See corresponding article on page 347.

Nothing's simple about malnutrition: complexities raised by epidemic neuropathy in Cuba[1,2]

Barbara A Bowman, Caryn Bern, and Rossanne M Philen

In this issue of the Journal, Macias-Matos et al (1) present remarkable data documenting widespread thiamine depletion in the Cuban population in 1993 during the epidemic of optic and peripheral neuropathy that affected more than 50 000 Cubans. The findings are striking: depending on the biochemical assessment method used, 30–70% of the 650 subjects examined had abnormal thiamine status. The prevalence of biochemical thiamine depletion was much higher at one study site, Pinar del Rio, than in Havana, paralleling observed disease incidence.

However, on closer examination, their results illustrate the complexity of human malnutrition. For example, the severity of biochemical thiamine depletion was comparable in subjects with neuropathy and unaffected control subjects. Furthermore, in some individuals with neuropathy, biochemical thiamine status did not normalize even after 3 wk of intensive multivitamin and nutritional therapy (1). These findings compel us to examine the historical perspective, nutritional pathophysiology, and public health significance of this tragic epidemic and to consider the challenges for prevention and control.

In the past, similar epidemics have occurred among prisoners of war during World War II and the Korean conflict, and in civilian populations during wartime when there was limited food availability, eg, in Havana during the Spanish-American War and in Madrid during the 1937–1939 Spanish civil war (2–4). In prisoner-of-war camps diets were based on rice and starchy vegetables and were sparse in animal products (2, 5). Observations of the clinical response to various treatments consistently showed that isolated therapy with any single vitamin was ineffective, whereas marked improvement was seen after treatment with brewer's yeast (2), which contains several vitamins and other nutrients. The 1991–1993 epidemic in Cuba fits this characteristic pattern: it occurred in a setting with very limited food availability and a monotonous diet based on rice, beans, cassava, and sugar, with very small amounts of animal products (6, 7). Multivitamin treatment was effective in most cases, and disease incidence decreased substantially after nationwide multivitamin supplementation was implemented (7).

Macias-Matos et al (1) state that ". . .underlying nutritional depletion, which is necessary but not sufficient to produce overt clinical signs and symptoms, is common wherever micronutrient deficiencies are widespread." The striking biochemical thiamine depletion documented in this study is consistent with other evidence that the Cuban population was at substantially increased nutritional risk, with inadequate dietary intakes of several micronutrients and macronutrients, and continuing weight loss (6, 7). This increased nutritional risk was temporally associated with acute food and energy shortages attributable to Cuba's deteriorating economic situation. Because of the functional and metabolic interactions among nutrients, it is likely that the depleted biochemical thiamine status documented by Macias-Matos et al reflects concomitant depletion of many other nutrients.

The epidemic was associated with multiple factors, both nutritional and toxic. A subsequent comprehensive study in Pinar del Rio, which included anthropometric, biochemical, clinical, and dietary assessment, showed that risk for optic neuropathy was associated with tobacco use (particularly cigar smoking), decreased dietary intakes of several nutrients (methionine, vitamin B-12, riboflavin, and niacin), and lower serum concentrations of antioxidant carotenoids (7). Lower dietary intakes of animal protein and B-complex vitamins were among the most significant predictors of nutritional risk. Food sources, and hence dietary intakes of these nutrients, are highly intercorrelated and their metabolic functions are interrelated.

What is the significance for public health and for prevention of future epidemics? Unfortunately, we cannot conclude from Macias-Matos et al's study that "simple" thiamine deficiency was the cause of the epidemic; indeed, it is clear that for individuals, thiamine status did not even explain the occurrence of illness. At the population level, however, the high prevalence of thiamine depletion is almost certainly linked to the conditions that caused higher incidence rates in Pinar del Rio than in other parts of Cuba. When a risk factor is very common in a population, its presence in an individual will not be highly predictive of disease, but its prevalence in a population may reflect the level of risk in the population (8). A good example of this is the relation between serum cholesterol concentrations and atherosclerotic cardiovascular disease. Rose (8) calls this the concept of the "sick population" as opposed to the "sick individual."

These observations support the implementation of efforts to sustain improved nutritional status that address food as a source of classes of nutrients, rather than single nutrients. Dietary

[1] From the Centers for Disease Control and Prevention, Atlanta.

[2] Address reprint requests to BA Bowman, Centers for Disease Control and Prevention, Chronic Disease Prevention Branch, Division of Nutrition and Physicial Acitivity, 4770 Buford Highway, Mailstop F-26, Atlanta, GA 30341.

diversification and enrichment of a staple food product with water-soluble vitamins, as suggested by Macias-Matos et al, are likely to be more effective in the long term than multivitamin supplementation of the population, an effective short-term measure that is costly and depends on continued individual adherence.

Work along several lines is needed to extend the important observations of Macias-Matos et al. Their findings remind us of the need to develop improved laboratory methods of nutritional assessment, as well as the need for better approaches to integrate data from the complementary methods of assessment. The biochemical methods used by Macias-Matos et al are classic, but rarely used and notoriously difficult to standardize; data to support consensus values for interpretive norms are sparse. In addition, if analysis of these or other presupplementation serum specimens is ongoing, it would be extremely useful to examine other nutrients, especially those identified elsewhere as the strongest predictors of risk: riboflavin, niacin, vitamin B-12, and antioxidant carotenoids, especially lycopene. A multivariate analysis of such findings might help to disentangle the effects of nutrients whose intake could not be separated in dietary assessments. Potential folate depletion should also be examined; folate-responsive optic and peripheral neuropathy has been described (9, 10), and folate status is likely to have been impaired in the subjects described in this study.

The ramifications of this exploration of biochemical thiamine status are far-reaching. Macias-Matos et al remind us that human nutritional status, although remarkably resilient and adaptive, is also complex and potentially precarious. Worldwide, many people exist daily in high-risk nutritional situations. Adequate nutrition requires access to varied foodstuffs of adequate quality; the diversity and quality of a population's diet, in turn, reflect the socioeconomic, political, and ecologic conditions under which people live. Thus, long-term solutions to global problems of dietary inadequacy depend on multiple factors, including socioeconomic and political change. Facilitating such change will be far more complex than traditional nutritional interventions, particularly given the compelling historical perspective of epidemic neuropathy in Cuba (11).

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