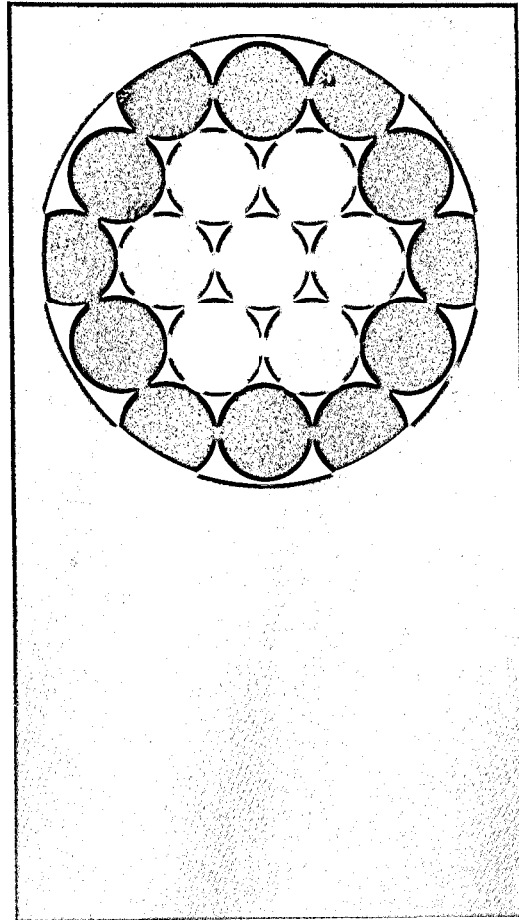



Clinical Neuropharmacology

www.clinicalneuropharm.com



000097771669 WNF 12/01/03
NATL LIB MED INDEX SER RECO
BLDG 3S
5600 ROCKVILLE PIKE
BETHESDA, MD 20894-0002

AUTO**ALL FOR ADC 207
3
12

112007

PROPERTY OF THE
NATIONAL
LIBRARY OF
MEDICINE

 LIPPINCOTT WILLIAMS & WILKINS

Argentum Pharm. v. Research Corp. Techs., IPR2016-00204
RCT EX. 2082 - 1/19

FOUNDING EDITOR

Harold L. Klawans, M.D.

EDITOR-IN-CHIEF

Christopher G. Goetz, M.D.

*Department of Neurological Sciences
Rush-Presbyterian-St. Luke's Medical Center
1725 West Harrison Street
Chicago, Illinois 60612, U.S.A.*

Tel: 312-942-8010 Fax: 312-942-2380

SECTION EDITORS

CEREBROVASCULAR DISEASE

Betsy B. Love

Alkeny, Iowa

MOVEMENT DISORDERS

Peter A. LeWitt

West Bloomfield, Michigan

CRITICAL CARE NEUROLOGY

Thomas P. Bleck

Charlottesville, Virginia

NEUROTOXICOLOGY

Robert G. Feldman

Boston, Massachusetts

PATIENT MANAGEMENT

Neelum T. Aggarwal

Chicago, Illinois

EPILEPSY

Jacqueline A. French

Philadelphia, Pennsylvania

PRE-CLINICAL NEUROPHARMACOLOGY

Michel Hamon

Paris, France

PSYCHOPHARMACOLOGY

Stephen I. Deutsch

Washington, D.C.

SLEEP DISORDERS

Cynthia L. Comella

Chicago, Illinois

NEUROIMMUNOLOGY

Robert P. Lisak

Detroit, Michigan

EDITORIAL BOARD

Yves Agid

Paris, France

J. Eric Ahlskog

Rochester, Minnesota

James W. Albers

Ann Arbor, Michigan

Burton Angrist

New York, New York

Arlene Barr

Chicago, Illinois

John M. Bertoni

Omaha, Nebraska

Thomas R. Browne

Boston, Massachusetts

Louis R. Caplan

Boston, Massachusetts

Paul Carvey

Chicago, Illinois

Deborah T. Combs Cantrell

Dallas, Texas

P. J. Cowen

Oxford, England

John Davis

Chicago, Illinois

Kenneth L. Davis

Bronx, New York

Paula Dore-Duffy

Detroit, Michigan

Christopher M. Filley

Denver, Colorado

Jes Gerlach

Roskilde, Denmark

Ludwig Guttman

Morgantown, West Virginia

Gregory L. Holmes

Boston, Massachusetts

Chung Y. Hsu

St. Louis, Missouri

Amos D. Korczyn

Tel Aviv, Israel

Kinya Kuriyama

Kyoto, Japan

Malcolm H. Lader

London, England

Steven R. Levine

Detroit, Michigan

Margery H. Mark

New Brunswick, New Jersey

Merrill Mittle

La Jolla, California

Jean-Louis Montastruc

Toulouse, France

John G. L. Morris

Sydney, Australia

Michael A. Moskowitz

Boston, Massachusetts

Robert M. Post

Bethesda, Maryland

Kedar N. Prasad

Denver, Colorado

Pierre Rondot

Paris, France

Kathleen Shannon

Chicago, Illinois

Ira Shoulson

Rochester, New York

Caroline M. Tanner

Sunnyvale, California

Michael J. Thorpy

Bronx, New York

Herman M. van Praag

Maastricht, The Netherlands

Leon A. Weisberg

New Orleans, Louisiana

B. J. Wilder

Gainesville, Florida

Richard J. Wyatt

Washington, D.C.

PUBLICATION AND ADVERTISING STAFF

Nancy Megley

Publisher

Matthew McGrath

Production Editor

January Bartle

Account Manager

Ray Thibodeau

Vice President Advertising Sales

Renée Artuso

Advertising Sales Representative

The Point of Difference, Ltd

International Advertising Representative

Argentum Pharm. v. Research Corp. Techs., IPR2016-00204

RCT EX. 2082 - 2/19

Clinical Neuropharmacology

A Journal of Reviews and Original Investigations in the
Pharmacology of Central Nervous System Dysfunction

Volume 26, Number 1, January - February 2003

CONTENTS

BRIEF REPORTS

- 1 Topiramate for the Treatment of Kleptomania: A Case Series and Review of the Literature**
Pinhas N. Dannon
- 5 Acute Delirium, Delusion, and Depression During IFN- β -1a Therapy for Multiple Sclerosis: A Case Report**
J. L. Goëb, A. Cailleau, P. Lainé, F. Etcharry-Bouyx, D. Maugin, Ph. Duverger, B. Gohier,
K. Rannou-Dubas, F. Dubas, and J. B. Garré

ORIGINAL ARTICLES

- 8 Clozapine in Parkinson's Disease Psychosis: 5-Year Follow-up Review**
Colin Klein, Jacob Gordon, Lea Pollak, and J. Martin Rabey
- 12 Beneficial Effect of Donepezil Augmentation for the Management of Comorbid Schizophrenia and Dementia**
Rafael Stryjer, Rael D. Strous, Faina Bar, Edith Werber, Ginette Shaked, Yosef Buhiri,
Moshe Kotler, Abraham Weizman, and Jose M. Rabey

(continued on next page)

This journal is listed in *Index Medicus/MEDLINE*, *Current Contents/Clinical Medicine*, *Science Citation Index*, *Neuroscience Citation Index*, *SCISEARCH*, *Research Alert*, *Reference Update*, *Current Awareness in Biological Sciences*, *Biosis*, *Excerpta Medica/EMBASE*, *PASCAL/CNRS*, and *PsycINFO*

Clinical Neuropharmacology (ISSN: #0362-5664) is published bimonthly by Lippincott Williams & Wilkins, Inc., at 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116. Business and production offices are located at 530 Walnut Street, Philadelphia, PA 19106-3621. Periodicals postage paid at Hagerstown, MD and at additional mailing offices. Copyright © 2003 by Lippincott Williams & Wilkins, Inc.

Address for subscription information, orders, or change of address (except Japan, India, Bangladesh, Sri Lanka, Nepal and Pakistan): 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116; phone 1-800-638-3030; fax 301-223-2400; in Maryland, call collect 301-223-2300. In Japan, contact LWW Igaku-Shoin Ltd., 3-23-14 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan; phone: 81-3-5689-5400; fax: 81-3-5689-5402. In India, Bangladesh, Sri Lanka, Nepal and Pakistan, contact Globe Publication Pvt. Ltd. B-13, 3rd FL, A Block, Shopping Complex, Naraina Vihar, Ring Road, New Delhi 110028, India; phone: 91-11-579-3211; fax: 91-11-579-8876.

Annual subscription rates worldwide: \$272.00 Individual Domestic, \$329.00 Individual International, \$519.00 Institutional Domestic, \$591.00 Institutional International. (The Canadian GST tax of 7% will be added to the subscription price of all orders shipped to Canada. Lippincott Williams & Wilkins' GST Identification Number is 895524239. Publications Mail Agreement #616346.) Subscriptions outside the United States must be prepaid. Subscriptions outside North America must add \$6.00 for airfreight delivery. Prices subject to change without notice. Copies will be replaced without charge if the publisher receives a request within 90 days of the mailing date, both in the U.S. and worldwide. Visit us on-line at www.lww.com.

Postmaster: Send address changes to *Clinical Neuropharmacology*, P.O. Box 1550, Hagerstown, MD 21740.

Argentum Pharm. v. Research Corp. Techs., IPR2016-00204
RCT EX. 2082 - 3/19

- 18 **Minocycline and Other Tetracycline Derivatives: A Neuroprotective Strategy in Parkinson's Disease and Huntington's Disease**
Madhavi Thomas, Wei Dong Le, and Joseph Jankovic
- 24 **Effect of Late Initiation of Levodopa Treatment in Patients With Long-Standing Parkinson's Disease**
Ruth Djaldetti, Therese A. Treves, Doron Merims, Hava Sroka, and Eldad Melamed

REVIEWS

- 28 **Treatment of Multiple Sclerosis and Related Disorders: What's New in the Past 2 Years?**
John H. Noseworthy
- 38 **Clinical Pharmacology of Antiepileptic Drugs**
Carl W. Bazil and Timothy A. Pedley

Manuscripts should be sent to: Christopher G. Goetz, M.D., Department of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, 1725 West Harrison, Chicago, IL 60612, U.S.A. [For editorial assistance or questions contact Bernadette Gillard at Rush-Presbyterian-St. Luke's Medical Center, telephone (312) 942-8010.]

Lippincott Williams & Wilkins, Inc., cannot be held responsible for errors or for any consequences arising from the use of the information contained in this journal. The appearance of advertising in this journal does not constitute an endorsement or approval by Lippincott Williams & Wilkins, Inc., of the quality or value of the product advertised or of the claims made for it by its manufacturer.

PERMISSION TO PHOTOCOPY ARTICLES: This publication is protected by copyright. Permission to photocopy must be secured in writing from: Permissions Dept., Lippincott Williams & Wilkins, Inc., 530 Walnut Street, Philadelphia, PA 19106-3621; FAX: 215-521-8902; or Copyright Clearance Center (CCC), 222 Rosewood Dr., Danvers, MA 01923; (978) 750-8400, FAX (978) 750-4470; or UMI, Box 49, 300 North Zeeb Road, Ann Arbor, MI 48106-1346; FAX: 313-761-1203.

Argentum Pharm. v. Research Corp. Techs., IPR2016-00204
RCT EX. 2082 - 4/19

Clinical Pharmacology of Antiepileptic Drugs

Carl W. Bazil and Timothy A. Pedley

The Comprehensive Epilepsy Center, The Neurological Institute of New York, Columbia University, New York, New York, USA

Antiepileptic drugs (AEDs) are the mainstay of treatment for the majority of patients with epilepsy. However, not all patients with seizures require treatment with AEDs, and many patients with some forms of epilepsy, especially children, need only 1 or 2 years of drug therapy (1). Thus, important questions for the treating physician to have in mind are “When to start AEDs?” and “When can AEDs be safely withdrawn?”

Nonetheless, it is safe to say that, as a group, patients with epilepsy typically receive one or more drugs, usually for many years. Therefore, it is essential that physicians have a good understanding of the clinical pharmacology of these agents, including their mechanisms of action, utilization patterns, and potential for interactions with other therapeutic agents.

SELECTION OF ANTIEPILEPTIC DRUGS

Table 1 lists the drugs currently used to manage different types of seizures. Table 2 gives the usual dosage, effective plasma concentration, half-life, and common side effects for the most commonly used of these agents (2).

Carbamazepine, phenytoin, primidone, and phenobarbital are equally effective for partial and secondarily generalized seizures, although one may be effective when another is not (3). Valproate is also as effective for secondarily generalized seizures but is somewhat less effective than carbamazepine (and, presumably, phenytoin) in managing simple or complex partial seizures (4). Despite relatively equal antiepileptic potency, however, these drugs differ substantially in terms of side effects, pharmacokinetic properties, and cost. Similar comparative data are generally lacking for

AEDs introduced after 1994. Phenytoin, with its relatively long half-life, which usually allows the drug to be given once or twice daily after midadolescence, has traditionally been preferred to drugs with shorter half-lives (5). However, concern about phenytoin’s occasional undesirable cosmetic effects (gingival hypertrophy, hirsutism, and coarsening of facial features) and other adverse consequences associated with long-term therapy have led to the preferential use of carbamazepine or one of the newer drugs (*e.g.*, lamotrigine, topiramate, zonisamide) as initial treatment in many patients today. Carbamazepine, despite its short half-life, can be given twice daily if an extended-release formulation (*e.g.*, Tegretol-XR, Carbatrol) is used. Phenobarbital and primidone are rarely used now, except in special circumstances, because of the high incidence of sedation and cognitive side effects at therapeutic doses and plasma concentrations (3).

As a group, generalized-onset seizures respond best to valproate (6). Valproate can be used effectively as monotherapy in about 80% of patients, even when several types of generalized-onset seizure coexist. Lamotrigine and topiramate are appropriate alternatives when valproate fails (7). A growing number of neurologists prefer lamotrigine to valproate because of a more favorable adverse effect profile. Phenytoin and carbamazepine are also effective against generalized tonic-clonic seizures, but the response is less reliable than with valproate (2). However, they are ineffective against absence or myoclonic seizures, which commonly coexist with generalized tonic-clonic seizures, which means another drug (*e.g.*, ethosuximide, clonazepam) must be used. Furthermore, phenytoin, gabapentin, and especially carbamazepine can actually aggravate nonconvulsive generalized-onset seizures (7).

MONOTHERAPY OR POLYTHERAPY?

Medical treatment of epilepsy in adults is generally less satisfactory than in children, especially when confronted with partial and secondarily generalized seizures. Fewer than 50% of such patients with recurrent seizures remain seizure free for more than 12 consecu-

Most of the material contained in this review was presented at the 54th Annual Meeting of the American Academy of Neurology and was included in a syllabus prepared for the Therapy in Neurology course given on April 15, 2002. It is reproduced here with the permission of the American Academy of Neurology.

Address correspondence and reprint requests to Dr. Timothy A. Pedley, 710 W. 168th St., The Neurological Institute of New York, Columbia University, New York, NY 10032, USA; E-mail: tap2@columbia.edu.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.