BLOOD VOLUME IN NORMAL INFANTS AND CHILDREN

By DAN C. DARROW, HERBERT C. SOULE, and THOMAS E. BUCKMAN

(From the Pediatric Service of the Boston City Hospital and Washington University, and St. Louis Children's Hospital)

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Knowledge concerning blood volumes has been limited until recent years by the lack of any reliable method that could be applied to living patients. Information about the blood volume is desirable both for the study of anemia and of disturbances in the water metabolism. The work reported in this and the three subsequent papers was undertaken from the latter viewpoint.

There are two reliable methods of determining blood volumes which may be applied to patients. They are (*a*) the carbon monoxide method, first adapted to man by Haldane and Smith (1) and (*b*) the dye method of Keith, Rowntree and Geraghty (2). The former method gives results that are probably a little lower than the actual blood volume whereas the latter gives results a little higher than the actual blood volumes. The high results by the dye method have been shown by Smith (3) to be due to transfusion of part of the dye into the lymph. However, the amount of dye disappearing in the lymph is small and fairly constant and the method is accurate for comparative results.

Our knowledge of blood volumes has been recently reviewed by Erlanger (4). In the present paper, only such results as seem to concern this work will be mentioned. The findings of the various workers seem fairly concordant and indicate that adults tend to have about 50 milliliters of plasma and 83 milliliters of blood per kilogram of body weight, as determined by the dye method (Keith, Rowntree and Geraghty (2) Bock (5), Brown and Rowntree (6)). Bock has emphasized the fact that the plasma volume is more constant than the blood volume and has found it to be about 50 milliliters per kilogram of body weight in conditions showing such widely varying volumes of red cells as pernicious anemia and polycythemia. However, a minimum volume of red cells is necessary to maintain the plasma volume.

Robertson and Bock (7) found in soldiers who had lost large amounts of blood that the plasma volume returns quickly to normal unless the volume of the red cells has reached a certain low minimum. If the loss of the red cells is below this minimum, the plasma volume cannot be maintained until the red cell volume has been restored. Obese adults have low plasma volumes per kilogram of body weight (Brown and Keith (8)) but the plasma volume per square meter of surface area of obese adults was found to be essentially the same as for normal adults. A formula relating the blood volume to the surface area times a constant was worked out by Dreyer and Ray (9), the constant being different for different species of animals. These workers felt that since fat is a relatively avascular tissue, surface area would be a better measure of blood volume than weight.

Reports of actual blood volume determinations in infants are confined to three papers. None have been reported on older children. Lucas and Dearing (10) determined blood volumes by the dye method on infants during the first year of life. Their results expressed in milliliters per kilogram of body weight are: blood volume in newly born infants 107 to 195, average 147; plasma volume in newly born infants, 42 to 77, average 59; blood volume in older infants, 90 to 126, average 110; plasma volume, 57 to 78, average 67. In the first weeks of life, a wider variation in the plasma volume was found than later, and the whole blood volume was higher. However, the high whole blood volume in the newly born is entirely accounted for by the high volume of the red cells. The plasma volume is actually lower in the newly born than in infants over six weeks old. Bakwin and Rivkin (11) obtained similar results. They found the average for the blood volume to be 101 milliliters per kilogram of body weight and for the plasma 69 milliliters. In nineteen cases, the average blood volume was 1700 milliliters per square meter of surface area. Marriott and Perkins (12) found 91 cc. of whole blood per kilogram of body weight in seven normal babies, under one year of age, and 80 cc. per kilogram of body weight in babies with severe undernutrition. All the papers agree in finding slightly higher blood volumes per kilogram of body weight in babies than has been found in adults.

The blood volumes here reported were estimated by the method of Keith, Rowntree and Geraghty (2). The cell volumes were determined by hematocrit tubes made from small burettes which were 5 millimeters in diameter and calibrated. Oxalated venous blood kept under mineral oil was used to minimize the errors due to loss of carbon dioxide. Serum or plasma protein concentration was estimated in some of the later determinations by the Abbe refractometer (13). The surface area was computed by the formula of Lissauer (14) for the infants under one year of age. In the other patients, the surface area was obtained from the table of Benedict and Talbot (15) based on this formula.

The data of the present study were obtained from essentially normal infants and children. The older children were suffering from fractures, or had recovered from some minor illness. The babies had recovered from upper respiratory infections or were in the hospital for some minor complaint. Most of the infants were slightly undernourished and fed on modified cows' milk. The results reported here and to be reported in the subsequent papers indicate that moderate undernutrition makes no difference in the plasma volume per kilogram of body weight. The data found on these patients are given in detail in tables 1 and 2, but the general trend and significance may be appreciated best by examining the two charts.

Chart 1 represents the blood and plasma volumes in milliliters per kilogram of body weight as related to age. As there were not enough determinations to permit conclusions concerning the blood and plasma volumes during the first six weeks of life, the lower relative plasma volume at this age is represented in accordance with previous work (Lucas and Dearing (10) and Bakwin and Rivkin (11)). The plasma volume per kilogram of body weight as related to age describes a curve as indicated on chart 1. This curve starts at about 50 milliliters per kilogram of body weight and rises rather rapidly to 62 milliliters by the sixth month of life, remains high well into the second year, and then gradually returns to 50 milliliters by the beginning of the fourth year. Thereafter the plasma volume per kilogram of body weight agrees well with the adult figure, cited above. The whole blood volume tends to describe a similarly shaped curve, but, due to variations in the volumes of the red cells, the whole blood volume cannot be predicted very accurately. In general the blood volume per kilogram is 25 to 35 milliliters more than the plasma volume for the

TABLE 1

Case number	Date	Diagnosis	Sex	Age	Weight	Surface area	Volumes per cent of cells	Blood volume			Blood volume per kilogram			Blood volume per square meter of surface	
								Blood	Plasma	Cells	Blood	Plasma	Cells	Blood	Plasma
					kgm.	*sq. m.*		*ml.*	*ml.*	*ml.*	*ml.*	*ml.*	*ml.*	*ml.*	*ml.*
1	July 26, 1923		F.	1 wk.	3.6	0.24	45.0	284	156	128	79.0	43.0	36.0	1,180	647
2	December 13, 1922		M.	1 mo.	3.4	0.23			221			65.0			950
3	July 13, 1923	Undernutrition	F.	2 mos.	3.1	0.21	27.0	214	156	58	69.0	50.4	18.7	984	710
4	July 20, 1923	Undernutrition	M.	2 mos.	4.2	0.27	27.5	301	218	83	71.7	52.0	19.7	1,120	814
5	September 10, 1923	Undernutrition	M.	2 mos.	3.5	0.24	27.0	271	198	73	77.7	56.5	21.1	1,180	835
6	April 7, 1924	Normal	M.	6 wks.	3.3	0.23			180			54.0			785
7	August 8, 1925	Normal	F.	10 wks.	3.7	0.24	30.0	321	225	96	87.5	61.1	26.0	1,340	920
8	December 3, 1922	Undernutrition	M.	3 mos.	3.0	0.21	19.0	240	194	46	80.0	64.5	15.3	1,140	905
9	December 1, 1922	Undernutrition	M.	3 mos.	4.2	0.27	34.0	400	264	136	95.3	63.0	32.4	1,480	985
10	November 29, 1922	Undernutrition	M.	3 mos.	3.0	0.21	25.0	215	161	54	71.6	53.6	18.0	1,020	753
11	September 17, 1923	Undernutrition	F.	3 mos.	3.5	0.24	24.0	246	188	58	70.3	53.7	16.5	1,040	794
12	July 12, 1923	Normal	F.	5 mos.	4.7	0.29	34.5	389	255	134	82.6	54.3	28.5	1,340	883
13	July 19, 1923	Normal	F.	5 mos.	4.3	0.27	29.0	372	264	108	86.5	61.4	25.2	1,380	967
14	September 13, 1923	Normal	F.	6 mos.	5.4	0.32	28.4	475	340	135	88.0	63.0	25.0	1,530	1,070
15	September 19, 1923	Undernutrition	F.	9 mos.	7.2	0.38	33.5	662	440	222	91.8	61.0	30.8	1,740	1,145
16	September 20, 1924	Undernutrition	F.	1 yr.	5.5	0.32	28.5	475	340	135	86.7	62.0	24.7	1,480	1,060
17	November 27, 1925	Normal	M.	1 yr. 2 mos.	10.5	0.50	35.5	969	624	345	92.3	59.5	32.9	1,940	1,250
18	December 1, 1925	Normal	M.	1 yr. 2 mos.	8.6	0.44	29.0	665	473	192	76.5	55.0	22.4	1,510	1,078
19	December 17, 1925	T. B. adenitis	M.	1 yr. 2 mos.	9.5	0.47	32.6	739	498	241	77.8	52.5	25.4	1,570	1,060
20	December 10, 1925	Undernutrition	M.	1 yr. 2 mos.	6.3	0.34	28.0	511	368	143	81.1	58.4	22.7	1,500	1 080
21	December 8, 1925	Undernutrition	M.	1 yr. 4 mos.	9.6	0.46	30.0	647	453	194	67.4	47.2	20.2	1,410	986
22	September 15, 1923	Normal	M.	1 yr. 6 mos.	10.0	0.49	31.1	897	618	280	89.8	61.8	28.0	1,830	1,260
23	June 23, 1923	Normal	M.	2 yrs.	12.6	0.57	34.2	1,058	696	362	84.0	55.3	28.7	1,860	1,220

24	September 14, 1923	Normal	F.	2 yrs.	14.0	0.62	30.6	1,038	720	318	74.0	51.4	22.7	1,670	1,160
25	December 6, 1924	Undernutrition	F.	2 yrs.	7.2	0.39	46.0	759	408	351	105.2	56.5	48.6	1,940	1,050
26	December 10, 1924	Undernutrition	F.	2 yrs.	8.6	0.44	30.0	672	470	202	78.4	54.8	23.6	1,530	1,068
27	September 21, 1923	Normal	M.	2.7 yrs.	13.0	0.59	37.5	1,024	640	384	78.8	49.2	29.6	1,740	1,085
28	September 22, 1923	Normal	M.	3 yrs.	14.6	0.63	30.2	960	670	290	65.7	46.0	19.8	1,540	1,060
29	July 7, 1923	Normal	F.	4 yrs.	15.0	0.65	38.0	1,200	744	456	80.0	49.6	30.4	1,840	1,140
30	June 19, 1923	Normal	M.	5 yrs.	14.4	0.63	36.4	1,170	745	426	81.4	51.7	29.6	1,850	1,185
31	July 10, 1923	Normal	M.	5 yrs.	27.2	1.00	31.9	1,982	1,350	632	72.9	49.6	23.2	1,982	1,350
32	June 5, 1923	Normal	F.	6 yrs.	24.0	0.92	43.4	2,340	1,327	1,013	97.5	55.3	42.3	2,540	1,440
33	June 27, 1923	Normal	M.	6 yrs.	20.0	0.83	34.7	1,347	880	567	67.4	44.0	23.4	1,630	1,065
34	July 25, 1923	Normal	M.	6 yrs.	18.4	0.76	34.0	1,394	920	474	75.7	50.0	25.7	1,840	1,210
35	August 2, 1923	Normal	M.	6 yrs.	19.0	0.79	33.5	1,407	936	471	74.0	49.2	24.8	1,780	1,180
35	August 6, 1923	Normal	M.	6 yrs.	18.4	0.77	33.5	1,407	936	471	76.4	50.8	25.6	1,820	1,210
36	July 21, 1923	Normal	M.	6 yrs.	17.0	0.74	33.6	1,327	880	447	78.0	51.7	26.2	1,790	1,190
37	June 8, 1923	Normal	F.	7 yrs.	21.0	0.84	34.4	1,450	951	499	69.0	45.3	23.7	1,720	1,134
38	June 13, 1923	Normal	F.	7 yrs.	18.9	0.76	31.4	1,430	981	449	75.7	51.9	23.8	1,880	1,290
39	July 12, 1923	Normal	M.	7 yrs.	24.1	0.93	34.0	1,818	1,200	618	75.4	49.8	25.6	1,950	1,290
40	July 10, 1923	Normal	M.	8 yrs.	22.2	0.88	36.0	1,595	1,020	575	71.8	46.0	25.8	1,810	1,160
41	July 11, 1923	Normal	M.	8 yrs.	28.4	1.06	35.4	2,150	1,390	760	75.8	49.0	26.8	2,020	1,310
42	July 20, 1923	Normal	M.	8 yrs.	27.2	1.05	33.6	2,119	1,404	713	77.9	51.6	26.2	2,020	1,340
43	July 28, 1923	Normal	M.	8 yrs.	23.0	0.906	38.0	1,761	1,092	669	76.6	47.5	29.0	1,945	1,200
44	August 1, 1923	Normal	M.	8 yrs.	23.4	0.91	31.8	1,870	1,275	595	80.0	54.5	25.4	2,030	1,400
45	July 10, 1923	Normal	M.	9 yrs.	22.7	0.89	37.0	1,676	1,056	620	73.8	46.5	27.3	1,880	1,190
46	July 19, 1923	Normal	F.	9 yrs.	21.5	0.82	37.0	1,562	984	578	72.6	45.8	26.8	1,900	1,200
47	July 23, 1923	Normal	M.	9 yrs.	24.0	0.93	37.0	1,911	1,204	707	79.8	50.3	29.5	2,030	1,290
48	July 4, 1923	Normal	M.	10 yrs.	24.5	0.94	35.0	1,877	1,220	657	76.6	49.7	26.8	2,000	1,300
49	July 5, 1923	Normal	F.	10 yrs.	29.0	1.05	38.0	2,338	1,450	888	80.6	50.0	30.6	2,220	1,380
50	July 23, 1923	Normal	M.	10 yrs.	33.0	1.18	39.0	2,598	1,584	1,014	78.7	48.0	30.7	2,200	1,340
51	July 28, 1923	Normal	M.	10 yrs.	22.3	0.84	38.0	1,826	1,132	694	81.9	50.8	30.1	2,180	1,350
52	July 25, 1923	Normal	M.	11 yrs.	30.0	1.11	33.0	2,240	1,500	740	74.7	50.0	24.6	2,090	1,350

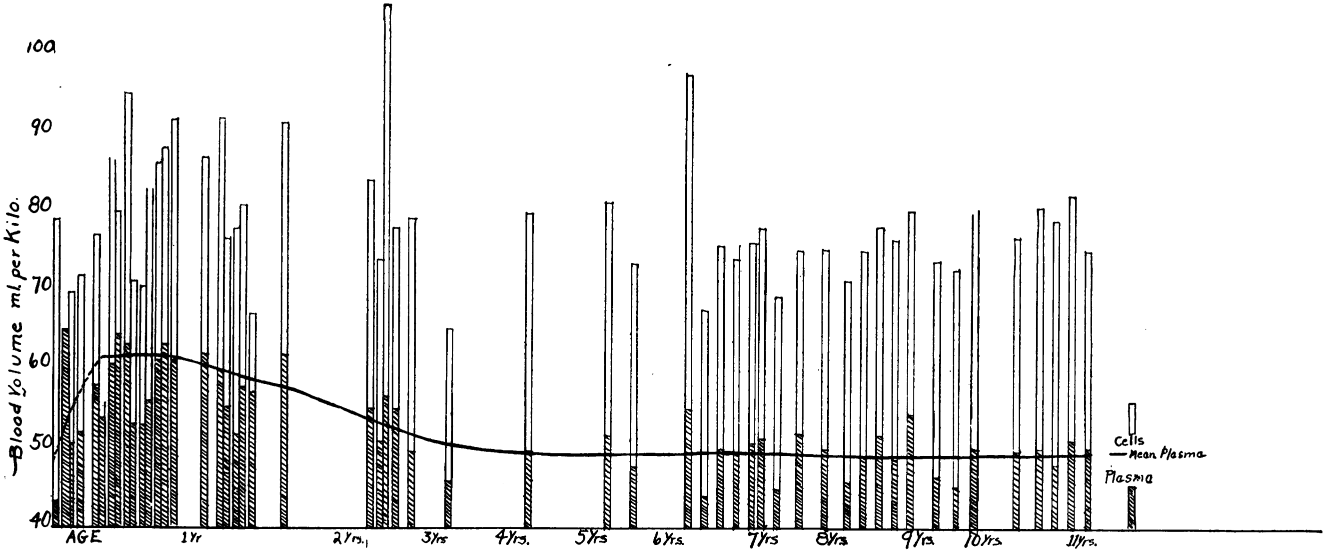

CHART 1. THE RELATION OF BLOOD AND PLASMA VOLUMES PER KILOGRAM AT DIFFERENT AGES

respective age. An exception to this statement is not shown in chart 1, but is brought out best in the paper of Lucas and Dearing (10). During the first 3 to 4 weeks of life, the proportion of the blood represented by the red cells is 45 to 70 per cent; while during the rest of the first year of life, it is only 30 per cent. The high proportion of red cells makes the total blood volume correspondingly high. It will be noticed also that the plasma volume per kilogram of body weight varies more widely during the first year of life, than later. This variability cannot be explained from our present knowledge of infant physiology. This physiological constant must, therefore, be classified with the other physiological constants that manifest greater variability in infants than in adults.

TABLE 2

Case number	Protein		Case number	Protein	
	Per cent	Grams per kilogram		Per cent	Grams per kilogram
5	6.62	3.74	19	8.65	4.54
7	7.96	4.86	20	6.98	4.08
16	7.26	4.50	21	8.05	3.80
17	7.42	4.40	25	7.78	4.40
18	7.63	4.20	26	9.60	5.25

The red cell volume per kilogram of body weight after the first six weeks of life, is about 25 to 35 milliliters. This is somewhat lower than in adults, and is in keeping with the lower hemoglobin and red cell count.

The total serum protein per kilogram of body weight is given on a few cases in table 2. The average for the second year is 4.2 grams per kilogram of body weight, whereas Bakwin and Rivkin (11) found 3.6 grams for the first year. From our knowledge that the serum protein concentration remains about the same after the first year of life, one may assume that the average for the rest of life will be about 4 grams per kilogram of body weight. This figure, though probably not very exact, will be useful for comparison with the findings obtained from patients suffering from various diseases.

The blood and plasma volume per square meter of body surface as related to age is shown in chart 2. It is realized that the methods for

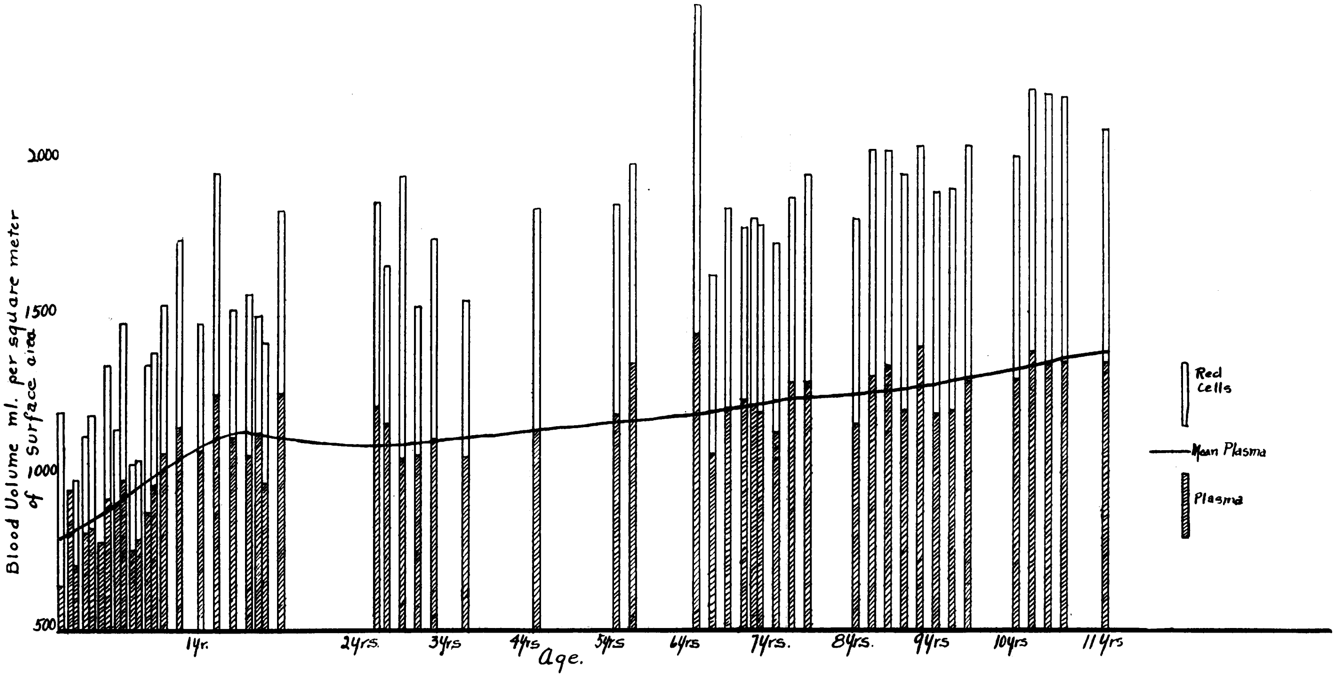

CHART 2. THE RELATION OF BLOOD AND PLASMA VOLUMES PER SQUARE METER OF SURFACE AREA AT DIFFERENT AGES

computing the surface area are not yet sufficiently accurate to give a very exact estimate of the surface area in a given child. However, the figures are sufficiently accurate to show the general relation of the blood and plasma volume to the surface area. As will be noticed, the plasma volume per square meter of body surface as related to age rises rapidly during the first year from 750 milliliters to 1110 milliliters and then remains constant during the second year, perhaps decreasing a little. Thereafter, there is a steady rise to about 1375 milliliters, by the twelfth year of life. That this rise continues till adult life is indicated by the fact that the adult average of the plasma volume per square meter of surface area is 2000 milliliters (Brown and Keith (8)).

The variability of the red cell volume makes the curve of the blood volume per square meter of surface area more irregular. In general the whole blood volume describes a curve similar in shape to the one described by the plasma volume.

The question as to whether weight or surface area is better correlated with the plasma volume has not been settled and the data in this paper only bring out new facts. Table 3 shows the standard deviation[1] from the average and the percentage standard deviation from the average of the plasma volume as related to both weight and surface area. The plasma volume per kilogram of body weight was not used in the six youngest babies in making this table because the data for this age are not sufficiently numerous. No figures are given for the first year for the standard deviation of the plasma volume per square meter of surface area because at this age the average plasma volume per square meter is changing too rapidly to allow such a computation from the data of this paper.

[1] Standard deviation is calculated according to the well known formulae:

$$\delta = \sqrt{\Sigma \frac{(x - x_1)^2}{n}}$$

δ = standard deviation
x = mean measurement
x_1 = given measurement
N = number of measurements
Σ = Sum of the different quantities $(x - x)^2$.

Percentage standard deviation $= \frac{100\delta}{x}$.

The average of the percentage standard deviations for each age is the same (5.4) whether plasma volume is compared with weight or surface area. However, since weight is more variable than surface area, the same degree of correlation would indicate a closer relationship between weight and plasma volume, than surface area and plasma volume. However, there are not enough cases in this series to draw conclusions from small differences. The main fact brought out is that surface area cannot be correlated with the plasma volume unless the age of the individual is also taken into account, but weight may be correlated with the plasma volume after the third year, since the plasma volume is constant at 50 milliliters per kilogram of body weight, after this age (see charts 1 and 2).

TABLE 3

	Age										
	1	2	3	4	5	6	7	8	9	10	11
Standard deviation per kilogram of weight	4.8	3.7	3.1	3.1	0	2.1	3.7	2.7	3.9	4.0	1.0
Percentage standard deviation per kilogram of weight	7.7	7.5	5.7	6.2	0	4.1	7.4	5.4	7.8	8.0	2.0
Standard deviation per square meter of surface		89	65	13	0	127	126	61	72	90	21
Percentage standard deviation per square meter of surface		7.3	5.9	1.3	0	10.9	10.5	4.9	5.7	7.0	1.5

DISCUSSION

The shape of the curve of the plasma volume per kilogram of body weight as related to age suggests a relationship between the plasma volume and the metabolic rate. It will be noted that the shape of this curve is similar to that of the basal metabolic rate per square meter of surface area as related to age (Benedict and Talbot (16)). There is both a rise in the metabolic rate and in the plasma volume during the first year of life and both remain high during the second year. The basal metabolic rate drops rather rapidly till the beginning of the fourth year and continues to decrease slowly during the rest of childhood. The plasma volume per kilogram of body weight decreases rapidly till the fourth year but then seems to be quite constant.

However, the figures for adults tend to be slightly lower than those for children reported in this paper (see previous references) and the comparatively small number of cases reported here may not have been sufficient to indicate a slight tendency to a decrease in the plasma volume after the third year. Thompson (17) found in nine patients with myxedema that treatment with thyroid extract caused an increase in the total plasma volume as follows: average increase in the total plasma volume 22 per cent; average increase in the plasma volume per kilogram of body weight 28 per cent; average increase in plasma volume per square meter of body surface 22 per cent. Furthermore, the plasma volume while the patients were suffering from myxedema, in general, was low. These facts seem to indicate that the higher the metabolic rate, the larger the amount of water in the blood stream, and the lower the metabolic rate, the smaller the amount of water in the blood stream.

The fact that the metabolic rate is so closely related to the surface area and that the surface area has a relation to the plasma volume which varies with the age of the child demands some explanation. The work of Brown and Keith (8) on obese patients would lead one to expect a close correlation between plasma volume and surface area. These facts may be reconciled by assuming that the plasma volume is related primarily to the mass of the body tissues and that there is only a secondary relation between the plasma volume and the metabolic rate. Thus weight becomes the better measure of the plasma volume when individuals of widely different sizes are chosen, but with individuals of about the same weight, the surface area may be a better measure of the plasma volume than weight.

The red cells play an important part in the regulation of the blood volume. In normal individuals, the volume of the red cells is large enough to maintain the plasma volume. However, a minimum volume of red cells is necessary to carry and hold water in the blood stream. (Robertson and Bock (7) Keith (18)). The dependence of the body on red cells to transport water is suggested by the appearance of edema in severe cases of anemia. Based on the increased depression of the freezing point which accompanies an increase in the tension of the carbon dioxide to which blood is exposed, Buckman and Darrow (19) have advanced the hypothesis that amongst the other varied functions of the red cells must be added that of being the chief carrier of water.

The mechanism of maintaining and carrying the blood and plasma water may be explained in part as follows. Given an adequate volume of red cells circulating through the body, the following events tend to take place. When the oxygenated blood reaches the systematic capillaries, a certain amount of fluid is filtered out of the blood stream by hydrostatic pressure; the red cells lose oxygen and take up carbon dioxide, as a result of the increased tension of carbon dioxide This causes an increase in the osmotic pressure of the plasma and presumably of the red cells which become swollen with water taken from the plasma. The increased osmotic pressure of the plasma enables it to take up water from the tissues to replace the loss of water to the red cells. In the lung capillaries all the factors favor an accumulation of water in the pulmonary tissues. In addition to the hydrostatic filtration process, the loss of carbon dioxide decreases the osmotic pressure of the plasma and thus favors the transfusion of water into the alveolar tissues. This probably accounts for the fact that the lungs contain a higher proportion of water than any other body tissue. The extent of the tendency of the circulating blood to take up water from the systemic tissues will depend ultimately on the amount of carbon dioxide carried by the blood. Although, in the plasma alone, bicarbonate is formed on exposure to carbon dioxide, and this reaction is accompanied by an increase in the osmotic pressure and is a reversible reaction, it is the presence of hemoglobin in the red cells, which so greatly enhances the efficiency of this reaction. The hemoglobin under the influence of carbon dioxide loses oxygen and becomes more alkaline, and conversely, the presence of oxygen frees carbon dioxide through the formation of oxyhemoglobin which is more acid than reduced hemoglobin. This property of hemoglobin explains the efficiency of blood not only as a carbon dioxide but also as a water carrier. Thus the amount of water taken up by the blood from the tissues should be related to (1) the amount of carbon dioxide produced or the basal metabolic rate and (2) the efficiency of the blood as a carbon dioxide and water carrier which under ordinary circumstances is dependent on the circulating mass of red cells.

Based on the above described mechanism of water transport, one may conceive of six classes of disturbances which may affect the blood volume and water distribution. They are as follows: (1) disturbances in carbon dioxide production as in diseases of the thyroid gland, fever, etc., (2) disturbances of the transporting mechanism of the blood such as occurs in anemia and changes in the acid-base equilibrium leading to too high or too low initial bicarbonate levels, (3) disturbances in carbon dioxide and water excretion in the lungs, as in emphysema, pulmonary edema, heart disease, pneumonia, etc., (4) disturbances in the excretion of water by the sweat glands, gastrointestinal canal and kidneys as in heat stroke, diarrhea and perhaps some forms of nephritis, (5) disturbances in the water absorption as in vomiting, and perhaps some forms of diarrhea, (6) disturbances in the rate of blood flow.

The manner in which all the above types of disturbances may affect water balance is fairly obvious, and only the third and sixth need any elaboration. Since venous blood undergoes an increase in osmotic pressure over that of arterial blood which is directly proportional to the increase in bicarbonate content, it is apparent that the tendency of the venous blood to take up water from the tissues depends on the increase in the bicarbonate content of the venous blood over that of the arterial blood, what one might call the potential difference between arterial and venous blood. In some unpublished experiments by Buckman and Darrow it was found that an increase in bicarbonate of the plasma of one volume per cent is accompanied by a lowering of the freezing point of about 0.001 degree centigrade. This corresponds to an increase in osmotic pressure of 9.1 millimeters of mercury, and when one takes into account the usual difference in bicarbonate content of venous and arterial blood, one would expect an increase in osmotic pressure of venous blood over that of arterial blood of the same order of magnitude as the fall in hydrostatic pressure from arterial to capillary blood. It is obvious that, with the same rate of carbon dioxide production, the difference in bicarbonate content between arterial and venous blood will become less the more rapid the rate of blood flow. If the increase in bicarbonate or osmotic pressure becomes small enough, an equilibrium between the osmotic pressure of the tissue and plasma cannot take place in the short period of time that it takes the blood to pass through the tissues. Since hydrostatic pressures remain about the same, water tends to accumulate in the tissues at the expense of the plasma under such conditions. Apparently this is what happens with a too rapid rate of blood flow. Similarly with a slow circulation, the increase in osmotic pressure may be great enough to increase the rate of water diffusion back into the plasma. Thus, when the water carrying mechanism of the blood is compensated, apparently a slow rate of blood flow leads to increased plasma water content, and diminished tissue water content, whereas a rapid rate of blood flow leads to a diminished plasma water content and an increased tissue water content. However, due to the shape of the carbon dioxide curve, which shows diminishing increments in bicarbonate with increasing carbon dioxide pressure, the carbon dioxide carrying and water carrying mechanism would tend to break down with too slow a rate of blood flow, and, in such cases, one would expect an accumulation of water in both the tissues and plasma. Data supporting these views will be given in subsequent papers in cases of pneumonia and heart disease.

When carbon dioxide excretion is interfered with in the lungs, as in cases of pulmonary edema, the first obvious change in the blood is an increase in arterial bicarbonate and decrease in arterial oxygen. This lessens the difference in bicarbonate content of venous and arterial blood by making the blood work at a higher carbon dioxide pressure, and as noted above, this diminishes the efficiency of the carbon dioxide and water carrying mechanism of the blood. Thus pulmonary edema leads to diminished plasma water content, and increased tissue water content. Evidence of these changes is given in post-influenzal pneumonia and poisoning by war gases by Underhill and Ringer (20) and Underhill (21). In emphysema, the increased red cell concentration leads to greater efficiency of the carbon dioxide and water carrying mechanism of the blood. Only experimental observations can tell whether this is sufficient to overcome the tendency to diminished plasma volume one would otherwise expect.

The above mechanism can only be considered a partial explanation of the transportation and distribution of water. Increased pressure of carbon dioxide in the tissues increases the osmotic pressure of the tissues by a process similar to that observed in the blood, and thus alters the water distribution. Other means of varying the salt binding power of proteins must occur, but little is known of such processes. Furthermore, our present knowledge does not permit a discussion of the rôle played by differential excretion of electrolytes and other crystalloids by the kidneys, intestines and sweat glands. Also any disturbance in the distribution of colloids should produce a disturbance in the water balance. No explanation of water metabolism can be complete, without considering these factors in addition to the mechanism postulated in this paper.

SUMMARY

Blood volumes determined by the dye method are reported on normal infants and children up to twelve years of age. A curve of the plasma volume per kilogram of body weight as related to age shows a rise in the plasma volume from 50 to 62 milliliters during the first year of life, and a return to 50 milliliters, by the fourth year. Thereafter, the plasma volume remains constant at 50 milliliters per kilogram of body weight.

A curve of the plasma volume per square meter of surface area as related to age shows a rapid rise from 750 to 1100 milliliters during the first year of life, and thereafter there is a gradual increase to 1375 milliliters by the twelfth year.

The proportion of the blood represented by the red cells is about 30 per cent, except during the first six weeks of life, when it is 45 to 70 per cent. The whole blood volume cannot be predicted very accurately either from the weight or the surface area because of the variability of the cell volume.

The following hypotheses are advanced: (1) The amount of plasma is primarily dependent on the mass of the body tissues. (2) Within certain limits set by the mass of the tissues, the amount of water in the blood stream varies directly with the metabolic rate.

The mechanism by which the plasma volume is maintained and varied is given a partial explanation.

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