

and rehabilitation. The patient endorsed daily use of intravenous cocaine mixed with 400 mg–800 mg of quetiapine. Quetiapine was surreptitiously diverted from his wife's prescription. He reported crushing the quetiapine tablets and mixing the resulting powder with cocaine and water. He subsequently heated the mixture and drew the supernatant through a cotton swab into a syringe to administer intravenously. When asked why he engaged in this drug mixture, he stated that it achieved desired "hallucinogenic" effects.

Combining prescription medications and/or illicit drugs is a common practice to synergistically heighten the intoxication from the substances while potentially reducing undesirable side effects. The combination of intravenous heroin and cocaine (also known as "speedball") is a well-known strategy to both maximize the cocaine "rush," while mitigating its "crash" (5). It may be hypothesized that quetiapine was substituted for heroin in our case (to form a "Q-ball") because the sedative/anxiolytic effects of quetiapine may mitigate the dysphoria associated with cocaine withdrawal and to possibly provide a "hallucinogenic" effect.

The case presented highlights the unknown effects (such as a "hallucinogenic" experience) of combining substances with different pharmacological properties and subsequently circumventing first-pass metabolism through intravenous administration. Individuals who use oral medications intravenously have the potential to develop significant pulmonary complications secondary to the deposition of medication binders in lung parenchyma. Furthermore, the cardiovascular and arrhythmogenic properties of cocaine may be amplified in combination with quetiapine (which has a risk of QTc prolongation). Physicians should remain cognizant of potential medication diversion and misuse in noncorrectional settings.

#### References

1. Hussain MZ, Waheed W, Hussain S: Intravenous quetiapine abuse (letter). *Am J Psychiatry* 2005; 162:1755–1756
2. Del Paggio D: Psychotropic medication abuse in correctional facilities. *The Bay Area Psychopharmacology Newsletter* 2005; 8:1, 5
3. Della Volpe K: Intervention reduces abuse of psychotropic medications in correctional facility. *Pharmacy Practice News*, July 2005
4. The Vaults of Erowid. <http://www.erowid.org/> (accessed April 2006)
5. Smith JE, Co C, Collier MD, Hemby SE, Martin TJ: Self-administered heroin and cocaine combinations in the rat: additive reinforcing effects-supra-additive effects on nucleus accumbens extracellular dopamine. *Neuropsychopharmacology* 2006; 31: 139–150

BRIAN M. WATERS, M.D.  
KAUSTUBH G. JOSHI, M.D.  
*San Antonio, Tex.*

*The authors report no competing interests.*

#### Quetiapine Addiction?

TO THE EDITOR: Quetiapine is not a controlled substance and is not considered addictive. Yet there are several reports describing abuse among inmates in jails and prisons (1, 2).

The pharmaceutical formulary for the Ohio correctional system contains three second-generation antipsychotics, but quetiapine is not one of them. It may be prescribed with special authorization for patients with serious mental disorders who have not responded to formulary agents. However, inmates entering prison on quetiapine for other conditions, such as sleep and anxiety disorders, must have it tapered and discontinued.

The authors have treated a number of inmates who have engaged in drug-seeking and sometimes illegal behavior to obtain this medication. The following case is illustrative:

**A 39-year-old incarcerated male with hepatitis C and a history of opiate abuse was treated for generalized anxiety disorder. When seen by the prison psychiatrist, he was receiving quetiapine 800 mg and clonidine 0.9 mg at bedtime.**

**The psychiatrist was concerned about the risks of prescribing an antipsychotic medication for a patient with hepatitis without a serious mental disorder. The patient refused to discuss other treatment alternatives stating, "I need my Seroquel." Efforts to enlist his cooperation for a quetiapine taper were unsuccessful. He abruptly left a treatment team meeting and informed staff that he would purchase quetiapine illegally from other inmates and had done this before.**

We have treated other prisoners who have threatened legal action and even suicide when presented with discontinuation of quetiapine. We have not seen similar drug-seeking behavior with other second-generation antipsychotics of comparable efficacy. Emil R. Pinta, M.D. has worked as a prison consultant for 35 years and can only recall similar behavior to obtain controlled substances.

Hussain et al. suggest that quetiapine abuse may be more prevalent among prisoners because commonly abused drugs are less readily available (2). Another reason may be that quetiapine treats anxiety and sleeplessness associated with substance use withdrawal—with prisoners having high rates for these disorders (3). However, an internet search yielded a number of self-reports by individuals who believe they have become addicted to this agent (4). There is a popular rap song in which "seroquel" is included in a long list of addictive substances (5). In street jargon, quetiapine is known as "quell" and "Susie-Q."

Our experience indicates the need for additional studies to explore the addiction-potential of quetiapine. Quetiapine is an effective medication for treatment of schizophrenia, bipolar disorder, and related illnesses. We believe clinicians should be extremely cautious when prescribing this medication for nonserious mental disorders and for individuals with histories of substance abuse.

#### References

1. Pierre JM, Shnyder I, Wirshing DA, Wirshing WC: Intranasal quetiapine abuse (letter). *Am J Psychiatry* 2004; 161:1718
2. Hussain MZ, Waheed W, Hussain S: Intravenous quetiapine abuse (letter). *Am J Psychiatry* 2005; 162:1755–1756
3. Monnelly EP, Ciraulo DA, Knapp C, Locastro J, Sepulveda I: Quetiapine for treatment of alcohol dependence. *J Clin Psychopharmacol* 2004; 24:532–535
4. Addiction to Seroquel. [http://groups.msn.com/BipolarDisorderWebCommunity/seroquel.msnw?action=get\\_message1](http://groups.msn.com/BipolarDisorderWebCommunity/seroquel.msnw?action=get_message1)

5. Lil' Wyte lyrics-Oxy Cotton lyrics. <http://www.seeklyrics.com/lyrics/Lil-Wyde/Oxy-Cotton.html>

EMIL R. PINTA, M.D.  
Columbus, Ohio

ROBERT E. TAYLOR, M.D.  
Cambridge, Ohio

*The authors report no competing interests.*

## Safety of Aripiprazole: High Serum Levels in a CYP2D6 Mutated Patient

TO THE EDITOR: We present a patient with high serum levels of aripiprazole caused by a common genetic modification in CYP2D6.

**A 51-year-old female patient diagnosed with schizophrenia was admitted to our clinic. Little antipsychotic effect being observed, the dose of aripiprazole was increased from 15 mg to 30 mg per day. Within approximately 2 weeks, progressive symptoms of lethargy and memory loss were evident.**

**After testing blood samples, the serum level of aripiprazole in our patient turned out to be 2990 ng/ml, approximately seven times the expected plasma concentration at the maximum dose of 30 mg per day (1).**

Since aripiprazole is metabolized by CYP2D6 and CYP3A4 (2), testing for a genetic polymorphism in these genes was initiated, showing a substitution of G1934→A on both alleles of the CYP2D6 gene (homozygote CYP2D6\*4/\*4), corresponding with the suspected slow metabolism. Pharmacokinetic interactions with CYP3A4 were excluded, since our patient did not use concomitant medication, herbals or grapefruit juice. When aripiprazole was substituted by quetiapine 400 mg daily, the adverse symptoms improved.

The high serum levels of aripiprazole, not the adverse events, are disconcerting. Poor metabolization is seen frequently, with prevalence rates in Caucasians of 7% and of 1%–4% in Asians and black Americans (3, 4). Additionally, although aripiprazole is relatively safe in cases of acute intoxication (5), preclinical safety data revealed significant toxic effects in female rats, including 1) dose-dependent adrenocortical toxicity and 2) increased incidence of adrenocortical and combined carcinomas at three to 14 times, respectively, and 14 times the mean AUC at 30 mg a day (2). Our patient showed serum levels in the range of the toxic effects in animal

studies. The concordance rate of toxicity in humans with animal studies is 71% (6). Assuming our patient to represent all poor metabolizers, many patients would potentially be at risk of long-term toxicity because of the good tolerability of aripiprazole (1).

Since poor metabolizing occurs regularly, we recommend drug monitoring (expected plasmaconcentration at 15 mg and 30 mg daily: 206–278 ng/ml and 320–584 ng/ml, respectively [2]) after 14 days of treatment, when a steady state is expected as well as further safety studies in poor metabolizers.

## References

1. Mallikaarjun S, Salazar DE, Bramer SL: Pharmacokinetics, tolerability, and safety of aripiprazole following multiple oral dosing in normal healthy volunteers. *J Clin Pharmacol* 2004; 44: 179–187
2. Bristol-Myers Squibb BV: Aripiprazole Summary of Product Characteristics, 2004
3. Evans WE, Relling MV, Rahman A, McLeod HL, Scott EP, Lin JS: Genetic basis for a lower prevalence of deficient CYP2D6 oxidative drug metabolism phenotypes in black Americans. *J Clin Invest* 1993; 91:2150–2154
4. Mizutani T: PM frequencies of major CYPs in Asians and Caucasians. *Drug Metab Rev* 2003; 35:99–106
5. Carstairs SD, Williams SR: Overdose of aripiprazole, a new type of antipsychotic. *J Emerg Med* 2005; 28:311–313
6. Olson H, Betton G, Robinson D, Thomas K, Monro A, Kolaja G, Lilly P, Sanders J, Sipes G, Bracken W, Dorato M, Van Deun K, Smith P, Berger B, Heller A: Concordance of the toxicity of pharmaceuticals in humans and in animals. *Regul Toxicol Pharmacol* 2000; 32:56–67

MARIEKE OOSTERHUIS, PHARM.D.  
GERBEN VAN DE KRAATS, M.D.  
DIEDERIK TENBACK, M.D., PH.D.  
*Leiden, the Netherlands*

*All authors report no competing interests.*

## Comment on CME Courses

[I] wanted to pass on my thanks for this CME product. It's straightforward and easy to use. I am a military psychiatrist in Iraq for 6 mo[nths], and to know I can easily and cheaply pick up 3 CME hours per mo[nth] is a Godsend. Keep up the good work. Thanks again.

HENRY B. NELSON, M.D.  
*LSA Anaconda, Iraq*

*Reprints are not available; however, Letters to the Editor can be downloaded at <http://ajp.psychiatryonline.org>.*

## Corrections

In the Clinical Case Conference “An Interaction Between Aspirin and Valproate: The Relevance of Plasma Protein Displacement Drug-Drug Interactions” (*Am J Psychiatry* 2006; 163:1891–1896), the units for valproate blood levels were given as “ng/ml.” They should be “µg/ml.”

In the article “Differences in Brain Chemistry in Children and Adolescents With Attention Deficit Hyperactivity Disorder With and Without Comorbid Bipolar Disorder: A Proton Magnetic Resonance Spectroscopy Study” (*Am J Psychiatry* 2006; 163:316–318), the NIMH grant number in the acknowledgments should have been MH-01978.