Diurnal Variation in Blood Volume of Man

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There have been many studies on the blood volume in man under various circumstances, a few demonstrating the changes from day to day.[1-3] Repeated measurements during the day, however, have not been designed to detect the possibility of diurnal variation.[4,5] Such information is of importance in setting up standards, in making comparative studies and in clarifying the relationship to such influences as posture, physical activity and changes in environmental temperature.[6] The present study, therefore, was undertaken to obtain data on changes in blood volume during the course of a day.

MATERIALS AND METHODS

Twelve young men and women from the hospital personnel were volunteer subjects. Diet and fluid intake were unrestricted and daily activities were the usual for this group. The study was conducted during the winter months without exposure to outside temperatures. For each determination of blood volume, body weight to the nearest 50 gm. was recorded, after voiding, with approximately the same clothing worn. The subjects lay supine for about 15 minutes while measurements were made. Tests were done: (a) fasting, just after arising in the morning; (b) at midday, approximately 20 minutes after lunch; and (c) at bedtime, at least three hours after supper.

Blood volume was determined by isotope dilution using I^{131} iodinated human serum albumin (RIHSA) in prepackaged doses of 0.25 to 4.6μc. Ten milliliter samples of venous blood were drawn without stasis. After the "blank" sample was drawn, the needle was left in situ, RIHSA was injected and the syringe was rinsed twice by aspiration and reinjection of blood. Following a 10 to 15 minute allowance for mixing, a second sample was taken from a large vein of the opposite arm. Samples were placed in heparinized plastic well-counter tubes and counts were made. The same blood was used later for hematocrit determinations. Capillary hematocrit tubes were centrifuged for five minutes and read in an International microcrit reader calibrated to ± 1 per cent, the average of three tubes taken as the value.

The dilution equation was solved by measuring the I^{131} plasma tag in whole blood. Measurements and calculations necessary to derive whole blood volume were made using the Volemetron, a semiautomatic device devised by Williams and Fine.[7] The accuracy of this apparatus was verified for each test using the precalibrated standard supplied. Prior in vitro and in vivo determinations performed in our laboratory corroborated the reproducibility and the limits of accuracy of the method as originally reported. Since whole blood volumes thus determined allow measurement of plasma volume only indirectly, additional studies were done to corroborate changes in plasma volume observed during the course of the present experiments. In four subjects, following determination of blood volume and hematocrit, the counting tubes were centrifuged, the plasma separated and transferred to smaller counting tubes. Using RIHSA doses, previously matched with those injected, to load the memory bank of the machine, plasma volumes were determined directly. Results substantiated the changes in plasma volume calculated from the whole blood volume.

The significance of the changes observed was determined by the F test for linear regression and variance.[8]

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This work was carried out in part under contracts with the Atomic Energy Commission and the Medical Research and Development Command of the U. S. Army. The assistance of the National Institutes of Health is acknowledged.

Submitted for publication September 27, 1963.

Table 1. Changes in Whole Blood Volume and Hematocrit During the Day

				(A) Morning			(B) Noon			Changes A to B		(C) Evening			Changes A to C	
Subject	Age	Sex	Height Inches	Wt. kg.	Blood Vol. ml.	HCT. %	Wt. kg.	Blood Vol. ml.	HCT. %	Blood Vol.	HCT.	Wt. kg.	Blood Vol. ml.	HCT. %	Blood Vol.	HCT.
CR	26	M	72	86.7	5900	41.5	86.25	6100	42.5	+3.0	+2.0	84.55	6300	42.	+6.7	+1.2
CH	37	M	69	74.8	4500	47.5	75.45	4600	47.0	+2.0	-1.0	77.40	4700	44.	+4.5	-6.0
AG	25	M	75	109	7700	49.	109	8000	48.	+4.0	-1.0	108.8	8600	44.	+11.7	-10.0
JM	25	M	74	89.5	6000	44.	90.1	6100	43.	+1.0	-2.0	89.4	6900	43.5	+15.	-1.0
DF	34	M	71	83.65	4900	45.	84.0	5300	40.	+8.0	-11.0	83.9	5700	41.	+16.3	-9.0
LI	29	M	65	68	5800	47.5	67.9	5500	47.5	-5.0	0	69.0	5800	47.	0	-1.0
DL	29	M	73	74.5	5700	49.	75.1	5100	49.0	-11.0	0	75.2	5400	48.	-5.7	-2.0
JB	20	F	66	55.9	3400	40.5	56.0	3500	41.	+3.0	+1.0	56.5	3400	39.	0	-4.0
EH	24	F	65	65.8	4400	48.	66.5	4600	45.5	+5.0	-6.0	65.6	4700	45.5	+6.8	-5.2
LM	24	F	67	80.0	4800	37.	79.6	4800	37.5	0	+1.0	80.2	4700	38.5	-2.0	+4.0
KC	25	F	66	63.1	4300	38.5	64.0	4700	38.	+5.0	-1.0	64.0	5000	38.5	+16.	0
DP	20	F	62	55.1	3800	39.	54.8	3700	38.5	-3.0	-1.0	55.1	3800	38.	0	-2.6
								Average		+1.0	-1.5		Average		+5.7	-2.8

RESULTS

In Table 1 it may be seen that blood volume tended to increase and the hematocrit to decrease during the day. While the changes are not persuasive between morning and midday, they are more obvious at the end of the day. At that time blood volume had increased in 8 of 12 subjects (range 4.5 to 16.3 per cent), was unchanged in 2, and declined slightly in 2 (5.7 and 2.0 per cent), for an average increase of 5.7 per cent. The average fall in hematocrit was 2.8 per cent. The hematocrit declined in 9 subjects (range 1.0 to 10 per cent, was unchanged in 1 and rose in 2, 1.2 and 4.0 per cent respectively. These changes were highly significant at the level $\alpha = 0.01$. The F tests for variation and linear regression were 6.07 and 10.93 respectively for the increase in blood volume and 6.88 and 9.88 respectively for the fall in hematocrit. There were no significant differences with regard to weight or in relation to sex.

DISCUSSION

Blood volume showed a diurnal variation with a significant increase by evening. A diurnal variation in blood volume is not surprising in view of cyclic changes in other body parameters. That this might occur is suggested by Elwood's study of diurnal variation in hemoglobin[9] and his discussion of the work of others, which revealed progressive hemodilution throughout the day. An interesting result, but not an unexpected one, in some of these studies and in the present one was the lack of significant change during the first part of the day, change being apparent only upon comparison of the morning and evening results.

To account for the observed increase in blood volume, a brief consideration of the possible homeostatic mechanisms involved may be helpful. In the absence of acute change, these mechanisms depend largely upon variations in renal water and electrolyte excretion mediated mainly by alterations in secretion of aldosterone and of antidiuretic hormone.[10] Although knowledge of the means by which these operate is incomplete, there is evidence that the reduction in thoracic blood volume accompanying the erect position, acting through left atrial stretch receptors, may increase the total blood volume.[11] Orthostasis is accompanied by decreased urinary water and sodium excretion and by retention of infused normal saline. Blood volume regulation is a complex and dynamic process involving many other factors; nevertheless, it appears reasonable to consider

orthostasis important in the changes observed here. There was nothing to account for the absence of change in several members of the group studied, except for some unavoidable variation in daily work load which made orthostasis less uniform. More uniformity in activity would have simplified the assessment of change.

A further problem brought to light by this study was the lack, in several of the subjects, of hemodilution sufficient to compensate for the increases in blood volume observed. Since the red cell mass remains constant, it is difficult to account for the apparent relative increase in cells seen in these subjects. This study is not comprehensive enough to offer an explanation, but if this is a valid phenomenon, it may be assumed that the large vessel total body hematocrit ratio[12] is not constant throughout the day. It, too, may show diurnal variation, thus reflecting changes in blood volume.

SUMMARY

Isotope dilution with I^{131} iodinated human serum albumin was used to measure the blood volume of 12 ambulatory, normally active, healthy young adults during the course of a day. Volumes increased and hematocrit decreased significantly on the average with changes most marked by evening.

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