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Cassava-derived cyanide poisoning in South-Kivu: Two possible consequences in addition to konzo

Cyanide is a natural poison that blocks the use of oxygen essential to living cells, needed to produce energy for their metabolism. Cyanide poisoning can occur from smoke inhalation (cigarettes, fires), environmental pollution (chemical and synthetic industries), or consumption of cyanogenic plants. Cassava is a major crop in tropical regions because it is easy to grow, it gives high yields and it is resistant to drought. However, it contains two cyanogenic glucosides, linamarin and a small amount of loutastralin, which liberates cyanide by enzymatic degradation.¹ When bitter cassava is insufficiently processed, its consumption generally causes sublethal cyanide poisoning, but leading sometimes to death.² Cassava provides 70% of caloric intake (*data from FAO and USAID*) in the Democratic Republic of Congo (DRC). Furthermore, cassava is the staple food in South-Kivu Province in Eastern DRC and in many other tropical regions.³ Recently we⁴ and APAA Congo found that the population of South-Kivu Province was undergoing cyanide poisoning from poorly processed bitter cassava. In this article, we discuss other possible consequences of cassava-related cyanide intoxication in the region, based on local daily medical practice and previous reports, confronted with current knowledge on cyanide poisoning and its target organs. We hope to focus attention on the current disruption of cassava safety in South-Kivu and its consequences on the health of the people.

When toxic cassava is ingested, linamarin and its intermediate metabolites are broken down mainly by microbial enzymes in the gut. The freed cyanide binds first to blood compounds, then is secondarily released and undergoes enzymatic degradation, mainly in the liver, being converted into less toxic thiocyanate, which is excreted in the urine. Thiocyanate synthesis requires sulphur groups exclusively provided by proteins in the diet.⁵

Cassava toxicity is an aggravating factor in a number of tropical diseases. In malnourished people the cyanide detoxification pathway into thiocyanate is defective. Linamarin and/or its metabolites are incriminated in the upper motorneuron degeneration leading to konzo.⁶ Thiocyanate competes with iodine uptake in the thyroid gland, hence the correlation between cassava-derived cyanide intoxication and endemic goitre.⁷ The implication of cassava toxicity in the pathogenesis of so-called tropical (or malnutrition-related) diabetes is still controversial^{2,8,9} but recent publications tend to support this hypothesis.^{8,10} The mechanism would be the toxic effect of cyanide on the pancreatic islets in malnourished people.⁹

South-Kivu has one of the highest rates of malnutrition in DRC.¹¹ Also, this province has been deeply affected by the long-lasting conflict situation the country has faced for more than a decade. In this context several cases of spastic paraparesis highly resembling konzo have been reported in Luwhinja, Burhinyi and Kaziba (cases count in CCDN News No 5, P3), where there seems to be a high frequency of early onset diabetes mellitus. If the high rate of diabetes were confirmed, other environmental and genetic factors should be looked

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for, but the coincidence of diabetes with konzo is striking.

In the colonial period, the island of Idjwi in Lake Kivu was infamous for its high prevalence of endemic goitre due to iodine deficiency exacerbated by thiocyanate from insufficiently processed toxic cassava.⁷ Iodine supplementation greatly improved the situation, at times even leading to thyrotoxicosis due to excessive iodine intake.¹² Since the war in the 1990's, some health workers suspected a resurgence of endemic goitre due, according to them, to disruption in the supply of iodised salt. Random interviews of people in the northern part of Idjwi in 2005, 2007 and 2008, noted that bitter varieties of cassava are more and more consumed, but no case of konzo has been so far reported. People in Idjwi Island probably have a better nutritional status compared to people in areas where konzo was recently reported. Therefore they are better able to convert cyanide into thiocyanate and this tends to aggravate pre-existing iodine deficiency rather than causing konzo. Iodised salt supplementation is the first target in overcoming possible resurgence of endemic goitre, but the contribution of cassava toxicity should not be neglected.

In this article, we deliberately did not stress the link between cyanide toxicity from locally consumed cassava in South-Kivu Province and the outbreak of spastic paraparesis which is discussed elsewhere.⁴ We considered possible involvement of cassava cyanide intoxication as an aggravating factor (if not more) in diabetes mellitus and endemic goitre in different areas of this province. Our assumption is that according to the nutritional level of the population, cassava toxicity leads to different clinical pictures. In deeply malnourished people (as in Burhinyi and neighbouring areas), it would lead to konzo and possibly contribute to (tropical) diabetes mellitus, while in populations with better nutritional status (Idjwi Island) it would worsen a pre-existing iodine deficiency. These hypotheses need confirmation by rigorous epidemiological studies.

They suggest a new parameter to be taken into account in the management of diabetes and endemic goitre in South-Kivu; viz. cyanide intoxication from insufficiently treated cassava. Reducing cyanide content of cassava varieties consumed in South-Kivu by simple and cheap strategies,⁴ would

probably decrease the frequency of these two pathologies and their effect on families and communities. We also note that promoting the safe consumption of cassava in South-Kivu would improve the food security system in which this crop plays a central role. We are currently fundraising in order to initiate a large epidemiological study targeting this particular issue.

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Cyanide poisoning and konzo from cassava in South Kivu Province, DRC

Meetings have been organised in the villages of Biriba, Kawizi, Kigoma, Kiliba, Nyakabere, Runingu and Sange near Uvira, South Kivu Province, DRC, at which many people have been told about the cyanide present in cassava and its effects in causing konzo and cyanide poisoning (the symptoms of which are headache, dizziness, stomach ache, diarrhoea and vomiting and in extreme cases death). Konzo is an irreversible paralysis of the legs that occurs suddenly as a result of high intakes of cyanide. Konzo occurs particularly in children and women of child bearing age. Also a new wetting method for the removal of cyanide from cassava flour was described, which reduces the cyanide content 3-6 fold.¹⁻³ Coloured, laminated posters, which describe the effects of cyanide poisoning and konzo and show in simple pictures the wetting method were produced in the local language (Kifuliru) and distributed to the people.⁴

Some months later about 30 people (mainly women) in two of the villages (Kawizi and Kiliba) were interviewed individually and asked 9 different questions. The results of the surveys from the 2 villages are given in the following numbered statements with comments as required. It was found that:

1. Everyone ate cassava every day and more than one third had cassava more than once per day.

Comment. This shows the very great dependence of the village people on cassava as their staple food and confirms the FAO data on food consumption in 2005, which lists the daily per capita consumption of cassava in DRC as 650 g/day, the third highest after Mozambique and Angola.⁵

2. 60% understand that bitter cassava contains a poison and more than 80% get sick after eating food from bitter cassava.

3. 87% prepared cassava flour by soaking the peeled roots in water for about 4 days, followed by sundrying, grinding in a wooden pestle and mortar and sieving.

Comment. This is a good method of removing the cyanide from cassava.⁶

4. As a result of the earlier meetings and the distribution of the laminated posters, 46% of those surveyed had learned to use the wetting method, but only 23% used the wetting method and then only less than once a week.

5. The complaint of 75% of those who had tried the wetting method was that it took too long (5 hours) and some said that the wet flour required surveillance over that time to prevent spoilage by children or loss by stealing.

Comment. The wetting method is unpopular because of the long 5 hour period of treatment. We have laboratory results that show that the loss of cyanide in 5 hours in the shade (at 30° C) is about the same as 2 hours in the sun (at 50° C). We hope that a 2 hour treatment in the sun will be more acceptable to rural women. Use of the wetting method in other countries that have konzo is given on P4.

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Elimination of cassava toxicity by processing

Cassava is an important food crop in the tropical regions of Africa, Latin America and Asia. In India, cultivation and processing of cassava is confined mainly to Kerala, Tamil Nadu and Andhra Pradesh, where it is utilized for human and animal feed and industrial products. Because cassava produces moderate yields with low inputs and where other staples fail, it is recognised as a valuable food security crop and an insurance against famine. The presence of toxic factors in cassava has been known ever since the crop was used for human consumption. Toxicity is associated with the presence of cyanoglucosides (CNG), linamarin and lotaustralin, which are hydrolysed by an endogenous enzyme linamarase to cyanohydrins and cyanide, both of which are toxic.

The highest concentration of CNG is in the skin of the tuber and leaves and lower amounts in the tuber flesh.¹ The amount of CNG in the tuber is genetically controlled, but is influenced by environmental factors such as soil, rainfall, drought and shade.² The linamarin content of tubers of different cultivars varies widely. Cassava cultivars may be classified as low (<50 mg HCN equivalents/kg fresh root = ppm), medium (50–100 ppm), high (>100 ppm). The concentration of CNG is positively correlated with the bitter taste of the raw tuber flesh.³ In Kerala, most of the popular varieties contain <50 ppm CNG.

A great diversity of processing methods are followed in cassava consuming communities. These include peeling and slicing fresh tubers followed by boiling, baking, steaming, drying, blanching and drying, deep frying, fermentation or grating/pounding followed by drying. Most of these processing methods are effective in reducing CNG content.⁴ Depending on the nature of the process, they either lead to hydrolysis of CNG to release cyanohydrins and cyanide, which are volatilized and subsequently lost or the highly soluble CNG and its hydrolytic products are leached out by water.

When cassava tubers are cut into small pieces and cooked in water, up

to 80% of CNG is removed. The CNG is leached out into the water, hence it is necessary to decant the water completely. The volume of water should be adequate for optimum dissolution of CNG. When bitter tubers are cooked, it is customary to change the water two or three times until the bitterness is reduced as far as possible. Chopping cassava tubers into chips of about 10mm thickness, followed by sundrying, also removes up to 80% of CNG. In contrast to the boiling process, removal of CNG during drying is primarily controlled by the activity of linamarase and the time allowed for it to act before it dries out. Processes such as baking, steaming and frying lead to only 20% loss of CNG. This is due to inactivation of linamarase and the stability of linamarin at high temperatures. These processes are therefore recommended only for very low cyanogen cultivars. When cassava is grated/pounded and then sundried, it is possible to obtain a product with very low cyanide levels. The process of grating/pounding is effective as it allows the CNG to come into contact with linamarase resulting in its complete hydrolysis.⁴⁻⁶

Both the initial content of CNG and the method of processing influence the level and nature of cyanogens in the final product. Thus different processing methods must be used for high and low cyanide varieties. Cardoso et al (2005)⁶ compared the retention of cyanogens during different processing methods and calculated the maximum root total cyanide content for a particular processing method, in order to obtain products with WHO safe levels of 10ppm. The initial root cyanide level for the process of crushing or pounding followed by sundrying should not exceed 270 ppm, while for sundrying the initial level should be <16 ppm.

Consumption of inadequately processed cassava can lead to dietary cyanide exposure.⁷ The source of dietary cyanide can be linamarin and/or acetone cyanohydrin, which in the gut can be broken to free cyanide. The human body has two defence mechanisms against cyanide. Cyanide is trapped by the methemoglobin fraction in red blood corpuscles and is converted into thiocyanate in a reaction catalysed by rhodanese that uses dietary sulphur amino acids. The thiocyanate formed is removed in the urine. The association of cassava with increased goitre frequency is due to increased thiocyanate levels, since thiocyanate interferes with iodine uptake.⁸ However cases with high

thiocyanate exposure fail to develop goitre if iodine is adequate. Several other sources of cyanide exposure also lead to increased thiocyanate levels including tobacco smoke. No increased incidence of goitre in these cases has been reported.

Epidemiological studies do not support a relation between cassava consumption and pancreatic diabetes, since the incidence of the disease is equally prevalent in non cassava consuming populations⁹, but there is some controversy on this point.¹⁰ Tropical ataxic neuropathy (TAN) was recently reported in South India¹¹ and linked to possible cassava intake, but there needs to be a closer study of actual intakes of cassava cyanogen in these populations. People who have had a staple diet of low cyanide cassava for many years along with protein (eg fish) that is rich in sulphur-containing amino acids which ensures adequate detoxification of cyanide, are not at risk from the clinical disorders mentioned above.

To conclude, consumption of low cyanide cassava (<50 ppm) with normal processing does not pose a cyanide toxicity problem. High cyanide cassava varieties containing up to 270 ppm cyanide can also be made safe if processed by pounding and sundrying.

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Uptake by rural women of wetting method to remove cyanide from cassava flour

In 2005 a simple wetting method was developed which reduces the total cyanide content of cassava flour 3-6 fold.¹⁻³ The method involved mixing cassava flour with water and leaving the wet flour spread thinly on a basket in the shade for 5 hours. This allowed the enzyme (linamarase) to break

down the cyanide containing compound (linamarin) to produce hydrogen cyanide gas. As is traditional the wet flour was then mixed with boiling water to produce a stiff porridge.

The wetting method was found to be very acceptable to rural women in Mozambique. It required no extra work, no extra water or additional equipment, and the flavour of the thick porridge was preferred to that produced from untreated flour.^{3,4} The wetting method received the inaugural \$2 a day award by the Institution of Chemical Engineers (ICHEM) in 2007. We have found that the time of treatment may be reduced from 5 hours in the shade to 2 hours in the sun.⁵ We have developed coloured laminated posters (see below) in 3 European and 5 African languages which are available for free.⁶

The wetting method has the potential to eliminate cyanide poisoning and konzo from those people in Eastern, Southern and Central Africa who use cassava flour. But for this to happen it is necessary for the wetting method to be widely used by rural women. However, 4 years on since its discovery, the uptake of the wetting method by rural women has been very small indeed.

Mozambique. There are more than 2000 recorded konzo cases and in 2005 there were more than 100 new cases in Nampula and Zambezia Provinces due to drought. The wetting method was successfully field tested amongst rural women³ and the first poster produced by Dr Dulce Nhassico in Portuguese. This has subsequently been modified and translated into Macua, the language used in Nampula Province. Urinary thiocyanate results from school children in these provinces have been consistently high over the years during the cassava harvest, indicating that they are in danger of

getting konzo when the next drought strikes, because the cyanide content of cassava roots and cassava flour increases 2-3 times during drought.⁴ In 2007 the Australian Agency for International Development (AusAID) funded a one year program in Nampula Province on rehabilitation and prevention of konzo involving Mozambique Red Cross, Domingos Nicala and Julie Cliff.

Tanzania. Konzo occurred due to drought in Mtwara region in southern Tanzania in 2002-3 and there were 214 cases. There is a konzo rehabilitation and prevention program in progress in Mtwara Rural District and Newala and Mbinga Districts involving Tanzania Red Cross and Dr Nicholas Mlingi and co-workers at Tanzania Food and Nutrition Centre and supported by AusAID. The wetting method is being introduced to rural

women and 200 copies of laminated posters in Kiswahili have been used.

Democratic Republic of Congo (DRC). It is estimated that there are 100,000 cases of konzo in DRC due mainly to prolonged war and unrest which forces people to leave home and eat high cyanide cassava from the bush. APAA Congo had the poster translated into Kifuliruru. They organised meetings in many villages around Uvira

and told about poisonous cyanide in cassava, that causes konzo which is common there. Five hundred laminated Kifuliruru posters have been distributed and feed back obtained in villages about the uptake of the wetting method.⁵

Central African Republic (CAR). Konzo was found in CAR in 1994⁷ and a 2008 report concludes that konzo is a serious health problem in health region 2 of CAR and recommends that a prevention program be set up.⁸

Cameroon. Konzo was reported here in 1998.⁹ Recently many refugees from war in CAR were forced into Cameroon and many were found to

have konzo.¹⁰ We provided cyanide kits to Medecins sans Frontieres (MSF) and laminated posters in French.

Angola. There are anecdotal reports of konzo in Angola. Also Angola had the highest daily per capita consumption of cassava in 2005 (787g) compared with Mozambique (680g) and DRC (653g) in second and third place.⁴ Since Mozambique and DRC experience outbreaks of konzo, it is very likely that Angola does too.

Conclusion. It is clear from many studies that konzo occurs amongst the poorest of the poor rural people who are exposed to a monotonous diet of high cyanide cassava. The disease would be eliminated if these very poor rural people could be given a broader diet, but this has not happened over the past generation. Indeed the incidence of konzo in tropical Africa is likely to increase with increasing use of cassava in the future⁴, unless the amount of cyanide ingested from cassava is greatly reduced. The wetting method, which reduces the cyanide content of cassava flour 3-6 times is a simple practical solution for cassava flour, and is being introduced around Uvira in South Kivu Province of DRC. We appeal to our readers to help get uptake of the method by rural women, in order to reduce konzo and cyanide poisoning.

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