2006 in Review

The editors are pleased to offer a brief personal selection of some of the articles that they found particularly interesting and important in this year's *Journal*.

Zuvekas SH, Vitiello B, Norquist GS: Recent trends in stimulant medication use among U.S. children. Am J Psychiatry 2006; 163:579–585

The first article is an example of our publication of epidemiological studies that calibrate the practice of psychiatry. The Food and Drug Administration (FDA) was told last spring by a prominent cardiologist that a doctor's hand should tremble when he or she writes a prescription for stimulants for attention deficit hyperactivity disorder (ADHD) because of the possibility of severe cardiac side effects. The specters of iatrogenic addiction and the indiscriminant use of psychotropic drugs to enhance school performance were raised. This study, which was scheduled for publication several months later, showed that the prescription of stimulants to children has been remarkably stable over the past decade and that, if anything, too few children are treated. The final version of the April issue had already gone to our printer the morning that we decided that this article needed to be published sooner than its scheduled time. Fortunately, because the printers were at lunch and work had not yet started we could hold the issue for this article. Our professional editorial staff, who are listed on the masthead, are marvelous; they worked quickly with the authors to get the text ready for printing. The only article that we could displace immediately was a review article by Kenneth Kendler, M.D., who told us that the needs of children should come first. The article appeared while the FDA hearings were ongoing, and the FDA decided not to issue a more severe warning about the safety and use of drugs that have a unique value in the treatment of childhood mental disorder.

ROBERT FREEDMAN, M.D.

McGlashan TH, Zipursky RB, Perkins D, Addington J, Miller T, Woods SW, Hawkins KA, Hoffman RE, Preda A, Epstein I: Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. Am J Psychiatry 2006; 163:790–799

Although we await the clinical availability of medications for the treatment of schizophrenia based on an understanding of the underlying disease process, the ultimate goal remains the prevention of this common, chronic, and costly illness. The apparently complex set of genetic liabilities and environmental risk factors that give rise to schizophrenia does not augur well for the development of means for primary prevention in the foreseeable future. However, advances in the clinical identification of adolescents and young adults at high risk for schizophrenia suggest that secondary forms of prevention that could forestall, delay the onset of, or reduce the severity of psychosis might be achievable. Indeed, the findings by McGlashan and colleagues, although they did not achieve statistical significance, are consistent with the hypothesis that administration of an atypical antipsychotic delays the onset of psychosis in individuals with prodromal signs and symptoms of schizophrenia. Unfortunately, the medication-associated adverse effects raise concerns about the wide-scale adoption of this particular approach. Nonetheless, the study provides one of a hoped-for series of proof-of-concept demon-

strations that early medical intervention will lead to reduced illness burden and better functional outcomes for individuals with schizophrenia.

DAVID A. LEWIS, M.D.

Høglend P, Amlo S, Marble A, Bogwald KP, Sorbye O, Sjaastad MC, Heyerdahl O: Analysis of the patient-therapist relationship in dynamic psychotherapy: an experimental study of transference interpretations. Am J Psychiatry 2006; 163:1739–1746

There is a fair amount of evidence that psychoanalytic psychotherapy is effective. However, when we come to the questions of how it works, for which patients it is effective, or the clinically crucial question of which components of the treatment are important for which patients, there are almost no data. Opinions abound, but we need to know more about therapist's beliefs than about how to treat patients.

Transference, a core concept in psychoanalytic theory, refers to the persisting unconscious influence on current relationships (especially the therapeutic relationship) of themes from early relationships. Interpretations of transference are powerful tools in psychotherapy, crucial in contributing to insight but potentially disturbing the therapeutic alliance. Høglend and colleagues compared therapies conducted with and without transference interpretations. Contrary to their expectation, they found that the therapy used makes no difference. However, when they focused on subgroups of patients, they found that a subgroup is defined by life history rather than diagnostic category. Those with a pattern of poor object relations do better with transference interpretations. The work of Høglend et al. illustrates that systematic empirical research on dynamic therapy is possible and can contribute to clinically relevant questions.

ROBERT MICHELS, M.D.

Casey BJ, Durston S: From behavior to cognition to the brain and back: what have we learned from functional imaging studies of attention deficit hyperactivity disorder? Am J Psychiatry 2006; 163:957–960

Psychiatric illnesses such as schizophrenia are being recharacterized as problems in the brain's information-processing resulting from perturbed neurodevelopment. The key to future advances will be to first define the nature of these problems and to next trace their neurodevelopment. For ADHD, that first step has been accomplished: diverse symptoms of ADHD are attributed to the loss of inhibitory control over cognitive function. This understanding must be further refined to identify which neurons fail early in development, when symptoms first appear.

For me, the editorial by Casey and Durston captured the excitement as new studies in brain imaging bring this next step closer to reality. They suggested that three studies published in the same issue of the *Journal* identified failure in ADHD of the prefrontal cortex to respond to signals from the basal ganglia and cerebellum, suggesting that new or competing information has arrived. The prefrontal cortex makes a top-down executive decision to pursue or ignore this new information. When the prefrontal cortex fails to inhibit processing in other centers, then loss of cognitive control occurs, and ADHD symptoms result. This formulation, an elegant explanation for problematic behaviors in children, will spawn new research examining treatments' ability to reverse this pathophysiology.

DANIEL S. PINE, M.D.

Fenton WS, Chavez MR: Medication-induced weight gain and dyslipidemia in patients with schizophrenia. Am J Psychiatry 2006; 163:1697–1704

This article focused our attention on the metabolic syndrome, framed in the familiar face of a young man with schizophrenia whose weight ballooned from 145 to 203 lb over a decade of antipsychotic treatment. The face of this patient represents more than just a medication side effect. The metabolic syndrome is now a national epidemic, yet we have a unique challenge in treating our patients who face multiple risk factors.

Drs. Fenton and Chavez provided a valuable service by delineating the physiological pathways that underlie the syndrome, but they also addressed the problem in the context of the patient's life. In summarizing the case, it was the patient's social support and personal desire to improve his health that led to his adherence to a weight-loss program.

This leaves the field with the daunting task of effecting change in a population that may be only partially receptive to behavioral interventions. Yet a public health crisis is impending, and it is insidiously afflicting our youngest patients. Consider the article in this issue by Klein et al.: "A Randomized, Double-Blind, Placebo-Controlled Trial of Metformin Treatment of Weight Gain Associated With Initiation of Atypical Antipsychotic Therapy in Children and Adolescents." It is alarming that we are now using medications designed for age-related chronic diseases in our children, but we must be both preventive and proactive if we want to forestall the devastating consequences of the metabolic syndrome.

SUSAN K. SCHULTZ, M.D.

Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, Shores-Wilson K, Biggs MM, Balasubramani GK, Fava M, STAR*D Study Team: Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. Am J Psychiatry 2006; 163:28–40

McGrath PJ, Stewart JW, Fava M, Trivedi MH, Wisniewski SR, Nierenberg AA, Thase ME, Davis L, Biggs MM, Shores-Wilson K, Luther JF, Niederehe G, Warden D: Tranylcypromine versus venlafaxine plus mirtazapine following three failed antidepressant medication trials for depression: a STAR*D report. Am J Psychiatry 2006; 163:1531–1541

McEvoy JP, Lieberman JA, Stroup TS, Davis SM, Meltzer HY, Rosenheck RA, Swartz MS, Perkins DO, Keefe RSE, Davis CE, Severe J, Hsiao JK, for the CATIE Investigators: Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did not respond to prior atypical antipsychotic treatment. Am J Psychiatry 2006; 163:600–610

Stroup TS, Lieberman JA, McEvoy JP, Swartz MS, Davis SM, Rosenheck RA, Perkins DO, Keefe RSE, Davis CE, Severe J, Hsiao JK, for the CATIE Investigators: Effectiveness of olanzapine, quetiapine, risperidone, and ziprasidone in patients with chronic schizophrenia following discontinuation of a previous atypical antipsychotic. Am J Psychiatry 2006; 163:611–622

This year saw the publication of several large multicenter, federally funded clinical treatment studies carried out in "real clinical practice settings." The studies were designed by clinicians, asked clinically relevant questions, and were funded by NIMH. Phase 1 of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study was published in January (Trivedi et al.), and one of its follow-up articles later in the year (McGrath et al.). This multiphase depression treatment project set out to demonstrate remission rates of depression (not just "response") to antidepressant drugs with an established medication algorithm and measurement-based care. Moreover, STAR*D progressed through several treatment phases to test sequential medication algorithms for nonremitters. These data provide substantial generalizability of clinical treatment research findings to routine clinical practice, i.e., translating clinical research to clinical practice. These are data that clinicians need in their everyday practice, science that is important to clinical care. The Clinical Antipsychotic Trials for Interventions Effectiveness (CATIE) phase 2 studies of second-generation antipsychotic medications in schizophrenia (McEvoy et al. and Stroup et al.) were also performed in clinical practice settings; these studies provide new information about antipsychotic medications, particularly about side effects and, generally, about limited efficacy. Unfortunately, schizophrenia lacks a significant "remission" measure and as yet a tested treatment algorithm. Psychiatry is now generating scientific treatment data on medication use with comparative drug outcomes for application in clinical practice, like other areas of medicine.

CAROL A. TAMMINGA, M.D.

Address correspondence and reprint requests to Dr. Freedman, American Journal of Psychiatry, 1000 Wilson Blvd., Suite 1825, Arlington, VA 22209; ajp@psych.org (e-mail).

Disclosures of the American Journal of Psychiatry *editors are published in each January issue. Dr. Pine is serving in a personal capacity. The views expressed are Dr. Pine's own and do not necessarily represent the views of the NIH or the U.S. government.*