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# Effect of early, short-term supplementation on weight and linear growth of 4–7-mo-old infants in developing countries: a four-country randomized trial<sup>1-4</sup>

Kirsten B Simondon, Agnes Gartner, Jacques Berger, André Cornu, Jean-Pierre Massamba, José-Luis San Miguel, Coudy Ly, Isabelle Missotte, François Simondon, Pierre Traissac, Francis Delpeuch, and Bernard Maire

**ABSTRACT** The effect of supplementation on growth was tested by means of four similar controlled randomized trials in the Congo ( $n = 120$ ), Senegal ( $n = 110$ ), Bolivia ( $n = 127$ ), and New Caledonia ( $n = 90$ ). Four-month-old infants were randomly allocated to supplement or control groups. A cereal-based precooked porridge was offered twice daily for 3 mo and consumption was monitored. Both groups were free to eat local food. At 7 mo of age, all infants were still breast-fed in the Congo, Senegal, and Bolivia compared with 47% in New Caledonia. Mean daily consumption of the supplement varied among countries (558–790 kJ/d). Mean length at 4 mo was lowest in Bolivia, higher in Senegal and the Congo, and near the National Center for Health Statistics reference in New Caledonia. The mean 4–7-mo length increment was 0.48 cm higher for supplemented than for control infants in Senegal ( $P < 0.05$ ), whereas weight increments did not differ. No significant effect was found in the other countries. *Am J Clin Nutr* 1996;64:537–45.

**KEY WORDS** Nutritional supplementation, growth disorders, controlled trial, intervention, recumbent length, developing countries, infancy

## INTRODUCTION

Growth faltering is common among infants and children in poor areas throughout the world. The process of growth faltering begins during infancy or even during fetal life, and is thought to be due to poor dietary intake and morbidity (1). Therefore, nutritional supplementation would appear to be an obvious way of improving linear growth. However, conclusions from previous studies vary (2), partly because of differences in study design. Previous supplementation studies mainly involved large-scale food distribution or feeding programs in which the growth of children from intervention villages was compared with the growth of children from control villages (2). This design does not ensure comparability among groups. More recent studies have adopted protocols similar to controlled clinical trials using random allocation of children to groups. Home delivery of supplements without control of consumption makes it difficult to interpret results, particularly when no effect on growth is found because consumption by the infant is not established (2). Daily delivery of supplements in a

center is time consuming for the mothers but has been shown to permit better compliance on the part of infants of low socioeconomic status from large families living near the centers (3). The age of target children is an important factor to consider when interpreting results of supplementation (4) together with weaning status because supplementation might affect intake of breast milk (5). Nutritional status at enrollment should also be considered because prevention of growth faltering and treatment of significant stunting are very different matters (6). Supplementation of mothers during pregnancy and lactation, in addition to supplementation of the infant, has complicated interpretation of some studies because effects cannot be analyzed separately (4).

Infancy is thought to be the period of life when growth is the most sensitive to environmental stress, and stunting originates mainly during infancy (1). Recent age-specific reanalyses of major large-scale supplementation studies have also suggested that supplementation is most efficient during infancy and especially during the 3–6-mo interval in Bogota, Colombia (4), and in rural Guatemala (7).

Therefore, the aim of the present study was to test the prevention of linear growth faltering during early infancy by short-term nutritional supplementation of breast-fed infants. The study was designed to avoid the methodologic problems and pitfalls of previous supplementation trials, particularly those concerning allocation to experimental groups, high dropout rates, irregular participation, sharing of the supplement with other family members, and risk of unhygienic preparation and storage. The main hypothesis was that supplementation

<sup>1</sup> From ORSTOM, Institut Français de Recherche Scientifique pour le Développement en Coopération, Montpellier, France; Instituto Boliviano de Biología de Altura (IBBA), La Paz, Bolivia; DGRST, Ministère de la Recherche Scientifique, Brazzaville, Congo; Organisme de Recherche sur l'Alimentation et la Nutrition Africaines (ORANA), Dakar, Senegal; and Direction Provinciale des Affaires Sanitaires et Sociales (DPASS), Province des Iles Loyauté, New Caledonia.

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<sup>3</sup> André Cornu, coordinator of the trial in New Caledonia, died on October 23, 1994.

<sup>4</sup> Address reprint requests to KB Simondon, Nutrition Unit (UR 44), ORSTOM, BP 5045, 34032 Montpellier Cedex, France.

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would have a positive effect on linear growth during the supplementation period (4–7 mo) and the main outcome measure chosen was the 4–7-mo length increment. The study was conducted simultaneously and according to the same protocol in four developing countries on three continents, in two rural and two urban areas. The aim of this “multicenter” design was to test whether the effect of early supplementation was identical in various environments.

In this paper we describe the levels of supplement consumption by age and setting, and examine the effect of supplementation on local food consumption and growth in length and weight during the supplementation period. Interrelations among supplementation, morbidity, and growth during the supplementation period, and the long-term effect of supplementation on physical growth will be examined in separate publications.

## SUBJECTS AND METHODS

### Design

The effect of supplementation on growth from 4 to 7 mo was tested by random assignment of infants aged 4 mo into an intervention group and a control group. Supplementation was done twice daily at home and supervised by fieldworkers after hygienic preparation of a high-energy-density semiliquid supplement enriched with minerals and vitamins. Both groups were free to eat local food and all infants were breast-fed except for some of those in New Caledonia. The outcome variable was the 4–7-mo length increment.

### Study areas

The study was conducted in four areas in Central and West Africa, South America, and the South Pacific in 1993–1994. The Central African study was conducted in a periurban area, Mikalou, in Brazzaville, the capital city of the Congo. A census of eligible infants was conducted in four maternity hospitals before the study, because all births took place in hospitals. The study was conducted from May to November, 1993, during the dry season (25–35 °C). Education levels were high; only 5% of mothers ( $n = 145$  of 148) had received no schooling and 71% had attended secondary school. Almost one-half of the mothers had an occupation outside the home as students still in school (24%) or small traders (22%,  $n = 148$ ). Mean ( $\pm$  SD) heights were 159.9  $\pm$  5.8 cm ( $n = 148$ ) for mothers and 169.6  $\pm$  6.0 cm ( $n = 70$ ) for fathers. The mean ( $\pm$  SD) body mass index (in kg/m<sup>2</sup>) was 22.4  $\pm$  4.1 ( $n = 148$ ) for mothers. The mean ( $\pm$  SD) birth weight of study infants was 3.09  $\pm$  0.44 kg ( $n = 145$ ) and the mean ( $\pm$  SD) birth length was 48.7  $\pm$  1.5 cm ( $n = 102$  of 148, routine maternity hospital data).

The West African Sahel study was conducted in a rural area in the peanut basin in central Senegal, 150 km from the capital city of Dakar. Continuous demographic surveillance ensured precise knowledge of all births in the three big villages (1900–2800 inhabitants) and three groups of hamlets with  $\approx$ 1000 inhabitants/group. The study was conducted partly during the warm, dry season (30–43 °C), from March to June, and partly during the rainy season (30–35 °C), from July to September, 1993. Education levels were very low, with 73% of fathers ( $n = 115$  of 134) and 89% of mothers ( $n = 133$  of 134) of included infants having had no school education. Nearly 90%

of parents were farmers growing millet for subsistence and peanuts as a cash crop. Height was 160.7  $\pm$  5.4 cm ( $n = 133$ ) for mothers and 172.5  $\pm$  7.0 cm ( $n = 100$ ) for fathers. The mean body mass index of mothers was 22.0  $\pm$  2.3 ( $n = 133$ ) at the start of the study. Birth weights and lengths were unknown because all births took place in the home.

The South American study was conducted in Pasankeri, a poor periurban area of La Paz, the capital city of Bolivia, at an altitude of 3700–4000 m. A continuous census of all births was conducted during the study period by primary health workers. The study was conducted from April, 1993, to January, 1994, mainly during the dry, cold season (0–22 °C). Parents were Aymaras (> 90%), and mothers had fairly high levels of schooling (57% attended primary school, 30% attended secondary school, and 13% were illiterate;  $n = 152$  of 160). Mean height was 148.7  $\pm$  5.1 cm ( $n = 146$  of 160) in mothers and 162.0  $\pm$  5.2 cm ( $n = 71$ ) in fathers; the mean body mass index of mothers was 23.8  $\pm$  3.1 ( $n = 146$ ). Birth weights and lengths were unknown because most mothers migrated back to their villages to give birth.

The fourth study was conducted on the Island of Maré (650 km<sup>2</sup>, 5646 inhabitants), which is part of New Caledonia, a French overseas territory in the South Pacific. The study was conducted during the cold season, from July, 1993, to June, 1994 (20–30 °C). All parents were Melanesian. Mothers had high education levels (27% attended primary school, 55% attended secondary school, 19% attended technical schools; 100% were literate;  $n = 116$ ). The majority of mothers (84%,  $n = 116$ ) had no occupation outside the home. One-half of the fathers were farmers and one-third were salaried employees ( $n = 102$ ). Mean height was 160.3  $\pm$  5.7 cm ( $n = 116$ ) in mothers and mean body mass index was 26.2  $\pm$  5.2 ( $n = 116$ ). Mean birth weight was 3.33  $\pm$  0.45 kg ( $n = 116$ ) and mean birth length was 49.7  $\pm$  2.1 cm ( $n = 116$ , maternity hospital data).

Sanitary conditions were poor in all study areas. Outdoor pipe-borne water was available in all settings except for the Senegalese hamlets, which only had wells. Indoor pipe-borne water was available for a few families in Bolivia and the Congo. Small domestic animals, including chickens, sheep, goats, and pigs lived within the compounds in Senegal, Bolivia, and New Caledonia.

### Subjects

Selection criteria were as follows for the Congo, Senegal, and Bolivia: infants had to be single-born, still being breast-fed and not bottle-fed at 4 mo, have a length-for-age  $\geq -2.5$  Z scores of the National Center for Health Statistics (NCHS) reference, and have a weight-for-length  $\geq -2$  Z scores at 4 mo. They were not to be traveling at 4 mo and parents were to have no plans for emigration from the study area. Mothers had to give their informed, oral consent. In New Caledonia weaned infants were also included because of the small number of eligible infants, but the other inclusion criteria were the same as in the other countries.

Sample size was estimated such that a difference of 0.6 cm in the 4–7-mo length increment would be detected with a type I error of 0.05 and a power of 0.80 with a one-tailed *t* test. The SD of the 4–7-mo length increment was estimated at 1.2 cm on the basis of growth data from the study areas in Senegal and Bolivia. The sample size required was 50 infants/group. The

number of dropouts anticipated because of refusals, deaths, emigration etc, was estimated at 15/group; therefore, 65 subjects/group were considered necessary at inclusion.

In the Congo, 148 of 182 (81%) infants born during the inclusion period were included. In Senegal, 134 of 161 (83%) infants were included. In Bolivia, 160 of 212 (75%) infants were included and in New Caledonia, 116 of 138 (84%) infants were included. Noninclusion was generally due to travel or travel plans (14 in the Congo, 16 in Senegal, and 12 in New Caledonia) or refusal by parents (12 in the Congo, 6 in Senegal, 24 in Bolivia, and 5 in New Caledonia). Some infants could not be included because of a length-for-age  $< -2.5$  Z scores (3 in the Congo, 3 in Senegal, 3 in Bolivia), a weight-for-length  $< -2$  Z scores (1 in the Congo), twins (2 in the Congo and 2 in Senegal), lack of breast-feeding (1 in the Congo), bottle-feeding (21 in Bolivia), unknown date of birth (1 in the Congo and 1 in Bolivia), or hospitalization or illness requiring hospitalization (2 in Bolivia and 4 in New Caledonia).

The study was accepted by all national health authorities, but no specific ethical approval could be obtained because no ethical review committees existed in the different countries at the time of the study. The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983, and oral informed consent was obtained from all mothers of the study infants just before inclusion. Standardized oral information in local languages was followed by discussions among the mother, the principal investigator, and eye witnesses.

### Intervention

The supplement, which was purchased from Nutriset (Malaunay, France) at market price, contained precooked wheat, maize, millet, soybean flour, milk powder, soybean oil, palm oil, and sugar and was enriched with minerals and vitamins (Table 1).

Supplements were given at the infants' homes twice a day, 7 d/wk, by the mothers with the help of female fieldworkers, using preweighed, standard quantities of dry supplement and clean water, both brought by the fieldworker each day. The fieldworkers were in charge of one to seven infants each and went from home to home on foot. At the beginning of each meal they mixed a predetermined quantity of water with the dry supplement in a plastic cup, weighed the ready-made supplement, supervised and counseled the mother while she fed the infant using a teaspoon, and finally weighed the leftovers at the end of the meal. Before eating, infants were dressed with clean bibs, and before weighing leftovers, spillage on the face of the child and on the bib and cloth was added to leftovers. After they were weighed, leftovers were thrown away to avoid delayed consumption by either the infant or other family members because of the high risk of bacterial contamination. No food was given to other members of the family. The time of the meal was noted together with weights of the supplement before and after consumption, and the quantity consumed was estimated as the difference between weights before and after consumption. The timing of the meals varied between countries and between children but each child was fed at about the same time each day, unless the mothers asked for a change to the schedule. The first meal was given from 0800 to 1100 and the second from 1500 to 1900.

Introduction was progressive, with smaller amounts and higher dilutions proposed from 4 to 5 mo [25 g dry supplement

**TABLE 1**

Energy and nutrient contents of the supplement (per 100 g dry wt)

Energy	
(MJ)	1.7
(kcal)	410
Protein (g)	9
Lipids (g)	10
Carbohydrates (g)	67
Acid detergent fibers (g)	1.2
Phytates (g)	0.5
Calcium (mg)	800
Phosphorus (mg)	400
Potassium (mg)	400
Magnesium (mg)	100
Iron (g)	9
Copper (g)	1
Manganese (mg)	2
Zinc (mg)	8
Iodine ( $\mu\text{g}$ )	100
Selenium ( $\mu\text{g}$ )	11
Vitamin A	
( $\mu\text{g}$ )	390
(IU)	1300
Vitamin D	
( $\mu\text{g}$ )	1.25
(IU)	50
Vitamin E	
(mg)	5.4
(IU)	8
Vitamin C (mg)	30
Thiamine (mg)	0.8
Riboflavin (mg)	0.8
Vitamin B-6 (mg)	0.5
Vitamin B-12 ( $\mu\text{g}$ )	1.5
Niacin (mg)	10
Folic acid ( $\mu\text{g}$ )	125
Pantothenic acid (mg)	2.5

in 75 mL water per meal, ie, 429 kJ (103 kcal) in 100 g] than from 5 to 7 mo [50 g supplement and 135 mL water per meal, ie, 858 kJ/d (205 kcal) in 185 g].

### Anthropometry

Anthropometric measurements were taken at 4 mo ( $\pm 7$  d) and 4, 8, and 13 wk later, ie, at 4.9, 5.8, and 7.0 mo of age, hereafter referred to as 4, 5, 6, and 7 mo. In New Caledonia, where the last measurements were taken at 7.2 mo, length and weight at the age of 7.0 mo were estimated by linear interpolation. Recumbent length was measured three times at each visit with a Holtain infantometer (Holtain Limited, Crymch, United Kingdom; resolution: 0.1 cm) and the mean of measurements was used for analysis. If two measurements differed by  $> 0.5$  cm, a fourth measurement was taken and the outlier discarded. The infants were weighed naked on a baby scale (Seca, Hamburg, Germany; resolution: 10 g). Measurements were taken in the children's homes in the Congo, Senegal, and New Caledonia. In Bolivia, where weighing of the naked child required a heating system because of the cold climate, measurements were made at the local health clinic. There was one anthropometrist and one assistant at each setting; intercountry reliability was not assessed. The technical error of length measurements, using  $r \sqrt{(\sum d^2/2N)}$  (8) and the first two mea-



surements of each series of three at the age of 4 mo, was 0.21 cm in the Congo, 0.17 cm in Senegal, 0.09 cm in Bolivia, and 0.21 cm in New Caledonia.

### Diet

Consumption of complementary foods other than the supplement was evaluated weekly in the Congo, Bolivia, and New Caledonia by using qualitative 24-h recalls. In Senegal, the recalls were only done monthly for practical reasons. The mothers were asked whether the child had consumed 1) breast milk, 2) special local infant food, 3) commercial "Western" baby food other than the supplement, 4) milk substitutes, 5) family food, 6) water, and other liquids except for milk.

### Analysis

Randomization was done immediately after inclusion of each infant by drawing lots. Predefined criteria for exclusion from the study were death of the infant or mother, severe illness that might affect nutritional status, refusal to continue participation, missed measurements, or lack of supplementation for > 7 d. During the study, a mean of 19.9% of infants dropped out (Table 2). More supplemented infants than control infants dropped out, especially in the Congo (75%) and in New Caledonia (67%), because their parents refused to continue participation. In Senegal, one infant was excluded because of measles and one because of pertussis, whereas one in New Caledonia was excluded because of gastroesophageal reflux. Excluded infants did not differ from the infants included in the analysis in terms of age, sex, nutritional status at inclusion, education levels, occupation, or nutritional status of parents.

Data processing was done with EPI-INFO or DBASE III, whereas statistical analyses was done by using SAS (SAS Institute Inc, Cary, NC) and BMDP (BMDP Statistical Software, Los Angeles). Growth increments were standardized to exact monthly and 3-mo intervals. Statistical analysis used chi-square test, *t* tests, and sign test.

## RESULTS

One hundred twenty infants in the Congo, 110 in Senegal, 127 in Bolivia, and 90 in New Caledonia were used for the

analysis (Table 2). Thus, the required minimal number of infants per group, 50, was attained in all settings except New Caledonia.

Consumption of the supplement varied among individuals, among weeks of supplementation, and among settings. Mean daily intakes and SDs over the total period of supplementation were 790 ± 452 kJ/d (189 ± 108 kcal) in the Congo, 558 ± 194 kJ/d (133 ± 47 kcal) in Senegal, 672 ± 261 kJ/d (161 ± 62 kcal) in Bolivia, and 669 ± 293 kJ/d (160 ± 70 kcal) in New Caledonia. Mean daily intake by week of supplementation and by country is shown in Figure 1. Most infants consumed higher amounts of supplement from 5 mo of age because the amount of supplement offered was doubled (Congo: 40 of 53 infants, *P* < 0.001 according to the sign test; Senegal: 47 of 53, *P* < 0.001; Bolivia: 61 of 65, *P* < 0.001; New Caledonia 39 of 43, *P* < 0.001). During the first month (weeks 1–4), infants in Bolivia consumed small amounts of supplements (374 ± 154 kJ/d) whereas infants in the Congo consumed large amounts (632 ± 135 kJ/d). From week 5, the lowest consumption was in Senegal (619 ± 230 kJ/d) and the highest was in the Congo (858 ± 305 kJ/d). However, large variations among individuals were noted in all countries. The maximum individual value of consumption was the total amount offered (858 kJ/d from weeks 1 to 4 and 1716 kJ/d from weeks 5 to 13) in all countries and for all weeks, whereas the lowest individual values of weekly consumption were very low (≈100–200 kJ/d) because of illness, anorexia, or short (< 8 d) absences from home.

Feeding patterns were described by means of 24-h recalls. Breast-feeding was required for inclusion in the Congo, Senegal, and Bolivia, and all infants were still breast-fed at the age of 7 mo. As noted above, weaned children were also included in New Caledonia. At inclusion, 67% were breast-fed whereas 47% were still breast-fed at 7 mo (51% of supplemented infants and 43% of control infants). However, no infants were exclusively breast-fed in any country because all received water in addition to breast milk from the age of 4 mo. Bottle-feeding was virtually unknown in Senegal, seldom observed in the Congo, more frequent in Bolivia (12% at age 6 mo), and prevalent in New Caledonia (73% at age 6 mo).

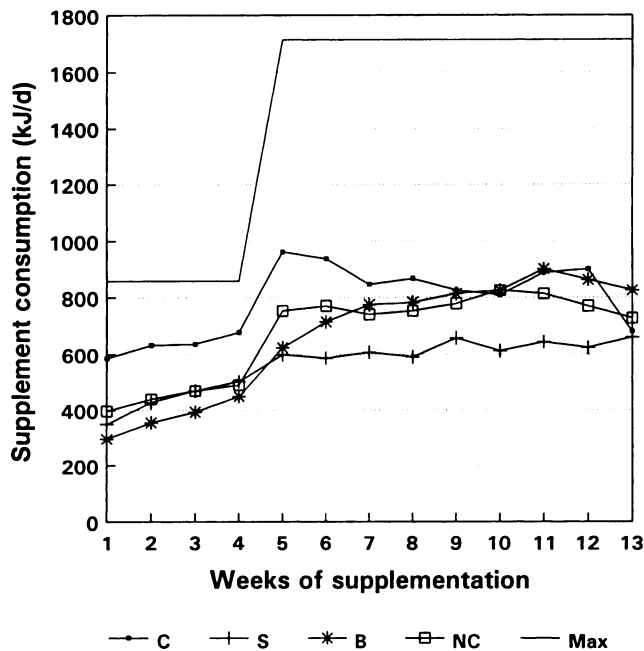
The type of local food given varied among countries. In the Congo, infants were mainly fed specific weaning food, ie,

**TABLE 2**

Number of supplemented and control infants excluded and in the analysis among included infants, by group, reason for exclusion, and country

Country and group	Included	Analysis	Excluded				
			All <sup>1</sup>	Death	Refusal	Absence	Illness
<b>Congo</b>							
Supplemented	74	53	21 [28]	2	12	7	0
Control	74	67	7 [9]	1	0	6	0
<b>Senegal</b>							
Supplemented	66	53	13 [20]	2	7	3	1
Control	68	57	11 [16]	3	2	5	1
<b>Bolivia</b>							
Supplemented	78	65	13 [17]	0	9	4	0
Control	82	62	20 [24]	0	15	5	0
<b>New Caledonia</b>							
Supplemented	63	43	20 [32]	0	8	11	1
Control	53	47	6 [11]	0	0	6	0

<sup>1</sup> Percentage in brackets.



**FIGURE 1.** Mean daily consumption of the supplement by supplemented infants in the Congo (C,  $n = 53$ ), Senegal (S,  $n = 53$ ), Bolivia (B,  $n = 65$ ), and New Caledonia (NC,  $n = 43$ ), with the total amount offered (max), by week of supplementation.

maize or cassava gruel (88% of control infants at 6 mo), either homemade or purchased. In Senegal, the family diet based on millet or rice was predominant from 6 mo (72% of control infants at 6 mo), whereas millet gruel was given to one-third of the children (31%). In Bolivia, infants were fed mainly soups and broth (79%) and mashed fruit and potatoes (65%). In New Caledonia, main food items were tubers (potatoes, sweet potatoes, and yam), rice and fruit.

At the age of 4 mo, almost all infants in the Congo had been given local food the preceding day, whereas few infants had received local food in the other countries (Table 3). No significant differences in feeding patterns were noted between groups before the start of supplementation (4 mo). The proportion of control children who had eaten local food increased rapidly with age in Senegal, Bolivia, and New Caledonia. Supplementation modified feeding patterns in the Congo and Senegal in that during the supplementation period (at 5 and 6 mo), fewer supplemented infants had received local additional food the preceding day, compared with control subjects. During the last days of supplementation (7 mo), almost all supplemented infants in the Congo and Senegal received local food, probably because mothers had been advised to introduce local food before the end of supplementation. In Bolivia and New Caledonia, supplemented infants appeared to have eaten local food as often as did control infants.

Growth patterns also varied from one country to another. In the control infants, growth in recumbent length in the Congo, Senegal, and Bolivia exhibited various degrees of retardation by as early as 4 mo (Figure 2). Infants were shortest in Bolivia, followed by Senegal, and then the Congo, whereas mean length was very similar to the NCHS reference in New Caledonia. Faltering continued during the study period. The mean weight-for-length of control infants was above the reference in all

**TABLE 3**

Prevalence of consumption of local additional food by supplemented and control infants

Country and age	Supplemented	Control
	%	
Congo		
4 mo	92.4	89.5
5 mo	58.8	95.5 <sup>1</sup>
6 mo	61.7	98.5 <sup>1</sup>
7 mo	91.7	95.3
Senegal		
4 mo	28.3	28.1
5 mo	20.8	40.4 <sup>2</sup>
6 mo	45.3	77.2 <sup>1</sup>
7 mo	80.8	75.4
Bolivia		
4 mo	18.8	27.4
5 mo	63.3	80.0
6 mo	90.2	90.0
7 mo	98.3	98.3
New Caledonia		
4 mo	26.7	40.8
5 mo	57.5	68.6
6 mo	79.2	88.8
7 mo	80.8	93.5

<sup>1,2</sup> Significantly different from supplemented infants (chi-square test): <sup>1</sup>  $P < 0.001$ , <sup>2</sup>  $P < 0.05$ .

countries at 4 mo, being highest in Bolivia, followed by New Caledonia, the Congo, and Senegal (Figure 2). In Senegal only, weight-for-length decreased sharply during the study period and was below the reference at 7 mo. The mean weight-for-age was above the reference in New Caledonia and close to the reference in the other three countries at 4 mo (results not shown). In conclusion, Bolivian infants were the shortest and heaviest, considering their length; Senegalese infants were both short and thin; Congolese infants were rather short but not thin; and New Caledonian infants were neither short nor thin.

At the age of 4 mo, just before supplementation began, supplemented and control infants did not differ significantly in weight or length in any country. However, some nonsignificant differences were observed. In Senegal, the mean length of supplemented infants tended to be lower than the mean length of control infants (Table 4). In New Caledonia, mean recumbent length tended to be higher for supplemented infants.

On the basis of monthly increments in recumbent length (Table 5), supplemented infants grew faster than control infants from 4 to 5 mo in Senegal ( $P < 0.01$ ) and from 5 to 6 mo in Bolivia ( $P < 0.01$ ). The 4–7-mo length increment differed significantly between groups in Senegal only (+0.48 cm,  $P = 0.021$ ). However, the higher growth rate of supplemented infants from 4 to 7 mo did not result in a higher mean length at the age of 7 mo because control infants tended to be longer than supplemented infants at 4 mo (–0.58 cm,  $t = 1.31$ ).

In the Congo, supplemented infants tended to be lighter in weight than control infants from age 4 mo (Table 6), and the difference increased from 5 to 6 mo, at which time the supplemented infants gained significantly less weight than the control subjects ( $P < 0.01$ , Table 7). The mean weight of supplemented infants was significantly lower than the mean weight of control infants at 6 and 7 mo. In Senegal, Bolivia, and New

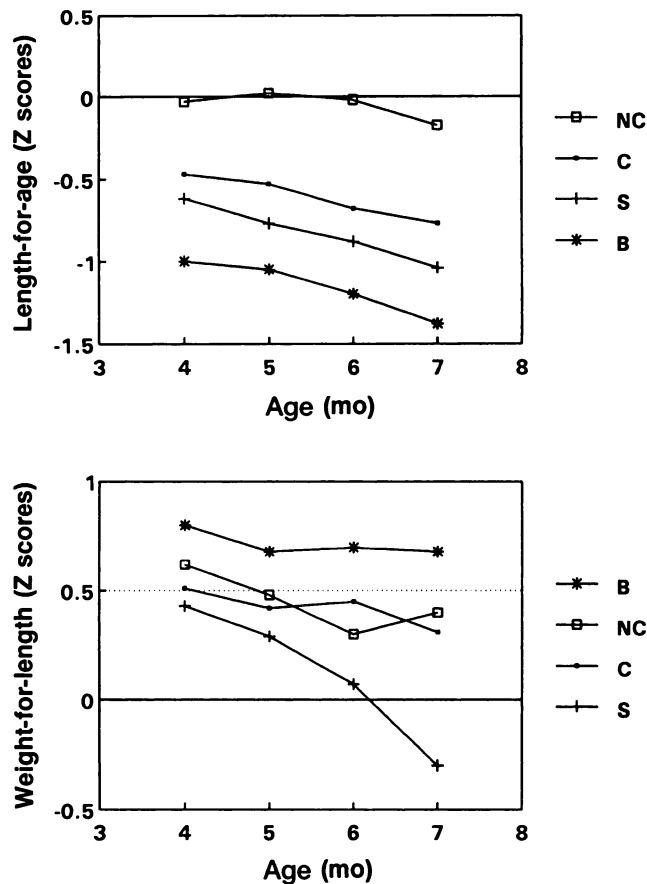


FIGURE 2. Mean length-for-age and weight-for-length Z scores of control infants in the Congo (C,  $n = 67$ ), Senegal (S,  $n = 57$ ), Bolivia (B,  $n = 62$ ), and New Caledonia (NC,  $n = 47$ ).

Caledonia, the mean weights were not different between groups during the study period. Supplemented infants tended to gain slightly more weight than control infants from 4 to 5 mo (60–80 g) in all three countries whereas control infants gained slightly more over the following months. As a result, the 4–7-mo weight increments were not different between groups in any of the four countries (Table 7).

## DISCUSSION

Nutritional supplementation had a significant effect of +0.48 cm on growth in length in Senegalese infants from 4 to 7 mo; no significant effects on growth in length in the Congo, Bolivia, and New Caledonia; and no effect on growth in weight in any country.

The study was conducted to assess the effect of nutritional supplementation on linear growth mainly. The 4–7-mo age interval is of particular interest because it is the age at which additional food is introduced to breast-fed infants and because the effect of supplementation on growth was found to be greatest during the 3–6 mo interval in previous supplementation trials (4, 7). Because it is not recommended that additional food be introduced before the age of 4 mo (9), the 4–7-mo age interval was chosen. Supplementation was continued until the age of 7 mo, an age at which virtually all infants receive daily complements in the studied countries. Comparison of mean

TABLE 4  
Recumbent length of supplemented and control infants, by age and country<sup>1</sup>

Country and age	Supplemented	Control	Difference <sup>2</sup>
<i>cm</i>			
Congo			
4 mo	61.36 ± 2.34	61.66 ± 2.23	-0.30
5 mo	63.16 ± 2.32	63.53 ± 2.33	-0.37
6 mo	64.56 ± 2.43	64.92 ± 2.44	-0.36
7 mo	66.09 ± 2.54	66.54 ± 2.51	-0.45
Senegal			
4 mo	60.59 ± 2.31	61.17 ± 2.07	-0.58
5 mo	62.69 ± 2.24	62.74 ± 2.13	-0.05
6 mo	63.93 ± 2.29	64.22 ± 2.09	-0.29
7 mo	65.63 ± 2.37	65.75 ± 2.77	-0.12
Bolivia			
4 mo	60.55 ± 1.76	60.25 ± 1.95	+0.30
5 mo	62.41 ± 1.76	62.22 ± 1.96	+0.19
6 mo	64.03 ± 1.78	63.48 ± 1.95	+0.55
7 mo	65.46 ± 1.91	64.94 ± 1.95	+0.52
New Caledonia			
4 mo	63.04 ± 1.95	62.55 ± 1.99	+0.49
5 mo	65.19 ± 2.23	64.80 ± 1.93	+0.39
6 mo	67.05 ± 2.39	66.49 ± 2.21	+0.56
7 mo	68.63 ± 2.42	68.07 ± 2.11	+0.56

<sup>1</sup>  $\bar{x} \pm SD$ .

<sup>2</sup> Supplemented minus control.

monthly length velocity of control infants to two reference populations, the NCHS reference (10) and a recent Danish reference (11) show that whereas length velocity was normal or close to normal in the Congo, Bolivia, and New Caledonia from 4 to 5 mo, it fell below the two references from 5 mo in the Congo and Bolivia, and from 6 mo in New Caledonia (Table 5). In Senegal, length velocity was lower than the references beginning at 4 mo. The NCHS reference is often considered inadequate for breast-fed infants because it is based on data from infants born a long time ago who were mainly bottle-fed and received complementary food early in life (12). The Danish reference is recent and composed of a high proportion of infants breast-fed over long periods (13).

Wasted children (weight-for-length < -2 Z scores) were not included in the study for obvious ethical reasons (they required supplements) but in 4-mo-old breast-fed infants, the prevalence of wasting was very low (only one infant was not included because of wasting). The prevalence of stunting (length-for-age < -2 Z scores) was higher than that of wasting, and 17 stunted infants were included in the study: 4 (3.3%) in the Congo, 5 (4.5%) in Senegal, and 8 (6.3%) in Bolivia. However, nine infants with a very low length-for-age (< -2.5 Z scores) were not included to avoid severely premature or short-for-term infants and chromosomal disorders. In Senegal, one of the three infants with a length-for-age < -2.5 Z scores had Down syndrome.

Initial comparability between groups was obtained through randomization similar to that in controlled clinical trials, but comparability of groups during the course of the study was not complete. First, the study was not blind because no placebo was given to the control infants. It was decided not to give any low-energy placebo-like supplement to the control group because of the possible risk of limiting their consumption of



TABLE 5

Total 4–7-mo increment and monthly increments in recumbent length of supplemented and control infants<sup>1</sup>

Country and age	Supplemented	Control	Difference <sup>2</sup>
<i>cm</i>			
Congo			
4–7 mo	4.75 ± 0.92	4.90 ± 1.26	–0.15
4–5 mo	1.90 ± 1.06	2.02 ± 1.02	–0.12
5–6 mo	1.51 ± 0.94	1.52 ± 1.17	–0.01
6–7 mo	1.36 ± 0.62	1.44 ± 0.78	–0.08
Senegal			
4–7 mo	5.03 ± 1.21	4.55 ± 0.94	+0.48 <sup>3</sup>
4–5 mo	2.30 ± 0.82	1.72 ± 0.86	+0.58 <sup>4</sup>
5–6 mo	1.33 ± 0.75	1.61 ± 0.81	–0.28
6–7 mo	1.46 ± 0.67	1.30 ± 0.58	+0.16
Bolivia			
4–7 mo	4.89 ± 0.83	4.64 ± 0.90	+0.25
4–5 mo	1.97 ± 0.76	2.08 ± 0.68	–0.11
5–6 mo	1.80 ± 0.79	1.39 ± 0.87	+0.41 <sup>4</sup>
6–7 mo	1.25 ± 0.66	1.25 ± 0.56	0.00
New Caledonia			
4–7 mo	5.47 ± 1.38	5.42 ± 1.27	+0.05
4–5 mo	2.32 ± 1.22	2.42 ± 1.14	–0.10
5–6 mo	2.03 ± 1.12	1.85 ± 1.10	+0.18
6–7 mo	1.39 ± 0.74	1.38 ± 0.87	+0.01

<sup>1</sup>  $\bar{x} \pm$  SD. Reference means of increments for both sexes combined (cm/mo): 4–5 mo, 2.03 (10) and 2.12 (11); 5–6 mo, 1.83 (10) and 1.81 (11); and 6–7 mo, 1.68 (10) and 1.58 (11).

<sup>2</sup> Supplemented minus control.

<sup>3,4</sup> Significantly different from supplemented infants (*t* tests): <sup>3</sup>  $P < 0.05$ , <sup>4</sup>  $P < 0.01$ .

nutritious food and thus deteriorating their nutritional status. Second, the study design required closer contact with the mothers of supplemented infants because of daily visits by fieldworkers in charge of supplementation, and it has been suggested that contact between mothers and a research team may in itself give some advantages to children in developing countries (14). However, fieldworkers visited the homes of control infants weekly, thus both groups had regular contact with the research team.

Amounts of supplement consumed were large in the Congo and small in Bolivia during the first weeks of supplementation, probably because of differences in traditional feeding patterns in these settings. In the Congo all infants had already been given complements by the age of 4 mo, compared with only 19% in Bolivia. The mean age at which weaning food is introduced is 2–3 mo in urban areas of the Congo (15) with several feedings a day, and previous studies in Brazzaville have shown that at the age of 4–5 mo, mean breast milk intake is only 460 ± 191 g/d in infants receiving no formula (mean number of breast-feedings: 7.6 ± 2.4; M-C Dop, unpublished observations, 1995). From the age of 5 mo, consumption of the supplement was lower in Senegal than in the other countries, possibly because of cultural differences in the mother-infant relation because children are not forced to eat more than at will in West Africa (16). However, the fieldworkers in charge of supplementation helped the mothers to assess whether their infants were fed to satiety, so other factors were probably involved.

TABLE 6

Weight of supplemented and control infants, by age and country<sup>1</sup>

Country and age	Supplemented	Control	Difference <sup>2</sup>
<i>kg</i>			
Congo			
4 mo	6.21 ± 0.83	6.46 ± 0.87	–0.25
5 mo	6.64 ± 0.89	6.95 ± 0.95	–0.31
6 mo	6.92 ± 0.93	7.38 ± 1.01	–0.46 <sup>3</sup>
7 mo	7.37 ± 0.96	7.74 ± 1.07	–0.37 <sup>3</sup>
Senegal			
4 mo	6.25 ± 0.79	6.26 ± 0.84	–0.01
5 mo	6.68 ± 0.79	6.61 ± 0.80	+0.07
6 mo	6.89 ± 0.81	6.88 ± 0.80	+0.01
7 mo	7.09 ± 0.91	7.06 ± 0.87	+0.03
Bolivia			
4 mo	6.16 ± 0.66	6.23 ± 0.63	–0.07
5 mo	6.71 ± 0.72	6.72 ± 0.68	–0.01
6 mo	7.10 ± 0.74	7.11 ± 0.66	–0.01
7 mo	7.48 ± 0.77	7.51 ± 0.70	–0.03
New Caledonia			
4 mo	6.85 ± 0.90	6.79 ± 0.81	+0.06
5 mo	7.44 ± 0.97	7.32 ± 0.84	+0.12
6 mo	7.78 ± 0.98	7.71 ± 0.94	+0.07
7 mo	8.16 ± 0.97	8.17 ± 0.96	–0.01

<sup>1</sup>  $\bar{x} \pm$  SD.

<sup>2</sup> Supplemented minus control.

<sup>3</sup> Significantly different from supplemented infants,  $P < 0.05$  (*t* tests).

In Senegal, supplemented infants showed a significantly higher mean 4–7-mo length increment compared with control infants. But length at the age of 7 mo was not different between the two groups because length at the age of 4 mo tended to be lower for supplemented infants. Therefore, it may be argued that the higher growth rate of supplemented infants was due to a higher growth potential of shorter infants and not to supplementation.

The higher length increment of supplemented infants was due to a higher growth rate during the first month of supplementation only, although faltering was obvious from 5 to 7 mo and although most infants consumed higher amounts of supplement from 5 mo than before 5 mo. Another important finding is that only linear growth, not weight, was significantly improved in Senegal. In 6–20-mo-old nonselected children from Indonesia, 3 mo of supplementation had a significant positive effect on weight only (17). It can be speculated that one or several nutrients, which limited skeletal growth in control infants and which was provided by the supplement, might have been responsible for the positive effect in Senegal rather than the energy intake (18).

Why did daily consumption of a mean of 669–790 kJ/d, with high amounts of protein, minerals, and vitamins, have no positive effect on growth in either the Congo, Bolivia, or New Caledonia? First, the statistical power of the study might have been insufficient to detect small effects. The study was conceived to detect effects from 0.6 cm with a power of 0.80. Given the actual sample sizes and observed SDs, the smallest effect that would have been detectable with this power was estimated to be 0.51 cm in the Congo, 0.38 cm in Bolivia, and 0.70 cm in New Caledonia. Second, the growth pattern of the Caledonian control infants was not very different from the references, so the food intake of control infants might have



TABLE 7

Total 4–7-mo increment and monthly increments in weight of supplemented and control infants<sup>1</sup>

Country and age	Supplemented	Control	Difference <sup>2</sup>
	<i>kg</i>		
Congo			
4–7 mo	1.17 ± 0.46	1.29 ± 0.49	–0.12
4–5 mo	0.46 ± 0.34	0.52 ± 0.28	–0.06
5–6 mo	0.30 ± 0.34	0.47 ± 0.28	–0.17 <sup>3</sup>
6–7 mo	0.41 ± 0.30	0.32 ± 0.28	+0.09
Senegal			
4–7 mo	0.84 ± 0.58	0.79 ± 0.41	+0.05
4–5 mo	0.47 ± 0.34	0.39 ± 0.23	+0.08
5–6 mo	0.22 ± 0.34	0.29 ± 0.24	–0.07
6–7 mo	0.18 ± 0.30	0.15 ± 0.24	+0.03
Bolivia			
4–7 mo	1.31 ± 0.34	1.26 ± 0.35	+0.05
4–5 mo	0.58 ± 0.30	0.52 ± 0.18	+0.06
5–6 mo	0.43 ± 0.25	0.43 ± 0.20	0
6–7 mo	0.32 ± 0.16	0.34 ± 0.15	–0.02
New Caledonia			
4–7 mo	1.29 ± 0.43	1.37 ± 0.39	–0.08
4–5 mo	0.63 ± 0.30	0.57 ± 0.22	+0.06
5–6 mo	0.37 ± 0.27	0.43 ± 0.25	–0.06
6–7 mo	0.34 ± 0.16	0.41 ± 0.22	–0.07

<sup>1</sup>  $\bar{x} \pm$  SD. Reference means of increments for both sexes combined: 4–5 mo, 0.54 (10) and 0.57 (11); 5–6 mo, 0.47 (10) and 0.50 (11); and 6–7 mo, 0.42 (10) and 0.44 (11).

<sup>2</sup> Supplemented minus control.

<sup>3</sup> Significantly different from supplemented infants,  $P < 0.01$  ( $t$  tests).

been close to requirements and thus explain the absence of effect in that country.

Low consumption of the supplement can hardly be responsible for the lack of effect in the Congo, Bolivia, and New Caledonia because the amount of supplementation was rather high for otherwise breast-fed infants. The mean daily intake was 669–790 kJ, ie, 153–181 g wet wt, which is 27–31% of energy requirements at the age of 6 mo (602 kcal/d (2520 kJ/d) (19). For comparison, the Senegalese infants consumed 558 kJ/d (22% of requirements) and supplemented infants in the INCAP (Instituto de Nutrición de Centro America y Panamá) Study in Guatemala had a mean daily intake of 334 kJ/d at the age of 6 mo, considering only participants (3). In the present study, consumption might have been higher if mothers had been able to offer the supplement at will, ie, at any time of the day, without the presence of the fieldworker. However, as stated above, hygienic handling of the supplement and information concerning the amounts consumed were major objectives in the present study, and the low education levels of most mothers did not enable them to attain these objectives by themselves.

Lack of effect in three of four countries may have been due to replacement of either local additional food and/or breast milk by the supplement. In the Congo, the supplement probably replaced some local food because more supplemented infants than control infants had no local food at 5 and 6 mo, but this was also the case in Senegal. In Bolivia and New Caledonia, proportions of supplemented and control infants fed local food were not significantly different, but supplemented infants may have consumed smaller amounts of food because no quantita-

tive information on dietary intake was available. No data on breast milk intake were available either, so the supplement might have replaced breast milk as was shown for 4–6-mo-old breast-fed infants in Honduras (5). If replacement occurred in this study, it may have been due to both social and biological factors. Social factors could be time- and money-saving strategies adopted by the mother of a supplemented child, such as breast-feeding less often or giving fewer meals or smaller amounts of other foods. The main possible biological factor would be the incapacity of the infant to consume higher total amounts of food than consumed before supplementation.

If some breast milk is replaced, supplemented infants are likely to have lower energy and nutrient intakes than control infants, especially during illness. Studies in Peru (20) and Indonesia (21) have highlighted the negative effect of fever and diarrhea on intake of non-breast-milk foods, and the absence of effect on breast-milk consumption.


It is unlikely that increased prevalences of morbidity in supplemented infants should be the reason for the lack of effect of supplementation, because great care was taken to avoid contamination of the supplement. However, because morbidity was monitored, this hypothesis will be tested.

A last hypothesis is that growth is not sensitive to higher intakes of either energy or nutrients during the particular age range under study, or that the effect on growth appeared later, after the age of 7 mo. Some authors assume that early postnatal growth is mainly determined by antenatal growth (22). In older age groups of malnourished children, a positive effect of supplementation on linear growth was described, eg, in 9–24-mo-old stunted children in Jamaica after 6 mo of supplementation (6).

The results of this study as well as the results of a recent trial in Honduras (5) disagree with earlier studies that suggested a rather strong, positive effect of supplementation on growth in both length and weight before the age of 6 mo: a recent age-specific reanalysis of the supplementation trial in Bogota, Colombia, found a 0.6-cm higher length increment and a 0.162-kg higher weight increment from the age of 3–6 mo in supplemented infants (4). However, the mothers of the infants had also been supplemented during pregnancy and lactation, and consumption of the supplement by the infants was not documented. It was remarkable that growth in length and weight significantly improved from birth to 3 mo, from 3 to 6 mo, and thereafter from 9 mo, whereas no effect on either weight or length was observed from 6 to 9 mo. The effect on growth from 0 to 6 mo might thus be explained partly by maternal supplementation, whereas supplementation of the infant would account for improved growth from the age of 9 mo. In the INCAP Study in rural Guatemala, supplementation from the age of 3 mo had a positive effect on the height and weight status at the age of 3 y (23, 24), but age-specific effects during infancy were not assessed.

In conclusion, the effect of nutritional supplementation on growth in length was modest, but significant, in one country (Senegal) and not significant in the three other countries (the Congo, Bolivia, and New Caledonia). The significant effect on growth in length was found in the country where length and weight increments were lowest, although this was also the country where mean consumption of the supplement was lowest. Further studies are needed to assess the degree of replacement of the usual diet by a supplement, the food items replaced,



and the reasons for replacement in partially breast-fed infants. These questions are important in terms of public health, in particular for nutritional interventions such as food-supplementation programs. 

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