

## Short report

# Vitamin B nutrition in the Nigerian tropical ataxic neuropathy

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**SUMMARY** Assessment of nutritional status of vitamin B components by plasma or blood levels indicated riboflavin deficiency and possibly thiamine deficiency in Nigerian patients who suffered from tropical ataxic neuropathy and neurologically normal Nigerians who subsisted on predominant cassava diet. Serum levels of folate, niacin, pyridoxine and panthothenic acid were normal. Vitamin deficiencies probably are minor factors, if any, in the pathogenesis of tropical ataxic neuropathy in Nigerians.

A syndrome of bilateral optic atrophy, bilateral nerve deafness, myelopathy and polyneuropathy had been reported from communities with poor nutrition particularly from tropical and subtropical countries. In Nigerians it is referred to as tropical ataxic neuropathy.<sup>1,2</sup> Chronic cyanide intoxication of predominantly cassava origin has been implicated as a major aetiological factor of tropical ataxic neuropathy in Nigerians and Tanzanians, and more recently in Mozambiqueans, among whom an epidemic occurred in 1981 which afflicted nearly 1000 patients following a severe drought when the concentration of cyanogenetic glycoside in cassava increases several folds. In Nigerians, deficiencies of vitamins especially the B group also have been incriminated as important aetiological factors on the basis of findings of abnormal pyruvate metabolism and low urinary excretion of some vitamins and their metabolites.<sup>1,2</sup> This communication reports results of assessment of nutritional status of the major components of vitamin B complex as measured by plasma/blood levels. We have previously shown that total serum level of vitamin B12 and vitamin B12 metabolism were normal in patients with tropical ataxic neuropathy.<sup>1,2</sup>

## Material and methods

The subjects were (a) 53 patients aged 20-60 years, 20 females (mean age in years + SD, was 50 + 8.5), and 33 males (51 + 6.3) who suffered from tropical ataxic neuropathy as previously described,<sup>2</sup> (b) a control group of 35 Nigerians aged 20-60 years, 15 females (49 + 6.3) and 20 males (50 + 8.5) who were neurologically normal and whose diet was similar in composition and quantity to that of the patients with tropical ataxic neuropathy and hereafter referred to as Normals on Cassava Diet (NCD), and (c) 87 healthy well nourished members of staff of University College Hospital (UCH) Ibadan and healthy donors who earned over 2000 Nigerian naira (about 1800 pounds sterling) per annum and hereafter referred to as Normals. The normals aged 20 to 60 years comprises 40 females (46 + 5.5) and 47 males (48 + 6.2). The patients who suffered from tropical ataxic neuropathy were studied before admission to UCH, Ibadan or before treatment. Members of Groups (a) and (b) ate cassava derivatives at least twice a day.

Total serum riboflavin was determined fluorometrically.<sup>3</sup> Thiamine nutritional status was assessed by the transketolase activity of the red blood cell haemolysate.<sup>4</sup> Standard liver function tests (determination of serum levels of alanine and aspartate transferases, alkaline phosphatase, bilirubin, thymol turbidity and flocculation) and measurements of serum proteins were done in all patients and subjects in whom transketolase activity of RBC haemolysate was assayed. Microbiological assays on sera were determined as follows: nicotinic acid using *Lactobacillus plantarum*,<sup>5</sup> folate using *Lactobacillus casei* (subspecies *rhamnosus*),<sup>6</sup> total vitamin B6 using *Saccharomyces carlsbergensis*,<sup>7</sup> panthothenic acid using *Lactobacillus plantarum*.<sup>8</sup> The

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Table Vitamin B nutrition in Nigerian tropical ataxic neuropathy. Mean serum concentrations + SEM of riboflavin, niacin, folate, B6 (pyridoxine), panthothenic acid and thiamine nutritional status assessed by red blood cell transketolase activity (expressed as mean + SEM: TPP effect in % and hexose formed in  $\mu\text{g/ml/hr}$ )

Groups	Riboflavin ng/ml	Nicotinic acid $\mu\text{g/ml}$	Folate ng/ml	Vitamin B6 ng/ml	Panthothenic acid ng/ml	$\mu\text{g/hexose formed/}$ ml/hr	TPP effect
Tropical ataxic neuropathy n = 53	19.3 + 0.90	2.22 + 0.025	8.05 + 2.49	26.06 + 3.45	364.16 + 11.2	911 + 49	18.84 + 1.51
Normals n = 87	28.21 + 0.78	2.23 + 0.01	9.29 + 1.39	25.83 + 2.49	363.87 + 73	846 + 50	10.06 + 1.00
Normal on cassava diet n = 35	20.0 ± 0.80	2.21 + 0.02	8.5 + 2.2	26.00 + 2.8	366.14 + 10.2	900 + 45	16.80 + 2.0

organisms were obtained from the National Collection of Industrial Bacteria, UK. Significance was determined by Student's *t* test.

## Results

The table shows that the mean serum riboflavin level was significantly lower in Nigerian patients with tropical ataxic neuropathy and in NCD than in normals. For thiamine nutritional status the TPP effect was significantly higher in patients with tropical ataxic neuropathy and NCD than in normals ( $p < 0.01$ ). In all in whom RBC transketolase activity was determined, liver function tests and serum protein levels were normal. Serum nicotinic acid, folate, total B6 and panthothenic acid levels were normal compared with controls.

## Discussion

There are geographical areas in Southern parts of Nigeria in which tropical ataxic neuropathy is very common. Such endemic foci were first defined by Money<sup>9</sup> who subsequently attempted to establish a correlation between the prevalence rates of the disease and avitaminosis B in field surveys of villages in the endemic area.<sup>10</sup> Signs classically attributed to deficiency of riboflavin such as angular stomatitis, glossitis and the orogenital syndrome are common and were found in 33% to 96% of Nigerian patients with tropical ataxic neuropathy.<sup>19</sup> These signs, however, are not specific for riboflavin deficiency and merely represent the effect of depressed oxidative metabolism in cells with rapid metabolic turnover such as those of the skin and mucosa: hence they are found in such conditions as iron deficiency (with impaired function of cytochrome oxidase system), deficiency of thiamine or B12, and they would on theoretical ground be present in state of chronic cyanide intoxication (with inactivation of ferricytochrome oxidase system). However cassava (*Manihot utilissima*), a poor source of the various components of vitamin B complex (especially riboflavin of which it contains 0.24 mg/g of fresh roots decreasing to 0.007 mg/g of "gari"<sup>11</sup>) constitutes the staple

food of the Nigerian patients with tropical ataxic neuropathy.<sup>12</sup> Although assessment of nutritional status of riboflavin by microbiological assay with *Tetrahymena thermophila* is more sensitive than the fluorimetric assay<sup>3</sup> used in this study, riboflavin deficiency is clearly demonstrated in patients with tropical ataxic neuropathy but it is also present in many Nigerians without neuropathy.<sup>12</sup> Erythroid hyperplasia, anaemia and vacuolisation of pronormoblasts which occur in riboflavin deficiency with reversion to normal after treatment, does not occur in Nigerian patients with tropical ataxic neuropathy.<sup>1</sup>

In this study patients with tropical ataxic neuropathy and neurologically normal Nigerians on cassava diet (NCD) showed evidence of marginal thiamine deficiency as assessed by the TPP effect in the estimation of RBC transketolase. It has been suggested that thiamine deficiency could be conditioned by chronic cyanide intoxication (which is present in patients with tropical ataxic neuropathy) as cyanide and its metabolites could inactivate and split thiamine into its pyrimidine and thiazole moieties.<sup>12,13</sup> This may explain why some improvement might have occurred in patients with tropical ataxic neuropathy who were treated with thiamine.<sup>10</sup> It has been suggested that microbiological assay by the flagellate *Ochromonas danica* is a more sensitive method of determining thiamine nutritional status.<sup>3</sup> Transketolase levels are said to be useful only in long-standing thiamine deficiency when levels are invariably low but increase after treatment with thiamine. Transketolase values are of little diagnostic value in presence of liver disease—levels are low and never recover presumably because of low transketolase apo-enzyme, a protein (for enzyme = coenzyme + apoenzyme). Although thiamine deficiency has been the subject of extensive investigation large gaps exist in our knowledge concerning the sequence of events that ultimately leads to severe neurological dysfunction and histopathological changes described in Wernicke-Korsakoff encephalopathy, peripheral neuropathy with or without beriberi heart disease. Most of the culinary derivatives of cassava are low in thiamine content

(about 0.005 mg/110 g)<sup>11</sup> and this may explain the mild thiamine deficiency status of neurologically normal Nigerians on cassava diet. There is some evidence that a genetically determined defect in the metabolism of thiamine in some individuals<sup>14</sup> may determine the occurrence of neurological deficit.

Deficiencies of pyridoxine, panthothenic acid and probably nicotinic acid and folate are known to cause neurological disorders. Serum levels of these vitamins were normal compared with controls and levels reported elsewhere,<sup>3</sup> although microbiological assay of nicotinic acid by the protozoan *Tetrahymena thermophila* is more sensitive than assay with *Lactobacillus plantarum* used in this study.<sup>3</sup>

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