## ALS in frontotemporal dementia (FTD)

Lomen-Hoerth et al. studied 36 sporadic FTD patients without a family or personal history of ALS. They found 5 (17%) who met criteria for definite ALS and an additional two with possible ALS. Five additional patients had prominent fasciculations and one of these progressed to ALS.

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## How many ALS syndromes?

*Commentary by Michael Swash*

The current research onslaught on ALS has revealed unexpected complexity. The old Charcot classification—ALS, and the related, overlapping syndrome of progressive muscular atrophy, primary lateral sclerosis, and progressive bulbar palsy—described recognized clinical syndromes. In the current working classification of the disease, there are pathogenesis-based and syndromic elements (table), even when other syndromes, notably the spinal muscular atrophies, are considered separately. Gradually, with increasing understanding, this confusion will be resolved. The role of multiple factors, genetic or acquired, in leading to phenotypic expression of the disease has been emphasized by the variability in the clinical syndromes in patients with SOD1 mutations, a feature that has led to the concept of "modifier genes," although these are as yet undefined. A puzzling feature of ALS has been the occurrence of frontotemporal dementia (FTD) in a proportion of patients with classical ALS.[1] It is uncertain whether this syndrome of FTD is separable from the milder frontal features that so often develop in people with ALS.[2] In this issue of *Neurology*, Lomen-Hoerth et al. emphasize this relationship. In 36 patients with FTD, 17% had definite ALS, and a further 36% had possible ALS. In a complementary study, the incidence of FTD in patients presenting with ALS was 31%. Pathologic studies suggest that cortical ubiquiti nated inclusions are frequent in people with ALS with or without dementia.[3] These two disorders thus seem part of a continuum rather than polar opposites, and may offer a clue to the puzzle of the genetic factors that result in the differing clinical syndromes of ALS and its additional features. One thing is clear; ALS is a disease of the brain as a whole and not just of motor neurons.

### References

1. Neary D, Snowden JS, Mann DMA. Cognitive change in motor neurone disease/amyotrophic lateral sclerosis. J Neurol Sci 2000;180:15–20.
2. Ludolph AC, Langen KJ, Regard M, et al. Acta Neurol Scand 1992;85:81–89.
3. Nakano I. Frontotemporal dementia with motor neurone disease (amyotrophic lateral sclerosis with dementia). Neuropathology 2000;20:68–75.

***Table*** *ALS syndromes and their known genetic loci*

| ALS syndrome | Locus | Inheritance | Clinical features |
|---|---|---|---|
| ALS 1 | Ch 21q, SOD1 gene | Dominant | Typical ALS |
| ALS 2 | Ch 2q 33, Alsin gene | Recessive | Juvenile <10 y, slow course |
| ALS 3 | Non-SOD | Heterogenous: 80% of inherited ALS | Variable |
| ALS 4 | Ch 9q34 | Dominant | Juvenile: possible homology with CMT with UMN signs |
| ALS 5 | Ch 15q 15 | Recessive | Childhood: LMN predominant |
| ALS 6 | Ch 18q 21 | Dominant | Typical ALS |
| ALS FTD | Ch 9q21-q22 | Dominant; sporadic | Onset 6th decade posterior column fiber loss |
| ALS X | Xp11-q12 | ? Dominant | ? |
| NF heavy chain | Ch 22q 12 | ? Dominant | Dementia, monomelic form |
| Western Pacific ALS | ? Inherited | | Dementia, PD |

This list is evolving; any possible contribution of genetic factors to sporadic ALS is currently speculative.

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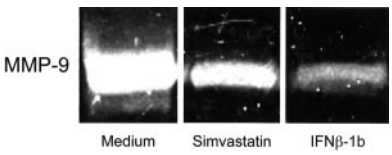
## Immunomodulation by statins in MS




Neuhaus et al. examined the immunomodulatory properties of statins on immune cells in MS. Statins had a distinct potent imunomodulatory profile with similarities to and differences from interferon-beta. Statins inhibited the stimulation of T cells and altered cytokine production. Statins deserve consideration as a treatment option in MS.

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*The accompanying editorial by Zamvil and Steinman notes that the beneficial effect of statins in cardiac transplantation has suggested a role the drugs other than their effect on atherogenesis. In addition to studies such as the Neuhaus work, there is evidence that statins prevent/reverse experimental allergic encephalomyelitis—the animal model of MS. They review how statins may work and reasons/ways they should enter clinical trial.*

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## Clinical practice guidelines

### Which stroke prevention guidelines are best?

Hart and Bailey compared 22 published guidelines for stroke prevention and found important differences in key management recommendations. Furthermore, reporting of the methods of guideline generation was often inadequate, making difficult the assessment of potential bias, validity, and applicability to clinical practice.

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### Neuropsychological testing to assess sports-related concussion

Hinton-Bayre and Geffen used three concussion management guidelines to assess 21 rugby players who suffered concussions. Using the guidelines for concussion severity grading systems of the AAN, the Colorado Medical Society, and the Cantu, none related to presence or duration of neuropsychological abnormalities.

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### Hard evidence vs expert consensus

*The editorial by Franklin and Zahn (co-chairs of the American Academy of Neurology's Quality Standards Subcommittee) that accompanies these two papers notes that, not surprisingly, stroke guideline recommendations based on expert consensus opinion are more inconsistent then those based on high-quality published evidence. The Hinton-Bayre and Geffen paper critiques consensus-based sports concussion severity grading scales, including the 1997 AAN guidelines; appropriately, the AAN recommendation had only weak endorsement. Franklin and Zahn consider areas where expert consensus may have a role: case definition and clinical practice processes.*

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## Medication overuse headache: Differences between acute headache drugs

In patients suffering from medication overuse headache (MOH, formerly drug-induced headache) Limmroth et al. identified monthly dosages and duration of drug overuse for different classes of antiheadache drugs. They found that triptans are associated with more rapid development of MOH than either ergots or analgesics.

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*The accompanying editorial by Silberstein and Welch points out that the MOH of triptans appears different from other MOH in that the headaches have migrainous features. They also consider the pathogenesis of MOHs providing evidence that hyperoxia leading to free radicals in the periaqueductal gray matter may contribute to headache development.*

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## MRI predictors of conversion to MS for clinically isolated syndromes

For patients presenting with a clinically isolated syndrome and >2 T2 lesions, enhancing lesions strengthened the prediction of clinically definite MS (CDMS). The CHAMPS Study Group based their results on a combined CDMS/MRI outcome that suggests the majority already have the disease process of MS, irrespective of additional MRI criteria.

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## Early-onset MS: Long-term follow-up

Out of 4000 patients, Baiko et al. found 116 (3.6%) who had onset of MS prior to age 16. Most were relapsing (97%), but a few had severe disease. After 20 years, 53% developed secondary progressive disease. As in adult MS, a high relapse rate predicted early onset of progression.

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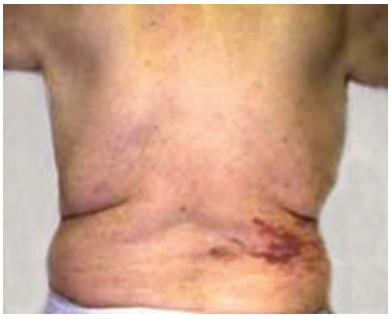
## Postherpetic neuralgia: Treatment with opioids vs tricyclic antidepressants



In a crossover study in 76 patients with postherpetic neuralgia, Raja et al. reported mean pain relief scores of 38%, 32%, and 11% with opioids, tricyclic antidepressants, and placebo. The superiority of opioids to placebo and the trend favoring opioids on some pain measures over tricyclic antidepressants indicates that neuropathic pain is not resistant to opioids.

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**October 8 Highlights**

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