Case report

A 56-year-old research engineer presented to the Hammersmith Hospital in 1972 with deteriorating balance, speech, and writing for nine months. Family history was negative. Examination showed titubation, slurred speech, horizontal nystagmus, cerebellar ataxia in the arms, and ataxia of gait. Tendon reflexes and sensation were normal. A cervical myelogram and vertebral arteriogram were normal. Air encephalography showed slight dilatation of the third ventricle and of cerebral cortical sulci. Malignancy, hypothyroidism, and other systemic diseases were excluded by full investigation, and late-onset idiopathic cerebellar degeneration was diagnosed. He deteriorated slowly over the next six years. By 1978 he could walk only with a stick.

He was given choline chloride 1 g four times daily by mouth. There was a dramatic improvement. He could walk without a stick even over irregular surfaces outdoors, which had been impossible for many years. More detailed observations were therefore made of his motor function both on and off choline. Without choline he walked on a wide base and needed a stick for support. He could not stand with his feet together, let alone perform Romberg's test or tandem standing. Within two days of starting choline he

Helices drawn with wrist unsupported. Left, untreated, right, on choline.

could do all these things and could hop on either foot alone. Ataxia also improved markedly in the arms: helices drawn with the wrist unsupported are shown in the figure, and the times taken for various tests of finger dexterity were reduced by 50% or more. Titubation improved, but there was no observable change in speech or nystagmus. He was stabilised on 5 g choline daily, which he felt was better than 4 g. When choline was stopped he deteriorated again within two days. Propantheline at 15 mg four times daily reduced the choline effect, and at 15 mg six times daily abolished it. Oral physostigmine 6 mg daily, instead of choline, did not benefit him.

Comment

Choline is a rate-limiting substrate for the synthesis of acetylcholine by cholinergic nerves. Oral choline increases choline concentrations in plasma and cerebrospinal fluid and also brain acetylcholine and acetylcholine receptor concentrations.² Its therapeutic effect in chronic tardive dyskinesia is thought to be due to enhanced cholinergic transmission,³ and the same conclusion may tentatively be drawn in the present case. The great improvement on oral choline was abolished by an anticholinergic drug, suggesting that the therapeutic effect was taking place at cholinergic synapses. No improvement was obtained with physostigmine, presumably because anticholinesterases produce only small rises in brain acetylcholine.

The site at which cholinergic transmission was being enhanced is a matter for speculation. Acetylcholine concentrations are low in the cerebellum compared with the rest of the brain.⁴ The climbing fibre input from the inferior olives may be cholinergic,⁵ but the evidence is scanty. The site of action may not necessarily be within the cerebellum. The implications of this report are twofold: it suggests that a defect of cholinergic transmission underlies some cerebellar movement disorders; and it offers the possibility of effective treatment for a hitherto untreatable syndrome.

¹ Kark, R A P, Blass, J P, and Spence, M A, *Neurology*, 1977, **27**, 70.

² Morley, B J, *et al*, *Nature*, 1977, **266**, 848.

³ Growdon, J H, *et al*, *New England Journal of Medicine*, 1977, **297**, 524.

⁴ Shea, P A, and Aprison, M H, *Journal of Neurochemistry*, 1977, **28**, 51.

⁵ Marani, E, and Voogd, J, *Journal of Anatomy*, 1977, **124**, 335.

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Anaphylaxis after oral penicillin

Allergic reactions to penicillin are not uncommon, but anaphylaxis is rare. Anaphylaxis after oral ingestion is rarer still, and many doctors are unaware of its existence. We describe here two patients who suffered near-fatal anaphylaxis after taking oral penicillin who were admitted within ten days of each other to the Leicester Royal Infirmary.

Case 1

A 29-year-old woman was prescribed penicillin V for a sore throat. Within three minutes after taking the first tablet she developed generalised pruritis and flushing, followed by abdominal cramps, nausea, and one episode of vomiting. When first seen 30 minutes after ingestion, she was responding only to commands and had severe peripheral cyanosis, a tachycardia of 120 beats/min, and blood pressure of 70/50 mm Hg. She was initially treated with 0.5 ml 1/1000 adrenaline subcutaneously, 200 mg hydrocortisone intravenously, and 10 mg chlorpheniramine intravenously, and subsequently with an infusion of hydrocortisone for 12 hours. She regained full consciousness over the next 30 minutes and her blood pressure returned to normal after three hours. On subsequent questioning she admitted having taken penicillin on several previous occasions.

Case 2

A 47-year-old man was prescribed talampicillin for a cough of one week's duration. Thirty minutes after taking the first tablet he developed facial oedema, pruritis, and nausea and then lost consciousness. When first seen at home he was severely cyanosed and was responding only to painful stimuli. He was given 10 mg chlorpheniramine intravenously together with 200 mg hydrocortisone, and a 19-G needle was inserted into his trachea. After transfer to hospital and further treatment with antihistamines and steroids his conscious level and respiration improved but he remained hypotensive for several hours before recovering fully. Subsequently he said that he had taken penicillin preparations on several other occasions with no adverse effects, the last time being three months previously.

Comment

These two patients suffered severe anaphylactic shock after oral ingestion of penicillin and both had been treated with penicillin preparations previously with no symptoms suggestive of allergy. The incidence of anaphylactic shock in all patients treated with penicillin is between 0.015 and 0.04%, with death occurring in 0.002% of cases.¹

Anaphylaxis after oral ingestion is, however, even less common than after parenteral administration, and Batson² could find only 28 cases in a survey of published reports up to 1960. There have been four reports of fatal anaphylaxis due to oral penicillin preparations.³ Patients who develop anaphylactic reactions have usually been treated with penicillin before—for example, 25 of the 28 patients in Batson's series and three out of four patients quoted by Spark³ had received previous treatment.

The main antigenic stimulus in penicillin allergy is now thought to come from the breakdown products of the penicillin molecule: the penicilloyl group, with the "minor antigenic determinants," such as Na-benzylpenilloate and Na-benzylpenicilloate, being particularly relevant in the development of anaphylactic reactions. Since all semi-synthetic forms of penicillin are built around the same molecular nucleus, this accounts for cross-allergy to different preparations, and activation of allergy in already sensitised individuals often requires only minimal amounts of penicillin, particularly with regard to anaphylactic reactions. This was well illustrated by our patients. We want to draw attention to this point and also to the fact that oral penicillin preparations can cause as rapid and as severe an allergic reaction as parenteral preparations.

¹ Idse, O, *et al*, *Bulletin of the World Health Organisation*, 1968, **38**, 159.

² Batson, J M, *New England Journal of Medicine*, 1960, **262**, 590.

³ Spark, R P, *American Journal of Clinical Pathology*, 1971, **56**, 407.

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