Eighteen-month Follow-up of Infants Fed Evaporated Milk Formula

James K. Friel, PhD, *Wayne L. Andrews,* MD, *Colin Edgecombe,* BSc, *Ursulla R. McCloy,* MSc, *Suresh L. Belkhode,* MSc, *Mary R. L'Abbe,* PhD, *Claude N. Mercer,* RT, *Allison C. McDonald,* RN

ABSTRACT

In parts of Canada including Newfoundland and Labrador and among Aboriginal peoples, infants still consume evaporated milk (EM) formulas for cultural and economic reasons. At 3 and 6 months, full-term infants fed EM (n=30) received low intakes of iron, thiamine, selenium and had higher weight velocity than breastfed (BF, n=29) infants. EM infants had greater anemia, lowered transketolase activity (thiamine) and lowered glutathione peroxidase (selenium) activity ($p<0.05$).

To determine the later effect of early feeding deficit on nutritional status, we examined these same infants at 18 months of age. At that time, there were no differences in dietary intakes of energy, protein, zinc, copper, selenium and iron, nor in plasma levels of zinc, copper, vitamin C, nor in red blood cell activity levels of glutathione reductase (riboflavin), transketolase, glutathione peroxidase, nor in superoxide dismutase. However, EM infants weighed more and were more likely to visit a physician, have anemia, and have iron depletion than were BF infants. We conclude that infants consuming evaporated milk formulas should receive iron supplements throughout infancy.

ABRÉGÉ

Dans plusieur régions du Canada y compris Terre-Neuve et le Labrador, et parmi les peuples autochtones, les bébés sont toujours nourris de lait évaporé pour des raisons culturelles et économiques. À trois mois et à six mois, les bébés nés à terme, nourris de lait évaporé (n=30) recevaient de moindres quantités de fer, de thiamine, de sélénium et pesaient plus que ceux nourris de lait maternel (n=29). Les bébés nourris de lait évaporé souffraient plus souvent d'anémie, d'un niveau d'activité réduit de transcétolase (thiamine) et d'un niveau d'activité réduit de glutathion peroxydase (sélénium) (p<0,05).

Afin de connaître les répercussions à long terme d'une alimentation déficiente chez le nourrisson, nous avons examiné les mêmes enfants à l'âge de 18 mois. À cet âge, il n'y avait aucune différence dans la consommation d'énergie, de protéine, de zinc, de cuivre, de sélénium et de fer, ni dans les niveaux de zinc, de cuivre, de vitamine C dans le plasma, ni dans les niveaux d'activité de glutathion réductase (riboflavine), de transcétolase, de glutathion, ni de superoxide dismutase dans les cellules rouges du sang. Cependant, les bébés nourris au lait évaporé pesaient plus et avaient plus souvent besoin de soins médicaux, souffraient d'anémie et avaient des niveaux plus bas de fer en comparaison avec des enfants nourris de lait maternel. Nous en concluons que les bébés nourris au lait évaporé devraient recevoir des suppléments de fer pendant leur petite enfance.

Until the mid-1950s,[1] the majority of infants in North America received formulas prepared with evaporated milk (EM). EM formulas as an alternative to breastfeeding (BF) are recommended "only when economic circumstances do not allow the purchase of commercially prepared formula."[2] However, in Newfoundland and Labrador as well as among Aboriginal peoples, EM formulas are still in use.[3,4]

EM is cow's milk (whole, 2% or skimmed milk) evaporated to approximately half the original volume and is not recommended for infants younger than 12 months.[5] Cow's milk may lead to increased allergy responses from protein,[6] increased gastrointestinal blood loss,[7] poorer protein digestion, increased solute loads,[8] low iron bioavailability[5] and possible dehydration.[1] Based on our previous report[3] indicating that at 6 months EM-fed infants were at risk for iron, copper, selenium and thiamine deficiency, we followed that same group at 18 months of age to determine later effects of early feeding.

SUBJECTS AND METHODS

The original group of full-term infants were recruited from the Grace Hospital in St. John's, Newfoundland during 1993. Infants weighed between 2500 and 4500 g at birth and were 38-42 weeks gestational age. Originally,[3] 3 groups of infants were followed: BF (n=29), formula-fed (n=30) and EM-fed (n=30). Mothers had to maintain their choice of feed for 3 months with minimal solid feeding. No information was provided except a handout from the public health nurses indicating that EM preparation for a 6-oz. bottle consisted of 2 oz. whole EM diluted with 4 oz. water, with 2 tsp. sucrose added to bring the energy content to 68 Kcal/100 mL.[2,9] Also 7.5 mg (0.3 mL) of iron should be added to the first bottle of EM formula of the day, as Fer-In-Sol (Mead Johnson, Ottawa, Ont). This occurred for only 24% of EM infants.

At 18 months of age (± one week), 30/30 EM infants and 28/29 BF infants originally enrolled completed anthropometric assessments, had a blood sample taken and had a 3-day dietary record completed for nutrient intakes.[3,9] Parents/guardians were asked about the frequency of hospital/doctor visits and the reasons, numbers and types of infections, gastrointestinal problems, allergies and the medication history of the child during the previous 18 months. Due to cost, only the human milk-fed and evaporated milk-fed infants were evaluated. Ethical approval was given by all Hospital and University ethics committees.

Infant weight was measured on a double beam balance. Recumbent lengths were measured using an infantometer. Head circumference was measured using a non-stretch plastic tape. Blood samples (2 mL) were collected by veinipuncture, separated and frozen at -70°C until analysis. Ferritin was analyzed using the Ferrizyme assay.[10] Hemoglobin, hematocrit and mean cell volume (MCV) were analyzed by Coulter counter.[3] Iron deficiency (ID) was defined as a ferritin value <10 ng/mL.[11] Iron defi-

Memorial University of Newfoundland, Janeway Child Health Centre, St. John's, NF and Nutrition Research Division, Food Directorate, Health Protection Branch, Health Canada, Ottawa, ON

Correspondence and reprint requests: James K. Friel, Department of Biochemistry, Memorial University, St. John's, NF, A1B 3X9, Tel: 709-737-7954, Fax: 709-737-2422, E-mail: jfriel@morgan.ucs.mun.ca

This project was supported by the Medical Research Council of Canada and the Janeway Research Foundation

ciency anemia (IDA) was defined as a hemoglobin of < 110 g/L or a hematocrit <33% and a ferritin value < 10 ng/mL.[12] An abnormal MCV is < 70 fL.[12]

Plasma zinc and copper were analyzed by atomic absorption.[13] Erythrocyte copper zinc superoxide dismutase (CuZnSOD) was assayed by an automated method.[14] Selenium status was determined by erythrocyte glutathione peroxidase (SeGHSPx) activity.[15] Thiamin status was assessed using the thiamin pyrophosphate effect (TPPE); marginal status was > 15%, and deficient status defined as > 25% stimulation.[16] Riboflavin was assessed by erythrocyte glutathione reductase (EGRAC) with an acceptable status defined as a value > 1.2.[17] Vitamin C in plasma was assayed using the method of Omaye.[18] For all tests, EM infants provided 30 samples and BF infants provided 29 samples except for plasma zinc and copper (EM=29) and vitamin C (BF=24). Weight, length and weight for length were calculated using the WHO/CDC computerized anthropometric program (CASP, Version 3).

Unpaired Students T-tests were used to assess differences between groups for socioeconomic data (as assessed by the Blishen score[19]), nutrient intakes, wellness data, biochemical and abnormal iron indices.[20] Statistical differences were assigned to p < 0.05.

RESULTS

There were no differences in mean weight (3550 ± 382 g), length (51 ± 2 cm) or head circumference (35 ± 1.2 cm) between the two groups at birth. EM was fed for 11.5 ± 1 months (n=30; 21 M, 9 F) and BF was fed for 7.5 ± 1 months (n=28; 15 M, 13 F). Mothers in the EM group were significantly younger (25 ± 5 yrs vs 30 ± 4 yrs), of lower social class (Blishen score = 22 ± 8 vs 41 ± 19) and lower education (4 ± 1 vs 6 ± 2 yrs post primary school) than were mothers from the BF group. At 18 months, EM infants had a trend towards greater number of reported doctor visits per year (EM, n=5 ± 4; vs BF n=3 ± 2, p=0.06). At 18 months, no differences were seen in incidence of hospital admission (0.3 ± 0.9), respiratory problems (5.5 ± 4.7), allergies (0.6 ± 1.4), gastroin-

TABLE I
Nutrient Comparison - Infant Feedings per 100 Calories

Nutrient	Human Milk*	Infant Formula†	EM‡ 1:2
Protein (g)	1.5	2.1	3.9
Fat (g)	5.4	5.4	4.4
Carbohydrate (g)	10	10.7	11.2
Linoleic Acid (mg)	540	1,300	151
Vitamin A (IU)	310	300	124
Vitamin D (IU)	3	60	52
Vitamin E (IU)	0.32	3	0.07
Vitamin B_1 (mcg)	29	100	29
Vitamin B_2 (mcg)	49	150	184
Vitamin B_6 (mcg)	28.5	60	47
Vitamin B_{12} (mcg)	0.07	0.25	0.50
Niacin (mcg)	208	1,050	1056
Folic Acid (mcg)	7	15	5
Pantothenate (mcg)	250	450	350
Biotin (mcg)	0.6	4.4	4
Vitamin C (mcg)	6	9	9
Calcium (mg)	39	77	140
Phosphorous (mg)	19	58	100
Magnesium (mg)	4.9	6	11
Iron (mg)	0.04	1.8 /0.22	0.11
Zinc (mg)	0.17	0.75	0.41
Manganese (mcg)	0.08	5	4.4
Copper (mcg)	35	90	11
Sodium (mg)	25	32	66
Potassium (mg)	73	96	177
Selenium (mcg)¶	2.5	2.3	1.0

* Tsang RC and Nichols BF.[22]
† Ross Laboratories product information, 1992.
‡ Nestle Enterprises Ltd., product information, 1991, Fomon,1 Health and Welfare Canada.[9]
¶ Litov and Combs,[23] Fomon[1]

TABLE II
Nutrient Intakes of Breastfed (BF) and Evaporated Milk-fed (EM) Infants at 18 Months

	BF (n=28)	EM (n=30)
Energy (kcal/d)	1224 ± 237*	1283 ± 398
Protein (g/d)	47 ± 13	46 ± 18
Fat (g/d)	46 ± 15	50 ± 22
Iron (mg/d)	8.3 ± 6.8	8.3 ± 5.4
Zinc (mg/d)	6.3 ± 1.4	6.0 ± 2.4
Copper (mg/d)	1.1 ± 0.4	1.0 ± 0.4
Se (mg/d)	57 ± 28	47 ± 21
B_1 mg/1000 kcal	0.8 ± 0.4	0.7 ± 0.3
B_2 mg/1000 kcal	1.4 ± 0.4	1.3 ± 0.5
Vit C (mg/d)	136 ± 84	129 ± 61

* X ± SD

TABLE III
Biochemical Indices of Breastfed (BF) and Evaporated Milk-fed (EM) Infants at 18 Months

	BF (n=28)	EM (n=30)
CuZnSOD (mU/mg Hb)	33 ± 5.5*	31 ± 4.7
SeGHSPx (mU/mg Hb)	35 ± 4.4	34 ± 3.7
TPPE (%)	2.6 ± 2.5	4.4 ± 2.7
Plasma Cu (ug/dL)	101 ± 20	118 ± 25
Plasma Zn (ug/dL)	78 ± 21	83 ± 15
EGRAC (%)	1.1 ± 0.1	1.1 ± 0.8
Plasma vit C (ug/mL)	13 ± 4	13 ± 4
Ferritin (ng/mL)	13.5 ± 6.3	16.4 ± 4.1
Hemoglobin (g/L)	123 ± 7	121 ± 10
Hematocrit	0.360 ± 0.023	0.359 ± 0.03
Mean cell Volume	78.5 ± 4.4	77.9 ± 4.2

*X ± SD

TABLE IV
Abnormal Iron Indices of Breastfed (BF) and Evaporated Milk-fed (EM) Infants at 18 Months

	BF (n=28) n	(%)	EM (n=30) n	(%)
Hemoglobin (<110 g/L)	1	(4)	5	(17)
Ferritin (<10 ng/mL)	9	(32)	11	(37)
Hematocrit (<33%)	0	(0)	4	(13)
Iron Deficiency Anemia	1	(4)	5	(17)
Mean Cell Volume (<70 fl)	1	(4)	2	(7)

testinal problems (1.4 ± 2.3), or use of antibiotics (3.3 ± 3.7). Z-score changes in weight in the BF group (-0.49 ± 0.37) were significantly lower between 3 and 6 months than in the EM group (0.01 ± 0.56). At 18 months, EM infants weighed significantly more (Z-scores, EM=0.53 ± 1.4) than did BF infants (-0.16 ± 0.9), however length (Z-scores, EM=0.46 ± 0.72; BF= 0.38 ± 1.06), weight for height (Z-scores, EM=0.56 ± 1.41; BF=-0.33 ± 0.98) and head circumference (EM=48 ± 1.7 cm; BF=49 ± 6.4 cm) did not differ.

The nutrient values of human milk, EM and a typical infant formula are presented in Table I. Nutrient intakes (Table II) and biochemical indices (Table III) did not differ between groups. However, there were a greater number of abnormal iron indices (Table IV) in the EM group. One EM infant had a low dietary vitamin C intake (5 mg) but his plasma vitamin C concentration (9.1 µg/mL) was acceptable.[21] One BF infant had a vitamin C intake of 152 mg/d yet had a low (medium risk) plasma vitamin C concentration of 2.3 µg/mL.[21] TPPE values for all infants were within the low risk category.[16] EGRAC values were marginal[17] for one infant in each group (Table III).

DISCUSSION

Energy and micronutrient intakes (Table II) reported here were similar to those reported previously in another Canadian study of 18-month-old toddlers.[22] Eighteen-month-old toddlers from a lower socioeconomic group in Denver[23] had almost identical intakes except for vitamin C (52 ± 42 mg/d) in the Denver study, still above the Canadian RNI.[24] EM infants consumed significantly more energy at 3 and 6 months of age[3] than did BF infants and had greater weight velocity between 3 and 6 months. EM infants are known to grow well[4] and BF infants show a decline in weight velocity in the first year.[25]

EM-fed infants are at risk for iron, thiamine, and selenium deficiency.[1,9,26,27] Whether this early risk would be realized in later childhood was the focus of this study. By 18 months there were 11/30 EM infants with ID (Table IV). Seven of these 11 infants at 18 months previously had ID at 6 months that was not resolved at 18 months.

In the EM group, 4 infants at 6 months and 5 infants at 18 months had iron deficiency anemia. Of the 5 infants who developed anemia by 18 months, none had anemia at 6 months. However, 6 of 11 EM infants with depleted iron stores at 18 months had depleted iron stores at 6 months. Iron intakes did not differ between EM and BF infants (Table II). On average, iron intakes were higher than recommended intakes,[24] however, 12/30 EM infants received less than the RNI.[24] Seventy-four percent of EM infants received no iron supplementation (iron-fortified formula or medicinal iron drops) in the first 6 months of life. Similar lowered iron status has been reported by others[28] in EM-fed infants. Seventy percent of the EM-fed infants (300/445) developed anemia by one year and by 18 months only 10 subjects did not have anemia. In the latter study as well as in the present study, solid foods alone were not enough to prevent iron deficiency anemia. In our study, only 1/6 infants who had received iron drops from birth had a low hemoglobin at 18 months. Clearly if EM-fed infants do not receive iron supplements early in life, poor iron status will persist into early childhood.

The CPS recommends that exclusively breastfed infants should receive extra iron as iron-fortified cereals or other iron-rich foods after 6 months of age.[29] None of our BF infants received iron supplements before 6 months. However, infant cereals did not provide enough iron. There were only 5 (BF) and 6 (EM) infants who consumed the recommended 20 g/d of iron-fortified infant cereal.[22] By 6 months 20% of BF infants had low hemoglobin and iron stores with 10% suffering from IDA. By 18 months only 1 BF infant had IDA, however 9 BF infants had depleted iron stores (Table IV), only 1 of whom was depleted at 6 months. Others[30] have reported that BF infants who do not receive iron supplements before 6 months are in marginal iron status. Fifteen percent of 9-month-old BF infants in Vancouver had iron deficiency anemia.[31] We think that iron supplementation of breastfed infants should start not once stores are depleted but earlier to maintain adequate stores. Because IDA is associated with long-lasting adverse effects on cognition, even mild ID in early infancy should be avoided.[1]

Selenium and thiamine deficiencies did not persist to 18 months. Low selenium intakes of 5 ± 1 µg/d at 3 and 10 ± 5 µg/d at 6 months[3] rose to 47 ± 21 µg/d (Table II) above the requirement of 20 µg/d,[24] once solids were introduced. There were no differences in SeGHSPx activity (Table III) suggesting that stores at birth suffice until the introduction of solid foods.

Thiamine intakes at 18 months (per 1000 kcal energy in the diet, Table II) did not differ from intakes at 6 months (0.66 ± 0.38 mg/1000 kcal). Intakes maintained adequate thiamine status in all infants (TPPE, Table III) even with 1 BM and 3 EM infants consuming less than the RNI.[24]

Intakes of vitamin C, riboflavin, zinc and copper were adequate (Table II) according to biochemical indices (Table III). Only 1 BM infant consumed less than the RNI for vitamin C and no infants in either group consumed less than the RNI for riboflavin.[24] Vitamin C added to EM is readily available.[32] EM infants consumed more vitamin C at 3 (EM=66 ± 28; BF=30 ± 2 mg/d) and 6 months (EM=90 ± 38; BM=49 ± 29 mg/d) than did BF infants. By 18 months of age, plasma and dietary vitamin C were similar.

Only 2 EM infants consumed less than the RNI of 4 mg/d for zinc, whereas 14 EM and 7 BF infants received less than recommended copper intakes of ~ 0.95 mg/d.[24] Nonetheless, there were no differences in plasma zinc, copper or CuZnSOD values (Table III).

Respiratory infections differed at 12[3] but not at 18 months. Decreased immune function earlier in infancy may occur when EM is the primary food, and may improve with the introduction of solids. Early feeding of EM was associated with more doctor visits. Because of lower socioeconomic status, it is difficult to attribute this to EM alone.

By 18 months of age, nutrient intakes between the two groups are nearly identical (Table II). Nonetheless infants in the EM group are at a clinical disadvantage for iron status (Table IV), suggesting that the results of early infant feeding habits have persisted into the toddler stage. If mothers choose to feed EM, their infants must receive iron supplementation from birth.

ACKNOWLEDGEMENTS

The authors acknowledge the support of the Janeway Child Health Centre and the Grace General Hospital and thank Dr. Albert Davis for his encouragement.

REFERENCES

1. Fomon SJ. *Nutrition of Normal Infants.* St. Louis: Mosby, 1993.
2. Health and Welfare Canada. *Feeding Babies.* Health Promotion Directorate, 1986.
3. Friel JK, Andrews WL, Simmons BS, et al. An evaluation of full-term infants fed an evaporated milk formula. *Acta Paediatrica* 1997;86:448-53.
4. Matthews K, Webber K, McKim E, et al. Infant feeding practices in Newfoundland and Labrador. *Can J Public Health* 1995;86(5):296-300.
5. American Academy of Pediatrics Committee on Nutrition. The use of whole cow's milk in infancy. *Pediatrics* 1992;89:1105-9.
6. Foucard T. Development of food allergies with special reference to cow's milk allergy. *Pediatrics* 1985;75:177-81.
7. Fomon SJ, Ziegler EE, Nelson SE, Edwards BB. Cow milk feeding in infancy: Gastrointestinal blood loss and iron nutritional status. *J Pediatr* 1981;98(4):540-45.
8. Ziegler EE, Fomon SJ. Potential renal solute load of infant formulas. *J Nutr* 1989;119(125):1785-88.
9. Health and Welfare Canada. *Nutrient Value of Some Common Foods.* Health Services and Promotion, Health Protection Branch, 1987.
10. Friel JK, Matthew JD, Andrews WL, et al. Comparison of two kits for measuring ferritin in blood. *Clin Pediatr* 1993;3:4-5.
11. American Academy of Pediatrics Committee on Nutrition. Iron deficiency. In: Forbes GR, Woodruff CW (Eds.), *Pediatric Nutrition Handbook* 2nd ed. Elk Grove, IL: American Academy of Pediatrics, 1985.
12. Yip R. The epidemiology of childhood iron deficiency. In: Dobbing J (Ed.), *Brain, Behaviour, and Iron in the Infant Diet.* London: Springer-Verlag, 1990;27-42.
13. Makino T, Takahara K. Direct determination of plasma copper and zinc in infants by atomic absorption with discrete nebulization. *Clin Chem* 1991;27:1445-47.
14. L'Abbe MR, Friel JK. Copper status of very low birth weight infants during the first 12 months of infancy. *Pediatr Res* 1992;32:183-88.
15. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. *J Lab Clin Med* 1967;70:158-68.
16. Brin M, Dibble MV, Peela EA. Some preliminary findings on the nutritional status of the aged in Onondaga county. *Am J Clin Nutr* 1965;17:240-45.
17. Tillotson JA, Baker EM. An enzymatic measurement of the riboflavin status in man. *Am J Clin Nutr* 1972;25:425-31.
18. Omaye ST, Turnbull JD, Sauberlich HE. Selected methods for the determination of ascorbic acid in animal cells, tissues and fluids. *Methods Enzyme* 1979;62:3-12.
19. Blishen BR, McRoberts HA. A revised socio-economic index for occupations in Canada. *Can Rev Soc Anthrop* 1976;13:71-84.
20. Nie NH, Hull CH, Jenkins JG, et al. (Eds.), *Statistical Package for the Social Sciences (SPSSx).* New York: McGraw Hill Inc., 1975.
21. Gibson RS. *Principles of Nutritional Assessment.* NY: Oxford University Press, 1990.
22. Yeung DL, Pennell MD, Hall J, Leung M. Growth and development of infants in Toronto and Montreal. *Can J Public Health* 1982;73:278-82.
23. Walravens PA. Nutritional sources of iron in infants and toddlers. In: LJ Filer, Jr. (Ed.), *Dietary Iron: Birth to Two Years.* New York: Raven Press, 1989;91-102.
24. Health and Welfare Canada. Nutrition Recommendations. The report of the scientific review committee. Minister of Supply and Services, 1990.
25. Heinig MJ, Nommsen LA, Peerson JM, et al. Intake and growth of breast-fed and formula fed infants in relation to the timing of introduction of complementary foods: The DARLING study. *Acta Paediatr* 1993;82:999-1005.
26. Tsang RC, Nichols BL. Appendix. In: *Nutrition During Infancy*. Philadelphia: Hanley and Belfus Inc., 1988.
27. Litov RE, Combs GF. Selenium in pediatric nutrition. *Pediatrics* 1991;87:339-51.
28. Andelman MB, Sered BR. Utilization of dietary iron by term infants. *Am J Dis Child* 1966;111:45-55.
29. Nutrition Committee. Meeting the iron needs of infants and young children: An update. *CMAJ* 1991;148(11):1451-54.
30. Owen GM, Garry PJ, Hooper EM, et al. Iron nutriture of infants exclusively breast-fed the first five months. *J Pediatr* 1981;99(2):237-40.
31. Innis SM, Nelson CM, Wadsworth LD, et al. Incidence of iron-deficiency anaemia and depleted iron stores among nine-month-old infants in Vancouver, Canada. *Can J Public Health* 1997;88(2):80-84.
32. Phillips MB, Wardlaw JM. Effect of preparation technique and storage time on vitamin C content of infant formulas made with vitamin-enriched commercial evaporated milk. *CMAJ* 1967;97:1384-88.

Received: June 29, 1998
Accepted: January 25, 1999