British Journal of Nutrition (2001), **85**, 641–642
DOI: 10.1079/BJN2001373

Invited commentary

Intake and status in healthy Havana men, 2 years after the Cuban epidemic neuropathy

There are two reasons why the nutrition of the people of Cuba is currently of special interest. The first is that the collapse of the Soviet Union in the mid 1980s had a disastrous effect on trading partnerships which Cuba had relied on, for at least two decades, especially with East Germany. It suddenly resulted in a major shortfall in essential food and oil imports, and the shortage of oil in turn affected the production and distribution of home-grown food, very seriously. The second reason, thought to be at least partly a consequence of the first, is that an epidemic of optic and peripheral neuropathy swept across the country during 1992–3, affecting around 50 000 individuals, about 0·4 % of the Cuban population (Roman, 1994; Thomas *et al.* 1995). It began in the wake of a severe storm 'the storm of the century' which further destroyed the already compromised food crops; it first emerged in the western sugar cane region of Pinar del Rio, and rapidly spread from west to east. Three main theories of causation were entertained: a toxic factor or factors, an infectious agent, or an unfamiliar manifestation of malnutrition.

The symptoms of the disease were clear-cut, unusual, and divisible into two main categories. The first to appear was an optic neuropathy which resulted in blurred vision, and this affected mainly adult males, especially smokers. The second, whose appearance lagged a few months behind the first, was a peripheral spastic neuropathy, which affected adult women more than men. For both categories, a history of recent weight loss was a significant risk predictor. One of the reasons why malnutrition was considered as a serious contender for the aetiology was that certain traditionally 'high risk' groups of the population that were receiving extra food rations provided by the State, namely young children, pregnant women and elderly people, all exhibited a very low incidence of the disease.

Although the characteristics of the epidemic were unprecedented in recent times, an epidemic with some similar features had been described in Cuba at the time of the Spanish blockade at the end of the nineteenth century (Madan, 1898); there were also some similarities with 'Strachan's syndrome', described in Jamaica around the same time (Strachan, 1897). Several outbreaks with shared characteristics have occurred in tropical countries at times of food shortage, during the twentieth century (Roman, 1994). A less widespread, but qualitatively similar, condition has been encountered very recently in Tanzania (Plant *et al.* 1997). Because malnutrition, and in particular an 'imbalanced' diet, poor in essential micronutrients was suspected as being at least one component of the risk complex, a massive supplementation programme was initiated during 1993–4. This aimed to provide a daily multi-vitamin supplement to the entire Cuban population for 1 year, using the medical profession as the means of distribution. Those already affected by the illness were treated by hospitalisation with improved nutrition, including high-level vitamin supplementation. Within a few months, the incidence of new cases had subsided to a very low level, similar to that before the epidemic, and the majority of the affected individuals showed clinical improvement, although some had residual long-term or permanent incapacity. Since there was no control group, it is not, of course, possible to say whether the improvements at the population or individual patient level would have been any different had the vitamin supplements not been given, but at least they were consistent with a beneficial effect.

This is the background to the paper by Arnaud and colleagues in the current issue of this Journal (Arnaud *et al.* 2001b), and to two other linked papers from the same group, published elsewhere (Barnouin *et al.* 2000; Arnaud *et al.* 2001*a*;). They describe a 1-year (March 1995–February 1996) multidisciplinary study of healthy adult men aged 25–59 years, randomly recruited from the medical registries of the La Lisa district of Havana City, under the auspices of 'Seguridad Alimentaria y Buena Alimentacion in Cuba' (SECUBA). This enterprise represented a collaboration between French and Cuban scientists and laboratories. The principal purpose of the study was to characterise, 2 years after the epidemic, the diets, nutrient intakes and biochemical status indices of a specific group of the Cuban population which had been at high risk of developing the optic form of the illness during the 1993 epidemic. It was designed to examine the effects of smoking habit and of season on these indices, and to this end the same individuals were studied twice during the dry season (March–April 1995 and January–February 1996) and twice during the rainy season (June–July and October 1995). About half of the 106–134 participants who provided complete sets of information were current smokers of cigarettes. The findings from all three papers are best considered together, since they are strongly complementary.

It is clear that both the estimated daily intakes, and the status indices, for a considerable number of key micronutrients, especially vitamins, were poor by western country standards (although not necessarily by those of developing countries). The dietary instrument used may have underestimated the intake of total food (energy)

(Arnaud *et al.* 2001*a*), which implies a possible underestimation of at least some of the micronutrient intakes, but the status measurements do not suffer from this uncertainty. They are supported by previous studies of similar groups in Cuba during the 1990s (The Cuba Neuropathy Field Investigation Team, 1995; Macias-Matos *et al.* 1996). Major seasonal fluctuations were observed, in both food and nutrient intakes and status indices, driven largely by the scarcity of fresh fruit, vegetables and eggs during the rainy season. In the paper in this Journal, biochemical deficiency was proven (on average) in at least a third of the participants, for four out of the five B-vitamins studied, namely thiamin, riboflavin, folate, and vitamin B_{12}. Of these B-vitamins, recorded low intakes, notably of riboflavin and vitamin B_{12}, were particularly associated with cases of optic neuropathy during the epidemic, as recorded by an American–Cuban study group (The Cuba Neuropathy Field Investigation Team, 1995).

Do these studies help to shed new light on the unresolved questions about the aetiology of the epidemic? They have confirmed the high prevalence of poor B-vitamin status and have produced new evidence about the complex seasonal cycles of micronutrient availability and biochemical status in men living in Havana (Arnaud *et al.* 2001*a*,*b*). They have also demonstrated a dramatic deleterious effect of smoking on riboflavin status and on some (but not all) classes of serum carotenoids, and a smaller but significant effect on total serum protein (but not on serum albumin) (Barnouin *et al.* 2000). Serum Cu levels and indices of oxidative damage were greater in smokers than in non-smokers.

Vitamin B_{12} presents an intriguing conundrum: total serum levels did not differ significantly between smokers and non-smokers, and the authors comment that 'it could be hypothesised that vitamin B_{12} participated to Epidemic Neuropathy etiological pathway through its cyanide detoxification capacity, but the vitamin should not be a precipitating factor…' (Barnouin *et al.* 2000). However, if an insult such as exposure to cigarette smoke were to alter the tissue distribution or balance of coenzyme and/or non-coenzyme forms of the vitamin, then a functional deficiency at a critical tissue site might arise even in the presence of an apparently normal serum concentration (Chisholm *et al.* 1967). The implication is that we may need to develop more discriminatory biochemical indices in order to resolve such uncertainties.

Clearly this is a detective story which is not yet fully solved. Nearly all of the circumstantial clues seem to point in the direction of malnutrition as being an important component of the risk complex, with a number of micronutrient deficiencies being on the list of suspects, along with the toxic effects of cigarette smoke. Whether the B-vitamins with their coenzyme roles, or nutrients such as specific carotenoids (and vitamin C) with their antioxidant roles, are the prime suspects, is still a matter for speculation. The new data obtained by Arnaud and the SECUBA team has added usefully to the fingerprint collection and has helped to characterise the particular nutritional vulnerability of this population.

C. J. Bates
MRC Human Nutrition Research
Elsie Widdowson Laboratory
Fulbourn Road
Cambridge CB1 9NL
UK

References

Arnaud J, Fleites P, Chassagne M, Verdura T, Barnouin J, Richard M-J, Chacornac J-P, Garcia Garcia I, Perez-Cristia R, Favier AE and the SECUBA group (2001*a*) Seasonal variations of antioxidant imbalance in Cuban healthy men. *European Journal of Clinical Nutrition* **55**, 29–38.

Arnaud J, Fleites-Mestre P, Chassagne M, Verdura T, Garcia Garcia I, Hernandez-Fernandez T, Gautier H, Favier A, Perez-Cristia R, Barnouin J & Neuropathy epidemic group (2001*b*) Vitamin B intake and status in healthy Havana men, 2 years after the Cuban epidemic neuropathy. *British Journal of Nutrition* **85**, 741–748.

Barnouin J, Perez Cristia R, Chassagne M, Verdura Barrios T, Arnaud J, Fleites Mestre P & Favier A (2000) Vitamin and nutritional status in Cuban smokers and nonsmokers in the context of an emerging epidemic neuropathy. *International Journal of Vitamin and Nutrition Research* **70**, 126–138.

Chisholm IA, Bronte-Stewart J & Foulds WS (1967) Hydroxocobalamin versus cyanocobalamin in the treatment of tobacco amblyopia. *Lancet* **2**, 450–451.

Johnson GJ, Mtanda AT, Kinabo NN, Sangawe JLF, Masesa DE & Negrel AD (1993) Optic nerve and macular atrophy of unknown origin in Tanzania. *Archives of Public Health* **51**, 561–571.

Macias-Matos C, Rodriguez-Ojea A, Chi N, Jiminez S, Zulueta D & Bates CJ (1996) Biochemical evidence of thiamine depletion during the Cuban neuropathy epidemic, 1992–1993. *American Journal of Clinical Nutrition* **64**, 347–353.

Madan D (1898) Notas sobre una forma sensitiva de neuritis periferica, ambliopia por neuritis optica retrobulbar (Notes on a form of peripheral neuritis and amblyopia due to retrobulbar optic neuritis). *Cronica Medico Qirurgica de La Habana* **24**, 81–86.

Roman GC (1994) An epidemic in Cuba of optic neuropathy, sensorineural deafness, peripheral sensory neuropathy and dorsolateral myeloneuropathy. *Journal of the Neurological Sciences* **127**, 11–28.

Strachan H (1897) On a form of multiple neuritis prevalent in the West Indies. *Practitioner* **59**, 477–484.

and The Cuba Neuropathy Field Investigation Team (1995) Epidemic Optic Neuropathy in Cuba – Clinical Characterization and Risk Factors. *New England Journal of Medicine* **333**, 1176–1182.

Thomas PK, Plant GT, Baxter P, Bates C & Santiago Luis R (1995) An epidemic of optic neuropathy and painful sensory neuropathy in Cuba: clinical aspects. *Journal of Neurology* **242**, 629–638.