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Flavor experiences during formula feeding are related to preferences during childhood

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Abstract

As part of a program of research designed to investigate the long-term effects of early feeding experiences, the present study exploited the substantial flavor variation inherent in three classes of commercially available infant formulas and determined whether flavor preferences during childhood differed as a function of the class of formula (i.e., milk, soy, hydrolysate) that 4- to 5-year-old children were fed during their infancy. Age appropriate, game-like tasks that were fun for children and minimized the impact of language development were used to examine their preferences for a wide range of food-related odor qualities including infant formulas, as well as the flavor of milk-based and hydrolysate formulas and plain, sour- and bitter-flavored apple juices. Formula type influenced children's flavor preferences when tested several years after their last exposure to the formula. When compared to children who were fed milk-based formulas ($n = 27$), children fed protein hydrolysate formulas ($n = 50$) were more likely to prefer sour-flavored juices, as well as the odor and flavor of formulas, and less likely to make negative facial expressions during the taste tests. Those fed soy formulas ($n = 27$) preferred the bitter-flavored apple juice. That the effects of differential formula feeding also modified children's food preferences is suggested by mothers' reports that children fed hydrolysate or soy formulas were significantly more likely to prefer broccoli than were those fed milk formulas. These data are consistent with the hypothesis that flavor experiences influence subsequent flavor preferences even several years following the early experience.

Keywords

Taste; Smell; Protein hydrolysate formula; Children; Preferences

1. Introduction

Although there is considerable speculation that early flavor experiences influence later food and flavor preferences in humans, much of the published research, which is not extensive, fails to provide strong evidence for such effects (reviews: Refs. [1,2]). For example, similarities in food preferences between children and their parents or siblings are often small or non-existent [3–6]. However, these studies are far from definitive since developmental differences in sensory perceptive behaviors between parent and offspring could obscure similarities in response as a function of shared experience. Perhaps a comparison of parent and offspring would result in substantial similarity if individuals were to be tested when the same age. In addition, most of the studies assessed preferences for food items, rather than flavors. In the

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former case, differences between children and adults, independent of experiential variables, could mask effects of common early flavor experiences.

We hypothesize that if there is an effect of early experience on later preference, it would involve flavors, not specific foods since experimental animal model studies demonstrate that early experiences with odors, a major component of flavor, in specific nursing-like contexts, results in long-term preferences [7–10]. Consistent with these findings, our prior research in humans has shown that, at least over the short-term, flavor experiences in amniotic fluid and mothers' milk, resulting from flavors transmitted from the mothers' diet, modify and serve to establish preferences [11,12].

A *prima facie* case for the importance of early flavor experience on long-term preference can be made from observations on culture-based flavor principles. It has been said that food habits and preferences are among the last characteristic of a culture that is lost during the immigration of an individual or group into a new culture [13]. Assuming there is truth to this generalization, why has past experimental and observational research on children's food habits largely failed to find strong effects of early exposure on later preferences and acceptance? We suggest that what is missing to adequately test this hypothesis is a model system where there are profound, controlled differences in early flavor experiences. Further, a research paradigm is needed to examine the flavor components (not just the foods) of that early experience and how they impact on later flavor likes and dislikes. Finally, such research should assess children's preferences directly because the mothers' accounts of their children's preferences are often inaccurate and biased [14].

As part of a program of research designed to investigate the long-term effects of early feeding experiences, the present study exploited the substantial flavor variation inherent in three classes of commercially available infant formulas experienced by infants: traditional milk-based formulas, formulas based on soy proteins, and those based on hydrolyzed proteins [15]. Although the flavor of each brand has its own characteristic profile, milk-based formulas are often described as having low levels of sweetness and 'sour and cereal-type' whereas soy-based formulas are described as tasting sweeter, more sour and bitter and having a relatively strong 'hay/beany' odor [16]. More obvious, to adults at least, is the extremely unpalatable, offensive taste and off odor of the hydrolysate formulas due primarily to its sourness and bitterness, perhaps because many amino acids taste sour or bitter [17], and to its unique volatile profile. In the study described herein, we evaluated the responses of 4- to 5-year-old children to a range of flavor and odor stimuli as a function of their prior experiences with these classes of formulas.

2. Methods

2.1. Subjects

Mothers of healthy, 4- to 5-year-old children were recruited from advertisements in local newspapers. Three groups of children ($n = 102$) were formed based on their early feeding history. Children in Group 1 were fed a milk-based formula exclusively during infancy ($n = 27$), those in Group 2 were fed a soy-based formula ($n = 25$), whereas Group 3 were fed protein hydrolysate formulas ($n = 50$). There were no significant differences among the groups in the number of months that these children were fed formula during their infancy ($F(2,99df) = 0.06$; $p = 0.94$; see Table 1). However, as expected, those children who were fed hydrolysate formulas often fed a milk- or soy-based formula during the first months (1.6 ± 0.2) of life and then, usually following their pediatrician's recommendation, switched to hydrolysate which they fed until they were, on average, $13.6 (\pm 0.7)$ months of age. The vast majority of children in the hydrolysate group (84%) began feeding this type of formula during the first 3 months of life. Likewise, 32% of those fed soy formulas fed milk-based formula during the first month (0.7

± 0.2) of life before being switched to soy; the remainder had fed soy formula from birth. None of the children who were fed milk-based formulas were ever fed soy or hydrolysate formulas and none of the child who were fed soy formulas ever experienced hydrolysates. Moreover, none of the children were fed any other type of formula (e.g., Pregestimil) in the neonatal period. All children were reported by their mothers to be healthy at the time of testing. Only one child was currently on medication (i.e., Claritin).

Salient characteristics of the three groups of children are listed in Table 1. There were no significant differences among the groups in the age of the mothers ($F(2,99df) = 1.11, p = 0.33$) and children ($F(2,99df) = 1.15, p = 0.32$), or in the body mass index ($F(2,89df) = 1.30, p = 0.28$) and ethnicity ($\chi^2 (4df) = 6.39; p = 0.17$) of the children. Nor was there any significant effect of the children's sex on any of the variables tested. The procedures used in this study were approved by the Office of Regulatory Affairs at the University of Pennsylvania and informed consent was obtained from each mother prior to testing.

2.2. Testing procedures

Using methodology developed by Schmidt and Beauchamp [18], we determined preferences for a wide range of nasally assessed food-related odors including those of infant formulas, as well as the orally assessed flavor of milk-based and hydrolysate formulas and differently flavored apple juices. Children were told that they were going to play a “taste and smell” game. If they liked the smell inside the bottle or the taste inside the cup, then they should give it to a stuffed toy of Big Bird™ (a likeable, well-known television character puppet), but if they do not like the smell or taste, they should give it to another well-known puppet, Oscar the Grouch™, “so that he can throw it in his trash can.” Prior to the actual testing and after the child acclimated to the room and personnel, the experimenter ascertained whether the child comprehended the task by asking him or her to point to the character who should receive a series of imagined liked and disliked items. Nine children were excluded because they could not understand the task.

Testing took place in a closed room specifically designed for sensory testing with a high air-turnover ventilation system. Each child sat at a small table designed especially for children on which the two Sesame Street character toys, Big Bird™ and Oscar the Grouch™ were placed; the side of the table (right versus left) that the characters were positioned was randomized. The mothers, who were unaware of the hypothesis being testing, completed questionnaires about their child's feeding habits and preferences (see below) and sat approximately 2 ft behind the child, out of view. This distance was chosen because previous work in our laboratory revealed that individuals could not smell the contents of the squeeze bottles when seated this far away from the odor source. Mothers were asked to refrain from talking during the testing session, which was confirmed by replays of videotapes. In addition, virtually every mother reported at the end of testing that they were not aware of, nor could they identify, any of the odors in the squeeze bottles or the different flavors of the juices.

On the first day of testing, we determined the child's preferences for a wide range of odors as well as the flavor of differently flavored apple juices. The odors, approximately matched for perceived intensity by adults, included: a milk-based formula (Enfamil, 3 ml; Mead Johnson, Evansville, IN); protein hydrolysate formula (Nutramigen 3 ml; Mead Johnson; Alimentum, 3 ml; Ross Products Division; Columbus, OH); pyridine (a sour milk-like odor; 3 ml of a 0.03% solution); bubble gum (3 ml of a 0.05% solution); and citral (a lemon odor; 3 ml of 10% solution). Children were also presented with a ‘blank’ bottle containing 3 ml of mineral oil.

Odor stimuli were presented individually to the child in an opaque, 250-ml poly-ethylene plastic squeeze bottles with flip-up caps. The experimenter held the stimulus bottle about 3 cm from the subjects' nares and gently delivered three puffs of air to the nostrils; the inter-stimulus

interval was approximately 30 s. Because previous research [18] revealed that children were reluctant to participate in a research study when the first odor stimulus was “unpleasant,” the trials began with a pleasant odor (e.g., bubble gum). Otherwise, the order of stimulus presentation was randomized.

After a 5-min break, the game was repeated but this time the child was asked to taste the contents of three cups which were identical in appearance but contained 30 ml of a differently flavored apple juice. The juices were presented individually in opaque sip cups and in counterbalanced order. One tasted sour (and perhaps had a distinctive odor) because of the addition of lemon juice to the apple juice (5 ml/30 ml; Eagle Family Foods, Columbus, OH); this juice is referred throughout as the sour-flavored one. A second juice tasted bitter because of the addition of naringen (0.03193 g/30 ml ACROS, New Jersey), a bitter compound from grapefruit rinds, whereas the third was unaltered (Motts Apple Juice, Stamford, CT). Children were told that they could drink as much as they wanted from the cup during the 1-min trial. A 30-s interval separated each of the three trials during which the child was offered a sip cup containing water and a small unsalted cracker to cleanse their palate.

These latter procedures were repeated on the second testing day but instead of apple juice, they were asked to taste, in counter-balanced order, the contents of identical (but a different color from those used for the juice test) opaque sip cups containing different formulas. Because pilot testing revealed that children and adults often dislike the flavor of these formulas, we decided to offer the children only two cups of formula. One cup always contained hydrolysate formula. For the hydrolysate group, the other cup contained Enfamil, whereas for the other two groups of children, the other cup contained the brand of formula that they were fed as infants (Enfamil ($n = 17$); Isomil ($n = 17$); Similac ($n = 8$); Prosobee ($n = 8$); Gerber ($n = 1$), Carnation Good Start ($n = 1$)). Twelve percent of the children refused to continue testing after tasting the first cup containing formula.

All but three of the test sessions were videotaped. During replays, trained raters, who were unaware of the experimental conditions, viewed the videotaped records and determined the number of sips taken and the frequency of negative facial expressions (e.g., nose wrinkling, brow lowering, upper lip raising, gaping, head turning) when tasting each cup of juice or formula.

2.3. Questionnaires

Mothers were given a list of a variety of foods and asked to indicate how often their child ate each of these food items and to list their child's most preferred vegetables and fruits. In addition, mothers completed an 8-item scale that measured their variety-seeking tendency with respect to foods [19] and a temperament and food neophobia scale designed for children [20].

2.4. Data analyses

The frequencies of subjects that classified each odor or juice as good (i.e., gave it to Big Bird) or bad (i.e., gave it to Oscar the Grouch) were determined. Pearson χ^2 tests were used to determine whether hedonic ratings varied as a function of the type of formula (i.e., milk, soy, hydrolysate) that the child was fed during infancy. A Repeated Measures ANOVA was conducted to determine whether there were differences between the groups on quantitative data (e.g., intake).

3. Results

3.1. Preferences for flavored apple juices

There was no significant differences among the groups in their preference for the plain apple juice (Pearson χ^2 (2df) = 1.48; p = 0.48). In contrast, the type of formula that children were fed as infants was related to their preferences for the sour-flavored apple juice (Pearson χ^2 (2df) = 6.81; p = 0.03; see Table 2). Children who were fed hydrolysates were more likely to prefer the cup containing the sour-flavored juice (Pearson χ^2 (1df) = 6.62; p = 0.01) and were less likely to make a negative facial expressions when tasting it (Pearson χ^2 (1df) = 4.05; p = 0.04) when compared to those fed milk-based formulas. Sour preferences for soy-fed children were intermediate to the other two groups but there were no significant differences in sour preferences or facial responses when comparing children who were fed soy to those fed hydrolysate (all p 's > 0.05) or those fed milk to those fed soy (all p 's > 0.05).

The type of formula that children were fed as infants also influenced their preferences for the bitter-flavored apple juices (Pearson χ^2 (2df) = 6.24; p = 0.04; see Table 2). Although there were no significant differences between the groups in the type of facial expressions made by the children when tasting the juice, children who were fed soy formulas were more likely to prefer the cup containing the bitter-flavored juice when compared to those fed milk formulas (Pearson χ^2 (1df) = 6.2; p = 0.01). Again, there were no significant differences in preferences or facial responses when comparing children who were fed soy to those fed hydrolysate (all p 's > 0.05).

Although there were no significant group difference in the amount of juice consumed by the children during the test session (F (2,96df) = 0.12; p = 0.88), the flavor of the juice significantly affected the amount of juice consumed (F (2, 192df) = 23.77; p = 0.000) and number of sips (F (2,192df) = 9.72; p = 0.000) taken during the testing session. As a group, children drank more of and took more sips while drinking the plain apple juice when compared to both the sour- and bitter-flavored juices (all p 's < 0.05).

3.2. Preferences for the flavor of formula and for odors

The type of formula children were fed as infants influenced their preferences for the flavor of formulas during the taste test (Pearson χ^2 (2df) = 8.28; p = 0.02) (Fig. 1), as well as the odor of the hydrolysate formula during the smell test (Pearson χ^2 (2df) = 8.61; p = 0.01). This difference between the groups was specific to the flavor and odor of hydrolysate formula since there was no significant difference among the three groups in their response to the other odors (all p 's > 0.10).

Children who were fed hydrolysate (Pearson χ^2 (1df) = 6.93; p = 0.008) or soy (Pearson χ^2 (1df) = 8.74; p = 0.003) formulas during infancy were more likely to judge the flavor of hydrolysate formulas as pleasant when compared to those fed milk-based formulas. In addition, those fed hydrolysate formula judged the odor of hydrolysates as more pleasant when compared to those fed milk (Pearson χ^2 (1df) = 8.34; p = 0.004). There were no significant group differences between children who were fed soy or hydrolysate formulas in their preference of the hydrolysate flavor or odor (all p 's > 0.05). Nor were there significant differences among the groups in the type of facial responses made or how much formula was consumed during the test session (all p 's > 0.05).

Consistent with previous findings [18], odor was a powerful variable in the children's preferences (Pearson χ^2 (5df) = 153.0; p < 0.000; data not shown). As a group, children preferred the bubble gum odor and citral odors but rejected the pyridine odor and odors of both milk-based and protein hydrolysate formulas.

3.3. Summary table for flavors

Fig. 2 summarizes the children's responses to the flavor of the sour- and bitter-flavored juices and the two types of formula. Here, we determined the number of times (out of four) that the children in each group liked (i.e., gave to Big Bird) the flavor of these juices and formulas. There was a significant effect of group on the number of times children liked these flavors ($F(2,99df) = 10.09$; $p = 0.0001$). Children who were fed hydrolysate or soy formulas during their infancy were significantly more likely to prefer three or all four of these cups whereas virtually none of those fed milk-based formulas did.

3.4. Food allergies, feeding habits and child temperament

As shown in Table 1, there was a significant difference among the groups in the percentage of children who had food allergies ($\chi^2(2df) = 7.7$; $p = 0.02$). One child in the soy group was allergic to strawberries and 18% of children in the hydrolysate group were allergic to either dairy ($n = 7$) or nuts ($n = 2$); virtually none of the children in the milk group were food allergic. Despite this difference, there were no significant differences between the groups in the mothers' reporting of how often the child ate a variety of vegetables (e.g., carrots, peas, green beans, peas, potatoes, broccoli) and fruits (e.g., apples, oranges, lemons, melons; all p 's > 0.05). However, there were significant differences between the groups in the mothers' ranking of their children's preference for broccoli (Pearson $\chi^2(2df) = 7.95$; $p < 0.02$). That is, mothers whose children fed hydrolysate (Pearson $\chi^2(1df) = 4.40$; $p < 0.03$) or soy (Pearson $\chi^2(1df) = 7.69$; $p < 0.005$) were more likely to rank broccoli as one of their children's most preferred vegetables when compared to those whose children were fed milk-based formulas.

And finally, there were no significant differences among the groups in the mothers' variety-seeking tendency with respect to foods ($F(2,99df) = 1.79$; $p = 0.17$). Nor were there differences among the three groups of children in the temperament dimensions of emotionality ($F(2,99df) = 0.46$; $p = 0.63$), shyness ($F(2,99df) = 0.33$; $p = 0.72$), sociability ($F(2,99df) = 2.49$; $p = 0.09$), negative reactions to foods ($F(2,99df) = 2.21$; $p = 0.11$) or activity ($F(2,99df) = 1.19$; $p = 0.31$).

4. Discussion

The type of formula fed during infancy influenced the flavor preferences of children who were tested several years after their last exposure to formulas with distinctive flavors. Specifically, children who were fed protein hydrolysate formulas were more likely to prefer the sour-flavored juice, as well as the odor and flavor of formulas, and less likely to make negative facial expressions during the taste tests, when compared to children who were fed milk-based formulas. Those fed soy formulas preferred the bitter-flavored apple juice more frequently than the other children. That the effects of differential formula feeding also modified children's food preferences is suggested by the mothers' reports that their children were significantly more likely to prefer broccoli than were those whose children fed milk formulas. A direct measure of children's food preferences is needed to confirm this, however.

Because we did not randomly assign children to groups (parents decided which formulas they would feed their infants), this was not a strict experimental study. Nonetheless, we attempted to match the groups as closely as possible to maximize the probability that any group differences were due only to differences in early formula feeding experiences. Because there were no significant differences among the three groups in the mothers' variety seeking scores, the differences observed in the children's behavioral responses to the flavors were unlikely to be due to the mothers' eating habits or attitudes toward foods. Neither do these differences appear to be due to temperamental differences among the children in the three groups. Nevertheless, controlled experimental studies where these formulas are introduced at differing

ages and later preferences are determined, are needed for confirmation. Such studies are ongoing in our laboratories.

In previous studies with these formulas [21–23], we suggested that there is a sensitive period between birth and 4 to 5 months of age when hydrolysate formulas can be easily introduced to infants. If the introduction of such formulas is delayed until later, infants exhibit strong indications of rejection and many mothers are apparently unable to induce their older aged infant to accept such formulas without very significant difficulty. However, if an infant receives exposure (of unknown length and amount) to hydrolysate formulas during the early period of acceptability, these formulas remain acceptable for a considerable period of time thereafter. The amount of exposure necessary at this earlier age is unknown but the data indicate that a single exposure, when the infant is younger than 2 months of age, is not sufficient to render the formula acceptable 5 to 7 months later [21].

The existence of sensitive period during development suggests, based on analogy to other sensitive periods in other biological systems (see Ref. [15] for review), that the effects of experience during this time should be particularly persistent. The data obtained herein, amongst children all of whom were introduced and fed this distinctive-tasting formula prior to 4 months of age, is consistent with this expectation. That the effects of early experience may persist even into adolescence and adulthood is suggested by the report that more than 50% of adolescent patients with phenylketonuria, who were fed a type of protein hydrolysate formula (which is specifically treated with charcoal to remove most of the phenylalanine) during infancy and childhood, were successfully able to return to the diet and formula after discontinuing this diet therapy at approximately 6 years of age [24,25]. Moreover, when this formula was reintroduced during adolescence, it was accepted relatively well and the adolescents reported that one of their most preferred flavors, which were often added to the formulas, was lemon [26]. Recall that in the present study, children fed hydrolysate formulas preferred the apple juice that was flavored with lemon juice (i.e., sour juice). That this preference did not generalize to the citral odor suggests that preference was for sour tastes and flavors, not lemon odor, although this was not conclusively proven.

Why should there be a sensitive period in the early flavor learning? Presuming there is an adaptive reason, it is obvious that it has nothing directly to do with these hydrolyzed or soy protein formulas. We suggest that these observations may expose a much more fundamental aspect of early flavor learning that is conveniently revealed by studies that exploit the substantial flavor variation inherent in the three classes of infant formulas. That is, we hypothesize that it is important for the pre-weanling human infant to accept and be particularly (but not exclusively) attracted to the flavors that are consumed by the mother. All else being equal, these are the flavors that are associated with nutritious foods, or at least foods as nutritious as the mother has access to, and the foods and flavors that the infant will be confronted with at weaning and probably thereafter. Under this hypothesis, much of the normal exposure would occur in utero and during breastfeeding where flavors mothers consume are transferred to the infants' chemosensory environment [12].

As indicated in Introduction, it has been difficult to demonstrate profound effects of early preweaning flavor experiences on later preference behaviors. We suggest that inherent variation in formula flavor provides a particularly apt model system because these formulas differ profoundly in flavor, because exposure is frequent and repeated, and because large numbers of infants are exposed to this very substantial differential early experience. Thus, if early experience were to influence later liking and choice, its effect should be most clearly revealed in this model system. The data obtained herein are amongst the strongest thus far indicating an effect of early flavor experience on later expressions of choice and liking.

The sensory world of children is different from that of adults [27]. Although there are clearly consistencies in taste preferences across children (e.g., preference for sweet tastes), the differences among them are often as striking as the similarities. What role genetic differences between individuals play in determining such preferences has not been determined. Sensitivity to the bitter taste of 6-*n*-propylthiouracil (PROP) is an inherited trait [28] and recent research demonstrated that sensitivity to PROP influences flavor preferences and food choice [29,30]. How such genetic differences in taste sensitivity or food allergic susceptibility traits (see Ref. [31]) interact with early experience in influencing food choice and flavor preference in infants and young children is an important area for future research.

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Fig. 1.

The percentage of children in each group who preferred the formula after tasting it. Grouping was based on the type of formula (milk, soy, hydrolysate) that the children fed during their infancy. Children were offered two cups of formula, one of which was hydrolysate (dark bars). For those in the hydrolysate and milk-based formula groups, the other cup (hatched bars) contained a milk-based formula, whereas it contained a soy-based formula for those in the soy group (Pearson χ^2 (2df) = 8.28; P = 0.02).

Fig. 2.

The cumulative percentage of subjects' positive responses to the flavor of the sour- and bitter-flavored juices and the two types of formula. We determined the number of times (out of four) that the children in each group liked the flavor of these juices and formulas. The groups differed in the type of formula (i.e., milk, soy, hydrolysate) that the children were fed during their infancy. Children who were fed hydrolysate or soy formulas during their infancy were significantly more likely to prefer the content of three or all four of these cups whereas virtually none of those fed milk-based formulas did ($F(2,99df) = 10.09$; $P = 0.0001$).

Table 1

Subject characteristics

Type of formula children were fed as infant	Group 1	Group 2	Group 3
	Milk	Soy	Hydrolysate
Children's age in years (Mean $\pm$ SEM)	4.8 $\pm$ 0.1	5.0 $\pm$ 0.1	4.8 $\pm$ 0.1
Children's body mass index (Mean $\pm$ SEM)	16.6 $\pm$ 0.3	15.8 $\pm$ 0.3	16.6 $\pm$ 0.4
Sex of children (♀/♂)	13/14	12/13	25/25
Number of months formula fed during infancy (Mean $\pm$ SEM)	11.7 $\pm$ 0.6	12.0 $\pm$ 0.7	12.0 $\pm$ 0.7
Percent of children who have food allergies	0%	4%	18% **
Mothers' age in years (Mean $\pm$ SEM)	32.9 $\pm$ 1.4	32.8 $\pm$ 1.2	34.7 $\pm$ 0.9
Ethnicity (percent of group)			
African-American	22.2	20.0	24.0
Caucasian	74.1	68.0	76.0
Other*	3.7	12.0	0.0
# Mother-children pairs	27	25	50

* Because of the small numbers of Hispanic and Asian children, they were categorized into the 'other ethnic' group for this analysis.

** Significant group differences.

Table 2

Effect of early flavor experiences on preference for differently flavored apple juices

Type of formula children were fed as infant	Group 1	Group 2	Group 3
	Milk	Soy	Hydrolysate
<i>Percentage of children who preferred contents of cup containing</i>			
Plain apple juice	81.5	92.0	82.0
Sour apple juice	33.3	48.0	64.0*
Bitter apple juice	29.6	64.0*	44.0
<i>Percentage of children who exhibited negative facial expressions while tasting</i>			
Plain apple juice	7.4	0.0	10.6
Sour apple juice	40.7	20.8	19.2*
Bitter apple juice	25.9	16.7	19.2
# Children	27	25	50

* $p < 0.05$ when compared to children who were fed milk-based formulas.