

CLINICAL STUDIES OF THE BLOOD VOLUME. II. THE RELATION OF PLASMA AND TOTAL BLOOD VOLUME TO VENOUS PRESSURE, BLOOD VELOCITY RATE, PHYSICAL MEASUREMENTS, AGE AND SEX IN NINETY NORMAL HUMANS

BY JOHN G. GIBSON, 2ND AND WILLIAM A. EVANS, JR.

(From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School, Boston)

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Medical literature contains several works on the blood volume in normal persons, based on findings with the dye method of Keith, Rowntree and Geraghty (1) or modifications thereof, (2, 3, 4). Our justification for presenting an additional study is that the principal errors inherent in the earlier techniques are minimized by the dye method we have employed. By this method, described in detail in a previous communication (5), the absolute plasma volume can be measured with considerable accuracy, and the calculation of total blood volume is based on the plasma volume and the hematocrit values of venous blood samples. It also seemed worth while to consider the normal blood volume in relation to physical measurements of the individuals and to certain aspects of hemodynamics, to determine what interrelations exist.

This study comprises an analysis of the plasma and total blood volumes, venous pressures and blood velocity rates determined in 90 adult individuals, 49 of whom were males and 41 females. These subjects were hospital patients with no evidence by history or on physical examination of cardiovascular or renal disease, blood dyscrasias or debilitating disorders, and members of the hospital staff in good health.

Plasma and total blood volumes, venous pressures and blood velocity rates were determined with the subjects in a basal state. Results are summarized in Table I.

Sex

The plasma and total blood volumes of all our subjects, considered by age and sex, are shown in Figure 1, and the corresponding plasma and total blood volume in cc. per kgm. of body weight in Figure 2. At once apparent is the striking

difference in volumes of males and females, the average absolute and per kgm. plasma volume of females being 22.5 per cent and 3.7 per cent less, and absolute and per kgm. total blood volume 28.8 per cent and 4.7 per cent less than that of males, respectively.

An extreme range of about 30 per cent above and below average plasma and total blood volumes is encountered in individuals, as shown in Figure 3, but no particular difference in range obtains between sexes. In about two-thirds of the cases in this series, plasma and total blood volumes were within 10 per cent above or below average values; of the remaining one-third, an approximately equal number were above and below that limit.

Age

Analysis of absolute and relative volumes by decades (see Figures 1 and 2), shows a tendency in both sexes for values to remain at or rise somewhat above the average levels of the series during middle life and to decline with advancing age. The increase in total volume in terms of body weight during middle age is more pronounced in males than in females, while the decrease after the fourth decade, apparent in both sexes, is greater in females than in males, being about 16 per cent below middle age values in women and 8 per cent in men.

Height, weight, and surface area

There is an increase in total blood volume with increasing individual height, weight and surface area as calculated from the nomogram of Boothby and Sandiford given by DuBois (6), the relationships being as shown in Figure 4. In relation to all three of these physical measurements, in about 70 per cent of our cases total volume is within 10

per cent above or below the average value for the group in both sexes. As regards weight only, those cases having volumes above these limits were predominantly muscular individuals, those falling below were for the most part tall and thin.

The relation of total volume in cc. per kgm. to variations in body weight is shown in Figure 5B, in which it will be noted that in both sexes, unit volume tends to rise with increase in weight of individuals, reaches a maximum at a lower weight level in females than in males, and thereafter

TABLE I

The absolute and relative plasma and total blood volume, physical measurements, venous pressure, blood velocity rate and hematocrit in adult normal men and women

Case number	Date	Age	Height	Weight	Surface area	Venous pressure	Blood velocity rate	Hemato-crit	Plasma volume		Total blood volume		
									cc.	cc. per kgm.	cc.	cc. per kgm.	
		years	cm.	kgm.	square meters	mm. H ₂ O	seconds						
MALES—49													
3	November 23, 1934	26	178.0	70.4	1.88			44.6	2620	35.2	4720	67.1	
6A	December 1, 1934	23	179.8	71.4	1.88			42.1	4045	56.8	6980	97.7	
17	April 4, 1935	22		77.3			115	16	42.4	3890	50.3	6760	87.3
20B	November 29, 1935	26	186.3	74.6	1.97		60		44.4	2830	37.9	5090	68.3
32A	May 26, 1935	37	176.4	70.4	1.85		70	18	45.0	2945	41.8	5350	76.0
34	June 7, 1935	21	165.1	68.2	1.74		90	19½	45.3	3090	45.3	5650	82.7
46A	June 23, 1935	28	190.5	71.8	1.98		90	17	46.7	2985	41.6	5600	78.1
58	July 4, 1935	62	177.0	65.2	1.82		65	19	44.4	3140	47.0	5640	86.5
66	July 16, 1935	41	161.4	63.2	1.67		40	18½	44.5	2760	43.7	4970	78.6
69	July 19, 1935	19	178.0	65.0	1.80		70	14	45.4	2420	37.2	4360	67.0
73	July 22, 1935	26	187.0	66.0	1.88		115	18	48.7	2980	45.2	5800	88.0
74	July 23, 1935	24	171.4	76.2	1.88		115	17	47.8	2700	35.4	5160	75.3
82B	June 19, 1936	30	162.5	63.3	1.67		80	17	43.0	2530	39.5	4480	70.2
86A	October 2, 1935	23	166.3	59.6	1.65		80	14½	44.1	2340	39.2	4180	70.2
127	December 12, 1935	26	184.0	84.2	2.10		70	14	43.2	3200	38.2	5650	67.2
130	December 17, 1935	58		78.2			130	16	51.8	2400	32.0	5180	66.3
131	December 18, 1935	89		55.2			75	19	36.0	3210	58.2	5010	90.8
138	January 14, 1936	27	182.9	78.0	1.99		100	22	44.3	3190	40.9	5730	73.7
140B	January 15, 1936	22	175.2	76.1	1.91		80	20	44.7	3040	39.9	5500	72.2
142	January 18, 1936	43	173.0	71.0	1.83		120	17	48.8	2690	38.0	5260	74.0
148	January 31, 1936	39		54.3			110		45.2	2380	44.0	4350	80.1
155	March 17, 1936	22	176.0	79.4	1.94		45	16	49.4	3080	38.8	6080	76.7
161	March 24, 1936	27	174.5	72.4	1.85		120	15	48.3	2840	39.2	5490	75.8
177	May 6, 1936	60		68.0			95	17	49.3	2550	37.6	5030	74.0
180	May 13, 1936	19	153.4	48.6	1.43		120	14	48.4	1855	38.2	3590	73.8
193	June 4, 1936	58	170.0	64.6	1.74		30	18	43.3	2940	45.5	5190	80.4
196	January 8, 1936	28	161.3	73.3	1.77		100	17	48.6	2760	37.7	5380	73.5
197	February 26, 1936	38	180.2	63.3	1.79		85		40.2	3500	55.2	5850	92.4
198	March 11, 1936	43	157.4	62.8	1.63		85		42.2	2280	36.3	3950	62.7
199B	May 27, 1936	31	173.6	63.0	1.75		110	20	42.0	3230	51.3	5570	88.5
200	April 1, 1936	44	160.0	43.7	1.41		65		40.9	2135	48.8	3610	82.6
201	April 22, 1936	37	171.3	59.8	1.69		75	16	46.0	2860	47.8	5300	88.6
202	May 27, 1936	44	168.6	68.7	1.78		60		42.4	3020	44.0	5250	76.3
203	May 27, 1936	45	180.1	89.0	2.24		110		39.8	3550	39.9	5910	66.3
209	June 20, 1936	24	185.4	78.2	2.01			18	42.5	4000	51.3	6970	89.2
210	June 22, 1936	24	178.7	73.0	1.90		70	18	41.8	3560	48.7	6110	83.7
212	June 23, 1936	27	185.3	83.0	2.06		65	23	44.5	3660	44.1	6600	79.5
215A	June 27, 1936	25	180.1	69.5	1.87		80		41.4	3170	45.6	5410	77.7
219	July 8, 1936	57	173.2	62.5	1.73		85		38.1	3040	48.7	4920	78.7
223	July 16, 1936	41	185.3	75.0	1.97		65		48.8	2790	39.6	5450	72.7
224	July 21, 1936	30	167.6	59.0	1.66				48.0	2765	46.9	5325	90.3
225	July 22, 1936	51	170.0	65.5	1.73				42.6	2485	38.0	4330	66.2
226	July 23, 1936	38		73.7					43.6	3670	51.3	6510	90.8
227	July 27, 1936	39	172.6	76.6	1.89		60		46.0	2915	38.1	5400	70.6
229	July 29, 1936	44	172.1	78.1	1.91		65		46.9	3260	41.7	6140	68.7
231A	August 6, 1936	42	167.3	66.0	1.74				45.8	2845	43.2	5250	79.6
255	December 3, 1936	39	166.4	55.0	1.60		75		42.3	2530	46.3	4420	80.3
257	December 8, 1936	30	188.3	93.6	2.18				47.5	3620	38.7	6890	73.6
275	January 11, 1937	20	161.5	53.2	1.54			14½	46.2	2180	41.0	4050	76.2
Average		35.5	173.8	78.6	1.821	81.4	17.34	44.67	2948	43.08	5335	77.7	

TABLE I—Continued

Case number	Date	Age	Height	Weight	Surface area	Venous pressure	Blood velocity rate	Hemato-crit	Plasma volume		Total blood volume	
		years	cm.	kgm.	square meters	mm. H ₂ O	seconds		cc.	cc. per kgm.	cc.	cc. per kgm.
FEMALES—41												
61	July 9, 1935	16	154.9	42.8	1.37	55	16	37.3	1880	44.0	3110	72.6
63	July 11, 1935	26	168.0	55.6	1.62	55	13½	43.4	2380	42.7	4190	75.3
72	July 21, 1935	26	163.8	56.8	1.60	60	14	37.9	2470	43.5	3970	70.0
83	September 19, 1935	28	163.7	48.2	1.50	80	14	41.0	2210	44.9	3750	76.2
120	December 15, 1935	31	167.7	68.6	1.77	90	14	39.7	2510	36.4	4150	60.4
122	December 6, 1935	41	149.8	48.8	1.42	90		39.5	1750	35.8	2990	59.3
136	January 14, 1936	28	166.3	61.5	1.68	95	17	37.6	2550	41.6	4100	66.7
141	January 16, 1936	22	170.0	57.0	1.63	60	19	38.7	2480	43.5	4050	71.0
143	January 20, 1936	55	176.3	49.0	1.43	45	18	41.7	1860	37.9	3190	65.1
145	January 23, 1936	42	155.0	80.8	1.79	95	18	42.1	2170	26.9	3750	46.3
149	February 17, 1936	27	167.4	70.0	1.78	110	16½	38.7	2360	33.7	3850	55.0
152	March 13, 1936	20	160.0	56.5	1.58	105	12	43.1	2120	37.9	3765	66.7
154	March 15, 1936	49	161.9	60.2	1.62	80	20	43.6	2360	39.2	4190	69.6
156	March 18, 1936	33	162.5	57.0	1.60	85	11	41.2	2860	50.1	4870	85.4
157	March 17, 1936	31	161.3	59.0	1.61	50	17½	38.0	2850	48.3	4610	78.1
158	March 19, 1936	34	143.0	44.0	1.31	50	17½	38.3	2300	52.3	3730	84.7
160	March 21, 1936	27	167.4	53.4	1.58	110	20½	37.9	2405	45.1	3875	72.6
164	April 1, 1936	31	162.8	66.0	1.71	100	13½	43.5	2390	36.2	4230	64.2
168	April 10, 1936	26	152.5	45.0	1.38	100	19	40.6	2045	45.3	3440	76.4
172	April 18, 1936	26		48.6		90	14	41.2	1925	39.7	3310	68.2
174	April 22, 1936	30	166.3	61.7	1.68	115	17	40.2	2820	47.3	4870	79.3
176	May 5, 1936	38	167.5	63.3	1.71	70	15	40.2	2490	39.9	4165	66.8
178	May 6, 1936	46	158.4	68.8	1.70	70	16	44.4	2300	33.4	4130	60.1
181	May 13, 1936	51	162.4	43.4	1.42	55	19	42.6	1772	40.9	3090	71.3
182	May 14, 1936	21	163.9	56.2	1.61	120	11½	41.5	2150	37.9	3640	64.7
184	May 15, 1936	27	156.3	50.0	1.47	80	18	38.5	1995	39.5	3240	64.8
186	May 21, 1936	37	152.2	58.0	1.54	95	17	38.2	2380	41.2	3860	66.6
206	June 10, 1936	52		62.2		90	24	43.0	2300	37.0	3435	55.3
207	June 10, 1936	21	162.4	59.2	1.62	70	13	37.8	2330	39.4	3750	63.4
208	June 16, 1936	23	160.0	47.0	1.47	65	15	33.7	2500	52.1	3770	80.3
211	June 23, 1936	19	167.4	54.0	1.59	65	17½	38.3	2550	47.2	4130	76.6
213	June 25, 1936	36	184.1	54.0	1.71	95	18	36.6	2820	52.2	4450	82.4
214	June 26, 1936	23	159.2	49.0	1.48	95	13	36.9	2460	50.2	3995	79.5
220	July 13, 1936	46	167.4	51.6	1.57	75	12½	43.8	2000	38.8	3570	69.3
221	July 15, 1936	35	162.6	59.0	1.62	95	16	36.3	2380	40.3	3730	63.2
222	July 16, 1936	37	161.3	49.6	1.50	60	16	38.7	2310	46.7	3770	76.1
247	November 17, 1936	48	165.1	63.8	1.69	75	14	42.5	2080	34.1	3620	56.7
258	December 11, 1936	23	161.3	46.3	1.45	95	11	39.7	2200	47.6	3650	78.9
262	December 23, 1936	21	156.3	46.0	1.40	50	15	39.1	1850	40.2	3030	66.0
266	September 17, 1936	20	157.0	43.4	1.39			43.1	1770	40.8	3115	71.7
272	January 8, 1937	20	151.8	47.4	1.40	60	22	37.9	2320	48.9	3740	78.7
Average		38.9	162.0	55.2	1.504	80.0	15.25	39.95	2284	41.5	3800	66.1

declines with further increase in weight, the decrease being more pronounced in women than in men. In relation to variations in height (Figure 5A) unit volume rises with increasing individual height, reaches a maximum value and remains quite constant with increases in height thereafter in both sexes. The composite relation of total volume to variations in both height and weight, namely, surface area (Figure 5C), clearly indicates the chief differences between the sexes in the relationship of volume to physical measurements; total blood volume in terms of surface

area is about the same in small men and women, but is considerably greater in large men than in large women. In addition, with increasing individual size, unit volume in males increases steadily at a gradually lessening rate, while in females it rises to a maximum well below the level of the male maximum value and declines rather sharply thereafter.

Venous pressure and blood velocity rate

We have observed no significant variations in either venous pressure or blood velocity rate with

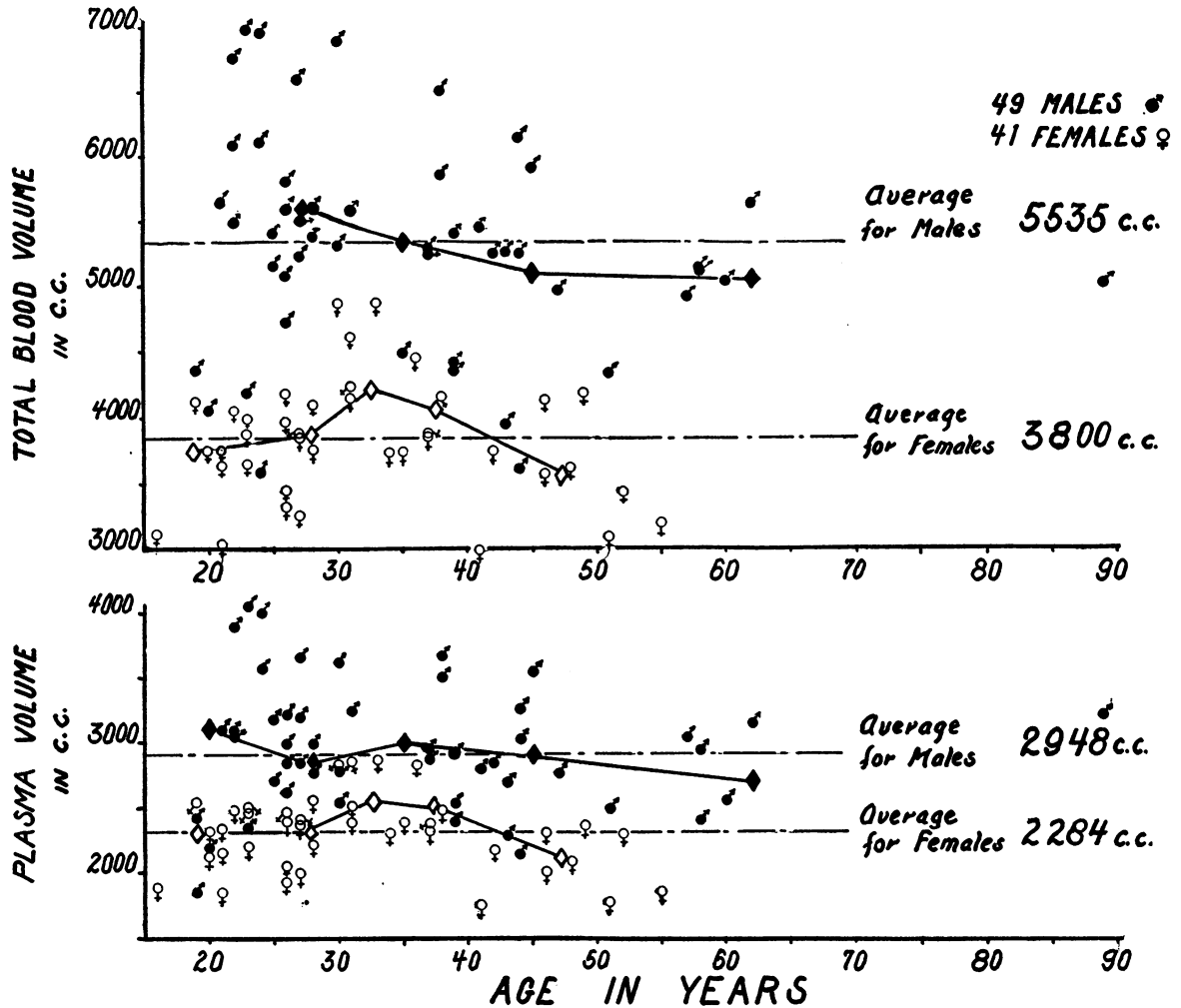


FIG. 1. PLASMA AND TOTAL BLOOD VOLUME IN 90 NORMAL MEN AND WOMEN WITH REFERENCE TO AGE

Both plasma and total blood volume of males is greater than that of females, and tend to diminish with advancing age in both sexes.

age in either sex (Figure 6). The degree of variation in individuals above and below average values for the whole group is less in the case of the blood velocity rate than in venous pressure in both sexes, but in both instances the extremes encountered in males and females are about the same. The average value of both determinations is appreciably lower in females than in males. The relation of total blood volume to variations in venous pressure and blood velocity rate is as shown in Figure 7. It is apparent that no interrelation between variations in these two measurements and blood volume exists in normal persons.

Red cell volume

In the method employed the red cell volume is based upon the hematocrit values of venous blood samples, being considered as the difference between total blood and plasma volumes. In this series the male hematocrit value ranged from 36.0 to 51.8 with an average value of 44.6; the female hematocrit from 33.7 to 43.8 with an average value of 39.9. Thus the average hematocrit value for females is 10.5 per cent less than that of males.

The computed average red cell volume of males is 2387 cc. and that of females 1514 cc., or 36.5 per cent less than that of males.

CRITIQUE

Our findings are at variance with those in the literature. Thus Keith, Rowntree and Geraghty (1), Rowntree and Brown (7), Kaltreider, Hurtado and Brooks (8) and Silbert et al. (9) reported higher average absolute and relative total blood volumes for males than the average values of this series, and Bock (10) and Seyderhelm

Some of the wide divergence in values found by the above authors may be due to the limited number of cases studied, since the extreme range encountered in this series, comprising more cases than were included in any of those series referred to above, is plus or minus 30 per cent from average values. Pitfalls of the earlier methods described by Gregersen, Gibson and Stead (16)

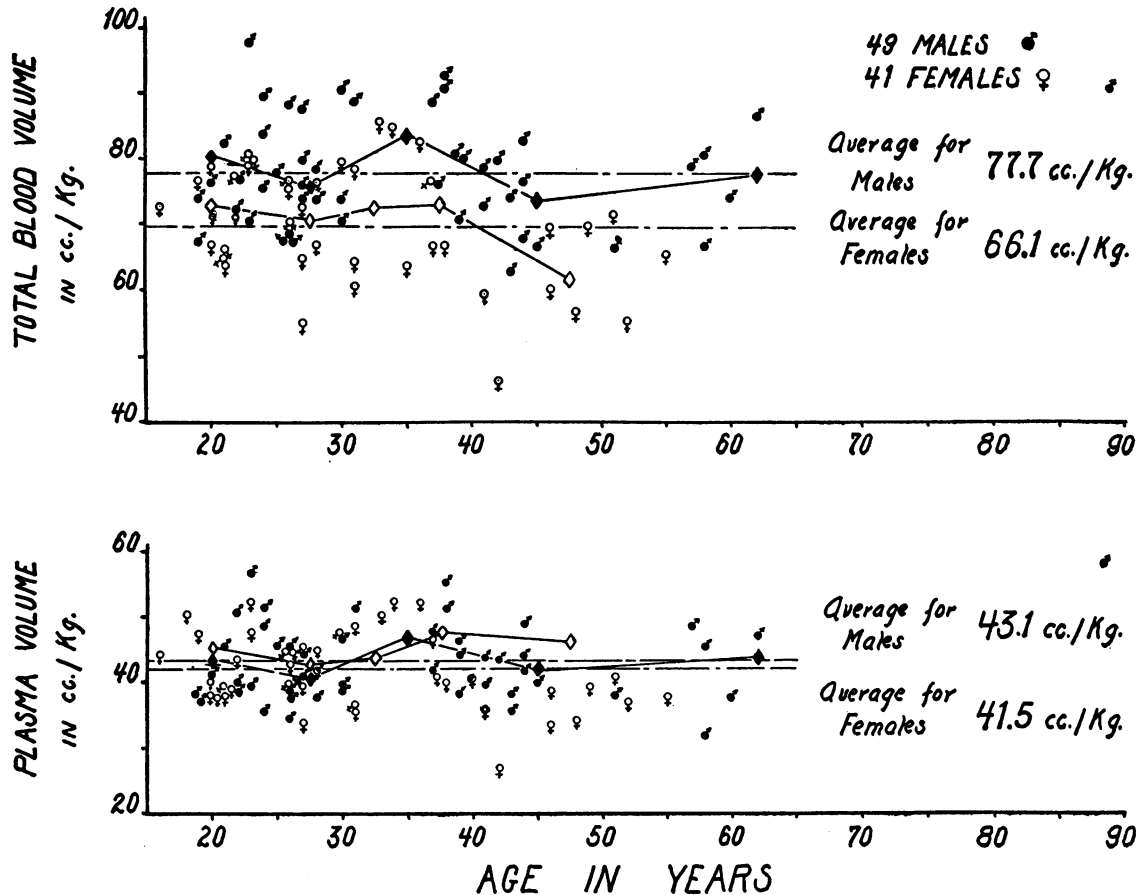


FIG. 2. PLASMA AND TOTAL BLOOD VOLUME IN TERMS OF BODY WEIGHT

The difference in total volume of males and females is due principally to the larger red cell volume of the male, the unit plasma volume of both sexes being nearly equal.

and Lampe (11) obtained higher relative total blood volumes. Wollheim (12) obtained a higher relative and lower absolute average total volume than our values. Kaboth (13) and Sparks and Haden (14) published values for women lower than those herein reported both as to absolute and relative total volume, while those of Uhlenbruck and Leyendecker (15) and Rowntree and Brown (6) were considerably higher.

and in a previous communication by us (5), account in large measure for this divergence. Thus, if the volume calculation is based on the dye concentration of a single blood sample taken before the dye is completely mixed in the blood stream, falsely low values will be obtained. Inequality of dye concentration between standard and unknown may produce large errors in either direction when the Dubosq colorimeter is used, as may

also errors due to hemolysis of dye free or dyed samples or both. While some of these errors may be compensating, it seems evident that values for normal blood volume as determined by the methods employed by the above authors cannot be regarded as reliable.

tissue as muscle and viscera and blood poor tissue as bone and fat. It is accordingly consistent that muscular persons should have relatively more and fat persons relatively less blood per unit of body weight than persons of more normal habitus and proportion of brawn and blubber. Thus Cases

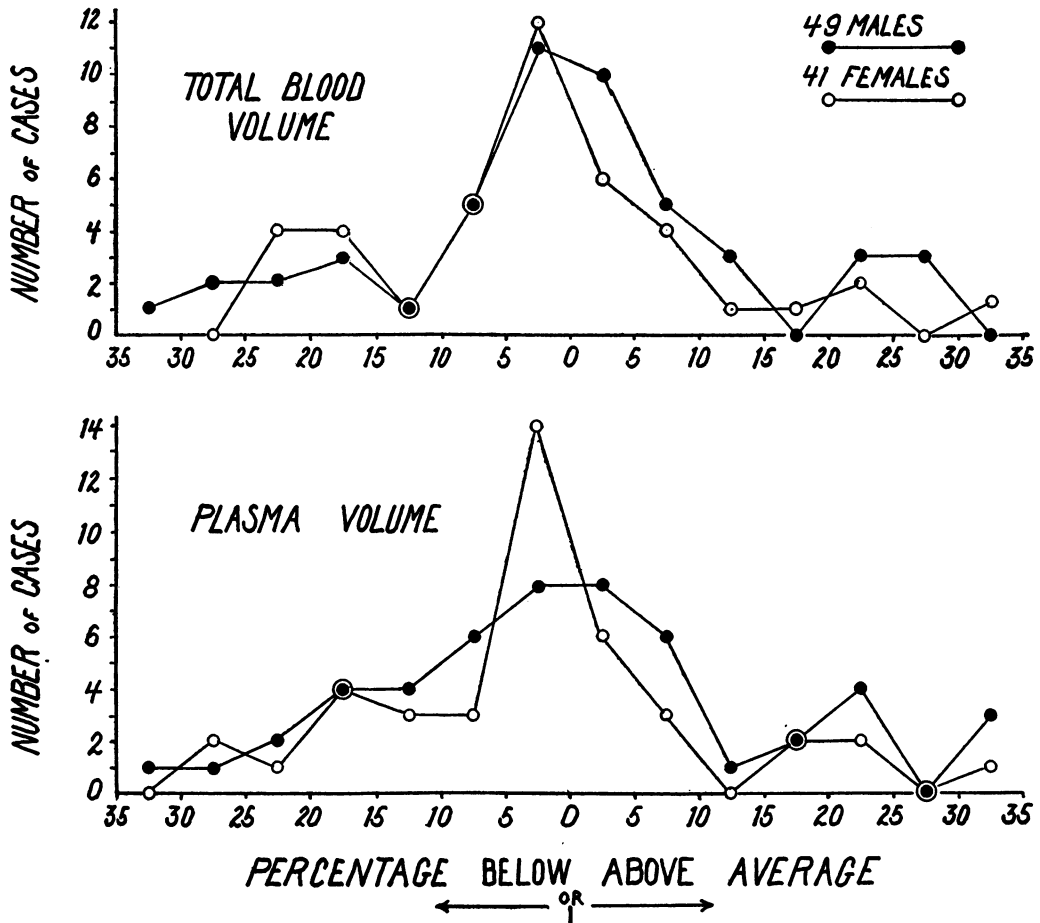


FIG. 3. DISTRIBUTION OF NUMBER OF CASES ABOVE AND BELOW AVERAGE VALUES FOR PLASMA AND TOTAL BLOOD VOLUME

About two-thirds of the cases are within 10 per cent above or below average values in both sexes.

Our analysis of the blood volumes of normal individuals, as determined by the method we have employed indicates that differences in plasma and total blood volume of individuals of comparable age, sex, height and weight may be considerable. That extreme variations in the amount of blood in the bodies of different persons exist is not incompatible with known individual differences in build, and varying proportions of such blood rich

6A, 156, 174, 209 and 224 are muscular persons leading physically active lives, and in all of these, both absolute and total volume per kgm. of body weight exceeds average values. Cases 140B, 145, 149, and 203, all obese persons, have absolute volumes equal to or above the average values, but less than the average value per unit of body weight. Cases 158, 208, and 226, all underweight, have absolute volumes slightly under, but

relative volumes much higher, than average values.

The greater blood volume of males than females is due chiefly to the higher red cell volume of the male, the plasma volume of the two sexes differing only slightly (Figure 1). This fact is in keeping with known observations of higher red

cell counts, hemoglobin and hematocrit values, basal metabolic rates (DuBois (6)), and vital capacities (Hutchinson (17) and Pratt (18)) of men as compared to women. It is of interest, however, that the total red cell volume of women as compared to that of men is considerably less

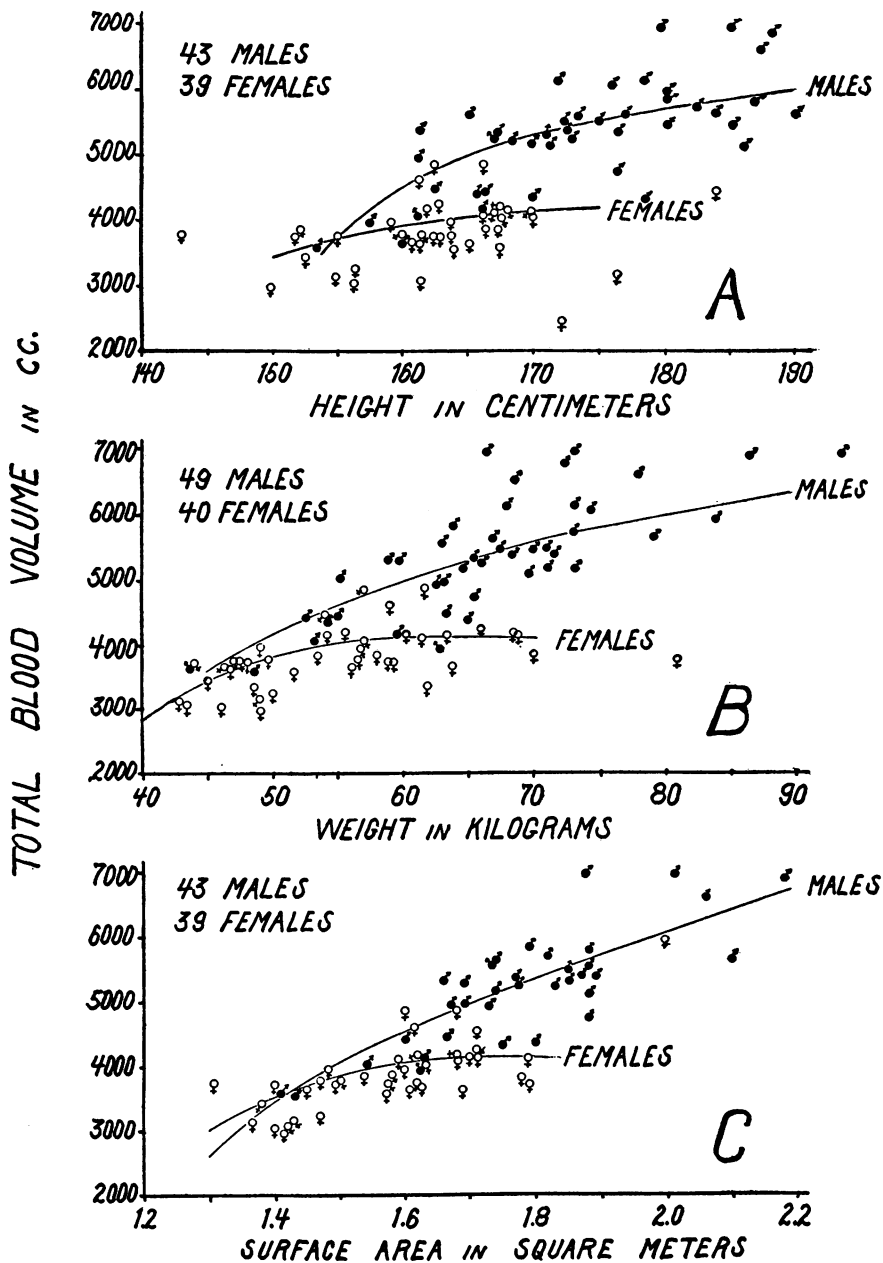


FIG. 4. RELATIONSHIP OF TOTAL BLOOD VOLUME TO HEIGHT, WEIGHT AND SURFACE AREA

With increase in size total volume in relation to surface area rises steadily in males, but tends towards a constant value in females.

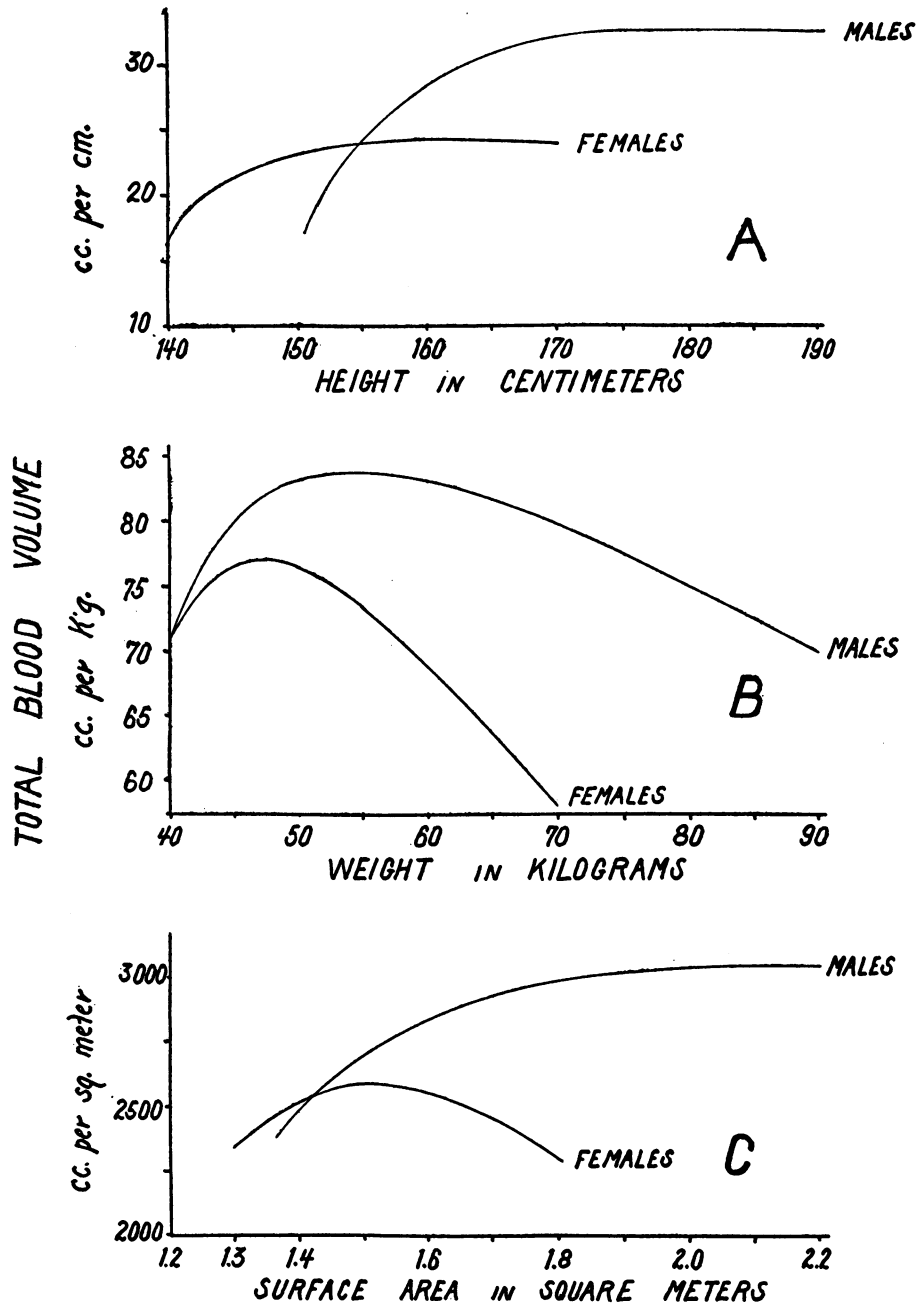


FIG. 5. RELATIONSHIP OF TOTAL BLOOD VOLUME IN UNIT TERMS TO DIFFERENCES IN INDIVIDUAL HEIGHT, WEIGHT AND SURFACE AREA

The diminution in unit volume with increasing weight is more pronounced in women than men. With increasing surface area, unit volume rises and tends toward a constant value in men, but decreases in large women.

than the percentage differences between normal values for red cell counts, hematocrits and hemoglobins would indicate. Thus while average hematocrit values in this series for women are only 10.5 per cent less than for men, the total red cell volume of women is 42.8 per cent less than that of men; the reason being the lower value of both the plasma volume and hematocrit of women. In this connection it should be pointed out that differences in absolute red cell volume of individuals

or of changes therein in the same individual cannot be determined on the basis of red cell counts or hematocrits alone. In each case, the plasma volume must be taken into consideration.

That there should be a considerable difference in the blood volume of men and women is not surprising when considered in terms of body weight, and the fact that men as a rule are more muscular and are apt to lead more physically active lives than women. In this connection cer-

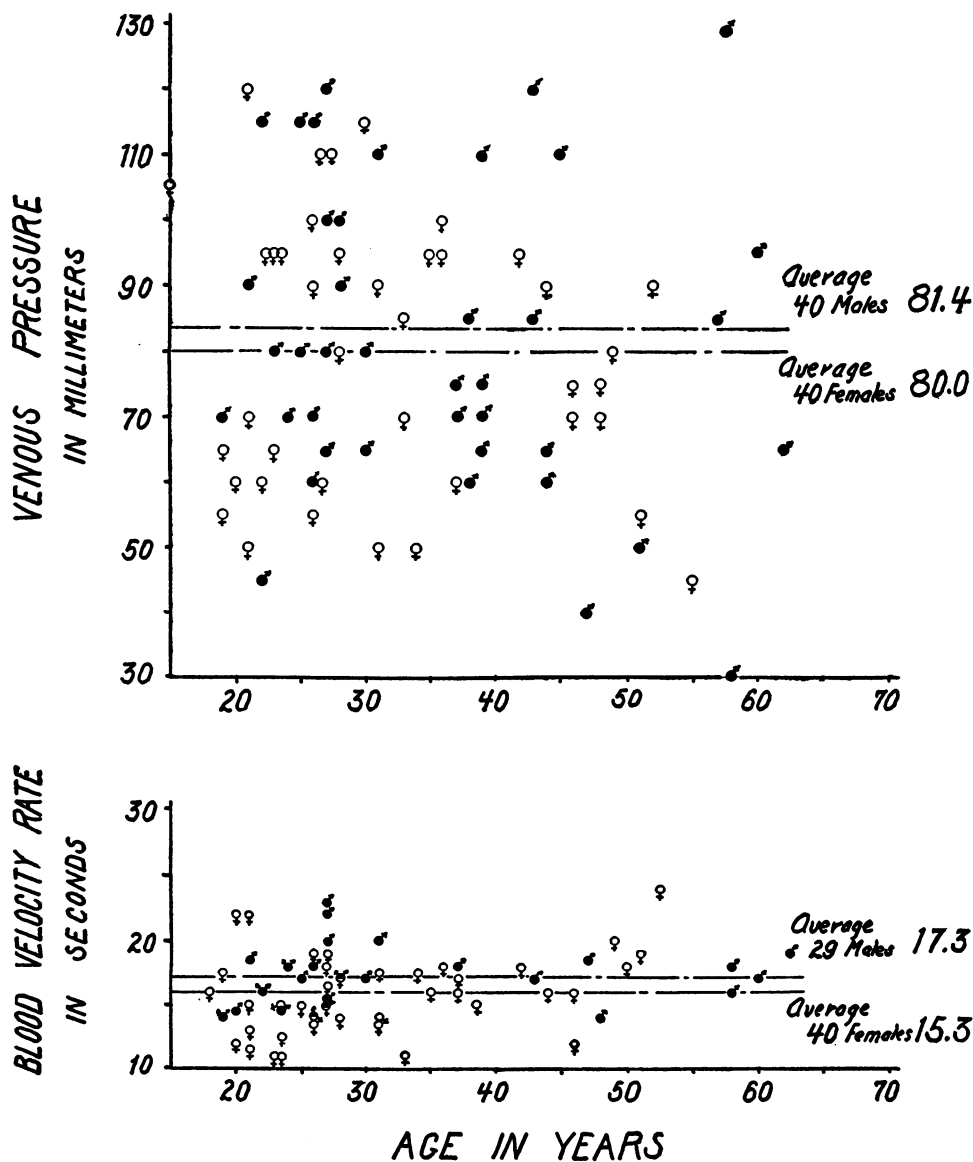


FIG. 6. VENOUS PRESSURES AND BLOOD VELOCITY RATES IN 90 NORMAL MEN AND WOMEN
No relationship of these determinations to age exists in either sex.

tain cases in this series are of interest as exceptions that prove the rule. Thus Cases 156 and 174, both athletic women, have high relative volumes well within the male range, while Cases 82B and 127, men of poor muscular development

during the life span. Thus Krogh's modification of the Sage standards of basal metabolism (6, p. 157) shows a decrease of 7 per cent in calories per hour between the ages of 25 and 55. A decrease of about 17 per cent in vital capacity dur-

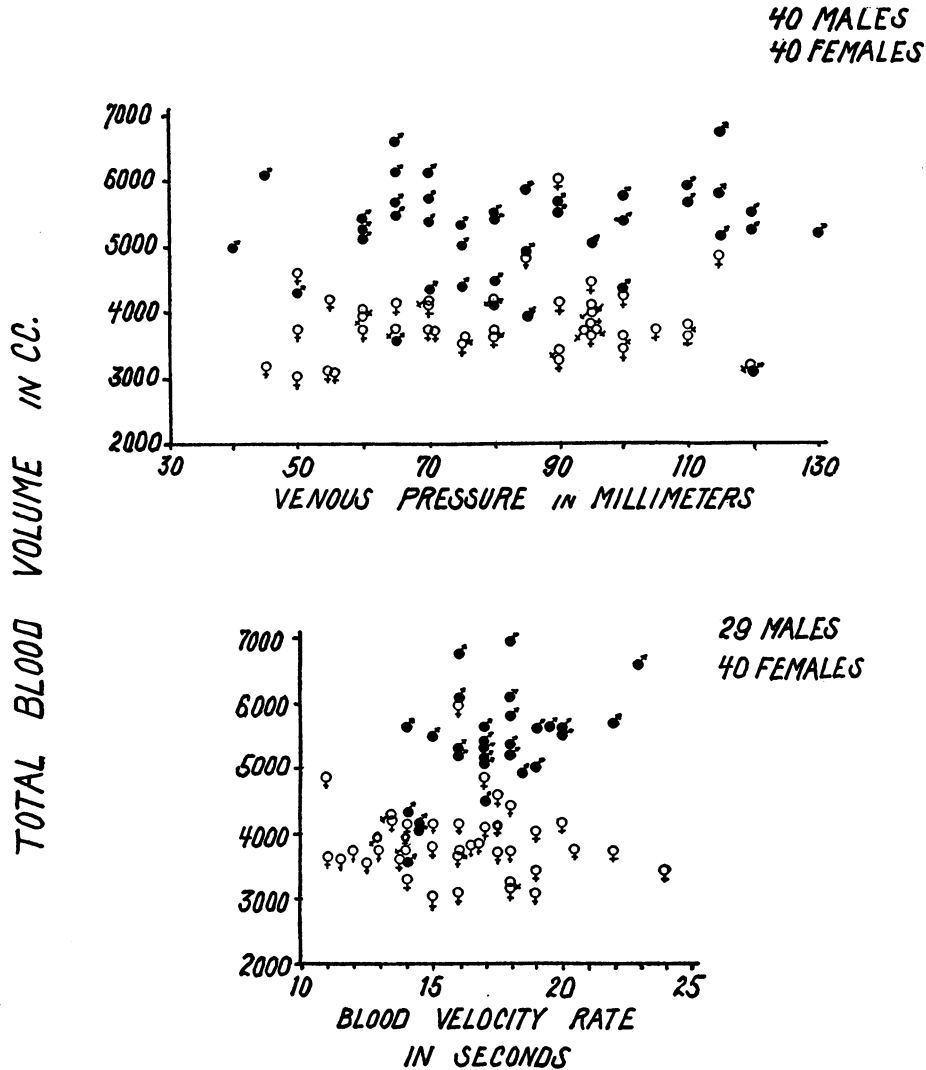


FIG. 7. RELATIONSHIP OF TOTAL BLOOD VOLUME TO VENOUS PRESSURE AND BLOOD VELOCITY RATE IN 90 NORMAL MEN AND WOMEN

No relationship to variations in these factors exists in either sex.

and sedentary habits, have relative volumes well below the male average.

The decline in total blood volume with increasing years, amounting to about 14 per cent in males and 10 per cent in females between the ages of 25 and 55 is in keeping with observations on changes in basal metabolism and in vital capacity

ing a similar age period is revealed in the studies of Hutchinson (17) and Pratt (18). It seems evident that the total quantity of blood in the normal body bears a definite relation to the oxygen requirement of the body.

The greater percentage decrease in volume in females than in males is consistent with known

changes in bodily condition taking place with advancing years, particularly in view of the tendency towards obesity occurring in women after the menopause.

The selection of a basis for the determination of normal values for comparative purposes in clinical investigation presents some difficulties. It is apparent that the blood volume of a given

for calculation of normal volume on the basis of height or surface area is shown in Figure 8.

CONCLUSIONS

- (1) Plasma and total blood volume, venous pressure and blood velocity rates were determined in 49 normal males and 41 normal females.
- (2) No relationship exists in normal persons

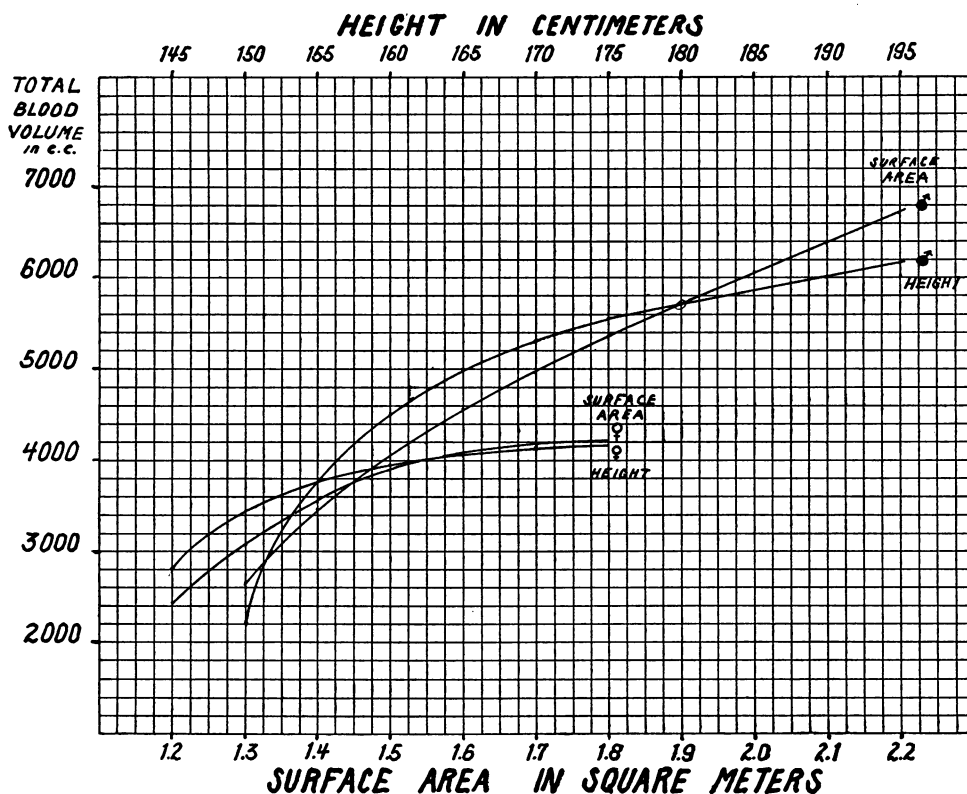


FIG. 8. CHART FOR DETERMINING NORMAL BLOOD VOLUME FOR MEN AND WOMEN ON THE BASIS OF HEIGHT OR SURFACE AREA (AS COMPUTED FROM THE NOMOGRAM OF BOOTHBY AND SANDIFORD)

individual may be predicted on the basis of height, weight or surface area only within wide limits. The average value found for males and females in this series does not reflect differences due to body size. We feel that in a group of patients, the average of normal values based on surface area in those cases exhibiting no marked disturbance in weight to height relationship, and on height in those cases presenting weight changes due to disease, offers a more useful estimate of normal volume than the average values for the entire group of normals herein reported. A chart

between variations in total blood volume, venous pressure and blood velocity rate.

(3) The total blood volume of normal males is greater than that of females, the difference being due to the greater red cell volume of males. The absolute red cell volume of females is less than that of males by a much greater degree than indicated by differences in red cell counts and hematocrit values.

(4) With increasing age there is a decline in the blood volume comparable to decreases in basal metabolic rates and vital capacities.

(5) In comparison to average values, the absolute total blood volume is high in muscular and obese persons, and low in thin individuals; the volume per unit of body weight is high in muscular and in thin individuals and low in obese persons.

(6) The blood volume of normal individuals varies within wide limits. The relationship to height or surface area offers a useful basis for estimation of normal volume in clinical investigation.

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