not have significant peripheral eosinophilia, which suggests that clozapine may cause alveolitis via more than one mechanism in susceptible individuals. Clinicians should consider clozapine-induced lymphocytic alveolitis in patients who develop pulmonary infiltrates while receiving clozapine treatment.

Reference

1. Benning TB: Clozapine-induced extrinsic allergic alveolitis. Br J Psychiatry 1998; 173:440–441

SIXTO A. ARIAS, M.D.
PAUL COHEN, M.D.
JEFF S. KWON, M.D.
Bridgeport, Conn.

The authors report no financial relationships with commercial interests.

This letter (doi: 10.1176/appi.ajp.2010.10101494) was accepted for publication in December 2010.

Aripiprazole Adjunctive to Antidepressant Therapy

TO THE EDITOR: We would like to clarify the dosing for aripiprazole adjunctive to antidepressant therapy in patients with major depressive disorder as suggested in the American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients With Major Depressive Disorder (1), published as a supplement to the October 2010 issue of the *Journal*. The medication product information states that for adjunctive treatment of major depressive disorder, aripiprazole should be initiated at 2–5 mg per day, with a target dose of 5–10 mg per day and a maximum dose of 15 mg/day. Dose adjustments of up to 5 mg/day should occur gradually, at intervals of no less than 1 week, and no dosage adjustments are needed for the current antidepressant.

The current guidelines state that adjunctive aripiprazole is typically initiated at 2.5–5 mg/day and titrated upward as tolerated to a maximum dose of 30 mg/day. In the study cited for this recommendation (2), adjunctive aripiprazole was initiated at 5 mg/day and, if tolerability permitted, increased to the target dose of 10 mg/day at the start of week 2. The dose could be reduced to 2 mg if necessary for tolerability. The maximal dose in the study was 20 mg/day. There is no recommendation in the product information for a maximum dose of 30 mg/day for aripiprazole adjunctive to antidepressants. When making treatment decisions, it is important to consider the doses that were studied in three large, placebo-controlled, double-blind clinical trials for aripiprazole adjunctive to antidepressants in the treatment of major depressive disorder (2–4), and these data provide the foundation for the recommended doses in the product information.

References

1. American Psychiatric Association: American Psychiatric Association Practice Guideline for the Treatment of Patients With Major Depressive Disorder. Am J Psychiatry 2010; 167(suppl):A34
2. Berman RM, Marcus RN, Swanink R, McQuade RD, Carson WH, Corey-Lisle PK, Khan A: The efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder: a multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychiatry 2007; 68:843–853
3. Marcus RN, McQuade RD, Carson WH, Hennicken D, Fava M, Simon JS, Trivedi MH, Thase ME, Berman RM: The efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder: a second multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol 2008; 28:156–165
4. Berman RM, Fava M, Thase ME, Trivedi MH, Swanink R, McQuade RD, Carson WH, Adson D, Taylor L, Hazel J, Marcus RN: Aripiprazole augmentation in major depressive disorder: a double-blind, placebo-controlled study in patients with inadequate response to antidepressants. CNS Spectr 2009; 14:197–206

RONALD M. MARCUS, M.D.
Wallingford, Conn.
RAYMOND SANCHEZ, M.D.
Princeton, N.J.
MARIANNE FROST, M.S.
Wallingford, Conn.
ROBERT D. MCQUADE, PH.D.
Princeton, N.J.

Dr. Marcus has received support from Bristol-Myers Squibb; and he is employed by Bristol-Myers Squibb. Dr. Sanchez has received support from Otsuka Pharmaceutical Development and Commercialization, Inc. Ms. Frost has received support from Bristol-Myers Squibb; and she is employed by Bristol-Myers Squibb. Dr. McQuade has received support from Otsuka Pharmaceutical Development and Commercialization, Inc; he is employed by Otsuka Pharmaceutical Development and Commercialization, Inc.; and he is a shareholder with Bristol-Myers Squibb.

This letter (doi: 10.1176/appi.ajp.2010.10101515) was accepted for publication in December 2010.

Response to Marcus et al. Letter

TO THE EDITOR: We thank Dr. Marcus et al. for bringing this error to our attention. The upper dose of aripiprazole studied for adjunctive treatment of major depressive disorder is 20 mg/day, and the upper recommended dose is 15 mg/day. A correction will be made in the guideline text published on PsychiatryOnline.com.

JOEL YAGER, M.D., CHAIR,
APA STEERING COMMITTEE ON PRACTICE GUIDELINES
Denver, Colo.
ALAN J. GELENBERG, M.D., CHAIR,
APA WORK GROUP ON MAJOR DEPRESSIVE DISORDER
Hershey, Pa.
LAURA J. FOCHTMANN, M.D., MEDICAL EDITOR,
APA PRACTICE GUIDELINES
Stony Brook, N.Y.

The authors' disclosures accompany the APA Practice Guideline.

This letter (doi: 10.1176/appi.ajp.2010.10101515r) was accepted for publication in December 2010.

Propofol Addiction Initiated by Anesthetic Use

TO THE EDITOR: Propofol is a safe anesthetic agent, acts rapidly, and allows a fast recovery from anesthesia. Despite its abuse potential by activation of the gamma-aminobutyric acid receptor type A ($GABA_A$), only several cases of propofol depen-

dency and abusive use for recreational intentions, mostly by medical professionals, have been reported since 1992 (1). We present the first case of propofol dependency initiated by repeated application of the drug within anesthetic use.

A 34-year-old female midwife was admitted to our hospital for propofol detoxification. The patient had no history of substance abuse or psychiatric disorders as well as no family history of substance use disorders. She suffered from a severe form of Crohn's disease, which resulted in her undergoing more than 28 necessary colonoscopies and surgeries between 1991 and 2008. Propofol was used for sedation and anesthesia in the majority of all her medical procedures. After her first surgeries, the patient described feeling "high and light-headed" and indicated that she "liked" the postanesthetic effect of propofol but had no craving for the drug between the surgeries.

In 2000, while faced with a variety of stressors and following renewed colonoscopies in which propofol was administered, the patient experienced a strong desire for the drug's euphoric and relaxing effects. She started self-medication with propofol, which she stole from her workplace. While keeping the dosage of each injection constant at 200 mg, she increased the frequency of the injections up to 5–7 times per day. For at least 1 year, the patient consumed propofol nearly everyday and was only limited by availability. During an inpatient treatment for Crohn's disease, she self-administered propofol twice through her central vein catheter and was found somnolent. However, she decided to visit our department for addiction treatment only after a colleague found the stolen propofol in her handbag (with the consequence being that she lost her job).

The present case indicates that propofol primarily used for anesthetic reasons has abuse potential even in patients without a history of drug abuse. Brazzalotto (2) found that 40% of 542 patients described feelings of pleasure after awaking from anesthesia with propofol, which is probably caused by a rapid activation of $GABA_A$ within mesocorticolimbic pathways.

It remains to be discussed why the vast majority of patients exposed to propofol apparently do not develop an addiction to the drug, contrary to our patient. One main contributing factor to the addiction seen in our patient might be the repeated exposure to the drug over several years. However, an important additional factor is that our patient (in contrast to the majority of anesthetized patients) was aware of propofol used for anesthesia, which caused the appreciated effect, and, moreover, was able to make the drug available for intentional use.

Based on the present report, vigilance should increase regarding the positively reinforcing effects of propofol, especially after repeated application in patients for whom propofol is available.

References

1. Wilson C, Canning P, Caravati EM: The abuse potential of propofol. Clin Toxicol (Phila). 2010; 48:165–170
2. Brazzalotto I: Propofol effects. Annales Francaises D Anesthesie et de Reanimation 1989; 8:388

ANNE KOOPMANN, M.D.
CHRISTOPH VON DER GOLTZ, M.D.
DERIK HERMANN, M.D.
FALK, KIEFER, M.D.
Mannheim, Germany

The authors report no financial relationships with commercial interests.

This letter (doi: 10.1176/appi.ajp.2010.10091293) was accepted for publication in December 2010.

Fatal Hepatotoxicity in an Elderly Patient Receiving Low-Dose Quetiapine

TO THE EDITOR: Quetiapine-related liver abnormalities are extremely rare occurrences. We report on a case of fatal hepatotoxicity caused by the lowest dose of quetiapine in an elderly patient.

"Ms. B" was a 77-year-old, fragile woman who was brought to the outpatient service of the geriatric clinic with symptoms of increasing fatigue, vomiting, and loss of appetite for 1 week. The patient had recently received treatment with low-dose quetiapine (12.5 mg twice daily) for 9 days, as prescribed by her psychiatrist, for symptoms of agitation and severe insomnia. She had no family or personal history of liver disease or abnormal liver biochemistry, and results of her liver function tests, conducted in our hospital 3 weeks prior, revealed aminotransferase levels within normal limits. The patient gave no history of alcohol use, substance abuse, or smoking, and she was not receiving any medication other than quetiapine.

On examination, she was afebrile, with a temperature of 36.8°C. She had a blood pressure measurement of 94/62 mm Hg, a heart rate of 112 beats/minute, a respiratory rate of 28 breaths/minute, and an oxygen saturation rate of 96% on a 2-liter nasal cannula. The patient was not alert, and she was disoriented. Her physical examination was unremarkable otherwise. However, laboratory findings were as follows: leukocyte count, 10.300 mm^3; hemoglobin level, 12.1 g/dl; hematocrit level, 37.4%; platelet count, 256.000/mm^3; erythrocyte sedimentation rate, 24 mm/h; C-reactive protein level, 3 μg/dl; serum creatinine concentration, 1.43 mg/dl; blood urea nitrogen concentration, 44.63 mmol/l; sodium level, 135.1 mmol/l; potassium level, 5.14 mmol/l; aspartate aminotransferase concentration, 1,415 U/l; (reference range: 10–35 U/l); alanine aminotransferase concentration, 1,565 U/l (range: 10–35 U/l); alkaline phosphatase level, 178 U/l (range: 38–155 U/l); gamma-glutamyl transferase level, 95 U/l (range: 7–32 U/l); total bilirubin, 4.77 mg/dl; direct bilirubin, 3.38 mg/dl; albumin concentration, 3.32; prothrombin time, 56.6 seconds; international normalized ratio, 4.12; and ammonia concentration, 104 g/dl. A diagnostic evaluation for viral, autoimmune, and metabolic diseases was negative, and an abdominal ultrasound using Doppler was not remarkable.

Following this extensive work-up, the patient's acute hepatic failure was attributed to an idiosyncratic reaction to low-dose quetiapine. Therefore, quetiapine was discontinued. Although her liver function improved in the following 7 days (aspartate transaminase concentration: 942 U/l, alanine transaminase concentration: 1,020 U/l), her condition continued to deteriorate significantly despite full supportive care in the intensive care unit. "Ms. B" died on the eighth day of her stay in the intensive care unit because of overwhelming multiorgan system failure.

The causal relationship between quetiapine and hepatotoxicity was evaluated using Naranjo criteria (1) (see the data supplement accompanying the online version of this case