We agree that excessive consumption of either sucrose-sweetened or high-fructose corn syrup (HFCS)-sweetened beverages could contribute to the epidemic. In his discussion of this issue, Jacobson supports the idea of an upper limit for intake of added caloric sweeteners (sugars) and uses the US Department of Agriculture value of 40 g/d for individuals eating 2000 kcal. Forty grams per day of sucrose or HFCS would contribute 160 kcal/d or 12.5% of the caloric value of a 2000-kcal diet. We would prefer a slightly lower figure of not >10% of energy from added sweeteners.

We interpret the data on the rapid rise of HFCS differently than does Jacobson and want to highlight that point. Consuming a sweetener with the fructose and glucose components separated as found in HFCS, compared with the conjoined molecule in sucrose, does 2 things. First, it changes the "sweetness" of the solution, because in the case of HFCS, separate molecules are competing for the same sweet-taste receptor, whereas with sucrose there is but a single molecule acting on this receptor. As we argued in our paper, the HFCS beverages are thus probably slightly sweeter and could never have exactly the same sweetness as do sucrose beverages. Second, the 2 molecules of glucose and fructose in HFCS give the solution a higher osmotic pressure than that in a beverage sweetened with the same weight of sucrose. This osmotic difference will influence the amount of fluid secreted in the stomach, and this occurs until the sucrose has been cleaved in the intestine to produce glucose and fructose. As we noted in the title to our paper, we believe that the use of HFCS in beverages is an added contributor to the obesity epidemic beyond what would occur if a person consumed soft drinks sweetened with sucrose.

How much the switch to HFCS from sucrose contributed to the increasing consumption of soft drinks in the United States we will never know. However, reduction of caloric intake from any source would be beneficial in combating the epidemic of obesity, and we believe that significant reduction in the use of caloric sweeteners, both HFCS and sucrose, would be beneficial. In our paper, we cited the clinical trial conducted by Raben et al (4), who showed that subjects with access to calorically sweetened soft drinks gained weight, whereas those drinking diet drinks lost weight, during a 10-wk trial. In a recent trial in children, consumption of soft drinks was associated with an increase in body mass index, whereas the rate of weight gain decreased in the intervention schools that reduced their intake of soft drinks (5).

Finally, after our paper was published, we noted that in Figure 1, the prevalence figures for obesity and overweight were incorrect. An erratum published in this issue of the Journal corrects those errors (1).

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Update on vitamin A–related deaths in Assam, India

Dear Sir:

A scientific debate was initiated in 2001 after >30 children died and many became ill in Assam (state), India, after a vitamin A campaign in which children were given a mega-dose of vitamin A (1–4).

Surveys conducted by the Indian Council of Medical Research in 1999 in Dibrugarh and Nagaon districts of Assam state, in which >11 000 children per district were evaluated with the use of the 30-cluster approach, found only 0.3% of children to have Bitot's spot, a marker of vitamin A deficiency. These data suggest that vitamin A deficiency was not a public health problem; however, in these 2 districts, vitamin A was administered by a campaign approach, as if there were an epidemic of vitamin A deficiency. After the deaths of children following vitamin A supplementation in these districts, Indian scientists opened a debate on the justification of supplementation with vitamin A via a campaign approach when there was no evidence of clinical vitamin A deficiency in these districts (6).

The deaths of children in Assam in 2001 were referred to the judiciary (7). The Guwahati High Court of Assam ruled that both the United Nations Children's Fund (UNICEF) and the government of Assam are to be blamed for the death of >30 children who were given vitamin A in the state. A 2-judge bench of the High Court pronounced its verdict in a public-interest case filed by 2 Assam residents against the state government and UNICEF. The court ordered the state government to pay compensation to the families of the children who died, at the rate of 20 000 rupees (US$400) in addition to the paltry 5000 rupees (US$100) that each family had already been paid. Chief Justice PP Navlekar and Justice AH Saikia said in their judgment that UNICEF had introduced stronger doses of vitamin A by replacing the traditional 2-mL dosing spoon with 5-mL medicine cups. The justices stated that the health workers involved were not properly trained and briefed and had administered greater doses than many of the sick children could tolerate. In the justices' judgment, there was an element of negligence in the way the Assam health department had administered the vitamin A, and that negligence led to the death of many children (8).

The court judgment addressed the questions that were raised by scientists as to the possible cause of the deaths of children in Assam (5). In an editorial recently published in the Journal, however, Solomons and Schümann (9) stated that the facts remain elusive, pending the filing of an official inquiry.

Developing countries should learn from what has happened in India and should take appropriate precautions to prevent similar episodes in the future. We should adopt the globally advocated policy of UNICEF—ie, assessment, analysis, and action—before we undertake a public health intervention (9).

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Reply to U Kapil

Dear Sir:

In his letter, Dr Kapil has done a service to the readership of the Journal in providing us an update on the final evaluation and legal evolution of the unfortunate situation that arose in the state of Assam in northeastern India in 2001, one that we previously commented on in our "collateral damage" commentary in these pages (1). We lament any suffering or loss of life resulting from iatrogenic factors. As trained physicians, Dr Kapil and we are linked in being imbued with the Hippocratic premise that actively doing harm to one's patients—even by accident—is a major moral proscription.

We need, however, to focus in on the aspects of negligence in the findings. In deference to cultural and religious sensitivities, instead of the animal-derived gelatin habitually used to compound the high-dose vitamin A capsules, India uses a titrated liquid syrup containing 100,000 IU vitamin A/mL. The field-campaign process in Assam in 2001 theoretically allowed for the delivery of up to 500 000 IU or 151 500 retinol activity equivalents (275 mg retinyl palmitate) of vitamin A in a single dose, if the 5-mL medicine cup had been filled. Placed into perspective, this would constitute a single dose of vitamin A that is unprecedented in the annals of human health-care exposures. The conventionally recommended vitamin A exposure for periodic dosing is 100 000 IU for infants 6–11 mo old and 200 000 IU for children 12–59 mo old, administered every 6 mo. The original safety trials for vitamin A supplements for young children, conducted in India, showed general security for a 300 000-IU dose in preschool children (2). Only recently, a 400 000-IU one-time dose of vitamin A has been advocated for immediate postpartum delivery to lactating mothers (3)—that is, adult women. Prorated over the 180 d in 6 mo, a dose of 275 mg retinyl palmitate would represent an average daily exposure of 842 retinol activity equivalents; the tolerable upper level of vitamin A for children aged 1–3 y has been set at 600 μg/d (4).

It is stated that, in the final years of the campaign to eradicate smallpox, many more people were dying of vaccine-related disseminated vaccinia than from native variola. Similarly, in the current, final throes of the efforts to eradicate polio, more cases of paralysis can be attributed to variant mutant strains in oral polio vaccine than to sporadic cases of the wild-type infection transmitted in the population (5). Although the equation for vitamin A is far from having shifted in these directions, some of the findings presented by Kapil provide food for thought as the vitamin A programs go forward. The Assam High Court judges found that children were exposed to "stronger doses of the VA [vitamin A] … that many of the sick children could not tolerate." Were the most malnourished and sickly children indeed those most vulnerable to harm from excessive vitamin A exposure? Kapil notes that, in the specific district setting of the child deaths in question, the background vitamin A status has improved and that vitamin A deficiency "was not a public health problem." Could it be, therefore, that an exposure to excessive high-dose vitamin A on top of a vitamin A–replete status would be the more problematic scenario? Supporting such a speculation, a presentation at Experimental Biology 2003 parsed the data on therapeutic trials of high-dose vitamin A in children hospitalized for acute infectious diseases; it was concluded that those with low vitamin A status on admission tended to benefit, but that no gains—and even adverse effects—befell those with adequate preadmission vitamin A status who were exposed to additional vitamin A in the hospital (J Griffith, unpublished data, 2003).

A poor-quality diet and recurrent infections are the permanent factors that keep the children of India at intrinsic risk of hypovitaminosis A. However, only several systematic semi-annual vitamin A supplementation rounds are needed to produce a stabilized and satisfactory vitamin A status (6), a situation apparently approached in parts of Assam, according to Kapil. Within the legal judgment, it seems that the postulate of Parcelsus—that everything can be toxic; it is just a matter of dosage—was found to have played out its unfortunate course among deprived populations in northeastern India. Harm may have been the concomitant result of intentions to do positive social and public health good.

Beyond establishing absolute safeguards against unintended overdosing of concentrated vitamin A to children, thought should be given to the efficacy-safety equation with respect to the perpetual maintenance of campaign-style vitamin A delivery, because these programs achieve their intended effect of raising the vitamin A status across the preschool population of deprived groups.

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