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## CME PSYCHCAST™

### **PRACTICAL MANAGEMENT STRATEGIES FOR ACUTE MANIA AND MIXED EPISODES OF BIPOLAR DISORDER: *PREVENTION OF MANIA AND MAINTENANCE TREATMENT IN BIPOLAR DISORDER***

#### **FACULTY**

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A related Expert Panel Supplement was published in  
***CNS Spectrums*** [*CNS Spectr* 14:12(12 Suppl 15):12-15.] and  
***Primary Psychiatry*** [*Primary Psychiatry* 16:12(12 Suppl 8):12-15].

CME .25

#### **ABSTRACT**

Bipolar disorder is a lifelong condition, which is diagnosed according to corroborative features such as family history, chronobiological sensitivities, treatment outcomes, longitudinal course, and patterns of recurrence. Each illness state is also classified as involving pure mania, hypomania, a mixed episode, a depressed phase, or euthymia. Mixed states are thought to comprise an important subgroup of syndromically ill individuals with bipolar disorder. Several dimensions of psychopathology, including thought-language problems, behavioral disturbances, mood symptoms, and chronobiological changes demand careful evaluation when considering the presentation of a patient with bipolar disorder. Once a comprehensive diagnostic assessment for acute or mixed mania has been completed, it is important to look at an evidence-based data set to guide treatment selection for mood stabilization. Pharmacotherapy is essential to its long-term management of bipolar disorder. Combination therapy, including at least one mood stabilizer, may be necessary to treat acute depression and mania and to further prevent both depressive and manic recurrences. The goal is to minimize frequency, duration, and severity of depressive and manic symptoms with a treatment regimen that is positioned to maximize treatment adherence and minimize side effects. Prevention of mania and maintenance treatment in bipolar disorder is largely routed in the decision to use monotherapy or combination therapy in the treatment regimen. Treatment must also include consideration of comorbidities such as anxiety, substance abuse, cardiovascular disease, and metabolic syndrome, which are pervasive in the bipolar disorder population.

In this Expert Review PsychCast™, Charles L. Bowden, MD, reviews prevention of mania and maintenance treatment in bipolar disorder, specifically addressing the ability to weigh efficacy against adverse effects.



This activity is jointly sponsored by the Mount Sinai School of Medicine and MBL Communications, Inc.



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**Termination date:** April 30, 2012

**Estimated time to complete this activity is:** 15 minutes.

## Acknowledgment of Commercial Support

Funding for this activity has been provided by an educational grant from Bristol-Myers Squibb.

## Activity Review Information

The activity content has been peer-reviewed and approved by

**M. Mehmet Haznedar, MD.**

Review Date: November 30, 2009

## Faculty Affiliation

**Charles L. Bowden, MD**, is clinical professor of psychiatry and pharmacology at the University of Texas Health Science Center in San Antonio.

## Faculty Disclosure Policy Statement

It is the policy of the Mount Sinai School of Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. Presenters must also make a meaningful disclosure to the audience of their discussions of unlabeled or unapproved drugs or devices. This information will be available as part of the course material.

## Faculty Affiliations and Disclosures

Dr. Bowden is a consultant to Bristol-Myers Squibb, Pfizer, sanofi-aventis, and Schering; and receives grant support from Repligen. Dr. Bowden's article mentions off-label usage of valproate for maintenance treatment of bipolar disorder.

CME Course Director James C.-Y. Chou, MD, is associate professor of psychiatry at Mount Sinai School of Medicine in New York City. Dr. Chou has received honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, and Pfizer.

Dr. Haznedar is assistant professor of psychiatry, at Mount Sinai School of Medicine. Dr. Haznedar reports no financial, academic, or other interest in any organization that may pose a conflict of interest.

## Learning Objectives

At the completion of this activity, participants should be better able to:

- Design therapeutic interventions to manage symptoms of acute mania and mixed episodes using appropriate dosing, switching, and combination strategies

## Statement of Need and Purpose

Bipolar disorder, a chronic episodic disease that is present in ~5.7 million Americans, is a complicated condition. No single medication or therapy is effective in treating bipolar disorder, and recent evidence suggests that subtypes of the disorder have been underrepresented due to the bipolar spectrum of expression. While the prototypic clinical picture concerns the "classic" bipolar disorder, mixed episodes with incomplete recovery and significant psychosocial impairment are more frequent and comprise up to 40% of acute bipolar hospital admissions. The clinical presentation of these mixed episodes is variable and eludes contemporary classification systems. Patients with mixed episodes tend to have a more severe course of illness compared to those with classic euphoric manias. They have less frequent remissions, higher rates of recurrence, more frequent substance abuse, poorer response to some medications, more extensive comorbidities, and increased potential for suicidality. Despite the available medications, treating mixed states remains a challenge and tends to require more complex treatment. Rational dosing is a problem as many trials do not address dosing questions. In addition, when and how to combine medications has not been studied nor is the issue of which medications should be discontinued during maintenance stages. Treatment ultimately depends on the patient's individual need and his or her psychiatric and medical comorbidities. The presence of a comorbid substance use disorder is associated with significantly lower rates of treatment adherence, higher anxiety disorder comorbidity, more suicide attempts, and poorer outcome, especially in terms of functioning and quality of life. Psychoeducation in combination with efficacious drug therapy may improve outcomes of patients with acute and mixed episodes of bipolar disorder.

## Target Audience

This activity is designed to meet the educational needs of primary care physicians and psychiatrists.

## Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Mount Sinai School of Medicine and MBL Communications, Inc. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.



## Credit Designation

The Mount Sinai School of Medicine designates this educational activity for a maximum of .25 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

## To Receive Credit for this Activity

Listen to this Expert Panel PsychCast™, reflect on the information presented, and complete the CME posttest and evaluation on pages 5 and 6. To obtain credit, you should score 70% or better. Early submission of this posttest is encouraged. Please submit this posttest by April 1, 2012 to be eligible for credit.

Selected content from this supplement will be available via ePocrates MobileCME in 2010.



# PREVENTION OF MANIA AND MAINTENANCE TREATMENT IN BIPOLAR DISORDER

By Charles L. Bowden, MD

## SLIDE LIBRARY

### SLIDE 1

*Guidelines for Combination Treatment of Mania*

Start with one medication in most cases

If manic symptomatology persists or develops with a partially successful drug, add a second antimanic drug

Good evidence for adding an antipsychotic to lithium or valproate or valproate to an antipsychotic in mania

Carbamazepine least suitable due to drug interactions

Lamotrigine and valproate better tolerated than lithium

### SLIDE 3

*Dosing: Too Much and Too Little*

#### Too Much

High dose that causes side effects or impairs function drives patient from treatment.

- A little hyperthymia is often a good thing

Attempting to rely on one drug to fix everything

Irrational polypharmacy

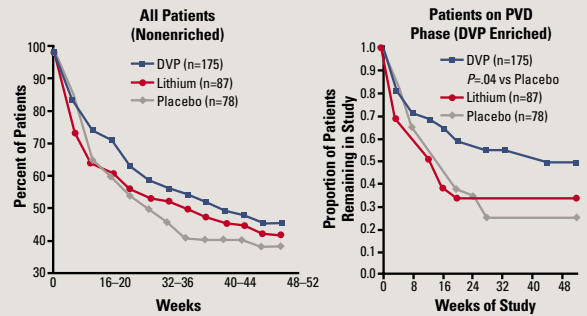
#### Too Little

No mood stabilizer

Unrealistic fear of side effects based on inadequate knowledge of drug's effects

### SLIDE 2

*Divalproex Versus Lithium Versus Placebo Prophylaxis: Mania or Depression Prevention*<sup>2,3</sup>



Evaluable patients (N=340).  
DVP=divalproex.

### SLIDE 4

*Adverse Cognitive Effects of Antipsychotics in Bipolar Patients*<sup>4,5</sup>

44 remitted bipolar patients<sup>4</sup>

Poor set-shifting, processing speed predicted by any antipsychotic use

COWA Total Words Correct

Effect Size  
-0.84  
P=.003

Sentence Completion

Effect Size  
-0.92  
P=.009

Stroop Color-Word

Effect Size  
-1.02  
P=.044

40 euthymic bipolar I patients from UCLA<sup>5</sup>

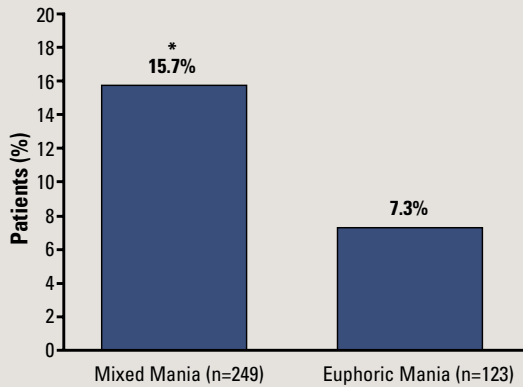
Significantly poorer executive function on WCST categories in subgroup taking antipsychotics

COWA=Controlled Oral Word Association; WCST=Wisconsin Card Sorting Test; UCLA=University of California at Los Angeles.

Dr. Bowden is clinical professor of psychiatry and pharmacology at the University of Texas Health Science Center in San Antonio. Disclosures: Dr. Bowden is a consultant to Bristol-Myers Squibb, Pfizer, sanofi-aventis, and Schering; and receives grant support from Repligen. This article mentions off-label usage of valproate for maintenance treatment of bipolar disorder.

**SLIDE 5**

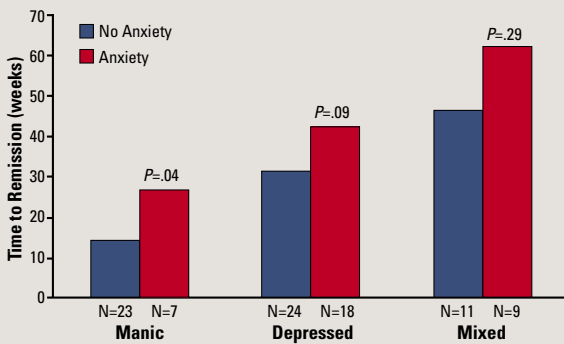
*Discontinuation Due to Side Effects in Mixed Versus Euphoric Mania in Maintenance Treatment: Results Similar for Lithium and Divalproex<sup>5</sup>*



\* $P < .05$ .

**SLIDE 6**

*Unresolved Anxiety Is a Correlate of Poor Recovery From Bipolar Disorder<sup>6</sup>*



**SLIDE 7**

*Behavioral Domains Provided By the Bipolar Inventory of Signs and Symptoms Scale (BISS)<sup>8</sup>*

Depression

Mania

Anxiety

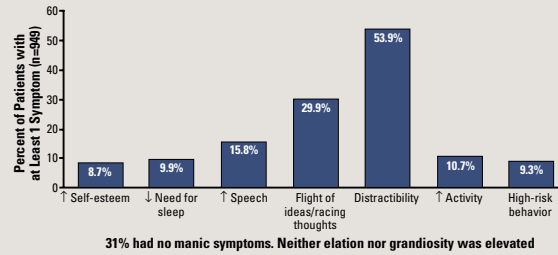
Irritability

Psychosis

Based on factor analysis of 246 BD patients: 28% mixed, 27% depressed, 17% hypo/manic, 7% subsyndromal, 21% recovered.

**SLIDE 8**

*Symptoms of Mania During an Index Bipolar Depressive Episode in the NIMH STEP-BD<sup>9</sup>*



31% had no manic symptoms. Neither elation nor grandiosity was elevated

NIMH STEP-BD=National Institute of Mental Health Systematic Treatment Enhancement Program for Bipolar Disorder.

**SLIDE 9**

*The LEGO Brain*

Domains fit together to form units which, if stable, resist dislodging and thus a resilience against destabilizing elements

This process occurs ontologically from genes to proteins to subcellular systems to cells to functional brain units

A similar approach with patients views units for sleep efficiency, affective instability, depression, irritability, anxiety, structured thinking, close relationships, and work/role as potentially stable elements

Patients can then gain confidence that a stable domain will remain so, that disturbances in a domain will be addressed in the therapeutic relationship, and that all will not fall apart

**SLIDE 10**

*Conclusion*

There are numerous options for treating mania

Options for treating bipolar depression are limited

Antipsychotics have a role in preventing relapses of mania and, in some cases, depression

Mixed presentations of bipolar disorder are particularly challenging

**References**

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## ***CME QUESTIONS***

- 1. Which steps may reduce subsyndromal manic symptomatology?**
  - A. Consider adjunct to first mood stabilizer
  - B. Review medications for possible destabilizing effects
  - C. Address sleep effectiveness
  - D. All of the above
- 2. Which of the following symptoms is least likely to be present in acute mania?**
  - A. Affective instability
  - B. Anxiety
  - C. Irritability
  - D. Sadness
- 3. Atypical antipsychotics are as effective as conventional antipsychotic and are better tolerated.**
  - A. True
  - B. False
- 4. Which is not a symptom of mania during a bipolar depressive episode?**
  - A. Distractability
  - B. Racing thoughts
  - C. Grandiosity
  - D. A decreased need for sleep

# REGISTRATION

APRIL 2010 CME POSTTEST



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## ANSWER FORM

CME PSYCHCAST™ – Practical Management Strategies for Acute and Mixed Episodes of Bipolar Disorder—*Prevention of Mania and Maintenance Treatment in Bipolar Disorder*

**TERMINATION DATE:** April 30, 2012

To receive credit, you should score 70% or better (participants will receive certification for their records in approximately 4–6 weeks). Early submission of this posttest is encouraged. Please submit this test by April 1, 2012, to be eligible for credit. If you have any questions about this, or any of our other CME materials, please e-mail CME@mblcommunications.com

*Please circle your answers*

1. A B C D    2. A B C D    3. A B    4. A B C D

## EVALUATION SECTION (please provide the information below and print clearly)

1=Minimally, 5=Completely

1. Please rate how well this CME activity met the stated learning objectives: 1 2 3 4 5

2. Please indicate how well this CME activity met your expectations regarding the following:

- A. Translating clinical information/trial data to patients I see in my practice 1 2 3 4 5
- B. Providing new information 1 2 3 4 5
- C. Increased my knowledge and/or skills in delivering patient care 1 2 3 4 5
- D. Communicated information in an effective, accessible manner 1 2 3 4 5

3. Compared to other CME activities in which I have participated this year, I would rate this activity as: 1=Needs Improvement, 5=Outstanding  
1 2 3 4 5

4. As a result of participating in this educational activity, I will (please check one)

- Change my practice     Seek additional information     Confirm my current practice

4a. If "change my practice," please describe: \_\_\_\_\_

5. Did this CME activity provide a balanced, scientifically rigorous presentation of therapeutic options related to the topic without commercial bias and influence? Yes  No

5a. If "no," please explain: \_\_\_\_\_

6. Do you feel these topics should be repeated/updated in future CME activities? Yes  No

6a. If "yes," what suggestions would you make to improve this activity? \_\_\_\_\_

7. Please indicate your three preferred formats for CME activities:

- Print media     Internet     Multimedia/video     Live meeting     PDA     Podcast

8. Please indicate three professional education gaps you would like to be addressed in future CME activities:

Topic 1: \_\_\_\_\_

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