

Childhood Bipolar Disorder

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Slides adapted from Robert Hilt, MD
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A Case

- 7 year old boy in your practice
- ADHD diagnosis at age 4
- Ritalin helped for a year, per mom
- Switched to Adderall last year as mom said Ritalin “stopped working”

Case Continued

- Even with Adderall 20mg QAM he is reported to be unimproved
- Mom says she can't control him at home
- **Today you get a history of labile moods, mom thinks he is bipolar (she saw this on Oprah)**
 - asks you to prescribe “something” to treat his bipolar mood swings

What To Do?

- What role should a primary care provider take regarding the question of child bipolar disorder?
 - Psychoeducation?
 - Referral?
 - Treatment?
- How does one assess for childhood bipolar disorder?
- When does it make sense to
 - Prescribe a mood stabilizer?
 - Refer to a therapist?
 - Refer to a psychiatrist?

Bipolar Is A Hot Topic

- Bipolar disorder in kids is much talked about
 - “Child Anxiety Disorder” on Google
 - 1,780,000 hits
 - “Child Bipolar Disorder” on Google
 - 2,170,000 hits
 - Child anxiety disorders are actually about 10 times more common than child bipolar disorder
- There has been a 40 fold increase in office visits for child bipolar disorder from 1994 to 2003 – What does this mean?

Childhood Frequencies

- Pediatric Population Prevalence Estimates:
 - Anxiety Disorders 5-18%
 - Depressive Disorders 15%
 - ADHD 12%
 - Learning Disability 5-10%
 - Conduct Disorder 1-10%
 - **Bipolar 0.6% to 1%**

Frequency of Childhood Bipolar

- Very controversial
- Some assert a high frequency of all children have bipolar disorder
 - “The Bipolar Child” by Papolos and Papolos
 - Assert present in 1 / 3 of all children with ADHD
 - Also states about 6% of all children are bipolar
 - “Is Your Child Bipolar” by McDonnell and Wozniak
 - States more than 3 million US kids have it
 - Around 4% of child population

Quoted Child Rates Don't Match Our Adult Knowledge

- Adult Lifetime prevalence rates of bipolar disorder 1 to 2%
- Greater diagnostic certainty with adults
- Note bipolar disorder is a lifelong diagnosis
- Smoky Mountain Study lessons
 - child bipolar NOS \neq bipolar adult
- **Kids with bad mood swings can not all have “true” bipolar disorder**

Bipolar Disorder Frequency Depends On Where/How You Look

- Prevalence of “true” adolescent bipolar
 - 0.6% of high school students
 - 7% of child psychiatry outpatients
 - 30% of child psychiatry inpatients manic symptoms
 - (less than 2% fit strict criteria for Bipolar 1 diagnosis)
 - “bad mood swings” = labile emotions \neq Bipolar Disorder

Case Continued

- The ‘unresponsive’ ADHD in a 7 year old boy?
 - Want better symptom detail than just “labile mood” and “won’t listen”
 - Want predisposing and perpetuating factors toward behaviors
 - Need timing of symptoms clarified
 - Location where symptoms occur

Case Continued

- Mom says he “never listens to me”
- Goes into rages easily whenever doesn’t get his way
- Throws things at mom, hits her
- Tried “everything,” even spanking when nothing else would help
- With dad or other adults he behaves better, though talks back sometimes

Case Continued

- In 2nd grade, teacher said he was not listening well in beginning of year, is better now
- In kindergarten he didn't follow rules well
- School not noting any academic failing
- Not having rages at school
- --Overall seems to be a problem at home more than at school
- Developmental milestones were OK

Case Continued

- Mom is primary caregiver
- 3 other young siblings
- Dad works, comes home late most nights
- Mom has few supports

How to answer Mom's Question if this is Bipolar Disorder?

- Psychoeducation based on DSM-IV
- Mania
 - 1 week of abnormal irritable or **expansive mood**
 - Plus 3 of the following:
 - Distractible, **grandiose**, little sleep, talkative, **indiscretions (hypersexuality)**, flight of ideas, increased goal directed activities
 - Need 4 of these if mood is just irritable
 - Hypomania
 - Above symptoms for 4 days, no hospitalizations

Consider the large differential for each of these Mania symptoms in kids:

- **D**istractible
- **I**ndiscretions (hypersexuality)
- **G**randiose
- **F**light of ideas
- **A**ctivity (goal directed) increase
- **S**leep need decrease (less than 3 hrs.)
- **T**alkative (pressured speech)

Which are common ADHD symptoms?

Diagnostic Perspective

- Experience with adult mania helps
- Compare child to a prototype “manic” patient
 - Pressured speech, not just talkative
 - Having no doubt about their grandiose ideas
 - True euphoria/grandiosity stands out
 - Imagine a 5th grader who insists on teaching the class
 - Thought process is fast and jumping around
 - Episode: many days in duration coupled with little need for sleep

Look for Patterns

- Mania/hypomania involves episodes
- Episodic patterns of mood changes
- Episode clear departure from baseline function with some hallmark symptoms
 - Elation
 - Hyperactivity
 - Grandiosity
 - Hypersexuality
 - Decreased need for sleep

Some Assert Child “Episodes” happen multiple times a day

- Not the usual adult pattern of symptoms
- Consider “rapid cycling” in kids if there is no trigger identifiable for the mood changes
- If child gets angry/frustrated with something before blowing up, that isn’t a “rapid cycle”
 - ADHD plus irritability should not generate a bipolar diagnosis

Usual Story of Bipolar I Disorder (with origins in childhood)

- Bipolar adults look back and note symptoms became bipolar-like in their teen years
- Many bipolar adults had major depression episodes as children
- The younger the child's first major depression, the more likely bipolar disorder is in the future

Bipolar Diagnostic Aides

- Rating Scales
 - Young Mania Rating Scale
 - Useful for monitoring symptoms over time
 - Not a diagnostic tool (very low specificity)
 - DISC or KSADS
 - Used in research, still have flaws
 - Impractical for your office practice
- Rating scales are **too misleading** to recommend for diagnostic use

Return to Case of 7 year old boy

- Rage episodes seem directed mostly at mom, when mom attempts to set limits at home
- Mood changes occur mostly in response to frustrations
- There are not any hallmark symptoms of grandiosity, euphoria, hypersexuality
- No history of days-long episodes
- He is very young to diagnose as bipolar
 - **have extra skepticism the younger the child is**

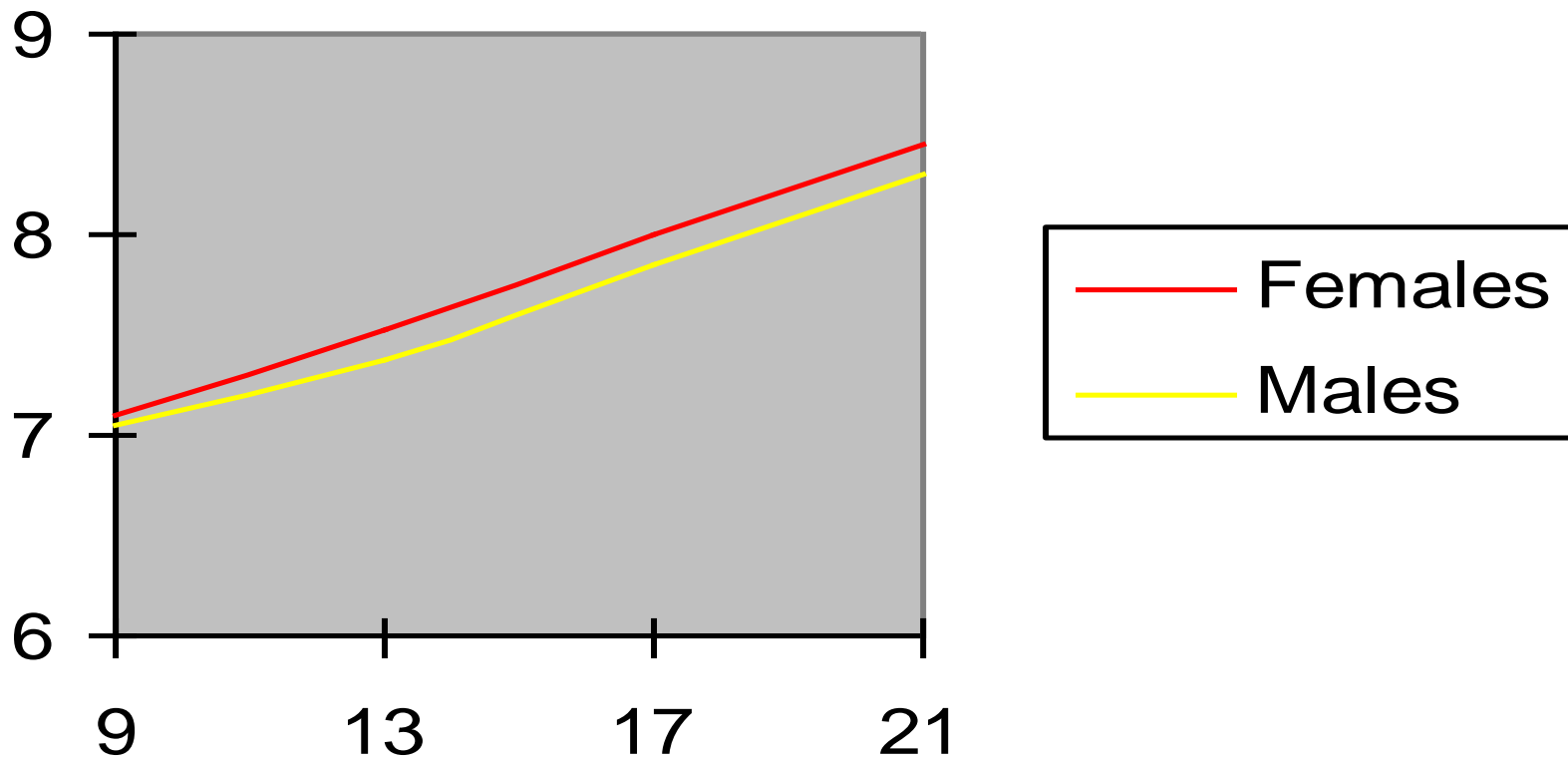
Winding up what to do with the Case

- Mom says his uncle is bipolar, “just like him”
- Avoid overcalling a positive family history
 - many adults who call themselves bipolar may not have that illness
 - first degree relative bipolar disorder, increases OR by 5
 - second degree relative bipolar, increase OR by 2.5
 - given a generous prevalence of 2% bipolar in the population, most children of a bipolar parent (~90%) will not have bipolar disorder
- You think something else may be going on, as he is oppositional and defiant with mom

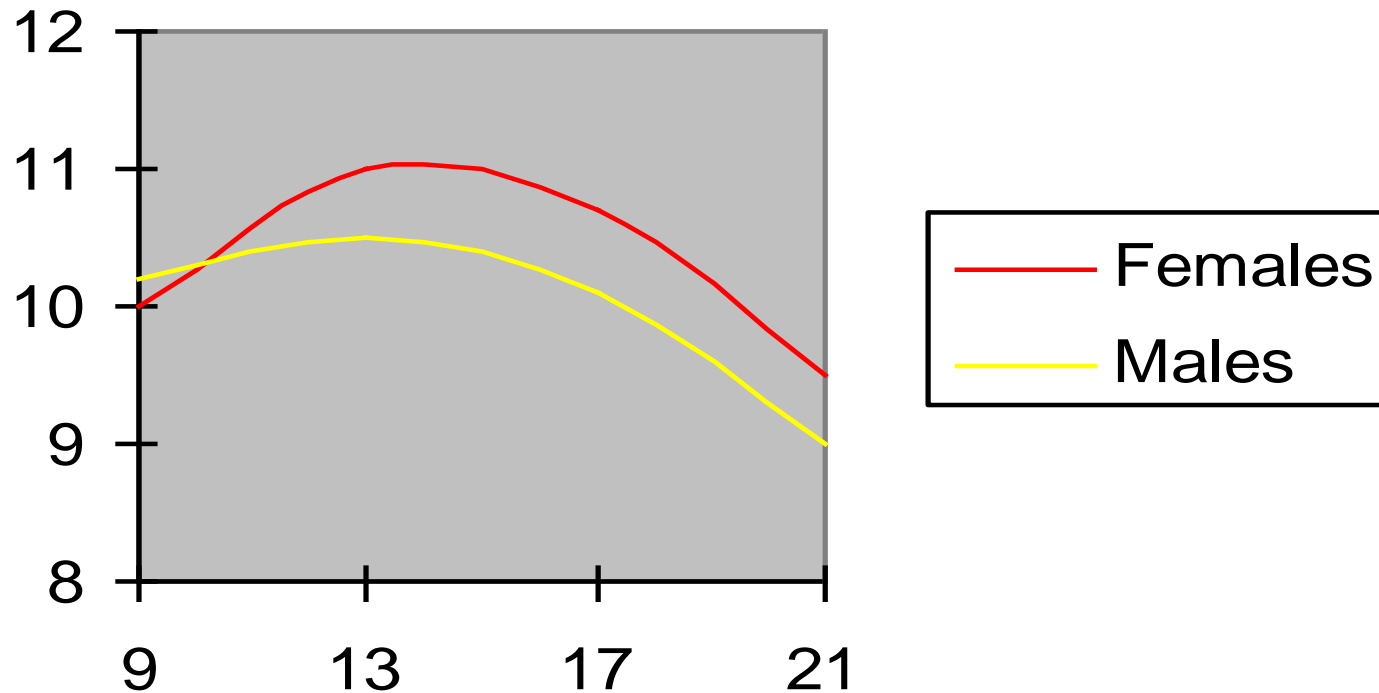
Irritability: Chronic vs Episodic

- ❖ Community sample of 776 children and adolescents
 - ❖ Assessed 1983, 1985, 1992
- ❖ Irritability rating scales extracted from existing database
 - ❖ Episodic irritability rating scale
 - ❖ Chronic irritability rating scale

Episodic Irritability by Age and Sex



Chronic Irritability by Age and Sex



Childhood Bipolar in a Community Sample

Those with *episodic* irritability were more likely than those with *chronic* irritability to have:

- A parent diagnosed with BD
- Experienced elation and/or grandiosity
- More of the B-criterion symptoms of mania
- Psychotic symptoms
- Had a depressive episode
- Made a suicide attempt

Conclusion (Leibenluft) : Episodic and chronic irritability are distinct constructs.

Episodic irritability is associated with BD

Irritability and Later Psychopathology

- ❖ Episodic irritability at T1 predicts:
simple phobia and mania at T2
- ❖ Chronic irritability at T1 predicts:
ADHD at T2 and MDD at T3

Irritability Conclusion

- Geller: Not all manic symptoms are created equal; some are more specific than others, eg grandiosity (Wozniak disagrees)
- Geller: Irritability is not diagnostic of BD; it is very common and shows high sensitivity, but poor specificity for BD (Wozniak: irritability may be primary mood symptom)
- Leibenluft: In diagnosing BD, *episodic* irritability is more suggestive of BD than is chronic irritability (Wozniak: episodicity not relevant)

Bipolar Disorder NOS: Our Fuzzy Diagnosis

- Contributions to the current bipolar “epidemic”
- Label often given to impulsive, aggressive kids
- Prognosis could be normal, MDD, or (rarely) true bipolar
- Diagnosis confused with:
 - ADHD
 - Oppositional Defiant Disorder
 - Intermittent Explosive Disorder
 - Fetal Alcohol Syndrome
 - Anxiety Disorders
 - Conduct disorder
 - Frontal lobe syndromes (head injury)

Bipolar NOS

- Why so commonly diagnosed?
 - Sounds better to us than “I don’t know”
 - If we give a child medicine as if bipolar, parents often report improvement
- Bipolar medicines have many non-specific effects
 - All decrease impulsivity and aggression
 - We see a response & think the bipolar label must have been correct

What if a “Bipolar” Child Really is Bipolar?

- Though rare in a PCP practice, becomes more likely the older the child is
- Typical pattern is early onset depression, and during teenage years getting first symptoms of mania
- True Bipolar Disorder is a big problem

Course Of True Bipolar Disorder

- Suicidalilty
 - *up to 15% eventually complete suicide*
- Substance Abuse in up to 60%
- Anxiety disorders in up to 50%
- Psychotic features in up to 50%
- Relationship Disruptions
- Work Disruptions
- Hospitalizations
- Progressive deterioration

Bipolar Treatment

- If clear manic episodes, strongly recommend referral to child psychiatrist
- Management difficult because:
 - High rate of substance abuse
 - High rate of medication non-compliance
 - Even with medication, recurrences happen
 - High rates of family disruption from the illness
 - Suicidal behavior is common

If No Child Psychiatrist Can Assume Care, Then What?

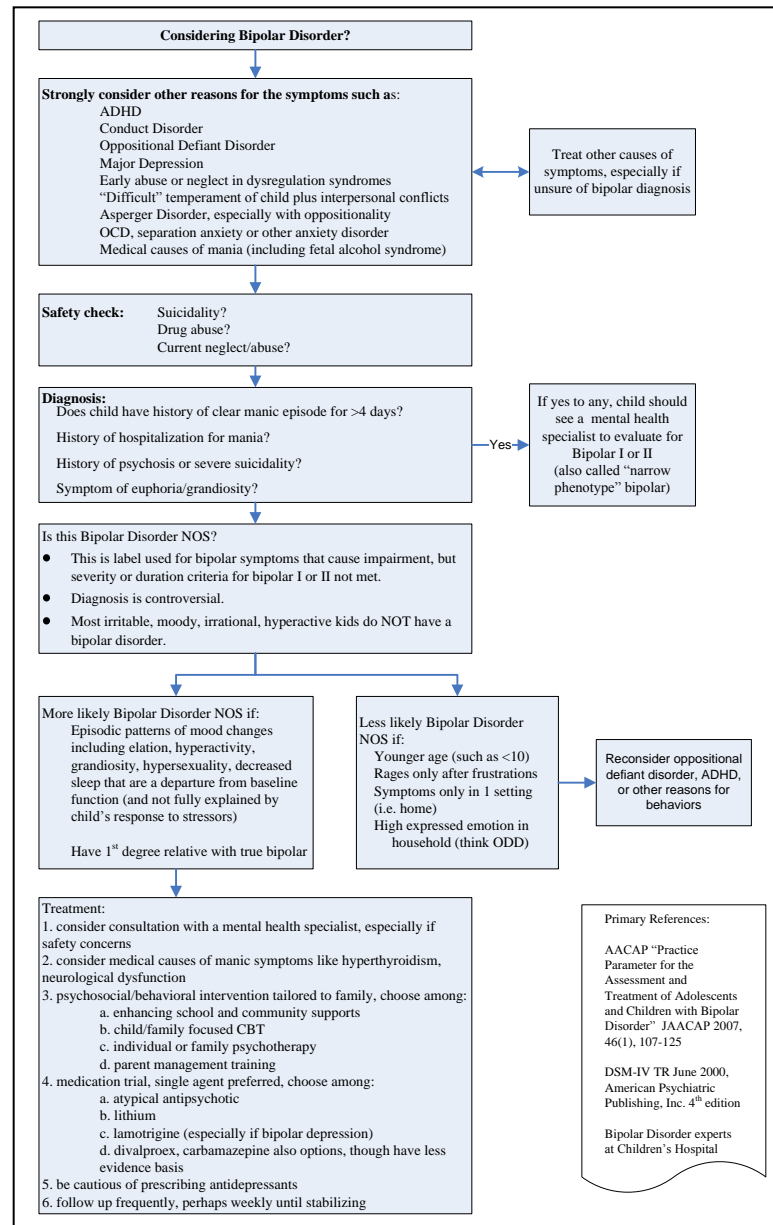
- Get collateral evaluations to help establish correct diagnosis
 - strongly advise against rushing to offer diagnosis of bipolar disorder
- Seek consultant advice on medication (when they are appropriate to consider)
- Preferred model of care:
 - MH specialist is primary prescriber
 - PCP is a partner in the treatment team
- Sometimes PCP is left holding the bag

Bipolar Treatments

(for when you are left holding the bag)

- Lithium
- Valproic Acid
- Atypical antipsychotics
- Combination therapy
- Antidepressants, if used cautiously
- Psychotherapy for:
 - depression treatment
 - coping skills
 - supporting medication treatment adherence
 - family support

Care Diagram





Treatment :

1. Consider consultation with a mental health specialist , especially if safety concerns
2. Consider medical causes of manic symptoms like hyperthyroidism , neurological dysfunction
3. Psychosocial/behavioral intervention tailored to family , including :
 - a. family psychoeducation
 - b. child/family focused CBT
 - c. enhancing school and community supports
 - d. individual or family psychotherapy
 - e. parent management training
4. Medication trial , single agent preferred , choose among :
 - a. atypical antipsychotic
 - b. lithium
 - c. lamotrigine (especially if bipolar depression)
 - d. divalproex , carbamazepine also options , though have less evidence basis
5. Be cautious of prescribing antidepressants
6. Follow up frequently , perhaps weekly until stabilizing

What Is A Mood Stabilizer?

- Note FDA does not use this term
- A mood stabilizer should:
 - treat both depression and manic phase of bipolar disorder
 - minimize recurrence of both depression and manic phases of bipolar disorder
- Since no one compound does this well, multiple meds are often used together

Mood Stabilizers are Non-Specific to Bipolar Disorder

- Maladaptive aggression
 - inappropriate intensity/frequency/duration
 - risperidone if conduct d/o, low IQ
 - (Effect Size 0.9, combined n=875)
 - lithium if conduct disorder
 - (ES 0.5, combined n= 195)
 - divalproex if conduct disorder
 - (crossover RCT, high dose better than low, n=71)
 - methylphenidate if comorbid ADHD
 - (ES 0.9, combined n=844)

Atypical Antipsychotics

	Dosage Form	Usual Starting Dose	Sedation	Weight Gain	EPS (stiff muscles)	Bipolar (+) child RCT evidence?	FDA bipolar approved?	Editorial Comments
Risperidone (Risperdal)	0.25,0.5, 1,2,3,4mg 1mg/ml	0.25mg QHS	+	+	+	Yes	Yes (Age >10)	Generic forms. More dystonia risk than rest
Aripiprazole (Abilify)	2,5,10,15, 25,30mg 1mg/ml	2mg QD	+	+	+/-	Yes	Yes (Age >10)	Long ½ life, can take weeks to build effect
Quetiapine (Seroquel)	25,50,100, 200,300, 400mg	25mg BID	++	+	+/-	Yes	Yes (Age >10)	Pills larger, could be hard for kids to swallow.
Ziprasidone (Geodon)	20,40,60, 80mg	20mg BID	+	+	+/-	No	No	Greater risk of QT lengthen, EKG check
Olanzapine (Zyprexa)	2.5, 5,7.5, 10,15, 20mg	2.5 mg QHS	++	++	+/-	Yes	Yes (Age >13)	Greatest risk of weight gain, ↑cholesterol

Table + and – from Fedorowicz VJ, Fombonne E. (2005), Lublin, H; et al (2005), and Correll CU et al (2009)

Risks common to all Atypical Antipsychotics

- sedation
- tardive dyskinesia
- cholesterol/blood sugar
- dystonia
- lower seizure threshold (mildly)
- QT interval change (~20ms for ziprasidone)
- weight gain (olanzapine > the rest)

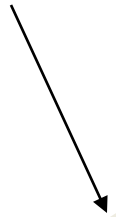
Lithium

- FDA approved for mania in pts >12
- Rapid absorption
 - peaks in 0.5 to 2 hours
- Half life ~ 24 hours
 - longer if poor renal function (renal excretion)
- Narrow therapeutic index
- Drug level 0.6 to 1.2 mEq/L
- Don't go past 1.4 mEq/L
- Don't combine with NSAIDs

Table 6.6 Lithium Carbonate Serum Level, Clinical Side Effects, and Toxicity

Therapeutic Lithium Levels (0.6–1.2 mEq/L)	Mild to Moderate Toxicity (1.4–2.0 mEq/L)	Moderate to Severe Toxicity (2.0–2.5 mEq/L)	Severe Toxicity ≥ 2.5 mEq/L
Central Nervous System Hand tremor Memory impairment Concentration difficulties	Central Nervous System Dizziness Drowsiness Dysarthria Agitation	Central Nervous System Coma Choreoathetoid movements Clonic limb movements Convulsions	Central Nervous System Seizures
Endocrine Hypothyroidism	Coarsening hand tremor Lethargy Muscle weakness Vertigo	Delerium EEG changes Fainting Hyperreflexia	Renal Oliguria Renal failure Death
Gastrointestinal Diarrhea Edema Nausea Weight gain	Gastrointestinal Abdominal pain Diarrhea Dry mouth Nausea Vomiting	Leg tremors Muscle fasciculations Nystagmus Vision blurred	
Renal Polydipsia Polyuria Nocturnal enuresis		Gastrointestinal Anorexia Nausea Vomiting	
Dermatological Acne		Cardiovascular Cardiac arrhythmia Sinus node dysfunction Pulse irregularities	

Early Signs



Adapted from Maxmen JS and Ward NG. *Psychotropic Drugs Fast Facts* (3rd ed.) New York: Norton, 2002, p. 255.

Lithium Monitoring

- Baseline
 - renal screen (BUN/creatinine)
 - thyroid function
 - cbc with diff
 - calcium/phosphorous
 - pregnancy test
 - EKG, only with Hx of arrhythmia or to assess Li toxicity
 - lithium level q 5-7 days until stable dose
- Q3 months
 - lithium level
- Q6 months
 - TSH, renal function

Depakote

- How well does it work?
 - fair, usually works best in adolescents in combination with an antipsychotic (better than either one alone)
 - some RCT's have suggested that it works better than lithium on manic symptoms
 - broad effects: also used for externalizing behavior disorders, conduct disorder

Carbamazepine

- Weak evidence of benefit in bipolar (McClellan and Werry, 1997)
- Used for aggression treatment by some
- drug/drug interactions
 - decreases BCP effectiveness
 - lithium may add neurotoxicity
- autoinduced metabolism, CYP450 3A4
- $\frac{1}{2}$ life 25-65 hours
- FDA approved for pediatric seizures

Oxcarbazepine

- FDA approved for adults with bipolar
- Adolescent bipolar trial negative
- less risks than with carbamazepine
 - less liver/blood toxicity
- levels don't correlate with efficacy or toxicity
- weight neutral

Lamotrigine

- Bipolar depression treatment
- Not helpful for manic phase
- CBC, LFT monitoring
- Significant Stevens-Johnson rash risk
- Slow titration (age >12)
 - 25 QD 2 weeks, 50 QD 2 weeks, 50 BID 2 weeks, target dose 100-200mg per day
 - $\frac{1}{2}$ life 33 hours
 - If miss more than a few days, safer to start back at beginning

Anticonvulsants Shown Not To Help Bipolar Adults

- topiramate (Topamax)
- gabapentin (Neurontin)
- levetiracetam (Keppra)
 - can cause psychiatric symptoms
- zonisamide (Zonegran)
- pregabalin (Lyrica)
- felbamate (Felbatol)
 - can cause psychiatric symptoms

Our Hope

- Labeling impulsive, difficult kids as bipolar will disappear
- **Most disruptive, irritable children do NOT have bipolar disorder**
- Recognize that Bipolar Disorder means a very troubled future

Our Hope For The Poorly Regulated Child

- Acknowledge the multiple etiologies for emotional dysregulation
 - Abuse, ADHD, ODD, mood disorders, anxiety disorders, personality disorders, learning disabilities, etc.
 - Parents need support/training to handle the extra challenge from difficult temperament
- When necessary, use symptom management medicines to decrease impulsive behavior and other target symptoms