

include the multiple environments that have influence on the child, such as the peer group, the school, the neighborhood community, and the media. Prospective studies with appropriate behavioral and social measures would document the developmental course of childhood obesity and complement efforts in basic and clinical science to uncover whether there are critical periods to be targeted in prevention or interventions efforts. One of the national health objectives of Healthy People 2010 is to reduce the substantial health disparities between ethnic groups in the United States. Data generated by prospective studies of minority families may be translated into targeted prevention and intervention models that focus on specific behavioral factors to promote and maintain a healthful lifestyle for successful weight control.

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ANOTHER SMALL STEP IN THE PATH TO CONTROLLING MICRONUTRIENT DEFICIENCIES. . .BUT WE STILL HAVE A LONG WAY TO GO

Using modern sophisticated stable isotope techniques, Mishan et al have clearly demonstrated bioavailability of iron and zinc from a multiple micronutrient-fortified beverage in 6- to 9-year-old Peruvian children.¹ Absorption of iron was in the range of 10% whether the beverage was ingested with food or between meals, and absorption of zinc was ~23% independent of the concurrent ingestion of food. The results of the study are important because this fortified beverage provides another option for preventing iron and zinc deficiencies.

The international focus on prevention of iron deficiency is not surprising²; iron deficiency is the most prevalent nutritional deficiency in the world today, and through its impact on the myelination of the developing central nervous system, infants and young

See related article, p 26.

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children with iron deficiency are likely to manifest impaired motor, cognitive and socio-emotional development. When these children enter school, they are more likely to fail grades and manifest behavioral problems. Moreover, the economic impact in adults, due to cognitive losses in childhood, is not trivial when considering the challenges faced by many developing countries. In fact, recently published estimates of the worldwide economic impact of childhood iron deficiency suggest a reduction of 4.5% of GDP through reduced learning and ultimately poorer paying jobs.³ In many developing countries, the prevalence of iron deficiency is as high as 80%, therefore the biologic, social, and economic impacts are immense.

Although the extent of zinc deficiency is harder to quantify, it is likely found in combination with iron deficiency and affects the body's immunologic defenses. Zinc supplementation in children with zinc deficiency decreases the morbidity associated with diarrheal diseases and pneumonia.⁴ Because of the biologic importance of these two micronutrients, there is both national and international emphasis in prevention of deficiencies.²

From a public health perspective, there are four potentially successful approaches for the prevention of micronutrient deficiencies. These include recommendations for dietary diversification to increase the intake of foods containing bioavailable sources of iron (eg, red meat, fish, and poultry), fortification of commodity-type foods (eg, wheat flour), use of dietary supplements, and targeted fortification. In Canada and the United States, we use a combination of strategies. For example, the food pyramid recommends the ingestion of a mix of foods from "food groups" including meat and poultry (both good sources of iron), wheat flour and products made from wheat flour (eg, pasta) that are fortified, breakfast cereals that are highly fortified, and "targeted" foods for infants (eg, infant cereals and formulas) that are highly fortified at levels designed to meet their specific micronutrient needs. In the developing world, however, especially for infants and young children, most of these options are not feasible. Meat, poultry, and fish are among the most expensive foods to purchase, so for the majority of "at-risk" families, this intervention is not an option. Although the fortification of food commodities like wheat flour is inexpensive, it too is unlikely to work with infants and children because the level of fortification is aimed at an adult population and the amount of food children eat is simply too small (compared with adults) to make an impact. Finally, targeted fortification (such as the use of infant cereals and fortified formula) is not successful because breast-feeding is recommended and practiced (appropriately) in most developing country settings and commercial infant foods are both too expensive and culturally unacceptable. Thus, from a public health perspective, one has to turn to nontraditional sources of micronutrients, like fortified beverages or "home-fortification."⁵

Although Mishan et al clearly demonstrate the biologic availability of the micronutrients from the fortified beverage, a more important practical issue that was not adequately addressed was the potential use of this new fortified

commercial product in populations at highest risk for iron and zinc deficiency. Children between the ages 6 and 9 years are not at high risk because growth (and growth in blood volume) is not particularly rapid. For example, had the authors completed this study in adolescent females, a high-risk population, the results would have been even more important. In the pediatric age range, infants 6 to 24 months of age and adolescent girls are at greatest risk of deficiency. Infants in the developing world are at risk for a number of reasons: (1) many are born with low stores because of maternal anemia; (2) early cord clamping impacts on iron endowment; (3) blood volume doubles in the second 6 months of life; (4) prolonged exclusive breast-feeding fails to meet iron and zinc needs; (5) chronic infection impacts food intake, parasitic infections lead to blood loss in stool; and (6) typical home-made complementary foods are poor sources of iron. Adolescent girls are at risk because of rapid growth (and increase in blood volume), menstrual blood loss, parasitic infection (with gastrointestinal blood loss) and iron-poor diets. But children between 6 and 9 years old do not fall into either of these high-risk categories.

The availability of medicinal or food products to solve the problem of iron and zinc deficiency is not really the issue. For example, iron drops are inexpensive and have been widely available for the past 150 years. Yet there is no documentation of successful, long-lasting iron deficiency prevention programs associated with their use. There are a number of reasons they have not been successfully used, including their strong "medicinal" taste, the staining of an infant's teeth with their use, and difficulty in measurement of doses. The real issue is finding a supplement or fortified food that is both efficacious and effective, meaning that it works to prevent the deficiency, is affordable, acceptable, and sustainable. Although Mishan et al have clearly demonstrated the bioavailability of the minerals in the multimicronutrient beverage, the next step is the real challenge. If it is going to be used in populations at risk, such as adolescent girls or women in the childbearing age, how will it be distributed? And will those really in need choose to buy it and be able to afford it? Certainly a protein-free sugar drink, even one with micronutrients would not be appropriate for young infants. For adolescents, a sweet noncarbonated multimicronutrient fortified beverage would likely be quite acceptable. However, with very limited spending money, would an adolescent choose to buy it? Probably not.

Iron deficiency has been characterized by the World Health Organization as one of the top 10 serious health problems in the modern world.² Zinc deficiency, too, is a major contributor to childhood morbidity and mortality. The solution to these massive problems will have to be creative, comprehensive and sustainable, and where possible, based on good science. Mishan et al have provided the good science. Who will provide the rest?

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CYSTIC FIBROSIS LUNG DISEASE: WHEN DOES IT START, AND HOW CAN IT BE PREVENTED?

Cystic fibrosis (CF) is a lethal inherited disorder that occurs in 1:3400 Caucasians born in the United States.¹ Epithelial cell ion transport abnormalities lead to pancreatic insufficiency and chronic, progressive pulmonary disease, characterized by early onset of airway inflammation² and infection. Since the 1960s, median estimated survival has increased from approximately 10 years to almost 32 years.³ This increase in survival is likely due to a number of factors, including treatment in specialty care centers, improved nutrition through widespread adoption of a liberal-fat diet,⁴ improved modalities for airway clearance, and better antibiotic therapy for chronic pulmonary infection and resultant infectious exacerbations.

Progressive pulmonary disease leading to respiratory failure remains the cause of death in the overwhelming majority of people with CF.³ The major marker of pulmonary disease used both for assessing the respiratory health of the population with CF and for outcomes of clinical trials is forced expiratory volume in one second (FEV₁). FEV₁ has been shown to be an important predictor of survival. However, as shown in the article by Brody et al in this issue of *The Journal*,⁵ significant findings of lung disease, observed on high-resolution computed tomography (HRCT) and quantitated by a validated scoring system, were present in a significant proportion of children with CF who had mild to moderate pulmonary disease as measured by FEV₁. Even more striking, almost one third of young children 6 to 10 years old who had no abnormality in FEV₁ or other spirometric measurements had HRCT abnormalities. Although air trapping was most commonly observed in children with normal spirometry, almost half of them had bronchiectasis.

Brody et al showed a statistically significant, but weak, correlation between pulmonary function and HRCT abnormalities in this population. This provides the clinician with further evidence that CF lung disease is demonstrable before the onset of spirometric abnormalities, and that spirometry alone may give an inaccurate view of the extent of CF lung disease. This has already been suggested by a number of

studies, including demonstration that there is significant neutrophil influx into the airways of asymptomatic infants and young children with CF² and other studies of HRCT in this population.^{6,7} From a clinician's point of view, this leads to troublesome questions in assessment and management of CF. In evaluating an infant or young child with CF, clinical findings such as respiratory symptoms, physical examination, plain chest radiography, and pulmonary function measured by spirometry appear insensitive to the onset of lung disease. Furthermore, even if a clinician assumes the presence of lung disease in very young children with cystic fibrosis, there is a lack of evidence to support the application of specific therapies targeted to CF lung disease in this population.

The therapeutic armamentarium available to clinicians who treat people with CF continues to expand. Recombinant human dornase alfa (Pulmozyme™) was shown to modestly improve FEV₁ and decrease pulmonary exacerbation frequency in a randomized, double-blinded, placebo-controlled study of children and adults with CF and an FEV₁ of 25% to 75% predicted.⁸ A later study, which included the cohort described in the study of Brody et al, found similar results in children 6 to 10 years old with a forced vital capacity ≥85% of predicted.⁹ Tobramycin for inhalation (TOBI™) was studied in two randomized, double-blind, placebo-controlled trials in children and adults with CF, chronic pulmonary infection with *Pseudomonas aeruginosa*, and FEV₁ ranging from 25% to 75% of predicted.¹⁰ In this population, chronic intermittent administration of TOBI led to increased FEV₁ and a decrease in pulmonary exacerbation frequency. In a 4-year, double-blinded, placebo-controlled study, high-dose ibuprofen was shown to improve nutrition and reduce decline of FEV₁ in children and adults 5 to 39 years of age.¹¹ Three published randomized, placebo-controlled studies have demonstrated that azithromycin, given to CF-affected children and

See related article, p 32.

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CF	Cystic fibrosis
FEV ₁	Forced expiratory volume in one second
HRCT	High-resolution computed tomography