ABSTRACT

The iron status and feeding practices of 434 infants in Vancouver were determined at 39±1 week of age. Iron-deficiency anaemia (haemoglobin ≤101 g/L, or ≤110 g/L with two or three abnormal results from tests of serum ferritin, zinc erythrocyte protoporphyrin and total iron binding capacity) occurred in 7% of infants. Low iron stores (serum ferritin <10 µg/L) occurred in about 24% of infants. Iron-deficiency anaemia was significantly associated ($p<0.001$) with duration of breastfeeding. The prevalence of iron-deficiency anaemia among infants breastfed for 8 months was 15%. At 39 weeks (9 months) of age, about 5% and 13% of the infants were bottle-fed with cows' milk or low iron infant formula, respectively, and this was also significantly associated ($p<0.02$) with low iron stores. Iron-fortified infant cereals had been introduced to 95% of the infants by six months of age. This study shows iron-deficiency anaemia is a problem among a significant number of nine-month-old infants in Canada, and is not explained by failure to introduce iron-fortified infant cereals.

ABRÉGÉ

On a déterminé les réserves en fer et les habitudes alimentaires de 434 nourrissons de Vancouver âgés de 39 semaines ±1 semaine. L'anémie ferriprive (taux d'hémoglobine < 101 g/L ou 110 g/L accompagné de deux ou de trois résultats anormaux du taux de la ferritine sérique, de la protoporphyrine érythrocytaire et du pouvoir sidéropexique) a été constatée chez 7 % des nourrissons. De plus, environ 24 % de la population à l'étude avait de faibles réserves en fer (ferritine sérique < 10 µg/L). Une association significative ($p < 0,001$) a été observée entre l'anémie ferriprive et l'allaitement maternel. La prévalence de l'anémie ferriprive chez les nourrissons allaités au sein pour une période 8 mois était de 15 %. À l'âge de 39 semaines (9 mois), environ 5 % et 13 % des nourrissons recevaient du lait de vache et une préparation à faible teneur en fer, respectivement, et on a constaté une corrélation significative ($p < 0,02$) entre cette alimentation et de faibles réserves en fer. Des céréales enrichies en fer étaient offertes à 95 % des nourrissons à compter de l'âge de six mois. Cette étude permet de constater que l'anémie ferriprive est un problème chez un nombre significatif de nourrissons âgés de neuf mois au Canada, problème que l'on ne peut pas attribuer à l'absence d'utilisation de céréales enrichies en fer.

Incidence of Iron-deficiency Anaemia and Depleted Iron Stores Among Nine-month-old Infants in Vancouver, Canada

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Considerable progress has been made in understanding the etiology of iron-deficiency anaemia in infants, and in designing strategies to reduce its incidence.¹ Although initially based on prevention of anaemia, ensuring adequate dietary iron intakes in infants and children has become of greater importance with the recognition that iron-deficiency may be associated with delayed psychomotor and cognitive development.²⁻⁵ Identification of iron-deficiency and treatment may reverse delays in psychomotor development,^{4,6} but some cognitive deficits may not be as easily corrected.⁷

The concentration of iron in human milk (0.3-0.5 mg/L) is low, but its bioavailability is high, consequently, iron-deficiency anaemia is not usually found in healthy breastfed infants under six months of age.⁸⁻¹⁰ The iron content of human milk is not sufficient to meet the estimated dietary iron requirements of 0.7 mg/day for infants over six months of age.¹¹ Thus it is recommended that breastfed infants be given additional dietary sources of iron from about four to six months of age.^{1,11,12} Because of the poor bioavailability of iron from infant formula,^{9,13} the Canadian Paediatric Society and American Academy of Pediatrics also recommend that infants who are not breastfed be fed formula with

6 mg iron/L or more.^{11,12} Further, cows' milk is not recommended for infants under 9-12 months,^{11,12,14,15} because of its low iron content (about 0.5 mg/L) and bioavailability, and the possibility that feeding with cows' milk may cause gastrointestinal blood loss in young infants.^{1,9,11,12,14-16}

The incidence of iron-deficiency anaemia among infants in the United States has declined to about 3% during the last two decades. This decline has been attributed to increased breastfeeding and increased use of iron-fortified infant formulae and cereals.¹⁷ Little information is available on the iron status of infants in Canada,¹⁸ although one study found haemoglobin values of <110 g/L in 27%, and serum ferritin values of <10 µg/L in 37% of 10 to 14-month-old infants from disadvantaged families.¹⁹ This study was done to determine the prevalence of iron-deficiency anaemia in a large group (434) of healthy, nine-month-old infants in Vancouver in relation to feeding practices and family background.

METHODS

Infants and recruitment

Contact with potential study participants was made by letter, followed by a telephone call to the parents of all term gestation infants born in Vancouver during the periods January 1 - March 2, 1993, or June 4 - July 8, 1993. Those willing to participate were given appointments to attend outpatient nutrition clinics to coincide with the time of the infant's 39th ± 1 week. All parents were telephoned 24 to 72 hours before the scheduled appointment to confirm or change appointments if necessary.

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TABLE I
Infant Sample

	Oct-Nov 1993	March-May 1994
Eligible infants	869	943
Parents contacted	578	579
% eligible	(66)	(61)
Appointments booked	301	290
% contact	(52)	(50)
Appointments attended	226	208
% booked	(75)	(72)

Eligible infants were identified from birth lists with 2,007 and 1,715 registered births for the Oct-Nov 1993 and March-May 1994 periods, respectively.

The study objectives and protocol could not be adequately described to the parent/guardian for 183 infants reached by telephone because of language difficulties. Other eligible infants were not reached because of incorrect address, or telephone number, or no response to telephone calls.

Dietary and family background

Information on infant feeding practices was obtained qualitatively with a diet history questionnaire. Each parent was instructed on how to complete the questionnaire. The completed questionnaires were checked by a nutritionist and any discrepancies or ambiguities corrected. For the purposes of this study, infants were considered breastfed as long as the intake of formula or other milk by bottle did not exceed 12 oz per week. Infants were considered never breastfed if they were not breastfeeding by seven days of age. Family background, including family income, parents' education, age and ethnic association was assessed with a confidential questionnaire which was not validated with the parent.

Determination of iron status

Capillary blood samples were taken by a trained phlebotomist from the B.C. Children's Hospital. Analysis of haemoglobin was done on ethylenediaminetetraacetic acid (EDTA)-anticoagulated whole blood using a TOA Sysmex NE-series 23 parameter blood counter (TOA Sysmex, Los Alamitos, CA). Serum ferritin was determined with a two-site radiometric assay (RAMCO, Houston, TX). Zinc erythrocyte protoporphyrin (ZPP) was measured in a haematofluorometer using the Proto Fluor Reagent System (Helena Laboratories, Beaumont, TX). Serum iron was quantitated using a diagnostic kit from

TABLE II
Prevalence of Iron-deficiency Anaemia and Low Iron Stores Among 39-week-old Infants in Vancouver

	Iron-deficiency Anaemia	Low Iron Stores	Uncertain	Normal
Number	30	106	43	254
Boys/Girls	17/13	63/43	25/18	124/130
% total	7	24	10	59

Iron-deficiency anaemia defined as, haemoglobin ≤ 101 g/L or ≤ 110 g/L + 2 or 3 abnormal indicators of iron status from ferritin, < 10 μ g/L, total iron binding capacity, > 60 μ g/L, ZPP, > 70 μ mol/mol haeme; low iron stores, ferritin ≤ 10 μ g/L without iron-deficiency anaemia; uncertain, haemoglobin 101-110 g/L with 0 or 1 indicator (other than ferritin) of low iron status; normal, haemoglobin > 110 g/L plus ferritin > 10 μ g/L.

Prevalence of iron-deficiency anaemia and of low stores significantly higher in boys than girls, $p=0.053$.

TABLE III
Prevalence of Iron-deficiency Anaemia and Low Iron Status Among 39-week-old Infants of Different Ethnic Backgrounds

	Canadian North American* (n=120)	Chinese (n=81)	Mother's Ethnic Background East Indian (n=43)	European (n=125)	Filipino (n=18)	Other Asian (n=23)	Other (n=23)
Iron-deficiency anaemia n=30	6 (5)	3 (4)	0 (0)	14 (11)	2 (11)	2 (9)	3 (13)
Low iron stores n=106	35 (29)	10 (12)	11 (26)	36 (29)	2 (11)	4 (17)	8 (35)
Uncertain n=43	9 (7)	7 (9)	5 (12)	15 (12)	2 (11)	2 (9)	3 (13)
Normal n=254	70 (58)	61 (75)	27 (63)	60 (48)	12 (67)	15 (65)	9 (39)

n = Number of infants, and in brackets the % within each iron class assignment for each ethnic group. Iron class assignment was significantly influenced by ethnic background, $p<0.05$.

* Includes First Nations and North American Indian.

Hoffman La-Roche Ltd., (Mississauga, ON). Unsaturated iron-binding capacity was determined with a diagnostic kit (Diagnostic Chemicals Ltd., Charlottetown, PEI) and total iron binding capacity (TIBC) calculated as the sum of the total iron and unsaturated iron binding capacity.

For this study, infants were considered to have iron-deficiency anaemia if the haemoglobin was ≤ 101 g/L, or ≤ 110 g/L with two or three indicators of low iron status from serum ferritin (≤ 10 μ g/L), total iron binding capacity (TIBC) (> 60 μ mol/L), and zinc erythrocyte protoporphyrin (ZPP) (> 70 μ mol/mol haeme). Infants without iron-deficiency anaemia with a serum ferritin of ≤ 10 μ g/L were considered to have low iron stores. Infants with a haemoglobin > 110 g/L and ferritin > 10 μ g/L, or a haemoglobin

> 101 g/L, ferritin > 10 μ g/L and a normal TIBC and ZPP were considered normal. All remaining infants (haemoglobin 102-110 g/L, with either an abnormal TIBC or ZPP test result) were considered uncertain. Infants with suspected iron-deficiency anaemia were retested, and in all cases potential haemoglobinopathies were ruled out and the test results were confirmed. The infants were then treated with ferrous sulphate (3 mg/kg per day) or diet counselling for two to three months, and retested. All the infants responded to treatment with a rise in haemoglobin. This was done through collaboration with each infant's doctor and not as part of this study.

Data analysis

Analysis of variance was used to determine potential differences in iron class

TABLE IV
Prevalence of Iron-deficiency Anaemia and Low Iron Status at 39±1 Week of Age Among Infants in Relation to the Duration of Breastfeeding*

Iron Status	Total n=433	Never n=74	Duration of breastfeeding				Mixed Feeds n=32
			<3 months n=92	4-6 months n=93	7-8 months n=50	>8 months n=92	
Iron-deficiency anaemia	30 (3)	1 (10)	3 (33)	10 (7)	2 (47)	14 (0)	0
Low iron stores	106 (7)	7 (27)	29 (22)	23 (13)	14 (26)	28 (5)	5
Uncertain	43 (16)	7 (26)	11 (19)	8 (21)	9 (19)	8 (0)	0
Normal	254 (22)	53 (21)	54 (9)	54 (16)	24 (16)	42	27

* Infants established on formula with no breastfeeding within seven days of birth were classified as never breastfed. Infants were considered breastfed as long as the intake of formula or other milk by bottle did not exceed 12 oz/wk. Infants who were breastfed and supplemented with 12 oz cows' milk or formula/wk for >1 month were classified as mixed feeds. The number of infants, with the percent of infants within a category of iron status in brackets, is given. One infant was not classified because of missing information on infant feeding; the infant had normal iron status.

over 25 years of age. The infants were also predominantly from middle and higher income families, with parents who had completed some post-secondary education. For example, 40% of the mothers had completed university and another 33% had undertaken vocational training. This study did, however, have the participation of infants from a broad range of ethnic groups; about 28% of the mothers reported that they were Canadian, 19% were Chinese, 29% European, 10% East Indian, 4% Filipino, 5% other Asian and 5% of other backgrounds (e.g., African, West Indian).

Thirty infants (about 7%) had iron-deficiency anaemia, 106 infants (about 24%) had low iron stores, and 255 infants (about 59%) had normal iron stores and haemoglobin values (Table II). All of the infants with suspected iron-deficiency anaemia were retested, the iron-deficiency confirmed, and all responded to treatment with a rise in haemoglobin and serum ferritin. Possibly, the potential for false positives in this study was limited by the use of multiple measures to classify iron status. As shown in Table II, iron-deficiency anaemia and low iron stores both tended to be more prevalent among infant boys than infant girls ($p=0.053$). The prevalence of iron-deficiency anaemia and low iron stores differed significantly ($p<0.05$) among infants of different maternal ethnic backgrounds (Table III). Iron-deficiency anaemia was more prevalent among infants with a mother of Caucasian rather than Chinese or East Indian background. Similarly, the prevalence of low iron stores was approximately two-fold higher among infants with a mother of Caucasian or East Indian rather than Chinese or Filipino background.

The iron class assignment also showed a significant relation to the duration of breastfeeding ($p<0.001$) (Table IV). Iron-deficiency anaemia occurred more frequently among infants who were breastfed for ≥ 3 months than among infants who were breastfed < 3 months. Of the 30 infants with iron-deficiency anaemia, 26 had been breastfed for ≥ 3 months, 4 had been breastfed for < 3 months; 14 (47%) were still breastfed at the time of testing. The prevalence of iron-deficiency anaemia

TABLE V
Prevalence of Iron-deficiency Anaemia and Low Iron Status in Infants at 39 Weeks in Relation to Use of and Age at Introduction of Iron-fortified Cereals*

Iron Status	n	Iron-fortified Infant Cereal				Total	Other Cereal (n=18)	Unknown (n=10)
		≤ 4 months	5 months	6 months (n=405)	> 6 months			
Iron-deficiency anaemia	30	5 (17)	15 (50)	5 (17)	2 (7)	27	1 (3)	2 (7)
Low iron stores	106	55 (52)	26 (24)	18 (7)	3 (2)	102	2 (2)	2 (2)
Uncertain	43	19 (44)	10 (23)	8 (20)	4 (9)	41	4 (2)	2 (5)
Normal	254	118 (46)	52 (20)	49 (19)	16 (6)	235	14 (6)	4 (2)

* Number of infants and, in brackets, the % of infants within a given iron class assignment. Information on age at introduction of iron-fortified infant cereals was not given for two infants; one was classified as uncertain and one had normal iron status.

assignment for duration of breastfeeding, age of introduction of breast milk substitutes, infant cereals and other food groups (including fruit, juice, vegetables, meat, and egg yolk), and family background. Chi-square and Goodman and Kruskal Tau tests were used to determine significant differences between the iron class assignment and grouped interval data for duration of breastfeeding, and age of introduction of cows' milk, infant formula, cereals and other food groups. All analyses were done using the Statistical Packages for the Social Sciences (SPSS), release 4.0 (SPSS Inc., Chicago, IL).

RESULTS

A total of 434 infants were screened for iron status (Table I). The infants screened represented about 38% of infants for whom a parent was contacted, and about 24% (434/1,812) of the eligible infants identified on the birth registries. The high 73% (434/591) participation by parents who agreed to be involved is probably due to the repeat telephone call 24 to 72 hours prior to the appointment date. Of the infants screened, 90% were from two-parent families and 89% of the mothers were

among the 92 infants who were breastfed at 9 months of age was 15%. The prevalence of iron-deficiency anaemia among the infants who were breastfed for ≤ 8 months was about 6%. Iron-deficiency anaemia was found in one infant who had never been breastfed; this infant had been fed a low-iron infant formula from birth. It must be noted that although iron deficiency was more common among the nine-month-old breastfed than formula-fed infants, the vast majority (85%) of nine-month-old breastfed infants did not have iron-deficiency anaemia.

Low iron stores (serum ferritin <10 $\mu\text{g/L}$) were also more common ($p<0.05$) among infants who had been breastfed, irrespective of duration, than among infants who had not (Table III). Feeding with low iron formula or cows' milk was also significantly ($p<0.02$) related to iron status. Of the 342 infants who were not breastfed at nine months of age, 63 (about 18%) had been bottle-fed with cows' milk or a low-iron infant formula for at least one month. Of these 63 infants, 44 (about 70%) had low iron stores ($p<0.05$).

Failure to introduce iron-fortified infant cereals was not related to iron status; 90%, 96% and 92% of the infants with iron-deficiency anaemia, low-iron stores and normal iron status, respectively, had been fed with iron-fortified infant cereal (Table IV). Only 10 infants (2%) had not been introduced to any cereals, and 18 had been fed cereals (e.g., oats) other than an iron-fortified infant cereal. No significant associations were found between the age of introduction of fruit juice, fruit, vegetables, meat or egg yolk and the iron status of the infants (data not shown).

DISCUSSION

This study shows a prevalence of 7% iron-deficiency anaemia among otherwise healthy nine-month-old infants in a predominantly middle-class setting in Vancouver. The infants at greatest risk, when identified by nutritional history, were those who were breastfed at the time of testing. Although breastfed infants receive adequate iron from human milk for the first four to six months after birth, breastfed infants over six months are

known to become increasingly vulnerable to iron deficiency with increasing age unless adequate additional sources of dietary iron are provided.²⁰

The prevalence of iron-deficiency anaemia among the nine-month-old breastfed infants in this study was about 15%. These results are very similar to work from Chile in which about 15 and 0.6%, respectively, of nine-month-old infants who were breastfed or fed iron-fortified formula, had iron-deficiency anaemia.²¹ The difference in iron-deficiency anaemia among infants from different ethnic groups in Vancouver, with the prevalence highest among Caucasian rather than Oriental or Asian infants, is probably explained by ethnic differences in breastfeeding, and the predominant use of iron-fortified formulae by mothers who choose not to breastfeed.

Breastfed infants who are not introduced to iron-fortified complementary foods in the second six months after birth are considered to be at risk for iron-deficiency anaemia.^{11,12,22} Although the efficacy of iron-fortified infant cereals has been questioned,²³ iron-fortified cereals clearly reduce the incidence of iron-deficiency anaemia among breastfed infants.²⁴ The incidence of 15% iron-deficiency anaemia among breastfed infants in Vancouver was not explained by delayed introduction of iron-fortified infant cereals beyond the recommended four to six months of age.¹¹ Indeed, 83% of the infants with iron-deficiency anaemia were fed iron-fortified infant cereals by four to six months of age. However, data on the quantity of cereal fed were not collected. Therefore, it is possible the amount or duration of cereal feeding among the breastfed infants with iron-deficiency anaemia was insufficient to meet their iron needs. Iron absorption also varies widely among infants,²⁵⁻²⁷ with the range of absorption of iron from breastmilk varying from 3 to 37%.²⁵ Whether variability in iron absorption has relevance to the aetiology of iron-deficiency in some breastfed infants is not known.

This study also found that low iron stores are common among nine-month-old infants who are breastfed or bottle-fed with cows' milk or a low iron formula. The physiological significance of low iron stores in infants without anaemia is not known.

Indeed it is reasonable to assume low iron stores reflect a normal developmental pattern which reverses as the diet becomes more varied and sources of haeme iron become more significant.

Only about 5% and 13% of the infants in this study had been bottle-fed with unmodified cows' milk or low iron formula, respectively. The low incidence of feeding with cows' milk and low iron infant formula, together with the widespread use of iron-fortified infant cereals in Vancouver suggest that recommendations from expert groups have had a positive influence on infant feeding practices. Previous studies have found much higher rates of cows' milk feeding; for example 72% of six-month-old infants in Toronto in 1977-78, and 38% of six to eight-month-old infants in Alberta in 1992 were fed unmodified cows' milk.²⁸

In summary, this study has shown that iron-deficiency anaemia remains a significant problem among nine-month-old infants, particularly those who are breastfed to at least nine months of age. Adverse effects on weight gain in iron-replete 12 to 18-month-old infants given ferrous sulphate were recently reported.²⁹ Routine iron supplementation for breastfed infants over six months may, therefore, not be an appropriate strategy to prevent iron-deficiency anaemia among breastfed infants. Studies to elucidate the reasons why some but not most breastfed infants have poor iron status are needed to allow development of nutrition strategies to meet the dietary iron needs of infants over six months, while supporting and maintaining longer breastfeeding.

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In Memoriam

ALEXANDER GORDON JESSAMINE, CD, MB, ChB (Abrdn), LMCC 1926-1997

Of Aberdeen, Scotland, St. John's, Nfld. and Ottawa, Dr. A.G. Jessamine died peacefully, happily and with release, at home on March 27, 1997.

Dr. Jessamine was born in Scotland and graduated from Aberdeen University. He spent three years as a medical officer with the Royal Army Medical Corps and in 1952 moved to Newfoundland. There he assumed the responsibilities of a chest physician in the Tuberculosis Service. From 1955 to 1959, he was the Assistant Superintendent of St. John's Sanatorium and then relocated to Ottawa, where he was head of the Tuberculosis Division for the Royal Ottawa Sanatorium. From 1968 to 1975, he held the position of Physician in Charge, Tuberculosis Prevention Service, Ontario Ministry of Health.

Much of Dr. Jessamine's long and illustrious career in public health was spent at the Laboratory Centre for Disease Control, where he was responsible for the Field Epidemiology Program. In 1987 he moved to the Sexually Transmitted Disease/HIV field, where he developed a strong national STD control program. He played a key role in establishing the Expert Interdisciplinary Advisory Committee on Sexually Transmitted Diseases (STDs), of which he was a member.

Teaching was always important to Dr. Jessamine, and from 1961 he held various academic positions and devoted a consider-

able amount of time to continuing medical education. He was an Assistant Professor in the Department of Medicine and an Adjunct Professor, Department of Epidemiology and Community Medicine, both at the University of Ottawa.

Dr. Jessamine was instrumental in establishing the STD Division within the Canadian Public Health Association (CPHA) and served as its chairperson and as a member of the CPHA Board of Directors for two three-year terms. He was involved with CPHA in the development of the CPHA AIDS Education and Awareness Program and provided valuable advice and support to CPHA in the early years of this program. He remained interested in its evolution and in 1994-95 served as a member of the Program's Advisory Committee.

Dr. Jessamine's work has been an inspiration to those in the public health field, especially in the areas of STDs and tuberculosis. For his boundless energy, enthusiasm and commitment to public health in Canada, CPHA awarded Dr. Jessamine its highest honour, the R.D. Defries Award and Honorary Life Membership in 1991.

Dr. Jessamine's kindness, sense of humour and broad smile will be fondly remembered by those who had the honour of working with him.

Funeral services were held on Monday, March 31. In memoriam donations to the Lung Association, Ottawa-Carleton Region, or Ottawa Regional Cancer Centre would be appreciated.