

**BIPOLAR DISORDERS AND COMORBIDITY:  
ASSESSMENT ISSUES**

**Presented by Linda S. Zamvil, M.D.**

Bipolar disorder begins early, though child psychiatrists have differing opinions about just how early it starts. Moreover, 60% of individuals who have bipolar disorder sometime in their lifetime will have a substance abuse problem. Substance abuse is the most common comorbid diagnosis for individuals with bipolar disorders.

In my work I have been able to follow three generations of some families for over a decade. Typically adolescents that are referred to me have had many diagnoses such as conduct disorders and attention deficit hyperactivity disorder (“ADHD”) but for many it is their mood disorders that have not been treated.

Bipolar disorder can be acquired but most often it is inherited. The phenomenon called genetic anticipation can be applied to bipolar disorders. A model for this phenomenon can be seen with Huntington’s Chorea. It is an illness that is handed down from generation to generation and appears earlier in each subsequent generation. Originally it was thought that Huntington’s was a mid-life illness; then it was seen in the 30’s and 20’s and now it is occurring in the teens. The same thing appears to be occurring with bipolar disorder with it being seen in younger and younger individuals. A parent with Huntington’s has a 50% chance of passing the disease to their offspring. Two parents who are bipolar, have a 75% chance that their child will have the illness.

**ASSESSMENT OF YOUNG CHILDREN**

In families where both parents have bipolar disorders, and there are grandparents on both sides who committed suicide, families that I see have concerns about whether their children have or will have the illness. Their children’s behavior needs to be assessed, as assessment is a critical initial step before a treatment plan can be determined. Are there signs of hyperactivity with insomnia? When they don’t sleep are they more energetic? Is the child aggressive? Does the child hear voices? If learning disabilities are present, are they meeting normal developmental

milestones? The initial assessment must include a consult with a neurologist and an EEG. Some of the children I work with also participate in research and receive MRIs.

After a thorough assessment a treatment plan must be developed. If a parent has responded to an agent such as Lithium and a nine-year-old child comes in for treatment of depression, the first appearance of depression is likely to be the beginning of a bipolar mood disorder. It is estimated that 20% to 40% of children presenting with depression will go on to be bipolar. A child with a known family history of bipolar mood disorder who presents with depression, with or without attention deficit disorder, should be suspected of having a bipolar mood disorder. That child may respond to a medicine like Lithium. Too often anti-depressants are prescribed to children who actually have bipolar disorders and this may cause cycling and make them worse. It is critical in any setting to provide a careful assessment first and then to prescribe appropriate medication.

Twenty percent of untreated people with bipolar disorder will commit suicide if they remain untreated. If a child has bipolar mood disorder, it is likely there is a diagnosed or undiagnosed relative. Sometimes it is a parent who may be abusing substances to self-medicate an untreated bipolar disorder or some other mood disorder.

Children with bipolar mood disorder are fearless high-risk takers. Adolescents can be grandiose, but these children are at another extreme. Their unsafe practices, whether it is driving an automobile, using illicit substances or dangerous sexual practices, can be significant.

Bipolar disorder is equally common in males and females. Adolescents with bipolar disorders tend to start substance abuse earlier. It is not uncommon for patients who have both mood disorder and substance abuse to say they started abusing at age nine or ten or eleven.

## **HISTORY**

Structured interviewing is important in the assessment of adolescents. Use of a structured format ensures that questions are asked of the child and the caretaker as well. Areas such as ADD, learning difficulties, anxiety and substance use should be covered in an assessment. In

addition, if there appear to be some indication of mood disorder, then questions must be asked not only about unipolar depression but also about mania.

Most children and adolescents who have this illness have multiple diagnoses. They do not have only a mood disorder and attention deficit disorder and substance abuse; they may also have oppositional defiant disorder, conduct disorder, panic disorder, obsessive compulsive disorder and post traumatic stress disorder.

### ***DEPRESSION***

The criteria for depression from the DSM IV are uncovered by such questions as, “How is your sleep? Too much or not enough? How are your interests? Do you have guilty feelings? What about your energy? Your concentration? Your appetite? Are you losing weight, gaining weight? Do you feel agitated? Are you tired and unable to move?”

### ***MANIA***

In addition to asking about depression, possible symptoms of mania should be questioned. Many adolescents seen with serious substance abuse problems often have “mixed bipolar.” They have depressive symptoms and manic symptoms at the same time. They may be distracted, as are those who have attention deficit disorder or any kind of depression. There may be an increase in goal directed activity. Suddenly these teens have three jobs; they are going to school; they are head cheerleaders; they are on the soccer team; they are presidents for their church youth group and many other things. They are doing a lot, more than one might expect or insist as a parent. This may be part of their mania and grandiosity. They may have racing thoughts or flight of ideas. They take part in activities with painful consequences, including substance abuse, running away and impulsive sexual practices. Hypersexuality is seen in males and females and can be seen in individuals and families where there has not been abuse or trauma.

Another early sign is sleeplessness. Some mothers say, “The first year my child never slept. Then after that he was the best sleeper in the world,” or, “My kid slept beautifully until age four or nine or thirteen.” It is not a predictor, but it is information that helps to understand

sleep/wake cycles. With this particular mood disorder there is a sleep/wake cycle reversal. Children who are night owls and prefer to be sleeping during the day or do not sleep at all should trigger the idea of possible bipolar mood disorder. Teenagers like to sleep, and they may choose to sleep from the middle of the night to late in the afternoon. That can be very normal. But those with the disorder are doing something not considered within the range of normal. They are in another league. It is chronic and it is disruptive. Talkativeness is another sign. A manic person cannot be interrupted. Often they talk incessantly. They may be difficult to follow. It is possible to see this in children as young as four years old.

Many children have what is called Bipolar II disorder. They have never had a full-blown manic episode but they have had multiple recurrent depressions and occasionally hypomanias. Too often, in today's standard of care, children with depression are considered unipolar, when in fact if the entire family history is looked at, they are really in the bipolar spectrum.

### **MEDICAL HISTORY**

Medical factors such as seizure disorders and other behaviors such as substance abuse can mimic bipolar. It is difficult to know for sure that a child is bipolar if he has a seizure disorder and is substance abusing and there is a family history. Fortunately the medicines that are used for manic depression, such as anti-convulsants, are helpful. In addition, the twelve-step treatments and education may be used, and a neurological work-up should be part of the assessment.

Many things can mimic a psychiatric illness such as a medication reaction, trauma, substance abuse or seizures. The *American Academy of Child and Adolescent Psychiatry* reported a case of a young woman who became manic after having had head trauma. This phenomenon is called post-concussive mania. A very careful and thorough assessment must include a careful history taking as well as medical evaluation.

### **FAMILY HISTORY**

Family history must be emphasized. If a child or adolescent presents with externalizing disorders, conduct disturbance, attention deficit hyperactivity disorder, and/or substance abuse, it

is important to learn if there is a relative who has been diagnosed with bipolar disorder. If so, it is best to be suspicious and watch. It does not mean they are going to have the same problem, but it should be in the differential diagnosis.

### **RAPID CYCLING**

Rapid cycling is having four or more episodes in one year. An example is a patient who refuses to go onto Lithium, takes anti-depressants and a small amount of Adderall for her attentional difficulties, and describes herself as going through rapid cycling, ups and downs that occur many times in a week or even a day, which is referred to as ultra rapid cycling. A mood stabilizer might be more effective to reduce the cycling.

Children who have this illness may have been in the hospital not just a couple of times but also sometimes five or more times. It can take a long time to get an accurate diagnosis.

### **CO-MORBIDITY**

It is rare to find an adolescent with only a substance abuse disorder. Usually there are multiple things affecting him or her. A child who cannot be excellent at school because of learning difficulties, cannot be excellent at sports, or excellent in his family because his family is not a nice place to be, or who has been abandoned and rejected, wants to be excellent at something. A child can get to be really good at substance abuse. That becomes his modus operandi. If this is the only arena where he can feel some sense of competence and gain some kind of good feeling in terms of peers and others, it is very hard to treat. It is very difficult to help the teen want to do something different.

Tim Wilens, MD looked at co-morbid conditions in his population of adolescents with and without substance abuse. Those with substance abuse had more diagnoses. Most had a psychiatric disorder before they got into the substance abuse and related problems.

In a sample of children with the diagnosis of attention deficit hyperactivity disorder, 22% met criteria for bipolar disorder. This was determined on the basis of structured interviews, though it was not confirmed at a later date by the psychiatrist.

Barbara Geller, MD, suggests that children or adolescents with language disorders, attention deficit disorder, oppositional defiant conduct disorder, or sexual abuse should be checked for bipolar disorder. Children or adolescents, who are very hypersexual, with no history of any sexual abuse, should be considered for bipolar disorder. With a teenager there is some overlap with schizophrenia. In a child with a psychotic depression and no diagnosis of bipolar, the most common cause of a psychotic depression is still manic depression, so it may be treated like that. Start with Lithium or Depakote, avoid antidepressants and consider an antipsychotic medication. This is particularly true if the family history is known or if there are relatives on these medicines.

Michael Strober, PhD, from UCLA feels that attention deficit hyperactivity disorder and bipolar disorder are part of the same spectrum. Developmental studies with imaging of children are showing that the brain does not work according to the DSM IV, and that the areas of the brain that are affected by these two illnesses are similar, with a lot of overlap. The neuro-circuitry and chemistry are similar. It may be that when a four to nine year-old is seen, it looks like attention deficit hyperactivity disorder, and when they are twelve or thirteen it begins to look like the mood disorder. There may be anxiety symptoms, and then other issues like substance abuse. The developmental stage of the child may play a role in the emergence of symptoms. A four year old may be hyperactive and aggressive. As the child matures into latency symptoms of anxiety may manifest. In adolescence the cognitive abilities of the child may allow the individual to display depressive symptomatology. It is not always a case of a pure diagnosis according to the DSM IV. It may be a series of emerging syndromes that evolve over the life cycle.

### ***DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER***

The diagnosis of attention deficit hyperactivity disorder is a clinical diagnosis. There is no lab test. There are no neuro-psychological tests. It is very helpful to have a teacher and/or parents' reports and to observe the child in multiple settings, to ascertain whether they have attention deficit hyperactivity disorder. All the questions from the DSM criteria should be asked. In addition, before treating a child with any medication, there should be a baseline medical work-up, in order to rule out other medical problems such as hyperthyroidism, lead poisoning, Wilson's disease or seizure disorder. Depending on the symptoms reported an EEG might be

required. However, an EEG will not always show that there is a seizure disorder. A positive EEG is helpful, but it is more common that most of the children will have negative neurological work-ups. This is true even if they have had all kinds of exposure in utero or if it is known that the parent was a drug abuser, alcoholic or cocaine addict.

### ***OTHER DIAGNOSES***

Many disorders may resemble bipolar disorder. Regions of the brain, the limbic system, and the temporal lobe are connected. It is possible that symptoms of disorders such as temporal lobe epilepsy might resemble bipolar disorder. An anti-convulsant is an agent that calms the brain down. Some people have paradoxical reactions to medicines that are supposed to calm them down, so caution is in order. In particular, it is difficult to know how a younger person will respond to a particular medication. With the very young, the medicine in my clinical practice that has given some of the best results is Catapres (clonidine). Sometimes an anti-psychotic like Risperdal is used and it works better than the stabilizers. Depakote and Lithium are used in little children as well. These medicines are given only to parents or caretakers who will be compliant, get the lab work and administer them in an appropriate way. It is important to note that the medications we use in children are the same we use in adults. However, the clinical studies in children are very limited and data that supports clinical practice is usually behind what most of us do in practice. The FDA has called for increased testing of medications in children and adolescents. Extrapolating from adult studies is not good enough since we know children metabolize medications differently than adults. Studies however, in young subjects, are difficult because of ethical considerations related to informed consent as well as using placebos in a controlled study where a child has a serious mental illness.

### **PHARMACOLOGICAL TREATMENT**

The effect of an anti-depressant on the brain is different from the effect of Lithium. Anti-depressants tend to be mood elevators. The anti-convulsants and Lithium are considered to be mood stabilizers. For some people, Lithium is a mood elevator. Many children who have been treated with anti-depressants are still depressed. They are more than depressed. They are psychotic. It is important to look at any diagnoses in the family of origin. But that is not possible with a child who may be adopted. It is a good idea to try Lithium to learn if the child suddenly

becomes better. Lithium is probably quieting something; it is known to have dopaminergic effects. Sometimes this is still more art than science, but giving agents that have a calming effect is preferred in this particular population.

Barbara Geller, MD has completed the only placebo-controlled study of Lithium with substance abusing adolescents and found that it was helpful. These children had bipolar disorder and substance dependence, primarily alcohol, while marijuana was secondary. Lithium was helpful.

Anti-depressants, whether they are SSRI's or the tricyclics can actually make things worse. Some say you cannot make a diagnosis based on a response to medication. However, most now agree that if people switch from a depression to a mania on an anti-depressant, they are more likely to have a bipolar disorder. There are still many who would disagree. Stressors can cause a bipolar episode e.g., a medical illness, break-up with a boyfriend or girlfriend, death of a loved one, or medication exposure.

### **AGE DIFFERENCES**

The initial episode looks different, depending on age. In a small child, depression may be the first thing seen. In an older adolescent, there might be more classic mania. Young children cycle very fast and are mixed. Parents will say that within one day, even within an hour, it is up and down. It changes often, day in and day out. It is chronic, continuous, and not episodic in the younger one. With adolescents and adults, in between the episodes, people do seem to function well. That leads to the question of whether an adolescent who responds to Lithium should be taken off it if he or she is doing really well. My personal feeling is no; this is a life threatening illness. Experience with the adult population, not the younger population, shows that people who have responded to Lithium and have been on it for thirty years go downhill when it is taken away. When it is readministered, they do not have the same response. If something is working, stay with it. Treat any side effects, but stay on the medicine. Like diabetics who need insulin to live, bipolar disorder requires medicines. Lithium is toxic, as are all these medicines, but with monitoring they are safe. It is safer to continue them than to take them away.

Children who take these medications can gain weight. Try to give options. Consult with a nutritionist and explore exercise before giving up if the medication is working. Thyroid function should be tested. If a child gets really bad psoriasis, try a switch to Depakote. Depakote, however, similar to the other medications causes weight gain.

Data from Brookside Hospital, where I used to run the child and adolescent programs, show that adolescents with a diagnosis of bipolar had more comorbid diagnoses. This was statistically significant. A bipolar individual has many systems in the brain that are awry. That is why it is important to calm the brain by first treating the bipolar disorder. Afterward, if there is attention deficit disorder, then treat that. If there is panic and anxiety, try something for that. If there are other learning difficulties, there must be remediation for that. If there is a history of trauma, then someone must help with that. Always start with the mood disorder and mood stabilization. That is the first line and the brain benefits from starting in that way.

### **About the Presenter**

Triple board certified in Adult, Child and Adolescent Psychiatry and Addiction Medicine, Linda S. Zamvil, MD, is the Director of Ambulatory Mental Health and Addictions at Cambridge Health Alliance and Medical Director of Cambridge Psychiatric Services. She is recognized for her special abilities with adolescent co-occurring disorders at many institutions and community hospitals in the Northeast. She is a frequently invited speaker through out the northeast in mental health communities, primary care communities and educational systems. Dr. Zamvil's current research focuses on the treatment of bipolar disorders in adolescents and children.

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