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Bipolar I disorder

Psychopathology, medical management and dental implications

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Bipolar I disorder, or BD, is a psychiatric illness (formerly known as manic-depressive disorder) that causes a person to experience recurrent episodes of elated and depressed moods separated by well-spaced intervals of euthymia—normal mood. During manic episodes, people appear euphoric and unusually cheerful and display heightened self-esteem and grandiosity that leads them to indiscriminately undertake multiple sexual, occupational, political or religious activities with a sense of conviction and purpose but without regard for the apparent risks or need to complete them.¹ This often is accompanied by restlessness, a decreased need for sleep, “pressured speech” that is loud, rapid and difficult to interpret, and increased sociability that is intrusive, demanding and domineering. When rebuffed or frustrated, however, irritability, anger and rage are likely to ensue.

People with bipolar I disorder who have a depressive episode are at high risk of developing rampant dental caries.

During a manic episode, more than 75 percent of patients who have BD experience psychotic symptoms such as auditory hallucinations, delusions and severely disturbed thought processes.² Delusions are erroneous but firmly held ideas. An example of a common delusion that occurs during a manic episode is patients’ claims of infallibility because of their special relationships to God. The disturbed thought process is inferred from these patients’ speech, which manifests rapid shifts between topics called “flight of ideas” that are loosely associated logically or are completely unrelated.

Patients’ euphoric moods may shift rapidly to the

Background. The authors review the clinical features, epidemiology, pathophysiology, medical management, dental findings and dental management of patients who have bipolar I disorder, or BD, previously known as manic-depressive disorder.

Types of Studies Reviewed. The authors conducted a MEDLINE search for the period 1995 through 2001 using the key terms “bipolar disorder,” “epidemiology,” “pathophysiology,” “treatment” and “dentistry.” The articles they selected for further review included those published in English in peer-reviewed journals; they gave preference to articles reporting randomized, controlled trials.

Results. BD is a psychiatric illness characterized by extreme mood swings. Mania is accompanied by euphoria, grandiosity, racing thoughts and lack of insight. Depression is characterized by marked sadness or loss of interest or pleasure in daily activities. The unpredictable mood swings can distress the person, can impair social function and quality of life and are associated with a significant increase in the risk for substance abuse and suicide. BD is common in the United States, with a lifetime prevalence rate of 1.6 percent and recurrence rate of more than 50 percent.

Clinical Implications. The prevalence of dental disease usually is extensive because of poor oral hygiene and medication-induced xerostomia. Preventive dental education, saliva substitutes and anticaries agents are indicated. To avoid adverse drug interactions with the usually prescribed psychiatric medications, special precautions should be taken when administering certain antibiotics, analgesics and sedatives.

depressive phase, during which patients experience dysphoria (feeling sad, helpless, pessimistic, agitated, anxious or any combination of the preceding), anhedonia (a loss of interest or pleasure in previously enjoyed activities such as hobbies and social or sexual interactions) or both. A sense of worthlessness or guilt accompanied by preoccupation

over minor failings and thoughts of suicide are common. Psychotic components of a depressive episode may include patients believing they deserve to be punished, refusing to eat and making multiple suicide attempts.

During a depressive episode, patients who have BD or their family members may note alterations in appetite that result in a weight loss or gain of more than 5 percent, insomnia characterized by early awakening or by difficulty falling or staying asleep, an inability to sit still (agitation), slowed speech and body movements (psychomotor retardation), extreme fatigue, and an impaired ability to think, concentrate or make decisions. Somatic complaints without physiological basis, such as bodily aches and pains, also are common.

These clusters of symptoms can be emotionally painful and interfere with patients' educations, occupations and social lives. During a manic episode, violent acting out and difficulties with the law or financial institutions often result from the patients' impulsivity, lack of insight and poor judgment. During both manic and depressive episodes, marital instability, alienation from family and an inability to hold a job are common. Approximately 50 percent of people who have BD also abuse illicit substances (for example, amphetamines, cocaine, hallucinogens such as lysergic acid diethylamide and opiates such as heroin and phencyclidine hydrochloride), alcohol or both.³⁻⁵ In addition, these people are at high risk of experiencing attention-deficit hyperactivity disorder, obsessive-compulsive disorder, other anxiety disorders and impulse control disorders such as pathological gambling and kleptomania concurrently.⁶ It is estimated that 25 to 50 percent of patients who have BD attempt to commit suicide and that 10 to 15 percent eventually commit the act.^{7,8}

EPIDEMIOLOGY

BD is common in the United States, with a lifetime prevalence of 1.6 percent; it is the sixth leading cause of disability worldwide.^{9,10} BD, however, may be even more common because an episode of depression may appear before a manic episode, and the disorder initially may be misdiagnosed as a major, unipolar depressive disorder until the manic episode evolves.¹¹ The prevalence of BD is approximately the same in both sexes; however, men are more likely to have a manic episode first, and women are more likely to experience a depressive episode first. In addition, the

frequency of depressive episodes, illicit substance abuse and suicide attempts is higher among women.^{12,13} The peak period of initial onset is between ages 15 and 24 years, and, if it is properly diagnosed and treated, it often is followed by a remission of approximately five years.¹⁴ Recurrence after five years is likely, as remission periods decrease progressively so that over the next five years the average patient has three more major episodes. In later years, the disease tends to stabilize, with the patient having approximately one episode per year.¹⁵

BD can present an emotional and financial burden on people who have BD and their families because of the 95 percent lifetime risk of recurrence, its chronicity and the potential for suicide. In addition, people who have BD have a mortality rate that is twice as high as might be expected in people who do not have BD, because of substance abuse, stress and smoking-related medical illnesses such as cardiovascular and respiratory diseases, and risk-taking behaviors that lead to accidents such as those arising from aggressive car driving.¹⁶ Thus, the illness poses a substantial public health burden with high costs in terms of lifetime medical expenses and lost productivity.¹⁷ In 1998 in the United States, the estimated cost of treating BD and the associated cost of impaired workplace productivity was \$24 billion.¹⁸

PATHOPHYSIOLOGY

The etiology of BD remains ill-defined, though it now is known that it may arise from a complex interaction of genetic predisposition, neurochemical influence, anatomical variation, substance abuse, and stressful perinatal and childhood experiences (for example, verbal, physical and sexual abuse).¹⁹⁻²¹ Although the exact gene or genes and mode of transmission remain illusive, BD's inheritability is demonstrated by the fact that if one parent has BD, there is a 25 percent chance that any of his or her children will have BD or major depressive disorder, and if both parents have BD there is a 50 to 75 percent that their children will have a mood disorder. Concordance rates for BD are 70 percent in monozygotic twins and 15 percent in dizygotic twins.²²

Neurochemical abnormalities have been implicated as contributing to the development of BD. Specifically, a paucity of the "inhibitory" neurotransmitter γ -aminobutyric acid, or GABA, and elevated levels of the neurotransmitters norepinephrine and dopamine at the synapses

between neurons in the brain's limbic system—which regulates mood and emotions—have been implicated as facilitating the excessive transmission of neuronal impulses resulting in a manic episode.²³ Meanwhile, inadequate levels of the neurotransmitters serotonin, norepinephrine and dopamine have been identified as hindering neuronal transmission resulting in a depressive episode.²⁴ Neuroimaging studies support this model by demonstrating abnormalities in blood flow and glucose metabolism in limbic system structures and in the amygdala—the area of the brain known to be involved in processing emotions.²⁵⁻²⁹

MEDICAL MANAGEMENT

An acute manic episode often constitutes a medical emergency and usually is treated in a hospital. Initially, high doses of a mood stabilizer such as lithium, valproate sodium or carbamazepine are prescribed; the latter two also are anticonvulsant medications. In addition to a mood stabilizer, an antipsychotic medication (risperidone, olanzapine or quetiapine) and a high-potency benzodiazepine (lorazepam or clonazepam) often are prescribed to attain a degree of control of acute agitation.^{30,31} People who cannot tolerate the medication may be given electroconvulsive therapy, or ECT.³²

Once the agitation is controlled, the antipsychotic medication and the benzodiazepine usually are discontinued. The dosage of lithium, valproate sodium, carbamazepine or a combination of these medications then is adjusted to obtain long-term mood stabilization and to prevent recurrence of both mania and depression. During this maintenance phase of treatment because of a less-than-optimal response, approximately 50 percent of patients also take an antidepressant (most commonly a selective serotonin reuptake inhibitor, or SSRI, or bupropion), 40 percent take a benzodiazepine, and 30 percent take an antipsychotic agent.^{33,34} Psychosocial interventions such as behavioral, cognitive and interpersonal therapy also are offered at this time and appear to augment the effects of the medications and forestall recurrence.³⁵

Risperidone, olanzapine and quetiapine are classified as second-generation antipsychotic medications. These medications are used to decrease agitation, control psychotic symptoms and promote mood stabilization. They derive their antimanic effect by blocking dopamine neural

transmission and their antidepressive effects by enhancing serotonin and norepinephrine neural transmission.³⁶⁻³⁹ The occurrence of extrapyramidal movement disorders is considerably less frequent than with first-generation antipsychotic medications such as chlorpromazine. However, when extrapyramidal movement disorders do arise, they often have an orofacial component such as acute dystonia creating mastication muscle spasms, pseudoparkinsonism resulting in a masklike face and drooling, and tardive dyskinesia manifesting as lip smacking and tongue protrusion. Occasionally, the use of these medications also is associated with the development of hypotension, orthostatic hypotension, weight gain, tachycardia, anticholinergic effects and sexual dysfunction.

Lorazepam and clonazepam may help control acute agitation, hyperactivity and insomnia by enhancing the activity of GABA—a major inhibitor of the norepinephrine and serotonin neurotransmitter systems in the central nervous system, or CNS. Occasionally, the use of these medications is associated with respiratory depression and hypotension.

The mood-stabilizing agent lithium may derive its antimanic effect from its ability to inhibit the release of the CNS neurotransmitters norepinephrine and dopamine from nerve terminals and synapses, and its antidepressant effect may be derived from its ability to increase CNS serotonin levels.⁴⁰ In some people, lithium may cause nausea, tremor, cognitive impairment and hypothyroidism, which may lead to a goiter—a diffuse, nontender, enlarged thyroid gland—and weight gain. Approximately 30 percent of patients who take lithium develop electrocardiogram changes, the most common of which are bradycardia and a benign, reversible reduction in the amplitude of T waves.⁴¹ Nephrotoxicity also may develop as evidenced by polyuria and polydipsia.

Valproate sodium and its enteric-coated divalproex formulation also is a mood-stabilizing agent. Its actions on inhibitory and excitatory amino acid systems and membrane-associated ion channels in the brain may be responsible for its stabilizing effect.⁴² Long-term use is associated with approximately 9 percent of patients developing leukopenia, 7 percent developing thrombocytopenia and a lesser percentage having a decrease in fibrinogen concentration.^{43,44}

Carbamazepine's mood-stabilizing effect also is believed to be derived from its ability to stabilize

TABLE 1

ADVERSE OROFACIAL REACTIONS TO SECOND-GENERATION ANTIPSYCHOTIC MEDICATIONS.*			
ADVERSE REACTION	MEDICATION		
	Risperidone	Olanzapine	Quetiapine
Xerostomia	+ [†]	+	+
Sialorrhea	+	+	+
Dysphagia	+	+	+
Sialadenitis	0 [‡]	0	0
Dysgeusia	+	0	+
Stomatitis	+	+	+
Gingivitis	+	+	+
Glossitis	0	+	+
Tongue Edema	+	+	+
Discolored Tongue	+	0	0
Bruxism	0	0	+
Miscellaneous	Toothache, tongue paralysis	Neck rigidity, facial edema, oral moniliasis, periodontal abscess	Buccoglossal syndrome, caries, oral ulcers, gingival hemorrhage

* Sources: Physicians' Desk Reference⁵⁴ and McEvoy.⁵⁵
[†] +: Yes.
[‡] 0: No.

episodes with severe agitation or severe depressive episodes that do not respond to medication.⁴⁹ The electrical currents used in ECT create massive neuronal electrical discharges in the CNS that result in a seizure. It is postulated that after a number of treatments, appropriate neuronal activity is restored.⁵⁰ ECT usually is given two to three times a week for several weeks until the patient improves. Approximately 90 percent of patients enter a remission within one to two weeks, which usually is quicker than for patients who take medications. Some psychiatrists recommend a dental examination for

sodium and potassium channels and the upregulation of GABA_B receptors.⁴⁵ Like valproate sodium, long-term use of carbamazepine is associated with decreased white blood cell and platelet counts.

SSRIs such as fluoxetine exert their antidepressant effect by preventing presynaptic neurons from reabsorbing serotonin from the synaptic cleft (the space between two neurons) for recycling. Thus, the concentration of serotonin in the cleft is heightened, and neuronal activity is enhanced.

Use of the majority of SSRIs frequently is associated with diarrhea, nausea, dizziness, insomnia, tremor, headache, sexual dysfunction (for example, decreased libido, ejaculatory dysfunction, erectile dysfunction and anorgasmia) and occasionally an increase in bleeding time.^{46,47} Bupropion, an atypical antidepressant, exerts its effects by preventing the reuptake of norepinephrine and dopamine from the synaptic cleft, thereby facilitating neural transmission.⁴⁸ SSRIs and bupropion are used much more frequently than the tricyclic antidepressant medications, as they are less likely to cause a switch to mania.⁴⁹

ECT is indicated for patients who have manic

their patients before ECT to determine if the anesthesiologist needs to adjust the procedure because of dentures or problem teeth.⁵¹ Positioning the electrodes farther away from the masseter muscles is associated with decreased dental injuries.⁵²

Psychosocial treatment provided as an adjunct to medication appears to decrease the likelihood and severity of recurrent episodes and improve the patient's quality of life. Initiated during or shortly after an acute manic or depressive episode, the therapeutic protocol encourages adhering to the drug regimen, educating the patient and family about the illness (for example, being able to recognize early signs of relapse) and offering practical techniques for coping with stressors such as loss of an important relationship or changes in work, school or home life.⁵³

DENTAL FINDINGS

In a review of the U.S. Food and Drug Administration's medication package inserts that accompany each medication used to treat BD and an analysis of the current medical literature, the

authors identified adverse orofacial reactions that may occur.^{54,55} The antipsychotic agents have been shown to cause xerostomia, dysgeusia and stomatitis (Table 1). The benzodiazepines are associated with both xerostomia and sialorrhea (Table 2). The mood-stabilizing agent lithium has been shown to cause xerostomia and dysgeusia, while valproate sodium and carbamazepine have been associated with xerostomia and glossitis (Table 3).^{56,57} A majority of the antidepressant medications have been shown to cause xerostomia (which affects approximately 18 percent of patients), stomatitis and glossitis, and a smaller percentage of these medications have been identified as causing sialadenitis, gingivitis, and edema and discoloration of the tongue (Table 4). Bupropion recently has been linked with causing hyperesthesia of the ophthalmic and maxillary divisions of the trigeminal nerve, although the mechanism remains ill defined.⁵⁸

Two studies have catalogued the extent of dental disease among patients who have BD (box, page 1215).^{59,60} Patients admitted to the hospital for the acute management of a manic episode frequently had oral mucosa and gingiva that were severely abraded and on occasion lacerated, secondary to overvigorous use of oral health devices such as toothbrushes, dental floss and water dental stimulators. Patients who had a history of three or more admissions for a manic episode often had advanced cervical toothbrush abrasion and occlusal attrition consistent with severe bruxism. Patients admitted during a depressive episode had an almost total disregard for proper oral hygiene. And those who had a history of three or more hospital admissions for a depressive episode had the highest decayed, missing and filled teeth, or DMFT, count, as well as the most severe periodontal disease.

People whose BD was in remission and who

TABLE 2

ADVERSE OROFACIAL REACTIONS TO BENZODIAZEPINES.*		
ADVERSE REACTION	MEDICATION	
	Lorazepam	Clonazepam
Xerostomia	0 [†]	+ [‡]
Sialorrhea	+	+
Dysphagia	0	0
Sialadenitis	0	0
Dysgeusia	0	+
Stomatitis	0	0
Gingivitis	0	+
Glossitis	0	0
Tongue Edema	0	0
Discolored Tongue	0	0
Bruxism	0	0
Miscellaneous	None	Coated tongue, feelings of a thick tongue, periorbital edema, toothache, pyrosis, jaw pain

* Sources: Physicians' Desk Reference⁵⁴ and McEvoy.⁵⁵
[†] 0: No.
[‡] +: Yes.

went to an outpatient dental clinic also were noted to have extensive dental disease. The most common chief complaint of these patients was xerostomia and a loss in taste acuity. Patients with the highest DMFT count and most advanced cases of periodontal disease had the longest history of lithium ingestion and the greatest number of hospital admissions for BD.

People who have a depressive episode are at high risk of developing rampant dental caries because of a mood-induced disinterest in performing oral hygiene procedures, decreased whole-mouth and parotid gland salivary output, a preference for carbohydrates and high *Lactobacillus* count.⁶¹⁻⁶⁴ In addition to and magnifying the severity of these problems are some of the adverse affects of the medications used to treat BD. Antipsychotic medications, mood-stabilizing agents and antidepressant medications cause xerostomia by interfering with salivary gland function, and lithium and valproate sodium cause an intense craving for carbohydrates.^{65,66} Patients often respond to their xerostomia and carbohydrate cravings by drinking large quantities of cariogenic sugared beverages.⁶⁷

TABLE 3

ADVERSE OROFACIAL REACTIONS TO MOOD-STABILIZING MEDICATIONS.*

ADVERSE REACTION	MEDICATION		
	Lithium	Valproate Sodium	Carbamazepine
Xerostomia	+†	+	+
Sialorrhea	0‡	0	0
Dysphagia	0	0	0
Sialadenitis	+	0	0
Dysgeusia	+	+	0
Stomatitis	+	0	+
Gingivitis	0	0	0
Glossitis	0	+	+
Tongue Edema	0	0	0
Discolored Tongue	0	0	0
Bruxism	0	0	0
Miscellaneous	Carbohydrate craving	Periodontal abscess, sinusitis, neck pain, carbohydrate craving	Erythema multiforme, carbohydrate craving

* Sources: Physicians' Desk Reference⁵⁴ and McEvoy.⁵⁵
 † +: Yes.
 ‡ 0: No.

People who have a depressive episode also are at high risk of developing periodontitis.⁶⁸⁻⁷¹ It is hypothesized that neglect of oral hygiene, increase in smoking and altered immune response facilitate increased colonization of pathological bacteria. This leads to the breakdown of the periodontal attachment.⁷²⁻⁷⁷ Periodontitis may be exacerbated in some patients who receive SSRIs, as these medications have been implicated in causing a movement disorder that includes bruxism.^{78,79} Bruxism may arise because these medications increase extrapyramidal levels of serotonin, thereby inhibiting dopaminergic pathways that control movements.⁸⁰

DENTAL MANAGEMENT

Some patients who receive psychiatric treatment for BD may be reluctant to admit it because of perceived stigma associated with mental illness. To overcome such barriers and obtain necessary information, dentists should exhibit a supportive, nonjudgmental attitude and advise patients that such information will be held confidential and is indispensable to the provision of safe dental care.

Patients who are experiencing an episode of mania or depression may be uncooperative and irritable during dental treatment, appear unappreciative and have numerous complaints that are inconsistent with objective findings. Before a patient begins dental treatment, the dentist should consult with the patient's psychiatrist after informing the patient. Dentists should ask the psychiatrist for the patient's current psychological status and psychiatric medication regimen. The dentist also should ask the psychiatrist about the patient's history of alcohol or substance abuse. Patients who have a history of alcohol abuse should undergo liver function tests that include blood serum levels of albumin and total proteins, a complete blood cell count and a

coagulation profile that includes prothrombin time and partial thromboplastin time.

Preventive dental education is paramount for these patients and their families. They should receive instruction in proper toothbrushing and flossing methods that maximize removal of dental plaque. Artificial salivary products should be prescribed for patients who have signs of xerostomia. Dental treatment should consist of subgingival scaling, root planing and curettage, caries control and restorative treatment. Profound local anesthesia should be achieved in these often-anxious patients before the procedures are performed.

Dentists should perform clinical examinations and oral prophylaxis at three-month follow-up visits and apply a fluoride gel with a fluorine concentration of at least 1.0 percent in patients who have BD. They also should correct any defects in the natural dentition or prostheses during recall visits, as patients may experience enhanced self-esteem as a result of dental treatment, which may contribute to the psychotherapeutic aspect of management.

Adverse drug interactions may occur between

TABLE 4

ADVERSE OROFACIAL REACTIONS TO ANTIDEPRESSANT MEDICATIONS.*						
ADVERSE REACTION	MEDICATION					
	Citalopram	Fluoxetine	Fluvoxamine	Paroxetine	Sertraline	Bupropion
Xerostomia	+ [†]	+	+	+	+	+
Sialorrhea	0 [‡]	0	0	0	0	0
Dysphagia	0	0	0	0	0	0
Sialadenitis	0	+	0	+	0	0
Dysgeusia	+	+	+	+	+	+
Stomatitis	+	+	+	+	+	+
Gingivitis	+	+	+	+	0	+
Glossitis	+	+	+	+	+	+
Tongue Edema	0	0	0	+	+	0
Discolored Tongue	0	+	0	+	0	0
Bruxism	+	+	0	+	+	+
Miscellaneous	None	Jaw pain, buccoglossal syndrome	Toothache	Caries, dysphagia	Dysphagia, gingival hyperplasia	Toothache, oral edema, dysphagia

* Sources: Physicians' Desk Reference⁵⁴ and McEvoy.⁵⁵
[†] +: Yes.
[‡] 0: No.

BOX

COMMON ORAL MANIFESTATIONS OF BIPOLAR I DISORDER.*

CAUSE	ORAL MANIFESTATION
Manic Phase	Toothbrush/dental floss abrasion of mucosa and gingiva Toothbrush abrasion of cervical aspects of teeth
Depressive Phase	Disregard of oral hygiene High decayed, missing and filled teeth count Severe periodontal disease
Medication Effects	Xerostomia/Sialorrhea Dysgeusia Stomatitis/Glossitis Bruxism

* Sources: Friedlander⁵⁸ and Friedlander and colleagues.⁵⁹

the medications used in dentistry and those used to treat BD.^{81,82} The antifungal agent ketoconazole has been shown to decrease the metabolism of quetiapine. Antihistamines, muscle relaxants, ketoconazole and opioid analgesics enhance the sedative effects of lorazepam and clonazepam. Erythromycin and aspirin inhibit the metabolism

of valproate sodium. Erythromycin, clarithromycin and propoxyphene may inhibit the metabolism of carbamazepine and permit the emergence of its side effects. Doxycycline is rendered less effective because carbamazepine has been shown to accelerate its metabolism. Nonsteroidal anti-inflammatory drugs and metronidazole decrease the renal clearance of lithium and can allow the build-up of toxic levels of the drug.^{83,84} Benzodiazepines such as diazepam and midazolam also must be used with caution because of the potential for excessive CNS depression when they are taken concurrently with lithium. Narcotic analgesics may be less effective than expected because lithium decreases the analgesic effect of opiates in some patients. Codeine, benzodiazepines and ery-



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thromycin should be used cautiously and in reduced dosages in patients receiving SSRIs because the antidepressant medications inhibit the metabolism of these medications.

CONCLUSION

We emphasize that dentists' working in concert with physicians and mental health professionals has much to offer patients who have BD. In this article, we provided dentists with an overview of BD's manifestations and complex pharmacological management so they can feel confident in offering patients who have BD a full range of dental treatment options. ■

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1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington: American Psychiatric Association; 1994:317-89.
2. McElroy SL, Keck PE Jr, Strakowski SM. Mania, psychosis, and antipsychotics. *J Clin Psychiatry* 1996;57(supplement 3):14-26.
3. Sherwood Brown E, Suppes T, Adinoff B, Rajan Thomas N. Drug abuse and bipolar disorder: comorbidity or misdiagnosis? *J Affect Disord* 2001;65(2):105-15.
4. Montgomery DB. ECNP Consensus Meeting March 2000 Nice: guidelines for investigating efficacy in bipolar disorder. *European College of Neuropsychopharmacology. Eur Neuropsychopharmacol* 2001;11(1):79-88.
5. Cassidy F, Ahearn EP, Carroll BJ. Substance abuse in bipolar disorder. *Bipolar Disord* 2001;3(4):181-8.
6. Hilty DM, Brady KT, Hales RE. A review of bipolar disorder among adults. *Psychiatr Serv* 1999;50:201-13.
7. Simpson SG, Jamison KR. The risk of suicide in patients with bipolar disorders. *J Clin Psychiatry* 1999;60(supplement 2):53-6.
8. Tondo L, Baldessarini RJ. Reduced suicide risk during lithium maintenance treatment. *J Clin Psychiatry* 2000;61(supplement 9):97-104.
9. Murray CJ, Lopez AD. The global burden of disease: Summary. Cambridge, Mass.: Harvard School of Public Health; 1996.
10. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1994;51(1):8-19.
11. Goldberg JF, Kocsis JH. Depression in the course of bipolar disorder. In: Goldberg JF, Harrow M, eds. *Bipolar disorders*. Washington: American Psychiatric Press; 1999:129-48.
12. Leibenluft E. Women and bipolar disorder: an update. *Bull Menninger Clin* 2000;64(1):5-17.
13. Zarate CA Jr, Tohen M, Baraibar G, Zarate SB, Baldessarini RJ. Shifts in hospital diagnostic frequencies: bipolar disorder subtypes,

- 1981-1993. *J Affect Disord* 1997;43(1):79-84.
14. Sachs GS, Thase ME. Bipolar disorder therapeutics: maintenance treatment. *Biol Psychiatry* 2000;48:573-81.
15. Sachs GS. A 25-year-old woman with bipolar disorder. *JAMA* 2001;285:454-62.
16. Osby U, Brandt L, Correia N, Ekblom A, Sparen P. Excess mortality in bipolar and unipolar disorder in Sweden. *Arch Gen Psychiatry* 2001;58:844-50.
17. Simon GE, Unutzer J. Health care utilization and costs among patients treated for bipolar disorder in an insured population. *Psychiatr Serv* 1999;50:1303-8.
18. Begley CE, Annegers JF, Swann AC, et al. The lifetime cost of bipolar disorder in the US: an estimate of new cases in 1998. *Pharmacoeconomics* 2001;19(5 Pt 1):483-95.
19. Meltzer HY. Genetics and etiology of schizophrenia and bipolar disorder. *Biol Psychiatry* 2000;47(3):171-3.
20. Huxley NA, Parikh SV, Baldessarini RJ. Effectiveness of psychosocial treatments in bipolar disorder: state of the evidence. *Harv Rev Psychiatry* 2000;8(3):126-40.
21. Kupka RW, Nolen WA, Altshuler LL, et al. The Stanley Foundation Bipolar Network. 2: preliminary summary of demographics, course of illness and response to novel treatments. *Br J Psychiatry* 2001;178(supplement 41):S177-S83.
22. Gurling H, Smyth C, Kalsi G, et al. Linkage findings in bipolar disorder. *Nat Genet* 1995;10(1):8-9.
23. Papadimitriou GN, Dikeos DG, Karadima G, Avramopoulos D, Daskalopoulou EG, Stefanis CN. GABA-A receptor beta3 and alpha5 subunit gene cluster on chromosome 15q11-q13 and bipolar disorder: a genetic association study. *Am J Med Genet* 2001;105:317-20.
24. Manji HK, Lenox RH. The nature of bipolar disorder. *J Clin Psychiatry* 2000;61(supplement 13):42-57.
25. Strakowski SM, Del Bello MP, Adler C, Cecil DM, Sax KW. Neuroimaging in bipolar disorder. *Bipolar Disord* 2000;2(3 Pt 1):148-64.
26. Noga JT, Vladar K, Torrey EF. A volumetric magnetic resonance imaging study of monozygotic twins discordant for bipolar disorder. *Psychiatry Res* 2001;106(1):25-34.
27. Keck PE Jr, McElroy SL, Arnold LM. Bipolar disorder. *Med Clin North Am* 2001;85:645-61.
28. Brown ES, Bobadilla L, Rush AJ. Ketoconazole in bipolar patients with depressive symptoms: a case series and literature review. *Bipolar Disord* 2001;3(1):23-9.
29. Ferrier IN, MacMillan IC, Young AH. The search for the wandering thymostat: a review of some developments in bipolar disorder research. *Br J Psychiatry* 2001;178(supplement 41):S103-6.
30. Grunze H, Erfurth A, Amann B, Giupponi G, Kammerer C, Walden J. Intravenous valproate loading in acutely manic and depressed bipolar I patients. *J Clin Psychopharmacol* 1999;19:303-9.
31. Licht RW, Bysted M, Christensen H. Fixed-dosed risperidone in mania: an open experimental trial. *Int Clin Psychopharmacol* 2001;16(2):103-10.
32. Sachs GS, Printz DJ, Kahn DA, Carpenter D, Doucherty JP. The Expert Consensus Guidelines Series: medication treatment of bipolar disorder 2000. *Postgrad Med* 2000 (special no):1-104.
33. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biol Psychiatry* 2000;48:593-604.
34. Sernyak MJ, Godleski LS, Griffin RA, Mazure CM, Woods SW. Chronic neuroleptic exposure in bipolar outpatients. *J Clin Psychiatry* 1997;58(5):193-5.
35. Levine J, Chengappa KN, Brar JS, et al. Psychotropic drug prescription patterns among patients with bipolar I disorder. *Bipolar Disord* 2000;2(2):120-30.
36. Cookson J. Use of antipsychotic drugs and lithium in mania. *Br J Psychiatry* 2001;178(supplement 41):S148-56.
37. Guille C, Sachs GS, Ghaemi SN. A naturalistic comparison of clozapine, risperidone, and olanzapine in the treatment of bipolar disorder. *J Clin Psychiatry* 2000;61:638-42.
38. Glick ID, Suppes T, DeBattista C, Hu RJ, Marder S. Psychopharmacologic treatment strategies for depression, bipolar disorder, and schizophrenia. *Ann Intern Med* 2001;134(1):47-60.
39. Glick ID, Murray SR, Vasudevan P, Marder SR, Hu RJ. Treatment with atypical antipsychotics: new indications and new populations. *J Psychiatr Res* 2001;35(3):187-91.
40. Schou M. Perspectives on lithium treatment of bipolar disorder: action, efficacy, effect on suicidal behavior. *Bipolar Disord* 1999;1(1):5-10.
41. Bucht G, Smigan L, Wahlin A, Eriksson P. ECG changes during lithium therapy: a prospective study. *Acta Med Scand* 1984;216(1):101-4.

42. Johannessen CU. Mechanisms of action of valproate: a commentary. *Neurochem Int* 2000;37(2-3):103-10.
43. Muller-Oerlinghausen B, Retzow A, Henn FA, Giedke H, Walden J. Valproate as an adjunct to neuroleptic medication for the treatment of acute episodes of mania: a prospective, randomized, double-blind, placebo-controlled, multicenter study. *European Valproate Mania Study Group. J Clin Psychopharmacol* 2000;20(2):195-203.
44. Bowden CL, Calabrese JR, McElroy SL, et al. A randomized, placebo-controlled 12-month trial of divalproex and lithium in treatment of outpatients with bipolar I disorder. *Divalproex Maintenance Study Group. Arch Gen Psychiatry* 2000;57:481-9.
45. Ketter TA, Post RM. Clinical pharmacology in pharmacokinetics of carbamazepine. In: Joffe RT, Calabrese JR, eds. *Anticonvulsants in mood disorders*. New York: Dekker; 1994:43-92.
46. Edwards JG, Anderson I. Systematic review and guide to selection of selective serotonin reuptake inhibitors. *Drugs* 1999;57:507-33.
47. Spigset O. Adverse reactions to selective serotonin reuptake inhibitors: reports from a spontaneous reporting system. *Drug Saf* 1999;20:277-87.
48. Goodnick PJ, Dominguez RA, DeVane CL, Bowden CL. Bupropion slow-release response in depression: diagnosis and biochemistry. *Biol Psychiatry* 1998;44:629-32.
49. Frances AJ, Kahn DA, Carpenter D, Docherty JP, Donovan SL. The expert consensus guidelines for treating depression in bipolar disorder. *J Clin Psychiatry* 1995;59(supplement 4):73-9.
50. Daly JJ, Prudic J, Devanand DP, et al. ECT in bipolar and unipolar depression: differences in speed of response. *Bipolar Disord* 2001;3(2):95-104.
51. Dubovsky SL. Electroconvulsive therapy. In: Kaplan HI, Sadock BJ, eds. *Kaplan and Sadock's comprehensive textbook of psychiatry*. 6th ed. Baltimore: Williams & Wilkins; 1995:2129-40.
52. Bailine SH, Rifkin A, Kayne E, et al. Comparison of bifrontal and bitemporal ECT for major depression. *Am J Psychiatry* 2000;157(1):121-3.
53. Scott J. Cognitive therapy as an adjunct to medication in bipolar disorder. *Br J Psychiatry* 2001;178(supplement 41):S164-8.
54. Physicians' desk reference. 56th ed. Montvale, N.J.: Medical Economics; 2002.
55. McEvoy GK. *AHFS drug information 2002*. Bethesda, Md.: American Society of Health-System Pharmacists; 2002.
56. Madinier I, Berry N, Chichmanian RM. Drug-induced oral ulcerations (in French). *Ann Med Interne (Paris)* 2000;151:248-54.
57. Tritsarolis K, Gromada J, Jorgensen TD, Nauntofte B, Dissing S. Reduction in the rate of inositol 1,4,5-trisphosphate synthesis in rat parotid acini by lithium. *Arch Oral Biol* 2001;46:365-73.
58. Amann B, Hummel B, Rall-Autenrieth H, Walden J, Grunze H. Bupropion-induced isolated impairment of sensory trigeminal nerve function. *Int Clin Psychopharmacol* 2000;15(2):115-6.
59. Friedlander AH. Lithium/bipolar disorder: their effects on salivary flow, dental caries and periodontal disease. In: Birch NJ, ed. *Lithium: Inorganic pharmacology and psychiatric use—Proceedings of the Second British Lithium Congress*, Wolverhampton, England, Sept. 6-9, 1987. Oxford, England: IRL Press; 1988:77-8.
60. Friedlander AH, Friedlander IK, Birch NJ. Prevalence of dental diseases among patients on long-term lithium therapy. In: Birch NJ, Padgham C, Hughes MS, eds. *Lithium in medicine and biology*. Carnforth, England: Marius Press; 1993:91-7.
61. Amsterdam JD, Settle RG, Doty RL, Abelman E, Winokur A. Taste and smell perception in depression. *Biol Psychiatry* 1987;22:1481-5.
62. Anttila SS, Knuutila ML, Sakki TK. Depressive symptoms favor abundant growth of salivary lactobacilli. *Psychosom Med* 1999;61:508-12.
63. Wallin MS, Rissanen AM. Food and mood: relationship between serotonin and affective disorders. *Acta Psychiatr Scand* 1994;377(supplement):36-40.
64. Christensen L, Somers S. Comparison of nutrient intake among depressed and nondepressed individuals. *Int J Eat Disord* 1996;20(1):105-9.
65. Chacko RC, Marsh BJ, Marmion J, Dworkin RJ, Telschow R. Lithium side effects in elderly bipolar outpatients. *Hillside J Clin Psychiatry* 1987;9(1):79-88.
66. Nemeroff CB. An ever-increasing pharmacopoeia for the management of patients with bipolar disorder. *J Clin Psychiatry* 2000;61(supplement 13):19-25.
67. Elmslie JL, Mann JI, Silverstone JT, Williams SM, Romans SE. Determinants of overweight and obesity in patients with bipolar disorder. *J Clin Psychiatry* 2001;62:486-91.
68. Elter JR, Beck JD, Slade GD, Offenbacher S. Etiologic models for incident periodontal attachment loss in older adults. *J Clin Periodontol* 1999;26(2):113-23.
69. Monteiro da Silva AM, Oakley DA, Newman HN, Nohl FS, Lloyd HM. Psychosocial factors and adult onset rapidly progressive periodontitis. *J Clin Periodontol* 1996;23:789-94.
70. da Silva AM, Newman HN, Oakley DA. Psychosocial factors in inflammatory periodontal disease: a review. *J Clin Periodontol* 1995;22:516-26.
71. Kurer JR, Watts TL, Weinman J, Gower DB. Psychological mood of regular dental attenders in relation to oral hygiene behaviour and gingival health. *J Clin Periodontol* 1995;22(1):52-5.
72. Corvin A, O'Mahony E, O'Regan M, et al. Cigarette smoking and psychotic symptoms in bipolar affective disorder. *Br J Psychiatry* 2001;179:35-8.
73. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. *J Clin Periodontol* 2001;28:283-95.
74. Krall EA, Garvey AJ, Garcia RI. Alveolar bone loss and tooth loss in male cigar and pipe smokers. *JADA* 1999;130(1):57-64.
75. Moss ME, Beck JD, Kaplan BH, et al. Exploratory case-control analysis of psychosocial factors and adult periodontitis. *J Periodontol* 1996;67(10 supplement):1060-9.
76. Schleifer SJ, Keller SE, Bartlett JA, Eckholdt HM, Delaney BR. Immunity in young adults with major depressive disorder. *Am J Psychiatry* 1996;153:477-82.
77. Kinane DF. Aetiology and pathogenesis of periodontal disease. *Ann R Australas Coll Dent Surg* 2000;15:42-50.
78. Gerber PE, Lynd LD. Selective serotonin-reuptake inhibitor-induced movement disorders. *Ann Pharmacother* 1998;32:692-8.
79. Wise M. Citalopram-induced bruxism. *Br J Psychiatry* 2001;178:182.
80. Bostwick JM, Jaffee MS. Buspirone as an antidote to SSRI-induced bruxism in 4 cases. *J Clin Psychiatry* 1999;60:857-60.
81. Hersh EV. Adverse drug interactions in dental practice: interactions involving antibiotics. *JADA* 1999;130:236-51.
82. Ketter TA, Flockhart DA, Post RM, et al. The emerging role of cytochrome P450 3A in psychopharmacology. *J Clin Psychopharmacol* 1995;15:387-98.
83. Haas DA. Adverse drug interactions in dental practice: interactions associated with analgesics. *JADA* 1999;130:397-407.
84. Callahan AM, Marangell LB, Ketter TA. Evaluating the clinical significance of drug interactions: a systematic approach. *Harv Rev Psychiatry* 1996;4(3):153-8.