

Methylphenidate significantly reduces lapses of attention during on-road highway driving in patients with ADHD. *J Clin Psychopharmacol* 2014 Jun 27. [Epub ahead of print]).

COMMENTARY. ADHD young adults are twice as likely to be cited for unlawful speeding and have more crashes and more accidents involving bodily injury, when compared to non-ADHD adult control subjects. These findings support a need for continued treatment of ADHD into adolescence and adulthood. Improvement of driving performance of adolescent drivers with ADHD was demonstrated using a driving simulator while taking Concerta compared to placebo [1] or immediate-release MPH [2].

#### References.

1. Cox DJ, et al. *Pediatrics*. 2006 Sep;118(3):e704-10.
2. Cox DJ, et al. *J Am Acad Child Adolesc Psychiatry*. 2004 Mar;43(3):269-75.

### **GUANFACINE EXTENDED RELEASE IN ADHD**

Investigators at Massachusetts General Hospital, Boston, MA, performed a multicenter, 9-week, double-blind, placebo-controlled, dose-optimization study of guanfacine extended release (GXR, <4 mg/d) adjunctive to a long-acting psychostimulant for ADHD continued in 461 subjects. Patients were randomized to receive GXR in the morning (GXR AM), GXR in the evening (GXR PM), or placebo.

GXR treatment groups showed significantly greater improvement from baseline compared with placebo plus psychostimulant. Small mean decreases in pulse, systolic, and diastolic blood pressure were observed in GXR treatment groups. Morning or evening GXR administered adjunctively to a psychostimulant showed significantly greater improvement and generated no new safety signals. (Wilens TE, et al. A controlled trial of extended-release guanfacine and psychostimulants for attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2012;51(1):74-85).

COMMENTARY. A similar randomized, double-blind trial of guanfacine extended release (Intuniv) administered either in the morning ((n=107) or evening (n=114) was associated with significant improvements in ADHD symptoms. Once-daily GXR monotherapy is effective, administered AM or PM [1]. The rapid-release guanfacine (Tenex) is often prescribed as an alternative to Intuniv because of cost and insurance denial. Tenex is often effective in the hyperactive/ADHD younger child with sleep disorder or tics, but drowsiness during the day may lessen the ability to focus in school. The effect of Intuniv on school performance and grades requires further study.

#### References.

1. Newcorn JH, et al. *J Am Acad Child Adolesc Psychiatry*. 2013 Sep;52(9):921-30.

### **ADVERSE EFFECTS OF MEDICATIONS FOR ADHD**

#### **CARDIAC AUTONOMIC DYSFUNCTION AND STIMULANT THERAPY**

Investigators at University of Minnesota, Minneapolis, report cardiac autonomic dysfunction and arterial stiffness among children and adolescents with ADHD treated

with stimulants. Compared with controls, ADHD patients had greater resting systolic BP, diastolic BP, and increased sympathetic tone. (Kelly AS, et al. **J Pediatr** 2014 Jul 8).

COMMENTARY. Variable pediatrician attitudes and cardiac screening practices prior to stimulant treatment of ADHD among US-based pediatricians reflect the limited evidence base and conflicting guidelines. In a survey of randomly selected US pediatricians with AAP membership, 25% agreed that the risk of sudden cardiac death (SCD) and 30% that legal liability were sufficiently high to warrant cardiac assessment; 75% agreed that physicians were responsible for informing families about SCD risk; 71% recognized interpreting a pediatric ECG as a barrier; 93% completed a routine H & P; 48% completed an in-depth cardiac H & P; 15% ordered an ECG; and 46% discussed stimulant-related cardiac risks [1].

Several factors influence the risks and cardiac screening practices, including: a cardiac murmur, the patient's sports activities, and an ECG with modifications of uncertain significance. We refer to a cardiologist for an opinion a child with a murmur, especially if engaged in strenuous sports activities, and an ECG abnormality of uncertain significance. Patients with a structural heart defect or prolonged QT interval are excluded from drug therapy for ADHD and are offered behavioral and alternative therapies.

#### References.

1. Leslie LK, et al. *Pediatrics*. 2012 Feb;129(2):222-30.

### PRIAPISM WITH MEDICATION FOR ADHD

Investigators at Auburn University, Huntsville, AL, and other centers, reviewed reports in the literature (1966-May 15, 2014) of priapism associated with methylphenidate (MPH), amphetamines, and atomoxetine used in treatment of ADHD. MPH is implicated in a recent FDA safety announcement warning as a result of 15 case reports (mean age 12.5 years). Prolonged erections and priapism occurred with immediate- and long-acting products, dose increases, and drug withdrawal periods. Priapism also occurred in 4 patients taking amphetamines and one 11-year-old patient taking atomoxetine for ADHD. Discontinuation is warranted if this adverse drug reaction occurs. (Eiland LS, Bell EA, Erramouspe J. **Ann Pharmacother** 2014 Jun 30).

COMMENTARY. Priapism is a painful, prolonged erection that does not return to a flaccid state within four hours, despite the absence of both physical and psychological sexual stimulation. The duration time of an erection to be called priapism is controversial and some classify priapism as 6 hours. Priapism is a medical emergency that should be treated in the ED. Based on my experience in treating children with ADHD, this adverse effect must be very rare and may not warrant special mention in counseling a young child with parents at the initiation of treatment. Referral of parents to the modified drug package insert should be sufficient warning.

Other drugs known to cause priapism rarely include sodium valproate [1] and risperidone [2], cited as single case-reports in the literature.

#### References.

1. Bansal S, Gupta SK. *Indian J Pharmacol*. 2013 Nov-Dec;45(6):629-30.
2. Paklet L, et al. *Ther Adv Psychopharmacol*. 2013 Feb;3(1):3-13.