contrast, patients who had had Henoch-Schönlein purpura with renal disease and had recovered fully had normal cryoglobulin concentrations, whereas those who had nephritis after an episode of purpura had significant cryoglobulinaemia. These observations suggest that the chronic glomerulonephritis that may follow acute Henoch-Schönlein purpura is a result of persisting immune complexes and that those patients who will develop nephritis may be identified by their continuing cryoglobulinaemia.

Although some patients with purpura or nephritis had normal cryoglobulin concentrations, their cryoglobulins contained proteins such as IgA, C4, C3, and properdin, which are never, or only rarely, detected in cryoglobulins isolated from normal subjects.[5 9] The constitution of a cryoglobulin may therefore be as important in indicating its pathogenetic significance as its serum concentration. Among our patients with nephritis IgA was much more prevalent (35%) than in other types of nephritis,[4 10] though not more so than in vasculitis.[5] The high incidence in Henoch-Schönlein purpura is of obvious interest in view of the frequent demonstration of IgA in the diseased glomeruli[11 12] and skin lesions of patients with Henoch-Schönlein purpura[13 14] and their raised serum IgA levels.[15 16] The role of IgA in Henoch-Schönlein purpura is not clear; it may be present in affected tissues and cryoglobulins as antibody against an infectious organism or other antigen which has entered via the respiratory or gastrointestinal mucosa. Alternatively the IgA may be altered by an infectious organism so that it becomes antigenic and causes immune-complex formation. This mechanism has been implicated in cases of poststreptococcal nephritis in which the IgG component of some cryoglobulins lacked sialic acid: the streptococci were found to be capable of producing this chemical change in vitro.[10] IgG so altered becomes autoantigenic, and experimentally induces nephritis and cryoglobulinaemia.[10] Bacteria can remove sialic acid from IgG by their secretion of neuraminidase, and this property may therefore allow immune-complex disease to follow infections. Although respiratory tract infections often precede Henoch-Schönlein purpura, no organisms have been specifically associated with the disease, and if the condition has an immune-complex aetiology the antigen awaits definition.

The finding that C1q, C4, and C3 were present in cryoglobulins only in association with IgA also suggests that IgA has some particular role in Henoch-Schönlein purpura. IgA can activate complement via the alternative pathway[17] or the classical pathway.[18] Furthermore, an IgA-IgG-IgM cryoglobulin which activated complement via both classical and alternative pathways has been described.[19] In our in-vitro studies the IgA-containing cryoglobulins activated complement exclusively by the classical pathway, but this does not exclude the possibility that they may activate the alternative complement pathway in vivo. That this occurs in Henoch-Schönlein purpura has been postulated from the high prevalence of glomerular properdin (a constituent of the alternative pathway) and IgA in patients with Henoch-Schönlein nephritis,[20] and, indirectly, from the occurrence of Henoch-Schönlein purpura in patients with C2 deficiency.[21-23]

Our finding of properdin in cryoglobulins from eight patients supports the view that the alternative pathway is also activated, although properdin was not specifically associated with IgA-containing cryoglobulins. Recent experiments have indicated that properdin may attach non-specifically to activated C3.[24] This mechanism may explain its presence in the glomeruli and cryoglobulins in Henoch-Schönlein purpura, though it does not account for the higher incidence of glomerular properdin in this condition than in other forms of nephritis.

We are indebted to many colleagues for allowing us to investigate patients under their care, and to Dr Ralph Counahan for providing follow-up data on several patients.

Financial support from the British Council for MGF and from the Wellcome Trust for DGW is gratefully acknowledged.

References

1 *British Medical Journal*, 1977, **1**, 190.
2 Lowry, O H, *et al*, *Journal of Biological Chemistry*, 1951, **193**, 265.
3 Peters, D K, *et al*, *Clinical and Experimental Immunology*, 1972, **11**, 311.
4 Levy, M, *et al*, *Actualités Néphrologiques de l'Hôpital Necker*. Paris, Flammarion Medecine-Sciences, 1972.
5 Cream, J J, *Clinical and Experimental Immunology*, 1972, **10**, 117.
6 Druet, P, *et al*, *Clinical and Experimental Immunology*, 1973, **15**, 483.
7 Griswold, W R, *et al*, *Proceedings of the Society for Experimental Biology and Medicine*, 1974, **145**, 117.
8 Barnett, E V, *et al*, *Annals of Internal Medicine*, 1970, **73**, 95.
9 Weisman, M, and Zvaifler, N, *Journal of Clinical Investigation*, 1975, **56**, 725.
10 McIntosh, R M, *et al*, *Quarterly Journal of Medicine*, 1975, **44**, 285.
11 Urizar, R E, and Herdman, R C, *American Journal of Clinical Pathology*, 1970, **53**, 258.
12 Berger, J, *Transplant Proceedings*, 1969, **1**, 939.
13 Baart de la Faille-Kuyper, E H, *et al*, *Lancet*, 1973, **1**, 892.
14 Asamer, H, *et al*, *Schweizerische Medizinische Wochenschrift*, 1974, **104**, 1188.
15 Tanaka, M, Fujisawa, S, and Okuda, R, *Annals of Pediatrics of Japan*, 1969, **15**, 19.
16 Trygstad, C W, and Stiehm, E R, *Pediatrics*, 1971, **47**, 1023.
17 Götze, O, and Muller-Eberhard, H J, *Journal of Experimental Medicine*, 1971, **134**, 90S.
18 Iida, K, *et al*, *Immunochemistry*, 1976, **13**, 747.
19 Wands, J R, *et al*, *New England Journal of Medicine*, 1976, **294**, 121.
20 Evans, D J, *et al*, *British Medical Journal*, 1973, **3**, 326.
21 Sussman, M, *et al*, *Clinical and Experimental Immunology*, 1973, **14**, 531.
22 Gelfand, E W, Clarkson, J E, and Minta, J D, *Clinical Immunology and Immunopathology*, 1975, **4**, 269.
23 Einstein, L P, *et al*, *New England Journal of Medicine*, 1975, **292**, 1169.
24 Chapitis, J, and Lepow, I H, *Journal of Experimental Medicine*, 1976, **143**, 241.

(*Accepted 18 May 1977*)

SHORT REPORTS

Paralysis of palate in a child

Isolated paralysis of the palate in children is now a rarity. Here I report a case in which this was possibly caused by a Coxsackie A9 infection.

Case report

A boy of 12 began to have difficulty with swallowing, and fluids he took regurgitated through his nose. At the same time his voice assumed a nasal intonation. He was referred to the otorhinolaryngology clinic, where it was found that his soft palate was virtually paralysed, there being only a slight flicker of movement on the left side. His voice was distinctly nasal, and an enlarged, non-tender lymph node was felt at each angle of the jaw. Apart from this he had no complaints, and showed no abnormal signs. He had never been seriously ill, and had received standard inoculation for diphtheria and poliomyelitis. Towards the end of last summer he had camped with a troup of Boy Scouts for two weeks before the onset of his palatal paralysis, and during that time he had bathed in the river Tame. None of his companions at the camp was adversely affected. Within a week of being seen in outpatients his difficulty in swallowing disappeared and only slight right palatal weakness and barely perceptible twang of his voice remained. Soon afterwards the palate appeared to be back to normal, but the enlarged nodes were slow to subside.

Investigations included culture of postnasal swab, which did not produce any pathogens; routine complement fixation tests in the virus laboratory (not including those for the Coxsackie viruses), which showed no abnormalities; and culture of a sample of stool, which yielded Coxsackie virus type A9.

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.

[1] Margoffin, R L, Lenette, E H, and Schmidt, N J, *Pediatrics*, 1961, **28,** 602.
[2] Lennette, E H, Margoffin, R L, and Knouf, E G, *Journal of the American Medical Association*, 1962, **179,** 687.
[3] Sells, C J, Carpenter, R L, and Ray, C G, *New England Journal of Medicine*, 1975, **293,** 1.

(*Accepted 23 March 1977*)

Solihull Hospital, West Midlands
A M NUSSEY, MD, FRCP, consulting physician

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.

[1] World Health Organisation Scientific Group, *Report*, No 478. Geneva, WHO, 1971.
[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.
[4] Teale, J D, *et al*, *Lancet*, 1974, **2,** 553.
[5] Teale, J D, and Marks, V, *Lancet*, 1976, **1,** 884.

(*Accepted 18 March 1977*)

St Mary's Hospital, London W2 1NY
C P O GARRETT, MB, BS, senior house officer

Poisons Unit, Guy's Hospital, London SE1 9RT
R A BRAITHWAITE, PHD, senior biochemist

Department of Biochemistry, University of Surrey, Surrey GU2 5XH
J D TEALE, PHD, research fellow

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