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ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) MEDICATION: A GROWING LIST OF CHOICES

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Attention-Deficit Hyperactivity Disorder (ADHD) Medication: A Growing List of Choices*

by [Ernest J. Bordini, Ph.D.](#)
 Clinical Psychology Associates of North Central Florida
 2121 NW 40th Terrace Suite B Gainesville FL 32605
 (352) 336 - 2888



CPANCE.COM
 2121 NW 40th Terrace Suite B Gainesville FL 32605
 (352) 336 - 2888

and Abimbola Farinde, PharmD., MS (Walden University, Minneapolis, MN)
Controversy about ADHD and medication becomes a renewed conversation in many families. Television and internet marketing promotes medicine for child and adult ADHD, and the evening news raises warnings about medication recalls and concern about ADHD medication overprescription. There will always be those opposed to any psychoactive medication for children and there will always be those who see a pill as a solution for everything. This article hopes to provide some basic information about the diagnosis of ADHD and the role of medication in treatment. This article discusses the role of stimulant medication, older and newer FDA-approved ADHD medication, as well as a brief review of some medications which are more rarely used for ADHD.

Attention-deficit Hyperactivity Disorder (ADHD) is not a new diagnosis. It was referred to as hyperkinesis, minimal brain damage, and Attention-deficit Disorder (ADD) with and without hyperactivity in the past. The current nomenclature

consists of ADHD predominantly hyperactive-impulsive type, predominantly inattentive type, and combined type. It is the most common neurodevelopmental psychiatric disorder. Males are diagnosed more frequently than females, and scientists agree that there is a genetic component in many cases. The primary symptoms are high levels of overactivity, difficulty sustaining attention, difficulty completing tasks such as homework, and disorganization. These must rise to the level in which they are problematic relative to age peers and result in difficulties in functioning. The symptoms need to be present since childhood.

Since there are no symptoms of ADHD that are unique to ADHD and the main question is "Are the problems unusual for age and ability?" it is easy to over-diagnose or under-diagnose the disorder. Since the disorder is one that persists into adulthood, diagnosis has serious implications for school, current and future medical insurance costs, and involves consideration of possible long-term medication. In addition other disorders such as handwriting difficulties, other behavior and mood difficulties often co-exist. Clearly, this diagnosis warrants careful psychodiagnostic evaluation. More information about symptoms and assessment is available at ADHDASSESSMENT.COM, CPANCF.COM and CHADD.ORG.

The National Institute of Mental Health conducted large study, called the Multimodal Treatment Study of Children with ADHD, involved close to 600 children with ADHD treated for a 14-month period. Children who were treated with medication, alone, and children who received both medication management and behavioral treatment had the best outcomes with respect to improvement of AD/HD symptoms. Combination treatment provided the best results with respect to ADHD and other areas of functioning (Swanson et. al., 2001).

While some children may get by with accommodations, many have sufficiently severe difficulties that they will require medication. Fortunately, studies are generally consistent with the American Academy of Pediatrics findings that 70-80% of children respond positively to medication. However, it also emphasizes use of behavior therapy such as parent training and group sessions. The American Academy of Child & Adolescent Psychiatry (1999) has historically emphasized that psychiatric medication should not be used alone for ADHD or other conditions. It states that medication should be part of a more comprehensive approach and treatment plan that usually includes psychotherapy as well as parent training or involvement in the therapy.



STIMULANT MEDICATIONS

By far the most frequently prescribed medications for ADHD in children are the psychostimulant medications. This is not new. Stimulant medications were first administered to children with behavior and learning problems in the late 1930's. At first it was thought that the stimulants had a paradoxical effect, calming hyperactive children.

We now understand that stimulant medication increase certain neurotransmitters which act to improve the brain's ability to inhibit and control behavior and the ability to focus and shift attention. Stimulants increase the brain's neurotransmitter levels of dopamine, norepinephrine, and serotonin, usually on a short-term basis (3-5 hours). Higher levels of dopamine are believed to reduce hyperactivity, while an increase in norepinephrine improves attention.

I often use the analogy of adding steering and brake fluid to an automobile. All the parts may be there, but adding the fluids, if they are low, makes stopping, starting and staying on the right road much easier than if the levels are critically low.

Medications will not make a child a perfect child, make them do anything they don't want to do, or allow them to accomplish things they do not have the abilities to do. Quality assessment is critical for establishing appropriate expectations. Parent training and [child therapy](#) are critical for dealing with motivational or behavioral issues.

There are eight decades of research and clinical experience which have demonstrated stimulants are generally safe and effective as prescribed. Studies have demonstrated reduced levels of out-of-seat behaviors, improved on-task performance, reduced distractibility, fewer spelling and math errors, and even improved handwriting. What time has developed is a large variety of stimulants with slow release forms, and new non-stimulant medications.

Though a slow-release stimulant (Ritalin SR) had been around for some time, it was reported to be somewhat unpredictable in terms of duration, and did not become as popular as the newer slow-release stimulant preparations. Some of these newer medications are quite sophisticated in terms of their release mechanisms. Some can allow for an immediate dose, and a second release in 3-4 hours.

An older medication, Cylert (magnesium pemoline) was available since around 1975 as a frequent alternative stimulant medication to shorter-acting medication and was often used in ADHD children who developed tics with other stimulants. It is structurally dissimilar to the amphetamines and methylphenidate stimulants discussed below. It often did not produce a therapeutic effect for 3-4 weeks. Since regular blood work is necessary due to more serious risks of liver failure and sometimes high blood pressure, this is now rarely used and

never became as popular as the current long-acting stimulant medication. Some reported of liver failure and limited use likely caused the manufacturer to discontinue Cylert in 2005, but it is available under its generic name, pemoline.

It is important to note that despite the multitude of stimulant medications, the American Academy of Pediatrics has found that each stimulant improved core symptoms equally. Thus, the differences between these medications largely involve absorption rates which affect blood levels that are important to the type of effect the stimulants have and affect how long the medication lasts.

Longer acting medications avoid the necessity to be called out of class for medication during the school day. Longer-acting stimulants may also help with completion of homework after school. In some cases a child is switched to a longer-acting stimulant to reduce some of the side effects such as afternoon irritability resulting from more rapid decreases in the stimulant blood level from short-acting doses. The trend toward the use of longer acting medication for ADHD is also probably partially due to increased awareness that problems in impulsiveness, inattention, hyperactivity impact on peer and family relationships as well as extracurricular activities.

Clinical use of the longer-acting stimulants have led some to report that individual duration of the effective response can vary from the duration which the medications are designed for. Thus, in the accompanying table in this article a range is given.

Stimulant and other medications sometimes do have side effects, though opponents to psychoactive medication for children often make wild claims. Stimulants do reduce appetite and therefore some weight loss or failure to gain an expected amount of weight can be seen if care is not taken to provide a good breakfast before the morning dose and sometimes shift meals to a later time. Also, research has shown that children generally regain growth when off these medications.

The second most common misconception is that stimulants turn children into “zombies”. Proper doses of medication increase concentration, decrease hyperactivity and seem to exert a calming effect, sleepiness or unresponsiveness is not typical unless the child is greatly over-medicated. When discussing side effects, it is important to understand all medication have side effects -just take a look at the side effects for aspirin or Tylenol. As with any medication, a small number of children can show unusual reactions, but since the medication is relatively short-acting these are usually short-lived. Other side-effects such as headaches and irritability usually disappear after a week or two. Sleep onset difficulties can occur if the medication is taken too

late in the day or lasts too long, but with properly scheduled dosing this should not be a problem.

Some physicians were reluctant to prescribe stimulants in individuals who tended to be anxious, since the stimulants increase physiological arousal. Clinical experience has largely found this to be only true for more severe anxiety disorders, and mild levels of anxiety usually do not contra-indicate stimulant use if an accurate diagnosis of ADHD is made. As co-existing disorders may influence which medication may be selected for treatment, it is important to perform a comprehensive assessment.

A final misconception is that children treated with stimulant medication will become addicted or will abuse other drugs later in life. Many of these medications can be abused, so close monitoring is required. However, follow-up studies generally indicate this is not true, and some studies find untreated children are more likely to abuse drugs in later life. It is likely that children with ADHD and who also show oppositional or conduct problems constitute a high-risk group for drug abuse as well as other illegal and destructive behaviors in later adolescence and adulthood. This highlights the importance of parent training to reduce oppositional behavior as early as possible to prevent evolution into more serious conduct problems which can be quite difficult to treat.

Common Stimulant Medication Used to Treat ADHD

Common Stimulant Side Effects

-appetite reduction
-headaches
-stomach aches
-trouble getting to sleep
-restlessness or irritability
- drowsiness or excessive staring (rare)
-tics (involuntary motor movements; rarely chronic; sometimes temporary)
- hallucinations or bizarre behavior (rare)
Other than Cylert, described previously, there are two general classes of stimulant medications, amphetamine stimulants and methylphenidate stimulants.

Amphetamine Stimulants

• Adderall (dextroamphetamine & levoamphetamine); ages



3+; duration 3.5 - 8 hrs

- ε *Adderall XR; ages 6+; duration 8-10 hrs; initial release 1 hrs with additional release 3-4 hrs; introduced*
- ε *Canada has withdrawn approval of Adderall due to concerns about reports of heart problems and sudden deaths. It remains approved in the U.S. and unlikely will be subject to closer scrutiny for these complications.*
- ε *Dexedrine (dextroamphetamine sulfate, Dextrostat) Ages 3+ Duration 4-5 hr Onset 20-30 min. introduced in 1950s*
- ε *Dexedrine Spanules, Ages 3+, Duration 6-12 hrs, somewhat variable duration, initial release 1 hr and 2nd release in 3-4 hrs*
- ε *Vyvanse (Lisdexamfetamine): age 6+, half-life ~ 1 hour, time to peak effect ~ 1 hr.*

Methylphenidate Stimulants:

- ε *Ritalin (methylphenidate); Ages 6+; Duration 4 hrs; Onset of action 15-20 min, introduced in the 1950s*
- ε *Ritalin SR (methylphenidate); Ages 6+; Duration 3-6 hrs; duration reported to vary greatly*
- ε *Ritalin LA (methylphenidate); duration 8 hrs; 1/2 released initially and 1/2 in 4 hrs*
- ε *Daytrana (methylphenidate); Ages 6+; half-life elimination: d-methylphenidate: 3-6 hours, L-methylphenidate: 1-3 hours*
- ε *Focalin (dexmethylphenidate) Short-acting, duration 4-6 hours*
- ε *Quillivant XR (methylphenidate): Ages 6+; early peak (~1 Hour) with high fat meal*
- ε *Methylin Chewable Tablet and Oral Solution (another form of methylphenidate)*
- ε *Methylin ER; extended release form introduced 2000*
- ε *Concerta (methylphenidate); ages 6+; duration 10-12 hours; introduced 2000*
- ε *Metadate ER (methylphenidate); duration 8 hrs; has two peaks; introduced 2000*
- ε *Metadate CD (methylphenidate); smoother curve than CD; introduced in 2001*
- ε *Focalin (dextro-methylphenidate hydrochloride); more potent than levo-methylphenidate and twice as potent as methylphenidate.*

ANTIDEPRESSANT MEDICATION

There are a number of classes of antidepressant medications, each with different side-effect profiles, advantages and disadvantages. The FDA advises that adults, teens, and children who take antidepressants should be closely watched for warning signs of suicide. It adds that it does not recommend that people stop using these medicines.

Tricyclic Antidepressants

Tricyclic antidepressants were long known to be effective for treating depression, also by increasing neurotransmitter levels. These were also often used, though not necessarily FDA-approved for an alternative means of treating ADHD children who developed tics, could not otherwise tolerate stimulants, who may have some co-existing problems such as insomnia, bedwetting, depression, or anxiety, or whose parents feared Ritalin might turn their children into the dreaded "green zombie". However, these medications were more inherently dangerous than the stimulants since overdose raised serious issues of cardiac arrest.

Though many children were safely treated, a small number of cardiac-related deaths were reported, some of which involved children who had cardiac problems. This, combined with safer new antidepressants, the Selective Serotonin Re-uptake Inhibitors (SSRI's) such as Prozac, greatly reduced the use of these medications in children.

Even many current medicines approved for the treatment of ADHD come with an FDA warning about possible heart-related or mental health problems. Events have been rare, but it continues to be important to inform your physician about any family history of high blood pressure or heart disease, and of course any history of such in your child.

Common tricyclic antidepressants included imipramine, desipramine, amitriptyline, nortriptyline (also marketed as Pamelor and Aventyl) and Clomipramine. Side effects were lowered blood pressure, irregular or rapid heartbeat, fatigue, stomach upset, dizziness, dry mouth, with some medication sleep difficulties, and rarely confusion and seizures. Abruptly stopping the medication could result in increased blood pressure, agitation and sleeplessness.

Selective Serotonin Re-uptake Inhibitors (SSRIs)

The popularity of the tricyclic antidepressants began to wane with the introduction of medications such as Prozac (fluoxetine) which were effective in more selectively targeting Serotonin, the SSRIs. These have not been FDA approved for ADHD, and like the tricyclics, probably were less effective at treating some of the core symptoms of inattention and hyperactivity than the stimulants.

Common SSRI side effects are constipation or diarrhea, sometimes nausea, headaches or dizziness, and in adults and late adolescents, sexual side effects could occur. Sleep is sometimes improved, but the more activating SSRIs are sometimes associated with sleep onset difficulties. These generally may take 3-5 weeks to reach full effect, and are sometimes started with a low dose to reduce the initial side effects. The effects of the medication are long-term. At first it

was thought that rapid discontinuation of these was far less problematic than the older antidepressants, but similar reactions have been reported especially for the SSRIs which have a shorter half-life.

Not all of the SSRI's are alike, some tend to be more activating and some tend to be more sedating. For example Effexor (venlafaxine) has effects on both serotonin and norepinephrine. Serotonin is believed, among other things, to have an important role in depression. Use of these medications as second-line medications for treating ADHD began as the popularity of tricyclic antidepressant use for children waned. More recently there have been some warnings concerning use of Paxil or Zoloft with children. Along with the tricyclic medications, not all have been FDA approved for children or adolescents. Refer to the [CPANCF.COM Articles and Archives section](#) for a more detailed discussion of the controversy about [antidepressant use in children](#).

Atypical Antidepressants:

Wellbutrin (bupropion hydrochloride) stimulates dopamine, but may be less effective than stimulants with respect to core ADHD inattentive symptoms. It has been FDA approved for treatment of depression and to help stop cigarette smoking (also marketed as Zyban). It is relatively short-acting from 4-6 hours, with longer acting forms available which may last 6-8 hours. Though not FDA approved for ADHD or children under 18, use of Wellbutrin became popular for treatment of adolescent and adult ADHD since it was not a controlled substance and tended to be of some help with mood problems. Common side effects include insomnia and headaches.

Anti-Hypertensive medication:

Another alternative to stimulants evolved with the use of medication that was traditionally used to lower blood pressure, the anti-hypertensive medication. This class of drugs can be very dangerous if there is an overdose, due to the effect on the cardiovascular system.

Catapres, Kapvay (clonidine), which blocks norepinephrine auto-receptors probably became the most popular of these, though it also is not FDA approved for ADHD. Medication effects last 4-6 hours, though a patch also became available which was designed to last 5-6 days. Clinical experience suggested that it tended to help more with hyperactive and impulsive or explosive behavior, and in some cases it was prescribed with an antidepressant or stimulant in difficult cases. Tenex / Intuniv (guanfacine) These medications, like clonidine, seems to work on anger and hyperactivity more than

inattention. This also was not FDA approved for ADHD. Use began to wane to a degree after a report of a small number of deaths when combined with Ritalin. These medications tended to produce drowsiness and if they are discontinued, they should be discontinued slowly. Common side effects were dry mouth, headaches, abdominal pain, and nausea. Since these are used to lower blood pressure, cardiac evaluation should be performed prior to prescription. Blood pressure, heart rhythm, and heart rate should be periodically monitored. Tenex is estimated to last approximately 6 hours, and Intuniv approximately 24 hours.

Adrenergic Agonists

Provigil (modafinil), released in 1998, is a medication which saw increased use for ADHD while it's manufacturer is in the process of obtaining approval for treatment of ADHD (possibly 2005). It is a drug traditionally used to treat narcolepsy and the fatigue associated with sleep apnea. Successful double-blind placebo-controlled studies and studies in adults have been reported.

- *Provigil (modafinil); 15 hour half-life; released in 1998*
- *Nuvigil (made of one of the isomers of Provigil); longer-acting than Provigil; possible release (2006)*

It is presumed Provigil has its main effect on the hypothalamus and seems to improve alertness without some of the side effects of more traditional stimulants. It is an Alpha-1-adrenergic agonist and believed to increase the receptiveness of brain's alpha-1 receptors to the neurotransmitter noradrenaline resulting in increased alertness, memory and energy. Common side effects are reported to include headache, nausea, diarrhea, upset stomach, headache, nausea, nervousness, anxiety, trouble sleeping, dizziness, or back pain. It may reduce the effectiveness of birth control pills.

It must be noted that approval for use of Provigil for ADHD in children was rejected in 2006. Adverse reactions included a small number of skin reactions, one of which was severe, possibly representing Stevens–Johnson syndrome (one in 933). The manufacturer's label now discourages any use of Provigil by children.

Selective Norepinephrine Re-uptake Inhibitor

Strattera (atomoxetine) was FDA-approved in 2002. It is an ADHD medication which inhibits pre-synaptic re-uptake of norepinephrine. It is FDA approved for ages 6 and above. While some studies show it is as effective as the stimulants and tolerated as well as the stimulants there are some greater cautions. There are some reports that it may also improve mood or mood swings, particularly with higher doses. Though

response is immediately seen with stimulants, full effects with Strattera may not be seen for 3-4 weeks. It is long-lasting and around-the-clock response can be achieved with one or two doses a day.

Strattera side effects are not unlike other stimulants or some of the antidepressants and consist of some reports of headache and sometimes dizziness, gastro-intestinal complaints such as stomach aches, nausea or vomiting and decreased appetite, dry mouth. While improvement in mood is usually seen, some individuals reported mood swings and/or fatigue and some reported nervousness or sleep difficulties. Some adults experience difficulty with urination, erectile difficulties, prostate difficulties, menstrual irregularities, or insomnia. The FDA has issued an advisory about the risks of liver injury, orthostatic hypotension, and syncope with Strattera. Parents should notify the prescribing physician if the child has complaints of nausea, belly pain, dizziness, or yellowing of the skin. Strattera should not be taken with MAO-inhibitors, and there are some cautions regarding individuals with either high or low blood pressure and for those with kidney or liver difficulties. An FDA advisory also suggests parents and other caregivers closely watch for warning signs of suicide in children and teens taking Strattera.



Mood Stabilizers

Mood stabilizers are sometimes used when other approaches fail or when there seems to be cyclical mood changes. Increased use seems to be associated with an increasing trend of the diagnosis of bipolar disorder in children and adolescents, a very controversial topic.

While it is true that a greater than average number of ADHD children and adolescents will develop bipolar disorder (manic-depression) in adulthood, a full clinical presentation of Bipolar Disorder - Type I is uncommon before early adulthood. Since hyperactive symptoms and even inattentive symptoms overlap a great deal with manic symptoms, and only a short duration is required to diagnosis a brief manic episode referred to as a hypomanic episodes, it is easy to misdiagnose ADHD and Bipolar Type II. Like ADHD, this is assumed to be a chronic disorder, but with more severe consequences and implications in adulthood with respect to potential employment, functional outcome, and even the ability to obtain future health insurance.

Since the risk of overdiagnosis of bipolar in ADHD children is high and the implications serious, some people have been critical and feel that this is rapidly becoming the “fad” alternative diagnosis in ADHD children. In the author’s opinion this should only be diagnosed after careful psychiatric and psychological evaluation.

Some of these medications such as carbamazepine (Tegretol or Epital), Topamax (topiramate), Lamictal (lamotrogine) and gabapentin (Neurontin) all act and have been used as anticonvulsants (used for seizure control) and mood stabilizers. There has been some clinical use for ADHD, though these also are not FDA approved for ADHD. It must also be noted that some of these medications can actually interfere with certain types of motor and cognitive performance and carry a number of more serious warning and side effects than the stimulants.

Antipsychotic Medication

Perhaps one of the more recent controversies has been the off-label use of powerful antipsychotic medication for treatment of aggression or other symptoms in ADHD children.

Antipsychotic drugs are associated with increased risks for major metabolic syndrome and involuntary, repetitive movements (tardive dyskinesia) or for developing TdP (torsade de pointes).

There are complex children with underlying psychotic tendencies where this may be appropriate, and as with all medications, for severely aggressive children there are also risks of not treating. However, serious concerns have been raised, some of which involves concerns that they are being prescribed for behavior disturbance as opposed to psychotic symptoms or features.

According to a 2012 study from Columbia University, there have been concerns that use of antipsychotic drugs such Seroquel, Abilify, and Risperdal has been found to increase risk of developing Type 2 diabetes from 3 to even 5-7 times that of other children and adolescents. There has been a Federal probe into the use of antipsychotic drugs, such as Risperdal and Zyprexa involving possible overuse of antipsychotic medication for poor children who are in the Medicaid system.

Snake Oil

Finally, there is very little support that supplements, vitamins, food additives have any general use in effective treatment for ADHD children. While there may be very few children who

have a particular response to medication, the marketing of these products is understandable. Many people fear traditional medicines and the large market created by this frequently diagnosed childhood condition attracts all sorts of snake-oil vendors, unlicensed helpers, and unproven and often costly treatments. As a general guide, if results are promised, a treatment is touted as a cure-all for a wide variety of conditions, dramatic improvements described in testimonials, or the individual providing the service is not licensed by the state, caveat emptor (buyer beware).

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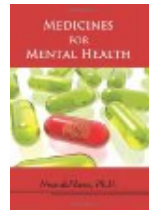

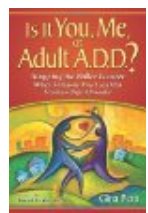


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