## Neurofilament light chain antibodies reflect cerebral atrophy in MS

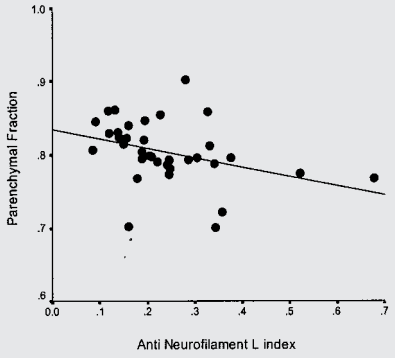
Eikelenboom et al. evaluated levels of heavy and light neurofilaments (NfH and NfL) and their antibodies (anti-NfL and -H) in 51 MS patients in relation to MRI measures. Anti-NfL index was associated with cerebral atrophy, indicating that these antibodies may serve as a marker of tissue damage, particularly axonal loss.
**see page 219**

## NF-light: Disease marker or just another antibody in MS?

*Commentary by John R. Richert, MD*

For years the pathologic immune target(s) in MS have been assumed to be myelin-associated. Although Charcot noted axonal damage in MS, the extent of axonal pathology has been only recently appreciated using quantitative techniques, such as confocal microscopy and MRS. This realization has refocused our attention on axonal damage and its role in cerebral atrophy and its clinical consequences in MS.

The Eikelenboom et al. study presents a cross-sectional evaluation of potential correlations between several CSF markers and MRI disease measures in MS. The most striking finding was the inverse correlation between the intrathecal production of antibody against neurofilament light chain and brain parenchymal fraction. This extends the recent finding of Silber et al. that such antibodies correlated with EDSS[1] and now shows that disease correlation can be detected in the relapsing-remitting phase of MS. The specificity of this antibody to "neurofilament light" supports the notion that early axonal damage contributes to atrophy and clinical disease progression. However, the question of whether this antibody represents the cause or merely the effect of axonal pathology remains unanswered.




*Correlation between anti neurofilament-L index and MRI.*

The degree of scatter of the data among patients in this study suggests that quantitating CSF NF-light may not yet be useful in evaluating an individual patient in the clinic. Neither is there evidence yet to suggest that determination of this antibody will predict subsequent clinical course. In the absence of longitudinal studies, it is also not clear when anti-NF-light appears relative to the clinical course or the development of cerebral atrophy. Nevertheless, this study bolsters the concept that irreversible axonal damage occurs early in MS and provides further rationale for early aggressive treatment of this disease.

### Reference

1. Silber E, Semra YK, Gregson NA, et al. Patients with progressive multiple sclerosis have elevated antibodies to neurofilament subunit. Neurology 2002;58:1372–1381.

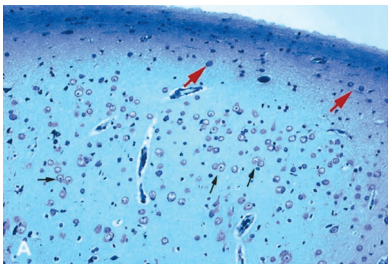
*continued on page 160*

## Why does epilepsy become intractable? Is intractability preventable?

Berg et al. demonstrate that surgically treated partial epilepsy in adults is frequently of childhood onset and provide evidence suggesting that the initial course of patients who ultimately become refractory to treatment may appear quite benign. They consider implications for designing prospective studies and possibilities for preventive therapies.

**see page 186**



*Temporal isocortex with regions of focal dysplasia.*

The Bocti et al. assessment of neuropathology in 22 children who underwent temporal lobe resections found a high incidence of mesial temporal sclerosis (12/15) and cortical dysplasia (14/22). Dual pathology was present in 8/12 children with mesial temporal sclerosis. These findings suggest that temporal lobe epilepsy in children may have a basis distinct from that in adults.

**see page 191**

*"Some patients with recent-onset seizures appear to have 'refractory' epilepsy de novo even before the first AED is prescribed, while others perhaps develop a progressive seizure disorder."*

*The accompanying editorial by Brodie and Leach considers the implications of the difficulty in predicting medical intractability of epilepsy. They consider new data suggesting that the pharmacoresistance of an epileptic focus may reflect overexpression of multidrug transport systems, notably P-glycoprotein, which may prevent AEDs from reaching their site of action in an epileptic focus.*

**see page 162**

## Epilepsy after subarachnoid hemorrhage

Epilepsy occurred in 7% of SAH patients alive at 1 year; was predicted by cerebral infarction and subdural hematoma; and was associated with poor functional recovery and reduced quality of life. Claassen et al. conclude that focal pathology is the principal cause of epilepsy after SAH.

**see page 208**

## Febrile seizures and mesial temporal sclerosis—no association in long-term follow-up

Tarkka et al. quantitated amygdala and hippocampal formation MRI volume on 24 patients with a prolonged first febrile seizure, 8 with an unprovoked seizure after the first febrile seizure, and 32 controls with a single simple febrile seizure selected from 329 febrile seizure patients prospectively followed for a mean of 12.3 years. None had mesial temporal sclerosis.

**see page 215**

## No evidence for "blocking factor" in MS and GBS

Despite repeated reports of "blocking factors" that interfere with neuronal function in MS and Guillain-Barré syndrome, blocking activity of these factors has been difficult to reproduce and their molecular identity has remained enigmatic. A recent report of sodium channel blockade by a pentapetide in the CSF in MS and Guillain-Barré syndrome elicited great interest. Here Cummins et al. report that investigators at three centers could not reproduce the putative blocking activity of this factor. The concept of blocking factors as contributors to pathophysiology in these disorders thus remains unsubstantiated.

**see page 224**

*continued on page 161*

## Early onset familial AD: Mutation frequency in 31 families

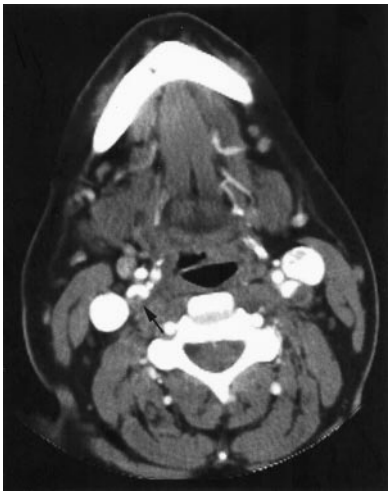
Janssen et al. demonstrated amyloid precursor protein and presenilin 1 mutation in 82% of definite and 77% of probable AD patients who fulfilled recognized criteria for autosomal-dominant inheritance. Some of the remaining ~20% of probands were homozygous for APOE $\epsilon$4, but other gene mutations are likely in others.

**see page 235**

## Outcome of carotid dissection with transient and permanent severe stenosis or occlusion

Kremer et al. restudied 161 patients a year after transient stenosis produced by internal carotid artery dissection. Clinical and ultrasound evaluation indicate a benign long-term prognosis with low annual rates of stroke: in patients with persistent stenosis ipsilateral carotid territory (0.7%) and any stroke (1.4%) and in those with transient severe stenosis or occlusion ipsilateral stroke (0.3%) and any stroke (0.6%).

**see page 271**



*Axial neck CTA of Case A, showing filing defect (arrow) in proximal right ICA.*

### Stroke mechanisms in inherited disorders of homocysteine metabolism

Kelly et al. investigated mechanisms of ischemic stroke and genetic features in young adults with homocystinuria. In all cases, a mild phenotype was present. Stroke was the initial clinical manifestations of homocystinuria in two of three index cases. Stroke mechanisms were intracarotid thromboembolism, carotid dissection, and cardiac embolism. All cases had deficiency of cystathionine beta-synthase.

**see page 275**

### Treatment of acute migraine with droperidol

In a placebo-controlled, double-blind study Silberstein et al. found that IM droperidol was effective: the 2.5-mg dose relieved headache in 87% of patients. Akathesia and somnolence were common; none of the patients were found to have QT prolongation on EKG.

**see page 315**

## Ophthalmoplegia complicating scorpion sting

Hamid Sadeghian reports a patient who developed transient bilateral oculomotor nerve palsy following sting of the scorpion *Mesobuthus eupeus*.

**see page 346**

**January 28 Highlights**

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