New York — Options are available for children with attention-deficit hyperactivity disorder who do not respond to treatment with stimulants or are troubled by side effects, but they must be chosen and used carefully, Laurence L. Greenhill, M.D., said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

First the diagnosis should be reviewed, as many conditions that will not respond to stimulants can overlap or mimic ADHD. These include oppositional defiant disorder, anxiety disorders, depression, occasionally bipolar disorder, and psychotic conditions.

“And don’t forget substance abuse disorder, which is a pretty good neutralizer of some stimulant treatments,” Dr. Greenhill said. Dr. Greenhill, who is professor of clinical psychiatry at Columbia University, New York, and director of research for the pediatric psychopharmacology unit at the New York State Psychiatric Institute.

The preferred second-line drug is atomoxetine (Strattera), a nonstimulant, highly specific norepinephrine reuptake inhibitor. This is not a controlled substance, so it is also useful for parents who are uncomfortable giving their child a schedule II drug, he said.

As a 24-hour drug, atomoxetine significantly improves behavior and activities in both evening and early morning.

“The most important thing you can do for your patients is to start this drug slowly and give it twice a day when you are titrating it,” Dr. Greenhill said. Patients are much less likely to experience severe somnolence if the drug is titrated over a week, despite the fact that the labeling says upward titration to a full dose of 1.2 mg/kg per day can begin after 3 days on the initial dose of 0.5 mg/kg per day.

If the full dose is given rapidly, there is a good chance that a formerly disruptive ADHD child will fall asleep in class. “As much as that might be a refreshing change for a teacher who’s been battling the noise, nothing gets a parent out of work faster than the school nurse calling and saying, ‘We can’t keep your son awake—come and get him.’ That only has to happen once and the parents will stop the atomoxetine really fast, because they’ve never had this problem before,” Dr. Greenhill said.

Third-line treatments include the α2 agonists and bupropion. Clonidine (Catapres) may be useful in treating very hypertensive or aggressive patients, but it may take several weeks to take effect and does not improve inattention symptoms. There also are risks of cardiovascular adverse effects, depression, and decreased glucose tolerance.

Guanfacine (Tenex) is a longer-acting α2 agonist that has a more favorable side effect profile than clonidine, but it has been studied only in open trials. Studies of this drug in primates suggest that it acts more on postsynaptic α2 receptors in the prefrontal cortex than in the brainstem where clonidine works. This may prove helpful, but there’s much more work to be done, Dr. Greenhill said.

Bupropion may be useful for comorbidities and is not a controlled substance, but the effect size of this drug appears to be limited. Adverse effects include irritability, insomnia, and tics.

The usual effective dose is about 300 mg/day, but seizures can result if the dose exceeds 450 mg/day. “So make sure the patient hasn’t been prescribed Zyban, the other form of bupropion, for smoking cessation,” he said.

Dr. Greenhill disclosed that he has relationships with several manufacturers of drugs used to treat ADHD, including Eli Lilly & Co., the manufacturer of atomoxetine.

AdHD Stimulants: No Link to Propensity for Later Drug Abuse

BY DOUG BRUNK
San Diego Bureau

YOSEMITE, CALIF. — Will my child become a dope fiend?

That’s a common question Robert S. McKevey, M.D., fielded from parents of children who are prescribed a class II stimulant for attention-deficit hyperactivity disorder (ADHD).

“The answer is no,” Dr. McKevey said at a pediatric conference sponsored by Symma Medicus. “The risk of kids who have properly diagnosed ADHD taking stimulants and becoming dope fiends is no different than if you had ADHD. The kids at risk are those who have ADHD” and are not on a prescribed drug treatment.

“Nonstimulant medications are an option for antisocial teens with ADHD, although, at least in my view, they’re not as effective as stimulants,” noted Dr. McKevey, director of child and adolescent psychiatry at Oregon Health and Science University, Portland.

“Nonstimulant choices include atomoxetine, bupropion, clonidine, guanfacine, and the tricyclic antidepressants imipramine and nortriptyline.

Another question he commonly fields from parents is the effect of stimulants on children who have a chronic tic disorder such as Tourette’s syndrome. “When I was in training, if you had tics, you had a history of tics, or even a family history of tics, we didn’t start you on stimulant medication,” he said.

“Now there are a couple of studies that show that if you have tics and you take stimulants, it’s probably OK as long as the tics don’t worsen. In many cases, the tics seem to decrease in severity.”

Drug preparations in the stimulant class are derived from methylphenidate or dextroamphetamine. Methylphenidate is more widely used in the United States, but Dr. McKevey noted that both agents are equally effective.

You can’t yet predict response, but it’s possible that pharmacogenetics studies will give us a hand on that,” he said. “If one of them doesn’t work, you try the other.”

A key point to remember about both agents is that they have very short half-lives. “Maximal benefit on behavior can occur 1-2 hours for agents derived from methylphenidate and 3-4 hours for agents derived from dextroamphetamine.”

The sustained-release formulations appear to be as effective as the standard short-term formulations. The doses vary with the individual. There is some thought that academic performance (such as that associated with inattention) may respond to a lower dose than does restlessness and impulsivity, he said.

New, long-acting preparations are available once-daily dosing. These include Concerta, Metadate CD, Adderall XR, Methyldopa, Patch, and Focalin.

The most common adverse effect of stimulants is decreased appetite, which occurs in about 80% of children who take them. “The decreased appetite and weight loss can be stunning in some kids,” he remarked. “I’ve seen some very skeletal looking little boys, and it can make you quite nervous.”

Long-term stimulant use may result in a 1-cm decrease in height per year during the first 3 years of use, “but some of that is caught up,” Dr. McKevey said. “More recent studies suggest there is perhaps a 1-cm decrease [in height] overall if you take stimulants long term.”

Insomnia is another common side effect, “so you tend to give it earlier in the day. You have to monitor heart and blood pressure. The things you’re monitoring are height, weight, and blood pressure. It’s pretty straightforward, but yearly, I usually check the white blood cell count,” he said.

He also warned against unproven thera- O...