

# **NEONATE AND INFANT NUTRITION AND IMMUNITY**

In relation to the diet of the pregnant mother, the foetus, the neonate and the young baby, the main areas of concern are:

1. the nutritional status of the mother in pregnancy i.e. folic acid and its methylation derivatives, essential fats, essential vitamins and minerals for the growth of the foetus
2. the nutritional status of the premature neonate
3. the nutritional status of the breast fed baby
4. the nutritional status of the bottle fed baby
5. the introduction of foods to the developing gastrointestinal tract and the priming of the immune system of the neonate and infant.

## **FOLIC ACID AND THE FOETUS**

See methylation pathways and cell division.

## **ESSENTIAL FATS IN PREGNANCY AND INFANCY**

Long chain polyunsaturated fatty acids (LC-PUFA) are essential for both structure and function in the neonate.

- Their structural role:
  - LC-PUFAs are an essential part of phospholipids, so play a role in the formation of membranes and the brain.
- Their functional role:
  - They function as specific precursors for the production of eicosanoids, i.e. prostaglandins, thromboxanes, and leukotrienes. These eicosanoids are powerful regulators of numerous cell and tissue functions. These include:

- thrombocyte aggregation
  - inflammatory reactions
  - leukocyte functions
  - vasoconstriction and vasodilatation
  - blood pressure
  - bronchial constriction
  - uterine contraction.
- Role in predisposition to disease:
    - Infant dietary lipid intake has a profound affect on cholesterol metabolism and has been shown to be associated with cardiovascular morbidity and mortality later in life.i

## **CHEMISTRY OF LC-PUFAs**

Two important long-chain polyunsaturated fatty acids (LC-PUCA), that are important for cognitive development, are docosahexaenoic acid (DHA, a  $\omega$ -3 fatty acid) and arachidonic acid (AA, an Omega-6 fatty acid).

### ***DOCOSAHEXAENOIC ACID***

DHA has a 22-carbon chain with 6 double bonds, making it one of the most highly unsaturated fatty acids in the human body. The metabolism of  $\alpha$ -linolenic acid (ALA) to DHA involves a series of reactions that involve desaturase enzymes (cofactors being zinc, pyridoxal 5 phosphate, folic acid, NADH, manganese and O<sub>2</sub>), that add double bonds to the molecule, and elongation enzymes (cofactors niacin, pantothenic acid, magnesium and insulin), that add 2-carbon units (methylation). ii

- DHA is a major component of the retina, reaching concentrations of 30–40% of the total fatty acids in the rod photoreceptor in the human retina.
- DHS is also involved in dopamine and serotonin metabolism

There is a growth spurt in the human brain during both the last trimester of pregnancy and the first postnatal months, with a large increase in the cerebral content of AA and DHA.

Both the foetus and the newborn infant are dependant on the maternal supply of DHA and AA.

## ***SUPPLEMENTATION OF LC-PUFAs***

There seems to be no detectable reduction in plasma  $\omega$ -3 LCPUFA concentrations during pregnancy.

There is however, a definite decline during the early postpartum period. This postpartum decrease in the maternal plasma DHA concentration is a gradual process, appears to be independent of lactation. The decline can be reversed with DHA supplementation (200-400 mg/d).<sup>iii</sup>

The supplementation of  $\omega$ -3 fish oils as opposed to supplementation with corn oil ( $\omega$ -6) oils showed a statistically significant increase in mental acuity at 4 years of age. <sup>iv</sup>

The **overall** levels of the  $\omega$ -6 and  $\omega$ -3 18C poly-unsaturated fatty acids in the mother's milk are closely dependent on their concentrations in maternal plasma, which is in turn related with the mother's dietary intake. The levels of AA and DHA in milk, however, are the result of a sequence of transfer and metabolic processes, not directly related to the mother's diet. Studies indicate that the major portions of milk PUFAs are not derived directly from the maternal diet, but stems from endogenous body stores. Thus, not only the woman's current but also her long-term dietary intake is of marked relevance for breast milk fat composition. <sup>v</sup> This confirms our observation that the breast milk and placenta will strip DHA from the mother's stores, so it is essential to have built up levels of DHA ahead of the birth process and breast feeding. <sup>vi</sup>

Premature infants can synthesize some DHA, AA and other  $\omega$ -3 and  $\omega$ -6 LC-PUFAs from the dietary EFAs, LA and ALA, but their rate of doing so, is unclear.

Plasma, erythrocyte and brain lipid levels of DHA are known to be lower in infants whose diets do not contain DHA.

It is therefore suggested that human infants have a conditionally essential need for DHA and probably for AA.

The following factors that need to be taken into account are:

- The maternal diet and supplementation of  $\omega$ -3 fats
- The maternal and infant desaturase and elongase enzyme function and the provision of their enzyme co-factors.

## ***BREAST MILK VERSUS FORMULA MILK***

Several recent studies document the beneficial effect of breast-feeding on the later neuro-developmental outcomes. The complete mechanisms involved are still in need of elucidation, but there is growing evidence that the fatty acid (FA) composition of mother's milk plays a role. The composition of all infant body fats, from circulating erythrocyte lipids to brain phospholipids, is linked to the early type of feeding.

In one study, breast-fed infants had higher tissue LC-PUFA (AA, EPA (eicosapentaenoic acid) and DHA than standard formula-fed infants and that the formula fed infants had lower visual and neuro-developmental test scores.

Human milk contains AA, EPA and DHA, while most available formulas, especially those intended for full-term infants, do not.

The preformed supply of DHA (i.e. Neuromins from marine algae) bypasses the regulating step of  $\delta$ -6 desaturase enzyme in DHA's formation from ALA. In fact, ALA in high doses (as in vegetable oils) actually inhibits the  $\delta$ -6 desaturase enzyme and so is counter-productive.

Fish oils supply DHA but little AA.

Pre- or postnatal deficits of AA and DHA together with **underdeveloped antioxidant protection** (superoxide dismutase enzyme [SOD] is not fully activated until term) contribute to cell membrane function problems, as well as endothelial and neurovisual developmental problems such as:

- Intraventricular haemorrhage,

- Periventricular leucomalacia
- Retinopathy of prematurity
- Bronchopulmonary dysplasia.

At birth, 70% of the foetal energy production is focused on its brain development, so that the brain and its blood vessels are growing at high speed. These pathologies associated with DHA and AA deficiencies and the SOD antioxidant deficiency can have serious long term consequences. At present there are no lipid nutritional supplements for the preterm neonate that can supply this need. All preterm infant foods are based on full term milk, the composition of which is very different than the placental nutrition.vii

For pregnant and lactating women: specific recommended levels of PUFA are unknown at this time. However a leading paediatric consultant says that “it seems prudent for pregnant and lactating women to include some food sources of DHA in their diet in view of their assumed increase in LC-PUFA demand and the relationship between maternal and foetal DHA status”. viii

**TABLE 1.** Fatty acid composition, as percentage of total fatty acids, of plasma phospholipids in preterm infants at 57 wk post conception age ix

	Breast milk ( <i>n</i> = 8)	CO ( <i>n</i> = 13)	SO ( <i>n</i> = 17)	SMO ( <i>n</i> = 14)
Total saturated fatty acids (%) <sup>2</sup>	43.0 ± 1.5	42.4 ± 1.3	43.1 ± 1.2	43.5 ± 1.2
Total monounsaturated fatty acids (%) <sup>3,4</sup>	10.5 ± 3.0 <sup>a</sup>	8.6 ± 0.7 <sup>b</sup>	7.5 ± 0.7 <sup>b</sup>	7.7 ± 0.9 <sup>b</sup>
20:3n-9	0.08 ± 0.17	0.08 ± 0.05	0.05 ± 0.03	0.03 ± 0.03
n-6 Fatty acids (%)				
18:2n-6 <sup>4</sup>	29.7 ± 4.4 <sup>a</sup>	35.2 ± 2.8 <sup>b</sup>	34.0 ± 1.6 <sup>b</sup>	31.4 ± 2.2 <sup>a</sup>
18:3n-6	0.04 ± 0.05	0.04 ± 0.02	0.04 ± 0.02	0.02 ± 0.02
20:2n-6 <sup>4</sup>	0.54 ± 0.06 <sup>a</sup>	0.74 ± 0.09 <sup>b</sup>	0.62 ± 0.11 <sup>c</sup>	0.52 ± 0.07 <sup>a</sup>
20:3n-6	2.13 ± 0.63	1.85 ± 0.35	1.79 ± 0.48	1.65 ± 0.30
20:4n-6 <sup>4</sup>	6.31 ± 1.61 <sup>a</sup>	7.91 ± 1.69 <sup>b</sup>	8.30 ± 1.58 <sup>b</sup>	5.69 ± 1.25 <sup>a</sup>
22:4n-6 <sup>4</sup>	0.37 ± 0.22 <sup>a</sup>	0.68 ± 0.20 <sup>b</sup>	0.56 ± 0.25 <sup>b</sup>	0.23 ± 0.19 <sup>a</sup>
22:5n-6 <sup>4</sup>	0.52 ± 0.47 <sup>a,b</sup>	0.67 ± 0.16 <sup>b</sup>	0.36 ± 0.13 <sup>b</sup>	0.09 ± 0.02 <sup>c</sup>
Total n-6 LCPUFAs <sup>4</sup>	9.88 ± 2.08 <sup>a</sup>	11.87 ± 1.89 <sup>a</sup>	11.66 ± 2.00 <sup>a</sup>	8.20 ± 1.47 <sup>b</sup>
n-3 Fatty acids (%)				
18:3n-3 <sup>4</sup>	0.28 ± 0.09 <sup>a</sup>	0.10 ± 0.08 <sup>b</sup>	0.37 ± 0.08 <sup>c</sup>	0.24 ± 0.05 <sup>a</sup>
20:5n-3 <sup>4</sup>	1.26 ± 0.61 <sup>a</sup>	0.10 ± 0.10 <sup>b</sup>	0.24 ± 0.09 <sup>b</sup>	1.94 ± 0.4 <sup>c</sup>
22:5n-3 <sup>4</sup>	1.14 ± 0.33 <sup>a,b</sup>	0.43 ± 0.17 <sup>c</sup>	0.93 ± 0.22 <sup>b</sup>	1.29 ± 0.30 <sup>a</sup>
22:6n-3 <sup>4</sup>	3.52 ± 1.07 <sup>a</sup>	0.62 ± 0.12 <sup>b</sup>	1.77 ± 0.30 <sup>c</sup>	5.11 ± 1.13 <sup>d</sup>
Total n-3 LCPUFAs <sup>4</sup>	6.36 ± 1.74 <sup>a</sup>	1.59 ± 0.48 <sup>b</sup>	3.11 ± 0.55 <sup>c</sup>	8.68 ± 1.56 <sup>d</sup>
Ratio of n-6 to n-3 LCPUFA <sup>4</sup>	1.75 ± 0.73 <sup>a</sup>	7.95 ± 2.05 <sup>b</sup>	3.84 ± 0.88 <sup>c</sup>	0.97 ± 0.27 <sup>a</sup>

<sup>1</sup> ± 1SD; LCPUFAs, long-chain polyunsaturated fatty acids (contain >18 carbons); SO, Soy-oil-based formula; CO, corn-oil-based formula; SMO, soy- and marine-oil-based formula. Values with different superscript letters within rows are significantly different from each other by post-hoc Neuman-Keuls procedure, *P* < 0.05.

<sup>2</sup>Includes 14:0, 15:0, 16:0, 17:0, 18:0, 20:0, 22:0, and 24:0.

<sup>3</sup>Includes 16:1, 18:1, 20:1, 22:1, and 24:1.

<sup>4</sup>*P* < 0.0005, ANOVA.

## **FORMULA MILK**

For healthy infants: breastfeeding is the preferred method of feeding, which supplies preformed LC-PUFA.

If infant formulas for term infants are needed, they should contain at least 0.2% of total fatty acids as DHA and 0.35% as AA. The highly unsaturated nature of DHA (with 6 double bonds) makes it particularly susceptible to lipid peroxidation. Because the generation of damaging free radicals is associated with extensive lipid peroxidation, there is some concern regarding the safe use of LC-PUFAs in infant formula.

The exact ratio of  $\omega$ -3 to  $\omega$ -6 fats is controversial. I suspect that recommended  $\omega$ -3 /  $\omega$ -6 ratio of 5:7 for early life may be high.

The adult recommendation for the ratio of  $\omega$ -3 to  $\omega$ -6 fats is a much lower ratio of about 1.4. Since there is a much higher need for DHA in neonate neural development, this does not make sense, the ratio should be at least that of the adult ratio if not more.

Preterm infants, since they are born with much less total body DHA and AA, need an infant formula that includes at least 0.35% DHA and 0.4% AA. Higher levels have not been evaluated and are probably necessary. x It is not just DHA, AA is also necessary. It is estimated that the neonate can only supply about 23% of its total plasma arachidonic acid by day 4 from vegetable oil based formulas. xi

## ***COGNITIVE DEVELOPMENT***

Research has shown that LC-PUFAs are associated with improved visual and cognitive development: breast-fed children had higher IQ scores compared with children who received an infant formula that did not contain LC-PUFAs. Because breast milk contains LC-PUFAs and the formulas in these studies did not, it is possible that LC-PUFAs may contribute to improved cognitive development. xii

## ***IMMUNE DEVELOPMENT***

Mothers whose children were found to be allergic have been shown to have lower levels of EPA, DPA and DHA in their breast milk compared to the milk from

mothers of non-allergic children. xiii

Low levels of  $\omega$ -3 PUFA in human milk, and particularly a high AA: EPA ratio in maternal milk and serum phospholipids in the infants, were related to the development of symptoms of allergic disease at 18 months of age. The milk PUFA composition was shown to influence the composition of PUFAs in infant serum phospholipids.

These findings showed that low ALA and  $\omega$ -3 LC-PUFAs, but **not** the levels of S-IgA antibodies to allergens, are related to the development of atopy in children.

## **THE ROLE OF PROBIOTICS IN NEONATE AND INFANTS**

Probiotics (lactobacillus GG)<sup>xiv</sup> were given to mothers two weeks prior to the birth and for the first six months of infant life in a double-blind, randomised placebo-controlled trial. There was a significant reduction in allergic symptoms in these children compared to controls. The children were chosen from mothers who had at least one first-degree relative (or partner) with atopic eczema, allergic rhinitis, or asthma.

Chronic recurring atopic eczema, the main sign of atopic disease in the first years of life, was significantly reduced in the probiotic supplemented infants.<sup>xv</sup>  
See Findings endnote <sup>xvi</sup>

## **FUNCTIONS OF GASTROINTESTINAL FLORA**

Gastrointestinal microflora promotes potentially antiallergenic processes in the following ways:

T-helper-type 2 immune system is dominant in both foetuses and neonates. It is the growth of the healthy gut microflora that should be the major postnatal counter-regulator of the Type 2 immune system.

The GI tract is colonised immediately at birth and when fully established, the viable cells of fully established gut microflora outnumber the cells of the human

host by a factor of ten.<sup>xvii</sup>

In this study, the improvement in symptoms in neonates was greater than usually seen with probiotic administration later in life.

### **Known side effects of probiotics:**

There are few known side effects; there are occasional cases of septicaemia and of liver abscess, but this is usually in immunodeficient patients.<sup>xviii</sup>

In one study there was an unexplained excess mortality in athymic neonatal mice given *Lactobacillus casei* GG, whereas similarly immunodeficient adult mice were unaffected.<sup>xix</sup> Further investigation is needed to clarify what is happening in this situation.

## **OVERVIEW OF PROBIOTIC USE IN ALLERGY:**

Probiotics are thought to have the following effects in the prevention and treatment of allergies:

- Probiotics increase T-helper-1-type immunity;<sup>xx</sup>
- Probiotics reverse increased intestinal permeability, <sup>xxi</sup> a characteristic of children with atopic eczema and food allergy.<sup>xxii</sup>
- Probiotics they play a key role in the induction of oral tolerance i.e. they inhibit specific immunological responsiveness to what they infant eats;<sup>xxiii</sup> this is important so that the infants do not become allergic to all the foods that they are exposed to.
- Probiotics enhance gut-specific IgA responses, which are often defective in children with food allergy.<sup>xxiv</sup> IgA is an essential component of the gut mucosal immune defence (GALT) <sup>xxv</sup>. These gastrointestinal microbes are the earliest and biggest stimulus for development of gut-associated lymphoid tissue (GALT).
- They also help to promote gut barrier function and restore normal gut micro ecology with lactic acid bacteria,<sup>xxvi</sup> significant deficiencies in healthy gut flora having been shown in allergic individuals.<sup>xxvii</sup>
- They reduce inflammation associated with allergic diseases both in vitro

and in vivo. xxviii'xxix

- They initiate the generation of transforming growth factor  $\beta$  (TGF- $\beta$ ) and interleukin 10 (IL-10) xxx'xxx' ' xxxii. TGF- $\beta$  has an essential role in suppression of T-helper-2-induced allergic inflammation (i.e. pro-inflammatory activity) xxxiii and these cytokines are thought to be more crucial than T-helper-1-type inducers xxxiv in the prevention and treatment of atopic diseases.
- Probiotics may block receptors in the intestinal mucosa and thus preventing adhesion of the pathogenic bacteria from becoming established.
- Probiotics may have eliminated other pathogenic bacteria just by competitive exclusion through production of their own antibacterial substances.
- Probiotics may cause changes in the pH or chemical composition of the colonic lumen that are unfavourable to pathogenic bacteria or they may promote the repair and nourishment of the gut mucosa.

The GI tract of the neonate is sterile, but there is a rapid colonisation of the gut until a stable indigenous gut microflora is established.xxxv A reduced ratio of bifidobacteria to clostridia in early gut microflora has been shown to precede the development of atopy and atopic disease. In these cases, the T-helper 2 type cells becoming dominant.xxxvi

Dietary antigens also strongly affect the neonatal gastrointestinal system and correct food ingestion is balanced by a healthy gut flora. It seems that children who are able to deal with different foods have transient increases of cytokines that promote production of IgE antibodies, whereas children who are unable to raise these IgE antibodies are more likely to develop atopic disease.

# **MECHANISM OF ACTION OF PROBIOTICS AND IMMUNE COMPETENCE**

The mother's and the neonate's gut flora in the developed world are discordant.

xxxvii

In the non-developed world and the 19th Century European infant, Bifidobacteria and Lactobacillus are the dominant flora.

In the developed world, the dominant flora are a variety of hospital-acquired organisms.

This trend is exacerbated by procedures such as caesarean section or admission to special-care units.<sup>xxxviii xxxix</sup>

Since colostral and breast-milk lymphocytes are dominated by gut-derived populations, it is quite possible that the newborn mucosal immune system is exposed to mismatched input during initial priming in the developed world.

It is thought that the first bacteria to colonise a previously sterile gut may establish a permanent niche by inducing specific and lasting glycosylation of the glycocalyx as well as by modulating enterocyte gene expression, thus putting later bacteria at competitive disadvantage.

It is highly probable that these differences in the gut flora between caesarean-born and vaginally born infants are permanent.<sup>xi</sup> There is also some evidence to suggest that first-night nursing away from the mother may be associated with increased likelihood of allergy in later life and that the neonates gut flora is primed by the handler in that first night.<sup>xii</sup> So the mother should be the first significant handler of the neonate.

It seems very likely that this early probiotic supplementation, both prenatal and postnatal supplementation, may stabilise gut flora at a higher concentrations than if such probiotics are supplemented later in life.

## **DIETARY EXCLUSION**

Dietary exclusions in the mother, pre- and post-natal, can provide a significant

and important clinical benefit in a substantial minority of children, since increasing numbers of infants are becoming sensitised to maternally ingested antigen despite exclusive breast feeding.<sup>xlii</sup> This is because of the poor immune system of the mother.

## **ALLERGENS OF INFANCY AND EARLY CHILDHOOD**

The typical allergens of infancy and early childhood are:

- egg,
- milk,
- peanut,
- wheat,
- soya.

## **ALLERGENS OF OLDER CHILDREN AND ADULTS**

The allergens responsible for **severe** reactions in older children and adults are mainly caused by:

- peanut,
- tree nuts,
- seafood,
- allergy to fruits and vegetables is common, but usually not severe.<sup>xliii</sup> <sup>xliv</sup>
- allergy/hypersensitivity to wheat and dairy is common but undiagnosed

Care should be taken with reintroduction of allergic foods, as when a food to which the patient is sensitised is removed from the diet during a chronic disorder, reintroduction can induce severe reactions.<sup>xlvi</sup>

Useful contacts for families where there are severe reactions are from support groups such as the Anaphylaxis Campaign, UK ([www.Anaphylaxis.org.uk](http://www.Anaphylaxis.org.uk)) and the Food Allergy and Anaphylaxis Network, USA ([www. foodallergy.org](http://www.foodallergy.org)).

Symptom wise, it is claimed that most children (about 85%) lose their sensitivity to most allergenic foods (egg, milk, wheat, soya) within the first 3-5 years of life <sup>xlvii</sup>; that food-specific IgE concentrations generally fall with tolerance <sup>xlviii</sup>; and

that even children with multiple, severe allergies usually achieve tolerance xlix. By contrast, adults with food allergy can have long-lived sensitivity. In allopathic medicine, they are noticing that the persistence of childhood food allergy seems to be increasingly common.l

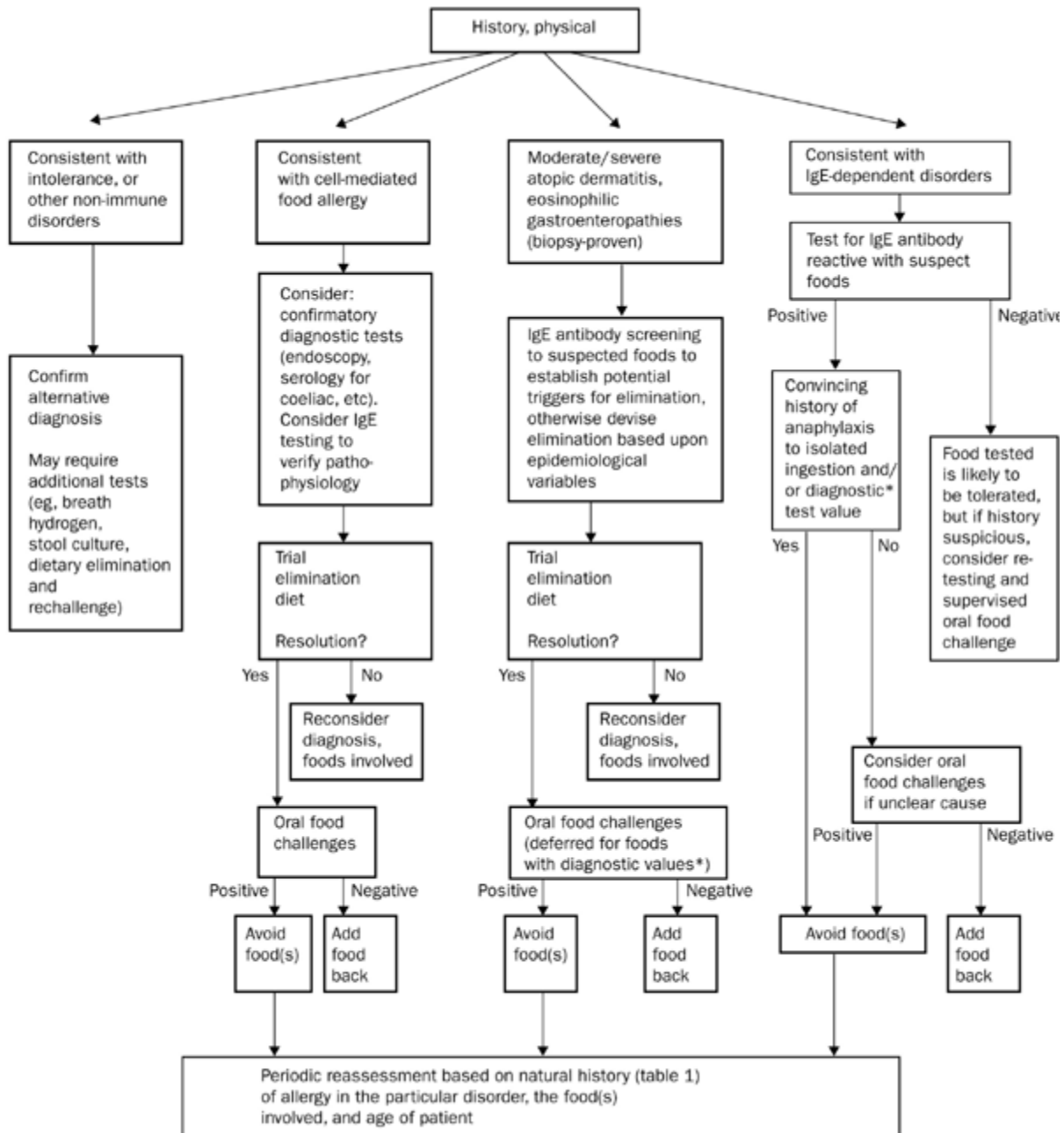
Our experience is that the allergies remain, but the symptoms are changed and that they lay down problems in later life with increases in stress physiology and the initiation of free radical pathology.

## THERAPEUTIC STRATEGIES

- Breastfeeding (6-12 months). li
  - Since maternally ingested foods can pass in an immunologically intact form into breast milk lii and produce reactions in the infant, liii, it is necessary to use **exclusion diets** and **digestive enzymes** in pregnancy and when breast feeding. Studies have shown that infants from atopic families whose mothers exclude highly allergenic foods from their diets during lactation generally have less atopic dermatitis and food allergy than those whose mothers' diets are unrestricted. liv lv However, such differences might not extend beyond early childhood so a true effect on long-term prevention is uncertain. Allopathic opinion is that dietary restrictions during pregnancy generally seem ineffective lvi but this is probably because they are not including other therapeutic modalities.
- Use of hypoallergenic formula (not soya) for supplementation.
- The delayed introduction of solid foods beyond the 5th month of life. lvii
  - The US recommendations lviii when one or both parents and siblings are atopic include:
    - elimination of peanut and nuts with consideration of elimination of other foods during breastfeeding,
    - consideration of elimination of peanut during pregnancy,
    - the delayed introduction of allergenic foods

- milk to 12 months
- egg to 24 months
- peanuts, nuts, and fish to 36 months.

This strategy is thought to reduce food allergy, atopic dermatitis, and food sensitisation by 30-50% in the first 2 years; however there is usually no significant difference in atopic parameters by age 4 and 7 years. <sup>lix</sup> Again this is probably due more to the poor diet, refined carbohydrate diet and damage to the gut wall from vaccines than to the failure of the care taken in pregnancy and breast feeding.



Allopathic: General scheme for diagnosis of food allergy

This group of strategies are universally accepted as associated with a reduction in atopic disease. ix | xi

<b>INFANT FEEDING RECOMMENDATIONS</b>	
1. All infants are best fed by breast feeding	
2. Mothers should avoid foods they are allergic to, especially dairy and wheat, the major allergens; plus sugar and alcohol because of the changes they make to the mother's gut wall permeability	
3. Cows milk should be avoided until at least 12 months	
4. If formula is used, challenge for allergy. Consider support with probiotics.	
5. Solid foods should not be introduced before 4 months as early use of solids is associated with obesity later in life. At 4 months they start to show teeth and that they are not satisfied with just breast milk.	
6. Additives to foods	Do not add: <ul style="list-style-type: none"> <li>• Salt</li> <li>• Sugar</li> <li>• Natural (honey) or unnatural sweeteners (modified starches)</li> </ul>
7. Introduce foods in an order so that one can identify any food reactions i.e. by introducing a new food every 5 days as on a rotation diet	Start with cereals: <ul style="list-style-type: none"> <li>• Oats</li> <li>• Barley</li> <li>• Wheat</li> <li>• Rye</li> <li>• Millet</li> </ul>
8. Do not use processed foods 9. Use organic food	Reduce the pesticide residues in the infant brain as they have never been tested on infants
10. After cereals, introduce organic vegetables	Use as wide a range of vegetables as possible to add diversity to the diet and taste of the infant
11. After the introduction of a wide range of vegetables, introduce meat (organic and free range) and fish (wild, not farmed).	Use white meat more than red meat Use deep sea fish as much as possible Delay fish in children of allergic parents until 36 months
12. After fish and meat, introduce fresh fruits	Use both raw and cooked with <u>no</u> sweeteners Add citrus fruits last at about 9 months
13. Eggs can be introduced after about 24 months	Start with egg yolks Add whole eggs after 3 more months
14. Peanuts, nuts, and fish in children of allergic parents should not be introduced before 36 months	

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- xvi **Findings** Atopic eczema was diagnosed in 46 of 132 (35%) children aged 2 years. Asthma was diagnosed in six of these children and allergic rhinitis in one. The frequency of atopic eczema in the probiotic group was half that of the placebo group (15/64 [23%] vs. 31/68 [46%]; relative risk 0.51 [95% CI 0.32-0.84]). The number needed to treat was 4.5 (95% CI 2.6-15.6).
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