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Joshua D. Feder, MD
Editor-in-Chief

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Learning Objectives

After reading these articles, you should be able to:

1. Evaluate the risk of antidepressant-induced suicidality in children and adolescents.
2. Assess and treat the effects of bullying in school-age patients.
3. Describe the current role of antidepressants in treating child and adolescent patients.
4. Summarize some of the current findings in the literature regarding psychiatric treatment for children and adolescents.

Antidepressant-Induced Suicidality: What It Is and What You Should Do

Candace Good, MD, Child & adolescent psychiatrist, SunPointe Health, State College, PA.

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

Do antidepressants actually cause children to be suicidal? If so, how do we detect it, and what should we do about it? In this article, we'll give you a brief review of the most recent findings on antidepressant-induced suicidality (AIS) in children and adolescents, and then move on to some practical tips for how to evaluate and prevent this problem.

Review of data on antidepressant-induced suicidality

In 2004, the FDA required a black box warning about suicidality in children
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In Summary

- It is important for clinicians to consistently monitor their child and adolescent patients for the potential of antidepressant-induced suicidality.
- Although it is more common for suicidal ideation to occur within the first month of starting an antidepressant, suicidality can emerge at any time during treatment.
- Educate your patient's family about potential antidepressant side effects such as trouble sleeping, increased activity, or impulsivity, which can lead to patients feeling worse or acting on suicidal thoughts.

Q&A With the Expert

Current Use of Antidepressant Medication in Children Danella Hafeman, MD, PhD

Assistant Professor of Psychiatry at the University of Pittsburgh School of Medicine

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

Editor's note: The issue of emergent suicidal thinking has weighed on us since the 2004 black box warning—amplified by the re-analysis of the now infamous study 329, which found the emergence of previously under-reported suicidal thinking. How do we offer hope for effective use of medication while balancing the potential risks? Dr. Danella Hafeman has made a close study of it all and sheds light on the problem.

CCPR: Can you tell me about your current work?

Dr. Hafeman: I'm a child psychiatrist at the Child and Adolescent Bipolar Spectrum (CABS) clinic at the University of Pittsburgh. While



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Antidepressant-Induced Suicidality: What It Is and What You Should Do

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and adolescents for all antidepressants. This was based on a meta-analysis of 23 antidepressant clinical trials with a total of 4,300 children and adolescents. While no actual suicides occurred in these trials, suicidal thinking was reported by 4% of kids taking medication vs 2% on placebo (Hammad TA, *Arch Gen Psychiatry* 2006;63(3):332–339). Although the difference was not statistically significant, the FDA mandated the black box warning in 2004, extending it to young adults (ages 18–24) in 2007. After the warning, there was a precipitous drop in antidepressant prescription rates and

in diagnoses of depressive disorders in youth, and some reports emerged of increasing suicide rates. For example, one retrospective study published in 2014 found a reduction of 31% in the use of antidepressants in adolescents in the second year after the warning, and the authors estimated 2 additional suicide attempts per 100,000 adolescents and 4 per 100,000 young adults (Lu CY et al, *BMJ* 2014;348:g3596).

While the FDA's actions may have had the unintended negative consequence of discouraging effective medication treatment, the preponderance of data indicate that AIS is a real issue in some patients and that it is an important potential side effect to monitor.

How to prevent AIS

Before you start antidepressants in children, check for common risk factors for suicidality. These include substance abuse, conduct disorder, prior suicidal ideation (SI) or attempts, and guns in the home. Because bipolar disorder is associated with SI, carefully assess whether the patient has symptoms and/or a family history of bipolar disorder. There are also some standardized screening instruments that are useful when assessing for SI: the Suicidal Ideation Questionnaire (SIQ-Jr) (for purchase information, see: <https://www.parinc.com/Products/PKey/413>) and the Patient Health Questionnaire (PHQ-A) (see: <http://uacap.org/uploads/3/2/5/0/3250432/phq-a.pdf>).

Choosing medications

Unless the depression is quite severe, it's best to begin treatment with psychotherapy. Address stressors and dynamic issues in school and family, as well as lifestyle factors such as sleep, exercise, and behavior activation strategies. While good psychotherapy is effective for depression, medication can be life-saving when a child is severely depressed, and particularly when there is suicidal thinking present.

Fluoxetine has the best data for antidepressant efficacy and may be the safest as well. Cipriani and colleagues looked at 34 randomized clinical trials of acute MDD, totaling 5,260 participants (ages 9–18) on 14 different antidepressants (Cipriani A et al, *Lancet*

2016;388(10047):881–890). Only fluoxetine was significantly more effective than placebo, and only venlafaxine was associated with an increased risk of SI. Fluoxetine was also more tolerable than duloxetine and imipramine. The researchers noted that when SI is present, it tends to occur early, particularly within the first month. Be sure to have close follow-up early on, asking about SI with questions such as, “Have you had any thoughts of hurting yourself?” and, “Have you had any thoughts of not wanting to live?”

Start low, go slow

The commonsense approach of “starting low and going slow” is supported by a large population study indicating that deliberate self-harm (DSH) can be dose-related (Miller M et al, *JAMA Intern Med* 2014;174(6):899–909). This study looked at 162,625 patients ages 10–64. It compared those who had dosages of fluoxetine 20 mg, sertraline 50 mg, or citalopram 20 mg vs people on higher dosages of those antidepressants. The overall rate of DSH in the patients on the higher dosages was 1 in 136 in the first 3 months of treatment, but patients ages 10–24 on those higher dosages had twice that rate of DSH.

How to talk to family about AIS

Ask about family history of antidepressant use and outcomes to learn what might work for your patient and what challenges and concerns family members might have. Tell families that antidepressants can be very helpful, reducing suicidal ideas and behavior, and although their risk of causing self-harm is low, watchfulness is advised just in case. Ask family members to alert you right away if self-harm occurs, and to watch for other possible side effects of antidepressants, including trouble sleeping, increased activity, or impulsivity—these can lead to patients feeling worse or acting on suicidal thoughts.

Evaluating SI or self-harm

If a child has made concerning statements, assess them carefully. Passive SI

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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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Antidepressant-Induced Suicidality: What It Is and What You Should Do

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is common in children, and you might hear statements such as, “I wish I were dead” or, “I wish I were not here.” If a child is indeed thinking about self-harm, follow up by asking if the child has thought of ways to possibly do so. Ask specifically if the child has actually done anything to prepare for an attempt, such as securing a knife, pills, or a rope, or looking for places to jump. Remember that asking gradually and sequentially about suicidal ideas and plans is extremely unlikely to “give the child

dangerous ideas.” It is far worse to have failed to ask.

Try to figure out how likely it is that the antidepressant is contributing to SI. Was the medication started within about 3 weeks of the SI onset? While 3 weeks or sooner is common, suicidality can emerge at any time. Are there other side effects, such as agitation or insomnia, which might have preceded and caused the SI? Are there other contributors that probably have nothing to do with the medication, such as family turmoil,

bullying, or school stress? Often the only way to be certain that the medication is the culprit is to reduce the dosage and see if the suicidal thinking abates.

CCPR VERDICT: When children are depressed, start with therapy. Add antidepressants if symptoms are severe, and partner with family members to watch for new or increased suicidal thinking or behavior.

Expert Interview—Current Use of Antidepressant Medication in Children

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we are primarily a clinic for bipolar disorder, we see a lot of kids with unipolar mood disorders, kids who have seen many providers. I am also a researcher, and my studies focus on children and adolescents at risk for bipolar disorder.

CCPR: What is the current state of knowledge about antidepressants in children? What is the research telling you?

Dr. Hafeman: I think our shared clinical experience is that these medications work for many children and adolescents. So, it was surprising that a recent meta-analysis by Cipriani and colleagues found that antidepressants did not generally fare better than placebo (Cipriani A et al, *Lancet* 2016;388(10047):881–890). Fluoxetine did a bit better, but not much. This was concerning, but it doesn't tell the whole story. Another researcher, John Walkup, explains that Cipriani's study included multiple small industry-sponsored trials of kids who had more minor depressive episodes. Those are kids who tend to respond to whatever we do, and so it's no surprise that the placebo rate was upwards of 50% (Walkup JT, *Am J Psychiatry* 2017;174(5):430–437).

CCPR: What can you tell us about the more severe cases that we tend to see?

Dr. Hafeman: The National Institutes of Health (NIMH)-funded Treatment of Adolescent Depression Study (TADS) showed fluoxetine was very helpful in about 60% of adolescents with more significant levels of depression (Silva MJ et al, *JAMA* 2004;292(7):807–820). The positive effect of treatment was even better for those who also had cognitive behavioral therapy (CBT). In that study, the placebo response rate was about 35%.

CCPR: Wow, what a difference. What else have you learned about antidepressants in younger children?

Dr. Hafeman: The TADS study only included children 12 and older. However, a prior randomized controlled study on fluoxetine with kids as young as 7 showed a positive effect with no differences in how the children or adolescents responded (Emslie GJ et al, *Arch Gen Psychiatry* 1997;54(11):1031–1037). So, despite the Cipriani meta-analysis, the rigorous NIMH-funded trials really do support using SSRIs. All the trials also show that the optimal treatment is SSRIs plus an evidence-based therapy, such as CBT or interpersonal therapy.

CCPR: How do you select the right SSRI for a child?

Dr. Hafeman: Fluoxetine has the most data. It was around when the large NIMH trials were happening. We don't have large studies with other medications. Fluoxetine has a very long half-life, which can be helpful if kids or adolescents aren't taking it every day. Also, kids metabolize medications more quickly, so some of the medications with a quicker half-life, such as paroxetine, can lead to withdrawal. On the other hand, sometimes you might actually want a medication with a shorter half-life if you think kids might have activation, sleep problems, or elevated mood, or if they have a family history of bipolar disorder. The shorter half-life means that, if they respond poorly, it won't take a long time for those side effects to go away.

CCPR: Any other important factors in choosing medications?

Dr. Hafeman: One other thing to consider when choosing an SSRI is drug interactions. If the child has other medical conditions and is on other medications, you might consider something such as escitalopram, because there aren't as many drug-drug interactions. But aside from avoiding paroxetine due to its propensity for withdrawal syndromes, there's really not much evidence to choose one versus another SSRI. I also ask what other family members have responded to, and while studies have shown that it doesn't matter substantially, parents who have responded to a specific medication might be more comfortable having their child use it.

CCPR: What about SNRIs?

Dr. Hafeman: There's not as much evidence for SNRIs in adolescents, but the TORDIA trial reported no difference between another SSRI and an SNRI. SNRIs had more cardiac side effects, including elevations in blood pressure, so sticking with SSRIs, at least at first, makes sense (Brent D et al, *JAMA* 2008;299(8):901–913). You might consider an SNRI after the first 2 trials of SSRIs, though there are limited data for this.

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Expert Interview—Current Use of Antidepressant Medication in Children

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CCPR: Can you help us distinguish between antidepressant-induced mania and behavioral activation?

Dr. Hafeman: These are pretty different adverse events. If children develop mania on SSRIs, the clinical consensus is that they are at much higher risk for bipolar disorder (Barbuti M et al, *J Affect Disord* 2017;219:187–192). In fact, if the SSRI-induced mania lasts after the SSRI is out of the system, then the patient meets criteria for bipolar disorder based on DSM-5. Depending on the situation, it probably makes sense to switch to a mood stabilizer at that point. And if you're trying another SSRI, you have to go really slowly and be very careful. Activation manifests differently, with hyperactivity and bounciness. It tends to happen early and sometimes resolves a little bit. Some kids have been very anxious and subdued, and then you give them medication and they're more outgoing. It's more likely to happen for younger kids and in kids with a family history of bipolar disorder, but even that is unclear. Starting low and going up slowly helps avoid activation and other side effects. Activation can vary greatly among SSRIs, so I'll consider switching.

CCPR: You spoke about faster metabolic rates in kids. Can you tell us more?

Dr. Hafeman: You also see that with other medications: for example, with stimulants. I can't tell you the number of kids that we see that definitely have depression and have been on perhaps 3 different antidepressants—like Prozac 20 mg, Zoloft 25 mg, and Celexa 10 mg. Going up to higher doses makes sense, but only if they are still symptomatic and not having side effects.

CCPR: What about bupropion?

Dr. Hafeman: Bupropion doesn't have as much evidence for treatment of depression in kids. It can be helpful for kids who have sub-threshold depression and difficulties with attention. Anecdotally, when kids have sort of a more sluggish depression, a lot of them will feel better on bupropion. I think that's the activating norepinephrine/dopaminergic effect, although not in the sort of activation we were talking about with the SSRIs.

CCPR: Any other antidepressants that you use? How about mirtazapine?

Dr. Hafeman: Mirtazapine can be helpful for sleep, appetite, and anxiety. The evidence for depression in kids is pretty minimal. I don't use it first line, even if there are those other problems that you're pretty convinced are related to depression. An SSRI is the place to start. But if there are other reasons to avoid SSRIs, mirtazapine can be a good choice. We use it a fair amount with medically sick kids, who have a lot of those problems along with a lot of anxiety.

CCPR: What are your thoughts on the black box warning about potential suicidality?

Dr. Hafeman: An FDA meta-analysis found slightly higher rates of suicidal ideation and attempts as compared to placebo groups (Friedman RA, *NEJM* 2014;371(18):1666–1668). There weren't actually any completed suicides. These were short-term studies, and perhaps the finding was due to side effects, such as behavioral activation. After the black box warning, not only did the rates of prescriptions dramatically go down for SSRIs, but the rates of diagnosis of depression went down too. Suicide rates as a whole went sharply up. Even so, the possibility of suicidal ideation arising from use of the medication, for whatever reason, is a serious concern.

CCPR: So, what do we tell families?

Dr. Hafeman: I tell my patients and families that antidepressants treat depression, and that depression is the biggest cause of suicide. But it's also really important for families to have a safety plan to be aware of potential suicidality and closely monitor.

CCPR: What does good follow-up look like, and how do we overcome the barriers?

Dr. Hafeman: Ideally, we would see people once a week after starting an SSRI. That is difficult for everyone: patient, family, and provider. I try to see them within a month, and if they're higher risk, I see them once a week or have them talk with the nurse. It's important to have the door open for people to call with any emergent side effects or anything that might come up.

CCPR: Can you talk more about your team approach to treating children with depression?

Dr. Hafeman: In our clinic, usually the doctor and the nurse see patients together. It helps us get a good diagnosis*, comorbidities, and the family situation in the very first step. Then you have follow-up to look at side effects and monitoring. But the smarter follow-up is an ongoing assessment of this child and the family—the longitudinal assessment. We are also in touch with the therapist, who has a different picture of the child, and the school. Those conversations make my visits with the patient go faster, because I know what's going on. The time it takes to communicate with all those people is difficult, but it's important for good care. *(*Ed note:* Some medical disorders also drive symptoms—see table on page 6 on endocrine disorders that can mimic depression.)

“Sometimes you might actually want a shorter half-life medication if you think they might have activation, sleep problems, elevated mood, or if they have a family history of bipolar disorder. The shorter half-life means that, if they respond poorly, it won't take a long time for those side effects to go away.”

Danella Hafeman, MD, PhD

Q & A
With
the Expert

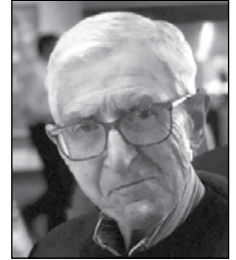
Depression in Transition to Adulthood: A Case Study Calvin Colarusso, MD

Clinical Professor of Psychiatry, volunteer faculty. Author of the book The Third Individuation: Psychoanalytic Study of the Child, Yale University Press, 1990.

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

Editor's note: Recently, CCPR presented the following hypothetical case to leading child and adolescent development authority Calvin Colarusso, MD, for his advice on how to help a young man presenting with a possible major depressive disorder (MDD).

The case: As he struggles to complete his senior college research project, a 23-year-old majoring in chemistry has a recurrence of severe depressive symptoms. He talks of his uncertainty about what he will do after graduating. He is overcome by worry about whether he can find a job, and whether he should apply to graduate school or wait. He is unable to concentrate in class, and he is having significant trouble eating and sleeping. He has no acute intent to harm himself, but at times he feels that, if he is unable to make good on his expensive education, life won't be worth living. The patient has had 3 similar episodes in the past. When he was thinking about college, one occurred during high school. As he was adjusting to being away from home, another happened in the fall of his freshman year. Another episode occurred a year ago just after finishing a semester abroad and leaving new friends and experiences.



Dr. Colarusso: What are the highlights of his earlier life?

CCPR: His history is notable for good grades, usual types of friends and activities, and very close relationships to both parents. His mother was a successful business professional, who then stayed home with the children. The father is an engineer, whose company over the past several years has had significant ups and downs. The patient tended to avoid teen parties and dating. He worked in a grocery store during high school and played varsity basketball and baseball. Medical history is positive for a couple of minor concussions sustained in sports with no clear residual symptoms, although one was temporally related to the first significant depression episode in high school. There is an older brother, who has learning challenges, and a younger sister with good function.

Dr. Colarusso: How has the patient been doing recently?

CCPR: He's been doing pretty well. His grades are quite good. He sees a counselor at school once or twice per semester to monitor his overall function, which is what the school offers as part of tuition. The patient says he finds this helpful.

Dr. Colarusso: What about friends and dating?

CCPR: He has friends and is socially active, but he prioritizes his school work: He typically goes out 1–3 times per week, depending on how heavy his workload is. He uses alcohol roughly 2–3 times per week, consuming an average of 3 beers each time. He also smokes marijuana about once a week “to relax”; however, he does not like the added suspiciousness that the drug creates when he uses it. He says that he has seen several girls over the course of his high school and college career, but he is not dating seriously, and this is not a current focus for him.

Dr. Colarusso: It's pretty clear that he has depression, and he would very likely meet criteria for a DSM-5 diagnosis of major depressive disorder with anxious features. But going beyond the surface diagnosis, there are clues in his developmental history that beg for more information.

CCPR: What other things should we be asking about?

Dr. Colarusso: Invest some time in taking a more detailed social and sexual history. Look closely at the quality of his relationships with his parents, his siblings, and his peers. Ask about how he did in school early on, and whether he had trouble separating from his parents. Also, his lack of interest in dating may be an important piece here. Be sure to ask more about why he hasn't wanted to date, about his attraction or not to women and men, and his family attitudes toward dating and sexuality.

CCPR: What developmental aspects are at play here?

Dr. Colarusso: Although 23 years old, he is dealing with the adolescent developmental task of separation from his mother and father and establishing that comfortable sense of autonomy associated with developmental transitions, such as leaving home for college and then leaving college for the work world. He's having trouble managing these things with less stress

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Expert Interview—Depression in Transition to Adulthood: A Case Study

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and without a depressive response. It is possible that separation issues—such as going to kindergarten or going away to camp—played a role in his early development.

CCPR: How so?

Dr. Colarusso: Entering the adult work world after years of education and dependence is a daunting task for many. He may be affected by patterns of thinking and emotional reactions that he developed early on and has carried with him over the years. In particular, my guess is that he may be having trouble living up to the expectations of his successful parents and at least one of his siblings. This can be intimidating and make the transition more difficult.

CCPR: Where do relationship dynamics impact the presentation of this patient as well as our understanding of his predicament?

Dr. Colarusso: Although there is very little information to go on, he also seems to be struggling with the adolescent and young adult task of establishing a comfortable sexual life. I say this because this is the age when most young adults have a very heightened sexual drive. Even when he's had more freedom from parental oversight, this patient seems to have been less engaged in this fundamental aspect of development for several years. To dampen his anxiety, he appears to be using alcohol and marijuana. If you are pressed for time and focused mainly on medication assessment, it's the kind of thing that you might overlook. But it would be unfortunate to miss addressing such an issue that could easily be driving the depression.

CCPR: How do these perspectives apply in a practical way to treatment?

Dr. Colarusso: It's very common for younger adults (ages 20–40) to have these kinds of unresolved adolescent developmental tasks. Aside from using medication for depression, if needed, I would approach therapy by asking the patient if he notices an inner conflict between wanting to be on his own and fearing the idea of being on his own. From there, ask him about past experiences that felt similar and had similar themes, perhaps when sleeping away at camp or a friend's home. Do not be surprised when other themes become clear as well, such as sexual feelings. Meanwhile, be attuned to any transference that arises in the therapy sessions. You might find that the patient's manner and communication with the therapist have similarities to the present and past challenges. Once these are all openly talked about, the patient has a more conscious ability to problem-solve and choose how to move forward. This is a simplified summary of how dynamic approaches to therapy unfold; however, most psychiatrists should be familiar with these ideas as they put the patient's symptoms into the context of lifelong development.

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

“Be attuned to any transference that arises in the therapy sessions. You might find that the patient’s manner and communication with the therapist has similarities to the present and past challenges. Once these are all openly talked about, the patient has a more conscious ability to problem-solve and choose how to move forward.”

Calvin Colarusso, MD



Endocrine Disorders That Can Mimic Depression

| Endocrine Disorder | Symptoms | Diagnostic Tests |
|----------------------------|---|--|
| Hypothyroidism | Constipation, thinning hair, dry skin, edema, cold sensitivity, hoarse voice, fatigue, weight gain, sleep disturbance | TSH, T4 (thyroxine) |
| Hyperparathyroidism | Kidney stones, headache, GERD, palpitations, bone aches, increased blood pressure, poor sleep, anhedonia, impaired concentration, irritability, decreased libido | Serum calcium, parathyroid hormone |
| Cushing’s syndrome | Hirsutism, truncal obesity, acne, hypertension, facial flushing, purple striae, poor concentration, premature awakening, decreased libido | Serum cortisol, dexamethasone suppression test, 24-hour urine cortisol |
| Addison’s disease | Hyperpigmentation, salt cravings, low blood pressure, vomiting, weakness, fatigue, weight loss, neurovegetative symptoms | Morning cortisol level, serum sodium and potassium |

Note: Symptoms in bold face are symptoms that overlap with depression.

Source: Carroll VK and Rado JT, *Curr Psychiatr* 2009;8(8):43–54.

Bullying and Suicidality: Some Practical Tips

Joshua D. Feder, MD. Child and family psychiatrist, Solana Beach, CA, Editor-in-Chief of The Carlat Child Psychiatry Report.

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

What can you do when one of your patients reports being bullied? Research has shown that being bullied increases the risk of depression, anxiety, and suicidality in children. In this article, we'll give you some tips for how to ask about bullying, how to assess its impact, and how to help your patients and their families deal with the problem.

How bullying affects children and adolescents

Bullying is unfortunately common. About 30% of school-aged children and teens report being bullied, and 70% report seeing bullying (<https://nces.ed.gov/pubs2013/2013329.pdf>). Kids who are bullied are more likely to have psychiatric problems than other children. A prospective, 15-year study of 2,120 children in Quebec (Geoffroy M et al, *CMAJ* 2018;190(2):E37–E43) found that children who suffered severe and chronic bullying had 2.5 times the risk of depression and 3.5 times the risk of both anxiety disorders and suicidality than controls.

The relationship between bullying and suicidality is complex—not the direct “bullicide” often cited in media. Experiences of rejection and exclusion and feelings of isolation and despair contribute to suicidal thinking. Those who become suicidal tend to have multiple risk factors, such as family turmoil, poor grades, and peer difficulties. Children who are both victims and bullies are at the highest risk for suicidal thinking and behavior. Social media bullying doubles the risk of self-harm or suicidal behavior (John A, *J Med Internet Res* 2018;20(4):e129).

How to assess for bullying

Children and teens are often embarrassed to bring up the topic of bullying, so it's important to routinely ask about

it during evaluations. Younger children may not understand what the word means, so you might ask, “Has anyone hurt you? Have they yelled at you or called you bad names?” When you see injuries, ask, “Was this an accident or on purpose?” Sometimes bullied children take a different way home or avoid certain places, such as the library or the bathroom. Such behavior may paradoxically lead to adult punishment for avoidance behavior or for wetting or soiling. Ask, “How come you are not using the bathroom at school?” Children who are having trouble sleeping may be worried or having nightmares; in these cases, ask, “Is something scaring you?”

For older children, you don't need to be as cautious about phrasing—you can use the word “bullying,” then have the patient elaborate on what that means—but in these older kids, be sure to also ask about cyber or social media bullying.

As in all abuse situations, accept the child's or teen's report as the true reality. While some kids misperceive situations (eg, kids with externalizing disorders may see neutral expressions as critical), most of the time this is not the case. Either way, our job is to complete the psychiatric assessment. Look especially for depression, anxiety, and suicidality, and seek collateral data by assessing the perspectives of parents, teachers, and peers to hone in on an accurate set of diagnoses. Parents can have an important role in this process. In particular, they can ask their teens: “Who's texting you? Why are you turning the phone away? What don't you want me to see?”

What to do for the patient who reports bullying

Treat the syndromes that you find, using psychotherapy or medications for depression and anxiety, and consider referring your patient for trauma-focused cognitive behavioral therapy (TFCBT), a well-researched therapy for trauma of many types. Address other contributing factors, particularly conditions that set the child apart from others (eg, ADHD and autism spectrum disorder), with treatments like

social skills training. Use medications as you usually would for psychiatric conditions, but avoid benzodiazepines, since recent research indicates that these might worsen PTSD.

Advise parents that their child requires care and protection. Many parents might encourage their child to strike back; however, this is shown to lead to more bullying difficulties. There are better approaches. Carol Gray is a well-known educator who has written extensively on managing bullying. I recommend using her evidence-informed technique of coaching the child to use one well-practiced, neutrally delivered verbal response, such as, “I'm not staying for this,” then turning and walking away from a bully and going to a trusted adult. There is excellent research showing that children and teens who witness bullying have a very good chance of stopping the bullying if they speak up forcefully, telling the bully, “Stop it!” This research demonstrates that when bystanders speak up, most of the time bullies back down.

What if your patient reports bullying but doesn't want you to tell the parents? This is one of those times when motivational interviewing can help: Ask the child about the advantages vs disadvantages of keeping such a secret. Some children worry that they are “tattling” on the bully and thus might incite reprisals. Help the child move toward a more balanced view, hopefully one that allows you to act with the child to inform parents and authorities in a manner that is safe and productive.

Advocating at school

Child psychiatrists can have a powerful impact on schools in addressing bullying. Get parental consent and call the principal to talk about the situation. It is a rare event for schools to hear from an outside, interested professional, and your advice will carry weight. Here are some talking points that you might consider.

1. Encourage good supervision. The most important intervention at a

Continued on page 8

Bullying and Suicidality: Some Practical Tips

Continued from page 7

- school is to provide better, more engaged, and often more structured supervision during lunch, recess, and other times and places when children and teens are likely to have conflict.
2. Make sure there are safe people to go to. Children need to have relationships with adults whom they trust, and who can actually advocate for and protect them at school.
 3. Discourage having the child face the bully to “work it out.” Many
 4. Make sure the school is addressing the needs of all the children

schools believe that such meetings are helpful for both parties, affording them the experience of working out their problems. In my experience, the meetings are rarely helpful. They tend to result in perfunctory and meaningless apologies at best, and often the bullying continues. This may also disincentivize the victim from reporting subsequent bullying.

involved, including perpetrators (often a group) and bystanders.

5. In rare instances, a school change may seem necessary, despite losing contact with friends and disrupting the child's education. Weigh the option carefully.

CCPR
VERDICT:

Always ask about bullying as part of your routine assessment and advocate with schools to address it.



Expert Interview: Current Use of Antidepressant Medication in Children

Continued from page 4

CCPR: What is your path for deciding whether to increase, change, or augment a medication?

Dr. Hafeman: Make sure the patient is on a good dose of the medication before calling it a failed trial. That takes time, and families want their kid to be better right now, which is understandable. Sometimes, kids with anxiety will need even higher doses.

CCPR: What if you just feel the medication is not working?

Dr. Hafeman: Revisit the diagnosis and make sure that it really is a major depression as opposed to ADHD or substance use or mania. If it's the first trial of an SSRI, I will switch to another SSRI. That's what's supported by the TORDIA study. Revisit therapy—more kids will respond when something such as CBT is added. Avoid multiple medications, with exceptions. For example, I've had children who don't want to get off their SSRI because it's helped their anxiety. Because it has a totally different mechanism, consider adding bupropion. There isn't great evidence in kids on augmentation. Case studies show that quetiapine can be helpful (Pathak S et al, *J of Child and Adol Psycho* 2005;15(4):696–702). Synthroid, other atypicals, and even lithium have been used for treatment-resistant depression in kids. There is a risk-benefit analysis for each option.

CCPR: How do you talk with parents regarding their concerns about antidepressant medication?

Dr. Hafeman: I ask them, “What are your thoughts about medication?” If the parents want to start with an evidence-based therapy first and hold off on the medication—aside from severe circumstances—that is a reasonable approach and it is supported by research. The response rate isn't as high for CBT, but it's higher than placebo (Arnberg A et al, *Behav Therapy* 2014;43(4):275–288). Also, make sure not to confuse baseline problems with side effects. Kids get headaches, and if they attribute the next headache they get to the SSRI, then that will be problematic. I'll always say, “Anything can cause stomachaches or headaches,” and I'll always go over the black box warning. I'll go over the possibility of activation. I tell families how they can get in touch with me, and I emphasize that I want them to be in touch with me as needed. You can talk about the pros and cons of medication, but it's important to talk about how not medicating depression can be absolutely deadly. Medication can be life-saving, and it's important to highlight that with families. Even when there is no suicidality, adolescence and pre-adolescence are extremely important times for a child's learning, development, social interactions, for developing a sense of self. If you're really depressed, you just cannot do these things. It's very important to not underestimate the detrimental effects of depression.

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



“You can talk about the pros and cons of medication, but it's important to talk about how not medicating depression can be absolutely deadly. Medication can be life-saving, and it's important to highlight that with families.”

Danella Hafeman, MD, PhD

Research Updates
IN PSYCHIATRY

ANXIETY

CBT vs Pharmacotherapy for Childhood Anxiety

REVIEW OF: Wang Z et al, *JAMA Pediatr* 2017;171(11):1049-1056

Managing childhood anxiety can sometimes leave clinicians in a quandary. There is a paucity of evidence comparing different treatment approaches, and current guidelines on the subject are old and make inconsistent recommendations. To address this dilemma, researchers at the Mayo Clinic performed a systematic review and meta-analysis comparing pharmacotherapy with cognitive behavioral therapy (CBT) in children with anxiety disorders.

Investigators identified 115 studies with a total of 7,719 participants. All studies evaluated CBT, pharmacotherapy, or the combination of both for treatment of a diagnosed childhood anxiety disorder. The average participant age was 9.2 years (range 5.4 to 16.1), and slightly over half (55.6%) were female. Data were pooled using a random-effects meta-analysis.

Selective serotonin reuptake inhibitors (SSRIs) had significantly better outcomes than placebo for reduction in primary anxiety symptoms reported by parents or clinicians, as well as increased remission (relative risk [RR], 2.04) and response (RR, 1.96). Likewise, when compared with placebo, serotonin-norepinephrine reuptake inhibitors (SNRIs) also had a significantly greater reduction in clinician-reported primary anxiety symptoms. The use of tricyclic antidepressants or benzodiazepines was not associated with a significant improvement in anxiety symptoms.

Treatment with CBT compared with no therapy significantly improved primary anxiety symptoms reported by clinicians, parents, and children, as well as remission (RR, 4.08) and response (RR, 4.72). Moreover, combining CBT with an SSRI resulted in significantly better response rates than treatment with an SSRI alone.

Mild or moderate adverse effects were reported with medication use

but not with CBT. However, none of the trials were large enough or long enough to evaluate suicide risk with SSRIs or SNRIs.

CCPR'S TAKE

This study provides insight into optimal treatment strategies for children with anxiety disorders. SSRIs or CBT are both effective therapies; SNRIs may also be useful alternatives to SSRIs, although the evidence supporting their efficacy is less robust. This study also supports the premise that there is an added benefit in combining CBT with pharmacotherapy. However, the authors caution that more research is needed to evaluate the comparative effectiveness of therapies—specifically, head-to-head evaluations of medication and CBT.

Importantly, these results allow clinicians to offer patients and their families several options for effective treatment of childhood anxiety. For most patients, we would suggest that offering a choice between pharmacotherapy or CBT is the best approach, explaining the risks and benefits of both. This allows patient and family preferences to guide the development of a treatment plan.

—Stephanie Fenwick, PharmD. Dr. Fenwick has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

ADHD

Amphetamine Extended Release Oral Suspension for ADHD

REVIEW OF: Childress AC et al, *J Child Adolesc Psychopharmacol* 2017;28(5):306-313

In 2015, the FDA approved Dyanavel XR (amphetamine extended release oral suspension), which was the first long-acting liquid version of amphetamine on the market. To provide some context, Quillivant XR, a long-action liquid methylphenidate formulation, was approved in 2012 and appears to be fairly popular for kids who can't or won't swallow pills. Seeing a market opportunity, Tris Pharmaceuticals developed Dyanavel XR

and funded a placebo-controlled trial that was successful enough to gain FDA approval. Recently, this study was published, and some readers might be curious to look at the quality of the data.

The study took place at 5 investigational sites in the US. A total of 108 boys and girls with ADHD (ages 6–12) were initially enrolled in a 5-week open-label phase in which all patients were given Dyanavel XR, starting at 2.5–5 mg and titrated up to a target dose of 10–20 mg/day. Nine of the children dropped out of this first phase, and 99 continued on to the placebo-controlled phase of the study. Participants were randomly assigned to either Dyanavel XR (51 patients, mean dose 17.3 mg) or placebo (48 patients). After 1 week on the medication, the children's ADHD symptoms were evaluated with a teacher-rated instrument called the SKAMP (for the Swanson, Kotkin, Agler, M-Flynn, and Pelham Rating Scale).

The primary outcome variable was improvement in SKAMP scores from pre-dose to post-dose of medication. Dyanavel XR was more effective than placebo beginning 1 hour after the dose and continuing for 13 hours. The effect size was a very robust 1.8, in line with effect sizes reported in similar trials of other long-acting stimulants. In terms of side effects, patients on Dyanavel XR reported decreased appetite (26%), insomnia (13%), and affect lability (9%), with no substantial differences in blood pressure or pulse between the treatment and control group.

CCPR'S TAKE

Not too surprisingly, Dyanavel XR is an effective stimulant treatment for ADHD. This study was not huge but was well-designed, and the results were judged to be robust enough to merit FDA approval. It's another arrow in our ever-expanding quiver of stimulant options, and this liquid formulation will likely be just as popular as Quillivant XR. Being a brand-name option, its cost is high. For families that want cheaper liquid stimulants, go with either generic ProCentra

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Research Updates
IN PSYCHIATRY

Continued from page 9

(short-acting dextroamphetamine) or Methylin oral solution (short-acting methylphenidate).

—*Rehan Aziz, MD.* Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

DEPRESSION

Resilience Networks in Adolescent Females at Risk for Major Depression

REVIEW OF: Fischer AS et al, *JAMA Psychiatry* 2018;75(5):493–502

One of our biggest in-office challenges is how to enhance teen resilience, the process of adapting to and recovering from stressful life experiences. Some neuroscientists hypothesize that resilience is related to the limbic system, which plays a vital role in emotion processing, motivation, and learning. According to one theory, when people can exert better modulation of the limbic

system, they are at lower risk of depression. A group of researchers recently looked at these neural pathways in adolescent females, and there were some intriguing results.

Fischer and colleagues examined brain pathways of resilience in adolescent females at familial risk for depression. They conducted a longitudinal study at Stanford University from 2003 to 2017. Sixty-five subjects participated: 20 at high risk of MDD in whom depression did not develop (resilient), 20 at high risk in whom depression developed (converted), and 25 at low risk of MDD with no history of psychopathology (control). Outcomes measured via functional MRI scans included connectivity in the limbic, salience, and executive control networks. Participants were imaged once, on average at age 19, 6 years after beginning the study.

The researchers found that resilient adolescent females had greater connectivity between the limbic and executive

control systems than did subjects who developed depression or even controls. The strength of the connection was correlated with positive life events.

CCPR'S TAKE

This study is consistent with the hypothesis that high-risk but resilient adolescent females have greater executive system control over emotions and behavior arising from the limbic system, which perhaps insulates them against depression. What are the treatment implications of this small study? Theoretically, since positive life events were correlated with better neural resilience, we might want to focus on therapeutic approaches that have an activity-oriented style and are designed to strengthen adaptive coping and cognitions, thereby helping teens foster positive life experiences.

—*Rehan Aziz, MD.* Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

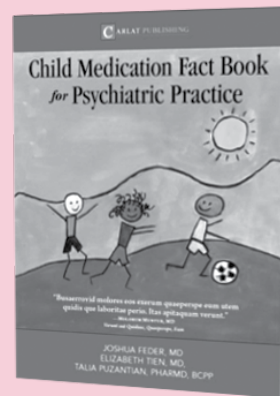
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Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatChildReport.com. Note: Learning Objectives are listed on page 1.

1. According to a 2016 study on major depressive disorder, which of the following medications was associated with an increased risk of suicidal ideation? (LO #1)
 - a. Amitriptyline
 - b. Paroxetine
 - c. Fluoxetine
 - d. Venlafaxine
2. According to Dr. Hafeman, SNRIs have been shown to be more effective in children than SSRIs with fewer cardiac side effects, such as elevations in blood pressure. (LO #3)
 - a. True
 - b. False
3. Approximately ____ of school-aged children and teens report being bullied. (LO #2)
 - a. 10%
 - b. 20%
 - c. 30%
 - d. 40%
4. According to a recent study, how did the rate of deliberate self-harm (DSH) in patients ages 10–64 taking higher doses of fluoxetine, sertraline, or citalopram compare to patients ages 10–24? (LO #1)
 - a. DSH occurred at a higher rate in older patients
 - b. DSH occurred at a higher rate in younger patients
 - c. DSH occurred at a higher rate in older patients within the first 3 months, then rates for both groups were equal
 - d. There was no difference in DSH rates between the older and younger groups of patients
5. One negative side effect of using Dyanavel XR for ADHD in children is increased heart rate that requires periodic monitoring for patients under 12 years of age. (LO #4)
 - a. True
 - b. False
6. According to a recent study, combining antidepressants with cognitive behavioral therapy (CBT) for anxiety is associated with which outcome? (LO #4)
 - a. 10% less suicide risk
 - b. Significant improvement in anxiety symptoms
 - c. No significant improvement in anxiety symptoms
 - d. 20% less suicide risk
7. According to Dr. Hafeman, in one study of adolescents with depression, _____ was found to be helpful in about 60% of patients with more significant levels of depression. (LO #3)
 - a. Citalopram
 - b. Escitalopram
 - c. Sertraline
 - d. Fluoxetine
8. According to a 2018 study, what effect does social media bullying have on the risk of self-harm or suicidal behavior in children and adolescents? (LO #2)
 - a. It increases the risk by 10%
 - b. It increases the risk by 35%
 - c. It increases the risk by 100%
 - d. There is no causation between social media bullying and self-harm or suicidal behavior

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

**Next Time in *The Carlat Child Psychiatry Report*:
ADHD in Children and Adolescents**

Note From the Editor-in-Chief

In this issue, we look at the complex relationship between bullying and suicidality and offer a range of ideas on how to help your patients with this all-too-common problem, both in the office and in advocating for your patients, with resources to boot. We also take on the issue of suicidality related to the use of antidepressants—is it real? What do we do about it? We interviewed Dr. Danella Hafeman, who talks about the current bottom line on whether antidepressants work for depression in kids. Finally, we have a case study interview with Dr. Cal Colarusso, a renowned psychoanalyst who ran UCSD's child fellowship training program for many years, looking at the care of a depressed college student through a developmental lens. We think this helps us to consider our patients' symptoms in a lifelong context—let us know what you think!



Regards,
Josh Feder, MD
jfeder@thecarlatreport.com

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