Treatment Strategies for Bipolar Disorder: CALM SEA

To the Editor: A prior shorter mnemonic (CALM, published previously in the *Companion*[1]) helped clinicians organize the pharmacologic treatment options for bipolar disorder. The current mnemonic CALM SEA incorporates a review of biorhythm and endocrine issues, as well as an image of the goal.

C = Control Cycling, starting with manic and mixed symptoms, especially insomnia, irritability, agitation, impulsivity, and anxiety, as these disrupt work situations and social supports (burn bridges), and even subsyndromal mixed mania has been associated with increased risk for suicidal behavior.[2,3] Uncontrolled cycling renders patients' lives chaotic, unpredictable, and unmanageable.

A = Antidepressants. Use conventional antidepressants (preferential unipolar antidepressants[4]) sparingly and selectively beyond 10 weeks. Adjunctive antidepressants have demonstrated benefit beyond 10 weeks of treatment in only 15% to 20% of bipolar patients, and only in the Stanley Foundation Bipolar Network studies.[4–8] Two important recent Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) studies[9,10] showed no separation of adjunctive antidepressants from adjunctive placebo. Further, another STEP-BD study with 1,742 patients followed for up to 1 year showed that "patients who received antidepressants were 3.8 times as likely to experience rapid cycling," ie, 4 or more mood episodes ($P = .001$), and "2.0 times as likely to have 2 or 3 episodes ($P = .0001$) . . . compared to patients who did not receive antidepressants."[11(p374)] For longer term use, consider preferential bipolar antidepressants,[4] eg, lamotrigine, quetiapine, lithium, or olanzapine,[4,12] with appropriate monitoring.

L = Longitudinal/long-term view. A longitudinal/long-term view of mood episodes over months to years is pivotal to making the diagnosis of bipolar disorder in the first place, to understanding the patient's intrinsic or baseline pattern of mood cycling, and to accurately gauging the patient's response to treatment.

M = Mood stabilizers, especially lithium, divalproex, and carbamazepine, remain the core building blocks of effective bipolar disorder regimens.[13] Lamotrigine provides an extremely helpful floor against recurrent depression but lacks robust antimanic coverage.[4,14]

S = Sleep. Consistent, regular-onset, full-duration, uninterrupted, restorative sleep is an essential component of any recovery from bipolar disorder and can generally be reestablished using primarily the sedative and antimanic properties of lithium, divalproex, or carbamazepine, with or without atypical antipsychotics. Antidepressants may aggravate insomnia,[15] and gradual antidepressant taper over months often relieves it.[16,17]

E = Endocrine/metabolic hot spots can be remembered as TSH:

- **T**-Thyroid augmentation may relieve cycling or depression[18,19] with even mild hypothyroidism, or even euthyroid state. Monitor TSH periodically, especially in lithium-treated patients.
- **S**-Steroid treatments may trigger mood episodes, usually mania or mixed states.
- **H**-Hormonal shifts (especially in women), such as puberty/menarche, postpartum, and perimenopause/menopause, may initiate mood episodes.

A = Activity. Regular activity, exercise, and social activity, including "'social zeitgebers,' ie, persons, social demands, or tasks that set the biological clock,"[20(p948)] comprise the important complement of regular sleep in maintaining a regular sleep-wake cycle and "lifestyle regularity,"[21] indispensable components of recovery.[20–22] Therefore, it may be advantageous to explain this to patients and their family or support system so that they can structure activity and social interaction as part of their recovery.

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