Natalizumab Therapy and Multiple Sclerosis

Stuve and colleagues (page 169) review recent experience with natalizumab therapy for multiple sclerosis. Three patients who were treated with natalizumab developed progressive multifocal leukoen cephalopathy (PML). The pathogenesis of natalizumab-associated PML may be different from that of non-natalizumab-associated PML. There are currently no treatment guidelines for patients receiving natalizumab therapy who might develop PML or other infections. They discuss incisively the biologically feasible potential interventions for patients diagnosed with PML or other infections while receiving natalizumab therapy.

Bilateral Ocular Paralysis

Keane (page 178) presents his review of the causes of bilateral ocular paralysis. He reports that Fisher syndrome (13 cases) and Guillain-Barré syndrome (5 cases) compose 58% of the 31 cases described.

Neuronal Damage in Brain Inflammation

Aktas et al (page 185) review current knowledge related to inflammatory-based neuronal damage in multiple sclerosis, trauma, Alzheimer disease, Parkinson disease, and stroke. They emphasize that developing and testing new concepts for directly protecting neurons and axons in neuroinflammatory diseases will be important and necessary for improving the outcome of patients.

Determinants of Cerebral Atrophy Rate in Multiple Sclerosis

Jasperse and colleagues (page 190) studied magnetic resonance imaging determinants that explain the subsequent rate of cerebral atrophy in recently diagnosed cases of multiple sclerosis. They found that the mean annualized cerebral atrophy rate was 0.9%. They report that in patients recently diagnosed with multiple sclerosis, the extent of accumulated brain tissue loss and overall lesion load partly explain the subsequent rate of cerebral atrophy. Editorial perspective is provided by J. Theodore Phillips, MD, PhD.

Gray Matter Perfusion in Multiple Sclerosis

Microvascular changes have been noted in patients with multiple sclerosis and advances in perfusion magnetic resonance imaging allow their measurement in vivo. Inglese et al (page 196) assessed the presence of perfusion abnormalities in the deep gray matter of patients with relapsing-remitting and primary progressive multiple sclerosis and the relationship of the perfusion impairment on clinical disability and fatigue (Figure). They report a significant decrease in cerebral blood flow in the deep gray matter of patients with multiple sclerosis with a correlation between perfusion impairment and the severity of fatigue.

Cerebral Hematoma Requiring Emergency Surgery

Rabinstein and Wijdicks (page 203) analyzed the likelihood of recovery and prognostic factors in patients with massive anticoagulation-associated intracerebral hemorrhage treated with surgical evacuation after reversal of anticoagulation. They conclude that emergency surgery for selected patients with large anticoagulation-associated intracerebral hemor-
rhage is compatible with a favorable outcome despite the presence of clinical and radiological signs of herniation before the evacuation. The details are important and their data and review are compelling.

**Drug-Related Gambling in Parkinson Disease**

Voon et al (page 212) evaluated factors associated with pathological gambling in Parkinson disease (PD). In a comprehensive study of 21 patients with PD with pathological gambling after medication onset compared with 42 patients with PD without compulsive behaviors, they report that patients with PD with younger PD onset, higher novelty-seeking traits, and a personal or family history of alcohol use disorders pose a greater risk for pathological gambling if they are taking dopamine agonists.

**Two Novel Epilepsy-Linked Mutations Causing a Loss of Function of LGI1**

Leucine-rich glioma-inactivated 1 (LGI1) gene mutations have been identified in families with autosomal dominant lateral temporal epilepsy (ADLTE). Chabrol et al (page 217) report the clinical and genetic studies in 2 families with ADLTE and the functional consequences of 2 novel mutations in LGI1. Two novel disease-linked mutations, p.Leu232Pro and c.431+1G>A, were identified in LGI1. They report that there is a significant decrease in the secretion of the mutant protein by mammalian cells and that LGI1-related epilepsy results from a loss of function.

**Molecular Analysis and Prenatal Prediction of Spinal Muscular Atrophy**

Chen et al (page 225) analyzed 87 patients and 132 parents from 77 Chinese families with spinal muscular atrophy (SMA) for the SMN1 deletion using restriction fragment length polymorphism studies and denaturing high-performance liquid chromatography for 11 fetuses. The frequency of SMN1 deletions detected was 93.5% (72/77). Four fetuses had the SMN1 deletion and the pregnancies aborted. The genetic status of the fetuses and live-born babies was the same as determined prenatally. The prenatal assessment employed is efficient and accurate.

**Differentiation Between Primary Lateral Sclerosis and Amyotrophic Lateral Sclerosis**

Taraglia et al (page 232) considered which clinical features at onset and during follow-up could help differentiate between amyotrophic lateral sclerosis (ALS) and primary lateral sclerosis (PLS). At presentation, stiffness was the only symptom that was significantly different between PLS and ALS; it was higher in PLS. During follow-up, limb wasting was rare in patients with PLS. Disease duration was significantly longer in patients with PLS, and over 16 years of follow-up, mortality rate was better in patients with PLS. Further, a patient presenting with spasticity and not developing wasting within 3 years most likely has PLS.

**Amyotrophic Lateral Sclerosis and Frontotemporal Dementia Linkage to Chromosome 9p**

Valdmanis et al (page 240) studied 3 families with the amyotrophic lateral sclerosis (ALS) and frontotemporal dementia syndrome (FTD) mapping to chromosome 9p. The gene mapping studies in these families reduced considerably the ALS/FTD candidate region located on 9p.

**Diffusion Tensor Imaging of White Matter in Frontotemporal Dementia**

Two major clinical variants of frontotemporal dementia (FTD) have been described, frontal variant (fvFTD) and temporal variant (tvFTD). Borroni and colleagues (page 246) have analyzed white matter and gray matter tissue organization in fvFTD and tvFTD by means of diffusion tensor imaging and voxel-based morphometry. They show in this study that fvFTD and tvFTD are associated not only with selective local gray matter reductions but also with significant white matter damage in the early disease phase. They find that the different white matter patterns contribute to the different clinical syndromes in FTD and could be responsible for the further progression of atrophy in the later disease stages.

**Autonomic Dysfunction and Poor Prognosis of Multiple System Atrophy**

Tada et al (page 256) found in a retrospective review of 49 Japanese patients with pathologically confirmed multiple system atrophy that the early development of autonomic dysfunction is an independent predictive factor for rapid disease progression and shorter survival time.