Functional Ingredients in the Complementary Feeding Period and Long-Term Effects

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Abstract

The complementary feeding period is a critical stage for growth and development. Infants in developing countries and selected individuals in developed countries may benefit from micronutrient supplementation, but long-term effects are still poorly explored. We have some evidence, coming from observational studies, of the role of iron in the second semester of life for optimal brain development and functioning through early adulthood, but the advantage seems to be restricted to those infants who are effectively iron-deficient. For long-chain polyunsaturated fatty acids we have limited observations from randomized trials that they could promote the maturation of visual acuity in the short-term, without direct evidence linking supplementation during the complementary feeding period to later functional measurements. Probiotics and prebiotics, as well as other micronutrients, such as zinc, represent new promising areas of investigating effects on the immune system. The medium- and long-term effects need to be extensively explored, and any type of association recorded to check the safety of dietary supplements, considering their overconsumption, starting at early ages, in western countries.

Introduction

Nutritional factors during early development might have not only short-term effects on growth, body composition and body functions but also long-term effects on health, disease and mortality risks in adulthood, as well as development of neural functions and behavior, a phenomenon called ‘metabolic programming’. The interactions of nutrients and gene expression form the basis of many of these programming effects [1]. Therefore, interest in functional ingredients for the enhancement of the genetic and environmental

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potentials for health, growth and development is emerging within the pediatric community.

During the intrauterine life and the early phases of the extrauterine life nutrients that have been demonstrated (in either animal or human studies) to have the potential for later functional advantages (from growth and neurodevelopment to the efficiency of the immune system) include minerals and trace elements (iron, zinc, iodine, copper and selenium), vitamins (vitamin A, folic acid, vitamin B₁₂, vitamin C, vitamin D₁, vitamin E), the essential fatty acid linoleic acid, and long-chain polyunsaturated fatty acids [LCP-UFA; including arachidonic acid (ARA) and docosahexaenoic acid (DHA)] [1]. Recently, also probiotics and prebiotics have been added to the concepts of functional nutrients, that is compounds having positive effects on biological processes and functional mechanisms, leading to a general advantage for the individual in terms of health and quality of life.

Now, new questions arise as to whether also the complementary feeding period may represent a further ‘sensitive’ period, in which selected nutrients might advantageously program the growing organisms, in both developing and well-developed countries. For the purposes of our discussion we will consider as ‘complementary feeding period’ the interval included between 4–6 and 18–24 months of age.

Clearly, different approaches are required according to the environmental background:

- Developing countries show primary needs to improve general health conditions, first of all growth, development and incidence of disease, closely connected to the nutritional status of young infants. Within this context, micronutrient supplementation has gained considerable attention, for a relatively low cost-benefit ratio, and the possibility to prevent conditions (such as iron deficiency anemia) that could impact later developmental abilities.

- Well-developed countries as well as countries in rapid transition offer opportunities to enrich diets with functional ingredients to maximize the individual genetic potential for growth, while decreasing the risk for the early appearance of unfavorable markers of the metabolic syndrome. The LCP-UFA as well as bioactive intestinal agents are two examples. Since the primary goal of a health intervention is the avoidance of any damage, we must take care that dietary supplements are not associated with untoward effects, and also assess their effective utility.

**Functional Ingredients and Complementary Feeding in Developing Countries**

In most developing countries the main (or even only) available weaning foods are represented by local staple cereal foods such as maize, rice or cassava.
In these communities, where energy-protein malnutrition is endemic, the 6- to 24-month period is the most critical for nutritional interventions and the introduction of specifically designed supplements can prevent the onset of wasting in a large proportion of children [2]. Malnutrition at an early age may have long-term effects on growth achievement as well as the incidence of disease and brain development (with identifiable anatomic changes), leading to lower levels of intellectual achievement in school-age children and final intelligence quotient scores [3]. As a matter of fact, while the minimal requirements for energy and protein intakes are seldom met and represent a primary health determinant, interventions based on micronutrient supplements are planned in order to improve health conditions, growth and developmental outcomes. Several studies have been conducted in developing countries by supplementing from 6- to 12- to 24-month (or even longer) infants at high risk of malnutrition. In these settings micronutrients (mostly iron, less often zinc, sometimes mixed with other micronutrients) have been introduced at the starting of the complementary feeding period to look at short-term effects on biological markers and health outcomes while no information is available on later effects [4].

To specifically assess the effects of iron supplements, anthropometric measurements, developmental indices, blood indicators of iron status (blood levels of hemoglobin, iron, ferritin), incidence of disease together with adverse reactions have commonly been considered. The assessment of other biological markers as well as later effects, such as growth and intellectual (educational) achievement, and markers of disease, including the early indicators of metabolic impairment are clearly necessary to optimize interventions. A rapid transition towards affluent conditions puts infants from developing countries at particular risk of growth acceleration and related unfavorable biological and anthropometric parameters [5, 6]. In general, growth progression is not influenced by micronutrient supplementation in the complementary feeding period (except in a few reports) since the energy and protein deficiencies represent the major limiting factors. Developmental progresses with supplements are more easily found at short-term assessments [7, 8], but many reports indicate that there is no convincing evidence that iron treatment has an effect on mental development in children aged less than 2 years [9]. Future studies from developing countries should supply data on the medium- and long-term outcomes of dietary supplements in the period of dietary diversification, to define the cost/benefit ratio of nutritional interventions.

Functional Ingredients and Complementary Feeding in Developed and Rapidly Progressing (‘Transition’) Countries

Even if surveys on several dietary supplements are available in more advantaged settings, very few studies have been published concerning nutrients
supplemented during the complementary feeding period and assessment of functional effects at medium-term (18–24 months of age) and long-term (at preschool age at least).

Only for iron do we have some evidence from observational studies, while for LCPUFA we are merely able to collect partial observations from randomized controlled trials (RCT). For other functional nutrients (such as probiotics, prebiotics, zinc and some minerals/vitamins) we have still more partial and indirect evidence, and it is, therefore, mostly speculation.

**Iron**

Iron deficiency in the 6- to 24-month period represents a challenging question even in affluent environments, and its effects may be more easily isolated, since energy and protein intakes are generally more than adequate. This time period is characterized by the peak hippocampal and cortical regional development, as well as myelinogenesis, dendritogenesis and synaptogenesis in the brain [4], all critical processes that, if early deranged, may justify the bases for later anatomo-functional consequences (table 1). Case-controlled studies usually include assessment before and immediately after iron supplementation and/or therapy [4]. Therefore, the issue of the medium- and long-term functional value of iron supplements in the complementary

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**Table 1.** Structural correlates from experimental models (mostly animals) of long-term functional effects of early iron deficiency in humans [as reviewed in 4]

<table>
<thead>
<tr>
<th>Reduced brain iron</th>
<th>Areas and functions differently involved</th>
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<tbody>
<tr>
<td>Alterations of brain metabolism</td>
<td>Failure of iron incorporation into protein structures, Altered dendritic structure, mainly in hippocampal areas, Poorer recognition memory</td>
</tr>
<tr>
<td>Alterations of myelination</td>
<td>Decrease in myelin lipids and proteins, Decreased proliferation of oligodendrocytes (fewer?, less functional?), Slower conduction in the auditory and visual systems, Other poorer outcomes?</td>
</tr>
<tr>
<td>Alterations of neurotransmission</td>
<td>Deranged metabolism of enzymes involved in neurotransmitter synthesis (serotonin, norepinephrine, dopamine), Alterations of dopamine receptors and transporters connected to the extent of iron loss, Social/emotional alterations, affective changes, Altered experience-dependent processes, Altered interactions with the environment</td>
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<tr>
<td>Altered gene and protein profiles</td>
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feeding period may be summarized in some fundamental points from observational studies in humans:

- The mean cell hemoglobin levels during infancy, and more markedly during the 6- to 12-month period, have been associated with neurodevelopmental indices at either preschool age [10–15] or school age [16–18].
- Lozoff et al. [19] found that early iron deficiency is still associated with lower performance in arithmetic and writing achievement and motor function, together with affective and social/emotional differences, during early adolescence (11–14 years of age). A widening gap for mental scores through 19 years of age has also been observed, which was particularly marked for children from more disadvantaged families [20].
- A recent, more sophisticated investigation showed longer wave latencies using auditory brainstem response and visual evoked potentials in 4-year-old children identified as having iron deficiency anemia at 6, 12 and 18 months [21].

Since no study included original RCT, observations generally result from the follow-up of infants who had formerly been anemics compared to those who had higher hemoglobin levels. On the whole, it seems that the prevention of iron deficiency anemia is critical to prevent later neurodevelopmental impairments (fig. 1). The hypotheses on the structural and biochemical correlates for the long-term effects are summarized in table 1.

The question then arises whether an indiscriminate supply of dietary iron as a supplement should be planned at 6–12 months of age or whether a screening procedure would be preferable in order to identify effectively iron-deficient infants requiring a dietary supplementation. To plan an indiscriminate supply, one should make sure that no untoward effects will follow for those who are already iron sufficient. There are reports of untoward effects of iron supplements on the incidence of disease [22] and weight and/or length progression [23] for previously iron-replete infants. On the other hand, if infants are going to be screened for iron status to individualize the intervention, we need to consider the ethical problem of an invasive procedure for blood sampling. We also need to consider a nutritional paradox: infants breastfed for an extended period are prone to have a low iron status [24], but breastfeeding itself has been associated in a duration-dependent fashion with higher intelligence quotient scores in adults [25].

An alternative way to solve the question could be represented by the early introduction of a natural food, such as meat, in subjects more exposed to iron deficiency (breastfed infants). Two recent studies (the first, an observational follow-up survey and the second, an RCT) have shown associations between meat intake at 4–16 months [26] and at 5–7 months [27] with more favorable psychomotor developmental indices at 22 months and behavioral indices at 12 months, respectively. Accordingly, the development of cereal iron fortification [28] might improve the mineral bioavailability from vegetables, adding a
new relevant dietary source of the mineral for infants in the complementary feeding period.

Long-Chain Polyunsaturated Fatty Acids

The issue of LCPUFA as functional nutrients in childhood nutrition is relatively more recent than the iron issue. Since also the concept of RCT in nutrition as gold standard for the scientific evidence is relatively recent, more RCTs are available for LCPUFA, but only some performed in the first semester of life have been assessed in the long-term, while the few conducted in the second semester have been limited to observations in the short-term.

The biochemical and structural changes attributable to the dietary enrichment with LCPUFA at the possible origin of neural functional effects are summarized in table 2. Since the accretion of LCPUFA in the human brain goes on during the postnatal period up to at least 2 years of age [29], particularly in the case of DHA [30], we could infer that LCPUFA supplied through this
entire period of the rapid development of the brain and membranes might influence the neurodevelopmental outcome and also some more general adaptive functions of membranes and tissues. Unfortunately, a direct association of LCPUFA supplementation in the 4- to 6- to 12- to 24-month period and functional measurements in the long-term is lacking. The major points are summarized as follows (fig. 2):

- Most studies on LCPUFA effects consider the exclusive milk feeding period (in either preterm or term infants) with assessment in the short-term, that is at the end of the supplementation period. A few studies have investigated the effects of LCPUFA-enriched formula feeding in the first 4–6 months of life beyond the supplementation period, that is at 10 months of age and at medium-term (18–24 months), with either positive effects [31, 32] or no effects [33, 34], respectively.
- One study considered the effects at 5 years on blood pressure values, who were lower in a group fed an LCPUFA-enriched formula in the first 4 months of life [35]. The neurodevelopmental performance of the same infants was evaluated at 5 years, but the results have not yet been published.
- One RCT showed that a dietary LCPUFA enrichment of human milk through the maternal diet is associated with higher intelligence quotient scores at 4 years of age [36].

**Table 2.** Structural correlates from experimental models (mostly cultured cells) of functional effects of early dietary LCPUFA supply in humans [as reviewed in 37]

<table>
<thead>
<tr>
<th>Structural correlates from experimental models (mostly cultured cells) of functional effects of early dietary LCPUFA supply in humans [as reviewed in 37]</th>
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<tbody>
<tr>
<td>Altered membrane fluidity, volume and packing</td>
</tr>
<tr>
<td>Changed lipid phase properties</td>
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<tr>
<td>Modified membrane lipid-protein interactions within specific microdomains</td>
</tr>
<tr>
<td>→ Changed physical properties and membrane excitability</td>
</tr>
<tr>
<td>→ Modified ability of membrane proteins to bind ligands and activate enzymes</td>
</tr>
<tr>
<td>→ Altered receptor activity, antigenic recognition, signal transduction</td>
</tr>
<tr>
<td>→ Modified electrical properties of membranes</td>
</tr>
<tr>
<td>→ Development of synaptic processes (ARA)</td>
</tr>
<tr>
<td>→ Modulation of neurotransmitter uptake and release (DHA)</td>
</tr>
<tr>
<td>→ Direct effect on the expression of genes regulating cell differentiation and growth</td>
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<tr>
<td>→ Growth stimulation on retinal neurons, higher rhodopsin concentrations (DHA)</td>
</tr>
<tr>
<td>→ Overexpression of retinal genes (DHA)</td>
</tr>
<tr>
<td>→ Overexpression of ion channels involved in retinal synaptogenesis (DHA)</td>
</tr>
<tr>
<td>→ Overall contribution to the development and maturation of retina (other brain regions?)</td>
</tr>
<tr>
<td>Modification of eicosanoid function</td>
</tr>
<tr>
<td>→ Decreased inflammatory processes and platelet aggregation</td>
</tr>
<tr>
<td>→ Influence on arterial wall compliance and blood pressure</td>
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Three trials showed favorable functional effects of the dietary enrichment of LCPUFA through a formula [37, 38] or eggs [39] during the complementary feeding period with neurophysiological tests exploring visual acuity at 12 months, that is there was only short-term assessment. There have been similar findings in infants affected by phenylketonuria and followed up for 12 months in an LCPUFA supplementation trial, in which an association between plasma DHA levels and better visual acuity measured with visual evoked potentials was found in the course of 1 year [40].

Hopefully more long-term assessments of early LCPUFA dietary supplementation could become available in the near future, but a lack of a consistent pattern of the results has already been anticipated due to the 'differences in the levels, nature and duration of supplementations, the use of

Fig. 2. LCPUFA supply: medium- and long-term effects from trials in the first semester and short-term effects from trials in the complementary feeding period. *Differing regarding sources and biochemical forms (phospholipids vs. triglycerides) and internal ratios (ARA:DHA ranging from 1:1 to 2:1) and absolute content of LCPUFA. PKU = Phenylketonuria.
tools that are insufficiently sensitive to measure small changes in performance, and the complexities caused by the longevity and reversibility of diet-induced changes in developmental outcomes’ [41, 42].

**Other Micronutrients, Probiotics and Prebiotics**

Zinc and other micronutrients have been considered for trials in both developing and developed countries, closely associated with the issue of iron supplementation, and, accordingly, no observations in either the medium- and long-term are available. Some contrasting observations might be explained on the basis of the co-presence of subjects with adequate zinc status and others with poorer stores who probably benefited most from the supplementation. A marginal zinc status in breastfed groups at the beginning of the complementary feeding period could represent an additional explanation for the observations linking the amount of meat eaten in the complementary feeding period to later developmental indices [26, 27] and suggests the need for further research.

An increasing interest in the potential effects of probiotics and prebiotics administered at early ages is developing today. It is speculated that the manipulation of the infants’ intestinal flora, either directly, with specific probiotic strains, or indirectly, by administering prebiotics, could develop patterns more favorably connected with less allergic reactions, fewer infective episodes (gastrointestinal, but also respiratory), and less gastrointestinal disturbances (constipation, colic episodes). The model is the breastfed, compared to the formula-fed, infant. While some RCTs with prebiotic- and/or probiotic-enriched formulas are available for the first months of life, there are fewer trials regarding the complementary feeding period, concerning oligofructose-enriched cereals [43, 44]; other studies, however, have considered the effects of administering probiotic strains within a formula [45, 46]. Available results are limited to the period of the supplementation trial, and are suggestive of possible preventive effects on the expression of allergy and the incidence of fever and diarrhea, particularly for probiotics. In any case, no studies are available on medium- and long-term effects.

**Dietary Supplementation: Useful or Useless?**

It is a well-known, common dietary practice to give children dietary supplements in the 4- to 24-month period of age. Inadequate iron and zinc intakes are highly prevalent in developing countries, especially during the period of complementary feeding when micronutrient requirements are high and breast milk contributes little. Severe diarrheal episodes, especially in case of persistent symptoms, represent a further condition requiring supplementation of dietary zinc [47]. More data are needed on the routine inclusion of zinc in iron supplements given to children with the simultaneous inclusion
of other micronutrients, to prevent negative interactions [48]. Once more, we need to expand our knowledge on the effects in the medium (preschool age) and long (school age) term.

In well-developed, rich countries it is a relatively common practice to add dietary supplements to infants’ nutrition, starting at 4–6 months of age. More than half of the US preschool children take vitamin and mineral supplements [49]. Children who are given supplements tend to have mothers who are older, more educated, married, insured, and receiving care from a private health care provider, have a greater household income, and took in turn supplements during pregnancy. Child health characteristics associated with supplement use included first birth order and having eating problems or poor appetite. The sociodemographic and health predictors identified for supplement use therefore suggest that groups at risk for nonuse are likely the same groups whose circumstances might suggest the need for supplementation.

According to a recent survey from the US [50], 8% of infants aged 4–5 months received some type of dietary supplements, and the prevalence of supplement use increased with age to 19% among infants aged 6–11 months and 31% among toddlers aged 12–24 months. The vast majority of supplement users (97%) received only one type of supplement, most commonly a multivitamin and/or mineral supplement. Vitamin/mineral supplement use among infants and toddlers was associated with being a first-born child, particularly if reported as being a ‘picky eater’. Accordingly, healthy infants and toddlers can achieve recommended levels of intake from food alone, and dietetics professionals should encourage caregivers to use foods rather than supplements as the primary source of nutrients in children’s diets. Since vitamin and mineral supplements could help infants and toddlers with special nutrient needs or marginal supply to achieve adequate intakes, care must be taken to ensure that supplements do not lead to an excessive intake, especially for nutrients that are widely used as food fortificants, including vitamin A, zinc, and folate. Another recent survey from the US has reached quite similar results and conclusions [51]. Among micronutrients, zinc intake is becoming excessive in preschool American children [52]. Paradoxically, early vitamin supplementation (within the first 6 months) has been associated with an increased risk of asthma in black children and food allergies in exclusively formula-fed children [53].

**Conclusions**

The complementary feeding period is a critical stage for growth and development. Infants in developing countries and selected individuals in developed countries may benefit from micronutrient supplementation, but long-term effects are still poorly explored, except for iron. Supplemented LCPUFA of the n-3 series (DHA) might promote visual acuity maturation up to 12 months
with potential long-lasting effects. Probiotics, prebiotics and zinc represent new promising areas of investigation. Not only the medium- and long-term effects need to be explored, but also any type of association recorded to check the safety of dietary supplementation, considering their overconsumption from early ages in affluent countries.

References

Discussion

Dr. Calcado: Do you think there is enough evidence nowadays to put lactating mothers on n-3 supplementation, to increase DHA in breast milk in order to improve cortex and retinal chemical composition?

Dr. Agostoni: The question is: if I supplement lactating mothers, would I supplement the pregnant mothers? I would follow the suggestion from the literature showing an effect starting with 200 mg DHA/day from 18–20 weeks of gestation. The data suggest that during intruterine life the growing fetus in the third trimester of life accumulates 40–60 mg/day of n-3 LCP and this could be roughly translated into 200 mg DHA to the mothers starting before the third trimester of life.

Dr. Biasucci: I have two considerations for you. The first one concerns the possibility of supplementing pregnant mothers, and the second one is related to the crucial and critical period of complementary feeding. What is your opinion regarding a natural approach, which would also be acceptable in developing countries, such as educating mothers to use fish in their babies’ diets, more than artificial or pharmacological supplementation?

Dr. Agostoni: Certainly I agree. In our Cambodian study, the main solid food during the complementary feeding period was made up of a soup with cereals in which some fish is added. Indeed they have 3-fold the DHA levels of an Italian reference population [1]. The second point is not just fish but egg yolk. Egg yolk is an excellent source of phospholipids with DHA and arachidonic acid. I remember a paper in the American Journal of Clinical Nutrition 15 years ago when I started as a nutritionist showing that in several areas in China egg yolk is started at 3 months [2]. Even if both fish and egg are not the best preferred indications of immune allergologists, I underline that there is no evidence from a normal healthy population.
Dr. Domellöf: I would like to expand on the iron issue. As was mentioned, several studies suggest that iron supplementation is beneficial for neural development but, on the other hand, excessive iron supplementation of infants who are already iron-sufficient might lead to poor growth and may also increase the risk for infections, especially in endemic malaria regions. So how do you suggest that we determine which children should receive extra iron supplements?

Dr. Agostoni: You mean our experience with sprinkles [3]. What am I suggesting? I like the term ‘holistic approach’, first of all to support breastfeeding because it is the main source of available iron and it does no harm; at the point that when you take the supply of iron from human milk into consideration you are getting some contradictions looking at intake recommendations. As a second suggestion I would say meat because meat is also an excellent source of many functional components such as zinc, iron and the LCP supplied even in minimal amounts. In very good work you have nicely shown that there is a strict regulation of iron absorption according to individual status and to the dietary source utilized. To optimize absorption, vitamin C must also be considered to improve the ratio in special preparations, and zinc with copper to prevent negative interactions. I think that it is possible even using internal resources in developing or transition countries; hopefully this will be a policy of the future.

Dr. Solomons: I don’t have an answer but I have several questions. One has to do with the philosophical question of why is the more rapid development of infants beneficial. I guess when humans were also prey as well as hunters and when other animals such as birds of prey or anacondas in the Amazon were looking around for young infants to eat it would seem to me that the infant who was more quite, less exploratory, had less visual acuity so it wasn’t fascinated by what he was seeing, would have been the less likely to be eaten. On the other hand, the advanced infant, looking around, crawling at the edge of his cliff, would have been the suitable prey. So it may be that at that time nature wanted babies to be more quiet. Now we are rethinking the issue of whether fast or slow is better. I would say that developmental mind landmarks have a similar kind of philosophical question. The second has to do with the ethics of screening for iron status versus the ethics of giving iron without screening, and it is a very interesting question. Dr. Haschke mentioned that there are technological solutions, I would suggest that there are technological solutions to iron screening, and Dr. Rainer Gross, who passed away a month ago, was working in Indonesia on a transducer, a skin Doppler, which could look at the underlying capillaries with energy and photons [4]. This essentially could do a hematocrit in a flowing capillary, so this kind of technological solution would eliminate any invasion, if you will, to the screening. I am convinced that between the two options that screening is preferable to indiscriminate iron supplementation.

Dr. Agostoni: Thank you for the second point, it is quite interesting indeed to develop a noninvasive method for assessing hematocrit. As to the first question about evolution, it could perhaps be advantageous to have fast adaptation to technologies, internet and e-mails and so on.

Dr. Brown: I want to speak on the second point that Dr. Solomons raised. I was going to speak about the iron issue more from a perspective of the methodologic dilemma that we face, namely that the beneficial effects of iron seem not surprisingly to occur in iron-deficient infants and young children, and the adverse effects occur in those who initially are iron replete. So if we are looking for either beneficial or adverse effects of an intervention, we can only interpret the results of those studies if we interpret them in light of initial status. In a study that does not do that, the beneficial and adverse effects may cancel each other out, and so we can get any result without looking at the modifying effect of initial status. That then has implications on sample size and whether we have statistical power in these studies to actually detect these.
effects. I would argue that the adverse effects of iron in iron-replete children may occur not only in malaria endemic zones but in other parts of the world like Chile, Honduras, Sweden and Indonesia. We won't see those effects if we are not looking at iron in relation to initial status.

Dr. Agostoni: Yes, I agree. It is perhaps easier to define an optimal dosage for LCP and the dose-related effects, also taking the initial status into consideration.

Dr. Brunser: I want to raise a point about genetic polymorphism, which is important because in the same locus there may be alleles that are not exactly similar, and this generates dispersion of values. Nobody is entirely equal to his neighbor and this has advantages because these slight differences represent different adaptation possibilities. From our point of view, this creates problems because we have to increase the number of individuals incorporated into our studies to obtain significant differences: it is this background ‘noise’ that has to be kept in mind when analyzing results. This is complicated for us because larger numbers of individuals have to be studied to demonstrate significant differences.

Dr. Turck: I am not sure that I quite understood your answer to the following question: should we supplement lactating mothers with DHA? Did you say yes?

Dr. Agostoni: I said that if we decide to supplement, we should start at 18–22 weeks of gestation because we have to ensure an adequate supply of LCP to the fetus that, from this time onwards to the end of pregnancy, receives progressively increasing levels of LCP. It is like giving folic acid after the periconceptional period; its preventive effects are clearly reduced. If we give DHA during lactation, the mother may benefit, but I am not sure if the infant will benefit. If we give DHA in the last trimester of pregnancy we benefit the mother and probably also the infant, so I would supplement the mother.

Dr. Turck: To me supplementation is needed when an individual cannot fulfill his/her requirements from the regular diet. There may be problems, financial or socio-cultural or even technical problems to obtaining DHA from the diet, but I think that we are not only raising a scientific issue but also an ethical issue. If we start to advise that lactating mothers be supplemented with DHA then the idea emerges that, in a sense, lactation becomes a sickness because we may need supplementation in several specific nutrients. So the question is difficult to answer and I think we have to be very cautious in the type of advice that we give to lactating mothers, at least for this issue with DHA.

Dr. Agostoni: I would say there are two categories mostly exposed to a poor transfer of DHA to the fetus. The first are mothers with intrauterine growth retardation who have very low DHA transfer [5]. The second category is smokers. It has been shown that infants born to smoking mothers have a poor DHA status [6]; smokers transfer lower DHA levels to the fetus. But the effects of maternal dietary supplementation have still to be investigated.

Dr. Haschke: All these discussions on the 2:1 ratio of arachidonic acid versus DHA is related to the American population because they are meat eaters. If you look at Japan, the ratio in breast milk of arachidonic acid to DHA is quite different, it is 1:1 or even less. So I think we should pay more attention to what people are eating in different regions. To follow up on the study which I mentioned yesterday by Dr. Bergmann which was presented at ESPGHAN this year, they started to supplement mothers with DHA at 30 weeks of gestation, and it was clearly shown that the DHA status of the mother was related to the DHA content in breast milk. And finally at birth and at 3 month of age, a clear effect of the supplementation was seen in the offspring. Again the ratio of arachidonic acid to DHA in breast milk was 1:1 or even below. So we have to learn more about supplementation, but it has an effect in certain populations.
**References**


