

CASSAVA

Solving the toxicity puzzle

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The root crop cassava is the major source of carbohydrates for some 300 million people in tropical regions. With a total production of about 100 million tons, it is the world's seventh most important crop, after the principal cereal grains, potatoes and sweet potatoes. Production is constantly increasing, and is expected to double in 30 years or so.

This background underlines the importance of the findings reported by a team of Belgian physicians, who have demonstrated after several years of research that under certain circumstances the consumption of cassava can provoke goiter, cretinism, and mental retardation. Cassava contains a substance which, once ingested, inhibits iodine uptake by the thyroid gland. In regions where food contains only marginal amounts of iodine, there is a risk that cassava will trigger thyroid insufficiency that could have severe consequences on the development and the functioning of the nervous system.

The survey that led to this finding started nearly 10 years ago on Idjwi Island, situated in Lake Kivu, Zaire, and inhabited by some 30,000 people scattered throughout 69 villages.

It showed that there was a severe and uniform shortage of iodine throughout the island. So the researchers were surprised by their first, then unexplained, finding: in certain villages, particularly in the south, there were hardly any cases of goiter; in others, mostly in the northern part of the island, the condition was endemic, with more than half the population affected by goiter, cretinism, or mental retardation.

A team of researchers from the Saint Pierre Hospital, Brussels, working with Zairian physicians from the Zaire Scientific Research Institute, set out to solve this mystery. A first study of iodine uptake by the thyroid gland and of iodine excretion in urine was carried out on more than 600 men, women, and children in different villages. The results showed there was no significant difference between endemic areas, and goiter-free ones. Some factor other than iodine shortage had to be involved.

Another survey, based on geological data, was undertaken. It was known that the soil in the endemic areas was of a different composition than the soil in goiter-free areas, and the

researchers speculated that these differences might be reflected in the composition of plants grown and eaten by the islanders. This lead, however, also turned out to be disappointing: the soil composition had no detectable effect on goiter.

The researchers then undertook a detailed study of food crops grown on the island: bananas, sweet potatoes, groundnuts, cassava, pumpkins... The goal here was to find out whether the ingestion of one plant or another could affect iodine uptake by the thyroid.

It was then that cassava appeared as the number-one suspect. People whose diet included large amounts of cassava were found to absorb via the thyroid gland an amount of iodine well under the normal. Analyses of urine and serum samples also revealed that the islanders who regularly ate cassava had a high level of thiocyanate, an anti-thyroid substance associated with the consumption of certain vegetables. Cassava is one of them: it contains cyanogenic glucosides which are transformed by hydrolysis into toxic cyanides. After ingestion, these cyanides are rapidly detoxified, and give rise to thiocyanate. Experiences with rats confirmed this anti-thyroid effect and showed, more precisely, that the uptake of radioactive iodine by this gland was inversely proportional to the concentration of thiocyanate in the blood.

The prime function of the thyroid gland is to secrete hormones that regulate tissue oxydation processes. Iodine is an essential constituent of these hormones. Thyroid activity is thus dependent on the amount of iodine in our food. Normally, the absorption of 100 micrograms of iodine a day is sufficient to ensure adequate thyroid function.

If there is a shortage of iodine, or if iodine uptake is inhibited, the thyroid gland is stimulated by a regulatory process in which a pituitary hormone secreted by a gland located at the base of the brain plays a key role. It is the thyroid stimulating hormone (TSH) that "instructs" the thyroid to resume normal function but, in the absence of iodine, provokes an increase in volume of the thyroid, that is, a goiter. This hypertrophy does not necessarily represent a sufficient adaptation to prevent thyroid hormone shortage. The patient suffers from thyroid insufficiency; he lacks hormones to regulate certain metabolic processes, notably those that concern the central nervous system. When this insufficiency occurs during the first months of life it can disturb the maturation and development of the nervous system.

In the worst cases the result is extreme mental retardation and impairment of psychomotor development. The patient may be unable to walk, even to stand. Paralysis, particularly of the legs, and deafness can be so severe that some of them lead an almost vegetative life.

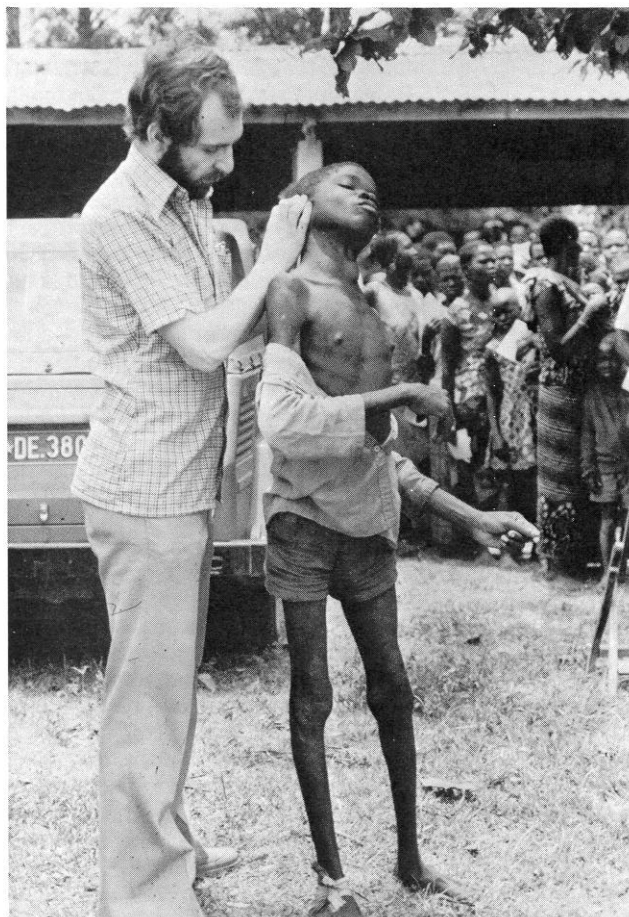
If iodine shortage occurs only after the first month of life, the thyroid may have accumulated sufficient iodine to function almost normally. There are no signs of thyroid insufficiency, but it is possible nevertheless that mental development is retarded. The patient, although he has neither the visible signs nor other symptoms of goiter, will not have attained his full intellectual capacities.

It could also happen, say the researchers, that an anomaly of the central nervous system is caused during gestation by thyroid dysfunction before birth. This hypothesis is supported by the observation that when an expecting mother in an endemic region receives iodine, her child will not be affected by either goiter or cretinism. Thus, in several countries, the utilization of iodized salt has made it possible to eliminate these diseases; but in others, the problem remains — notably in parts of Central Africa, where salt is hardly ever used in cooking, and where cassava is a staple food.

In addition, it is particularly impossible to evaluate the incidence of the less severe forms of mental retardation; these could lower the level of intelligence of an individual, and, on the scale of an entire population, become a major obstacle to development. In the past ten years or so, epidemiological studies in rural regions of Africa, South America and Asia, have revealed that endemic goiter is much more widespread than had been believed. It is estimated today that some 200 million people throughout the world are affected by this disease to varying degrees.



Above: mother and child in Mali — the child may also suffer an abnormal thyroid condition in later years. Below: goiter is endemic in parts of Zaire — this young boy already shows signs of thyroid enlargement.



The risk of provoked hypothyroidism is not limited to tropical countries, as other vegetables also contain cyanogenic glucosides. The most frequently encountered are amygdalin in bitter almonds and the pit of some fruits, dhurrine in sorghum, and linamarin in cassava and other plants including *brassicaceae*, of which cabbage is a member.

There are several regions in Europe where the amount of iodine in food is barely sufficient, and where cabbage is consumed in large amounts. This is the case in certain parts of central Europe, and regions bordering the Mediterranean. Last year Dr François Delange, one of the Belgian research team, in collaboration with Sicilian physicians, carried out a study showing that a high level of thiocyanate — and of goiter — exists on some parts of Sicily.

What can be done to prevent these diseases?

It is known that mental retardation and other sequels of congenital hypothyroidism can be avoided if iodine treatment is started early, during the first days of life. However, it is almost impossible to make the diagnosis of thyroid insufficiency at birth on the basis of clinical signs.

Dr Delange, together with Dr Claude Thilly, another member of the Belgian team, recently perfected a technique that determines the level of the pituitary hormone TSH from a single drop of dried blood. The level of this hormone increases when thyroid function is insufficient and the test thus allows the diagnosis of thyroid insufficiency in newborn infants.

Last year the Belgian researchers undertook another study, in the region of Ubangi in the north-eastern part of Zaire, where goiter is endemic in a population of about one million. They have found that goiter affects 60 to 70 percent of the population, and that up to ten percent of the inhabitants (depending on the location of the villages, on nutrition, and socio-economic conditions) suffer from cretinism. In the Ubangi region, as on Idjwi Island, the consumption of cassava is associated with a high level of thiocyanate and a decreased iodine uptake.

A vast campaign is now being undertaken to eradicate goiter and cretinism in this highly endemic region. Treatment consists of intramuscular injections of iodine in an oily solution that is resorbed slowly, and diffuses the iodine throughout the organism, over a period of three to seven years. Some 300,000 injections have already been given, and 700,000 more are scheduled. This long-term project is supported by the Belgian General Administration of Cooperation and Development, the Ministry of Science Policy, and the Medical Fund for Scientific Research.

The IDRC, which has supported research into cassava toxicity in the region since 1974, is now funding a second phase of this research. The aim is to define precisely the nutritional conditions required in man to induce goiter and cretinism, and to study the mechanism responsible for mental retardation resulting from a cassava-based diet. This will include specifically the role of thyroid failure in early life, and the direct toxic effect of cyanide on the central nervous system.

The potential impact of these findings and of the diagnosis and treatment campaigns is evident. At stake are not only the state of health of vast populations, but the intellectual capabilities of men and women carrying the heavy burden of endemic mental retardation, as they strive to overcome the difficult conditions of their lives.

If the goitrogenic effect of cassava, demonstrated in Zaire, is confirmed in other tropical regions, new avenues of research must be explored aside from the agricultural efforts aimed at increasing productivity: research in medical prevention, treatment of cassava before it is eaten, and development of cassava lines that cannot trigger thyroid insufficiency. □

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