Microvascular decompression entails a risk of death (although this is small) and other serious complications requiring surgery (much more often) in the face of a painful, but benign disorder. Perhaps, "trauma surgery" would be best to ensure equal results with a much lower complication rate. A minimally invasive approach (endoscopy) could be studied in this regard.

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About the original description of cerebellar tonsil herniation by Pierre Marie

Transfalcial and transtentorial herniation and the engagement of the cerebellar tonsils into the foramen magnum are well recognised consequences of increased intracranial pressure. They were discovered through both experimental findings carried out in the 19th century,¹ and pathological and clinical experiences reported in the first decades of this century.² Harvey Cushing (1869-1939) is usually acknowledged as the first clinician who, in 1902, correlated the clinical picture of neurological disturbances and cardiorespiratory failure with the herniation of the cerebellar tonsils into the foramen magnum.³ However, when in his book on pontocerebellar angle tumours Cushing made use of the notion of "cerebellar pressure cone",⁴ he was employing a term first introduced into the English language by Collier,⁵ as Cushing himself acknowledged in an earlier article.⁶

Here we report on the observations of Pierre Marie (1853-1940) that bear on the same issue and antedate those of both Cushing and Collier. On 1 July 1899, during a session of the Société de Biologie, Pierre Marie⁷ reported on two cases of cerebral haemorrhage that resulted in secondary compression of the cerebellum. In the first case, a haemorrhage of the external segment of the lenticular nucleus flattened the superior face of the left cerebellar lobe and shifted the vermis to the right. In the second case, a thalamic

haemorrhage resulted in compression of the superior face of the left cerebellar hemisphere and caused a protrusion of the cerebellar tonsils that "appeared to have engaged the occipital foramen".

Pierre Marie drew attention to the pathophysiological research of Leonard Hill. "In his *Hunterian Lectures* in 1896, he showed that the brain does not transmit the pressure on one point in all directions. Indeed, a clear pressure difference is created between the main cranial cavity and the posterior fossa. According to Hill, the pressure gap is due to: (1) the viscosity of the cerebral substance; (2) the interposition of the falx cerebri and the tentorium cerebelli. This explains why a haemorrhage lesion exerts a localised compression on a particular part of the cerebrum, instead of creating a uniform pressure growth on the whole cerebral mass, as some think. In the present circumstance, the compression is exerted on a cerebellar hemisphere.

Furthermore, according to Leonard Hill "the compression exerted by the haemorrhaged cerebellar hemisphere upon the superior surface of the cerebellum can have very serious consequences. In fact, if the compression is sufficiently strong, the downward push on the cerebellum causes the engagement of its inferior surface into the foramen magnum. In this process the cerebellum takes the form of two cones constituted by the cerebellar tonsils. As a result the medulla oblongata is trapped within the foramen magnum, and if the pressure is strong enough its vessels will be compressed to the point of failing to supply the organ. Hence a severe bulbar ischemia will ensue."⁷

Pierre Marie concluded his communication by considering the possibly severe consequences of cerebellar tonsillar penetration into the occipital foramen and the resulting bulbar hypoperfusion, exactly devising the mechanism of cerebellar herniation. In the next year, Pierre Marie reported the pathological findings of another two cases of raised intracranial pressure.⁸ In the first case with a thalamic haemorrhage the rise in intracranial pressure caused the caudal shift of a cerebellar tonsil, that consequently "engaged into the occipital foramen". The second case was of increased intracranial pressure of unknown origin, disclosed by pronounced hydrocephalus. "Both cerebellar tonsils had shifted into the occipital foramen such as to form a sort of cone enclosing the bulbous for more than half of its circumference." In his conclusions, Pierre Marie suggested that the compression of the medulla could have contributed to the fatal outcome.

A few years later, in 1905, Louis Pierre Marie Alquier (1872-1956) described two further cases of cerebellar tonsils herniation into the occipital foramen.⁹ In Alquier's article the discussion of Jean Athanase Sicard (1872-1929) and Pierre Marie on the topic is reported. Mentioning his personal experience in similar cases, Pierre Marie also made the somewhat surprising suggestion that Alquier's pathological findings might be attributed to a postmortem process. We could find no further contribution by Pierre Marie on this topic in his subsequent scientific production.

Recently, Fisher¹⁰ has pointed out that cerebellar herniation is not necessarily a terminal event, except, in cases in which cerebellar herniation occurs in posterior fossa infarcts, acute subdural haematomas, or during a lumbar puncture. In such cases, acute herniation is justifiably considered among the determinant factors of clinical outcome. The first

clinical description of this important phenomenon was made by Pierre Marie.

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Blepharospasm induced by flunarizine

Flunarizine is a calcium channel antagonist that has been widely prescribed for vertigo, cerebral or peripheral vascular diseases, migraine, and epilepsy.^{1,2} At doses of 10-40 mg/day, it can produce side effects such as parkinsonism or abnormal involuntary movements, especially in elderly people.^{1,2} A case of blepharospasm in a 67 year old woman who had been taking 20 mg/day flunarizine for 18 months has been reported.² However, the cause of the disorder in this instance may be questionable as this patient had also been treated with cinnarizine and her dystonic movements did not disappear 13 months after the discontinuation of both drugs.² We have seen a 30 year old woman who was treated with 10 mg/day flunarizine for migraine prophylaxis. After two months of treatment she developed a progressive blepharospasm which eventually prevented her from reading or watching television. Three weeks after the appearance of symptoms, flunarizine was withdrawn, and the patient made a gradual and complete recovery over the next month.

Dopaminergic, cholinergic, serotonergic, or other poorly understood mechanisms might be implicated in the pathogenesis of blepharospasm.³ Flunarizine has been reported to have antihistaminic, antiserotonergic, and antidopaminergic activities.² This interference with dopaminergic transmission seems to be both complex and particularly

relevant. On the one hand, flunarizine blocks dopamine receptors and might have a toxic effect on dopaminergic neurons.⁴ On the other hand, its calcium channel antagonism leads to inhibition of dopamine neurotransmission.⁴ In addition, the antihistaminic activity of flunarizine may also have some importance. The blepharospasm that occasionally follows the use of decongestants has been explained by the antihistaminic component of these drugs.⁵ Whatever the mechanisms involved, the early development of blepharospasm in a young adult on a low dose of flunarizine would suggest that individual susceptibility played a part in its emergence. The present case would favour the inclusion of flunarizine among the causes of isolated blepharospasm.

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Expression of tenascin in astrocytic tumours: too much ado about nothing?

The stroma of astrocytic tumours has been investigated in the past years by various authors. Among the proteins of the extracellular matrix tenascin is considered a very important molecule because of presumed links with the malignancy of the tumours and

with the angiogenesis^{1,2} and also a possible target for therapy. To verify these opinions we have performed an immunohistochemical analysis of 10 astrocytic tumours of the cerebral hemispheres. The series of patients comprised six men and four women, ranging in age from 43 to 72 years; seven underwent gross total resection and three subtotal resection. The study focused on the following molecules of the extracellular matrix: tenascin, laminin, fibronectin, and type IV collagen. The results were evaluated in relation to the following indices: grading according to the St Anne/Mayo System,³ proliferating cell nuclear antigen labelling index,⁴ dimensions of the tumour evaluated radiologically (CT and MRI) and expressed according to the criteria of the manual for staging of cancer by means of the parameter "T".⁵

Primary monoclonal antibodies were purchased from Dako and staining was performed by the labelled streptavidin biotin staining method on 10% formalin fixed and paraffin embedded tissue.

The tumours were grade II in two cases (one gemistocytic), grade III in three cases, and grade IV in five cases. Tenascin was present in the extracellular matrix in all grade IV astrocytomas and in the gemistocytic astrocytoma. In two grade III astrocytomas and in all grade IV astrocytomas the basement membranes of the vessels with or without endothelial proliferation showed a positive immunohistochemical staining for tenascin (figure). Tenascin and fibronectin were detected in some neoplastic cells of grade IV tumours and also in the gemistocytes. Laminin, fibronectin, and collagen type IV were found around the vessels of tumours of all grades. The PCNA labelling index was <1% in tumours of grade II and grade III. In grade IV tumours the areas of highest PCNA staining did not correspond to the greater expression of tenascin on serial sections. In some areas with strong staining for tenascin the PCNA labelling index was <5%, whereas the total percentage in grade IV tumours ranged from 5% to 18%.

Evaluation of the parameter "T" failed to provide a correlation between the size of the tumour and the presence of the molecules of the extracellular matrix. For instance, a grade IV tumour evaluated as T1 expressed the

tenascin as well as a grade IV tumour evaluated as T4.

In conclusion, we have shown that tenascin does not correlate with the indices of malignancy we have studied—namely, grading, PCNA labelling index, and size of the tumour. The presence of tenascin in the extracellular matrix could only be a signal of progression of astrocytic tumours. This could explain its presence in the gemistocytic astrocytoma, which is well known as a tumour with a high probability of progression.

Furthermore, it is well known in oncology that the size of the tumour must correlate with neoangiogenesis.⁶ Our hypothesis is that if the expression of tenascin does not correlate with the dimension of the tumour it cannot really correlate with the angiogenesis.

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Multiple sclerosis associated with duplicated CMT1A: a report of two cases

The concomitant involvement of both the peripheral and central nervous system myelin is rare and may occur in the course of inherited lysosomal storage diseases. In inflammatory autoimmune diseases of the peripheral nervous system or CNS, a mild involvement of central or peripheral myelin has sometimes been reported.^{1,2} In such conditions, a single pathogenetic mechanism has been tentatively considered as responsible for the nervous tissue damage and the association of peripheral nervous system and CNS demyelinating disorders due to different pathogenetic mechanisms has never been reported.

We describe two patients with definite multiple sclerosis and hereditary peripheral neuropathy of Charcot-Marie-Tooth type 1A (CMT1A).

Patient 1, a 38 year old woman, was admitted to hospital because of episodes of gait disturbances and optic neuritis. Neurological

Glioblastoma. Immunohistochemical staining for tenascin is in the basement membrane zone of tumour vessels and also in the extracellular matrix (originally $\times 125$).