Gabapentin in ALS: No benefit and possible worsening

The phase III controlled trial by Miller et al. (p. 843) failed to confirm a previously observed phase II trial benefit of gabapentin. Merging phase II and III trials actually suggested worsened vital capacity with the drug. ◆ The accompanying editorial by McDermott and Rowland (p. 826) considers the many lessons this trial teaches clinicians pursuing research on ALS (and other neurologic diseases). They also note the problems inherent in pharmaceutical industry–sponsored trials.

Ataxia and seizures from coenzyme Q10 (CoQ10) deficiency

Muscle CoQ10 deficiency has been recognized in rare patients with myoglobinuria, encephalopathy, or ragged-red fibers (RRF). Musumeci et al. (p. 849) describe low muscle CoQ10 levels in six patients with unexplained familial ataxia who also had seizures. All six responded to CoQ10 supplementation: less ataxia, fewer seizures, and better strength. None of the six had RRF on muscle biopsy.

Neurofibromatosis-1 (NF-1)

The NF-1 gene product neurofibromin regulates the growth of neural elements; when abnormal owing to the mutations that cause NF-1, tumors result. Many types of tumor are associated with NF-1, among them, fibrillary astrocytomas (fibA). Li et al. (p. 885) examine the expression of cancer-related genes in patients with pilocytic astrocytomas—looking for similar abnormalities to those found with fibA. Because none were found, the basis for these tumors remains unclear. ◆ The accompanying editorial by Ruggieri and Packer (p. 827) reviews the clinical picture of NF-1 and considers the reasons for its extraordinary phenotypic variability and the reasons the benign tumors that result from a mutation in the remaining normal NF-1 gene (loss of heterozygosity) subsequently become malignant.

Painful peripheral neuropathies: Characterization of the autonomic nervous system (ANS)

Novak et al. (p. 861) studied 92 patients with painful peripheral neuropathy. Because patients with neuropathic pain have small fiber involvement, ANS involvement would be anticipated. Clinical ANS findings included cutaneous vasomotor and sudomotor dysfunction, hypertension, and impotence. Autonomic reflex testing was abnormal in over 90% and more abnormal in those with abnormal nerve conduction.

Tibial muscular dystrophy (TMD): A titinopathy?

Late-onset distal myopathy usually presents in the 4th to 5th decade with anterior compartment, distal leg weakness—hence, the name TMD. Haravuori et al. (p. 869) report that calpain3 is virtually absent in TMD biopsies. Because calpain3 is a ligand of the very large protein titin, and because the titin gene is localized to the chromosome 2q locus linked to TMD, titin is a likely candidate gene. There is also reason to suspect that homozygous mutations at the TMD locus can cause a limb girdle muscular dystrophy.

TNF-α polymorphism and carbamazepine (CBZ) hypersensitivity

Pirmohamed et al. (p. 890) studied 60 patients who had hypersensitivity to CBZ: 37 nonserious and 23 serious (e.g., severe rash, liver dysfunction, fever) vs two large control groups (epilepsy patients including 63 on CBZ and normal subjects). They determined the frequency of variant alleles of TNF-α and human leukocyte antigen (HLA) DR3 and DQ2. One TNF-α allele (TNF2) was associated with serious CBZ hypersensitivity. Although the association was not independent of the HLA haplotypes, the data suggest that CBZ hypersensitivity occurs in genetically predisposed subjects. The association with TNF-α suggests a possible role for this cytokine in severe allergic reactions.

DWI vs neuropathology in ischemic stroke

Kelly et al. (p. 914) retrospectively studied 11 consecutive patients with clinically suspected acute stroke (within 14 days) who had diffusion MRI within 4 weeks of symptoms and who had autopsy within 16 weeks. Diffusion MRI identified 23 of 25 pathology-documented infarcts, but suggested infarction in two instances when none was documented. Neither diffusion MRI or pathology revealed evidence of recent infarction in two cases who initially presented with abrupt onset of strokelike symptoms, but who were assigned final clinical diagnoses other than acute stroke.

Does flu vaccination in MS provoke T-cell response to brain antigens?

Natural infections are associated with MS exacerbations. Moriabadi et al. (p. 938) studied the responses to influenza A vaccination in MS patients and controls. MS patients had a heightened number of T cells responsive to influenza protein but no increase in T cells responsive to myelin basic protein (MBP) or oligodendrocyte protein. In contrast, MBP responses were heightened after natural infection in several MS patients.

