Race-Related Differences in Peripheral Blood and in Bone Marrow Cell Populations of American Black and American White Infants

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The present study confirms that in healthy infants, a racial difference exists in peripheral blood hemoglobin levels, total leukocyte, and total neutrophil counts. Racial differences in the composition of the bone marrow are negligible. The only demonstrable difference is confined to the erythroid cell population. No significant difference exists in the incidence of myeloid cells or small lymphocytes.

Racially related differences in a variety of hematologic parameters have recently been documented. From large nutritional surveys,[1-3] and healthy populations of soldiers[4] and college athletes[5] it has been demonstrated that hemoglobin levels are 0.5 to 1.0 gm/100 ml lower in American black populations when compared with their American white counterparts. A race-related difference has also been demonstrated in total leukocyte counts of the peripheral blood of healthy adults[6-9] and children.[10] In all reports the total leukocyte counts and granulocyte counts were significantly lower in the American black populations. Such findings in the peripheral blood prompted the present study to determine whether or not differences also exist within the bone marrow.

We examined the peripheral blood and bone marrow aspirates of a population of 88 infants who had participated in a broad prospective nutritional and developmental survey between 1966 and 1968. Since the dietary intake of these infants was strictly controlled and their health was closely monitored through a special clinic, the population provided a unique opportunity to determine whether or not similar race-related differences were already demonstrable in the peripheral blood at such an early age. Furthermore, we also tested whether race differences existed in the bone marrow.

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Materials and Methods

Full-term infants delivered after uncomplicated pregnancies were selected from the newborn nursery. Their mothers gave informed consent to participation in an 18-month longitudinal survey which involved a comprehensive nutritional and developmental evaluation with anthropometric, biochemical, and hematologic parameters. Evaluations were carried out at monthly intervals from birth to six months and, thereafter, at three-month intervals to the age of 18 months. Health care included vaccinations with combined diphtheria, pertussis, and tetanus and trivalent oral polio vaccines at 2, 4, and 6 months and with live measles vaccine at 12 months. All infants resided at sea level in Seattle throughout the study.

At each visit a dietary history and 24-hour dietary recall were recorded. The following laboratory studies relevant to the present report were performed: hemoglobin concentration, hematocrit, total and differential peripheral blood counts, tibial bone marrow aspiration, serum iron, total iron-binding capacity, total serum protein, and protein electrophoresis. The hemoglobin concentration was measured in duplicate using the cyanmethemoglobin method. Hematocrit measurements were made in triplicate using the microhematocrit method. The total leukocyte count was determined in a hemocytometer on duplicate venous blood samples. The same venous blood and the bone marrow aspirate were then smeared on cover slips and stained with Wright's stain. Peripheral blood neutrophil and lymphocyte counts were calculated from the differential count of 100 leukocytes. One thousand nucleated cells of the bone marrow aspirate were classified according to a method and criteria described previously.[11] Sickle cell preparations were performed for all black infants to exclude heterozygous carriers of the sickle cell gene.

Twenty black and 18 white infants who had completed at least 12 months of the study with normal observations were selected for the present analysis. Individual monthly values were excluded if: (1) there was some clinical evidence of a major or minor illness, (2) serum protein and protein electrophoresis were outside the accepted range of normal, (3) serum transferrin saturation was less than 16 percent,

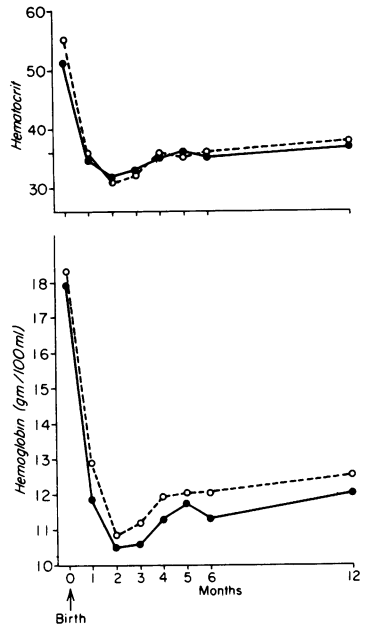

Figure 1. Comparison of hematocrit and hemoglobin levels in the peripheral blood of black (solid circles) and white (open circles) infants, expressed as median percentages.

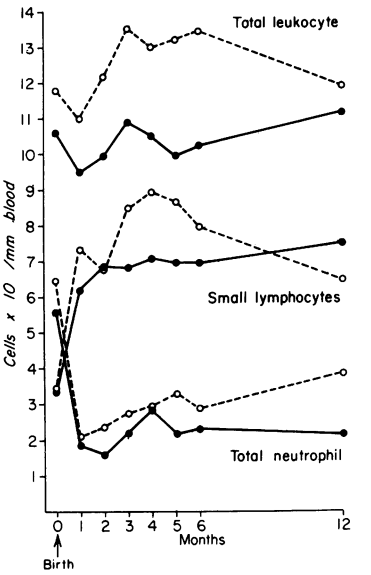

Figure 2. Comparison of the total leukocyte count, small lymphocyte, and total neutrophil count in the peripheral blood of black (solid circles) and white (open circles) infants expressed as median percentages.

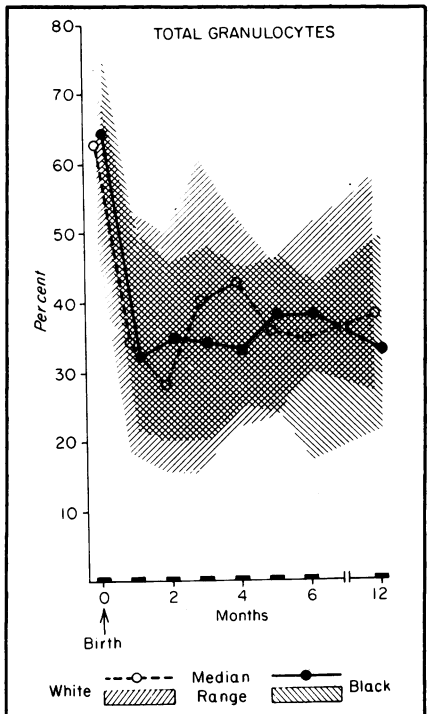

Figure 3. Total myeloid cells in the bone marrow of black and white infants.

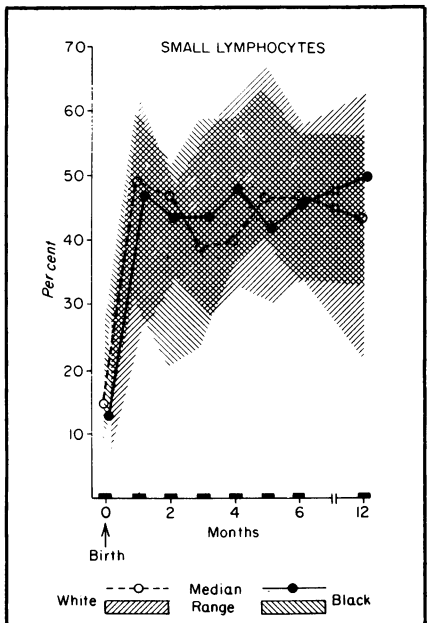

Figure 4. Small lymphocytes in the bone marrow of black and white infants.

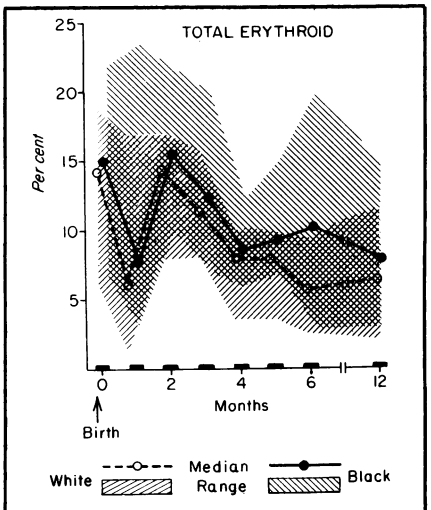

Figure 5. Total nucleated erythroid cells in the bone marrow of black and white infants.

(4) the bone-marrow sample was inadequate or unsuitable for morphologic analysis. It will be clear from Table 1 that a substantial number of infants failed to meet these criteria from time to time.

Monthly comparisons of the two racial groups are restricted to the first six months of life. Thereafter, a significant number were found to have less than 16 percent transferrin saturation, thus reducing the total number of monthly observations to a point at which no meaningful statistical comparisons could be made. An additional comparison was also made at the age of 12 months. If at this age, the infant did not meet all predetermined criteria, the normal data from nine to 15 months were substituted. We felt justified to follow this procedure because after the age of four months, the peripheral blood and bone marrow cell populations become relatively stable and remain unaltered until the age of 18 months.[11]

Analysis of race related differences was restricted to hemoglobin, hematocrit, total leukocyte, neutrophil, and lymphocyte counts of the peripheral blood, and to total erythroid, myeloid, and small lymphocyte cell populations of the bone marrow. Nonparametric tests were chosen because the distributions of many cell groups were not gaussian at certain ages. The Mann-Whitney U test, as a nonparametric analog of the t test, was used to evaluate significance of the racial differences.[12]

Results

Figures 1-5 show graphically the hemoglobin, hematocrit, peripheral blood, and bone marrow cell populations of black and white infants in the first 12 months of life. Median values and ranges for each month are recorded in Tables 1 and 2. In the tables, monthly values which show a significant racial difference ($P < .05$) are marked †.

The median values for *hemoglobin* are consistently lower through the 12 months of this study in the American black infants (Figure 1). This dif-

Table 1. Peripheral Blood Data of Black and White Infants Expressed as Median Percentages and Ranges

Month	Race	N	Hemoglobin (gm/100ml)	Hematocrit	Peripheral Blood Total Leukocytes X 10^3	Peripheral Blood Total Neutrophilis X 10^3	Peripheral Blood Total Lymphocytes X 10^3
0*	White	12	18.3 (17.3-20.3)	55.25 (49.5-64.0)	11.15 (6.2-18.6)	6.47 (2.79-8.76)	3.35 (2.43-8.37)
	Black	15	17.8 (14.7-21.2)	51.5 (45.0-68.0)	10.6 (6.6-15.0)	5.55 (2.91-9.04)	3.29 (1.50-6.00)
1	White	16	12.9 (11.3-13.9)	36.0 (31.5-41.5)	11.0 (6.2-18.4)	2.02 (1.04-12.28)	7.35 (5.29-10.66)
	Black	18	11.85 (8.9-16.0)	34.75 (24.0-48.0)	9.45 (6.6-13.5)	1.80 (0.42-3.92)	6.13 (4.07-9.86)
2	White	12	10.7 (9.2-12.0)	31.0 (29.0-36.0)	12.2 (5.7-15.5)	2.36 (1.14-4.05)	6.70 (3.53-11.30)
	Black	15	10.5 (9.4-13.1)	32.0 (25.5-39.0)	9.9 (3.4-14.9)	1.66 (0.58-3.60)	6.79 (2.38-9.24)
3	White	11	11.2 (9.8-12.0)	32.0 (29.5-36.5)	13.5 (8.2-25.0)	2.70 (1.44-4.39)	8.51 (5.17-11.07)
	Black	8	10.6 (9.6-12.4)	33.1 (27.5-35.5)	10.85 (7.2-13.7)	2.21 (1.01-3.97)	6.76 (4.39-8.98)
4	White	7	11.9 (11.2-12.6)	36.0 (34.0-37.0)	13.0 (9.2-13.9)	2.99 (1.81-3.90)	8.98 (4.51-10.29)
	Black	7	11.3 (9.8-12.0)	35.0 (31.0-36.0	10.5 (6.3-19.7)	2.95 (0.88-5.07)	7.04 (4.66-13.74)
5	White	8	12.0 (10.9-12.6)	35.3 (32.5-37.0)	13.25 (9.0-16.7)	3.31 (1.71-4.29)	8.62 (5.94-11.69)
	Black	7	11.7 (10.6-12.4)	36.0 (33.0-38.0)	9.9 (8.6-18.4)	2.18 (1.44-3.50)	6.93 (5.68-11.78)
6	White	10	12.0 (11.1-12.8)	36.0 (33.5-37.0)	13.40 (9.8-17.4)†	2.88 (1.10-7.05)	7.96 (5.10-11.88)
	Black	9	11.3 (10.3-13.1)	35.0 (33.0-39.5)	10.2 (8.7-15.7)	2.35 (1.50-7.05)	6.91 (1.39-11.30)
12**	White	12	12.5 (10.9-13.5)†	37.75 (33.0-40.0)	11.8 (9.6-21.6)†	3.84 (1.63-10.80)†	6.57 (4.06-10.34)
	Black	13	12.0 (8.6-12.4)	36.5 (32.0-40.0)	11.2 (4.8-13.2)	2.17 (0.72-4.65)	7.58 (3.36-9.75)

N - Number of infants
*Refers to the first four days immediately following birth
**Refers to the closest normal value to 12 months in the 9-15 month period
†Significant to the 0.05 level using the Mann-Whitney U test

Table 2. The Incidence of Major Cell Types in the Bone Marrow of Black and White Infants Expressed as Median Percentages and Ranges

Month	Race	N	Total Erythroid	Total Granulocytes	Small Lymphocytes
0*	White	12	14.30 (6.3-19.6)	62.45 (45.7-74.0)	14.25 (9.5-29.0)
	Black	15	15.0 (7.3-22.9)	64.3 (50.2-76.1)	13.6 (7.2-22.0)
1	White	16	6.05 (1.2-17.2)	34.70 (17.8-54.5)	48.85 (31.6-59.9)
	Black	18	7.80 (3.1-23.4)	32.50 (22.1-48.9)	47.60 (26.4-61.6)
2	White	12	14.30 (8.6-17.7)	28.25 (15.6-49.0)	47.05 (20.0-52.5)
	Black	15	15.3 (9.3-21.8)	35.2 (19.8-45.9)	43.8 (34.3-48.7)
3	White	11	11.1 (8.5-15.9)	40.2 (16.3-61.0)	39.4 (22.8-58.6)
	Black	8	12.25 (6.9-19.8)	34.35 (19.8-49.0)	44.15 (28.1-58.3)
4	White	7	7.9 (3.4-10.1)	43.8 (22.1-52.5)	40.3 (36.3-58.5)
	Black	7	8.3 (5.7-12.4)	33.0 (24.6-45.4)	48.6 (33.0-64.6)
5	White	8	8.05 (3.2-10.4)	36.00 (23.3-46.2)	47.60 (39.6-63.8)
	Black	7	9.4 (7.1-14.9)	37.3 (21.7-46.7)	42.4 (30.6-67.2)
6	White	10	5.80 (2.6-9.6)†	34.75 (29.8-50.7)	47.55 (34.4-57.1)
	Black	9	10.4 (2.8-20.7)	37.8 (17.1-42.9)	46.4 (34.0-58.4)
12**	White	12	6.55 (2.0-12.6)	38.0 (27.4-58.1)	44.50 (33.0-57.1)
	Black	13	8.0 (3.2-15.5)	33.1 (21.1-49.2)	49.9 (21.6-63.2)

N - Number of infants
*Refers to the first four days immediately following birth
**Refers to the closest normal value to 12 months in the 9-18 month period
†Significant to the .05 level using the Mann-Whitney U test

ference achieves statistical significance ($p < .05$) at the age of 12 months. *Hematocrit* values (Figure 1) show no consistent racial trends and this is confirmed by statistical analysis. The median values for the *total leukocyte* and *total neutrophil* counts are also consistently lower in black infants (Figure 2). These findings have statistical significance at 6 and 12 months for total leukocytes, and at 12 months for total neutrophils. *Small lymphocyte* counts show no consistent racial correlation (Figure 2) which is confirmed by statistical analysis.

In is clear from the graphs that no consistent racial differences can be demonstrated in the prevalence of bone marrow total myeloid (Figure 3) and small lymphocyte cell populations (Figure 4). This impression is confirmed by statistical analysis (Table 2). On the other hand, the total erythroid population (Figure 5) in black infants was significantly greater at six months of age ($p < .05$). The median values of erythroid percentages were also consistently higher in the black infants at all other ages (Table 2).

Discussion

The analysis of peripheral blood values and bone marrow cell populations in newly born and young infants is particularly suited for the detection of racial differences. Such subjects have experienced limited impact from extrauterine factors that might be responsible for environmentally induced differences in hemopoietic cell distributions. The extensive documentation of normalcy in the present population of infants adds considerable significance to this study. The material analyzed in this report is limited to observations made on infants who were defined as normal by serial anthropometric, nutritional, hematologic, and biochemical assessments. The age at which such observations were made was likewise carefully controlled and could be precisely matched for the two racial groups.

This report confirms that as do older individuals, American black infants have a consistently lower hemoglobin level than their American white counterparts. This lower hemoglobin level in black infants is compatible with the relative erythroid hyperplasia of their bone marrow. The cause of this hyperplasia, however, cannot be iron deficiency because infants were excluded whose serum transferrin saturation was less than 16 percent. This 0.5-1.0 gm difference in hemoglobin levels has been found at all ages, even when corrected for sex, dietary intake, socioeconomic status, and place of residence.[1-4] Surely some compensatory mechanisms must exist to counteract this relative deficiency of hemoglobin since a significant difference has even been demonstrated in healthy athletes.[5] There are reports of a higher 2-3 DPG level in healthy black males and females.[13] It is conceivable that this could cause a shift to the right in the hemoglobin oxygen dissociation curve so that a lower level of hemoglobin would be sufficient to supply adequate oxygen delivery to the tissues.[14]

Racial differences in peripheral blood leukocyte counts have also been well documented.[6-10] As in the older individuals, this population of black infants had consistently lower total leukocyte and total neutrophil values. There is no evidence that these differences are of any functional significance. It is of interest, however, that one would more frequently encounter a black infant with a neutrophil count in the neutropenia range (< 1,500). It would appear that a new lower limit of normal should be established for black children.

The racial differences in peripheral blood leukocyte counts were not reflected in the prevalence of bone marrow myeloid or small lymphocyte cell compartments. It is not possible to offer an explanation for this discrepancy. It may be that the racial difference exists within the marginal pool of leukocytes or in the blood volume/hemopoietic marrow volume ratio. There are no data, however, to substantiate these propositions. The significance of longitudinal changes in these bone marrow cell populations have already been discussed for the entire group of infants.[11]

Acknowledgement

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Statement Regarding Investigations on Humans

The studies were carried out in 1966-1968 prior to the precise codification and implementation of current regulations involving the participation of human subjects in experimentation. They were conducted, however, in conformity with all of the principles of the Declaration of Helsinki. Parents were informed in complete detail of the nature of the study, observed all procedures, had the opportunity of withdrawing at any time without penalty and the actual subjects, being minors, had a disinterested infant advocate in the form of a public nurse who had no other relationship to the investigations. The studies were observed, reviewed, and the procedures observed by senior administrative personnel within the Department of Pediatrics and all clinical procedures were carried out by senior investigators who served as patient physicians and had had many years experience in performing the clinical procedures. That the procedures were in every way acceptable to the families involved was indicated by the fact that no parent withdrew from the study for reasons other than moving from the area.