On the Internet at www.leeheymd.com

MEDICAL MEMO

Kevin Leehey, M.D. Child, Adolescent, and Adult Psychiatry; Board Certified

What is a Mood Stabilizer ?

Mood Stabilizers are treatments that prevent or lessen the ups (mania and hypomania) and downs (depression) of Bipolar Disorder (BD). Primarily these are medications, but psychotherapy, avoiding mood altering substances, and regulating sleep, eating, and exercise all are important. By "affect " clinicians refer to our feelings, emotions at the moment such as happy, sad, mad whereas by "**mood**" clinicians mean our emotional experience or state over a longer prolonged period of time – days, weeks, or months. For affect think the weather at the moment and for mood think the climate or season. Thus Mood Disorders mean prolonged clinical states like Depression (Major Depression must meet criteria for at least 2 weeks), the Hypomania of Bipolar II (at least 5 days) and the Mania of Bipolar I (at least a week); not briefer sad, mad, happy feelings. Mood Stabilizers are used when these longer mood disorders cause significant disruption and impairment in a person's life.

A good way to understand and rate the range of Moods is to use a rating scale ranging from a lowest low of -10 to a highest high of +10 where -10 is the worst most severe extreme Major Depression you have ever felt or could ever imagine, -2 to +2 is the "normal" range clinicians call euthymic, and +10 is the most severe extreme Mania possible. Feeling happy about a good event like a raise at work, your team winning, your loved one doing well, she or he said "yes", etc may be a +2. Sad about a death in the family, getting laid off, your team lost a big game, the semester grades went badly, etc may be a -2. Mild Depression is -3 to -4, moderate is -5 to -6, disabling severe Major Depression is -7 and worse which may include psychosis (hallucinations, delusions, and severely disordered thinking). Hypomania is more up than is normal (mild mania) and fits +3 to +4, while moderate Mania is +5 to +7 and severe, even psychotic Mania is up to +10 where as one person commented "not only can you talk to God, but you are God". Mood Stabilizers seek to keep or help us stay in the -2 to +2 of everyday life and certainly try to help us not spin out past +5 or crash below -5.

See both my **Bipolar Disorder** and **Depression Medical Memos** or DSM-5 for a detailed explanation of Mania and types of Depression. Also please see both my **Mood Stabilizers** and **Atypical Antipsychotics Medication Charts** which detail the medications discussed below. Additional information about the atypical antipsychotic medicines' usage, benefits and possible side effects, both short and long term, is detailed in my **Medical Memo "Antipsychotic Medicines"**.

All of the mood stabilizer medications are what I refer to as "big guns" meaning they are typically used primarily to treat severe mental illness and are strong medicines that may have significant side effects requiring closer follow-up than other meds, sometimes including blood and other tests. These medicines are used for all age groups and are given daily. We think of mood stabilizers as falling into 2 main groups 1) lithium and the AEDs (Anti-Epileptic Drugs = seizure meds) and 2) the atypical antipsychotics.

The classic and original medicine mood stabilizer is the naturally occurring element **lithium** that has been used and studied extensively for Bipolar Disorder, Schizo-affective disorder, and as a booster to treat depression for more than 50 years. Lithium stabilizes, treats, and maintains benefits for both the depression and manic phases of BD. Lithium has the best research evidence for maintenance and preventing recurrences. It works very well for many, but not all, has the most research backing (rivaled only by divalproex) and for all ages. It lowers suicide risk and works best for those with BD consisting of more separate episodes of depression and mania including periods of euthymia ("normal" mood) in between. The benefits must be balanced with possible disadvantages. Lithium can cause many mostly nuisance side effects, requires blood tests, is dangerous in overdose, and has a low therapeutic index (meaning there is a relatively small distance between the top beneficial blood level and toxicity). Side effects are often none or minor, tend to be dose related, and may change with time. Relatively common usually mild side

effects include gastrointestinal (GI) upset, loose bowels, and tremor. Less common are low thyroid, acne, sun sensitive rash, weight gain, and polyuria/polydipsia (an urge to drink excess fluids associated with a need to urinate frequently). Less common potentially serious side effects can include affecting heart rhythm, kidney function, and if the dose is too high or in overdose, ataxia (unsteady walking) and confusion. Lithium can be used in pregnancy but with caution due to increased risk of a rare heart defect, Ebstein's anomaly. Lithium can be used at any age with extra caution if health problems exist (especially kidney and heart arrhythmias) and in geriatric and child age groups. Blood tests are done periodically to monitor especially blood level and thyroid.

AEDs, (Anti-Epileptic Drugs) all began, and continue, as seizure medicines for epilepsy. Their effects, which include stabilizing the cell membranes of neurons in the brain, have proven to often help stabilize moods as well. **Divalproex (valproic acid, valproate, Depakote)** rivals lithium as a mood stabilizer for both the depressed and manic phases of BD. It may help more than lithium for mixed depression and manic states, anxiety, and more rapid cyclers (those who have shorter more frequent episodes). Divalproex works differently and has a different set of side effects than lithium and thus may work for those who do not respond adequately to lithium, and vice versa. Thus combining lithium and divalproex may work better than either alone. Side effects are often none or minor and are dose related and may change with time. Because divalproex, lamotrigine, and carbamazepine were extensively used as seizure meds in children and adolescents by neurologists before being adopted by psychiatrists as mood stabilizes we have a lot of experience using them to help kids. Relatively common usually mild side effects include GI upset, and either increased or decreased energy. Less common but significant are weight gain, tremor, thinner hair for a few, and at higher doses reversible ataxia or slower cognition (thinking). Potentially serious side effects can include low platelets, polycystic ovaries, and liver or pancreas injury. Blood tests are done to monitor especially blood level and liver. Divalproex (and carbamazepine) have about a 1% risk of harm to the fetus (birth defects) while pregnant. This is the highest risk of any psychiatric medicine and can be lessened to some extent by taking folic acid before and throughout pregnancy.

Lamotrigine (Lamictal) is another AED often used especially for the depressed phase of BD. It is less helpful for the manic phase. Thus it is not typically used alone for Bipolar I but can be for Bipolar II, the form with only hypomania, not full mania. Lamotrigine advantages include few to no side effects (the least side effects of all mood satbilizers) at typical doses and generally no weight gain. The roughly one in 10,000 risk of a potentially dangerous delayed hypersensitivity rash is managed by a low and slow tapering up the dose process for all ages and especially in youth under age 16. Side effects may include mild increased or decreased energy and at higher doses, ataxia.

Other AEDs sometimes used in psychiatry but not often as first choice mood stabilizers include carbamazepine (Tegretol), oxcarbazepine (Trileptal), topiramate (Topamax), and gabapentin (Neurontin). Each has their pros and cons and uses.

Both typical and **atypical antipsychotic medicines**, known as "**atypicals**", were developed for the psychosis of schizophrenia, psychotic symptoms of severe Major Depression or Mania, schizoaffective disorder, and both mania and hypomania. Antipsychotics are generally the fastest and most effective treatments for mania. Generally, any of the typicals and atypicals treats mania effectively. Atypicals have a broader range of benefits with at least several of the current 10 US options also helping depression (quetiapine, Latuda, olanzapine, risperidone, Abilify, clozapine) and a few probably acting as mood stabilizers too. First line treatments of the acute phase of BD depression based on research now include quetiapine (Seroquel), olanzapine (Zyprexa) plus fluoxetine (Prozac), lurasidone (Latuda), or lithium plus lamotrigine. 2nd line are divalproex, aripiprazole (Abilify), lamotrigine alone, or olanzapine alone. 3rd line is adding an antidepressant with a mood stabilizer also present.

As we think about mood stabilizer treatments we must consider both the acute and maintenance phases. The **acute phase** is the days and weeks, even months of active symptoms of depression, mania, or mixed symptoms and can be from mild to disabling and even life threatening. Once the person is back to baseline (-2 to +2) and no longer actively ill, this is the **maintenance phase**. Our goal then is to maintain mental health and prevent or at least minimize the recurrent episodes that are a hallmark of BD I and II. Medications are generally crucial, often essential, during acute mental illness. Although without medication, as with pneumonia, diabetes, and heart attacks, the condition will run its course and will often recover, the agony, life disruption, and costs for the patient and family can be huge and too often life threatening in the meantime. It is difficult at best to do therapy, supplements, and non medicine treatments during severe acute phases. People who are hypomanic or manic or who long to return to what they

liked about hypomania (+3 to +4) and mild to moderate mania (+4 to +6) often deny problems, avoid any type of therapy that may limit their ebullient grandiose creative energy, and too often stop their medicines while not recognizing or ignoring the costs of spinning out into disruptive or severe mania or wearing themselves out and crashing into often deep depressions. This cycle can occur over and over again. This is why continuing treatment in the maintenance phase is so crucial. Lithium has the most evidence for benefit in the maintenance phase lessening recurrence of both mania and depression; followed by divalproex. Research so far on lamotrigine shows some maintenance benefit regarding depression, maybe hypomania, but not mania. Unfortunately, we currently have little research evidence regarding the effectiveness of atypicals for the prevention of new episodes during the maintenance phase. Thus we proceed with clinical impressions and experience while scientific data develops.

So let's talk **non medicine treatment and prevention**. Psychoeducation is #1. You are pursuing that right now by reading this. The patient and his/her loved ones and formal and informal treatment team do better by learning about the condition – what it is and isn't, how to recognize early warning signs, what to do and not do, treatment, and how to minimize recurrences. Avoidance of mood altering drugs like alcohol, marijuana, and other drugs is vital. Next important, in my opinion is a focus on sleep – getting about 8 hours nightly, 6 or less can be an early sign of mania while 10 or more can be a warning sign of depression. In fact, skipping a night's sleep can push a person with BD into mania ! From our sleep schedule follows our eating schedule, exercise habits, and overall self care including avoidance of alcohol and other drugs. Most of us struggle to accept that we cannot get away with what our peers seem to do with impunity. Social Rhythm therapy emphasizes the centrality of lifestyle, how we interact with others, and self care. Cognitive Behavioral Therapy (CBT) and other psychotherapies also address relapse prevention, healthy outlets for emotion, and more. Therapies can include family, other loved ones, and other persons important to the patient's well being. Non medicine biologic treatments may include "natural" supplements. There is some evidence in favor of fish oil (omega 3 fatty acids) especially for women with depression and in the maintenance phase. NAC (N-Acetyl-Cysteine) may help some for depression and maintenance especially those with history of substance problems and trichotillomania (hair pulling). Optimizing thyroid may make depression easier to treat, especially for women. "Not pills" adjunct options for depression include exercise, CBT, light therapy, rTMS, and when most severe ECT.

Please remember, this article and my medication charts give general information about the pros and cons, side effects, risks, and benefits of options, are not exhaustive or complete, and do not replace detailed informed consent discussions and follow up with your doctor(s).

Kevin Leehey, M.D.
Child, Adolescent and Adult Psychiatry

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www.leeheymd.com

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