0031-3998/93/3405-0680$03.00/0
PEDIATRIC RESEARCH

Vol. 34, No. 5, 1993
Printed in U.S.A.

Prevalence of Iron Deficiency in Swedish Adolescents

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ABSTRACT. The prevalence of iron deficiency was determined in Göteborg, Sweden, in a sample of 15- to 16-y-old girls (n = 220) and boys (n = 207) using serum ferritin (SF). In a recent study in women on the relationship between SF and stainable bone marrow iron, it was established that at a cutoff value for SF of <16 μg/L in 75% of women with no iron stores SF concentration was below this value (sensitivity 75%), whereas in 98% of iron-replete women it was above this cutoff value (specificity 98%). The present study showed that in 40% of the girls and 15% of the boys SF was below this cutoff value, indicating iron deficiency. Low SF concentration was associated with significant decreases in transferrin saturation, Hb concentration, mean corpuscular Hb, and mean corpuscular volume. The results from this cross-sectional study showed that, with decreasing SF, the decrease of values for these parameters occurred already before SF had reached the level 16 μg/L, suggesting that SF can be validly used as a single criterion of iron deficiency. Using the cutoff value SF < 16 μg/L, the figures for the prevalence of iron deficiency in adolescents in different countries were compared and found to be rather similar in Australia, Canada, the United States, and Sweden. High iron requirements combined with the present low-energy life-style leading to an insufficient supply of dietary iron may be a reasonable main explanation for the paradoxical, high prevalence of iron deficiency in adolescents in affluent societies. (*Pediatr Res* 34: 680–687, 1993)

Abbreviations

MCH, mean corpuscular Hb
MCV, mean corpuscular volume
SF, serum ferritin
TS, transferrin saturation

Evidence is accumulating that iron deficiency may impair not only physical activity, especially endurance, but also mental functions such as learning (1–4). Brain iron content increases during the whole of early life and into adulthood. Only 10% of brain iron is present at birth and 50% at about the age of 10, and brain iron content increases up to the age of 20–30 y (5). Animal studies suggest that a lower iron content in the brain due to iron depletion is difficult to restore by iron therapy later (6). Several recent observations have thus increased awareness of the importance of preventing the development of iron deficiency (7, 8).

Iron requirements are very high in adolescents of both sexes, especially during the growth spurt periods (9). In girls, the menarche imposes further requirements to cover menstrual iron losses (10). In boys, there are also additional needs relating to the increase in Hb concentration at the time of puberty (11).

Studies on the prevalence of iron deficiency were previously based mainly on Hb determinations and focused on the prevalence of anemia caused by iron deficiency. The distributions of the classic hematologic parameters of iron status, *e.g.* Hb concentration, red cell indices (MCH and MCV), and TS, are wide in normal subjects and show a marked overlap with the corresponding distributions in iron-deficient subjects. These methods can therefore only validly be used when the severity of iron deficiency is marked. In highly industrialized countries where this severity is usually mild, these methods are therefore too insensitive both in the single patient and in epidemiologic studies. This may lead to underestimation of the prevalence of iron deficiency if a reasonably high specificity is ascertained.

The introduction of SF determinations to evaluate iron status made it possible to make more valid estimates of the prevalence of iron deficiency (12). A relationship between SF levels and iron stores is well established, and low SF values are only observed in iron deficiency (13). Some diseases such as infections, liver diseases, and hyperthyroidism, however, may give too high values in relation to iron stores also in iron-deficient subjects. Temporary reduction of caloric intake has the same effect (14). The choice of cutoff value to separate iron-deficient and iron-replete subjects has been difficult, however. Originally, <12 μg/L was chosen on the basis of a statistical analysis of an extensive sample of 326 adults using certain criteria to select normal subjects (15). More recent studies partly relating SF to findings of stainable iron in bone marrow smears suggested that higher cutoff values should be used and values between 15 and 27 μg/L have been proposed (16–25). In a study in our laboratory on a randomly selected sample of 207 women all aged 38 y, we measured both SF and content of stainable iron in bone marrow smears (26). We found that at a cutoff level of <16 μg/L, SF had both a high specificity (98%) and a high sensitivity (75%), *i.e.* 98% of iron-replete subjects (with stainable bone marrow iron; n = 105) had SF values ≥ 16 μg/L and that 75% of iron-deficient subjects (with no stainable bone marrow iron; n = 69) had values below 16 μg/L. In this sample of women, the diagnostic efficiency (correct positive and correct negative results in relation to all results) of SF at this cutoff value (<16 μg/L) was 91%.

Although a low SF concentration indicates low iron stores, it may be argued that absence of iron stores per se might not be associated with an increased risk of an insufficient supply of iron to tissues; therefore, iron-deficient erythropoiesis, rather than the absence of iron stores, should be the basis used to classify subjects as being iron deficient and developing functional impairments related to this deficiency. Theoretically, this is a logical position.

Received June 17, 1992; accepted April 1, 1993.
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Supported by The Freemason Foundation for Research on Children and Adolescents, Swedish Medical Research Council Project B88-19X-04721-13B.

The problem, however, is the above-mentioned difficulty in demonstrating in the single, iron-deficient subject significant changes of the classic laboratory parameters that reflect an insufficient supply of iron to the erythropoiesis, due to the marked overlap in laboratory values between normal and iron-deficient subjects. The great intra- and interindividual variation, *e.g.* in TS, makes it impossible, at least at an early stage of iron deficiency, to identify single individuals with no iron stores who also have a compromised supply of iron to tissues.

According to presently generally accepted concepts, the delivery of iron to the erythroid bone marrow will not be inadequate until iron stores are exhausted. Due to the overlapping mentioned, there is no doubt that during the development of iron deficiency it will take some time before an iron-deficient erythropoiesis can be detected in the individual. It is not known, however, whether this inability to establish an iron-deficient erythropoiesis early corresponds to a true intermediate, transitional stage of no functional importance.

In 1990, studies were made in a representative sample of 15- to 16-y-old boys and girls in Göteborg to examine the prevalence of iron deficiency among adolescents and to try to clarify its causes and possible consequences. The purpose of the present paper was limited to studying the prevalence of iron deficiency based on SF determinations. Moreover, the intention was to examine at which SF concentration signs of an iron-deficient erythropoiesis were observed in boys and girls.

MATERIALS AND METHODS

The present sample was drawn to be representative of 15- to 16-y-old boys and girls in Göteborg covering different socioeconomic and living conditions. Areas were chosen varying from high-income one-family housing to multiapartment houses with lower income families. Göteborg is the second biggest city in Sweden with about 430 000 inhabitants. It has Sweden's main port and is principally engaged in trade and industry. The study was done in 1990 in late spring when the incidence of infections is usually low. In 1990, there were in total 5280 boys and girls in the 9th grade. Four schools in different areas were selected, and all 9th-grade boys and girls in these schools were selected for the study, comprising 260 boys and 255 girls. They were all informed in detail by a specially assigned nurse. Written information was sent via the pupils to all parents, who had to give written approval for the drawing of blood samples. Permission was granted for 220 girls (86% of those invited in the original sample) and 207 boys (80% of those invited in the original sample).

SF. The SF values used in the study were determined by a double-antibody polyethyleneglycol RIA (Diagnostic Products Corp., Los Angeles, CA). The assay was calibrated against World Health Organization 1st International Standard, IS 80/602. The performance of the RIA in our hands has been reported (14). Judging from results of quality control in a large-scale international immunoassay program, the precision may be classified as good or excellent and the bias is not significantly different from zero (*i.e.* overall mean). The assays in the present study were done immediately after the completion of the clinical study. In the standard curves, 95% binding of the radioligand is typically obtained at a concentration of about 3–4 μg/L, and 50% binding at about 90 μg/L. Single determinations of the specimens from the participants and duplicate determinations of three different controls (in-house serum pools) at the start and at the end of the assay runs were done. The values for the controls in the three consecutive runs were in good agreement with the values usually obtained. In 42 runs during 1 y, the coefficient of variation within assays and the total between assays were as follows: at a mean concentration of 15.2 μg/L, 6.1 and 7.1%, respectively; at 63 μg/L, 3.2 and 4.1% respectively; and at 642 μg/L, 4.3 and 5.7%, respectively.

Considering the importance of the accuracy and precision of the SF analysis in the present study, all sera were also analyzed using an immunochemiluminometric assay (MagicLite Ferritin, Ciba Corning Diagnostics Corp., Medfield, MA) previously reported to correlate well with the RIA (27). Although our experience of this assay is limited, the results were expected to give further information on the validity of the results obtained with the RIA for which completely different reagents are used.

Hematologic methods. Hb concentration, MCV, MCH, and red cell distribution width were analyzed with an automatic system, Technicon H2 equipment (Technicon Instruments Corp., Tarrytown, NY). Serum iron was determined according to Ichida *et al.* (28) using bathophenantroline sulfonate as binder. Total iron-binding capacity was determined by adding excess ferroammonium citrate to serum and removing excess iron with the ion-exchanger Amberlite IRA 400 (Rohm and Haas Co., Philadelphia, PA). TS was the ratio of serum iron to total iron-binding capacity expressed as a percentage.

Statistics. All statistical analyses were made using a Statview II computer program (Abacus Concepts Inc., Berkeley, CA) and the Excel Version 2.2 computer program (Microsoft, Redmont, WA). Mean values were compared using the *t* test. Graphical analysis of data (29) was also done using a specially designed computer program [locally weighted least squared error fit method in Kaleidagraph, Mac II, version 2.1 (Synergy Software, PCS Inc., Reading, PA)].

RESULTS

The laboratory findings in the total material of boys and girls are given in Table 1. Table 1 also shows the distributions of the laboratory parameters to make possible comparisons with results obtained in other studies (18, 30, 31). The distributions of log SF in boys and girls are shown in Figures 1 and 2.

The RIA (Diagnostic Products Corp. method) was used throughout the study and run against an international standard as mentioned in Materials and Methods. The sera were also analyzed using an immunochemiluminometric assay. The mean SF value with the latter method was 0.64 μg/L lower. The correlation between individual results obtained with the two methods was high, $r = 0.984$.

Among the boys, 31 (15%) of 207 had SF below 16 μg/L, and the corresponding values for the girls were 88 (40%) of 220. Judged visually, there was a bimodal distribution of the values for log SF concentration in the boys, with some skewness to the left. In the girls, there was also some skewness to the left that might reflect the two groups of iron-replete and iron-deficient girls.

Different analyses were made to examine the relationship between iron stores and the presence of iron-deficient erythropoiesis. The material was divided into three groups for each sex based on expected iron status: group I, with SF $<$ 16 μg/L, was considered to contain almost exclusively iron-deficient subjects. Group III, with SF $>$ 30 μg/L, was expected to contain mainly iron-replete subjects. Group II, with SF between 16 and 30 μg/L, was an intermediate group. This group can be estimated to contain mainly normal subjects, but about 10–30% of the total number of subjects in this group may be iron deficient. This division was based on results in a previous unpublished study in 203 women on the relationship between SF and stainable iron in bone marrow smears showing that only 2% of normal subjects have SF $<$ 16 μg/L, about 25% of iron-deficient subjects having SF values above this level but only 6% having SF values $\geq$ 30 μg/L.

The hematologic findings in these groups are shown for girls in Table 2 and for boys in Table 3. It was evident that Hb concentration, TS, MCH, and MCV were significantly lower in the iron-deficient group (group I) compared with the other two groups (groups II and III), both when the groups were compared separately and when groups II and III were pooled. Comparisons between groups II and III showed a significant difference only

Table 1. *Distribution of different laboratory parameters in whole samples of boys and girls*

	Mean	SD	*n*	Percentile				
				10th	25th	50th	75th	90th
Boys								
Hb (g/L)	147	8.31	203	135	142	147	152	157
TS (%)	32.7	10.25	197	21.2	25.7	31.7	38.6	46.3
MCH (pg)	29.4	1.43	203	27.7	28.6	29.2	30.2	31.0
MCV (fL)	88.4	3.87	203	83.5	85.5	88.1	90.9	93.2
RCDW (%)*	13.0	0.95	202	12.3	12.5	12.9	13.2	13.5
SF μg/L	26.4†	1.71‡	207	13.2	22	29	40.8	52
Girls								
Hb (g/L)	134	7.63	216	123	129	134	139	143
TS (%)	29.9	10.7	215	17.2	22.8	29	35.2	43.4
MCH (pg)	29.6	1.43	215	27.8	28.8	29.5	30.6	31.3
MCV (fL)	90.1	3.86	216	84.8	87.6	90.3	92.8	94.8
RCDW (%)	12.8	0.71	217	12.1	12.4	12.7	13.2	13.6
SF (μg/L)	18.2†	1.98‡	220	7.5	12	18.2	28.5	41.5

* RCDW, red cell distribution width.
† Geometric means.
‡ Antilog of logarithmic values.

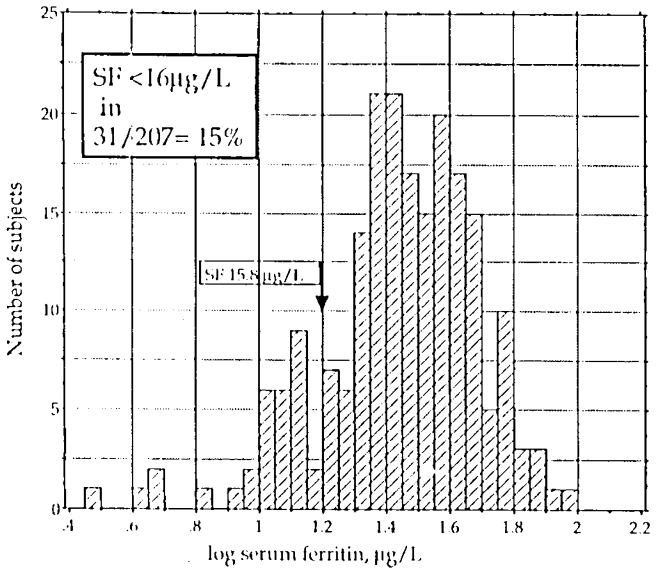

Fig. 1. Distribution of log SF concentration in 207 boys aged 15–16 y. Log SF 16 = 1.2; 20 = 1.3; 30 = 1.48; 40 = 1.6.

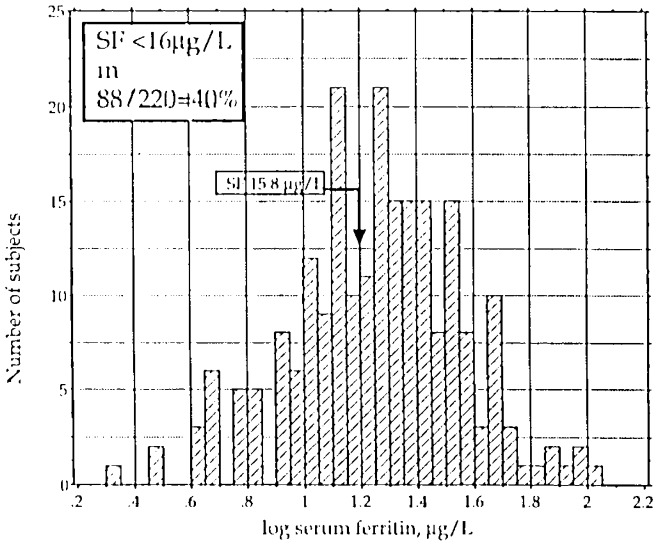

Fig. 2. Distribution of log SF concentration in 220 girls aged 15–16 y. Log SF 16 = 1.2; 20 = 1.3; 30 = 1.48; 40 = 1.6.

for Hb concentration. No significant differences were seen for red cell distribution width.

In another analysis of the relationships between SF and iron status parameters, the materials for boys and for girls were divided into deciles for SF concentration, and means for Hb concentration, MCH, MCV, and TS were calculated in each decile. The results in the graph in Figure 3 show the decile values of these parameters at the mean SF concentration in each decile. With decreasing SF, there is a consistent decrease in all four parameters. Visually, the decrease seems to start well above the cutoff value for SF < 16 μg/L (log value 1.2) in both boys and girls. Analyzing the linear regression between the hematologic parameters and log SF in the range covering the seven lowest SF deciles (to SF 26 μg/L in girls and 37 μg/L in boys), the correlation coefficients for MCH, MCV, Hb concentration, and TS were all significant. The *p* values for boys were <0.01, <0.01, <0.01, and <0.02, respectively. The corresponding *p* values for the girls were <0.01, NS, <0.02, and 0.05, respectively. To obtain further information about the SF concentration at which the hematologic parameters started to decrease, the data were also analyzed graphically using the weighted least square fit method and a special computer program (Fig. 4). This method is less sensitive for single outliers. For the girls, there was a continuous decrease in Hb concentration, MCH, MCV, and TS at least from log SF 1.3 and possibly from log SF 1.4, thus corresponding to an SF concentration of about 20 μg/L. For the boys, the continuous decrease in hematologic values started already at log SF 1.5 or even higher, *i.e.* in the SF range 30–40 μg/L.

The results from these studies indicate that, with decreasing SF, signs of an iron-deficient erythropoiesis already appeared before SF had reached the level (<16 μg/L) considered to be associated with depleted iron stores.

Common infections, such as a common cold with fever, may increase the SF level (32–34). For this reason, the number of subjects in the different groups who had a history of upper respiratory infection during the preceding month (Table 4) were recorded. A χ^2 analysis showed that the frequency of infections was higher in the groups with SF ≥ 16 μg/L, suggesting that preceding infections had to some extent shifted the SF values upward.

DISCUSSION

Iron status is best described as a continuous variable from iron overload to different degrees of iron depletion in different tissues.

Table 2. *Hematologic parameters in girls in different SF intervals*

	SF interval (μg/L)												Statistical comparisons							
	Group I (SF <16)			Group II (SF 16–29)			Group III (SF ≥30)			Groups II + III (SF ≥16)			Group I *vs* group II		Group I *vs* group III		Group II *vs* group III		Group I *vs* groups II + III	
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	*t*	*p*	*t*	*p*	*t*	*p*	*t*	*p*
Hb (g/L)	132	8.5	87	134	7.2	74	136	5.9	51	135	6.7	125	2.37	<0.02	2.67	<0.01	1.08	NS	3.27	<0.005
TS (%)	28.0	12.6	87	30.7	8.9	74	32.1	9.0	53	31.3	8.9	127	2.23	<0.05	2.67	<0.01	0.87	NS	3.27	<0.005
MCH (pg)	29.2	1.41	87	29.9	1.26	77	29.9	1.54	51	29.9	1.38	128	3.34	<0.001	2.72	<0.01		NS	3.62	<0.001
MCV (fL)	89.3	3.71	87	90.6	3.9	78	90.6	3.90	51	90.6	3.89	129	2.87	<0.01	2.25	<0.025		NS	3.08	<0.001
RCDW (%)*	13.0	0.80	87	12.7	0.56	79	12.8	0.69	53	12.7	0.62	132	3.07	<0.01	1.74	NS	0.91	NS	3.02	<0.005

* RCDW, red cell distribution width.

Table 3. *Hematologic parameters in boys in different SF intervals*

	SF interval (μg/L)												Statistical comparisons							
	Group I (SF <16)			Group II (SF 16–29)			Group III (SF ≥30)			Groups II + III (SF ≥16)			Group I *vs* Group II		Group I *vs* Group III		Group II *vs* Group III		Group I *vs* Groups II + III	
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	*t*	*p*	*t*	*p*	*t*	*p*	*t*	*p*
Hb (g/L)	142	9.8	31	146	7.3	75	149	7.9	97	148	7.7	172	2.48	<0.02	3.94	<0.001	2.12	<0.05	3.62	<0.001
TS (%)	27.9	10.2	29	32.2	9.5	73	34.4	10.4	95	32.5	10.1	168	2.02	<0.05	2.95	<0.005	1.75	NS	2.25	<0.025
MCH (pg)	28.5	1.22	31	29.5	1.62	74	29.6	1.23	98	29.6	1.41	172	3.09	<0.01	4.32	<0.001	0.46	NS	4.33	NS
MCV (fL)	87.3	3.61	31	88.4	4.15	74	88.8	3.7	98	88.6	3.89	172	1.28	NS	1.97	<0.05	0.66	NS	1.79	NS
RCDW (%)*	13.3	0.82	31	13.0	0.95	74	12.9	0.97	97	12.9	0.96	171	1.28	NS	1.78	NS	0.88	NS	1.99	NS

* RCDW, red cell distribution width.

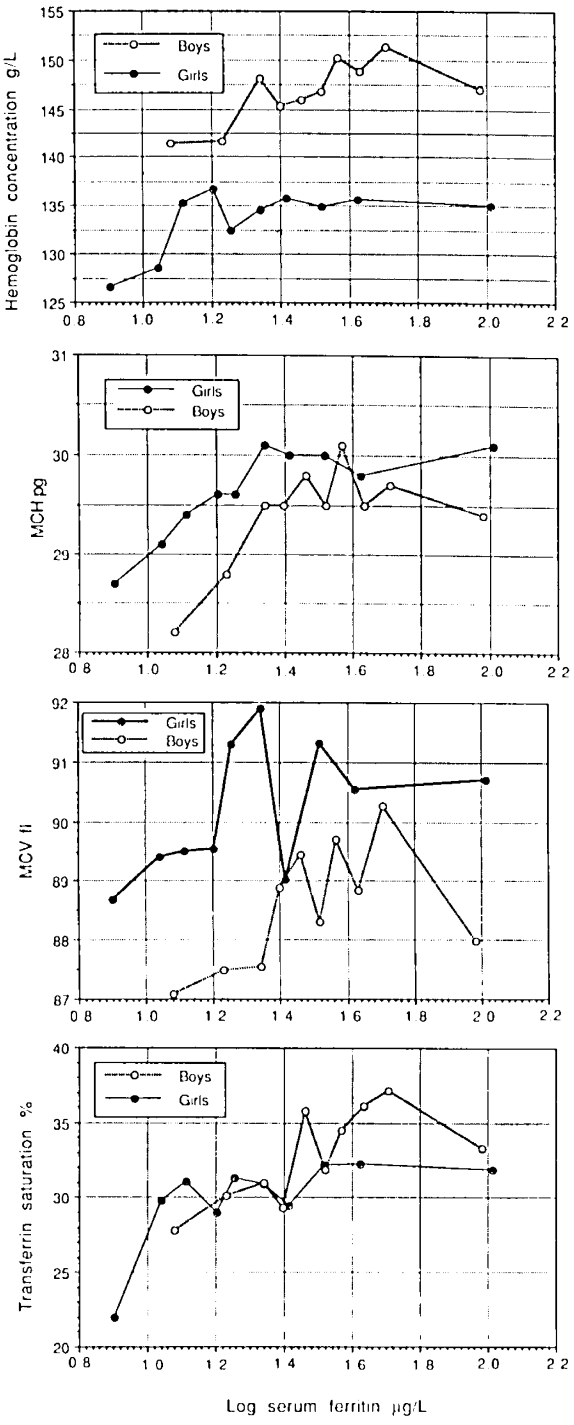

Fig. 3. Hb concentration, MCH, MCV, and TS in relation to log SF concentration in girls and boys. The materials of boys and girls were divided into deciles based on log SF concentration. In each decile, the mean values for the hematologic parameters were plotted against the mean log SF value in each decile. Log 16 µg/L = 1.2 (for decision limit for SF concentration, see text). Log SF 16 = 1.2; 20 = 1.3; 30 = 1.48; 40 = 1.6.

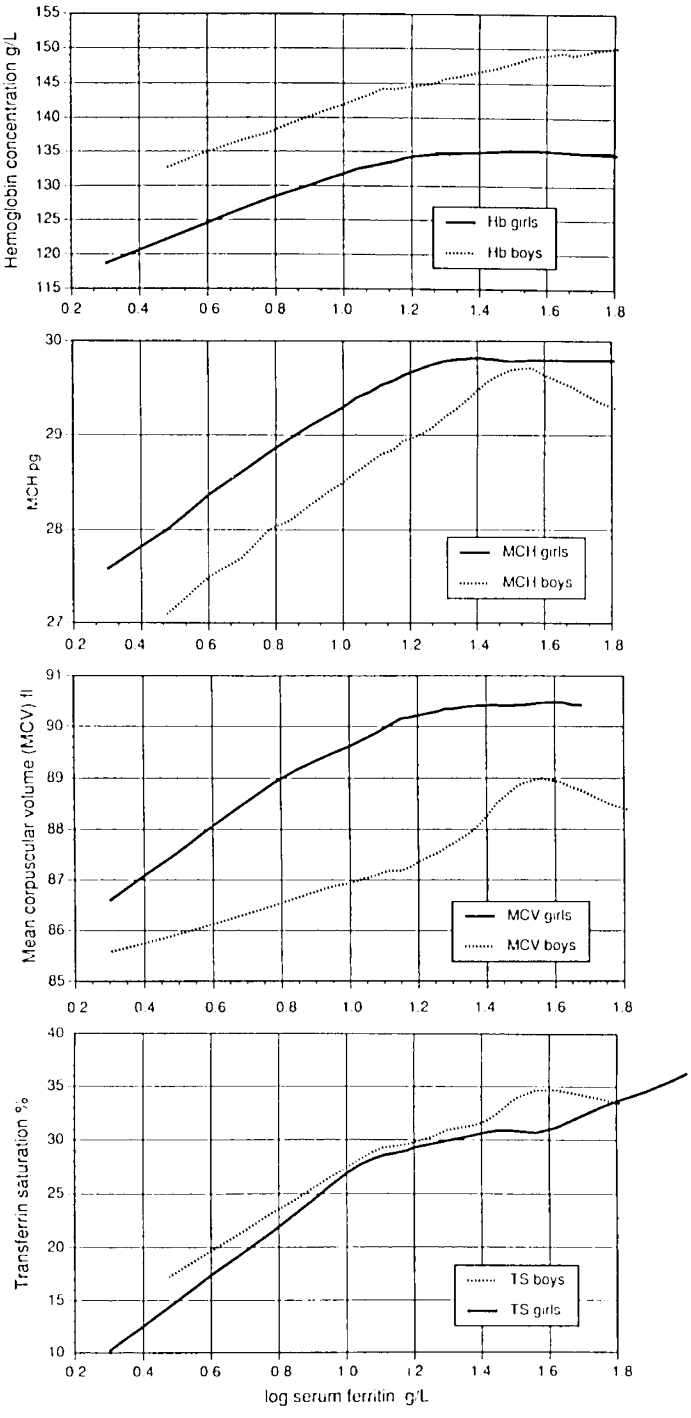

Fig. 4. The relationship between log SF and Hb concentration, MCH, MCV, and TS in girls and boys using a locally weighted least square error fit (for explanation, see text). Log SF 16 = 1.2; 20 = 1.3; 30 = 1.48; 40 = 1.6.

Empty iron stores are just a point on this scale of importance for two reasons. One is that the supply of iron to tissues from this point downward may be compromised; the other is that this point is conceptually easily definable and also readily detectable by laboratory methods such as the absence of stainable iron in bone marrow smears and by a low SF.

As mentioned, the cutoff value for SF used (<16 µg/L) was based on a study in 38-y-old women in whom iron status was established by the absence or presence of reticuloendothelial iron in technically adequate bone marrow smears. The prevalence figures of iron deficiency observed in girls and boys (40 and 15%, respectively) were high using the cutoff value of SF < 16 µg/L. The possibility that this value might be too high was therefore carefully considered. The relationship between SF and iron stores might, for example, be different in adolescents and in adults. This hypothesis was examined by relating SF in adults and adolescents to another independent parameter, TS, expected to be related to the size of the iron stores. It is well established that TS is very high in states of iron overload and low in severe iron

Table 4. *Prevalence of recent infection in adolescents grouped according to SF interval*

	All subjects			SF interval (μg/L) <16			16–29			≥30				
	Previous infection		Total in group	Previous infection		Total in group	Previous infection		Total in group	Previous infection		Total in group		
	n	%	(*n*)	*n*	%	(*n*)	*n*	%	(*n*)	*n*	%	(*n*)	χ^2 value	*p*
Boys	41	20.9	206	2	6.5	31	12	16	75	27	27	100	11.38	<0.01
Girls	46	20.9	220	11	12.5	88	20	25.3	79	15	28.3	53	6.33	<0.05

deficiency anemia. The correlation between TS and SF was highly significant in the boys, the girls, and the adult women ($p < 0.0001$). As shown in Figure 5, the regression lines for the relationship between TS and SF were very similar in the adult women and in the boys and girls and there was no statistically significant difference between the three regression lines. The relationship between SF and iron stores is thus very probably the same in adolescents and adults and implies that the same cutoff value for SF should be used. The validity of the cutoff value used presently is also supported by the independent findings that SF values below this cutoff value were associated with signs of an iron-deficient erythropoiesis. The balance of evidence thus implies that the prevalence of iron deficiency in adolescents, in fact, is very high.

Theoretically, the absence of iron stores per se may not be associated with any negative effects as long as iron absorption can balance the physiologic requirements needed to cover iron losses and growth. Iron deficiency can be considered to occur when there is an insufficient supply of iron to tissues, *i.e.* when insufficient amounts of iron-transferrin reach the transferrin receptors on various cell surfaces. To establish that iron deficiency is really present, one would thus require both depletion of iron stores and signs of a compromised supply of iron to an easily accessible tissue, such as red cells. This is difficult to establish in the individual subject due to the previously mentioned marked overlap in normal and iron-deficient subjects between the distributions of various parameters that are influenced by the iron supply to the erythron such as Hb and red cell indices.

It was thus important to examine at what SF concentration there were signs of an iron-deficient erythropoiesis. The increase in MCH, MCV, and Hb concentration with increasing SF certainly indicates that the critical point for the supply of iron to the erythron is positioned above the SF value 16 μg/L (Tables 2 and 3). The regression analyses of the hematologic parameters at different SF deciles more strongly suggest that iron-deficient erythropoiesis starts well above a SF level of 16 μg/L. Moreover, the graphical analyses based on a locally weighted least square method showed that the decrease in Hb concentration, MCH, and MCV started at an SF concentration of about 20 μg/L in girls and about 30–40 μg/L in boys.

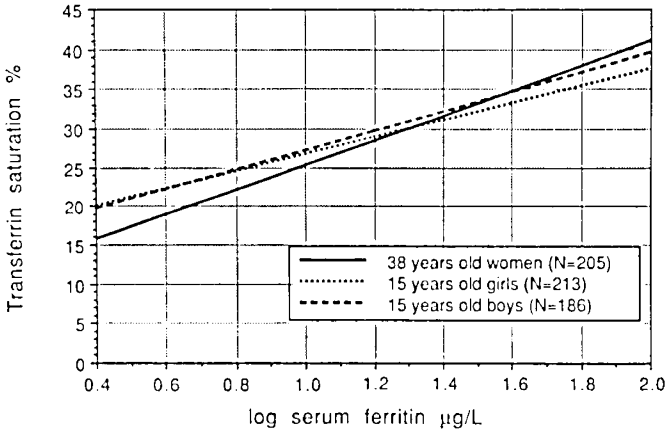

Fig. 5. Regression lines for the relationship between TS and log SF concentration in the present material of girls and boys and a sample of 38-y-old women previously studied (see text). All correlation coefficients were highly significant ($p < 0.0001$), and there was no statistically significant differences between slopes or intercepts of the three lines.

The findings of signs of an iron-deficient erythropoiesis at SF levels well above the selected cutoff value may simply be explained by individual differences in the SF level at which iron stores are exhausted. The unexpected observations that differences in the severity of iron depletion (Hb concentration, MCH, MCV, and TS) were associated with statistically significant differences in the concentration of subnormal SF values would suggest that iron stores might never be completely exhausted, not even in severe iron deficiency anemia. This conceptually quite different explanation would fit with the fact that some ferritin can always be demonstrated biochemically in the liver and bone marrow, even when iron deficiency anemia is present, and no stainable iron can be demonstrated microscopically (35). This hypothesis implies that the release of iron from stores becomes successively more difficult and is influenced by the amounts of iron remaining in stores. This hypothesis would also be consistent with the strong relationship between iron stores, SF, and TS observed from severe iron deficiency anemia to iron overload.

The present findings that hematologic parameters start to decrease at SF values >16 μg/L strongly suggest that iron stores are depleted or negligible at the cutoff value used for SF (<16 μg/L) and that at this point the erythropoiesis is limited by an insufficient supply of iron. Therefore, an SF value <16 μg/L can be validly used as the sole indicator of iron deficiency. This will certainly simplify the diagnosis of iron deficiency, especially in epidemiologic studies. In clinical practice, however, it is important to emphasize that an SF value >15 μg/L cannot be used to exclude deficiency. One reason is that there is a certain probability that patients with higher SF values, especially in the range of 16–30 μg/L, are iron deficient.

The other fact to be considered is that in patients with iron deficiency, SF values may falsely be too high due to recent infections, inflammatory diseases, liver diseases, or starvation. Several studies have shown that common infections may increase the SF level (32–34). This was also illustrated by the present findings that the proportions of subjects with a recent infection were higher in groups II and III with the higher SF values, suggesting that infections may have caused a shift of SF toward higher values resulting in some underestimation of the prevalence of iron deficiency (Table 4).

The iron status in different populations can be validly studied by comparing the distributions of the SF concentration in representative samples. The figures for 15-y-old girls in Canada (Nutrition Canada National Survey) were estimates obtained by interpolation from an enlarged published graph (18). The distributions of SF in girls were rather similar in Canada, the United States [N-HANES II study (30)], and Sweden (present sample), whereas the ferritin values were higher in 15-y-old girls in Australia [National Dietary Survey of Schoolchildren (31)]. The

prevalence of iron deficiency in the 15- to 16-y-old girls in the present sample was 40% (88 of 220) based on a cutoff value for SF of <16 μg/L. Corresponding figures for girls in the United States, Canada, and Australia, using the same cutoff value, would be 42%, 40%, and 23%. The reason for the lower prevalence of iron deficiency in the Australian girls is not known.

In boys, the SF values were consistently lower in Canada except at the 90th and 95th percentiles. At the lower end of the distribution curves, up to the 25th percentile, the distributions in the United States, Australia, and Sweden were rather similar. The prevalence of iron deficiency in the 15- to 16-y-old boys in the present Swedish sample (SF <16 μg/L) was 15% (31 of 207). Corresponding figures for boys in the United States, Australia, and Canada were 10%, 9%, and 32%. It should be mentioned that, in the Canadian study, 32 of 98 boys (32.7%) had an SF value below 15 μg/L in the whole age group, 10–19 y. The reason for the divergent, higher prevalence of iron deficiency in Canadian boys is unknown. It is of interest that another study in another region of Canada (Quebec) also reported similarly high figures of iron deficiency for both boys and girls. A weighed mean prevalence was 38% in 189 boys aged 13–18 y, and 39.5% in 180 girls (36).

Several bias factors may influence the validity of comparisons of the prevalence of iron deficiency in different groups examined by different laboratories. Examples are the effects of sampling methods, seasonal variations, and differences in infection rate. Previously, an important source of error was differences between calibrators used in different kits for SF determinations. An international standard was introduced in 1981 by the International Committeé for Standardization in Haematology, made available by the National Institute for Biological Standards and Control, a WHO International Laboratory for Biological Standards in London. Since then, most, but possibly not all, laboratories have been using methods calibrated with this standard. Even before this time, however, some participating laboratories were using adequate standards.

Present results suggest that some of the previous methods used in estimating the prevalence of iron deficiency, for example in the N-HANES II study, led to a considerable underestimation of the condition (37, 38). In the previously mentioned sample of 38-y-old women, the distribution of SF in those with no stainable iron in their bone marrow smears indicated that only about 60% of the iron-deficient subjects would be correctly classified as iron deficient at the cutoff value of <12 μg/L for SF used in the N-HANES II study. It was also found that if multiple hematologic criteria of iron deficiency had to be fulfilled to establish the diagnosis, the degree of underestimation of the true prevalence of iron deficiency would be even greater (26).

Iron requirements in adolescents are high, and much iron is needed to cover basal iron losses, requirements for growth, and, for girls, menstrual iron losses as well. Based on extensive longitudinal studies on growth and development in children, especially in Britain (39, 40) and Sweden (41), the maximal whole-year velocity standard for both weight and height in boys is seen around the age of 13–14 y. It has been suggested that the growth spurt in boys should be of short duration (42). In both the British and Swedish materials, however, there was a continued marked growth in both height and weight even 3 y after attaining the maximal growth velocities. Sexual maturation is associated with an increase in Hb concentration with a continuous, marked increase between the age of 13 and 16 y (43). About 4–5 times more iron is required for this Hb mass increase than for the growth of other tissues. Total iron requirements in boys are thus high for a period of 3–4 y. In girls, the growth spurt is seen about 1–2 y earlier than in boys and the 50th percentile maximal height is attained at about the age of 15–16 y, whereas body weight continues to increase. The average age for menarche in Sweden is around 13 y (SD ± 1 y) or about 1 y after peak growth. In the present material, eight of the 220 girls (3.6%) had not yet had their menarche. The average age of menarche was 12.9 y (SD 1.0 y). In single individuals, growth and iron requirements may be very high and of shorter duration. For most adolescents, however, total iron requirements are high for a considerable period of time. This conclusion is supported by findings in a longitudinal study of SF in adolescent girls (44).

It may seem paradoxical that a nutrient deficiency disorder should be common among adolescents in highly industrialized countries with an excess of foods. It should be remembered, however, that although iron requirements are very probably the same today as they were for our ancestors, the food intake is much lower with our present low-energy life-style. Moreover, the composition of our diet has not been sufficiently adjusted to this life-style. Available information suggests that our ancestors had not only a higher intake of energy and iron but probably also a higher bioavailability of their dietary iron with a higher content of animal protein and ascorbic acid (45).

Present findings strongly suggest that more emphasis must be placed on the prevention of iron deficiency. Adolescents are one of the important target groups who must be better covered by intervention measures such as school lunch programs and the adequate iron fortification of foods even in highly industrialized countries.

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