



Fig CT scans with contrast enhancement: (a) 26 days (b) 13 months after acute carbon monoxide poisoning. Arrow indicates bilateral areas of low-density in the globus pallidus.

scan, 26 days after carbon monoxide poisoning, revealed marked low-density areas in the globus pallidus (fig a). Over the next week, the patient became very apathic and remained so for ten days. The relatives noticed obsessional behaviour concerning her clothing which lasted for one month. The EEG returned to normal. A year later, she was normal and the CT scan was normal (fig b).

In the cases of severe carbon monoxide poisoning presented by Sawada *et al.*,¹ low-density areas suggesting selective degeneration of the globus pallidus were observed on CT scans performed a few hours after injury. Nardizzi has described a later appearance (8th day) of CT scan changes in the globus pallidus consisting in an abnormal enhancement with contrast medium.³ Our case emphasises that globus

pallidus low-density areas can also appear late after carbon monoxide poisoning (in our case 26 days). The early and the late CT scan lesions originate from different processes. The early lesion may be due to glial alterations similar to those found in the globus pallidus by Foncin in 1978⁴ after carbon monoxide poisoning. Hypodense lesions in the globus pallidus, which in our case disappeared a year later, accompanied by behavioural changes, have also been described by Laplane⁵ in a case of bilateral pallido-striatal necrosis due to encephalopathy after a wasp sting.

A DESTEE
V COURTEVILLE
PH DEVOS
P BESSON
P WAROT

Service de Clinique Neurologique (Pr P Warot) CHU, 2, avenue Oscar Lambret, F 59037 Lille cedex.

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Isoniazid and action tremor in multiple sclerosis

Sir: Isoniazid has been reported to help the action tremor of patients with multiple sclerosis.¹ We used isoniazid to treat five consecutive patients with this problem and followed the patients up for eighteen months.

All patients had clinically definite multiple sclerosis.² They all had a tremor of both

arms which although inconspicuous at rest was very marked on assuming a posture. It often spread to involve the whole body. Where the finger-nose test was possible there was no increase in tremor at the extremes of movement. The patients were all wheelchair bound, mainly because of the tremor, and the functional ability of their arms was measured by recording their ability to feed, wash and dress themselves. The tremor was assessed by four simple bedside tests: drawing a straight line between two crosses, measuring the amount of water spilt from a glass held in the outstretched hand, building a tower of three bricks, and assembling nine boxes of descending size inside one another. Between five and ten days practice was given before starting isoniazid, 300 mg daily in divided doses. The daily dose was increased by 300 mg every three days up to 1200 mg daily or the occurrence of side effects.

Pyridoxine 150 mg daily was given concurrently. Acetylator status was measured before starting treatment³ and liver function tests were performed at weekly intervals during it.

The tremor improved in four of the five patients while on isoniazid. Functionally two found it easier to walk with a Zimmer aid and two others propelled their wheelchairs more easily (see table). Three patients gained the ability to drink from a cup and two the ability to feed themselves. All four patients showed an improvement in two or more of the functional tests. The patients who improved did so within three days of starting treatment and if the drug was discontinued they reverted to their previous state in a similar time period. The remaining patient showed no improvement over a two week period and the drug was then discontinued.

All four patients who improved developed weakness of the lower limbs of upper motor neuron distribution. In one who was on carbamazepine for a seizure disorder, this was associated with extensor plantars, marked drowsiness, and elevation of aspartate transaminase and alanine transaminase to four times normal. When the dose of isoniazid was reduced and the anticonvulsant changed to primidone these symptoms and signs disappeared and the tremor remained controlled. The other three patients who were weak complained of mild drowsiness. Reducing the dose of isoniazid abolished the weakness and drowsiness but still controlled the tremor. Aspartate transaminase and alanine transaminase were increased to twice normal

Table Clinical details and results of isoniazid treatment

Case	Age (yr)	Sex	Duration of tremor (yr)	Acetylator status	Optimum daily dose (mg)	Functional ability	Bedside tests
1	46	F	4	Slow	700	+	++
2	34	F	3	Rapid	900	+	+
3	26	M	6	Rapid	600	+	++
4	32	M	5	Rapid	1200	-	-
5	47	F	1	Slow	1200	+	+

-, no improvement; +, mild improvement; ++, marked improvement.

all patients on their maintenance dose of isoniazid, an effect noted previously.⁴

We followed-up the patients helped by isoniazid for a period of eighteen months. One patient (case 1) maintained her improvement; she made several attempts to stop the drug but each time the tremor got worse and her hand function deteriorated; there has been no recurrence of weakness. Case 3, who had developed the drowsiness and extensor plantar responses, developed a less severe form of the same condition and asked for the drug to be discontinued even though his tremor then became much worse. Cases 2 and 5 both developed increasing weakness of the legs which was not affected by stopping the isoniazid. In case 2 the weakness was accompanied by severe spasticity.

Isoniazid definitely helped the action tremor in four of our patients. Its beneficial effect was rapidly lost when the drug was stopped and it is unlikely that this was a placebo effect or related to drowsiness since all the patients had been previously treated with other drugs including levodopa, diazepam, chlorpromazine, sodium valproate, with no subjective or objective benefit. Dose-related weakness of pyramidal type also occurred in all the patients who benefited and on follow-up two developed paraparesis not affected by stopping the drug. Weakness has not been mentioned as a side effect of isoniazid when it has been used in comparable doses to treat multiple sclerosis or Huntington's disease.⁵ Possibly isoniazid produces weakness by unmasking a sub-clinical lesion of the pyramidal tract, a lesion which became clinical in two patients due to progression of their disease. We feel that isoniazid has a place in the management of action tremor in some multiple sclerosis patients. Its usefulness may be limited by side effects and it would seem prudent to discontinue the drug if weakness increases.

JAMES MORROW
HELEN MCDOWELL
CATHERINE RITCHIE
VICTOR PATTERSON

Department of Neurology
Royal Victoria Hospital
Grosvenor Road
BELFAST
BT12 6BA, UK

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Drug-induced alpha coma

Sir: Alpha frequency rhythms in the electroencephalogram (EEG) in comatose patients was initially described in intrinsic brainstem lesions,¹⁻⁴ and more recently in patients who suffered from cerebral hypoxia following cardiopulmonary arrest.⁵⁻⁸ A review of the literature on drug-induced alpha pattern coma disclosed nine cases.^{7,9,12} We report an additional case of drug-induced alpha coma, and discuss the clinical significance of this pattern, and the value of brainstem auditory evoked responses (BAERs) in this condition.

A 43-year-old female was brought to the emergency room on March 30, 1983, in a deep coma, after being found unresponsive by her husband. Apparently, her husband left the home for approximately an hour and on return, found her to be uncon-

scious. Subsequent to her admission, an empty bottle of glutethimide was found which originally contained 25-30 pills. The patient had a long history of psychiatric illness and had made two attempts at suicide in the past. She had been treated with thioridazine, benzhexol, and hydroxyzine pamoate.

On admission, she had a blood pressure of 95/60 mmHg, a heart rate of 76/min, and a rectal temperature of 34°C. The patient received 2 l of oxygen per minute by nasal catheter and her arterial blood gases revealed pO₂ of 83.4 mmHg, pCO₂ 54.5 mmHg and pH 7.26. Her blood pressure was maintained by intravenous fluid. She was given 0.8 mg of naloxone hydrochloride, 50 mg of diphenylhydramine and 100 mg of thiamin intravenously. After intubation, she was placed on a respirator. Neurological examination revealed an unconscious patient with reaction only to noxious stimuli. There were no spontaneous movements of the extremities, but painful stimuli elicited decorticate posturing. Her pupils were in mid-position and reacted slightly to light. Oculocephalic, oculovestibular, ciliospinal and corneal reflexes were absent. She was flaccid in the lower extremities but the tone was increased slightly in the upper extremities. All muscle stretch reflexes were symmetrical but hypoactive. There were no pathological reflexes. There was no nuchal rigidity.

Multi-drug screening tests established intoxication with glutethimide. Urine was positive for glutethimide metabolite. Blood glutethimide level was 2.28 mg/dl (toxic level, 1.09-9.7 mg/dl). Chest radiographs, ECG and computed tomography of the head were normal. The patient was comatose for four days. EEG was initially performed 24 hours after admission. It showed diffuse 9-10 Hz rhythmic activity of 40-120 μ v in amplitude, most prominent over fronto-central regions. The background activity showed only a slight reactivity to painful stimuli which evoked brief theta-delta activity. The second EEG tracing was obtained four days later when the patient