

Maternal & Infant Nutrition Briefs



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A research-based newsletter prepared by the University of California for professionals interested in maternal and infant nutrition



Antioxidants for Prevention of Pre-eclampsia

Pre-eclampsia, characterized by hypertension and proteinuria, is an important cause of preterm delivery and maternal morbidity and mortality. No intervention has been proven to prevent or delay the onset of pre-eclampsia. According to the toxemia theory, an abnormal placenta releases into the mother's blood stream substances that lead to maternal vascular endothelium damage and dysfunction. What could cause this vascular damage? Some have suggested that oxidative stress, through free radicals, may be involved. In the plasma of women with pre-eclampsia, levels of antioxidants are low, and evidence of lipid peroxidation has been found. The purpose of this study was to determine whether early supplementation with vitamins C and E could improve maternal vascular function and prevent pre-eclampsia in women at-risk.

The study used a double-blind, randomized trial in which the women were given either 1000 mg of vitamin C and 400 IU of vitamin E daily or a placebo starting at 20-22 weeks. The researchers selected pregnant women at-risk of pre-eclampsia, based on either history of pre-eclampsia or an abnormal two-stage uterine-artery doppler waveform scan at 18-22 weeks. The doppler scan is thought to be an indicator of placenta function and predictive of later pre-eclampsia, intrauterine growth retardation, and placental abruption. Outcomes included 1) occurrence of pre-eclampsia and 2) plasma indicators of maternal endothelium and placental function. To assess the latter, the researchers looked at the ratio of plasminogen-activator inhibitors (PAI-1: PAI-2) in the mother's blood. In normal pregnancies, this ratio decreases over time but remains high in pre-eclampsia due to the endothelium damage and placenta malfunction. Levels of vitamin C and E in the blood were also examined monthly.

Among the 283 women, only 8% of the vitamin group developed pre-eclampsia, compared to 17% of the controls ($p= 0.02$, odds ratio 0.39, 95% CI 0.17-0.90). Over the course of the pregnancy, vitamin supplementation increased plasma vitamin C levels by 32% and vitamin E

levels by 54%, compared to baseline values. Vitamin supplements were also associated with a 21% drop in the PAI-1:PAI-2 ratio, compared to the control group ($p=0.015$).

The authors suggest that previous studies may have failed to find benefits of vitamin supplements because therapy was started too late in the pregnancy. While the results look very promising, the doses used are relatively high, and safety for the infant has not been rigorously examined. The authors conclude that their results need to be confirmed in a much larger multicenter trial.

Source: Chappell LC, Seed PT, Briley AL, Kelly FJ, Lee R, Hunt BJ, Parmer K, Bewley, Shennan AH, Steer PJ, Poston L. 1999. Effect of antioxidants on the occurrence of pre-eclampsia in women at increased risk: a randomized trial. *Lancet* 354: 810-815.

Birth Weight Predicts Size at Three-to-Six Years of Age

With obesity on-the-rise in children, many health providers would like to be able to identify those children at-risk and target them for early preventive efforts. Some small prospective studies have shown that birth weight status, both low and high, is associated with growth patterns up to 8 years of age. The purpose of this study was to determine whether these relationships hold up in an ethnically diverse sample of U.S. children.

The analysis was done on 3428 children (3-6 yrs.) using data from the third National Health and Nutrition Examination Survey (NHANES III). Only nonHispanic white, nonHispanic black, and Mexican-American children were included in the study, because the reference data to classify birth weight status is specific to those groups. Weight, height, head and mid-arm circumferences, and skinfold measurements were obtained from the NHANES III, and birth weight, length of gestation, and ethnicity, from birth certificates. Small-for-gestational age (SGA) was defined as a birth weight < the 10th percentile for gestational age. Large-for-gestational age (LGA) included those with birth weights > the 90th percentile. Those between the 10th-89th percentiles were considered appropriate-for gestational age (AGA). To make comparisons across age, gender, and race/ethnic groups, the anthropometric data were examined in terms of standard deviation units (SDU) above or below the mean. For example, weight-for-age at the 10th, 50th, and 90th percentiles would have a SDU of -1.28, 0, and +1.28, respectively.

In all measures of body size and linear growth, SGA children consistently remained below the mean and showed little change from 3 to 6 yrs of age. Measures of fatness (i.e., skinfolds) fluctuated for SGA children and only indicated deficits in the oldest children. In contrast, LGA children showed patterns of growth that continued to diverge strongly from mean over the same period. The triceps and subscapular skinfolds measurements indicated that LGA children accumulated significant amounts of body fat during the same time period. Thus, birth weight relative to gestational age appears to influence growth of 3 to 6 year olds. In particular, LGA status may be a useful indicator to consider in developing a risk profile for overweight in young children.

Source: Hediger ML, Overpeck MD, McGlynn A, Kuczumarski RJ, Maurer KR, and Davis WW. 1999. Growth and fatness at three to six years of age of children born small- or large-for-gestational age. *Pediatrics*. 104 (3): e33 at <http://www.pediatrics.org/cgi/content/full/104/3/e33>.

Safety Issues Related to Formula Preparation and Use

Although many mothers give their babies formula, little is known about how mothers prepare and handle formula. While experts may disagree to some extent about ideal practices, the following steps are generally recommended: 1) follow manufacturer's directions on amounts of water to add to powdered or concentrated formula; 2) avoid using warm tap water to reduce danger of lead toxicity; 3) do not add cereal to the bottle; 4) do not put the baby to bed with a bottle; 5) avoid heating bottles in a microwave to prevent burns; 6) sterilize nipples, bottles, and water (to destroy *Cryptosporidium*); and 6) do not leave prepared formula at room temperature for more than 2 hours.

To determine the extent to which mothers comply with these recommendations, the researchers of this study examined data from the United States Food and Drug Administration Infant Feeding Practices Study (IFPS), carried out between February 1993 and October 1994. Questionnaires about infant feeding practices were mailed to the mothers at 2, 5, and 7 months after delivery. Consequently, the 1,140 respondents were more likely to be white, older, married, and of higher education and income than mothers in other more nationally representative surveys. Although 68% of the mothers give their babies formula by 2 months, only 21% received advice from health professionals on how to handle formula. The findings described below suggest that health professionals need to be more consistent about reinforcing proper infant feeding practices.

- Mothers who receive professional advice are less likely at 2 months to dilute formula, use warm tap water, or heat bottles in the microwave than those who do not receive advice.
- At 2 months, 33% use warm tap water; 43% do not boil the water; 14% leave bottles at room temperature for more than 2 hours; 39% heat bottles in the microwave; 35% add cereal to the bottle; 10% put the baby to bed with a bottle; and 10% overdilute the formula. In all cases, the percentage of mothers engaging in these practices is higher at 5 months than at 2 months post-delivery.
- Partially breast-feeding mothers are less likely than nonbreast-feeding women to use warm tap water, heat bottles in the microwave, add cereal to the bottles, and put the baby to bed with a bottle.
- Compared to primiparas, multiparas are more likely to use warm tap water, heat bottles in the microwave, and skip boiling the water, particularly from 5 months on.
- Risk of diarrhea is 63-72% higher among older infants whose mothers leave bottles at room temperature for more than 2 hours, compared to infants of mothers who do not.

Source: Fein SB and Falci CD. 1999. Infant formula preparation, handling, and related practices in the United States. *JADA* 99 (10): 1234-1240.

Does Breast-feeding Reduce the Risk of Child Obesity?

Finding strategies that can help prevent childhood obesity is very important. There are several reasons why breast-feeding might be expected to help prevent obesity. Energy and protein intakes are lower in breast-fed than in formula-fed infants. Some studies have found a link between high intakes of protein during infancy and later body mass index. Formula-fed babies also have significantly higher levels of plasma insulin than breast-fed babies. Higher

insulin levels would be expected to stimulate fat storage and the development of fat cells. However, most previous studies of breast-feeding and later risk of obesity have been carried out in relatively small samples and were unable to find a protective effect of breast-feeding. Some researchers from Bavaria, Germany has revisited the question of whether breast-feeding reduces obesity risk using a sample of 9,357 children, aged 5-to-6 yrs.

All children in Bavaria must have a health examination before entry to school. The data for this analysis came from an additional questionnaire that parents in two rural areas were asked to complete. From the questionnaire, the researchers were able to determine the duration of exclusive breast-feeding, defined as not being fed any other food other than breast milk. All children were weighed and measured. Using German growth reference data, the researchers defined overweight as a body mass index (BMI) above the 90th centile and obese, as BMI above the 97th centile.

After controlling for low birth weight, parent education, and smoking during pregnancy, exclusive breast-feeding for at least 6 months or more reduced risk of overweight and obesity by 30% and 40%, respectively. The researchers also reported a "dose-dependent" relationship between longer duration of exclusive breast-feeding and lower prevalence of being overweight or obese. However, some important limitations to this study must be mentioned. Maternal obesity was not considered in the analysis but may be related to both genetic tendencies toward obesity and difficulties in initiating breast-feeding (see Nov/Dec 1997 of Maternal and Infant Nutrition Briefs). Another study from Italy found similar protective effects against obesity in young but not older children. Finally, parent education may not be adequate to control for all social class effects that influence both the breast-feeding decision and development of obesity in this population. While this study includes the largest sample yet to examine the question, other factors, not measured in this study, may still be confounding the relationship between breast-feeding and obesity.

Sources: von Kries R, Koletzko B, Sauerwald T, von Mutis E, Barnert D, Gruner V, and von Voss H. 1999. Breast feeding and obesity: cross sectional study. *BMJ* 319: 147-150.
Franzese A, Iannucci MP, Valerio G, Buongiovanni C, Criscuoli C, Impagliazzo N, Pisacane A. 1999. Does breast feeding protect against obesity in adulthood? *BMJ* 319: 151.

Maternal and Infant Nutrition Briefs is a research-based newsletter prepared by Dr. Lucia Kaiser (llkaiser@ucdavis.edu), a Cooperative Extension Specialist in the Department of Nutrition, University of California at Davis. This newsletter is written for health professionals interested in nutrition of mothers and young children.

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