## ETHICS OF GENETIC COUNSELING IN EPILEPSY

The ethical issues raised by families involved with epilepsy are reviewed from the Faculty of Medicine and Research Centre for Public Law, Universite de Montreal, Canada; and the Foundation for Genetic Medicine, Reston, MD. The mode of inheritance in most cases of epilepsy is complex, with genetic heterogeneity and variable expression. The clinical uses of genetic testing include medical management, diagnosis, prevention, and determination of risk to future children in family planning. Genetic research facilitates the recognition of new epilepsy syndromes and the development of new antiepileptic drugs. From an ethical viewpoint, the potential benefits of diagnosis and treatment must be weighed against the potential harm of genetic labeling. Genetic testing should be performed only if it promotes the wellbeing of the individual. The risks of guilt, blame, stigmatization, and discrimination emphasize the need for further research on the ethical issues raised by genetic testing. Genetic counselors must advise patients and families of the economic and social risks of participating in genetic research and genetic testing. The multifactorial nature of epilepsy etiology and our limited understanding of the disorder can foster misinterpretation of the genetic findings by insurers and employers and lead to unwanted financial and emotional hardships. (Godard B, Cardianal G. Ethical implications in genetic counseling and family studies of the epilepsies. **Epilepsy & Behav** 2004;5:621-626). (Respond: E-mail: Beatrice.godard@umontreal.ca).

COMENT. The recommended approach to genetic counseling concerning epilepsy is a case-by-case determination of the benefit and harm of testing and the need to protect the individual privacy and wellbeing.

**ANKH gene, autosomal dominant early childhood seizures and chondrocalcinosis.** ANKH is added to the list of genes involved in idiopathic seizure disorders, in a report from Belfast City Hospital; Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire; and City Hospital, Nottingham, UK. All members of an English family affected with chondrocalcinosis (CCAL) experienced seizures in early childhood, usually febrile seizures, and they developed recurrent attacks of arthritis and synovitis as adults. A mutation within the ANKH gene on chromosome 5p is associated with CCAL and can predispose to genetic epilepsy and febrile seizures. The seizures are usually benign and resolve by 2 to 4 years of age without neurologic sequelae. The seizure syndrome with CCAL and ANKH gene mutation resembles generalized epilepsy with febrile seizures plus (GEFS+), except that none had seizures after 4 years. ANKH codes for a transmembrane protein involved in regulation of extracellular pyrophosphate ion levels. (McKee S et al. **Epilepsia** 2004;45:1258-1260).

## EPILEPSY SURGERY FOR TUBEROUS SCLEROSIS

The surgical amenability of epileptogenic lesions in tuberous sclerosis complex is reviewed in the light of novel presurgical assessment in a report by investigators at University of Rome, Italy; Stanford University, Palo Alto, CA; and Central Illinois Neurohealth Sciences, Bloomington, IL, USA. In carefully selected patients, neurosurgical

resection of the epileptogenic tubers and epileptogenic foci is successful in the control of seizures in 78% (range 43-100%), and results in reduction of seizure frequency in 20% (10-45%). Quality of life is improved in 95% as a result of seizure control or reduction in medication. Accurate presurgical testing is essential and involves surface video-electroencephalogram, MRI, positron emission tomography, single-photon emission computed tomography, magnetoencephalography, and invasive EEG monitoring. Early detection and resection of medically refractory epileptogenic tubers can prevent deterioration of cognitive functioning, improve behavior and socialization, and offer a better qualiy of life. (Romanelli P, Verdecchia M, Rodas R, et al. Epilepsy surgery for tuberous sclerosis. **Pediatr Neurol** 2004;31:239-247). (Respond: Dr Paolo Curatolo, Pediatric Neurology, University of Rome "Tor Vergata,"V le Oxford 81, 00133, Rome, Italy).

COMMENT. Early effective seizure control may significantly reduce the adverse effects on cognition and development associated with refractory recurrent seizures in tuberous sclerosis. With new presurgical investigative techniques, it is now possible to select patients who may be amenable to resection of multiple epileptogenic tubers. In patients not suitable for resection, anterior callosotomy, vagal nerve stimulation, and radiosurgery are alternative methods suggested.

## RISK-BENEFITS OF OXCARBAZEPINE VS CARBAMAZEPINE

The clinical differences between oxcarbazepine (OXC) and carbamazepine (CBZ) are reviewed in terms of efficacy, tolerability, and interaction with other drugs in a study at Universitat Bonn, Berlin, Germany. OXC (Trileptal) is used as monotherapy or adjunctive therapy for the treatment of partial seizures with or without secondary generalization in adults and children above 4 years (USA) or 6 years (Europe) of age. The mechanism of action of OXC resembles CBZ in involving sodium channel blockade; it differs in the type of calcium channel modulation. OXC metabolizes by reduction to the monohydroxy derivative (MHD) and is excreted in the urine after conjugation as a glucuronide, with no autoinduction. CBZ is oxidized to 10, 11-epoxide and is hydrolyzed in the liver. Hepatic metabolism of OXC and enzyme induction are minimal, so that drug combinations show little interaction. OXC is better tolerated and its risk-benefits are superior to CBZ. It causes fewer skin rashes than CBZ; rashes occurred in 3% of patients taking OXC compared to 7% of those treated with CBZ. Cross-reactions may occur, and in patients with known hypersensitivity to CBZ, therapy with OXC should be avoided. The efficacy of oral contraceptives may be impaired by OXC, and risks of teratogenicity remain to be determined. Hyponatremia (<135mEq/L) has occurred more frequently with OXC (30/104 patients, 29%) than with CBZ (69/479 patients, 14.4%). Clinically significant hyponatremia (<125mmol/L) occurred in 2.7% of adults with previously normal values; it is less common in children (0.2%). (Schmidt D, Elger CE. What is the evidence that oxcarbazepine and carbamazepine are distinctly different antiepileptic drugs? **Epilepsy & Behav** 2004;5:627-635). (Respond: E-mail: dbschmidt@t-online.de).

COMMENT. The authors recommend OXC as preferable to CBZ because of proven efficacy and lower incidence of side effects. In a multicenter, randomized, double-blind, parallel group trial of 62 newly diagnosed children ages 5 to 17, OXC (Trileptal) in a mean