# Maternal & Infant Nutrition Briefs

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**New Recommendations on Hypoallergenic Infant Formulas**

Symptoms of food protein allergy that are commonly associated with immunoglobulin E (Ig-E) reactions include hives, rash, wheezing, runny nose, and vomiting. Other problems, such as irritation or inflammation of the gastrointestinal tract, may also occur but not through mechanisms involving immunoglobulin E. Finally, in some cases, extreme irritability or colic may be the only symptom. The American Academy of Pediatrics (AAP) has recently published its recommendations on the use of hypoallergenic infant formulas for these conditions.

In their statement, AAP outlines the steps to be taken in clinical testing and labeling of new hypoallergenic formulas. AAP also states that breast milk is the best nutrition for the first six months of life and should be offered throughout the first twelve months or longer. They do not recommend goat's milk as an acceptable alternative for infants allergic to cow's milk. Finally, they review some studies of preventing allergy in high-risk infants and conclude that soy-based and currently available partially hydrolyzed formulas are not hypoallergenic by their criteria. Extensively hydrolyzed and free amino acid-based formulas are considered to be hypoallergenic. AAP's specific recommendations include the following:

1) Breast milk is the optimal nutrition source during the first year or longer. Breastfeeding infants with symptoms of food protein allergy may benefit from restriction of cow's milk, egg, fish, peanuts, and tree nuts in the mother's diet. If changes in the mother's diet are not effective,
then hypoallergenic or soy-based formulas may be an alternative where infants have Ig-E associated symptoms. Soy-based formulas are not recommended for non-Ig-E syndromes, such as enterocolitis;

2) Formula-fed infants with confirmed cow's milk allergy may benefit from either a hypoallergenic formula or soy-based formula, as described for the breastfed infant;

3) Infants at high-risk of allergy due to family history may benefit from exclusive breastfeeding or hypoallergenic formulas. Evidence that partially hydrolyzed formulas prevent development of allergy is weaker. For breastfed infants at high risk of allergy, AAP recommends that, in addition to maternal dietary restrictions (same as # 1 above), solid foods should be delayed until six months of age. Dairy products should be delayed until one year; eggs, until two years; and peanuts, nuts, and fish, until three years of age. No maternal dietary restrictions, except for possibly peanuts, are necessary during pregnancy; and

4) Breastfeeding mothers on a restricted diet should consider taking vitamin and mineral supplements.

**Source:** American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic Infant Formulas. Pediatrics 106 (2): 346-349.

### Effects of Gestational Diabetes on Child Weight

Gestational diabetes affects 2-3% of all pregnancies. A previous study found that certain maternal factors, including gestational diabetes, increase fatness in infants at birth and one year. The purpose of this study was to examine the long-term effects of gestational diabetes on relative weight and fatness of the same children, at 4 to 7 years of age.

The findings come from a prospective, longitudinal study of children of mothers who either had gestational diabetes (GDM) or normal pregnancies (controls). Most of the mothers were white, middle-class women, and neither education nor marital status differed between the groups. The study excluded children who were small-for-gestational age, had birth defects, or had been placed in intensive care after delivery. Within each group, infants were identified as either being of normal birth weight (AGA) or large-for-gestational age (LGA, > 90th percentile). The researchers measured blood pressure, postprandial blood glucose levels, weight, height, and skinfolds of these 207 children at 4, 5, 6, and 7 years of age.

Although blood pressure and glucose levels were similar, group differences in body mass index (kg/m2) significantly increased over time ($p < 0.009$. High birth weight children of diabetic mothers were heavier and had more body fat than all other children. Interestingly, normal weight children of diabetic mothers tended to have the lowest body mass index and skinfold measurements of all children. This finding may be due to tighter control of blood sugar in women who were leaner at the start of their pregnancies, compared to women with GDM who delivered large babies. Another possibility is that normal weight children of diabetic mothers experience an rebound in body fatness later.

These findings differ from those among the Pima Indians where diabetes during pregnancy increased the risk of child obesity in both high birth and normal birth weight children. More research is needed on the long-term consequences of gestational diabetes and the impact of good control of blood sugar during pregnancy.

**Source:** Vohr BR, McGarvey ST, Tucker R. Effects of maternal gestational diabetes on offspring adiposity at 4-7 years of age. Diabetes Care 22:1284-1291.

### Early vs. Late Iron Supplementation in Premature Infants

Premature infants are at risk of iron deficiency due to their lower stores of iron at birth. In

1985, the American Academy of Pediatrics recommended that low birth weight infants be given 2-3 mg of iron/kg/day, starting at 2 months of age, or at least when the infant reaches 2000 gm in weight. That recommendation has not been updated, although many smaller infants survive today than in the 80's. Pediatricians are cautious about not giving ferrous iron too soon to avoid oxidative stress from free radicals that could damage the retina and lungs. However, blood transfusions also pose a risk of infection and other health problems. The purpose of this study was to compare the effects of early vs. late iron supplementation in 133 premature infants, with birth weight < 1301 gm.

The infants were randomly assigned to receive 2 mg/kg/ day of ferrous sulphate as soon as they could tolerate 100 ml/kg/ day of enteral feeding (early) or at 61 days of age (late). For the early group, the average age of starting iron was 16 days. All infants were fed either fortified breast milk or a standard premie formula. Equal numbers of infants in both groups received transfusions before 7 days, and a restrictive protocol determined whether transfusions were given after 7 days. The main outcome was iron deficiency at 61 days, as indicated by low serum ferritin or percent saturation of transferrin. Infants in early and late groups were similar in birth weight, gestational age, and clinical risk factors at the start of the study.

At 61 days, mean serum ferritin levels were not different among the two groups, although a greater percentage of the late-iron group was iron deficient compared to early-iron babies (40.0% vs. 14.7%). Also, more infants in the late-iron group were given transfusions after 14 days (53.5% vs. 39%). The researchers did not find any adverse effects of early iron supplements on enterocolitis, retinopathy, or infections.

This is the first randomized trial of early vs. late iron supplementation in premature infants. The findings suggest that early iron may be well-tolerated and could even reduce the need for transfusions, but the authors did not report any breakdown of effects by type of infant feeding. Thus, more research is needed to repeat these results and determine the optimal timing of iron dosing for premature infants.

**Source:** Franz AR, Mihatsch WA, Sandert S., Kron M, and Pohlandt F. Prospective randomized trial of early vs late enteral iron supplementation in infants with a birth weight of less than 1301 grams. Pediatrics 2000; 106:700-706.

### Emotional Stress and Birth Defects

Can a stressful life event, such as the sudden death of an older child, increase the risk of delivering a baby with birth defects? Since psychosocial stress affects the nervous, cardiovascular, metabolic, and immune systems, one might expect negative effects on the unborn child. Cranial neural crest cells may be more vulnerable to stress, because internal factors influence their growth and development. Cortisone, a hormone released during stress, increases risk of cleft palate, other skull defects, and spina bifida in mice. A recent Danish study provides new evidence in humans that severe emotional stress may be associated with birth defects, particularly those affecting the skull and face.

This study involved linking several national databases, including the Medical Birth Registry, the Fertility database, the National Mortality Registry, and the National Hospital Discharge Registry. In this way, the researchers were able to identify not only birth outcomes and socioeconomic data for each pregnant woman, but also whether or not the woman's partner or older child had died or been admitted to the hospital during her pregnancy. Using criteria set by the American Psychiatric Diagnostic System, the researchers defined a severe life event as death or first hospitalization for cancer. The final sample included 3560 pregnancies exposed to severe life events and 20, 229 randomly selected unexposed pregnancies (controls). The outcomes included cranioneural crest defects (eg. cleft lip and/or palate, ear defects) and other birth defects.

Women who experienced a stressful event tended to be older, less educated, single mothers. Controlling for these factors, women exposed to severe life events were 1.5 times as likely than controls to deliver a baby with cranioneural crest defects (95% C.I .1.05-2.27). Women exposed to 2 events in subsequent pregnancies were 2.6 times as likely to deliver a baby with cranioneural crest defects (95% C.I.: 1.06-8.43). Women who had an older child die unexpectedly during their first trimester were 8.36 times as likely as controls to deliver a baby with cranioneural crest defects (95% C.I.: 2.4-29.0) and were at greater risk of other birth defects, as well.

The authors conclude that severe emotional stress, especially the death of a child, during pregnancy may cause birth defects. No data are available to explain how stress might cause birth defects, but cortisone may affect cranioneural crest cells by limiting the supply of oxygen or raising maternal blood glucose levels. The roles of poor diet and/or alcohol intake remain to be determined.

**Source:** Hansen D, Lou HC, and Olsen, J. Serious life events and congenital malformations: a national study with complete follow-up. Lancet 2000; 356: 875-80.

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