Vapniarca revisited: Lessons from an inhuman human experience.

Fernand Lambein, Delphin Diasolua Ngudi, Yu-Haey Kuo

Lab. Physiological Chemistry, Faculty of Medicine and Health Sciences, Ghent University, Kluyskensstraat 27, B-9000 Ghent, Belgium.

Email: (1) Fernand.Lambein@rug.ac.be

In the previous issue of this Newsletter, a contribution on "Homeopathy, longevity, and *Lathyrus sativus* toxicity"[(5)], indicated that the problem of the economic value of this crop and the medical consequences of its over-consumption involved nutritional aspects that need better consideration. To better understand the essence of the problem, and to further this discussion we revisited some older literature focusing on observations or statements concerning human nutrition.

In the old Loudon's "Encyclopaedia of Plants" re-edited in 1855[(7)], the well-known edict of the Duke of Wurtenberg of 1671 forbidding the use of grass pea in bread is mentioned. It also adds: "and this not being observed, was enforced by two other edicts under his successor Leopold in 1705 and 1714", underlining the popularity of this food in Europe three hundred years ago. And further a nutritional observation: "Mixed with wheat flour in half the quantity, it makes a very good bread, that appears to be harmless. But bread made with this flour only has brought on a most surprising rigidity of the limbs in those who have used it for a continuance; insomuch that the exterior muscles could not by any means be reduced, or have their natural action restored". Loudon also made allusion to the effect of the environment and the soil on the variable toxicity of the seed.

The most remarkable account comes from the description of the epidemic in the German prisoners of war camp in Vapniarca, a town in Ukraine occupied by Germany during the second world war. There the highest incidence of neurolathyrism on record developed between December 1942 and the end of February 1943[(3)]. Dr A. Kessler, who was among the prisoners, noted many details on the diet and neurological symptoms of the prisoners and the lathyrism victims. This was published in the German language in 1947. Additional information on the camp conditions can be found on the web:

http://motlc.wiesenthal.com/pages/t081/t08153.html

What is termed in the website as "horse fodder" consisted of 200 gram boiled grass pea seed and 200 gram barley bread containing 20 % chopped straw. This was given to 150 inmates who were moved from Bukovina to Vapniarca 3 to 6 months before the arrival of 1200 inmates on 16 September 1942. Of these, 680 came from other camps, while the others were recent arrests. At that time, the diet of all inmates was changed to 400 gram boiled grass pea seed per day and the same 200 gram barley bread.

In November 1942 one of the earlier inmates, who had been in the camp for five months (three months on a diet of 200 gram grass pea and 160 gram barley, and two months on a diet of 400 gram grass pea and 160 gram barley), developed symptoms of lathyrism. Three more cases developed in December 1942, and on December 29, the first of the group arrivals of September 16 developed the symptoms. One week later on January 5, already 19 lathyrism cases were apparent. On January 23, the consumption of grass pea was halted. New cases continued to become apparent until March 1, with a peak on January 20, 1943. Together, 60% of the inmates had developed various levels of neurolathyrism, the highest incidence ever reported in the literature. A number of these patients are now under the care of Dr Dan Cohn in Tel Aviv[(9)].

Like Loudon before, Kessler also mentioned the effect of the environment on the toxicity of the seed. Information on the atmospheric conditions of the time might give some information on the potential content of ODAP in the grass pea seed. We can conservatively estimate that the content was about 0.25 % (seeds recently harvested in Poland have a range of 0.03 to 0.33 % ODAP, the lower values apparently for selected lines; A. Winiarska, pers. comm.). This means that a daily intake of 500 mg of ODAP per day under severe conditions of malnourishment and physical exhaustion did not cause apparent signs and symptoms of neurolathyrism in those inmates during a period of 3 to 5 months. After September 16, 1942, when the diet was

changed to 400 gram of grass pea seed and the same amount of the same bread, the inmates absorbed about 1 gram of ODAP per person per day. From that moment the latency period of 2 to 3 months of continued intake was still needed for apparent cases of neurolathyrism to occur.

From this dramatic episode in history we may deduce that a threshold level of ODAP intake may be close to 500 milligram per day per adult person. This has to be taken with extreme caution, as some of those earlier inmates worked outside during the day, and some had relatives nearby who could visit. In both these cases, small amounts of additional unspecified food could be received and consumed, changing the balance of the dietary intake, while the total intake of ODAP was probably unaffected. Our assumption that the seeds consumed before and after September 16 were the same also has no proof. An additional factor is the preparation of the seeds: if the water after boiling was discarded this would give an important reduction of the toxin ingested.

We calculated the amino acid score, that gives a measure of the balance of essential amino acids and for which the FAO gives the standard. For the diets as described, and not considering the unspecified additions mentioned above, we find an important decrease from 61% in the earlier diet to less than 50% of the optimal ratio in the diet after September 16, 1942. The amino acid score for pure grass pea seeds is around 20 %. The minimal requirement for essential amino acids was met in both diets, except for sulphur amino acids. The diet before 16 September had only 798 mg of cysteine plus methionine, when an adult male needs 1100 mg. The diet after 16 September had about 1067 mg of cysteine plus methionine. The important variation in the diet on 16 September may have been in the ratio of ODAP to essential amino acids. An important point is that the quantitative daily requirement for essential amino acids is considerably lower for women than for men. Perhaps there is possibly a simple explanation for the difference in susceptibility between males and females on the basis of this intake of essential amino acids. The bread mentioned in Loudon's Encyclopaedia containing half grass pea and half wheat and causing no deleterious effects, should have had an amino acid score and a ratio of ODAP to essential amino acids close to the diet before 16 September.

When comparing with the dietary aspects of konzo, a disease with similar socio-economic background as lathyrism and exactly the same final stage of spastic paraparesis of the legs[(1)], we can make a nutritional comparison. Cassava, the dietary cause of konzo is quantitatively a much poorer source of protein than grass pea seed, containing only 1 to 1.5 %. For the detoxification of the cyanide intake (from the cassava), sulphur atoms derived from sulphur amino acids are needed and are no longer available to feed the biochemical pathways protecting against oxidative stress. Konzo is prevalent only in areas where little other food is available and especially in periods of food scarcity when treatment to reduce cyanide by soaking is insufficient. In areas where 25% of corn is added to the daily diet of cassava, konzo is not prevalent. The amino acid score of cassava is only 14.1 and increases to 48.7 with addition of 25% corn. Still then, the daily requirement for essential amino acids is not met when 500 g of this mixture is consumed per day. Less than 40% of the daily requirement of cysteine plus methionine is supplied by this diet; the lysine supplied is only 65% of the daily requirement and tryptophan only 28%. This mixed diet has a higher amino acid score, but is still not well balanced. Although both cassava and grass pea have an obvious deficiency in essential amino acids, the rate of susceptibility to konzo between males and females is different from neurolathyrism. Points of similarity may be found further in the biochemical pathways and physiological effects, where metabolites involved in the biosynthesis of nitric oxide and its modulation can be derived from the diet. Spencer and co-workers have studied the effects of sulphur amino acid depletion on the metabolism of cyanide[(10)].

While there is an obvious point to learn, that we should respect old literature, we should not overemphasise the conclusions from such a one-sided approach of the problem. As mentioned in the contribution in the previous Newsletter issue [(1)], many aspects need further research, such as i) the micro-nutrients essential for our defence against oxidative stress[(6)], ii) the potential depletion of these micro-nutrients through chelation with ODAP, iii) the potential presence of minor toxins that may have a synergistic physiological effect together with ODAP, iv) the neurological and physiological effects of ODAP other than the well established excitation of the AMPA receptors[(2,4,8)] and v) the effects

of ODAP and other metabolites such as homoarginine on nitric oxide metabolism and apoptosis.

The threshold level of safe intake of ODAP as deducted from the Kessler report is probably the only such information in the literature. Also this needs a careful approach as the level of ODAP in the grass pea seed of 1942 is unknown. Perhaps the archives of the Vapniarca camp, or the survivors of this tragedy may shed further light on this inhuman human experience.

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