Ann. Ist. Super. Sanità, vol. 31, n. 4 (1995), pp. 411-418

Artificial feeding: progresses and problems

Giorgio L. PIACENTINI, Attilio L. BONER, Carmen C. RICHELLI and Dino GABURRO

Clinica Pediatrica, Università degli Studi, Verona

Summary. - The introduction of infant formulas represents an important result in the field of the newborn and infant artificial feeding, reducing the gap with maternal feeding. In the last decade technological evolution allowed to obtain milk formulas which became more and more similar to human milk starting from cow's milk, thus obtaining a composition adequate to the digestive and nutritional requirements of the newborn and of the infant, starting from the model of the breast feeding (infant formulas). The major differences between human and cow's milk have been corrected by dilution, skimming, addition of carbohydrates, acidification. From an allergenic viewpoint, in a recent study, we observed that no significant differences can be observed in the development of atopic symptoms for children supplemented with different substances in the first 5 days of life or receiving cow's milk infant formulas in the first three months of life, compared to those breast fed. In the case of the development of intolerance or allergy to cow's milk proteins, the substitution of the cow's milk based formula with hydrolysed or soy formulas is required. Maternal feeding represents the best choice for the nutrition of the newborn; however, when it is not possible, milk formulas despite they still show marked differences with human milk, concerning both nutrients and defensive factors, allow to reach satisfactory results about both nutrition and health.

Key words: artificial feeding, nutrition, newborn, allergy.

Riassunto *(Allattamento artificiale: progressi e problemi)*. - L'introduzione delle formule adattate rappresenta un risultato importante nel campo dell'alimentazione del neonato e del lattante, riducendo il divario rispetto all'allattamento al seno. Negli ultimi dieci anni, in particolare, l'evoluzione tecnologica ha consentito di ottenere formule sempre più simili al latte umano partendo, come base, dal latte vaccino. In questo modo si sono ottenute formulazioni adeguate alle necessità digestive e nutrizionali del neonato e del lattante prendendo come esempio la composizione del latte umano. Le principali differenze sono state corrette mediante procedure di diluizione, scrematura, addizione di idrati di carbonio, acidificazione. Da un punto di vista allergologico, in uno studio recente, abbiamo osservato che non esistono significative differenze in termini di sviluppo di sintomatologia allergica per bambini che hanno ricevuto diversi tipi di supplementazione durante la permanenza al nido nei primi 5 anni di vita rispetto a quelli alimentati al seno. Nel caso di sviluppo di intolleranza alle proteine del latte vaccino è necessario sostituire questo tipo di latte con formule a base di soia. L'allattamento al seno rappresenta la scelta migliore per la nutrizione del neonato; tuttavia, quando esso non è possibile, le formule artificiali, pur presentando ancora notevoli differenze rispetto al latte di donna, consentono risultati soddisfacenti sia da un punto di vista della nutrizione che della salute generale del bambino.

Parole chiave: allattamento artificiale, nutrizione, neonato, allergia.

Introduction

It is currently widely accepted that the quantity and the quality of food intake are of extreme relevance, in particular during the period of the maximum body growing and maturation.

The first year of life, and the first months in particular, represents a critic period since the organism is growing very fastly.

It was, indeed, calculated that in the first months the body weight increases at least 1 g per hour (25-30 g per day) and the weight of the brain 2 g per day.

Inadequate food regimens - either food lacks or excesses - during this period of life may be rather frequently responsible for some extent of damage both on the nutritional state and, as a consequence, on the health status, both at a short- and a long-term.

As it happens for all the mammalians, for the humans the first period after the birth is characterised by almost exclusive milk feeding.

Milk constitution

Milk is the specific product of the mammalian gland. It is constituted by a complex, fluid, colloidal system which contains proteins and tricalcium phosphate in a disperse phase, lipids and liposoluble vitamins as an

emulsion, lactose, salts and hydrosoluble vitamins in solution.

The mammalian milk is peculiar for each species. However, quite recently, the man was able to substitute human milk (natural milk feeding or breast feeding) with milk obtained from other mammalians (artificial or unnatural feeding) for newborn's alimentation.

Different kinds of milk have been employed (goat, ass, camel and others), but cow's milk represents the most common alternative to human milk for the alimentation of the newborn.

As relevant differences between human milk and cow's milk composition have been observed (Table 1), a different extent of manipulation has been introduced in order to correct the most evident discrepancies. The main modifications consists in dilution, skimming, addition of carbohydrates and acidification.

In the last decade, technological evolution allowed to obtain milk formulas which became more and more similar to human milk starting from cow's milk [1].

It has been therefore possible to obtain a formulation adequate to the digestive and nutritional requirements of the newborn and of the infant starting from the model of the breast feeding. These preparations are commonly defined as infant formulas.

When the maternal milk is not available, this kind of formula represents an alternative for the feeding in the first 4 (or 6) months of life.

The infant formulas are available both as powder - to be reconstituted in water - and as liquid preparations, all of which give warranty for the composition and the sterility of the preparation.

Their mean composition is reported in Table 2.

The actual formulations of the infant formulas allows to recognise the favourable modification which have been obtained starting from the original composition of cow's milk. Many of these formulas are also enriched with carnitine and/or taurine; some of them with long chain polyunsaturated fatty acids; all of them are enriched with vitamins and in particular with vitamin D.

From an energetic viewpoint, there is an equivalence between infant formulas and human milk, so that the volume of the daily rate is practically coinciding with that of the breast-fed infants.

The quantitative and qualitative similarity of the nutrients allow a flexible administration of the meals during the time of the day in a way similar to the breast feeding, also for the artificial feeding.

However it is not rare to have a mild dyspepsia, in particular when the mother prepares the milk using too high quantity of powder, with an erroneous final concentration of the artificial milk.

It is also possible to observe a higher rate of regurgitation or vomiting, gaseous colics and fluid stools which may appear grumous and hyperacid.

This dyspepsia may exist even in case of a correct preparation of the milk and this is thought to be due to temporary lactase and "lipolytic powers" defect or to motility disorders [2].

Problems related to artificial feeding

Despite the effort to make artificial milk similar to human milk, different aspects still remain, which can be shortly summarised as follows [3-5]:

- the growth is similar: in the first three months the growth is about 8-9 g/kg/die both in the breast fed and in the bottle fed infants; nevertheless, the artificially fed infants require higher energy consumption (15% higher);

- different studies on morbility, of course not so easy to be performed, presented discordant results, but none of them reported higher morbility in the breast fed infant;

- artificial milk has a standard formulation which is always constant, whereas maternal milk composition may change. During each single feeding there is an increase in the lipids at the end of the feeding which is in favour for an autoregulation in the assumption of milk; during the period of the lactation there is a change from the colostrum, through the transition milk, to the definitive milk which provides the infant with the specific nutrients in the different periods of life;

- infant formulas, even if less of cow's milk, have a high level of proteins (casein) which increases the renal load of dissolved substances, and also of phenylalanine and tyrosine, aminoacids for which the newborn presents low metabolic capability;

- human milk does not contain β-lactoglobulin which is, in contrast, present in infant formulas and which is considered highly allergenic;

- infant milk formulas are low in oligosaccarides that may exert different functions, among which a facilitation of the lactic component of intestinal flora (bifidobacteria);

- human milk contains higher level of long chain fatty acids, both unsaturated and polyunsaturated, and very long chain fatty acids which play a role in myelinization process and in the development of visual function, respectively;

- artificial formulas, even in less degree than cow's milk, still present different contents of minerals than human milk. For example, Fe and Ca are present in lower quantity in human milk, but they present a significantly higher bioavailability;

- content of enzymes in human milk is higher; maternal milk lipase promotes the digestion of lipids, while protease do the same for proteins;

Table 1. - Human milk and cow's milk composition (values for 100 ml of milk)

Constituent	Unit	Human milk	Cow's milk
Specific weight		1031	1032
pH		7.1	6.8
Calories	kcal	7.1 (65-75)	69 (66-79)
	kj	297 (272-314)	289 (276-330)
Proteins			
Total rate	g	1.0 (0.9-1.4)	3.3 (3.1-4.0)
Casein/serum proteins	%	40/60	82/18
Casein		0.25	2.7
Serum proteins		0.64	0.60
Essential aminoacids	mg		
Phenylanine		48	172
Isoleucine		68	228
Histidine		22	95
Leucine		100	350
Lysine		73	277
Methionine		25	88
Threonine		50	164
Tryptophan		18	49
Valine		70	245
Non essential aminoacids	mg		
Aspartic acid		116	166
Glutamic acid		230	688
Alanine		35	75
Arginine		45	129
Cystine		22	32
Glycine		0	11
Proline		80	250
Serine		69	160
Tyrosine		61	179
Non proteic nitrogen	mg	50	28
Urea		25	1.3
Creatine		3.7	9
Creatinine		3.5	0.3
Uric acid		0.5	0.8
Glucosamine		4.7	?
a-aminic nitrogen		1.3	4.8
Ammonium		0.2	0.6
Others		-	7.4
Lipids			
Total rate	g	3.8 (3.5-4.0)	3.7 (3.5-5.2)
Saturated/unsaturated fatty acids		45/55	65/35
Saturated fatty acids			
(% total fatty acids)		45	65
Butyric acid		-	2-4
Caproic		-	< 1
Caprylic		-	0.4-0.6
Capric		1.8	1.9-3
Lauric		6.7	2-4.3
Myristic		6.5	11-13
Palmitic		20.4	25-32
Stearic		6.5	10-15.2

Table 1 (continued)

Constituent	Unit	Human milk	Cow's milk
Unsaturated fatty acids (% total fatty acids)	g		
Palmitoleic acid		55	35
Oleic		3.1	2-3
Linoleic		36.5	30-35
α-Linoleic		11	1.7
Arachidonic		0.9	traces
Eicosapentaenoic		0.5	traces
Decosaesaenoic		0.2	-
		0.3	-
Cholesterol	mg	20-25	10-15
Glucides			
Total rate	g	7.0 (6.5-7.5)	4.8 (4.5-5.0)
Lactose		6	4.8
Oligosaccarides		1.1	0.1
Minerals			
Total rate	mg	200 (150-250)	720 (700-750)
Cl		42	102
K		54.6	136.5
Na		16.1	57.5
Ca		33	137
P		15	92
Ca/P		2.1	1.3
Mg		4	13
Fe		0.05	0.03-0.06
Zn		0.3	0.4
Cu		0.03	0.008
I		0.003	0.021
Mn		0.001	0.003
Se		0.002	0.0025
Vitamins			
A	UI	200	100-170
D	UI	2.2	1.4
E	UI	0.2-0.5	0.04
K	µg	1.5	6
B_1	mg	0.016	0.044
B_2		0.04	0.175
B_6		0.01	0.02-0.06
B_{12}	µg	0.03	0.4
Folic acid	µg	5	6
PP	mg	0.15-0.19	0.09
Pantothenic acid		0.2	0.35
C		4-5.5	1.1
Biotin (H)	µg	0.1-2.5	3.5

- human milk gives to the baby important defensive factors:

- *immunoglobulines*, in particular IgA (mainly IgAs), which exert a protective function against virus and bacteria of the intestinal site, but also in the respiratory tract;
- *lactoferrin*, practically absent in milk formulas, which has a bacteriostatic action versus *E. coli* and staphylococci;
- *lysozime*, a nonspecific antimicrobial factor present at low concentration in cow's milk;
- *lysosomes* (30 times higher in human milk than in cow's milk), which along with lactoferrin and oligosaccarides facilitate the bifidobacteria and depress the Gram negative component;
- *complement C3* that facilitates phagocytosis;
- *nucleotides*;
- *cellular defence factors* (very high in the colostrum) as macrophages, lymphocytes and neutrophils;
- lastly, other factors commonly classified as modulators of growth: *epidermic growing factor* (EGF), *nerve growing factor* (NGF) *and neuropeptides.*

Table 2. - Mean energetic contribution and main nutrients of various kinds of milk (in 100 ml)

Constituent	Unit	Human milk	Cow's milk	Milk formulas
Calories	kcal	71 (65-76)	69 (66-79)	67.6 (64.3-72)
	kj	297 (272-314)	289 (276-330)	289 (373-301)
Proteins	g	1.0 (0.9-1.4)	3.3 (3.1-4.0)	1.6 (1.4-1.8)
Serum proteins/casein	ratio	60/40	18/82	57/43
Glucides	g	7.0 (6.5-7.5)	4.8 (4.5-5.0)	7.4 (6.9-8.8)
Lactose		6.0	4.8	6.6 (3.7-7.6)
Oligosaccarides		1.1	0.1	1-2 (maltodestrines)
Lipids		3.8 (3.5-4.0)	3.7 (3.5-5.2)	3.5 (3.1-3.7)
Saturated/unsaturated fatty acids	ratio	45/55	65/35	46/53
Linoleic acid	% total fatty acids	11	1.7	13
α-linoleic acid	%	0.9	traces	1.4
Minerals	g	0.2 (0.15-0.25)	0.72 (0.7-0.75)	0.3 (0.2-0.4)
Cl	mEq	1.2	2.9	1.16 (0.5-1.6)
K		1.4	3.5	1.8 (1.7-2.4)
Na		0.7	2.5	0.9 (0.7-1.2)
P		15	92	31.4
Ca	mg	33	137	51 (42-65)
Ca/P		2.1	1.3	1.6 (1.4-2)
Fe		0.05 (0.02-0.08)	0.05 (0.03-0.06)	0.6 (0.1-0.8)
Zn		0.30 (0.05-1.2)	0.4 (0.2-0.6)	0.4 (0.2-0.5)
Cu		0.03 (0.01-0.06)	0.008 (0.005-0.0018)	0.034 (0.015-0.041)
I		0.003	0.0021	0.01 (0.005-0.075)
Mn		0.001	0.003	0.006 (0.004-0.01)
Vit. D	IU	2.2 (0.4-10)	1.4 (0.3-4)	42 (32-64)

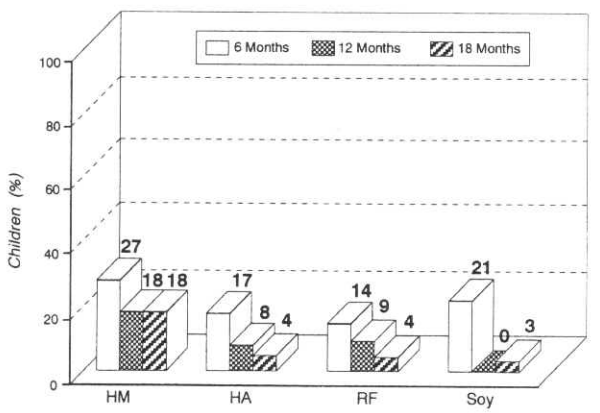

Fig. 1. - Dietary food regimen in the first days of life and incidence of atopic dermatitis at 6, 12 and 18 months (family history positive for atopic diseases. Human milk no. = 11, hypoallergenic formula no. = 24, regular formula no. = 22, soy no. = 29).

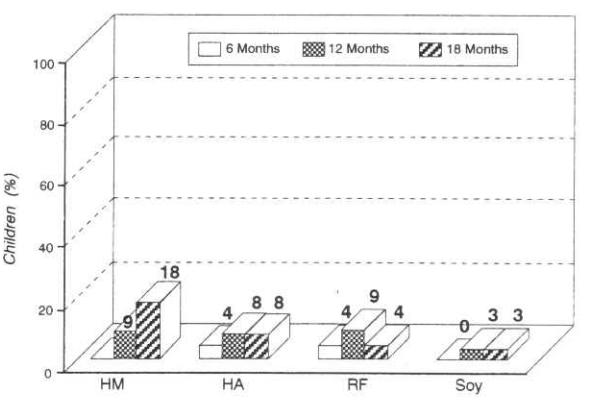

Fig. 2. - Dietary food regimen in the first days of life and incidence of respiratory symptoms at 6, 12 and 18 months (family history positive for atopic diseases. Human milk no. = 11, hypoallergenic formula no. = 24, regular formula no. = 22, soy no. = 29).

It must also be remembered that, while these important defensive factors are almost completely absent in artificial milk formulas, some toxic substances for the infant may be present also in human milk.

This can be observed in particular with the use of not idoneous pharmacological treatments, "social toxics" or radionuclides, but these, at least theoretically, are avoidable and controllable events.

The problem of toxic substances in milk which derive from contaminations is more complex. In fact, this kind of substances may be found, even if in different ways and extent, both in human and cow's milk, and they are very difficult to be controlled.

An example of this kind of contamination may be the use of toxic substances employed in agriculture (insecticides, anticryptogamics, fungicides) or just present in the environment (for instance Pb) and in water (atrazine).

Allergy-related aspects of artificial feeding

Prevention

Cow's milk allergy represents a relevant problem in pediatrics.

The development of food allergy in general is the result of interactions between genetic and environmental factors, including food. The first contact with relevant antigen determinants may happen even before the birth since antigens may cross the placental barrier and induce sensitisation in the foetus. The foetus may, indeed, produce non-specific IgE from the 11th week of gestation and specific IgE may be detected in the cord blood [6, 7].

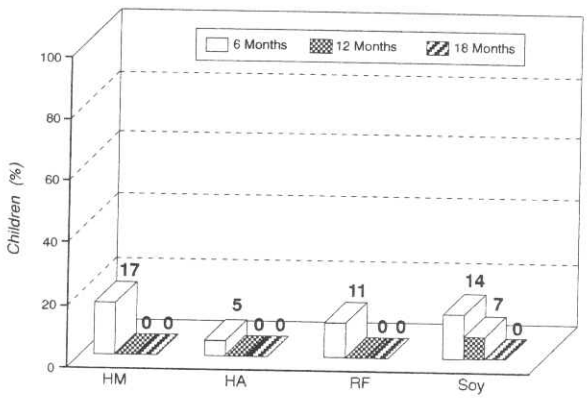

Fig. 3. - Dietary food regimen in the first days of life and incidence of atopic dermatitis at 6, 12 and 18 months (family history negative for atopic diseases. Human milk no. = 6, hypoallergenic formula no. = 19, regular formula no. = 18, soy no. = 14).

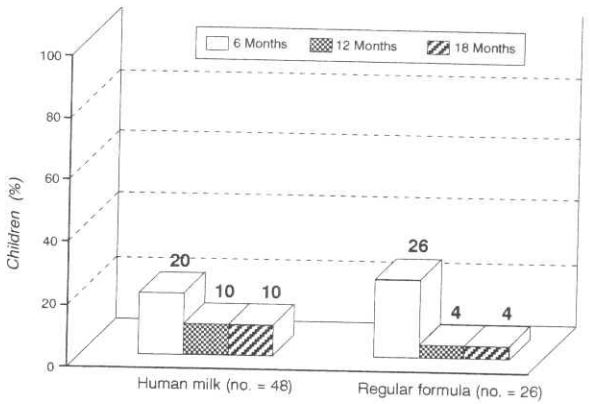

Fig. 4. - Dietary food regimen in the first days of life and incidence of atopic dermatitis at 6, 12 and 18 months (family history positive for atopic diseases).

The newborn is therefore able to produce specific IgE, to bind them to mast-cells and to develop type I reactions. Specific IgE to food have been shown to be demonstrable earlier than those to aero-allergens, which are rarely found before the age of 2.

The infant may become sensitised to food when assuming allergens via the breast feeding or artificial feeding (in particular β-lactoglobulin).

During the first three months of life the infant is highly susceptible to food sensitisation also because of the immaturity of the gastrointestinal barrier which is functionally effective after the third month. The development of food tolerance in the normal infant has been suggested to be mediated by the M cells of the intestinal mucosa, which have been described to be involved in the antigen presenting process to the gut associated lymphoid tissue and in the consequent production of IgA.

However the enhanced epithelial permeability in the first three months of life alone cannot fully explain the development of food sensitisation, which is probably influenced by other factors, such as the time of antigen exposure, metabolic characteristics of the subject, concomitant infections, immaturity of the immune system.

When breast milk is not available, different substitutes of human milk have been proposed as hypoallergenic alternatives. It has been reported that soy formulas can prevent the onset of atopic manifestations in children at risk. However, other studies did not show any protective effect of soy compared to cow's milk. Moreover, soy contains relevant immunogens which have been found to be responsible for sensitisation in children fed with soy because of an intolerance to cow's milk proteins [8].

Alternatively, protein hydrolysate formulas have been tried as another form of prophylaxis of allergic reactions to food in children for which maternal feeding was not possible [9].

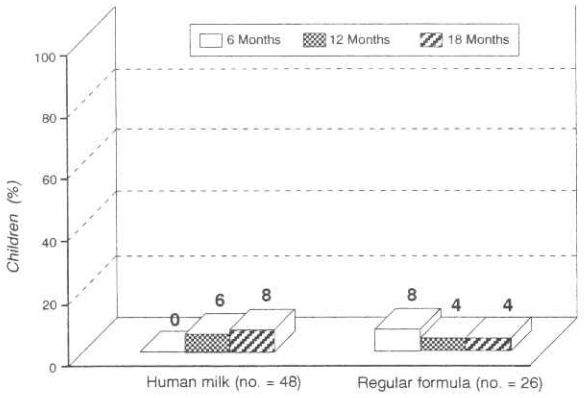

Fig. 5. - Dietary food regimen in the first days of life and incidence of respiratory symptoms at 6, 12 and 18 months (family history positive for atopic diseases).

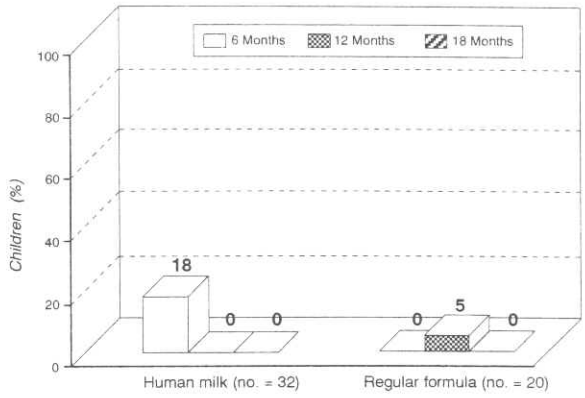

Fig. 6. - Dietary food regimen in the first days of life and incidence of atopic dermatitis at 6, 12 and 18 months (family history negative for atopic diseases).

Despite some studies that support the use of these preparations in the prevention of cow milk allergy, at the present there still are some doubt on the real prophylactic effect due to the low number of children included in the clinical trials and to the heterogeneous design of the studies.

A further open issue is represented by the supplementary feeds of the breast milk in the first days of life.

We have recently performed a perspective study aimed to evaluate the effects of different supplementations in the first days of life, followed by exclusive breast or artificial feeding for the first three months of life on the development of allergic symptoms in a group of 1149 newborns with different family histories for allergic diseases.

The subjects were selected among those who were born in our hospital with a gestational age between 37 and 42 weeks not presenting significant neonatal diseases. The children were randomly allocated in one of the following groups receiving, while in the nursery, in addition or instead of maternal feeding, one of the following regimens: 1) hypoallergenic (HA) formula, 2) soy formula, 3) regular infant formula, 4) glucose solution.

Children were re-evaluated at the age of 3, 6, 12 and 18 months in order to check whether they presented clinical manifestations of atopic diseases.

At the birth 470 children (41%) presented a family history positive for atopic diseases.

At the present we have data for 556 children at 3 months, 456 at 6 months, 312 at 12 months and 143 at 18 months. The present analysis was performed on the 143 children who completed the study, 86 of which had a positive and 57 a negative family history for allergic diseases.

Figs 1 and 2 show respectively the incidence of atopic dermatitis and asthma at 6, 12 and 18 months for the different regimen of supplementation received in the first 5 days of life for the children with positive family history for atopy. No significant difference can be observed among the 4 groups.

Fig. 3 shows the data for the group with a history negative for allergic diseases.

The effect of artificial feeding versus breast feeding in the first three months of life were also evaluated in the children with a family history positive for allergic diseases.

Figs 4 and 5 respectively show the incidence of atopic dermatitis and asthma, with no difference between the two groups. No difference between the two alimentation regimens was observed in the group with negative history for allergic diseases (Fig. 6).

The data so far analysed show an incidence of allergic disease in our study population in a range of about 20% for the group of children with a positive family history and 5-8% in the group with a negative family history. These data are according with the percentages reported in the literature.

At present we can conclude that, in the 143 children who completed the study, no preventive effect of different food regimen could be observed. In particular it seems that no relevance is tributable to the supplementation given in the first days of life and that breast feeding does not present a protective effect on the development of atopic manifestations.

Treatment

In the case of children who present allergy or intolerance to cow's milk proteins, the substitution of cow's milk based formula with soy formulas is required, and it is preferable to the use of even extensively hydrolysed cow's milk formulas, for which have been reported some case of anaphylactic reaction [10].

Conclusions

In conclusion, the introduction of the most recent artificial milk formulas represents an essential step for the perfectioning of artificial feeding.

The milk formulas allow the infant to reach a satisfactory nutritional and health state, but many problems, both immunological and nutritional, are still unsolved.

Therefore the model of maternal breast feeding presents a proved superiority.

However, when maternal feeding is not possible it is essential giving the mother those information and the serenity she needs to correctly perform the artificial feeding.

Submitted on invitation.
Accepted on 30 October 1995.

REFERENCES

1. GABURRO, D. 1955. *A quale prezzo il lattante sopporta un allattamento artificiale.* Parte II. Atti 7° Congr. Naz. Nipiol, Roma, Aprile 1954. Arti grafiche valsesiane, Varallo Sesia.

2. GABURRO, D. 1978. Il lavoro digestivo-metabolico nell'allattamento artificiale con particolare riferimento ai grassi. *Minerva Pediatrica* **30**: 397-406.

3. GABURRO, D. 1988. Nutrizione clinica in pediatria. *Riv. It. Ped.* **14**: 628-634.

4. MAGGIONI, G. & SIGNORETTI, A. 1991. *L'alimentazione del bambino sano e malato.* 2. ed., Il Pensiero Scientifico Editore, Roma.

5. MAGLIETTA, V. 1994. *Puericultura*. 4. ed., Casa Editrice Ambrosiana, Milano.

6. GABURRO, D., PIACENTINI, G. & BONER, A.L. 1990. Razionale immunologico nella strategia preventiva dell'allergia alimentare. *Riv. Ital. Pediatr.* **16**: 383-390.

7. LILJA, G., DANNAEUS, A. & FALTH-MAGNUSSON, K. 1988. Immunoresponse of the atopic woman and foetus effects of high and low dose food allergen intake during late pregnancy. *Clin. Allergy* **18**: 131-142.

8. WILSON, N.W. & HAMBURGER, R.N. 1988. Allergy to cow's milk in the first year of life and its prevention. *Ann. Allergy* **61**: 323-326.

9. COMMITTEE ON NUTRITION. 1989. Hypoallergenic infant formulas. *Pediatrics* **83**: 1068-1069.

10. ELLIS, M.H., SHORT, J.A. & HEINER, D.C. 1991. Anaphylaxis after ingestion of a recently introduced hydrolized whey protein formula. *J. Pediatr.* **118**: 74-77.