Need for iron supplementation in infants on prolonged breast feeding

Iron status, as measured by blood counts and indices, serum iron, transferrin saturation, and serum ferritin values, was studied longitudinally in 56 infants on prolonged breast feeding, and compared to that of 29 infants receiving cow milk formula prepared at home and of 47 infants receiving a proprietary infant formula. The first two groups received no iron supplementation, whereas the proprietary formula was supplemented with iron. Although breast feeding was found to be sufficient to meet iron needs during the first 6 months of life, supplemental iron would be necessary during the second half of infancy in order to guarantee the optimal iron status.

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IRON DEFICIENCY in infancy can be prevented by consumption of iron-enriched milk formulas[1-3] that supply the amounts of iron recommended by the Committee on Nutrition, American Academy of Pediatrics.[4, 5] The concentration of iron in breast milk is similar to that of cow milk or unfortified cow milk formulas[6, 7] but recently the iron in breast milk has been found to have a uniquely high bioavailability.[8-10] The need for additional iron in infants on prolonged breast feeding is therefore likely to be less than in those fed unfortified cow milk formula. The purpose of the present study was to determine whether breast-fed infants require supplemental iron and how their iron status compares to that in bottle-fed infants with and without iron supplementation.

SUBJECTS

The subjects were 238 healthy newborn infants of gestational age between 38 and 42 weeks and with a birth weight over 3.0 kg. They were born at the Helsinki University Central Hospital and were examined at the Children's Hospital at 2 weeks and at 1, 2, 4, 6, 9 and 12 months of age.

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Study groups. Breast feeding was initially recommended to every mother. However, of those voluntarily weaned, some were started on a home-prepared cow milk formula and the others on a proprietary infant formula. Infants were assigned to these two potential milk regimens randomly at the time of birth. From the total of 238 infants, a breast-fed group and two bottle-fed control groups were later selected as follows.

Abbreviations used	
Hgb:	hemoglobin
Hct:	hematocrit
MCH:	mean corpuscular hemoglobin of red blood cells
MCV:	mean corpuscular volume of red blood cells
MCHC:	mean corpuscular hemoglobin concentration
SI:	serum iron
TIBC:	total iron-binding capacity
S%:	transferrin saturation
SF:	serum ferritin

Breast milk group. Breast milk was the only source of milk for 56 infants until 6 months of age, after which they were gradually weaned either to proprietary formula or cow milk (Table I).

Cow milk group. Cow milk formula prepared at home was started prior to one month of age in 29 infants and continued until 6 months of age, after which commercial cow milk was consumed. Partial breast feeding continued on the average until 2.5 months of age.

Formula group. Proprietary infant formula containing 11 mg iron/liter as ferrous gluconate was started in 47

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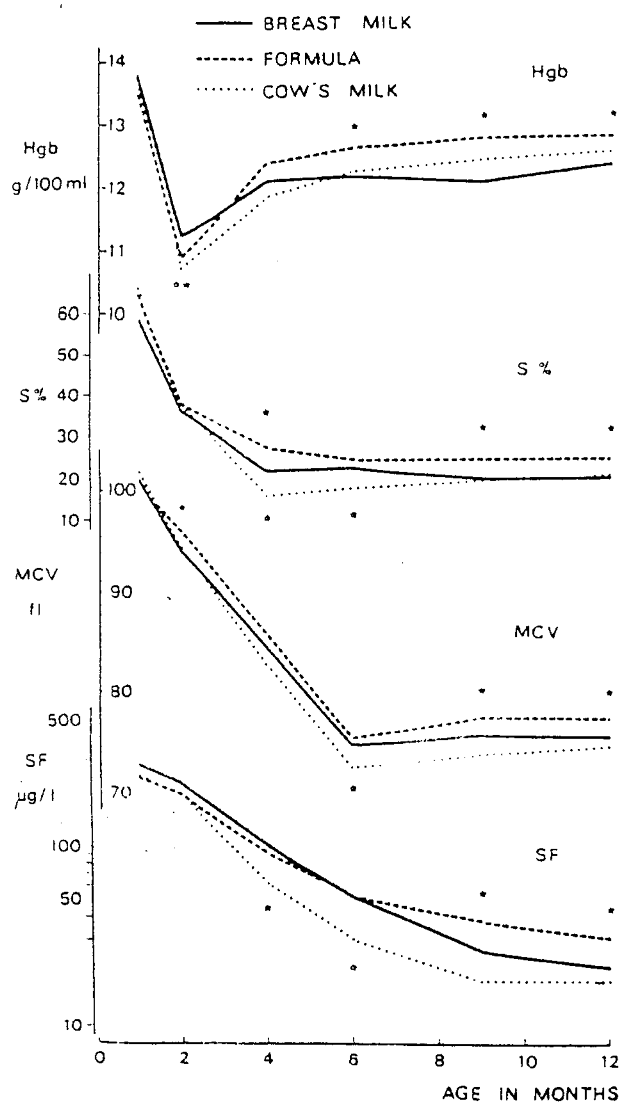

Fig. 1. Mean values for Hgb, S%, MCV, and SF of the breast milk group and the two control groups at different ages. Significant differences between the breast milk group and the formula group are shown with solid asterisks, and those between the breast milk group and the cow milk group with open asterisks. The level of significance varied from $P < 0.05$ to $P < 0.001$, most of the differences being of the highest significance. The values for Hct behaved like Hgb, and those for MCH behaved like MCV. There were no differences in the reticulocyte count or MCHC. The differences in S% were due to both SI and TIBC. SI was highest in the formula group, whereas the values in the breast milk group and the cow milk group were similar. On the other hand, TIBC was highest in the cow milk group.

infants prior to the age of one month and continued until one year of age. Partial breast feeding was discontinued on the average by 3 months of age in this group.

Criteria and instructions. The three study groups were similar in birth weight, and there were no significant differences in the hematologic values at 2 weeks of age except in serum ferritin, which was slightly higher in the breast milk group.

Table I. Infants of the breast milk group (n = 56)

	Age (mo)		
	6	*9*	*12*
Exclusively breast-fed	56	8	1
Partially breast-fed	–	34	6
Formula started	–	13	15
Cow milk started	–	34	39
Study discontinued	–	1	1

Table II. Percent of infants with two or more criteria of iron deficiency, defined by Hgb below 11 gm/dl (10 gm/dl at 4 months), MCV below 70 fl, S% below 10%, or SF below 10 µg/l

	Age (mo)			
	4	*6*	*9*	*12*
Formula group	–	–	–	–
Breast milk group	–	–	4	7
Cow milk group	7	7	4	4

All infants were given the same dietary instructions for introduction of solid foods: cooked vegetables at 3.5 months, cereals at 5 months, meat and eggs at 6 months, and table food at 9 months of age. At 2 weeks of age, daily vitamins were started: vitamin D, 1,000 IU; vitamin A, 1,500 IU; and vitamin C, 20 mg.

Wheat flour in Finland is supplemented with 0.045 mg of iron/gm, which was the only source of supplementary iron in the breast-fed and cow milk-fed infants. In contrast, the infants weaned to the proprietary formula received iron-supplemented infant cereals, in which the level of iron fortification was 0.1 mg/gm of dry cereal, compared to 0.45 mg/gm in the United States.

Four infants were excluded from the study because of anemia and the consequent initiation of iron therapy: one infant of the cow milk group at 4 months of age (Hgb 9.3 gm/dl, S% 5), another at 9 months of age (Hgb 9.8 gm/dl, S% 8), and two infants of the breast milk group at 9 months of age (Hgb 10.1 gm/dl, S% 8, and Hgb 10.3 gm/dl, S% 15, respectively).

METHODS

At every visit about 2.5 ml of venous blood was drawn from a scalp vein: 1 ml was placed into EDTA and 1.5 ml into an iron-free tube. The serum was removed and frozen within one or two hours.

Hemoglobin and red blood cell indices were determined in a Model S Coulter Counter. The reticulocytes were counted microscopically. Serum iron and total iron-binding capacity were measured spectrophotometrically in duplicate.[11, 12] Serum ferritin was determined in triplicate by a radioimmunometric assay.[13]

The means and standard deviations as well as the Student t test were used in the statistical analyses. The serum ferritin values had a normal distribution after logarithmic transformation, and the analyses were performed using the logarithms. The final results were converted back to the antilogarithms.

Criteria of iron deficiency. The following lower limits of normal were used in defining values indicating possible iron deficieny: hemoglobin 11.0 gm/dl,[14] MCV 70 fl,[15] transferrin saturation 10%,[16] and serum ferritin 10 μg/l.[7] These limits were used separately and independently of each other, as will be explained later.

RESULTS

Breast milk proved to be superior to cow milk in regard to the mean hematologic values such as hemoglobin, erythrocyte count, red blood cell indices, transferrin saturation, and serum ferritin. Differences between the lower values in the cow milk group were found at 4 months of age in transferrin saturation ($P < 0.005$) and serum ferritin ($P < 0.001$), and at 6 months of age for most of the measurements (Fig. 1). The mean values of the breast milk group and the formula group were quite similar up to 6 months of age, the age at which the entire breast milk group was still being exclusively breast-fed (Fig. 1). At 9 months of age a number of differences appeared, with lower values in the breast milk group than in the formula group. At that age more than half of the infants of the breast milk group had been weaned to cow milk (Table I). Those eight infants exclusively breast-fed at 9 months did not, however, have more normal values than the others within the group already weaned to cow milk.

The differences in laboratory values between the cow milk group and the formula group appeared at 4 months of age, were of greatest magnitude, and persisted throughout the time of the study.

Within the breast milk group, the low values for hemoglobin, MCV, transferrin saturation and serum ferritin were less common than in the cow milk group prior to and including the age of 6 months. The iron-supplemented infants rarely had any laboratory evidence of exhausted iron stores (Fig. 2). When infants with two abnormal laboratory values were defined as iron deficient, deficiency by these criteria appeared in the breast milk group at 9 months of age and in the cow milk group at 4 months of age, but not at all in the iron-supplemented formula group (Table II).

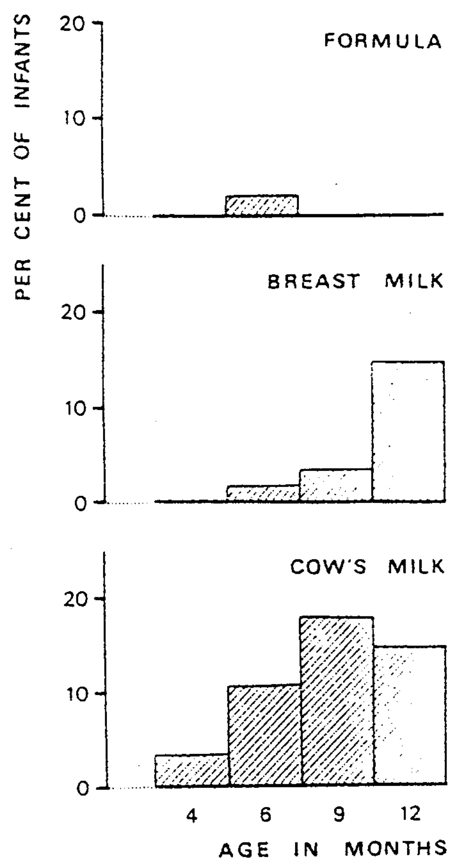

Fig. 2. Proportion of infants with suspected iron deficiency within the three milk groups, as defined by serum ferritin concentration below 10 μg/l.

DISCUSSION

The results indicate that supplemental iron should be considered for breast-fed infants after 6 months of age. In contrast, infants who are weaned to cow milk early need iron supplementation even sooner, at 4 months of age or earlier. This difference between infants fed breast milk and those fed cow milk is most likely due to the higher bioavailability of breast milk iron.[10]

When breast feeding is continued for 9 months or more, it may be insufficient to maintain optimal iron status. Recent evidence suggests that the iron concentration in breast milk declines during the course of lactation.[17] Further, after 6 months of age the amount of ingested breast milk obviously tends to decrease, since solid foods play an increasing role in the diet. It is also possible that the unusually high bioavailability of breast milk iron is modified by the introduction of various solid foods.[18] The above mentioned reasons might explain why, in the present study, the eight infants still on breast milk at 9 months of age did not have any better values than those weaned to cow milk, whereas in the paper of McMillan et all the four infants fed only breast milk for periods longer than 6 months had no obvious evidence of iron deficiency.

Thus it seems that nonfortified solid foods do not provide a source of sufficient iron in infants on prolonged breast feeding. Among the solid foods ingested by infants, iron-fortified cereals would provide a major source of iron and could be expected to prevent iron deficiency during the latter half of infancy; this aspect was not studied in the present paper.

The values of the iron-supplemented formula group were used in this study as a reference standard and were considered to represent optimal iron status. However, the precise definition of the physiologic iron status in infancy is still uncertain. Anemia should be avoided, but high iron stores may also be unnecessary.[19, 20]

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