

Red blood cell indices and iron status according to feeding practices in infants and young children

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With the electronic counters routinely used, it has become practical to determine the concentration of hemoglobin, red cell indices, and RDW concurrently in association with transferrin saturation and ferritin in accordance with feeding practices. The 1028 infants and children aged 6 to 24 months, who had been mainly admitted with acute infectious or inflammatory diseases, were divided into three groups, i.e., children who were exclusively breast-fed more than 6 months (group A), those who had been given iron-fortified formula milk since birth (group B), and those who had been given breast milk for 5-6 months and then switched to the iron-fortified formula (group C). Children with anemia comprised 34.8% (104/299) of group A, significantly more than 5.6% (34/608) of group B and 6.6% (8/121) of group C ($p < 0.001$, respectively). Children with MCV < 70 fl comprised 39.5% (118/299) of group A, significantly more than 7.1% (43/608) of group B and 13.2% (16/121) of group C. Out of the total 146 patients with anemia, 82.2% ($n = 120$) had laboratory evidence of iron deficiency, which was mostly suggested by a dietary history. The sensitivity of MCV values < 70 fl in IDA patients was 90.0%; specificity was 53.8%. The sensitivity of RDW values $\geq 15\%$ was 83.3%; specificity was 57.7%. The positive predictive value could be increased to 97.8% by combining MCV < 70 fl and RDW $\geq 15\%$. The sensitivity of serum ferritin concentrations < 10 ng/ml was 62.4% and specificity was 100%. The sensitivity of transferrin saturation $< 12\%$ was 72.3% and specificity was 81.3%. By combining the hemoglobin with MCV and RDW in screening for iron deficiency, the diagnostic accuracy of IDA can be increased. We support the use of appropriately iron-fortified weaning foods or the routine iron supplement starting at 6 months of age in exclusively breast-fed infants. \square Anemia, breast milk, formula, infant, iron deficiency, red cell indices

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The prevalence of IDA (iron deficiency anemia) has decreased sharply during the past two decades (1, 2). The decline probably results from the improvement in infant nutrition in general, including iron supply, and particularly from increased duration of breast-feeding and the introduction of iron-fortified formulas and solids (3-5). However, IDA still remains the most common single nutrient deficiency disorder in the world and has peak prevalence among infants, affecting an estimated 25% of all babies (6). The highest rates occur in the less developed regions of the world. Furthermore, an even greater percentage of individuals of all ages reflects the biochemical changes of iron deficiency that precede the development of anemia, because anemia is a late manifestation of iron deficiency. In Korea, anemia is thought to be prevalent among infants and young children.

Iron stores become depleted by about 4 months of age in term infants unless replenished by an adequate exogenous supply of iron. The introduction of solid foods has been implied as a cause of a marked decrease in iron

bioavailability from human milk (7), especially when solid foods are given near the time of a breast-feeding. Although it is generally accepted that prolonged breast-feeding offers substantial protection against the development of IDA (8, 9), Siimes and coworkers (10) found that 6 of 36 infants who were exclusively breast-fed for 9 months eventually did become iron deficient. In another study, 15 to 40% of infants who were fed only human milk and unfortified solid food had developed iron deficiency by infancy and early childhood (11-13). Compared with 250 mg/yr, the calculated amount of absorbed iron required during the first year of life (14), the total iron potentially incorporated by an exclusively breast-fed infant during the same period may be calculated to be 57.3 mg/yr (13).

With the electronic counters routinely used in large clinical laboratories, it has become practical to determine the concentration of hemoglobin and red cell indices and red cell distribution width (RDW) concurrently. We report the results of a survey of a pediatric inpatient population that examines the relationship of

Table 1. Characteristics of the infants and mothers entered in the study.

	Group A	Group B	Group C
Maternal age (years, mean \pm SD)	28.5 \pm 2.5	28.0 \pm 2.2	28.2 \pm 3.6
Birth weight (kg, mean \pm SD)	3.43 \pm 0.35	3.48 \pm 0.32	3.47 \pm 0.41
Disease entity of the inpatients (%)	299 (100)	608 (100)	121 (100)
Diseases of the respiratory tract			
Upper respiratory infection	9 (3.0)	20 (3.3)	5 (4.1)
Acute otitis media	12 (4.0)	16 (2.6)	3 (2.5)
Croup	17 (5.7)	39 (6.4)	10 (8.3)
Acute bronchiolitis	26 (8.7)	78 (12.8)	11 (9.1)
Pneumonia	78 (26.1)	154 (25.3)	34 (28.1)
Bronchial asthma	12 (4.0)	28 (4.6)	5 (4.1)
Diseases of the gastrointestinal tract			
Diarrheal diseases	94 (31.4)	155 (25.5)	31 (25.6)
Intussusception	3 (1.0)	4 (0.7)	2 (1.7)
Acute hepatitis	2 (0.7)	1 (0.2)	0
Diseases of the nervous system			
Meningitis	7 (2.3)	5 (0.8)	0
Cerebral palsy	0	1 (0.2)	0
Fibrile seizures	2 (0.7)	23 (3.8)	1 (0.8)
Non-febrile seizures	3 (1.0)	6 (1.0)	0
Other infectious diseases			
Urinary tract infection	14 (4.7)	24 (3.9)	3 (2.5)
Measles with or without pneumonia	8 (2.7)	27 (4.4)	4 (3.3)
Viral exanthem and/or enanthem*	4 (1.3)	9 (1.5)	4 (3.3)
Septicemia	3 (1.0)	6 (1.0)	2 (1.7)
Suppurative lymphadenitis	3 (1.0)	1 (0.2)	0
Miscellaneous			
Kawasaki disease	1 (0.3)	7 (1.2)	3 (2.5)
Reye syndrome	0	1 (0.2)	0
Urticaria	1 (0.3)	0	1 (0.8)
Idiopathic thrombocytopenic purpura	0	2 (0.3)	2 (1.7)
Drug intoxication	0	1 (0.2)	0

* Included herpangina, hand-foot-mouth disease, or other viral rashes.

current feeding practices and the iron status of patients. We compare the effects of three infant feeding regimens as determined by hematologic profiles.

Subjects and methods

During a two-and-a-half-year period from March 1992 to August 1994, infants and children aged 6 to 24 months who had been admitted to Inha General Hospital in Seongnam city in Korea were investigated for evidence of iron deficiency. Blood samples were obtained by venipuncture. Hemoglobin, hemocrit, mean corpuscular volume (MCV), and red cell distribution width (RDW) were determined with the use of a Coulter S-PLUS IV (Coulter Electronics Inc., USA).

Patients with dehydration, chronic illness, previous transfusion history or major congenital anomalies were excluded from the study. We excluded those infants whose birth weight was < 2500 gm. The children were divided into three groups according to the feeding practices, i.e., children who were exclusively breast-fed more than 6 months (group A), those who were given iron-fortified formula milk since birth (group B), and those who were given breast milk for 5–6 months and then

switched to the iron-fortified formula at 6 months of age (group C). As shown in Table 1, there were no significant differences in the maternal ages at delivery or in birth weights between each group. The main causes of eligible inpatients aged 6 to 24 months were acute infectious or inflammatory diseases (93.6% in group A, 93.1% in group B and 90.9% in group C), followed by allergic diseases (bronchial asthma, urticaria), non-febrile seizures, thrombocytopenic purpura and drug intoxication. Parents were interviewed during infants' admission or telephoned after the discharge of their children regarding socioeconomic status and dietary characteristics. The iron-fortified milk powder commercially available in Korea contained 6–9 mg per 100 g (1.16–1.74 mg per 100 kcal) of iron as ferrous sulfate and 50 mg of ascorbic acid per 100 g.

All children with a hemoglobin < 10 g/dl were classified as having anemia according to Hong (15). The iron status in patients who were supposed to have iron deficiency (suggested dietary history, MCV < 72 fl, MCH < 24 pg, or RDW > 14.5) was determined by measuring hemoglobin, transferrin saturation, and serum ferritin (16, 17). Cut-off values for the laboratory tests were as follows: MCV < 70 fl, RDW \geq 15%, serum ferritin level < 10 μ g/l, and transferrin saturation

Table 2. Hematologic values among exclusively breast-fed (group A), formula-fed (group B) and switched from breast-feeding (group C) groups.

	Group A (n = 299)	Group B (n = 608)	Group C (n = 121)
Hb (g/dl) (range)	10.1 ± 1.6* (5.2 ~ 14.1)	11.9 ± 1.1 (7.6 ~ 15.2)	11.9 ± 1.2 (5.9 ~ 14.4)
Hct (%) (range)	31.1 ± 4.1* (20 ~ 45.7)	35.3 ± 3.1 (22.4 ~ 45.7)	35.3 ± 3.5 (21.5 ~ 43.3)
MCV (fL) (range)	66.7 ± 9.1* (45.9 ~ 89.7)	76.9 ± 7.3 (51.6 ~ 95.6)	74.9 ± 5.2 (57.2 ~ 84.6)
MCH (pg) (range)	21.8 ± 3.8* (12.4 ~ 33.9)	25.6 ± 2.1 (16.4 ~ 35.1)	25.1 ± 2.1 (16.6 ~ 28.3)

The values are mean ± SD.

* $p < 0.005$ compared with groups B and C, respectively.

< 12%. The diagnosis of IDA was established when infants with hemoglobin level < 10 g/dl had ferritin < 10 µg/l or transferrin saturation < 12%, whereas patients with a TIBC value below 200 mg/ml was excluded from IDA because it is characteristic of inflammatory disease (17). Serum iron and total iron-binding capacity were determined spectrophotometrically (Iatron, Japan). Transferrin saturation is calculated by dividing the concentration of serum iron by TIBC and multiplying by 100. Ferritin assay was done by

microparticle enzyme immunoassay (Abbott Laboratories, USA).

Mean, standard deviation, Student's *t*-test were used in the statistical analysis. Differences in proportions were tested for statistical significance by chi-square test. The sensitivity of an iron deficiency criterion is the proportion of all individuals with IDA who have a positive result on each test. The specificity of an iron deficiency criterion is the probability of a negative test result in an individual who is not iron-deficient.

Results

A total of 1028 patients (M:F = 1.6:1) aged 6 months to 24 months were included in the study. Table 2 shows the age distribution among the children and the proportion who remained breast-fed (group A, $n = 299$), those who received fortified formula (group B, $n = 608$), and those who were switched to fortified formula feeding from breast milk feeding after 5 to 6 months of age (group C, $n = 121$) according to the feeding practices.

The mean hemoglobin value of group A was 10.1 ± 1.6 g/dl (mean ± SD), significantly lower than 11.9 ± 1.1 g/dl of group B and 11.9 ± 1.2 g/dl of group C ($p < 0.005$, respectively). The mean MCV values in group A were 66.7 ± 9.1 fl (mean ± SD), significantly lower than in group B of 76.9 ± 7.3 fl and in group C of

Table 3. Incidence of anemia (Hb < 10 g/dL) in exclusively breast-fed (group A), formula-fed (group B) and switched from breast-feeding (group C) groups.

Age (mon)	Group A (%)	Group B (%)	Group C (%)	Total (%)
6 ~ 9	28/79 (35.4)	7/181 (3.9)	2/31 (6.5)	37/291 (12.7)
10 ~ 12	26/75 (34.7)	8/168 (4.8)	1/26 (3.8)	35/269 (13.0)
13 ~ 15	25/66 (37.8)	7/105 (6.6)	1/20 (5.0)	33/191 (17.2)
16 ~ 18	10/35 (28.6)	6/63 (9.5)	2/27 (7.4)	18/125 (14.4)
19 ~ 21	9/28 (32.1)	2/38 (5.3)	1/4 (25)	12/70 (17.1)
22 ~ 24	6/16 (37.7)	4/53 (7.5)	1/13 (7.6)	11/82 (13.4)
Total (%)	104/299* (34.8)	34/608 ⁺ (5.6)	8/121 (6.6)	146/1,028 (14.2)

* $p < 0.001$ compared with groups B and C, respectively.

⁺ $p < 0.5$ compared with group C.

Table 4. Prevalence of anemia, microcytosis and red cell anisocytosis in exclusively breast-fed (group A), formula-fed (group B) and switched from breast-feeding (group C) groups.

	Group A (n = 299)	Group B (n = 608)	Group C (n = 121)	Total (n = 1,028)
Hb < 10 g/dL	104 (34.8)*	34 (5.6)	8 (6.6)	146 (14.2)
MCV < 70 fL	118 (39.5)	43 (7.1)	16 (13.2)	177 (17.2)
RDW ≥ 15%	132 (44.1)	59 (9.7)	18 (14.0)	209 (20.3)
Hb < 10 g/dL and MCV < 70 fL	86 (28.8)	13 (2.1)	5 (4.1)	104 (10.1)
Hb < 10 g/dL and RDW ≤ 15%	94 (31.4)	15 (2.5)	5 (4.1)	114 (11.1)

* Numbers in parentheses represent percentages.

Table 5. Sensitivity and specificity of the various parameters for iron deficiency in patients with anemia.

Parameter	Cut-off point	Sensitivity (%)	Specificity (%)
MCV (fl)	70	90.0	53.8
RDW (%)	15	83.3	57.7
Ferritin (ng/ml)	10	62.6	100
Transferrin saturation (%)	12	72.3	81.3

74.9 ± 5.2 fl, ($p < 0.005$, respectively). There were no significant differences in hemoglobin and MCV between male and female. (The mean hemoglobins were 11.4 ± 1.5 g/dl and 11.3 ± 1.6 g/dl, respectively; the mean MCVs were 72.5 ± 7.7 fl and 73.5 ± 7.3 fl, respectively).

Of 1028 children 146 (14.2%) were found to have anemia (hemoglobin < 10.0 g/dl). Children with anemia comprised 34.8% (104/299) of group A, significantly more than 5.6% (34/608) of group B and 6.6% (8/121) of group C ($p < 0.001$, respectively). Children who were anemic at 6 to 9 months comprised 35.4% (28/79) compared with 3.9% (7/181) of group B and 6.5% (2/31) of group C. Similar differences between group A and other groups after 9 months were also observed (Table 3).

As shown in Table 4, children with MCV < 70 fl ($n = 177$) comprised 39.5% (118/299) of group A, significantly more than 7.1% (43/608) of group B and 13.2% (16/121) of group C. Among 209 (20.3%) children who had RDW ≥ 15%, the prevalence rate of group A was 44.1% (132/299), compared with 9.7% (59/608) of group B, and 14.0% of group C (17/121). Out of 146 patients with anemia, 82.2% ($n = 120$) had laboratory evidence of iron deficiency, and 17.8% ($n = 26$) appeared to have anemia caused by acute infection or inflammation (8 cases of pneumonia, 6 of gastroenteritis, 3 of bronchiolitis, 3 of bronchial asthma, 2 of croup, and 4 of other infectious diseases). Iron deficiency is suggested in 97.9% (95/97) by a dietary history, i.e., exclusive breast-feeding more than 6 months, use of unfortified formula or excessive cow milk consumption more than 500 ml per day during infancy, and unbalanced diets mainly limited to cow milk after infancy.

The sensitivity of MCV values < 70 fl in IDA patients was 90.0%; specificity was 53.8% (Table 5). The positive predictive value of MCV < 70 fl was 90.0%, and negative predictive value, 53.8%. The sensitivity of RDW values ≥ 15% was 83.3%; specificity was 57.7%. The positive predictive value of RDW ≥ 15% was 90.1%, and negative predictive value, 42.9%. The positive predictive value could be increased to 97.8% by combining MCV < 70 fl and RDW ≥ 15%. The sensitivity of serum ferritin concentrations < 10 ng/ml was 62.4% and specificity 100%. The sensitivity of

transferrin saturation < 12% was 72.3% and specificity was 81.3%.

Discussion

Iron deficiency and IDA are more common in youngsters during infancy and early childhood, when important aspects of brain development occur. Unfortunately, determination of iron deficiency in the absence of anemia in clinical practice is limited by the fact that most physicians still rely on measurement of hemoglobin concentration or hematocrit to detect the child who is hematologically at risk (18). Traditionally, even treatment and further evaluation for anemia has been reserved for individuals with hemoglobin that are below the "normal" range, partly because of difficulty in blood sampling in infants and young children and because of parents' reluctance to have them examined. Because of the wide range of hemoglobin concentrations and the overlap of values in normal, non-anemic persons and iron-deficient individuals, the number of iron-deficient individuals hidden within the normal range of hemoglobin concentrations is probably as great as the number of iron-deficient individuals who can be recognized as anemic (19). In addition, when anemia is mild, the differentiation of iron deficiency from other causes becomes more difficult because the changes in results of iron-related tests are of small magnitude and inconsistent (17).

Our data for breast-fed infants are in accord with other recent studies showing that there is a substantial risk of iron deficiency anemia after 6 months of age unless a source of extra iron is provided (10, 12). Pizarro et al. (12) showed prevalences of anemia at 9 months of age of 22.5% in breast-fed infants, 3.8% in infants fed iron-fortified formula, and 29.4% in those fed cow milk without added iron. According to Calvo et al. (13), at the ninth month, the prevalence of anemia was 27.8% in the breast-fed group and 7.1% in the formula group. Compared with other reports, our data showed a slightly a higher incidence of anemia. As the reason, the prevalence of anemia was significantly higher among children suffering from or recovering from acute infectious illness than among healthy children (20). After measles vaccination, mean decrease of hemoglobin was 0.2 to 0.4 g/dl and the decrease of hemoglobin > 1.0 g/dl was observed in 8.6% of infants (21). Therefore, the prevalence of anemia from our study possibly exaggerated the real incidence of IDA, because we studied an inpatient population in which illnesses such as respiratory tract infection, otitis media, and gastroenteritis were common events in early childhood.

However, subnormal values of MCV are observed when iron deficiency becomes severe and are fairly specific indicators of iron deficiency once thalassemia trait and the anemia of chronic diseases have been excluded. There was no evidence that MCV values

were different from those of whites (16). In the adults with polycythemia undergoing phlebotomy, 3 to 6 weeks later RDW rose above normal; 2 to 4 weeks after RDW rose, MCV fell below the 80 fl (22). Even when anemia has not yet become apparent, relatively early iron deficiency may be suggested by low MCV (23), which is apparent in our study that prevalence by MCV < 70 is greater than that by hemoglobin < 10 g/dl. Using the MCV model applied to children aged 3 to 10 years the prevalences of anemia were more like those given by the MCV < 70 fl model than by the ferritin model (24). Since the incidence of hemoglobinopathy and thalassemia is extremely rare in Korea, the most frequent cause of microcytosis is probably IDA, followed by chronic disease. So we believe that the prevalence of anemia in our study was not much exaggerated and that most anemia was caused by iron deficiency on the grounds of feeding history and low MCV values. Rather, the incorrect classifying of "anemic" individuals as normal is thought to be considerable because we determined 10 g/dl as the cut-off value. For 1-year-old infants, the lower limit of the 95% range is estimated to be 11 g/dl for hemoglobin (16, 25, 26), although 10.0 to 10.5 g/dl was used as the cut-off value of hemoglobin for children aged 6 to 23 months in some studies (10, 27). This study shows that the MCV and RDW in combination are useful initial screening tests in the evaluation of anemias in infants and young children.

As serum ferritin reflects a depletion of stored iron, earlier manifestation of iron deficiency and higher prevalence than the MCV model, it is known to be more suitable for assessing iron deficiency than the serum iron concentration, the TIBC and the percentage saturation of transferrin. But this is not the case in our patients aged 0.5 to 2 years, who had been mainly admitted with the problems of infection or inflammation, because even mild upper respiratory infections are associated with an elevation in serum ferritin (20). And the serum ferritin is known to be of lesser value when iron deficiency is common. Transferrin saturation is not an adequate gold standard for iron deficiency and is sometimes misleading because transferrin saturation reflects the biologic variability and laboratory errors of both the serum iron and TIBC (17).

In our study, IDA and iron deficiency were common among infants exclusively fed human milk beyond 6 months of age. Dietary history of a large group of infants was highly predictive of their risk of anemia (12). Our results can be applied to selecting an appropriate approach to the detection of iron deficiency in individual infants on the basis of their nutritional history. The prevention of iron deficiency by iron fortification of infant foods (28) is appealing because it is easily targeted to the age group at greatest risk and is less costly and more effective than the detection and treatment of anemia in individual infants by use of test battery for IDA. It is easier for mothers to make a

one-time change to an iron-fortified formula than consistently giving a daily iron supplement. And we support the use of appropriately iron-fortified weaning foods or the routine iron supplement starting at 6 months of age in exclusively breast-fed infants and perhaps somewhat earlier if solid foods have been started. Moreover, the accumulating evidence that IDA in infancy is associated with irreversible psychomotor delay provides strong motivation for complying with these recommendations to avoid iron deficiency during late infancy (29, 30).

The improved pattern of infant feeding and nutritional status related to iron can probably be attributed to the concerted effort in nutritional education of the pediatric community, which resulted in the heightened parental awareness of nutritional issues related to iron and improved feeding practices for infants (27). Therefore, it is urgent to inform the public of our knowledge about the relationship between diet and iron nutrition, including the substitution of iron-fortified formulas for unfortified formulas and cow's milk, greater frequency and duration of breast-feeding, more prolonged use of iron-fortified formulas and increased use of iron-fortified infant cereals.

References

1. Dallman PR, Yip R. Changing characteristics of childhood anemia. *J Pediatr* 1989;114:161-4
2. Yip R, Walsh KM, Goldfarb MG, Binkin NJ. Declining prevalence of anemia in childhood in a middle-class setting: a pediatric success story? *Pediatrics* 1987;80:330-4
3. Saarinen UM, Siimes MA, Dallman PR. Iron absorption in infants: high bioavailability of breast milk iron as indicated by the extrinsic tag method of iron absorption and by the concentration of serum ferritin. *J Pediatr* 1977;91:36-9
4. Committee on Nutrition. Iron-fortified infant formulas. *Pediatrics* 1989;84:1114-5
5. Dallman PR. Progress in the prevention of iron deficiency in infants. *Acta Pediatr Scand* 1990;365 Suppl:28-37
6. De Maeyer E, Adiels-Tegman M. The prevalence of anemia in the world. *World Health Stat Q* 1985;38:302-16
7. Oski FA, Landaw SA. Inhibition of iron absorption from human milk by baby foods. *AJDC* 1980;134:459-60
8. McMillan JA, Landaw SA, Oski FA. Iron sufficiency in breast-fed infants and the availability of iron from human milk. *Pediatrics* 1976;58:686-91
9. Woodruff CW, Latham C, McDavid S. Iron nutrition in the breast-fed infant. *J Pediatr* 1977;90:36-8
10. Siimes MA, Salmenpera L, Perheentupa J. Exclusive breast-feeding for 9 months: risk of iron deficiency. *J Pediatr* 1984;104:196-9
11. Grindulis H, Scott PH, Belton NR, Wharton BA. Combined deficiency of iron and vitamin D in Asian toddlers. *Arch Dis Child* 1986;61: 843-8
12. Pizarro F, Yip R, Dallman PR, Olivares M, Hertrampf E, Walter T. Iron status with different infant feeding regimens: relevance to screening for anemia. *J Pediatr* 1991;118:687-92
13. Calvo EB, Galindo AC, Aspres NB. Iron status in exclusively breast feeding infants. *Pediatrics* 1992;90:375-9
14. Stekel A, Olivares M, Pizarro F, Chadud P, Lopez I, Amar M. Absorption of fortification iron from milk formulas in infants. *Am J Clin Nutr* 1986;43:917-22
15. Hong CY. Studies on normal values for red blood cells of Korean infants and children. *J Korean Pediatr Assoc* 1961;2:23-42

16. Dallman PR, Siimes MA. Percentile curves for hemoglobin and red cell volume in infancy and childhood. *J Pediatr* 1979;94:26-31
17. Dallman PR, Yip R, Oski FA. Iron deficiency and related nutritional anemias. In: Nathan DG, Oski FA, editors. *Hematology of infancy and childhood*. 4th ed. Philadelphia: WB Saunders, 1993:413-50
18. Miller V, Swaney S, Deinard A. Impact of the WIC program on the iron status of infants. *Pediatrics* 1985;75:100-5
19. Cook JD, Alvarado J, Gutnisky A, Jamra M, Labardini J, Layrisse M, et al. Nutritional deficiency and anemia in Latin America: a collaborative study. *Blood* 1971;38:591-603
20. Reeves JD, Yip R, Kiley VA, Dallman PR. Iron deficiency in infancy: the influence of mild antecedent infection. *J Pediatr* 1984;105:874-9
21. Olivares M, Walter T, Osorio M, Chadud P, Schlesinger L. Anemia of a mild viral infection: the measles vaccine as a model. *Pediatrics* 1989;84:851-5
22. McClure S, Custer E, Bessman D. Improved detection of early iron deficiency in nonanemic subjects. *JAMA* 1985;253:1021-3
23. Bessman JD, Gilmer PR, Gardner FH. Improved classification of anemias by MCV and RDW. *Am J Clin Pathol* 1983;80:322-6
24. Expert Scientific Working Group. Summary of a report on assessment of the iron nutritional status of the United States population. *Am J Clin Nutr* 1985;42:1318-30
25. Hunter RE, Smith NJ. Hemoglobin and hematocrit values in iron deficiency in infants. *J Pediatr* 1972;81:710-13
26. Saarinen UM, Siimes MA. Developmental changes in red blood counts and indices of infants after exclusion of iron deficiency by laboratory criteria and continuous iron supplementation. *J Pediatr* 1978;92:412-6
27. Yip R, Binkin NJ, Fleshood L, Trowbridge FL. Declining prevalence of anemia among low-income children in the United States. *JAMA* 1987;258:1619-23
28. Cook JD, Bothwell TH. Availability of iron from infant food. In: Stekel A, editor. *Nutrition in infancy and childhood*. New York: Raven Press, 1984:119-43
29. Walter T, de Andraca I, Chadud P, Perales CG. Iron deficiency anemia: adverse effects on infant psychomotor development. *Pediatrics* 1989;84:7-17
30. Volpe JJ. Neuronal proliferation, migration, organization and myelination. In: *Neurology of the Newborn* 2nd ed. Philadelphia: WB Saunders, 1987:33-68

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