MEDICAL EVALUATION OF NUTRITIONAL STATUS[1]

III. HEMOGLOBIN AND ERYTHROCYTE VALUES FOR ADOLESCENTS IN HIGH-INCOME FAMILIES

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AMONG the dietary deficiencies that are reported in studies of food consumption for low-income families is an inadequate iron intake. During periods of growth the need for iron is especially high, and, therefore, the detection of this nutritional deficiency has been one part of the examination of a large number of high school students in New York City. The children were examined in a cooperative investigation of methods for appraising nutritional status. The purpose of the study and the procedures included in the examination have been described (1).

The present report is the first of a series in which the hematological findings for about 3,000 adolescent boys and girls will be discussed. The data in this report will be limited to those for a carefully selected group of about 300 boys and girls between 12 and 18 years of age. A detailed study of hemoglobin and erythrocyte values in this smaller group is necessary as a basis for the interpretation of findings for less privileged children in the larger group. This analysis represents only the first step in an attempt to give a more precise description of the hemoglobin and erythrocyte values that are characteristic of each sex and age during the adolescent period than has been found in the literature.

Iron-deficiency anemia has been extensively studied by hematologists, and the changes in hemoglobin content of the blood and changes in the number and size of erythrocytes have been described. The principal characteristic of iron-deficiency anemia is a reduction

[1] This paper is the third of a series from a cooperative investigation by the New York City Department of Health; the United States Public Health Service, Division of Public Health Methods; the Cornell University Medical College, Department of Public Health and Preventive Medicine and Department of Pediatrics; and the Milbank Memorial Fund.

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of the hemoglobin content of the blood. With this reduction there is a decrease in the hemoglobin content of the erythrocytes (hypochromia), and a diminution in cell size (microcytosis). The number of cells declines only slightly unless the deficiency has been chronic. Since all hypochromic, microcytic anemia is not due to an inadequate intake of iron, the etiology of such a condition must be determined by additional study; but the presence of hypochromia provides a basis for selecting cases of anemia.

It is obvious that the classification of an individual's blood-findings with respect to whether there is a *reduction* in hemoglobin level or in the number or size of erythrocytes is dependent upon well-established levels that are expected for persons whose blood-findings are not lowered. This expected value is commonly termed the "normal" or "standard" level, and, since some variation from this level is considered of no significance, a "normal" limit of variation, or an acceptable range, is used. It is fundamental to the interpretation of any finding as subnormal that the "normal" level and the limits used should represent values that are physiologically satisfactory.

Normal values in general use have been derived from hematological determinations on presumably healthy persons. For the data thus assembled, various statistical constants provide the values designated as "normal." Thus, the average value usually becomes the "normal" level and is the base line, that is the 100 per cent value, against which the deviation of any finding is measured. The "normal" limits are variously selected; they may represent some percentage of the observed values or some arbitrary amount of deviation from the average, such as 10 or 15 per cent. The application of the term "normal" to these averages and limits has the inevitable result that they acquire significance as values that are satisfactory to health. Consequently, the problem of determining standards that are desirable for health is oversimplified and its complex nature is obscured.

In this Study there is interest in detecting the cases with mild or slightly subnormal blood levels. For this purpose it is necessary to obtain the best possible indication of the hemoglobin and erythrocyte values that are to be expected for adolescent children apparently in good health. The approach is, in general, that mentioned above, namely, the analysis of frequency distributions of values obtained from examinations of carefully selected children. Some difference in individual values no doubt is without significance. But an attempt will be made to identify some of the characteristics or factors which may affect the hemoglobin or erythrocyte values in order that the effect of such factors may be taken into account when the findings on a given individual are interpreted as within the expected range or as lower than should be expected.

Since the reason for having standard or "normal" values is to appraise individual values, it is important that standards be derived from a sample that is representative of persons to whom they are applied. For example, if hemoglobin determinations are made for a group of white boys and girls aged 10 to 12 years in New York City, and all are considered as one group, the mean, standard deviation, and other statistical measures are specific for that group but do not necessarily give values which are typical of each sex and age, all nationality groups, and of children in other climates. Similarly, if individual characteristics, such as height, weight, or rate of growth, affect the hemoglobin level, a group of 12-year-old boys may not be representative of all 12-year-old boys. As distributions of values become available for groups which are homogeneous with respect to characteristics that influence the hemoglobin level, standard values can be set up which are more applicable to an individual, and what was previously an insignificant variation may become significant, and vice versa. Thus, knowledge of factors associated with variation makes it possible to take account of such factors and to evaluate the findings for an individual child against levels observed in children with similar characteristics that affect the hemoglobin level.

Such a measure of deviation from an expected value remains, however, a statistical expression of the probability or chances that any given hemoglobin value will occur among persons with specific characteristics. If the observed hemoglobin level is so low that it may be expected to occur only rarely, on the basis of available knowledge, it is taken as presumptive evidence that there is a deficiency of hemoglobin. The greater the odds against a given finding, the more significance may be attached to it.

It will be apparent that the levels selected at which individuals are classified as showing a hyper- or hypo-state are necessarily arbitrary; that is, there must be a decision as to how rare a particular value must have been in observed populations before it is considered as abnormal. Even if very large numbers of persons from a homogeneous population have been examined, there is no break in the frequency distribution to indicate the limits of normal, physiologic variation and to suggest which values are influenced by some degree of deficiency. The use of the term "normal" for selected levels is unfortunate, in the opinion of the writer. A terminology that would be more precise and specific is not readily suggested, but it seems possible that the meaning implied would be conveyed better by the term "standard." Standard is applied more commonly to measures that have an arbitrary basis, but it has the weakness that it does not imply the statistical concepts used in establishing the levels designated as standards. It is necessary to define a suggested standard with respect to the characteristics of the population to which it applies, and with respect to its statistical interpretation.

Another aspect of the problem of determining what hemoglobin or erythrocyte values indicate a mild or borderline deficiency is to determine what are the effects of a specific value. It is established that a marked deficiency of hemoglobin is deleterious to health and produces definite symptoms. But no sharp point of demarcation can be set at which no ill effect occurs. Further study of subjects who show slight deviations from average levels may reveal effects that are not at present recognized. Such study may suggest additional diagnostic methods for detecting or classifying cases that will be more specific than a selection based on the statistical measure of the probabilities of the occurrence of a given finding. Functional and pathological effects of severe anemia have been studied, but persons with a mild deficiency of hemoglobin have received little attention. Study of the associated effects of a mild deficiency is an important part of the study of methods for appraising the nutritional status of an individual, but it is outside the scope of this report. It is mentioned chiefly because of its bearing on the acceptance of "normal" blood findings, as at present derived, as synonymous with a demonstrated good nutritional state.

An additional aspect of the interpretation of average values as satisfactory values arises from the fact that there is no basis for believing that average values observed for apparently well persons are ideal or optimal values. It has been found that infants with presumably normal hemoglobin values would utilize iron if given in proper form; and this has suggested that optimal levels may be higher than observed average values. Similarly, by giving iron supplements to adolescents with average hemoglobin, or slightly less, the utilization of additional amounts might be demonstrated.

Data on Standards for Adolescents

The data published on hemoglobin and erythrocyte values for adolescent children are scant and not in close agreement. Furthermore, this age period has been studied as a whole, with little or no attention to significant differences from year to year. In 1916, Williamson (2) collected data on hemoglobin content of the blood for over 900 persons of each sex and all ages from birth to over 75 years of age. He gave average values, based on 15 to 20 cases, for boys and for girls in the age groups 11-15 and 16-20 years. For boys, the average at 16-20 years was 16 per cent higher than that for ages 11-15 years; and for girls, the corresponding percentage was only 4 per cent, but the 11-15 year old girls had an average hemoglobin value 9 per cent above the average for ages 6-10 years. Although the absolute values obtained by Williamson are now considered too high, the sex-age curves prepared by him have been widely used to indicate the *relative* hemoglobin level for children as compared with adult levels. In a recent book on hematology, Haden (3) reproduced the Williamson curves as a guide to determining the hemoglobin percentage typical of each sex and age period relative to the 15.4 grams of hemoglobin per 100 c.c. reported by him as normal for adult men. No specific recommendation is made for normal values during puberty when rapid changes in the hemoglobin level are shown.

By a series of studies on different groups in Oregon, Osgood and his coworkers (4) brought together data for each sex and for ages from 4 to 30 years. Determinations included erythrocyte counts, volume per cent of erythrocytes, hemoglobin in the blood, and a number of derived values. The average values for each sex, by single years of life, show a definite increase for all three determinations in the 'teen ages, with the exception of erythrocyte counts for girls. However, Osgood has not discussed the advisability of changing standards by age in this period, perhaps because his cases at each year were too few to afford dependable averages. Dividing the data into two broad age groups for each sex, he has suggested standards for ages 4 to 13 years and an adult level to be used from 14 to 30 years and older. The hemoglobin level suggested for both sexes under 14 years of age is 12.0 grams per 100 c.c., but the average level reported for the examined children 13 years of age is 12.89 for boys and 12.92 for girls. The adult level (14 years and older) recommended is 15.8 grams for boys and 13.8 for girls, although the averages for examined boys were about 14.6 and 15.3 grams[2] at ages 14 and 15 years respectively, and, for examined girls, the averages at single years of age from 14 years to 18 years varied from 14.0

[2] Values were read from the chart for ages over 13 years and are not exact.

grams to 14.6 grams, consistently higher than the standard. The standard range suggested is 14 to 18 grams for boys 14 years and older and 11.5 to 16 grams for girls. Obviously, among 14-year-old boys whose average hemoglobin level was only 14.6 grams, there will be a relatively large percentage with values below 14.0 grams (lower limit) as compared with 16 and 17-year-old boys whose average values equalled the standard average of 15.8 grams. Thus, these standards would not have the same meaning at each age in terms of the expected frequency of a given hemoglobin level.

The same age and sex division for standards is made by Osgood for erythrocyte counts, the "normal" level for both sexes 4 to 13 years of age being 5.0 million, for boys 14 years and older 5.4 million, and for girls 14 years and older being 4.8 million. In this case, too, the standards do not seem wholly satisfactory as criteria for evaluating the count at ages near the dividing line. The sex-age curves for volume per cent of red cells (hematocrit) obtained by Osgood, did not follow closely either the hemoglobin or the cell count curves. For females, there are two levels recommended as standards but the division is shifted to age 17 years; and for males, an additional age group is made, a special level for males 14 to 19 years being inserted between that for boys up to 14 years and that for men. This average level from 14 to 19 years is by no means adequate to represent each year of age since there was a steadily increasing volume of cells during the age period.

Data on healthy subjects have been reported also by Mugrage and Andresen (5, 6) from studies in Denver, Colorado. Both the hemoglobin and red cell values reported for adolescents in Denver differ markedly from those found in other studies, and it has been commonly accepted that the blood levels are affected by high altitude. Some data are available from several other studies on adolescent boys and girls, but no one study affords a satisfactory description of changes during this age period. All data are in agreement, however, that during adolescence there is a transition from the values found in childhood to those found for adults and that the change is rapid, especially for boys.

Present evidence indicates the necessity for careful study of hemoglobin and erythrocyte values for each year of age for each sex in order to determine standard limits that are equally applicable at each age. Although the use of only a few standards makes for simplicity, average values for several ages which are characterized by significant differences do not permit careful evaluation of the blood findings for an individual in terms of the extent of his deviation from the standard level. To obtain standards which would provide the basis for identifying persons with lowered blood values and would have comparable meaning at each age, the data presented in the following pages were collected.

The Sample

The blood findings presented in this report are for a group of privileged children selected as being without apparent infection, disease, or nutritional deficiency. Nearly all were Jewish children, though not orthodox, attending a private high school in New York City (Fieldston School) and were from relatively high-income families. About 350 children were examined in February and March, 1940, but the blood findings for only 295 children have been used for the following tabulations. The results of the complete examination and of special tests for specific nutritional deficiencies were reviewed, and the hematological records for forty-one children were excluded on the basis of some acute or chronic condition that might possibly affect the hemoglobin level or red cell count.[3] A few other records were omitted for children who were older or younger than the specific ages included in this analysis because they were too few for special study. The boys included were from 12 to 18 years of age and the girls were from 12 to 17 years of age. Be-

[3] Nutritional deficiencies accounted for nine cases excluded; eight with ascorbic acid content of the blood less than 0.4 mg. per cent and one case of ariboflavinosis. Other causes for exclusion were heart conditions, sugar, albumin, hyaline and granular casts in the urine, positive serology, osteomyelitis, and enlarged cervical lymph nodes.

cause of the careful selection of children, it is believed that the findings may be considered representative of boys and girls from Jewish families in New York City who are without signs of infection or other illness.

Data and Laboratory Procedures

The hematological values to be discussed include the hemoglobin in whole blood, erythrocyte count, and erythrocyte volume per cent; and three values derived from these direct determinations; namely, mean hemoglobin content per erythrocyte, the mean hemoglobin concentration per 100 c.c. of erythrocytes, and the mean red cell volume. All determinations were made on a blood specimen taken by venipuncture at about 8:30 a.m. before the child had breakfast.

The technique of the erythrocyte count followed standard procedure. Trenner pipettes diluting 1 to 200 and Levy counting chambers with improved Neubauer double-ruling were used. The blood specimen was thoroughly mixed in its vial, and each of two pipettes was filled with Hayem's solution as diluent. The one pipette was shaken for 60 seconds in a Hauser shaker just before being used to charge each of the two ruled areas of one chamber. The other pipette was similarly treated and used to charge the two ruled areas of the second counting chamber. Thus, four ruled areas were prepared for counting, and a photograph of each was made with the euscope (7). This instrument affords a simple mechanism for making a photograph, measuring 4 by 5 inches, on bromide paper. Cells in five groups of 16 of the smallest squares or in a total of 80 small squares (0.02 c.mm. of diluted blood), were counted on each photograph. The cumulative total was read from a tally counter which is equipped with a needle-like pointer and counts automatically as each cell is pierced with this pointer. The count was verified by examining each square to determine whether all cells had been punched and whether those on the lines had been properly counted in or out of the ruled area. Thus, errors in counting are eliminated, but the sampling error remains. No counts were arbitrarily discarded on the basis of large differences between counts for the several ruled areas.

The volume per cent of packed red blood cells was determined by hematocrit according to the method of Wintrobe (8). The tube was centrifuged at 3,000 revolutions per minute for one-half hour.

The hemoglobin determination is based upon the colorimetric determination of oxyhemoglobin by the Evelyn method, using the photoelectric colorimeter (9). The K_2 value used in calculating the results from galvanometer readings was determined by standardization of the instrument against bloods of various hemoglobin concentration as determined by their oxygen capacity (10, 11).

Results of Hematological Examinations on a Privileged Group

Frequency distributions for boys and for girls at each year of age are given in appendix tables for the following hematological values: Table I, hemoglobin in whole blood; Table II, erythrocyte counts; Table III, volume of packed red cells, percentage; Table IV, mean volume of red cells, cubic microns; Table V, mean hemoglobin content per cell, micromicrograms; Table VI, concentration of hemoglobin in red cells, grams per cent. These tables give in detail the data for the 155 boys and 140 girls in high-income families from which average values and other statistical constants have been derived.

For each of the six hematological values, similar statistical measures that describe the frequency distributions are presented as a basis for discussion. In addition to the mean value at each age, the standard error of the mean and the standard deviation of the distribution, several values are given which divide the total distribution into various percentages. Thus, the median value indicates the level at which 50 per cent of the observed values were greater and 50 per cent were smaller; the first and third quartile values indicate, respectively, the level at which 25 per cent of the observed values were smaller and 25 per cent were greater. Between the first quartile level and the third quartile level, there is included the middle 50 per cent of observed values. Similarly, the first and ninth deciles shown in the table represent the levels below and above which 10 per cent of the distribution of values was found; and 80 per cent of the distribution is included between the first and ninth deciles.[4] The levels for these various percentage limits are portrayed graphically for each set of values.

The median and average values are equal when the observed values above and below the median level vary by the same amount. A higher median indicates that the distribution is skewed downward, or weighted by relatively low individual values in the distribution; and a lower median indicates a greater spread of values in the upper half of the distribution. Thus, the median provides a central value on which the effect of a few extreme observations has been eliminated, and seems especially useful for these data, since extreme variations may well be atypical. On the other hand, the mean and the standard deviation provide a better basis for estimating the probability of the occurrence of specific high or low values if the sample distribution is typical and not greatly skewed.

Hemoglobin in Whole Blood. The trend in hemoglobin values for boys and girls from 12 to 17 years of age is clearly seen in Figure 1. The difference by sex is very marked. The median line for girls shows only slight variations from age to age, the highest median value being 13.9 gms. per 100 c.c. at age 14 years and the lowest, 13.6 gms. at age 17 years. But the median line for boys rises steadily and sharply from 13.7 gms. at age 12 years to 15.4 gms. at ages 17-18 years. At 12 years of age the mean hemoglobin value for girls (Table 1) was slightly higher than that for boys but the difference

[4] The percentage levels, computed in the usual way for grouped data, represent *estimated levels* for the frequency distributions, and not *observed values* for persons at the specified point in the arrayed series of observed values. The decile limits are subject to great variability when computed for frequencies as small as the eighteen to thirty-four cases available for this analysis.

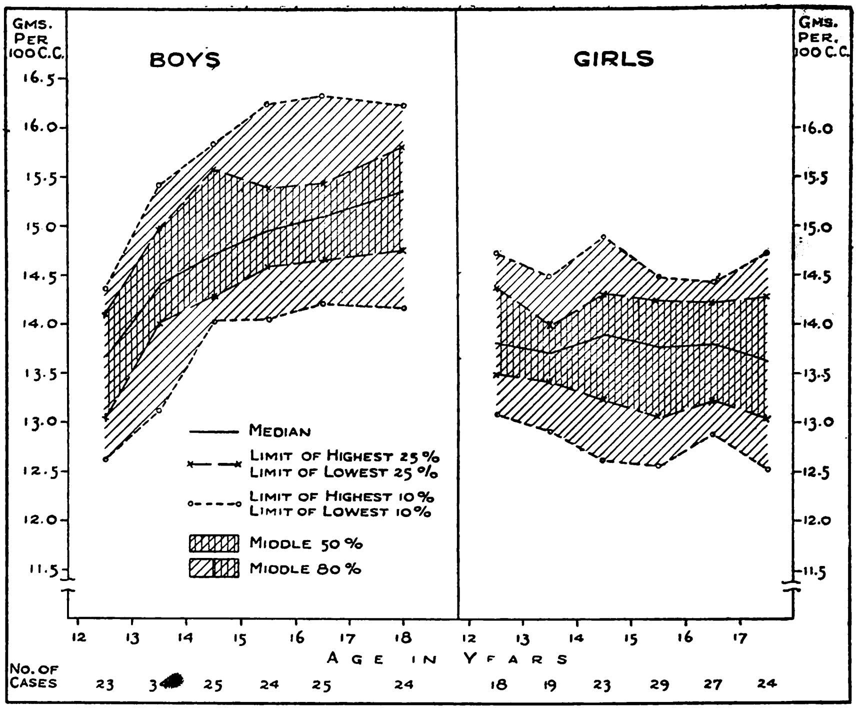


Fig. 1. Hemoglobin in whole blood. Selected percentiles for frequency distributions of values for boys and for girls at specific ages.

was not statistically significant.[5] At all other ages, the hemoglobin level was lower for girls and the difference was highly significant at every age.

For 12-year-old girls in this sample, the median hemoglobin value was 13.8 grams per 100 c.c. (mean 13.9 gms.) and was as high as that usually reported and used for standard for adult women. Comparison of the width of the shaded area above and below the median line for girls, in Figure 1, reveals a tendency for the area above the line to be slightly wider at ages 12 and 13 years, but after 13 years of age the area below the median becomes wider, indicating that the distributions were slightly skewed. The interpretation

[5] The consistent practice in this discussion with reference to statistical significance will be to consider *differences* as not statistically significant if, on the basis of the t value, the probability is greater than .05; if the probability is between .05 and .02, differences will be termed significant; if the probability is .02 or less, the difference will be termed *very*, or *highly* significant.

Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles		Deciles	
					First	Third	First	Ninth
Boys								
12	23	13.62 ± 0.14	0.65	13.66	13.04	14.11	12.61	14.36
13	34	14.44 ± 0.15	0.88	14.40	14.02	14.99	13.12	15.42
14	25	14.87 ± 0.16	0.79	14.70	14.28	15.58	14.04	15.84
15	24	15.10 ± 0.17	0.83	14.95	14.58	15.38	14.05	16.25
16	25	15.19 ± 0.15	0.75	15.09	14.64	15.44	14.20	16.32
17–18	24	15.29 ± 0.16	0.77	15.35	14.75	15.81	14.15	16.22
Girls								
12	18	13.92 ± 0.14	0.59	13.81	13.49	14.37	13.08	14.72
13	19	13.72 ± 0.14	0.60	13.70	13.41	13.99	12.90	14.48
14	23	13.79 ± 0.20	0.94	13.89	13.22	14.32	12.60	14.88
15	29	13.68 ± 0.15	0.81	13.76	13.05	14.24	12.56	14.48
16	27	13.73 ± 0.15	0.79	13.80	13.22	14.21	12.88	14.42
17	24	13.69 ± 0.17	0.83	13.62	13.03	14.28	12.52	14.72

Table 1. Grams of hemoglobin per 100 c.c. of blood according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table I.

of this skewness is not clear, but there is always a possibility that some low values at the extreme limits represent slight deficiencies.

For boys, the greatest increase in hemoglobin between any two successive years of age is shown at ages 12 and 13 years. The difference in the mean hemoglobin content of the blood at these ages was 0.82 grams and is highly significant. Although the differences between successive ages were not significant statistically for any other ages, the consistent increase with age provides unquestionable evidence of a significant physiological trend during this age period.

The width of the shaded area above the median line for boys at ages 14-16 years, inclusive, indicates some skewness in the frequency distributions toward higher values. This suggests all the boys of one specific chronological age had not progressed toward the higher values to the same extent, and, at these intermediate ages, the spread in the higher values is widened by boys with more rapid progress in their physiological change.

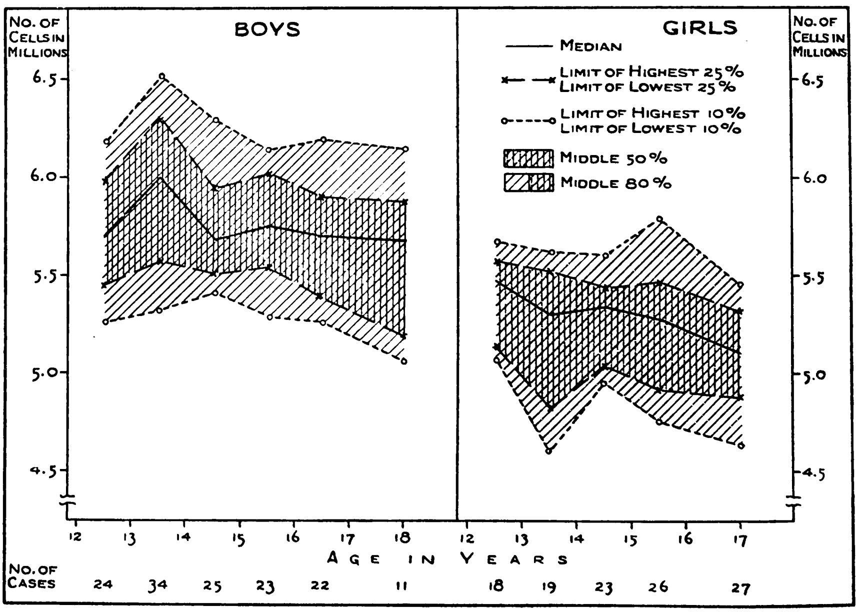
Erythrocyte Counts. The statistical measures for the frequency

Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles		Deciles	
					First	Third	First	Ninth
Boys								
12	24	5.68 ± 0.07	0.37	5.70	5.45	5.98	5.27	6.18
13	34	5.94 ± 0.08	0.47	6.00	5.57	6.30	5.32	6.51
14	25	5.76 ± 0.06	0.31	5.68	5.51	5.94	5.41	6.29
15	23	5.74 ± 0.09	0.43	5.79	5.54	6.02	5.28	6.14
16	22	5.69 ± 0.08	0.37	5.70	5.38	5.90	5.26	6.19
17–18	11	5.54 ± 0.14	0.47	5.68	5.19	5.88	5.06	6.14
Girls								
12	18	5.38 ± 0.06	0.27	5.47	5.14	5.57	5.07	5.67
13	19	5.18 ± 0.09	0.40	5.30	4.82	5.52	4.60	5.62
14	23	5.27 ± 0.06	0.28	5.34	5.04	5.44	4.96	5.61
15	26	5.26 ± 0.07	0.36	5.28	4.92	5.47	4.77	5.79
16–17	28	5.09 ± 0.06	0.32	5.11	4.88	5.32	4.64	5.46

Table 2. Number of erythrocytes per c.mm. in millions according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table II.

distributions of red blood cell counts are presented in Table 2 and Figure 2.

Fig. 2. Erythrocyte count per c.mm. of blood. Selected percentiles for frequency distributions of counts for boys and for girls at specific ages.



The mean count of red cells for boys was higher than that for girls by about 0.5 million cells or more at each age over 12 years, and the difference was highly significant at every age. At 12 years the difference was 0.3 million, and it also was very significant.

The trend in the number of red cells from age to age was very different from the trend in hemoglobin values, both for boys and for girls, as can be clearly seen in Figure 2. The median line in Figure 2 for girls shows a definite, though somewhat irregular, downward trend over the age period. Differences in the mean value from one age to the next were not statistically significant, but the difference between the mean count at age 12 years (5.4 million) and at ages 16-17 combined (5.1 million) was very significant. Skewness shown by the shaded area in the chart is toward the lower values and in the direction in which a trend is indicated.

For boys, the median line in Figure 2 is approximately 5.7 million red blood cells at every age except 13 years. At 13 years the median red cell count rose sharply to about 6.0 million and then dropped back to the 5.7 million level. The difference in the mean count at 12 years and that at 13 years was 0.26 million and is significant, but the difference between the mean at 13 years and at 14 years was not significant. Differences between average counts were less at these ages than differences between the medians due to a shifting in the skewness of the distribution from low values at age 13 to high values at age 14 years. This increase in red blood cells, which coincided by age with the period of most rapid increase in hemoglobin, apparently represents a significant though temporary shift in the erythrocyte level.

Hematocrit. Changes in the volume per cent of packed red cells from age to age are depicted graphically in Figure 3 and the mean, median, and measures of dispersion of the distribution are given in Table 3.

For girls, the median line in Figure 3 is very irregular and shows no constant trend. However, the highest average value (and median

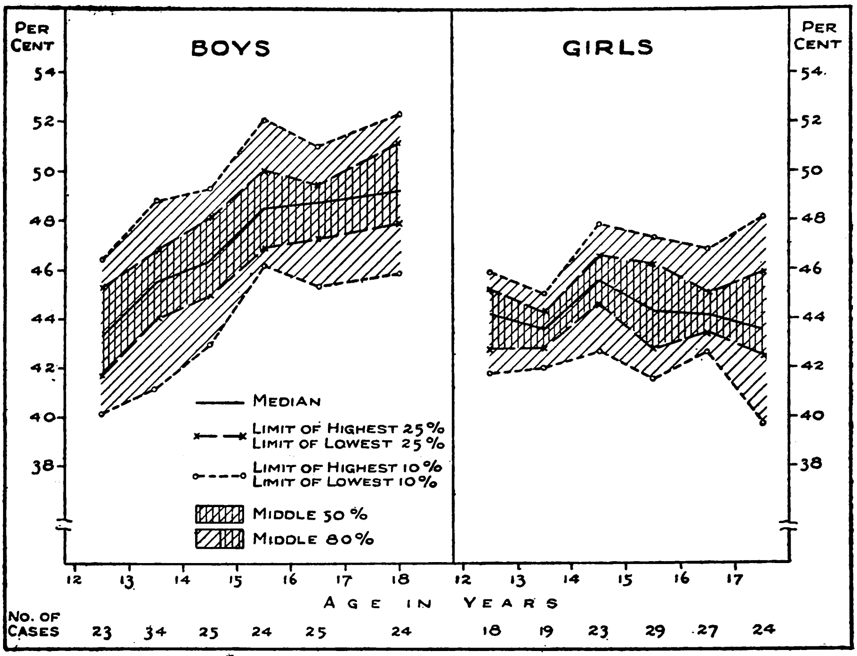


Fig. 3. Percentage volume of packed red cells (hematocrit). Selected percentiles for frequency distributions of values for boys and for girls at specific ages.

value) for girls was at age 14 years, and it was significantly higher

Table 3. Percentage volume of packed red cells (hematocrit) according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table III.

Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles First	Quartiles Third	Deciles First	Deciles Ninth
Boys								
12	23	43.35 ± 0.48	2.30	43.33	41.69	45.25	40.15	46.40
13	34	45.32 ± 0.44	2.58	45.50	44.00	46.75	41.20	48.80
14	25	46.40 ± 0.50	2.50	46.38	44.95	48.08	43.00	49.33
15	24	48.75 ± 0.51	2.51	48.50	46.93	50.50	46.20	52.10
16	25	48.52 ± 0.40	2.02	48.78	47.25	49.47	45.33	51.00
17–18	24	49.25 ± 0.51	2.49	49.25	47.90	51.17	45.90	52.37
Girls								
12	18	43.94 ± 0.39	1.67	44.25	42.75	45.20	41.77	45.90
13	19	43.63 ± 0.33	1.45	43.57	42.79	44.25	41.95	45.05
14	23	45.52 ± 0.58	2.79	45.58	44.62	46.58	42.65	47.85
15	29	44.48 ± 0.43	2.30	44.33	42.71	46.25	41.47	47.28
16	27	44.63 ± 0.46	2.36	44.15	43.45	45.04	42.64	46.80
17	24	43.88 ± 0.59	2.91	43.50	42.50	45.90	39.70	48.10

than the average values at ages 12 and 13 years and at 17 years. This, again, would suggest that a real change in hematocrit was occurring during this period. If the size of the red cells remained the same, the volume per cent of cells would vary with the number of cells, but since the hematocrit trend from age to age does not follow closely the trend in the red cell count, the explanation must be looked for in the mean size of cells.

The median line for boys (Fig. 3) indicates a rapidly increasing volume of red cells from ages 12-15 years, inclusive, and a further gradual increase at older ages. It resembles the median line for hemoglobin in whole blood, but there are minor differences in the steepness of the curve at some ages.

Size of Red Cells. The mean volume of red cells in cubic microns was estimated by the usual method of dividing the hematocrit percentage by the red cell count. The formula is:

$$\frac{\text{Volume per cent of packed red cells x 10}}{\text{R. B. C. in millions per c.mm. of blood}} = \text{mean cubic microns.}$$

The averages, medians, and other values for the several distributions of individual findings are shown in Table 4, and the percentage limits are given also in Figure 4.

The median line in Figure 4 which portrays the change in the mean cell volume for girls from age to age shows a definite upward trend from 12 to 14 years, and the increase thereafter is slight. Thus, the median for red cell size at age 12 years was 82.1 cubic microns and increased to 86.2 at age 14 years. During these years we have seen that there was no evidence of a significant change in hemoglobin in the blood, but the red cell count showed some reduction and the hematocrit increased. The indication seems definite that during adolescence one part of the hematological change is the size of red cells and this change was in progress over a number of years after the increase in hemoglobin in whole blood had been completed. The larger mean size of cells for girls than for boys at

Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles		Deciles	
					First	Third	First	Ninth
Boys								
12	22	76.50 ± 0.78	3.65	76.70	74.75	78.25	71.60	81.30
13	34	76.56 ± 0.84	4.92	76.17	73.38	79.33	71.97	82.22
14	25	80.84 ± 1.14	5.70	80.00	77.25	83.88	75.00	88.00
15	23	85.61 ± 1.75	8.42	84.67	80.25	87.92	76.80	99.20
16	22	85.32 ± 1.40	6.56	85.50	80.00	91.00	76.10	92.43
17–18	11	87.73 ± 1.78	5.92	87.25	85.25	88.75	80.60	94.40
Girls								
12	18	82.06 ± 0.85	3.63	81.83	80.25	83.75	77.30	87.10
13	19	84.63 ± 1.39	6.08	84.00	79.25	86.75	77.80	94.60
14	23	86.17 ± 1.15	5.51	85.88	83.08	88.75	79.65	93.20
15	26	84.92 ± 0.96	4.88	85.83	80.25	88.00	78.30	90.90
16–17	27	87.78 ± 0.94	4.91	87.00	84.69	91.62	81.35	94.93

Table 4. Red cell mean volume in cubic microns according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table IV.

age 12 years also suggests that some change in cell size for girls occurred before age 12 years.

The change in red cell size for boys, shown from ages 12 years to 18 years, is greater than that for girls but is of the same nature. There was no increase in the average cell size for boys aged 13 years as compared with those aged 12 years, although hemoglobin in whole blood increased and the number of cells increased. But at ages 14 and 15 years the median value for mean cell volume was much higher than in the preceding year of age. This increase in cell size for boys was concurrent with a continued rising hemoglobin level, whereas in the case of girls the hemoglobin level was not changing. Since boys experience their adolescent growth and development at a later age than girls, the 12 and 13-year-old boys examined probably give a picture of the first changes in the hemoglobin and erythrocyte values; but the 12 and 13-year-old girls in this Study seem already to have progressed beyond the earliest changes.

At the same chronological age, from 12-14 years inclusive, the

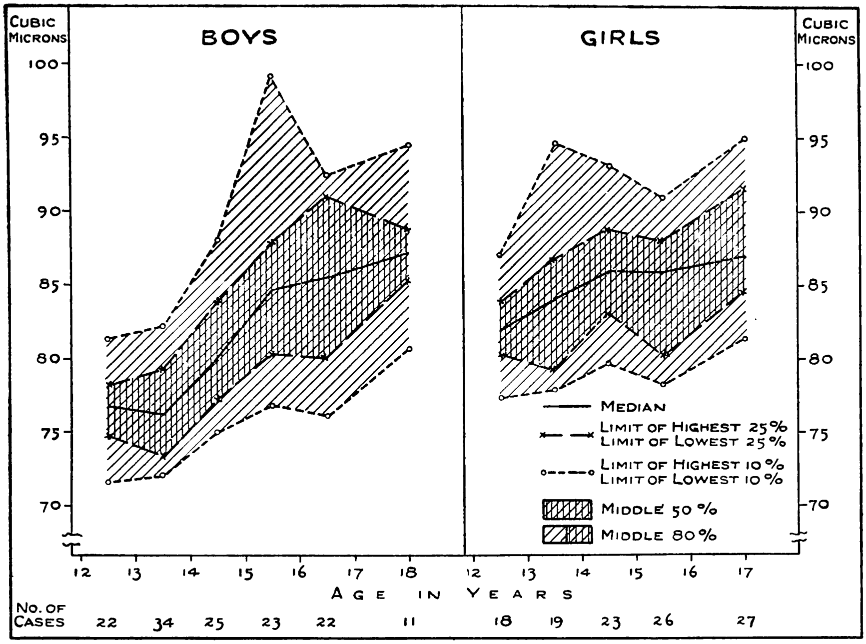


Fig. 4. Mean volume of red blood cells. Selected percentiles for frequency distributions of mean volume for boys and for girls at specific ages.

averages for mean cell size for boys were much smaller than for girls and the differences were highly significant. At age 15 years and older the differences for the two sexes were not significant. Thus, the increase in red blood cell volume started at a later age for boys but progressed more rapidly, and by age 15 years little difference remained.

Mean Hemoglobin Content per Cell. From the hemoglobin content of whole blood and the red cell count, the mean hemoglobin content per cell is calculated as follows:

$$\frac{\text{Hemoglobin, grams per 100 c.c.} \times 100}{\text{R. B. C. in millions per c.mm. of blood}} = \text{mean hemoglobin content per cell, micromicrograms.}$$

The average and median values and other statistical measures for the distributions of findings for each sex-age group are shown in Table 5 and Figure 5.

In general, we should expect the trend in the hemoglobin con-

Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles First	Quartiles Third	Deciles First	Deciles Ninth
Boys								
12	22	24.00 ± 0.30	1.42	23.95	23.10	25.01	22.05	25.43
13	34	24.38 ± 0.25	1.46	24.09	23.39	25.14	22.75	25.88
14	25	25.77 ± 0.29	1.44	25.99	24.86	26.64	23.70	27.53
15	23	26.47 ± 0.51	2.44	26.20	25.08	27.22	23.60	28.80
16	22	26.52 ± 0.32	1.48	26.45	25.39	27.30	24.98	28.35
17–18	11	27.38 ± 0.51	1.69	26.87	26.39	28.58	25.98	29.40
Girls								
12	18	26.00 ± 0.31	1.32	25.95	25.03	26.58	24.40	27.25
13	19	26.46 ± 0.43	1.86	25.76	24.89	28.08	24.27	29.22
14	23	26.08 ± 0.33	1.60	26.20	25.08	26.88	23.78	27.80
15	26	26.12 ± 0.29	1.49	26.53	25.08	27.14	23.72	27.68
16–17	27	27.20 ± 0.30	1.53	27.20	25.92	28.55	25.38	28.89

Table 5. Mean hemoglobin content per cell in micromicrograms according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table V.

tent per cell to follow closely that noted for red cell size with advancing age of boys and girls during adolescence. The median lines in Figures 4 and 5 are quite similar but there are some small differences in the changes at several ages. This is not surprising since it is apparent that the red blood cells are in a state of transition and neither the size nor the content are on a stable basis during this age period. Both were definitely increasing and it is not clear from these data whether this increase was complete for the oldest groups, 16-17 years for girls and 17-18 years for boys.

At ages 12 and 13 years the differences between the mean hemoglobin content per cell for boys and for girls were highly significant statistically. At age 14 years and at older ages the differences between average values for the sexes were small and not significant.

Mean Hemoglobin Concentration in Cells. The saturation of the red cells with hemoglobin is estimated as follows:

$$\frac{\text{Hemoglobin, grams per 100 c.c. x 100}}{\text{Volume of packed red cells, per cent}} = \text{Hb. concentration (grams per cent)}$$

The values describing the frequency distributions of hemoglobin

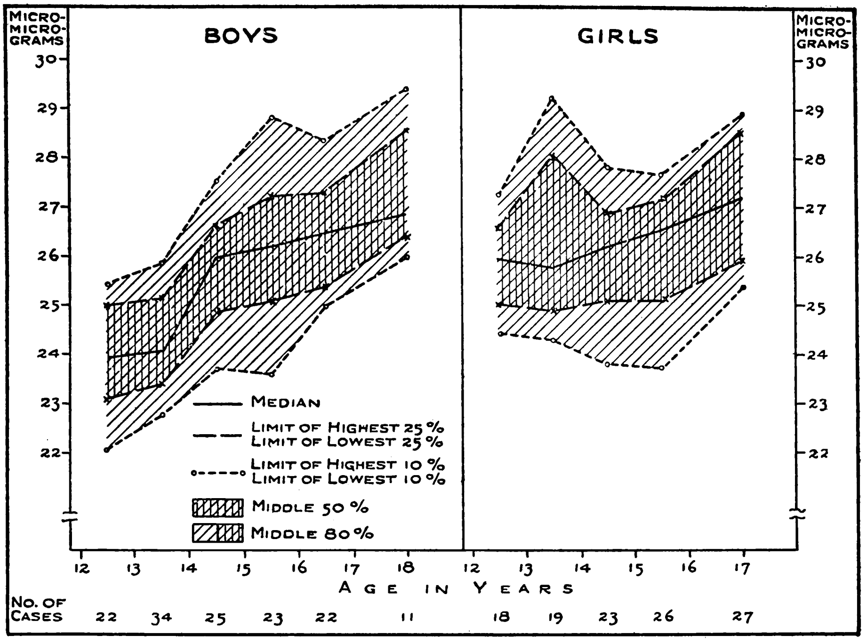


Fig. 5. Mean hemoglobin content per red blood cell. Selected percentiles for frequency distributions of mean content for boys and for girls at specific ages.

concentration in the red cells for boys and girls at each age are

Table 6. Percentage concentration of hemoglobin in red blood cells according to sex and age for Jewish children in high-income families. Mean and standard deviation and selected percentiles for frequency distributions shown in Appendix Table VI.

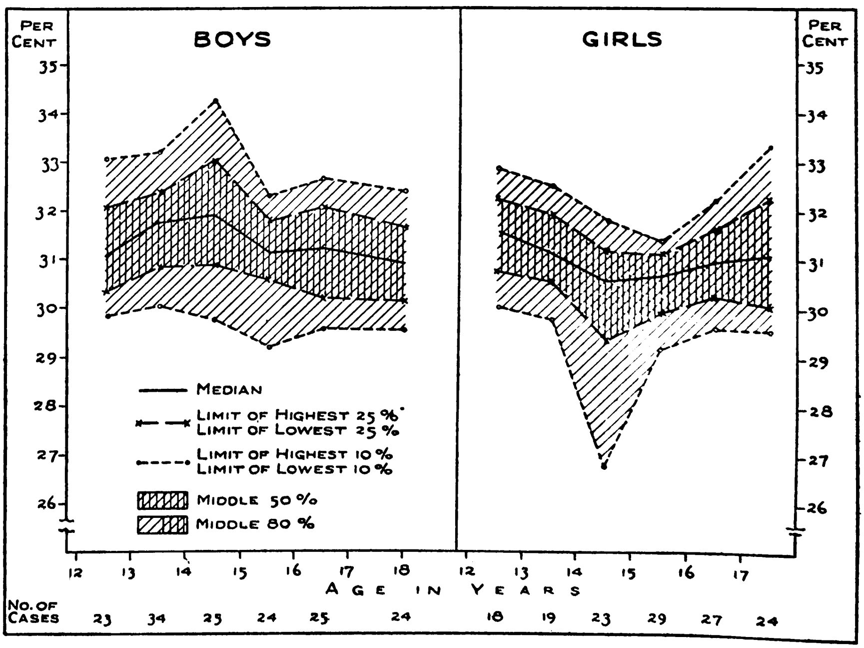
Sex and Age	Number of Cases	Mean and Standard Error	Standard Deviation	Median	Quartiles First	Quartiles Third	Deciles First	Deciles Ninth
Boys								
12	23	31.35 ± 0.30	1.43	31.06	30.32	32.06	29.83	33.07
13	34	31.79 ± 0.24	1.39	31.79	30.86	32.39	30.07	33.22
14	25	32.00 ± 0.34	1.71	31.92	30.88	33.05	29.75	34.25
15	24	30.96 ± 0.26	1.28	31.14	30.59	31.79	29.20	32.30
16	25	31.12 ± 0.25	1.27	31.25	30.21	32.09	29.58	32.67
17–18	24	31.08 ± 0.29	1.44	30.94	30.17	31.70	29.57	32.42
Girls								
12	18	31.56 ± 0.23	0.97	31.64	30.80	32.29	30.10	32.90
13	19	31.21 ± 0.23	1.02	31.19	30.59	31.95	29.80	32.55
14	23	30.09 ± 0.42	2.02	30.60	29.38	31.22	26.80	31.85
15	29	30.59 ± 0.17	0.91	30.72	29.96	31.17	29.22	31.44
16	27	30.67 ± 0.41	2.13	31.00	30.29	31.68	29.62	32.26
17	24	31.21 ± 0.35	1.70	31.10	30.07	32.30	29.56	33.37

shown in Table 6 and Figure 6. The differences in the averages by age are relatively small but some of them were significant.

For girls, the concentration of hemoglobin in the cells declined from age 12 years to 14 years. The differences between the averages at 12 and 14 years and at 13 and 14 years were, respectively, very significant and significant. This coincides with the ages at which we have noted a rapid increase in mean cell volume and a more gradual increase in the mean hemoglobin content per cell.

For boys, there was a rise in the concentration value at ages 13 and 14 years, followed by a decline to a value which remained constant for ages 15 years and older. The differences in the average value at age 14 years and the lower averages at older ages were significant. This temporary change in the concentration of hemoglobin in the cells apparently was the result of rapid changes already noted in hemoglobin in whole blood and in content per cell asso-

Fig 6. Percentage concentration of hemoglobin, grams per 100 c.c. of red blood cells. Selected percentiles for frequency distributions of values for boys and for girls at specific ages.



ciated with a somewhat slower increase in the mean cell volume.

The mean hemoglobin concentration in red cells has been found to be very constant in studies on various groups. Even for this adolescent group the changes were not great but they are of interest because they indicate a somewhat unstable equilibrium associated with the transition from values in childhood to those in adult life.

Summary

Hemoglobin and erythrocyte values for 155 boys, aged 12 to 18 years inclusive, and for 140 girls, aged 12 to 17 years inclusive, have been presented. All were attending a private school in New York City and were mostly from Jewish families with relatively high incomes.

The statistical basis on which standards for hemoglobin and erythrocyte values are established was discussed; and it was pointed out that the interpretation of individual findings requires that the standards used be (a) derived from data on a population with characteristics, which affect the blood levels, that were similar to those of the persons under investigation, and (b) of comparable meaning, in terms of statistical significance of limits.

For girls in this Study, the change from childhood levels apparently began before age 12 years. In the age period 12-17 years, some of the changes were:

Hemoglobin in whole blood was about the same at every age, the averages at specific ages varying from 13.9 gms. per 100 c.c. to 13.7 gms.

The number of red cells per c. mm. of blood decreased with age from 5.4 to 5.1 millions.

Mean red cell volume increased from 82.1 cubic microns at age 12 to 87.8 at 16-17 years combined.

Hemoglobin content per cell increased slightly with age, from 26.0 to 27.2 micromicrograms.

Concentration of hemoglobin in red cells varied significantly at these ages.

For boys, hemoglobin and erythrocyte values during the age

period 12-18 years showed greater changes than for girls for all determinations except the concentration of hemoglobin in cells. Some of the changes in average values for boys were as follows:

Hemoglobin in whole blood increased from 13.6 gms. per 100 c.c. at age 12 years to 15.3 at ages 17-18 combined, and most of the increase was at ages 13 and 14 years.

A rise in the number of red cells at age 13 years was followed by a decline to a fairly constant count of about 5.7 million.

Mean red cell volume increased from 76.6 cubic microns at age 13 years to 85.6 at 15 years, and was 87.7 at 17-18 years of age.

Mean hemoglobin content per cell increased from 24.0 micromicrograms at age 12 years to 27.4 at ages 17-18 years.

Significant differences between average values for boys and girls were:

Hemoglobin level higher for boys at every age except 12 years.

Red cell count higher for boys at every age.

Mean volume of red cells smaller for boys aged 12, 13, and 14 years, not significantly different at older ages.

Mean hemoglobin per cell lower for boys aged 12 and 13 years, not significantly different at older ages.

The marked changes during adolescent period make it necessary to use different standards by sex and year of age. Furthermore, it must be borne in mind that average values by chronological age do not take fully into account the stage in physiological change which we have found affects hemoglobin and red blood cell values.

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Appendix Table I. Grams of hemoglobin in whole blood according to sex and age for Jewish children in high-income families in New York City.

GRAMS PER 100 C.C.	BOYS						GIRLS					
	Number at Each Age With Specified Finding						Number at Each Age With Specified Finding					
	12	13	14	15	16	17–18	12	13	14	15	16	17
TOTAL	23	34	25	24	25	24	18	19	23	29	27	24
11.0–11.9									1	1	1	
12.0–12.9	5	2	1				1	2	2	5	2	5
13.0–13.9	10	5		2	1	2	10	12	9	10	12	9
14.0–14.9	8	18	15	10	9	6	7	5	9	12	11	9
15.0–15.9		8	8	9	11	12			2	1	1	1
16.0–16.9		1	1	2	4	4						
17.0–17.9				1								

Appendix Table II. Erythrocyte counts according to sex and age for Jewish children in high-income families in New York City.

NUMBER OF RED CELLS IN MILLIONS PER C. MM.	BOYS						GIRLS				
	Number at Each Age With Specified Finding						Number at Each Age With Specified Finding				
	12	13	14	15	16	17–18	12	13	14	15	16–17
TOTAL	24	34	25	23	22	11	18	19	23	26	28
4.4–4.5				1				1	1		1
4.6–4.7						1	1	3		2	4
4.8–4.9	1							2	1	5	5
5.0–5.1		1			1	1	4	2	5	2	6
5.2–5.3	3	3		2	4	3	2	3	5	7	6
5.4–5.5	6	4	8	3	3		6	4	7	6	5
5.6–5.7	3	3	6	4	4	2	4	4	4	1	
5.8–5.9	4	5	5	5	5	2	1			1	1
6.0–6.1	4	6	1	6	2	1				2	
6.2–6.3	3	5	5		2	1					
6.4–6.5		4		2	1						
6.6–6.7		2									
6.8–6.9		1									

Per Cent	Boys: Number at Each Age With Specified Finding						Girls: Number at Each Age With Specified Finding					
	12	13	14	15	16	17–18	12	13	14	15	16	17
Total	23	34	25	24	25	24	18	19	23	29	27	24
38												1
39	1								1			1
40	2	2					1					2
41	2	2	1					1	1	3		
42	4	1	1				3	2		3	2	2
43	3	1	1			1	2	6	2	6	5	6
44	3	5	1	1			4	7	1	3	10	2
45	3	6	5		3	1	5	2	6	3	6	2
46	3	8	4	2	1	1	3		6	5	1	5
47	2	2	4	7	3	1			3	4	1	
48		3	3	2	3	5		1	2	1		1
49		2	3	4	9	4					1	2
50		2	1	2	3	3				1		
51				3	1	3						
52			1	1	1	3						
53					1	2						
54				2					1		1	

Appendix Table III. Volume of packed red cells (hematocrit) according to sex and age for Jewish children in high-income families in New York City.

Appendix Table IV. Red cell mean volume according to sex and age for Jewish children in high-income families in New York City.

Cubic Microns	Boys: Number at Each Age With Specified Finding						Girls: Number at Each Age With Specified Finding				
	12	13	14	15	16	17–18	12	13	14	15	16–17
Total	22	34	25	23	22	11	18	19	23	26	27
64		1									
67		1									
69–71	2		1								
72–74	3	10	1	1	1					1	
75–77	10	10	5	2	2		2	1	1		
78–80	4	4	6	3	3	1	3	5	3	6	1
81–83	2	6	5	4	1	1	8	2	3	1	5
84–86	1	1	4	5	7	2	2	6	7	7	7
87–89		1	1	4	2	5	2	1	4	7	3
90–92			1		4		1	2	2	3	6
93–95				1		1		1	2	1	4
96–98			1		2			1			1
99–101				1		1			1		
102				1							
108				1							

Micro-Micrograms	Boys: Number at Each Age With Specified Finding						Girls: Number at Each Age With Specified Finding				
	12	13	14	15	16	17–18	12	13	14	15	16–17
Total	22	34	25	23	22	11	18	19	23	26	27
20.0–20.9	1										
21.0–21.9	1	1									
22.0–22.9	2	4	2	1							
23.0–23.9	7	10	1	2	1				3	4	1
24.0–24.9	5	9	4	2	1	1	4	5	2	2	
25.0–25.9	5	7	5	6	7		5	6	5	5	6
26.0–26.9	1	1	8	3	4	5	6	1	8	7	6
27.0–27.9			5	6	6	1	2	2	3	7	4
28.0–28.9		2		1	1	2		2	1	1	8
29.0–29.9					2	1	1	3	1		1
30.0–30.9						1					1
31.0–31.9				1							
32.0–32.9											
33.0–33.9				1							

Appendix Table V. Mean hemoglobin content per cell according to sex and age for Jewish children in high-income families in New York City.

Appendix Table VI. Hemoglobin concentration in red cells according to sex and age for Jewish children in high-income families in New York City.

Grams Per Cent	Boys: Number at Each Age With Specified Finding						Girls: Number at Each Age With Specified Finding					
	12	13	14	15	16	17–18	12	13	14	15	16	17
Total	23	34	25	24	25	24	18	19	23	29	27	24
21											1	
25									1			
26									1			
27				1					1			
28					1				1			2
29			2	2	1	2		1	2	4	1	
30	7	6	2	2	6	6	3	3	4	7	6	7
31	8	7	6	11	6	9	5	8	10	16	11	5
32	4	14	6	7	8	5	7	5	2	1	7	5
33	3	5	5	1	3	1	3	2		1	1	3
34		1	2						1			1
35			1									1
36	1		1			1						
37		1										