carried out four times. On day 6, the patient regained consciousness but remained immobile and confused. Neurological examination on day 7 disclosed a positive Babinski's sign and bilateral hyperreflexia. On day 8, rigidity of all limbs, akinesia, and rest tremor of about 6 Hz in both hands were noticed for the first time. Therefore, the diagnosis of diffuse hypoxic encephalopathy was suspected but on day 10 pyramidal signs disappeared. On day 11, the concentration of PChE reached the normal range. The same day the patient was taken off mechanical ventilation but because of persistent salivation, disturbance of swallowing, and consecutive aspiration it was needed again for 24 hours. Even after complete pulmonary and cardiovascular stabilisation the patient remained completely immobile, unable to turn around in bed or to speak. Because rigidity, tremor, akinesia, and bradyphrenia persisted on day 24 the diagnosis of parkinsonism was suspected and treatment with amantadine intravenously (300 mg/day) was started. Within 1 day there was marked improvement of consciousness, orientation, mobility, and speech. Furthermore, salivation, and disturbance of swallowing improved and, therefore, feeding by tube was no longer necessary. Only 6 days later, on day 30, the patient left the intensive care unit and moved to the neurological department. Due to a continuous improvement treatment with amantadine was stopped on day 40. After discontinuation no relapse occurred. When the patient was discharged on day 61 he had completely recovered from parkinsonian symptoms.

Between day 33 and day 53 various additional diagnostic examinations such as MRI, [^{18}F]-fluorodesoxyglucose-positron emission tomography ([^{18}F]-FDG-PET), [^{18}F]-fluorodopa-PET ([^{18}F]-F-DOPA-PET) and [^{123}I]-iodobenzamide-single photon emission computed tomography ([^{123}I]-IBZM-SPECT) were performed but showed no pathological findings. In addition, on clinical examination and electrophysiological studies there were no signs of an intermediate syndrome or delayed polyneuropathy. Furthermore, the patient had no history of parkinsonism and antidopaminergic therapy, and family history was unremarkable.

This is a description of a patient who developed the complete picture of severe parkinsonism after acute OP poisoning with demeton-S-methyl-sulphone, an S-substituted phosphorothiate. Parkinsonian symptoms were noticed 8 days after intoxication, markedly improved after treatment with amantadine, and resolved spontaneously within 9 weeks.

We suggest that parkinsonism was due to a transient pharmacological effect. Organophosphate poisoning causes irreversible AChE inhibition resulting in raised acetylcholine (ACh) concentrations. The striatum contains large aspiny cholinergic interneurons which are likely to stimulate efferent enkephalin-containing GABA projections to the globus pallidus externus leading via increased glutamatergic excitation in the subthalamic nucleus to a reduced cortical glutamate stimulation (indirect pathway of the corticostriatopallidothalamocortical circuit). Therefore, it can be speculated that reduced striatal AChE activity resulted in a decrease of cortical glutamate stimulation which clinically mimicked a dopamine deficiency syndrome. This hypothesis is supported by the fact that the patient recovered completely and no relapse after discontinua-

tion of amantadine medication occurred. Amantadine was preferred to other antiparkinsonian treatment because there was no evidence for a dopamine deficiency and, furthermore, can be administered intravenously. The benefit of amantadine might be due to its antilutaminergic effect in the subthalamic nucleus as well as its presumed NMDA receptor mediated antagonism on ACh release on striatal interneurons.

We looked for various alternative explanations for the presented parkinsonism. In MRI, however, there were no hypoxic lesions and [^{18}F]-FDG-PET disclosed normal striatal glucose metabolism. [^{18}F]-F-DOPA-PET and [^{123}I]-IBZM-SPECT did not show a reduction of presynaptic striatal F-DOPA uptake or a decrease of postsynaptic dopamine D2 receptor capacity. Therefore, it seems to be very unlikely that parkinsonism in this patient was due to hypoxic encephalopathy, idiopathic Parkinson's disease, or postsynaptic dopaminergic changes.

Although acute organophosphate poisoning is relatively common only a few case studies are available describing central nervous symptoms suggesting an involvement of the extrapyramidal system. Extrapyramidal manifestations were noticed early in the course of the disease and spontaneously disappeared within a few weeks in those patients who survived.¹⁻⁴ Therefore, it can be speculated that such symptoms will often be overlooked or will be masked by other complications. So far it is unclear whether the occurrence of extrapyramidal symptoms depends on the type of the organophosphate agent or on the severity of poisoning.

In conclusion, transient parkinsonism must be added to the sequelae of acute organophosphate poisoning persisting even after cholinergic symptoms have resolved. Although parkinsonian symptoms spontaneously improved the diagnosis should not be missed because complications such as aspiration, pneumonia, thrombosis, and prolonged mechanical ventilation could be prevented by appropriate treatment.

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Oropharyngeal palsy in Guillain-Barré and Fisher's syndromes is associated with muscle weakness in the neck and arm

Guillain-Barré syndrome is an immune mediated peripheral neuropathy characterised by acute onset of symmetric limb weakness and areflexia. Patients with typical Guillain-Barré syndrome had greater leg weakness than arm weakness, with an ascending progression.¹ Some patients with Guillain-Barré syndrome, however, present muscle weakness only at the oropharynx, neck, and proximal upper limb muscles, and a descending pattern of weakness appears as illness progresses.² Ropper² proposed that the second group of patients had a variant of Guillain-Barré syndrome, "pharyngeal-cervical-brachial weakness (PCB)". Ophthalmoplegia and cerebellar ataxia, however, are often noted in patients with PCB. Therefore, it is unclear whether PCB is an "atypical" Fisher's syndrome or a distinct variant entity of Guillain-Barré syndrome. To clarify this, we investigated the relation of neck and limb weakness with cranial nerve involvements. We report here that oropharyngeal palsy in Guillain-Barré syndrome has a significant association with neck and arm-dominant weakness whereas ophthalmoplegia does not.

We made prospective examinations of 113 patients with Guillain-Barré syndrome and 39 patients with Fisher's syndrome who had been referred to our neuroimmunological laboratory between December 1996 and February 1998 with cranial nerve dysfunction and weakness in the neck and limbs on the day of admission. All the patients fulfilled the accepted clinical criteria for these syndromes. Diagnosis of Fisher's syndrome was also made in patients who initially presented with ophthalmoplegia, ataxia, and areflexia and later developed generalised muscle weakness. On admission, 53 patients with Guillain-Barré syndrome or Fisher's syndrome (Guillain-Barré syndrome, 14 (12%); Fisher's syndrome, 39 (100%)) had ophthalmoplegia, and 48 (Guillain-Barré syndrome, 41 (36%); Fisher's syndrome, seven (18%)) had oropharyngeal palsy. Generalised muscle weakness was present in six (15%) patients with Fisher's syndrome. Of the 48 patients with Guillain-Barré syndrome or Fisher's syndrome who had oropharyngeal palsy, 36 (75%) and 20 (42%) respectively had neck and arm-dominant weakness, compared with 33 (32%) and 13 (13%) of the 104 patients without oropharyngeal palsy (table). Patients with oropharyngeal palsy showed a significant increase in the frequency of neck weakness (χ^2 test, $p<0.0001$) and arm dominant weakness ($p<0.0001$). By contrast, leg dominant weakness was less common in patients with oropharyngeal palsy (11 (23%)) than in patients without (50 (48%)) ($p=0.003$). There was no significant association of ophthalmoplegia with neck or arm dominant weakness ($p=0.5$ and $p=0.9$ respectively).

Statistical analysis showed that muscle weakness in the neck and upper limbs was frequent in patients with Guillain-Barré syndrome or Fisher's syndrome who had oropharyngeal palsy. This may account for the distribution of muscle weakness that occurs in PCB. According to the clinical criteria of Ropper *et al* for PCB,¹ it should be diagnosed

Relation of oropharyngeal palsy to neck and limb weakness in Guillain-Barré and Fisher's syndromes

	Oropharyngeal palsy		<i>p</i> Value	Odds ratio	95% CI
	Present (<i>n</i> =48)	Absent (<i>n</i> =104)			
Ophthalmoplegia	18 (38%)	35 (34%)	0.6		
Neck weakness	36 (75%)	33 (32%)	<0.0001	6.5	3.1–13.6
Arm dominant weakness	20 (42%)	13 (13%)	<0.0001	5.0	2.3–10.9
Leg dominant weakness	11 (23%)	50 (48%)	0.003	0.3	0.1–0.7

Differences in proportions were examined by χ^2 test. 95% CI=95% confidence interval.

only in patients who have a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs but no weakness or areflexia in the legs. In his original report,² however, one of the three patients with PCB had generalised areflexia. Moreover, the patient with Guillain-Barré syndrome described by Mizoguchi *et al*,³ whose initial symptoms were lower cranial nerve dysfunction and upper limb weakness, later developed generalised muscle weakness. These patients with PCB with generalised areflexia or weakness indicate that the preservation of the tendon reflex and muscle power in the legs depends on the severity of the involvement of the limbs. None of the patients in our study met the clinical criteria proposed by Ropper.¹ However, the close association of weakness of the pharynx, neck, and upper limbs in Guillain-Barré syndrome and Fisher's syndrome indicates that PCB is a distinct variant of Guillain-Barré syndrome, because ophthalmoplegia, a cardinal sign in Fisher's syndrome, is not associated with oropharyngeal palsy, neck weakness, or arm dominant weakness.

Our finding is also supported by detection of serum antibodies against GT1a ganglioside in patients with PCB which show different reactivity from those in patients with Fisher's syndrome.⁴ IgG anti-GT1a antibodies in patients with PCB are not absorbed by GQ1b ganglioside whereas those in patients with Fisher's syndrome are.⁴ Because only GT1a is recognised by serum IgG from the patient who had a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs,⁴ we speculate that anti-GT1a and anti-GD1a antibodies respectively contributed to the development of PCB and generalised weakness in the patient described by Mizoguchi *et al*.³

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Cumulative meta-analysis of aspirin efficacy after cerebral ischaemia of arterial origin

In 1996 we reported in this *Journal* that there was virtually no difference in relative risk reduction for low (<100 mg/day), medium (300 to 325 mg/day), and high (>900 mg/day) doses of aspirin in the prevention of vascular events in patients with cerebral ischaemia of arterial origin.¹ A meta-analysis of the cumulative data showed a modest 13% (95% confidence interval (95% CI) 4% to 21%) relative risk reduction. Recently the final data of the second European Stroke Prevention Study (ESPS-2) were reported.² One of its comparisons was between 50 mg aspirin daily and placebo in patients after cerebral ischaemia; the relative risk reduction of 13% (95% CI 0% to 24%) was exactly the same as that resulting from our previous meta-analysis. This similarity allows the calculation of an update of the meta-analysis. The overall relative risk reduction of course remains 13%, but the 95% CI has narrowed to 6% to 19%. The figure shows the results of the updated cumulative meta-analysis, in chronological order. These data once more underscore the need for more efficacious treatment strategies. For this reason we started the European and Australian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT).³

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Cumulative meta-analysis in chronological order (1977 to 1996) with relative risks and corresponding relative risk reductions with 95% CIs. Each line represents the relative risk and 95% CI of that study combined with all previous studies.

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CORRESPONDENCE

Hemifacial spasm

We have looked with interest at the scan of a patient with hemifacial spasm by Reigosa and Rios.¹ Indeed, this is a very nice MRI which shows an arterial loop and the internal auditory meatus. However, this loop is not the cause of hemifacial spasm.

Typical hemifacial spasm, which begins in the orbicularis oculi and gradually progresses down the face, is caused by a blood vessel on the non-fascicular portion of the facial nerve on the caudal or anterior aspect, including the intrapontine nerve. Atypical hemifacial spasm, which starts in the buccal muscles and progresses up the face, is caused by a blood vessel on the posterior or rostral side of the nerve. This is much less common. The compression is also at the brainstem. A distal artery, as shown in the scan, does not cause hemifacial spasm. The syllogism that Reigosa and Rios bring out—namely, that botulinum toxin helped and that this picture showed the pathology, is inadequate. They do not have a completed explanation.

This patient's spasm will recur because the cause has not been treated. The spasm has an excellent chance of responding to a microvascular decompression of the facial nerve performed by a neurosurgeon who has experience in the nuances of the operative procedure.

Nevertheless, Reigosa and Rios have shown a beautiful scan.

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Pego Reigosa replies:

We thank Jannetta and Kassam for their interest in our article.¹ We think that the vascular loop that appears in the MR image is indeed the cause of the hemifacial spasm of our patient, as it is the only abnormal finding of the neuroimaging studies performed. Furthermore, we did not find compression of the nerve at other levels where it is more often encountered, as is the caudal aspect of the VII cranial nerve next to the pons.

Moreover, it is evident that the hemifacial spasm will reappear or recur. For this reason,