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Mantakassa: an epidemic of spastic paraparesis associated with chronic cyanide intoxication in a cassava staple area of Mozambique. 2. Nutritional factors and hydrocyanic acid content of cassava products*

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An outbreak of spastic paraparesis which mostly affected women and children occurred in a northern province of Mozambique in 1981. The epidemic was related to chronic cyanide intoxication associated with a diet consisting almost exclusively of cassava. A prolonged drought in the area had exhausted all food resources except cassava, especially the bitter varieties. A nutritional, toxicological and botanical investigation was carried out in two of the five districts affected. The main findings were that cyanide levels were unusually high in the cassava plant as a consequence of the drought with daily intakes estimated at 15-31.5 mg HCN. Detoxification of the bitter varieties by sun-drying was inadequate because of the general food shortage, and metabolic detoxification was probably reduced owing to the absence of sulfur-containing amino acids in the diet. The raw and dried uncooked cassava was eaten mostly by women and children. The nutritional status of the population, however, was not very poor and symptoms of advanced undernutrition were rarely seen.

An outbreak of spastic paraparesis occurred between May and October 1981 in Nampula Province, northern Mozambique, and involved five districts: Memba, Erati, Nacala, Maiaia and Monapo. The disease was called *mantakassa*, which means paralysis in the local language. The outbreak occurred in a drought-stricken rural area, where the staple food was cassava, and affected mostly women and children. The epidemiological, clinical and laboratory findings suggested that the disease was associated with cyanide intoxication and cassava consumption (see Part 1). Recently a neurological disease associated with chronic cassava intoxication was described in Nigeria (*1*). Mantakassa also shows clinical and epidemiological similarities with lathyrism in India (*2*).

This second part of the study describes the nutritional, toxicological, and botanical investigations that were performed to test the possibility of a food-related cause. These investigations were carried out in September and October 1981 in the districts of Memba and Maiaia. The objective was to study the agricultural and nutritional situation in normal years, to compare this with the changes that occurred in 1981, and to investigate the relationship between cassava consumption and the high thiocyanate levels found in patients with the disease.

The fieldwork was done in the short time available with limited resources. The sample size for the nutrition investigation was small and the results could not, therefore, be subjected to statistical analysis. They do, however, indicate that nutritional and other factors could have played a part in the etiology of the disease.

Ecological description of the area

The area affected by the drought in 1981 can be divided into three distinct ecological and agricultural zones: coastal, intermediate, and interior. The usual rainy season extends from December to March with a mean annual rainfall of about 700 mm along the coast, increasing to 1000 mm in the interior (Fig. 1). Table 1 shows the distribution of crops in the three zones, based on a national agricultural survey carried out in Mozambique in 1961-66 (*3*). This distribution has not changed.

* Part 1 appears on pages 477-484 in this issue of the *Bulletin*. Requests for reprints should be sent to: Secção de Epidemiologia, Direcção Nacional de Medicina Preventiva, Ministério da Saúde, Maputo, Mozambique.

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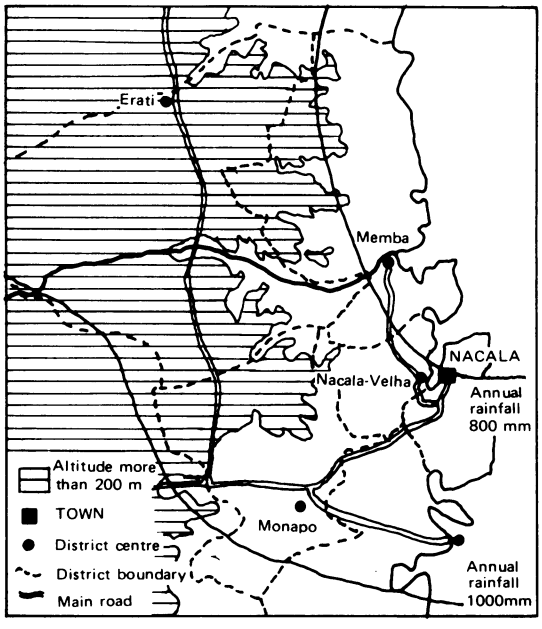

Fig. 1. Altitude and mean annual rainfall in the area affected by the drought.

The dry and sandy *coastal* zone, 10–12 km wide, has a severely limited agricultural capacity. Cereals are rarely grown while cassava occupies 86% of the cultivated area. The predominant cash crops are cashew and sisal. The *interior* zone, which is situated more than 60 km from the coast at an altitude of more than 200 m above sea level, has good agricultural conditions. Although much sorghum is grown, cassava is still the main staple food; cotton is the cash crop. The *intermediate* zone lies between 10 km and 80 km from the coast at an altitude of 50–200 m above sea level. The vegetation consists of secondary deciduous forest with deciduous parkland, open bushland, and spiny savanna (*4*). The number of cashew trees per peasant is among the highest in northern Mozambique; this zone also marks the eastern limit where cotton can be grown. Cassava accounts for 68% of the cultivated area of food crops, with smaller proportions for maize and sorghum. The main protein suppliers in the diet are beans and groundnuts.

The present study refers mainly to the intermediate zone where the disease incidence was highest.

History of cassava in Mozambique

Cassava was probably introduced into Nampula Province, around 1760, from the French colonies in the Indian Ocean (*5*). It became established as the main staple crop along the coast in the period between then and the beginning of the present century. From 1926 onwards, the Portuguese colonial power introduced a system of forced cultivation of cash crops, like cotton and cashew, which had a negative effect on the subsistence economy. It was during this period that cassava gained prominence as a staple food crop. Its cultivation calendar did not coincide with that for cotton, which resembled that for cereals. The peasants were also obliged to grow cassava for commercial purposes, to help feed the growing number of plantation and urban workers (*6*). In recent years, cash crop production has diminished owing to a combination of factors such as the abolition of forced labour after the country's independence and a breakdown of the commercial network.

As a consequence of the slave trade, cassava became the staple food in many parts of Africa. It yielded more energy per hectare and per man-hour than cereals; and the fact that its edible parts were not needed for sowing and that it was remarkably resistant to drought and pests contributed to its spread. Today, it provides around 40% of the food energy requirements in Africa.

Table 1. Distribution of crops in the family sector in the three agricultural zones

Crops	% of area with crops		
	Interior zone	Intermediate zone	Coastal zone
Cassava	59.5	68.5	86.0
Sorghum	18.6	6.6	2.6
Maize	3.3	5.8	1.8
Rice	3.3	0	2.6
Peanuts	10.5	11.0	2.1
Beans	4.2	8.0	3.8
Cotton (as % of the area with traditional crops)	27.2	22.2	0
Cashew (mean number of trees per peasant)	21.9	51.0	45.3

MATERIALS AND METHODS

From August to October 1981 information was obtained on the agricultural and nutritional situation from a variety of sources — local authorities, farmers, teachers, traders, and the general population. Systematic investigations were made of the nutritional situation and samples of cassava products were collected from the following affected areas:

— a communal village, Acordo de Lusaka, 20 km south of Memba;

— the administrative division of Calawane, 40 km northwest of Memba; and

— the administrative division of Muentaze, 20 km south of the port town of Nacala.

The communal village was chosen for study because it had a high incidence of the disease with 28 cases in a population of 815. Seventeen of the affected families were interviewed, as well as sex- and age-matched controls in 17 neighbouring families. Eight affected families in Calawane, which had an incidence of 10.7 per 1000 inhabitants, and 6 affected and 4 neighbouring families in Muentaze were also interviewed.

The nutrition investigation included the collection of information on current agricultural practices, nutritional habits and customs before and during the drought, and socioeconomic conditions. In addition, a review of family food consumption during a 24-hour period and an assessment of nutritional status using anthropometry were carried out in the communal village. Weight-for-height and weight-for-age parameters were used to indicate the degree of "wasting" (*7*) or recent loss of body weight due to reduced food intake; the cut-off points were 75% and 90% for weight-for-height and 60% and 80% for weight-for-age of the Harvard Standards, which correspond to those currently in use by the Ministry of Health in Mozambique.

Various samples of fresh and processed tubers and leaves of cassava were collected for cyanide analysis using uniform collection methods. Fresh samples were placed in a plastic bag immediately after collection, labelled and frozen on the same day, then transported to the laboratory in cold boxes and frozen again immediately on arrival. Dry samples were placed in paper bags until they were analysed, without any special storage or transport conditions. The samples were collected from many different parts of the affected area and were analysed for cyanide content at the National Food and Water Hygiene Laboratory of the Ministry of Health in Maputo, using the alkaline titration method (*8*) and the direct potentiometric method with a cyanide specific electrode (AMEL 201 I).

Samples of domesticated and wild plants consumed by the inhabitants were also collected, identified, and recorded.

RESULTS

Cassava cultivation and diet in normal years

Cassava constitutes about 80% of the staple food in the affected area. Twelve cultivated varieties were identified, two of which were considered to be bitter. It was estimated that the latter accounted for about 30% of the cassava cultivated, but this was higher in some areas. *Gurue*, the more common of the bitter varieties, had been rejected when first introduced in the 1950s, but in recent years was more readily accepted because of its high yield and resistance to drought and attacks from wild animals.

The entire cassava crop is harvested and replanted in August. The fresh cassava is cut into 20-cm-long pieces, sun-dried for 2–3 weeks, and then stored for up to 12 months. The population believes that this long drying period is necessary to make the cassava safe for consumption. Fig. 2 shows that families always reserved some of the previous year's dried cassava to cover the current harvest and drying period.

In these areas the population uses only the sun-drying method of detoxification for bitter cassava; this is eaten uncooked or boiled or, most commonly, after pounding into flour which is mixed with boiling water to make a thick paste called *chima*. The fresh sweet varieties are eaten raw or boiled; they are also dried and processed as for the bitter varieties. Cooked cassava is usually eaten with a relish made from the leaves of the sweet cassava, pumpkin or sweet potato plants, beans, groundnuts, dried fish, tomatoes or coconut depending on availability. People normally eat two meals per day; one normally contains a cereal when this is available in the period after the cereal harvest. Meat and game are rare in the diet; pork is not eaten for religious reasons. Various fruits are eaten but the cashew apple is used to prepare an alcoholic drink. Cashew nuts are roasted and seldom used in cooked dishes.

Effect of the drought on the harvest

The rainy season normally extends from December to March, but in 1979–80 the rains failed and in 1980–81 the area had the lowest rainfall ever remembered or recorded. Fig. 3 shows the low flow of

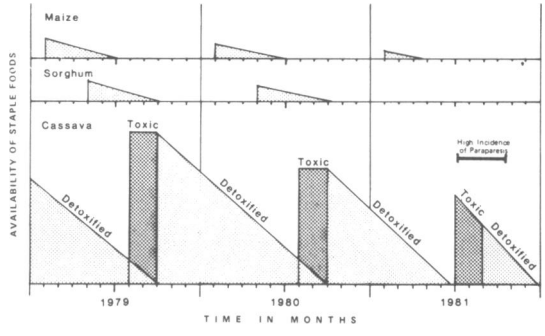

Fig. 2. Availability of staple foods (maize, sorghum, and cassava) from 1979 to 1981 in the area affected by drought.

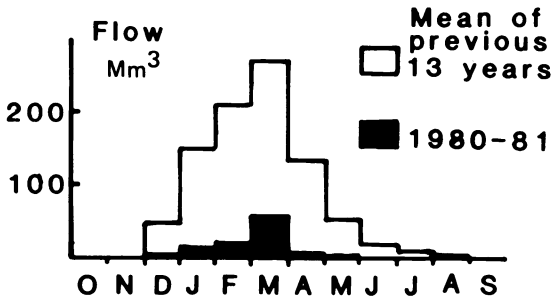

Fig. 3. Flow of the Mecuburi river in the affected area in 1980–81, compared with mean values during the previous 13 years (abscissa shows months from October (O) 1980 till September (S) 1981).

the Mecuburi, the principal river in the most affected area in 1981, which was due to the severity of the drought.

Fig. 2 shows the period of availability after harvesting of the three main staple food crops (maize, sorghum and cassava) from January 1979 to October 1981. Two important points should be noted: firstly, in 1981 cassava was harvested as early as June, while normally it is harvested in August; and second, in the middle of 1981, only the freshly harvested, toxic cassava was available, whereas in 1979 and 1980 some of the previous year's harvest lasted until September.

The production of cereals and legumes was very low or completely lost owing to the drought. Sweet varieties of cassava also suffered severe losses but the bitter varieties produced a reasonable harvest. As a result of the poor harvests, edible wild plants, 110 of which were collected for identification, became an important constituent of the diet.

By the end of June 1981 all normal means of procuring food were exhausted and it became necessary to harvest the cassava. People complained that the surviving sweet cassava had turned bitter, and that the bitter varieties were more bitter than usual. The fresh tubers were cut into 1×1 cm pieces and/or pounded and dried for 1–2 days only. As other foods were scarce, the population began to consume this inadequately dried cassava.

Because the cashew crop also had failed and work was difficult to obtain, ready cash was in short supply. Thus, even when food was occasionally available, some families did not have the means to buy it.

Diet during the drought

Table 2 presents the results of the 24-hour recall on food consumption, which was carried out in the communal village. The low economic status of the affected families is demonstrated by their failure to join the food Consumer Cooperative which required a monetary contribution, and by the fact that these people depended on gifts of food from family and friends. Some affected families also ate fresh bitter cassava and augmented the quantity of flour with pounded, dried cassava peelings. This latter practice was introduced only in 1981. Most families ate twice a day but some, including children, sometimes ate only once a day. In Calawane and Muentaze, the dietary situation was similar, the only exceptions being one family that ate maize and two others that ate dried fish and beans, in Muentaze.

Table 2. Results of a 24-hour recall of food consumption by affected and control families in Acordo de Lusaka, Memba District, in October 1981

	No. of families with positive response	
	Affected families (n = 17)	Control families (n = 17)
Ate "chima" (made from dried bitter cassava)[a]	17	17
Ate dried, uncooked cassava[a]	16	6
Ate cereals	1	1
Ate beans	1	2
Ate relish (containing cassava leaves)[a]	13	12
Ate fish or meat	0	6
Ate wild plants (in the last month)	1	6
Member of the food Consumer Cooperative	0	6
Depended on gifts of food	6	1

[a] Median estimated drying time of cassava was 7 days for both the affected families and the control families.

Almost all the affected families recalled having acute symptoms 4–6 hours after ingestion of meals containing cassava from the 1981 harvest. However, at the time of the investigation the incidence of acute intoxication had decreased.

Nutritional status

Table 3 shows the results of the investigation of nutritional status of families in Acordo de Lusaka. There is little difference between the status of the affected families and the controls.

Toxicology

Table 4 shows the hydrocyanic acid (HCN) content of the cassava samples using the alkaline titration method. Comparison of this method with the direct

Table 3. Nutritional status in Acordo de Lusaka, Memba District, in October 1981

	No. of persons or children	Parameter[a]	Percentage undernourished	
			Moderate	Severe
Affected families	65	W/H	49	12
Control families	37	W/H	38	11
Village children:				
0–1 year old	29	W/A	45	14
1–6 years old	121	W/H	32	2

[a] W/H = weight for height; W/A = weight for age.

Table 4. Hydrocyanic acid (HCN) content of cassava samples from the affected area

Type of cassava sample	No. of samples	HCN (mg/kg)		
		Mean value	Standard deviation	Range
Fresh leaves:				
bitter varieties	6	377	110	224–469
sweet varieties	14	347	178	71–495
Fresh roots:				
bitter varieties	15	327	153	186–446
sweet varieties	20	138	55	54–235
Dried roots:				
bitter varieties	12	95	47	64–178
sweet varieties	3	46	9	35–54
Flour	5	40	9	26–43
Cooked cassava	10	38	22	19–87

potentiometric method gave a maximum variation of 10%. HCN values were highest for the fresh leaves, with no significant difference between bitter and sweet varieties; the mean HCN value was higher in fresh roots of the bitter than sweet varieties ($P < 0.01$) but there was considerable overlap. Progressively lower mean values were found in the dried samples, the reduction in cyanide content being 70% for the bitter varieties and 67% for the sweet varieties. The greatest range of variation in HCN values occurred in the fresh bitter roots.

The relationship between the cyanide content, the length of drying time, and humidity showed that the cyanide levels appeared to decrease rapidly with drying (within one week) and then remained stationary. Even with prolonged drying of two months and over, the HCN levels were still high: 85 mg/kg for bitter cassava and 35 mg/kg for sweet cassava.

DISCUSSION

Historical factors

The problem encountered in 1981 had its real beginnings in the colonial period when cassava was first introduced into the area. Virtual dependence on this one crop was created at the expense of subsistence production of cereals, legumes, etc. This, in turn, created a dependence on commercially available food which consequently generated the need to earn money through sale of cash crops or manual labour for wages. In recent years the commercially available food has diminished for several reasons such as a decline in cash crop production because of unfavourable weather conditions, the abolition of forced cash crop production, and a breakdown in the commercial network. Owing to the shortage of cash and of food on sale, the dietary supply of protein-rich foods containing the sulfur necessary for metabolic detoxification of cyanide was probably reduced.

Pressure of demand from the coastal and urban centres for food from the interior continued during the drought, thereby encouraging the rural population to sell the dried cassava and other food that they had.

Agricultural potential

The non-coastal areas most affected by the 1981 drought and outbreak of mantakassa had always had a limited agricultural potential and a relatively high population density, but this did not prevent them from exporting food to other areas. The coastal zone, in comparison, could not produce sufficient food and imported it from the interior, although fishing provided a useful supplement. The coastal zone was least affected by the outbreak, possibly because of the continued supply of fish which provided both the sulfur-containing amino acids needed for metabolic detoxification of cyanide, and the means for exchanging food with the interior. The urban populations, on the other hand, ate mainly dried cassava from the interior and were therefore prone to the risk of intoxication.

Detoxification

Unlike other cassava-producing areas where the cassava is left in the ground and harvested as required, the crop in Nampula is harvested over a short period which is followed by extensive drying and storage periods. The practice in Nampula probably

evolved both to fit in with the dates for cotton cultivation during the year and to allow sufficient time for the cassava to dry out adequately, especially in the case of the bitter varieties. As sun-drying is the only method of detoxification used, the drying period is particularly important.

In a review of traditional detoxification methods, Coursey (*9*) states that "sun-drying can only be applied to cassava containing small amounts of glycoside". It is therefore surprising that in an area where bitter cassava had for a long time been cultivated, other more efficient detoxification methods (such as soaking) were not practised. In other areas of Mozambique, however, methods such as soaking and grating are used (*10*). Soaking has been shown to reduce the glycoside content by about 90%, while sun-drying and boiling were less effective (*11*). Also, a study among six ethnic groups in Zaire (*12*) discussed the importance of detoxification methods in relation to cyanide intake; a direct relationship was found between the incidence of goitre attributed to a high cyanide intake linked with a low iodine supply, and the methods of preparation used. Soaking, again, gave more favourable results.

Diet and nutritional status

Before the drought, the diet in the affected area was probably well balanced in terms of energy and nutrient requirements. The drought then caused a severe reduction and imbalance in the diet, which mostly affected the women of reproductive age and children who probably consumed the raw and dried uncooked cassava, which are higher in cyanogenic glycosides, in the course of collection and preparation. The children were affected because they often accompany women in their tasks. In contrast, the men normally ate well-cooked cassava. Lactating women who had a high incidence of the disease may also have eaten more raw cassava which was believed to stimulate lactation.

Studies in a cassava-eating population in Zaire (*13*) have shown that the thiocyanate level in breast milk, although low, was not negligible but breast-fed babies did not present with the disease. The protein in the breast milk could have exerted a protective effect; in older children, however, the introduction of other foods possibly raised their cyanide intake. Vanderpas et al. (*14*) reported that when cassava juice was introduced as a first weaning food, the serum thiocyanate levels rose.

Table 2 shows that a larger proportion of the affected families ate dried uncooked cassava which could have been an important factor in raising the cyanide intake. The similarity in nutritional status between the affected and control groups confirms the general lack of food in the area. Protein-rich foods, particularly, were insufficient and could have resulted in diminished metabolic detoxification. In spite of the general food shortage, the usual symptoms of advanced undernutrition such as growth failure, oedema, wasted muscles, and apathy were rarely seen. However, many cases of kwashiorkor did appear in February 1982 after the rains failed again at the end of 1981.

The high serum thiocyanate levels in both patients and controls must have been due to chronic cyanide intoxication. Factors in the diet such as high cyanogenic glycoside levels in the cassava plant and inadequate detoxification of the cassava, as well as insufficient metabolic detoxification due to a dietary deficiency of sulfur-containing amino acids, may have triggered the disease.

As none of the wild plants identified is known to be neurotoxic, it is unlikely that they played a role in the etiology of the disease. They did provide some food during the critical period, but the drought considerably reduced this source too.

Toxic levels in cassava products

The cyanide levels found in the cassava samples in this investigation are high when compared with those found by other authors (*15*, *16*). In this study, 55% of the sweet fresh roots were extremely toxic and the remainder moderately so, which may have been due to the drought conditions increasing the cyanogenic glycoside content (*17*). The mean values were higher in the roots of the bitter varieties. In general, the dried samples had lower cyanide levels, but even with two months of drying some values were still high. This finding confirms the opinion of Coursey (*9*), mentioned above.

To relate the values found in the samples to the amount of cyanide ingested, the dietary habits of the population must be considered. The highest values were found in fresh leaves but these are normally eaten cooked which probably detoxifies much of the cyanide. If it is assumed that 90% of the diet was composed of cassava, then with a daily adult energy intake of 7.53 megajoules (MJ) (1800 $kcal_{th}$) the quantity of cassava consumed would have been in the range of 500–700 g per day. Most of the dried bitter cassava samples had a cyanide content of 80–100 mg/kg, while for the cooked samples the range was 30–45 mg/kg. A calculation based on a diet containing dried bitter cassava gives an approximate daily intake of 15–31.5 mg HCN. These levels of intake may be compared with the adult lethal dose of cyanide of 50 mg and could explain the frequent acute reactions after meals. Over a period of time, the consumption of such quantities could result in chronic cyanide intoxication, which was found in both patients and controls. Given the dependence of this population on cassava, and the proneness of the area to drought, people

possibly consume sufficient cassava to result in chronic cyanide intoxication even under more normal conditions. They could therefore be at risk from other diseases reported in association with chronic cyanide intoxication such as chronic neurological disease (*1*), endemic goitre and cretinism (*12*), and diabetes (*18*).

Cassava and economic development

As one of the cheapest sources of food energy available, cassava plays a very important role in countries such as Mozambique, where peasant populations are subjected to unreliable climatic conditions and need security in their food supplies; owing to its hardiness and natural resistance, it often provides this security. The solution to the problem of cyanide intoxication, however, is not the prohibition of cassava but a careful study of the agricultural situation so that other drought-resistant crops including cereals and legumes, and varieties of cassava with lower cyanogenic glycoside levels may be introduced. At the same time, efforts to promote economic and social development in the areas prone to such disasters offer the only long-term solution.

CONCLUSIONS

The following evidence links the chronic cyanide intoxication found in patients to cassava consumption:

— raised levels of cyanogenic glycoside levels in the cassava plant, including sweet varieties, which were due to the drought;

— higher levels than usual of cyanide in processed cassava products because of inadequate detoxification;

— the almost total dependence on cassava in the diet during the drought period, and reduced metabolic detoxification of cyanide because of the lack of protein-rich foods.

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RÉSUMÉ

LE MANTAKASSA: ÉPIDÉMIE DE PARAPARÉSIE SPASMODIQUE ASSOCIÉ À UNE INTOXICATION CYANURÉE CHRONIQUE, DANS UNE RÉGION DU MOZAMBIQUE OÙ LE MANIOC EST L'ALIMENT DE BASE. 2. FACTEURS NUTRITIONNELS ET TENEUR EN ACIDE CYANHYDRIQUE DES PRODUITS DU MANIOC

Une épidémie de paraparésie spasmodique ou *mantakassa* (de son nom local) a éclaté en 1981 dans cinq districts d'une province septentrionale du Mozambique. C'est dans une région agricole assez pauvre et touchée par la sécheresse que l'incidence la plus forte a été observée. Les principales victimes étaient les femmes et les enfants. Etant donné la rareté des denrées alimentaires, la population s'est presque exclusivement nourrie de manioc, de variétés amères en particulier. Parmi les douze variétés de manioc cultivées dans la région, deux seulement sont amères à proprement parler; mais par suite de la sécheresse toutes les variétés se sont révélées plus amères qu'à l'ordinaire. Le manioc se détoxique normalement par séchage au soleil et stockage pendant une durée qui va jusqu'à un an. Mais en 1981, à cause de la pénurie alimentaire, le manioc a été récolté de bonne heure, concassé et séché au soleil un ou deux jours seulement avant d'être consommé.

L'existence d'un lien possible entre la consommation de manioc et une intoxication cyanurée a été explorée dans les zones les plus touchées au moyen d'investigations portant sur la nutrition, la toxicologie et la botanique. Sur le plan de la nutrition, les familles touchées et les témoins ont été étudiés sous l'angle des facteurs agricoles, économiques et sociaux et des habitudes alimentaires avant et pendant la sécheresse, notamment la nature de la consommation journalière. L'analyse d'échantillons de produits du manioc a révélé, tant dans les produits séchés que dans les produits frais, une teneur anormalement élevée en hétéroside, qui libère par hydrolyse de l'acide cyanhydrique. Le taux de cyanure résiduel dans les échantillons déshydratés atteignait respectivement 85 et 35 mg/kg dans les variétés amères et douces.

La ration de cyanure a été estimée à 15–31,5 mg par personne et par jour. De plus, il s'est produit une pénurie d'aliments riches en protéines contenant des acides aminés soufrés qui auraient pu renforcer la détoxification métabolique du cyanure. Les symptômes d'une intoxication aiguë ont été ressentis 4 à 6 heures après les repas comportant du manioc de la récolte de 1981. Plus de 100 variétés de plantes sauvages consommées ont été récoltées et identifiées; aucune

n'a de propriétés neurotoxiques connues. Les familles économiquement défavorisées et qui ont consommé du manioc séché cru et mangé moins de viande ou de poisson étaient relativement plus nombreuses parmi les familles atteintes que parmi les témoins. Les femmes et les enfants ont probablement consommé davantage de manioc séché non cuit, car ce sont eux qui sont chargés de la récolte et de la préparation. Aucune différence importante n'a été notée entre les groupes atteints et les groupes témoins en ce qui concerne l'état nutritionnel; des signes de dénutrition grave ont rarement été observés. Le lien entre l'intoxication cyanurée chronique et la consommation de manioc ressort de diverses observations, parmi lesquelles il convient de citer l'absorption anormalement élevée de cyanure pendant la sécheresse, par suite de la teneur accrue de la plante en hétéroside libérant de l'acide cyanhydrique, et le manque d'acides aminés soufrés dans le régime alimentaire.

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