

## Aripiprazole in Schizotypal Personality Disorder: A Case Report

**Sir:** Schizotypal personality disorder (SPD) is characterized by odd, eccentric behavior; inappropriate or constricted affect; odd beliefs or magical thinking; circumstantial, metaphorical, or stereotyped thinking manifested by odd speech; anxiety in social situations; and cognitive or perceptual distortions.<sup>1</sup> Studies have been conducted on the efficacy of haloperidol,<sup>2</sup> thiothixene,<sup>3</sup> olanzapine,<sup>4</sup> and risperidone<sup>5</sup> in SPD. However, efficacy of aripiprazole in SPD has not been reported.

Aripiprazole is a novel antipsychotic with a unique mechanism of action. It is a partial agonist of D<sub>2</sub> and D<sub>3</sub> dopamine receptors and 5-HT<sub>1A</sub> serotonin receptors, which are, respectively, responsible for its efficacy on positive, negative, and cognitive symptoms of schizophrenia and its antidepressant and antianxiety actions.<sup>6-8</sup> Hence, it is called a dopamine-serotonin system stabilizer.<sup>9,10</sup> Aripiprazole has been approved by the U.S. Food and Drug Administration in the treatment of schizophrenia.

A search of English-language publications in PubMed using the keywords *schizotypal personality disorder* and *aripiprazole* retrieved no published reports or articles. Herein, we describe a patient with SPD of 5 years' illness duration who had never been treated with any medications and who responded to treatment with aripiprazole.

**Case report.** Mr. A, a 22-year-old engineering student of middle-class socioeconomic status and urban background, presented to our hospital in August 2007 with an insidious onset and continuous course of illness of 5 years' duration characterized by odd and eccentric behavior, oddities in speech, avoidance of social situations, deteriorating academic performance, idiosyncratic repetitive behaviors, and magical thinking. His family members were concerned about his odd and eccentric behavior, social dysfunction, and academic decline. The above symptoms could not be attributed to any clear-cut psychotic disorders, mood disorders, substance use disorders, or general medical conditions. He had never received treatment for the symptoms. The patient's history and family history were noncontributory.

Structured assessment conducted at baseline using the Structured Clinical Interview for DSM-IV Axis I Disorders<sup>11</sup> and Structured Clinical Interview for DSM-IV Axis II Personality Disorders<sup>12</sup> revealed that Mr. A had schizotypal personality disorder. The Schizotypal Personality Questionnaire (SPQ)<sup>13</sup> revealed social anxiety, odd beliefs, odd behaviors, blunted affect, suspiciousness, lack of close friends, and magical thinking. A baseline score of 4 on the Clinical Global Impressions-Severity of Illness scale (CGI-S)<sup>14</sup> was noted. Other baseline psychodiagnostic assessments were also conducted, such as the Object Sorting Test, Thematic Apperception Test, and Rorschach Inkblot Test, which revealed the absence of pathognomonic signs of psychosis. After giving informed consent, Mr. A was started on treatment with aripiprazole 10 mg at night.

At 2-month (week 8) follow-up, the patient reported a 70% decrease in his symptoms, started attending his engineering college regularly, and showed interest in his studies. His family members reported marked improvement in his social and academic functioning. They also reported that his odd ideas, eccentric behaviors, magical thinking,

and suspiciousness were reduced to minimal. His interaction with friends and his mood also improved. His CGI-S score was 3 (mildly ill), and his CGI-Improvement score was 2 (showing much improvement).

This patient with SPD had a 5-year duration of untreated illness and was assessed with structured instruments. He responded to treatment with 10 mg of aripiprazole. Currently, thiothixene, haloperidol, risperidone, and olanzapine have been documented to be effective in treatment of SPD. This case report assumes importance in the light of the paucity of aripiprazole studies in SPD. However, the choice of antipsychotic medications is largely based on side effect profile. Available data on aripiprazole reveal that it is an effective medication with a benign adverse effect profile.<sup>9,10</sup> Aripiprazole, being a dopamine-serotonin system stabilizer, is hence an ideal drug to target the odd and eccentric behavior, stereotyped thinking, social anxiety symptoms, and obsessive symptoms of SPD. Future double-blind, placebo-controlled studies examining the effectiveness of aripiprazole in the treatment of SPD are needed.

*The authors report no financial or other relationship relevant to the subject of this letter.*

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### Vigilance Needed in Recognizing Behavior Changes in Patients Taking Statins

**Sir:** Evidence from randomized trials suggests that statins are very safe.<sup>1</sup> Consequently, their widespread use is highly promoted, even in high doses, and among adults of all ages. However, we feel caution is warranted, particularly when striving for aggressive low-density lipoprotein (LDL) cholesterol targets.

In general, subjects in statin trials have been free of many chronic diseases, such as prevalent cancer, severe renal impairment, and neurodegenerative and depressive disorders. In clinical practice, individuals with the aforementioned problems and other chronic ailments are commonly treated with statins to achieve LDL cholesterol-lowering targets. Hence, it is sometimes dangerous to extrapolate trial results to real-world practice.

High-dose simvastatin alters cholesterol turnover in the brain.<sup>2</sup> Low-dose simvastatin has caused significant decreases in positive affect in elderly volunteers.<sup>3</sup> Additionally, violent behavior has been associated with hypocholesterolemia resulting from a novel apolipoprotein B gene mutation.<sup>4</sup> Furthermore, victims of violent suicides were found to have lower frontal cortex gray-matter cholesterol content than victims of nonviolent suicides.<sup>5</sup>

Statins were introduced in 1987. During the 1990s, in Scotland, there was a sharp increase in antidepressant prescribing by physicians.<sup>6</sup> It is certainly plausible that the increase in the use of antidepressants might have occurred as a result of statin-induced lower cholesterol levels, leading to more depression. As the prescribing of statins becomes more widespread and cholesterol-lowering goals more aggressive, practicing clinicians must be vigilant in recognizing behavior changes, particularly in elderly and depressed individuals.

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### Risperidone- and Aripiprazole-Induced Leukopenia: A Case Report

**Sir:** Leukopenia and agranulocytosis are life-threatening side effects of antipsychotics, but routine white blood cell (WBC) count monitoring is not indicated, with the exception of clozapine. Studies have shown that < 3% of patients treated with clozapine develop granulocytopenia.<sup>1,2</sup> Although several case reports have been published regarding leukopenia and/or neutropenia associated with risperidone,<sup>3</sup> olanzapine,<sup>4,5</sup> quetiapine,<sup>6</sup> and ziprasidone,<sup>7</sup> data are still lacking. Lithium, on the other hand, has been used successfully to treat leukopenia associated with cancer chemotherapy,<sup>8</sup> carbamazepine,<sup>9</sup> and clozapine.<sup>2</sup>

We report a case of risperidone- and aripiprazole-induced leukopenia successfully treated with lithium. We suggest careful monitoring of WBC counts in patients who have a history of antipsychotic-induced leukopenia, as they can be more prone to leukopenia with other antipsychotics.

**Case report.** Mr. A, a 32-year-old African American man with a long history of schizophrenia, paranoid type (DSM-IV criteria), and no significant medical history, had been treated with risperidone 2 mg orally at night for a few years. He reported no side effects from his medication and continued to attend a vocational program and hold a summer job. Mr. A was followed at a community mental health clinic for medication management.

On review of his annual physical examination and laboratory workup in September 2006, it was noted that his WBC count was  $2.8 \times 10^9$ , with an absolute neutrophil count (ANC) of  $1.27 \times 10^9$ . The other results of Mr. A's physical examination were normal, and he had no signs of any infection. Risperidone-induced leukopenia was suspected, but the patient refused to change his medication. He agreed to decrease the risperidone dose to 1 mg at night and repeat his bloodwork in a few weeks. His WBC count and ANC remained low, at  $2.7 \times 10^9$  and  $1.22 \times 10^9$ , respectively, and finally risperidone was discontinued. The patient agreed to start treatment with aripiprazole 10 mg daily and undergo repeat laboratory testing in 6 months. He

reported no side effects during this time and was evaluated at least every 4 weeks.

Aripiprazole was discontinued after 6 months, as Mr. A's WBC count and ANC continued to decrease and were  $2.4 \times 10^9$  and  $0.85 \times 10^9$ , respectively. The patient was referred for full hematologic workup and medical treatment. After 2 weeks with no antipsychotic medication, he decompensated and was hospitalized due to paranoid delusions, irritable mood, and auditory hallucinations. At the time of inpatient admission, his WBC count was found to be  $6.4 \times 10^9$ , and his ANC was  $4.67 \times 10^9$ . The patient was put back on treatment with aripiprazole 10 mg daily with good response and discharged from the hospital.

Follow-up upon discharge at the mental health clinic showed that his WBC count and ANC had decreased again to  $2.9 \times 10^9$  and  $1.29 \times 10^9$ , respectively. After extensive discussion with the treatment team and a review of the literature, aripiprazole was discontinued. It was decided to treat Mr. A with an antipsychotic along with lithium as it has been reported to correct leukopenia of various etiologies. The patient refused to try aripiprazole or risperidone again but agreed to treatment with paliperidone 6 mg and lithium 300 mg daily. He responded well to the medication change, and his WBC count increased to  $3.3 \times 10^9$  and ANC increased to  $1.42 \times 10^9$ .

The patient has refused to adjust medication dosages further but continues to attend a vocational program and keep his summer job. His hematologic workup is pending at this point.

The exact pathophysiology of psychotropic-induced blood dyscrasias is still unclear, but direct toxic effect, immune reactions, and peripheral destruction of cells have all been implicated.<sup>10</sup> Individual risk factors that have been suggested are being African Caribbean, being young, and having a low baseline WBC count, especially in cases of leukopenia associated with clozapine.<sup>2</sup> Neutrophils can either circulate in the blood vessels or be marginalized alongside the vessel wall. African Caribbean individuals have apparently lower WBC counts due to increased margination.<sup>2,5</sup> It has been proposed that lithium can cause leukocytosis and reverse leukopenia by direct stem cell stimulation,<sup>9</sup> stimulation of granulocyte-macrophage colony-stimulating factor,<sup>11</sup> stimulation of cytokines,<sup>12</sup> and demargination.<sup>13</sup>

It is an interesting finding that, as in our case, many patients who developed leukopenia as a result of one antipsychotic were also leukopenic after taking another antipsychotic.<sup>5-7</sup> This might be due to some genetic vulnerability in these individuals. In the light of these data, we suggest careful monitoring of WBC count even while using newer antipsychotics, especially if the patient has a history of leukopenia associated with antipsychotic use. Lithium can improve the WBC count in some of these cases if used appropriately.

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#### Aggressive Behavior After Ingestion of a High Dose of Sildenafil

**Sir:** Only 1 study pertaining to the use of sildenafil in men with erectile dysfunction who are undergoing treatment with antipsychotic drugs has been performed.<sup>1</sup> There are only 2 reports about adverse effects of high doses of sildenafil in this population.<sup>2,3</sup> We report a case of a man, treated with different psychotropic drugs, who exhibited serious aggression after having ingested a high dose of sildenafil.

**Case report.** Mr. A, a 50-year-old patient with a 5-year history of a psychotic disorder due to a head trauma, with delusions, and with personality change due to a head trauma, combined type (both according to DSM-IV), was admitted to a psychiatric hospital in May 2007 because of suicidal thoughts and low mood. He was complaining about his erectile dysfunction, which had begun after he had started taking antipsychotics a year before. He was convinced that erectile dysfunction was the main reason for his low mood and diminished will to live. Mr. A sometimes used vardenafil, with no success. At the time of admission, he was receiving quetiapine, mirtazapine, and valproate. After 10 days in the hospital, his suicidal thoughts decreased, and his mood improved.

He went home for a 2-day holiday and came back very agitated. He shouted that he needed a woman and that he would have all the women in the world; he started harassing the nurses and took off all his clothes. He reported taking 400 mg of his father's sildenafil at home the day before. Agitation progressed

into a tremendous rage, and he had an aggressive outburst during which he broke 2 chairs and a window. He had to be physically restrained and was calmed down with haloperidol (15 mg daily) and diazepam (40 mg daily) administered parenterally.

This agitated condition persisted for the next 6 days, with only moderate response to continuous treatment with haloperidol and diazepam. Mr. A's mood fluctuated, he shouted obscenities, and he was aggressive toward everyone in the ward. In the next 4 days, his condition improved; however, he started feeling depressed and had paranoid ideas. Upon his discharge after 3 weeks, he was in a better mood without paranoid ideas, his agitation had subsided, and he regretted his behavior.

In the U.S. Food and Drug Administration Adverse Event Reporting System, sildenafil has been implicated as a suspected cause of neurological, emotional, and psychological disturbances.<sup>2</sup> The mechanism of those adverse events is still unknown, and different hypotheses are being tested: inhibition of phosphodiesterase type 5 in the brain, reduction in the concentration of nitric oxide in the hippocampus, accumulation of cyclic guanosine monophosphate, impact on neuronal communications, and others.<sup>3</sup>

The link between aggressive behavior and sildenafil treatment is not convincing, but, nevertheless, extra caution may be needed when sildenafil is used for the management of sexual dysfunction in patients with organic brain disorders who are undergoing treatment with psychotropic drugs.

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#### A Case of Pancreatitis Associated With Aripiprazole in the Absence of Hyperglycemia

**Sir:** Several atypical antipsychotic medications, including clozapine, olanzapine, and risperidone, have been associated with pancreatitis.<sup>1</sup> Cases of pancreatitis have also been associated with the use of haloperidol. An analysis of reports of pancreatitis associated with atypical antipsychotics published in 2003 utilized data from the U.S. Food and Drug Ad-

ministration's MedWatch Safety Information and Adverse Event Reporting Program (January 1981–February 2002) and MEDLINE (through February 2002). Aripiprazole<sup>2</sup> was not available until November 15, 2002, and thus was not included in this analysis.

While the case has not been conclusively proven, aripiprazole is thought to have fewer metabolic effects than other atypical antipsychotics, and one report has even discussed aripiprazole's ability to "reverse" the metabolic adverse effects of other antipsychotic agents.<sup>3</sup> The metabolic effects seen with atypical antipsychotics include hyperglycemia, new onset or exacerbations of type 2 diabetes mellitus, and diabetic ketoacidosis.<sup>4</sup>

Although pancreatitis has been reported in conjunction with atypical antipsychotic-induced hyperglycemia,<sup>5</sup> no cases of aripiprazole-induced pancreatitis have been reported, and prescribing information for aripiprazole<sup>2</sup> does not carry a warning concerning pancreatitis. There is only 1 case report in the literature linking aripiprazole to hyperlipasemia complicating diabetic ketoacidosis, and no cases of isolated pancreatitis related to aripiprazole use have been reported. We describe a case of aripiprazole-associated pancreatitis without hyperglycemia.

**Case report.** Ms. A, a 44-year-old white woman with bipolar disorder, presented to the primary care clinic with a 4-day history of epigastric pain, nausea, and early satiety. The patient had initiated use of aripiprazole 2 months prior in addition to oxcarbazepine, venlafaxine, and clonazepam. At presentation, the serum lipase level was 545 U/L (reference range: 23–300 U/L), the serum amylase level was 75 U/L (reference range: 30–110 U/L), the serum sodium level was 126 mmol/L (reference range: 137–145 mmol/L), the serum chloride level was 90 mmol/L (reference range: 98–107 mmol/L), the serum glucose level was 76 mg/dL (reference range: 65–105 mg/dL); and serum levels of CO<sub>2</sub>, urea nitrogen, creatinine, and potassium were measured, and the results were normal. The results of a complete blood count were normal except for a white blood cell count of  $3.8 \times 10^3$  (reference range:  $3.9\text{--}11.6 \times 10^3$ ); the results of liver function tests and calcium levels were within normal limits, except for the serum albumin level (4.7 g/dL [reference range: 3.5–4.6 g/dL]) and serum total bilirubin level (0.1 mg/dL [reference range: 0.2–1.3 mg/dL]). A serum triglyceride level drawn 11 months prior was 61 mg/dL (reference range: 30–149 mg/dL). The results of a test to detect helicobacter pylori antibody immunoglobulin G levels were negative.

Ms. A had a remote history of alcohol abuse, in remission for 6 years, and no current substance use. She had no prior history of cholelithiasis, pancreatitis, or gastrointestinal disorders. The results of an abdominal ultrasound were negative for gallstones or common bile duct dilation. Ms. A was treated as an outpatient with fluid restriction, liquid diet, and analgesics. The results of an abdominal computed tomography scan were negative for pancreatic abnormalities and hepatic pathology. The results of an endoscopic ultrasound were negative for overt pancreatic or biliary abnormalities. Due to unstable psychiatric status, the aripiprazole was not discontinued until 8 weeks after initial presentation. Approximately 10 weeks after Ms. A's initial presentation, the serum lipase level was persistently elevated (1169 U/L), and she developed vomiting that required a 2-day hospitalization, during which a repeat abdominal ultrasound was performed and the results found to be normal. Tests for anti-nuclear antibodies and immunoglobulin G subclass 4 levels, were conducted, to rule out autoimmune pancreatitis and results were normal.

Two months after the hospitalization, a repeat measure of serum lipase level was found to be 508 U/L. At that time the patient had been restarted on an antipsychotic medication, risperidone, due to unstable moods. Her abdominal symptoms persisted, with mild epigastric pain and nausea. One month later the risperidone was discontinued, and 4 weeks later a serum lipase level was found to be normal, and her symptoms resolved.

Although Ms. A's serum amylase and lipase levels were less than 3 times the upper limit of normal, the clinical presentation was consistent with acute pancreatitis.<sup>6</sup> A thorough evaluation for another etiology of the pancreatitis was completed, and gallstone, alcoholic, tumor, and autoimmune causes were excluded, suggesting that aripiprazole may have been a contributing factor. Ms. A's recovery was protracted because of continued use of the possibly offending medication and a subsequent switch to an alternative atypical antipsychotic (risperidone) associated with pancreatitis. Once all atypical antipsychotics were discontinued, her symptoms resolved, and serum lipase normalized.

A previous case report associated aripiprazole with hyperlipasemia in the presence of severe hyperglycemia.<sup>5</sup> Throughout Ms. A's illness, results from tests for serum glucose levels were normal, suggesting that the mechanism for pancreatitis is independent of the atypical antipsychotic metabolic effects on glucose levels. Further studies are needed to evaluate the association of aripiprazole and acute pancreatitis and to clarify the pathophysiological cause.

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## CALM: A Mnemonic for Treatment Options for Bipolar Disorder

**Sir:** The treatment of bipolar disorder remains a challenge, with some clinicians using antidepressants frequently,<sup>1</sup> others promoting antipsychotics,<sup>2</sup> and some advocating primarily lithium or anticonvulsants.<sup>3</sup> For the practicing clinician, these debates can be confusing. We have devised the following mnemonic to help organize the treatment options for bipolar disorder: CALM.

**C** = Control manic and mixed symptoms. First and foremost, control manic and mixed symptoms (especially insomnia, irritability, agitation, and anxiety). Control of these symptoms is pivotal to treatment success. Agitation and irritability disrupt work situations and social supports, and even subsyndromal manic symptoms during bipolar depression have been associated with increased risk for suicidal behavior.<sup>4,5</sup>

**A** = Antidepressants. Use antidepressants very selectively, if at all. Recent randomized data from the STEP-BD (Systematic Treatment Enhancement Program for Bipolar Disorder) study showed adjunctive acute use of antidepressants to be of no help even in pure bipolar depression,<sup>6</sup> and in bipolar depressed patients with as few as 2 or more concomitant manic symptoms, adjunctive antidepressant use was associated with "significantly higher mania symptom severity at the 3-month follow-up."<sup>7</sup>

**L** = Longitudinal/long-term view. Take a longitudinal/long-term view of bipolar illness and treatment response. The long-term view of mood episodes over months to years is a key to making the diagnosis of bipolar disorder in the first place. Viewing only current cross-sectional symptoms may also interfere with the ability to accurately gauge the patient's response to treatment.

**M** = Mood stabilizers. Emphasize mood stabilizers—especially lithium, divalproex, carbamazepine, and lamotrigine—as these remain the core building blocks of effective bipolar disorder regimens.

*Dr. Sparhawk is on the speakers bureaus for AstraZeneca, Bristol-Myers Squibb, Cephalon, Forest, GlaxoSmithKline, Janssen, Otsuka, Pfizer, and Wyeth; has received research support from AstraZeneca, Bristol-Myers Squibb, Cephalon, GlaxoSmithKline, Janssen, Eli Lilly, Neurocrine, Sepracor, and Wyeth; and is on the advisory and/or consultant boards for AstraZeneca, Bristol-Myers Squibb, Forest, GlaxoSmithKline, Janssen, and Eli Lilly. Dr. Ghaemi currently receives research grants from GlaxoSmithKline and Pfizer; is on the speakers bureaus for GlaxoSmithKline, AstraZeneca, Pfizer, Janssen, and Abbott; and has served on the advisory boards of GlaxoSmithKline, Janssen, Pfizer, Shire, and Abbott. Neither he nor his family holds equity positions in pharmaceutical corporations.*

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### Suicide Attempt and Psychosis Revealed After an Apparent Traffic Accident: A Case Report

**Sir:** Although suicidal behavior has been known to occur in patients with known schizophrenia and other psychotic disorders,<sup>1</sup> the occurrence and frequency of underlying acute psychosis in victims of suicide attempts have not been well described.

I report the case of a trauma victim who had been hit by a car in an incident that initially appeared to be accidental; he was later revealed to have acute psychosis that had led to a suicide attempt.

**Case report.** Mr. A, a 36-year-old man, was brought to the emergency room (ER) in August 2007 after being hit by a car in traffic. He had some lacerations on his head and a broken femur. While being treated in the trauma unit, he was found to be talking to himself.

Neurology was consulted but was unable to find any neuro-anatomical cause for the patient to be talking to himself. Psychiatry was consulted, and a detailed history was obtained. Mr. A then revealed that the accident was, in fact, a suicide attempt. He had been hearing the voices of his friends and family talking outside the wall. He was sad that they were saying bad things about him and hated him but were not willing to come in. He felt that his life was worthless.

Interestingly, the patient was seen in the ER of another institution for suicidal ideation only 1 night prior to this event. Unfortunately, he managed to escape from the ER that day after he suddenly became very suspicious of the ER staff. He felt deceived and disheartened. This heightened his feelings of worthlessness, and he ran into moving traffic to kill himself.

Apparently, Mr. A had been having troubles for the past few years. He had been divorced twice and was staying with his mother. He believed that his mother poisoned his food. Every time his mother said, "I love you, son," he heard a small voice that followed immediately and said, "You know it is not true."

He was admitted to an inpatient psychiatric unit and started on risperidone treatment.

This case illustrates an example of the high risk of suicidality associated with first presentation of frank psychosis. One Irish study<sup>2</sup> showed that about 10% of patients present with suicide attempt as their first presentation of psychosis, and about 18% of patients will have a suicide attempt within 4 years of

their diagnosis, of which 3% die from suicide. Suicide attempt, in fact, seems to be one of the common presentations of psychotic disorder. It is prudent to investigate any situation that may actually represent a suicide attempt and obtain a detailed history to look for any clues of psychosis.

*Dr. Ojha reports no financial or other relationship relevant to the subject of this letter.*

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### Metabolic Side Effects of Risperidone in Children and Adolescents With Early-Onset Schizophrenia

**Sir:** Atypical antipsychotics have a favorable risk/benefit profile in early-onset schizophrenia,<sup>1</sup> but their endocrine and metabolic side effects (weight gain, obesity, and related metabolic abnormalities, such as hyperglycemia and dyslipidemia) are of particular concern,<sup>2</sup> especially with children.<sup>3,4</sup> These side effects may evolve to a metabolic syndrome with a high-risk state for future cardiovascular morbidity and mortality.<sup>5</sup> Sex- and age-adjusted body mass index (BMI) percentiles and BMI z scores are crucial to assess weight gain and obesity in children and adolescents.<sup>6</sup> Numerous studies have assessed weight gain during antipsychotic treatment,<sup>7</sup> yet these studies are limited because of their short duration and because of their methodology: indeed, adjusted BMI percentiles and BMI z scores were calculated in only 1 study.<sup>8</sup>

**Method.** This pilot study focuses on the metabolic effects of risperidone in children and adolescents up to 16 years of age. Patients included in the study were referred to our Department of Child and Adolescent Psychiatry at the University Hospital Center of Lille for early-onset schizophrenia (according to the Schedule for Affective Disorders and Schizophrenia for School Age Children for DSM-IV<sup>9</sup>) from June 2005 to June 2007. They had received no antipsychotic treatment prior to their inclusion. Weight, height, waist circumference, blood pressure, fasting triglyceride levels, fasting total and high-density lipoprotein (HDL) cholesterol levels, and fasting glucose levels were measured. Sex- and age-related BMI percentiles and adjusted BMI z scores were obtained from tables from the Centers for Disease Control.<sup>10</sup> Statistical analyses were performed using the SAS software (SAS Institute, Inc., Cary, N.C.). All p values < .05 were considered statistically significant. The linear mixed model was used to analyze repeated measurements. This study has been approved by the regional Comité de Protection des Personnes Nord-Quest IV.

**Results.** Fifteen schizophrenic adolescents (11 males, 4 females) aged 11 to 16 years (mean = 13.3 years, SD = 2.4 years) were included. Risperidone was given from 1 mg/day to a maximum of 6 mg/day. Data were obtained for 10 patients at month

3, for 8 patients at month 6, and for 5 patients at month 12 of follow-up. Statistical analysis shows a significant link between prescription of risperidone in early-onset schizophrenia and increases of BMI ( $p = .043$ ), sex- and age-adjusted BMI percentile ( $p = .033$ ), and BMI z scores ( $p = .025$ ). Clinically, one 15-year-old male, receiving risperidone up to 6 mg/day, presented with hyperprolactinemia-induced gynecomastia after 6 months of follow-up (neurologic examination was normal), while his BMI increased from 16.2 kg/m<sup>2</sup> to 28 kg/m<sup>2</sup> (BMI z score increased from  $-0.97$  to  $1.95$ ). Furthermore, one 14-year-old female, receiving 2 mg/day of risperidone, presented a 100 mg/dL increase of fasting total cholesterol (up to 248 mg/dL, normal range: 150–200 mg/dL) during the first 3 months of treatment, along with just a small increase of her BMI (from 17.1 kg/m<sup>2</sup> to 18.2 kg/m<sup>2</sup>). At 6 months of follow-up, her dose of risperidone was decreased to 1 mg/day, and within 3 months her total cholesterol level also decreased to 224 mg/dL. Glucose, cholesterol, and blood pressure remained at normal levels for all the other patients.

Despite the limited number of children included, our results confirm a strong link between prescription of risperidone in early-onset schizophrenia and risk of obesity. Clinicians and caregivers need to be aware of the potential endocrine and metabolic adverse effects of atypical antipsychotics and systematically ask for family history of metabolic disorder, lifestyle, diet, and habits. Alternative treatment should be considered in some cases.<sup>11</sup> With adolescents, the sole monitoring of weight gain, and even of BMI, underestimates the gain of corpulence. One methodological implication of our study is that adjusted BMI z scores seem to be the best suited to assess long-term drug-induced weight gain.

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*Dr. Bordet is a consultant to Genfit and has served on the speakers/advisory boards for Lundbeck, Janssen, Cilag, Bristol-Myers Squibb, Sanofi Aventis, and Pfizer. Drs. Goëb, Marco, Duhamel, Jardri, Kechid, Delion, and Thomas report no additional financial affiliations or other relationships relevant to the subject of this letter.*

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#### Corrections

In the letter to the editor "Separation Anxiety Disorder and School Refusal in Childhood: Potential Risk Factors for Developing Distinct Psychiatric Disorders?" by Karl Kralovec, M.D., et al. (volume 10, issue 1, pp. 72–73), Dr. Kralovec's surname was misspelled. The online version of the letter has been corrected.

In the letter to the editor "Exacerbation of Obsessions With Modafinil in 2 Patients With Medication-Responsive Obsessive-Compulsive Disorder" by Oguz Tan, M.D., et al. (volume 10, issue 2, pp. 164–165), Dr. Huseyin Bulut's surname was misspelled. The online version of the letter has been corrected.

The staff regrets these errors.