On Politics and Health: An Epidemic of Neurologic Disease in Cuba

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■ Political decisions may cause disease. During 1992 and 1993, an epidemic of neuropathy in Cuba—largely overlooked by U.S. physicians—affected more than 50 000 persons and caused optic neuropathy, deafness, myelopathy, and sensory neuropathy. Patients with the neurologic disease responded to B group vitamins, and oral vitamin supplementation of the population curbed the epidemic. Dietary restrictions and excessive carbohydrate intake were the immediate cause of the epidemic; however, the primary cause might have been political. Political changes in eastern Europe had major repercussions on Cuba's economy and food supply. In turn, these changes compounded the effects of internal political decisions in the island, leading toward isolationism and economic dependence on the former Soviet Union. Also, for more than 30 years, the United States has maintained an economic embargo against Cuba. In 1992, the U.S. embargo was tightened by the Torricelli amendment (or the Cuba Democracy Act), which prohibited third-country subsidiaries of U.S. companies from trading with Cuba and prevented food and medicines from reaching the island; this amendment produced a virtual economic blockade. Penuries resulting from all these political events resulted in the largest epidemic of neurologic disease in this century. Physicians may need to use their influence to modify political decisions when these decisions result in adverse health consequences. The American Academy of Neurology has issued a plea to encourage physicians and other health personnel to support efforts leading to lifting of the U.S. embargo against Cuba for humanitarian reasons.

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Epidemic diseases of the nervous system often accompany food and vitamin deprivation brought on by the devastation of war. Examples include deaths from beriberi among the defenders of Bataan and Corregidor (1–3) during the infamous "death march" in the Philippines, early in World War II; and outbreaks of lathyrism, amblyopia, deafness, and sensory neuropathy described, from 1936 to 1939, among the civilian population of Madrid during the Spanish Civil War (4). Adverse health effects of an economic embargo or a blockade between nations not at war, a contemporary problem, have only been recently reported (5, 6). The largely overlooked epidemic of neuropathy observed in Cuba during 1992 and 1993, affecting more than 50 000 patients, was the largest epidemic of neurologic disease in this century. This article briefly describes political conditions leading to the outbreak of neurologic disease in Cuba and describes the symptoms and treatment of these patients.

The Epidemic

Cuba (the major island of the Greater Antilles) is 111 000 km^2 in size and has almost 11 million inhabitants. In November of 1991, index cases of neurologic disease appeared in Pinar del Río, which is the rural, tobacco-growing, westernmost province of the island. The first 8 patients were middle-aged men with progressive visual loss and painful dysesthesias in the feet and hands. Between 14 and 36 new cases per month were seen in the same province; by July of 1992, 168 cases were diagnosed. Tobacco–alcohol amblyopia was considered the most likely cause of the disease. In August of 1992, in the city of Cienfuegos, 22 prison inmates were hospitalized with edema and painful dysesthesias of the feet and legs, difficulty in walking, sensory ataxia, and weakness. Onset of these symptoms was preceded by dysentery and profound weight loss. Beriberi was suspected, and patients responded to treatment with thiamine, other B group vitamins, and appropriate diet. At the end of 1992, optic and peripheral neuropathy had been diagnosed in 472 patients from 6 of the 14 provinces of Cuba: Pinar del Río, La Habana, Cienfuegos, Holguín, Sancti Spíritus, and Santiago de Cuba. Three months later, the number had escalated to 4461 patients.

On 20 March 1993, a task force coordinated by the Civil Defense for Disaster Relief, the Ministry of Public Health, and the Cuban Academy of Sciences was organized. Six research groups were formed, including epidemiology, toxicology, basic sciences, nutrition, clinico-therapeutic, and food resources. Between March and April 1993, an island-wide initiative was launched to increase case ascertainment and to promote early treatment. Approximately 18 000 family doctors of Cuba's unique community-based primary health care system (7) were used

for this effort; each family doctor cares for approximately 100 families. This health initiative resulted in a 40% surge in diagnosis of incident cases, increasing the cumulative total to 11 797 patients (5, 6). During March, April, and May of 1993, the epidemic curve reached an irregular plateau with a cumulative total of 45 584 patients. By early June 1993, a precipitous drop in incidence finally occurred that was temporally associated with distribution to the entire population of Cuba of a vitamin supplement containing B group vitamins, folate, and vitamin A. Distribution began in the first week of May 1993. During the last half of 1993, incident cases gradually abated; by the end of the year, the epidemic had vanished.

According to the Centers for Disease Control and Prevention (CDC) (5), as of 14 January 1994, the total number of cases was 50 862, and the national cumulative incidence rate was 461.4 per 100 000 persons (566.7 for women and 368.5 for men) for all forms of the disease. According to the preponderance of visual or peripheral nerve symptoms, cases were classified for epidemiologic purposes as optic forms (26 446 patients, 52%) or as peripheral forms (24 416 patients, 48%); however, combined forms of the disease were also common. Age-specific incidence rates were lowest in children younger than 15 years of age and in elderly people aged 65 years and older. Few cases were also noted among adolescents and pregnant women. Most cases (87%) occurred in persons between 25 and 64 years of age. Optic forms predominated in persons 45 to 64 years of age and were slightly more common in men. In contrast, peripheral forms occurred most commonly in women between 25 and 44 years of age. Overall, most of the patients (69%) lived in urban areas. No fatalities were attributable to the neurologic epidemic. The geographic distribution showed a west-to-east pattern of decreasing incidence with very high rates in Pinar del Río and few cases in Guantánamo. Evidence of contact was low among patients, and contagion was not evident.

A study (8) of 4437 patients from Pinar del Río found a strong association of the optic form of the disease with weight loss (79%) and smoking (74% of the patients smoked). Further, up to 81% of the patients with peripheral forms and 85% of those with combined forms of the disease mentioned weight loss before the onset of symptoms. Additional case–control studies included 708 age- and sex-matched pairs nationwide. Distribution by age, sex, and clinical form in these samples resembled national trends. These studies confirmed the increased risk for disease development in those with a history of smoking (odds ratio [OR], 4.9; 95% CI, 2.5 to 9.3), of irregular consumption of food (missing one or more meals per day with lower intake of animal protein, fat, and vitamin B–rich foods) (OR, 4.7; CI, 2.5 to 8.8), of smoking and drinking (OR, 3.5; CI, 1.7 to 7.4), of weight loss (OR, 2.8; CI, 2.2 to 3.6), of excessive sugar consumption (OR, 2.7; CI, 2.0 to 3.7), and of heavy drinking (OR, 2.3; CI, 1.0 to 5.4). Pesticide exposure or contact in the same household with persons affected by the disease did not increase the risk for the disease. In September of 1993, a collaborative study was done by the Cuban Task Force and U.S. scientists from the CDC, the Food and Drug Administration (FDA), Emory University, and the Neuroepidemiology Branch of the National Institutes of Health. This case–control study in Pinar del Río compared 150 patients with an equal number of controls. Preliminary results confirmed the findings of the Cuban studies.

Clinical Aspects

Various clinical features were observed in the course of the epidemic (6), including optic neuropathy, sensory peripheral neuropathy, dysautonomic neuropathy, dorsolateral myeloneuropathy, sensorineural deafness, dysphonia and dysphagia, spastic paraparesis, and mixed forms. In confirmed cases, patients were hospitalized for treatment with intravenous B group vitamins and folic acid. In addition to this basic therapy, other forms of treatment were tested. Less than 0.1% of the patients were left with moderate-to-severe sequelae. Investigation, diagnosis, and treatment of this large-scale patient load required a 30% increase in the number of hospital beds; urgent importation and airlifting of medications and supplies; production of clinical neurophysiologic equipment; and purchase (against major difficulties imposed by the economic embargo) of reagents and materials for research laboratories in Cuba.

Optic Neuropathy

Patients had symptoms of blurred vision and photophobia with slowly progressive loss of vision in both eyes. Visual acuity ranged from moderate (20/80) to severe loss (5/400). Ishihara color test scores ranged from 7.5 to 0 (of a total score of 8), indicating a loss of perception of green and red colors. Tangent field testing with a white target showed central scotomata (up to 5 degrees) that were larger when testing with red and green targets (up to 8 degrees from fixation), often showing cecocentral scotomata. On fundus examination, optic discs were normal in most patients. A few patients presented with slight hyperemia and capillary tortuosity. A typical finding in Cuban patients, first recognized by Sadun and colleagues (9), was the presence of a wedge-shaped loss of fibers of the maculopapillary bundle. Although observed in other conditions, this finding was considered pathognomonic in the context of the Cuban epidemic. Patients with advanced disease had temporal optic disc pallor.

Peripheral Neuropathy

Patients presented with symptoms of "burning feet" and painful dysesthesias also involving the hands and, rarely, affecting the face and perioral region. Hyperpathic pain at night interfered with sleep. Nerves were painful upon palpation. In general, no motor paralysis was present, but patients often reported easy fatigability and muscle pains with exercise. Most patients had a decrease in or a loss of vibratory perception distally in the limbs, and some also had a decrease in or a loss of soft touch, pinprick, and temperature in a "stockings and gloves" distribution. Tendon reflexes were lost or decreased distally. No obvious muscle wasting or paralysis was noted. Biopsy specimens of the sural nerve showed an axonal neuropathy affecting predominantly large-diameter myelinated axons (10).

Dorsolateral Myeloneuropathy

Patients with dorsolateral myeloneuropathy presented with sensory symptoms similar to those described above. However, impotence in men, weakness of the legs, difficulty in walking, and an increase in urinary frequency were also noted. Nocturia, urgency, and involuntary micturition were common. Reflexes were brisk in the knees with crossed-adductor responses, contrasting with decreased ankle reflexes. Spasticity and Babinski signs were usually absent. Proximal motor weakness was present in approximately one third of the patients. A few patients developed spastic paraparesis. In severe cases of the disease, decreases in vibratory perception and position sense in the feet, unsteadiness on the Romberg test, and sensory ataxia were all noted on physical examination.

Sensorineural Deafness

Patients had symptoms of hearing loss and high-pitched tinnitus, usually in association with either peripheral sensory symptoms or visual loss (or both). Pure-tone audiometry tests showed bilateral high-frequency (4 to 8 kHz) hearing loss, usually symmetrical; approximately 25% of these patients had a subclinical hearing deficit. Few associated vestibular symptoms were noted in most patients. In general, a minimal return of hearing occurred in response to treatment.

Other Signs and Symptoms

In addition to weight loss and lack of appetite, many patients had symptoms reminiscent of the chronic fatigue syndrome, including loss of energy, irritability, difficulties with concentration and memory, and sleep disturbances. Some patients presented with dysautonomic symptoms, such as excessive body sweating, coldness, and hyperhidrosis of the hands and feet. Rarely, hoarseness and dysphagia were present. Palpitations, occurring either spontaneously or after minimal efforts, were relatively common. Edema of the feet was observed with some frequency.

Overall, clinical and laboratory tests did not indicate the presence of infection or inflammation. In some patients, cerebrospinal fluid examinations showed mild alterations of the blood–brain barrier, but these results were normal in most patients. No consistent abnormalities were noted for endocrine, hematologic, renal, or liver function tests or for electrolyte levels. In a group of 105 patients with several forms of the disease and in asymptomatic controls, serum thiamine levels and thiamine pyrophosphate activity were normal in only 38% of the patients and 45% of the controls, indicating widespread deficiency of thiamine in the population (8).

Analysis of the diet in the population during the second trimester of 1991 in Pinar del Río (8, 11) showed that the percentages of daily allowances were reduced below recommended values: 33% for vitamin A, 50% for thiamine, 57% for vitamin B_6, 62% for vitamin B_{12}, and 29% for folic acid. These percentages are similar to those that Lincoff and colleagues (12) found in a group of 20 patients from Cuba who had optic neuropathy. These patients denied consuming milk or dairy products, chicken, pork, or red meat in the several months before the evaluation. Their diet consisted of rice, 2.3 kg/mo; beans, 560 g/mo; sugar, 2.7 kg/mo; eggs, 1/wk; fish, 1 serving/wk; bread, 1 to 2 servings/d; vegetables, 1 serving/d; yuca (cassava), 1 serving/wk; fried plantains, 1 serving/wk; fresh fruit, 1 serving/wk; cake or cookies, 1 serving/wk; tea or coffee, 1 to 3 servings/wk; and rum, 1 to 3 servings/wk. The above was the standard, highly monotonous diet for the entire Cuban population—distributed by ration cards—that provided the following U.S. recommended daily allowances (12): a total of 816 kcal (41%), 15.6 g of protein (36%), 180 g of carbohydrates, 3.4 g of fat, 88 g of sugar, 4.0 g of alcohol, 240 IU of vitamin A (6%), 0.39 mg of thiamine (40%), 0.23 mg of riboflavin (19%), 3.49 mg of niacin (27%), 0.43 mg of vitamin B_6 (21%), 0.21 mg of vitamin B_{12} (7%), 110 μg of folate (27%), 42.9 mg of vitamin C (71%), 0.09 IU of vitamin D ($< 1\%$), 42.3 μg of vitamin K (40%), 156 mg of calcium (20%), and 154 mg of magnesium (30%).

Factors Causing the Disease

Nutritional Deprivation

This epidemic disease was characterized by selective involvement of just a few neuronal groups and axons, including the maculopapillary bundle; axons in the dorsal columns (fasciculus gracilis); and concurrent distal axonal degeneration of large myelinated peripheral sensory axons, high-frequency spiral ganglion neurons of the cochlea, and distal-most pyramidal tract fibers. A metabolic lesion is the most likely cause of this selective injury, affecting neurons requiring high energy consumption.

Numerous neurotoxins, such as agents capable of producing amblyopia or scotomata, were excluded. In particular, methyl alcohol, organophosphate pesticides, trichloroethylene, and chronic cyanide intoxication from cassava in the diet were carefully excluded. A Coxsackievirus was isolated in Cuban laboratories, but this could not be confirmed at the National Institutes of Health or two other laboratories in the United States. Genetic predisposition, in particular, mitochondrial DNA point mutations associated with Leber disease, was excluded in the group of patients from Pinar del Río (13).

The nutritional origin of the epidemic appears inescapable: Early treatment of patients with B group vitamins produced complete remission. Distribution of vitamins to the entire population of 11 million Cubans rapidly curbed the epidemic (5, 6). Moreover, the clinical syndromes observed in Cuba were identical to those described among Allied prisoners of war in Japanese prison camps in the Far East during World War II (1942 to 1945) and among U.S. prisoners of war during the Korean War (14). All the clinical variants observed in Cuba were described in the 1940s by physicians who were also detained in the prisoner-of-war camps (15, 16) or were reported after repatriation (17, 18). In the 1940s, these syndromes were called camp blindness, happy feet, and camp deafness. Large epidemic outbreaks of these neurologic disorders occurred, usually in association with poor diets based on rice and complex carbohydrates and containing minimal protein and a lack of B group vitamins. Tropical heat, heavy physical labor, dysentery, and malaria were some of the precipitating factors.

Political Factors

Cuba was not at war at the time of the epidemic. However, a series of political events created an unusual "war-time" situation in the island, which was called the special period or *período especial.* All the cities on the island had day and night blackouts, food distribution was restricted to ration cards, public transportation virtually stopped, work in industries and offices came to a standstill, and tractors were replaced by oxen. The collapse of the Soviet Union and socialist countries (which represented 85% of Cuba's foreign trade) halted imports—most importantly, oil, foods, feed for livestock, fertilizers, and pesticides. Lack of foreign currency and credits compounded the problems (19, 20). These events magnified the negative results of internal political decisions in Cuba that led to isolationism and economic dependence on the former Soviet Union. The efforts of the Cuban government to maintain the health of the population during the special period were only partially successful. Children, pregnant women, and the elderly received vitamin and protein supplementation and were largely protected from the neuropathy. However, the population had increased requirements for the B group vitamins—in particular, thiamine—resulting from environmental heat, increased physical activity, and sugar consumption. These requirements were not supplemented.

In 1992, the 30-year-old U.S. economic embargo against Cuba was tightened by the Torricelli amendment (Cuban Democracy Act), which prohibited third-country subsidiaries of U.S. companies from trading with Cuba. The economic embargo became, in effect, a blockade of medicines and food. Medicines that usually are not restricted by embargoes were limited because the Act stipulated that all shipments required on-site U.S. inspection to verify that the medications were imported for their intended use. Cuba imported soybean and other grains as a protein source for the population. However, the cost of food importation increased because Cuba had to buy from distant countries such as China and Brazil (a provision of the Act prevented vessels with foreign flags that docked in Cuban ports from loading or unloading in a U.S. port for at least 6 months) (20).

Conclusion

As a physician working for the World Health Organization mission to Cuba, I found profound injustice in the occurrence of this huge epidemic of nutritional cause in a population not at war. Although the U.S. economic embargo against Cuba was not the primary cause of this epidemic, it certainly contributed to its development, complicated its investigation and treatment, and continues to hamper its prevention. No justifiable political reasons exist for continuing to maintain the embargo against Cuba after the end of the Cold War and the normalization of diplomatic relations with Vietnam. Nor can the United States, a nation with a long tradition of generous giving to those in need—in Africa, the former Soviet Union, the Third World—and with a clean record of respect for human rights and self-determination, continue (for internal political reasons) to use an embargo that has already contributed to neurologic injury in the Cuban population. The American Academy of Neurology (19, 20) has endorsed a plea to lift the embargo on food and medicines for humanitarian reasons. Other voices (21) have also joined in this request because of the overall deterioration of health conditions in Cuba associated with the U.S. embargo.

Adverse health effects notwithstanding and despite international rejection of the U.S. embargo at the United Nations General Assembly, a bill has been recently introduced by Senator Helms to tighten even more the U.S. embargo against Cuba. Physicians may need to remind their representative that the repercussions of political decisions on the well-being and the health of the Cuban people must not be overlooked.

Disclaimer: The opinions expressed here are those of the author and do not necessarily represent the opinion of the U.S. Government, the Cuban Government, the World Health Organization, The American Academy of Neurology, or the American College of Physicians.

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