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978-0-521-71413-6 - Antipsychotics and Mood Stabilizers: Stahl's Essential Psychopharmacology, Third Edition

Stephen M. Stahl

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Antipsychotics and Mood Stabilizers

The best-selling *Stahl's Essential Psychopharmacology* – fully revised and updated throughout – continues its tradition of being the preeminent source of information in its field. More than one-third longer than the previous edition, this third edition of *Antipsychotics and Mood Stabilizers* draws from the revised chapters in *Stahl's Essential Psychopharmacology* to form a resource that is essential reading for all clinicians treating psychosis as well as for all students who need to know the mechanisms of drug actions. Straightforward and eminently readable, this edition can be read cover to cover by experts and novices alike.

Stephen M. Stahl is Adjunct Professor of Psychiatry at the University of California at San Diego. He has conducted numerous research projects awarded by the National Institute of Mental Health, the Veterans Administration, and the pharmaceutical industry. Author of more than 350 articles and chapters, Dr. Stahl is an internationally recognized clinician, researcher, and teacher in psychiatry with subspecialty expertise in psychopharmacology.

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Stahl's Essential Psychopharmacology

Third Edition

Stephen M. Stahl

University of California at San Diego

With Illustrations by
Nancy Muntner

Editorial Assistant
Meghan M. Grady



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In memory of Daniel X. Freedman, mentor, colleague, and scientific father.

To Cindy, my wife, best friend, and tireless supporter.

To Jennifer and Victoria, my daughters, for their patience and understanding of the demands of authorship.

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Preface to the Third Edition

This booklet is a set of the two chapters from the third edition of *Stahl's Essential Psychopharmacology* that deal exclusively with psychosis and schizophrenia and their treatment with antipsychotic drugs. The knowledge base of psychopharmacology for psychosis and schizophrenia has expanded considerably since publication of the second edition of this book, and the third edition attempts to reflect these changes.

In most developed countries, antipsychotics have become the most expensive therapeutic market, not only for psychiatry, but for medical therapeutics in general. Since prescribers are rapidly expanding their utilization of the newer antipsychotics for the treatment of disorders other than psychosis, such as for the treatment of bipolar disorder and various treatment-resistant disorders of anxiety and mood, it is particularly important to understand how the drugs categorized here as "antipsychotics" work. This therapeutic area of psychopharmacology occupies one of the largest sections of the full textbook and is perhaps the section that has undergone the most change since publication of the second edition. Given the importance of this area of psychopharmacology, many readers may be interested in this area alone; therefore, we offer the two chapters on psychosis and on antipsychotics as a stand-alone spinoff of the third edition of *Stahl's Essential Psychopharmacology*.

Psychopharmacology has not only experienced incredible growth since publication of the second edition of this textbook; it has also experienced a major paradigm shift from a limited focus on neurotransmitters and receptors to an emphasis as well on brain circuits, neuroimaging, genetics, and signal transduction cascades. The third edition of *Stahl's Essential Psychopharmacology* attempts to reflect this transformation in the field, and elements of this paradigm shift are incorporated into each of these chapters in this booklet. Many new antipsychotics have been introduced in recent years, and many more are now in clinical testing, and these are covered in this new edition. These two chapters on psychosis and antipsychotics have been extensively reorganized, rewritten, and illustrated with roughly twice the number of figures in every chapter. However, what has not changed is the didactic style of the first and second editions, which continues in this third edition.

The text is purposely written at a conceptual level rather than a pragmatic level and includes ideas that are simplifications and rules, while sacrificing precision and discussion of exceptions to rules. Thus, this is not a text intended for the sophisticated subspecialist in psychopharmacology. Also, it is not extensively referenced to original papers, but rather to textbooks and reviews and a few selected original papers, with only a limited reading list for each chapter. For those of you interested in specific prescribing information about the most common one hundred or so psychotropic drugs, this information is available

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in the companion textbook, *Essential Psychopharmacology Prescriber's Guide*. A spinoff of this book just on antipsychotics (and mood stabilizers) is also available, called *Essential Psychopharmacology Prescriber's Guide of Antipsychotics and Mood Stabilizers*.

Now, you also have the option of going to Essential Psychopharmacology Online at www.essentialpsych.org. We are proud to announce the launch of this new website, which is due to premiere in the fall of 2008. Access to this website will allow you to search within the entire Essential Psychopharmacology series that includes not only the third edition of *Stahl's Essential Psychopharmacology*, but also *Essential Psychopharmacology Prescriber's Guide*. This site will be updated regularly and should therefore provide an up-to-date source for what you need to know about the essentials of psychopharmacology between publication of subsequent editions of these books.

Much of the new content in this text is based on updated lectures, courses, slides, and articles by the author. Many of the new illustrations are now available as animations on the Neuroscience Education Institute's website, as are the lectures, slides and articles, continuing medical education (CME) credits, tests, certifications, and much more. I invite you to explore this interactive reference by visiting the Neuroscience Education Institute's website at www.neiglobal.com. If you are interested in comprehensive materials, you can choose to have access to both websites.

In general, this text attempts to present the fundamentals of psychopharmacology in simplified and readily readable form. Thus, this material should prepare the reader to consult more sophisticated textbooks as well as the professional literature. The organization of the information here also applies principles of programmed learning for the reader, namely repetition and interaction, which has been shown to enhance retention.

Therefore, it is suggested that novices first approach this text by going through it from beginning to end, reviewing only the color graphics and the legends for these graphics. Virtually everything covered in the text is also covered in the graphics and icons. Once having gone through all the color graphics in these chapters, it is recommended that the reader then go back to the beginning of the book and read the entire text, reviewing the graphics at the same time. After the text has been read, the entire book can be rapidly reviewed again merely by referring to the various color graphics in the book. Finally, as a member of the Neuroscience Education Institute, you can utilize the content available online at www.neiglobal.com to obtain continuing medical education credits for this activity or as a helpful interactive reference. Many of the graphics are animated and available on this site. Also, you can search topics in the field covered in the Essential Psychopharmacology book series on Essential Psychopharmacology Online.

This mechanism of using the materials will create a certain amount of programmed learning by incorporating the elements of repetition, as well as interaction with visual learning through graphics. Hopefully, the visual concepts learned via graphics will reinforce abstract concepts learned from the written text, especially for those of you who are primarily "visual learners" (i.e., those who retain information better from visualizing concepts than from reading about them).

For those of you who are already familiar with psychopharmacology, this book should provide easy reading from beginning to end. Going back and forth between the text and the graphics should provide interaction. Following review of the complete text, it should be simple to review the entire book by going through the graphics once again. In addition, the Neuroscience Education Institute's website further expands the Essential Psychopharmacology learning experience and Essential Psychopharmacology Online allows quick searches of topics in this field.

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For those of you interested in the specific updates made in the third edition, the psychosis chapter has much expanded coverage of the neurotransmitter glutamate and of the interactions among glutamate, serotonin, and dopamine. The NMDA (N-methyl-d-aspartate) receptor hypofunction hypothesis of schizophrenia is extensively discussed, as are the various genetic advances occurring in schizophrenia research. Included are sections on matching the symptoms of psychosis and schizophrenia to various hypothetically malfunctioning brain circuits. Several new antipsychotics are also included in this third edition, as well as numerous new agents of novel mechanism on the horizon for the treatment of psychosis and schizophrenia. There is extensive coverage of cardiometabolic risks and sedation related to antipsychotics, particularly certain of the newer atypical antipsychotics.

This is an incredibly exciting time for the fields of neuroscience and mental health, creating fascinating opportunities for clinicians to utilize current therapeutics and to anticipate future medications that are likely to transform the field of psychopharmacology. Best wishes for your first step on your journey into this fascinating field of psychopharmacology.

Stephen M. Stahl, M.D, Ph.D.

CME Information

Release/Expiration Dates

Original release date: March 2008

CME credit expiration date: original expiration February 2011 (if this date has passed, please contact NEI for updated information)

Target Audience

This activity was designed for health care professionals, including psychiatrists, neurologists, primary care physicians, pharmacists, psychologists, nurses, and others, who treat patients with psychiatric conditions.

Statement of Need

The content of this educational activity was determined by rigorous assessment, including activity feedback, expert faculty assessment, literature review, and new medical knowledge, which revealed the following unmet needs:

- Psychiatric illnesses such as schizophrenia have a neurobiological basis and are primarily treated by pharmacological agents; understanding each of these, as well as the relationship between them, is essential in order to select appropriate treatment for a patient
- The field of psychopharmacology has experienced incredible growth; it has also experienced a major paradigm shift from a limited focus on neurotransmitters and receptors to an emphasis as well on brain circuits, neuroimaging, genetics, and signal transduction cascades

Learning Objectives

Upon completion of this activity, you should be able to:

- Apply neurobiologic and mechanistic evidence when selecting treatment strategies in order to match treatment to the individual needs of the patient
- Utilize new scientific data to modify existing treatment strategies in order to improve patient outcomes in schizophrenia

Accreditation and Credit Designation Statements

The Neuroscience Education Institute is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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The Neuroscience Education Institute designates this educational activity for a maximum of 16.0 *AMA PRA Category 1 Credits*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Activity Instructions

This CME activity is in the form of a printed book and incorporates instructional design to enhance your retention of the information and pharmacological concepts that are being presented. You are advised to go through the figures in this activity from beginning to end, followed by the text, and then complete the posttests and evaluations. The estimated time for completion of this activity is 16 hours.

Instructions for CME Credit

To receive a certificate of CME credit or participation, please complete the posttest (you must score at least 70% to receive credit) and evaluation available online only at <http://www.neiglobal.com/ep3>. If a score of 70% or more is attained, you can immediately print your certificate. There is a fee for the posttest (certificate included) for non-NEI members.

NEI Disclosure Policy

It is the policy of the Neuroscience Education Institute to ensure balance, independence, objectivity, and scientific rigor in its educational activities. The Neuroscience Education Institute takes responsibility for the content, quality, and scientific integrity of this CME activity.

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Neither the Neuroscience Education Institute nor Stephen M. Stahl, MD, PhD has received any funds or grants in support of this educational activity.

Individual Disclosure Statements

Authors/Developers

Stephen M. Stahl, MD, PhD

Adjunct Professor, Department of Psychiatry

University of California, San Diego School of Medicine, San Diego, CA

Dr. Stahl has been a consultant, board member, or on the speakers bureau for the following pharmaceutical companies within the last three years: Acadia, Alkermes, Amylin, Asahi Kasei, Astra Zeneca, Avera, Azur, Biovail, Boehringer Ingelheim, BristolMyers Squibb, Cephalon, CSC Pharmaceuticals, Cyberonics, Cypress Bioscience, Dainippon, Eli Lilly, Forest, GlaxoSmithKline, Janssen, Jazz Pharmaceuticals, Labopharm, Lundbeck, Neurocrine Biosciences, NeuroMolecular, Neuronetics, Novartis, Organon, PamLab, Pfizer, Pierre Fabre, sanofi-aventis, Schering-Plough, Sepracor, Shire, SK Corporation, Solvay, Somaxon, Takeda, Tethys, Tetragenix, Vanda Pharmaceuticals, and Wyeth.

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Meghan Grady

Director, Content Development

Neuroscience Education Institute, Carlsbad, CA

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Editorial and Design Staff

Nancy Muntner

Director, Medical Illustrations

Neuroscience Education Institute, Carlsbad, CA

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Participants have an implied responsibility to use the newly acquired information from this activity to enhance patient outcomes and their own professional development. The information presented in this educational activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this educational activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities. Primary references and full prescribing information should be consulted.

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