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Selection from: The Treatment of Bipolar Disorder and Schizophrenia in Children and Adolescents

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The Treatment of Bipolar Disorder and Schizophrenia in Children and Adolescents (Slides and Transcript) CME

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Disclosures

The Treatment of Bipolar Disorder and Schizophrenia in Children and Adolescents

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from W&HMD

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Slide 1.

Robert L. Findling, MD: Hello, I'm Dr. Robert Findling, Professor of Psychiatry and Pediatrics, Case Western Reserve University. I am also the Director of the Division of Child and Adolescent Psychiatry at University Hospital's Case Medical Center in Cleveland, Ohio.

I would like to welcome you to a Medscape CME Spotlight panel discussion to educate physicians and allied health professionals, "The Treatment of Bipolar Disorder and Schizophrenia in Children and Adolescents." Here we will explore the clinical characteristics of these major mental illnesses as they appear in the young and discuss the treatments for them, both pharmacologic and nonpharmacologic. We will also review medication-related side effects.

I am joined today by 2 colleagues. I am first joined by Alexandra Sporn. Welcome. Dr. Sporn is an Assistant Professor of Clinical Psychiatry at Columbia University, College of Physicians and Surgeons, as well as the New York State Psychiatric Institute in New York City. I am also joined by Dr. Roy Boorady, who is an Assistant Professor of Child and Adolescent Psychiatry at the NYU Child Study Center and the NYU School of Medicine, also in New York City. Welcome, Alex. Welcome, Roy.

Learning Objectives

- Summarize the clinical characteristics of schizophrenia and bipolar disorder in children and adolescents
- Review new and emerging efficacy data on the pharmacologic treatment of these disorders
- Discuss the metabolic side effects of drugs that are used to treat these illnesses
- Describe nonpharmacologic adjuncts to medication-based treatment

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Slide 2. Learning Objectives

I do want to mention for our viewers that the learning objectives for this program are first to summarize the clinical characteristics of schizophrenia and bipolar disorder in children and adolescents. We will review new and emerging efficacy data on the pharmacologic treatment of these disorders in children and adolescents. We will also discuss concerns and metabolic side effects of drugs that are used to treat these illnesses, and, finally, we will describe nonpharmacologic adjuncts to treatment that are oftentimes medication based.

First of all, welcome again, and let's start by looking at the diagnostic challenges in working with children and adolescents who suffer from these major mental illnesses. Certainly bipolar disorder is really a controversial topic and so, Roy, perhaps you would want to talk a little bit about the challenges of this and how you might address them in your own clinical practice?

Diagnosing Childhood Bipolar Disorder

- Developmental differences
 - Irritability tends to be more prominent in mania and hypomania in children and adolescents
- Cyclic course and chronicity
- DSM-IV criteria, such as:
 - Changes in sleep
 - Changes in appetite
 - Racing thoughts in mania

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Slide 3. Diagnosing Childhood Bipolar Disorder

Roy J. Boorady, MD: I think recognizing and diagnosing bipolar [disorder] in children and adolescents is a challenge. One of 2 things that come to mind concerns the developmental differences that children and adolescents have vs adults, so the symptoms that we might be used to in looking at mania or hypomania in adults can be very different in children and adolescents. Another factor that comes to mind is then how to disentangle or differentiate mania, say, or hypomania from just mood, irritability, or instability. With children and adolescents, they may not have discrete episodes and may be combined into one in terms of depression and mania. One thing we are seeing in children and adolescents is that irritability might be more of a presenting factor than your classic sort of mania or hypomania.

Dr. Findling: So with all of these challenges, certainly I would imagine as a skilled clinician, you probably have some good pearls to share with folks to help disentangle and tease apart some of these real challenges that people consistently face. What are some of your real keys to helping sort this out?

Dr. Boorady: What I do is look at the course of the illness and the chronicity of it; that is one pearl. I think another guideline is, as much as you can with the parents, disentangle what the child or adolescent presents with and try to look at discrete episodes. I also still fall back on a lot of the DSM-IV criteria, so I do try to look for changes in sleep or changes in appetite, or racing thoughts, and other symptoms that may overlap with other comorbidity in children and adolescents.

Dr. Findling: I would certainly tell you that in my own practice, that is exactly what I do, specifically looking for longitudinal courses. I think one of the things that I certainly heard as you were talking is that at the end of the day, bipolar disorder is a mood disorder, so it is associated with mood perturbations. Without a mood perturbation, you don't have bipolar illness. And, certainly, you keep on talking about the cyclic nature of the condition, despite the fact that patients are chronically impaired, and the cyclic mood perturbations and chronicity are, I think, really important points. Alex, I see you nodding your head, and I can only imagine that there are also challenges associated with schizophrenia diagnostically in the young.

Diagnosing Childhood Schizophrenia

- Two seemingly contradictory problems
 - Overdiagnosing
 - Underdiagnosing
- Necessary criteria
 - DSM-IV criteria, such as:
 1. Delusions and hallucinations (often less elaborate than in adults)
 2. Disorganized speech or behavior
 3. Negative symptoms (flattened affect, lack of motivation, and so on)
 - Onset before age 13 years

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Slide 4. Diagnosing Childhood Schizophrenia

Alexandra L. Sporn, MD: Oh, absolutely. For one thing, childhood schizophrenia is very rare. It is about 300 times rarer than adult-onset schizophrenia, and so we actually encounter 2 kinds of problems, which are contradictory in a sense, in diagnosing childhood schizophrenia. One is overdiagnosing, which is when you see a child who is hallucinating or having strange ideas or having some social difficulties [that] may be interpreted as negative symptoms, and some clinicians tend to overdiagnose it. On the other hand, the true real childhood schizophrenia often goes underdiagnosed because nobody thinks about it. Actually, clinically, the actual diagnosis is when the child meets full DSM-IV criteria for schizophrenia before the age of 13. Again, it is very rare.

Dr. Findling: But in adolescents, it is more common.

Childhood-Onset Schizophrenia

(Onset Before Age 13 Years)

Early-Onset Schizophrenia

(Onset Before Age 16 Years)

- Very rare
- Continuous with adult schizophrenia
- More severe than adult-onset illness
- Fewer environmental influences
- More pronounced brain changes
- "Hearing voices" ≠ schizophrenia

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Slide 5. Childhood Onset Schizophrenia (Onset Before Age 13)

Dr. Sporn: It is much more common in adolescents. Generally, the onset of schizophrenia is late adolescence and early 20s. But when you do encounter children with schizophrenia, they usually present with very severe positive symptoms (hallucinations, delusions) and also negative symptoms, and usually they are sicker people than adult schizophrenics. The challenges that we do encounter are with kids with psychosis not otherwise specified, which we call colloquially multidimensional impairedness. These kids have psychotic symptoms [that] are not as persistent as in schizophrenia. They also have emotional lability, they often have aggressive outbursts, they often have social difficulties, but they are different from negative symptoms of schizophrenia in the sense that the kids usually want to have friends and want to socialize, they just can't quite do it well, so that is the main thing.

Dr. Findling: So certainly one of the similarities in bipolar disorder and schizophrenia is they are reasonably uncommon in children, more common during adolescence. The challenges have to do with their symptom overlaps and the fact that this group of youngsters doesn't quite fit adult criteria, whether it be in a bipolar spectrum illness or the multidimensionally impaired. So now, ultimately, presuming that we have followed your wisdom and gotten these youngsters appropriately diagnosed, certainly we want to treat them.

Roy, do you want to start off and talk a little about the treatment of bipolar disorder in the young, perhaps at least focusing initially on pharmacotherapy?

Treating Childhood Mania

- Strive for monotherapy
- Follow AACAP* algorithms for:
 - BPD-I, manic or mixed, without psychosis
 - BPD-I, manic or mixed, acute, with psychosis
- Comorbidity
 - ADHD
 1. 70% to 90% of prepubertal children
 2. 30% to 40% of adolescents
 3. Treat bipolar disorder symptoms first
 - Oppositional Defiant and Conduct Disorders
 1. Treat bipolar disorder symptoms first
 - Substance Abuse
 1. Treat both disorders simultaneously
- Consider atypical antipsychotics for a robust response

*Kowatch R et al. *J Am Acad Child Adolesc Psychiatry*. 2005;44:213-235.

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Slide 6. Treating Childhood Mania

Dr. Boorady: Sure. I think as with adults, polypharmacy or multiple medications might be more the norm than the exception, and though we try to manage these symptoms with single therapy, I think children and adolescents do end up on multiple medications. The approach usually is to treat the mania and the hypomania first. If there is any depression, treat that next, and then whatever comorbid disorder might be there. I know the American Academy of Child and Adolescent Psychiatry released some guidelines for the treatment recently and listed lithium, divalproic sodium, and atypical antipsychotics as treatments. What we find clinically in our practice is that the atypical antipsychotics tend to be more robust in the treatment response, especially for mania, because with the mania can come a lot of aggression and irritability. So I think first line or first choice would be the atypical antipsychotics and then after that would be anything to treat the depression.

Treating Childhood-Onset Schizophrenia

Long-term Outcomes

- Clinical trials (n=65): haloperidol* vs clozapine*, olanzapine* vs clozapine*, aripiprazole* vs risperidone
- Great majority remains severely ill
- 2- to 6-year follow-up results:
 - "Good Responders" - 28%
 - Predictors of good response:
 1. Family acceptance
 2. Appropriate medication management (clozapine or other "hardcore" neuroleptics)
 3. Appropriate school placement
 - "Good responders" still had poor Clinical Global Impression score, low functioning (group homes, supervised living, supervised work)

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* Not FDA approved for this indication

Slide 7. Treating Childhood-Onset Schizophrenia: Long-term Outcome

Dr. Findling: It is interesting that you focused in on antipsychotics because certainly one of the other topics has to do with schizophrenia. Alex, I know we are talking about childhood schizophrenia, adolescent schizophrenia. Certainly your work with the most treatment resistant are important, but could you walk us through general approaches and then maybe the approach to the treatment-resistant youngster?

Dr. Sporn: Yes. Generally, children are much harder to treat than adults, because A, you are faced with more side effects, which I guess we are going to speak about later, and B, it is harder to delineate symptoms you actually would target first, just as Roy said. So, obviously, if you are faced with a child who is having positive symptoms of schizophrenia, such as hallucinations and delusions, those are your primary target, and generally we start with atypical antipsychotics. Most of them tend to work quite well for not-so-treatment-resistant cases.

Atypical Antipsychotics in Children

- Aripiprazole and risperidone have the most favorable side-effect profiles
- Clozapine is most effective
- Efficacy, tolerability, and safety need to be balanced

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Slide 8. Atypical Antipsychotics in Children

My first choice would be probably aripiprazole or risperidone, just because of a more favorable side effect profile of aripiprazole to start with. Very often, we, as Roy just said, end up with polypharmacy because we have to manage other symptoms, such as anxiety, aggression, sleep disturbances, and so forth, so we end up quite commonly with polypharmacy. In more treatment-resistant cases, like the ones I have encountered while working at the NIMH, we end up with really hardcore old neuroleptics, such as haloperidol or others, even though we tend not to use them more as adjuncts rather than the primary medication. And also at NIMH, I participated in several studies [that] involved using clozapine in children or adolescents with schizophrenia; and, actually, just as in adults, it is the most effective medication for schizophrenia and can be used quite safely in youngsters as well.

Dr. Findling: So everyone keeps on talking about safety. It is interesting; you can't talk about this treatment without at least wanting to talk about safety. So let's move to that. Roy, when you are thinking about treating youngsters with bipolar disorder in your practice, what are the side effects or, particularly with antipsychotics, metabolic considerations that you grapple with as you consider treatment not only acutely but over the long term?

In Treating Bipolar Disorder ...

- Avoid sedation
- Minimize metabolic side effects:
 - Weight
 - Blood pressure
 - Triglycerides
 - Lipids
 - Fasting blood glucose
- Take into account family history, including:
 - Cardiovascular disease
 - Obesity and diabetes
- Monitor metabolic risk factors every 3 months

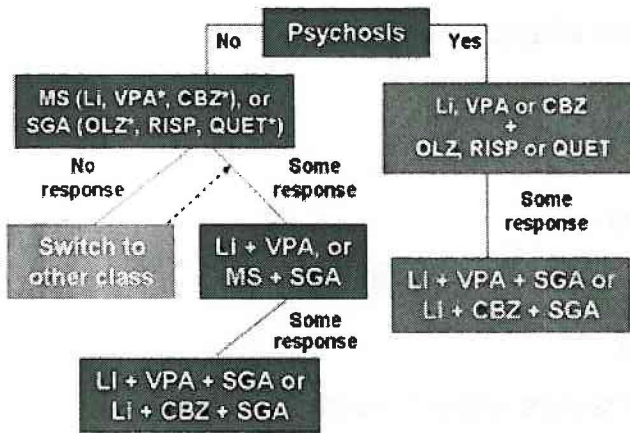
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Slide 9. In Treating Bipolar Disorder...

Dr. Boorady: I would probably say the top 2 side effects are sedation and the metabolic sequelae of the medications. In terms of managing them, I know recently there have been some guidelines as the issue of metabolic side effects has been discussed more within the field and as we brought in other specialists, including endocrinologists, to help us. If I am going to start a child on an atypical antipsychotic, I am going to be worried about the metabolic symptoms. At baseline, we check weight, blood pressure, fasting blood glucose, and lipid profile. What is also very important is a family history of cardiovascular illness and dyslipidemias. And you want to monitor obesity and diabetes every 3 months, and check body mass index, because children are growing in height along with weight, I have been using those as sort of guidelines in initiating treatment with the atypicals.

Dr. Findling: And you also mentioned polypharmacy. Does that come into play when you are thinking about side effects with these youngsters?

Treatment of Acute Mania in Pediatric Bipolar Disorder



Madsen V et al. *Expert Opin Pharmacother*. 2007;8:1801-1819.

*Not FDA approved for this indication

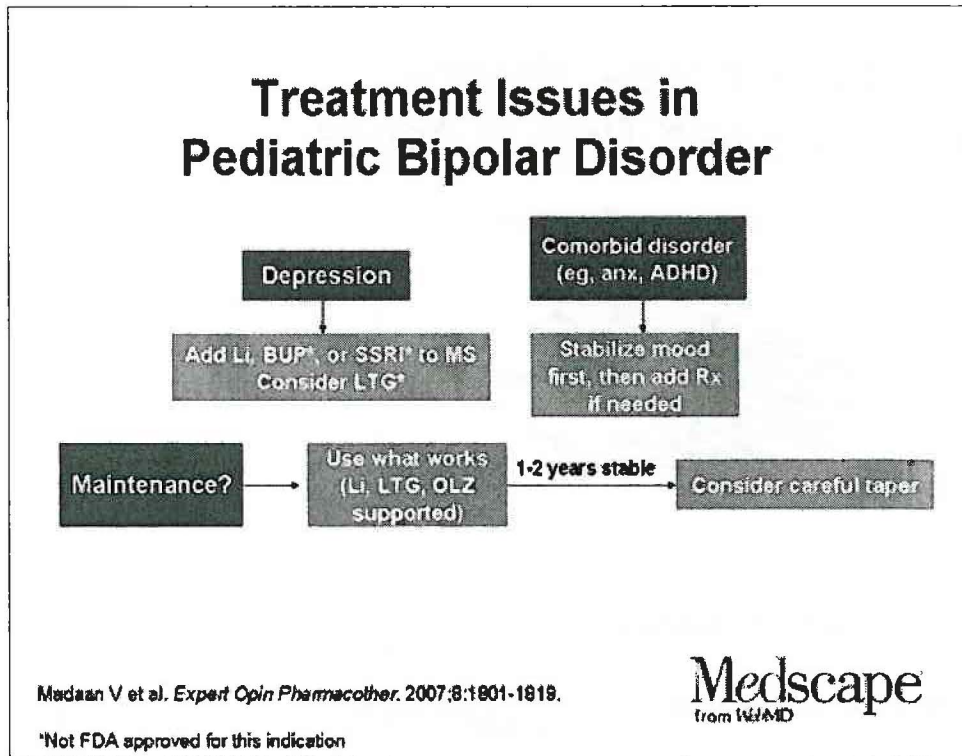
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Slide 10. Treatment of Acute Mania in Pediatric Bipolar Disorder

Dr. Boorady: Absolutely -- probably more so, as kids might be on more than one agent that could cause things [such] as weight gain and sedation. So if you have a child on atypical antipsychotics, they might also be on another mood stabilizer. I know I mentioned lithium and so on. These other agents are also going to have side effects of weight gain, sedation, and so on.

Dr. Findling: And certainly as you think about that, and you are talking about monitoring, are there specific treatment options you prefer or parents seem to be concerned about? When we talk about metabolic side effects and laboratory values, what do parents hone in on or what do the kids hone in on as concerns to them?

Dr. Boorady: The weight gain and sedation, sedation in terms of feeling fatigued, or how that might affect them in school or social settings. It can be very impairing to be tired and sedated during the day. And you may have to take some of the older mood stabilizers multiple times throughout the day and check blood levels, so they can be a little bit cumbersome to manage.



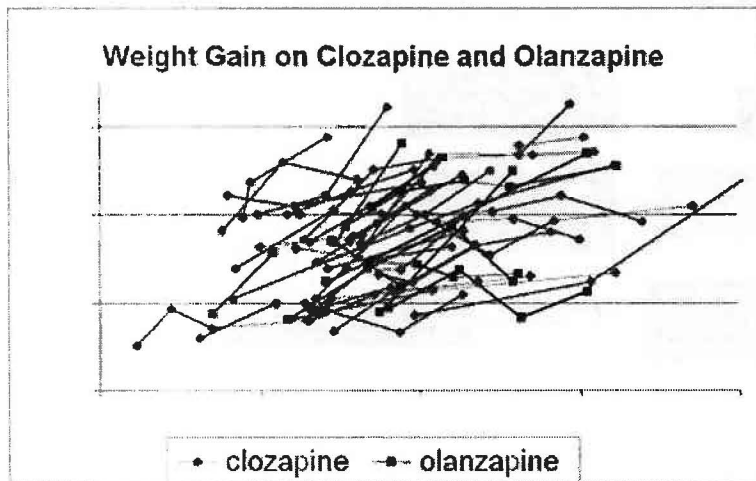
Slide 11. Treatment Issues in Pediatric Bipolar Disorder

Dr. Findling: But yet I'm almost hearing from you that despite these potential shortcomings, you still prescribe medications. I think one of the things that shouldn't get lost in the equation as we are talking about side effects is what you have both talked about, which is that these youngsters are oftentimes very impaired, whether their primary diagnosis is bipolar disorder or schizophrenia. So we are not talking about treating trivial conditions but major mental illnesses that are potentially life-shattering. I think that always needs to be put into any equation as we talk about side effects that you have already talked about, and before we move forward.

Alex, you certainly have a lot of experience with antipsychotics and treatment of schizophrenia in the young. What would you say are the key issues perhaps that distinguish or actually are similar between the 2 patient populations?

Dr. Sporn: I want to agree with your point that when we are talking about severe mental disorders, we always have to weigh the pros and the cons. We shouldn't forget that the benefit we achieve comes with certain side effects, which sometimes outweigh, in the eyes of parents or the eyes of the public, the benefits that the child gets with his major medical condition being treated.

Weight Gain on Antipsychotics Much More Pronounced Than in Adults



Sporn AL et al. *J Am Acad Child Adolesc Psychiatry*. 2005;44:825-833.

Medscape
from WJMD

Slide 12. Weight Gain on Antipsychotics...

Again, with atypical antipsychotics, the most common side effects that we see in treating children with schizophrenia or other forms of psychosis are obviously weight gain and metabolic side effects.

Antipsychotic-Induced Akathisia

- Restlessness, inability to sit still; often causes aggression; can be mistaken for exacerbation of psychosis or suicidal ideation
- More common than in adults
- Unlike in adults, is often induced by atypical antipsychotics
- 40% incidence of akathisia on clozapine and olanzapine
- Can be successfully treated with beta-blockers
- 100% akathisia remission on propranolol (dose: 20-40 mg/day)

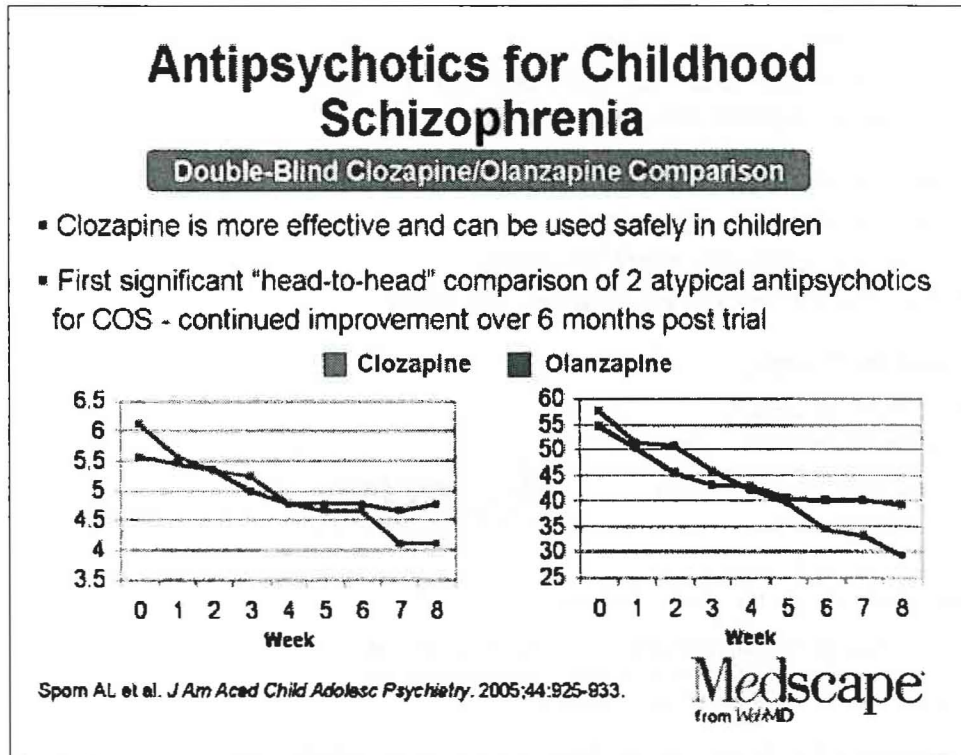
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Slide 13. Antipsychotic-Induced Akathisia

Another side effect that we have commonly seen, even with atypical antipsychotics, is akathisia. Akathisia rarely happens in adults but is much more common in children and adolescents. This is probably because the dopaminergic system of children and adolescents is not as mature, so it is

more vulnerable to the side effects. We try to ameliorate that by adding beta blockers such as propranolol or atenolol, which works quite well in kids and pretty much doesn't cause any side effects on its own because the blood pressure is very easily regulated in itself. It has been quite helpful because akathisia in kids can also happen even with SSRIs [selective serotonin reuptake inhibitors], and this has often been confused with suicidality or irritability or aggression.

Dr. Findling: So it is a major consideration.



Slide 14. Antipsychotics for Childhood Schizophrenia

Dr. Sporn: It is a major consideration. In terms of the weight gain, again, atypical antipsychotics, especially olanzapine and clozapine, but also the other ones. Again, it is much more pronounced than in adults. There have been a couple of interesting studies with using metformin, which is an antidiabetic pill, to counter these side effects, and as far as I know, there is one study going on now at NIMH with metformin.

Dr. Findling: So certainly approaches include pharmacologic. Are there other things you think about for weight gain approaches when you talk to families during treatment, other than prescribing metformin? Of course, you are laughing, because of course you do.

Dr. Sporn: Of course we do. It is exercise, it is diet. On the unit, we actually keep locks on the refrigerators because very often when kids are put on antipsychotics, we just can't control their appetite, and we are talking about really sick kids with very little control over their emotions and desires. But yes, when parents are instructed appropriately and they are targeted with the program, it can be managed. It can be arranged.

Goals of Psychosocial Treatment of Bipolar Disorder

- **Family-Focused Therapy**
 - Increase communication
 - Educate patient about prodromes and develop a plan to intervene
 - Examine beliefs about medication and adherence
- **Interpersonal and Social Rhythm Therapy**
 - Stabilize daily routines and sleep-wake cycle
 - Improve personal relationships and insight into moods
 - Use Social Rhythm Metric to track sleep, activities, and mood
- **Cognitive-Behavioral Therapy**
 - Restructure dysfunctional beliefs
 - Monitor moods and prodromes
 - Intervene constructively to alter moods

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Slide 15. Goals of Psychosocial Treatment for Bipolar Disorder

Dr. Findling: You notice how we are moving forward. We talked about medicines and we talked about medicine side effects, and we are now moving a little bit towards nonpharmacologic management of weight gain, and maybe that is another thing to highlight.

Certainly I don't think clinicians in their practices simply prescribe medicines to these youngsters, so maybe, Roy, we should start off with our last topic, which is really that to achieve optimal patient outcomes, adjunctive treatments that are nonpharmacologic are always almost employed and recommended. Talk a little bit about the nonpharmacologic treatment and approaches to a youngster with bipolar illness.

Psychosocial Treatment of Pediatric Bipolar Disorder

- Useful adjunct to pharmacotherapy
- Few manual-based treatments
- Booster sessions
 - Accelerate recovery in adolescents in 24-month follow-up
 - Prevent the effects of CBT group (vs other treatment groups) from disappearing

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Slide 16. Psychosocial Treatment of Pediatric Bipolar Disorder

Dr. Boorady: I think the treatment is extremely necessary in these cases because we are catching these illnesses early on and they have a very chronic course. I favor educating families and educating the child and adolescent themselves. I also do a lot of outreach and I educate schools and teachers about our current knowledge about bipolar [disorder] and what this might mean down the road. I am not talking just in your initial 3 to 6 months of treatment, but 1 year from now, 2 years from now, and 3 years from now, about what it is children are going to achieve as they get older. I think educating is important.

Child- and Family-Focused Cognitive-Behavioral Therapy (CFF-CBT)

12-session manual-based treatment

- Seven core ingredients:
 - Routine
 - Affect regulation
 - Self-efficacy and coping
 - Coping with depressive cognitions
 - Social skills building
 - Interpersonal problem-solving
 - Social support

- Therapy involves:
 - Acute treatment
 - Maintenance treatment with booster sessions

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Slide 17. Child- and Family-focused Cognitive Behavioral Therapy (CFF-CBT)

And then within that is family therapy and, I think, for the child or adolescent, more of an interpersonal, almost behavioral, therapy where we can incorporate discussions of exercise, of nutrition, of peer and social interaction, and within the kind of behavioral modification also incorporate mood charting, where a child or adolescent can be accountable for and get an understanding of what mood they are feeling related to maybe events that are happening during the day and keep a mood log or journal, I think, to help them sort of take charge of their illness. And then with bipolar [disorder], you really are after -- because they might be on more than one medication -- you are after the child or adolescent adhering to the treatment, so compliance and adherence to the medication is also key.

Dr. Findling: So certainly we don't just prescribe medicines to youngsters, children or adolescents with schizophrenia, certainly there is a lot to worry about that doesn't respond to medicine. When thinking about these youngsters, what kind of nonpharmacologic considerations are really paramount to you?

Recommended Psychosocial Treatments for Pediatric Schizophrenia

- Psychoeducation for the patient
 - The illness and treatment options
 - Relapse prevention
 - Basic life skills training
 - Social skills training
 - Problem-solving skills training

- Psychoeducation for the family
 - The illness and treatment options
 - Prognosis
 - Strategies to cope with the patient

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Slide 18. Recommended Psychosocial Treatment for Pediatric Schizophrenia

Dr. Sporn: Right. Actually, the first hurdle that we meet while treating these children is to have the family accept the diagnosis of either schizophrenia or bipolar disorder or any other major psychiatric illness. That is the turning point of [the] beginning of the treatment. That very often delineates how well the treatment will progress. Actually, we did a small study also with this group of kids at NIH, and it seems that family acceptance was 1 of the 2 best predictors of the outcome, surprising as it is, but it is very important because as long as family is along and as long as they are helping and doing everything possible in accepting the diagnosis and possible implications, the treatment will go much better. The important parts of that [are] obviously [a] very structured environment, where the kid definitely knows what he or she has to do and what not to do, and we always say that illness does not explain bad behavior, the child should know what to do, what not to do, and even if they do things for wrong reasons, they have to be put back on track. A very important thing is the school system; we work very hard to find acceptable school systems for the children with a variety of diagnoses, so it is obviously special education, it is a lot of one-on-one teaching with a child, or a teacher's assistant with a child.

Additional Psychosocial Treatments That May Be Indicated

- Special education
- Vocational programs
- Community support with social acceptance, such as:
 - Day programs
 - School programs
 - Boy Scouts, Girl Scouts
 - Gym

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Slide 19. Additional Psychosocial Treatments That May be Indicated

Also the social acceptance is obviously very important to the kids, so getting them in special programs, whether it is a church program, parochial program, school program, gym, or a kind of boy scout group, [is important]. And, interestingly, healthy children are very open to incorporating someone with major mental difficulties in the environment, they actually, after like 2 or 3 visits, it becomes very natural and it works great with kids with social difficulties. It is the same thing with kids with autism or developmental disorders of other sorts. So, yes, obviously that is very important, and also very important is getting them health benefit services if it looks like the child by the age of 16 or 17 is not likely to function independently. It is very important to get them into the guardianship program, get it before they turn 18, because after they turn 18 sometimes it is almost impossible to do, logically.

Dr. Findling: So there is a lot to it.

Dr. Sporn: Yeah, there is a lot. It is a multifaceted system, and everybody has to be in touch and working very hard with it.

Summary

- **Diagnosis is difficult**
- **Medication is lynch pin for treatment**
 - Atypical antipsychotics for both conditions
 - Lithium and anticonvulsants for bipolar disorder
- **Side effects of medications must be considered**
- **Multimodal approach best**
 - Medication
 - Psychosocial treatment

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Slide 20. Summary

Dr. Findling: And this is very hard work, certainly. We have really covered a lot today, but I think the place to begin with is just to review. The key points to remember are that both bipolar disorder and schizophrenia, even though they do occur in the young, are serious mental illnesses that can be associated with pronounced, profound, protracted impairment and human suffering, and for that reason an accurate diagnosis as a starting point is key. One of the real obstacles to treating youngsters with bipolar disorder and schizophrenia pertains to the difficulties with the diagnosis, which is a key starting point. There are risks in overdiagnosing and stigmatizing folks that you both alluded to, while at the same time there are real concerns about missing something and thereby missing an opportunity to make a difference in a youngster's life earlier. Certainly the lynch pins or the fundamental interventions for these youngsters still really do revolve around medications -- the atypical antipsychotics certainly for both conditions as well as some other adjuncts or even lithium and anticonvulsants for bipolarity. But despite their growing body of evidence to support their utility, there is also at the same time a growing body of evidence really pertaining to their side-effect profile that is really requiring thoughtful, careful, and measured assessment during the course of treatment. And certainly, finally, these are still children. These are still teenagers. And focusing on treatments that don't just really consider pharmacotherapy but really employ a multimodal approach is really what both of you advocate for really effectively.

Alex and Roy, let me first of all thank you for joining me in this very stimulating discussion. I would also like to thank you, the audience, for tuning in to this program today.

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