

# Corticosteroid psychosis: Stop therapy or add psychotropics?

## Off-label antipsychotics, mood stabilizers, and anticonvulsants could help

**M**rs. E, age 31, develops rapid, pressured speech and insomnia for 4 consecutive nights, but reports a normal energy level after receiving high-dose methylprednisolone for an acute flare of systemic lupus erythematosus (SLE).

Her medical history indicates an overlap syndrome between SLE and systemic sclerosis for the last 5 years, migraine headaches, and 4 spontaneous miscarriages, but she has no psychiatric history. Her family history is negative for psychiatric illness and positive for diabetes mellitus, hypertension, and coronary artery disease.

Mrs. E lives with her husband and 10-year-old son. She admits to multiple stressors, including her health problems and financial difficulties, which recently led to the family's decision to move to her mother-in-law's house. Mrs. E denies using illicit drugs, cigarettes, or alcohol.

Mrs. E is admitted to the hospital, and her corticosteroid dosage is reduced with a switch to prednisone, 60 mg/d. She is started on risperidone, 1 mg at bedtime, which is titrated without adverse effect. Her psychotic symptoms improve over 4 days, and she is discharged on prednisone, 60 mg/d, and risperidone, 0.5 mg in the morning and 2 mg at night.

After completing her corticosteroid course, Mrs. E experiences complete resolution of psychiatric symptoms and is tapered off risperidone after 6 months.

Corticosteroid use can cause a variety of psychiatric syndromes, including mania, psychosis, depression, and delirium. A meta-analysis reports severe psychotic reactions in 5.7% of patients taking corticosteroids and mild-to-moderate reactions in 28% of patients.<sup>1</sup> Hypo-



### **Andrew J. Muzyk, PharmD**

Clinical pharmacist

### **Shannon Holt, PharmD**

Clinical pharmacist

### **Jane P. Gagliardi, MD**

Assistant professor of psychiatry and behavioral sciences  
Assistant professor of medicine

....

Duke University School of Medicine  
Durham, NC



## Corticosteroid psychosis

### Clinical Point

High corticosteroid dose is the primary risk factor for psychosis but does not predict onset, severity, type of reaction, or duration

Table 1

## Grading scale for corticosteroid-induced psychiatric symptoms

| Grade   | Symptoms   |
|---------|--|
| Grade 1 | Mild, nonpathologic, and subclinical euphoria            |
| Grade 2 | Reversible acute or subacute mania and/or depression     |
| Grade 3 | Bipolar disorder with relapses possible without steroids |

Source: Reference 4

mania, mania, and psychosis are the most common psychiatric reactions to acute corticosteroid therapy.<sup>2</sup> This article reviews case reports and open-label trials of antipsychotics, mood stabilizers, and anticonvulsants to treat corticosteroid-induced mania and psychosis and outlines treatment options.

### Symptoms

Corticosteroid-induced psychosis represents a spectrum of psychological changes that can occur at any time during treatment. Mild-to-moderate symptoms include agitation, anxiety, insomnia, irritability, and restlessness, whereas severe symptoms include mania, depression, and psychosis.<sup>3</sup> Case reports reveal:

- mania and hypomania in 35% of patients with corticosteroid-induced psychosis
- acute psychotic disorder in 24% of patients, with hallucinations reported in one-half of these cases
- depression, which is more common with chronic corticosteroid therapy, in 28% of patients.<sup>4</sup>

Delirium and cognitive deficits also have been reported, although these symptoms generally subside with corticosteroid reduction or withdrawal.<sup>4,5</sup>

Psychiatric symptoms often develop after 4 days of corticosteroid therapy, although they can occur late in therapy or after treatment ends.<sup>6</sup> Delirium often resolves within a few days, psychosis within 7 days, and mania within 2 to 3 weeks, whereas

depression can last for more than 3 weeks.<sup>4</sup> A 3-level grading system can gauge severity of corticosteroid-induced psychosis; grade 2 or 3 warrants treatment (Table 1).<sup>4</sup>

### Risk factors

High corticosteroid dose is the primary risk factor for psychosis. The Boston Collaborative Drug Surveillance Program reported that among individuals taking prednisone, psychiatric disturbances are seen in:

- 1.3% of patients taking <40 mg/d
- 4.6% of patients taking 40 to 80 mg/d
- 18.4% of patients taking >80 mg/d.<sup>7</sup>

However, the corticosteroid dosage does not predict onset, severity, type of reaction, or duration.<sup>3,7</sup> Female patients are at higher risk of corticosteroid-induced psychosis, even after one controls for medical conditions diagnosed more often in women, such as SLE and rheumatoid arthritis.<sup>3</sup> Previous episodes of corticosteroid-induced psychosis, history of psychiatric illness, and age are not associated with corticosteroid-induced psychosis.<sup>3</sup>

### Treatment

Management includes tapering corticosteroids, with or without adding medications to treat the acute state. Decreasing corticosteroids to the lowest dose possible—<40 mg/d—or gradually discontinuing therapy to prevent triggering adrenal insufficiency may improve psychotic symptoms and avoids the risk of adverse effects from adjunctive medications.

Psychopharmacologic treatment may be necessary, depending on the severity of psychosis or the underlying disease, particularly if corticosteroids cannot be tapered or discontinued. Evidence from open-label trials (Table 2)<sup>8-12</sup> and case reports indicates that psychotic symptoms could be prevented and treated with off-label antipsychotics, mood stabilizers, and anticonvulsants.

Consider your patient's underlying medical condition when selecting psychotropics. For example, try to avoid prescribing:

- antipsychotics to patients with cardiac conduction abnormalities

ONLINE ONLY

Discuss this article at <http://CurrentPsychiatry.blogspot.com>

Table 2

## Corticosteroid-induced psychosis: Adjunctive treatment studies

| Medication and source                                      | Patient population  | Results   |
|--|---|---|
| <b>Olanzapine</b><br>(Brown et al, 2005 <sup>8</sup> )     | 12 outpatients experiencing manic or mixed symptoms received olanzapine, mean 8.5 mg/d                            | Reductions on YMRS, HRSD, and BPRS with no change in extrapyramidal symptom side-effect scales, weight, or glucose measurements |
| <b>Lithium</b><br>(Falk et al, 1979 <sup>9</sup> )         | 27 patients diagnosed with multiple sclerosis or retrobulbar neuritis treated with corticotropin received lithium | 38% of lithium patients developed psychiatric symptoms compared with 62% of controls  |
| <b>Phenytoin</b><br>(Brown et al, 2005 <sup>10</sup> )     | 39 patients received phenytoin, 300 mg/d, or placebo at prednisone therapy initiation                             | Patients receiving phenytoin reported a smaller increase in ACT score compared with controls                                    |
| <b>Levetiracetam</b><br>(Brown et al, 2007 <sup>11</sup> ) | 30 outpatients receiving corticosteroids randomized to levetiracetam, 1500 mg/d, or placebo                       | No significant change in HRSD, YMRS, or ACT scores  |
| <b>Lamotrigine</b><br>(Brown et al, 2003 <sup>12</sup> )   | 5 patients on chronic corticosteroid treatment received open-label lamotrigine, mean dose 340 mg/d                | No significant difference in HRSD, YMRS, or the depression subscale of the Internal State Scale                                 |

ACT: Internal State Scale Activation subscale; BPRS: Brief Psychiatric Rating Scale; HRSD: Hamilton Rating Scale for Depression; YMRS: Young Mania Rating Scale

- lithium to patients who need diuretic or angiotensin-converting enzyme inhibitor therapy or those with underlying renal insufficiency.

When appropriate, collaborate with the provider who prescribed the corticosteroids because tapering or discontinuation might not be possible.

### Antipsychotics

**Open-label trial.** Olanzapine reduced psychiatric symptoms in a 5-week, open-label trial of 12 outpatients experiencing manic or mixed symptoms secondary to corticosteroids.<sup>8</sup> At baseline, patients had a mean score of 15.25 on the Young Mania Rating Scale (YMRS) on a mean prednisone dose of 14.4 mg/d. After receiving olanzapine, 2.5 mg/d titrated to a maximum 20 mg/d (mean 8.5 mg/d), subjects demonstrated a significant decrease on the YMRS ( $P = .002$ ), Hamilton Rating Scale for Depression (HRSD) ( $P = .005$ ), and Brief Psychiatric Rating Scale (BPRS) ( $P = .006$ ) with no change in extrapyramidal side-effect scales, weight, or glucose measurements.

**Case reports.** Among antipsychotics, olanzapine has the greatest number of case reports for treating corticosteroid-induced psychosis, mainly for mania.<sup>13-15</sup> Benefit with olanzapine was demonstrated at dosages from 2.5 to 15 mg/d and improvement occurred within days to weeks. Several patients remained symptom-free with olanzapine and continued corticosteroid therapy.

Other reports describe benefit with risperidone for a variety of psychiatric symptoms—including hypomania, hallucinations, and delusions—associated with corticosteroid therapy.<sup>16-19</sup> Risperidone dosing ranged from 1 to 4 mg/d, and symptoms improved within days to weeks.

One case report describes quetiapine for the treatment of corticosteroid-induced mania.<sup>20</sup> The patient's symptoms improved within 10 hours of initiating quetiapine, 25 mg/d, and YMRS score decreased from 31 before therapy to 5 at discharge. No case reports exist for ziprasidone or aripiprazole.

### Mood stabilizers

**Cohort study.** One study suggests that lithium may be effective for preventing

### Clinical Point

Benefit with olanzapine was seen at dosages from 2.5 to 15 mg/d, and improvement occurred within days to weeks

continued on page 67



voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: *Skin and subcutaneous tissue disorders* – Angioedema. **DRUG INTERACTIONS: Central Nervous System (CNS)-Active Agents**– The risk of using Pristiq in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when Pristiq is taken in combination with other CNS-active drugs [see *Warnings and Precautions* (5.13)]. **Monoamine Oxidase Inhibitors (MAOIs)**– Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Pristiq (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of a MAOI [see *Contraindications* (4.2)]. **Serotonergic Drugs**– Based on the mechanism of action of Pristiq and the potential for serotonin syndrome, caution is advised when Pristiq is administered with other drugs that may affect the serotonergic neurotransmitter systems [see *Warnings and Precautions* (5.2)]. **Drugs that Interfere with Hemostasis (eg, NSAIDs, Aspirin, and Warfarin)**– Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are administered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol**– A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine**– Inhibitors of CYP3A4 (ketocazole)– CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. **Inhibitors of other CYP enzymes**– Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs**– **Drugs metabolized by CYP2D6 (desipramine)**– *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. **Drugs metabolized by CYP3A4 (midazolam)**– *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. **Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9, and 2C19**– *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter**– *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy**– There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy**– Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. **Teratogenic effects—Pregnancy Category C**– There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. **Non-teratogenic effects**– Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [see *Warnings and Precautions* (5.2)]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [see *Dosage and Administration* (2.2)]. **Labor and Delivery**– The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers**– Desvenlafaxine (0-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use**– Safety and effectiveness in the pediatric population have not been established [see *Box Warning and Warnings and Precautions* (5.1)]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use**– Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients; however, in the short-term, placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients >65 years of age compared to patients <65 years of age treated with Pristiq [see *Adverse Reactions* (6)]. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [see *Dosage and Administration* (2.2) and *Clinical Pharmacology* (12.6)]. If Pristiq is poorly tolerated, every other day dosing can be considered. SSRIs and SNRIs, including Pristiq, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [see *Warnings and Precautions* (5.12)]. Greater sensitivity of some older individuals cannot be ruled out. **Renal Impairment**– In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [see *Dosage and Administration* (2.2) and *Clinical Pharmacology* (12.6) in the full prescribing information]. **Hepatic Impairment**– The mean  $t_{1/2}$  changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. The recommended dose in patients with hepatic impairment is 50 mg/day. Dose escalation above 100 mg/day is not recommended [see *Clinical Pharmacology* (12.6)].

**OVERDOSAGE: Human Experience with Overdosage**– There is limited clinical experience with desvenlafaxine succinate overdose in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose > 600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdose include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (eg, prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdose may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdose, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage**– Treatment should consist of those general measures employed in the management of overdose with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference (PDR®).

This brief summary is based on Pristiq Prescribing Information W10529C009, revised September 2009.

continued from page 63

and treating corticosteroid-induced psychosis. A retrospective cohort study examined records of patients diagnosed with multiple sclerosis or retrobulbar neuritis who were treated with corticotropin.<sup>9</sup> Corticotropin has been reported to cause psychotic reactions in up to 11% of patients through a mechanism thought to mirror corticosteroid-induced psychosis (*Box, page 68*).<sup>21-23</sup> Psychiatric symptoms developed in 38% of patients treated with lithium compared with 62% of controls. No patients pretreated with lithium maintained at 0.8 to 1.2 mEq/L reported mood disturbances or psychotic reactions.

**Case reports.** Among mood stabilizers, lithium has the greatest number of case reports on its use for prevention and treatment of corticosteroid-induced psychosis. In these reports, patients pretreated with lithium did not experience a relapse of psychosis related to chronic corticosteroid therapy.<sup>24-27</sup> Case reports also describe benefit with valproic acid and carbamazepine.<sup>28-30</sup>

## Anticonvulsants

**Trials.** In a 1-week trial, 39 patients without previous psychiatric diagnosis or psychotropic use were randomly assigned to phenytoin, 300 mg/d, or placebo as prednisone therapy was initiated.<sup>10</sup> Compared with placebo, the phenytoin group reported a smaller increase on the Internal State Scale Activation subscale (ACT), a self-report measure of mania symptom severity. No significant differences were found on the YMRS or HRSD scales. Based on the ACT scale finding, the authors concluded that phenytoin attenuated manic or hypomanic effects of prednisone.

A study of levetiracetam, 1500 mg/d, showed no significant change in HRSD, YMRS, or ACT scores from baseline to end point for either levetiracetam or placebo.<sup>11</sup>

A 12-week, open-label trial of lamotrigine in 5 patients receiving corticosteroids continuously for 6 months showed no significant difference in mood changes as measured by the HRSD, YMRS, or the depression subscale of the Internal State Scale.<sup>12</sup>

**Case reports** show that lamotrigine and gabapentin have been used effectively to prevent manic symptoms in patients receiving corticosteroid therapy.<sup>31,32</sup>

## Treatment recommendations

Establishing a treatment algorithm for corticosteroid-induced psychosis is hampered by the lack of prospective placebo-controlled trials. However, most case



## Corticosteroid psychosis

### Clinical Point

Consider adding a low-dose atypical antipsychotic to corticosteroid therapy; lithium may be second-line with precautions

### Box

## Pathophysiology of corticosteroid-induced psychosis

How corticosteroids cause psychosis is not well understood. One theory suggests that corticosteroids act at steroid-specific receptors and suppress filtering by the hippocampus of irrelevant stimuli.<sup>21</sup>

Supporting this theory of hippocampal change, a study of 17 patients receiving corticosteroid therapy for >6 months found decreased hippocampal volume compared with a control group.<sup>22</sup> Other possible causes include suppressed hypothalamus-pituitary axis and enhanced dopamine neurotransmission.<sup>23</sup>

reports describe benefit from administering atypical antipsychotics and lithium.

Consider adding a low-dose atypical antipsychotic with which case studies report quick symptom resolution and patients tolerating these agents. Monitor carefully for metabolic changes, a risk associated with antipsychotics and corticosteroids. Lithium would be a good second-line therapy because of its demonstrated benefit for both prophylaxis and treatment of psychiatric disturbances.

Lithium use can be complicated and dangerous in patients who have underlying diseases associated with renal dysfunction, however—such as nephrotic syndromes and SLE—leading some authors to suggest valproic acid or carbamazepine instead.<sup>33</sup> In addition, corticosteroid-induced changes in sodium balance could increase the risk of lithium toxicity.<sup>34</sup>

When patients cannot tolerate atypical antipsychotics or lithium, case reports sup-

## Related Resources

- Cerullo MA. Expect psychiatric side effects from corticosteroid use in the elderly. *Geriatrics*. 2008;63(1):15-18.
- Sirois F. Steroid psychosis: a review. *Gen Hosp Psychiatry*. 2003;25:27-33.
- Patten SB, Neutel CI. Corticosteroid-induced adverse psychiatric effects: incidence, diagnosis, and management. *Drug Safety*. 2000;22(2):111-122.
- Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. *Mayo Clin Proc*. 2006;81(10):1361-1367.

### Drug Brand Names

|                                      |                          |
|--------------------------------------|--------------------------|
| Aripiprazole • Abilify               | Olanzapine • Zyprexa     |
| Carbamazepine • Tegretol             | Phenytoin • Dilantin     |
| Corticotropin • Acthar               | Prednisone • Deltasone   |
| Gabapentin • Neurontin               | Quetiapine • Seroquel    |
| Lamotrigine • Lamictal               | Risperidone • Risperdal  |
| Levetiracetam • Keppra               | Valproic acid • Depakene |
| Lithium • Lithobid, Eskalith, others | Ziprasidone • Geodon     |
| Methylprednisolone • Medrol          |                          |

### Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

port the use of valproic acid, carbamazepine, lamotrigine, or gabapentin to treat symptoms of corticosteroid-induced psychosis.

### References

1. Lewis DA, Smith RE. Steroid-induced psychiatric syndromes: a report of 14 cases and a review of the literature. *J Affect Disord*. 1983;5:319-332.
2. Bolanos SH, Khan DA, Hanczyc M, et al. Assessment of mood states in patients receiving long-term corticosteroid therapy and in controls with patient-rated and clinician-rated scales. *Ann Allergy Asthma Immunol*. 2004;92:500-505.
3. Warrington TP, Bostwick JM. Psychiatric adverse effect of corticosteroids. *Mayo Clin Proc*. 2006;81(10):1361-1367.
4. Sirois F. Steroid psychosis: a review. *Gen Hosp Psychiatry*. 2003;25:27-33.
5. Newcomer JW, Craft S, Hershey T, et al. Glucocorticoid-induced impairments in declarative memory performance in adult humans. *J Neurosci*. 1991;14:2047-2053.
6. Hall RC, Popkin MK, Stickney SK, et al. Presentation of the steroid induced psychosis. *J Nerv Ment Dis*. 1979;167:229-236.
7. The Boston Collaborative Drug Surveillance Program. Acute adverse reactions to prednisone in relation to dosage. *Clin Pharmacol Ther*. 1972;13:694-698.
8. Brown ES, Chamberlain W, Dhanani N, et al. An open-label trial of olanzapine for corticosteroid-induced mood symptoms. *J Affect Disord*. 2004;83:277-281.

## Bottom Line

First-line treatment for corticosteroid-induced psychosis is to taper or discontinue corticosteroid therapy. If this is not possible because of comorbid disease or severe psychosis, consider adding low-dose atypical antipsychotics in patients with manic or hypomanic symptoms. Consider mood stabilizers such as lithium or valproic acid as second-line treatment in patients with normal renal function.

9. Falk WE, Mahnke MW, Poskanzer DC. Lithium prophylaxis of corticotropin-induced psychosis. *JAMA*. 1979;241:1011-1012.
10. Brown ES, Stuard G, Liggin JD, et al. Effect of phenytoin on mood and declarative memory during prescription corticosteroid therapy. *Bio Psychiatry*. 2005;57:543-548.
11. Brown ES, Frol AB, Khan DA, et al. Impact of levetiracetam on mood and cognition during prednisone therapy. *Eur Psychiatry*. 2007;22:448-452.
12. Brown ES, Frol A, Bobadilla L, et al. Effect of lamotrigine on mood and cognition in patients receiving chronic exogenous corticosteroids. *Psychosomatics*. 2003;44(3):204-208.
13. Goldman LS, Goveas J. Olanzapine treatment of corticosteroid-induced mood disorders. *Psychosomatics*. 2002;43(6):495-497.
14. Brown ES, Khan DA, Suppes T. Treatment of corticosteroid-induced mood changes with olanzapine. *Am J Psychiatry*. 1999;156(6):968.
15. Budur K, Pozuelo L. Olanzapine for corticosteroid-induced mood disorders. *Psychosomatics*. 2003;44(4):353.
16. Herguner S, Bilge I, Yavuz Yilmaz A, et al. Steroid-induced psychosis in an adolescent: treatment and prophylaxis with risperidone. *Turk J Pediatr*. 2006;48:244-247.
17. DeSilva CC, Nurse MC, Vokey K. Steroid-induced psychosis treated with risperidone. *Can J Psychiatry*. 2002;47:388-389.
18. Kato O, Misawa H. Steroid-induced psychosis treated with valproic acid and risperidone in a patient with systemic lupus erythematosus. *Prim Care Companion J Clin Psychiatry*. 2005;7(6):312.
19. Kramer TM, Cottingham EM. Risperidone in the treatment of steroid-induced psychosis. *J Child Adolesc Psychopharmacol*. 1999;9:315-316.
20. Siddiqui Z, Ramaswamy S, Petty F. Quetiapine therapy for corticosteroid-induced mania. *Can J Psychiatry*. 2005;50(1):77-78.
21. Naber D, Sand P, Heigl B. Psychopathological and neuropsychological effects of 8-days' corticosteroid treatment. A prospective study. *Psychoneuroendocrinology*. 1996;21(1):25-31.
22. Brown ES, Woolston DJ, Frol A, et al. Hippocampal volume, spectroscopy, cognition, and mood in patients receiving corticosteroid therapy. *Biol Psychiatry*. 2004;55:538-545.
23. Schatzberg AF, Rothschild AJ, Langlais PJ, et al. A corticosteroid/dopamine hypothesis for psychotic depression and related states. *J Psychiat Res*. 1985;19(1):57-64.
24. Sabet-Sharghi F, Hutzler JC. Prophylaxis of steroid-induced psychiatric syndromes. *Psychosomatics*. 1990;31(1):113-114.
25. Siegal FP. Lithium for steroid-induced psychosis. *N Engl J Med*. 1978;299(3):155-156.
26. Goggans FC, Weisberg LJ, Koran LM. Lithium prophylaxis of prednisone psychosis: a case report. *J Clin Psychiatry*. 1983;44(3):111-112.
27. Merrill W. Case 35-1998: use of lithium to prevent corticosteroid-induced mania. *N Engl J Med*. 1999;340(14):1123.
28. Himelhoch S, Haller E. Extreme mood lability associated with systemic lupus erythematosus and stroke successfully treated with valproic acid. *J Clin Psychopharmacol*. 1996;16(6):469-470.
29. Kahn D, Stevenson E, Douglas CJ. Effect of sodium valproate in three patients with organic brain syndromes. *Am J Psychiatry*. 1998;145(8):1010-1011.
30. Abbas A, Styra R. Valproate prophylaxis against steroid induced psychosis. *Can J Psychiatry*. 1994;39(3):188-189.
31. Preda A, Fazeli A, McKay BG, et al. Lamotrigine as prophylaxis against steroid-induced mania. *J Clin Psychiatry*. 1999;60(10):708-709.
32. Ginsberg DL, Sussman N. Gabapentin as prophylaxis against corticosteroid-induced mania. *Can J Psychiatry*. 2001;44:455-456.
33. Wada K, Yamada N, Yamauchi Y, et al. Carbamazepine treatment of corticosteroid-induced mood disorder. *J Affect Disord*. 2001;65:315-317.
34. Saklad S. Management of corticosteroid-induced psychosis with lithium. *Clin Pharm*. 1987;6(3):186.

# MAINTAINING WELLNESS IN PATIENTS WITH BIPOLAR DISORDER

moving beyond efficacy to effectiveness

## PARTICIPATING FACULTY

### S. Nassir Ghaemi, MD, MPH

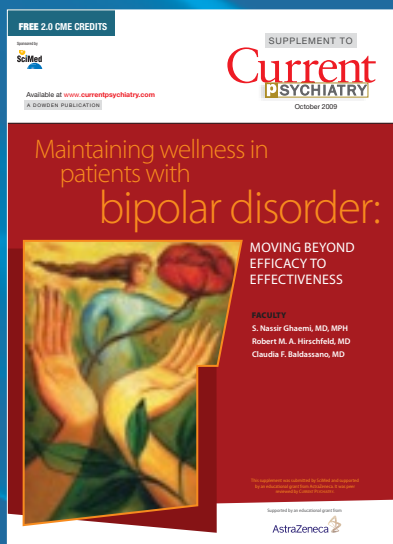
Director, Mood Disorders and Psychopharmacology Programs  
Professor of Psychiatry  
Tufts Medical Center  
Boston, Massachusetts

### Robert M. A. Hirschfeld, MD

Titus H. Harris Chair  
Harry K. Davis Professor  
Professor and Chairperson  
Department of Psychiatry and Behavioral Sciences  
University of Texas Medical Branch  
Galveston, Texas

### Claudia F. Baldassano, MD

Assistant Professor of Psychiatry  
Director, Bipolar Outpatient Program  
Hospital of the University of Pennsylvania  
Philadelphia, Pennsylvania



FREE  
2.0 CME  
credits

Available at  
CurrentPsychiatry.com

A CME-certified supplement enduring from the 2009 CURRENT PSYCHIATRY/AACP Symposium. This activity is sponsored by SciMed and supported by an educational grant from AstraZeneca. It was peer reviewed by CURRENT PSYCHIATRY.