BLOOD VOLUME ALTERATIONS IN CONGESTIVE HEART FAILURE

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A considerable body of data indicates that the plasma volume, as measured by dye dilution methods, is generally increased in congestive heart failure (1–4). However, recent investigations, utilizing P^{32} (5, 6) or Cr^{51} (7) tagged red cells, indicate that there is little or no increase in total blood volume, plasma volume, or red cell volume in most cases of heart failure.

According to presently accepted concepts, the total body relative cell volume,

$$\frac{\text{RBC volume}}{\text{RBC volume} + \text{plasma volume}},$$

is appreciably lower than the relative cell volume of the blood withdrawn from the large vessels (hematocrit value) (8–16), and the ratio between these two is not necessarily constant (17). It is, therefore, theoretically possible for total erythrocyte volume and venous hematocrit value to remain unchanged in the presence of a significant increase in plasma volume, if the ratio,

$$\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}},$$

decreases. Some such mechanism suggests itself if the aforementioned discrepancies are to be satisfactorily resolved.

It was, therefore, considered to be of interest to reinvestigate the status of the blood volume in heart failure by performing simultaneous red cell and plasma volume determinations before and after compensation in a variety of cases of decompensated heart disease.

METHODS

Subjects were hospitalized male patients in whom the diagnoses (Table I) and the presence of congestive heart failure were verified by at least two observers. Fifty-seven studies were made on 26 subjects. Treatment of the heart failure followed conventional lines, employing in various combinations, bed rest, low salt diet, digitalis substances, and diuretics as dictated by individual requirements. No attempt was made to regulate therapy in any special manner. A period of bed rest in the recumbent position for at least three hours preceded all determinations. Peripheral venous pressures and circulation times were determined in all cases simultaneously with the blood volume studies. Peripheral venous pressures were obtained in the recumbent subject with the manometer zeroed at a level 8 cm. posterior to the manubro-sternal junction. Decholin sodium was employed for determination of the arm to tongue circulation times.

Erythrocyte volumes and plasma volumes were measured with P^{32} tagged erythrocytes and dialyzed solutions of I^{131} labeled human serum albumin, respectively. The methods employed were the same as those previously described (16) except that weighed amounts of the tagged red cell suspensions and iodoalbumin solutions were administered within a minute of each other through the same needle. Each syringe was rinsed four times with the venous blood. The syringes were then assayed for residual radioactivity which was found to be negligible. Heparinized blood samples were withdrawn from a vein in the opposite arm 15, 20, and 25 minutes after injection. The P^{32} was assayed with a thin glass walled Geiger counter with a sensitivity of 32:1 for P^{32} as compared with I^{131}, and the I^{131} with a thick bismuth cathode Geiger tube which is almost insensitive to P^{32}. Sufficient counts were recorded for each assay to reduce the statistical error of counting to less than 1.5 per cent.

Venous hematocrit values were obtained by centrifugation at 3000 rpm. for 30 minutes and then multiplied by 0.98 to correct for trapped plasma (18). Since erythrocyte and plasma volumes were calculated from assays of whole blood samples, any systematic error in the correction factor was not critical to determinations of the ratio,

$$\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}}.$$[2]

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[2] This point is clarified by the following example. Assume that 2,000,000 counts of P^{32} and I^{131} each have been injected, that the counts per ml. whole blood due to P^{32} and I^{131} are 500 and 400, respectively, and that the observed venous hematocrit is 50 per cent. Utilizing a correction factor of 2 per cent for trapped plasma results in calculated values of 1960 ml. RBC volume and 2550 ml. plasma

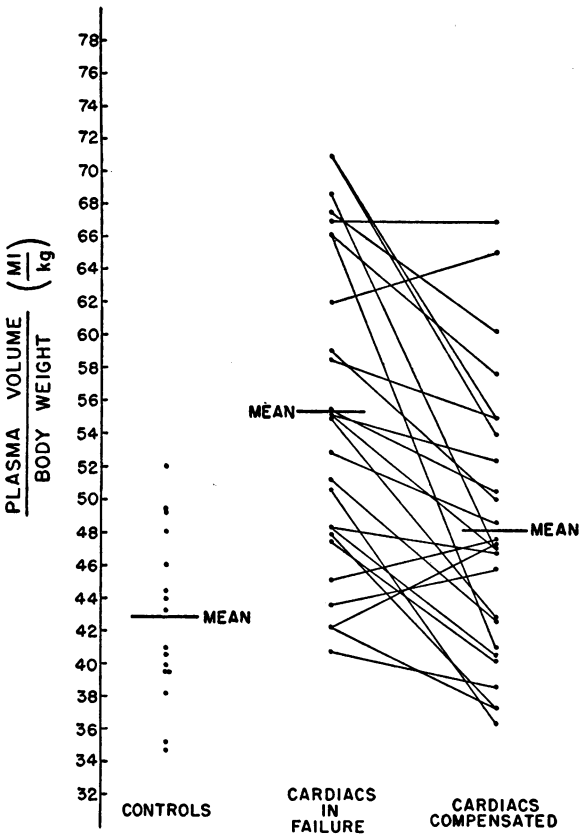

FIG. 1. COMPARISON OF PLASMA VOLUMES OF CONTROL SUBJECTS WITH THOSE OF PATIENTS IN HEART FAILURE AND AFTER COMPENSATION

There was no significant trend in the concentrations of the labeled plasma or tagged cells between 15 and 25 minutes. This confirms previous observations (16, 19) that, even in heart failure, mixing is essentially complete by this time.

RESULTS

Blood volumes are given as absolute values in milliliters (Table I) and as ml. per Kg. body weight (Figure 1). It has been shown that gain or loss in weight has no significant influence *per se* on plasma volume (20). Even in moderately severe caloric starvation accompanied by losses of 25 per cent of the body weight (21), plasma volume remains unchanged in absolute values, thus increasing greatly in proportion to body weight. Cachexia will then tend to magnify any increase in blood volume when calculated in terms of body weight. Conversely, edema may obscure such changes. With a single exception (Case 26, C. C.) cachexia was not present in the subjects reported here. Therefore, the weights after restoration of compensation were taken as closest to the "normal" weights of the cardiac subjects and used as reference for all determinations in these cases.

Plasma and erythrocyte volumes

In 22 of the 26 patients studied, compensation was accompanied by a decrease in total blood volume ranging from 3.5 per cent to 23.0 per cent (Table I). In four of the subjects (Nos. 11, 17, 25, 26) there was an increase in total blood volume following therapy of heart failure. However, in one of these (No. 17, I. S.) clinical improvement was equivocal and, in another (No. 11, L. I.), subsequent relapse into failure was associated with a marked increase in plasma volume which was retained after recompensation. The decrease in blood volume in the 22 patients was chiefly attributable to loss of plasma volume but in most of these, a fall in red cell volume was also noted. The plasma volumes in failure and following compensation were compared with a group of non-cardiac controls on the basis of volume per kilogram body weight (Figure 1). The mean plasma volume for the group of 16 non-cardiac subjects was 42.0 ± 1.19 [8] ml. per Kg. which agrees well with other "normal" values obtained in this laboratory and elsewhere. The mean plasma volume for the group of 26 patients in heart failure was 55.6 ± 1.83 ml. per Kg. and, after complete or partial compensation, was 48.2 ±1.61 ml. per Kg. The average decrease in plasma volume was 430 ml. (12.2 per cent). The mean value for erythrocyte volumes during decompensation (39.2 ± 1.83 ml. per Kg.) was higher than that of a group of seven control subjects (32.2 ± 1.83 ml. per Kg.), and the mean fall following compensation was 170 ml. (7 per cent).

volume. The ratio, $\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}}$, is then

$$\frac{\frac{1960}{1960 + 2550}}{.49} = .887.$$

If instead, a correction factor of 10 per cent is used, then

$$\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}} = \frac{\frac{1800}{1800 + 2750}}{.45} = .879.$$

[8] All values are expressed as mean values ± standard error of the mean.

TABLE I—*Data pertaining to blood volume in cardiac patients*

	A	B	C	D		E	F	G	H
							Blood volume (*ml.*)		
Case	Date 1953	Clin. cond.*	Weight	V.P.†	C.T.‡	Edema§	RBC	Plasma	Total
			Kg.	*mm. H_2O*	*Sec.*				
1. J. Mc.	5/26	F	71.1	140	32	0	2510	3480	5990
	6/12	C	66.0	100	22	0	2570	3210	5780
2. W. C.	5/12	F	73.9	300	30	2+	2600	3340	5940
	5/29	C	65.2	140	30	0	2520	2780	5300
3. H. S.	2/17	F	92.6	220		4+	3680	4570	8250
	3/20	P.C.	78.3	160		1+	3220	4300	7520
4. E. I.	3/18	F	64.1	400	30	4+	2220	3900	6120
	3/27	C	55.0	80	14	0	1985	3030	5015
5. I. B.	12/17/52	F	61.0		35	4+	2025	3400	5425
	1/7	F	54.5	250	30	2+	2160	3425	5585
	2/6	P.C.	50.8	160	35	0	1810	3400	5210
6. J. C.¶	2/4	F	69.5	156	26	1+	1820	3410	5230
	3/11	P.C.	60.4	96	30	0	1490	3050	4540
7. C. C.	1/21	F	75.8	140	30	2+	2140	3660	5800
	2/3	P.C.	72.3	135	23	0	1880	2630	4510
8. A. W.	6/3	F	74.8	230	30	4+	1650	4290	5940
	6/22	C	63.6	80	17	0	1515	3840	5355
9. C. W.	1/14	F	78.3	230	33	3+	3700	4420	8120
	1/30	C	66.9	160	23	0	3510	2740	6250
10. J. R.	5/22	F	83.0	280	25	4+	2600	4300	6900
	6/8	C	78.2	100	18	0	2410	3685	6095
11. L. I.	1/26	F	56.3	180	40	2+	2040	2375	4415
	2/6	C	49.0	110	20	0	2080	2300	4380
	4/6	F	53.6	280	40	4+	1875	2680	4555
	4/22	C	52.6	120		0	2000	2820	4820
12. J. D.	5/12	F	71.8	180	30	4+	1945	4120	6065
	5/27	C	60.0	120	18	0	1875	2820	4695
13. E. W.	1/14	F	96.8	220	28	4+	3600	3620	7220
	2/20	C	83.6	140	23	0	2860	3150	6010
14. G. S.	5/1	F	73.1	220	32	2+	2055	3220	5275
	5/11	C	66.8	130	22	0	2170	2720	4890
15. A. K.	6/4	F	57.7			2+	3010	3360	6370
	6/29	C	50.9	120		0	2475	2940	5415
16. F. W.	3/24	F	71.4	140	20	0	2205	2820	5025
	4/22	C	69.0	110	18	0	1880	2660	4540
17. I. S.	3/20	F	59.0	120	30	0	2275	2620	4895
	4/17	C?	60.0	120	25	0	2315	2755	5070
18. F. A. D.	12/11/52	F	93.6	160	30	4+	4155	3770	7925
	12/22/52	P.C.	84.6	120	25	2+	3520	3880	7400
	12/30/52	P.C.	83.5	110	25	1+	3550	3980	7530
19. H. M.	3/6	F	71.7	120	30	2+	2950	3660	6610
	4/6	C	66.4	80	25	0	2380	3480	5860
20. J. M.	3/13	F	57.3	130	30	0	1830	3090	4920
	4/3	C	52.3	80	13	0	1595	2620	4215
21. F. P.	6/18	F	52.7	140	20	2+	2260	2290	4550
	7/1	C	47.7	60	10	0	2120	1780	3900
22. C. D.	4/10	F	75.5	140	30	2+	1960	3470	5430
	4/24	C	73.0	120	15	0	2270	2930	5200
23. H. K.	5/19	F	78.2	230	50	4+	3250	4910	8160
	5/29	P.C.	64.5	80	30	0	3290	3480	6770
24. R. C.	5/20	F	62.2	210	27	3+	2040	3100	5140
	5/27	C	56.3	140	17	0	1920	2410	4330
25. A. S.	4/18	F	82.3	220	18	0	2030	3450	5480
	4/24	C	81.8	140	16	0	2210	3890	6100
26. C. C.¶	3/18	F	59.1	200	20	2+	1630	3420	5050
	3/27	C	55.0	108	24	0	1370	3610	4980
	7/14	C	57.4	120	18	0	1800	3820	5620
Mean		F					2490	3510	6000
		C					2320	3080	5370

* C—Compensated. F—Failure. P.C.—Partially Compensated.

† V.P.—Venous Pressure.

‡ C.T.—Circulation time with Decholin®.

§ Grading of edema: 1+ = mild ankle edema; 2+ = ankle and pre-tibial edema, moderate; 3+ = marked edema of the lower extremities; 4+ = generalized anasarca (severe edema of lower extremities, sacrum, skin including abdominal wall, and ascites).

¶ Cases No. 6 (J. C.) and No. 26 (C. C.) have not been included in the mean values for RBC volume and total body relative cell volume/peripheral hematocrit value ratio (L/M), because of other factors tending to decrease erythrocyte volume. For explanation see Text.

TABLE I—*Continued*

I	J	K	L	M	N	O	P
% Change in blood volume			RBC	Peripheral hematocrit			
RBC	Plasma	Total	RBC and plasma	value	L/M	Diagnosis‖	Remarks
			%	%			
+ 2.4	− 7.8	− 3.5	41.9	44.9	0.932	ASHD	
			44.5	45.6	0.975	Diabetes	
− 3.1	−16.8	−10.8	43.8	50.6	0.864	ASHD	
			47.5	52.0	0.915		
−12.5	− 5.9	− 8.9	44.6	51.2	0.873	ASHD	
			42.8	49.7	0.860	HHD	
−10.6	−22.3	−18.1	36.3	43.0	0.845	ASHD	
			39.6	47.6	0.830	HHD	
			37.4	47.4	0.788	ASHD	
−10.6	0	− 4.0	38.8	46.0	0.843	HHD	
			34.7	39.0	0.893		
−18.1	−10.6	−13.2	34.8	41.0	0.850	Amyloid	Melena during study
			32.9	42.4	0.775	HD	
−12.2	−28.2	−22.2	36.9	45.8	0.806	ASHD	
			41.6	45.5	0.915	Luetic HD	
− 8.2	−10.5	− 9.9	27.7	30.4	0.912	HHD	
			28.3	31.1	0.910		
− 5.1	−38.0	−23.0	45.5	55.5	0.820	HHD	
			56.1	62.0	0.905		
− 7.3	−14.3	−11.7	37.7	42.7	0.880	HHD	
			39.6	43.6	0.908		
+ 2.0	− 3.2	− 0.8	46.2	55.1	0.840	HHD	
			47.5	53.0	0.895		
+ 6.7	+ 5.2	+ 5.8	41.3	47.7	0.865		Returned in failure
			41.5	47.6	0.872		
− 3.6	−31.5	−22.5	32.1	36.9	0.867	HHD	
			39.9	42.2	0.946		
−20.5	−13.0	−16.8	49.8	57.0	0.875	HHD	
			47.6	53.0	0.899		
+ 5.6	−15.5	− 7.3	38.9	45.6	0.850	HHD, RHD, ASHD	
			44.4	48.6	0.915		
−17.8	−12.5	−15.0	47.2	50.3	0.940	RHD	
			45.7	50.1	0.911		
−14.7	− 5.7	− 9.7	43.8	49.0	0.895	RHD	
			41.4	46.8	0.885		
+ 1.8	+ 5.2	+ 3.6	46.5	54.0	0.860	RHD	Partial clinical improvement
			45.6	49.0	0.932		
			52.5	57.2	0.914	RHD	
−14.5	+ 5.6	− 5.0	47.5	56.1	0.850	ASHD	
			47.1	53.1	0.888		
−19.3	− 4.9	−11.3	44.6	50.8	0.878	RHD	
			40.5	47.8	0.850		
−12.8	−15.2	−14.3	37.2	44.6	0.831	RHD	
			37.8	42.0	0.900		
− 6.2	−22.3	−14.3	49.6	51.8	0.957	Cor Pulmonale	
			54.3	53.4	1.020		
+15.8	−15.5	− 4.2	36.1	43.5	0.829	Primary Pulm. Hypert.	
			43.6	46.5	0.940	Cor Pulmonale	
+ 1.2	−29.1	−17.0	39.8	45.7	0.868	Undiagnosed	
			48.6	52.2	0.931	Nutritional?	
− 5.9	−22.3	−15.8	39.8	45.6	0.872	Unknown etiology	
			44.3	49.7	0.892		
+ 8.9	+12.7	+11.3	36.9	42.7	0.865	Unknown etiology	
			36.2	40.2	0.900		
			32.3	38.4	0.840	Luetic HD	
+10.4	+11.7	+11.3	27.5	40.0	0.689	Carcinoma mouth	
			32.1	38.8	0.825		
− 6.9	−12.2	−10.5			0.868		
					0.908		

‖ ASHD—Arteriosclerotic Heart Disease; HHD—Hypertensive Heart Disease; RHD—Rheumatic Heart Disease.

Ratio of total body relative cell volume to venous hematocrit values

In the majority, compensation was associated with an increase in the ratio,

$$\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}}$$

(Table I, column N, Figure 2). In addition, in one instance, a decrease in this ratio was noted following relapse into congestive failure. Furthermore, the mean ratio in 24 patients in congestive heart failure (0.868 ± 0.008) was considerably lower than that of a control group of non-cardiac subjects (0.937 ± 0.009) and rose following compensation (0.908 ± 0.008). Two subjects are not included in these calculations because of the influence of other factors on red cell volume. In one (No. 6, J. C.) there was gastrointestinal bleeding during the study, and in the other (No. 26, C. C.) a changing blood picture accompanied roentgen therapy of a laryngeal carcinoma.

Our observations fail to show a correlation between the magnitude of the fall in venous pressure and that of the plasma volume.

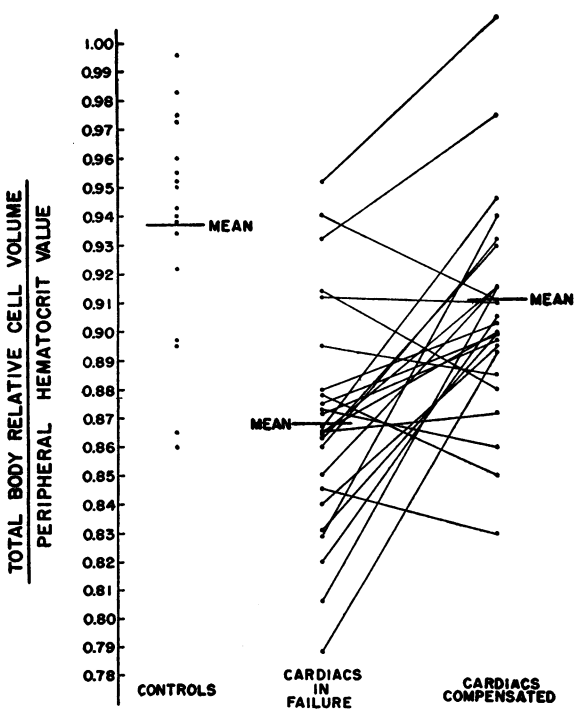

FIG. 2. COMPARISON OF THE RATIOS, $\frac{\text{TOTAL BODY RELATIVE CELL VOLUME}}{\text{PERIPHERAL HEMATOCRIT VALUE}}$ OF CONTROL SUBJECTS WITH THOSE OF PATIENTS IN HEART FAILURE AND AFTER COMPENSATION

Cases No. 6 (J. C.) and No. 26 (C. C.) are not included. For explanation see Text.

DISCUSSION

The accurate measurement of plasma volume remains a matter of some dispute. Direct determinations with plasma soluble dyes (9–14, 22–24) or radioiodinated albumin (16) have in general shown values higher than those calculated from measured red cell volumes and the venous hematocrit values. This discrepancy has been interpreted by some (9–14, 16, 22) as resulting from a true difference between the relative cell volume of the entire body and that of the large vessels. Others (5, 6, 25) have concluded that the dye methods are in error and that total body relative cell volume does not differ significantly from the venous hematocrit value (5). Although there is no positive data to support the latter concept (5), several arguments derived from indirect evidence must be evaluated.

The origin of the dispute lies in the observation that the plasma soluble substances employed have a space of distribution greater than that of tagged erythrocytes. To conclude from this alone that the former must be distributed extravascularly is to imply that the relative cell volume is the same throughout the body. However, splenic blood, which is rapidly exchangeable with injected Fe-tagged erythrocytes, has a much higher hematocrit value than blood in the large vessels (26). In subjects with markedly enlarged spleens, the ratio,

$$\frac{\text{total body relative cell volume}}{\text{venous hematocrit value}},$$

is frequently over 1.00 (27), a circumstance which is very rarely observed in other subjects. In the normal dog this ratio averages almost 1.00 as determined by Evans Blue and P^{32} tagged erythrocytes. Yet it cannot be concluded that in this species the relative cell volume is the same in all vessels, for the ratio decreases to 0.90 following splenectomy (28). Furthermore, there is direct evidence that the relative cell volume of minute vessels is lower than that of the large vessels. Krogh (29) noted that there is a marginal lining of plasma in small vessels through which there

flows an axial stream of whole blood, and Fåhraeus (30) demonstrated a similar phenomenon in glass capillary tubes by observing that the relative amount of plasma increases as the diameter of the tube is reduced. Ebert and Stead (31) demonstrated a lower hematocrit value in blood obtained from the small vessels of the forearm than in the large vessels.

Other critics of the dye methods have pointed to an early rapid leak out of the vascular system, attributed to delayed binding by serum albumin (13), or to phagocytosis of a foreign substance (32). These objections cannot be applied to I^{131}-labeled serum albumin. Schultz, Hammarsten, Heller, and Ebert (33) demonstrated that the amount of I^{131}-labeled albumin appearing in thoracic duct lymph during the period of plasma volume determination does not significantly influence the measurement of plasma volume. In the dog, at least, intravenously administered tagged serum proteins equilibrate more rapidly with thoracic duct lymph than the lymph from the neck or limbs (34).

The arterial time concentration curves of I^{131}-labeled albumin and P^{32} tagged erythrocytes do not differ significantly between 1 or 1½ minutes and 15 minutes, and venous concentrations of I^{131}-labeled albumin do not change significantly between 4 and 20 minutes after injection (16). Therefore, if the difference between the spaces of distribution of I^{131}-labeled albumin and tagged red cells is to be attributed to leakage from the blood stream, this leakage must be completed within a very few minutes. The liver has been suggested as the site of an early leak of T-1824 dye from the blood stream (25). The possibility of rapid I^{131}-labeled albumin accumulation by the liver has previously been evaluated (35) by recording a continuous radioactive assay over the liver from the time of injection. After an initial rapid rise during the first minute, the level of radioactivity remained at a plateau without significant change for the next hour. This observation was confirmed in two cardiac patients of the present series. The possibility of leak into the liver during the first minute was investigated in the rabbit. Following simultaneous injection of P^{32}-tagged rabbit erythrocytes and I^{131}-labeled human serum albumin into the portal vein, the apparent volumes of distribution in the liver during the first circulation, as determined from hepatic vein samples, did not differ by more than 2 per cent.

The studies of other investigators (26) showed a higher I^{131}-albumin/Fe-tagged erythrocyte ratio in most organs than in the large blood vessels. Thus, if an early rapid loss of I^{131}-albumin from the blood stream is to explain these findings, this loss must occur throughout the body. It appears unlikely, that within the first few minutes, iodinated albumin exchanges with a diffusely distributed extravascular albumin pool, equivalent in magnitude to approximately 15 per cent of the total plasma albumin. Furthermore, the similar volumes of distribution of bovine serum proteins, T-1824 and pneumococcus polysaccharide S III (36) in animals and of I^{131}-labeled serum albumin and gamma globulin in humans (37) indicate that any such diffusely distributed compartment which equilibrates so rapidly with plasma should be regarded as associated physiologically with plasma volume regardless of its anatomic boundaries.

It might be claimed on theoretical grounds that I^{131} serum proteins or protein bound dyes do not measure exactly the plasma volume since there is a concentration of plasma proteins during filtration of fluid from the arterial ends of the capillaries. However, since the capillary bed comprises only about 5 per cent of the total blood volume (38) and the average hemoconcentration is not likely to exceed that in the glomerular capillaries (about 20 per cent), the error in the plasma volume determination due to non-uniform protein concentration is of the order of 1 per cent. In our opinion, therefore, until direct evidence to the contrary is presented, the determination of plasma volume with I^{131}-labeled albumin must be considered to be on a more valid basis than estimates calculated from measured red cell volumes and peripheral vessel hematocrit values.

Recently, other investigators (5–7) concluded that there was no consistent expansion of blood volume in heart failure. In fact, following compensation, an increase in blood volume was not infrequently noted (6). However, these conclusions were derived from studies with tagged red cells and were based on the assumption that total body relative cell volume is identical with the peripheral vessel hematocrit value. In the present study there were a number of cases in which a decrease in plasma volume following compensation

TABLE II

Comparison of measured changes in plasma volume with changes calculated from erythrocyte volumes and peripheral hematocrit values

Case	Measured change in plasma volume	Calculated change in plasma volume
	ml.	*ml.*
1. J. Mc.	− 270	− 10
11. L. I.	− 75	+180
20. J. M.	− 470	− 65
22. C. D.	− 540	+120
21. F. P.	− 510	−250
2. W. C.	− 560	−200
7. C. C.	−1030	−280
14. G. S.	− 500	−155
9. C. W.	−1680	−790
12. J. D.	−1300	−760
23. H. K.	−1430	−750
10. J. R.	− 615	−380
13. E. W.	− 470	−160
Mean of all cases studied	− 430	−170

would have remained undetected or would have been interpreted as an increase if calculations from erythrocyte volumes and hematocrit values alone were relied upon. In several other cases the magnitude of fall in plasma volume would have appeared much less striking (Table II). The mean fall in plasma volume for the entire group would have been calculated as 6 per cent compared to the measured decrease of 12.2 per cent. The results of the present investigation thus suggest why workers using tagged red cells alone failed to find much change in plasma volume following treatment of heart failure. However, regardless of the methods of calculation employed, the values for red cell and plasma volume in congestive heart failure, which have been obtained in the present study, indicate definite increases above normal.

The cause of the increased plasma volume in heart failure is not established. Starling (39) believed that a fall in cardiac output leads to reflex vasoconstriction, and that the consequent reduction in intracapillary pressure results in absorption of interstitial fluid into the circulation. Evidence in favor of this view has been reviewed elsewhere (40). Warren and Stead (41) have postulated that the increase in interstitial fluid tension produced by edema promotes an increase in plasma volume by upsetting the balance of factors regulating net transcapillary fluid exchange. Little support is offered to this concept by the results obtained in the present study, since plasma volumes frequently remained at higher than normal levels following cardiac compensation even in the absence of edema.

The mechanism of the observed decrease in circulating red blood cell volume with compensation is not clear. Waller, Blumgart, and Volk (42) found evidence of red cell destruction in heart failure. However, Watson (43) failed to observe any increase in fecal urobilinogen in cardiac decompensation. Mollison (44) has remarked on the absence of a normal hemolytic mechanism operating to rid the body of excess erythrocytes, and Fryers and Berlin (45) have demonstrated in rats that additional red cells formed in response to low barometric pressure have a normal life span after return to sea level environment. However, a decrease in red cell volume of as much as 25 per cent over a one month period can be accounted for by a cessation of blood formation, since the average normal red cell life span is about 120 days (44). Other investigators (46) have shown that in human subjects who move from high altitudes to sea level, the red cell iron turnover rate decreases to one-tenth of the initial value, approaching that seen in aplastic anemia. Therefore, the magnitude of the fall in erythrocyte volume observed in this series could be explained by reduced or arrested red cell formation without increased red cell destruction. Hyperplasia of the bone marrow in congestive heart failure with return to normal after compensation has been noted by Ott (47). Hypoxia of the marrow due to poor blood flow or low arterial O_2 tension, secondary to heart failure, is the probable stimulus for the increased erythropoiesis.

SUMMARY AND CONCLUSIONS

1. Red cell and plasma volumes were determined independently in 26 subjects in heart failure and after compensation.

2. Mean values for red blood cell volumes and plasma volumes were elevated above those of control subjects and fell with compensation.

3. The ratio, $\frac{\text{total body relative cell volume,}}{\text{venous hematocrit value}}$ was observed to be decreased in failure and to rise with compensation in the majority of cases.

4. When plasma volumes are indirectly calculated from measured red cell volumes and hemato-

crit readings, significant changes may remain undetected.

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