Bipolar Disorder Demystified
Learning Objectives:

1. The physician will be able to recognize/distinguish bipolar/manic symptoms from other symptoms of mental illness.
2. The physician will be able to initiate treatment and monitor for complications.
3. The physician will be able to avoid pitfalls for treatment of general medical conditions to prevent a manic episode from occurring in individuals susceptible to a manic episode.
What is Bipolar Disorder?

A severe mental illness characterized by symptoms of at least one manic or hypomanic episode and may or may not be associated with having a depressive episode in a person’s lifetime. It is cyclical in nature and progressive.¹
Bipolar and Related Disorders

The Diagnostic and Statistical Manual of Mental Disorders has sandwiched Bipolar related disorders between the Schizophrenia Spectrum disorders and Depressive disorders to recognize the relationship between these disorders. ¹
The Big Three

For today’s purposes, we are going to focus on Bipolar I and Bipolar II disorder with mention of Cyclothymia.
What is the difference?

In a nutshell, to meet criteria for Bipolar I disorder, your patient has had to have met the criteria for at least one Manic episode in his or her lifetime. That episode should have been severe enough to warrant hospitalization or to cause significant impairment in functioning (this can include incarceration). ¹
What is the difference?

In the Bipolar II patient, you must have met criteria for a hypomanic episode, and while impairment in level of functioning is impaired, it is less severe than that of the Bipolar I patient. In addition, the Bipolar II patient has had to have had a depressive episode in his or her lifetime.¹
What is the difference?

In the Cyclothymic patient, he or she has experienced manic episodes without ever having had a depressive episode. \(^1\)
What is Mania?

Manic vs. Hypomanic

The difference between the two are time and severity. For the “A” criteria of a manic episode, the symptoms last at least a week or hospitalization is necessary.¹
Manic vs. Hypomanic

For the “A” criteria in the hypomanic episode, the symptoms last at least four consecutive days, change in functioning is noticeable by others, but not severe enough to cause major impairments. ¹
The “A” Criteria

The patient has a “distinct period and persistently elevated, expansive, or irritable mood AND persistently increased goal-directed activity or energy”\(^1\)
What does that look like?

Elevated and Expansive

Irritable
Children and Adolescents

Irritable and destructive

Depressive episode tends to have physical complaints. ²
Goal-Directed Activity

Taking on more new projects or commitments than normally, because pesky things like sleep or common sense would stand in his or her way.
The “B” Criteria

During this episode of abnormal mood and activity/energy, one must also have at least three (four if mood is only irritable) of the following seven criteria.¹
1. Self-Esteem

The self-esteem is inflated or grandiose.

They can be benign expansions of the truth or floridly reaching delusional levels.
Example of inflated self-esteem:

In meeting with Mr. Jones to see what he’d like to work on, he at first presented humbly with “small” body language. As our discussion progressed, his eye contact frequency increased, body language enlarged and he became more boastful about his education. He was proud of his education and boasted of having learned Algebra, Calculus, Trigonometry, Cosmology, Physics and Psychology, but neglected to mention that he had only earned his GED. He would like to try phase groups, but he felt isolated by his intelligence and stated that he was educationally baffling even to psychologists.
2. Decreased Need for Sleep

Feels rested after only a few hours
3. Speech

More talkative than usual
or

pressured to keep talking.

Warning: What is cultural?
4. Flight of Ideas
Racing Thoughts

The Patient’s train of thought is characterized by shifting from one topic to another. There may be some connection between ideas, albeit tenuous, but may be understandable. When moderate to severe, it can be elevated to illogical.
What does that look like?

“The sky is blue. Blue is my favorite color. My mom took me to Color-Me-Mine once. I painted a mug. Don’t drive through Los Angeles; you’ll get mugged.”
What does it look like?

Patient: I came to see you to the psychiatrist’s office because you have the time to listen to me GPs don’t have the time to listen to me because he’s not very clever he takes some interest in me sometimes but sometimes he doesn’t I’ve got real important stuff to show you because there is real important stuff here.

Psychiatrist: What is your name?
Patient: Names? Names are games, diddley dang whatisyourname? (laughing)
What does it look like?

Often times the patient may tell you that his or her thoughts are racing and like the previous example, that is evident. Sometimes the patients thoughts are so rapid that he or she can’t keep up with the thoughts and may have trouble himself being able to express any thoughts.
5. Distractibility

Attention is too easily drawn to unimportant or irrelevant external stimuli.
6. Increase in Goal Directed Activity/Energy

If the patient is only experiencing a hypomanic episode, this can be advantageous to his or her career.
Psychomotor agitation

Purposeless non-goal-directed activity. It can also be manifested by pacing, hand wringing or picking at the patient’s nails, hair, etc.
7. Excessive involvement in activities that have a high potential for painful consequences
Engaging in unrestrained buying sprees
Sexual Indiscretions
Foolish Business Investments
Test Film

https://www.youtube.com/watch?v=wuk8AOjGURE
Test Question

1. In the film, Good Morning Vietnam, in this scene, Robin Williams’ character demonstrates which of the following manic symptoms?
   a. racing thoughts
   b. pressured speech
   c. elevated and expansive mood
   d. All of the above
What it isn’t
Not secondary to a substance.
Not due to a general medical condition.
It is not better explained by another major psychiatric disorder.
Is it mania? Or is it meth?

Methamphetamines, amphetamines, cocaine, and PCP can all give manic like presentations.
Prescription Medications that Induce Manic Symptoms

All Antidepressant medications have been implicated in inducing manic-like or manic episodes. ³,⁴ L-Dopa, Corticosteroids, Anabolic-androgenic steroids ³ Tramadol ⁵ Isoniazide ⁶ Clarithromycin, Ciprofloxacin and Ofloxacin among other antimicrobials ⁶
Thyroid Induced Mania

Either by supplementation or by Grave’s Disease itself can induce a manic-like episode or exacerbate mania. 7,8
Borderline Personality Disorder

“Mood Swings” is NOT bipolar disorder.

If her mood is like the weather and not the season, she could be a borderline.
Demi Lovato on Her Bipolar Disorder: “It's a Daily Thing”
Lovato tells *Cosmopolitan for Latinas*, which named her its "Fun, Fearless Latina of the Year."
At 21, Lovato has overcome many hurdles – including an eating disorder, drug abuse, self-mutilation, rehab and a nervous breakdown – but the pop singer remains open about her struggles, hoping to inspire others, especially young people. ¹⁰
Diagnostic criteria for 301.83 Borderline Personality Disorder

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

(1) frantic efforts to avoid real or imagined abandonment.  **Note:** Do not include suicidal or self-mutilating behavior covered in Criterion 5.

(2) a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation

(3) identity disturbance: markedly and persistently unstable self-image or sense of self

(4) impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating).  **Note:** Do not include suicidal or self-mutilating behavior covered in Criterion 5.

(5) recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior

(6) affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)

(7) chronic feelings of emptiness

(8) inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)

(9) transient, stress-related paranoid ideation or severe dissociative symptoms
I Hate You, Don’t Leave Me

I hate you, don’t leave me
I feel like I can’t breathe
Just hold me, don’t touch me

And I want you to love me
But I need you to trust me
Stay with me, set me free

But I can’t back down, no, I can’t deny
That I’m staying now ’cause I can’t decide
Confused and scared I am terrified of you

I admit, I’m in and out of my head
Don’t listen to a single word I’ve said
Just hear me out before you run away
‘Cause I can’t take this pain

No
I’m addicted to the madness
I’m a daughter of the sadness
I’ve been here too many times before
I’ve been abandoned and I’m scared now
I can’t handle another fall out
I am fragile, just washed up on the shore

They forget me, don’t see me
When they love me, they leave me

I hate you, don’t leave me
I hate you, don’t leave me
‘Cause I love when you kiss me
I’m in pieces, you complete me

But I can’t back down, no, I can’t deny
That I’m staying now ’cause I can’t decide
Confused and scared I am terrified of you

I admit, I’m in and out of my head
Don’t listen to a single word I’ve said
Just hear me out before you run away
‘Cause I can’t take this pain
No, I can’t take this pain

I hate you, don’t leave me
I hate you, please, love me!!
Violent mood swings... Chronic depression...
Self-destructive tendencies...

I HATE YOU—
don't leave me

UNDERSTANDING THE BORDERLINE PERSONALITY

JEROLD J. KREISMAN, M.D., & HAL STRAUS
STIGMA
Take a break?
Prevalence

- **12-month Prevalence**: 2.6% of U.S. adult population\(^1\)
- **Severe**: 82.9% of these cases (e.g., 2.2% of U.S. adult population) are classified as “severe”\(^2\)
Average Age-of-Onset: 25 years old

Demographics
(for lifetime prevalence)

- Sex: Not Reported
- Race: Not Reported
- Age:

Percent of U.S. Adult Population

<table>
<thead>
<tr>
<th>Age</th>
<th>18-29</th>
<th>30-44</th>
<th>45-59</th>
<th>60+</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.9</td>
<td>4.5</td>
<td>3.5</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

12
Demographics

In bipolar illness, Men and women are equal...but not really.\textsuperscript{13}
Bipolar disorder is an equal opportunity illness. It does not discriminate.
Demographics

Economic factors

#6

$45 Billion $^{14,15,16}$
Comorbidities

Most Common Psychiatric Disorders

- Anxiety
- Substance Use disorders (Alcohol and Cannabis) \(^{18}\)
- Conduct Disorders

Most Common General Medical Conditions

- Migraine
- Thyroid disorders
- Obesity
- Type II Diabetes
- Cardiovascular Disease \(^{19}\)
Mortality

Women 9.0 years
Men 8.5 years
than the general population.
All Cause 2-fold greater $^{21}$
Mortality

Cardiovascular disease
Diabetes mellitus
COPD
Influenza/pneumonia
Unintentional injuries
Suicide
Cancer for women only \(^{21}\)
Mortality

Don’t blame it on the medications.

No treatment increases mortality.\textsuperscript{20}
Mortality

Access
Unhealthy lifestyle factors
Smoking
Substances
Obesity$^{20}$
Mortality

Suicide

Women 10 fold
Men 8 fold

1 in 5 Completes \(21\)
Mortality Due to Suicide

Risk Factors

Prior Suicide Attempt

Degree of which the patient rates the severity of the acute illness $^{22,23}$

Cigarette Smoking $^{23}$
Mortality Due to Suicide

Lithium is better than Depakote \(^{24}\)

Patients are at highest risk for suicide when stopping or lowering Lithium. \(^{25}\)
Causality
Causality

Genetics

Heritability overall is about 60%

Risk to offspring is 27% for one parent and 50-65% in both for bipolar and up to 75% for any affective disorder.

Second degree relatives 5%$^{25}$
Causality

Genetics

No single gene

226 Empirically significant genes

6 Neurological Pathways
Causality

Head Injury

28% more likely to be diagnosed with bipolar disorder \(^{26}\)
Causality

Inflammatory/Immunologic Response

The theory of bipolar disorder as an illness of accelerated aging: Implications for clinical care and research \(^{42}\)

Immunosenescence is associated with human cytomegalovirus and shortened telomeres in type I bipolar disorder. \(^{27}\)
Causality
Causality
Treatment
Noncompliance
64%
Most frequent cause of recurrence
Treatment

Lithium
Acute Mania
1800 mg divided BID (ER) TID/QID (IR)

Maintenance
900 -1200 mg per day

Start divided but end the day United
Treatment/Lithium

as effective as divided dosing

spare renal concentrating capacity, thereby diminishing the risk of diabetes insipidus

reduce the long-term risk of lithium-induced renal insufficiency

greater adherence

better tolerability\textsuperscript{29}
Treatment/Lithium Levels
Measure trough levels 4-7 days after initiating or changing dose
Goal levels
Acute 0.9-1.4 mEq/L
Maintenance 0.8-1.2 mEq/L
Treatment/Lithium

Toxicity
>0.8 mEq/l

Gastrointestinal Symptoms
Nausea, Vomitting, Diarrhea, Stomach Pains

Neurologic
Dizziness and weakness
Treatment/Lithium Toxicity

Coarse Tremor
Slurred Speech
Confusion
Hyperreflexia
Psychosis
Treatment

Depakote

Dosing Patient’s weight + 0

Trough plasma concentration between 50 and 125 mcg/mL
Treatment

Depakote

Common Side Effects: Nausea, Vomitting, Dizziness, Somnolence and Weight Gain

Thrombocytopenia
Bipolar patients taking Depakote were 2.7 times as likely to commit suicide as those taking lithium. 30
Treatment

Tegretol (Carbamazepine)
Initiate at 3-5 mg/kg/day divided
Increase up to 10-20 mg/kg/day divided

Trileptal (Oxcarbazepine)
Initiate 300 mg BID
Increase up to 2400 mg (3200)
Treatment

Tegretol
Trough between 6 & 8 mg/L
Should not exceed 10 mg/L $^{31}$

Trileptal
Monitoring not indicated
Treatment

Side Effects

Tegretol
Loaded

Trileptal
Fewer & Better Tolerated$^{32}$
Other Anticonvulsants

Neurontin (Gabapentin) Double-blind studies failed to demonstrate efficacy.
Gabitril (Tiagabine)
Keppra (Levetiracetam)
Topamax (Topiramate)
Treatment
Lamictal
NOT for Acute Mania
Prevents recurrence of mania/depression
Treatment of Bipolar Depression$^{33}$
Treatment

Lamictal

“Go low. Go slow. But go!”

-Howard Graitzer, DO
Treatment
Lamictal
Treatment

Lamictal

25 mg/day X 2 weeks, then 50 mg/d X 2 weeks, then 100 mg X 1 week, up to 200 mg per day. Above 200 mg has not been found efficacious. \(^{34}\)
Treatment

Avoid Antidepressants

Flip into mania “ 35,37

May not be any more efficacious than placebo36
Treatment

Second Generation Antipsychotics
Zyprexa (Olanzapine)
Risperdal (Risperidone)
Invega (Paliperidone)
Seroquel (Quetiapine)
Abilify (Aripiprazole)
Saphris (Asenapine)
Latuda (Lurasidone)
Geodon (Ziprasidone)

[^38]
Treatment

SGA

Effective in Acute Mania

Do not induce Depressive Episodes

Have AD Effect $^{38}$
Treatment

Second Generation Antipsychotics
Zyprexa (Olanzapine)
Risperdal (Risperidone)
Invega (Paliperidone)
Seroquel (Quetiapine)
Abilify (Aripiprazole)
Saphris (Asenapine)
Latuda (Lurasidone)
Geodon (Ziprasidone)
Treatment

Long Acting Depot

Risperdal Consta 25, 37.5, 50 mg q2wks

Invega Sustenna 234, 156, 117 Q 4 wks

Abilify Maintena 400 mg q 4 wks
Treatment

Side Effects

EPS
Metabolic
Sexual Dysfunction
Hyperprolactinemia
Cardiac Arrhythmias
Treatment

Namenda (Memantine) 20-30 mg qd $^{38,39}$
Treatment
Mirapex (Pramipexole)
Adjunct treatment
Rapid Cycling
Test Question #2

It is 3 am and you are moonlighting in the emergency room when a 64 year old woman is brought in by the county sheriff for assessment. She is demanding, talking at a rapid rate, chain smoking, and when she removes her wrap-around sunglasses, she looks like this:
Test Question #2
Test Question #2

She is prescribed Lithium, Zyprexa and Paxil. After admitting her to the psychiatric ward for stabilization, which medication option is the best move to stabilizing her mania?

a. Stop the lithium and prescribe Depakote.
b. Increase the Zyprexa to 50 mg at bedtime.
c. Taper or discontinue the Paxil.
Test Question #3

You are working in the county jail. One of the prisoners tested positive for TB exposure several weeks ago. Prophylactic treatment has been initiated. A correction officer informs you that this patient is hostile, cursing, hasn’t slept but two hours per night, and is exposing himself to female officers. What agent may be the culprit in causing his behavior?

a. Pruno
b. Methamphetamines
c. isoniazid
d. All of the above
References

10. Cosmopolitan for Latinas, WADE ROUSE, 05/01/2014
References

References


21. Comorbidities and Mortality in Bipolar Disorder: A Swedish National Cohort Study. Casey Crump, MD, PhD; Kristina Sundquist, MD, PhD; Marilyn A. Winkleby, PhD; Jan Sundquist, MD, PhD, JAMA Psychiatry. 2013;70(9):931-939.


24. Suicide Risk in Bipolar Disorder During Treatment With Lithium and Divalproex, Frederick K. Goodwin, MD; Bruce Fireman, MA; Gregory E. Simon, MD; Enid M. Hunkeler, MA; Janelle Lee, MHA, DrPH; Dennis Revicki, PhD, JAMA. 2003;290(11):1467-1473.


References


30. California Department of State Hospitals, Psychopharmacology Network, Michael Cummings, MD

31. Suicide Risk and Treatments for Patients With Bipolar Disorder, Ross J. Baldessarini, MD; Leonardo Tondo, MD, JAMA. 2003;290:1517-1519.


35. Primary Psychiatry, October 1, 2009, Optimal Dosing of Lithium, Valproic Acid, and Lamotrigine in the Treatment of Mood Disorders, Anna Lembke, MD

37. CNS Drugs. 2007;21(9):727-40. Bipolar II disorder: epidemiology, diagnosis and management. Benazzi F.


39. Arch Gen Psychiatry. 2007;64(4):442-455. Second-Generation Antipsychotic Agents in the Treatment of Acute Mania: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Harald Scherk, MD; Frank Gerald Pajonk, MD, PhD; Stefan Leucht, MD, PhD


