nerve palsy were present. Perimetry showed full visual fields and visual acuity was 6/9 in both eyes. Magnetic resonance imaging showed appreciable tumour recurrence. Foci of haemorrhage were evident throughout the lesion, which was compressing both cavernous sinuses, although there was no chiasmal compression. A further endonasal transphenoidal hypophysectomy was performed. Overtly haemorrhagic and necrotic pituitary adenoma was identified at operation and later verified histologically. Two months after this procedure the left third nerve palsy had begun to resolve.

Haemorrhage within pituitary adenomas is a common finding either at the time of operation or on subsequent histopathological examination and is often subclinical.[2 3] It has been suggested that in cases of subclinical haemorrhage, tissue necrosis is an uncommon finding whereas it is common in those presenting with clinical apoplexy. Repeated minor haemorrhage within vascular adenomas probably accounts for the clinically occult group, whereas swelling secondary to ischaemic oedema or haemorrhagic infarction in an adenoma which has outgrown its blood supply, is proposed as the more likely sequence of events in cases of clinical apoplexy.[4] The second mechanism seems to have been responsible for the three cases presented here, where extensive necrosis was uniformly seen. The absence of severe headache, obtundation, and altered visual acuity accords with the finding that whereas ophthalmoplegia is compatible with an alert state, defects in visual acuity are more often associated with impaired consciousness.[5]

The mortality and morbidity of untreated classical pituitary apoplexy is high, whereas the results of expedient surgical intervention for pituitary apoplexy are generally good. Misdiagnosis of pituitary apoplexy even in its more typical presentation is common, however, and it is therefore important that those involved in the initial evaluation of patients are aware of the variability in clinical presentation and the need for early and appropriate radiological evaluation. Magnetic resonance imaging combines high diagnostic accuracy with excellent anatomical detail particularly in the coronal plane (figure).

The case for urgent surgical decompression in the presence of obtundation and actual or threatened visual loss is generally supported. In the alert patient presenting with ophthalmoplegia in the absence of visual field deficit or impaired acuity the surgical role is less clearly defined and many advocate conservative management in this instance. Steroid treatment and close clinical observation is certainly associated with spontaneous improvement in some cases, although there do not seem to be any reliable predictive criteria on which such patients can be identified. The clinical course is unpredictable and the possibility of rapid deterioration with blindness or death must be borne in mind and weighed against the surgical alternative. The transphenoidal approach in experienced hands is extremely well tolerated and surgery ensures immediate decompression of the parasellar structures and affords the opportunity to obtain tissue for histological evaluation to aid subsequent management.

Extraocular muscle palsies may occur as the sole manifestation of infarction or haemorrhage in pituitary adenomas. Early recognition of this "non-apoplectic" mode of presentation allows prompt neurosurgical management, hopefully averting permanent ophthalmoplegia and the possibility of life threatening upward extension of the pituitary mass, while permitting definitive treatment of the underlying adenoma.

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Excitotoxic amino acid neurotransmitters are increased in human cerebrospinal fluid after subarachnoid haemorrhage

Experimental evidence[1] suggests a role for glutamate neurotoxicity in many neurodegenerative disorders, but few clinical studies have been conducted to substantiate this hypothesis.[2 3] We have measured excitatory and inhibitory amino acid neurotransmitters including glutamate, aspartate, taurine, and alanine in human CSF in the acute stage of subarachnoid haemorrhage in relation to clinical outcome.

The study protocol was approved in advance by the local ethics committee and informed consent was obtained from a relative. Ten patients who had a subarachnoid haemorrhage due to a ruptured cerebral aneurysm were included in this study (table) and their ruptured aneurysm was clipped within 48 hours of ictus. A ventricular catheter was placed, CSF was intermittently drained to maintain the intracranial pressure below 20 mm Hg, and CSF samples were collected from day 3 to day 8 after the haemorrhage and for at least two days after operation. Samples were deproteinised and stored at –80°C until analysis. Control CSF samples were collected and stored in the same way from patients without neurological disorders who underwent spinal taps for spinal anaesthesia.

The CSF samples were diluted 10 times with distilled water and 30 μl aliquots were used. Amino acids were measured three times for each CSF sample by high performance liquid chromatography with an electrochemical detector (ECD-100; EICOM, Kyoto, Japan) after a 4·6 mm (diameter) × 150 mm reverse phase precolumn (Eicompak, MA-50DS, EICOM, Kyoto, Japan) derivatisation procedure with *o*-phthaldialdehyde and ethylmercaptan. The liquid phase was 0·1 mol phosphate buffer (pH 6·0) with a 30% methanol gradient. Standards of aspartate, glutamate, taurine, and alanine in concentrations of 9, 90, and 900 pmol (Wakojunyaku, Tokyo, Japan) were measured every eight to 12 CSF sample analyses to obtain calibration curves. The retention time was identified from the standard chromatograms and the area was used for the calculation of CSF amino acid neurotransmitters. We estimated the maximal error of the glutamate concentration to be 30% in some of our samples based on the data reported by Ferrarese *et al*.[4] We expressed the results as mean (SD) and compared the concentrations between patients and control subjects by Mann-Whitney *U* test.

Symptomatic cerebral vasospasm was defined with transcranial Doppler and, together with neurological deficits, was graded as mild, moderate, or severe. The outcome was assessed at three months after subarachnoid haemorrhage according to the Glasgow outcome scale. The patients were divided into two groups; good outcome, if the Glasgow outcome score showed good recovery or moderately disabled, and poor outcome, if it showed severely disabled or dead. The amino acid neurotransmitters were compared between the two groups by Student's *t* test.

Patients and normal controls were compared. Mean values of glutamate, aspartate, and alanine increased some threefold ($p < 0·05$). The taurine increased 1·7-fold but the difference was not significant. Five patients made a good recovery, one was moderately disabled, two severely disabled, and two died of delayed ischaemia due to vasospasm (table). Differences in amino acid neurotransmitter concentrations were compared between those who had good outcomes and those with poor outcomes. Concentrations of the amino acid neurotransmitters tended to be higher in the poor outcome group, but these differences were not significant.

Persson *et al* evaluated the cortical extracellular glutamate concentration in a patient with severe subarachnoid haemorrhage by a microdialysis method[5] and found a 25-fold increase in glutamate, aspartate, and taurine under conditions of energy perturbation as indicated by the simultaneously measured lactate:pyruvate ratio and suggested that a massive accumulation of glutamate and aspartate in the extracellular space may contribute to neuronal injury in subarachnoid haemorrhage.[5] We measured concentrations of amino acids in the ventricular CSF, which can be regarded as a pool into which substances diffuse from the extracellular space. As the amino acids were diluted in the CSF in the ventricles, their concentrations in the extracellular space may be higher than those measured in the CSF.

The concentration of extracellular glutamate that is toxic to neurons is poorly defined particularly as any such effects are enhanced by compromising energy generation.[6] In vitro experiments with cultured neurons have suggested that concentrations of 5–100 μmol/l glutamate are toxic to neurons.[1] Olney *et al* reported that direct injection of 500 nmol (as 1 μl of a 500 mmol/l glutamate solution over five minutes) into the rat striatum was necessary to cause delayed local neuronal degeneration.[3] The relation between the amount of increase of amino acid neurotransmitters in CSF and

Summary of patients with subarachnoid haemorrhage: clinical profiles, and amino acid neurotransmitter (AANT) concentrations in CSF

Case	Age /sex	H and K grade	GCS	Day of Operation	Day of Deterioration	Day of sampling	Vasospasm	GOS	AANT concentrations (μM) ASP	GLU	TAU	ALA
1	53/M	2	15	1		4	+	GR	5·26	9·28	7·68	60·3
2	56/M	2	14	1		3	+	GR	0·22	2·57	5·74	64·43
3	62/F	3	11	1		8	+	GR	2·13	9·32	15·6	129·1
4	52/M	3	13	0		3	+ +	MD	1·02	0·88	4·65	155·4
5	64/M	3	14	1	3	5	+ +	SD	2·02	3·11	8·94	132·4
6	48/M	3	13	1		6	+	GR	0·54	3·76	5·98	60·94
7	41/F	4	7	1		5	+	GR	1·48	0·77	4·35	110·0
8	79/F	4	6	1	5	5	+ + +	D	0·24	9·45	5·33	40·3
9	55/M	4	5	0	3	2	+ + +	D	2·00	3·24	12·9	145·4
10	65/F	4	11	1	4	5	+ + +	SD	4·29	7·85	14·8	151·0
							Mean (SD)		1·9(1·7)*	5·0(3·6)*	8·6(4·3)	105·3(44)
							Control (n = 16)		0·6(0·5)	1·6(0·7)	5·8(1·8)	31·9(6·2)

*$p < 0.05$ v controls.
H and K = Hunt and Kosnik grade; GOS = Glasgow outcome scale; GCS = Glasgow coma scale; ASP = aspartate; GLU = glutamate; TAU = taurine; ALA = alanine; Day = postsubarachnoid haemorrhage day; + = mild (100–149 cm/s); ++ = moderate (150–199 cm/s); +++ = severe (≥200 cm/s); GR = good recovery; MD = moderately disabled; SD = severely disabled; D = dead.

outcome requires study of a larger population of patients but our preliminary results provide a rational basis for such studies and for trials of excitotoxic amino acid antagonists.

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Incidence of internal carotid artery dissection in the community of Dijon

Dissection of the cervical internal carotid artery is one of the major causes of ischaemic stroke in patients under 50 years old.[1] Reliable epidemiological data are not numerous. Only one defined population study on internal carotid artery dissection has been published.[2]

We examined the occurrence of spontaneous internal carotid artery dissection in the population of the city of Dijon from 1985 to 1993, by means of the stroke Registry of Dijon[3] which records all first strokes, and also asymptomatic stenosis, occlusion, and dissection of internal carotid artery occurring in the population of the city of Dijon. The diagnosis was ascertained by an ultrasonic Doppler examination of the cervical carotid arteries, and a carotid angiography. Patients with a history of cervical trauma were not included. For the calculation of incidence, the whole population of Dijon was considered to be at risk, with 135 000 inhabitants in 1985 and 150 000 inhabitants in 1992, and was used as the denominator for the study.

From 1985 to 1993, 36 internal carotid artery dissections were diagnosed. The average annual incidence for all age groups was 2·9 per 100 000 population (95% confidence interval 1·9–3·9). There were no statistically significant annual variations (three cases in 1985, four in 1986, three in 1987, five in 1988, four in 1989, five in 1990, three in 1991, four in 1992, five in 1993). The mean age was 39·9 (7·5) years for the 21 women, 43·7 (5·7) years for the 15 men. All had headache or neck pain; 19 patients presented with cerebral ischaemic symptoms, four with retinal ischaemic symptoms; one patient had had a subarachnoid haemorrhage. Oculosympathetic palsy was noted in 12 patients, and 12th cranial nerve palsy in one. Isolated headache was the single symptom in three cases (8·3%). The diagnosis of dissection was suspected with ultrasound in 34 cases (with demonstration of a double lumen in eight cases), and proved with angiography in all cases, with MRI in only the last four patients. No necropsy cases of spontaneous cervical internal carotid artery dissection were found during this period. No bilateral cervical internal carotid artery dissections, or associated vertebral artery dissection were found. Arterial hypertension was seen in 19 cases. Dysplastic cervical or renal arteries were found in 15 cases. Association with tobacco and pill consumption was present in 15 out of 21 female cases. Evolution was marked by slight neurological sequelae in four cases. Headache resolved in all patients. Recurrent arterial dissections were not found at follow up ranging from three months to nine years.

These 36 cases represent 2% of 1784 patients with stroke collected in this population of Dijon and 10·1% of the 356 stroke patients under 50 years old. This confirms that internal carotid artery dissection is a major cause of cerebral infarction in those under 50 years old.[1]

The average annual incidence of spontaneous internal carotid artery dissection for all age groups was 2·9 per 100 000 inhabitants, similar to that in the city of Rochester.[2] This compares with 2·2 per 100 000 for aneurysmal subarachnoid haemorrhage in Dijon.[3]

Before ultrasound was introduced many cases remained undiagnosed. Biller *et al*[4] reported a spontaneous cervical internal carotid artery dissection in 0·13% of 4531 patients with acute stroke and Bogousslavsky *et al*[5] reported dissection in 2·5% of 1200 patients with acute stroke.

A community based study in Rochester, Minnesota, 1987–92 gave a similar incidence of 2·6 per 100 000.[2]

Headache, ischaemic cerebrovascular disease, and oculosympathetic palsy were the most common manifestations of spontaneous internal carotid artery dissection. Some internal carotid artery dissections do not present with ischaemic stroke (10% in the study of Shievinck *et al*,[2] 8·3% in the present study).

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