COMMENT. Variants in the *CACNA1H* gene are associated with a range of generalized epilepsy syndromes, but additional genes or environmental factors also may influence epilepsy susceptibility in some individuals. These genetic variants can contribute to a risk of epilepsy but are not themselves the cause. (Lowenstein D, Messing R. Editorial. **Ann Neurol** Dec 2007;62:549-551).

## ATTENTION DEFICIT DISORDERS

### CONTROLLED STUDY OF GUANFACINE XR IN ADHD

A multicenter, double-blind, placebo-controlled, fixed-dosage escalation study of an extended release formulation of guanfacine is reported from the Massachusetts General Hospital, Boston, and other centers in the US and UK. A total of 345 patients aged 6-17 years were randomly assigned to 1 of 3 guanfacine dosage groups (2, 3, or 4 mg/each AM) or placebo for 8 weeks. All groups of children taking guanfacine showed significant improvement in hyperactivity/impulsivity and inattentiveness subscales of the ADHD Rating Scale IV, Clinical Global Impression, Parent's Global Assessment, and Conners' Parent and Teacher Rating Scales-Revised. Adverse events included headache, somnolence, fatigue, abdominal pain, and sedation. Treatment was discontinued because of somnolence in 4.2%, sedation in 3.5%, and headache in 1.5%. Somnolence occurred in 15.8-27.6% patients with doses of 0.04-0.12 mg/kg. Blood pressure and pulse rate decreased as dosages were increased, by a maximum of -10.1 mm Hg (week 4) and -8 bpm (week 4). Mean changes in ECG (PR and QRS intervals) were unremarkable, mean changes in QTcF intervals were 3.7-9.1 msec (dose related), and no patient had a QT interval =/> 480 msec. Seven discontinued treatment because of ECG abnormalities, 4 because of QTc interval prolongation, one in each treatment group. Mean changes in height and weight were unremarkable, and group and individual cortisol and human growth hormone levels showed no excessive suppression or elevation. Guanfacine XR was considered safe and effective compared with placebo. (Biederman J, Melmed RD, Patel A, et al. A randomized, double-blind, placebo-controlled study of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. **Pediatrics** January 2008;121:e73-e84). (Respond: Joseph Biederman MD, Pediatric Psychopharmacology, Yawkey Center, Suite 6A, Massachusetts General Hospital, Boston, MA 02114).

COMMENT. Guanfacine is considered a more selective a2-adrenoceptor agonist than clonidine, binding preferentially to receptors in the prefrontal cortex. It has a longer plasma half-life and is less sedating and less hypotensive. The extended release formulation of guanfacine appears to be superior to the immediate release, and is effective in a once daily dosage. In practice, guanfacine XR may be superior to stimulant medications in the younger child with hyperactive behavior and ODD, but the sedative side effect can be troublesome in children of school age. Pretreatment cardiac evaluation with ECG and regular cardiac monitoring are advisable. The potential increase in risk of cardiac complications should limit or discourage the use of a combination of stimulant medication and clonidine or guanfacine.