

ASSESSMENT, DIAGNOSIS, AND MANAGEMENT OF BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS—IN BRIEF:

Epidemiology and Diagnosis:

- Adults (NCS Replication Study, Merikangas et al. 2007)
 - Bipolar I Disorder: 1.0%
 - Bipolar II Disorder: 1.1%
 - Bipolar Subthreshold: 2.4%
- Adolescents
 - Bipolar Disorder: 1.0-1.4% (e.g., see Shaffer D et al. 1996 [MECA]; Kessler RC et al., 2011)
- Children
 - Rare (less than 1%)
- **DSM-5 Criteria:**
 - A *DISTINCT PERIOD* of abnormally and persistently elevated, expansive, **or** irritable mood; *accompanied by increased energy/activity*, lasting at least 1 week or resulting in hospitalization
 - (or any duration if hospitalization because of mania is necessary)
 - At Least Three:
 - Inflated self esteem or grandiosity
 - Decreased need for sleep
 - More talkative than usual
 - Flight of ideas or racing thoughts
 - Distractibility
 - Increase in goal-directed activity or psychomotor agitation
 - Excessive involvement in pleasurable activities potential for painful consequences
 - Causes a **marked impairment** in occupational or social functioning
- **Developmental Differences in Diagnosis:**
 - Similarities exist between adults and children with Bipolar Disorder
 - elated mood, grandiosity, hypersexuality, decreased need for sleep, flight of ideas, racing thoughts, social intrusiveness (*Geller et al. J Child and Adolescent Psychopharmacology 10:157-164, 2000*)
 - Consider the importance of developmental differences in presentation (for example, grandiosity in a child presents differently than in adults, simply on the basis of intelligence, life experience, and linguistic competence)
- **Distinguish between unipolar and bipolar depression**
 - First mood episode of Pediatric (ages 6-17) Bipolar Disorder is often a depressive episode
 - MDD in children often associated with high rates of irritability...i.e., children with depression can present with irritable mood, not depressed mood
 - Children and adolescents with major depressive disorder can have very labile mood
- **Family History**
 - Take a careful family psychiatric history
 - Bipolar disorder in one parent = 5x odds of bipolar disorder in child (but still only ~5% prevalence; *LaPalme et al., 1997*), still less than likelihood of ADHD

- Bipolar disorder in parents, grandparents, and siblings is clinically meaningful but doesn't rule out "bad" ADHD (ADHD comorbid with conduct and oppositional problems), which is actually more common among children of bipolar relatives
- The presence of bipolar disorder in more distant relatives may not confer greater genetic risk
- No clear family history doesn't rule out pediatric bipolar disorder
- **Summary:**
 - In evaluating pediatric bipolar disorder look for classic criteria, i.e., a DISTINCT EPISODE, different from the child's normal state, characterized by:
 - elevated mood, grandiosity, decreased need for sleep, racing thoughts
 - Look for high rates of psychiatric co-morbidity, especially ADHD, ODD, Conduct Disorder and Learning disabilities
 - Do a Careful family history
 - Focus on first and second degree relatives
 - Rating scales do not help you diagnose pediatric bipolar disorder. Instead, do a careful history, examining the presence of a DISTINCT EPISODE, different from the child's normal state

What to do in the case of an acute episode of Pediatric Mania:

- **Refer for hospitalization and emergency psychiatric evaluation**
 - Start an atypical, such as Risperidone, target dose 2-4 mg/day, divided doses
 - Start 0.5 mg qhs, add 0.5-1mg q. 3-4 days if well-tolerated
 - Onset of action: 7 days; full efficacy in 4-6 weeks
 - Assess Side effects: weight gain, sedation, elevated prolactin
 - At baseline: fasting glucose, lipids, BMI, girth, dietary consultation
 - Taper at 6 months
- **Ongoing Management**
 - For long-term management, most children with true bipolar disorder (e.g., an episode of acute mania) will require a combination of medications, e.g., a mood stabilizer such as lithium and/or valproate, and an SSRI. Atypicals can often be tapered after the acute manic episode has resolved, e.g., after 6 months.
 - Continue to assess the possibility of side effects on kidney and thyroid function.
- **Summary**
 - Please refer to specific individual treatment guidelines for recommendations for specific conditions if they are comorbid with bipolar disorder.
 - When unsure whether to add or change a psychiatric medication, please consult with the on-call psychiatrist on the Psych TLC hotline:
 - **The free Psych TLC** service is available for:
 - Consultation on psychiatric medication related issues including:
 - Advice on diagnosis and initial management for your patient
 - Titration of psychiatric medications
 - Side effects of psychiatric medications
 - Combination of psychiatric medications with other medications
 - Referral and services consultation regarding children with mental health issues
 - A licensed mental health professional (MHP) and a child and adolescent psychiatrist (CAP) are available via telephone to provide consultation and

support to PCPs from 8am-5pm, M-F. Simply call **(844) 547-5688** or **(501) 320-7270** to contact the Psych TLC Call Center. One of our expert MHPs will obtain basic information from you about the child and then set up a convenient time for Peter S. Jensen, MD, or another child & adolescent psychiatrist to call you back, usually within 30 minutes to 2 hours.

Treatment Guidelines for Mood Stabilizers in Children and Adolescents

—Medications are off-label for the treatment of bipolar disorder in children and adolescents. As research in this population is limited, recommendations are based, in part, on medications for children with seizure disorders and adults with bipolar disorder.

Generic Name*	Trade Name (Preparations Available, mg)	Starting Dose (mg/day, bid or tid)	Titration	Target dose (mg/day, bid or tid)	Therapeutic Serum Level	Adverse Events	Lab Tests**	Levels of Evidence***	FDA Approval
Lithium (Li)	Li carbonate (150, 300, 600); Li citrate elixir (8 mEq [300 mg]/5 mL); Sustained release forms: Lithobid (300); Eskalith (450)	<25 kg: 300 25-40 kg: 600 >40 kg: 900	↑ 300 mg/d Q 3-5 days	Based on serum level & response: <25 kg: 600 25-40kg: 750-900 >40 kg: 1200 (Therapeutic index is narrow)	0.6-1.2 mEq/L	<i>Common:</i> ataxia, fatigue, tremor, acne, hair loss, hypothyroidism, polydipsia, nausea, diarrhea, weight gain, polyuria <i>Rare:</i> hypothyroidism, hepatic toxicity	CBC, BUN, creatinine, UA (BL & Q 6 months), TFTs (BL & Q 6 months), EKG, serum Li level 12 hrs. after dose (Q 1-2 wks until stable, then Q 1-2 months)	A, B	BD: >12 y.o.
Valproic Acid (Divalproex Sodium)	Depakene (125, 250, 500); Depakote (125, 250, 500)	<25 kg: 250 25-40 kg: 375 >40 kg: 500	↑ 10 mg/kg/d Q 3 days	Based on serum level & response: <25 kg: 500 25-40 kg: 750 >40 kg: >1000	50-120 mg/L	<i>Common:</i> sedation, hair loss, nausea, vomiting, weight gain, muscle weakness <i>Rare:</i> hepatic toxicity, pancreatitis, polycystic ovary, thrombocytopenia	CBC & LFTs (BL, months 1 & 2, then Q 4-6 months), serum levels (5 days to reach steady state) 8-12 hrs. after dose	B, C	BD: Adults (acute) SZ: >10 y.o.
Carbamazepine	Tegretol (100, 200); Tegretol XR (100, 200, 400)	<25 kg: 100 25-40 kg: 200 >40 kg: 400	↑ 100 mg Q 5 days	Based on serum level & response: <25 kg: 400 25-40 kg: 800 >40 kg: 1200	8-11 mg/L	<i>Common:</i> CYP inducer (↓ levels of certain psych meds), dizziness, drowsiness, rash, headache, diplopia, nausea, leukopenia <i>Rare:</i> hepatic toxicity (esp. <10 y.o.), bone marrow suppression, agranulocytosis	CBC, LFTs, blood levels (Q wk. to adjust dosage, then Q 3-6 months), eye exams, UA, BUN	B, C	SZ: children/ adults
Lamotrigine	Lamictal (25, 100, 200)	12.5 qd >40 kg: 25	↑ 25 mg Q 7- 15 days	Based on response: 75- 400	N/A	<i>Common:</i> ataxia, dizziness, somnolence, headache, diplopia, nausea, vomiting <i>Rare:</i> Stevens-Johnson syndrome (potentially life-threatening rash)	CBC, LFTs, monitor plasma levels during dose adjustments	C	BD: adults (maintenance) SZ: children / adults (adjunctive)
Topiramate	Topamax (25, 100)	>40 kg: 12.5-25	↑ 25 mg Q 3- 7 days	50-400	N/A	<i>Common:</i> CYP inducer (↓ levels of certain psych meds), cognitive diffs (dulling, word retrieval, attention), sedation, dizziness, emotional lability, weight loss	Serum bicarbonate levels	C, F	SZ: >2 y.o. (adjunctive); >10 y.o.
Oxcarbazepine	Trileptal (150, 300, 600)	8-10 mg/kg/d 20-29 kg: 160-300 30-39 kg: 300-400 >40 kg: 400+	↑ 5 mg/kg/d Q 3 days	20-29 kg: 600-1200 30-39 kg: 900-1500 >39 kg: 900-2100	N/A	<i>Common:</i> ataxia, dizziness, fatigue, somnolence, tremor, diplopia, nausea, vomiting, dyspepsia	Monitor for hyponatremia, serum sodium levels	D, E	SZ: >2 y.o. (adjunctive); >4 y.o.
Gabapentin	Neurontin (100, 300, 400)	>12 y.o.: 300 3-12 y.o.: 5-10 mg/kg/d	↑ up to 300 mg/d Q 3-5 days	Based on response: >12 y.o.: 900-1800 3-12 y.o.: 25-35 mg/kg/d	N/A	<i>Common:</i> ataxia, sedation, somnolence, asthenia, behavioral disinhibition at high doses	Creatinine clearance (for those with renal problems)	F	SZ: >3 y.o. (adjunctive)

BD=bipolar disorder; BL=baseline; BUN=blood urea nitrogen; CBC=complete blood cell count; EKG=electrocardiogram; LFT=liver function test; SZ=seizure disorders; TFT=thyroid function test

*Medications ordered by strength of evidence supporting their use in children and adolescents with bipolar disorder. **If not otherwise specified, lab tests should be performed at baseline and periodically thereafter.

***A=efficacy in child/adolescent placebo-controlled, randomized clinical trials; B=efficacy in adult randomized clinical trials; C=positive results in open child/adolescent trials and retrospective analysis; D=child/adolescent case reports; E=no different than placebo in child/adolescent studies; F=not helpful in controlled adult studies

Adapted from: Kowatch & DeBello MP (2006); Kowatch et al. (2005); Martin et al. (2003); McClellan et al. (2007); PDR (2007).