RED CELL AND PLASMA VOLUMES IN NORMAL ADULTS

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Despite numerous published methods for predicting normal red cell and plasma volumes, little is known of the range of normal in subjects of given body dimensions. In this study, reported results of red cell and plasma volumes in 481 normal men and 303 normal women have been used to calculate mean volumes and standard deviations (s.d.) for any given body surface area (male and female results being kept separate). All of these mean volumes, each ±2 s.d., have been plotted against body surface area. The resulting graphs of means and 95% confidence limits have tended to be curvilinear. Standard deviations have increased with increasing mean volumes, but coefficients of variation (s.d./mean) have shown considerable constancy at 11–12%. The mean values observed in this series have often differed substantially from those predicted from published formulas. Use of the presently observed means with the 11–12% coefficients of variation allows compilation for any surface area of a range of normal against which a clinically obtained volume can be compared.

Many systems have been published for predicting "normal" red cell and plasma volumes using as standardizing factors one or more dimensions of body size such as weight, height, or surface area (*1–12*). Regression equations incorporating such body dimensions have been prepared from data obtained from healthy people. Data from men and women have in general been grouped separately because of the higher average male blood volume but other factors such as age (*13,14*), physical activity, and habits (*12,15*) appear to be of little importance in predicting the "normal" value. Weight or height alone has had less predictive value than more complex functions (*8*).

Most predictive equations agree fairly closely for people of average body size and there seems little to choose between them. A common feature is the assumption of a rectilinear regression of blood volume against the chosen parameter(s) of body size with "95% confidence limits" sometimes presented as parallel lines ±2 s.d. of the regression line. Inspection of the regressions suggests that the assumptions of rectilinearity are unfounded.

Meaningful interpretation of a red cell or plasma volume value clearly requires knowledge not only of the mean but also of the range for normal people of the same sex and body dimensions. Large numbers are necessary to obtain such data. In the present study all the suitable available published data on healthy individuals have been combined to allow an estimate of the range of normal values, relative to body surface area, for red cell and plasma volumes in men and women.

Received July 1, 1974; original accepted Aug. 15, 1974.

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METHOD

The available literature (*1,3–5,8,11–13,16–18*) was searched for individual results of red cell and plasma volume determinations in healthy men and women whose body surface area was given or could be calculated. Only reports in which the tracer method used was described in satisfactory detail and conformed to accepted present day standards (*19,20*) were used. Red cells were labeled with either sodium ^{51}Cr-chromate or ^{32}P. Plasma volume estimations were performed with the use of albumin labeled with either radioiodine or Evans Blue. It has been abundantly demonstrated (*20,21*) that the two red cell labeling techniques produce identical results as do the two methods for quantifying plasma volume. Because of small numbers in some subgroups of patients, it was sometimes necessary to derive a value for plasma volume from a measured red cell volume and the venous hematocrit or vice versa. For these derivations, the following equation was used: PV is RCV (100 − 0.91 Hct)/0.91 Hct, where PV is plasma volume, RCV is red cell volume, and Hct is venous hematocrit, expressed as a percentage. A value of 0.91 was taken as the ratio between whole-body and venous hematocrit (*16*). Where published figures used a different factor from 0.91, or none at all, they were corrected to a result using 0.91. Hematocrits measured with a centrifuge technique were further corrected by a factor of 0.96 to correct for trapped plasma (*22*). Some published series had been corrected for intravascular mixing of tracer by extrapolation of a series of points back to zero time. For the sake of uniformity, all present results were based as closely as possible on a single blood sample taken 10–15 min after injection, and where published results had been extrapolated back to zero time, the extrapolation was ignored and the 10–15 min value used instead.

Only data from normal volunteers were considered. Male and female results were analyzed separately. Red cell or plasma volume values were grouped according to subjects' body surface area at intervals of 0.01 m^2, e.g., the 1.81 m^2 category consisted of people with surface areas in the range 1.805–1.814 m^2. The nomogram of Du Bois and Du Bois (*23*) was used to calculate body surface area from height and weight.

TABLE 1. AGE DISTRIBUTION*

Age (yr)	Men	Women
15–19	29	14
20–29	215	124
30–39	131	51
40–49	42	28
50–59	19	21
60–69	8	6
70–79	27	41
80–89	8	17
90+	2	1

* Numbers of subjects.

When a particular surface area category contained eight or more directly determined values for red cell or plasma volumes (i.e., values derived without recourse to a calculation involving the venous hematocrit), no indirectly determined results were used. When there were fewer than eight direct determinations, all the available indirect determinations were used to bring the total up to or greater than eight. Where the total of indirect and direct determinations was less than eight, the group was not considered (except at the extremes of the surface area ranges when results from two adjacent surface area categories were combined if necessary and expressed for the mean surface area of those two categories).

When eight or more red cell or plasma volume values were available in a particular surface area category (i.e., $n \geqq 8$), the mean ($\overline{X}$) and standard deviation (s.d.) of those values was calculated using the formula

$$\text{s.d.} = \sqrt{\frac{(X - \overline{X})^2}{n - 1}}$$

TABLE 2. EQUATIONS GIVING THE HIGHEST CORRELATION COEFFICIENTS (r) RELATING MEAN RED CELL OR PLASMA VOLUME (V), MEAN −2 s.d. AND MEAN +2 s.d. TO BODY SURFACE AREA (S)

Subjects, red cell and plasma vols	Mean − 2 s.d.	r	Mean	r	Mean + 2 s.d.	r
Men, red cell volume	$V = 443e^{0.6825S}$	+0.76	$V = 1486S^2 - 4106S + 4514$	+0.95	$V = 2388S^2 - 7147S + 7488$	+0.88
Men, plasma volume	$V = 1261e^{0.5900S}$	+0.86	$V = 995e^{0.6085S}$	+0.95	$V = 581e^{0.7658S}$	+0.74
Women, red cell volume	$V = 223S^2 + 256S + 55$	+0.64	$V = 1167S - 479$	+0.94	$V = 936S^{1.305}$	+0.70
Women, plasma volume	$V = -1074S^2 + 4901S - 3251$	+0.66	$V = 1278S^{1.289}$	+0.91	$V = 1014S^2 - 924S + 1734$	+0.78

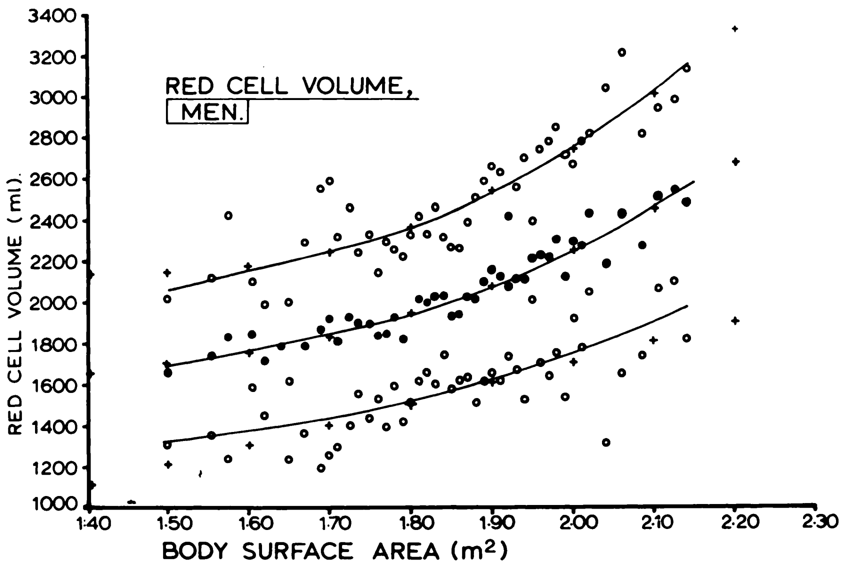

FIG. 1. Mean red cell volumes, normal men, plotted against surface area (closed circles). Ninety-five percent confidence limits (mean ± 2 s.d.) are plotted for each surface area category as open circles. Regression lines are drawn by eye. Representative values obtained with use of formulas in Table 2 are shown by symbol +.

Values for all the means and all the 95% confidence limits (mean ± 2 s.d. for each particular surface area category assuming a normal distribution) were then plotted against surface area. Regression equations based on least-squares rectilinear, exponential, parabolic, and power functions were obtained with the use of a desk-top computer.

RESULTS

Data were available from 481 normal men and 303 normal women whose ages are listed in Table 1. "Best-fit" curves, fitted by eye, for mean red cell and plasma volumes, mean +2 s.d., and mean −2 s.d., plotted against surface area in men and women are shown in Figs. 1–4. With the men, the regressions are obviously curvilinear. Data points are fewer and are based on generally smaller numbers in each surface area category with the women and their regressions more nearly approximate straight lines. In each case, the calculated regression equation giving the highest correlation coefficient is listed in Table 2. With the sole exception of the female mean red cell volumes, the best fit was not the rectilinear regression but was either parabolic, exponential, or in two instances with the women, a power function. Complex computer methods were not used to derive more

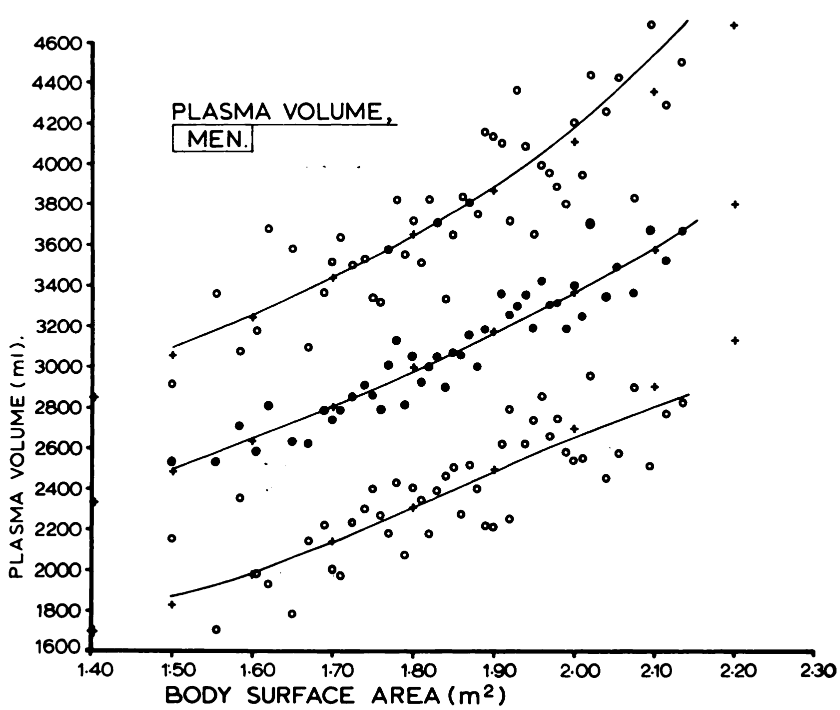

FIG. 2. Plasma volumes, normal men, as in Fig. 1.

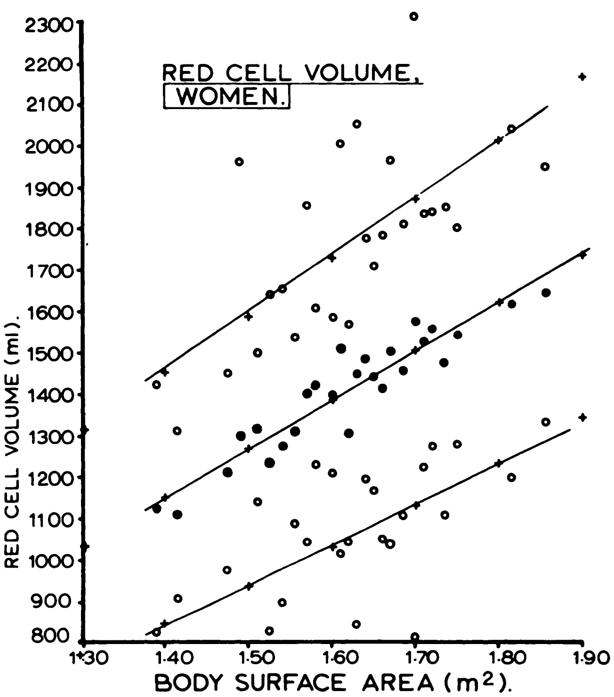

FIG. 3. Red cell volumes, normal women, as in Fig. 1.

closely fitting curves than this simple family of four. Representative values obtained from the closest-fitting of these curves are also plotted in Figs. 1–4 in which they can be seen to bear in general a close relationship to the eye-fitted curves, particularly in the middle of the surface-area ranges. Where fitting by eye was difficult, the calculated curves were used to give assistance but otherwise the eye-fitted curves were used to derive the mean values listed in Table 3.

When the calculated coefficients of variation in each surface area category were meaned, the results shown in Table 4 were obtained (coefficient of variation = s.d./mean). This table also lists the value (C) obtained by averaging the coefficients of variation weighted for the number of data points in each calculation by the formula:

$$C = \frac{1}{n} \begin{array}{l}\Sigma \text{ (coefficient of variation)} \times \text{ (no. of} \\ \text{data points) (n = grand total number} \\ \text{of data points)}\end{array}$$

Table 5 shows the considerable uniformity of coefficients of variation (read from Figs. 1–4) regardless of the surface area category.

DISCUSSION

The purpose of this investigation was to derive figures for means and dispersion about the means of normal red cell and plasma volume values for any given body surface area. As demonstrated in Table 5, considerable uniformity of coefficient of variation was found and it is suggested that Tables 3 and 4 might form a useful means of assessing the range of normal against an investigator's own derived value for a particular patient.

As detailed in Table 6, the various previously presented predictive equations based on surface area produce rather widely varying results often remote from the mean values collected in the present series. This series has the advantage of more data than were used by other investigators; moreover, Figs. 1–4 are based not on predictive equations but on the actual data obtained from several hundreds of normal volunteers. A deficiency in the predictive methods is that they have assumed rectilinear regressions. This assumption may appear justified in a small series with few extremes of body size but in the present data it is clear that regressions are not simple rectilinear functions. From Table 6 it can be seen that, compared with the present results, most of the predictive equations underestimate male red cell and plasma volumes at either extreme of the surface-area range and tend to overestimate female volumes at the lower extreme and underestimate them at the upper extreme of the surface-area range.

Figures 1–4 also demonstrate that the dispersions of values about the respective means are not rectilinear. The actual, though not the relative, deviation increases with increasing body surface area. Thus, figures for standard deviation quoted in earlier reports, based on lines parallel to the derived rectilinear regressions, are inappropriate. Moore, et al (*24*) have analyzed a number of earlier reports of this type and found the following figures for coefficient

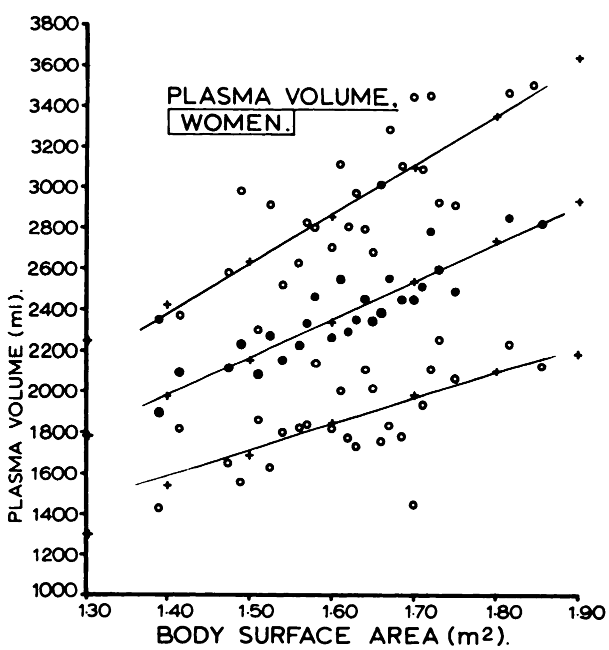

FIG. 4. Plasma volumes, normal women, as in Fig. 1.

TABLE 3. MEAN VALUES FOR RED CELL (RCV) AND PLASMA VOLUMES (PV) (IN ML) RELATED TO BODY SURFACE AREA (S, IN M²) FOR MEN AND WOMEN

	Men		Women			Men		Women	
S	RCV	PV	RCV	PV	S	RCV	PV	RCV	PV
1.39	—	—	1,136	1,964	1.77	1,907	2,922	1,588	2,666
1.40	—	—	1,148	1,982	1.78	1,917	2,940	1,599	2,682
1.41	—	—	1,162	2,000	1.79	1,927	2,958	1,610	2,702
1.42	—	—	1,172	2,018	1.80	1,938	2,976	1,622	2,720
1.43	—	—	1,184	2,039	1.81	1,951	2,994	1,634	2,740
1.44	—	—	1,196	2,058	1.82	1,964	3,013	1,645	2,760
1.45	—	—	1,208	2,076	1.83	1,977	3,031	1,657	2,778
1.46	—	—	1,220	2,094	1.84	1,990	3,050	1,670	2,796
1.47	—	—	1,232	2,112	1.85	2,003	3,069	1,681	2,815
1.48	—	—	1,242	2,132	1.86	2,016	3,087	1,692	2,838
1.49	—	—	1,254	2,148	1.87	2,029	3,106	1,704	2,854
1.50	1,684	2,498	1,268	2,168	1.88	2,042	3,125	—	—
1.51	1,692	2,513	1,280	2,184	1.89	2,055	3,144	—	—
1.52	1,699	2,529	1,291	2,204	1.90	2,070	3,164	—	—
1.53	1,707	2,544	1,302	2,222	1.91	2,087	3,183	—	—
1.54	1,715	2,560	1,315	2,242	1.92	2,104	3,202	—	—
1.55	1,722	2,575	1,326	2,258	1.93	2,121	3,222	—	—
1.56	1,730	2,591	1,338	2,278	1.94	2,138	3,242	—	—
1.57	1,737	2,606	1,349	2,296	1.95	2,156	3,261	—	—
1.58	1,745	2,621	1,362	2,314	1.96	2,173	3,280	—	—
1.59	1,752	2,637	1,376	2,336	1.97	2,191	3,299	—	—
1.60	1,760	2,652	1,386	2,354	1.98	2,208	3,318	—	—
1.61	1,768	2,667	1,398	2,374	1.99	2,226	3,337	—	—
1.62	1,776	2,682	1,408	2,392	2.00	2,244	3,358	—	—
1.63	1,784	2,697	1,421	2,410	2.01	2,266	3,380	—	—
1.64	1,792	2,712	1,434	2,428	2.02	2,288	3,402	—	—
1.65	1,800	2,727	1,445	2,444	2.03	2,310	3,424	—	—
1.66	1,809	2,742	1,458	2,462	2.04	2,332	3,446	—	—
1.67	1,817	2,757	1,468	2,480	2.05	2,354	3,468	—	—
1.68	1,826	2,772	1,480	2,500	2.06	2,375	3,490	—	—
1.69	1,834	2,787	1,492	2,520	2.07	2,397	3,513	—	—
1.70	1,842	2,802	1,504	2,538	2.08	2,419	3,536	—	—
1.71	1,851	2,819	1,516	2,558	2.09	2,441	3,558	—	—
1.72	1,861	2,837	1,527	2,576	2.10	2,463	3,580	—	—
1.73	1,870	2,854	1,540	2,592	2.11	2,486	3,604	—	—
1.74	1,880	2,871	1,552	2,612	2.12	2,510	3,628	—	—
1.75	1,889	2,888	1,563	2,630	2.13	2,535	3,653	—	—
1.76	1,898	2,905	1,576	2,648	2.14	2,560	3,679	—	—
					2.15	2,586	3,704	—	—

Continued in column 2

of variation of volumes as a function of body weight: men, red cell volume, 14%; plasma volume, 14.5%; women, red cell volume, 12%; plasma volume, 14%. As might be expected from a different parameter of body size and with smaller numbers of subjects, these coefficients of variation differ from those obtained in the present series but there is constancy between them. The ranges of normal based on twice the weighted mean coefficients of variation in the present series (Table 4) are: red cell volume—men, ±24% of mean; women, ±25% of mean; plasma volume—men and women, ±22% of mean.

The present series might be criticized on the validity of constructing curves for ±2 s.d. confidence limits. Each point contributing to these curves represented an actual confidence limit obtained from the data available for that particular surface area category. Sometimes, because of lack of numbers, groups as small as eight subjects had to be accepted and standard deviations (and coefficients of variation) based on such small numbers are inevitably open to inaccuracy. However, it was assumed that the mean coefficient of variation obtained from all the differ-

TABLE 4. MEAN COEFFICIENTS OF VARIATION

Subjects, red cell and plasma vols	%
Men, red cell volume	11.21
red cell volume (weighted for frequency)	11.85
plasma volume	11.22
plasma volume (weighted)	11.38
Women, red cell volume	12.56
red cell volume (weighted)	12.63
plasma volume	10.86
plasma volume (weighted)	10.94

ent surface-area categories reflected in accuracy the large numbers comprising the entire series. Despite the scatter present in some of the curves (particularly those of the women whose numbers were fewer), they were fitted by eye. The scatter was most noticeable at extremes of body surface area because of relative paucity of data and any inaccuracy due to this scatter would also have been reflected in more complex curve-fitting maneuvers. There appears to be little to choose between the predictive accuracy of height/weight or surface-area regressions (*8*) but the published standard deviations of regressions based on surface area are almost invariably slightly less than corresponding standard deviations based on height, weight, or height/weight formulas (*25*).

The present system of defining mean normal blood volumes is based on direct observation only and thus appears preferable to systems using predictive equations; furthermore, it allows the use of an almost uniform coefficient of variation to predict the normal range when body surface area is known.

TABLE 5. COEFFICIENTS OF VARIATION READ AT REGULAR INTERVALS FROM THE GRAPHS IN FIGS. 1–4

Subjects	S (m^2)		Coeff. of var. (%), RCV	Coeff. of var. (%), PV
Men	1.6		11.08	11.98
	1.7		11.01	11.70
	1.8		10.85	11.22
	1.9		10.81	11.06
	2.0		11.19	11.35
	2.1		11.56	12.29
		Mean	11.08	11.60
Women	1.4		13.56	10.04
	1.5		12.99	10.45
	1.6		12.62	10.88
	1.7		12.29	11.22
	1.8		12.00	11.58
		Mean	12.69	10.83

S is surface area; RCV is red cell volume; PV is plasma volume.

TABLE 6. PREVIOUSLY PUBLISHED EQUATIONS FOR PREDICTING RED CELL AND PLASMA VOLUMES (V, IN ML) ON THE BASIS OF BODY SURFACE AREA (S, IN M²), COMPARED WITH RESULTS IN THE PRESENT SERIES

Subjects, red cell and plasma vols	Equation, V =	Results for V over S range*		
		V; S = 1.5	V; S = 1.8	V; S = 2.1
Men, red cell volume				
Samet, et al (1957)	1,299S — 469	1,480	1,869	2,259
Wennesland, et al (1959)	1,550S — 890	1,435	1,900	2,365
Brassinne (1968)	1,070S + 56	1,661	1,982	2,303
Retzlaff, et al (1969	1,100S	1,650	1,980	2,310
Present series	—	1,684	1,938	2,463
Men, plasma volume				
Samet, et al (1957)	1,487S + 68	2,299	2,745	3,191
Wennesland, et al (1959)	1,580S — 520	1,850	2,324	2,798
Moens, et al (1962)	2,294S — 928	2,513	3,201	3,889
Brassinne (1968)	1,846S — 522	2,247	2,801	3,355
Retzlaff, et al (1969)	1,630S	2,445	2,934	3,423
Present series	—	2,498	2,976	3,580
Women, red cell volume		V; S = 1.4	V; S = 1.6	V; S = 1.8
Samet, et al (1957)	6,187S + 267	1,133	1,257	1,381
Brown, et al (1962)	1,138S — 397	1,196	1,424	1,651
Brassinne (1968)	749S + 168	1,217	1,366	1,516
Retzlaff, et al (1969)	840S	1,176	1,344	1,512
Present series	—	1,148	1,386	1,622
Women, plasma volume				
Steinbeck (1954)	2,596S — 1,451	2,183	2,703	3,222
Samet, et al (1957)	1,667S — 324	2,010	2,343	2,677
Brown, et al (1962)	1,747S — 733	1,713	2,062	2,412
Brassinne (1968)	1,241S + 353	2,090	2,339	2,587
Retzlaff, et al (1969)	1,410S	1,974	2,256	2,538
Present series	—	1,982	2,354	2,720

* The last three columns give results for V over the commonly encountered range of S.

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