PLASMA TRANSFUSIONS IN THE TREATMENT OF HAEMORRHAGE

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During the past two years investigations have been made on the circulatory changes occurring during neurosurgical and other operations associated with considerable loss of blood. The material studied comprised 130 neurosurgical and fifty-six general surgical patients. The investigations, which consisted primarily in measurements of the external blood loss, serial red cell counts throughout operation, and, where possible, blood-volume estimations before and immediately after operation, will shortly be published elsewhere in some detail.

Two Important Observations

Of the many interesting observations made two are of immediate practical importance: (1) As a result of haemorrhage the individual red blood corpuscles increase very appreciably in size, often by 30 to 50 per cent. or even more. (2) Following haemorrhage very considerable numbers of the patient's red blood corpuscles become side-tracked within the body—probably in the muscle capillaries. Often more than 20 per cent. of the number circulating originally were found to be "missing" in this way.

It is generally admitted that haemorrhage leads to dilution of the blood by the rapid passage of tissue fluids into the circulation. My own investigations support this view very clearly, and by serial blood counts taken every few minutes it has been possible to watch this dilution occurring. I consider that these fluids, lacking as they do the specific plasma proteins and some at least of the normal inorganic constituents of the plasma, have a lower osmotic pressure than normal plasma, and therefore than the corpuscles. Consequently much of this fluid passes by osmosis into the corpuscles, which therefore increase in size. Partly because of the lowered blood pressure and partly because of the mechanical effect of the swollen corpuscles, the blood stream through the capillaries is first slowed, and later in many of them actually stops, numerous capillary loops becoming resting-places for cells because the intravascular pressure is not sufficient to keep them in movement.

A New Form of Auto-transfusion

These observations and conclusions suggested the enormous possibilities of a new form of auto-transfusion having as its object the return to the circulation of the patient's own missing corpuscles. In most of the cases studied the number of corpuscles missing was equal to the number which would have been given by the transfusion of about a litre of whole blood. If one can restore a sufficient number of a patient's own missing corpuscles it is obviously unnecessary to give him a whole-blood transfusion from a donor. After a number of animal experiments, in which gratifying results were obtained, plasma transfusions were given to a series of patients who had lost varying amounts of blood. The results were so satisfactory that it is felt that the urgency of the present situation as regards casualty surgery calls for their publication at an earlier stage in the investigation than would normally be considered.

Plasma transfusions have been widely advocated for the treatment of shock, but without the evidence which has been gained during the present investigations their use in

haemorrhage might seem a fruitless if not actually harmful form of therapeutics. Bond and Wright (1938), however, found lyophile serum very effective in restoring the blood pressure and general condition in eight dogs which they had bled experimentally. The practical advantages of plasma over whole-blood transfusions in casualty surgery are:

1. There is no need to group the patient. Time is therefore saved and the plasma can be actually running into a vein within five minutes of the patient's admission to hospital.
2. The plasma can be kept in liquid form for long periods without deterioration. Several of the samples used in this series were two to three months old. Of course, if the plasma is dried it may possibly be kept almost indefinitely.
3. There is no need for elaborate refrigerator storage.

The plasma used in this series of cases was removed from stored blood on the seventh to eleventh day after its collection and was diluted with an equal volume of normal saline in Baxter vacoliter bottles. It was given rapidly—500 c.cm. in twenty to thirty-five minutes—and without any regard for the patient's blood group. In only one case was there any suggestion of a reaction. This patient ran a temperature of 100° to 101° for thirty-six hours. I was uncertain whether this was in response to the operation or to the transfusion.

Results in a Series of Cases

To date, plasma transfusions have been given to twenty-one patients who had lost varying amounts of blood. Very definite clinical improvement occurred in every case. In five cases the plasma was given for urgent reasons and no technical assistance was available for haemocytometry. In these cases the only concrete evidence of improvement which was recorded was a sustained rise in the blood pressure. In the other sixteen cases serial red cell counts were taken before, during, and after the transfusion (not fewer than ten counts being made on each case), and in a number of them blood-volume and mean-corpuscular-volume estimations were also made. The cell counts

Case		R.B.C. (Capillary) per c.mm.	Mean Corpuscular Volume (μ^3)
1	Pre-operative	4,750,000	100.2
	Before plasma	4,100,000	123.5
	After plasma	4,600,000	105.0
2	Pre-operative	4,910,000	99.7
	Before plasma	4,295,000	112.3
	After plasma	4,780,000	103.7
3	Pre-operative	4,800,000	95.5
	Before plasma	4,210,000	116.8
	After plasma	4,600,000	105.0
4	Pre-operative	3,970,000	
	Before plasma	4,390,000	
	After plasma	3,610,000	
5	Pre-operative	4,300,000	
	Before plasma	5,490,000	90.1
	After plasma	4,210,000	115.3
6	Pre-operative	4,900,000	91.7
	Before plasma	3,900,000	
	After plasma	2,990,000	
7	Pre-operative	3,360,000	
	Before plasma	4,800,000	100.0
	After plasma	3,900,000	124.2
8	Pre-operative	4,400,000	116.5
	Before plasma	4,650,000	
	After plasma	3,360,000	
9	Pre-operative	3,750,000	
	Before plasma	4,850,000	100.0
	After plasma	3,100,000	158.5
10	Pre-operative	3,850,000	121.7
	Before plasma	5,250,000	
	After plasma	4,380,000	
11	Pre-operative	4,690,000	
	Before plasma	5,210,000	89.7
	After plasma	4,580,000	105.0
12	Pre-operative	4,700,000	95.4
	Before plasma	3,900,000	
	After plasma	2,990,000	
13	Pre-operative	3,360,000	
	Before plasma	5,500,000	85.4
	After plasma	3,390,000	134.8
14	Pre-operative	4,550,000	91.1
	Before plasma	3,100,000	142.3
	After plasma	3,700,000	105.7

given in the preceding table were taken on capillary blood. Those described as "after plasma" were taken five to fifteen minutes after the transfusion was completed. The mean-corpuscular-volume estimations were made at the same time but on venous blood. Each of the cases was given 500 c.cm. of plasma saline, twenty-five to thirty-five minutes being taken over the transfusion.

The following patient (Case 16) was given one litre of plasma, and made the most dramatic response I have yet seen. I first saw her at the end of operation, when a cerebellar tumour the size of a tangerine had been removed. She had lost a large amount of blood and was in a very bad condition—very pale and with no palpable pulse. After 600 c.cm. had been given in thirty minutes her colour had improved and her pulse had not only returned but registered a systolic pressure of 98 mm.

Case 16 Post-operative	(2.30 ... 3,150,000)	600 c.cm. plasma from 2.30 to 3.0 400 c.cm. plasma from 3.0 to 4.0
	(2.55 ... 3,415,000)	
	(3.15 ... 3,620,000)	
	(3.45 ... 3,395,000)	
	(5.00 ... 4,175,000)	

Discussion

It will be seen that in each of these cases the transfusion of plasma was followed by a rise in the red cell count. Mathematically, of course, the addition to the circulation of 500 c.cm. fluid might be expected to reduce the cell count by upwards of 10 per cent. This rise in cell count must have been due to the return to the circulation of some or all of the side-tracked stationary corpuscles.

It will also be seen that in those cases in which it was measured the mean corpuscular volume was found to return towards normal after the transfusion. This fall in mean corpuscular volume is probably very important. One can imagine that the rapid addition to the circulation of 500 c.cm. plasma would mechanically cause a rise in blood pressure and wash back into the circulation many of the missing corpuscles. By using Barger's capillary-tube technique I have found that the osmotic pressure of the transfused plasma is higher than that of the recipient's. This is due partly to the fall in osmotic pressure of plasma which takes place as a result of haemorrhage, and partly to a rise in the osmotic pressure of the stored plasma before it is removed from the corpuscles. The latter is probably due to the rise in the potassium content shown by Downman, Oliver, and Young (1940) and by Aylwood, Mainwaring, and Wilkinson (1940). The osmotic pressure of the patient's plasma is raised by the transfusion of fluid of higher osmotic pressure, and therefore fluid now passes out of the red cells again and their mean corpuscular volume is reduced. This may well be the turning-point in clinical improvement, as it breaks the vicious circle formed by low blood pressure, dilution, and swollen corpuscles. The smaller cells, the greater oxygen capacity of the blood, and the raised blood pressure enable the body thenceforward to keep the corpuscles in circulation.

Though this series of cases is small its consistency provides strong evidence of the value of this method of treatment, and the previous investigations supply a rational explanation for its success. If the results obtained are confirmed on a larger series of cases it is likely that in the near future, especially in military surgery, transfusion with plasma will become a routine measure in the treatment of haemorrhage. A possibility which should not be ignored is that equally good results might be obtained from some artificial solution.

Meanwhile, in many parts of this country banked blood has fallen into disrepute. It is urged that transfusion

centres should again take blood from all available donors and that on about the eighth day after collection the plasma should be filtered, pooled, and stored in as great quantities as possible.

Summary and Conclusions

1. Investigations, to be reported elsewhere, have shown that after haemorrhage the individual red blood corpuscles swell very appreciably in size and that large numbers of them become side-tracked out of the circulation in muscle capillaries.

2. These observations suggested a new form of auto-transfusion for haemorrhage, aimed at restoring these corpuscles to the circulation.

3. Evidence is produced that this can be effected by plasma transfusions, which should therefore rival whole-blood transfusions in the treatment of acute haemorrhage.

4. It is suggested that plasma transfusions should become a routine measure in the treatment of severe haemorrhage.

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DELAYED TRAUMATIC INTRACEREBRAL HAEMORRHAGE

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The report of a single case is of questionable value, especially when, as in the following instance, the diagnosis is unproved. Some justification, however, may be found for these notes in the discussion of a clinical problem which is rarely encountered and is perhaps not so simple as at first sight it appears.

A Recent Case

Sergeant A., aged 42, was thrown from his motor-cycle on December 22, 1939, at 9 a.m. He has no memory of the accident, but remembers being within a mile of the place where it occurred, and that the roads were slippery with ice. His next memory is of coming to his senses six hours later in a civil hospital, to which he had been taken by ambulance. He had abrasions and contusions on the right forehead and nose. A cut in the forehead was stitched, his head was radiographed, and his wife was permitted to take him home by car, a distance of twelve miles. He remained in bed at home for a week. During this period he had no headache or other symptoms. His convalescence was uneventful, and he returned to duty on January 22, 1940. On January 28 he slipped while walking on ice, and fell, sustaining a cut at the base of the nose. He was dazed for half an hour afterwards.

At 7.30 a.m. on March 2, having been on duty during the previous night, he was sitting at a table when he was seized