New Developments in the Pharmacologic Treatment of Schizophrenia: Editor’s Introduction

by John M. Kane

Abstract

In this issue we have tried to bring together a series of reviews describing new developments in the pharmacologic management of schizophrenia. Important progress is being made not only in medication development, but also in furthering our ability to use available treatments and treatment combinations in the most effective manner. Topics discussed include: the role of blood levels; alternative somatic treatments for nonresponding patients; the role of clozapine; putative mechanisms of action of novel antipsychotics; an overview of potential antipsychotic drugs under development; new findings in maintenance treatment; a review of the impact of neuroleptic treatment on the long-term course of schizophrenia; and a discussion of obstacles which must be overcome to ensure that the promise of treatment research can be fully realized.

Schizophrenia remains the most devastating of the mental illnesses. Its treatment requires the integration of a variety of treatment modalities as well as systems of long-term care that can provide continuity and appropriate responses to the individual’s problems and potential at various stages of the illness.

An increasingly broad array of scientific perspectives and expertise is being brought to bear on the challenge that schizophrenia presents, with the hope of setting the stage for future breakthroughs. At the same time, even incremental advances in treatment can have enormous impact on the lives of thousands of patients and their families as well as on the costs to society associated with this illness.

This issue of the Schizophrenia Bulletin presents an overview of new developments in the pharmacologic management of schizophrenia. These advances represent not only new medications and new concepts in medication development, but also important ongoing efforts to improve our ability to use available treatments and treatment combinations in the most effective manner.

Given enormous individual variability in absorption and metabolism of antipsychotic drugs, the role of plasma levels in the use of these medications has been an important research question for several years. Definitive conclusions have been lacking, however, largely because of the enormous difficulty in carrying out clinical trials with the necessary methodologic rigor. Van Putten et al. (1991, this issue) review current knowledge in this area and suggest that for some drugs (perphenazine, haloperidol, fluphenazine, and chlorpromazine) plasma levels that produce good antipsychotic effect without undue side effects have been tentatively identified. However, the extent to which very high plasma levels are associated with poor antipsychotic response remains unclear. On the other hand, the measurement of plasma levels does not explain the lack of drug responsiveness among many schizophrenic patients.

Christison et al. (1991, this issue) provide a very valuable review of alternative somatic treatment strategies for patients who fail to respond to adequate trials of antipsychotic medication. Clinicians treating patients with schizophrenia are faced every day with the challenge of choosing treatment approaches for...
such patients with the hope of bringing about some improvement. Although the available data in many instances leave much to be desired, tentative guidelines are provided.

The release of clozapine in the United States in February of 1990 provided not only the first new antipsychotic drug introduced in this country in 15 years, but also the first compound shown to be more effective than a comparison drug in carefully selected, treatment-refractory patients. However, while the use of clozapine offers some real hope for the most severely ill patients, it poses a variety of problems for both patient and clinician. Safferman et al. (1991, this issue) provide a review of current knowledge about the efficacy and adverse effects of this drug and also highlight the need for further research.

Clozapine is an important compound not only because of its apparent potential to help some severely ill, treatment-refractory patients, but also because it possesses several novel or atypical properties preclinically and clinically (e.g., reduced incidence of drug-induced parkinsonism and tardive dyskinesia). As a result, it has served as a model for exploring different mechanisms of action for putative antipsychotic drugs. Meltzer (1991, this issue) provides a perspective on the mechanism(s) of action of novel antipsychotic drugs and highlights the need for comparative studies of different "atypical" compounds. He also stresses the need for clinical testing of various concepts of the role of specific drug-induced neurotransmitter receptor phenomena in producing different clinical effects.

Following this background, Gerlach (1991, this issue) provides an overview of potential new antipsychotics under development, summarizing what is known regarding their classification, efficacy, and adverse effects. His review highlights the extensive current activity in antipsychotic drug development and should leave the reader with the sense of excitement and opportunity that currently exists in this field.

There is no question that antipsychotic drugs play an enormously important role in the maintenance treatment of schizophrenia and have a tremendous impact in reducing rates of relapse and rehospitalization. However, important questions continue to be addressed regarding optimum strategies for maximizing benefit and minimizing risk in this treatment approach. In the past decade, we have seen a second generation of long-term clinical trials focusing on an array of issues in maintenance treatment. Schooler (1991, this issue) provides a summary of current knowledge about alternative maintenance treatment strategies (particularly dosage reduction and intermittent treatment) in terms of both efficacy and impact on the incidence of tardive dyskinesia.

Although numerous controlled maintenance treatment trials have demonstrated the value of continued antipsychotic treatment, these trials have lasted only 1 to 2 years, a relatively short interval in the treatment of a schizophrenic illness. Without controlled trials lasting for much longer periods, which are clearly not feasible, it has been difficult to quantify the impact of long-term neuroleptic treatment on the overall course of a schizophrenic illness. Wyatt (1991, this issue) has drawn the best available information on this topic from an extensive literature review and concludes that antipsychotic drug treatment has had a positive effect on the long-term course of this illness.

The final article by Kane (1991, this issue) provides a brief review of some of the important challenges that need to be met to further critically important treatment development research. At a time when the potential gains from clinical research are greater than ever, obstacles may loom larger than ever as well. Strategies need to be developed and supported to ensure that the promise of treatment research can be fully realized.

References


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Schizophrenia: Questions and Answers

What is schizophrenia? What causes it? How is it treated? How can other people help? What is the outlook?

These are the questions addressed in a booklet prepared by the Schizophrenia Research Branch of the National Institute of Mental Health.

Directed to readers who may have little or no professional training in schizophrenia-related disciplines, the booklet provides answers and explanations for many commonly asked questions of the complex issues about schizophrenia. It also conveys something of the sense of unreality, fears, and loneliness that a schizophrenic individual often experiences.

The booklet describes "The World of the Schizophrenic Patient" through the use of analogy. It briefly describes what is known about causes—the influence of genetics, environment, and biochemistry. It also discusses common treatment techniques. The booklet closes with a discussion of the prospects for understanding schizophrenia in the coming decade and the outlook for individuals who are now victims of this severe and often chronic mental disorder.

Single copies of *Schizophrenia: Questions and Answers* (DHHS Publication No. ADM 90-1457) are available from the Public Inquiries Branch, National Institute of Mental Health, Room 15C-05, 5600 Fishers Lane, Rockville, MD 20857.