

# PEDIATRIC NEUROLOGY BRIEFS

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### PEDIATRIC NEUROLOGY AT THE MILLENNIUM A CELEBRATION OR A CHALLENGE?

One definition of the millennium is an anniversary or celebration of "a period of freedom from imperfections in human existence." We have not reached this utopian ideal but, in the relatively short space of time since the specialty of pediatric neurology was envisioned and vigorously developed, in the 1950s, much progress has been accomplished, much for the better but with limiting reservations.

**CELEBRATION.** *Childhood epilepsies* are more accurately diagnosed and better controlled, but not without adverse side-effects. The utility of the International Headache Society (IHS) criteria for the definition of *migraine* headaches in children has been challenged because of the lack of agreement between pediatric neurology studies and the IHS diagnostic criteria, based on adult data. The hyperactive and inattentive child with *ADHD* is benefited by methylphenidate, but not without controversy concerning the wisdom of 'medicalizing' a behavior, frequently regarded by social scientists and the media as a variant of normal. The neurologic basis for *dyslexia* and other learning disabilities is better understood with the help of neuroimaging techniques. *Tourette syndrome and tics*, ignored in neurology textbooks in the 1950-60s, are a common subject for research and review in neurology journals since the 1970s. As a downside of this observation and a result of one successful therapeutic advance, an apparent increase in prevalence of tics may be linked to the increased use of stimulant medications in the United States.

Advances in *genetics of neurologic disease* have been particularly valuable in the diagnosis of neuromuscular disorders, sometimes without the necessity for an invasive muscle biopsy. Discoveries relating molecular genetic programming of the embryonic neural tube to *cerebral malformations* have helped in our understanding of the causes of congenital hydrocephalus, holoprosencephaly, and heterotopias. The role of the pediatric neurologist in the *neonatal unit* has changed from a mainly passive consultant to an active participant in the treatment of seizures, diagnosis of congenital myopathies, and prediction of cerebral palsy in infants with asphyxia. *Neuro-oncology* is an important new

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subspecialty, aiding the neurosurgeon in the management of tumors and the hematologist in the neurologic complications of leukemia. Interest in *cerebrovascular disease* has increased with the introduction of less invasive methods of diagnosis, such as magnetic resonance imaging, magnetic resonance angiography, and transcranial Doppler. In *traumatic head injury*, improved obstetrics has lessened the frequency of birth head injury, road vehicle accidents and non-accidental injury have increased as causes of childhood head injury, and modifications of the Glasgow Coma Scale aid in the evaluation and prognosis.

*Infectious disease* has increased in importance in pediatric neurology practice and research as a result of HIV-1 infection, the AIDS epidemic, and its frequent CNS complications. The use of protease inhibitors has reduced AIDS mortality and the frequency of AIDS progressive encephalopathy. The availability of the polymerase chain reaction (PCR) test facilitates the early diagnosis of viral infections of the CNS. The role of *toxins* in the cause of neurologic disorders is recognized: lead poisoning rarely results in acute encephalopathy, but abatement methods have not completely prevented the cognitive impairments linked to low-level exposures. *Heredo-degenerative, metabolic, and demyelinating diseases* are estimated to account for approximately 20% of pediatric neurology practice in the United States. Recent advances include the documentation of clinical diagnostic criteria for newly recognized syndromes, some with specific MRI findings, diagnostic enzyme assays and enzyme replacement therapy, prenatal detection of disease, evidence of a genetic basis for Rett syndrome, and the use of 5-hydroxytryptophan and vitamin E among treatment regimens. Finally, despite some scepticism, interest in the role of *nutrition and diet* in the cause and treatment of neurologic disorders has expanded, including folate deficiency and spina bifida, and the ketogenic diet in the treatment of epilepsy.

#### **CHALLENGES FOR THE 21ST CENTURY** include the following:

- neurogenetics and studies of the genetic heterogeneity of the epilepsies and febrile seizures, and specific gene replacement and neuropharmacological treatments in epilepsy;
- the cause of ADHD, neurotransmitter analyses, dopamine transporter genes and MPH response, and development of more specific therapies;
- the early recognition, pathogenesis, and prevention of learning disabilities, including dyslexia;
- the role of gene regulators and mutant analysis in the investigation of neural development and prevention of cerebral and spinal cord anomalies;
- genetic screening and gene therapy of neuromuscular diseases and ethical considerations;
- advances in treatment of neonatal asphyxia, neonatal seizures, and birth injuries;
- advances in neuroimmunology and chemotherapy in brain tumors;
- DNA targetting and molecular studies of drug resistant organisms, and advances in antibiotic therapy for drug resistant CNS infections and new antiviral agents;
- Pathogenesis of degenerative, metabolic, and demyelinating diseases, and their treatment;
- Collaboration with colleagues in radiology and electrophysiology, advancing the use of neuroimaging, PET, and EEG in diagnosis and management of neurologic disease;
- Recognition of toxic and nutritional disorders of the nervous system, and the role of dietary factors in therapy.

To meet these challenges and achieve these goals, the pediatric neurologist must be trained as a scientist as well as a clinician. Training program directors should encourage fellows with a demonstrated aptitude and motivation in laboratory research. The National Institutes of Health, politicians, and hospital administrators need to provide necessary monies from budget surpluses or through industrial collaboration, allowing residents and young clinicians the time and facilities to pursue projects of research. University Children's Hospitals should be located in close proximity to or within the university complex, permitting frequent discourse and communication of clinician with basic scientist. Time expended in travel between hospital and outlying suburban clinics or the university center is counter-productive. While quantity may be augmented, quality in the standard of service to the patient may be diminished. At this time of escalating health care costs, the realization of these proposals and ideals may appear impractical but, nonetheless, essential, if advances in pediatric neurosciences and "freedom from imperfections" in our patients are to be achieved in the 21st century. *J. G. Millichap, M.D., Editor.*

COMMENT. My readers and colleagues will have additional and alternative views regarding reasons for celebration of our past accomplishments and challenges for the future. The above comments and views are meant as a basis for further discussion of the pediatric neurologist's role in the year 2000 and beyond.

Special millennium articles written by invited distinguished colleagues in adult neurology are presented by the editors of the Archives of Neurology Jan 2000;57;50-64. Among eighteen presentations, the views and opinions of the pediatric neurologist are sadly lacking. It appears that pediatric neurology, after 50 years progress and development, is still not fully accepted as an equal partner in the neurosciences.

## NEUROBEHAVIORAL DISORDERS

### STIMULANTS VS BEHAVIOR THERAPY IN ADHD

A 14-month randomized clinical trial in 579 children, aged 7 to 9.9 years, with ADHD Combined type, compared the effects of four different treatment programs (Multimodal Treatment Study). This cooperative study was performed by 6 independent research teams in collaboration with the National Institutes of Mental Health, and the Office of Special Education, Washington, DC. Treatment assignments were *medication alone, psychosocial behavior therapy, combined medication and behavior therapy, and community care*. Assessments analysed were ADHD symptoms, oppositional/aggressive symptoms, social skills, internalizing symptoms (anxiety and depression), parent-child relations, and academic achievement in reading, math, and spelling. Behavioral treatment included parent and child training, and school-based intervention. Medication management was methylphenidate (MPH), 28-day, double-blind, daily-switch titration, using 5 repeats of placebo, 5, 10, and 15 or 20 mg t.i.d. The optimal dose of MPH for each subject (average, 38 mg/d) was used in subsequent treatment of 73% of 289, and an alternative drug (dextroamphetamine (10%), pemoline (1%) etc) was prescribed in the remaining patients who failed to respond to MPH.

All 4 groups showed reductions in symptoms of variable degrees during the course of the study. Medication and combined treatment were significantly superior to behavioral treatment and community care in controlling ADHD symptoms. Combined behavioral and stimulant treatment was not superior to medication alone for core ADHD symptoms, but had modest benefits in treating non-ADHD symptoms (ODD etc). Short-term benefits from MPH therapy persist