against any tentorial herniation as a cause of the oculomotor palsy.

Wilson *et al*¹ recently described three patients with internal carotid artery occlusions who also had transient ocular motor palsies, generally recovering within hours. However, pupil dilatation and ptosis were observed for up to three weeks. The most likely mechanism was transient impairment of the nutrient circulation of the ocular motor nerves. For example, the oculomotor nerve receives its blood supply from an anastomotic plexus of small arteries which in turn is supplied from branches of the internal carotid artery within the cavernous sinus, from multiple branches of the maxillary artery, as well as from the ophthalmic artery anteriorly, and from the posterior cerebral and basilar arteries posteriorly.^{2,3} This rich blood supply from multiple sources could explain why oculomotor palsy is so unusual, even transiently, after carotid occlusions or carotid ligations for the treatment of aneurysms,⁴ since occlusion of several components of the nerve's nutrient supply is probably required to produce significant ischaemia. Thus in the oculomotor palsy in diabetes mellitus there are diffuse small vessel abnormalities in the vasa nervorum.³ Similarly, flow was absent in the ophthalmic and internal carotid arteries in our case and in those of Wilson *et al*. Whether the resulting oculomotor palsy is transient or permanent may perhaps depend on the adequacy of the collateral blood supply from the posterior circulation, or on the extent of segmental occlusion of the plexus of small vessels along the nerves themselves.

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Penicillamine treatment of Wilson's disease and optic neuropathy

We report a case of optic neuropathy associated with penicillamine treatment of Wilson's disease.

A twenty six year old woman presented with a one year history of progressive shaking of her hands and four months of shaking of her head. As a result she had had to give up her job on a production line. There was no family history of neurological or liver disease. She had a history of tachycardia and had taken disopyramide 100 mg three times a day for three years. A mitral regurgitation murmur had been noted in the past.

On examination her pulse was 80/minute and regular, and blood pressure was 115/60. There was a mid and late systolic murmur

loudest at the left sternal edge. Higher functions were intact, but her manner was disinhibited. Visual acuity was 6/9 on the right and 6/6 on the left. Fundoscopy showed normal optic discs. Slit lamp examination showed Kayser-Fleischer rings. The other cranial nerves were normal. She had titubation, tremor of the upper limbs, worse on the right and aggravated by movement, and cogwheel rigidity of both wrists. Reflexes, power and sensation were normal.

Serum copper was 7.0 micromol/l (Normal: 12-26 micromol/l), caeruloplasmin 70 mg/l (Normal: 190-450 mg/l) and 24 hour urinary copper was 5.1 micromol/24 hours (Normal <0.8 micromol/24 hours). Biochemical screen, plasma glucose, and chest and skull radiographs were all normal. Haemoglobin was 119 to 136 g/l, white blood count 2.2 to 3.9 × 10⁹/l with polymorphs 1.0 to 2.3 × 10⁹/l and platelets 85 to 116 × 10⁹/l. The bone marrow was mildly hypocellular, with reduced numbers of erythroid and myeloid cells and megakaryocytes. A CT brain scan showed low densities in the thalami and cerebral peduncles. Echocardiography showed mild mitral valve prolapse.

A diagnosis of Wilson's disease was made and D-penicillamine 50 mg three times a day was started.

Three weeks after starting penicillamine the patient presented with failing vision. A week after starting treatment she had developed a "red light" in the centre of both visual fields and then progressive blurring of vision. On examination both optic discs were pale and both pupils reacted sluggishly to light. Corrected visual acuity was 6/24 on the right and 6/18 on the left. Near vision was N18 bilaterally. Visual evoked potentials (VEP) showed latencies of 102 ms on the right and 112 ms on the left (Normal <115 ms). Brainstem auditory (BAEP) and somatosensory evoked potentials (SSEP) were bilaterally delayed. The wave form of the BAEPs was small. Electroretinogram and autoimmune profile were normal.

Penicillamine was stopped and pyridoxine 50 mg twice a day was started. Nine days later near vision was N10 in both eyes. Trientine dihydrochloride 600 mg three times a day was started. Three weeks after stopping penicillamine colour vision had returned to normal. A week later pupillary reactions were improved and near vision was N6 (right) and N4 (left). The VEPs showed improved amplitude, but the latencies were unchanged. Three months after stopping penicillamine the VEP latency on the left had improved to 99 ms and on the right was 106 ms. The BAEPs and SSEPs were unchanged. After seven months the visual acuity was 6/12 on the right and 6/9 on the left. After a year of trientine the tremor had greatly improved. She has since returned to work and her manner appears normal.

No case of untreated Wilson's disease with optic neuropathy has been described. BAEPs are commonly delayed in Wilson's disease, but delayed VEPs have been found in only a minority of cases with neurological involvement.¹ Recovery of VEP latency with treatment has been shown in one study. The abnormal VEPs may be related to cerebral hemisphere involvement.¹

Optic neuropathy in Wilson's disease treated with DL-penicillamine and D-penicillamine has been attributed to penicillamine induced pyridoxine deficiency: in two cases the optic neuropathy developed only after months at higher doses of penicillamine and

improved with pyridoxine. Against this theory is a third case,² which developed while on prophylactic pyridoxine. In all cases there was an improvement of the Wilson's disease with penicillamine treatment, making the Wilson's disease itself unlikely to be the cause of the optic neuropathy.

Optic neuropathy has been described in association with D-penicillamine treatment of chronic active hepatitis for two months and rheumatoid arthritis for six months and for a year. The last was associated with development of antinuclear antibody titre of 1/320 and improved with steroids.³

This case differs from the others described as the duration of treatment before the development of optic neuropathy is much shorter. Pyridoxine deficiency is unlikely, because of the low dose and short duration of treatment. The short history and negative autoimmune profile make autoimmune disease unlikely. Neurological deterioration in the first month of penicillamine treatment of Wilson's disease has been recognised recently⁴ and the time course in this case would be consistent although optic neuropathy has not been described in this situation. Worsening of extrapyramidal signs is often seen in this syndrome, but was absent in this case. The neurological deterioration may be due to redistribution of copper. Trientine therapy has not been associated with neurological deterioration. Neuro-ophthalmic complications of desferrioxamine, including one case with optic neuropathy, have been associated with raised cerebrospinal fluid copper levels and attributed to redistribution of copper.⁵ Another explanation of the optic neuropathy in this case consistent with the short history would be an idiosyncratic hypersensitivity reaction. Although optic neuropathy is a rare complication, physicians should regularly assess the visual acuity of their patients on penicillamine, particularly when starting treatment or increasing the dose.

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Serum erythropoietin levels in von Hippel-Lindau syndrome

No serum marker exists in von Hippel-Lindau syndrome (HLS), an autosomal-dominant inherited cancer-prone disorder

associated predominantly with heman-gioblastomas of the central nervous system (Hbl), angiomas of retinae (AR), renal cysts, renal cancer, pancreatic cysts, pheochromocytoma and epididymal cystadenoma. Since paraneoplastic production of erythropoietin (EPO) or of erythropoiesis stimulating factors has been described in cerebellar Hbl,⁴ renal cancer,² renal cysts,⁵ and pheochromocytoma,¹ we investigated whether the serum EPO concentration is an indicator of HLS, which might facilitate an early diagnosis of affected individuals.

Our study included 44 patients (23 females, 21 males) with positive gene carrier status of HLS. Their mean age was 38.7 (16–79) years. Five of the patients had Hbl, 25 had AR, two had renal cancer, three had renal cysts, seven had pheochromocytomas; four had a history of surgical treatment for Hbl, and 11 for pheochromocytoma. Fifteen subjects presented with multiple lesions. Three asymptomatic individuals were identified as gene carriers by pedigree analysis.

Serum for EPO radioimmunoassay was prepared from venous blood sampled without anticoagulant. The assay was carried out in duplicate using human urinary EPO standard, ¹²⁵I-labelled recombinant human EPO (specific activity 11–33 TBq/mmol; Amersham Buchler, Braunschweig, Germany) and antiserum (1:5000) from a rabbit immunised with human urinary EPO. The antibody-bound ¹²⁵I-EPO was precipitated with polyethylene glycol 6000 (160 g/l). The mean within and between assay coefficients of variation were 7% and 19% in the EPO range 40–50 mU/ml. The detection limit was 5 mU/ml.

Comparative measurements of immunoreactive EPO were performed on serum samples from 14 normal subjects (five females, nine males; age 20–38 years). Their EPO values were essentially normally distributed with a mean (1 SD) of 18.1 (7.5) mU/ml. Thus with the assay described, 95.5% of all normal values are in the range 3.1–33.1 mU/ml, mean (2 SD).

Serum EPO was elevated (> 33.1 mU/ml) in two of five (40%) patients with Hbl, in two of 25 (8%) with AR, in one of seven (14%) with pheochromocytoma, but in none of the patients with renal and pancreatic lesions. No significant correlation was found between elevated EPO values and serum haemoglobin concentrations. One patient with AR and one patient with a history of pheochromocytoma surgery presented with erythrocytosis (haemoglobin > 180 g/l), but serum EPO was normal in both cases.

We conclude that EPO is not a suitable marker for identifying patients affected with HLS, either in asymptomatic or in symptomatic individuals, and subsequently does not support our recently published clinical screening programme.³

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Application of gadolinium-DTPA magnetic resonance imaging for detection of a filum terminale myxopapillary ependymoma allowing successful surgical resection

Myxopapillary ependymomas of the spinal cord are histologically distinct low-grade gliomas which arise almost exclusively in the regions of the conus medullaris and filum

terminale.^{1,2,4,5} Radiographic confirmation of these tumours has traditionally relied upon myelography and, more recently MRI.^{3,4,7} We report a further case that demonstrates the diagnostic value of Gadolinium-DTPA enhanced MRI.

A 41 year old male teacher of gymnastics presented with a one and a half year history of low back pain which radiated intermittently and alternately to the right and left buttocks and thighs, and was exacerbated by Valsalva manoeuvres. He did not complain of focal motor weakness, sensory or sphincteric disturbances.

Physical examination of the patient's lumbosacral region as well as his neurological examination were unremarkable. He had normal strength, sensation and rectal tone, as well as active and equal deep tendon reflexes throughout, with downgoing plantar reflexes and a normal gait. Lasegue's test was negative bilaterally.

Plain radiographs and unenhanced CT scans of the entire lumbosacral spine were repeated at our institution and were unremarkable. Intravenous enhanced lumbosacral (L1–S1) CT also failed to show any intraspinal enhancing mass. Spin-echo

Figure (a) Spin echo pulse sequence, T1 (TR/TE = 600/20) and (b) T2 (TR/TE = 2500/80) weighted sagittal MRIs of the lumbar spine: the tumour was not apparent on T1, however, on T2 weighted image an intradural tumour extending from approximately mid L2 to the superior border of L3 could be seen. Note the signal intensity of the CSF below the mass which was brighter than the CSF above the tumour. (c) Post Gd-DTPA injection T1-weighted sagittal MRIs of the lumbar spine: the location, margin and extent of the intradural tumour was readily identifiable due to the striking enhancement of the tumour. (d) Light microscopy of the tumour revealing papillary low columnar cells surrounding a central core of hyaline containing small vessels (Haematoxylin and Eosin $\times 40$).