CHANGES IN BLOOD VOLUME FOLLOWING TRANSFUSIONS OF SERUM OR PLASMA AND FATE OF INJECTED PROTEIN

A PRELIMINARY REPORT

BY

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The widespread use of intravenous serum or plasma in recent months has aroused interest in the effect of these transfusions on the blood volume and in the fate of the transfused protein. The present observations on changes in the blood volume and the fate of the serum protein were made on normal patients and on a series of patients with peripheral vascular disease who, in the course of another investigation, were receiving weekly injections of serum or plasma (Hayward, 1942).

Changes in plasma volume following injection of saline and dextrose solution have been studied by Gilligan, Altschule, and Volk (1938), using both dye methods and changes in the haemoglobin and haematocrit. They found that the increase in plasma volume after such transfusions is a transient one, usually lasting for only two hours. They also confirmed that changes in the haemoglobin and haematocrit give a reliable index of changes in plasma volume.

Few observations on the effect of transfusion of serum or plasma on the blood volume of normal patients are available, although the use of this substance is widespread. Freeman and Wallace (1938) gave serum intravenously to dogs and found that the blood volume was restored to normal within 24 hours. Using cats, Robertson (1938) found that when blood serum was injected fluid left the vascular system during the injection and continued to leave afterwards, so that an hour after the injection the blood volume was about 15% above the normal. Scimone (1940), in similar experiments on rabbits, found that injected serum disappeared from the circulation in 2 hours, with a return of blood volume to normal. Harper and his fellow workers (1941) concluded that after plasma transfusion in man the haematocrit remained below the level before transfusion for a period up to four days. Hill, McMichael, and Sharpey-Schafer (1940) found that in 2 cases injection of concentrated (4 times normal) serum caused a dilution of the blood volume lasting for over three days.

The importance of the plasma protein in regulating blood volume has been emphasized by Chang (1932). He found that in nephrosis the blood volume was reduced and any rise in plasma protein concentration was accompanied by a rise in plasma volume, and concluded that the plasma protein concentration is one of the regulating factors of circulating volume.

The fate of the injected protein is interesting. There is good evidence from animal experiment that transfused serum protein can be utilized in body metabolism, and will maintain a protein-fasting animal in nitrogenous equilibrium (Holman, Mahoney, and Whipple, 1934). Animals show no increase in urinary nitrogen excretion after transfusion of plasma protein, and it is therefore possible that the protein is stored as such rather than broken down (Weech, Goettsch, and Reeves, 1933; Daft, Robschey-Robbins, and Whipple, 1938).

Methods

In the present series of cases changes in blood volume after, serum or plasma transfusion have been followed by means of estimations of the haemoglobin and haematocrit readings. Most of the haemoglobin estimations were made by the Haldane method. The instrument used was checked against the oxygen capacity method, and 100% was found to equal 18.5 c.cm. of oxygen per 100 c.cm. of blood. Repeated estimations on the

same sample of blood showed the standard deviation to be 2.0, and the results reported are taken to be $\pm 4\%$. A certain number of the haemoglobin estimations were made on the Sahli principle, using a Neoplan haemoglobinometer. On this instrument 100% represented 19.4 c.cm. of oxygen per 100 c.cm. of blood, and the standard deviation of estimations was 2.0. These results were also taken to be $\pm 4\%$. All the estimations in any series were undertaken by the same observer, using the same instrument on venous blood obtained at the same time each day, and the patients were confined to bed throughout the tests.

The haematocrit readings were made on heparinized blood, and the tube was spun for thirty minutes, always using the same centrifuge. Multiple determinations showed that the results could be reproduced to $\pm 1\%$.

Blood-urea determinations were made by Archer's modification of the urease-nesslerization method, and estimations of the plasma protein by the biuret method, both described by Harrison (1937).

The serum used was pooled serum and had a total protein content of about 7 gm. per 100 c.cm. In a few cases citrated plasma was given, the protein content of which varied from 4.06 to 6.25 gm. per 100 c.cm.

Results

The initial blood volume was presumed to be normal in most of the patients—in only 5 was there any reason to suppose that it might be low (Cases 22 and 25, low plasma protein oedema; Cases 4 and 6, Buerger's disease; Case 29, nephrosis). In most cases the haemoglobin, and therefore the blood volume, after transfusion of 800 to 1,200 c.cm. of serum or plasma returned to normal in from two to five days (see Table), although in two cases the initial volume was regained in 24 hours. Statistically the haemoglobin values fall immediately after transfusion and

Table showing Changes in the Haemoglobin (Hb) and Haematocrit (Hc) Reading following Intravenous Serum or Plasma

Case		Volume of Fluid Transfused (c.cm.)	On Day of Transfusion		Days Following Transfusion					
			Before	Immediately After	1	2	3	4	5	6
1	S	1,115	Hb 104	79	93	100	100	105		
			Hc 50.3	42.2		48.6				
2	S	800	Hb 97	90	90	99	91	108		
			Hc 48.2	43.6	42.4	44.6	40.9	48.4		
4	i	800	Hb 120	102	107	110	116			
	ii	800	Hb 107	94	96	92	95	107	108	
			Hc 50.9	45.2	44.5	44.5	43.9	47.0	48.0	
5	i	800	Hb 100	80	85	95				
	ii	800	Hb 100	87	85	94	99			
	iii	800	Hb 98	84	91	90	93	94	94	99
	iv	800	Hb 118*	101	101	104	112			
6	i	1,600	Hc 55.0*	45.9	46.0	50.2	53.0			
	ii		Hb 112	92	100	105	101	107	100	
			Hc 51.2	43.3	45.8	47.5	45.0	48.6	43.2	
8	i	800	Hb 114	102	93	95	103	110	114	
	ii	1,080	Hc 50.0	43.4	40.0	43.8	46.2	45.6	48.3	
			Hb 122	109	110	122	118			
11	S	800	Hc 51.5	42.3	46.2	49.8	52.5	49.9		
13	S	800	Hb 87	65	73	80	80	81	81	
19	i	800	Hb 92	87	87	95				
	ii	800	Hb 81	75	80	83	95			
		800	Hb 96	72	83	93				
20	S	1,000	Hb 103	86	88	90	98	102	102	
21	S	1,200	Hb 75	62	65	65	70	74		
22	S	800	Hb 106	72	100	102				
23	S	800	Hb 100	102†	97	108	103			
			Hc 50.9	42†	41.1	46.9	43.6			
24	P	1,080	Hb 78	70	70	67	68	76		
			Hc 33.9	30.0	31.1	31.8	33.7	33.4		
25	S	800	Hb 113	107	110	105	109			
			Hc 55.4	47.0	50.8	47.8	52.8			
26	P	1,080	Hb 97	82		84	82			
			Hc 37.8	34.8		38.8				
27	P	1,080	Hb 107	90	98		86			
			Hc 46.4	40.9	43.5		38.1			
28	i	1,080	Hb 101	98	99		95	105	105	
	ii	1,080	Hc 48.0	45.4	43.1		43.7	46.0	46.2	
		+400 normal saline	Hb 105	94	96	92	101			
			Hc 45.6	40.8			47.9			
29	i	1,000	Hb 131	118	113		95			
	ii	1,000	Hb 108	104	105					

* Hb=112 and Hc=54.0 the previous day.

† 6 hours after transfusion.

Hb and Hc expressed as percentages.

All estimations carried out on venous blood. The case reports of some of these patients will be found, under the same number, in the article by Hayward (1942).

S=Pooled serum.

P=Citrated plasma.

return to their pre-transfusion level in three days. On the fourth and fifth days there is no significant lowering of the average haemoglobin value.

The changes in the haematocrit readings confirm the results obtained from haemoglobin determinations. The haematocrit readings did not always return to their initial values when the haemoglobin had returned to normal. Such a difference, if real, must mean that while the haemoglobin content of the individual cells remains unchanged the cell volume decreases. A similar phenomenon has been observed after the intravenous injection of gum acacia (Heckel and others, 1938) and of saline and dextrose (Gilligan, Altschule, and Volk, 1938). No explanation has been given for this curious phenomenon.

The total protein concentration of the circulating plasma was studied in 17 cases after the transfusion of serum (7% protein) or plasma (4 to 6.25% protein). In no case was any significant change found to occur in the plasma protein concentration either immediately after the transfusion or during the period of restoration of the blood volume to its original level, so that the transfused fluid and protein are removed from the circulation together. In 9 of these cases the plasma albumin, and in 6 the plasma fibrinogen, were also studied with similar results. Cases 22 and 25 were examples of oedema due to a low plasma protein concentration of unknown aetiology. Both received 800 c.cm. of serum containing 7% protein, which might be expected to cause a rise of about 0.5% in the plasma protein content. No such rise occurred; the excess of protein must have been removed almost as rapidly as it was injected. The figures actually observed for the total plasma protein on these 2 cases were:

	Case 22	Case 25
Before transfusion	4.5%	4.7%
Immediately after transfusion	4.5%	4.7%
1 day after transfusion	4.25%	4.7%
2 days	—	4.7%
3 days	4.25%	—

The fate of the injected protein is obscure. None appeared in the urine following any transfusion. If metabolism of the excess protein occurs rapidly, some change in the blood urea may be found. The blood urea was studied after 11 transfusions of serum; the results revealed no consistent rise in the blood urea.

Conclusions

Following the transfusion of 800 to 1,200 c.cm. of serum or plasma the initial blood volume is regained in from 2 to 5 days.

The added serum protein is removed from the circulation, none is lost as protein in the urine, and concentration of the blood to its original volume produces no increase in the plasma protein figures. The ultimate fate of the protein is still uncertain.

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F. R. Moore (*U.S. Naval Bull.*, 1941, **39**, 386) records his observations on eighty cases of gonorrhoea, showing that sulphathiazole is a much more satisfactory drug than either sulph-anilamide or sulphapyridine. The percentage of cures was higher, while the average time on the sick list was nearly 45% less than with sulphapyridine and 60% less than with sulph-anilamide. There was only one reaction following sulphathiazole, compared with fifteen after sulphapyridine and seventeen after sulph-anilamide.

THE LOW NAIL

BY

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In two of the most recent textbooks on fractures published in this country opinion on the treatment of the trochanteric or extracapsular fracture of the neck of the femur differs somewhat. Watson-Jones (1941) advises internal fixation with a Smith-Petersen nail where possible, but considers that the pertrochanteric fracture lies so close to the cortex of the outer surface of the femur that the distal fragment is too thin for successful nailing. Perkins (1940) considers traction in the long axis of the limb sufficient, but admits that recurrence of angulation with shortening is common. In elderly patients he advises that only the saving of life is of importance and that the treatment of the fracture need not be attempted.

Low Fracture of Neck of Femur

Surgical teaching gives the impression that treatment of the low or basal fracture of the neck of the femur is not difficult, as this fracture invariably unites, whatever measures are undertaken. Presumably this is in pleasant contrast with the medial fracture of the neck, which before the use of the Smith-Petersen nail often failed to unite in spite of treatment. Recent progress in fracture therapy has opened our eyes to the fact that mere union of this fracture does not produce a perfect or even a fair result.

In the treatment two factors are paramount:

1. *The Viability of the Patient.*—These patients are frequently old and therefore liable to complications, of which the most usual are bed-sores and pulmonary affections. Nursing the patient on a Thomas splint may be difficult or impossible, and requires at least three months of immobilization. The word "difficult" is used advisedly because this is not impossible, but it calls for such skilled nursing as cannot be available everywhere. Frail and elderly patients do not tolerate plaster-of-Paris easily, and the comfort and the complete relief from pain advertised by the advocates of plaster are often not forthcoming. Here again skilled nursing and the most constant attention by the surgeon are required.

2. *The Maintenance of Position during the Period of Union.*—Even with the most careful nursing and application of splint or plaster cast, adduction or external rotation of the distal fragment will take place in the majority of patients. This is a gloomy fact, possibly unwelcome to practitioners well versed in the art of self-deception. It may be said that full movement is unnecessary for these old patients, that the patient is really lucky to survive and get union, and that a limp and a stiff knee are but small handicaps. No one would quarrel with this attitude were it not for the fact that perfect position, rapid union, and painless convalescence may be obtained in a very high percentage by successfully nailing with a Smith-Petersen nail.

If one grants that these premisses are forthcoming there can be no doubt which is the best treatment. A patient whose fracture has been soundly nailed can sit up, turn over, lift the leg, and bend the knee, and by this mobility avoids bed-sores, pulmonary complications, and stiff joints. Furthermore, the nearly vertical position of the nail permits earlier weight-bearing than in the medial fracture, as the shearing strain is better guarded against. Why, then, is low nailing not in vogue?

The chief disadvantages so far published are: (1) It is not necessary, because the fracture joins up in any event; but the disadvantages of mere union have already been pointed out. (2) The operation is difficult because the cortical bone splinters into the fracture: this technical difficulty can be overcome. (3) It is a more formidable operation than the medial nailing, requiring a more extensive exposure.

The operation here described is not severe and takes less than one hour.

Description of Operation

The optimum time is considered to be the third day after fracture, when the primary shock has worn off and before bed-sores or pulmonary complications have appeared. This is, of course, an elastic period. Preliminary "vetting" by a physician