Genomic Profiling of Neurological Diseases Using Blood: The Future

Sharp and colleagues (page 1529) provide a state-of-the-art review of human neurological disease genomic profiling using genomic sequencing data and microarray analyses. Genomic profiles of patients with ischemic stroke, Tourette syndrome, Duchenne muscular dystrophy, and spinal muscular atrophy are presented. Genomics define specific patterns of gene expression for specific diseases that will indicate the molecular basis of disease pathogenesis and provide insight into future therapies.

Docosahexaenoic Acid and Protection Against Alzheimer Disease: The Framingham Heart Study

Schaefer et al (page 1545) determined the role of plasma phosphatidylcholine (PC) docosahexaenoic acid (DHA) content and the risk of developing dementia of the Alzheimer disease type. Participants in the study in the upper quartile of the baseline PC DHA quartile, as compared with subjects in the lower 3 quartiles, had a relative risk of developing all-cause dementia of 0.53 and Alzheimer disease of 0.61 (Figure). Subjects in the upper PC DHA quartile had a mean DHA intake of 0.18 g/d and a mean fish intake of 3.0 servings per week ($P<.001$) in a study of 488 participants. Based on these data from the Framingham Heart Study, fish consumption provides an important dietary means to reduce the risk of Alzheimer disease. Editorial comment is provided by Martha Clare Morris, ScD.

Intranasal Zolmitriptan in Acute Cluster Headache

Cittadini et al (page 1537) evaluated zolmitriptan nasal spray in the acute treatment of cluster headache in a placebo-controlled, double-blind, crossover study. A well-designed and analyzed study was conducted, and they report that intranasal administration of 5-mg and 10-mg doses of zolmitriptan is effective within 30 minutes and well tolerated in the treatment of acute cluster headache.

Diabetes Mellitus and Risk of Developing Alzheimer Disease: Results From the Framingham Heart Study

Akomolafe et al (page 1551) compared the risk of developing Alzheimer disease in subjects with and without diabetes mellitus. They report that diabetes is not an independent risk factor for Alzheimer disease in the overall Framingham Heart Study sample, but it was a strong independent risk factor for Alzheimer disease among persons at a relatively lower initial risk for developing Alzheimer disease.

Human T-Lymphotropic Virus 1–Associated Myelopathy: A 14-Year Follow-up Study

Oindo and colleagues (page 1560) determined the longitudinal changes in patients with human T-lymphotropic virus 1 (HTLV-1)–associated myelopathy/tropical spastic paraparesis (HAM/TSP). They find that HAM/TSP is a rapid motor disability disease. Older age at onset and high HTLV-1 proviral load are 2 important independent factors associated with poor prognosis. Monitoring HTLV-1 proviral load is highly advisable in future therapeutic trials.

Effectiveness of Mitoxantrone in Treating Multiple Sclerosis

The mechanism of effectiveness of mitoxantrone in treating patients with multiple sclerosis was investigated by Kopadze and colleagues (page 1572). They found that mitoxantrone treatment of patients with multiple sclerosis decreased the migratory capacity of CD14$^+$ monocytes as well as CD4$^+$ and CD8$^+$ T lymphocytes. Similar effects were seen when peripheral blood mononuclear cells were preincubated with 4-hydroperoxy-cyclophosphamide. Thus, these elegant studies show that mitoxantrone achieves its clinical efficacy, at least in part, by inhibiting the migration of inflammatory cells into and within the central nervous system.
Interferon Inhibitory Activity in Patients With Multiple Sclerosis

The role of interferon inhibitory activity and soluble interferon-α/β receptor in determining the response of patients with multiple sclerosis to interferon beta therapy was studied by Chadha and colleagues (page 1579). Of considerable importance, they report that the levels of interferon inhibitory activity are associated with increased multiple sclerosis disease activity and with responsiveness to interferon-beta therapy in anti-interferon beta neutralizing antibody-negative patients with multiple sclerosis.

Apolipoprotein E ε4 and Age at Onset of Sporadic and Familial Alzheimer Disease

The presence of the apolipoprotein E ε4 allele was studied by Olarte et al (page 1586) to determine its role for the earlier age at onset in familial Alzheimer disease cases compared with sporadic Alzheimer disease cases in Caribbean Hispanic individuals. They report that apolipoprotein E ε4 had a consistent lowering effect on the age at onset in familial Alzheimer disease but was attenuated in sporadic Alzheimer disease. These compelling data indicated that among individuals with a family history of Alzheimer disease and the apolipoprotein E ε4 allele, additional genetic or environmental factors may be accelerating the onset of dementia.

Genomewide Scan Implicates a Novel Locus at 3q28 in Familial Alzheimer Disease

Lee and colleagues (page 1591) conducted a genomewide scan in 1161 members from 209 Caribbean Hispanic families with late-onset Alzheimer disease. Of note, 7 loci were identified with logarithm-of-odds scores greater than 2.0 among these families with late-onset Alzheimer disease. The highest logarithm-of-odds score was found at 3q28, highlighting this region as a locus of interest for further genetic exploration.

Effect of Transcranial Magnetic Stimulation on Action Naming in Patients With Alzheimer Disease

The primary aim of this intriguing study by Cotelli and colleagues (page 1602) was to assess the effect of repetitive transcranial magnetic stimulation to the dorsolateral prefrontal cortex on picture naming in patients with Alzheimer disease. They report that repetitive transcranial magnetic stimulation to the dorsolateral prefrontal cortex improved accuracy in action naming. This procedure may be of considerable value as a novel approach in the treatment of language dysfunction in patients with Alzheimer disease and other related disorders.

Novel Mutations in the Guanosine Triphosphate Cyclohydrolase 1 Gene in DYT5 Dystonia

Ohta et al (page 1605) investigated the relationship between mutation of the guanosine triphosphate cyclohydrolase 1 (GCH1) gene and the etiology of DYT5 dystonia and accumulated data on mutation in the Japanese population for the genetic diagnosis of the disease. They found several novel GCH1 mutations in patients with DYT5 dystonia. In some of them, GCH1 enzyme activity was proved to be impaired. These detailed studies extend our knowledge of the clinical and molecular basis of DYT5 dystonia.

Neuropathy in Sjögren Syndrome

Gransson et al (page 1612) studied the involvement of the peripheral nervous system, including small-diameter fibers, in patients with primary Sjögren syndrome. They found that peripheral neuropathy occurs in a large proportion of patients with primary Sjögren syndrome, in most cases as a subclinical demyelinating neuropathy. They show as well that small-diameter nerve fiber neuropathy is not a frequent finding in these patients.

Cardiac and Pulmonary Findings in Bethlem Myopathy

In their study, van der Kooi et al (page 1617) systematically investigated patients with Bethlem myopathy, an autosomal dominantly inherited myopathy manifesting with skeletal muscle weakness and contractures, to determine the presence and degree of cardiac and respiratory involvement. They did not find cardiac involvement in Bethlem myopathy and all patients with compromised respiratory function were still ambulant.

Benign Behavioral Variant by Magnetic Resonance Imaging in Frontotemporal Dementia

Davies et al (page 1627) assessed the clinical course and prognosis in patients with frontotemporal dementia lacking evidence of brain atrophy on magnetic resonance imaging. They concluded that patients with frontotemporal dementia with normal magnetic resonance images follow a more benign course than cases with atrophy at presentation. They also noted that behavioral symptoms in such cases differ from the neurodegenerative pathology typically associated with frontotemporal dementia.