"Relative Polycythemia" or "Pseudopolycythemia"

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The laboratory diagnosis of polycythemia depends on the demonstration of an elevation in hematocrit or in the hemoglobin content of the peripheral blood. Since these determinations are really expressions of concentrations, observed elevations may be induced by either an increase in the red cell mass or a decrease in the plasma in which the cells are suspended. Although states of hemoconcentration are frequently encountered in acute dehydration from any cause, the presence of a chronic, relatively asymptomatic state of hemoconcentration was not appreciated until the clinical use of blood volume determinations. Recent literature has applied the term "relative polycythemia" to discussions of patients suspected of polycythemia but found to have a normal red cell mass and a smaller than normal plasma volume. The term "pseudopolycythemia" probably is more descriptive of the current view of such patients.

Examples of this type of patient were recognized by Keith, Rowntree, et al.,[1,2] who reported 3 cases of "polycythemic hypovolemia" in which the elevations of hemoglobin and hematocrit were attributed mainly to a decrease of the plasma volume. Geisbock[3] called attention to the association of an elevated red blood cell count and hemoglobin with hypertension and named the condition "polycythemia hypertonica." Since blood volume determinations were not done in his cases, it is not possible to determine the exact type of polycythemia he described. Bassen[4] described 2 cases of "pseudopolycythemia," with a low total plasma volume. The first case would fit the syndrome of alveolar hypoventilation with secondary polycythemia, which has become familiar in recent years. The second case probably had a true elevation of the total red cell mass. Our present clinical interest in this condition was revived by Lawrence et al.,[5] who reported on a study of 18 cases of "relative polycythemia." This was also called "stress polycythemia" because many of the patients had hypertension and psychosomatic complaints. Since the primary criteria they used for diagnosis was a decrease in the plasma volume, 11 of the 18 patients had hematocrits below 55%, and 6 of the 18 had hemoglobins of less than 16.5 gm. These cases would not ordinarily have been suspected of having polycythemia on the basis of the hematocrit or hemoglobin values.

Submitted for publication Jan. 24, 1962; accepted June 5.

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Material and Methods

Our present report includes 10 patients studied in the Iowa City Veterans Administration Hospital between 1954 and 1961. This undoubtedly does not represent the true incidence of this condition, because only cases of suspected or borderline polycythemia had determinations of red cell mass. To be included in our series, the patient must have had

TABLE 1.—*Normal Values—50 Cases*

	Hgb.	Hct.	Ml. per Kg. of Body Weight			Ml. per Sq. Meter of Body Surface*		
			Bld. Vol.	RCM	Plasma	Bld. Vol.	RCM	Plasma
Mean	14.6	46	61.9	29.2	32.6	2,417	1,142	1,275
S.D.	1.0	3	6.0	2.9	4.4	231	134	152
Mean ± 2 S.D.	12.6-16.6	40-52	49.9-73.9	23.4-35.0	23.8-41.4	1,955-2,879	874-1,410	971-1,579

* Based on 41 cases; height on 9 subjects not available.

an elevated hematocrit and a normal total red cell mass, expressed per kilogram of body weight. Normal values for hematocrit and red cell mass were determined in this hospital previously in a group of 25 healthy hospital staff members and 25 ambulant patients with no hematologic disorders. The total blood volume was determined by the Cr^{51}-labeled red cell technique as described by Huff.[6] Plasma volumes and red cell mass were calculated from the venous hematocrit.

The findings in the group of 50 normal controls are listed in Table 1.

Clinical and Laboratory Findings

The main clinical and laboratory findings of the 10 patients are listed in Tables 2 and 3. Almost all of the patients had ruddy complexions and were obese. These findings combined with the elevated hematocrit caused the possibility of polycythemia to be considered. Although the degree of elevation of the hemoglobin and of the hematocrit was only slight to moderate, the elevations were

TABLE 2.—*Clinical Findings*

Pt.	Age	Ruddy Complexion	Cyanosis	Blood Pressure		Weight, % Excess *	Thrombo-embolism	Primary Diagnosis
				Maximum	Minimum			
1	62	+	+	160/90	110/70	29	0	Chronic interstitial pneumonitis
2	61	0	±	150/90	140/80	31	0	Obstructive emphysema
3	37	+	+	190/120	168/104	15	+	HASHD †
4	63	+	0	185/120	175/105	29	+	HASHD, CVA
5	67	±	0	220/120	140/80	12	0	HVD
6	65	+	0	220/110	142/92	69	0	Diabetes mellitus
7	66	+	0	148/92	120/70	34	+	ASHD
8	70	+	+	138/84	138/84	40	+	ASHD, CVA
9	54	+	0	124/100	100/64	28	0	Duodenal ulcer
10	63	+	0	165/90	110/60	—	+	ASHD, CVA

* Normal values from the Metropolitan Life Insurance Company data, 1959.

† HASHD indicates hypertensive arteriosclerotic heart disease; CVA indicates cerebral vascular accident; HVD indicates hypertensive vascular disease; ASHD indicates arteriosclerotic heart disease.

TABLE 3.—*Laboratory Findings*

Pt.	Hgb. *	Hct. *	Ml. per Kg. of Body Weight			Ml. per Sq. Meter of Body Surface †		
			Bld. Vol.	RCM	Plasma	Bld. Vol.	RCM	Plasma
1	18.2	55.0	50.9	28.0	22.9	2,137	1,176	961
2	18.4	56.0	59.8	34.1	25.7	2,549	1,454	1,096
3	18.3	60.0	50.0	28.0	22.0	1,952	1,093	859
4	19.5	62.0	56.6	35.1	21.5	2,404	1,491	914
5	18.0	56.0	48.2	26.7	21.5	1,867	1,045	822
6	16.4	55.0	46.3	26.4	19.9	2,283	1,301	982
7	17.0	57.0	60.6	33.3	27.3	2,646	1,455	1,191
8	17.8	55.0	45.6	25.1	20.5	2,076	1,142	934
9	17.6	53.0	42.4	22.9	19.5	1,771	956	814
10	18.2	58.0	59.1	35.5	23.6	—	—	—

* These are averages of determinations on different days within a 2-week period.

† Height on one patient not available.

definite and persistent. Of the 10 patients, 6 had diastolic blood pressure over 90 mm. of mercury. Only 3 of these, however, had hypertension of a degree or constancy to be considered clinically significant. Thromboembolic phenomena were encountered in 5 of the 10 patients. These included 3 cerebral thromboses, 4 coronary thromboses, one arterial embolism to the leg, and one venous thrombosis of the leg.

Comment

Most of the blood volume data in the literature are expressed in relationship to body weight. This method was employed in the selection of our patients. For clinical purposes, the blood volume correlates fairly well with body weight in normal individuals; however, such correlations are on less firm ground in the obese person. Rowntree et al.[2] found that blood volumes correlated better in the obese with body surface than with body weight. On this basis, 3 of our 10 patients had red cell masses slightly above 2 standard deviations from normal (Table 3). The magnitude of change in the other 7 patients was insignificant. The expected normal blood volumes can probably be best estimated from the lean body mass and percentage of adipose tissue.[6,7] Direct measurements of body fat and lean body mass were not made on our group of patients. However, determinations of lean body mass (from body water measured with D_2O) in this hospital indicated that Allen's [8] nomograph relating lean body mass to height and weight was as equally applicable to a group of American males in Iowa City as to the population from which it was derived. The blood volume for the 41 control subjects can, therefore, be expressed in regression equations as follows [9]:

$$\textit{Red cell mass (ml.)} = 36.4(\textit{kg. of lean body mass}) + 16.1(\textit{kg. of adipose tissue mass}) - 175.$$

$$\textit{Plasma volume (ml.)} = 34.1(\textit{kg. of lean body mass}) + 9.2(\textit{kg. of adipose tissue mass}) + 387.$$

Using the above formulae, the expected range ("95% confidence limits") of red cell mass and plasma volume for the patients with relative polycythemia was calculated and summarized in Table 4. When compared on this basis, 4 patients had red cell masses within the expected range, 3 patients had red cell masses above, and 2 below, this expected range. These deviations ranged from 18% below to 28% above the regression line for normal red cell mass.

The accuracy of the calculated lean body masses and adipose masses does not warrant the designation of this expected normal range as 95% confidence limits. The magnitude and opposite direction of these deviations from expected total red cell mass are interpreted as confirming the probable normality of the red cell masses for this group of patients. However, the possibility is illustrated that

TABLE 4.—*Expected Range of Red Cell Mass and Plasma Volume* *

Pt.	Height (Cm.)	Lean Body Mass (Kg.)	Adipose Tissue (Kg.)	% Fat	Observed Red Cell Mass (Ml.)	95% Confidence Interval	Observed Plasma Vol. (Ml.)	95% Confidence Interval
1	162	48.0	28.0	37	2,130	1,862.0-2,184.0	1,740	2,071.0-2,493.0
2	167	52.0	29.0	36	2,760	2,038.2-2,331.8	2,080	2,234.6-2,619.4
3	162	46.0	22.2	32	1,910	1,704.5-2,007.5	1,500	1,961.4-2,358.6
4	172	56.0	29.0	34	2,980	2,188.0-2,472.0	1,830	2,377.8-2,750.2
5	173	59.0	14.6	20	1,960	2,099.1-2,316.9	1,540	2,390.3-2,675.7
6	171	63.0	45.6	42	2,850	2,217.4-2,946.6	2,150	2,477.1-3,432.9
7	171	56.0	29.9	35	2,910	2,192.5-2,495.5	2,380	2,373,4-2,770.6
8	181	66.0	34.4	34	2,520	2,520.6-3,041.4	2,060	2,612.7-3,295.3
9	173	57.0	27.1	32	1,920	2,212.9-2,459.1	1,640	2,418.6-2,741.4

* Height was not available on one patient.

Lean body masses and adipose tissue masses were calculated for these patients on the basis of heights and weights from Allen's nomograph. [8] From the linear regression equations for red cell mass and plasma volume, derived from 41 control subjects, the 95% confidence limits for a normal individual were calculated. [9] These confidence limits vary, as the individual deviates from the population mean for lean body mass and adipose tissue.

some of these patients might be slightly polycythemic, when body fat is taken into account. Future efforts at clarifying "relative polycythemia" should gather data on this point.

Plasma volumes were smaller than normal in most of the 10 patients reported, whether related to body weight, body surface area, or lean body mass and fat. Blum et al.[10] studied 10 cases of relative polycythemia and found that the body hematocrit was normal (not elevated as suggested by the peripheral venous hematocrit) in 9 when the red cell mass was determined with Cr^{51}, and the plasma volumes were determined independently with I^{131} albumin. The peripheral hemoconcentration was secondary to an alteration in the distribution of plasma. Their study certainly confirms the inconstant relationship between venous and body hematocrit noted by others in abnormal states.[11-14] The fact remains that there is at least a peripheral hemoconcentration in these patients, as well as generalized hemoconcentration in some cases.

The physiologic mechanisms involved in either persistent peripheral hemoconcentration or reduced plasma volume remain unknown. No studies have been reported concerning serum protein synthesis or degradation rates in such patients. Increased capillary permeability has been reported as the cause of acute plasma hypovolemia,[15] but no studies have been reported on chronic plasma hypovolemia. Obviously it would be of interest to know the response of such patients to plasma or plasma-expander transfusions.

Relative polycythemia is usually considered a benign condition, requiring no treatment. However, 50% of Lawrence's cases showed hypertension. This frequency of hypertension was identical with that in 157 cases of polycythemia vera reported in the same article.[16] Other authors have also found a high incidence of hypertension in polycythemia vera.[17-19] Of the 10 patients in the present series, 6 had elevated blood pressure, and 3 had clinically significant hypertension. Causal relationship between polycythemia vera and hypertension has not been established.[20] Similarly, such a relationship in relative polycythemia may also be coincidental. Further studies are clearly needed.

One of the most serious complications in polycythemia vera has been thromboembolism. Five of our patients had such complication during life, and it was the cause of death in both of the patients who died. Since 8 of our patients were over 60 years old and were obese, such complications might well be anticipated, but the frequency of occurrence in this small group equals or exceeds that reported in larger series of polycythemia vera.[17,18,21-24] The possible importance of an elevated peripheral hematocrit in increasing blood viscosity and thrombotic potential is worthy of careful reexamination. The newer knowledge of non-Newtonian flow characteristics of blood has altered the textbook concept of the relationship of blood viscosity to hematocrit.[25] Burch[26] has found that patients with myocardial infarction have a high normal peripheral hematocrit and has suggested that this is a significant factor in elevating blood viscosity in areas of reduced velocity of blood flow. It is conceivable, therefore, that the elevated hematocrit may be contributing to the thromboembolic complications seen in relative polycythemia.

Repeated blood volume determinations over a period of 3½ years in one patient showed the persistence of the condition. The red cell mass increased from 33.3 ml. per kilogram to 39.4 ml. per kilogram. The plasma volume remained low. Whether this will develop eventually into a case of polycythemia vera can only be answered in time.

Only one of our 10 patients was noted to be anxious and presented a picture of a person under emotional stress. The others were calm, cooperative, and apparently well adjusted. Attempts to determine whether they were also under some hidden stress were not made.

Summary and Conclusions

1. Ten cases of relative or pseudopolycythemia seen over a period of 7 years were reviewed. The diagnosis was based on an elevated hemoglobin or hematocrit and a normal red cell mass expressed per kilogram of

body weight. The red cell mass was found to be normal in 4, slightly elevated in 3, and reduced in 2 when body fat and lean body mass were used to establish normal ranges. Eight patients had subnormal plasma volumes.

2. Clinically significant hypertension was found in 3 and major thromboembolic episodes in 5. Two died of myocardial infarction. Whether these complications were coincident findings of old age is uncertain. Further studies of such patients are necessary to determine the validity of considering this a syndrome.

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