toddlers are fed 10 times the amount of naturally occurring fructose ingested by adults.

What is a reasonable guess for the daily intake of total fructose for an infant from the Stone Age? Zero. They must have been fed mother’s milk, the sugar in which is lactose, which digests to galactose and glucose only. Note that the ratio between the amount of fructose our infants are being fed today and the amount they were fed when our genes were adapting to the environment approaches infinity.

Bray et al pointed out many differences between fructose and glucose, with more troubles from fructose. “It is becoming increasingly clear that soft drink consumption may be an important contributor to the epidemic of obesity, in part through the consumption of larger portion sizes of these beverages and through the increased intake of fructose from high-fructose corn syrup and sucrose.” Bray et al referenced Elliott et al (5), who cited more differences between glucose and fructose in their major review. They concluded in part, “...on the basis of the available data regarding the endocrine and metabolic effects of consuming large quantities of fructose and the potential to exacerbate components of the insulin resistance syndrome, it is preferable to primarily consume dietary carbohydrates in the form of glucose (free glucose and starch).” Others concluded that, “if plasma triacylglycerols are a risk factor for cardiac disease, then diets high in fructose may be undesirable...efforts to reduce fructose intake should focus on reducing the amount of fructose added to beverages and foods in the American diet. A reduction in added fructose would be facilitated by an acceptable replacement sugar. Such a sugar might be glucose (6).” Wharton and Hampl (7) concluded that, “Native Americans face some of the highest rates of obesity and diabetes in the world...little attention has been paid to reducing fructose, particularly in the form of HFCS [high-fructose corn syrup] in beverages...numerous studies have documented that beverages are a leading contributor to energy intakes among Native Americans...one approach may be by promoting sugar-free beverages.” The titles of the studies by Levi et al (8) and Suarez et al (9) point to additional alarming troubles associated with fructose intake. Basic biochemistry indicates that glucose and fructose have different chemical properties. Of the 3 major sugars that digest into the human bloodstream, the 2 that are vital to humans, galactose and glucose, are both aldoses, whereas fructose is a ketose—this sugar is the one that the human liver tries hard to keep at essentially a zero concentration in the blood. Murray et al (10) wrote that, “Biomedically, glucose is the most important monosaccharide and ingestion of large quantities of fructose has profound metabolic consequences because it bypasses the regulatory step catalyzed by phosphofructokinase. This allows fructose to flood the pathways in the liver, leading to enhanced fatty acid synthesis, increased esterification of fatty acids, and increased VLDL secretion, which may raise serum triglyceride and ultimately raise LDL cholesterol concentrations.” Could fructose contribute to nonalcoholic fatty liver disease? With all the documented troubles from fructose, it is clear that the low glycemic index of fructose is misleading at best. The main source of fructose for infants and toddlers is fruit juice and soda. The nutrition-facts labels indicate that both sources are essentially the same, that is, sugar water that digests to nearly equal amounts of glucose and fructose. Of course, more trouble results from the faster sugar ingestion from a water solution than from sugar in solid foods, as noted by Bray et al.

Three summarizing facts call for immediate resolution: 1) we are flooding our infants and toddlers with fructose, 2) we are doing this through their entire postnatal brain growth spurt, and 3) infants and toddlers are being flooded with severe health problems, including brain disorders. How effective is the liver of infants and toddlers in keeping fructose out of their blood? How effective is their blood-brain barrier in keeping fructose out of their brain? Would there be any harm from withholding fructose until an age at which this population could handle whole fruit? How much does the surging worldwide sale of sugar water contribute to the surging obesity epidemic? Should fructose be withdrawn from the list of “generally recognized as safe” substances?

Nicholas J Krilanovich

310 Myrtle Street
Apartment 306
Mount Vernon, WA 98273
E-mail: njkrilanucla@hotmail.com

REFERENCES

Reply to NJ Krilanovich

Dear Sir:

Krilanovich has written a stimulating and provocative letter to the Editor with a call to action based on our critique of high-fructose corn syrup (HFCS). He has pointed out a significant error in our Figure 1 (1) and emphasized the potentially detrimental effects of fructose during the period of brain maturation in children. His letter serves to highlight this additional area of concern, and we applaud him for that.

At the end of our article (1) we stated that, “...we believe that an argument can now be made that the use of HFCS in beverages should be reduced and that HFCS should be replaced with alternative non-caloric sweeteners.” On the basis of the special issues relating to fructose and children that were highlighted by Krilanovich, which we did not dwell on, we support his suggestion that a reduction or elimination of fructose from HFCS as well as in sucrose in beverages available to infants and children could be a high-priority nutritional policy.
We thank Krilanovich for pointing out the error in our Figure 1. He is absolutely correct that the prevalence of obesity was 30.5% in 2000, not 26%. We submitted an amended figure to the Journal, which was published in response to an earlier letter (2). As Krilanovich noted, the correct value makes the rise in the prevalence rates of obesity more evident and the temporal relation of the increasing use of HFCS clearer.

Since our paper was published, a subsequent analysis of carbohydrate intake in relation to the prevalence of diabetes was published by Gross et al (3). Their observations dovetail with ours. They showed a decline in carbohydrate intake of from 500 g per capita in 1910 to 362 g per capita during the first three-quarters of the 20th century. Thereafter, carbohydrate intake returned to the same level as earlier in the 20th century. HFCS represents almost all of the increased carbohydrate during this latter period. Their study also nicely highlights the temporal relation of this change in carbohydrate intake with the rising incidence of diabetes.

Nature prefers glucose and rejects fructose. Fructose does not enter the brain or pancreas to any appreciable degree. Yet fructose is considerably sweeter than either glucose or sucrose. As Krilanovich points out, infants and young children in our society are exposed to higher intakes of fructose than were our ancestors. The fructose from HFCS used in beverages differs from the fructose combined to form sucrose in 2 ways. First, it is free fructose and as such is sweeter molecule for molecule than is sucrose or glucose—the other half of the sucrose molecule. In addition, HFCS solutions have a higher osmotic pressure than do equimolar sucrose solutions, because there are 2 molecules in the HFCS solution (fructose and glucose) compared with a single molecule in sucrose. This enhanced sweetness and high osmolality may serve to stimulate the taste receptors more intensely and to “imprint” this intense taste in the plastic neurocircuitry of young and growing brains, a change that may increase the desire for sweet taste throughout life. If this is even a remote possibility, the suggestion by Krilanovich to eliminate the exposure of food and children to fructose might be worth serious consideration. As we know, intrauterine exposure to maternal smoking (4) or diabetes (5) enhances the risk of obesity and overweight later in life. Their study also nicely highlights the temporal relation of this change in carbohydrate intake with the rising incidence of diabetes.

Nature prefers glucose and rejects fructose. Fructose does not enter the brain or pancreas to any appreciable degree. Yet fructose is considerably sweeter than either glucose or sucrose. As Krilanovich points out, infants and young children in our society are exposed to higher intakes of fructose than were our ancestors. The fructose from HFCS used in beverages differs from the fructose combined to form sucrose in 2 ways. First, it is free fructose and as such is sweeter molecule for molecule than is sucrose or glucose—the other half of the sucrose molecule. In addition, HFCS solutions have a higher osmotic pressure than do equimolar sucrose solutions, because there are 2 molecules in the HFCS solution (fructose and glucose) compared with a single molecule in sucrose. This enhanced sweetness and high osmolality may serve to stimulate the taste receptors more intensely and to “imprint” this intense taste in the plastic neurocircuitry of young and growing brains, a change that may increase the desire for sweet taste throughout life. If this is even a remote possibility, the suggestion by Krilanovich to eliminate the exposure of infant and children to fructose might be worth serious consideration. As we know, intrauterine exposure to maternal smoking (4) or diabetes (5) enhances the risk of obesity and overweight later in life. Thus, we support Krilanovich in encouraging a review of whether this is even a suggestion that this is so, then access by infants and young children to beverages with fructose should be curtailed during critical periods of brain growth and development.

George Bray

Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808-4124
E-mail: brayga@pbrc.edu

Samara Nielsen
Barry Popkin

University of North Carolina–Chapel Hill
Chapel Hill, NC

REFERENCES

Vitamin B-6 status and coronary artery disease

Dear Sir:

We found the recent article by Friso et al (1) potentially intriguing. An association between vitamin B-6 status and coronary artery disease (CAD) in humans has been discussed for decades, but to date there has been no satisfactory biochemical explanation for this association (see, for example, reference 2). In their study, Friso et al stated “…we excluded subjects with conditions known to influence B-vitamin metabolism …”; however, they included smokers and nonsmokers in both their CAD-free subjects and their CAD patients (see Table 1 in their article). Although they further stated that they performed multivariate logistic regression analyses that controlled for smoking and other indexes, such a regression analysis does not preclude an increasing percentage of smokers in each of the successive quartiles of pyridoxal-5'-phosphate (PLP) concentrations (see Figure 1 in their article). Because smoking is a well-documented determinant of PLP concentrations (3–6), we would have anticipated that the PLP data would also have been stratified by smoking load or that the incidence of smokers and nonsmokers would have been reported for each quartile in Figure 1. These data should be fairly easy for the authors to check.

In addition, more information on the intake of vitamin B-6 from the diet and from supplements needs to be provided. Moreover, because of the inverse association between circulating PLP concentrations and the activity of plasma alkaline phosphatase, the activity of alkaline phosphatase needs to be provided for both groups of subjects. After these analyses, if the associations of PLP with smoking and other indexes, such a regression analysis does not preclude an increasing percentage of smokers in each of the successive quartiles of pyridoxal-5'-phosphate (PLP) concentrations (3–6), we would have anticipated that the PLP data would also have been stratified by smoking load or that the incidence of smokers and nonsmokers would have been reported for each quartile in Figure 1. These data should be fairly easy for the authors to check.

Robert D Reynolds

Department of Human Nutrition
University of Illinois at Chicago
Chicago, IL 60612
E-mail: reynolds@uic.edu

James E Leklem

Department of Nutrition and Food Management
Oregon State University
Corvallis, OR 97333
E-mail: j.leklem@comcast.net