Psychiatry and Clinical Neurosciences 2011; **65**: 549–560 doi:10.1111/j.1440-1819.2011.02260.x

Review Article

Psychiatric complications of treatment with corticosteroids: Review with case report

Heather A. Kenna,* MA, Amy W. Poon, MD, C. Paula de los Angeles, BA and Lorrin M. Koran, MD

Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, Stanford, USA

Corticosteroids are widely used in modern medicine but can result in troubling psychiatric side-effects. Physicians and other medical professionals should be aware of the potential for these side-effects, possible means of prevention, and efficacious treatments. Herein, we review adult case report data published during the past quarter-century on adverse corticosteroid-induced psychiatric effects, and present a case of corticosteroid-induced psychotic depression. PubMed and PsychLit databases were searched using the terms 'corticosteroids', 'steroids', and the generic names of corticosteroid medications with terms for psychiatric symptoms or syndromes, including psychosis, mania, hypomania, depression, apathy, anxiety, panic, depersonalization, delirium, confusion, hallucinations, delusions, paranoia, cognitive impairment and dementia. Fifty-five cases and a number of clinical trials investigating the incidence and treatment of these psychiatric symptoms and syndromes were identified. Data on incidence, drug dose, risk factors, course of illness and treatment (when present) were tabulated. We conclude that the cumulative data indicate that psychiatric complications of corticosteroid treatment are not rare and range from clinically significant anxiety and insomnia, to severe mood and psychotic disorders, delirium and dementia. While tapering or discontinuation of the corticosteroid treatment may remedy these adverse side-effects, psychotropic medications are often required because of the medical necessity of the corticosteroid or the severity of the psychiatric symptom. Further studies are needed to better understand the deleterious psychiatric effects associated with corticosteroids.

Key words: corticosteroids, delirium, mood, anxiety, psychosis.

CORTICOSTEROIDS ARE A widely used and highly effective treatment for a number of conditions, including immunologic and inflammatory disorders,[1] systemic lupus erythematosus (SLE) and systemic vasculitis,[2,3] asthma and chronic obstructive pulmonary disease,[4,5] cancer,[6] acute and chronic back pain,[7,8] and in the prevention of postoperative swelling in head and neck surgery.[9–11] Unfortunately, troubling psychiatric side-effects are sometimes seen in patients treated with corticosteroids.[12–14] The pathophysiology of negative reactions to corticosteroid administration or withdrawal is not well understood, but clinical practice may benefit from greater awareness of these potential adverse events and of methods to possibly prevent and to treat them.

*Correspondence: Heather Kenna, MA, Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, 401 Quarry Road, Room 2360, Stanford, CA 94305-5723, USA. Email: hkenna@stanford.edu

None of the authors have any conflicts of interest to report.
This manuscript was not sponsored by any grant funding support.
Received 3 February 2011; revised 11 July 2011; accepted 23 July 2011.

CORTICOSTEROID-INDUCED SYMPTOMS AND SYNDROMES

The psychiatric signs, symptoms and syndromes associated with corticosteroid treatment include (DSM-IV substance-induced) mood disorders (hypomania, mania, mixed states, depression), anxiety and panic disorder,[15,16] delirium, suicidal thinking and behavior in the context of affective syndromes or

delirium,[12,17–20] aggressive behavior[21] (including attempted murder[22]), insomnia and agitation with clear consciousness, depersonalization; and, isolated cognitive impairments (impaired attention, concentration, memory and word-finding difficulties).[14,17,23–26] In addition, the existence of a reversible, corticosteroid-induced dementia has been confirmed.[27–30] Rarely, corticosteroids have been abused for their euphoria-producing effects, producing drug dependency.[31–33] The term 'psychosis' has been variably applied to many of these clinical presentations, without distinguishing, for example, mania or psychotic depression from delirium.

Corticosteroid-induced cognitive deficits in the absence of psychotic symptoms commonly involve declarative or verbal memory.[34–40] Similar reversible deficits in declarative memory have been reported in Cushing's disease and are greater in more severe cases,[41–43] suggesting that excess endogenous and exogenous corticosteroids produce similar cognitive impairment. Reversible cognitive deficits and mood symptoms have been reported in healthy control subjects after administration of prednisone,[40] dexamethasone,[37,39] and cortisol.[38] By contrast, a small ($n = 10$) double-blind, placebo-controlled, crossover-design study utilizing prednisone 0.5 mg/kg/day in SLE patients with mild symptoms who had not received corticosteroids for at least 6 months demonstrated beneficial effects on cognition, mood and SLE symptoms.[44]

In older patients, corticosteroid-induced dementia has been misdiagnosed as early Alzheimer's disease and can occur in patients who have not experienced a steroid psychosis and are free of mood symptoms.[45] Deficits occur in memory, attention, concentration, and mental speed and efficiency, and in severe cases, formal IQ is substantially reduced.[28,45] Occupational performance is diminished, but the patients do not appear 'manifestly demented, amnestic, or disoriented, or . . . toxic or intoxicated' (p. 372).[45]

INCIDENCE OF PSYCHIATRIC SYMPTOMS AND SYNDROMES

Almost 40 years ago, The Boston Collaborative Drug Surveillance Program[46] reported 'psychiatric reactions' in 1.3% of 463 patients treated with 40 mg/day or less of prednisone, 4.6% of 175 patients dosed with 41–80 mg/day, and 18.4% of 38 patients receiving doses higher than 80 mg/day. A decade later, Lewis and Smith[12] reported a weighted average 5.7% incidence of severe psychiatric symptoms across 13 studies involving 2555 patients treated with corticosteroids. A subsequent review by Steiffel *et al.*[6] of major psychiatric symptoms in cancer patients treated with high-dose corticosteroids noted a 5–10% incidence. In contrast to patients with other medical conditions, cancer patients seemed more likely to develop delirium rather than affective syndromes, and these authors postulated that this difference may arise from the patients' frequent medical complications, from the co-administration of narcotics, and from the neurological effects of the cancers themselves. Nishimura *et al.*,[47] reviewing 139 treatment episodes in 135 patients with SLE but without current overt central nervous system manifestations, observed 14 cases (10.1%) of new-onset DSM-IV disorders, primarily manic episodes ($n = 9$, 6.5%).

In the older literature, psychotic symptoms were reported in 58% of the 55 cases reviewed by Ling *et al.*[14] Nearly 72% of their 55 cases included mood symptoms. In the review by Lewis and Smith,[12] 'disturbances in reality testing' were reported in 71% of the 79 cases (which included 44 of the 55 cases from the review of Ling *et al.*[14]), but only 14% (11/79) had 'a psychotic disorder without evidence of significant mood changes or features of a delirium.' Depression was present in 32/79 (40.5%), mania in 22/79 (27.8%), a mixed state in 6/79 (7.6%) and delirium in 8/79 (10%) of the sample. A review by Sirois[48] reporting on steroid 'psychosis' published between 1970 and 1983, before publication of the current edition of the American Psychiatric Association's DSM-IV-TR, found a syndromal breakdown of 35% mania, 28% depression, 12% mania and depression, 13% delirium, and 11% psychosis.

A number of more recent publications support the conclusion that symptoms of hypomania or mania are the most common psychiatric adverse effect of corticosteroid treatment.[12,13,18,20,47,49] Some recent studies have suggested, however, that the risk of depression increases with prolonged or chronic exposure.[48,50–52] Patients who experience corticosteroid-induced depression during one treatment course may experience drug-induced mania in a subsequent course, and vice versa.[53]

Appenzeller *et al.*[54] report episodes of acute psychosis meeting DSM-IV criteria in 17.1% (89/520) of SLE patients followed for periods of from 4 to 8.8 years. Corticosteroid-induced psychoses accounted for 31.5% (28/89) of the cases of psychosis (a 5.4%

incidence in the entire sample), of whom 10 (35.7%) had more than one psychotic episode.

Gift *et al.*[55] found significantly greater self-reported depression scores in 20 patients with chronic obstructive pulmonary disease receiving 20–40 mg/day of prednisone for 10–14 days than in 20 not receiving corticosteroids, but did not include any measure of hypomanic/manic symptoms. Swinburn *et al.*,[56] in a study of 20 similar patients given 30 mg/day of prednisolone, found only a small reduction in anxiety and depression after 3 days of prednisolone (before lung function improved) and no significant mood change after 2 weeks of treatment.

ONSET OF PSYCHIATRIC SYMPTOMS

Early studies[12,14,26] suggested and later studies[13,39,57] confirmed that the psychiatric side-effects of corticosteroid treatment have a rapid onset. Lewis and Smith[12] reported a median time to onset of 11.5 days; 39% of cases had onset during the first week and 62% within 2 weeks. Hall *et al.*[26] noted that 86% of patients with psychiatric side-effects developed these symptoms within 1 week of starting treatment. Ling *et al.*[14] reported that the psychiatric sequelae of corticosteroid treatment generally occurred within 2 weeks. In a study of 50 ophthalmic patients receiving high-dose corticosteroids, Naber *et al.*[13] reported development of psychiatric symptoms within 3 days of initiating corticosteroid treatment (when present). Another study by Nishimura *et al.*[47] found a mean of 12.5 days for onset of symptoms in their 14 cases, noting a range of 2–28 days after starting treatment. Lastly, a study of healthy subjects by Wolkowitz *et al.*[39] reported onset of psychiatric sequelae within 5 days of corticosteroid administration.

The corticosteroids dexamethasone and betamethasone have half-lives of 36–54 h.[58] As a result, they may accumulate and induce psychiatric symptoms that begin after the last dose has been given.[9,10]

CORRELATION BETWEEN DOSE AND OCCURRENCE OF PSYCHIATRIC SYMPTOMS

The early study of the Boston Collaborative Drug Surveillance Program demonstrated the striking dose–response correlation of corticosteroids. Similarly, Chan *et al.*[59] reported psychosis in 8% of patients receiving prednisone 90 mg/day compared to 3% of patients receiving 30 mg/day. The more recent literature confirms that the likelihood of inducing psychiatric symptoms follows a dose–response correlation. Nishimura *et al.*[47] noted that all 20 SLE patients who developed psychiatric symptoms (primarily hypomania, mixed states or depression) were receiving at least 40 mg/day of prednisolone. An additional 97 patients receiving these doses did not develop psychiatric symptoms. Wada *et al.*,[18] describing 18 patients who developed mood disorders or psychosis after receiving 30–60 mg/day of prednisone-equivalent, also reported a strong association with dose, although they noted that some patients had a recurrence of depression or mania related to psychosocial stressors rather than to dose changes or to resumption of corticosteroids. Appenzeller *et al.*[54] reported that all patients with corticosteroid-induced psychosis were taking prednisone 0.75–1.0 mg/kg/day, which translates into total doses as high or higher than those just noted.

Olsen *et al.*[60] found a significant correlation between mood lability and prednisone dose in mg/kg during a 6-week taper from 40 mg/d to zero in 32 patients with alopecia areata. Naber *et al.*[13] used the Profile of Mood States scale, a European psychiatric symptom scale developed by the Association of Methodology and Documentation in Psychiatry, a semi-structured interview and a battery of neuropsychological tests to study the psychological and cognitive effects of methylprednisone or fluocortolone (50–300 mg/day to start, tapered to 18–100 mg/day by day 8) in 50 ophthalmologic patients, all of whom were initially free of psychiatric disorders. Although 36% (18/50) developed DSM-III-R mania ($n = 13$) or depression ($n = 5$) during treatment, the authors found no correlation between the daily dose of steroid and the daily ratings of mood symptoms. No patient developed psychosis, delirium or severe cognitive deficits.

In almost all of the cases of corticosteroid-induced dementia located in the present search of the literature, the corticosteroid dose has been at least 60 mg/day of prednisone-equivalent. Varney *et al.*[45] reported one case in which dementia was documented 2 weeks after the prednisone dose was reduced to 20 mg/day after a 4-month course of 100 mg/day; irregular improvement occurred over the following 24 months, while prednisone was continued at 20 mg/day.

OTHER RISK FACTORS

Other than dose, no strong predictors of risk have emerged. However, psychiatric risk may be increased by drugs that increase circulating levels of corticosteroids. Clarithromycin, for example, is an inhibitor of the cytochrome P450 enzyme (CYP) 3A4 that metabolizes prednisone's biologically active metabolite, prednisolone. Finkenbine and Gill[21] reported a case of mania induced by adding clarithromycin to prednisone; the mania resolved over 5 days when both drugs were stopped. Finkenbine and Frye[21] report a case of psychotic paranoia that required the addition of olanzapine, plus a prednisone taper and the discontinuation of clarithromycin, which was followed over the next 6 days by a clearing of the paranoia.

Nishimura *et al.*,[47] studying 135 patients with systemic SLE, found cerebral spinal fluid/serum albumin ratio (a marker of blood–brain barrier damage) to be a significant risk factor for corticosteroid-induced psychiatric disorder (odds ratio 33.3). Chau and Mok,[61] studying 92 SLE patients, of whom 5% experienced a corticosteroid-induced psychosis or mania, found that hypoalbuminemia distinguished those who suffered this side-effect from those who did not. Appenzeller *et al.*[54] reported that after multiple regression analysis, hypoalbuminuria (odds ratio 2.2) was the only variable significantly associated with corticosteroid-induced psychosis in their series of SLE patients.

Some earlier studies,[12,18,62] but not all,[13,63] reported a higher prevalence of steroid-induced psychiatric problems in women. In part, the higher prevalence may have reflected their greater propensity to seek medical care, more common experience of certain psychiatric disorders, such as major depression and most anxiety disorders, or the higher prevalence of certain medical disorders, such as SLE in women; the female preponderance persisted in one study (2) even after cases of SLE were excluded.

A previous history of psychiatric disorder does not seem to increase the risk of an adverse psychiatric reaction.[6,64] Early studies reported that prior episodes of steroid-induced psychiatric symptoms may or may not be followed by recurrence during future treatment courses[12,26,65] and that risk does not appear to be associated with a particular age group.[12,14] Nothing in the modern literature contradicts these findings.

PATHOPHYSIOLOGY

The pathophysiological mechanisms giving rise to the psychiatric symptoms associated with corticosteroid treatment remain unclear. Speculations regarding these mechanisms are discussed elsewhere[5,20,39,40,47,66] and include corticosteroid effects on dopaminergic and cholinergic systems,[67,68] decreases in serotonin release,[69] and toxic effects on hippocampal neurons[39] or on other brain regions.[28]

RESULTS OF OUR REVIEW OF CASES

The following review of the adult case report data on corticosteroid-induced psychiatric side-effects targets those published since the last major review of this kind in 1983 by Lewis and Smith,[1] with the goal of ascertaining whether recent experience with corticosteroids has produced new conclusions regarding the clinical pictures and their management. We searched the PubMed and PsychLit databases by combining the search terms 'steroids', 'corticosteroids' and the generic names of corticosteroid steroid medications with terms for psychiatric symptoms or syndromes including psychosis, mania, hypomania, depression, apathy, anxiety, panic, depersonalization, delirium, confusion, hallucinations, delusions, paranoia, cognitive impairment and dementia. Our search produced 55 cases along with a number of trials investigating the incidence and treatment of these conditions. Our review focuses on the nature of these adverse events, their incidence, correlation to drug dose, risk factors, course and treatment; we also summarize the findings from earlier studies and reviews. A caveat is that case reports are likely to be influenced by publications bias – more dramatic or consequential symptoms or syndromes are more likely to be written up and accepted for publication. Thus, the analyses we present are unlikely to represent accurately the milder symptoms that may occur or the true population incidence rates of more serious reactions. Still, our analyses may provide value to the clinician treating such patients.

Our search produced 55 cases with the following syndromes: hypomania/mania; depression; delirium; subsyndromal symptoms, such as hallucinations and agitation/anxiety, and panic disorder. Of these cases, 34 (61.8%) were psychotic, that is, had hallucinations and/or delusions coupled with impaired reality testing or lack of insight. Suicidal ideation was present in 22 cases (40%), of whom half were psy-

chotic and half not; one patient committed suicide.[53] In addition, the search produced three cases of steroid-induced reversible dementia confirming the 1984 observations of Varney *et al*.[27–30,45] and six cases of psychoses apparently induced by rapid steroid discontinuation.[70–76] The dementia cases were atypical of the corticosteroid cases we identified in that only two patients were younger than age 50 (ages 25 and 44 years), symptom onset was often not reported until after months of corticosteroid treatment, and recovery, not always complete, often took more than 6 months after corticosteroid discontinuation.

We analyzed the 55 non-dementia cases of psychiatric syndromes induced by corticosteroid administration to characterize the patients, the drugs involved, the psychiatric symptoms and treatments. A summary of these cases is provided in Table 1. Although in some cases, particularly cases associated with SLE, contributions of the underlying disease or of psychosocial stressors could not be ruled out, the results of our analysis largely resemble those of earlier case series analyses.[12–14]

Patients' ages ranged from 18 to 93 years, with a mean of 44.5 ± 17.7 years. As in some earlier reviews,[12,62] but not all,[13,63] more cases involved women (34/55, 61.8%) than men. Symptoms began a mean of 12.2 ± 13.7 days after starting corticosteroids ($n = 50$), and within 1 week in 60% (30/50), but onset ranged from 1 to 60 days after starting the drug.

Hypomania or mania was the most common presentation, present in 54.5% (30/55) of cases. Clinical depression was present in 23.6% (13/55), of whom two patients were also delirious, and delirium was present in 20% (11/55). Suicidal ideation was reported in 36.4% (20/55), of whom a little less than half (9/20) were also psychotic. 'Psychosis', or a psychotic mania, psychotic depression or delirium was reported in 61.8% (34/55), quite close to the 58% incidence reported in an early study by Ling *et al*.[14] and lower than the 71% incidence reported in the early study of Lewis and Smith.[12]

Among our 53 cases in which the corticosteroid was identified, prednisolone was administered in 20 (mean dose = 46.5 ± 28.5 mg/day, [$n = 19$]), prednisone in 16 (41.4 ± 24.7 mg/day [$n = 15$]), methylprednisone in seven (38.1 ± 44.3 mg/day), dexamethasone in seven (15.3 ± 6.2 mg/day [$n = 6$], with one outlier at 100 mg/day), betamethasone in two (2 mg/day and 4 mg/day), hydrocortisone in one (50 mg/day), and triamcinolone in one (80 mg/day + prednisone 10 mg/day). The mean (±SD) prednisone-equivalent dose, excluding the dexamethasone outlier, was 63.6 ± 46.2 mg/day, and the range 5–200 mg/day. This mean prednisone-equivalent dose supports the suggestion in the literature that psychiatric side-effects are more likely to occur at higher corticosteroid doses.

Focusing on individual syndromes and cases for which data are available, we found that delirium ($n = 9$) had a mean (±SD) onset of 7.0 ± 9.3 days after starting the corticosteroid (range 1–30 days), mean (±SD) prednisone-equivalent dose of 62.2 ± 45.5 mg/day, and mean (±SD) recovery time of 9.6 ± 9.3 days (range 1–25 days). For depression, mean onset was 12.4 ± 10.2 days (range 2–30 days) ($n = 12$), mean prednisone-equivalent dose 73.2 ± 48.4 mg/day (range 5–160 mg/day), and mean recovery time 20.9 ± 10.5 days (range 7–42 days) ($n = 8$ cases, with one still ill at time of reporting and three unknown). For hypomania/mania ($n = 28$), these statistics were: mean onset ($n = 24$), 14.0 ± 16.7 days (range 1–60 days), mean prednisone-equivalent dose ($n = 25$) 44.8 ± 45.6 mg/day, and recovery time ($n = 19$) 21.3 ± 18.8 days. Hypomania/mania seems to occur at somewhat lower doses than delirium. Compared to earlier reports, our findings indicate similar mean recovery times for delirium (several days), depression (4 weeks) and hypomania/mania (3 weeks). Without distinguishing various syndromes, Appenzeller *et al*.[54] noted a median time to recovery of 13.3 ± 5.2 days in SLE patients suffering corticosteroid-induced psychoses. Some patients were treated with psychotropic drugs and some recovered simply by virtue of corticosteroid discontinuation.

CASE REPORT

The following case illustrates the difficulty that may be experienced in treating corticosteroid-induced depression, particularly when medical stressors continue and the corticosteroid cannot be quickly reduced. It also illustrates the need in such cases for prolonged use of psychotropic treatment, and the ultimate good prognosis. The authors received informed consent to publish her case.

> Mrs S, an 85-year-old widowed, socially active woman with no prior psychiatric history, developed temporal arteritis with abrupt and permanent loss of vision in her right eye and blurred vision in her left. Subsequently, she began oral prednisone

Table 1. Summary of identified cases ($n = 55$)

Symptomatic category	Sex	Age	Underlying disease(s) or condition	Prednisolone dose or prednisolone dose equivalent (p.d.e.)/day
Depression				
Ferris *et al.* 2003[9]	Female	62	Undergoing parotidectomy	160 mg (p.d.e.)
Ismail *et al.* 2002[2]	Female	64	Asthma	30 mg
Ito *et al.* 2003[77]	Female	37	Acute myeloid leukemia	50 mg
Jenkins *et al.* 2000[66]	Female	53	Meningioma	106.7 mg (p.d.e.)
Terao *et al.* 1994[78]	Male	42	Systemic lupus erythematosus	40 mg
Terao *et al.* 1994[78]	Male	18	Systemic lupus erythematosus	15 mg
Terao *et al.* 1997[79]	Female	24	Systemic lupus erythematosus	50 mg
Terao *et al.* 1997[79]	Female	66	Polyarteritis nodosa	60 mg
Wada *et al.* 2000[53]	Female	31	Systemic lupus erythematosus	30 mg
Wyszynski *et al.* 1993[80]	Female	46	Sjögren's syndrome	156.3 mg (p.d.e.)
Yoshimura *et al.* 2001[81]	Male	70	Pneumonia	100 mg
Yoshimura *et al.* 2001[81]	Female	50	Pneumonia	80 mg
Hypomania/mania				
Benyamin *et al.* 2008[82]	Male	67	Chronic neck pain	100 mg (p.d.e.)
Bloch *et al.* 1994[83]	Male	26	Multiple sclerosis	30 mg
Brown *et al.* 1999[84]	Female	21	Asthma	30
Brown *et al.* 2001[49]	Female	43	Behçet's disease	30 mg
Cerullo *et al.* 2006[85]	Male	69	Unidentified cancer	Not reported
d'Orban 1989[86]	Male	26	Undergoing maxillary osteotomy	60 mg (p.d.e.)
Finkenbine *et al.* 1997[87]	Female	30	Sinusitis	30 mg
Franco *et al.* 2000[88]	Male	59	Post-stroke cardiac transplantation	20 mg
Ginsberg *et al.* 2001[89]	Female	59	Asthma	35 mg
Hong *et al.* 2006[90]	Female	48	Sheehan's syndrome	15 mg
Johnson *et al.* 1996[76]	Female	36	Asthma, pregnancy	20 mg
Kato *et al.* 2005[91]	Female	46	Systemic lupus erythematosus	40 mg
Lopez-Medrano *et al.* 2002[3]	Female	20	Systemic lupus erythematosus	60 mg
Lopez-Medrano *et al.* 2002[3]	Female	21	Systemic lupus erythematosus	30 mg
Lundberg *et al.* 2000[92]	Male	32	Hodgkin's lymphoma	100 mg
Muzyk *et al.* 2010[93]	Female	31	Systemic lupus erythematosus	60 mg
Preda *et al.* 1999[94]	Female	41	Nephritis	40 mg
Siddiqui *et al.* 2005[95]	Male	52	Liver transplant	225 mg (p.d.e.)
Viswanathan *et al.* 1989[96]	Male	38	Post-renal transplant	15 mg
Wada *et al.* 2000[53]	Female	40	Dermatomyositis	60 mg
Wada *et al.* 2000[53]	Female	19	Minimal-change nephrotic syndrome	30 mg (p.d.e.)
Wada *et al.* 2000[53]	Female	21	Dermatomyositis	50 mg
Wada *et al.* 2000[53]	Female	23	Ulcerative colitis	26.67 mg (p.d.e.)
Wada *et al.* 2000[53]	Female	47	Systemic lupus erythematosus	Not reported
Wada *et al.* 2000[53]	Male	68	Intractable nephrotic syndrome	15 mg
Wada *et al.* 2000[53]	Male	53	Systemic lupus erythematosus	40 mg
Wada *et al.* 2000[53]	Male	42	Kidney transplant rejection	666.7 mg (p.d.e.)
Delirium				
Ahmad *et al.* 1999[4]	Female	55	Chronic obstructive pulmonary disease	60 mg
Artukoglu *et al.* 2007[97]	Female	32	Biopsy for humeral mass operation	53.33 mg (p.d.e.)
Benazzi *et al.* 1997[98]	Female	70	Systemic lupus erythematosus	5 mg (p.d.e.)
Galen *et al.* 1997[10]	Male	26	Facial osteotomies	666.7 mg (p.d.e.)
Jenkins *et al.* 2000[66]	Male	93	Renal cell carcinoma	133.3 mg (p.d.e.)
Koh *et al.* 2002[99]	Male	40	ER-breathing difficulty	82 mg
Mada *et al.* 2009[100]	Female	72	Adrenal insufficiency	12.5 mg (p.d.e.)
Okishiro *et al.* 2009[101]	Male	67	Pulmonary emphysema	13.33 mg (p.d.e.)
Silva *et al.* 1995[102]	Male	45	Dental operation	100 mg (p.d.e.)
Stoudemire *et al.* 1996[31]	Female	40	Chronic obstructive pulmonary disease	40–100 mg
Panic				
Charbonneau *et al.* 1997[16]	Female	31	Erythema multiforme	5 mg
Raskin *et al.* 1984[15]	Female	35	Hirsutism	Not reported
Hallucinations				
Daragon *et al.* 1997[103]	Male	72	Rheumatoid arthritis	74 mg (p.d.e.)
Gallerani *et al.* 2008[104]	Male	64	Hypertension	40 mg (p.d.e.)
Paranoia				
Finkenbine *et al.* 1998[21]	Male	50	Emphysema	20 mg

60 mg/day. While tapering down to 40 mg/day 1 month later, she developed significant depressive and psychotic symptoms that resulted in her hospitalization for apparent steroid-induced psychosis. The psychosis resolved several weeks later and the patient was discharged, but continued to become increasingly depressed. Her depressive symptoms were marked anhedonia, apathy, and poor concentration, and she was disheveled in appearance with poor grooming and loss of function. Although her prednisone dose was lowered to 10 mg/day, she continued to decline. Four months later, after making suicidal statements and becoming assaultive toward her 24-h caregiver, she was hospitalized again, this time for almost 2 months. She was severely depressed, hopeless, nihilistic, with delusional guilt, visual hallucinations, poor insight and self-neglect. In hopes of saving the remaining vision in her left eye, methotrexate was added to her prednisone 10 mg/day. She was stabilized and discharged on olanzapine 7.5 mg alternating with 10 mg q.h.s., bupropion XL 300 mg/day, duloxetine 90 mg/day, benztropine 0.5 mg q.h.s., and, lorazepam 0.5 mg bid p.r.n. Two weeks later upon follow up, Mrs S was neatly groomed and cheerful. She denied depressed mood, anhedonia and suicidality. In the following months, her mood remained stable and she resumed social activities while continuing her hospital discharge medications. Olanzapine and duloxetine were gradually decreased, while bupropion, benztropine and lorazepam were discontinued after 4 months.

TREATMENT OF CORTICOSTEROID-INDUCED PSYCHIATRIC SYMPTOMS

The literature on the treatment of corticosteroid-induced psychiatric symptoms is limited to multiple case reports and a few small trials. These provide clinical guidance, but require larger double-blind, placebo-controlled trials to meet the standard of evidence-based medicine.

Many authors[49,64,105] emphasize the importance of educating patients and their families about the risks of corticosteroid-induced psychiatric side-effects and of seeing patients soon after these drugs are begun, since these adverse effects may have rapid onset. The common occurrence of suicidal ideation (and less often, suicidal behaviors) must be kept in mind and preventive measures considered.[106] When psychiatric symptoms occur, contributions of the underlying medical condition(s), other drugs or treatments, withdrawal from drugs such as alcohol and benzodiazepines, medical complications, such as infections, metabolic derangements or paraneoplastic syndromes, and contributions of psychosocial stressors, including the illness itself, will have to be taken into account and managed.

As has often been pointed out, treatment of corticosteroid-induced psychiatric symptoms should start whenever possible with dose reduction or stopping the drug.[12,14,48,49,54,64,105] Without specifying the diagnoses associated with particular drugs, Lewis and Smith[12] report that simply tapering the corticosteroid dose to zero resolved the psychiatric symptoms in 94% of 36 cases. Appenzeller *et al*. reported that simply tapering off the drug was effective in half their cases.[54] Warrington and Bostwick[105] cite endocrine experts[107] who recommend tapering the corticosteroid dose to 40 mg/day of prednisone equivalent when discontinuation is not possible, followed as quickly as is safe by a taper to a physiological dose of 7.5 mg/day. The possibility of inducing psychiatric symptoms by tapering too quickly must be born in mind.[14,72,75,108] Even slow taper, however, has led to the onset of depression in patients who were euthymic on prednisone, with the depression lasting 6–8 weeks after completing the taper.[109]

Corticosteroid-induced hypomania, mania and mixed mania have been successfully treated with a typical antipsychotic or mood stabilizer, most often haloperidol,[18,53,54,76,102] haloperidol plus lithium,[2] risperidone,[3,91,93] quetiapine,[95] olanzapine,[24,92,110,111] olanzapine with valproate,[18,112,113] carbamazepine,[18] lithium,[18,114,115] lamotrigine plus clonazepam,[94] or clonazepam alone in a case where lithium had been ineffective.[96] In some cases a combination of an antipsychotic and a benzodiazepine has been required. In a 5-week, open-label trial of olanzapine 2.5–20 mg/day (mean 8.5 mg/day) for mania or mixed mania symptoms secondary to corticosteroids, Brown *et al*.[62] observed marked improvement in 11 of 12 outpatients; one patient withdrew for lack of efficacy. Renal function must be considered when contemplating the use of lithium and potential drug interactions are always a consideration.

Corticosteroid-induced depression has responded to lithium alone,[77–79] lithium added to mianserin, amitriptyline,[18] intravenous clomipramine,[18] fluoxetine,[80] venlafaxine,[2] and, low-dose fluvoxamine.[81]

Psychotic depression has responded to electroconvulsive therapy[2] and to combinations of sertraline, risperidone and lorazepam,[9] or paroxetine, risperidone and lorazepam.[2] In the 1970s, Hall *et al.*[26,116] recommended against the use of tricyclic antidepressants after observing increased mood lability or symptoms consistent with delirium in some patients; others have also reported poor response.[114,117] Selective serotonin reuptake inhibitors may be preferable due to their lower side-effect profile. Prednisolone, the active metabolite of prednisone, may increase plasma levels of fluvoxamine,[81] so that smaller-than-usual antidepressant doses may be utilized.

Corticosteroid-induced delirium, like delirium of other causes, may respond to haloperidol[4,100] or an atypical antipsychotic,[99] although the addition of other agents, such as a benzodiazepine may be necessary.[90,99]

In one case,[15] corticosteroid-induced panic disorder with agoraphobia responded within 2 weeks to tranylcypromine 20 mg/day coupled with behavioral therapy. In a second case, these symptoms responded within an unspecified interval to fluvoxamine and supportive psychotherapy.[16]

As noted earlier, corticosteroid-induced dementia resolves much more slowly following drug discontinuation than do other syndromes and may leave residual cognitive decrements. Although improvement may be apparent 1 month after discontinuation,[28,45] deficits in learning and memory may persist for 6 months or more.[27,30,45] Symptoms may also remit despite continued corticosteroid treatment. A patient who experienced a manic psychosis on 125 mg/day of cortisone had symptoms of impaired memory, attention and concentration 1 week after recovery while euthymic on 1 mg/day of dexamethasone, but normal mental status when examined 9 months later, despite being maintained in the interim on 0.5–1.5 mg/day of dexamethasone.[45] Interestingly, memantine, used in treating Alzheimer's disease, has been reported in a double-blind, crossover trial of modest size to decrease adverse effects of corticosteroid treatment on declarative memory.[118] A small, double-blind, placebo controlled study also suggested improvement in declarative memory as a result of treatment with lamotrigine, although the drug was not well-tolerated.[119]

For patients who have experienced a corticosteroid-induced psychosis or other severe adverse psychiatric effect, the clinician may wish to attempt a preventive intervention when the steroid is again needed. A number of strategies to prevent psychotic symptoms are described in case reports and one case series, but whether these symptoms would have returned absent these interventions is unknown. Falk *et al.*[120] treated 27 patients receiving corticotrophin for multiple sclerosis or retrobulbar neuritis with prophylactic lithium carbonate (serum levels 0.8 to 1.2 mEq/l) and compared them to a historical control group not receiving concurrent lithium. Psychosis had occurred in 14% (6/44) of the historical control group, but was seen in none of the lithium-treated group. Two patients discontinued lithium for side-effects. Goggans *et al.*[121] reported that a patient with a history of steroid psychosis had no recurrence during a second course of prednisone 60 mg/day preceded and accompanied by lithium 900 mg/day. In another case, lithium did not prevent the onset of mania with a first course of prednisone, but when prednisone was resumed 3 weeks later with concurrent lithium, the mania did not recur.[122] A woman who had experienced two previous psychotic episodes followed by persistent melancholic depression safely underwent a third steroid course while treated with protriptyline, lithium and haloperidol (administered for only a few days).[123] Bloch *et al.*[83] reported that a patient who had become psychotic during two prior courses of corticosteroid treatment had no symptoms during a third course (methylprednisolone 1 g tapered to zero over 10 days, followed by prednisone 30 mg/day) so long as chlorpromazine 150 mg/day was co-administered. When it was tapered off, the patient became hypomanic and it had to be resumed. A patient who had experienced a manic episode when treated with prednisone 40 mg/day tolerated two subsequent courses while taking gabapentin 900 mg/day starting 1 day before resuming corticosteroids.[89] In a bipolar patient whose lithium had to be discontinued because of worsening interstitial nephritis, lamotrigine plus clonazepam was effective in treating mania present on hospital admission and in preventing an exacerbation when the patient was placed on high-dose prednisone.[94] Valproate has been reported to prevent steroid-induced psychosis in one case.[112] In a double-blind, placebo-controlled trial of 30 patients, acetaminophen 4000 mg/day did not differ from placebo with respect to change in depressive symptoms.[124]

DIRECTIONS FOR FUTURE RESEARCH

Brown and Suppes[57] highlight limitations of the current literature on the psychiatric adverse reactions

to corticosteroid treatment – most large studies have not included formal psychiatric assessment, most studies that incorporated such assessment were small and, thus, the interpretation and generalization of their results are difficult, and useful, patient-specific risk factors remain unknown.[57] As noted above, the case report literature on which much of our knowledge depends cannot be regarded as definitive.

Wada *et al*.[18] suggest the individual susceptibility to mania versus depression and other corticosteroid-induced psychiatric symptoms be studied. These authors also note a paucity of information on long-term outcome, on the risk of recurrence of symptoms and on the optimum treatments for corticosteroid-induced psychiatric syndromes.[18]

Given the potential severity and cost of corticosteroid-induced psychiatric side-effects, controlled trials of preventive strategies would be quite useful. In addition, recent advances in genetic mapping could be utilized to help identify a risk-promoting role for particular genes or polymorphisms, although the sample sizes needed are daunting.

CONCLUSION

Psychiatric complications of corticosteroid treatment range from anxiety and insomnia to severe mood disorders, delirium and dementia. The psychiatric symptoms typically come on within 1–2 weeks after starting high-dose corticosteroid steroid treatment and the most common serious adverse event reported is hypomania or mania, though various forms of psychotic syndromes, taken together, are even more common. Hypo-albuminemia appears to be a risk factor worth attending to, as does co-administration of drugs that may slow the metabolism of the corticosteroid, for example, P450 (CYP) 3A4 inhibitors. Although steroid taper or discontinuation can remedy these adverse effects, psychotropic medications are often required, either because of the inability to discontinue the steroid treatment or the severity of the psychiatric symptoms. The psychotropic medication classes that are effective for particular idiopathic psychiatric syndromes also appear to be effective in cases induced by corticosteroid treatment.

Although much remains to learn about adverse psychiatric reactions to corticosteroid treatment, physicians, patients and their families should work together to improve awareness of the limited available knowledge and to stimulate research aimed at improved methods of prevention, recognition and treatment.[82,84–88,97,98,101,103,104]

REFERENCES

1. Da Silva JA, Jacobs JW, Kirwan JR *et al*. Safety of low dose glucocorticoid treatment in rheumatoid arthritis: published evidence and prospective trial data. *Ann. Rheum. Dis.* 2006; **65**: 285–293.
2. Ismail M, Lyster G. Treatment of psychotic depression associated with steroid therapy in Churg-Strauss syndrome. *Ir. Med. J.* 2002; **95**: 18–19.
3. Lopez-Medrano F, Cervera R, Trejo O, Font J, Ingelmo M. Steroid induced psychosis in systemic lupus erythematosus: a possible role of serum albumin level. *Ann. Rheum. Dis.* 2002; **61**: 562–563.
4. Ahmad M, Rasul FM. Steroid-induced psychosis treated with haloperidol in a patient with active chronic obstructive pulmonary disease. *Am. J. Emerg. Med.* 1999; **17**: 735.
5. Brown ES, Suppes T, Khan DA, Carmody TJ 3rd. Mood changes during prednisone bursts in outpatients with asthma. *J. Clin. Psychopharmacol.* 2002; **22**: 55–61.
6. Stiefel FC, Breitbart WS, Holland JC. Corticosteroids in cancer: neuropsychiatric complications. *Cancer Invest.* 1989; **7**: 479–491.
7. Curatolo M, Bogduk N. Pharmacologic pain treatment of musculoskeletal disorders: current perspectives and future prospects. *Clin. J. Pain.* 2001; **17**: 25–32.
8. Deyo RA. Drug therapy for back pain. Which drugs help which patients? *Spine* 1996; **21**: 2840–2849.
9. Ferris RL, Eisele DW. Steroid psychosis after head and neck surgery: case report and review of the literature. *Otolaryngol. Head Neck Surg.* 2003; **129**: 591–592.
10. Galen DM, Beck M, Buchbinder D. Steroid psychosis after orthognathic surgery: a case report. *J. Oral Maxillofac. Surg.* 1997; **55**: 294–297.
11. Fleming PS, Flood TR. Steroid-induced psychosis complicating orthognathic surgery: a case report. *Br. Dent. J.* 2005; **199**: 647–648.
12. 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.
13. Naber D, Sand P, Heigl B. Psychopathological and neuropsychological effects of 8-days' corticosteroid treatment. A prospective study. *Psychoneuroendocrinology* 1996; **21**: 25–31.
14. Ling MH, Perry PJ, Tsuang MT. Side effects of corticosteroid therapy. Psychiatric aspects. *Arch. Gen. Psychiatry* 1981; **38**: 471–477.
15. Raskin DE. Steroid-induced panic disorder. *Am. J. Psychiatry* 1984; **141**: 1647.
16. Charbonneau Y, Ravindran AV. Successful treatment of steroid-induced panic disorder with fluvoxamine. *J. Psychiatry Neurosci.* 1997; **22**: 346–347.

17. Lewis A, Fleminger JJ. The psychiatric risk from corticotrophin and cortisone. *Lancet* 1954; **266**: 383–386.
18. Wada K, Yamada N, Sato T *et al*. Corticosteroid-induced psychotic and mood disorders: diagnosis defined by DSM-IV and clinical pictures. *Psychosomatics* 2001; **42**: 461–466.
19. Breitbart W. Suicide in cancer patients. *Oncology* 1987; **1**: 49–55.
20. Braunig P, Bleistein J, Rao ML. Suicidality and corticosteroid-induced psychosis. *Biol. Psychiatry* 1989; **26**: 209–210.
21. Finkenbine RD, Frye MD. Case of psychosis due to prednisone-clarithromycin interaction. *Gen. Hosp. Psychiatry* 1998; **20**: 325–326.
22. d'Orban PT, O'Connor A. Women who kill their parents. *Br. J. Psychiatry* 1989; **154**: 27–33.
23. Rome HP, Braceland FJ. The psychological response to ACTH, cortisone, hydrocortisone, and related steroid substances. *Am. J. Psychiatry* 1952; **108**: 641–651.
24. Brown ES, Khan DA, Nejtek VA. The psychiatric side effects of corticosteroids. *Ann. Allergy Asthma Immunol.* 1999; **83**: 495–503; quiz 503–494.
25. Bender BG, Lerner JA, Kollasch E. Mood and memory changes in asthmatic children receiving corticosteroids. *J. Am. Acad. Child Adolesc. Psychiatry* 1988; **27**: 720–725.
26. Hall RC, Popkin MK, Stickney SK, Gardner ER. Presentation of the steroid psychoses. *J. Nerv. Ment. Dis.* 1979; **167**: 229–236.
27. Varney NR. A case of reversible steroid dementia. *Arch. Clin. Neuropsychol.* 1997; **12**: 167–171.
28. Sacks O, Shulman M. Steroid dementia: an overlooked diagnosis? *Neurology* 2005; **64**: 707–709.
29. Sacks O, Shulman M. Steroid dementia: a follow-up. *Neurology* 2007; **68**: 622.
30. Norra C, Arndt M, Kunert HJ. Steroid dementia: an overlooked diagnosis? *Neurology* 2006; **66**: 155.
31. Stoudemire A, Anfinson T, Edwards J. Corticosteroid-induced delirium and dependency. *Gen. Hosp. Psychiatry* 1996; **18**: 196–202.
32. Ortega LD, Grande RG. Cushing's syndrome due to abuse of dexamethasone nasal spray. *Lancet* 1979; **2**: 96.
33. Brown ES. Chemical dependence involving glucocorticoids. *Ann. Clin. Psychiatry* 1997; **9**: 185–187.
34. Lupien SJ, McEwen BS. The acute effects of corticosteroids on cognition: integration of animal and human model studies. *Brain Res. Rev.* 1997; **24**: 1–27.
35. Keenan PA, Jacobson MW, Soleymani RM, Mayes MD, Stress ME, Yaldoo DT. The effect on memory of chronic prednisone treatment in patients with systemic disease. *Neurology* 1996; **47**: 1396–1402.
36. Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol. Rev.* 1992; **99**: 195–231.
37. Newcomer JW, Craft S, Hershey T, Askins K, Bardgett ME. Glucocorticoid-induced impairment in declarative memory performance in adult humans. *J. Neurosci.* 1994; **14**: 2047–2053.
38. Newcomer JW, Selke G, Melson AK, Hershey T, Craft S, Richards K, Alderson AL. Decreased memory performance in healthy humans induced by stress-level cortisol treatment. *Arch. Gen. Psychiatry* 1999; **56**: 527–533.
39. Wolkowitz OM, Reus VI, Weingartner H *et al*. Cognitive effects of corticosteroids. *Am. J. Psychiatry* 1990; **147**: 1297–1303.
40. Wolkowitz OM, Rubinow D, Doran AR *et al*. Prednisone effects on neurochemistry and behavior. Preliminary findings. *Arch. Gen. Psychiatry* 1990; **47**: 963–968.
41. Mauri M, Sinforiani E, Bono G *et al*. Memory impairment in Cushing's disease. *Acta Neurol. Scand.* 1993; **87**: 52–55.
42. Starkman MN, Gebarski SS, Berent S, Schteingart DE. Hippocampal formation volume, memory dysfunction, and cortisol levels in patients with Cushing's syndrome. *Biol. Psychiatry* 1992; **32**: 756–765.
43. Starkman MN, Schteingart DE. Neuropsychiatric manifestations of patients with Cushing's syndrome. Relationship to cortisol and adrenocorticotropic hormone levels. *Arch. Intern. Med.* 1981; **141**: 215–219.
44. Denburg SD, Carbotte RM, Denburg JA. Corticosteroids and neuropsychological functioning in patients with systemic lupus erythematosus. *Arthritis Rheum.* 1994; **37**: 1311–1320.
45. Varney NR, Alexander B, MacIndoe JH. Reversible steroid dementia in patients without steroid psychosis. *Am. J. Psychiatry* 1984; **141**: 369–372.
46. [No Authors Listed]. Acute adverse reactions to prednisone in relation to dosage. *Clin. Pharmacol. Ther.* 1972; **13**: 694–698.
47. Nishimura K, Harigai M, Omori M, Sato E, Hara M. Blood-brain barrier damage as a risk factor for corticosteroid-induced psychiatric disorders in systemic lupus erythematosus. *Psychoneuroendocrinology* 2008; **33**: 395–403.
48. Sirois F. Steroid psychosis: a review. *Gen. Hosp. Psychiatry* 2003; **25**: 27–33.
49. Brown ES, Chandler PA. Mood and cognitive changes during systemic corticosteroid therapy. *Prim. Care Companion J. Clin. Psychiatry* 2001; **3**: 17–21.
50. Herbert J. Neurosteroids, brain damage, and mental illness. *Exp. Gerontol.* 1998; **33**: 713–727.
51. Mitchell A, O'Keane V. Steroids and depression. *BMJ* 1998; **316**: 244–245.
52. Bolanos SH, Khan DA, Hanczyc M, Bauer MS, Dhanani N, Brown ES. 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.
53. Wada K, Yamada N, Suzuki H, Lee Y, Kuroda S. Recurrent cases of corticosteroid-induced mood disorder: clinical characteristics and treatment. *J. Clin. Psychiatry* 2000; **61**: 261–267.

54. Appenzeller S, Cendes F, Costallat LT. Acute psychosis in systemic lupus erythematosus. *Rheumatol. Int.* 2008; **28**: 237–243.
55. Gift AG, Wood RM, Cahill CA. Depression, somatization and steroid use in chronic obstructive pulmonary disease. *Int. J. Nurs. Stud.* 1989; **26**: 281–286.
56. Swinburn CR, Wakefield JM, Newman SP, Jones PW. Evidence of prednisolone induced mood change ('steroid euphoria') in patients with chronic obstructive airways disease. *Br. J. Clin. Pharmacol.* 1988; **26**: 709–713.
57. Brown ES, Suppes T. Mood symptoms during corticosteroid therapy: a review. *Harv. Rev. Psychiatry* 1998; **5**: 239–246.
58. Clinician's Ultimate Reference. Available from URL: http://www.globalrph.com/corticocalc.htm (last accessed 19 August 2011).
59. Chan L, French ME, Oliver DO, Morris PJ. High- and low-dose prednisolone. *Transplant. Proc.* 1981; **13**: 336–338.
60. Olsen EA, Carson SC, Turney EA. Systemic steroids with or without 2% topical minoxidil in the treatment of alopecia areata. *Arch. Dermatol.* 1992; **128**: 1467–1473.
61. Chau SY, Mok CC. Factors predictive of corticosteroid psychosis in patients with systemic lupus erythematosus. *Neurology* 2003; **61**: 104–107.
62. Brown ES, Chamberlain W, Dhanani N, Paranjpe P, Carmody TJ, Sargeant M. An open-label trial of olanzapine for corticosteroid-induced mood symptoms. *J. Affect. Disord.* 2004; **83**: 277–281.
63. Nielsen J. Home visits by psychiatrists. *Compr. Psychiatry* 1963; **44**: 442–460.
64. Patten SB, Neutel CI. Corticosteroid-induced adverse psychiatric effects: incidence, diagnosis and management. *Drug Saf.* 2000; **22**: 111–122.
65. Clark LD, Quarton GC, Cobb S, Bauer W. Further observations on mental disturbances associated with cortisone and ACTH therapy. *N. Engl. J. Med.* 1953; **249**: 178–183.
66. Jenkins CA, Bruera E. Difficulties in diagnosing neuropsychiatric complications of corticosteroids in advanced cancer patients: two case reports. *J. Pain Symptom Manage.* 2000; **19**: 309–317.
67. Black AC. Biochemical mechanisms of steroid-induced psychosis. *N. Y. State J. Med.* 1982; **82**: 1024.
68. Gilad GM, Rabey JM, Gilad VH. Presynaptic effects of glucocorticoids on dopaminergic and cholinergic synaptosomes. Implications for rapid endocrine-neural interactions in stress. *Life Sci.* 1987; **40**: 2401–2408.
69. Beshay H, Pumariega AJ. Sertraline treatment of mood disorder associated with prednisone: a case report. *J. Child Adolesc. Psychopharmacol.* 1998; **8**: 187–193.
70. Campbell KM, Schubert DS. Delirium after cessation of glucocorticoid therapy. *Gen. Hosp. Psychiatry* 1991; **13**: 270–272.
71. Venkatarangam SH, Kutcher SP, Notkin RM. Secondary mania with steroid withdrawal. *Can. J. Psychiatry* 1988; **33**: 631–632.
72. Judd FK, Burrows GD, Norman TR. Psychosis after withdrawal of steroid therapy. *Med. J. Aust.* 1983; **2**: 350–351.
73. Mercadante S, Villari P, Intravaia G. Withdrawal acute psychosis after corticosteroid discontinuation. *J. Pain Symptom. Manage.* 2007; **34**: 118–119.
74. Alpert E, Seigerman C. Steroid withdrawal psychosis in a patient with closed head injury. *Arch. Phys. Med. Rehabil.* 1986; **67**: 766–769.
75. DeSilva CC, Nurse MC, Vokey K. Steroid-induced psychosis treated with risperidone. *Can. J. Psychiatry* 2002; **47**: 388–389.
76. Johnson I. Steroid-induced prepartum psychosis. *Br. J. Psychiatry* 1996; **169**: 522.
77. Ito M, Onose M, Yamada T, Onishi H, Fujisawa S, Kanamori H. Successful lithium carbonate treatment for steroid-induced depression following bone marrow transplantation: a case report. *Jpn. J. Clin. Oncol.* 2003; **33**: 538–540.
78. Terao T, Mizuki T, Ohji T, Abe K. Antidepressant effect of lithium in patients with systemic lupus erythematosus and cerebral infarction, treated with corticosteroid. *Br. J. Psychiatry* 1994; **164**: 109–111.
79. Terao T, Yoshimura R, Shiratuchi T, Abe K. Effects of lithium on steroid-induced depression. *Biol. Psychiatry* 1997; **41**: 1225–1226.
80. Wyszynski AA, Wyszynski B. Treatment of depression with fluoxetine in corticosteroid-dependent central nervous system Sjogren's syndrome. *Psychosomatics* 1993; **34**: 173–177.
81. Yoshimura R, Ueda N, Nakamura J. Successful treatment of steroid-induced depression with low dosage of fluvoxamine. *Aust. N. Z. J. Psychiatry* 2001; **35**: 855–856.
82. Benyamin RM, Vallejo R, Kramer J, Rafeyan R. Corticosteroid induced psychosis in the pain management setting. *Pain Physician* 2008; **11**: 917–920.
83. Bloch M, Gur E, Shalev A. Chlorpromazine prophylaxis of steroid-induced psychosis. *Gen. Hosp. Psychiatry* 1994; **16**: 42–44.
84. Brown ES, Khan DA, Suppes T. Treatment of corticosteroid-induced mood changes with olanzapine. *Am. J. Psychiatry* 1999; **156**: 968.
85. Cerullo M. Corticosteroid-induced mania: Prepare for the unpredictable. *Curr. Psychiatry* 2006; **5**: 43–50.
86. d'Orban PT. Steroid-induced psychosis. *Lancet* 1989; **2**: 694.
87. Finkenbine R, Gill HS. Case of mania due to prednisone-clarithromycin interaction. *Can. J. Psychiatry* 1997; **42**: 778.
88. Franco K, Chughtai H. Steroid-induced mania in post-stroke patient involving the right basal ganglion and right frontal region. *Psychosomatics* 2000; **41**: 446–447.

89. Ginsberg DL, Sussman N. Gabapentin as prophylaxis against steroid-induced mania. *Can. J. Psychiatry* 2001; **46**: 455–456.
90. Hong SI, Cho DH, Kang HC, Chung DJ, Chung MY. Acute onset of steroid psychosis with very low dose of prednisolone in Sheehan's syndrome. *Endocr. J.* 2006; **53**: 255–258.
91. 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**: 312.
92. Lundberg JC, Lee M, Chionchio SB, Theobald DE, Saltzer EB. A steroid-induced disorder in a patient with non-Hodgkin's lymphoma. *Cancer Pract.* 2000; **8**: 155–159.
93. Muzyk A, Hold S, Gagliardi J. Corticosteroid psychosis: stop therapy or add psychotropics? *Curr. Psychiatry* 2010; **9**: 61–63, 67–69.
94. Preda A, Fazeli A, McKay BG, Bowers MB, Mazure CM. Lamotrigine as prophylaxis against steroid-induced mania. *J. Clin. Psychiatry* 1999; **60**: 708–709.
95. Siddiqui Z, Ramaswamy S, Petty F. Quetiapine therapy for corticosteroid-induced mania. *Can. J. Psychiatry* 2005; **50**: 77–78.
96. Viswanathan R, Glickman L. Clonazepam in the treatment of steroid-induced mania in a patient after renal transplantation. *N. Engl. J. Med.* 1989; **320**: 319–320.
97. Artukoglu F. Single dose dexamethasone induced postoperative psychosis. *Canad. J. Anesth.* 2007; **54**: 43461.
98. Benazzi F. Resistant depression associated with lupus erythematosus and steroid therapy. *Can. J. Psychiatry* 1997; **42**: 530–531.
99. Koh YI, Choi IS, Shin IS, Hong SN, Kim YK, Sim MK. Steroid-induced delirium in a patient with asthma: report of one case. *Korean J. Intern. Med.* 2002; **17**: 150–152.
100. Mada S, Palmer C, Mhando Y, Rao P, Erukulapati R, Nag S. Severe acute psychosis precipitated by replacement dose hydrocortisone in newly diagnosed panhypopituitarism. *Endocrine Abstracts.* 2009; **19**: P228.
101. Okishiro N, Tanimukai H, Tsuneto S, Ito N. Can 'steroid switching' improve steroid-induced psychosis in a patient with advanced cancer? *J. Palliat. Med.* 2009; **12**: 487–490.
102. Silva RG, Tolstunov L. Steroid-induced psychosis: report of case. *J. Oral Maxillofac. Surg.* 1995; **53**: 183–186.
103. Daragon A, Vittecoq O, Le Loet X. Visual hallucinations induced by intraarticular injection of steroids. *J. Rheumatol.* 1997; **24**: 411.
104. Gallerani M, Boari B. Hallucinations and tremors due to oral therapeutic doses of erythromycin and methylprednisolone. *Intern. Emerg. Med.* 2008; **3**: 283–285.
105. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. *Mayo Clin. Proc.* 2006; **81**: 1361–1367.
106. Ismail K, Wessely S. Psychiatric complications of corticosteroid therapy. *Br. J. Hosp. Med.* 1995; **53**: 495–499.
107. Richter B, Neises G, Clar C. Glucocorticoid withdrawal schemes in chronic medical disorders. A systematic review. *Endocrinol. Metab. Clin. North Am.* 2002; **31**: 751–778.
108. Fricchione G, Ayyala M, Holmes V. Steroid withdrawal psychiatric syndrome. *Ann. Clin. Psychiatry* 1989; **1**: 99–108.
109. Wolkowitz OM. Long-lasting behavioral changes following prednisone withdrawal. *JAMA* 1989; **261**: 1731–1732.
110. Goldman LS, Goveas J. Olanzapine treatment of corticosteroid-induced mood disorders. *Psychosomatics* 2002; **43**: 495–497.
111. Budur K, Pozuelo L. Olanzapine for corticosteroid-induced mood disorders. *Psychosomatics* 2003; **44**: 353.
112. Abbas A, Styra R. Valproate prophylaxis against steroid induced psychosis. *Can. J. Psychiatry* 1994; **39**: 188–189.
113. Himelhoch S, Haller E. Extreme mood lability associated with systemic lupus erythematosus and stroke successfully treated with valproic acid. *J. Clin. Psychopharmacol.* 1996; **16**: 469–470.
114. Blazer DG, Petrie WM, Wilson WP. Affective psychoses following renal transplant. *Dis. Nerv. Syst.* 1976; **37**: 663–667.
115. Siegal FP. Lithium for steroid-induced psychosis. *N. Engl. J. Med.* 1978; **299**: 155–156.
116. Hall RC, Popkin MK, Kirkpatrick B. Tricyclic exacerbation of steroid psychosis. *J. Nerv. Ment. Dis.* 1978; **166**: 738–742.
117. Malinow KL, Dorsch C. Tricyclic precipitation of steroid psychosis. *Psychiatr. Med.* 1984; **2**: 351–354.
118. Brown ES, Vazquez M, Nakamura A. Randomized, placebo-controlled, crossover trial of memantine for cognitive changes with corticosteroid therapy. *Biol. Psychiatry* 2008; **64**: 727–729.
119. Brown ES, Wolfshohl J, Shad MU, Vazquez M, Osuji IJ. Attenuation of the effects of corticosteroids on declarative memory with lamotrigine. *Neuropsychopharmacology* 2008; **33**: 2376–2383.
120. Falk WE, Mahnke MW, Poskanzer DC. Lithium prophylaxis of corticotropin-induced psychosis. *JAMA* 1979; **241**: 1011–1012.
121. Goggans FC, Weisberg LJ, Koran LM. Lithium prophylaxis of prednisone psychosis: a case report. *J. Clin. Psychiatry* 1983; **44**: 111–112.
122. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 35-1998. A 54-year-old woman with a progressive gait disturbance and painful leg paresthesias. *N. Engl. J. Med.* 1998; **339**: 1534–1541.
123. Sabet-Sharghi F, Hutzler JC. Prophylaxis of steroid-induced psychiatric syndromes. *Psychosomatics* 1990; **31**: 113–114.
124. Brown ES, Denniston D, Gabrielson B, Khan DA, Khanani S, Desai S. Randomized, double-blind, placebo-controlled trial of acetaminophen for preventing mood and memory effects of prednisone bursts. *Allergy Asthma Proc.* 2010; **31**: 331–336.