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Promoting Quality, Safety, and Efficiency

CLINICAL PRACTICE

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“As a community-based primary care physician I see the emergence of hospitalists as an opportunity. But I have serious concerns.”

FROM

“It’s not my patient. I’m just covering.”

HOWARD O. KERPEN, MD

FREE ONLINE CME CREDITS

Advocating for consumers— and caregivers, too

▶ PETER V. LEE, JD

“It’s not my patient. I’m just covering.”

▶ HOWARD O. KERPEN, MD

Measuring up: Quality improvement efforts yield success

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Improving clinical quality and efficiency with simple practice adjustments

▶ CHRISTINE POCHA, MD, PHD

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INDUSTRY-SUPPORTED ARTICLE

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psychotic and mood disorders
in primary care

ABOUT THIS ISSUE

We are so excited about the launch of our new and improved Web site for *Current Clinical Practice* (www.currentclinicalpractice.com) that we want you to see it for yourself. So, in this issue, we are providing a brief abstract of each journal article and asking you to go online to read the full text and complete the CME posttest electronically.

Beyond journal articles, on the new Web site you'll find high-quality industry-supported CME supplements on clinical topics. This month's topic is "Recognizing and managing psychotic and mood disorders in primary care," offering additional CME credits. You'll also find an interactive Instant Poll, a list of our most-read articles, a library of related articles drawn from Dowden Health Media's medical journals, links to important pay-for-performance and quality conferences, and much more.

We hope you are as pleased with the depth and utility of the new Web site as we are, and we look forward to bringing you more information about performance and quality improvement in medicine in 2009.

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Advocating for consumers—and caregivers, too The Consumer-Purchaser Disclosure Project

Peter V. Lee, JD

Executive Director for National Health Policy, Pacific Business Group on Health
Co-chair, Consumer-Purchaser Disclosure Project
San Francisco, California

Patients want objective appraisals of the care doctors provide. And employers want to know that their dollars are buying the highest quality and most efficient care. In response, health plans and private vendors have created tools to help individuals find “better” doctors. But the results are often incomplete and difficult to trust.

Until recently, the voices heard most often in the health care arena belonged to hospitals, health plans, and physicians. The Consumer-Purchaser Disclosure Project was created to give a louder voice to individuals, consumer groups, and employers, and to promote the availability and use of valid performance information.

Working with the American Medical Association, the American Academy of Family Physicians, and the American College of Physicians, the Disclosure Project identified a number of points that health care plans must incorporate in reporting physician performance. The Patient Charter, launched by the Project in April 2008, incorporates these points. Many major health plans have already agreed to follow the Patient Charter (<http://healthcaredisclosure.org/activities/charter/>).

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“It’s not my patient. I’m just covering.” Hospitalists, PCPs, and the fragmentation of medical care

Howard O. Kerpen, MD

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Not long ago, I was rounding on one of my patients in the hospital of an academic medical center. Because my patient was suffering from hypertension in addition to a number of other conditions, I sought out the teaching attending—a hospitalist and recent graduate of our internal medicine program—to discuss a current article on the pathogenesis of resistant hypertension. Her response took me aback. “With all due respect, Dr Kerpen, I really don’t have to know about that.” I had an epiphany—her apathetic attitude was yet another example of the “It’s not my patient, I’m just covering” fragmentation of patient care that is evident not just in our hospital but perhaps in medicine as a whole. Does the proliferation of the hospitalist movement represent this fragmentation and the non-patient-centered approach being observed in the rest of medicine?

Wachter and Goldman coined the term “hospitalist” in 1996 to describe a physician whose role is to care for hospitalized patients and return responsibility to their “regular” doctor upon discharge. Since then, hospitalists have become the fastest growing group of physicians in the United States, and if this trend continues their numbers will swell to between 20,000 and 30,000.

As a community-based primary care physician with responsibilities for patient care and education in addition to hospital quality, I see the emergence of hospitalists as an opportunity. But I have serious concerns.

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Measuring up: Quality improvement efforts yield success

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AMA Vice President

Clinical Quality and Patient Safety

The Physician Consortium for Performance Improvement
Chicago, Illinois

It is gratifying when the hoped-for benefits of a new approach materialize. When secondary rewards are realized as well, that is a boon. Such is the case with the Physician Quality Reporting Initiative (PQRI) launched in 2007 by the Centers for Medicare & Medicaid Services.

Of the more than 109,000 health care providers who participated in the 2007 program, 56,700 (52%) successfully completed reporting requirements and earned the 1.5% bonus on total Medicare payments, a payout of more than \$36 million to participating physicians. Overall, the level of involvement in the 2007 initiative was strong, especially considering the relatively rapid ramp-up for the program and the small financial incentive. Though official figures are not yet available for 2008, a preliminary assessment indicates that participation this year is even stronger than last.

PCPI'S CONTRIBUTION TO THIS PROGRESS

Of the 175 measures endorsed by the National Quality Forum and selected for inclusion in the 2009 PQRI program, 126 (72%) have been developed by the AMA Physician Consortium for Performance Improvement (PCPI).

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RESEARCH ARTICLE

4

Improving clinical quality and efficiency with simple practice adjustments.

How one VA clinic's dedicated care team created a novel patient-education forum and streamlined scheduling

Christine Pocha, MD, PhD

Medical Director, Hepatitis C Resource Center

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Minneapolis, Minnesota

PURPOSE: The high prevalence of chronic hepatitis C virus (HCV) among veterans requires significant health care resources. Our goal was to improve clinic efficiency to insure that the delivery of health care was prompt and available to more patients.

METHOD: We collected data retrospectively from workload reports in 2004 and 2006. Interventions included creating a care team and a group education class, optimizing the scheduling process to streamline the provider visit, and implementing order menus.

RESULTS: In 2004 and 2006 respectively, appointment slots numbered 880 and 735, with 677 and 700 slots filled. Used capacity increased by 18%, and clinic efficiency rose by a factor of 2.25; the no-show rate decreased by 5%. The HCV education class opened 82 appointment slots for new consultations (or 164 for follow-ups). Corrected for no-shows and cancellations, 2340 minutes of clinic time were saved. The number of patients followed for HCV treatment increased by 77%.

CONCLUSION: Clinic management and patient care in the hepatology clinic improved. A dedicated team is the keystone for continuity of care for patients with chronic diseases. The HCV group class assured standardized education. This project may easily be applied to other specialty clinics.

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LEARNING OBJECTIVES

After reviewing this material, clinicians should be better able to:

- Achieve early and accurate diagnosis of patients with mood disorders
- Utilize available screening tools effectively
- Understand the mechanisms of action, hepatic effects, and other metabolic effects of available agents and their potential impact on treatment
- Develop an effective treatment plan that includes monotherapy or combination therapy
- Select the most appropriate agent(s) for short- and long-term treatment to meet individual patient needs

TARGET AUDIENCE

Psychiatrists, primary care physicians, and other health care professionals who treat patients with psychotic and mood disorders

CME ACCREDITATION STATEMENT

The University of Cincinnati designates this educational activity for a maximum of 2.5 AMA PRA Category 1 credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. This CME activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the sponsorship of the University of Cincinnati College of Medicine. The University of Cincinnati College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

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THE FACULTY HAS REPORTED THE FOLLOWING:

DR NASRALLAH reports that he is on the advisory board of Abbott, AstraZeneca, Cephalon, Janssen, Pfizer, and Vanda Pharmaceuticals; is a consultant for AstraZeneca, Janssen, Pfizer, and Vanda Pharmaceuticals; receives grants from AstraZeneca, Forest Laboratories, Janssen, Otsuka America Pharmaceutical Inc., Pfizer, Roche, and sanofi-aventis; and is on the speakers bureau of AstraZeneca, Janssen, and Pfizer.

DR BLACK reports that he is a consultant for Forest Laboratories and Jazz Pharmaceuticals and receives grant(s) from Forest Laboratories.

DR GOLDBERG reports that he is on the advisory board, speakers bureau, and serves as a consultant for AstraZeneca, Eli Lilly & Co, and GlaxoSmithKline.

DR PARISER reports that he receives grants from Pfizer and is on the speakers bureau for AstraZeneca, GlaxoSmithKline, and Pfizer.

DR MUZINA reports that he is on the advisory board of AstraZeneca and Bristol-Myers Squibb; and is on the speakers bureau of AstraZeneca, Bristol-Myers Squibb, Pfizer, Sepracor, and Wyeth.

PLANNING COMMITTEE: Kay Weigand, University of Cincinnati; and Kristen Georgi, Charles Williams, and Katherine Wandersee for Dowden Health Media have disclosed no relevant financial relationship(s) with any commercial interests.

No off-label uses of drugs or devices are discussed in this supplement.

None of the atypical antipsychotic agents have been approved in the psychosis or agitation of dementia, and the FDA has issued a class-effect black-box warning regarding the increased mortality in geriatric patients treated with atypical antipsychotics compared to those treated with placebo.

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CURRENT CLINICAL PRACTICE

Recognizing and managing psychotic and mood disorders in primary care

INTRODUCTION > HENRY A. NASRALLAH, MD

The diagnosis and management of psychotic and mood disorders is an evolving process and an important clinical topic for primary care clinicians (PCPs). Although many reports exist on the prevalence and treatment of depression in primary care, far less information is available about patients in this setting with depression accompanied by symptoms of mania or hypomania.¹

To facilitate a dialogue on the identification and treatment of psychotic and mood disorders, we invited 4 expert faculty members to present actual patient cases followed by a panel discussion in which the collective experience of all the faculty lends further practical insights into the nuances of management of such patients in both inpatient and outpatient settings. In particular, these cases underscore the importance of being alert to critical clues in a patient's history or the family's history. A larger version of this panel discussion appears in a supplement to the December 2008 issue of CURRENT PSYCHIATRY. We've extracted the portion that we felt would be of most interest to primary care providers.

The case selected for presentation here is by David Muzina, MD, and concerns a 20-year-old man who was referred for psychiatric evaluation by his PCP and psychologist for treatment of mood swings, anxiety, and confusion. He had been given sertraline and then venlafaxine, but discontinued both medications on his own. His symptoms began rather abruptly 14 months earlier, coinciding with an intense program of weight lifting and supplement use to change his self-described smallness. Profound, persistent sadness and feeling "dead inside" were his chief complaints, and they had led to a break-up with his girlfriend, which distressed him greatly and preoccupied his thinking. He also believed his parents were hiding from him the truth of a significant birth defect.

Following the case presentation is a faculty discussion of several pivotal issues in the management of mood disorders:

- Pitfalls to avoid during the diagnostic evaluation
- Pros and cons of monotherapy and combination therapy
- Mechanisms of action of available medications and implications for an effective treatment plan
- Suggestions for enabling patient compliance with prescribed regimens

We hope the insights you glean from this exchange of practical clinical issues will enhance and confirm your own approach to diagnosing and treating patients with psychotic and mood disorders.

REFERENCE

1. Das AK, Olfson M, Gameroff MJ, et al. Screening for bipolar disorder in a primary care practice. JAMA. 2005;293:956-963.

Depression and anxiety: Distinguishing unipolar and bipolar disorders

Presented by

DAVID J. MUZINA MD CLEVELAND CLINIC, CLEVELAND, OHIO

The use of steroids and supplements can complicate the clinical picture in a young man with mood swings, anxiety, and depression referred for psychiatric evaluation by his primary care clinician and psychologist.

Identifying information: A 20-year-old single man was referred by his primary care physician and a psychologist for medical management of mood swings, anxiety, and confusion.

Chief complaint: The patient reported unremitting sadness that had lasted more than a year, and said that he generally felt “dead inside” or “like a zombie.” He was often ruminative and irritable, with difficulty concentrating.

History of present illness: The young man’s sadness and disagreeable sensations were relieved only for periods of 3 to 4 days when he felt more worried than sad. It was during these intervals of worry that he grew more ruminative, tired, and irritable, and said he could not “sort out” his thoughts.

The patient could not recall when he last felt well enough to have fun with friends. He ruminated about the past, often trying to change it in his mind and thereby causing himself to become confused about what was real and what he might have imagined to be real. In particular, he was preoccupied with the recent loss of a relationship with a girl, which began in high school. He blamed the loss on his moodiness. However, he also acknowledged that he briefly dated her younger sister, a short time after which the girlfriend abruptly stopped returning

his calls, telling him it was payback for dating her sister. The patient spent a great deal of time online looking at his ex-girlfriend’s MySpace social-interaction page, which only caused him to feel worse.

He blamed himself for everything that was wrong in his life and struggled with thoughts that people were talking and thinking about him negatively. Because he believed he was physically too small, he exercised regularly to stay in good shape.

Medications and allergies: The referring primary care physician and psychologist had prescribed sertraline 100 mg/d for 3 weeks. They then switched him to venlafaxine 225 mg/d which he took for 4 to 5 weeks. However, the patient stopped taking both drugs on his own initiative because they made him feel numb, and he also thought they made him feel more depressed. In the week before the initial psychiatric evaluation, his father had given him some sleeping medications because he was often tense, keyed up, and unable to relax in the evenings and around bedtime. They did not help. Otherwise, this young man had not been taking any medications during the previous 6 months.

Psychiatric history: The patient had never been hospitalized and denied

any suicidal or homicidal ideation. As mentioned, he sometimes thought he could undo the past by some ritualistic mental action.

The young man was an only child and spent a lot of time talking about this. He denied any history of childhood trauma. However, he held an unusual suspicion that his parents were hiding a birth defect from him, and that this defect was in some manner related to his current issues and difficulties. He did not give any more details about this suspicion, saying, “Every time I ask them about it, they tell me I’m crazy and just make a joke about it.” His mother reported that it took about 10 years to conceive, but there were no complications with the pregnancy or delivery.

The patient received no intervention during the first 6 months of the current episode, when his family doctor was contacted. The doctor referred the patient to a psychologist for counseling, and the psychologist quickly referred him back to the doctor, believing that the young man needed a prescription for antidepressant medication.

His mother said he was drinking alcohol more regularly while on his medications, and that he was probably not fully compliant with the antidepressant regimens. He was never prescribed benzodiazepines for his anxiety and tension, apparently due to concern about abuse potential.

Medical history: The patient reported no medical problems connected with his mental symptoms, and he specifically denied any history of cardiovascular disease, seizures, or head injury.

Family history: The mother had been diagnosed with situational anxiety and depression and was taking fluoxetine. A paternal aunt was taking sertraline for a diagnosis of panic disorder. There was no known family history of schizophrenia, bipolar disorder, or suicide.

Social history: The patient had always been social, had no developmental delays, and did well academically until his senior year in high school when his grades declined. He withdrew from friends and began experiencing anxiety and periods of sadness. It was during this time that he was working out more vigorously and using dietary supplements.

The patient still lived at home with his parents. Although he finished high school, he did not enroll in college. He had no specific plans for the future and was working part-time at a fast food restaurant.

Review of systems: He had not experienced panic attacks, excessive physical rituals or compulsions, nightmares, or flashbacks. He worried chronically in the past year, experiencing poor sleep, restlessness, and muscle tension.

On direct questioning, the patient denied hallucinations, thought insertion, or broadcasting. However, referential thinking did seem to weave through some of his history.

There were no clear periods of euphoria or classic manic symptoms. He often had been irritable and had a difficult time separating the irritability from the depression. Periodically, his anxiety rose above the daily baseline of tension and on-edge feelings to include confused thinking, which he described not as racing thoughts but as having many simultaneous thoughts that aggravated the tension and interrupted sleep.

The last 6 months were dominated by fragmented sleep, decreased appetite and libido, pervasive guilt with passive thoughts of death, but absolutely no suicidal ideation.

Substance use history: He rarely used alcohol, but admitted to drinking more heavily during his senior year of high school. He also denied any illicit substance abuse. He had used the supplements purchased over the counter and online; however, he denied using injectable steroids. He would also augment his workouts with large amounts of energy drinks.

Although he denied current use of dietary supplements, he admitted to having done so in the past. He had used several herbal preparations as well as creatinine, protein supplements, and androstenedione that he would buy at nutrition stores or on the Internet to increase his testosterone levels and promote muscle growth. He conceded that he might have been more irritable, aggressive, and volatile while taking the supplements for his workouts. Though he claimed not to be using these supplements at present, he still had them and refused to discard them, saying he did not want to waste more than \$300.

Physical examination: The patient was in good general health, clearly well-developed with increased muscle mass. Neurologic exam was unremarkable.

Mental status examination: This was largely within normal limits, although the patient exhibited a restricted affect when discussing his ex-girlfriend, in contrast to expected sadness or tearfulness. His thought process was logical, linear, and goal-directed. Cognitive testing, while limited to a brief Mini Mental State Exam, detected only some difficulty doing the serial seven test, but his effort was poor.

Assessment: The initial psychiatric impression was that while there were a number of diagnostic considerations,

this young man most likely suffered from a mood disorder. Although he was never clearly manic, the presence of significant irritability and “crowded” thoughts along with the cyclical nature of his symptoms suggested Bipolar II disorder.

Provisional diagnosis:

- AXIS I:** Bipolar disorder, mixed episode, with psychotic features
- R/O substance-induced mood disorder with psychotic features
 - R/O paranoid schizophrenia
 - R/O schizoaffective disorder, bipolar subtype

AXIS II: Deferred

AXIS III: None

AXIS IV: Problems with primary support group; problems with social environment; educational problems; problems with access to health care services

AXIS V: 21

Treatment: Baseline blood work, including thyroid function, heavy metals, metabolic panels, and toxicology screens were ordered. Although the patient’s presentation and family history suggested mood disorder rather than thought disorder, an MRI of the brain and projective testing were obtained to better evaluate a potential first-break psychosis. All test results were within normal limits.

The patient was referred to a 5-week mood disorders intensive outpatient program. Given the acute severity of his condition and the suspicion that he would require longer-term maintenance therapy for bipolar disorder, combination treatment with quetiapine (dosed up to 300 mg at bedtime during the first week) and lamotrigine (gradually titrated up to 200 mg/d over 5 weeks) was initiated.

PANEL DISCUSSION

DR MUZINA: There are numerous clinical features and historical clues that may aid in the distinction of bipolar from unipolar depression in many patients (see Table). For this patient, the clinical presentation of depression with mood swings and anxiety, as well as a family history of mood disorder, early age of illness onset, presence of potential psychotic features, and irritability with crowded thoughts all pointed to the potential presence of bipolar disorder.

The initial treatments with the antidepressants sertraline and venlafaxine may have been reasonable options, given the consideration of unipolar depression and anxiety. However, if clinical suspicion of bipolar disorder exists in such a patient and psychiatric consultation is not available, the primary care clinician might consider quetiapine monotherapy (which has evidence to support its use for bipolar disorder, major depression, and generalized anxiety disorder) or combining the traditional antidepressant with any mood stabilizer, such as lithium or valproate.

DR. NASRALLAH: The sudden onset of depression and anxiety in a previously well-adjusted young person can suggest several diagnostic possibilities and present a complicated clinical puzzle demanding careful exploration. Are there any comments on the initial steps in evaluating a referred patient such as this one?

DR PARISER: Having patients complete the Mood Disorder Questionnaire (MDQ) can be quite helpful, but it is important that they understand you are assessing symptoms experienced *during* an episode.¹ You are not asking them to report symptoms experienced randomly at different points in their lives.

Sometimes I also ask family members to fill out the MDQ as a means of recounting their observations of the patient. As long as I get consent from a patient in refractory cases, I will do everything I can to talk with one or more family members to help fill out the patient's history. These cases are very challenging.

DR BLACK: He has also been in therapy for 6 months. My experience in such cases is that it is hard for patients to describe the nature of the therapy, so I seldom know exactly what the therapist has been doing with them. After 6 months, it is either time to get a new therapist or to stop it altogether.

DR PARISER: That is a good point. How many obsessive-compulsive disorder patients have you discovered who are in dynamic therapy?

DR BLACK: Quite a few.

DR PARISER: Another important point this raises is that we should do our own therapy. Issues such as the ones in this case can overlap, and it takes time to tease them apart. Unfortunately, even when talking to a therapist about prior counseling, it is often difficult to get a firm idea about what has been happening. For one thing, the therapist may be a little defensive.

DR MUZINA: All of these points are valid. The therapy, as best I could tell, focused chiefly on the patient's soured relationship with the former girlfriend. His mother was involved with 1 or 2 of those sessions at the outset. One of the therapist's principal concerns was that the patient was depressed and anxious—and perhaps even bipolar—because he had taken a couple of antidepressant medications without benefit.

Also, there was some concern that he might have a predilection for stalking. There was no evidence that he was stalking the ex-girlfriend, except perhaps the frequency of going online to visit her MySpace page.

DR BLACK: Because the patient did not tolerate the antidepressants and stopped taking them on his own, it is hard to know whether he is truly treatment-refractory or if something else is going on. He has never been adequately medicated. It also sounds like sertraline was administered at a dose too low to have an impact.

I wonder, too, if he may have some kind of body dysmorphic disorder—a feeling that his muscles are too small. I believe Pope, Hudson, and colleagues called it *bigorexia*.² Or does the patient have some other kind of personality disturbance? He was preoccupied with the young woman; checking her out online. I have certainly seen that sort of thing in individuals with personality disorders.

DR MUZINA: Yes, I had the same thoughts about personality disorder. From what I was able to gather in the first 90-minute visit, nothing he or his mother said strongly suggested a primary personality disorder diagnosis.

DR BLACK: I have one other comment. He was taking power drinks to help with exercise and muscle building. These products contain stimulants. I wonder if he might be a stimulant abuser, even though he may not see it that way.

DR MUZINA: I agree. There is a reason why locker rooms for competitive athletes have tubs of these energy drinks

TABLE Distinguishing bipolar from unipolar depression

Symptom	Bipolar	Unipolar
Substance abuse	Very high	Moderate
Family history	Almost uniform	Sometimes
Seasonality	Common	Occasional
First episode <25 years	Very common	Sometimes
Psychotic features <35 years	Highly predictive	Uncommon
Rapid on/off pattern	Typical	Unusual
>3 recurrent major depressive episodes	Common	Unusual
Antidepressant-induced mania/hypomania	Predictive	Uncommon
Mixed depressions (presence of hypomanic features within the depressive episode)	Predictive	Rare

Kaye NS. Is your depressed patient bipolar? *J Am Board Fam Pract.* 2005;18(4):271-281. Reproduced by permission of the American Board of Family Practice. © 2005 American Board of Family Practice.

available before and during games. It is not just to boost energy but to increase the desire to go out and play hard. The drinks claim to improve performance, especially during times of increased stress or strain, to increase concentration and improve reaction speed, and to stimulate the metabolism. The ingredients almost always include caffeine; they will throw in amino acids and things like taurine and pyridoxine, ostensibly to help with performance and concentration.

DR NASRALLAH: Could he have been taking the anabolic and herbal preparations before he broke up with his girlfriend? Is it possible his depression, irritability, and volatility could have been instigated by anabolic steroid use?

DR MUZINA: Yes. The timeline, as I was able to put it together, was that midway through his senior year of high school he was working out heavily and using these supplements along with friends. And he was dating the young woman. All of this continued the first 6 months after graduation. So the complaint of having felt sad over 14 months before I saw him certainly suggests that the substances could have been affecting him before any relationship problems developed with the girlfriend.

DR NASRALLAH: Then it is possible this patient could have a bipolar spectrum disorder exacerbated by steroid use (TABLE).³

DR BLACK: A toxicology screen would be appropriate, and not only for steroids. In a patient like this, you wonder what else he was putting into his body.

DR PARISER: And what about duty to warn? He was getting

into e-mail, is that correct? Cocaine could even be an issue, in addition to steroids—that would be worrisome.

DR MUZINA: He was blocked from the e-mailing functionality on the social network. But that does not stop one from posing as someone else and being assigned a friend in one of these social networks. So, he could still be finding a way to track what another person is doing and still be looking at the pictures and blogs.

DR PARISER: Dr Muzina, does the patient recognize anything strange in what he was doing, or is it egosyntonic? Has he admitted this is something he should not be doing, or does he see nothing wrong with looking the ex-girlfriend up on My Space and violating boundaries?

DR MUZINA: I do not know if he recognizes his behavior as strange. His own words were, “I know I shouldn’t be doing this because she is no longer my girlfriend. She told me she doesn’t want to talk with me or communicate with me anymore, and I’ve been told by my mom, my family doctor, and a psychologist that I should just let this all go.” There was sort of an irresistible urge still to go online to check out those photos and see what she had been doing recently. Even though he knew he should not be doing it because he had been told it was not a good thing to do.

DR NASRALLAH: A bipolar patient of mine was jilted by a boyfriend. For several weeks, she would drive her car around his block as many as 50 times in a few hours just hoping to see him come out of his apartment. I have seen this kind of behavior in many bipolar patients who simply will not let go. Their manic energy and grief combine to

cause this kind of behavior. That is why it seemed to me this patient, in exhibiting what I call “mini-stalking,” may not know how to let go of the object of his affection.^{4,5}

DR BLACK: When you said that his father gave him sleeping pills, do we know if he was not sleeping because he was psychometrically active at night, or whether he was tired the next day?

DR MUZINA: No, he was not particularly tired the next day. He described what I thought was anxiety: lots of tension and being wound up. In some ways, it was almost an obsessive urge to log on and look at his ex-girlfriend’s Web page. He knew he should not be doing that. These thoughts were coming to him in the evening and that prevented him from sleeping. One of the first things I discussed with his mother was limiting his Internet access or turning the wireless network off when everyone went to bed.

DR PARISER: He would meet most of the research diagnostic criteria for agitated depression, which does not exist in the DSM. The tension, the psychomotor agitation, the questions that are what are called “crowded thoughts.”⁶ Whether it is a variant of psychosis or of bipolar disorder, it is certainly not a simple unipolar presentation, and it is likely aggravated to some extent by substances. From a management standpoint, agitated depression warrants greater concern about the patient acting on impulses and calls for prescribing an antipsychotic.

DR NASRALLAH: I am wary of the term agitated depression. Any time a patient with presumed unipolar disorder is said to have agitated depression I want to rule out bipolar II disorder that has irritability, anger, and hostility as features. Using the MDQ and differentiating between agitated depression and bipolarity is useful for diagnostic accuracy. But in a sense, it is less useful for management because we have a treatment that addresses both situations.

A quandary for many practitioners is whether to use or avoid an antidepressant in bipolar disease. But the quetiapine-lamotrigine combination Dr Muzina is using with this patient would work in either case.

DR BLACK: Another aspect to this patient’s case is the

possibility of paranoia. I worry about the kind of intrusive behavior he has exhibited, and using an atypical antipsychotic may be appropriate.

DR PARISER: The psychological testing you have requested should yield answers about his potential for psychotic thinking, especially under stress, and as to whether any Cluster A personality disorder exists.

DR NASRALLAH: Dr Muzina, did you feel that this patient exhibited some psychotic or prepsychotic features?

DR MUZINA: Yes. He made me more uncomfortable than most patients do, and I supposed he was not giving me the whole story. He alluded to what could be psychotic or developing psychotic symptoms.

DR PARISER: What about traumatic brain injury? Any number of organic issues, including frontal lobe involvement, might be considered. You said there was no history of closed head trauma or anything like that?

DR MUZINA: None that he told me and none that his mother reported.

DR BLACK: Dr Nasrallah, I think you may have taught me that agitated depression in the late teens can often herald the onset of bipolar disorder. Nothing in this case absolutely indicates bipolar disorder, but there are clues suggesting it could evolve that way.

DR PARISER: That would be good news in terms of diminishing the possibility of Cluster A disturbance.

DR NASRALLAH: Yet, do not underestimate the potential for destructive behavior in this young man who had low self-esteem and was so worried about his dysmorphic features. He was obsessed about the lost girlfriend and was tracking her in what amounts to a mini-form of stalking. But I do not think that predicts psychosis as much as it does a bipolar-related stress. I think medication and psychotherapy will get him out of it. So, unless anyone has further comment, I think we’re all agreed on the therapeutic approach Dr Muzina has chosen for this patient. ■

REFERENCES

1. Kim B, Wang HR, Son JI, et al. Bipolarity in depressive patients without histories of diagnosis of bipolar disorder and the use of the Mood Disorder Questionnaire for detecting bipolarity. *Compr Psychiatry*. 2008;49:469-475.
2. Pope HG Jr, Katz DL, Hudson JI. Anorexia nervosa and “reverse anorexia” among 108 male bodybuilders. *Comp Psychiatry*. 1993;34:406-409.
3. Talih F, Fattal O, Malone D Jr. Anabolic steroid abuse: Psychiatric and physical costs. *Cleve Clin J Med*. 2007;74:341-352.
4. Whyte S, Petch E, Penny C, et al. Who stalks? A description of patients at a high security hospital with a history of stalking behavior. *Crim Behav Ment Health*. 2008;18:27-38.
5. Southworth C, Dawson S, Fraser C, et al. A high tech twist on abuse: Technology, intimate partner stalking, and advocacy. Safety Net Project at the National Network to End Domestic Violence Fund. 2005. www.mincava.umn.edu/documents/commissioned/stalkingandtech/stalkingandtech.pdf. Accessed September 29, 2008.
6. Maj M, Pirozzi R, Magliano L, et al. Agitated depression in bipolar I disorder: prevalence, phenomenology, and outcome. *Am J Psychiatry*. 2003;160:2134-2140.

Issues associated with the use of atypical antipsychotic medications

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First-generation (“conventional”) antipsychotic agents are often associated with troubling extrapyramidal symptoms (EPS), including pseudoparkinsonism, erectile dysfunction, and tardive dyskinesia.^{1,2} Newer atypical antipsychotic medications are generally regarded as offering improved efficacy and fewer EPS relative to conventional agents, as well as having broad application for the treatment of both schizophrenia and bipolar disorders. However, concern has grown in recent years about the metabolic effects of these agents, particularly with respect to weight gain, hyperglycemia, dyslipidemia, and development of diabetes.^{3,4} This article will review current evidence pertaining to the metabolic effects of atypical antipsychotics with an emphasis on weight gain, which clinicians are highly likely to encounter in their practices. Other metabolic and pharmacokinetic aspects of atypical antipsychotics will be briefly discussed as they pertain to dosage, drug interactions, and mechanism of action.

Atypical antipsychotics have been defined as agents that produce minimal catalepsy in animal models and minimal EPS or movement disorders at therapeutic doses, and which significantly reduce positive and negative symptoms of schizophrenia.^{5,6} The major atypical antipsychotic agents currently available in the United States are listed in **TABLE 1**.

While the incidence of both obesity and diabetes is soaring among the general population, these conditions are more prevalent in patients with schizophrenia, even those who have no history of antipsychotic drug use.⁷ Prevalence rates for both diabetes and obesity are approximately 1.5 to 2 times higher in people with schizophrenia and other affective disorders than in the general population.⁴ This suggests that people with psychiatric illness may be somehow predisposed toward metabolic disorders, although the precise mechanisms are not well understood. Many confounding factors inevitably enter the picture, including baseline weight, family history, diet and exercise habits, concomitant medications, and comorbid diseases.⁸ Importantly, the propensity toward weight

gain and development of hyperlipidemia or diabetes during atypical antipsychotic treatment appears to vary widely among individuals.⁹ Thus, it is difficult to predict which patients will be affected and the precise role drug treatment might play in this process.

Potential mechanisms of metabolic dysfunction in psychiatric patients

Various hypotheses have been discussed to explain the metabolic changes observed in patients using antipsychotic drugs.⁸ Some proposed mechanisms pertain to the direct impact of these drugs on glucose homeostasis, such as an interaction between glucose and 5-HT serotonin receptor antagonism, damage to the pancreatic islet cells, or sympathetic nervous system dysregulation.¹⁰ There are numerous case reports of patients who rapidly develop hyperglycemia after initiation of drug therapy, primarily when using olanzapine or clozapine.¹¹⁻¹⁴ This effect often abates after the drug is discontinued. However, it is important to remember that development of diabetes is most likely to occur secondary to obesity.^{4,9} Smoking, a common behavior among those with affective disorders, confers an additional risk for diabetes and cardiovascular disease.¹⁵

What causes medication-related weight gain? People with psychiatric disease are prone to the same mismatch of caloric intake and energy expenditure that is causing obesity in the general population. Additional causal factors proposed include regaining of weight lost during psychiatric illness; food cravings; alterations in resting metabolic rate; and reduced physical activity.^{9,16} The last could be exacerbated by medication side effects such as somnolence. In addition, the binding affinities of atypical antipsychotics with specific neurotransmitters may alter the sensations of hunger and satiety (eg, alpha-adrenergic stimulation is thought to stimulate the appetite).¹⁶ Finally, many drugs used in combination with atypical antipsychotics, including lithium and divalproex, are known to cause significant weight gain.¹⁷

TABLE 1 Atypical antipsychotics and FDA-approved indications

Drug	Common trade names	Approved indications
Aripiprazole	Abilify	Schizophrenia (acute and maintenance treatment in adults); bipolar I disorder (acute and maintenance treatment of manic and mixed episodes with or without psychotic features—adult and pediatric); major depressive disorder (adjunct to antidepressants); agitation in schizophrenia or bipolar mania
Clozapine	Clozaril	Treatment-resistant schizophrenia (second-line agent); reducing risk of recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder
Olanzapine	Zyprexa	Schizophrenia; bipolar disorder (acute and maintenance); combination therapy with valproate or lithium in bipolar disorder; agitation associated with schizophrenia and bipolar I mania
Quetiapine	Seroquel	Bipolar depression; bipolar mania (bipolar I, as either monotherapy or adjunct therapy to lithium or divalproex); maintenance treatment of bipolar I disorder (as adjunct to lithium or divalproex) acute and maintenance treatment of schizophrenia (Seroquel XR)
Risperidone	Risperdal	Schizophrenia; manic symptoms of acute manic or mixed episodes associated with bipolar I disorder. (Available as solution for depot injection.)
Ziprasidone	Geodon	Schizophrenia; bipolar mania; acute agitation in schizophrenia

Source: Manufacturers' prescribing information.

Review of data on weight gain among atypical antipsychotics

To address growing concerns and put the mounting case-based and clinical trial evidence into perspective, the American Diabetes Association (ADA) and the American Psychiatric Association (APA) convened with 2 other national organizations to develop a consensus statement on the metabolic impact of atypical antipsychotic agents.⁴

The ADA/APA statement ranked clozapine and olanzapine as being associated with the greatest risk of weight gain, diabetes, and dyslipidemia.⁴ Risperidone and quetiapine were put into an intermediate risk category for weight gain, while aripiprazole and ziprasidone were, at the time, too new to categorize. More recent data have shown ziprasidone and aripiprazole to be relatively weight-neutral.⁸

However, the consensus statement must be interpreted with caution. Criticism has been leveled at the report from many corners, including the Division of Neuropharmacological Drug Products of the FDA, which argued that insufficient data were available to appropriately “rank” obesity/diabetes risks for the atypical antipsychotic agents.¹⁸ Other authors pointed out that efficacy considerations of these drugs are a critical and overlooked component of the discussion and that the data used to compare the agents did not adequately control for key lifestyle factors such as overreliance on “junk food.”^{19,20}

Data from CATIE study

The large-scale Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study enrolled nearly 1500 patients with schizophrenia at 57 US centers between 2001 and 2004.³ The study compared efficacy variables and weight gain in the course of treatment with olanzapine, perphenazine, quetiapine, and risperidone. Ziprasidone was added later in the study. Weight change (defined as kg/month of treatment) in phase I of the CATIE trial is shown in **TABLE 2**.

The CATIE investigators found that among the patients randomized to olanzapine, 30% experienced weight gain in excess of 7% of baseline, compared with 16%, 14%, 12%, and 7% of those randomized to quetiapine, risperidone, perphenazine, and ziprasidone, respectively. Exposure-adjusted changes in cholesterol or triglyceride blood levels were highest for olanzapine, followed by quetiapine and perphenazine, with decreases noted for ziprasidone and risperidone. With any of the agents, these effects must be balanced against the benefits of the drug in individual patients.

Results from other controlled studies

As Glick states in his analysis of the CATIE trial, long-term tolerability and efficacy of antipsychotic therapy is the goal of schizophrenia management to insure treatment adherence and garner maximum benefit.²¹ In most clinical trials of antipsychotics, core symptoms of

TABLE 2 Weight change from baseline to last observation in phase 1 of the CATIE trial

Antipsychotic	Mean lb per month of treatment	Mean weight change (lb)	Range (lb)
Olanzapine	2.0	9.4 ± 0.9	-14 to 42
Quetiapine	0.5	1.1 ± 0.9	-25 to 25
Risperidone	0.4	0.8 ± 0.9	-24 to 24
Perphenazine	-0.2	-2.0 ± 1.1	-29 to 22
Ziprasidone	-0.3	-1.6 ± 1.1	-24 to 18

CATIE = Clinical Antipsychotic Trials of Intervention Effectiveness.

Source: Lieberman JA, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia.

N Engl J Med. 2005;353:1209-1223.

schizophrenia are balanced against drug side effects. However, symptoms of schizophrenia vary significantly from person to person, and antipsychotic medications themselves can adversely affect functioning.

Of concern is that much of the data on weight gain from antipsychotic agents comes not from controlled trials like CATIE but from uncontrolled trials. A meta-analysis conducted by Allison and colleagues compared data on weight change after 10 weeks of treatment among patients receiving conventional and atypical antipsychotics and placebo.²² These authors observed that many of the studies “report their weight gain in an incomplete, idiosyncratic, and poorly defined manner,” noting that this area of research would benefit from standardization. Again, clozapine (12 studies) and olanzapine (7 studies) resulted in the highest weight gain, and risperidone resulted in moderate weight gain (26 studies). Ziprasidone was weight-neutral (22 studies) and available data were insufficient to evaluate quetiapine (3 studies).²²

Monitoring patients for weight gain, dyslipidemia, and diabetes

Should patients be switched to another agent if weight gain is observed? If so, how much is too much? The ADA/APA consensus report recommended considering a switch if a patient gains weight ≥5% above baseline at any point during therapy (TABLE 3).⁴ However, this view might be somewhat simplistic given the challenges involved in identifying a drug regimen that controls symptoms optimally for that individual.^{1,20,23} Switching agents can potentially introduce new problems, with the possible loss of therapeutic benefit, need for additional dosage monitoring, and potential to introduce adherence problems and/or other adverse effects.

The ADA/APA report does provide some prudent monitoring steps that serve as a useful guideline for practitioners while maintaining patients on atypical antipsychotics (TABLE 4).

Other metabolic issues related to atypical antipsychotics

While weight gain and glucose metabolism have received much recent attention, several other issues pertaining to atypical antipsychotic metabolism bear mentioning, a few of which are highlighted below.

Role of cytochrome P450 enzymes in antipsychotic metabolism

Cytochrome P450 (CYP) enzymes have significant involvement in the metabolism of atypical antipsychotics. Clozapine is primarily metabolized by CYP1A2; risperidone mainly by 2D6; quetiapine and ziprasidone mainly by 3A4; and aripiprazole by 2D6 and 3A4.²⁴ This hepatic metabolism increases the potential for drug–drug interactions with other agents that inhibit or induce CYP enzymes. These interactions could alter antipsychotic plasma levels and result in reduced effectiveness of the antipsychotic agent or increased risk of adverse events.²⁵ Since many drugs used concomitantly with antipsychotics work along these pathways (for example, ketoconazole and fluconazole are highly potent inhibitors of P450 3A), the prescriber should exercise caution and be aware of potential interactions.

Effect of smoking on plasma levels of antipsychotics

Cigarette smoking is a highly prevalent habit in patients with schizophrenia, with rates estimated as high as 88%.²⁶ These patients tend to smoke heavily and many also use excessive caffeine or other addictive

TABLE 3 Atypical antipsychotics and metabolic abnormalities

Drug	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/-	-	-
Ziprasidone*	+/-	-	-

+ = Increased effect; - = No effect; D = Discrepant results. *Newer drugs with limited long-term data.

American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. © 2004 American Diabetes Association. Diabetes Care®, Vol 27, 2004; 596-601. Reprinted with permission from The American Diabetes Association.

TABLE 4 Monitoring metabolic profiles in patients receiving atypical antipsychotic drugs

Recommendations from the American Psychiatric Association/
American Diabetes Association Consensus Report

- Baseline monitoring of BMI, personal/family history, waist circumference
- Baseline monitoring for symptoms of hyperglycemia (advise patients of hyperglycemia symptoms)
- Reassess weight change at 4, 8, and 12 weeks after initiation or change in antipsychotic therapy and quarterly thereafter
- Reassess fasting plasma glucose, lipids, and blood pressure at 3 months and annually thereafter

Adapted from American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care. 2004;27:596-601.

substances.²⁷ The role of these habits in dosage adjustment and therapeutic response may be overlooked.²⁸ Smoking is known to increase metabolism of drugs that act primarily via CYP1A2, notably clozapine and olanzapine.²⁹ Modification of clozapine or olanzapine dosages may be necessary in smokers.³⁰ In addition, it is important to consider that patients who are forced to stop smoking while hospitalized are likely to return to the habit after discharge, potentially altering the metabolism of these drugs.

Drug metabolites and new mechanisms

In some cases, a better understanding of the metabolic pathways of antipsychotic agents has contributed to new knowledge about their mechanisms of action and have yielded new pharmacologic agents. For example, the recently approved antipsychotic paliperidone is the active

metabolite of risperidone. According to the authors of a recent Cochrane Review on this agent, it remains unknown whether this metabolite confers any benefit over the “parent compound,” risperidone.³¹

An active metabolite of quetiapine (N-desalkylquetiapine) has recently been found to exert an inhibitory effect on the norepinephrine transporter (NET), which is an important site of therapeutic action for several antidepressants. Goldstein and colleagues reported that inhibiting NET leads to elevation of noradrenaline levels in specific brain areas.³² This effect is likely to account for the antidepressant activity of quetiapine and helps explain its efficacy in unipolar depression.^{33,34}

Conclusion

Although the effects of atypical antipsychotic medications are often lumped together, it is important to consider this a heterogeneous group of medications. They can produce highly differing results, depending on individual patient variables and number of external factors. Clozapine and olanzapine are the most commonly associated with weight gain, risperidone and quetiapine with moderate effects, and aripiprazole and ziprasidone the least, but other factors that lead to weight gain should be taken into account. In addition, efficacy, dosage, and adherence are critical components that must be weighed as part of the decision to switch a patient to a different therapy. Dosage of atypical antipsychotics is a complex matter, and metabolic interactions with other drugs and agents such as cigarette smoke must be taken into account as well. With more research into the metabolism of these drugs, new pathways have been identified that add to our understanding of their specific mechanisms of action. ■

REFERENCES

- Citrome L, Volavka J. The promise of atypical antipsychotics: fewer side effects mean enhanced compliance and improved functioning. *Postgrad Med.* 2004;116:49-63.
- Davis JM, Chen N. Old versus new: weighing the evidence between the first- and second-generation antipsychotics. *Eur Psychiatry.* 2005;20:7-14.
- Lieberman JA, Stroup TS, McEvoy JP, et al, for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med.* 2005;353:1209-1223.
- American Diabetes Association; American Psychiatric Association; American Association of Clinical Endocrinologists; North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care.* 2004;27:596-601.
- Markowitz JS, Brown CS, Moore TR. Atypical antipsychotics. Part I: Pharmacology, pharmacokinetics, and efficacy. *Ann Pharmacother.* 1999;33:73-85.
- Kinon BJ, Lieberman JA. Mechanisms of action of atypical antipsychotic drugs: a critical analysis. *Psychopharmacology (Berl).* 1996;124:2-34.
- Ryan MC, Collins P, Thakore JH. Impaired fasting glucose tolerance in first-episode, drug-naïve patients with schizophrenia. *Am J Psychiatry.* 2003;160:284-289.
- Baptista T, DeMendoza S, Beaulieu S, et al. The metabolic syndrome during atypical antipsychotic drug treatment: mechanisms and management. *Metab Syndr Relat Disord.* 2004;2:290-307.
- Citrome L, Vreeland B. Schizophrenia, obesity, and antipsychotic medications: what can we do? *Postgrad Med.* 2008;120:18-33.
- Goldstein LE, Sporn J, Brown S, et al. New-onset diabetes mellitus and diabetic ketoacidosis associated with olanzapine treatment. *Psychosomatics.* 1999;40:438-443.
- Kohen I, Gampel M, Reddy L, et al. Rapidly developing hyperglycemia during treatment with olanzapine. *Ann Pharmacother.* 2008;42:588-591.
- Duiverman ML, Cohen D, van Oven W, et al. A patient treated with olanzapine developing diabetes de novo: proposal for hyperglycaemia screening. *Neth J Med.* 2007;65:346-348.
- Cohen D. Atypical antipsychotics and new onset diabetes mellitus. *Pharmacopsychiatry.* 2004;37:1-11.
- Clark C, Burge MR. Diabetes mellitus associated with atypical antipsychotic medications. *Diabetes Technol Ther.* 2003;5:669-683.
- McCreadie RG. Use of drugs, alcohol, and tobacco by people with schizophrenia: case-control study. *Br J Psychiatry.* 2002;191:321-325.
- Zimmerman U, Kraus T, Himmerich H, et al. Epidemiology, implications, and mechanisms underlying drug-induced weight gain in psychiatric patients. *J Psychiatr Res.* 2003;37:193-220.
- Isojarvi JT, Laatikainen TJ, Knip M, et al. Obesity and endocrine disorders in women taking valproate for epilepsy. *Ann Neurol.* 1996;39:579-584.
- Boehm G, Racoosin JA, Laughren TP, et al. Consensus development conference on antipsychotic drugs and obesity and diabetes: response to consensus statement. *Diabetes Care.* 2004;27:2088-2089.
- Citrome L, Volavka J. Consensus development conference on antipsychotic drugs and obesity and diabetes: response to consensus statement. *Diabetes Care.* 2004;27:2087-2088.
- Isaac MT, Isaac MB. Consensus development conference on antipsychotic drugs and obesity and diabetes: response to consensus statement. *Diabetes Care.* 2004;27:2088.
- Glick ID. Understanding the results of CATIE in the context of the field. *CNS Spectr.* 2006;11(7 suppl 7):40-47.
- Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry.* 1999;156:1686-1696.
- Citrome L. Efficacy should drive atypical antipsychotic treatment. *BMJ.* 2003;326:283.
- Urichuk L, Prior TI, Dursun S, et al. Metabolism of atypical antipsychotics: involvement of cytochrome p450 enzymes and relevance for drug-drug interactions. *Curr Drug Metab.* 2008;9:410-418.
- Conley RR, Kelly DL. Drug-drug interactions associated with second-generation antipsychotics: considerations for clinicians and patients. *Psychopharmacol Bull.* 2007;40:77-97.
- Hughes JR, Hatsukami DK, Mitchell JE, et al. Prevalence of smoking among psychiatric outpatients. *Am J Psychiatry.* 1986;143:993-997.
- Williams JM, Foulds J. Successful tobacco dependence treatment in schizophrenia. *Am J Psychiatry.* 2007;164:222-227.
- Dratcu L, Grandison A, McKay G, et al. Clozapine-resistant psychosis, smoking, and caffeine: managing the neglected effects of substances that our patients consume every day. *Am J Ther.* 2007;14:314-318.
- Derenne JL, Baldessarini RJ. Clozapine toxicity associated with smoking cessation: case report. *Am J Ther.* 2005;12:469-471.
- Dalack GW, Becks L, Hill E, et al. Nicotine withdrawal and psychiatric symptoms in cigarette smokers with schizophrenia. *Neuropsychopharmacology.* 1999;21:195-202.
- Nussbaum A, Stroup TS. Paliperidone for schizophrenia. *Cochrane Database Syst Rev.* 2008;April 16:CD006369.
- Goldstein JM, Christoph G, Grimm S, et al. Unique mechanism of action for the antidepressant properties of the atypical antipsychotic quetiapine. Poster presented at: American Psychiatric Association, 160th Annual Meeting; May 19-24, 2007; San Diego, CA. Poster NR336.
- Jensen NH, Rodriguiz RM, Caron MG, et al. N-desalkylquetiapine, a potent norepinephrine reuptake inhibitor and partial 5-HT1A agonist, as a putative mediator of quetiapine's antidepressant activity. *Neuropsychopharmacology.* 2008;33:2303-2312.
- Pira L, Mongeau R, Pani L. The atypical antipsychotic quetiapine increases both noradrenaline and dopamine release in the rat prefrontal cortex. *Eur J Pharmacol.* 2004;504:61-64.

POSTTEST QUESTIONS

A score of 70% or higher is required to receive a CME certificate.

Select the single letter response that best answers the question or completes the sentence.

1. Pope, Hudson, et al labeled a type of body dysmorphic disorder in which the patient believes his muscles are too small as:

- a. Bromosis
- b. Bigorexia
- c. Somatoform disorder
- d. Narisexia

2. A feature of bipolar depression that WOULD NOT commonly occur with unipolar depression is:

- a. Substance abuse
- b. Family history of the disorder
- c. Seasonality
- d. Psychotic features at <35 years of age

3. Drugs that produce minimal extrapyramidal side effects at therapeutic doses and significantly reduce symptoms of schizophrenia are:

- a. Typical or first-generation antipsychotics
- b. Selective serotonin reuptake inhibitors
- c. Antineuroleptics
- d. Atypical or second-generation antipsychotics

4. Causal factors for medication-related weight gain in patients taking antipsychotic drugs include all EXCEPT:

- a. Food allergies
- b. Alterations in metabolic rate
- c. Altered sensations of hunger/satiety
- d. Reduced physical activity/somnolence

5. A consensus statement from the American Diabetes Association and the American Psychiatric Association associate which drugs with the greatest risk of weight gain, diabetes, and dyslipidemia?

- a. Aripiprazole and ziprasidone
- b. Risperidone and quetiapine
- c. Clozapine and olanzapine
- d. Perphenazine and quetiapine

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Please circle the letter that best reflects your agreement with the statements below, using the following scale:

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