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CHILD PSYCHIATRY

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UNBIASED INFORMATION FOR CHILD PSYCHIATRISTS

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Editor-in-Chief

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IN THIS ISSUE

Hidden Medical Disorders

Learning objectives for this issue:
1. Explain the research and theories behind post-concussive syndrome. **2.** Describe the role of vitamin D in depression. **3.** Detail the relationship between the endocrine system and psychiatric illnesses in children and adolescents. **4.** Understand some of the current findings in the literature regarding psychiatric treatment.

Post-Concussive Syndrome, Traumatic Brain Injury, and Disruptive Behavior Disorders

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Dr. Harris has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Head injuries occur in 110 to 400 out of every 100,000 adults each year, but are much more common in children—around 692 per 100,000 children younger than 15. Mild traumatic brain injury (TBI) occurs in 75% to 85% of these cases. While serious emotional, cognitive, and behavioral changes are known sequelae of severe TBI, it appears at least in some cases, mild TBI has more significant and longer term effects than previously believed.

Severe TBI

Severe TBI is generally defined as brain injury resulting in loss of consciousness (LOC) for greater than six hours and a Glascow Coma Scale (GCS) score of three to eight. Documented behavioral effects of severe TBI include more disruptive behavior in general, new onset conduct disorder in particular (Gerring JP et al, *Brain Inj* 2009;23(12):944–955), and increases in

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Vitamin D Deficiency and Depression in Children

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Should you be ordering vitamin D levels in your patients? Vitamin D studies have proliferated recently. The recent finding that vitamin D receptors are found in the brain, along with the well known association between low sunlight exposure and seasonal affective disorder, has led doctors to wonder whether there is an association between vitamin D deficiency and depression.

What is Vitamin D?

Vitamin D is a fat-soluble vitamin that has two forms—vitamin D_2 or ergocalciferol, and vitamin D_3 or cholecalciferol. Vitamin D_3 is produced in the skin upon exposure to ultraviolet B radiation from sunlight. Variations in age, skin pigmentation, latitude, time of day of exposure, and time of the year affect the actual amount of exposure. In general, for a fair-skinned person, adequate amounts of vitamin D can be generated by exposing the arms and legs to direct sunlight for five to 30 minutes twice a week (Parker G and Brotchie H, *Acta Psychiatr Scand* 2011;Apr 12, online ahead of print). Vitamin D_3 can also be obtained from animal dietary sources, such as deep sea fatty fish, egg yolks, liver, or fortified foods.

Vitamin D_2 can be found in plant dietary sources, such as shitake mushrooms, and is commercially produced for fortification by irradiation of yeast. Less than 10% of vitamin D is derived from dietary sources. Both vitamin D_2 and D_3 are converted to the prohormone 25-hydroxyvitamin D (25(OH)D) in the liver, and vitamin D status is determined by measurement of serum 25(OH)D levels.

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Post-Concussive Syndrome, Traumatic Brain Injury, and Disruptive Behavior Disorders

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aggressive behavior (Cole WR et al, *Brain Inj* 2008;22(12):932–939).

Cognitive effects have been noted for all core academic skills, leading to a reported 79% of kids with severe TBI having failed grades or received special education services within two years post-injury (Ewing-Cobbs L et al, *J Clin Exp Neuropsychol* 1998;20(6):769–781). Emergence of new onset ADHD (so-called secondary ADHD or SADHD) is a documented phenomenon (Max JE et al, *J Am Acad Child Adolesc Psychiatry* 2005;44(10):1041–1049), and reports of increases in depressive and anxiety disorders have also been made.

Mild TBI

Definitions of mild TBI vary, but perhaps the simplest is brain injury resulting in any LOC less than 30 minutes, or amnesia, confusion, or disorientation, and a GCS score greater than 12. It is essentially synonymous with the colloquial term "concussion."

The outcome of mild TBI is far more controversial. Post-concussive syndrome (PCS) is a term frequently used to refer to a constellation of symptoms noted after mild TBI, including complaints of headache, dizziness, fatigue, depressed or anxious mood, sleep disturbance, light sensitivity, forgetfulness, irritability, emotional instability, and concentration difficulties. (It is called post-concussional disorder in DSM-IV.)

Estimates of PCS are 6% to 35% in mild TBI in children. Symptoms of PCS appear to resolve in large part for most patients within the first few months post-injury, but there is evidence for persistent PCS and other behavior problems in a minority of children with mild TBI (Taylor HG et al, *Neuropsychol* 2010;24(2):148–159). For example, one study found a significant increased risk for psychiatric illness in children with no prior history of psychiatric illness in the three years after mild TBI, especially hyperactivity in the first year after mild TBI (Massagli TL et al, *Arch Phys Med Rehab* 2004;85(9):1428–1434).

Controversy surrounds the diagnosis of post-concussive syndrome. There is a question as to whether the symptoms experienced can truly be attributed to brain injury *per se.* Studies have shown increased rates of pre-trauma behavior problems (eg, ADHD), and that some symptoms (eg, SADHD, behavioral problems) have occurred at similar rates following orthopedic non-brain injury and following mild TBI.

Therefore the question is whether behavior problems attributed to mild TBI are cause or effect, and if the answer is effect, effect of what? Are children with behavior problems more likely to be injured in general? Or does the experience of being injured, and not the organ system injured, cause the symptoms described as post-concussive syndrome?

One study attempted to answer these questions by looking at 186 children ages eight to 15 with mild TBI and a comparison group of 99 kids with uncomplicated orthopedic injuries. Patients and their parents were asked to rate their symptoms within three weeks after injury and at one, three, and 12 months post-injury. The mild TBI group had higher ratings of symptoms consistent with post-concussive syndrome both at baseline and at follow-up than the orthopedic injury group. Notably, parent ratings of cognitive symptoms did not peak until three months after a brain injury. More severe ratings were associated with motor vehicle related trauma, loss of consciousness, neuro-imaging abnormalities and hospitalization (Taylor op.cit). The study, however, did not discuss in detail what symptoms were most commonly reported or elevated, so it's difficult to draw more specific conclusions.

Clinically, however, it is clear that many clinicians and families report worsening behavior, concentration, and impulse control in the months after even mild head injury. It is important to our patients and their families to hear that these symptoms are probably related to the injury, and more importantly, will likely improve over time. In my experience, symptoms improve greatly over the first few weeks, then often resolve over the next six months.

For those who don't improve, careful psychiatric treatment, both psychosocial and possibly psychopharmacological may be warranted. Medications to treat symptoms of inattention and impulsivity (eg, stimulants) or aggression and irritability (eg, valproic acid) are anecdotally helpful. At the moment, there are no clear clinical guidelines as to how to treat these children, beyond the basics of all good psychiatric care—thoughtful individualized assessment, monitoring, and symptom management. It is also very important to minimize the chance of recurrent TBI, as this may lead to even more severe consequences (Byard RW and Vink R, *Forensic Sci Med Pathol* 2009;5(1):36–38).

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EDITORIAL INFORMATION

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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.

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Vitamin D Deficiency in Children

The reference range for normal vitamin D levels varies from lab to lab and continues to be a matter of debate. The Institute of Medicine (IOM) and the American Academy of Pediatrics have defined vitamin D *deficiency* as a serum level less than 11 ng/ml. (Bone disease is usually evident at these levels.) Vitamin D *insufficiency* has been defined by levels lower than 20 ng/ml. Levels between 21 ng/ml and 29 ng/ml may be defined as *relative insufficiency.* A 25(OH)D level greater than 30 ng/ml is usually considered optimal (some would argue greater than 40 ng/ml, but most experts consider the goal range to be 30 ng/ml to 60 ng/ml).

Most pediatricians assume that children receive adequate amounts of vitamin D from sunlight and dietary sources such as milk. The universal feeling is that receiving adequate sun exposure is problematic only in extremes of latitude, in winter, for those who are of very dark complexion, and in people with extreme clothing coverage. Interestingly, however, a recent study conducted in an area with excellent ambient sun exposure and conducive to year-round outdoor activity (the American Southwest) showed high levels of insufficiency (14% of healthy children had vitamin D levels of less than 20 ng/ml, 49% had levels lower than 30ng/ml, and only 15% had sufficient levels of greater than 40 ng/ml) (Szalay EA et al, *J Pediatr Orthop* 2011;31(4):469–473).

Pediatricians commonly recommend regular use of sunscreen to minimize damage caused by sun exposure. Sunscreen with a sun protection factor (SPF) of eight or greater effectively prevents vitamin D production by the skin. On top of that, the amount of time that children play outside continues to decrease. A 2006 survey in Minnesota found that 40% of children regularly watch television by age three months, and 90% watch regularly by age two (Jordan A, *Dev Behav Pediatr* 2004;25(3):196–206). Children between two and 17 years of age may spend more than six non-school hours per day with electronic media. These factors combined may result in today's children having an elevated risk of vitamin D insufficiency compared to previous generations of children.

Testing for Serum 25(OH)D Levels and Using Vitamin D Supplementation

The lab test to measure vitamin D levels can range in cost from $25 to $250. Given recent data regarding high rates of vitamin D deficiency in children, coupled with the fact that obtaining adequate vitamin D from food is nearly impossible (to obtain 1,000 international units per day (IU/d) of vitamin D, a child would need to drink ten eight-ounce glasses of milk or eat two to three servings of salmon plus several glasses of milk daily), supplementation might be more cost-effective than mass testing of levels.

In 1997, The IOM established adequate intake levels for vitamin D at 200 IU/d for infants and children, a level assumed to maintain serum vitamin D levels if the child receives no vitamin D through sun exposure. This recommendation was doubled to 400 IU/d in 2008 as higher intake levels were shown to prevent rickets. In 2010, after reviewing more recent data, the IOM increased the recommended daily allowance to 600 IU for children and adults (and 800 IU/d for those over age 70) (Dietary Reference Intakes for Calcium and Vitamin D. Eds, Institute of Medicine of the National Academies, Food and Nutrition Board 2010. *Chapter 5. Dietary reference intakes for adequacy: calcium and vitamin D.* National Academies Press. 291–340).

In children without adequate sun exposure or to correct a deficiency, 800 to 1,000 IU/d may be required to maintain adequate levels. The dosage found in most children's multivitamins is 400 IU/d, and this amount of intake likely has little effect on serum vitamin D levels. As a reference point, 400 IU/d raises the vitamin D level in a healthy adult by 3 ng/ml to 5 ng/ml, depending upon the baseline level. To increase the blood level from 20 ng/ml to 32 ng/ml in an adult, an additional 1,700 IU/d of vitamin D may be needed (Barger-Lux MJ et al, *Osteoporos Int* 1998;8(3):222–230). Therefore, the current recommended allowances may be set at unrealistically low levels if the goal is to prevent or to treat insufficiency or deficiency.

For vitamin D supplementation, you should use vitamin D_3, as vitamin D_2 has only one third the potency of D_3. Vitamin D_3 can be purchased by itself in small tablets, capsules, gummy forms or liquid.

Vitamin D in any form, as a fat-soluble vitamin, does have potential for toxicity, although this is rarely seen with levels below 150 ng/ml. An extensive review of multiple studies found that vitamin D toxicity in adults was not evident in trials using less than 10,000 IU/d (Szalay EA et al, *op.cit*). Consequences of vitamin D toxicity include hypercalcemia (clinically presenting as nausea, vomiting, increased thirst, depression), kidney stones, and soft tissue and vascular calcifications.

Vitamin D and Depression

So what does all this have to do with psychiatry? One word: depression. A number of cross sectional clinical and epidemiologic studies have investigated whether there is a relationship between vitamin D levels and depressive symptomatology or illness in adults. Nine out of 13 such studies found that low levels of vitamin D were significantly associated with higher rates of depression diagnoses or depressive symptoms. Because vitamin D deficiency may be related to living in areas with decreased sunlight or in higher latitudes, it has been theorized that vitamin D deficiency may play a role in the development of seasonal affective disorder. However, two studies were not able to show a difference in vitamin D levels when patients with seasonal affective disorder were compared to controls. Additionally, bright light therapy did not show any improvement in vitamin D levels. None of these studies included pediatric populations.

Only one controlled study of vita-

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Q&A With the Expert

Expert Interview

The Endocrine System and Psychiatric Medications

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Dr Lee has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

CCPR: Dr. Lee, in addition to your clinical practice, you do research on reproductive development and the effects of endocrine disruptors on growth and puberty. You're a great resource for us because, as child psychiatrists, we have a lot of overlap between our practice and endocrinology, and often we're not sure what to do. Our biggest issue is often the thyroid, because lithium suppresses it, and because thyroid disorders can cause psychiatric symptoms, right?

Dr. Lee: Sometimes thyroid disorders do present with psychiatric symptoms. With Graves' disease behavioral manifestations are very common, and can be the presenting symptoms. In children, these manifest as moodiness, irritability, and labile behavior. Therefore a child with hyperthyroidism may have mood swings, school performance issues, and difficulty concentrating that might be confused with ADHD.

CCPR: If we have a child who is presenting with symptoms that we are concerned might be thyroid, what kind of history do we need to ask about?

Dr. Lee: Let's talk about the two forms of thyroid disease separately. For hypothyroidism, the symptoms are very subtle and maybe something as simple as constipation. Poor growth in height is often the major finding. Children don't usually have excess weight gain or obesity, because although hypothyroidism slows metabolism, it also decreases appetite.

CCPR: And hyperthyroidism?

Dr. Lee: Hyperthyroidism tends to be more symptomatic. One of the behavioral signs is mood swings where they burst out crying, for example. Deterioration in school performance is a big complaint—inability to concentrate and distractibility. There is often a history of diarrhea, weight loss or difficulty gaining weight, and hyperphagia.

CCPR: What about the contribution of a family history of thyroid disease? Is that something that we should ask about?

Dr. Lee: Thyroid disease is so common that that you often hear that a distant relative has thyroid disease, and there definitely is a genetic component. I think the relevant point in child psychiatry is that, particularly for lithium, there is limited data suggesting that those patients who have a family history of thyroid disease or who have thyroid autoantibodies themselves have a higher risk of developing thyroid dysfunction with lithium therapy. So the relative risk is greater if you have a baseline genetic risk (Bochhetta A et al, *J Clin Psychopharm* 2001;21(6):594–598; Baethage C et al, *J Psych Neurosci* 2005;30(6):423–427).

CCPR: So if we wanted to test for a thyroid problem, what tests do you recommend?

Dr. Lee: For hypothyroidism, the most important is TSH, and that will measure if the pituitary gland senses that the body is not receiving enough thyroid hormone. To measure thyroid hormone levels, depending on your local lab, you can request either free T4 or total T4. For hypothyroidism, you don't need to measure total T3, because that tends to be well preserved in the normal range even in children who are profoundly hypothyroid. However, for Graves' disease, you do need to measure all three hormones—TSH, either free T4 or total T4, and total T3. There is hardly ever any need to measure free T3, because it is very short lived and serum concentrations are not meaningful.

CCPR: We all know that lithium suppresses thyroid. What is the danger of that and over what time course?

Dr. Lee: Lithium has direct effects on the thyroid gland. It causes suppression of thyroid hormone synthesis as well as thyroid hormone release. If someone is being started on lithium, I think it is important to obtain baseline labs, then to retest every six months, or sooner if the lithium dose is being increased significantly. This is because thyroid hormone has such a profound effect on children's growth. If someone is on lithium for the long term, I would start thyroid hormone replacement as soon as the TSH becomes abnormal. Thyroid hormone is easy to give and the goal is to maintain a euthyroid status.

CCPR: So would we be better off starting our own thyroid hormone or referring to an endocrinologist? What are the risks if we get it wrong?

Dr. Lee: I think a referral to an endocrinologist for management is preferable. However, this depends on how comfortable individuals feel with management of thyroid dysfunction. If your patient is thyrotoxic, he or she won't be comfortable, and you could have behavioral consequences of the elevated thyroid hormone. If you use a subtherapeutic dose, then the child is still symptomatic.

CCPR: What do you usually start at for thyroid?

Dr. Lee: Dosage starts at 12 mg/kg for an infant and changes through childhood. An adolescent receives approximately 1.5 mg/kg, so the dosing is both age and weight based.

CCPR: Let me switch hormones. How cautious do we need to be about prolactin?

Dr. Lee: If prolactin is only minimally elevated, and there has been no clinical effect on reproductive function, then you don't need

to address it. For example, a woman may have serum concentrations that are one to two times the normal range with absolutely normal cycling. If prolactin becomes more elevated, for example, greater than three times the normal level, you are likely to see some effects on reproductive function.

CCPR: And does too much prolactin in a boy affect puberty?

Dr. Lee: Yes. It can delay the progression of puberty.

CCPR: While we are in the reproductive realm, can we talk a little bit about Depakote and how it may cause polycystic ovarian syndrome. What should we monitor for?

Dr. Lee: What has been reported with valproate is irregular menstrual cycles. So it may be a good idea for adolescents who are already menstruating to keep track of the first and last days of their cycles when they are started on a drug such as valproate. This way you can identify abnormal menstrual patterns early. Other symptoms such as hirsutism or acne are due to elevated androgens.

CCPR: Adolescents hate Depakote and most other mood stabilizers because they cause acne and weight gain. There is evidence that metformin can prevent weight gain associated with antipsychotic use. Do you think that metformin is appropriate to use in children?

Dr. Lee: Unless you have clear insulin resistance, there is no good data showing metformin's efficacy for weight loss in children on antipsychotics. For teenage girls with PCOS, there is some benefit (Ojaniemi M et al, *Horm Res Paediatr* 2010;74(5):372–375).

CCPR: Is metformin risky to use?

Dr. Lee: The major side effect is lactic acidosis, which has symptoms of nausea and weakness, but it is fairly rare. There are frequent acute side effects of GI distress and discomfort, which sometimes lead to kids stopping it soon after starting or being nonadherent to therapy.

CCPR: Let's talk about growth hormone. Do you know of any link between growth hormone deficiency and psychiatric symptoms?

Dr. Lee: In general most of the kids that I follow on growth hormone do very well and don't have psychiatric symptoms. However, there has been some association with growth hormone deficiency and depression (Okumura A et al, *J Paediatr Child Health* 2009;45(11):636–640).

CCPR: Are there other endocrine problems that we should consider when we see a child with psychiatric symptoms that don't quite fit the usual?

Dr. Lee: Sometimes Cushing's syndrome can cause a psychosis and is a very, very difficult endocrine condition to diagnose. Cushing's in children is a diagnosis that often is made two or three years after initial symptoms. So that is one possibility if you have a child who has had excess weight gain and poor linear growth. Excessive glucocorticoids will compromise linear growth. If a child who is still growing has weight gain that isn't accompanied by normal growth, as you'd typically see with obesity, then you should consider Cushing's disease. Poor growth in height, combined with subtle hirsutism and muscle pseudohypertrophy should signal that it might be an endocrine cause.

CCPR: Thank you, Dr. Lee.

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Vitamin D Deficiency and Depression in Children

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min D supplementation in non-seasonal depression has been published. In that study, 441 overweight and obese patients were randomized to receive 20,000 or 40,000 IU of vitamin D_3 or placebo weekly for one year. Although patients were not necessarily clinically depressed (rather, had depressive symptoms as measured by Beck Depression Inventory), at baseline, those with vitamin D levels lower than 16 ng/ml had greater depressive symptomalogy than those with higher levels. The two groups receiving vitamin D supplementation had significant improvement in their scores, whereas the placebo group did not (Jorde R et al, *J Intern Med* 2008;264(6):599–609).

Vitamin D supplementation has been studied in two controlled studies of seasonal affective disorder (SAD). In the first study (n=15), eight patients received a one-time 100,000 IU dose of vitamin D and seven received light therapy for one month. Vitamin D levels increased significantly in both groups: in 74% of those supplemented and in 36% of those who

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Vitamin D Deficiency & Depression: Take Home Facts

- Vitamin D deficiency and insufficiency in children may be quite common.
- The IOM and the AAP have defined vitamin D deficiency as a serum level <11 ng/ml; insufficiency as levels of <20 ng/ml; and relative insufficiency as levels between 21 ng/ml and 29 ng/ml. A vitamin D serum level >30ng/ml is usually considered optimal.
- Historically, the recommended vitamin D intake levels have been too low and were recently increased.
- There is some evidence that vitamin D deficiency may contribute to depression; however, current studies cannot convincingly support this theory.
- Similarly, there is some evidence that supplementation may improve depressive symptoms; however, due to paucity of data (and absolute lack of data in children), conflicting results and limitations in study size and design, an evidence-based recommendation to supplement cannot be made.
- No studies investigated the role of vitamin D supplementation in addition to antidepressant treatment, so no conclusions can be made with regard to its role as an augmenting agent.
- Given the high rates of deficiency and insufficiency and the relative safety of 400 IU/day to 800 IU/day, a case could be made for supplementation in children who have tested with low serum vitamin D levels whose lifestyle and geography may predispose them to vitamin D insufficiency, if not for depression then for overall bone health.

Research Updates IN PSYCHIATRY

ADHD

Is Nicotine an Effective Treatment for ADHD? Three Studies Weigh In

If you want to watch a new drug wend its way to market, you might start watching the literature for ABT-809, a nicotinic receptor partial agonist and proposed novel approach to the treatment of ADHD. To that end, two recent clinical trials are interesting reads.

The nicotinic receptor has five subunits that can vary from location to location, and presumably from purpose to purpose. It seems that different subunit combinations mediate different behaviors and different neurotransmitters, and that makes them an interesting focus for drug design. The alpha-4, beta-2 nicotinic receptor appears to induce the release of dopamine stored at neural synapses and induces the firing of dopaminergic neurons. When people quit smoking, they have a variety of symptoms, including lack of concentration. People with ADHD are more likely to be smokers (although this may be our own making—prior stimulation with amphetamine makes nicotine more reinforcing in rats), and smoking relieves the symptoms of ADHD in patients who have it. Nicotine has also been shown to improve attention in Alzheimer's patients, improve abnormal sensory gating and attention in patients with schizophrenia, and enhance working memory.

To refresh your memory, a partial agonist reduces the response of the target cell rather than completely blocking it, more like a dimmer than a light switch. ABT-089 is a partial agonist of the alpha-4, beta-2 subtype of the nicotinic receptor, which seems to play a role in depression, locomotion (specifically too much locomotion), pain, and fear-associated learning, among other things (Piccioto et al, *Neuropsychopharmacology* 2000;22(5);451–465).

In the first study, which focused on adults with ADHD (Apostol G et al, *Psychopharmacology (Berl)* 2011;Jul 12, online ahead of print), five different doses of ABT-089 were evaluated in a double-blind, randomized cross-over design. That is, within each group, half of patients were given placebo for four weeks and half active compound. Then there was a two week wash out period in which neither was administered. Finally, for the next four weeks, the subjects were given the opposite of what they had previously received: placebo if they had drug, drug if they had placebo. There were about 20 subjects in each group. Doses were 2 mg, 5 mg, 15 mg, 40 mg and 80 mg daily. All subjects met criteria for ADHD and nothing else and were washed out from any psychotropic medication they had been using. The primary outcome was CAARS:Inv, an adult ADHD scale with subscales in inattention and hyperactivity. There were several drop-outs and interestingly, many of these were smokers.

To cut to the chase, there was a statistically significant improvement in total CAARS:Inv scores in the higher doses, with effect sizes of 0.29 for the 40 mg group and 0.30 for the 40 mg, BID group (in other words: very small effect sizes). To be fair, the effect seen was only at the tail end of treatment, so it is possible that after more time, the effect would be larger. Adverse effects are always hard to gauge, as things happen to people whether or not they are taking medication—or think they are. However, three patients had serious adverse events: vasovagal syncope, myocardial infarction, and gallstones. While the investigators did not feel that these were related to drug (and the patients were on the lower doses of medication), the compound does modulate cholinergic activity, so you never can tell. Irritability was the most frequent "non-serious" adverse event.

In the pediatric paper (Wilens TE et al, *J Am Acad Child Adolesc Psychiatry* 2011;50(1):73–84.e1), two similar studies were reported together. Both enrolled subjects between ages six and 12 with ADHD (per the KSADS-PL). One study used doses equivalent, in mg/kg, to the first four adult doses. The second study used the equivalent of the 80 mg dose. Rather than a cross-over design, the subjects were given six weeks of drug or placebo or atomoxetine (Strattera). There were about 40 subjects per group. Using the outcome of Attention-Deficit/Hyperactivity Disorder Rating Scale-IV: Home Version, and the secondary outcome of Clinical Global Impression–Attention-Deficit/Hyperactivity Disorder-Severity Scale, the study found no statistical difference in ABT-089 vs placebo, but the atomoxetine group did improve.

CCPR's Take: In comparison to the Apostol et al adult study, the Wilens et al pediatric study suggests that ABT-089 is really not effective in children. The authors remind us that the blood-brain barrier differs in permeability from children to adults, and offer this as one possible explanation. It will be interesting to see if, like atomoxetine, ABT-089 goes on to achieve FDA approval in adults despite poor early trials. If so, it is likely that less well informed practitioners will use it in kids. Fortunately, you don't have to be one of them.

SCHIZOPHRENIA

Early Onset Psychosis May Lead to Better Outcomes

A long term study comparing patients with early onset psychosis to those with later onset psychosis may have some good news for child psychiatry. While previous studies have shown worse or equivalent outcomes for younger onset patients, this study demonstrated a protective effect. Three hundred and sixty-six patients diagnosed with schizophrenia spectrum disorders were interviewed at a mean follow up of 7.4 years after onset. All patients had an age of onset between 14 and 30 years old and were treated at the same clinic in Melbourne, Australia. The study compared patients with a first episode of psychosis before age 18 to those with the first episode after age 18.

Diagnosis between onset and follow up was not any more likely in either group, but patients in the early onset group were more likely to have been free of psychosis for the past two years. The younger onset group had better

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CME Post-Test

CME Notice: The test below is intended to be for **practice only.** All subscribers must take their tests online at www.thecarlatchildreport.com. If you cannot take your test online, please call 866-348-9279 or email info@thecarlatreport.com.

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Below are the questions for this month's CME 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. Approximately how many kids with mild traumatic brain injuries will develop post-concussive syndrome (Learning Objective #1)?
   a) 2% to 5% b) 15% to 25% c) 75% to 85% d) 6% to 35%

2. If a child has a 25(OH)D level of 40 ng/ml, which of the following would best define him (LO #2)?
   a) He has a vitamin D deficiency b) He has a vitamin D insufficiency
   c) His vitamin D level is optimal d) His vitamin D level is dangerously high

3. According to Dr. Mary Lee, a child with hypothyroidism may have mood swings and school performance issues that can be confused with ADHD (LO #3).
   a) True b) False

4. In the Wilens T et al study of ABT-089 as a treatment for ADHD, the children in the ABT-089 treatment group showed what improvement over those in the placebo group (LO #4)?
   a) no statistically significant improvement over placebo b) 5% improvement over placebo group
   c) 24% improvement over placebo group d) 40% improvement over placebo group

5. In the Amminger GP et al study of early onset psychosis, at follow-up participants in the younger onset group were more likely to be employed or in school and to be employed half time or more (LO #4).
   a) True b) False

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Vitamin D Deficiency and Depression in Children

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received light therapy. All patients in the vitamin D group showed improvement in all depression outcome measures compared to those treated with light therapy, none of whom showed significant changes in mood scores (Gloth FM et al, *J Nutr Health Aging* 1999;3(1):5–7). The second controlled study was conducted with women in England with SAD and who were greater than 70 years of age. In this six-month study, 912 patients received calcium with 800 IU/d of vitamin D and 1,205 received no supplementation. No significant differences were noted in mental health outcome measures in either group (Dumville JC et al, *J Nutr Health Aging* 2006;10(2):151–153).

CCPR'S VERDICT

There is pretty clear evidence that vitamin D insufficiency is a big problem. However, the current evidence does not definitively establish an association between vitamin D deficiency and risk for depression. Plus, there are no data in children in particular to support the notion of vitamin D supplementation for depression. In fact, after reviewing the data available on use of vitamin D, the IOM issued a report in 2010 concluding that there was not adequate evidence to suggest a causal role or a treatment role for vitamin D in non-bone-health related uses, including depression. Nonetheless, since moderate vitamin D supplementation is harmless and cheap, many child psychiatrists may choose to recommend it as we await more definitive data.

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outcomes in other ways as well: younger onset patients were more likely to be employed or in school and to be employed half time or more. Younger onset patients were also more functional in social relationships.

Although there is talk in the field about the potential protective effect of early use of antipsychotics (Liu et al *Schizophr Res* 2010;23(1):37–44; Preti A et al, *Schizophr Res* 2010 Oct;123(1):30–36) the research has been disappointing. The authors make an interesting but different hypothesis as to what is the critical difference between the two groups, citing the participating clinic's treatment priorities for early onset patients: to stay in school and maintain normal adolescent developmental milestones. They recommend intensive psychosocial and cognitive-behavioral interventions that address the developmental needs of the age group (Amminger GP et al, *Schizophr Res* 2011;Jul 6, online ahead of print).

CCPR's Take: This paper shows that early onset psychosis does not necessarily portend a worse outcome for patients with schizophrenia or schizophrenia spectrum disorders. We know that intensive early psychosocial interventions for early psychosis actually work, and the risks of psychosocial interventions are low. It's easy to get caught up in the anxiety that the positive symptoms of first episode psychosis generate, and join the family in wanting them to be gone as quickly as possible. Our patients are best served by our ongoing anticipatory guidance after the psychosis itself passes, and a firm understanding that every adolescent wants to be as "normal" as possible.

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