Blood Volume Changes in Cyanotic Congenital Heart Disease and Polycythemia Rubra Vera

By David Vérel, M.D.

It is well known that in polycythemia rubra vera the total blood volume increases as the hematocrit level rises beyond approximately 55 per cent.1,2 This increase masks the extent of the polycythemia and insures that the plasma volume is not greatly diminished despite an increase in red cell volume to twice or three times the normal value. The changes in adults suffering from cyanotic congenital heart disease have not been precisely defined. It is less easy to compare the blood volume in this condition with expected normal values because the limits of the normal blood volume are poorly defined by reference to height or weight.3 Statistically valid limits of blood volume have been determined in adult subjects by means of height, weight, girth, and fat thickness.4 In this paper patients of adult stature suffering from polycythemia rubra vera and from congenital heart disease are compared with normal adults.

Methods

Red cell volume was measured with radioactive phosphorus52 or radioactive chromium51-labeled red cells by a modification of the methods of Reeve and Veall5 and of Mollison and Veall.6 Approximately 10 ml. of red cells were withdrawn with sterile precautions and placed in a sterile stoppered ampoule. The red cells were centrifuged, and the supernatant plasma was added to 100 ml. of sterile ice-cold normal saline. Three milliliters of isotonic acid-citrate-dextrose mixture were added to the red cells and to this approximately 15 microcuries of radioactive phosphorus52 or 50 microcuries of radioactive chromium51 were added. The cells were then incubated for 30 minutes at 37°C, if phosphorus was used, and at room temperature, if chromium was used. The cells were then washed three times with cold saline-plasma mixture. An accurately measured volume of 20 ml. was then injected into the patient intravenously and two samples were taken at 10-minute intervals. Suitable standards were prepared and the radioactivity of the samples, the standards, and the saline in which the cells were suspended were counted in a Type N 550 Eko* well-type scintillation counter for the chromium and a standard liquid-type Geiger-Müller tube for the phosphorus.

Plasma volume was measured in a few patients in each group with either Evans blue radioactive iodine131, labeled albumin, or high molecular weight dextran.6 In other cases the plasma volume was calculated from the red cell volume with use of a body venous hematocrit ratio of 0.92 for patients in whom the hematocrit value was below 60 per cent. In those exceeding 60 per cent a body venous hematocrit ratio of 0.94 was employed, since this gave a more precise estimate.7,8 The hematocrit value was estimated in duplicate on all samples by spinning in 10-cm. Wintrobe tubes in a centrifuge at 15-cm. radius for 55 minutes at 3,000 r.p.m. The hematocrit values were corrected for plasma by the method of Chaplin and Mollison.9 Height, weight, and girth were measured by standard methods, fat thickness was measured below the angle of the scapula with a caliper. Blood volume was predicted from these measurements by the formula of Hicks et al.3

Results

Blood volume measurements were made on 12 patients with congenital heart disease. Their ages ranged from 16 to 46 years, the venous hematocrit values from 44.0 to 83.2 per cent, and the red cell volume from 1,890 to 5,170 ml. The calculated blood volumes ranged from 3,940 to 8,000 ml. (table 1).

Similar measurements were made on 12 patients with polycythemia rubra vera who had not been subjected to venesection. Their ages ranged from 35 to 66, the venous hematocrit values from 50.0 to 68.8 per cent, and the red cell volume from 2,550 to 6,460 ml. The calculated blood volume ranged from 4,800 to 9,400 ml. (table 2).


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The body measurements in the two groups were comparable. The blood volume and red cell volume predicted from these body measurements are shown for each patient. In each case the estimation of blood volume has a standard deviation of 383 ml.3

The red cell volumes, venous hematocrit values, and body builds in these two groups are comparable with each other and may be compared with the data of the normal subjects published by Hicks et al.3 It is therefore possible to use a predicted normal value for each patient obtained from the body measurements as a basis of comparison. The age of the patients was not found to have a measurable effect in determining blood volume,3 so that the difference between the two groups of patients does not invalidate their comparison. For the purposes of comparison the data are most conveniently expressed as a ratio of the

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function measured to the predicted normal value. Throughout, this ratio has been expressed as a percentage of the normal value (tables 1 and 2).

**Discussion**

Measurements of blood volume in congenital cyanotic heart disease have been reported by Cassels and Morse (1947) and by Hallock (1940). Both found a variable increase in the total blood volume due to a rise in the red cell volume, the plasma volume being usually diminished. Cassels and Morse suggested that abnormal circulation in congenital heart disease required an elevation of circulating blood volume, the addition to the normal quantity being due to the volume shunted in one direction or the other through an abnormal communication. The observations reported in this paper do not support this view.

When the total blood volume in the patients reported here is expressed as a percentage of normal and related to the venous hematocrit level, it is clear that in congenital heart disease the total blood volume may remain within normal limits up to a hematocrit level of over 80 per cent (fig. 1). Only in two cases (nos. 2 and 7) did the total blood volume rise significantly above the predicted normal value; in both cases the red cell volume itself had risen close to the predicted normal volume, so that an increase of blood volume was inevitable if the plasma volume was to be retained. In the remaining patients the increase in red cell volume was not so gross. A similar tendency may be observed in the patients reported by Cassels and Morse and by Holman. In all three patients reported by Cassels and Morse the total blood volume exceeded the predicted normal volume by more than 100 per cent and the total red cell volume itself was considerably above the predicted normal blood volume. It seems likely therefore that the increases in blood volume reported previously and in this paper are not related to the quantity of blood shunted but rather to the degree of polycythemia. This response differs from that found in the patients with polycythemia rubra vera in whom the rapid increase in total blood volume is found as the hematocrit level rises above 55.
per cent. This confirms the well-known observations of Gibson and Evans.\(^1\)

When the changes in the red cell volume found in polycythemia rubra vera and congenital heart disease are compared (fig. 2), it is seen that at any hematocrit level the red cell volume in polycythemia rubra vera is higher than that in congenital heart disease. This is a simple result of the increase in total blood volume seen in polycythemia rubra vera, which conceals the true extent of the polycythemia.

The changes in plasma volume expressed as percentages of the predicted normal volume are shown in figure 3. In polycythemia rubra vera there is no very consistent change in plasma volume, which ranges between 75 and 126 per cent of normal, although, as might be expected, the majority of plasma volume measurements are below normal. In congenital heart disease the response is quite different. A remarkably consistent fall in plasma volume occurs as hematocrit values rise, until the hematocrit is about 80 per cent when the plasma volume is about half its normal value or less. The correlation coefficient is significant \((r=-0.920)\). These data can be used to calculate with a fair degree of confidence the plasma volume in subjects suffering from congenital heart disease. The regression equation derived from the data is \(%PV=\ -1.15\ (\%Ht) +147.5.\) If the normal blood volume is calculated by the data of Hicks et al.\(^3\), the plasma volume may therefore be inferred from the formula \(PV=BV \times 58/100 \times K,\) in which \(K=\ (147.5-1.15\ (\%Ht)).\) The correlation between the measured and predicted plasma volumes is shown in table 3.

These observations may be important in the surgery of congenital heart disease. The figures in table 3 indicate that in subjects of adult stature the plasma volume may be as low as 1 liter when a plasma volume of 2.4 liters might be expected. In such patients less than half the normal quantity of fibrinogen circulates in the blood and the total available quantities of platelets and prothrombin are comparably reduced. These changes may well be involved in the hemolytic tendency reported in certain patients with congenital heart disease following surgery. It is clear that further research is indicated into the changes occurring during readjustment from this abnormal status after surgery.

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**Table 3**

*Comparison of the Plasma Volume*

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*Calculated from the formula \(PV=\) predicted B.V. \(\times 58/100\) \((147.5-1.15\ Ht).\)
BLOOD VOLUME IN POLYCYTHEMIA

Summary

The blood volume has been measured in 12 adult patients with cyanotic congenital heart disease and in 12 patients with polycythemia rubra vera by radioactive isotopes. In congenital heart disease the total blood volume was found to be within normal limits provided the red cell volume had not risen so high as to make an increase in total blood volume inevitable. In polycythemia rubra vera the total blood volume increased rapidly once a hematocrit level of 55 per cent had been exceeded. Increasing polycythemia in congenital heart disease was found to be associated with the predictable fall in plasma volume, and a formula for estimating the plasma volume from the predicted normal blood volume and the hematocrit is presented. It is suggested that the low plasma volume that may be found in very polycythemic patients may be partly responsible for their known tendency to postoperative hemorrhage.

References


Obstacles encountered in research, however, sometimes yield quite as important results as those which were anticipated. In 1897, when I was using the recently discovered X-rays in studying the movements of the stomach, I was greatly disconcerted by occasional interference with my observations. Although some animals displayed the rolling waves of the stomach wall with the utmost definiteness, others showed no movements whatever. The whole purpose of my effort, of course, was to see the waves and to learn their effects. Their failure to appear in animals which had been carefully prepared was a serious check on my progress. Only after some time did I note that the absence of activity was accompanied by signs of perturbation and that when serenity was restored the waves promptly reappeared. This observation, a gift for my troubles, led to a long series of studies on the effects of strong emotions on the body.—Walter B. Cannon, M.D. The Way of An Investigator. New York, W. W. Norton & Co., Inc., 1945, p. 38.

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