Serum neutralisation test for this type of virus carried out two months after the patient was first seen was positive in a 1/4 dilution.

Discussion

Despite full immunisation, poliomyelitis may still occur, though it is comparatively rare. Margoffin *et al*[1] found, however, that 25 of the 497 patients clinically classified as suffering from paralytic poliomyelitis excreted various types of Coxsackie viruses. (A9 in three, B2 in six, B1 in one, B4 in eight, B5 in six, and B4 combined with B5 in one case) and that, with exception of two patients in this subgroup —in whom the evidence was equivocal—serological and other inquiries were against a polio infection. The findings in this early survey were extended shortly afterwards by Lenette *et al*,[2] who added Echo type 9 and mumps viruses as potential causes of paralytic manifestations. More recently Sells *et al*[3] have stated that "with the virtual elimination of poliomyelitis, the central nervous syndromes associated with Coxsackie and Echo viruses have attracted increasing attention." They listed Coxsackie A 1-11, 14, 16-18, B types 1-6, and at least 24 of the recognised Echo viruses as having been implicated. Their review supported the conclusion of previous investigations that neurological sequelae of these non-polio enteroviral infections become less damaging with increasing age, the immature brain being principally vulnerable.

Paralysis of the palate in the patient described is likely to have been caused by a Coxsackie A9 infection, the source of which may have been river water, which was much depleted by a severe drought. The excellent spontaneous recovery which took place in this boy is in keeping with the good prognosis expected at his age.

I thank Mr Hazeley Anderson, consultant ear, nose, and throat surgeon, for referring the patient to me, and Dr T H Flewett, consultant virologist, for his help.

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(*Accepted 23 March 1977*)

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Unusual case of tetrahydrocannabinol intoxication confirmed by radioimmunoassay

The major manifestations of acute tetrahydrocannabinol (THC) intoxication include paranoia, hallucinations, confusion, restlessness, and excitement. Additionally there may be delerium, disorientation, and impaired consciousness.[1 2] These symptoms sometimes occur after quite small doses, particularly in "naive" users of the drug. Rarely, however, do toxic symptoms last more than a day.

Case report

A 19-year-old student on holiday in London was found by friends in his hotel room collapsed and unresponsive with arms flexed and legs extended. On admission to hospital he was found to be in grade III coma and sweating (axillary temperature 37·5°C). His eyes were open but "not seeing." The pupils were constricted and equal in their reaction to light, and gaze was downwards to the right. He exhibited the features of decorticate rigidity, with flexed arms and extended legs. Muscle tone in all limbs was increased and tendon reflexes were all brisk (plantar responses equivocal). Neck movement was stiff in all directions but did not show tonic reflex patterns. There was also sustained right ankle clonus. Respiration was irregular but pulse and blood pressure were normal. Radiography of the cervical spine and lumbar puncture showed nothing abnormal, and Kernig's sign was absent. Haematological and biochemical values were all normal. Drug intoxication was suspected and samples of blood and urine were sent for toxicological analysis.

Twelve hours after admission the patient was less rigid and began to respond to pain. Over the next two days he was unable to speak coherently and suffered hallucinations, becoming difficult to control and at times violent. Chlorpromazine was prescribed and his condition improved, so that four days after admission he was responding normally. He was discharged next day. Subsequently he admitted to having smoked a quantity of material that he called "THC" a few hours before the onset of his symptoms.

Toxicological analysis of blood and urine obtained on admission included tests for alcohol, barbiturates, benzodiazepines, glutethimide, methaqualone, methadone, phenothiazines, tricyclic antidepressants, and other miscellaneous hypnotic and psychotropic drugs. All gave negative results. Owing to the persistence and nature of the symptoms and the circumstantial evidence of drug ingestion a blood sample obtained on admission was analysed by radioimmunoassay[3] for cross-reacting cannabinoid (CRC) concentration, a result of 180 μg/l being obtained.

Comment

Reports of serious cannabis or THC intoxication resulting in loss of consciousness are rare, and the present case therefore represents a severe toxic episode of this kind. The persistence and nature of the symptoms were serious, particularly with regard to the hallucinatory changes.

The plasma CRC concentration of 180 μg/l some eight hours after intake may be compared with one of 70 μg/l in a volunteer immediately after smoking a cigarette impregnated with 5 mg of pure THC.[4] The volunteer experienced moderate effects attributable to cannabis. A specimen of blood taken from a driver killed in a motor-car accident had a CRC concentration of 315 μg/l.[5]

This case illustrates some of the problems in diagnosing an unusual type of drug intoxication, but one that may become more common should the illicit use of refined cannabis material increase.

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[2] Graham, J D P, editor, in *Cannabis and Health*, p 271. London, Academic Press, 1976.
[3] Teale, J D, *et al*, *Journal of Pharmacy and Pharmacology*, 1975, **27**, 465.
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(*Accepted 18 March 1977*)

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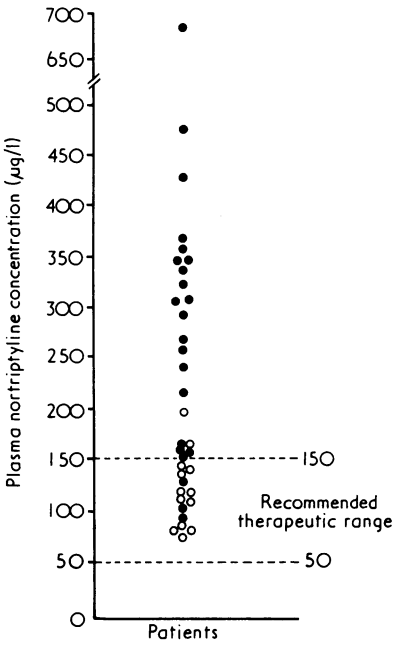
Routine nortriptyline levels in treatment of depression

An important question about tricyclic antidepressant drugs is whether doses that lead to high plasma levels are ineffective or even prevent recovery. Several studies have indicated this possibility with nortriptyline,[1–4] and a therapeutic range of 50-150 μg/l has been recommended.[3] High plasma levels can result from low doses and it has been argued that therapeutic success could be improved if more attention were paid to plasma concentrations.

Patients, methods, and results

Thirty-six depressed inpatients (16 men, 20 women) at two hospitals were treated with a constant dose of 75-150 mg nortriptyline daily, as decided by the treating psychiatrist. The average age of the men was 51 (range 23-70) and of the women 57 (range 21-74). Five further patients were excluded

because of concomitant treatment with antidepressants or drugs known to change plasma levels. Three were on monoamine oxidase inhibitors and two on phenothiazines and their levels of nortriptyline and responses to the drug did not seem to differ from those of the other patients. Five of the 36 patients were also taking lithium and 24 were receiving benzodiazepines, mainly nitrazepam. Plasma nortriptyline levels were measured after two or more weeks. Recovery, defined as a pronounced persistent improvement in depressive symptoms observed three to six weeks after starting treatment, was assessed globally at Preston Hall Hospital by the treating psychiatrist, who did not know the plasma levels, and at the Maudsley-Bethlem Hospital by assessing the case papers, which had usually been written before the plasma levels were known, though blindness might not always have been maintained. Plasma levels were measured using a method similar to that of Kragh-Sørensen *et al.*[5] Interlaboratory reproducibility studies were performed.



Relation between plasma nortriptyline levels and clinical response. ● = Non-responders. O Responders.

The mean daily dose (101·2 mg) adjusted for body weight produced a higher dose for women (1·81 mg/kg) than for men (1·53 mg/kg), and men seemed to respond better. There was a ninefold variation in individual plasma nortriptyline concentrations from 77 μg/l to 684 μg/l. Patients with levels within the range 50-150 μg/l responded significantly better than those with higher levels (χ^2 17·9; DF = 1; P<0·0001; see figure). Only two of the 22 patients with levels above 150 μg/l responded, while 11 of the 14 with levels of 50-150 μg/l did so. The mean daily dose of the responders (1·39 mg/kg) was significantly (P<0·01) lower than that of the non-responders (1·86 mg/kg).

Comment

It is surprising that on an average daily dose of 100 mg 61% of our patients produced plasma nortriptyline levels above 150 μg/l, while Kragh-Sørensen *et al*[3] found that only 43% of 30 patients on a dose of 150 mg daily developed such levels. His patients were a little younger than ours, but we failed to show a correlation with age. The British health system, whereby patients are referred to hospital-based psychiatrists by general practitioners who have already attempted treatment, may preselect non-responders with high levels. The correct dose for this study's population would have been 60 mg/day—much lower than that commonly used. Although in any group of psychiatric patients some spontaneous or non-drug-related remissions may be expected, the group of patients with high plasma levels consisted overwhelmingly of those who did not recover. This confirms the view[5] that plasma nortriptyline levels above about 150 μg/l inhibit recovery.

Most patients with high drug levels showed no clinical signs of their high concentrations, though two developed confusional states. High plasma nortriptyline concentrations can be produced by moderate doses, and only the laboratory can detect the presence of these high levels. We therefore recommend the routine measurement of plasma nortriptyline levels in patients taking the drug.

We thank Dr Felix Post for his help; S Dawling, M Tashin, D Montgomery for technical help; and the medical and nursing staff of both hospitals.

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[3] Kragh-Sørensen, P, *et al*, *Psychopharmacologica*, 1976, **45**, 305.
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(*Accepted 29 April 1977*)

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Meningitis and endophthalmitis caused by Streptococcus suis type II (group R)

Streptococcus suis, type II, is now recognised to be an important cause of meningitis, septicaemia, and purulent arthritis in young pigs.[1] Human infections are rare, but have been reported in Holland and Denmark[2 3] and the first British case has been recently described.[4] In the case reported here the patient presented with severe bilateral endophthalmitis as well as other reported manifestations of *Str suis infection*.

Case report

A 46-year-old maintenance engineer at a pork-pie factory presented with a three-day history of malaise, fever, right-sided deafness, tinnitus, frontal headache, and discharging eyes. He also complained of swelling of both wrists and pain in both elbows. He was febrile, drowsy, and deaf (more in the right ear). He had a severe bilateral endophthalmitis and secondary glaucoma with left purulent conjunctivitis. His throat was inflamed with areas of superficial ulceration. No skin wounds were found. Both wrists were tender and swollen, but no fluid could be aspirated from them; his elbows were normal apart from slight redness. He had no neck stiffness and Kernig's sign was negative. Cerebrospinal fluid (CSF) examination disclosed a pleomorphic cell count (polymorphonuclear leucocytes 331/mm^3, lymphocytes 29/mm^3, and protein 0·8 g/l). Gram-positive cocci in pairs and short chains were seen in the CSF and in aqueous fluid aspirated from the anterior chamber of the left eye. Cultures of these fluids and blood grew a β-haemolytic streptococcus, which gave a weak reaction with Lancefield Group-D antiserum (both after acid extraction and autoclaving) but was not resistant to bile. The organism was not isolated from the throat swab. The isolate was examined by the Streptococcus Reference Laboratory, Colindale, and by Dr S D Elliott, Cambridge, and was identified as *Str suis*, Type II. The minimum inhibitory concentration of penicillin and of ampicillin was 0·03 mg/l.

The meningitis and septicaemia were treated with benzylpenicillin, 20 000 units intrathecally immediately and 4 million units intravenously every four hours for two days, followed by amoxycillin, 0·5 g 6-hourly. The endophthalmitis and glaucoma responded to acetazolamide, 250 mg, and prednisolone, 10 mg every six hours—together with local eyedrops of atropine, bacitracin, and Maxidex. Benzylpenicillin, 0·5 megaunits, was given subconjunctivally followed by ampicillin, 100 mg, and betamethasone, 4 mg, on alternate days. Systemic antibiotic therapy was continued for a total of six weeks. The patient recovered but was left with high tone deafness, unsteadiness of gait, and impairment of vision in the left eye.

Discussion

Previous case reports of *Str suis*, type II, in man have described septicaemia and meningitis, and in one case meningitis was present