

# ARCHIVES OF NEUROLOGY

The ARCHIVES OF NEUROLOGY is a member of the consortium of AMA journals listed below. The complete text of all AMA journals is available online from Dialog Information Services and Ovid Technologies, Inc.

## The Journal of the American Medical Association (JAMA)

Archives of Dermatology  
Archives of Facial Plastic Surgery  
Archives of Family Medicine  
Archives of General Psychiatry  
Archives of Internal Medicine  
Archives of Neurology  
Archives of Ophthalmology  
Archives of Otolaryngology—Head & Neck Surgery  
Archives of Pathology & Laboratory Medicine  
Archives of Pediatrics & Adolescent Medicine  
Archives of Surgery

The ARCHIVES OF NEUROLOGY (ISSN 0003-9942) is published monthly by the American Medical Association, 515 N State St, Chicago, IL 60610, and is an official publication of the Association. The ARCHIVES OF NEUROLOGY reaches more than 13 800 readers in over 79 countries each month. Periodicals postage paid at Chicago, IL, and at additional mailing offices. GST registration number 12622 5556 RT. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 318973.

Printed in the USA.

**SUBSCRIPTION RATES**—The personal subscription rates for the ARCHIVES OF NEUROLOGY are \$195 for 1 year (12 issues) in the United States and US possessions; \$295 in the Americas; £175 outside the Americas. The institution rates for 1 year are \$325 in the United States; \$425 in the Americas; £275 outside the Americas. Special rates for residents and medical students are available. Address all subscription communications to: Subscriber Services Center, American Medical Association, PO Box 10946, Chicago, IL 60610-0946. Phone: (800) 262-2350. Fax: (312) 464-5831. E-mail: ama-subs@ama-assn.org. For mailing addresses outside the United States and US possessions, see International Subscription Information.

**CHANGE OF ADDRESS**—POSTMASTER, send all address changes to ARCHIVES OF NEUROLOGY, c/o Subscriber Services, American Medical Association, 515 N State St, Chicago, IL 60610. Please notify us of address change at least 6 weeks in advance to ensure uninterrupted service. Include both old and new addresses, a recent mailing label, and new ZIP code. For mailing addresses outside the United States and US possessions, see International Subscription Information.

**SUBSCRIBER SERVICES**—For information about subscribing to any of the AMA publications, change of address, missing issues, or purchasing back issues, please contact Subscriber Services Center, American Medical Association, PO Box 10946, Chicago, IL 60610-0946, or call (800) 262-2350 or (312) 670-SUBS (670-7827) between 8:30 AM and 4:30 PM CST. Fax: (312) 464-5831. E-mail: ama-subs@ama-assn.org. For mailing addresses outside the United States and US possessions, see International Subscription Information.

**INTERNATIONAL SUBSCRIPTION INFORMATION**—Subscriptions outside the United States and US possessions are served according to geographic region. Please address correspondence to the following 2 offices based on delivery address: (1) For delivery in North America, Central America and South America, contact Subscriber Services, AMA, PO Box 10946, Chicago, IL 60610-0946. Phone: (312) 670-7827. Fax: (312) 464-5831. E-mail: ama-subs@ama-assn.org. (2) For delivery outside the Americas: Subscription Department, JAMA & Archives Journals, American Medical Association, Tower House, Sovereign Park, Market Harborough, Leicestershire LE15 9EF, England. Phone: +44 (0) 1858-438880. Fax: +44 (0) 1858-434958.

**REPRINTS**—Authors place their reprint order at the time the edited typescript is reviewed and should allow 4 to 6 weeks for delivery following publication. Requests for individual reprints should be sent directly to the author at the address shown in the article.

For bulk reprint orders for distribution by commercial organizations, please contact Wanda Bartolotta, 500 Fifth Ave, #2210, New York, NY 10110. Phone (212) 354-0050. Fax: (212) 354-1169. E-mail: wanda\_bartolotta@ama-assn.org. For reprint orders in limited quantities for distribution by educational organizations and for author reprints, please contact Reprints Coordinator, 515 N State St, Chicago, IL 60610. Phone: (312) 464-4594. Fax: (312) 464-4849.

**PERMISSIONS**—Contact Rhonda Bailey, Permissions Assistant, 515 N State St, Chicago, IL 60610. Phone: (312) 464-2513.

**ADVERTISING PRINCIPLES**—Each advertisement in this issue has been reviewed and complies with the principles governing advertising in AMA scientific publications. A copy of these principles is available on request. The appearance of advertising in AMA publications is not an AMA guarantee or endorsement of the product or the claims made for the product by the manufacturer.

**WORLD WIDE WEB ADDRESS**—<http://www.ama-assn.org>

**NEUROLOGY HOME PAGE**—<http://www.archneurol.com>

## Publication Staff Offices: 515 N State St, Chicago, IL 60610

### Editorial Processing Department

**Division Director:** Cheryl Iverson  
**Director:** Paula Glitman  
**Copyediting Manager:** Lise M. Stevens  
**Freelance Copyediting Manager:** Diane L. Cannon

**Freelance Copyediting Coordinators:** Gwen Chaffin  
Connie Manno

**Electronic Editing Specialist:** Paul Frank

**Assistant Electronic Editing Specialist:** Monica Mungle

**Senior Copy Editors:** Dee E. Egger  
Vickey Golden

**Copy Editors:** John McFadden  
Jennifer L. Reddy

**Editorial Assistant:** Wanda Hill

### Scientific Publications & Multimedia Applications

**Assistant to the Editor:** Helga Fritz

### Scientific Online Resources

**Director:** Margaret Winker, MD  
**Electronic Media Department Director:** Michelle Kurzynski  
**Web Development Editor:** Keith Huff  
**Assistant Editor:** Nikhil Torsekar  
**Staff Assistant:** Marla A. Hall

### Production & Distribution Division

**Director:** Vanessa Hayden  
**Manager, Journal Manufacturing:** Diane Darnell  
**Journal Manufacturing Analyst:** Nona Malchin  
**Office Manager:** Karen Branham  
**Production Assistant:** Shannon Epplert

### Advertising & Production Department

**Director:** Karen Adams-Taylor  
**Production Specialist:** Terri Hanley  
**Manager, Advertising Services:** Carole Piszker  
**Manager, Production Services:** Susan Price  
**Supervisor, Production Services:** Debbie Camp  
**Production Associates:** Mary Ann Donley  
Sarah Powell  
Denise Steinhauser  
Jo Anne Turner  
Carmela Ware  
**Production Assistant:** Amelia Zamudio

### Distribution

**Distribution Manager:** Paul Gasielki  
**Distribution Analyst:** Michelle Robinson

### Advertising

**National Sales Manager:** Peter G. Messina  
**AMA Classified Advertising Department:** Thalia Moss, 800-262-2260.



### Specialty Journal Division Office

**Manager, Marketing Services:** Geoffrey A. Flick  
**Assistant to the Publisher:** Christine Hearne

### Circulation & Content Marketing Division

**Administrative Assistant:** Millette Jackson-Bates

### Circulation Processing Department

**Director:** Robert Herling  
**Subscriber Services Manager:** Susan Stoken  
**Circulation Systems Manager:** Alfred Tomaselli  
**Circulation Specialists:** Reginald Jordan  
Kathryn Osten

### Circulation Development Department

**Director:** Bina Oza  
**Circulation Marketing Managers:** Audrey Mathies  
**Circulation Marketing Specialists:** Sandra Garzon  
Michael McGraw

### Licensing & Permissions Department

**Director:** Norman Frankel  
**Permissions:** Rhonda Bailey  
**International Coordinator:** Sharon Ali

### Electronic Production Department

**Electronic Production Specialists:** Brenda Chandler-Grayer  
Karl Elvin  
Amy Evers  
Fred Furtner  
Mary Ann Kuranda  
Sandra Lopez

**Manager, Graphics:** Charl Richey  
**Electronic Imaging Specialists:**

Joe Amft  
Noel Chaparro  
Carolyn Hall  
Maria Kowalkowski  
Chris Meyer  
JoAnne Weiskopf  
**Manager, Proofreading:** David Antos  
**Proofreaders:**

Daniel James  
Rachel Novickas  
Teresa H. Omiotek  
Mary Kay Timerella  
Barbara Wojtowicz  
**Manager, Database & New Media:**

Mary Ellen Johnston

**Indexer:** Bruce McGregor

**New Media Specialists:**

Clifford O. Barrett  
Gail Barrett  
Joel Brammeier  
Regina Brownlee  
La son J. Diggs  
Melanie Parenti  
Angela Smits  
**Production Assistant:** Ruth Sprague

### Advertising Office:

**East:** Kelly Lezynski,  
119 Cherry Hill Rd, 3rd Fl,  
Parsippany, NJ 07054  
(973) 263-9191.

**Midwest/West:** J. P. Cahill & Associates,  
341 S Waiola Ave  
La Grange, IL 60525  
(708) 352-1450.

# ARCHIVES OF NEUROLOGY

JUNE 2000

VOLUME 57, NUMBER 6

PAGES 769-908

## EDITORIALS

**Finding the Beginning or Predicting the Future?** 783  
*Richard Mayeux, MD, MSc;*  
*Scott A. Small, MD*

**Inflammation in Neurodegenerative Disease: Good, Bad, or Irrelevant?** 786  
*Lawrence S. Honig, MD, PhD*

## NEUROLOGICAL REVIEWS

**Autotoxicity and Alzheimer Disease** 789  
*Patrick L. McGeer, MD, PhD;*  
*Edith G. McGeer, PhD*

**Mechanisms of Neurodegenerative Disorders: Part 1, Protein Aggregates** 793  
*Benjamin Wolozin, MD, PhD;*  
*Christian Behl, PhD*

**Mechanisms of Neurodegenerative Disorders: Part 2, Control of Cell Death** 801  
*Benjamin Wolozin, MD, PhD;*  
*Christian Behl, PhD*

## ORIGINAL CONTRIBUTIONS

**The Preclinical Phase of Alzheimer Disease: A 22-Year Prospective Study of the Framingham Cohort** 808  
*Merrill F. Elias, PhD, MPH;*  
*Alexa Beiser, PhD;*  
*Philip A. Wolf, MD;*  
*Rhoda Au, PhD;*  
*Roberta F. White, PhD;*  
*Ralph B. D'Agostino, PhD*

**Cortical Inflammation in Alzheimer Disease but Not Dementia With Lewy Bodies** 817  
*Claire E. Shepherd, PhD;*  
*Emma Thiel, BSc;*  
*Heather McCann, DipApplSc;*  
*Antony J. Harding, PhD;*  
*Glenda M. Halliday, PhD*

**Apolipoprotein E Polymorphism and Alzheimer Disease: The Indo-US Cross-National Dementia Study** 824  
*Mary Ganguli, MD, MPH;*  
*Vijay Chandra, MD, PhD;*  
*M. Ilyas Kamboh, PhD;*  
*Janet M. Johnston, PhD;*  
*Hiroko H. Dodge, PhD;*  
*B. K. Thelma, PhD;*  
*Ramesh C. Juyal, PhD;*  
*Rajesh Pandav, MBBS;*  
*Steven H. Belle, PhD;*  
*Steven T. DeKosky, MD*

American Medical Association

Physicians dedicated to the health of America



Copyright 2000 by the American Medical Association. All rights reserved.  
Reproduction without permission is prohibited.

All articles published, including editorials, letters, and book reviews, represent the opinions of the authors and do not reflect the policy of the American Medical Association, the Editorial Board, or the institution with which the author is affiliated, unless this is clearly specified.

**Catherine D. DeAngelis, MD, MPH**  
Editor in Chief, Scientific Publications  
& Multimedia Applications

**Robert L. Kennett**  
Vice President, Publishing

**Peter L. Payerli**  
Publisher

**E. Ratcliffe Anderson, Jr, MD**  
Executive Vice President,  
Chief Executive Officer

**Lynn E. Jensen, PhD**  
Chief Operating Officer

**Robert A. Musacchio, PhD**  
Senior Vice President,  
Publishing & Business Services

**Effect of Anti-inflammatory Medications on Neuropathological Findings in Alzheimer Disease**

Glenda M. Halliday, PhD;  
Claire E. Shepherd, PhD;  
Heather McCann, DipHealthSc;  
Wayne G. J. Reid, PhD;  
David A. Grayson, PhD;  
G. Anthony Broe, FRACP;  
Jillian J. Kril, PhD

831

**Region-Specific Neurotrophin Imbalances in Alzheimer Disease: Decreased Levels of Brain-Derived Neurotrophic Factor and Increased Levels of Nerve Growth Factor in Hippocampus and Cortical Areas**

Christoph Hock, MD;  
Klaus Heese, PhD;  
Christine Hulette, MD, PhD;  
Carlyn Rosenberg, MS;  
Uwe Otten, MD

846

**The Course of Cognitive Impairment in Preclinical Alzheimer Disease: Three- and 6-Year Follow-up of a Population-Based Sample**

Brent J. Small, PhD;  
Laura Fratiglioni, MD, PhD;  
Matti Viitanen, MD, PhD;  
Bengt Winblad, MD, PhD;  
Lars Bäckman, PhD

839

**Progression of Parkinsonism and Loss of Cognitive Function in Alzheimer Disease**

Robert S. Wilson, PhD;  
David A. Bennett, MD;  
David W. Gilley, PhD;  
Laurel A. Beckett, PhD;  
Julie A. Schneider, MD;  
Denis A. Evans, MD

855

**ARCHIVES**  
OF  
**NEUROLOGY**

*Editor:*

**Roger N. Rosenberg, MD**  
Department of Neurology  
University of Texas Southwestern  
Medical Center  
5323 Hines Blvd  
Dallas, TX 75390-9108

*Associate Editors:*

**Hassan M. Fathallah-Shaykh, MD**  
Dallas, Tex  
**Christopher G. Goetz, MD**  
Chicago, Ill  
**Susan T. Iannaccone, MD**  
Dallas, Tex  
**David E. Pleasure, MD**  
Philadelphia, Pa  
**E. S. Roach, MD**  
Dallas, Tex  
**Ira Shoulson, MD**  
Rochester, NY  
**John N. Whitaker, MD**  
Birmingham, Ala

*Assistant Editors:*

**Lawrence S. Honig, MD, PhD**  
Dallas, Tex  
**Matthew Menken, MD**  
Somerset, NJ

*Editorial Assistant:*

**Jenny Kang**  
Dallas, Tex  
**Editorial Office**  
(214) 648-9383  
fax: (214) 648-9388  
e-mail: archneurol@mednet.swmed.edu

*Section Editors:*

*Neurological Review Editor:*  
**David E. Pleasure, MD**  
Philadelphia, Pa

*Controversy in Neurology/  
Consensus in Neurology Editor:*  
**John N. Whitaker, MD**  
Birmingham, Ala

*Basic Science Seminars  
in Neurology Editor:*  
**Hassan M. Fathallah-Shaykh, MD**  
Dallas, Tex

*NeuroTherapeutics Editor:*  
**Ira Shoulson, MD**  
Rochester, NY

*History of Neurology Editor:*  
**Christopher G. Goetz, MD**  
Chicago, Ill

*Neurology and Public Health Editor:*  
**Matthew Menken, MD**  
Somerset, NJ

*Book Review Editor:*  
**Susan T. Iannaccone, MD**  
Dallas, Tex

*Web Editor:*  
**Lawrence S. Honig, MD, PhD**  
Dallas, Tex

*CME Editor*  
**Matthew Menken, MD**  
Somerset, NJ

*Editorial Board*

**James I. Ausman, MD, PhD**  
Chicago, Ill  
**Louis R. Caplan, MD**  
Boston, Mass  
**Steven T. DeKosky, MD**  
Pittsburgh, Pa  
**Mahlon R. DeLong, MD**  
Atlanta, Ga  
**James A. Ferrendelli, MD**  
Houston, Tex  
**John H. Growdon, MD**  
Boston, Mass  
**Vladimir Hachinski, MD, DSc**  
London, Ontario  
**Audrey S. Penn, MD**  
Bethesda, Md  
**Stanley B. Prusiner, MD**  
San Francisco, Calif  
**Bruce R. Ransom, MD, PhD**  
Seattle, Wash  
**Thomas R. Swift, MD**  
Augusta, Ga  
**Kenneth L. Tyler, MD**  
Denver, Colo  
**Paul C. Van Ness, MD**  
Dallas, Tex

*International Advisory Committee*

**Johan A. Aarli, MD**  
Bergen, Norway  
**Oded Abramsky, MD, PhD**  
Jerusalem, Israel  
**Samir F. Atweh, MD**  
Beirut, Lebanon  
**Paula Coutinho, MD, PhD**  
Porto, Portugal  
**Alexandra Dürr, MD**  
Paris, France  
**Bruno Estanol, MD**  
Mexico City, Mexico  
**Cesare Fieschi, MD**  
Rome, Italy  
**Hans J. Freund, MD**  
Düsseldorf, Germany  
**Wang Guo-Xiang, MD**  
Beijing, China  
**Sang-Bok Lee, MD, PhD**  
Seoul, Korea  
**Colin Masters, MD**  
Melbourne, Victoria, Australia  
**Sergio Novis, MD**  
Rio de Janeiro, Brazil  
**Michael Piradov, MD**  
Moscow, Russia  
**Nippon Pongvarin, MD, FRCP**  
Bangkok, Thailand  
**Anthony H. V. Schapira, DSc, MD, FRCP**  
London, England  
**Bhim S. Singhal, MD**  
Bombay, India  
**Erik Stalberg, MD**  
Uppsala, Sweden  
**Eduardo Tolosa, MD**  
Barcelona, Spain  
**Shoji Tsuji, MD, PhD**  
Niigata, Japan

**Left Frontotemporal Hypoperfusion Is Associated With Aggression in Patients With Dementia** 861  
*Nobutsugu Hirano, MD;*  
*Michael S. Mega, MD, PhD;*  
*Ivo D. Dinov, PhD;*  
*Fred Mishkin, MD;*  
*Jeffrey L. Cummings, MD*

**Association Between Severe Cerebral Amyloid Angiopathy and Cerebrovascular Lesions in Alzheimer Disease Is Not a Spurious One Attributable to Apolipoprotein E4** 869  
*John M. Olichney, MD;*  
*Lawrence A. Hansen, MD;*  
*C. Richard Hofstetter, PhD;*  
*Jae-Hong Lee, MD;*  
*Robert Katzman, MD;*  
*Leon J. Thal, MD*

**Assessing Financial Capacity in Patients With Alzheimer Disease: A Conceptual Model and Prototype Instrument** 877  
*Daniel C. Marson, JD, PhD;*  
*Stephen M. Sawrie, PhD;*  
*Scott Snyder, PhD;*  
*Bronwyn McInturff, MS;*  
*Tracy Stalvey, MPH;*  
*Amy Boothe;*  
*Traci Aldridge;*  
*Anjan Chatterjee, MD;*  
*Lindy E. Harrell, MD, PhD*

**OBSERVATION**

**Early-Onset Alzheimer Disease Caused by a New Mutation (V717L) in the Amyloid Precursor Protein Gene** 885  
*Jill R. Murrell, PhD;*  
*Ann M. Hake, MD;*  
*Kimberly A. Quaid, PhD;*  
*Martin R. Farlow, MD;*  
*Bernardino Ghetti, MD*

**IMAGES IN NEUROLOGY**

**Active Intracerebral Hemorrhage From the Lateral Posterior Choroidal Artery** 889  
*Federico C. Vinas, MD;*  
*Chris Kazmierczak, MD;*  
*William M. Coplin, MD*

**HISTORY OF NEUROLOGY: SEMINAL CITATION**

**Aphasia** 892  
*Joseph C. Masdeu, MD, PhD*

**BOOK REVIEWS**

**Motor Disorders** 896  
*David Goldblatt, MD*

**Epidemiology of Pain** 897  
*Ronald M. Glick, MD*

**Diagnosis and Management of Dementia: A Manual for Memory Disorder Teams** 898  
*Marc W. Haut, PhD, ABPP-cn*

**LETTERS TO THE EDITOR**

**Topography, Histology, and Seminology in Dementia** 899  
*Richard J. Caselli, MD*

**In Reply** 899  
*Julene K. Johnson, PhD;*  
*Elizabeth Head, PhD;*  
*Ronald Kim, MD;*  
*Arnold Starr, MD;*  
*Carl W. Cotman, PhD*

**REGULAR DEPARTMENTS**

**This Month in Archives of Neurology** 781

**Calendar** 888

**Index to Advertisers** 901

**ARCHIVES CME** 902

**Classified Advertising** 905

**Instructions for Authors—**  
 See January 2000 issue, page 145, or visit the Web site at [www.archneurol.com](http://www.archneurol.com).