

## EDITOR'S NOTE

This column reflects our commitment to provide you, the primary care physician, with information that will prove helpful in making informed decisions about the care of your patients who suffer from psychiatric disorders. We will highlight abstracts of high interest to you from our sister publication, *The Journal of Clinical Psychiatry*, and summarize pertinent articles from the general scientific literature. We hope that this section is clinically relevant to your practice and that it will encourage you to expand your horizons.

## Recognition and Prevention of Inhalant Abuse

Anderson CE, Loomis GA

Inhalant abuse is a prevalent and often overlooked type of substance abuse in adolescents. According to survey results, nearly 20% of adolescents in middle school and high school have experimented with inhaled substances. The method of delivery is inhalation of a solvent from its container, a bag, or a soaked rag. Solvents include almost any household propellant or cleaning agent, glue, lighter fluid, and paint thinner. Typically, inhalant abuse causes a feeling of euphoria and can become addictive. Acute effects include asphyxia, sudden sniffing death syndrome, and serious injuries (e.g., burns, frostbite, falls). Chronic inhalant abuse can damage neurologic, hepatic, cardiac, and renal systems, and abuse during pregnancy can cause fetal abnormalities. Diagnosis of inhalant abuse is difficult and relies almost solely on a high index of suspicion and a thorough history. Because there are no reversal agents for inhalant intoxication, treatment is generally supportive. It is essential to educate young persons and their parents in order to decrease inhalant experimentation.

(*Am Fam Physician* 2003;68:869-874,876)

## The Effects of Mirtazapine on Plasma Lipid Profiles in Healthy Subjects

Nicholas LM, Ford AL, Esposito SM, et al.

**Background:** The novel antidepressant mirtazapine has been linked to elevated random plasma total cholesterol (TC) levels. The purpose of this study was to evaluate in a more controlled and precise approach the putative effects of mirtazapine on plasma lipids. **Method:** In a double-blind design, 50 healthy subjects (30 women and 20 men) were randomized to receive either mirtazapine (N = 28) or placebo (N = 22) for a 4-week period. The study was conducted from June 1997 to September 1998. The initial dose for the mirtazapine group was 15 mg daily, which was increased to 30 mg daily at the beginning of the second week. Body weight and plasma lipoprotein profiles, including TC, low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides, were determined at baseline and at weekly intervals throughout the study period. **Results:** At baseline, there were no group differences in any of the measures. There was a statistically significant increase of 2.5% in mean body weight over the course of the study in the mirtazapine group that appeared to reach a plateau at 3 weeks, while no increase was observed in the placebo group. Mirtazapine subjects also showed significantly increased TC at week 4 ( $p = .016$ ) and a transient rise in triglycerides that normalized by week 4. No significant changes in any of the other lipid parameters, including HDL, LDL, and TC/HDL ratios, were observed within either group. Changes in TC were significantly and positively correlated with changes in weight ( $p < .01$ ). **Conclusion:** These results suggest that while mirtazapine may be associated with increased TC, it does not increase LDL levels or affect the ratio of TC to HDL.

(*J Clin Psychiatry* 2003;64:883-889)

## Psychotic Symptoms in Alzheimer Disease: Evidence for Subtypes

Cook SE, Miyahara S, Bacanu SA, et al.

**Objective:** A phenotype with distinct neurobiology and genetic architecture is identified in the psychotic symptoms of Alzheimer disease (AD). This article investigated whether AD with psychosis is a composite of subtypes or homogeneous. **Methods:** Factor and cluster analyses of the psychotic-symptom items of the CERAD Behavioral Rating Scale in 188 probable and possible AD subjects who had displayed at least 1 psychotic symptom were performed. **Results:** A 1-factor solution that comprised auditory and visual hallucinations, misidentification delusions, and the misidentification of people resulted from the exploratory factor analysis. Persecutory delusions were often present and were independent of the misidentification/hallucination factor. Similar results were yielded from cluster analysis. **Conclusion:** Misidentification/hallucinations and

persecutory delusions may distinguish 2 subtypes of psychosis in AD. In order to determine whether these proposed subtypes remain stable and independent over time or merge into a single group over the illness course, longitudinal study is necessary. (*Am J Geriatr Psychiatry* 2003;11:406–413)

### Risperidone, but Not Olanzapine, Decreases Bone Mineral Density in Female Premenopausal Schizophrenia Patients

Becker D, Liver O, Mester R, et al.

**Background:** The hyperprolactinemia induced by conventional antipsychotics often leads to osteoporosis. The commonly used atypical antipsychotics risperidone and olanzapine vary in their hyperprolactinemic properties. Therefore, we compared hormone profiles and bone properties in female premenopausal schizophrenia patients treated with either risperidone or olanzapine. **Method:** In a cross-sectional study, consecutive premenopausal, female, DSM-IV schizophrenia patients who were treated with either risperidone (N = 12) or olanzapine (N = 14) for at least 2 years were included. Dual energy X-ray absorptiometry evaluated bone mineral density, and multisite quantitative ultrasound measured bone speed of sound. In addition, profiles of urinary excretion of deoxyypyridinoline and circulating levels of hormones and lipids were assessed. **Results:** Serum prolactin levels were higher in the risperidone-treated group as compared with the olanzapine subjects ( $123 \pm 144$  and  $25.9 \pm 25.7$ ,  $p < .05$ ). Whereas bone mineral density was similar in the treatment groups, bone speed of sound was lower in the risperidone group as compared with the olanzapine-treated group. Expressed as age-adjusted Z score, bone speed of sound at the radius was  $-0.31$  and  $0.58$ , respectively,  $p < .05$ , and at the phalanx,  $-1.41$  and  $0.04$ , respectively,  $p < .05$ . The bone speed of sound in the risperidone-treated patients inversely correlated with urinary deoxyypyridinoline excretion ( $r = 0.73$ ,  $p < .05$ ). **Conclusion:** Risperidone treatment, as opposed to olanzapine, for female premenopausal schizophrenia results in hyperprolactinemia and clinically relevant decrease in bone mineral density. The calculated relative risk for fragility fracture of women treated with risperidone as compared to those treated with olanzapine is 1.78 when bone speed of sound was measured at the phalanx and 1.23 when measured at the radius. (*J Clin Psychiatry* 2003;64:761–766).

### Transfer of Olanzapine Into Breast Milk, Calculation of Infant Drug Dose, and Effect on Breast-Fed Infants

Gardiner SJ, Kristensen JH, Begg EJ, et al.

**Objective:** Infant drug doses and breast-milk-to-plasma area-under-the-curve ratios for olanzapine were characterized in this study. Plasma concentrations and effects of the drug on breast-feeding infants were determined. **Method:** The study included 7 mother-infant nursing pairs. Olanzapine was measured in milk and plasma with high-performance liquid chromatography at a single time after dose ingestion (for 1 patient) at steady state or over a dose interval (for 6 patients). Infant drug exposure was estimated as the product of an assumed milk production rate and average drug concentration in milk and expressed as a percentage of maternal dose; both measures were normalized to body weight. **Results:** The median milk-to-plasma area-under-the-curve ratio was 0.38 for the 6 patients with data collected over

the dose interval. The median infant dose of olanzapine ingested through milk was 1.02% of the maternal dose. In the patient with single-point data, corresponding values were 0.75 and 1.13%. In the 6 infants with an evaluable plasma sample, olanzapine was not detected in the plasma. None of the infants experienced side effects, and all were healthy. **Conclusions:** Breast-fed infants were exposed to a calculated dose of olanzapine (approximately 1%) well below the 10% notional level of concern. Olanzapine was well below the detection limit in infant plasma and the infants experienced no adverse effects. These data support the use of olanzapine during breast-feeding. The authors recommend, however, that breast-fed infants be monitored closely and the decision to breast-feed be made after individual risk-benefit analysis.

(*Am J Psychiatry* 2003;160:1428–1431)

### Alcohol-Related Dementia: Validation of Diagnostic Criteria

Oslin DW, Cary MS

**Objective:** To validate the diagnostic criteria for alcohol-related dementia. **Methods:** Veterans consecutively admitted to a 240-bed VA nursing home care unit were included in the sample. Measures of cognition and functioning were included in baseline and follow-up assessments. The diagnosis and type of dementia were determined within 2 months of admission by a geropsychiatrist using chart review, patient interviews, and information from a structured collateral interview. Residents were followed for up to 2 years. **Results:** Data were collected on 192 residents, 158 (82%) of whom were diagnosed with dementia of some form. Diagnoses were as follows: alcohol-related dementia (ARD) in 16 residents (10.1%), vascular dementia (VD) in 46 (29.1%), probable Alzheimer dementia (AD) in 26 (16.5%), and mixed or dementia of undetermined origin in 70 (44.3%). A stabilization of both cognition and functional status was demonstrated in residents with ARD. Those with VD and AD, however, showed a general decline in both functional status and cognition. **Conclusion:** These results validate the diagnostic criteria for ARD and suggest that abstinence may be of clinical value in treating patients with alcohol dependence and dementia. Additional research should be conducted to confirm the value of abstinence.

(*Am J Geriatr Psychiatry* 2003;11:441–447)

### Ethnicity and Diagnosis in Patients With Affective Disorders

Strakowski SM, Keck PE Jr, Arnold LM, et al.

**Background:** Clinically, African American psychiatric patients are disproportionately diagnosed with schizophrenia compared with white patients. Why this occurs is unknown. Extending prior work, the authors hypothesized that first-rank symptoms distract clinicians so that they fail to identify affective disorders in African Americans. **Method:** 195 African American and white patients with at least 1 psychotic symptom (delusions, hallucinations, or prominent thought disorder) at admission were recruited from January 1, 1998, through May 31, 2001. Each patient received 3 independent DSM-IV diagnoses: a clinical diagnosis, a structured-interview diagnosis, and an expert-consensus diagnosis. The expert-consensus diagnoses were derived from the structured interviews, which were audiotaped and tran-

scribed, and medical records. After reviewing edited transcripts and medical records from which ethnic cues had been eliminated, 2 psychiatrists assigned expert-consensus diagnoses and first-rank symptom ratings. For the 79 patients who received an expert-consensus diagnosis of an affective disorder, clinical variables, diagnoses, and first-rank symptoms were compared between African American (N = 39) and white (N = 40) patients. **Results:** Seventy-nine (41%) of 195 patients were diagnosed with an affective disorder by expert consensus. African American men with an expert-consensus affective disorder were significantly ( $p < .03$ ) more likely than other patients to be diagnosed with a schizophrenia spectrum disorder by clinical assessment and structured interview. Although first-rank symptoms were more commonly identified in African American men, this finding did not explain the difference in diagnoses. Post hoc analyses suggested that African American men diagnosed with a schizophrenia spectrum disorder were more likely than other patients to have been identified during structured interview as having psychotic symptoms in the absence of affective symptoms. **Conclusion:** The apparent misdiagnosis of schizophrenia in African-Americans with mood disorders cannot be ascribed to differences in first-rank symptoms. However, it may be due to a perception that psychotic symptoms are more chronic or persistent than affective symptoms in these patients.

(*J Clin Psychiatry* 2003;64:747-754)

### Off-Label Applications for SSRIs

Stone KJ, Viera AJ, Parman CL

Due to their safety, tolerability, and demonstrated efficacy across a broad range of clinical conditions, selective serotonin reuptake inhibitors (SSRIs) are widely used. The use of SSRIs is supported in the medical literature for the treatment of many conditions outside of the U.S. Food and Drug Administration-approved indications. SSRIs are a reasonable alternative to traditional therapy for generalized anxiety disorder, and a side effect of SSRIs provides therapy for premature ejaculation. SSRIs are possibly effective in reducing the pain of diabetic neuropathy and may reduce the frequency and severity of migraine headaches. When combined with tricyclic antidepressants, SSRIs offer more potent therapy for fibromyalgia than either agent alone. In some patients with neurocardiogenic syncope that is refractory to standard therapies, SSRIs appear to be effective. Ongoing research and clinical experience continue to expand on the broad array of therapeutic applications for SSRIs. (*Am Fam Physician* 2003;68:498-504)

### The Role of Managed Care and Financing in Medical Practices: How Does Psychiatry Differ From Other Medical Fields?

Sturm R, Ringel JS

**Background:** During the past decade, the organization and financing of medical practice has experienced substantial changes. Today, traditional indemnity insurance is predominant only among Medicare enrollees, and the majority of individuals with private insurance are enrolled in managed care plans. There was substantial growth in the number of managed care companies specializing in behavioral health care and separating them out ("carved-out") from other medical care at the same time that managed care was growing in general. It is clear that these changes have influenced physicians and the way they

practice medicine; however, it is less clear whether there has been a differential effect across physician types. **Method:** Data were collected from the Community Tracking Study physician survey, a national survey of active physicians in the United States fielded between August 1998 and November 1999. Physicians had to have completed their medical training (which excludes residents, interns, or fellows) and be providing direct patient care for at least 20 hours/week in the contiguous United States to be eligible. The total number of completed interviews was 12,304, including 7,217 primary care physicians, 566 psychiatrists, and 4,521 other medical or surgical specialists. Our analysis is primarily descriptive presenting weighted means and odds ratios from multivariate models and is consistent with the previous literature. **Results:** Psychiatrists are significantly less likely than primary care physicians or other specialists to agree that clinical decisions in the interest of their patients do not reduce income. Psychiatrists, in comparison to primary care physicians, are less likely to agree that they have the freedom to make clinical decisions that meet their patients' needs or that it is possible to maintain continuing patient relationships over time that promote delivery of high quality care. Psychiatrists, in contrast to the perceived impacts on practice, tend to work in practices with a lower dependence on managed care than either primary care physicians or other specialists. Regarding individual physician compensation among nonowners, psychiatrists are less likely than other physicians to have their income adjusted based on individual productivity. **Conclusions:** Based on the available measures of financing and organization, psychiatrists are less dependent on managed care but are more concerned that managed care has a negative impact on patient-provider relationships than other physicians. Other aspects of managed care, such as preauthorization and gatekeeping that disproportionately affect specialists are driving psychiatrists' perceptions of the patient-provider relationship.

(*Soc Psychiatry Psychiatr Epidemiol* 2003;38:427-435)

### Effects of Treating Depression and Low Perceived Social Support on Clinical Events After Myocardial Infarction

Writing Committee for the ENRICHD Investigators

**Context:** Low perceived social support (LPSS) and depression after myocardial infarction (MI) are associated with higher morbidity and mortality; little is known about whether treatment can reduce this excess risk. **Objective:** To determine whether recurrent infarction and mortality are reduced by treatment of LPSS and depression with cognitive behavior therapy (CBT), supplemented with a selective serotonin reuptake inhibitor (SSRI) antidepressant when indicated, in patients enrolled 28 days after MI. **Design, Setting, and Patients:** MI patients (N = 2481 [1084 women, 1397 men]) were enrolled from 8 clinical centers in a randomized clinical trial conducted from October 1996 to April 2001. Modified DSM-IV criteria were used to diagnose major or minor depression, and severity was identified by the 17-item Hamilton Rating Scale for Depression (HRSD); the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Social Support Instrument (ESSI) was used to determine LPSS. Random allocation was to CBT-based psychosocial intervention or usual medical care. **Intervention:** Cognitive behavior therapy was started at a median of 17 days after the index MI for a median of 11 individual sessions over a 6-month time period, plus group therapy when feasible, with SSRIs for patients scoring higher than 24 on the HRSD or having a less than 50% reduction

in Beck Depression Inventory scores after 5 weeks. **Main Outcome Measures:** Composite primary endpoint of death or recurrent MI. Secondary outcomes included change in ESSi scores (for LPSS) and change in HRSD scores (for depression) at 6 months. **Results:** Psychosocial outcome improvement at 6 months favored treatment: mean (SD) change in HRSD score, -10.1 (7.8) in the depression and psychosocial intervention group versus -8.4 (7.7) in the depression and usual care group ( $p < .001$ ); mean (SD) change in ESSi score, 5.1 (5.9) in the LPSS and psychosocial intervention group versus 3.4 (6.0) in the LPSS and usual care group ( $p < .001$ ). After a 29-month average follow-up, there was no significant difference in event-free survival between psychosocial intervention (75.8%) and usual care (75.9%). There were no differences in survival between the usual care and psychosocial intervention arms in any of the 3 psychosocial risk groups (LPSS, depression, and LPSS and depression patients). **Conclusions:** Event-free survival was not increased by the intervention. Depression and social isolation were improved through the intervention; however, the relative improvement in the psychosocial intervention group compared with the usual care group was less than expected because the usual care patients improved substantially. (*JAMA* 2003;289:3106-3116)

### Psychopathology and Age at Onset of Conduct Problems in Juvenile Delinquents

Ruchkin V, Koposov R, Vermeiren R, et al.

**Background:** This study aimed to assess psychopathology among incarcerated Russian juvenile delinquents in relation to onset of conduct problems. **Method:** 358 male juvenile delinquents were interviewed from January to September 1999, using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version. Early behavior problems, current antisocial behavior, and psychopathology were also assessed through self-reports. The presence of conduct disorder (CD) and other diagnoses was determined according to DSM-IV criteria. **Results:** 73.2% of the incarcerated youths met criteria for CD. 23.5% of the total sample reported at least 1 criterion for CD being present before the age of 10 years. All participants from this early-onset group fulfilled the criteria for CD. This group also had significantly higher rates of psychopathology, and particularly of externalizing behaviors, as compared with youths whose conduct problems began at or after the age of 10 years. **Conclusion:** Poor psychosocial adaptation and future prognosis in juvenile delinquents with early-onset conduct problems may be related to their greater degree of psychiatric disturbance compared with later-onset delinquent youths. Need for psychiatric treatment should be carefully considered in prevention and rehabilitation efforts for troubled youths.

(*J Clin Psychiatry* 2003;64:913-920)

### The Use of Antidepressants in Alcohol-Dependent Veterans

Petrakis IL, Leslie D, Rosenheck R

**Background:** Although some research reports suggest antidepressants may be an effective treatment for alcohol dependence, their clinical use has been controversial. **Method:** By using comprehensive national administrative data from the Department of Veterans Affairs (VA) documenting psychiatric diagnoses and care under natural conditions in both mental health and non-mental health settings, the use of antidepressants was compared in alcoholic and non-alcoholic veterans. Data were collected from April 1, 2000, to Sept. 30, 2000. **Results:** Overall, patients with alcohol dependence were significantly more likely to be prescribed antidepressants than individuals without alcoholism (38.9% vs. 31.2%), but multivariate analysis showed that this was attributable to the higher rate of comorbid psychiatric diagnoses in this group. After controlling for diagnosis and other potentially confounding factors, alcohol-dependent individuals treated in specialty mental health clinics were in fact less likely to be prescribed antidepressants (odds ratio = 0.95,  $p < .0001$ ). Of patients treated with antidepressants, those with alcohol dependence were more likely to be prescribed newer antidepressants (odds ratio = 1.22,  $p < .0001$ ). Among patients treated in non-mental health clinics, there were no significant differences in rate of antidepressant use between alcohol-dependent and non-alcohol-dependent individuals with mental illness after controlling for other factors. **Conclusion:** The principal finding is that a diagnosis of alcoholism, independent of other factors, is associated with a decreased likelihood of receiving antidepressant treatment in VA mental health clinics, suggesting that prescribers have not embraced reports of their efficacy in alcohol dependence. In fact, this may reflect a disinclination to use medications to treat alcoholism in specialty mental health clinics but not in non-mental health clinics.

(*J Clin Psychiatry* 2003;64:865-870)

### Ginkgo Biloba

Sierpina VS, Wollschlaeger B, Blumenthal M

Ginkgo biloba is commonly used in the treatment of vascular dementia, early-stage Alzheimer's disease, tinnitus of vascular origin, and peripheral claudication. Systematic reviews suggest the herb can improve the symptoms of dementia, and multiple trials investigating the efficacy of ginkgo for treating cerebrovascular disease and dementia have been performed. Although generally well tolerated, ginkgo can increase the risk of bleeding if used in combination with antiplatelet agents, warfarin, and certain herbal medications. This review addresses clinical issues of dosing, safety, pharmacology, and use in the perioperative period.

(*Am Fam Physician* 2003;68:923-926)