

THE CARLAT REPORT

CHILD PSYCHIATRY

A CME Publication

Subscribe today!
Call 866-348-9279

UNBIASED INFORMATION FOR CHILD PSYCHIATRISTS

Special
Double Issue!
Worth 2 CME
credits!

Joshua D. Feder, MD
Editor-in-Chief

Volume 8 Issue 6&7

September/October 2017

www.thecarlatchildreport.com

IN THIS ISSUE

ADHD in Children and Adolescents

- An Integrative Approach to ADHD — 1
- Expert Q&A — 1
Anne Buchanan, DO
Choosing Medications for ADHD
- Table: Official 2017 Carlat ADHD Pediatric Stimulant Comparison Table — 6
- Research Updates: — 9
 - Is Modafinil an Effective Alternative for the Treatment of ADHD?
 - Can Strattera Improve Reading Skills in Children With Dyslexia?
 - Understanding Tantrums in Autism Spectrum Disorder
- CME Test — 11

Learning Objectives

After reading these articles, you should be able to:

1. Identify the benefits and side effects of medications used to treat the symptoms of ADHD in children and adolescents.
2. Discuss the value of using an integrative medicine approach for children and adolescents with ADHD.
3. Summarize some of the current findings in the literature regarding psychiatric treatment for children and adolescents.

An Integrative Approach to Attention Deficit Hyperactivity Disorder

Scott Shannon, MD. Assistant clinical professor in the Department of Psychiatry, University of Colorado

Dr. Shannon has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Integrative approaches to treating ADHD have become increasingly sought after by parents, especially those who are concerned about the side effects and potential overuse of psychostimulant medication. Surveys report that over 60% of child psychiatry patients are employing integrative tools on their own such as vitamins, specific diets, and herbal remedies. The most recent study of parents of children with

Continued on page 2

In Summary

- Many patients and clinicians support an integrative medicine approach to treating ADHD as an alternative or adjunct to conventional psychiatry.
- In addition to the three DSM presentations of ADHD, integrative medicine practitioners often use additional subtype variations, such as “angry and oppositional” or “food allergies and gut imbalance,” based on the complexities of individual patients.
- Common integrative medicine treatments include commonsense adjustments that focus on lifestyle issues, natural supplements, and psychotherapy as well as parenting interventions.

Q&A
With
the Expert

Choosing Medications for ADHD

Anne Buchanan, DO

Child psychiatrist at Maimonides Medical Center in Brooklyn, NY

Dr. Buchanan has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Can you tell us about your current practice?

Dr. Buchanan: I am responsible for pediatric ER and floor consults, I supervise the school crisis walk-in clinic, and I am responsible for high-risk intakes in the clinic.

CCPR: We hear a lot about overdiagnosis of ADHD. What are your thoughts?

Dr. Buchanan: We all hear that the problem is that every child with bad behavior is given a stimulant. In actuality, the saddest cases are the children who have not been identified despite chronic academic underperformance and behavioral problems. By the time they get to middle school, they have anxiety and depression. They come to clinic for, say, suicidal ideation, and as we peel back the history, we find untreated ADHD. So, while overdiagnosis and overmedication is a huge problem, so is underdiagnosis. If children come in before they end up repeating first grade for the third time, then



Continued on page 5

An Integrative Approach to Attention Deficit Hyperactivity Disorder

Continued from page 1

autism found that 88% used complementary and alternative medical (CAM) treatments in the previous three months of care (Smith DL et al, *Sleep Med* 2017 34:170–178).

Whether you are personally interested in the integrative approach or not, it's important to understand the basics, if only to be able to converse about the approach with patients. Integrative medicine (IM) focuses on supporting the innate healing powers of the body, whereas conventional medicine focuses on identifying illness/pathology and then using medications to treat illnesses or reduce symptoms. Integrative psychiatrists, such as myself, prefer the safest options, as these are the least likely to impair an individual's ability to recover. The Hippocratic dictum "first do no harm" resonates deeply.

IM is not without its disadvantages. Firstly and chiefly, the evidence base for efficacy is deficient by the

standards of conventional medicine. In part, this is due to a lack of financial incentives. Most natural remedies cannot be patented, and therefore it is rare for companies to invest the many millions of dollars required for large-scale clinical trials, as the resulting products would be unlikely to yield a good return on investment. Secondly, the IM approach demands more of the patient and can also take more of the practitioner's time. Symptomatic improvement usually takes longer for IM treatments, and parents may not be able to tolerate the wait, especially if their children are in crisis. Finally, many integrative treatments are not covered by insurance.

Nonetheless, many patients are seeking alternatives to conventional psychiatry, and practicing integrative psychiatry can be quite fulfilling. I'll give you a snapshot of my approach to assessment and treatment of ADHD.

Assessment

ADHD assessment in integrative practice is a bit more time-consuming, and may take 60–90 minutes. Like traditional evaluations, it is based primarily on a comprehensive interview, and includes results from ADHD symptom scales (I tend to prefer the Vanderbilt over the Connors scale, as the former is broader in scope). My assessment

protocol includes the following elements.

- Assessment of the child's six realms (environmental, physical, mental, emotional, social, and spiritual), which can be viewed as an expansion of the popular biopsychosocial approach in psychiatry.
- Identification of the child's strengths in addition to deficiencies.
- Focus on diet issues, food quality, food allergies, or gut issues. I will often refer to a nutritionist or naturopath (a clinician who emphasizes use of natural healing agents) as needed. About 30%–40% of my patients work collaboratively with a naturopath.
- An especially detailed examination of family issues, in order to assess for the need of a behavioral management and parenting program.
- Lab testing (typically on the more extensive side), in order to assess the need for supplements. I routinely check TSH, vitamin D (25 OH), ferritin, serum zinc, lipid profile (for low cholesterol), homocysteine (methylation), and high-sensitivity C-reactive protein (HS CRP). I will also order a

Continued on page 3

EDITORIAL INFORMATION

Publisher: Daniel Carlat, MD

Editor-in-Chief: Joshua D. Feder, MD

Deputy Editor: Talia Puzantian, PharmD, BCPP, is associate professor at the Keck Graduate Institute School of Pharmacy in Claremont, CA.

Editorial Director: Bob Croce

Executive Editor: Janice Jutras

Founding Editor: Caroline Fisher, MD, PhD, is training director and chief of child psychiatry at Samaritan Health Systems in Corvallis, OR.

Editorial Board:

Jonathan C. Gamze, MD, is a psychiatrist in private practice in Arlington Heights, IL.

Georgia Gaveras, DO, is the director of training and education in child and adolescent psychiatry and the director of the child and adolescent psychiatry consultation liaison service at Mount Sinai St. Luke's Hospital in New York, NY.

Peter Parry, MBBS, is consultant child & adolescent psychiatrist and senior lecturer at Flinders University in Adelaide, Australia.

John Preston, PsyD, is a professor emeritus at Alliant International University in Sacramento, CA.

All editorial content is peer reviewed by the editorial board. Dr. Feder, Dr. Fisher, Dr. Gamze, Dr. Gaveras, Dr. Parry, Dr. Preston, and Dr. Puzantian have disclosed that they have no relevant financial or other interests in any commercial companies pertaining to this educational activity.

This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists, and other health care professionals, with an interest in the diagnosis and treatment of psychiatric disorders.

New Editor-in-Chief!

We're pleased to introduce Joshua D. Feder, MD, as the new editor-in-chief of the *Carlat Child Psychiatry Report*. Dr. Feder attended Boston University School of Medicine, and did his internship and psychiatry residency at the Naval Regional Medical Center in San Diego, followed by a child and adolescent psychiatry fellowship at Tripler Army Medical Center in Honolulu. He was then stationed at the National Naval Medical Center in Bethesda, MD, and the Uniformed Services University of the Health Sciences, becoming chief of child psychiatry. After military service, Dr. Feder returned to San Diego, where he has an active clinical practice; he also serves as an adjunct professor at Fielding Graduate University and an associate clinical professor at UCSD School of Medicine. In addition to his clinical practice, Dr. Feder is active in developing technology to help people with autism and related challenges and serves as a senior consultant to the International Network for Peace Building with Young Children.



sleep study if there is snoring or extremely restless sleep.

- A detailed assessment of learning issues in order to recommend educational supports if needed.

Subtypes of ADHD

In the conventional view, there are three DSM presentations of ADHD: inattentive, hyperactive, and combined. But in reality, children with ADHD present with many variations. Integrative practitioners tend to be particularly attuned to these variations, and they often categorize patients into subtypes, each of which has implications for mechanism and treatment approaches. The following eight subtypes are based on a combination of my clinical experience and a review of current research. Not all patients fit a single subtype; many have qualities of more than one. Nonetheless, I find this a helpful system for better understanding the complexities of individual patients.

1. Classic ADHD. High energy, positive mood, and good sleep characterize these patients, who usually respond well to psychostimulants.

2. Anxious and over-focused. These children have an incredible ability to focus when they are alone. They can read a book for five hours straight, but decompensate in a social setting, becoming anxious and distracted. I consider a supplement like L-theanine or a medication like atomoxetine that both reduces anxiety and improves focus.

3. Angry and oppositional. These children may have mood issues with a volatile rejection of limits. Their parents may be too permissive or too harsh. I work on mood stability and parental limit setting. I recommend a behavioral management and parenting method called the Nurtured Heart Approach by Howard Glasser (see <http://difficult-child.com/> for more info).

4. Apathetic with learning issues. Some children with learning issues don't thrive in the typical classroom.

Processing speed may be low, or a true learning disability may exist. Over time, they may drift into a passive-avoidant approach to learning and withdraw from engagement. Parents and teachers flail at finding motivation. The path to reaching these children is by emphasizing their particular gifts and talents, which are almost always non-academic.

5. Lack of structure. These kids suffer from a lack of structure. They may respond to this by overusing electronic devices; their diet is often poor, and sleep is erratic. Here, the challenge is effective parental engagement.

6. Sleep issues. Many children are obese, and obstructive sleep apnea has become common. Since low iron levels have been correlated with sleep apnea, I routinely test ferritin to gauge total body iron stores and replenish as needed. Sometimes oxygen saturation and airway limitations are the issue. Several clinical trials have shown that surgery for enlarged tonsils has improved attentional symptoms. Most recently, a prospective study of 59 children with ADHD found that all but 8 demonstrated significant improvements in ADHD after a tonsillectomy (Ahmadi MS et al, *Int J Pediatr Otorhinolaryngol* 2016;86:193-195).

7. Food allergies and gut imbalance. These children often have a history of colic, reflux, eczema, and chronic otitis. Multiple courses of antibiotics may have disrupted the microbiome. These children may crave carbohydrates, especially sugars. An elimination diet and treatment of the gut issues can often bring dramatic relief.

8. Developmental delays. These children present with a history of significant delay in developmental milestones. Walking or talking may have lagged months behind. Exercise tolerance may be low; they wear out quickly and often nap.

Integrative treatment

Regardless of the subtype of patient, I view treatment in three

phases. The first involves commonsense adjustments; the second looks to specific complementary treatments based on subtype and often some form of psychotherapy or education; and the third is conventional medication treatment, if needed.

Commonsense adjustments

These strategies focus on lifestyle issues, which are helpful for both conventional and integrative practitioners to address.

- *School.* Are the school and teacher a good fit based on learning style, temperament, and other factors? Will a school change make a difference?
- *Sleep.* Is the child getting adequate sleep? Is there sleep apnea or sleep-disordered breathing?
- *Overstimulation.* Is the child overstimulated? Excessive electronics can create more attentional imbalance. Limit screen time (I recommend the book *Reset Your Child's Brain* by Victoria Dunckley, MD).
- *Outdoor activities.* Does the child spend time outside? Is the child getting enough sunlight, activity, and exercise? Exercise is a helpful tool for ADHD symptoms, according to a recent meta-analysis of eight studies (Cerrillo-Urbina AJ et al, *Child Care Health Dev* 2015; 41(6):779-788).
- *Breakfast.* A high-protein breakfast may be the single best piece of advice. High carb/low protein (e.g., waffles or pancakes) is worse for cognitive performance than no breakfast at all. I sometimes will humorously write out the following "prescription" that I refer to as my basic remedy for the American breakfast: "Protein, 15 to 20 grams in AM on empty stomach."
- *Other.* What else in the child's ecosystem seems out of balance and easy to correct? We need to honor

Continued on page 4

our intuitive ability to recognize imbalances.

Typical integrative treatments

1. Nutrition and diet. Children with ADHD often benefit from more well-balanced diets, including high-protein breakfasts. Another specific intervention is the elimination diet, focusing on foods that often cause allergic or other reactions, such as dairy, wheat, corn, citrus, chocolate, yeast, and soy. Typically the foods are eliminated for four weeks, then items are added back one at a time over a two-week period looking for relapse or reaction. One randomized controlled trial of 100 children with ADHD found this approach effective (Pelsser LM, *Lancet* 2011;377(9764):494–503). The mechanism of the food-ADHD connection is unclear, but it may be due to the immune system creating antibodies to food antigens, antibodies which then cross-react to parts of the brain, disrupting attention and other behaviors.

2. Natural supplements. The term “natural supplements” refers to non-prescription substances that are not regulated by the FDA. A few of these are supported by randomized controlled trials, but in many cases the evidence is weaker, such as small case series or small uncontrolled trials. Nonetheless, these supplements are safe, are likely to activate a robust placebo effect, and may have specific efficacy as well. There are several supplements that I frequently use in children with ADHD.

- **Eicosapentanoic acid (EPA).** EPA is likely the most efficacious fatty acid found in fish oil, and a meta-analysis found it to be moderately effective for ADHD symptoms (Bloch MH, *J Am Acad Child Adolesc Psych* 2011;50(10):991–1000). I prescribe 1 gram of EPA per day with a meal and find that it generally takes 3 months for the benefit to appear, as it is a nutritional effect, rather than a neurotransmitter effect.
- **L-theanine.** This component of green tea has been shown to

improve both anxiety, focus, and sleep. I use 200–400 mg twice daily, and I’ve found it particularly effective in the over-focused or traumatized child.

- **Acetyl-L-carnitine.** A multisite, placebo-controlled pilot study of 112 children with diagnosed ADHD found that acetyl-L-carnitine (which transports fatty acids into the mitochondria for energy) was ineffective overall, but subtype analysis found it effective in children with the inattentive subtype of ADHD (Arnold LE et al, *J Child Adolesc Psychopharmacol* 2007;17(6):791–802). In my experience, this works well for slowed, low-energy, inattentive, or learning-delayed children. I use 1–2 grams twice daily. I look for increased energy, reduced sleep needs, and more engagement. Acetyl-L-carnitine is often best combined with 100 mg of Coenzyme Q10 (CoQ10), which is an antioxidant.
- **Iron.** Iron is a needed cofactor for the production of dopamine in the CNS. I use chelated iron (which may be more easily absorbed than ferrous sulfate) 10–20 mg a day if low ferritin is present (under 30 ng/mL) on a standard blood test.
- **Zinc.** Two studies showed a positive effect in ADHD with zinc sulfate (Salehi B, *J Res Pharm Pract* 2016;5(1):22–26) but not with zinc gluconate. You can test RBC zinc to assess this common deficiency. Doses of at least 20 mg once per day are best if children test low. Zinc sulfate can cause nausea if given on an empty stomach.
- **Pycnogenol.** This supplement comes from the bark of French pine trees. It is a powerful antioxidant and has one randomized controlled trial with 61 children supporting its use in hyperactivity at 1 mg/kg (Tribaticka J et al, *Eur Child Adolesc Psychiatry* 2006;15(6):329–335). I typically recommend 25–50 mg twice daily in the classically hyperactive child.

- **Ginkgo biloba.** Ginkgo biloba has some limited evidence for efficacy in small, uncontrolled trials. I use 160 mg twice daily, and have found that it enhances cognitive function and alertness—but can disrupt sleep.
- **Bacopa.** This classic ayurvedic remedy from India has been used for centuries for learning and memory. An open-label trial of 31 children found it helpful (Dave UP et al, *Adv Mind Body Med* 2014;28(2):10–15), and a large randomized controlled trial is underway. I recommend one to two capsules twice daily for learning disabilities or memory problems.

3. Neurofeedback. Neurofeedback is a type of biofeedback that engages the child in real-time brain wave training designed to compensate for abnormalities demonstrated on a quantitative EEG. The child, through operant conditioning, learns to adjust brain wave patterns based on visual or other types of feedback. The FDA recently approved a device to diagnose ADHD based on the brain waves (the ratio of slow to fast waves), though the utility of this method is controversial. A large NIMH-sponsored multisite study on neurofeedback in the treatment of ADHD is currently in process (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4134464/>).

4. Parenting and behavioral interventions. In the Multimodal Treatment of ADHD (MTA) study, the best outcomes were found in the combined group that received both parenting support and medication. Parenting and behavioral treatments are a well-proven but underused treatment avenue in ADHD.

5. Psychotherapy and education. In addition to all of the evidence-based forms of psychotherapy, IM embraces any proven treatment that emphasizes skill building. Mind-body skills that enhance self-care and awareness, like meditation, are valuable approaches. Meditation builds awareness on many

Expert Interview

Continued from page 1

maybe we can change their paths. But there is, I think, a pretty significant minority of children who may not have as much of the disruptive behavior, and they kind of get just moved along—and in those cases, we really end up with a lot more problems down the line.

CCPR: So how do you do assessments?

Dr. Buchanan: We get history from the parent, from the child, and from the school. We have parents and teachers fill out rating scales, with another teacher form about the student's strengths and weaknesses. Academic records, IEPs, special education plans, and previous testing are really helpful. If we have concerns about learning issues or developmental problems, we then refer for additional assessment.

CCPR: How do you sort out learning disabilities and ADHD?

Dr. Buchanan: Teachers may describe ADHD symptoms in certain settings, such as during testing or during certain subjects, or parents might not see symptoms at home. A child might also tell me that concentration is not the problem, but rather that the material is simply "too hard." If I am suspicious of other psychiatric issues, we can do psychological testing. However, ADHD is often apparent with a proper history, collateral information, and observation of the child in the office.

CCPR: We hear from some pediatricians that they don't think the kids they are referring to us actually have ADHD. Is this a common problem at that level of care?

Dr. Buchanan: Yes, and it is also something we sometimes see in our clinic. ADHD is a catchphrase that teachers and guidance counselors know, and they will often use it as a label as part of a referral. But larger issues are often evident during the initial consultation, things that the school may not know about. Many children we see have ADHD, but many do not.

CCPR: Does your evaluation change depending whether it's a younger or older patient?

Dr. Buchanan: I find that younger children are often not as reliable as older kids in terms of self-reporting symptoms; however, we are still gathering the same records and the same information from parents and schools no matter the child's age.

CCPR: We've also read that poor sleep can play a role with kids. Can you tell us more about that?

Dr. Buchanan: Lack of sleep/poor sleep hygiene is a huge factor in worsening existing ADHD symptoms and making any kid more inattentive during the day. Although getting kids to sleep is by no means a new issue, the overall increase in screen time over the years certainly has contributed to this, and we always ask and counsel about sleep.

CCPR: Moving on to treatment, what is your approach to choosing medications?

Dr. Buchanan: Most child psychiatrists, including myself, consider stimulants first-line. I view alpha-agonists as second-line, or sometimes I use them as augmenters to a stimulant, such as when we see only a partial response from a stimulant or when we are limited in dosing due to side effects. Agents such as Strattera (atomoxetine) and Wellbutrin (bupropion) are generally third-line. I deviate from that depending on contraindications or comorbidities, but most kids do well on stimulants. Ultimately, the recommendations that we land on depend on individual tolerability.

CCPR: Which medications do you tend to start with?

Dr. Buchanan: Keeping in mind that insurance formularies often dictate medication choices, especially when initiating treatment, it's rare that I use newer formulations. I tend to start with a methylphenidate product, and I try a second one before going to an amphetamine product, because amphetamines can often be more potent, with more appetite suppression, irritability, and withdrawal symptoms. I generally start with any of the long-acting methylphenidate products—this would include medications such as Concerta, Metadate CD, Ritalin LA, and Focalin XR. For younger kids, I may consider starting with a short-acting, such as generic Ritalin (methylphenidate), as younger children may experience more side effects with stimulant medications and may not need as much coverage due to having fewer academic demands. The newer liquid, chewable, and dissolvable meds seem great for kids who struggle to swallow pills. However, insurance often doesn't cover them initially. With some generics and Adderall XR, Metadate CD, Focalin XR, and Ritalin LA, it works well to snip the capsule and pour the beads into a spoonful of something with decent consistency—not a liquid—to ensure the child gets all the beads. Parents can use yogurt, oatmeal, or peanut butter, for example.

CCPR: What dose do you tend to shoot for?

Dr. Buchanan: I always start with the lowest dose, as some kids will respond to it. I will go up to and over the maximum recommended dose if needed, as long as we see improvement and as long as there are no side effects. For Metadate, the first dose is 10 mg, and if by 30 mg we have side effects and no improvement, I would switch to something else. Otherwise, I go to a maximum of 60 mg. For Concerta, I start at 18 mg. I've gone up to the max of 72 mg and even higher in certain patients, as long as the medicine is tolerated and the symptoms are improving.

“Most child psychiatrists, including myself, consider stimulants first-line. I view alpha-agonists as second-line, or sometimes I use them as augmenters to a stimulant, such as when we see only a partial response or if we are limited in dosing due to side effects. Ultimately, the recommendations that we land on depend on individual tolerability.”

Anne Buchanan, DO

Official 2017 Carlat ADHD Pediatric Stimulant Comparison Table

Medication	Pediatric Dose (starting-max*)	Available Strengths (in mg except where noted)	Duration of Action (h)	Can It Be Split?	Generic Available?	Ages Approved for ADHD	Delivery System/Notes
Methylphenidates							
Short-acting							
Focalin (dexamethylphenidate)	2.5 mg BID-10 mg BID	2.5, 5, 10	3-4	Yes	Yes	6-17, adults	D-enantiomer of methylphenidate but twice as potent
Methylin CT	2.5 mg BID-20 mg TID	2.5, 5, 10	3-4	Yes	Yes	6-17, adults	Chewable tablets
Methylin Oral Solution	2.5 mg BID-20 mg TID	5 mg/5 mL, 10 mg/5 mL	3-4	NA	No	6-17, adults	Clear, grape-flavored liquid
Ritalin	2.5 mg BID-20 mg TID	5, 10, 20	3-4	Yes	Yes	6-17, adults	Immediate-release tablets
Intermediate-acting							
Ritalin SR (generic only)	10 mg q AM-60 mg q AM	10, 20	4-8	No	Yes	6-17, adults	Continuous-release tablets (less predictable because of wax matrix)
Long-acting							
Aptensio XR	10 mg q AM-60 mg q AM	10, 15, 20, 30, 40, 50, 60	8-12	Can be sprinkled; do not crush or chew	No	6-17, adults	ER capsules; 40% IR, 60% ER
Concerta (OROS – osmotic [controlled] release oral [delivery] system)	18 mg q AM-72 mg q AM (max 54 mg if < 12 yo)	18, 27, 36, 54	10-16	No; do not crush or chew	Yes	6-17, adults	Initial release, then continuous capsule. 22% IR, 78% ER; hard shell may make it more difficult to abuse.
Cotempla XR-ODT	17.3 mg q AM-51.8 mg q AM	8.6, 17.3, 25.9	8-12	No	No	6-17	Orally disintegrating tablets; 25% IR, 75% ER
Daytrana patch (methylphenidate transdermal system)	10 mg q AM-30 mg q AM. Remove after 9 hours.	10, 15, 20, 30	8-12	No	No	6-17	Continuous release patch. Duration can be shortened by decreasing wear time; effects persist up to 5 hours after removal.
Focalin XR (dexamethylphenidate XR)	5 mg q AM-30 mg q AM	5, 10, 15, 20, 25, 30, 35, 40	8-12	Can be sprinkled; do not crush/chew	Yes	6-17, adults	Capsules of 50% immediate-release beads & 50% delayed-release beads. Mimics BID dosing; twice the potency of methylphenidate.
Metadate CD	20 mg q AM-60 mg q AM	10, 20, 30, 40, 50, 60	8-12	Can be sprinkled; do not crush/chew	Yes	6-17, adults	30% immediate-release beads and 70% delayed-release beads; mimics BID dosing
QuillChew	20 mg q AM-60 mg q AM	20, 30, 40	8-12	Yes	No	6-17, adults	Chewable ER capsules; 30% IR, 70% ER
Quillivant XR	20 mg q AM-60 mg q AM	25 mg/5 mL	8-12	No	No	6-17, adults	Oral solution; 20% IR, 80% ER; shake well
Ritalin LA	20 mg q AM-60 mg q AM	10, 20, 30, 40, 60	8-12	Can be sprinkled; do not crush/chew	Yes	6-17, adults	50% immediate-release beads & 50% delayed-release beads

Amphetamines									
Short-acting									
Dexedrine (dextroamphetamine)	3-5 yo: 2.5 mg q AM-20 mg BID 6-16 yo: 5 mg q AM-20 mg BID	5, 10	3-5	Yes	Yes	3-16	Tablets		
Liquadd, ProCentra (dextroamphetamine)	5 mg q AM-20 mg BID	5 mg/5 mL	3-5	NA	Yes	3-16	Bubblegum-flavored liquid		
Intermediate-acting									
Adderall (mixed amphetamine salts)	3-5 yo: 2.5 mg q AM-20 mg BID 6-17 yo: 5 mg q AM-20 mg BID	5, 7.5, 10, 12.5, 15, 20, 30	6-8	Can be crushed	Yes	3-17, adults	Mixed salt of l- and d-amphetamine		
Long-acting									
Adderall XR (mixed amphetamine salts)	6-12 yo: 5 mg q AM-30 mg q AM 13-17 yo: 10 mg q AM-40 mg q AM	5, 10, 15, 20, 25, 30	8-12	Can be sprinkled; do not crush/chew	Yes	6-17, adults	50% IR, 50% ER mixed salt of l- and d-amphetamine; beads; mimics BID dosing		
Adzenys XR-ODT, Adzenys ER (amphetamine)	6-12 yo: 6.3 mg q AM-18.8 mg q AM; 13-17 yo: 6.3 mg q AM-12.5 mg q AM	3.1, 6.3, 9.4, 12.5, 15.7, 18.8, 1.25 mg/mL	8-12	No (ODT, liquid)	No	6-17, adults	ER orally disintegrating tablets: 3.1 mg is equivalent to 5 mg mixed salts product; increasing dose preparations are equivalent to 10 mg, 15 mg, 20 mg, 25 mg, and 30 mg respectively; oral liquid (available early 2018)		
Mydayis (mixed amphetamine salts)	12.5 mg q AM-25 mg q AM	12.5, 25, 37.5, 50	10-12+	Can be sprinkled; do not crush/chew	No	13-17, adults	pH-dependent ER formulation; effects may last up to 16 hours		
Vyvanse (lisdexamfetamine)	30 mg q AM-70 mg q AM	10, 20, 30, 40, 50, 60, 70	8-12	Can be dissolved in water	No	6-17, adults	Capsules; lisdexamfetamine is prodrug of dextroamphetamine		
Non-stimulants									
Intuniv (guanfacine extended-release)	1-4 mg daily (do not increase faster than 1 mg/wk)	1, 2, 3, 4	24	No	Yes	6-17	ER tablet; not a 1:1 conversion from IR		
Strattera (atomoxetine)	Dosage varies.**	10, 18, 25, 40, 60, 80, 100	24	No	Yes	6-17, adults	Norepinephrine reuptake inhibitor		
Tenex (guanfacine immediate-release)	1-4 mg daily (do not increase faster than 1 mg/wk)	1, 2	17	Can be crushed	Yes	Not FDA-approved for ADHD	Tablets		
Wellbutrin (bupropion)	1.4-6 mg/kg/day	IR: 75, 100; SR: 100, 150, 200; XL: 150, 300, 450	6-9	Yes	Yes	Not FDA-approved for ADHD	SR (12 hour) and XL (24 hour) versions exist		

* Maximum dose based on FDA recommendations (see this issue's interview with Dr. Buchanan for information regarding higher doses)

** Strattera dosing: Weight < 70 kg, start 0.5 mg/kg, target 1.2 mg/kg, max 1.4 mg/kg; weight > 70 kg, 40 mg-100 mg

Expert Interview

Continued from page 5

CCPR: Are you typically going up by a pill a week?

Dr. Buchanan: In an ideal setting, I would raise the dose each week. In busier clinics, seeing kids that often is difficult, so frequently the dose gets raised every other week.

CCPR: So you won't just tell parents to figure it out and come back in a month?

Dr. Buchanan: No, we don't do that. Families need education. For us, it's often a slow ramp up to get a parent to agree to medication. Private practice may be a different story because parents may come in already understanding the diagnosis, and if so, they might be more reliable in increasing the dose on their own and coming back in several weeks.

CCPR: What side effects do you see?

Dr. Buchanan: Mostly appetite suppression. We try to make sure kids eat their breakfast before taking medicine; we also educate the parents that children may not be hungry at lunch, so packing snacks for school is recommended if they get hungry later. We find that a lot of kids eat their traditional lunch after school and then are hungry again for dinner. As long as they get enough calories in 24 hours, I don't worry about timing. I recommend parents be flexible so that children are eating what they need to gain weight and grow. Another option is to lower the stimulant dose until appetite improves, and augment with an alpha-agonist to target residual ADHD symptoms. [EIC Note: When clinically appropriate, I use Periactin 4–12 mg or Remeron 7.5–30 mg, both dosed at night, to help with appetite and sleep. —JDF].

CCPR: What are your thoughts about the Daytrana patch?

Dr. Buchanan: Many kids have skin reactions with the patch, but it is as efficacious as other stimulants. The nice thing is that you can peel the patch and control when the effect is gone, depending on the child's schedule that day.

CCPR: When do you switch to an amphetamine?

Dr. Buchanan: If after two methylphenidates we are not seeing symptom control, I try an amphetamine. Some kids respond better to them. One reason to go with an amphetamine product from the beginning of treatment might be because a sibling is doing well on one.

CCPR: Out of, say, 100 patients in your practice, what percentage are on methylphenidates vs. amphetamines?

Dr. Buchanan: I would guess the ratio is 70%/30%.

CCPR: Is Vyvanse better in some way?

Dr. Buchanan: Both work well, but for some kids Vyvanse is better tolerated. But all amphetamines suppress appetite and have withdrawal irritability.

CCPR: Do you prescribe much Adderall?

Dr. Buchanan: We prescribe Adderall XR, but we avoid short-acting Adderall because it may have higher diversion and abuse potential. I see red flags whenever there are prescriptions lost or when there are requests for refills sooner than necessary. In New York, we are required to electronically prescribe everything, and we check the state monitoring program before prescribing any controlled substance, so this has cut down on funny business. As more states do this, diversion will be less of a problem. We can have parents or patients sign a contract that if they need to fill a script early, we will do so one time, but then after that we won't prescribe anymore.

CCPR: Tell me about alpha-agonists.

Dr. Buchanan: Guanfacine comes in short-acting Tenex and long-acting Intuniv. Clonidine is more sedating and has a long-acting formulation, Kapvay, as well as a long-acting Catapres patch. Alpha-agonists have the FDA indications to treat core symptoms of ADHD. They are not quite as good as stimulants for inattention and concentration, but they help hyperactivity and disruptive behaviors. ADHD kids often have issues with sleep from the ADHD and from stimulants, and alpha-agonists can help them settle down for bed.

CCPR: Do alpha agonists cause sedation the next day?

Dr. Buchanan: Clonidine is more sedating, so I will have parents split the lowest dose of Tenex (1 mg) into 0.5 mg for a bedtime dose, and if the kid is not sedated in the morning we will go with BID dosing, which seems to work well for many.

CCPR: When would you use an alpha-agonist as monotherapy?

Dr. Buchanan: Kids with cardiac histories may have a murmur or arrhythmia, and in those cases we are hesitant to use a stimulant. Or if a stimulant causes side effects like palpitations or high blood pressure or irritability, we might switch to an alpha-agonist.

CCPR: What do you tell families who ask about risk of sudden death with stimulants?

Dr. Buchanan: If the child does not have a personal history of any cardiac issues and there is no family history of sudden cardiac death, we reassure families that the risk of sudden death is low. We check blood pressure when starting or increasing a dose, and we wouldn't continue a child on something that made the parents feel uncomfortable, even if the vitals are OK. We don't send every kid for EKGs or cardiac clearance, but if there is something in the history that makes us concerned, then we will do that first.

CCPR: What about Provigil or Nuvigil?

Dr. Buchanan: I don't have experience with Provigil and Nuvigil, as they are generally not covered by managed Medicaid. I use Strattera or Wellbutrin. They are not as efficacious as the stimulants, but for kids who can't be on stimulants, they may help.

CCPR: What about psychotherapy or non-medication treatments?

Continued on page 9

Expert Interview
Continued from page 8

Dr. Buchanan: We have group therapy for every child for difficult behaviors, impulse control, and frustration tolerance. If a child is unmanageable in group, we have the child undergo individual therapy. We have groups for parenting and psychoeducation. Our psychiatrists collaborate closely with the group and individual therapists. A few kids are stable on medication only.

CCPR: How does therapy add to care?

Dr. Buchanan: The psychotherapeutic modalities won't fix the core symptoms of ADHD: focus, distractibility, and inattention. But kids with mild symptoms can learn cognitive strategies that mitigate their symptoms, helping with frustration tolerance, coping, resilience, and social skills. More importantly, kids with ADHD are often difficult to parent, and effective parenting can help so the child doesn't feel constantly punished, as punishment can lead to more acting out. The psychoeducation that the parents get is invaluable. The MTA study demonstrated that the combined treatment tends to be as good or better than medication alone, whereas psychosocial treatments alone tend to be not as good (*Arch Gen Psychiatry* 1999;56(12):1073–1086). We push for combined treatment for the best outcome.

CCPR: Thank you for your time, Dr. Buchanan.



Research Updates IN PSYCHIATRY

ADHD

Is Modafinil an Effective Alternative for the Treatment of ADHD?

REVIEW OF: Wang SM et al, *J Psychiatr Res* 2017;84:292–300.

Modafinil (Provigil) is FDA-approved for narcolepsy, obstructive sleep apnea, and shift work sleep disorder, but not for ADHD. Given that it has some of the same stimulating properties of psychostimulants, it should theoretically be effective. Wang and colleagues identified five randomized placebo-controlled trials testing modafinil for the treatment of ADHD in children and adolescents, and performed a meta-analysis of this data.

Of the 927 participants in these studies, 640 were randomly assigned to modafinil (doses ranged from 170–425 mg/day), and 287 were assigned to placebo. All five RCTs were short-term studies (all < 9 weeks). Patients on modafinil showed more improvement on ADHD scores than patients on placebo, with a standard mean difference vs placebo of -0.77 and -0.71 for the ADHD-RS-IV home and school versions, respectively. The standard mean difference is also known as the effect size, and this effect size is moderate to large. (For perspective, in previous meta-analyses, effect sizes for stimulants have been in the 0.6–0.8

range.) Modafinil patients experienced more insomnia and decreased appetite. Only four cases of serious adverse events (Stevens-Johnson syndrome, duodenitis, and two cases of dehydration) were reported in the modafinil group.

CCPR'S TAKE

Modafinil appears to work about as well as stimulants for children and adolescents with ADHD. It is a good off-label option for kids who don't respond or don't tolerate stimulants. Just be aware that there is a small (likely very small) risk of Stevens-Johnson syndrome.

—Ariana Ayón Verduzco, PharmD candidate (2018). Ms. Verduzco has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

LEARNING DISABILITIES

Can Strattera Improve Reading Skills in Children With Dyslexia?

REVIEW OF: Shaywitz S et al, *J Child Adolesc Psychopharmacol* 2016;27(1):19–28.

Dyslexia, a learning disability characterized by difficulty in reading skills, is highly prevalent, with rates between 5% and 17%. Treatments include non-medical interventions, which have limited success. Research suggests a critical role

for attentional mechanisms in the development of dyslexia. Previous small studies have shown stimulants as well as atomoxetine may improve reading in patients who have comorbid attention deficit hyperactivity disorder and dyslexia (ADHD+D). This new study is a larger, placebo-controlled trial to evaluate atomoxetine's efficacy in patients with ADHD+D as well as those with dyslexia or ADHD only.

The researchers randomized 209 children and adolescents, aged 10–16 years, into a placebo group (n = 89) and a treatment group (n = 120). The placebo group consisted of dyslexia-only (n = 29) and ADHD+D patients (n = 60), while the treatment arm consisted of dyslexia-only (n = 29), ADHD+D (n = 64), and ADHD-only (n = 27) patients. The patients were treated with either atomoxetine (starting at 0.5 mg/kg daily for 3 days, then 1.0–1.4 mg/kg per day) or placebo. Reading abilities were measured with a variety of standardized tests after 16 weeks. Both ADHD+D and dyslexia-only patients receiving atomoxetine showed statistically significant improvement in phonologic processing (sounding out words), basic reading skills, and reading vocabulary compared to those receiving placebo. Effect sizes were moderate to high (ranging from 0.5 to 0.73), and literacy improvement in comorbid patients was not correlated with improvements in ADHD symptoms.

Continued on page 10

Research Updates
Continued from page 9

CCPR'S TAKE

While the study shows promising results, it's not clear whether the improvement seen is clinically significant, whether it would be seen in a range of kids with varying levels of dyslexia, or whether it would be sustained over time. Nonetheless, atomoxetine is a well-tolerated medication and is one of the few agents shown to be helpful for dyslexia. Readers should know that the study was funded by Eli Lilly, the manufacturer of Strattera (atomoxetine), although there were no obvious signs of bias in research design or analysis.

—Ricardo Arechiga, PharmD candidate (2018). Mr. Arechiga has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

AUTISM

Understanding Tantrums in Autism Spectrum Disorder

REVIEW OF: Mayes S et al, *J Dev Phys Disabil* 2017;29(4):587-596

Why do children with autism spectrum disorder (ASD) have tantrums?

One theory is that these tantrums are due in part to children's frustration with not being able to express themselves. This theory has led to a treatment approach called "mand training." A mand is a verbal request, and mand training seeks to help children with ASD make simple requests more effectively. In theory, therefore, the improvement in communication would decrease the likelihood of frustration-induced tantrums. A recent study, however, reported results that are at odds with the tantrum-communication theory.

In this cross-sectional cohort study, 240 children ages 15–71 months with confirmed diagnoses of ASD were administered the Early Intervention Developmental Profile and WPPSI-III or Bayley verbal and nonverbal IQ tests depending on their level of function. Parents then reported on both tantrum frequency and speech intelligibility using the Pediatric Behavior Scales. ANOVA and ANCOVA analyses showed that expressive language, receptive language, and nonverbal IQ each accounted for 2%–3% of the variance in tantrum frequencies. Moreover,

children with expressive language age equivalent ≥ 24 months had more tantrums than those < 24 months, with a moderate effect size ($d = 0.4$).

CCPR'S TAKE

Although the study was limited by its reliance on parental reports of tantrums, the main finding is that impaired speech was not the primary cause of tantrums in these children. The article underlines the need to understand behavior from a more holistic perspective, rather than focusing on a single aspect of behavior. Include an assessment of sensory sensitivities, motor planning problems, and rigidity of thinking and expectations as well as the parent-child relationship. In addition, sometimes children resist behavioral training efforts because they may prefer to interact in ways that feel more meaningful to them.

—Joshua Feder, MD, editor-in-chief, *CCPR*. Dr. Feder has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

An Integrative Approach to Attention Deficit Hyperactivity Disorder

Continued from page 4

levels and has been shown to augment response to psychotherapy in anxiety and depression. It does this by enhancing our awareness of the repetitive loops of thought we engage in that pull us from our immediate experience. Enhanced immediate awareness forms the core of mindfulness. A recent review of mindfulness meditation in ADHD in young adults found 17 relevant studies, and these studies indicated positive results (Aadil M et al, *Cureus* 2017;9(5):e1269). For children, the evidence is less clear, but a large multisite study is underway.

Medications if needed

I use stimulants if other approaches fail. I try to avoid stimulants in over-focused, angry, or traumatized children, as I've found over the years that these children tend to be more prone to negative side effects such as autonomic overarousal, insomnia, and anxiety. Overall, I use the lowest possible dose and avoid progressive dose escalation.

Conclusion

Tremendous resources have been spent on ADHD research. Sadly, we have no reasonable path to prevention, and prevalence rates are significantly escalating. In my opinion, this indicates a need to move beyond the medication-only approach to treating ADHD that characterizes most current clinical care. Integrative psychiatry offers a different approach based on a holistic appreciation of the child.

CCPR
VERDICT:

Patients and parents are going to ask you about alternatives for ADHD, so whether or not you decide to use an integrative psychiatry approach, you should at least be familiar with some of the supplements used.

CME Post-Test

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatChildReport.com to take the post-test. You must answer 75% of the questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be completed within a year of each issue's publication date. As a subscriber to *CCPR*, you already have a username and password to log onto www.TheCarlatChildReport.com. To obtain your username and password, please email info@thecarlatreport.com or call 978-499-0583.

The Carlat CME Institute is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Carlat CME Institute is also approved by the American Psychological Association to sponsor continuing education for psychologists. Carlat CME Institute maintains responsibility for this program and its content. Carlat CME Institute designates this enduring material educational activity for a maximum of two (2) *AMA PRA Category 1 Credits™* or 2 CE credits for psychologists. Physicians or psychologists should claim credit commensurate only with the extent of their participation in the activity.

Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatChildReport.com. Note: Learning Objectives are listed on page 1.

1. Your patient with ADHD is 8 years old. You may want to consider using a short-acting methylphenidate versus a long-acting formulation for which of the following reasons? (LO #1)
 - a. Younger children have more side effects, so try short-acting stimulants first
 - b. Insurance companies are more likely to cover short-acting methylphenidates initially
 - c. Younger children often receive only partial response from long-acting methylphenidates
 - d. Short-acting methylphenidates tend to cause less next-day sedation in younger patients
2. Your patient with ADHD exhibits behaviors that fit within an anxious and overfocused subtype. According to Dr. Shannon, what supplement could be beneficial in reducing anxiety and improving focus for this patient? (LO #2)
 - a. L-theanine
 - b. Ginkgo biloba
 - c. Acetyl-L-carnitine
 - d. Ginseng
3. According to studies, combining psychosocial and medication treatments tends to be as good or better than medication alone for treating the symptoms of ADHD. (LO #1)
 - a. True
 - b. False
4. In a recent meta-analysis on modafinil for the treatment of ADHD in children and adolescents, patients assigned to modafinil showed which of the following results compared to the placebo group? (LO #3)
 - a. More insomnia and increased appetite
 - b. No change on ADHD scores
 - c. More improvement on ADHD scores
 - d. Less insomnia and decreased appetite
5. You would like to use a supplement for your ADHD patient to help with symptom control of hyperactivity. According to Dr. Shannon, one recommendation to try is: (LO #2)
 - a. Calcium plus vitamin D3, with optional magnesium
 - b. SAME (S-adenosylmethionine)
 - c. Pycnogenol
 - d. Vitamin E
6. Methylphenidate products tend to have more appetite suppression, irritability, and withdrawal symptoms than amphetamine products. (LO #1)
 - a. True
 - b. False
7. In a recent study on atomoxetine in children with comorbid ADHD and dyslexia (ADHD+D), both ADHD+D patients and dyslexia-only patients assigned to atomoxetine showed which of the following results compared to the placebo group? (LO #3)
 - a. Significant improvement in phonologic processing; no change in basic reading skills and reading vocabulary
 - b. Significant improvement in phonologic processing and basic reading skills; no change in reading vocabulary
 - c. No improvement in phonologic processing; significant improvement in basic reading skills and reading vocabulary
 - d. Significant improvement in phonologic processing, basic reading skills, and reading vocabulary
8. Which of the following long-acting stimulants can be administered in crushed form? (LO #1)
 - a. Focalin XR
 - b. QuilliChew
 - c. Concerta
 - d. Aptensio XR

Hone your psychiatry skills
and earn CME with...

The Carlat Psychiatry Report



This newsletter offers
all of the same great
features as *The Carlat
Child Psychiatry Report*,
but covering general
psychiatry.

One year: \$129

Two years: \$229

To subscribe, visit
www.thecarlatreport.com

THE CARLAT REPORT: CHILD PSYCHIATRY

P.O. Box 626
Newburyport, MA 01950

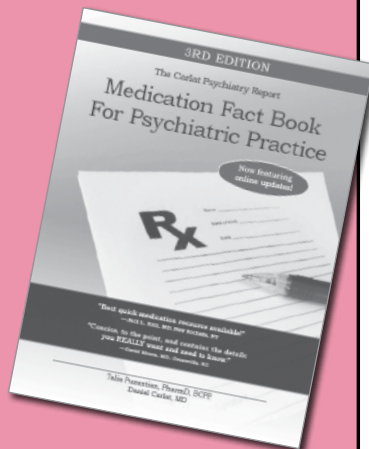
This Issue's Focus:
**ADHD in Children and
Adolescents**

Next Time in *The Carlat Child Psychiatry Report*: Focus on Adolescents

New Edition!

The Carlat Psychiatry Report Medication Fact Book 3rd Edition

- The latest on new medications (such as Rexulti, Vraylar, Namzaric, Belsomra, Addyi, and Xyrem)
- 101 medication fact sheets, 24 of which are brand-new
- 20 updated reference tables
- An 8-credit CME quiz



Order your copy online today!
www.TheCarlatReport.com/MedFactBook

- Yes! I would like to try *The Carlat Child Psychiatry Report* for \$129 for one year. I may cancel my subscription at any time for a full refund if not completely satisfied.
- Enclosed is my check made payable to *Carlat Publishing LLC*

Please charge my

Visa MasterCard Amex

Card # Exp. Date

Signature

Name

Address

City State Zip

Phone Email (required)

Please mail payment to:

The Carlat Child Psychiatry Report,

P.O. Box 626, Newburyport, MA 01950

Or call toll-free 866-348-9279 or fax to 978-499-2278