Serum cholinesterase activity was absent until day 20. He developed severe organophosphorus intoxication with coma, cholinergic crisis, and complete paralysis (intermediate syndrome). Mechanical ventilation was necessary for 33 days while he gradually recovered. During this time, repetitive nerve stimulation of the median nerve at frequencies of 2 to 50 Hz showed a prominent decremental response of the terminal compound muscle action potential (CMAP) until day 14. This decremental response then gradually subsided and disappeared by day 27.

He subsequently became alert and completely recovered from coma, tetraparesis, and weakness in the feet and hands at four weeks after the acute intoxication. Clinical examination showed signs of severe, symmetrical, distal, sensori-motor polyneuropathy. Findings included muscle wasting, reduced tendon reflexes of all distal leg and foot muscles with severe muscle atrophy. Deep tendon reflexes were absent in the legs although they had been present earlier, at the time of the cholinergic crisis. No plantar reflexes were present. Vibration sense was diminished mildly at the ankles. He was unable to stand or walk. CSF examination at this time was normal. Peroneal nerve stimulation of the bilateral head and the ankle showed no CMAP from the extensor digitorum brevis. Nerve conduction velocity of the median nerve was normal (52 m/s; CMAP 5.5 mV). Repetitive nerve stimulation studies at this time were normal. EMG of both anterior tibial muscles showed profuse fibrillations without voluntary motor unit potentials present. Therman EMG showed only few fasciculations with reduced recruitment. During the next five weeks, muscle strength gradually recovered, more completely in the hands than in the feet. Eventually he was able to walk without assistance, but distal weaknesses persisted in the legs. No pyramidal tract signs evolved.

In our patient, the intoxication with a pure formulation of an ethyl-parathion pesticide induced a severe axonal polyneuropathy which was clinically apparent four weeks after intoxication. Clinical and electrophysiological manifestations included distal extremity weakness, severe in the legs, associated with severe muscle atrophy as well as loss of reflexes in the legs, and nerve conduction velocity and EMG changes indicative of severe axonal loss and denervation. These findings are incompatible with the more acute weakness of the intermediate syndrome, occurring much earlier in the course of organophosphorus intoxication, and associated only with the electrophysiological features of neuromuscular junction blockade. The electrophysiological findings of this blockade had subsided and supervening axonal damage was confirmed by EMG and nerve conduction studies.

This case is similar to that reported by de Jager, et al in whom clinical and neurophysiological findings demonstrated a delayed neuropathy following severe ethyl-parathion intoxication. This compound is not known to irreversibly inhibit the cholinesterase target esterase and, in adult hens, no delayed neurotoxicity is seen. The reason for the neuropathy in these patients therefore remains uncertain. It has been argued that both the chemical structure of the organophosphorus compound and the degree and duration of intoxication contribute to the irreversible inhibition of the esterase. All delayed neuropathies following intoxication with compounds not normally neurotoxic—for example, ethyl-parathion and carbamates, have been seen after very severe or prolonged intoxications. This has occurred in only a few cases to date. Ethyl-parathion is imidazole-like and the structural comparison with the most toxic organophosphorus compounds is significant. It has been suggested that a delayed polyneuropathy may occur in humans with organophosphorus compounds that are not usually neurotoxic, if the intoxication is severe and sufficiently prolonged. The absence of corticospinal tract signs is noteworthy and is similar to previous reports of the delayed polyneuropathy resulting from ethyl-parathion and carbamates. This suggests that the pathogenesis of the polyneuropathy differs in these cases from the more classical delayed neurotoxicity, that is, irreversible inhibition of neuropathy target esterase.

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Reverse ocular bobbing due to combined phenoxyzidine and benzodiazepine poisoning

Observation of spontaneous eye movements may be of considerable value in the diagnosis of the unconscious patient. Slow roving eye movements, for example, imply a disorder sparing the brainstem oculomotor circuitry, whilst ocular bobbing (that is, rapid conjugate downward movement of the eyes followed by a slow return to the primary position, typically associated with a loss of horizontal eye movements) is usually due to structural pathology affecting the pons although cases due to metabolic or toxic encephalopathy have been described. Reverse ocular bobbing may be absent or be a jerky upward movement followed by slow return to the primary position) is generally a less reliable guide to the localisation of pathology. We describe two cases where reverse ocular bobbing occurred in coma due to covert combined phenoxyzidine and benzodiazepine poisoning.

Patient 1, a 14 year old schoolboy, was brought to a casualty department after his paing with a frequency of 1-2 Hz and dystarthy with difficulty in walking; they said he had been unhappy because his brother had recently had a relapse of schizophrenia but felt that he did not have access to his brother's medication. No one had seen him stare but open his eyes, grunted and moved his limbs semi-purposefully to a painful stimulus; there were no focal neurological signs. He had a history of series of episodes of involuntary limb and neck extension and unresponsiveness lasting several minutes. These were thought to be epileptic seizures and were treated with boluses of intravenous diazepam, 1 mg/kg, but then his CSF was found to have a very low sodium concentration, 77 mmol/l. He was transferred to this unit. He had mild cogygwe rigidity in the right arm and episodes of spontaneous reverse ocular bobbing with a frequency of 1 Hz and lasting one to two minutes and occurred several times per hour. A search of his clothing revealed a suicide note; his parents later reported that sixty 50 mg tablets (that is, 3 g of chlorpromazine) was found in his brother's supplies. He regained consciousness over the next 18 hours; he then experienced a series of typical ocularolytic crises with compulsive upward gazing of both eyes, which responded to anticholinergic therapy. He was transferred for psychiatric treatment.

Patient 2, a 26 year old woman, whose occupation afforded access to a variety of medical drugs, was brought to a casualty department in a stuporous state. She described a recent mild head injury and denied ingestion of drugs other than therapeutic doses of aspirin. Over the next six hours her consciousness level deteriorated, with no responses to pain and slow shallow respiration. Pupillary, vestibuulo-ocular, corneal and anal reflexes were absent; arterial blood gas values were normal; her blood salicylate level was 90 mg/dl. Urgent CT brain scan followed by CSF examination by lumbar puncture was normal and she was transferred to this unit. Examination remained unchanged except for spontaneous reverse ocular bobbing with a frequency of 1-2 Hz that occurred in bursts lasting several minutes; these bursts could be observed through her closed eyelids and were not affected by opening her eyelids. Toxicological testing subsequently revealed...
the presence of prochlorperazine and an unspecified benzodiazepine in her urine; a packet of Buccastem (Buccastem) from which 12 tablets (36 mg) had been removed was later found in her car but the source of the benzodiazepine was not identified. The abnormal eye movements resolved after twelve hours when she regained consciousness over 36 hours, declined psychiatric assistance and discharged herself from the ward.

In an unconscious patient the presence of oculogyric crises should raise the possibility of structural pathology in or around the pons. As these cases illustrate, however, other forms of spontaneous vertical eye movements may be due to toxic or metabolic encephalopathies and ideally consideration should be given to such causes before embarking upon invasive investigations. Self-poisoning is by far the commonest cause of coma in patients presenting to casualty departments, but can only often be diagnosed on the basis of circumstantial evidence and subsequent toxicological screening.

Both of these patients were exposed to the unusual combination of phenothiazines and benzodiazepines. The pharmacological basis of the eye movements is not clear. It is possible that they represent a form fruste of oculogyric crises induced by phenothiazines and modified by benzodiazepines. Typical phenothiazine-related oculogyric crises cause sustained upwards deviation of the eyes (often with a lateral component) associated with obsessional thoughts and a feeling of unease.1 One of the present patients developed these typical episodes on regaining consciousness. Whilst unconscious, both patients had episodes of uncontrolled rapid conjugate upwards deviation of the eyes, interspersed by slower drifts back to the primary position. Benzodiazepines have complex actions4 on the brainstem circuits which may be responsible for this maintenance and generation of vertical gaze both under normal circumstances and during oculogyric crises,1,5 and have been used to treat the latter.6 If the reverse oculoballism is indeed a form of oculogyric crisis one would expect it to be abolished by intravenous anticholinergic drugs, which almost always abolish typical oculogyric crises. This was not attempted during the episodes of reverse oculoballism here but, if validated in future cases, might form the basis of a simple bedside test for combined phenothiazine and benzodiazepine poisoning.

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