concentration is also increased approximately 50% in PD. Our findings concerning PD differ considerably from those of our previous studies of Alzheimer's disease, in which we found elevated Hg and Br but no alterations in Fe, Mn, or chromium levels [5]. The lack of change in Al concentration in PD supports the concept that neuronal loss and gliosis alone do not increase the amount of Al in brain [9].

The Zn level was not found to be significantly elevated or decreased in our patients. Our previous study of brain trace elements in normal adult patients (ages 22 to 85) indicated that brain Zn remains within narrow concentration limits throughout adult life [6], suggesting the existence of an efficient homeostatic mechanism in the adult brain for its regulation. Constantinidis and collaborators [1, 2] speculated that Zn is elevated in PD and plays a role in its pathogenesis. They found elevated levels of Zn in blood, urine, and hippocampus in patients with PD compared with patients with Alzheimer's disease and normal controls. We have not found Zn levels to be elevated in any areas of the brain in patients dying in the late stages of PD, and our data do not support the hypothesis of these researchers.

Our data indicate an imbalance in a number of trace elements in the brain in PD. Whether this represents an epiphenomen or is important in the pathogenesis of the disease remains a question for further study. The data can serve as reference points for others studying this relatively rare disorder.

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Biochemical Studies of Pyridoxal and Pyridoxal Phosphate Status and Therapeutic Trial of Pyridoxine in Patients with Carpal Tunnel Syndrome

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A number of recent studies report response of patients with carpal tunnel syndrome to pyridoxine treatment. Neurological and biochemical studies were therefore performed on six patients both before and after treatment with pyridoxine for at least 9 weeks. Free pyridoxal, pyridoxal phosphate, and total pyridoxal were assayed in plasma and neutrophils. The pyridoxal status was also estimated by assaying red cell aspartate aminotransferase. No evidence was obtained to suggest that these patients were deficient in either pyridoxal or pyridoxal phosphate. Although four of the patients claimed some partial symptomatic relief, there was no consistent improvement in clinical findings or neurophysiological measurements following pyridoxine treatment.

Smith GP, Rudge PJ, Peters TJ: Biochemical studies of pyridoxal and pyridoxal phosphate status and therapeutic trial of pyridoxine in patients with carpal tunnel syndrome. Ann Neurol 15:104–107, 1984

Carpal tunnel syndrome is a common neurological complaint and frequently necessitates surgical decompression. Therefore, the recent reports that affected patients show biochemical evidence of pyridoxal

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deficiency [1–5] and that following pyridoxine treatment "clinical evaluation showed a great improvement in their status, and anticipated surgery for some of the patients became unnecessary" [8] are of considerable potential interest.

We have developed a direct, highly sensitive biochemical method [9] for assaying leukocyte pyridoxal and pyridoxal phosphate levels as indices of tissue pyridoxine status. These measurements, together with assays of red cell aminotransferase activities as indirect indices of pyridoxine status, have been carried out in six patients with idiopathic carpal tunnel syndrome. The patients were treated with pyridoxine for between 9 and 26 weeks, and evidence of clinical and neurophysiological improvement was sought.

Materials and Methods

Six patients were initially investigated, but only five were studied in detail before and after pyridoxine treatment (see Table 1). All patients had idiopathic carpal tunnel syndrome of at least 3 months' duration. One patient had had unsuccessful surgical intervention. Two patients had bilateral symptoms. Patients were carefully screened for carpal tunnel syndrome secondary to such conditions as hypothyroidism and rheumatoid arthritis, by clinical examination and appropriate serological tests. They received no other treatment or medication during the study. Patients were treated with pyridoxine, 100 mg daily, for 9 to 26 weeks.

Leukocyte and plasma pyridoxal and pyridoxal phosphate were assayed as described previously [9]. Protein was determined by a modified Lowry procedure [7], and erythrocyte aspartate aminotransferase, in both the presence and the absence of added pyridoxal, was assayed as described by Williams [10].

Results

Two patients had bilateral and three patients unilateral symptoms of painful dysesthesias in the hand. All had sensory signs in the median nerve distribution, and one had weakness of adductor pollicis brevis (APB). None had signs of a generalized neuropathy.

Three patients improved symptomatically with pyridoxine therapy given for periods of 9 to 26 weeks; two were unchanged. The sensory impairment improved in two and was unchanged in three. The weakness of APB in one patient was unchanged. Results of the motor and sensory studies before and after treatment are shown in Table 1. After treatment, distal motor latency decreased in one patient and increased in three. The amplitude of the sensory action potential increased in three patients, decreased in one, and was unchanged in one. Latency decreased in three and was unchanged in two patients.

Before treatment, all patients had a normal plasma level of free pyridoxal, and four of the six patients had normal pyridoxal phosphate levels; two of the patients had increased pyridoxal phosphate levels, and four patients had increased total pyridoxal levels. One patient

Table 1. Results of Neurophysiological Studies of Patients with Carpal Tunnel Syndrome Before and After Pyridoxine Treatment

Patient No., Age (yr), Sex, Diagnosis	Side of Study	Time of Study	DML to APB (ms)	Sensory F2 to Wrist	
				Amplitude (μV)	Latency to Peak (ms)
1	L	Before Rx	4.6	2.5	4.4
23		After Rx	. . .[a]	10.0	4.1
Female	R	Before Rx	5.4	3.0	4.2
BCT		After Rx	. . .[a]	8.0	4.1
2	L	Before Rx	4.5	22.0	3.2
39		After Rx	3.2	22.0	3.1
Female	R	Before Rx	5.2	20.0	4.5
BCT		After Rx	4.0	20.0	4.0
3	L	Before Rx	5.6	12.0	4.8
65		After Rx	6.4	7.0	5.4
Male					
LCT					
4	R	Before Rx	4.6	4.0	4.4
48		After Rx	5.0	10.0	4.0
Female					
RCT					
5	R	Before Rx	4.4	3.0	3.5
65		After Rx	4.5	7.0	3.6
Male					
RCT					
Normal range			< 4.5	9.0–45.0	< 4.0

[a]Refused second study.

DML = distal motor latency; APB = adductor pollicis brevis; CT = carpal tunnel syndrome; B = bilateral; R = right; L = left.

Table 2. Biochemical Indices of Pyridoxine Status in Patients with Carpal Tunnel Syndrome

Patient No.	Plasma Levels (pmol/ml)			Leukocyte Levels (pmol/mg protein)			Erythrocyte Aminotransferase Activity			
	Py	Py-P	Total	Py	Py-P	Total	Time of Study	Aspartate Aminotransferase Level (IU/gm hemoglobin)	Vitamin Effect (%)	Activity Coefficient
1	20.5	11.3	31.8	29.8	12.5	42.3	Before Rx	4.01	16.3	1.11
							After Rx	8.0	19.5	1.24
2	9.2	12.4	21.6	< 1.0	20.9	20.9	Before Rx	5.04	22.2	1.29
							After Rx	8.72	14.8	1.17
3	23.8	10.8	34.6	3.9	5.72	9.57		...	...	...
4	8.13	5.08	13.2	3.2	11.1	14.2		...	...	...
5	15.1	26.4	41.5	4.76	7.94	12.7	Before Rx	3.55	38.5	1.62
							After Rx	11.6	10.3	1.11
6	26.7	18.5	45.2	20.0	13.9	33.9	Before Rx	6.82	17.4	1.21
							After Rx	5.28	17.6	1.21
Controls[a]										
Mean ± SD	14 ± 9.6	5.6 ± 6.7	20 ± 6.6	7.6 ± 2.5	13.4 ± 8.1	20.6 ± 8.6				
Range	5.5–30.0	0–16.4	10.0–30.0	4.0–10.3	3.2–23.2	12.6–33.5		2.0–6.40	0–50	1.0–2.0

[a]Control data from five normal adults aged 20 to 43 years from ref. 6.

Py = pyridoxal; Py-P = pyridoxal phosphate; SD = standard deviation.

had no detectable pyridoxal in his leukocytes; two patients had elevated levels, and three had levels within the normal range. All six patients had normal levels of pyridoxal phosphate, and only one patient showed a slightly lowered total pyridoxal level. In all cases the level of aspartate aminotransferase, the vitamin efficiency, and the activation coefficient were well within normal limits and showed no consistent change with pyridoxine treatment (Table 2).

Discussion

These studies provide no biochemical evidence of pyridoxine deficiency in six patients with idiopathic carpal tunnel syndrome. This conclusion is based on sensitive assays of pyridoxal and pyridoxal phosphate in both plasma and leukocytes, the latter reflecting tissue levels of the vitamin. In addition, assays of erythrocyte aminotransferase activity, both before and after incubation with pyridoxal phosphate, provide no evidence of vitamin deficiency. Sequential erythrocyte studies in four patients also provide no evidence of a response to pyridoxine, as would be expected if these patients were pyridoxine deficient.

Previous reports of pyridoxine status in patients with carpal tunnel syndrome were based solely on assays of erythrocyte aspartate aminotransferase activity [1–5]. These showed small but significant reductions in enzyme activities that reverted to normal values after only 2 weeks of treatment. The reason for the discrepancies between the two series of patients is not clear, but the variations presumably reflect differences in vitamin status of the two patient groups. In the Texas series [3], two patients had electrolyte disturbances and seven had "violent nocturnal muscle spasms in extremities," features that were absent in the present series. It is also possible that the "copious amounts of aspirin and other analgesics, a variety of sedatives, tranquillisers, diuretics and corticosteroids" that the patients in this study consumed [3] were responsible for the apparent pyridoxine deficiency.

Response to treatment in the series of Ellis and colleagues [3] was judged solely on the basis of clinical criteria, and, not surprisingly, as in the present series, there was symptomatic improvement. We suggest that this improvement is probably an artifact of selection. Patients tend to visit a physician at a time of severe or worsening symptoms, a fact that will bias any study if there is a tendency to spontaneous remission. Furthermore, patients tend to rest the affected hand when the symptoms are severe, a maneuver that is known to help symptomatically; hence the value of wrist splints and the interesting observation that operation on the right hand in right-handed patients with bilateral symptoms tends to cure both sides.

Le Quesne and Casey [6] showed that with adequate decompression of the carpal tunnel, the latency of the sensory action potential recorded at the wrist fell within 2 months and the amplitude significantly increased within 4 to 6 months of operation. In the present study there was no consistent pattern. Interpreta-

tion of the alterations in distal motor latency is more difficult, because it is not known how much of the delay results from impaired conduction in the segment of the carpal tunnel that is compressed and how much from slow distal conduction in the regenerated axons. There was no evidence of improvement in the conduction delay during the period of pyridoxine therapy in the present study, however. Similarly, clinical sensory examination did not demonstrate a consistent pattern following treatment.

A large double-blind controlled trial would be necessary to show that the symptomatic response to oral pyridoxine claimed by some patients was genuine. The evidence in the present study does not support the claim that pyridoxine deficiency, responsive to pyridoxine therapy, is an important factor in carpal tunnel syndrome.

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Creutzfeldt-Jakob Disease: A Case of 16 Years' Duration

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A 46-year-old man with Creutzfeldt-Jakob disease confirmed postmortem had a 16-year course of very slowly progressing incoordination and mental deterioration, suggesting Alzheimer's disease. The disease course transformed abruptly into a 7-week terminal phase of florid Creutzfeldt-Jakob disease. Dementing illnesses of unknown cause were present in the patient's paternal lineage.

Cutler NR, Brown PW, Narayan T, Parisi JE, Janotta F, Baron H: Creutzfeldt-Jakob disease: a case of 16 years' duration. Ann Neurol 15:107–110, 1984

In most patients the clinical course of Creutzfeldt-Jakob disease (CJD) progresses relentlessly to death in less than one year from the time of diagnosis [8]. However, in a small proportion of cases verified postmortem, patients have an unusually prolonged illness [4]. The disease course in one such patient is described in the following report.

A 46-year-old caucasian male mathematician had experienced gradual intellectual deterioration. According to his wife, this decline began approximately in 1967, when he was noted to be unexplainedly "slower." He began to exhibit mild clumsiness and had difficulty screwing a lightbulb into a socket and manipulating carpentry tools. Three years later, at age 34, the patient became aware of trouble with complex math and was forced to give up his teaching job. He would lose his way in familiar surroundings, and routine tasks took him longer and gave imperfect results. His clumsiness progressed to difficulty with tying shoelaces. Psychiatrists treated him for depression with psychotherapy.

During the next 5 years, the patient unsuccessfully attempted a succession of decreasingly demanding jobs; by 1977 his level of functioning had deteriorated to mainte-

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