RED CELL, PLASMA AND BLOOD VOLUME IN HEALTHY MEN MEASURED BY RADIOCHROMIUM (Cr^{51}) CELL TAGGING AND HEMATOCRIT: INFLUENCE OF AGE, SOMATOTYPE AND HABITS OF PHYSICAL ACTIVITY ON THE VARIANCE AFTER REGRESSION OF VOLUMES TO HEIGHT AND WEIGHT COMBINED *

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Methods employing radioactively tagged red cells have been widely adopted for measurement of blood volume. However, in comparison with the work which has been done with the dye (1–5) and carbon monoxide (6) methods, little attention has been given to the establishment of mean values for men and women or to study of the variance encountered among healthy subjects. Most clinical investigators have collected their own control data, based often on study of relatively few or not entirely healthy subjects (7–13).

A rather large scatter of data around mean prediction values has been found by all workers, regardless of methods employed, when values for whole blood volume (Vwb), red cell volume (Vrbc) and plasma volume (Vpl) are related to body weight, height, or combinations of these measures (1–5, 13, 14). Some of this variation presumably results from differences in body composition, since blood volume correlates both with body density (5, 15) and with lean body mass (16, 17). However, it has not been shown that predictions based on total body mass are less accurate than those based on lean body mass, which requires a separate measurement (15, 16). Consideration of fat thickness and girth measurement, in addition to height and weight, was found by Hicks, Hope, Turnbull and Verel to improve prediction (14). Gregersen and Nickerson (3) classified subjects according to somatotype and found that variance of blood volume per unit of body surface area was reduced to an important degree when dealing with extreme body types but not in the middle ranges. Divergent results have been reported concerning the influence of age and of physical training on blood volume (2, 18–23).

We have used the Cr^{51} method of Sterling and Gray (24, 25) to measure Vrbc and, indirectly from the hematocrit, Vwb and Vpl in 201 healthy prison inmates. Trivariate regression equations have been derived for the plane surfaces which relate the volumes to height and weight and a graphic system for their rapid application to practical problems has been developed. By analysis of individual differences, "residuals," from the mean regression planes, we have studied the effects of the following factors on the variability of the data: age, body build, habits of physical activity and, to a limited extent, seasonal changes.

SUBJECTS

The subjects were selected by careful screening from normally active volunteers. Most of them were white (see Table I for racial and national origins). Information from the prison health records was supplemented by interviews conducted by a physician from our group, by minifilm X-rays of the chest and by laboratory tests which included complete blood count, sedimentation rate, urinalysis, electrocardiogram and a serologic test for syphilis. Volunteers were rejected if the results of these tests were abnormal, if their blood pressures were above 140 mm. Hg systolic or 90 diastolic, or if they had recognizable disease or past history of illness, such as rheumatic fever or tuberculosis, which might be present

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TABLE I

Data in chronologic order from experiments on 201 healthy men

Subject*	Age	Height	Weight	Activity class I, II or III	Somatotype			Hematocrit†	Vrbc†
					En	Me	Ec		
	Years	*cm.*	*Kg.*					%	*L.*
F. Bl.	29	178	73.5	II	3	4′	3′	43.0	2.02
W. Ru.	25	180	68.0	I	2′	3	4′	43.0	1.96
B. Re.	27	174	64.3					42.8	2.11
A. Wa. (N)	31	173	67.1		1′	5′	3	41.1	1.62
R. Ke.	27	186	66.2	I	2	3	6	44.0	2.03
E. Yo.	25	183	72.5	II				44.2	2.31
J. Ki.	32	171	67.3	II	2	5	2	44.6	1.76
R. No.	29	180	72.5	I	3	4′	3′	47.6	2.16
D. Br.	24	187	76.6	II	3	4	4′	51.2	2.42
R. Cu.	29	180	80.2	I	3	5	2′	48.3	2.49
E. Sm. (N)	38	177	79.2					49.7	2.36
J. Li.	27	173	67.9	I	3	4′	3	44.5	2.01
W. Sm.	34	187	95.7					48.6	2.70
W. Bu.	37	182	66.2	I				46.2	2.01
J. St.	42	173	65.3	I	3	4	4	43.2	1.80
R. Wa.	33	180	71.6	I	2′	4	4′	46.4	2.26
W. Sm.	26	178	77.0		2′	5′	2	48.4	2.30
J. Je. (N)	33	177	87.0	I				46.9	2.37
P. Ki.	26	186	102.0	III	4	5′	1′	47.3	2.54
H. Po. (N)	50	174	110.2‡	II	3′	6′	1	43.6	2.41
R. Ha.	22	169	61.2	I	1′	5′	2	46.0	1.63
R. Su.	30	168	70.3	II				43.0	1.60
R. Sa.	22	183	77.1					45.9	2.35
I. Tu.	25	183	77.1					45.2	1.99
N. McK. (I)	32	183	70.7	II				42.9	2.13
H. Ca.	30	187	86.2	II	3′	4′	3	43.7	2.26
N. St.	33	168	53.9		2′	3	4′	43.4	1.66
D. Ma.	41	182	96.7	II				44.9	2.24
J. He.	35	183	65.7	II				46.5	1.91
G. Al.	43	173	67.6	I	3	4	3	42.6	1.97
W. Be.	26	173	56.6	II				40.1	1.46
M. Va.	21	170	69.3	III	3	5′	2	43.1	1.88
F. Pr.	25	165	58.9					43.2	1.52
M. Re.	27	173	70.3	I	4′	4	3	44.7	1.85
R. Ma.	24	174	63.4	II	3	3′	4	43.3	1.90
T. Ke.	20	183	76.6	I	3′	3′	4′	43.2	2.07
R. Pe. (M)	24	180	64.3	III	2	5	4	41.1	2.18
G. Yo.	34	163	54.9					49.8	2.13
G. Ol.	27	170	61.1	III	2′	4′	3′	43.3	1.79
B. Br.	23	185	85.7	III	3	5	2′	44.0	2.20
K. Kn.	29	180	72.1	I	3′	3′	4′	41.6	2.11
C. Fa.	25	176	65.7	III	2′	5	3	45.6	2.09
B. Ma.	24	171	65.7	III				48.0	2.11
R. Tu.	26	173	71.1	III	3	5	2′	44.2	1.89
J. Fr.	21	183	81.7					43.4	1.97
M. Sw.	31	178	76.2	II	3	4′	3′	48.7	2.08
E. Ri. (M)	35	171	69.2	II	3′	4	3	46.7	2.20
W. Er.	32	180	80.0	II	3′	4′	3′	43.0	2.58
F. Er.	33	171	75.5	II	4	4′	2′	44.4	1.87
S. Ti.	41	163	60.9	III	3	4′	3	47.7	1.55
L. Vi.	36	173	58.0	I	2′	4	4′	42.7	1.63
W. De.	44	170	70.0	III	3	4′	3	43.1	2.08
H. Sa.	26	171	73.0	III	2′	5′	1′	44.6	2.26
K. Sk.	21	182	76.8	II	2′	5	2′	42.7	2.17
B. Ma.	43	182	78.0	III	3′	3′	4	44.7	2.42
R. Bl.	29	175	81.8	III	2	6′	1	44.8	2.07
R. Mo.	31	178	77.3	II	2′	5	2′	46.6	2.26
J. Ca.	30	182	75.0	II	3′	4	4	48.3	2.37
C. Tu.	32	175	68.2	II	3	4	4	43.5	2.04
B. Sy.	35	183	80.0	II	2′	4′	3′	43.5	2.65
D. Hu.	24	185	90.5	II	3	5′	2	45.0	2.72
L. Lo.	35	184	87.3	I	4	3′	3	45.0	2.38
D. Bi.	22	180	87.8	II	4	5′	2	45.6	2.32

* (C) Chinese, (F) Filipino, (I) North American Indian, (M) Mexican, (N) Negro.
† Uncorrected for trapped plasma.
‡ Weight: height ratio exceptionally high. See Figures 1 and 4.

TABLE I—*Continued*

Subject*	Age	Height	Weight	Activity class I, II or III	Somatotype			Hematocrit†	Vrbc†
					En	Me	Ec		
	years	*cm.*	*Kg.*					%	*L.*
R. Al.	27	175	63.6	III	2′	3′	4	47.8	1.95
J. Da.	30	173	75.5	II	2′	5′	1′	46.1	2.33
L. An.	25	175	82.1	III	2	6′	1	49.2	2.17
W. Me.	25	192	84.6	III	2′	4	4	47.2	2.44
W. Co.	30	177	75.0	III	2	6	1′	43.4	1.86
P. Re.	29	179	62.3	I	2	3′	5	40.8	1.67
D. Sm.	21	187	71.0	II	2′	3′	4	42.3	2.08
F. Sh.	26	165	63.2	I	2′	5′	2	48.9	1.80
H. Fr.	37	167	70.0	II	3	5	2	48.8	1.81
J. Ve.	33	170	63.6	III	2	5	3	45.3	1.90
M. Wi. (N)	30	175	65.0	II	1′	5	4	45.7	1.87
W. McC. (N)	27	191	98.2	III	2′	6	2	43.3	2.58
P. Do.	32	175	71.0	III	2′	5	3	44.9	1.78
R. Wh.	26	180	77.3	III	4	4	3′	42.4	1.73
P. Ca. (M)	26	168	65.5	II	3′	4′	2′	48.4	1.93
F. Pe.	26	176	71.4	II	2′	5	2′	45.2	2.30
R. In.	33	175	71.0	III	3	4	3	42.5	1.75
C. Mo.	23	180	66.0	II	2′	3′	4′	45.4	1.84
J. Po.	45	163	63.6	I	3′	5	2	43.0	1.61
W. Tw.	22	185	78.2	III	3′	4	4	45.5	2.13
R. Ga.	32	177	81.4	I	4	4	2	40.2	1.83
L. Ba.	31	178	72.3	I	3	4′	4	44.6	1.95
B. Ho.	26	173	64.1	II	1′	5′	3	41.6	1.58
R. Bl. (M)	27	177	65.5	II	3	4	4′	48.1	1.93
H. Pi. (I)	22	177	70.9	I	3	5	3	44.2	1.82
S. Ro.	30	179	60.5	I	2	2′	5′	39.4	1.44
W. Ti. (N)	27	164	64.6	I	2	6	1′	48.4	1.95
M. Wa.	33	182	78.2	II	3′	3′	3′	47.6	2.03
E. Ch.	29	175	75.6	II	3	5	2	42.1	1.84
M. Pa. (F)	27	180	93.2	III	4	5′	2	52.8	2.69
C. Ho.	21	180	67.3	I	3′	3′	4	46.3	1.87
F. McG.	26	180	66.9	I	2′	2′	5	46.5	2.00
J. McC.	26	183	66.8	III	3	2′	5′	48.5	2.07
G. Lo. (C)	30	170	54.1	I	2′	2′	5′	47.2	1.72
C. Fi.	31	157	55.5	II	3	5	2′	48.2	1.54
E. Fl.	30	183	82.8	II	3	4′	3′	48.4	2.21
A. Ow.	28	179	86.8	III	3	6	2	44.9	2.13
P. Ca.	26	163	59.6	I	3	5	2	47.3	1.89
P. Li.	35	168	68.6	I	4	4	2′	45.9	1.70
E. Re. (N)	22	183	74.2	II	1′	5′	3′	42.6	1.91
E. Mu.	40	183	74.2	I	2′	3′	4′	46.3	2.32
R. Mi.	33	171	76.4	I	3′	5	2′	46.5	1.65
E. McN.	25	174	55.9	II	2	2′	5	43.6	1.82
J. Au.	26	179	80.9	II	4	4′	3	44.2	2.07
W. Jo.	26	175	59.2	I	2′	2′	5	45.5	1.53
J. Co.	27	177	85.9	II	4′	5	2′	54.0	2.62
R. Mo. (N)	27	180	70.0	II	2	4′	4	43.5	1.99
F. Sm.	35	166	69.6	I	3	5	2	41.9	1.60
J. Ja. (N)	32	171	69.2	I	2	5′	2′	53.5	2.15
P. Ca.	24	170	66.4	II				43.4	1.74
F. La.	34	188	81.0	II	2	4′	4	45.9	2.45
G. Fi.	24	175	80.5	I	4	5′	2	45.3	2.12
B. Fa.	27	179	68.2	II	2′	3′	4	44.0	1.79
C. Bi.	21	165	65.5	II	3	5′	1′	50.0	2.25
G. Tr.	29	180	91.0	III	4	5	2	44.9	2.24
A. Ko.	35	179	61.8	III	1′	4	5	40.7	1.63
H. Or. (N)	40	179	112.7‡	I	5′	4′	1′	53.0	3.02
R. Le.	37	170	74.1	II	3	5	2	46.7	2.03
T. Ke.	30	170	73.2	III	2′	6	2	46.2	2.05
V. Sl. (N)	32	173	74.2	II	3′	4′	2′	46.6	2.23
A. Si.	43	163	79.6	I	4	5	1	45.9	2.21
R. Ca.	36	175	70.5	II				44.8	1.94
J. Sm.	31	171	84.2	III	4′	4′	1′	44.3	2.18
W. Mo.	35	173	68.2	III	3	4′	3′	44.3	1.78
M. Du.	25	178	66.0	III	1	5′	3′	41.7	2.04
J. Ha.	45	171	63.7	I				40.5	1.66
J. Al.	27	184	71.8	I	2′	3′	4′	45.5	2.47
L. En.	29	173	67.3	I	2′	5	3	44.9	1.83

TABLE I—*Continued*

Subject*	Age	Height	Weight	Activity class I, II or III	Somatotype			Hematocrit†	Vrbc†
					En	Me	Ec		
	years	*cm.*	*Kg.*					%	*L.*
R. Gu.	26	163	78.7	III	3	7	1	46.9	2.14
W. Ki.	28	170	61.8	I				48.5	1.72
H. Co.	30	185	72.8	III	2′	3′	5	49.1	2.35
H. We.	21	173	66.8	I	3′	4′	3	48.8	1.72
A. Ma.	28	168	65.4	II	3′	4′	2′	47.6	2.05
R. Ba.	22	178	73.2	III	3	5	3	48.5	2.22
R. Bo.	25	180	63.2	I	2′	2′	5′	42.9	1.73
E. Ro.	27	173	63.7	II	3	4	4	46.5	1.78
R. Mo.	28	174	69.6	II	3	5	2′	43.9	1.88
W. Re.	37	178	95.5	II	5	4	3	44.9	2.43
T. La.	25	170	82.8	II	5	5	1′	45.2	1.98
J. Ri.	48	179	67.3	II	2	4	5	44.9	1.82
D. Hu.	19	178	64.1	II	2′	4	4′	43.1	1.73
V. Fl.	22	173	65.5	II	3	5	4	45.6	1.89
E. Ge.	30	170	63.2	I	3	4	3	42.8	1.73
E. Zu.	39	177	77.3	II	3	4′	3	48.6	2.12
A. Ma.	39	184	78.2	III	3′	3	4′	46.7	2.19
J. St.	24	180	64.6	I	2′	3′	5	44.6	1.80
D. Jo. (N)	26	178	70.0	II	1′	5′	3′	43.5	1.84
W. Ka.	23	184	74.1	I	3	4	4	39.8	1.91
R. Or.	22	170	72.8	III	3′	5′	2	48.4	2.10
R. Ma.	23	177	74.6	I	3	5	2′	44.8	2.11
W. Co.	28	170	58.2	I	2	4	4	45.0	1.90
R. Cu.	22	173	61.8	II	3	4	4	42.2	1.96
J. Ad.	27	183	74.1	II	2′	4′	4	42.0	2.28
D. Ra.	39	184	70.9	I	2	3′	5	43.9	2.01
G. Lo.	20	180	80.9	II	4	5	2	43.3	2.21
C. Ba.	21	178	66.4	II	2	4′	4	42.8	1.81
W. Th.	42	171	66.8	I	2′	4′	3′	40.9	1.87
J. An.	28	185	87.3	III	1′	6′	2′	45.8	2.48
R. McA.	25	175	67.3	II	2′	4′	3	43.5	2.07
C. Mo.	25	171	65.0	I	2′	5	2′	45.9	1.94
C. Fa.	29	165	71.0	III	2	6′	1	45.3	2.05
R. Sm.	37	170	64.1	II	2′	4′	2′	46.9	1.92
G. Br.	27	174	75.0	III	2	6	2	47.7	2.15
C. Fi.	29	180	81.4	I	3′	4′	2′	44.9	2.13
B. Kl.	25	175	83.7	II	5	4	2	45.0	2.23
C. Sl.	24	177	78.7	III				51.2	2.64
F. Sp.	30	184	75.5	I	3	4	4′	47.5	2.23
J. Sa.	29	169	66.8	II	3′	5	3	49.5	1.90
H. Wi. (N)	24	169	60.5	III	2	5	3′	40.3	1.60
R. Fa.	24	163	60.5	II				44.1	1.35
J. Ja.	24	180	69.1	III	2	4′	4	42.3	1.74
W. Jo.	33	174	68.2	I	3	4	3′	44.8	1.91
H. Co.	52	188	73.2	II	2	3	5	42.9	1.73
J. Jo.	28	191	66.4	I	1′	1′	6′	43.9	1.98
W. Sc.	25	177	66.8	I	3′	3′	3′	46.4	1.88
J. Ar.	27	178	66.4	II	2′	3′	4	45.2	2.07
J. St.	24	180	64.6	I	2	4	5	44.7	2.29
T. Pr.	36	189	90.5	III	2	5′	3	45.1	2.58
J. Me.	33	168	58.2	II	2	5	3	46.0	1.82
M. Bu.	23	173	63.6	II	2′	4	4	42.0	1.78
F. Br.	36	170	65.5	I	3	4	3	49.0	2.18
E. Ru.	29	169	62.3	II	2′	4′	3	45.2	1.81
R. Kr.	24	179	67.8	I	2	4′	4	44.0	1.95
D. Co.	28	173	62.3	II	1′	5	3′	46.1	1.94
R. Ce.	33	174	65.0	II	2	4′	3′	43.0	1.82
K. O'N.	23	183	86.8	II	4′	4′	2′	44.3	1.92
M. Si.	34	173	67.3	III	2	5	3	44.9	2.26
K. Kr.	25	188	83.7	I	2	5′	3	48.5	2.71
R. Cl.	30	182	80.4	II	2	5′	2′	47.6	2.47
S. DeR.	22	183	71.4	II	2	5	3′	43.2	2.15
D. La.	27	189	72.3	II	2	3	5′	44.9	2.16
J. Ca.	29	179	72.8	I	2	5	3	42.5	1.80
W. Sh.	32	173	66.4	I	2′	4′	3	41.5	1.59
R. Ro.	33	183	80.5	II	2	5′	3	45.1	2.36
W. Ch.	26	175	69.6	II	1	6	2′	44.2	2.14
S. Ga.	42	180	65.5	I				45.9	1.97
M. Br.	29	183	73.7	I	2′	4	4	47.1	2.09
C. We.	37	172	72.3	I	2′	5	3	46.1	2.08

in latent or chronic form. No cases of gross clinical obesity were included. The men had stayed in San Quentin State Prison, where there is little seasonal variation of outdoor climate, for various periods of time. None had stayed recently at high altitudes or in climates of extreme heat or cold. The series included 46 men who had donated blood once and seven who had donated blood twice in the year preceding the experiment. Donors were not accepted if they had given blood within 42 days; those who had donated twice were not accepted within 60 days of the last bleeding. The basis for the decision to include blood donors in the series of "normals" will be shown under Results.

PROCEDURE AND METHODS

On the day before the experiment, blood was taken for tagging and the laboratory screening tests were performed. The subject stayed in the prison hospital overnight and received no food or medication after retiring in the evening. He was also requested not to smoke. On the morning of the experiment, he reclined for at least 30 minutes before injection of the tagged cells and until the final sample for measurement of blood volume had been taken. Wintrobe hematocrit tubes were filled in duplicate from each blood sample within three hours of collection and centrifuged for 30 minutes at 3,000 rpm (radius 15 cm.). The height of the cell column was read to the top of the buffy coat, and no correction was applied for "trapped plasma."

The volume of cells (Vrbc) was measured by a modification of the Cr^{51} method of Sterling and Gray (24) which we have described elsewhere (25) and which will be analyzed in a forthcoming publication (26). Essentially, the procedure was as follows: *1)* About 15 ml. of the subject's blood was tagged with 100 to 200 μc. of $Na_2Cr^{51}O_4$, containing 0.1 to 1.0 μg. of Na_2CrO_4 per μc. The erythrocytes were then washed and resuspended in saline and stored overnight in the refrigerator.[1] *2)* Ten ml. of the cell suspension was delivered from a calibrated syringe and washed quantitatively into the subject's vein with not more than 30 ml. of saline, using an indwelling needle and a small infusion system. *3)* Two or three samples of blood were taken from the same needle beginning not less than 20 minutes after delivery of the tagged cells. The reported data are based on the averages of the derived values. A very slow infusion of saline provided for patency of the needle, but this was discontinued and at least 2 ml. of blood was taken from the vein and discarded before collection of any sample. *4)* Vwb was determined by comparing the radioactivity of each blood sample with that of the tagged cell suspension. Vrbc was derived by multiplying Vwb and the hematocrit of the same blood sample. Vpl was obtained by subtracting Vrbc from Vwb. No factor was introduced to correct the data for the probable difference between the hematocrit of venous blood and that of the body as a whole (29–31).

On the day of the experiment pulse and blood pressure were measured. The subject's height and weight in the nude were measured to the nearest half inch and pound, respectively, and he was photographed as prescribed by Sheldon (32) for determination of somatotype. His age to the nearest birthday was recorded and the medical interview was completed.

On the basis of the medical interview, supplemented by information from associates and supervisors, each subject was assigned to a physical activity group. Group I (light) included clerical workers, laboratory assistants, students and unemployed persons who did not participate in sports. Group II (moderate) consisted of janitors, garden and yard workers, messengers, cooks, electricians, and so forth. Group III (heavy) consisted of men who worked as plumbers, roofers, plasterers, laundry helpers and quarry and construction laborers. Because of activity in sports, a person who by occupation belonged in Group I might be placed in Group II. If he participated intensively in strenuous sports, such as weight-lifting, football, wrestling or boxing, a person whose work was light or moderate might be placed in Group III.

Each subject was classified[2] according to a scale of 13 (seven whole grades and six half grades, shown in Table I as primes) for each of the three somatotype components, endomorphy (obesity), mesomorphy (muscularity) and ectomorphy (linearity).

RESULTS

1. Volumes in relation to height and weight

Table II lists the mean values for Vrbc, Vpl and Vwb, with the regression equations describing the relationships of the volumes to the body measurements. The regression lines and planes were fitted by the method of least squares. For Vrbc, Vpl and Vwb, the coefficient of variation is smaller if the volumes are related to height and weight combined or to the calculated body surface area (Du Bois' formula), than if they are related to height or weight alone. The values for whole blood have a smaller coefficient of variation than those of the two components. The bivariate equations represent straight lines and the trivariate equations, planes without curvature.

In Figure 1, each of the 201 subjects is plotted

[1] Overnight storage of the cells makes it possible to inject them into the fasting subject at a convenient time before breakfast. *In vitro* tests and animal experiments have shown that handling the blood in this way does not affect the accuracy of the method (27, 28).

[2] We are greatly indebted to Dr. C. W. Dupertuis of Western Reserve University, who, at our request, kindly agreed to make an independent determination of somatotypes. No classification was considered correct unless approved by Dr. Dupertuis.

TABLE II

*Regression equations of Vrbc, Vpl and Vwb to weight alone, height alone, weight and height combined and to body surface area**

	Mean of all values	Predicted values	Standard deviation	Coefficient of variation
	ml.	*ml.*	*ml.*	%
Vrbc	2,030		290	14.2
		1) 22.4 × height − 1,930	250	12.2
		2) 21.4 × weight + 490	200	9.7
		3) 8.6 × height + 18.6 × weight − 830	190	9.4
		4) 1,550 × surface area − 890	190	9.4
Vpl	2,460		330	13.2
		5) 29.7 × height − 2,770	260	10.7
		6) 19.6 × weight + 1,050	260	10.7
		7) 19.9 × height + 13.1 × weight − 2,000	240	9.7
		8) 1,580 × surface area − 520	240	9.8
Vwb	4,490		570	12.6
		9) 52.1 × height − 4,700	450	10.1
		10) 41.0 × weight + 1,530	400	8.9
		11) 28.5 × height + 31.6 × weight − 2,820	370	8.1
		12) 3,140 × surface area − 1,410	360	8.1

* Height in cm.; weight in Kg.; surface area in square meters as calculated from Du Bois' formula. Values are uncorrected for trapped plasma and for differences between body hematocrit and venous hematocrit.

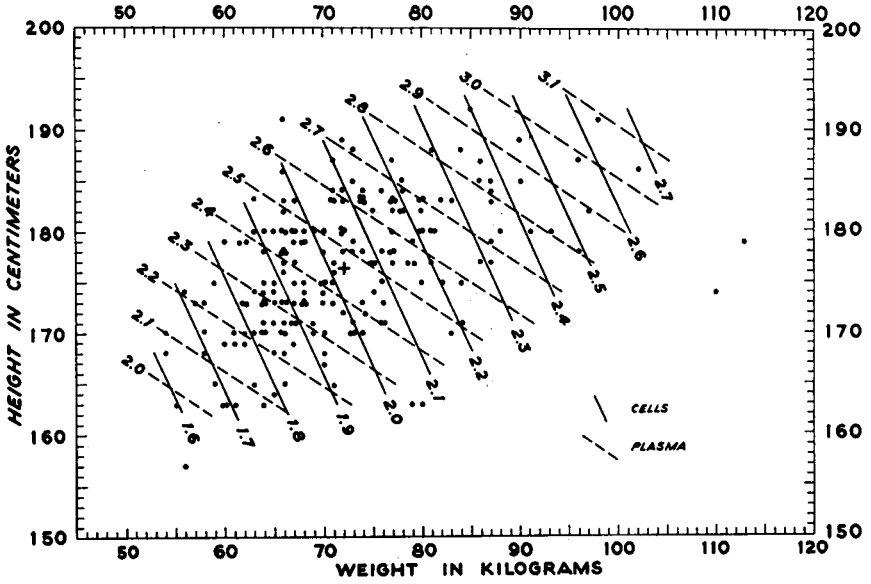

FIG. 1. RED CELL AND PLASMA VOLUMES IN RELATION TO HEIGHT AND WEIGHT

Each solid circle represents one subject, plotted according to his height and weight. The average of the heights and weights is shown by +. The solid and dashed contour lines give the mean predicted Vrbc and Vpl, respectively, to the nearest 0.1 L., calculated from Equations 3 and 7, Table II. The mean predicted volumes of a man 175 cm. tall and weighing 70 Kg. are: Vrbc = 1.98 L., Vpl = 2.40 L., and Vwb = 4.38 L. Values are uncorrected for trapped plasma and for differences between body hematocrit and venous hematocrit. Vrbc includes leukocytes and platelets.

The contour lines are constructed by introducing the successive mean values for Vrbc and Vpl in their respective regression equations (No. 3 and No. 7, Table II) and computing the height for a given weight or vice versa.

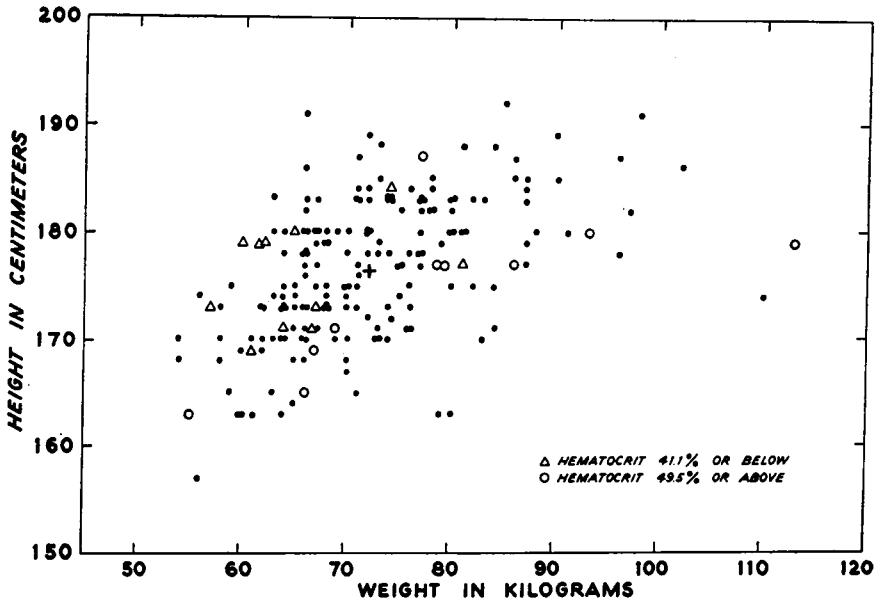

FIG. 2. RELATION OF HEIGHT AND WEIGHT TO HEMATOCRIT

Each subject is plotted according to height and weight as in Figure 1. The 11 men with the lowest hematocrits, 41.1 per cent or below and represented by △, appear mostly in the left upper area. The 10 men with the highest hematocrits, 49.5 per cent or above and represented by ○, appear mostly in the right lower area.

according to his height and weight. The location of the regression plane for Vrbc in relation to combined height and weight (Equation 3, Table II) is represented by the solid contour lines progressing from the left lower to the right upper corner of the chart. The regression plane for Vpl (Equation 7, Table II) is represented by the dotted contour lines. The contour lines for Vrbc are steeper than those for Vpl, indicating that Vrbc is relatively more dependent on weight than height, whereas the reverse is true of Vpl. Although the differences are small, the hematocrits of short, heavy men tend to be slightly higher than those of tall, thin men, as shown in Figure 2.

2. *Influence of factors other than height and weight as shown by analysis of "residuals"*

Analysis of the differences between the observed volumes in each subject and the average volumes for his height and weight, *i.e.*, "residuals," provided a means of testing the influence on blood volume of factors other than weight and height when considered independently. The predicted Vrbc and Vpl of each subject were calculated, using Equations 3 and 7, Table II. Each subject's residual Vrbc and Vpl were then found by subtracting his predicted from his observed volumes.

A positive correlation was found between residuals for Vrbc and Vpl ($r = +0.42$).

A) Age. Table III shows the distribution of ages and the mean residuals for Vrbc and Vpl of the subjects within each five year age group. The largest number of men were in their third and fourth decades; a few were over 40. Comparison of mean residuals with their standard errors indicates that age has little effect, except on the Vrbc of subjects in the highest age group.

TABLE III

Influence of age on Vrbc and Vpl

Age	Number of men	Residuals Vrbc		Residuals Vpl	
		Mean	S. E.*	Mean	S. E.*
years		*ml.*	*ml.*	*ml.*	*ml.*
19–24	42	−18	29	14	37
25–29	76	15	22	−5	27
30–34	45	4	28	−11	35
35–39	22	10	41	−22	51
40–44	11	40	57	88	72
45–52	5	−236	85	−42	106

* Standard error.

TABLE IV

*Classification of 177 men with respect to endormorphy, mesomorphy and ectomorphy and mean residuals in ml. of Vrbc and Vpl of grouped classes**†*

Endomorphy	Mesomorphy	Ectomorphy 1, 2			Ectomorphy 3, 4, 5			Ectomorphy 6, 7		
1, 2	1, 2				(6)	**−97**	*−148*	(1)	**−60**	*−150*
	3, 4, 5	(13)	**116**	*19*	(59)	**7**	*62*	(1)	**30**	*10*
	6, 7	(10)	**26**	*47*						
3, 4, 5	1, 2				(1)	**80**	*−330*			
	3, 4, 5	(37)	**−21**	*−33*	(46)	**−10**	*−27*			
	6,7	(3)	**−133**	*80*						
6,7										

* Number of individuals in parentheses; mean Vrbc residual in **bold** type; mean Vpl residual in *italic* type.
† The calculated linear regression equations of residuals on the three somatotype variables are as follows: *1)* Expected Vrbc residual (*ml.*) = − 27En + 1Me − 17Ec + 114; *2)* Expected Vpl residual (*ml.*) = − 38En + 25Me − 8Ec + 19.

B) Somatotype. A total of 177 individuals were somatotyped. They fell into 43 distinct groups when a scale of one to seven was used to describe each component (endomorphy, mesomorphy, ectomorphy). Analysis of residuals showed that the reduction in variance which results from considering somatotype when height and weight are fixed is numerically small and of doubtful statistical significance (p for Vrbc = 0.08, for Vpl = 0.23).

In Table IV, the degrees of endomorphy, mesomorphy and ectomorphy have been reduced even further by grouping together the less extreme classes (three, four and five) and the high and low extremes (one and two; six and seven). Thus, the number of combinations encountered in our material is reduced to 10 and the number of individuals per group is larger. Inspection of the table shows the predominance of muscularity in our subjects. The mean residuals show no strong trends, although there appears to be a tendency toward negative residuals in men of low muscularity, positive residuals in men of high muscularity, low linearity and low obesity and negative residuals in men of high muscularity and low linearity but moderate obesity.

TABLE V

Influence of physical activity on Vrbc and Vpl

Physical activity class	Number of men	Residuals Vrbc Mean	Residuals Vrbc S. E.*	Residuals Vpl Mean	Residuals Vpl S. E.*
		ml.	*ml.*	*ml.*	*ml.*
I	65	−19	24	−37	30
II	80	1	21	17	27
III	45	15	29	22	36

* Standard error.

C) Physical activity. Table V shows the fairly uniform distribution among Groups I, II and III of the 190 subjects who were classified according to physical activity. The residuals of both Vrbc and Vpl appear to increase with increasing physical activity but the effect is slight after allowances for weight and height. The differences are not statistically significant (for Vrbc, $p = 30$; for Vpl, $p = 0.15$).

D) Seasonal and within-month variations. Data were not collected primarily for evaluation of these factors. However, certain trends during the 25 months of study suggest that seasonal fluctuations of blood volume may occur even in the relatively uniform climate of San Quentin. For example, in 1954 and 1955, the mean Vrbc residual for the 30 observations between July 7 and November 9 was + 117 ml. (S.E. 35), and for the 51 observations between November 16 and February 8, it was − 70 ml. (S. E. 27). Mean residuals for plasma are similar, + 156 and − 130, respectively. It should be kept in mind that these two time intervals were selected from the entire 25 month period because they showed the most extreme deviations, suggesting a seasonal effect. By grouping the residuals according to the months in which observations were made, it was found that the variance within months was 15 per cent lower than the variance of all 201 residuals (p = 0.001). The relative uniformity of results within months, in contrast to the fluctuations during the entire study period, might be attributed to *a)* seasonal effects, *b)* the types of subjects encoun-

tered, or *c*) methodologic factors. Influence of the latter seems unlikely since the within-month effect was as great at the end of the study as at the beginning and since the personnel, procedures and methods were unchanged throughout.

E) *Blood donations.* Fifty-three blood donors were included in the series. Their residuals of Vrbc and Vpl are plotted in Figure 3 according to the interval of time between donation and experiment. The points are distributed evenly around the zero line which represents the predicted Vrbc or Vpl of each individual calculated from his height and weight. Most of the residuals were within plus or minus one standard deviation of the mean predicted volume so that the variation is no greater in this group than in the population as a whole. The residuals showed no tendency to increase or decrease progressively with time, between 42 and 180 days. For all donors, the mean residuals (ml.) were as follows: Vrbc = + 17 (S.E. 27), Vpl = − 17 (S.E. 33), Vwb = + 0.2 (S.E. 50).

3. *Repeat determinations*

In 15 men the blood volume was re-estimated one or more times after intervals of three to 31 weeks. The mean of the 20 differences for Vrbc was 73 ml. (range, 10 to 160 ml.) and for Vwb, 222 ml. (range, 10 to 710 ml.). These repeat measurements enable us to estimate the amount of variation due to measurement errors and short-term temporal changes. The estimated standard deviation of such variation was 64 ml. for Vrbc and 211 ml. for Vwb. The standard deviations about the regression planes described by Equations 3 and 11, Table II, are reduced only modestly by taking into account the degree of variance shown by the repeat measurements, which includes the errors of measurement and the changes in blood volume of individual subjects from time to time.[3] Thus, for Vrbc almost all of the predictive error seems to relate to intrinsic differences between subjects rather than to errors of measurement or temporal changes within subjects. For Vwb this is so to a lesser degree; this volume is either less stable or less accurately measured, or both.

DICUSSION

Only the observed venous hematocrit values were used in our calculations. It is recognized that the true Vrbc is slightly smaller than that calculated from the Cr^{51} space and observed hematocrit because of plasma trapping in the hematocrit

[3] The S.D. for Vrbc (Equation 3, Table II) is reduced from 190 ml. to $\sqrt{(190)^2-(64)^2}=179$ ml. and the S.D. for Vwb (Equation 11, Table II) is reduced from 370 ml. to $\sqrt{(370)^2-(211)^2}=304$ ml.

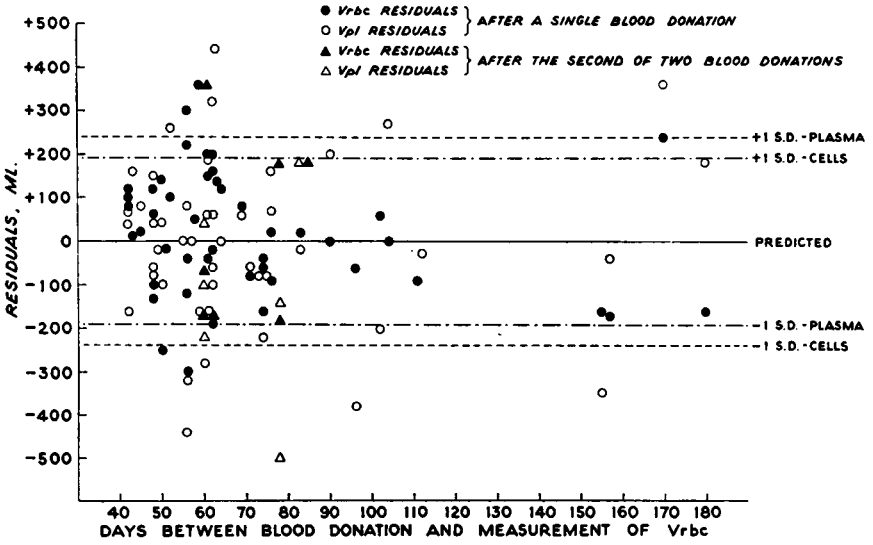

FIG. 3. RESIDUALS OF VRBC AND VPL FOR 46 MEN WHO HAD GIVEN ONE BLOOD DONATION AND SEVEN WHO HAD DONATED TWICE, ARRANGED ACCORDING TO THE TIME INTERVAL BETWEEN THE LAST DONATION AND THE BLOOD VOLUME MEASUREMENT

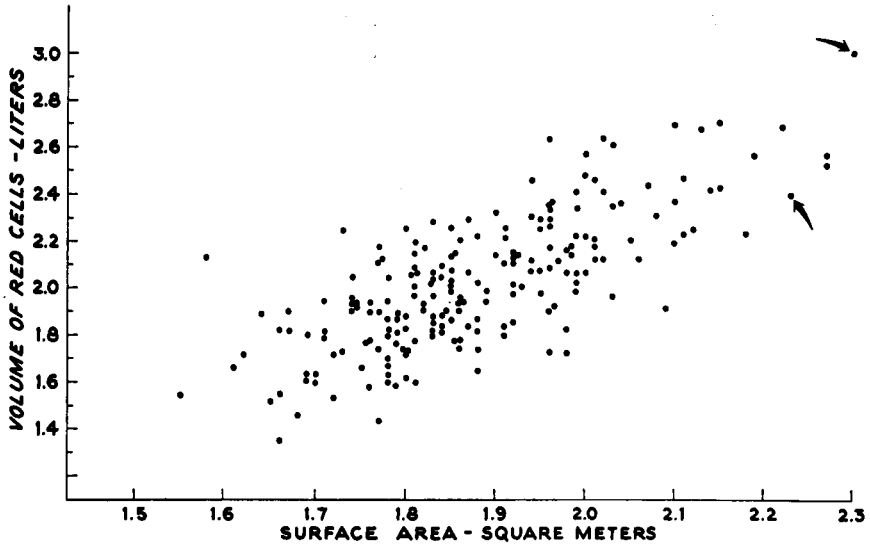

FIG. 4. VRBC OF 201 HEALTHY MEN IN RELATION TO BODY SURFACE AREA AS CALCULATED FROM DU BOIS' FORMULA

The linear regression Equation 4 (Table II) describes the data. Arrows point to two subjects whose weight: height ratios were exceptionally high and who appear to the far right of the population scatter shown in Figures 1 and 2. Data relating to these two subjects are marked by ‡ in Table I.

tube (33) and that Vwb and Vpl may be larger than they appear when calculated from Vrbc and a large vessel hematocrit (29, 30). Application of correction factors such as are used widely at present, 0.96 for trapping (34) and 0.91 for body: venous hematocrit ratio (31), would change the observed values only systematically. Correction factors which apply to data on healthy subjects do not necessarily apply to subjects with disease. Plasma trapping varies with the hematocrit level (35) and the body: venous hematocrit ratio is altered in some circulatory disorders (11, 35), with splenomegaly (36) and in pregnancy (37). Other investigators may conveniently compare their data with ours before they apply any desired correction factors. Vrbc as determined here is independent of the body: venous hematocrit ratio, but Vpl and Vwb are not. It should be noted that Vrbc as reported here includes leukocytes and platelets because hematocrits were read to the top of the buffy coat.

The finding that blood volume relates more closely to one or another combination of height and weight than to either measure alone is in accord with the results of several other studies (1–6, 13, 14). von Porat (4) proposed the use of $(\text{height})^3$ as a reference and Allen and co-workers (5) found that regression to $(\text{height})^3$ and weight gave the most adequate expression of their own and other published data. However, the function, $(\text{height})^3$, is nearly linear over the narrow range of heights encountered among adult men. The predicted Vwb is altered only 28 ml. at most by substitution of height for $(\text{height})^3$ in the equation of Allen and co-workers (5) over the range of heights encountered by these authors (1.57 to 1.89 M.).

The regression equations presented here should not be relied on for heights and weights outside the range covered by our observations, since there is no reason to suppose that the regression planes would continue to be the same beyond the observed domain. Furthermore, the accuracy with which the planes are estimated decreases as we depart from the center (indicated by a cross) of the height: weight scatter diagram (Figure 1).

For predicting "normal" volumes in individual cases, the graphic representation of the regression planes shown in Figure 1 has several advantages: *a*) No calculations are required; *b*) one can see at a glance whether the individual's height and weight are within the range covered by our calculations; and *c*) any existing peculiarities of height: weight relations of the individual under

consideration are revealed. That these may be obscured when calculated body surface area is used as the basis of prediction was pointed out many years ago by Rowntree and Brown (1) and by Gibson and Evans (2). For example, two heavy men are found to the far right of Figure 1. Although noticeably different from the rest of the population when located on the scatter diagram, they cannot be distinguished from the other large individuals in our series when the data for Vrbc are plotted against body surface area, as shown in Figure 4.

Regression of Vwb to height and weight accounted for only 56 per cent of the original variability of our data. The coefficient of variation (8.1 per cent) after this regression is of about the same magnitude as has been found in other studies after regression or correlation of blood volume to weight and height or to surface area. The magnitude of the coefficient depends on the homogeneity and size of the population under investigation. It was comparatively low in a group of average American medical students and considerably higher than ours in a group of subjects selected for extremes of somatotype (3). Our sample of adult males was of intermediate homogeneity, in that it included men from several racial origins whose ages extended to above 50 years and included physically active as well as sedentary persons, but only a few examples of extremely linear or obese body build. Most of the variation to be accounted for after consideration of height and weight is biologic rather than methodologic, as shown by our repeat studies and by similar experiences reported by workers using a variety of methods, for example, P^{32} (7, 12, 13), Cr^{51} (10), I^{131} (15), and T-1824 (5, 13, 16).

Within the population available to us for study, we have found that age, somatotype and habits of physical activity influence Vrbc and Vwb only slightly when considered independently from height and weight. This may be because each of these characteristics is strongly linked in its effect on blood volume with body size and composition. The effect of each characteristic is of course minimized when examined by analysis of residuals about the height × weight regression planes. Available evidence suggests that individual differences with respect to the content of fat and lean tissue in the body have only a modest effect on blood volume. This is probably because the blood content of fat tissue is not insignificant (5, 15). Hicks, Hope, Turnbull and Verel (14) found that consideration of fat thickness and girth in addition to height and weight lowered the coefficient of variation for Vwb from 9.6 to 7.6 per cent. Vwb, Vrbc and Vpl have been found to be directly related to body density (5, 15), and Muldowney (17) found a surprisingly good correlation between Vrbc and lean body mass, considering that both were determined indirectly. On the other hand, Inkley, Brooks and Kreiger (16) found no better correlation between Vpl and lean body mass, determined by densitometry or by antipyrine space, than between Vpl and total body mass, and Huff and Feller (15) were unable to improve the prediction of blood volume by determining body density and calculating the expected blood content of fat and lean tissues separately.

The data of Gibson and Evans (2) appeared to show that blood volume per unit body size was less in large than in small subjects, so that the curves relating volumes to height, weight and body surface area were flattened at the top. We have been unable to corroborate this finding; none of our regression lines or planes show evidence of curvature. The only apparent explanation for the difference is that our large subjects were relatively more muscular and less obese than theirs. In most other respects, our results are in remarkably good agreement with those of the early workers who used the dye methods. The positive correlation found between residuals for Vrbc and Vpl ($r = + 0.42$) means that a man whose Vrbc is larger than average for his height and weight will also tend to have a large Vpl. This is in contrast to the inverse relation between Vrbc and Vpl found in certain pathologic states, *e.g.,* anemia and polycythemia (38), and suggests that the normal biologic determinants of blood volume may be concerned with circulatory volume rather than with total circulating hemoglobin.

The apparent absence of age effect in the third to fifth decades is in agreement with several reports (6, 8, 13). The suggested tendency for the volumes per unit size to decrease in the sixth decade corroborates the findings of Gibson and Evans (2) and of Baker, Kozoll and Meyer (20). The question of age, however, requires further

study, inasmuch as both the above-mentioned studies (2, 20) and our own involved few subjects over 50 and since discordant results were found in two investigations particularly devoted to the problem of aging (18, 19).

We have found that muscularity (mesomorphy) has a slight positive effect, while both linearity (ectomorphy) and obesity (endomorphy) have negative effects on the residuals about the height × weight regression planes. Also, a slight progressive positivity of residuals was found with increasing grades of habitual physical activity. This supports Sjöstrand's hypothesis (39) that Vrbc is primarily dependent on total muscle mass and, equally well, the thesis that blood volume may be more dependent on lean than on total body mass. In contrast, Bass, Buskirk, Iampietro and Mager (22) found no increase in Vpl or Vrbc after three weeks of vigorous physical conditioning and Buskirk (23) was unable to demonstrate differences in Vpl or Vwb per unit of total or fat-free body weight in moderately or rigorously trained athletes and nonathletes. The demonstration by Kjellberg, Rudhe and Sjöstrand (21) of large differences between the blood volumes of athletically trained and untrained persons requires re-examination. The carbon monoxide method which they used is particularly unsuitable for this problem, since 15 per cent of the test dose of gas leaves the blood during the measurement and goes mostly to muscle pigments (25, 27).

SUMMARY

1. A group of 201 men were screened for health and classified as to age, habits of physical activity and somatotype. The red cell volumes (Vrbc) of these subjects were measured with Cr^{51} tagged cells; plasma (Vpl) and whole blood volumes were derived indirectly from venous hematocrits.

2. Regression equations were derived, expressing the relations of the volumes to body weight and height and to combinations of these measures. From these data a chart was devised from which the expected Vrbc and Vpl for a man of given height and weight can be found conveniently.

3. In the sample of population examined, age, elements of the somatotype and habits of physical activity were found to influence the variance of the data only slightly, after effects of height and weight had been accounted for.

ACKNOWLEDGMENT

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