Genetically engineered "golden" rice unlikely to overcome vitamin A deficiency

To the Editors:

The suggestion that "golden" rice, bioengineered to contain β-carotene (1), could have a "real impact on the health of children living in Southeast Asia" (2) deserves critical scrutiny from nutrition professionals. This rice, although not yet available commercially, has become the "poster child" of the food biotechnology industry's extensive public relations campaign to convince the public that the benefits of genetically engineered agricultural products outweigh any safety, environmental, or social risks they might pose. (3) National magazines promote golden rice as a means to prevent the more than one million annual deaths and cases of blindness that occur among children in developing countries as a result of vitamin A deficiency. (4) The creation of golden rice appears to confirm the belief that biotechnology is the key to solving world food and nutrition problems. (5)

Consideration of basic principles of nutrition suggests that rice containing β-carotene is unlikely to alleviate vitamin A deficiency. To begin with, the bioavailability of β-carotene is quite low—10% or less by some estimates. To be active, β-carotene—a provitamin—must be split by an enzyme in the intestinal mucosa or liver into two molecules of vitamin A. Like vitamin A, the provitamin is fat soluble and requires dietary fat for absorption. Thus, digestion, absorption, and transport of β-carotene require a functional digestive tract, adequate protein and fat stores, and adequate energy, protein, and fat in the diet. (6) Many children exhibiting symptoms of vitamin A deficiency, however, suffer from generalized protein-energy malnutrition and intestinal infections that interfere with the absorption of β-carotene or its conversion to vitamin A. (7) In numerous countries where vitamin A deficiency is endemic, food sources or β-carotene are plentiful but are believed inappropriate for young children, are not cooked sufficiently to be digestible, or are not accompanied by enough dietary fat to permit absorption. (8) In addition to doubts about cost and acceptability (2), biological, cultural, and dietary factors act as barriers to the use of β-carotene, which explains why injections or supplements of preformed vitamin A are preferred as interventions (8). The extent to which the β-carotene in golden rice can compensate for these barriers is limited. Vitamin A deficiency is undeniably the single most important cause of blindness among children in developing countries and a substantial contributor to illness and death from infectious diseases (9). Mortality rates are higher among children with even mild vitamin A deficiency, but fall by as much as 54% when vitamin A—not β-carotene—is supplemented or injected (8). Because such intervention methods are expensive and difficult to accomplish in the field, and because so many children exhibit signs of generalized protein-energy malnutrition, food-based approaches to improving vitamin A status seem especially desirable (10). The addition of one or two nutrients to an existing food does not constitute a food-based approach.

Furthermore, the use of β-carotene as a single-nutrient supplement itself raises questions. Although fruits and vegetables containing β-carotene are demonstrably protective against disease (11), the results of clinical trials of β-carotene supplements as a means to prevent cancer or cardiovascular disease have proved disappointing (12,13). Some laboratory studies support the idea that β-carotene produces biological effects that might protect against cancer (14), but others suggest that it might be co-carcinogenic (15). Still others argue that β-carotene is a pro-oxidant that may be harmful or beneficial, depending on circumstances (16). What all this means is that the short- and long-term effects of supplementation of β-carotene as a single nutrient—distinct from the foods that contain it—are as yet uncertain.

The complexity of the physiological, nutritional, and cultural factors that affect vitamin A status suggest that no single nutrient added to food can be effective as a remedy for dietary deficiencies. Instead, a combination of supplementation, fortification, and dietary approaches is likely to be needed (17), along with a substantial commitment to improve socioeconomic status. Food biotechnology may yet lead to products that improve nutrition and health, but at the moment its benefits remain theoretical.

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Response:

"This rice could have a real impact on the health of children living in southeast Asia, where vitamin A and iron deficiency are endemic, if it is accepted by farmers and local consumers." This sentence contains two caveats: "could" and "if it is accepted by farmers and local consumers." Acceptance of the product by farmers and consumers in developing countries cannot be assumed. Previous programs to eradicate vitamin A deficiency have had limited success.

Generally, programs that provide high-dose vitamin A supplements to children reduce the symptoms of vitamin A deficiency. However, less than 50% of the children in countries with endemic vitamin A deficiency are estimated to receive these supplements (1). FAO officials think that supplementation programs do not encourage the development of a "long-term, self-reliant prevention" program (2). Thus, a variety of food fortification and diet diversification programs have been attempted (3,4). For example, fortification of monosodium glutamate with vitamin A was found to be effective in raising serum vitamin A levels among children in the Philippines and Indonesia (5,6). Ultimately, however, consumer acceptance of the product was limited by a variety of technological and economic concerns (3). Similarly, consumer concerns and preferences (eg, about safety of a new product, the "discoloration" of the rice by β-carotene) and economic concerns may prevent "golden" rice from being widely utilized.

The literature on bioavailability of carotenoids is complex, and consensus has not been achieved. Supplementation of women with β-carotene was found to reduce the symptoms of vitamin A deficiency in women and their infants (7,8). Furthermore, several groups of investigators have demonstrated that ingestion of vegetables and fruits rich in β-carotene improved vitamin A status of children and women in Asia (9,10). de Pee, et al (9) estimated that 1 RE would be 12 μg β-carotene for leafy vegetables and carrots. This is lower than the estimated equivalency of carotenoids in Western-type diets. Many factors (particularly the amount of fat consumed with the carotenoids, the forms of carotenoids in foods, the vitamin A status of the subjects, the general condition of the subjects' guts) may have lowered the bioavailability of β-carotene among subjects in the studies cited (11).

I thank Dr Nestle for giving me an opportunity to make these points.

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ERRATA

Many astute readers noticed that a fork on the cover of January's *Journal* was labeled "Olesra." The correct spelling is "Olestra."

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