HAEMOLYSIS OCCURRING DURING PRESSURE TRANSFUSION OF STORED BLOOD

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Surgery today frequently necessitates the use of rapid transfusions of blood. Transfusion by gravity will not suffice when the rate of transfusion must exceed ± 20 - 40 ml./min. Various devices[1,2] have been designed to speed up transfusion. The method chosen is usually dependent on the type of blood container and the nature of the administration set.

One of the most commonly used methods employs an administration set incorporating a pressure pump (Fig. 1). The filter is contained in a chamber which is compressible by hand, the inlet at the top being occluded intermittently by a plastic ball valve. The manual squeezing provides the necessary increase in pressure required to speed up the transfusion. This device, where the filter and pump are situated in one chamber, has been shown to cause the most haemolysis in comparison with other pumps or where the pump chamber is separate from the filter.[1] It has also been demonstrated that the higher the resistance to transfusion, the greater the haemolysis.[2] If the mechanical fragility of the red cell increases then greater haemolysis will occur under the same circumstances.[2]

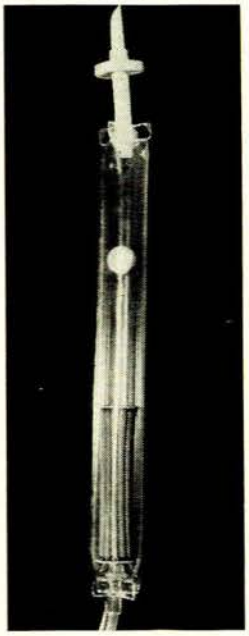

Fig. 1. Transfusion set with combined pressure pump and filter as used in experiments 1, 2 and 3.

The increasing practice of warming blood before transfusion raised the question of whether the mechanical fragility of the red cell was increased by warming. In most methods of warming described, the blood is warmed only after passage through the filter.[3-7] In radio frequency (RF) induction heating recently described,[8] the blood is warmed in the container and only warm blood passes through the filter. It was thus decided to ascertain whether RF heated blood, subjected to pressure transfusion through the plastic filter pump administration set, would show a greater degree of haemolysis than cold blood.

The following investigation was undertaken, divided into 4 experiments, to try and elucidate the problem.

Experiment 1

Twenty units of acid citrate dextrose (ACD) blood from malarial donors were paired according to storage age, 10 pairs thus obtained, with each member of a pair having the same storage age as its partner. This was done in an effort to obtain pairs of blood samples comparable in the amount of 'damage' sustained during storage.

One bottle of each pair was warmed by a RF induction heater with an automatic temperature controlling device,[9] to end temperatures varying between 32° - 36°C. The other bottle was left at room temperature for varying lengths of time, as it was not realized at first what an important role temperature of the transfused blood played. Each bottle of blood was then pressure transfused through a clean standard filter pump set (Fig. 1) against the same resistance. The resistance was provided at the end of the drip set by a No. 15 SWG Luer needle with a 13¾ cm. length of polythene tubing, gauge No. 3 (bore 1·5 mm.), attached to its point. (The pressures required to produce a rate of transfusion of 100 ml. of blood per minute were measured, under the same conditions, on a mercury manometer. For cold blood the pressure exerted with each manual squeeze ranged from 140 - 160 mm.Hg; for warm blood 80 - 120 mm.Hg.)

In this experiment, the rate of transfusion was kept as constant as possible for each unit in a pair, varying from pair to pair to between 90 - 180 ml./min.

Samples of blood were taken as atraumatically as possible, centrifuged, and haemoglobin values estimated by the method of Crosby and Furth.[10] The first sample from each bottle, referred to as the control value both for warmed and 'cold' blood, was obtained after gentle mixing through a clean, dry, No. 15 SWG needle, with a clean, dry, wide-bore polythene extension. Free flow by gravity was employed, the first 5 - 6 ml. were discarded and the sample collected into a clean, dry test tube, avoiding frothing. Immediately after warming, a second sample was obtained from the warm bottle in exactly the same way—this sample is obviously omitted where the blood was transfused without warming. A further 2 samples were taken after approximately 50% and 75% of the bottle had been pressure transfused. These 2 samples were obtained by removing the needle and the polythene extension from the end of the drip set and allowing 5 ml. to run by gravity into a clean, dry test tube. The samples collected thus consisted of blood that had already passed through the filter.

Experiment 2

This consisted of 14 units of blood, paired according to storage age. Each member of a pair was cross-matched against its partner. The 2 units were then mixed, allowed to stand for 24 hours in the blood bank refrigerator and then divided into 2 equal units of presumably identical composition.

Transfusion and sampling procedure was the same as in experiment 1 except that care was taken to keep the cold units as close to storage temperature as possible.

Experiment 3

Seven units of blood which were paired according to storage age, were transfused and sampled as in experiment 1, except that a high resistance was provided by doubling the length of the polythene tubing. The last unit was warmed and transfused similarly.

Experiment 4

Ten units of time-expired ACD blood were prepared, as in experiment 2. The aliquots were then transferred to plastic blood bags. Pressure transfusion was achieved by using a pressure infusor (Fig. 2). Pressures were kept constant at 300 mm.Hg for

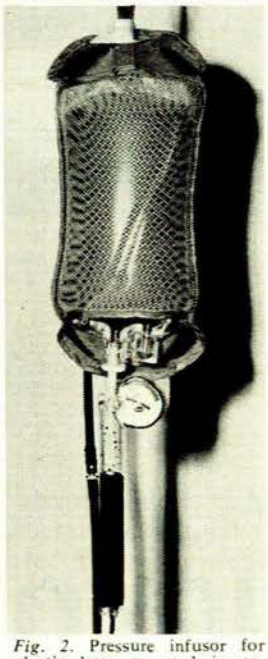

Fig. 2. Pressure infusor for plastic bags as used in experiment 4.

both warm and cold blood. The procedure of warming and sampling was the same as the preceding groups.

RESULTS

Experiment 1

A rise above the initial value of the plasma haemoglobin occurred during pressure transfusion of both warm and cold blood as expected. The mean rise in the warm blood was 18 mg./100 ml., compared with a mean rise of 41 mg./100 ml. in the cold blood. This difference in mean rises was not statistically significant, however. Some of the cold blood pressure transfused showed very small rises in plasma haemoglobin values (Table I). The explanation for this is, as mentioned earlier, that the cold blood remained at room temperature for considerable lengths of time, some of the cold blood reaching a temperature of 18 - 20°C before being submitted to pressure transfusion. The reduction in viscosity brought about by this rise in temperature facilitated transfusion considerably, hence the discrepancies. This error was corrected in the second experiment.

Experiment 2

In this group of units consisting of paired blood of identical composition, a similar rise in plasma haemoglobin values occurred during pressure transfusion (Table II). The mean rise above the control value of plasma haemoglobin in the RF warmed blood was 8 mg./100 ml. compared with a mean rise in the cold blood of 56 mg./100 ml. This difference was statistically significant ($P < 0.05$).

Experiment 3

The blood transfused against a high resistance showed marked increase in plasma haemoglobin values (Table III). The mean rise above the control value of plasma haemoglobin was 213 mg./100 ml. of blood in the cold blood, compared to warm blood which showed a mean rise of 68 mg./100 ml. of plasma haemoglobin. The difference was statistically significant ($P < 0.02$).

Experiment 4

Here, the plasma haemoglobin values showed very little elevation after pressure transfusion. This method of transfusion by external compression of the bag, i.e. having the pump chamber separate from the filter chamber is thus far less traumatic to the erythrocyte in spite of the high pressures applied. The mean rise in plasma haemoglobin

TABLE I. RISES IN PLASMA Hb. VALUES IN COLD AND WARM BLOOD UNDER PRESSURE TRANSFUSION

Storage age of blood in days	*Plasma haemoglobin values in mg./100 ml.*					*Rate of transfusion (ml./min.)*
	Warm blood			*Cold blood*		
	Sample No.	*Hb. value*	*Rise above control*	*Hb. value*	*Rise above control*	
	1	lost		10		
4	2	12	7	—	18	120
	3	15		23		
	4	19		28		
	1	11		30		
2	2	11	7	—	80	120
	3	13		80		
	4	18		110		
	1	17		11		
2	2	20	17	—	15	100
	3	21		16		
	4	34		26		
	1	31		34		
9	2	lost	38	—	132	140
	3	58		139		
	4	69		166		
	1	20		27		
9	2	21	4	—	5	160
	3	24		31		
	4	23		33		
	1	43		17		
4	2	67	37	—	37	140
	3	72		25		
	4	80		54		
	1	45		34		
6	2	47	7	—	37	160
	3	52		49		
	4	52		71		
	1	145		38		
13	2	150	22	—	34	120
	3	155		78		
	4	167		82		
	1	38		84		
12	2	41	10	—	14	180
	3	48		lost		
	4	45		98		
	1	68		66		
12	2	73	27	—	178*	100
	3	88		144		
	4	95		244		

*See text.

TABLE II. RISE IN PLASMA Hb VALUES IN COLD AND WARMED BLOOD OF IDENTICAL COMPOSITION

Storage age of blood in days	*Plasma haemoglobin values in mg./100 ml.*					*Rate of transfusion (ml./min.)*
	Warm blood			*Cold blood*		
	Sample No.	*Hb. value*	*Rise above control*	*Hb. value*	*Rise above control*	
6	1	26	1	23		
	2	27		—	25	180
	3	27		24		
	4	26		48		
6	1	42	19	37	53	170
	2	57		—		
	3	61		59		
	4	61		90		
6	1	40	6	47	54	170
	2	43		—		
	3	44		80		
	4	46		101		
3	1	20	6	19	351*	140
	2	23		—		
	3	26		129		
	4	26		370		
4	1	24	5	24	65	140
	2	24		—		
	3	29		79		
	4	27		89		
3	1	34	12	33	141	140
	2	36		—		
	3	43		100		
	4	46		174		
3	1	20	6	21	12	120
	2	22		—		
	3	26		24		
	4	25		33		

*See text.

TABLE III. PRESSURE TRANSFUSION AGAINST HIGH RESISTANCE

Storage age of blood in days	*Plasma haemoglobin values in mg./100 ml.*						*Rate of transfusion (ml./min.)*
	Warm blood			*Cold blood*			
	Sample No.	*Hb. values*	*Rise above control*	*Sample No.*	*Hb. values*	*Rise above control*	
5	1	21	13	1	30	258	120
	2	23		2	230		
	3	28					
	4	34		3	288		
9	1	66		1	28		
	2	68		2	135		
	3	132	99			214	100
	4	176		3	242		
	1	70		1	44		
10	2	77	92	2	177	176	120
	3	104					
	4	162		3	220		
	1	56					
15	2	57	354*	—	—	—	140
	3	177					
	4	410					

*See text.

in warm and cold blood were 16·8 mg./100 ml. and 8·5 mg./100 ml. respectively (Table IV). This difference was not significant. The rise in plasma haemoglobin occurring after warming is due to the fact that the RF heater had not been modified for safe warming of the plastic bags, but for experimental purposes, it was felt to be adequate.

Comparing the rates of transfusion obtained here for the same pressure applied, one finds quite a marked difference. A mean transfusion rate of 216 ml./min. in warm blood and a mean rate of 156 ml./min. in cold being obtained at 300 mm.Hg pressure. This difference is statistically significant ($P < 0.01$).

In calculating the mean values and assessing the statistical significance of the results, all values marked with an asterisk in the tables were omitted, as these values referred to instances where the filter was thought to be defective. In experiment 2 the value of the corresponding unit was also omitted from the statistical calculations.

There appeared to be no correlation between the storage age of the blood and the amount of haemolysis occurring, both to cold and warm blood. In the warmed blood there was a correlation ($R = +0.8656$) between rate of transfusion and haemolysis. This was not reproducible in the cold blood series (this included results from experiments

TABLE IV. RISE IN PLASMA Hb. VALUES IN ALIQUOTS OF BLOOD PRESSURE TRANSFUSED IN PLASTIC BAGS

Plasma haemoglobin values in mg./100 ml.

Warm blood						*Cold blood*				
				Hb. values mg./100 ml.					*Hb. values mg./100 ml.*	
Age of blood (days)	*Rate of trans. (ml./min.)*	*Pressure employed (mm. Hg.)*	*No.*	*Absolute values*	*Rise above control*	*Rate of trans. (ml./min.)*	*Pressure employed (mm. Hg.)*	*No.*	*Absolute values*	*Rise above control*
33	220	300	1	234·4	13·8	160	300	1	208·5	1·3
			2	244·8				2	205·5	
			3	244·8				3	206·8	
			4	248·2						
33	220	300	1	331·0	27·6	150	300	1	293·1	13·7
			2	341·3				2	293·1	
			3	344·8				3	306·8	
			4	358·6						
34	200	300	1	351·7	20·7	140	300	1	351·7	13·8
			2	372·4				2	351·7	
			3	386·2				3	365·5	
			4	372·4						
33½	220	300	1	300·0	15·2	170	300	1	262·0	6·9
			2	310·3				2	265·5	
			3	310·3				3	268·9	
			4	315·2						
33	220	300	1	358·6	6·9	160	300	1	324·1	6·9
			2	372·4				2	324·1	
			3	372·4				3	331·0	
			4	368·5						

1 and 2). The reason again is probably that some of the 'cold' blood had attained room temperature during the course of experiment 1, thus the lowered viscosity facilitated transfusion with less pressure required for faster rates of transfusion.

Fig. 3 is a composite graph showing the mean rises in plasma haemoglobin values in warm and cold blood. The

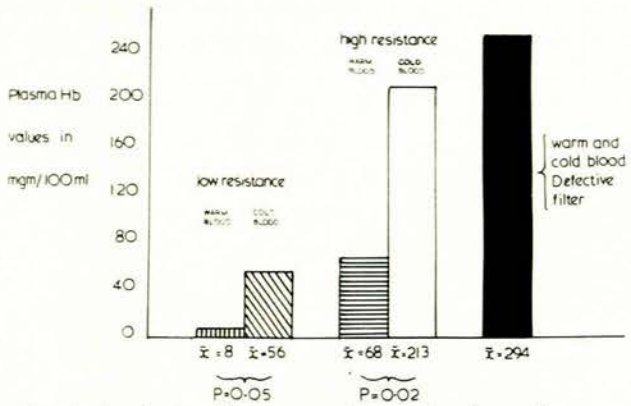

Fig. 3. Graph showing comparative rise in plasma haemoglobin values during pressure transfusion. O = control level in all cases.

column labelled 'defective filter' is derived from the values marked with asterisks in Tables I and II. The mean rise above control values was 294 mg. of Hb./100 ml.

DISCUSSION

From these results one may conclude that the mechanical fragility of the red cells, as tested by pressure transfusion in experiments 2, 3 and 4 is not increased by RF warming. It appears advantageous to warm the blood before transfusion when the filter pump administration set is used for pressure transfusion to avoid excessive haemolysis.

The end values of plasma haemoglobin obtained in some of the experiments (Tables I, II and III) are alarmingly high. In a rapid massive transfusion this may possibly lead to levels of plasma haemoglobin exceeding the clearance capacity of the haptoglobins, other proteins and the reticulo-endothelial system. This may lead to haemoglobinuria which, under certain circumstances, e.g. shock, dehydration and renal anoxia, may predispose to renal shutdown and renal damage.

Excessive trauma to the blood during pressure transfusion is easily avoided. Unfortunately, very little stress is placed on this aspect of resuscitation.

The factors leading to excessive haemolysis during pressure transfusion fall into 3 big groups:

1. *The Type of Pump Used*

Where the pump and the filter are incorporated in 1 chamber more haemolysis occurs than with the roller type pump, where the pump and filter are separate, as in plastic bags, or where air is introduced into the container under pressure.[2] (The last method, however, carries the serious risk of air embolism and is not advocated.)

2. *Increased Resistance to Transfusion*

Increased resistance to transfusion may occur for a variety of reasons:

(*a*) Increased length of the drip tubing. With the emphasis on hypothermia as a major cause of cardiac arrest during massive transfusion,[7] a variety of blood warmers has been described.[2-5] With one exception, the RF heater,[5] all consist of an extension of the drip tubing up to lengths of 24 - 30 ft. immersed in some form of heat exchanger, the warming thus occurring only after the blood has passed through the filter at storage temperature 4 - 10°C. This extension of tubing, according to Poiseuille's Law, leads to a decreased flow rate for the same pressure difference if compared with a drip set of standard length. Greater pressure is thus needed to allow rapid rates of transfusion with a resultant sharp increase in trauma to the cells.

(*b*) Internal diameter of the needle is of great importance in determining the resistance to flow. It appears self-evident that a needle with the largest internal diameter and shortest length possible should always be used. The argument may be raised

that in collapsed patients, one is not always able to insert large-size needles. However, here more than one intravenous route may be employed, obviating the need for pressure transfusion to some extent or a larger size needle or cannula should be inserted as soon as possible. A cut-down with a large diameter cannula inserted may prove even more satisfactory.

In operative cases, where one is anticipating a massive fast transfusion, more than one intravenous drip channel should be established to avoid excessive pressure transfusion.

(*c*) The vein selected for the venipuncture should be as large as possible. Venospasm must be eliminated if present. This is strikingly rare when warm blood is transfused. If there appears to be an obstruction higher up, retarding free transfusion, it should be removed if possible or another site selected for venipuncture.

(*d*) A small practical aspect which is often neglected is the importance of changing the filter set regularly. The consistent rise in plasma Hb. seen in all the experiments is, in part, due to clogging of the filter by fibrin deposits with an increased resistance to transfusion, calling for greater pressure to be exerted to achieve fast rates of transfusion.

(*e*) The faster rate of transfusion achieved in experiment 4 for the same pressure differences, emphasizes the role temperature plays in determining the viscosity of blood. Below 27°C there is a dramatic increase in viscosity of blood for the same shear rates and haematocrit.[11]

The less viscous warm blood requires very little pressure to traverse the filter, the drip tubing and the needle. This leads to less trauma to and haemolysis of the red cell.

3. *Defective Filter*

The third important aspect leading to increased haemolysis is the defective filter pump. Here the bobbin fails to occlude the inlet at the top end of the chamber during the squeezing process. A jet of blood is squirted back into the bottle. The resultant churning and frothing leads to gross cell destruction as seen in the values marked with asterisks. These filters also fail to produce rapid rates of transfusion and are best replaced immediately.

Associated with this is the incorrect use of the filter pump. The portion designed for squeezing is the part of the chamber above the filter. One frequently sees personnel squeezing the lower portion of the filter pump where the filter is situated.

CONCLUSION

Warming the blood by RF induction heating does not increase the mechanical fragility of the red cell, when stored blood is pressure transfused through 2 types of pressure transfusion units, i.e. the filter pump administration set and the plastic bag pressure infusor.

Pressure transfusion, using the filter pump administration set, leads to increased haemolysis both in warm and cold blood. Any factor increasing the resistance to transfusion increases the magnitude of the cell destruction. However, warmed blood, due to its decreased viscosity, suffers less than cold blood.

Defective filters appear to lead to excessive haemolysis, at the same time being ineffective in achieving rapid rates of transfusion.

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