	No. of Cases showing General Improvement	No. of Observations Made	No. of Cases showing Subjective Improvement	Pulse					Blood Pressure			
						Rate down 10 or more Beats per Minute	Rate up 10 or more Beats per Minute	Stationary (within 10 Beats per Minute of Original Figure)	Tension Volume Improved	Not Noted	Down 10 or more mm. Hg	Up 10 or more mm. Hg	Stationary (within 10 mm. of Original Figure)	Not Noted
Acute haemorrhage { Fresh	20	2.2	18		10	9	2	9	1		2	12	6	
{ Stored	32	1.9	26		9	19	7	5	1*	1	3	18	10	1
Non-acute haemorrhage { Fresh	22	2.1	17		12	5	4	12		1	4	7	10	1
{ Stored	34	1.9	24		16	12	2	20			5	8	13	8
Miscellaneous { Fresh	12	1.7	4	1	2	2	2	6		2		3	4	5
{ Stored	20	1.8	15		6	6	1	13	2*		5	5	10	

* This entry also appears in the group where rate is increased.

TABLE III.—*The Change in Haemoglobin Level Expressed as the Absolute Rise of Haemoglobin % Divided by the Number of Bottles of Blood Administered*

Type of Case and Type of Blood	Haemoglobin % at 24 Hours							Haemoglobin % at 48 Hours							Haemoglobin % at 5-7 Days						
	Fall	Station- ary	Rise					Fall	Station- ary	Rise					Fall	Station- ary	Rise				
			0-3	3-6	6-9	9-12	12-15 +			0-3	3-6	6-9	9-12	12-15 +			0-3	3-6	6-9	9-12	12-15
Acute haemorrhage .. { Fresh	2		2	1	3	1	1	1		2	2	1	2	2	1		1	1	2		1
{ Stored	8	1	2	4	1		1	7		2	2			1	9	1	4	3	2		
Non-acute haemorrhage { Fresh	1		1	3	2	1				1	3	5	1	1			1	5	3		3
{ Stored	3	1	2	6	6	1				2	4	6	1	2			7	7	1		2
Miscellaneous { Fresh		1	1	4	2					1	1	1				1	3	3			1
{ Stored			2	4	1	1				1	7	3	1	1	1	1	7	1			1

days. The figures for non-acute haemorrhage cases given stored blood are 37% (7 out of 19) at twenty-four hours, 60% (9 out of 15) at forty-eight hours, and 59% (10 out of 17) at five to seven days. Each proportion is slightly lower in the stored blood group. The corresponding percentages for the acute haemorrhage groups are: fresh blood 50 at each point of time, stored blood 12, 15, and 19 (again it must be noted that the basic numbers are very small). With the miscellaneous cases there is, however, no difference between fresh and stored blood, the percentages giving a "good" reaction, being 25, 50, and 20 for the former and 25, 38, and 18 for the latter.

With the number of observations available the differences between the fresh and the stored blood cases in the acute and non-acute haemorrhage groups are not, according to the statistical test, more than might easily occur by chance. The appropriate conclusion therefore seems to be that in many cases stored blood will certainly give a rise in the haemoglobin level as great as that produced in comparable cases by fresh blood; but more extensive figures than those available here will be necessary before it can be said whether it is as effective in all cases. Further, it may again be stressed that, especially in acute haemorrhage, a fall in haemoglobin may be due to dilution associated with clinical improvement. Therefore too much importance should not be attached to the divergent readings found in the small groups of acute cases given fresh and stored blood. Finally, 10 cases were available which had been given transfusions of equal amounts of fresh and stored blood, and in which there were no gross complicating factors. In 1 the haemoglobin response to fresh and stored blood was the same; in 6 there was a greater rise in haemoglobin with fresh blood; while in 3 the response to stored blood was the greater (Table IV).

TABLE IV.—*Patients receiving Transfusions of both Fresh and Stored Blood*

Case No.*	Fresh Blood			Interval (days)	Stored Blood	
	Hb Change†	Days after	Reaction		Hb Change	Reaction
1 A	7	7	0	7	7	0
2 B	7	7	0	8	13	Slight
3 A				7	6	Slight
4 B	4	7	Slight	7	—4	0
5 C	4		0	8	7	0
6 D	9	7	0			
7 A	7	24 hours	0	6	4	0
8 B				7	11	0
9 A	10	7	0			
10 B	9	24 hours	0	7	5	0
11 A				7	1	0
12 B	5	7	0	6	4	+
13 A	10	48 hours	0			
14 B	5	24 hours	0	24 hours	—7	0

* Letters A, B, C, D indicate the number and order of transfusions given to any one case.

† Expressed as the absolute rise of haemoglobin % divided by the number of bottles of blood administered.

Reactions Observed

The number of reactions observed with fresh and stored blood is given in Table V: even a mild rigor or serious head-

ache has been included. In no case was a really serious reaction with jaundice and haemoglobinuria noted. Two cases of transient jaundice occurred in patients with advanced carcinoma and one in a patient who had had a hysterectomy three days previously.

The proportions of patients showing reactions in the different groups are given in Tables V and VI. Division into sub-

TABLE V.—*Analysis of Reactions with Fresh and Stored Blood*

Type of Case and Type of Blood Given	Total Cases	Total Cases with Reactions	Rigor +	Rigor ++	Rigor +++	Vomit	Pain in Back or Head	Jaundice	Urticaria
Acute haemorrhage :									
Fresh, warm ..	17	1	1						
" cold ..	3	0							
Stored, warm ..	20	4	3					1*	
" cold ..	12	2	1		1				
Non-acute haemorrhage :									
Fresh, warm ..	16	1							1
" cold ..	6	1				1	1		
Stored, warm ..	20	3	2		1	1	2		
" cold ..	14	8	1	2	2				4
Miscellaneous :									
Fresh, warm ..	7	2		2	1				
" cold ..	5	1		1	1				
Stored, warm ..	10	3	2	1	1				
" cold ..	10	5	2	2		1	1	2*	1
Miscellaneous reactions only :									
Fresh, warm ..	3	0							
" cold ..	1	0							
Stored, warm ..	6	3	1	2	1				
" cold ..	3	3	1	1					

* Slight transitory.

groups by type of case and type of transfusion—fresh, stored, warm, or cold—results, of course, in very small numbers, so that the levels of the percentages must be interpreted cautiously. It is noticeable, however, that in each of the six comparisons between fresh and stored blood there is a higher rate of reactions in the latter. As the relative numbers of cases of the different groups treated with fresh and stored blood are approximately the same there is no fallacy in comparing the rates based upon the totals. They are as follows: With fresh warm blood the reaction rate was 9%, and with stored warm blood 23%; with fresh cold blood the rate was 13%, and with stored cold blood 46%. Taken alone neither difference is more than might be expected to occur by chance in such small samples, but as this difference was consistently observed in all the groups studied by type of case the excess in the stored blood groups is statistically significant. It will be seen that 31 reactions were recorded in the stored blood groups: if in each of the six subgroups in Table VI the rates for the corresponding fresh blood groups had prevailed there should have been 10. On the other hand, whether warming the blood is of advantage it is, on the available figures, difficult to say. With fresh blood there is an insignificant difference between the two reaction rates in the totals (9% and 13%) and no pronounced difference in any of the small subgroups. With stored blood there is a considerable difference in the totals (23% and 46%), to the disadvantage of cold blood; this is statistically significant. In one of the three subgroups (the acute haemorrhages) there is, however, no material difference. There is an indication, it may be concluded, that warming the blood is likely to reduce the number of reactions, but on these figures it is hardly more than an indication. (It may be noted that a consider-

TABLE VI.—Total Reactions in Relation to Type of Blood

Type of Case and Type of Blood	Cases	Reactions	Per cent.
Acute haemorrhage	Fresh, warm	17	1
	" cold	3	0
	Stored, warm	20	4
Non-acute haemorrhage	" cold	12	2
	Fresh, warm	16	1
	" cold	6	1
Miscellaneous	Stored, warm	20	3
	" cold	14	8
	Fresh, warm	10	2
Total	" cold	6	1
	Stored, warm	16	6
	" cold	13	8
Total	Fresh, warm	43	4
	" cold	15	2
	Stored, warm	56	13
	" cold	39	18
			46

ably larger proportion of the patients given stored blood had it cold: the addition of the warm and cold groups for comparison of the reactions produced by fresh and stored bloods would therefore be open to objection, and has been avoided.) If attention be confined to severe reactions—i.e., patients who had rigors ++ or rigors +++ (Table VII)—clearly no appre-

TABLE VII.—Severe Reactions (Rigors ++, Rigors +++) in Relation to Type of Blood

Type of Blood	Total Cases	No. of Reactions
Fresh, warm	43	2
" cold	15	1
Stored, warm	56	3
" cold	39	9

ciable difference is revealed between fresh warm blood, fresh cold blood, and warm stored blood. The reaction rates are all low—namely, 4.7, 6.7, and 5.4%. The only high rate is with stored blood administered cold—namely, 23.1%—and the experience is too small for much confidence to be placed in this observation.

It may be concluded, therefore, that severe reactions were no more frequent with warm stored blood than with warm fresh blood. Cold stored blood showed to some disadvantage, but further observations are needed to substantiate the case. Very minor reactions were, however, more often observed with stored blood, warm or cold, than with the corresponding fresh blood. There is no evidence that these reactions were the result of other differences between the groups of patients. The patients were fairly equally divided into the different type groups, their age and sex distribution were very similar, the amount of blood given was equivalent, and closely similar proportions were said to be improving, stationary, or deteriorating in clinical condition at the time of transfusion. The only difference observed was that in the group of patients given stored cold blood rather more were "group-to-group" transfusions than in the other groups. This might have been expected to reduce their reaction rate relatively. In the group of 10 patients who had transfusions of both fresh and stored blood at different dates two had a slight reaction following stored blood but not following fresh blood, while one had slight reactions following both fresh and stored blood.

Temperature Rise

An attempt was made to analyse the changes in temperature noted, since a rise is usually thought to indicate an unfavourable reaction to transfusion. Owing to complicating factors, such as pre-existent sepsis, associated operative intervention, or internal haemorrhage, the results are not easy to interpret except in chronic haemorrhage. In these cases observation of temperature was made in 15 instances with warm fresh blood and in 16 with warm stored blood (Table VIII). There was some rise of temperature in 7 patients in the former group and in 8 in the latter. A rise of 3° F. or more was observed in 3 instances in each group. Of 6 similar patients to whom cold fresh blood was given there was a temperature rise in 3, and in 14 given cold stored blood there was a rise in 7. (Relatively rather more instances of a considerable rise occurred in the latter group, but the numbers are too small

TABLE VIII.—Observations of Temperatures following Transfusion (up to 12 Hours after End of Transfusion)

Type of Case and Type of Blood	Total Cases	Rise by					Stationary	Not Recorded	Associated Reactions
		1° F.	2° F.	3° F.	4° F.	5° F.			
Acute haemorrhage*									
Fresh, warm	17	1	1	2	0	0	8	5	1
" cold	3	0	0	1	0	0	2	0	0
Stored, warm	20	3	2	1	0	0	8	6	4
" cold	12	0	2	1	1	0	3	5	2
Non-acute haemorrhage:									
Fresh, warm	16	2	2	1	0	2	8(c)	1	1
" cold	6	1	2	0	0	0	3	0	1
Stored, warm	20	3	2	2	0	1	8(b)	4(c)	3
" cold	14	2	0	5	0	0	7	0	8
Miscellaneous:									
Fresh, warm	7	0	1	0	0	1	4	1	2
" cold	5	0	1†	0	0	0	4	0	1
Stored, warm	10	0	3†	1†	0	0	4	2	3
" cold	10	3†	0	0	1	1†	5	0	5

* In every case where there was an appreciable rise of temperature this might have been accounted for by the patient's original condition—e.g., haematemesis and post-operative conditions.

† Pyrexial beforehand.

(a) Some other cause for pyrexia.

(b) Temperature recorded immediately afterwards but not again during 12 hours following.

(c) Temperature taken during transfusion but not in 12 hours following.

for any stress to be laid upon this.) Accepting a rise of any magnitude as evidence of a reaction, there is clearly no difference between the four groups of patients with non-acute haemorrhage. There appears to be equally little difference between the cases of acute haemorrhage in which warm fresh or warm stored blood was administered. In the former there was a rise in 4 out of 12 cases, and in the latter 6 out of 14. The numbers of observations in the groups given cold blood are too few to be informative, as are also those relating to the miscellaneous cases (Table VIII). In several instances the increased temperatures might well be due to other factors, and no certain conclusions can be drawn.

Relation of Quantity of Blood given to Reaction Rate

It was thought that the reaction rate might be related to the amount of blood administered or to the rate of administration. An analysis was therefore made of the data available on both these points. The figures of reactions observed in relation to the amount of blood administered are given in Table IX. The numbers in each of the sub-

TABLE IX.—Reactions related to Number of Bottles Administered

Type of Case and Type of Blood	Total Cases	R	1 Bottle		2 Bottles		3 Bottles		4 Bottles	
			Cases	R.	Cases	R.	Cases	R.	Cases	R.
Acute haemorrhage:										
Fresh, warm	17	1	4	0	10	1	1	0	2	0
" cold	3	0	0	0	3	0	0	0	0	0
Stored, warm	20	4	10	3	6	1	2	0	2	0
" cold	12	2	4	0	7	2	1	0	0	0
Non-acute haemorrhage:										
Fresh, warm	16	1	6	1	4	0	4	0	2	0
" cold	6	1	0	0	4	1	2	0	0	0
Stored, warm	20	3	3	0	13	2	2	0	2	1
" cold	14	8	2	1	12	7	0	0	0	0
Miscellaneous:										
Fresh, warm	7	2	2	0	4	2	1	0	0	0
" cold	5	1	2	0	3	1	0	0	0	0
Stored, warm	10	3	3	0	6	2	0	0	1	1
" cold	10	5	4	2	5	2	0	0	1	1

R = Reactions.

groups of this table are so very small that some method of summation is essential to discover whether the amount of blood administered bears any relation to the number of reactions recorded. For instance, in the acute haemorrhage cases given warm stored blood 4 of the 20 patients had some kind of reaction. If the amount of blood given does not influence the chance of a reaction occurring, then, with a sufficiently large number of observations, one-fifth of the patients given one pint would be expected

to show a reaction, one-fifth of those given two pints, and so on. The figure for the total would, in other words, be derived equally from each of the groups given different amounts. Therefore in the instance quoted the number of reactions expected would be one-fifth of the 4 given either three or four pints, or 2, 1.2, and 0.8 "patients" with reactions. Actually the numbers of patients with reactions in these subgroups were 3, 1, and 0. The comparison of these observed numbers with those expected on the assumption that the amount of blood given does not influence the reaction rate at all cannot unfortunately show whether the assumption is likely to be false or not. The experience is far too small. It is, however, possible to get the corresponding expected numbers of reactions on the same hypothesis for each of the groups of Table IXA—for the six different groups defined by diagnosis and type of blood administered. The addition of all these small expected numbers, none of which is large enough to be informative by itself, is then legitimate and will give the total number of reactions that might have been expected to occur in the patients given different amounts of blood, using throughout the hypothesis that the amount of blood given is not a factor in the occurrence of reactions. If that hypothesis is false then the total observed numbers of reactions in the patients given one pint, two, three, or four pints will differ significantly from the numbers calculated on the basis of it, as follows:

TABLE IXA

	1 Bottle	2 Bottles	3 or 4 Bottles	Total
Total No. of cases given different amounts of blood	40	77	23	140
Observed No. of reactions	7	21	3	31
Expected No. of reactions on assumption of no connexion between amount of blood given and occurrence of reactions	9	19	3	31

The observed distribution of reactions differs insignificantly from the expected, and it may be concluded that these observations reveal no association between the amount of blood given and the risk of a reaction occurring.

Relation of Rate of Administration to Reaction Rate

A similar calculation based on figures shown in Table X, where reactions are related to rate of administration per bottle, gives the following results (Table XA) (excluding one unspecified case). The sequence of such differences as are observed with these small numbers does not suggest any close association between rate of administration and occurrence of reactions. It must, however, be stressed that the experience is really insufficient to give decisive answers to these questions.

TABLE X.—Reactions Related to Rate of Administration per Bottle

Type of Case and Type of Blood		Total Cases	R	Rate of Administration in Hours																Rate not Recorded	
				0-1		1-1½		1½-1		1-1½		1½-2		2-3		Over 3					
				No.	R	No.	R	No.	R	No.	R	No.	R	No.	R	No.	R				
Acute haemorrhage	Fresh, warm	17	1	2	1	5	0	5	0	3	0	0		1	0	1	0				
	" cold..	3	0	0	0	0	0	0	0	3	0	0	0	1	0	0	0				
	Stored, warm	20	4	2	0	4	1	5	2	3	0	1	0	2	0	3	1				
	" cold	12	2	0	0	0	0	3	1	4	1	1	0	2	0	2	0				
Chronic haemorrhage	Fresh, warm	16	1	1	0	4	0	5	1	2	0	0	0	2	0	2	0				
	" cold..	6	1	1	0	0	0	1	0	1	0	1	1	2	0	0	0				
	Stored, warm	20	3	2	1	2	0	3	1	2	0	3	0	2	0	6	1				
	" cold	14	8	0	0	0	0	6	5	4	2	1	1	2	0	1	0				
Miscellaneous	Fresh, warm	7	2	1	0	1	0	0	1	0	1	0	1	0	0	2	1				
	" cold..	5	1	1	0	0	0	0	1	1	1	0	2	0	0	0	0				
	Stored, warm	10	3	0	0	2	0	1	1	0	1	1	2	0	4	1					
	" cold	10	5	0	0	1	0	4	3	2	1	2	0	1	1	0	0				

R = Reactions.

TABLE XA

	Under ½ hour	½-1 hour	1-1½ hours	1½-2 hours	2 hours or more	Total
Total No. of cases receiving blood at given rates	29	33	26	12	39	139
Observed No. of reactions	3	14	5	3	5	30
Expected No. of reactions on assumption of no connexion between rate of administration and occurrence of reactions	4	9	6	3	8	30

Summary and Conclusions

A study has been made of the effect of fresh and stored blood in cases in which the clinicians in charge considered that blood transfusion was indicated.

The six clinical observers attached to the four blood depots who were engaged in this investigation are unanimously agreed from a consideration of the clinical results that stored blood is as good as fresh blood in the treatment of acute haemorrhage. They are not so certain that stored blood is as valuable as fresh blood in the treatment of non-acute haemorrhage, but at the same time the available data present no evidence that stored blood is in fact of less value to such cases.

Analysis of the figures regarding gain in haemoglobin shows that in many cases stored blood will certainly give a rise in haemoglobin as great as that produced by fresh blood, but on the average in both the acute and non-acute haemorrhage cases the gain was greater with fresh than with stored blood. (In the miscellaneous cases no difference in the average gain was noted.) More extensive figures than those available here will be necessary before any final conclusion can be reached.

Mild reactions, excluding rises in temperature, occurred more commonly following stored than following fresh blood. The numbers of severe rigors observed after the use of warm fresh and stored blood were practically identical (4.7% and 5.4%).

In a total of 153 cases analysed in this investigation no severe haemolytic reactions were found and no fatal result attributable to transfusion occurred.

With regard to rise in temperature following transfusion, cases of non-acute haemorrhage are the most informative and, though the scale of the experience is small, these reveal no material difference between fresh and stored blood administered either warm or cold.

From a study of the occurrence of reactions it is considered that there is an advantage in warming the blood to approximately 37° C. before administration.

Analysis of the figures available reveals no association between either the amount of blood given and the risk

of reactions or the rate of administration and the risk of reactions. The experience is, however, insufficient to give a decisive answer.

The clinical observations were made on behalf of the Medical Research Council by Drs. Helen Brown, A. C. Dornhorst, G. W. Hayward, D. H. G. MacQuaide, P. L. Mollison, N. Whittaker. The observers were well aware that in the literature similar observations have been recorded on many of the points raised in the present report; they have, however, made no attempt to correlate these with their own findings. They wish to express their thanks to the staffs of hospitals in the London Sectors who placed clinical material at their disposal, and to Dr. Bradford Hill for his help in the statistical analysis of the data collected.

HYPERTONIC SODIUM SULPHATE: PRACTICAL APPLICATIONS

BY

J. C. LYTH, M.B., B.S.Lond.

My experience of the use of sodium sulphate as a hypertonic agent for wounds was first published in 1935.¹ In 1939, with war imminent, I appealed² for a trial of this method. In February, 1940,³ I recorded the results of this treatment alone in over 1,000 consecutive cases, with experiments and suggestions to explain its success.

It is now generally admitted that bactericidal antiseptics do more harm to the body tissues and leucocytes than they do to invading germs. The need is urgent for a ready and effective way of treating large numbers of infected wounds. I feel, therefore, that the following brief summary of the practical applications of this method may not be out of place.

Details of the Method

The Principle.—The surface of an infected wound is kept in contact with material soaked (and kept soaked) with the strongest tolerable solution of the optimal osmotic and diffusive agent available. For this purpose no other hypertonic agent hitherto used approaches sodium sulphate in efficiency; but other relatively feeble agents in use, with varying degrees of appreciation of the true nature of their reactions, are Epsom salts, common salt, Dakin's solution, urea, insulin, partially evaporated pus, saliva, and sweat.

The Solution.—To make a saturated solution of sodium sulphate (Glauber's salt) place a quantity (say 2 lb.) of the salt in a Winchester, fill up with cold reasonably sterile water, and shake. Add more water as the solution is used, so long as undissolved crystals remain. Do not dilute.

The Medium.—This may be of any material which will hold the solution—plain lint, or cotton-wool if cavities are deep and irregular. Loose particles of wool will not adhere.

The Covering.—This should consist of elastoplast wherever practicable; otherwise oiled silk or grease-proof paper and bandage will do. Clean shallow fresh wounds will heal under a bandage alone.

Method of Application: (a) *Fresh Clean Wounds, Non-penetrating.*—Do not wash with water or antiseptic. Bathe gently with the solution. Soak the material in the solution, apply to the wound, and cover completely with elastoplast. Leave the dressing twenty-four hours or longer if there is no pain, fever, or discharge. Before removing, soak the material with the solution. If no suppuration or inflammation occurs, repeat the dressing and leave for a further period; if septic, treat as below.

(b) *Penetrating, Dirty, or Already Septic Wounds.*—Remove obvious foreign bodies, but avoid disturbing exposed tissues—particles of dirt will work out later. Bathe with solution and apply dressing and elastoplast as above. Avoid unnecessary

changes of dressing, but *apply more solution at frequent intervals* (hourly if necessary) by turning back a corner of the covering, or through an elastoplast-covered window.

Never hesitate to apply this treatment, however deep the wound or minute the breach of surface. Two important accessories are, first, elevation by means of a sling for the arm and bed or a foot-rest for the leg; secondly, immobilization, using splinting or plaster when necessary.

Difficulties that Arise

Types of Injury.—In cuts requiring suture primary healing is invariable if dressing soaked in solution is applied over the stitches. If foreign bodies cannot be removed, treat as for penetrating wounds: septic inflammation may be prevented until removal later. Septic inflammation after tannic acid treatment of burns and scalds is immediately relieved, and large burns heal well under continuous application. No hesitation need be felt in using sulphonamide chemotherapy as well. Since the series published (Lyth, 1940) I have treated numerous cases with sulphonamides and with sulphapyridine along with this method without ill effect. Exception may be made in jaw injuries (see below).

Localities.—In the case of orifices and cavities (for example, nostril, external auditory meatus, axilla, interdigital hollows of hand or foot, orbits) pack with wool kept soaked with solution. The cornea tolerates the saturated solution, which can also be used in an eye bath. A simple way of covering the fingers and toes with elastoplast is to run a two-inch strip from base over tip and down to base, press the sides together, and cut off superfluous edges, making an adhesive finger-stall. For maxillo-facial injuries treat an external penetrating wound as above. Where the mouth is affected a specialist surgeon told me he is trying to arrange a form of irrigation which will avoid the swallowing of solution. I doubt whether sulphonamide drugs could be used concomitantly in jaw injuries.

Conclusion

First-aid posts and casualty clearing hospitals throughout Britain are now going into action; but it is not too late to equip them with a wound dressing far superior in results to any hitherto used, and one which is safe, easy to apply by semi-trained personnel, cheap, and ready to hand. There need be little or no suppuration of the grossly infected wounds we shall see; and débridement can be reduced to reasonable and practical limits. And once more: *No other hypertonic agent used approaches sodium sulphate in efficiency.*

REFERENCES

- ¹ Lyth, J. C. (1935). *British Medical Journal*, 2, 903.
- ² — (1939). *Ibid.*, 89.
- ³ — (1940). *Lancet*, 1, 216.

E. L. Kendig, jun., and T. W. Kirmsl (*Arch. Pediat.*, 1940, 57, 1) state that though typhoid fever has declined both in morbidity and mortality among adults in the United States during the past few decades, the mortality among infants and children remains relatively high. Ninety-five cases of typhoid fever were treated in the wards of the Children's Medical Services of Bellevue Hospital, New York, from 1924 to 1938, during which time over 30,000 patients were admitted. Apart from an epidemic in Manhattan in 1924-5 only sporadic cases were admitted; forty-one were girls and fifty-four boys. The ages ranged from 14 months to 12 years. The sources of infection were as follows: contact with known cases 28; swimming in water probably polluted, 10; visits to resorts 5; raw milk and oysters 2 each; ice-cream sticks and water supply 1 case each; other foods 3; source undetermined 43. There were 7 deaths, which were due to gastro-intestinal haemorrhage in 4, and pneumonia, myocarditis, and meningitis 1 case each.