

Working together to eliminate cyanide poisoning, konzo and tropical ataxic neuropathy (TAN).



# CCDN

## News

Cassava Cyanide Diseases Network

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## Konzo Count

The first description of konzo<sup>1</sup> was in 1928 in Bandundu Province in the south west of Belgian Congo, now Democratic Republic of Congo (D.R.Congo). There have been various epidemics since then and currently, largely as a result of warfare, konzo is present in four Provinces. In Bandundu Province there are 4.5 million inhabitants and in affected areas the prevalence can be as high as 20 per 1000 people. In the eastern province of Kivu, especially South Kivu, at Kaziba, Ifendula, Mulambu, Uvira, Burhinyi and Bunyakiri, they have no experience in the treatment of konzo, because it is new to them. Konzo is also reported from the centre of the country in the provinces of Western and Eastern Kasai. The

total number of cases is estimated to be as high as 100000, which may not be an exaggeration because of continuous warfare in D.R.Congo.

In Northern Mozambique there have been 2200 cases reported since 1981 mainly in Nampula Province. There were 214 cases last year at Mtwara, southern Tanzania, and another outbreak on Pemba Island, northern Tanzania, reported by WHO.<sup>2</sup>

There is abundant evidence that major outbreaks occur as a result of war, as in D.R.Congo, and drought which causes large increases in the total cyanide content of roots and flour.<sup>2</sup> However, sporadic cases of persistent konzo also occur amongst the poorest of the poor in agriculturally deprived rural areas.<sup>3</sup>

There needs to be a concerted effort by countries in which konzo occurs and international aid agencies to remove this scourge, by implementing strategies<sup>4</sup> to reduce the cyanide intake of these people.

*We thank readers of CCDN News who have provided*

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information on konzo and ask you to please continue to inform us of outbreaks and approximate number of cases.

#### References:

<sup>1</sup> Cliff, CCDN News1, June 2003 P.3.

<sup>2</sup> CCDN News 2, Dec 2003, P.3.

<sup>3</sup> Ernesto, Cardoso, Nicala, Mirione, Massaza, Cliff, Haque & Bradbury. Acta Trop. 82, 357-362, (2002).

<sup>4</sup> CCDN News 1, June 2003, P.2

### **Konzo or Neurolathyrism : Is There a Difference?**

Konzo is a spastic paraparesis of the legs that occurs after prolonged consumption of insufficiently processed cassava (*Manihot esculenta* Crantz)<sup>1</sup>. Neurolathyrism is a spastic paraparesis of the legs occurring after prolonged over-consumption of grass pea seed (*Lathyrus sativus* L.)<sup>2</sup>. Both diseases have mostly a sudden onset and are non-progressive and irreversible. In both conditions there are gradations of severity derived from the degree of walking difficulty. The clinical presentation of scissor gait in the mild cases, the need to use a stick for walking in the more severe cases and total loss of the use of legs in the most severe cases, the exaggerated reflexes, clonus, Babinski sign etc are all very similar. For proper diagnosis the patient's history is needed: a regular consumer of cassava or manioc develops konzo, a regular consumer of grass pea seed develops neurolathyrism. The occasional presence of optical neuropathy seems to be a complication of konzo only. In rare cases the neurolathyrism patient also develops osteolathyrism<sup>3</sup>. As there is no geographical overlap of the cassava and grass pea production there is also no geographical overlap of the two diseases.

The socio-economic conditions of the konzo patients and of the neurolathyrism patients are very similar as well. Both diseases can be considered a sign of poverty, lack of dietary variation and illiteracy<sup>4,5</sup>. In times of drought or military activity, the incidence of both diseases increases. Drought increases the level of linamarin in cassava and the level of neurotoxin in grass pea. Military activity reduces the access to alternative foods. The inhabitants of remote villages have little political voice and the problems of the poorest of the poor are not a high priority in the more affluent capital cities, that have a spongy effect on the state budget. Very often the patients with konzo as well as those with neurolathyrism become social outcasts and become completely dependent on their family for livelihood. In Addis Ababa (Ethiopia) it is not uncommon to see a beggar with neurolathyrism, although he developed the condition in a remote village. In Kay Kalengi, a remote village in the Bandundu province of D. R. Congo, a Spanish catholic nun is teaching the konzo patients how to use a sewing machine.

The cause of the two diseases is very different. Cassava belongs to the *Euphorbiaceae* family and is rich in carbohydrate but poor in lipids and protein. Grass pea is a legume belonging to the *Fabaceae* family and is rich in protein. The toxic secondary metabolite blamed for causing the disease is linamarin, a cyanogenic glycoside in cassava, giving rise to the respiration toxin cyanide; while in the case of grass pea it is a neuro-excitatory amino acid beta-ODAP ( $\beta$ -N-oxalyl-L- $\alpha,\beta$ -diaminopropionic acid). How such different compounds, affecting our metabolism in such different ways, can result in the same clinical presentation of spastic paraparesis is an

unresolved issue. The intricate cascade of reactions resulting in cell-death of motoneurons may involve oxidative stress, imbalance of micronutrients, depletion of essential amino acids and the mitochondria. These mitochondria are the generators of energy-rich molecules needed as fuel for the neuronal activity but they are also generating free radicals. The biochemical pathways leading from very different molecules to a similar clinical presentation, are becoming more complex with every new experimental approach<sup>6,7</sup>.

An important difference in the two diseases is the higher susceptibility of women at reproductive age for konzo, and the higher susceptibility of young men for neurolathyrism. The female hormones (especially 17 $\beta$ -estrogen) have been proposed as a protective factor for neurolathyrism, but can this be an aggravating factor for konzo? The absence of a suitable animal model to study both diseases makes it difficult to identify protective factors or to develop curative medicine.

A simple way to prevent these irreversibly crippling diseases may probably be achieved by broadening the monotonous diets leading to these diseases. Both crops, cassava and grass pea, are easy to cultivate, tolerant to drought and the cheapest food available. Unfortunately, they both are deficient in the essential sulphur amino acids methionine and cysteine, molecules that are important for our defence against oxidative stress. The protein of both crops is of poor quality because of this imbalance of essential amino acids. The leaves of cassava are rich in protein and used in sauce, but also this protein is of poor quality<sup>8</sup>. Cassava has the additional practical advantage

that it can be harvested any time of the year and thus needs no storage. Genetic engineering to produce cassava and grass pea varieties with better amino acid score and with reduced toxin without losing the positive traits may be possible in the near future.

For the time being education is probably the key issue in the prevention of both diseases. Especially education of the women is essential because they are preparing the food. In cassava growing countries in Africa, the women do the planting and the harvesting, they also do the soaking and the pounding, and even carry water from the river, while politics is an activity of the men. Hard physical labour by young men has been identified as a risk factor for neuroleptism in Ethiopia and Bangladesh. Physical activity and any neuronal activity produce reactive oxygen species and contribute to oxidative stress. Perhaps this can be part of the explanation why women are more susceptible to konzo?

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### Cyanide Content of Gari Samples from Cameroon

Manyu Division is part of South West Province in Cameroon. More than 80% of the rural dwellers in this province are farmers. Cassava is one of the tropical root crops grown and is a major source of energy. The cassava roots are boiled and eaten with palm oil or various soups. Also grated cassava mash is fermented into 'gari' or soaked roots are fermented into 'water-fufu' and 'ackpu'.

Gari is consumed raw soaked in cold water or cooked in hot water to give a pasty dough-like food eaten with various meat or fish soups. Many households consumed gari every day and some of the gari is transported for sale to urban areas of Cameroon.

Sixty gari samples were collected from four villages in Manyu Division and their total cyanide contents analysed using the cyanide kit B2<sup>1</sup>. The range of total cyanide contents was 1–20 mg HCN/kg DM (ppm). This is quite high, since WHO recommends a maximum of 10 ppm<sup>2</sup>. Hence there is a need for education of the rural people on the proper processing techniques to produce cyanide-free gari.

The rural dwellers of Manyu Division have been provided with mechanical graters and hydraulic presses for quick dehydration of the grated cassava mash. This will actually shorten the period of cassava processing into gari and might lead to the production of gari with very high cyanide content, because of the limited time for

the breakdown of linamarin by the enzyme linamarase. This makes it very urgent to educate the populace on the importance of allowing sufficient time for breakdown of linamarin in gari processing.

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- <sup>1</sup> Bradbury, Egan & Bradbury, J. *Sci. Food Agric.* 79, 593-601, (1999)
- <sup>2</sup>FAO/WHO, 1991 Joint FAO/WHO Food Standards Programme. *Codex Alimentarius Commission XII, Suppl.4*, FAO, Rome, Italy.

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### Processing of Cassava to Reduce Cyanide Content

One strategy proposed at a Workshop in Mozambique<sup>1</sup> to reduce the cyanide content of processed cassava is to improve processing methods used for conversion of roots to storeable cassava products such as flour, gari and farinha. Flour is used in East, Central and Southern Africa, the roasted product gari in West Africa and farinha in South and Central America.

The major methods of flour production in Africa involve sun drying of peeled roots followed by crushing in a pestle and mortar and sieving<sup>2</sup>. This method retains 25-33 % of the original linamarin present<sup>3</sup>. A second method is called heap fermentation in which the peeled roots are placed in a heap for about 3 days and fermentation occurs with breakdown of some linamarin. The product is then dried in the sun, crushed and sieved<sup>2</sup>. Heap fermentation removes about twice as much linamarin as does sun drying, but still 12.5 – 16.5 % of linamarin is retained. This large retention arises because of the lack of intimate contact between

the linamarin which is located inside each tiny plant cell and the hydrolysing enzyme linamarase that is located in each cell wall. It is calculated that in order to produce cassava flour with 10 mg HCN equivalents/ kg flour (ppm), the WHO safe level, using heap fermentation one would need to use sweet cassava roots containing not greater than 32 ppm linamarin<sup>3</sup>.

However if peeled cassava roots are either immersed in water for some days or are ground or grated into small pieces and left for some days, then the linamarase is able to break down nearly all of the linamarin. The cyanide is removed from the ground or grated cassava by squeezing out the waste liquor and drying (roasting) the product in a metal dish over a wood fire with removal of hydrogen cyanide gas. Grinding or soaking processes used in West Africa and South and Central America retain only 1.3 - 2.5 % of the cyanide originally present in the root. Thus, these methods are more than 10 times as effective as those used in East and Southern Africa to remove the cyanide present in the root<sup>3</sup>.

This shows the *inadequacy* of the sun drying and heap fermentation methods for removal of cyanide as compared with the soaking or grating methods used in West Africa.

It is therefore most important to develop improved methods of processing in East, Central and Southern Africa to reduce greatly the total cyanide content of flour,

in order to prevent the occurrence of konzo in children and young women of child bearing age<sup>4</sup>.

Konzo probably occurs because of a high peak intake of cyanide over a relatively short period of time, which produces very high levels of urinary thiocyanate. In Nigeria there have been no confirmed reports thus far of the incidence of konzo, probably because in general, gari contains much less cyanide than does cassava flour<sup>3</sup> and hence the per capita intake of cyanide from gari is much less in Nigeria than it is from flour in East, Central and Southern Africa.

On the other hand, tropical ataxic neuropathy (TAN), occurs amongst older people in Nigeria and has also been reported in Tanzania. TAN is thought to be due to intake of lower levels of cyanide from cassava over many years<sup>5</sup>, which results in increased but much lower levels of urinary thiocyanate than is observed in children from konzo-prone areas.

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<sup>1</sup>Ernesto, Cardoso, Nicala, Mirione, Massaza, Cliff, Haque & Bradbury. *Roots*, 8(1), 8-11, (2002).

<sup>2</sup>Cardoso, Ernesto, Cliff, Egan & Bradbury. *Int. J. Food Sci. Nutr.* 49, 93-99, (1998).

<sup>3</sup>Cardoso, Mirione, Ernesto, Massaza, Cliff, Haque & Bradbury. *J. Food Comp. Anal.* (2004), in press.

<sup>4</sup>Cliff, CCDN News 1, June 2003, P3

<sup>5</sup>Cliff, CCDN News 2, Dec.2003, P 4

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**CCDN News** is the Newsletter of the Cassava Cyanide Diseases Network (CCDN). The CCDN is a free, worldwide network commenced in June 2001, which is working towards the elimination of konzo, TAN and other cassava cyanide diseases.

CCDN News will consider for publication short articles and letters (1-3 pages A 4 double spaced) written in English concerned with the following subjects:

1. Cyanide poisoning, konzo, TAN, goitre and cretinism facilitated by cyanide intake from cassava and any other cyanide diseases.
2. Reduction of cyanide intake from cassava through agricultural and nutritional means such as by broadening the diet of cassava consumers through introduction of new crops, pulses, vegetables and fruits, and by reducing the cyanide content of cassava varieties through selection and breeding. The effect of environmental factors such as drought on cyanide levels in cassava.
3. Processing methods for conversion of cassava roots to stable food products of low cyanide content.
4. Chemical analysis to determine the total cyanide content in cassava roots and products and thiocyanate in urine.
5. Other relevant matters of interest.

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