third and nineteenth day from the beginning of the symptoms, the first one being normal and the second one showing an increase in protein (0.95 g/l) with 11 cells and negative titres to brucella, syphilis, toxoplasma, herpes simplex, varicella-zoster, and a negative anticryptococcal antigen determination.

The patient's clinical pattern began to improve two weeks after admission; she was discharged a week later. Follow up a month later revealed only a generalised areflexia and a slight dysmetria on the heel-knee test.

Electrophysiological studies (table) were carried out on the sixth and eighteenth day, which revealed absent sensory potentials. Motor NCS showed less abnormality than that of sensory nerves. There was delay in the distal motor latency in all the nerves tested and there was also reduction in motor amplitude in both median nerves, with a 25.3% drop in peak-to-peak amplitude between wrist and elbow, and a 39.2% drop in amplitude between wrist and axilla in the first right median nerve conduction study. Neither temporal dispersion nor motor conduction block in the remaining nerves was noted. EMG studies were normal. A third electrophysiological study performed a month after her discharge showed the recovery of the sensory nerve action potentials in the lower and upper extremities, although the amplitude and sensory conduction velocity of the nerves studied were lower than the normal values. The motor NCS, however, were similar to previous values. The EMG study of the right anterior tibialis and right first dorsal interosseous muscles showed compatible changes with minimum denervation.

Until recently the Guillain-Barré syndrome was an entity whose nosological characterisation relied upon a purely descriptive base, with relatively widely accepted diagnostic criteria.¹ Among these, the presence of muscular weakness is the most noticeable, indicating the main affection of the motor roots. However, a purely sensory clinical variant of this illness is also believed to be possible and the following features are necessary for it to be accepted:² rapid onset, distribution widespread and symmetrical, complete or near recovery, high CSF protein content, with few or no cells, and an electrophysiological study compatible with a demyelinating process in the peripheral nervous system.

There is still a certain controversy as to whether this clinical variant occurs. In a recent review of 42 patients with acute sensory neuropathy, the authors concluded that this condition is not part of the spectrum of inflammatory demyelinating neuropathies;³ nevertheless, it is noticeable that only 2 of the 42 patients had complete remission of symptoms and that the course of their disease was very protracted—from six to nine months.

A case of acute polyneuropathy has been published in which the sensory disorders were also prominent and very similar to those of our patient.⁴ The necropsy carried out after the patient's death from pulmonary embolism revealed inflammatory infiltration with segmental demyelination in the peripheral nerves, posterior roots and spinal ganglia, with a marked preservation of the anterior roots. These findings, except for the preservation of the motor roots, are identical to those which are described in the Guillain-Barré syndrome.⁵

Our patient had an acute sensory neuropathy after a presumed viral illness and vaccination with a monophasic course and nearly

complete recovery—both clinical and electrophysiological—in a short time; CSF protein content was high with a mild pleocytosis. The evidence suggests that this was probably an acute sensory inflammatory demyelinating polyneuropathy.

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- 1 Asbury AK, Bolis L, Gibbs CJ. Workshop on autoimmune neuropathies: Guillain-Barré syndrome. *Neurology* 1990;40:381.
- 2 Asbury AK. Diagnostic considerations in Guillain-Barré syndrome. *Ann Neurol* 1981;9(suppl):1-5.
- 3 Windebank AJ, Blehrud MD, Dyck PJ, Daube JR, Karnes JL. The syndrome of acute sensory neuropathy: clinical features and electrophysiologic and pathologic changes. *Neurology* 1990;40:584-91.
- 4 Dawson DM, Samuels MA, Morris J. Sensory form of acute polyneuritis. *Neurology* 1988;38:1728-31.
- 5 Prineas JW. Pathology of the Guillain-Barré syndrome. *Ann Neurol* 1981;9(suppl):6-19.

Cerebral venous thrombosis in paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare acquired disease of the haematopoietic system manifested by chronic haemolytic anaemia, leukopenia, and thrombocytopenia. Patients with PNH have an increased risk of developing systemic venous thrombosis, and obstruction of the hepatic veins, or Budd-Chiari syndrome (BCS) which is a highly fatal complication in about 30% of cases. PNH is also a well-established though extremely uncommon cause of cerebral venous thrombosis (CVT).¹⁻³ We describe a patient with PNH and BCS in whom CVT was angiographically documented. We comment upon the risks of anticoagulants in this unusual situation and the need to remember PNH among the possible causes of CVT.

A 34 year old woman was admitted to hospital because of malaise, low-grade fever, pleural effusion, hepatomegaly and ascites. The diagnosis of PNH was established by the presence of haemosiderinuria, positive Ham acid haemolysis and sucrose lysis tests. Hepatic venogram confirmed the existence of BCS. She received repeated blood transfusions and a year later a portocava shunt was performed. Three years later she complained of intensive fronto-occipital pain and clumsiness of the left limbs. Examination showed a mild distal paresis of the left leg with only minimal slowness of alternating movements in the left arm. There was impairment of position and pain perception with sensory extinction on the left side. The optic discs were slightly blurred. The visual fields were full with a moderately enlarged blind spot on both sides. CT scanning showed a right parietal infarction. Cerebral angiography revealed thrombosis of superior sagittal sinus, straight sinus, lateral sinuses, and internal cerebral veins. The patient made a complete recovery with dexamethasone and coumarin therapy.

In a comprehensive review of 38 cases, Bousser *et al*⁴ failed to list PNH among the

possible causes of CVT. PNH is commonly undiagnosed for a period of months to years, and its true incidence among patients with CVT is probably underestimated because detailed coagulation studies are not performed in most cases. This may be of the utmost importance when treatment with heparin is under consideration. The recent German randomised trial demonstrated the benefit of high-dose heparin in patients with CVT.⁵ Conversely, therapy with heparin has caused exacerbation of the hemolytic process in some patients with PNH,^{1,2} and thus might be deleterious in this particularly difficult situation.

PNH should be considered among other possible causes of CVT and ruled out by the appropriate laboratory investigations, especially when treatment with heparin is contemplated.

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- 1 Johnson RV, Kaplan SR, Blailock ZR. Cerebral venous thrombosis in paroxysmal nocturnal hemoglobinuria. *Neurology* 1970;20:681-6.
- 2 Spencer JAD. Paroxysmal nocturnal haemoglobinuria in pregnancy: case report. *Br J Obstet Gynaecol* 1980;87:246-8.
- 3 Benoit P, Lozes G, Destée A, *et al*. Hypertension intracranienne bénigne et maladie de Marchiafava-Micheli. *Rev Neurol (Paris)* 1986;142:782-5.
- 4 Bousser MG, Chiras J, Bories J, Castaigne P. Cerebral venous thrombosis. A review of 38 cases. *Stroke* 1985;16:199-213.
- 5 Villringer A, Garner C, Meister W, *et al*. High-dose heparin treatment in cerebral sinus-venous thrombosis (SVT). *Stroke* 1988;19:135.

Toxic reaction following the combined administration of fluoxetine and phenytoin: two case reports

Fluoxetine is a new antidepressant agent unrelated to the tricyclic antidepressants, whose structure corresponds to a straight chain phenylpropylamide. The drug selectively inhibits reuptake of serotonin but not noradrenaline and has a minimal muscarinic, dopaminergic, histaminergic or serotonergic effect.¹ The only described interaction^{1,3} is with L-tryptophan which enhances its therapeutic effects, but produces symptoms and signs of intoxication.² Presently there is no published work on the possible interaction between fluoxetine and anticonvulsant drugs.

We describe two patients, who developed symptoms and signs of intoxication with phenytoin a few days after initiating the use of fluoxetine.

An 84 year old woman was treated with phenytoin 300 mg daily, after removal of a chronic subdural haematoma. Two months later she developed a depressive syndrome. CT showed no alteration, and the plasma level of phenytoin was 15 µg/ml. Treatment with a dose of 20 mg/day of fluoxetine was given, increasing the dose to 40 mg/day after 10 days. Five days after the beginning of treatment she developed gait ataxia, vertigo, diplopia and alteration of consciousness. Examination also showed dysmetria of the limbs, multidirectional nystagmus, and alteration of judgement with visual hallucinations.

The plasma level of phenytoin was 35 µg/ml. The dose of phenytoin and fluoxetine was reduced gradually and there was progressive recovery from the signs and

symptoms, becoming completely normal after 4 weeks. Fluoxetine was reintroduced at the same dose and the depressive syndrome disappeared without recurrence of toxic effects.

A second case, a 57 year old woman, developed a generalised secondary partial epilepsy 3 months after an embolic cerebral infarct. Phenytoin was introduced at 400 mg/day. A year later the patient developed a depressive syndrome and fluoxetine was indicated at a dose of 20 mg/day. Previously the phenytoin plasma level had been 11.5 µg/ml. Ten days later she developed vomiting, difficulty with getting up and sitting and vertigo. The neurological examination showed trunk ataxia, limb dysmetria, and multidirectional nystagmus. Phenytoin plasma level was 47 µg/ml.

The fluoxetine was suspended and there was a progressive recovery of the signs and symptoms with a complete recovery in approximately three weeks. Four weeks after suspension of fluoxetine, the phenytoin plasma level was 20 µg/ml for the same described dose.

In human studies an alteration of the pharmacokinetics of fluoxetine was not found when administered simultaneously with other drugs (such as, ethanol, diazepam, chlorothiazide, tolbutamide and warfarin) and viceversa.³ In animal studies it was shown that fluoxetine is a potent inhibitor of hepatic microsomal metabolism,² this could be responsible for the increase of the phenytoin plasma level in these cases. The interval between the first administration of fluoxetine and the beginning of the phenytoin overdose symptoms, also suggests a mechanism of the metabolic alteration in the degradation of the anticonvulsant drug.

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- Cooper GL. The safety of fluoxetine. An update. *Br J Psychiatry* 1988;153:62.
- Fuller R, Rathbun R, Parli J. Inhibition of drug metabolism by fluoxetine. *Res Commun Chem Pathol Pharmacol* 1976;13:353-6.
- Lemberger L, Bergstrom R, Wolen R, et al. Fluoxetine: Clinical Pharmacology and Physiologic Disposition. *J Clin Psychiatry* 1985; 46:14-9.
- Stark P, Fuller R, Wong D. The pharmacologic profile of fluoxetine. *J Clin Psychiatry* 1985;46:7-13.
- Steiner W, Fontaine R. Toxic reaction following the combined administration of fluoxetine and L-tryptophan: five case reports. *Biological Psychiatry* 1986;21:1067-71.

Gamma vinyl GABA in the treatment of Levodopa-induced dyskinesias in Parkinson's disease

In non-human primates blockade of the GABAergic inhibitory strio-pallidal pathways to the lateral segment of the globus pallidus causes chorea, whereas stimulation causes a Parkinsonian syndrome.¹ This has led to renewed interest in the potential value of gabaminergic agents in the treatment of Parkinson's disease and the complications of levodopa therapy.

We have investigated the irreversible inhibitor of GABAtransaminase, gamma vinyl GABA (GVG) in the treatment of disabling

levodopa-induced chorea in 5 patients with Parkinson's disease. The patients had a mean age of 54 (41-74) years, a mean duration of disease of 11 (7-21) years, mean duration of levodopa therapy 9 (6-18) years and a mean levodopa dose of 760 (450-1400) mg/day. All the patients were also receiving subcutaneous apomorphine, 4 selegiline and 1 bromocriptine.

The patients' dyskinesias were assessed over a one week baseline period on optimum anti-Parkinsonian therapy. They were then given 2 Gm/day of GVG for one week and 3 Gm GVG for a second week. Assessment of dyskinesia severity was carried out using a 4-point scale after a standard therapeutic dose of sc apomorphine.

The patients also kept self-scoring diaries for three days of each week to assess the number of hours "on" with and without dyskinesias and the number of hours "off". Baseline assessments showed that dyskinesias were more severe later in the day in all patients. On GVG no change in dyskinesia severity occurred as judged by either the apomorphine challenges or the self-scoring diaries, but there was a mean increase in off hours from 3 to 4 hours.

Four patients were unable to tolerate more than 2 Gm GVG due to increased severity of Parkinsonian symptoms. The other patient also noticed worsening of Parkinsonism on 3 Gm GVG.

Contradicting results with progabide, a gabaminergic agonist, have been reported in levodopa-induced dyskinesias in Parkinson's disease.^{2,3} GVG was reported to aggravate Parkinsonism without improving tardive dyskinesias in psychotic patients on sustained neuroleptic therapy.⁴ GABA mimetic drugs therefore appear to have complex and contradictory actions in patients with movement disorders. This study is of interest in that aggravation of Parkinsonism occurred without significant reduction in dyskinesias suggesting that these two phenomena may not be inextricable.

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- Crossman AR. A hypothesis on the pathophysiological mechanisms that underlie levodopa or dopamine agonist-induced dyskinesia in Parkinson's disease. Implications for future strategies in treatment. *Mov Disord* 1990;5:100-8.
- Bartholini G, Lloyd KG, Worms I, Constantiniades J, Tisset R. GABA and GABAergic medication relating to striatal dopamine function and Parkinsonism. In: Posner JL, et al, eds. *Adv Neurol*, Vol 24, New York: Raven Press, 1979:253-9.
- Bergmann KJ, Limongi JCP, Lowe YH, Mendoza MR, Yahr MD. Potentiation of the L-dopa effect in Parkinsonism by a direct GABA receptor agonist. *Lancet* 1984;i:559.
- Gaio JM, Pollak P, Hommel M, et al. Clinical and biochemical effects of gamma-vinyl gaba in tardive dyskinesia. *J Neurol Neurosurg Psychiatry* 1987;50:1674-8.

Hypochromia iridis in acquired Horner's syndrome

The uncommon condition of congenital Horner's syndrome consists of ptosis, miosis, facial anidrosis and hypochromia of the affected iris.¹ This condition commonly results from injury to the brachial plexus at birth.^{2,3} The mechanism of the hypochromia

iridis is generally thought to be that of failure of pigment development rather than loss of pigment that has already formed. Hypochromia of the iris following acquired Horner's syndrome has been reported but is rare. We report a case of this rare but interesting manifestation of damage to the sympathetic nervous system to the eye.

A 17 year old man was involved in a motorcycle accident and suffered brachial plexus trauma, with loss of power and sensation in the right arm followed by pain. Examination 23 years later revealed partial C7 and complete C8 and T1 paresis with corresponding sensory loss. He had post-traumatic brachial plexopathy pain for which he was seeking advice. Examination also revealed a right Horner's syndrome with loss of pigment in the right eye, his left being coloured grey/green.

Several mechanisms by which alteration in sympathetic activity may influence iris pigmentation have been proposed.⁴ There may be failure of delivery of noradrenaline or other melanin precursors to the melanocytes in the iris, perhaps mediated via cyclic adenosine monophosphate. There may be loss of activation of prostaglandins, or their precursors, or some melanotropic moiety, that are involved in melanin synthesis. Several cases of depigmentation of the iris⁵ or heterochromia iridis, with spots on the affected iris,⁶ have been reported following injury to the sympathetic nervous system, but this condition in the acquired state appears to be rare, although it may often be unrecognised.

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- Hyodo T, Kare M, Shintomi Y. Two cases of congenital Horner's syndrome. *Folia Ophthalmol* 1983;34:387-90.
- Ogle JW. On the influence of the cervical portion of the sympathetic nerve and spinal cord upon the eye and its appendages, illustrated by clinical cases, with observations. *Medicochirurg Trans* 1850;41:397-440.
- Calhoun PF. Causes of heterochromia iridis with special reference to paralysis of the cervical sympathetics. *Am J Ophthalmol* 1919;2:255-69.
- Simon D, Austin J, Forslor L. Heterochromia pupillaris: implications of the spotted pale iris. *Neuro-ophthalmology* 1982;2:279-91.
- Mackley TA, Abbott K. Neurogenic heterochromia: report of an interesting case. *Am J Ophthalmol* 1965;59:927-8.
- Miller NR. Disorders of pupillary function, accommodation and lacrimation. *Wash and Hoyt's Clinical neuro-ophthalmology*, 4th ed. Baltimore: Williams and Wilkins, 1982: 500-7.

Shoulder pain from glomus tumour

Localised pain in the shoulder often suggests a brachial plexus neuropathy or cervical radiculopathy. Pain limited to a small area with sensory loss suggests a focal nerve lesion such as a neuroma. Glomus tumours typically cause arm pain distally;¹ they rarely occur proximally.

A 41 year old woman presented with point tenderness in the right posterior deltoid and lateral suprascapular area. The tender area, which had been present for several years, was less than 1 cm in diameter and located lateral to the spine of the right scapula. A friendly "touch on the shoulder" would cause an