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

CCDN News

Cassava Cyanide Diseases & Neurolathyrism Network

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CCDN Coordinator:
Dr. J. Howard Bradbury
EEG, Research School of Biology,
Australian National University
Canberra ACT 0200, Australia
Phone: +61-2-6125 0775
E-mail: howard.bradbury@anu.edu.au

Website:
www.anu.edu.au/BoZo/CCDN

Why are neurolathyrism and konzo neglected diseases?

Neurolathyrism and konzo are two spastic paraparesis / tetraparesis diseases with identical clinical symptoms which have not yet been reported to occur in the same geographical area. Neurolathyrism is associated with prolonged over-consumption of grass pea seeds (*Lathyrus sativus* L.), a drought-tolerant legume crop grown in Ethiopia and in the Indian Sub-continent (Bangladesh, Pakistan, Nepal, India) while konzo is associated with frequent consumption of insufficiently processed bitter cassava (*Manihot esculenta* C.) roots and cassava flour and cases are found in Sub Saharan Africa (DRC, Angola, Cameroon, CAR, Tanzania and Mozambique). If the two diseases were to occur in the same area, it would be difficult to distinguish one from the other except that the onset of neurolathyrism has been reported to occur later than konzo and men are predominant in neurolathyrism compared to konzo where children above two years old and women at childbearing age are more affected than men. Epidemiology and dietary information would be needed to differentiate the two.

Both diseases are permanent and affect many thousands of people among poor rural populations. There are no accurate numbers of cases since both diseases are not considered reportable by the World Health Organization (WHO). Poverty and illiteracy of the victims, and remoteness of the areas of incidence make underreporting common. There are few reliable statistics on the prevalence of both conditions and mostly estimations have been made.[1] Little attention has been given by governments in afflicted countries. The affected populations have low socio-economic status and mostly live in remote rural areas where they have no decision power and no political voice. No comprehensive epidemiological studies have been planned and conducted. These diseases are not seen by Ministries of Health as a major national health problem.[2]

The International Classification of Diseases (ICD), which is the international standard diagnostic classification for all general epidemiological, many health management purposes and clinical use by WHO Member States, does not include monitoring of the incidence and prevalence of neurolathyrism and konzo. There is no specific ICD code for both crippling conditions.[3] A specific and more accurate code would allow for the surveillance of the number of cases in the population if these conditions become reportable by WHO.[4]

WHO has a much more complex classification of terms and concepts used in disability, the so called International Classification of Functioning, Disability and Health (known as ICIDH-2) which is complementary to the ICD-10 (10 standing for the tenth revision). The applicability of the ICIDH-2 framework has demonstrated the possibility of its use as a common language among researchers in the field of motor disorders. However, a revision was suggested of its taxonomy, and a definition provided of operational criteria to clarify the content of different qualifiers, to assess the level of functioning or disability.[5]

Neurolathyrism and konzo are incurable, irreversible disabilities that persist exclusively in the poorest and the most marginalized communities and often reduce the victims to beggars and a burden to the local economy. These diseases can be prevented at a relatively low cost using rapid interventions (such as the wetting method in the case of konzo[6]) and can be largely eliminated but they are often

neglected or forgotten. Insufficient money is spent on research and there is no existing cure for both diseases, except a well balanced diet which can prevent malnutrition and further attacks. A first and important step in the prevention of these diseases would be their recognition as reportable diseases as proposed by Haimanot et al[2] for neurolathyrism in Ethiopia. Initiatives to recognize these diseases as reportable have to be taken by the national authorities who should organize active surveillance and timely reporting.

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Diasolua Ngudi, D. ddiasolu@yahoo.com
and Lambein, F.
Fernand.Lambein@ugent.be
IPBO- Ghent University, Ghent, Belgium

Prevention of new cases of konzo in a village in DRC

Konzo is an irreversible paralysis of the legs that occurs mainly in children and young women as a result of intake of cyanogens from bitter cassava.[1] The wetting method which reduces the total cyanide content of cassava flour 3-6 fold, was developed in 2005 to reduce cyanide poisoning and konzo[2,3] and was shown to be acceptable to rural women in Mozambique.[4] Subsequently the wetting method was taught to more than 200 rural women in villages where konzo has occurred in Tanzania[5] and has now been used in Kaykalenge village of Democratic Republic of Congo (DRC) to prevent the occurrence of new cases of konzo and reduce the percentage of children in danger of getting konzo.

In Kaykalenge village (population 1250), Popokabaka Health Zone, Bandundu Province, DRC, a medical team found 34 cases of konzo, of which 17 were contracted in 2009. Since poisonous cyanide is detoxified in the body to produce soluble thiocyanate which is removed in the urine, a urinary thiocyanate analysis gives a measure of the amount of cyanide ingested in preceding days. Those people with urinary thiocyanate concentrations in excess of 300 µmole/L we consider to be in danger of getting konzo. Urinary thiocyanate analyses on 100 school children of Kaykalenge village showed that 49% were in danger of contracting konzo.

Ten of the senior women of the village were taught to use the wetting method and they in turn each showed 15-20 women how to use the method. Laminated, illustrated posters which describe the method in the local language (Kiyaka) were distributed to the women of the village.[6] In the wetting method the dry flour is placed in a bowl and the level that it reaches is marked on the inside of the bowl. Water is then added with stirring until the wet flour comes up to the mark on the bowl. The wet flour is then placed in a thin layer on a basket and left in the shade for 5 hours or in the sun for 2 hours to allow hydrogen cyanide gas to escape. The damp flour is cooked in boiling water in the traditional way to make the thick porridge (fufu). Sometimes the women of Kaykalenge village put the basket of wet flour in the sun when they went to work and left it there until they returned in the afternoon. They also preferred the taste of the fufu made from treated flour because the bitter taste of the cyanide compound (linamarin) had been removed by the wetting treatment.

The rural women of Kaykalenge continued to use the wetting method and during the dry season May-August 2010 when konzo usually occurs there were no new cases of konzo. Furthermore, 100 urinary thiocyanate analyses at Kaykalenge school showed that the percentage of children in danger of getting konzo had been reduced from 49% to 28%.

The results obtained thus far show that it is possible to prevent the occurrence of konzo in a konzo-prone village by the introduction and use of the simple wetting method to remove cyanogens from cassava flour. This is a preliminary report and the study in Kaykalenge village is continuing.

We believe that this is the first example of prevention of konzo. It is hoped that this use of the wetting method to reduce cyanogen intake from cassava flour may serve as a model that can be used throughout the konzo countries of Africa, to remove the scourge of konzo from Africa and the world.

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Banea, JP,[1] Mandombi, C,[2] Bradbury, JH,[3] Nahimana, G, [1] Kuwa, N,[1] & Didier, T.[2]
[1] Programme National de Nutrition (PRONANUT), Kinshasa, DRC.
jpbanea@yahoo.fr
[2] Zone de Sante de Popokabaka, DRC.
[3] EEG, Research School of Biology, Australian National University, Australia.
Howard.Bradbury@anu.edu.au

Mild processing of cassava leaves to retain nutrients

Cassava leaves are a very important food source in tropical Africa with high use (above 60% consumption) in DRC, Congo, CAR, Angola, Rwanda, Burundi, Liberia, Sierra Leone and Guinea, moderate use (above 40% consumption) in Senegal, Cameroon, Chad, Uganda, Tanzania, Zambia, Mozambique and Madagascar and low use (<40% consumption) in other countries of tropical Africa.[1] Leaves are available throughout the year and are a good source of protein, minerals and vitamins. The Congolese say that cassava is “all sufficient” because they get “bread from the (starchy) roots and meat from the leaves.”[1]

However there is a problem because the leaves contain large amounts (80-1860 ppm)[2] of cyanogenic glucosides (mainly linamarin and a small amount of lotaustralin – methyl linamarin) which the plant synthesises to deter animals that attack the plant. If a leaf is attacked then linamarin present is broken down to glucose and acetone cyanohydrin, catalysed by the enzyme linamarase and the acetone cyanohydrin is decomposed in a second reaction to hydrogen cyanide (HCN) gas and acetone, catalysed by the enzyme hydroxynitrile lyase.

The consumption throughout the year of large amounts of processed cassava leaves contributes to the cyanide intake of the people, but is minimised, if there are very good methods of removal of cyanogens. A current method is to pound cassava leaves for about 15 min in a pestle and mortar and then boil them in water for 15-60 min.[2-4] For intact leaves boiling in water for 1-2 h is also used to remove cyanogens. However, although boiling in water (with or without pounding) effectively removes cyanogens from cassava leaves, it also greatly reduces their nutrient content. Thus boiling for 30 min reduced the protein content by 58% and the methionine content by 71%[5] and 10 min boiling reduced the vitamin C content by 60%.[2] Losses of vitamin A and of B-vitamins thiamin, riboflavin and nicotinic acid are also considerable.[6]

It is important to retain as much as possible of these nutrients, particularly protein and the S-containing amino acids (methionine and cysteine), which are necessary to detoxify ingested cyanide (CN) to produce thiocyanate (SCN), that is removed in the urine. A shortfall of S-containing amino acids could slow the detoxification of cyanide, allowing a build up of cyanide in the body and the sudden onset of konzo.

Konzo is an irreversible paralysis of the legs that occurs mainly in children and young women and is associated with a very high intake of cyanogens from bitter cassava combined with low protein intake.[7] In a village with 34 cases of konzo, we have shown that new cases of konzo can be prevented through reduction of cyanogen intake, by consistent use by the village women of the wetting method to remove cyanogens from cassava flour.[8] It is hoped that development of new mild methods of removal of cyanogens in cassava leaves, that allows retention of key nutrients including S-containing amino acids, will help further to reduce the incidence of konzo.

1. Pounding followed by washing at room temperature

Cassava leaves (10g) were analysed for total cyanide, pounded in a laboratory pestle and mortar and analysed for cyanide. The pounded leaves were washed with 20 mL of water and the pounded leaves analysed. The washing treatment and analyses were repeated 3 more times with 20 mL water. The mean % cyanide remaining from analyses on four different cultivars after pounding was 29%, and after washes 1, 2, 3, 4, was 13%,8%, 6% and 3% respectively. Thus the pounding treatment followed by 2 washes at ambient temperature, reduced the cyanide content to 8%, which should be sufficient for normal use, but for cassava leaves with very high total cyanide content (>1000 ppm) it may be necessary to wash 4 times to reduce the cyanide content to an acceptable level.

2. Immersion of cassava leaves in water at 50° C

Two 10g samples of cassava leaves were analysed and mixed with 100 mL of water at about 50° C and allowed to stand for 2 h at 50° C. In one case the experiment was continued at 50° C withdrawing further leaf samples for analysis at 3, 4 and 5 h. In the second case the leaves were analysed after 2 h and the water was changed. Fresh water (100 mL) at 50° C was added and the leaves analysed after 3, 4 and 5 h. Averaged over 4 cultivars it was shown that after 4 h immersion of leaves there was 17 % cyanide retained, but the change of water after 2 h reduced the cyanide retained to 7%. The water wash solutions used in experiments on pounded leaves and on intact leaves, contained considerable amounts of cyanogens and must be discarded.

Conclusions

1. The best method to remove cyanogens from cassava leaves whilst retaining key nutrients is to pound them for at least 10 min in a pestle and mortar and then wash them at least twice, in twice their weight of water. The pounded leaves are fresh green in colour.

2. Removal of cyanogens from intact leaves can be achieved by immersing them in ten times their weight of water for 2 h at 50° C, replacing the water with fresh water at 50° C and immersing for 2 h more, a total of 4 h. If no thermometer is available a finger can be placed in the water and if it can be held there for > 2 min the temperature is 50° C or less. At 54° C the finger must be removed after only 5 sec.

3. It is hoped that adoption of these mild methods to remove cyanogens from cassava leaves, which conserve protein and particularly S-containing amino acids, may help to limit the occurrence of konzo in tropical Africa.

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Bradbury, JH and Denton, IC
EEG, Research School of Biology, Australian National University, Canberra, 0200, Australia
Howard.Bradbury@anu.edu.au
iancd@yahoo.com

Konzo in Angola?

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Subject

Tropical spastic paraparesis - Angola: (Lunda Norte)

A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the International Society for Infectious Diseases
<http://www.isid.org>
Date: Wed 13 Oct 2010
Source: AllAfrica, Angola Press Agency (Angop) report [edited]
http://allafrica.com/stories/201010130688.html

Angola: possible illness hitting Caungula District revealed

The medical commission created by the Chancellery of the state run Agostinho Neto University (UAN) suspects that the illness that has been hitting Caungula District, in the eastern Lunda-Norte Province, is tropical spastic paraparesis [TSP], ANGOP [Angola Press Agency] has learnt. This was stated in a press conference by the dean of the Medicine Faculty with UAN and coordinator of the mentioned commission, Miguel Bettencourt, who travelled to the locality.

"In a clinical assessment made mainly in the villages of Monakaje and Lukwokeza, at Caungula District, it was concluded that the disease tropical spastic paraparesis (TSP), an illness that has already been reported in Mozambique and in the Democratic Republic of the Congo (DRC). At this moment, it is not possible to say what is the cause of this illness, although there are indications that it is caused [either] by the bitter manioc which contains cyanide, a chemical and toxic element, [or] HTLV [human T-cell lymphotropic virus] infection."

The expert said that the illness is characterised by reduction of muscular strength of the arms, marked by a rigidity of the legs, hindering thus the movements. "This situation is worrying and with serious social and economic results, particularly in Monacaje village, where 40 per cent of the cases were recorded, among children and adults," he explained.

Samples of the blood of patients, as well as of the manioc, have already been sent to a laboratory in South Africa.

communicated by:
Thomas James Allen
<tjallen@pipeline.com>

In the case of the outbreak of illness in Caungula District, in the eastern Lunda-Norte Province of Angola it is uncertain whether the outbreak can be attributed to HTLV-1 infection or is a consequence of manioc poisoning.
The outcome of diagnostic testing in South Africa is awaited.

Editors Comment:
This outbreak is likely to be konzo and if so, it is the first reported outbreak in Angola. There were anecdotal reports by H. Rosling of previous konzo in Angola, cited by Cliff et al.,[1] and a prediction in 2009 that konzo would be found there, because of the very high per capita consumption of cassava in Angola.[2] If konzo is confirmed in Angola, this is further evidence of the increasing geographical spread of konzo in tropical Africa, which has recently been noted within Mozambique,[3] Tanzania[4] and DRC.[5]

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