

Cerebrovascular Diseases

Edited by

Martin Reivich • Howard I. Hurtig

Cerebrovascular Diseases

Thirteenth Research (Princeton) Conference

Editors

Martin Reivich, M.D.

*Professor of Neurology and Radiology,
and Director Cerebrovascular
Research Center
University of Pennsylvania
School of Medicine
Philadelphia, Pennsylvania*

Howard I. Hurtig, M.D.

*Associate Professor of Neurology
University of Pennsylvania
School of Medicine, and
Chief Department of Neurology
Graduate Hospital
Philadelphia, Pennsylvania*

Raven Press, 1140 Avenue of the Americas, New York, New York 10036

© 1983 by Raven Press Books, Ltd. All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system, or transmitted, in any form or recording, or otherwise, without the prior written permission of the publisher.

Made in the United States of America

International Standard Book Number 0-89004-876-2
Library of Congress Catalog Card Number 82-40298

The material contained in this volume was submitted as previously unpublished material, except in the instances in which credit has been given to the source from which some of the illustrative material was derived.

Great care has been taken to maintain the accuracy of the information contained in the volume. However, Raven Press cannot be held responsible for errors or for any consequences arising from the use of the information contained herein.

Materials appearing in this book prepared by individuals as part of their official duties as U.S. Government employees are not covered by the above-mentioned copyright.

CEREBROVASCULAR DISEASES

Thirteenth Research (Princeton) Conference

TRANSACTIONS OF THE THIRTEENTH RESEARCH (PRINCETON) CONFERENCE
ON CEREBROVASCULAR DISEASE
HELD UNDER THE AUSPICES OF THE
AMERICAN NEUROLOGICAL ASSOCIATION
AND THE
AMERICAN HEART ASSOCIATION, STROKE COUNCIL
WILLIAMSBURG, VIRGINIA, FEBRUARY 28-MARCH 2, 1982

CONFERENCE SUPPORTED BY A GRANT FROM THE
NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISEASES
AND STROKE,
(NATIONAL INSTITUTES OF HEALTH)

Princeton Conferences on Cerebrovascular Diseases

FIRST CONFERENCE, January 24–26, 1954

Irving S. Wright, Chairman; E. Hugh Luckey, Editor

SECOND CONFERENCE, January 16–18, 1957

Irving S. Wright, Chairman; C. H. Millikan, Editor

THIRD CONFERENCE, January 4–6, 1961

C. H. Millikan, Chairman; R. G. Siekert and J. P. Whisnant, Editors

FOURTH CONFERENCE, January 8–10, 1964

C. H. Millikan, Chairman; R. G. Siekert and J. P. Whisnant, Editors

FIFTH CONFERENCE, January 5–7, 1966

C. H. Millikan, Chairman; R. G. Siekert and J. P. Whisnant, Editors

SIXTH CONFERENCE, January 10–12, 1968

James F. Toole, Chairman; R. G. Siekert and J. P. Whisnant, Editors

SEVENTH CONFERENCE, January 7–9, 1970

James F. Toole, Chairman; J. Moossy and R. Janeway, Editors

EIGHTH CONFERENCE, January 5–7, 1972

Fletcher H. McDowell, Chairman;

F. H. McDowell and R. W. Brennan, Editors

NINTH CONFERENCE, January 9–11, 1974

Jack P. Whisnant, Chairman;

J. P. Whisnant and Burton A. Sandok, Editors

TENTH CONFERENCE, January 7–9, 1976

Peritz Scheinberg, Chairman and Editor

ELEVENTH CONFERENCE, March 5–7, 1978

Erland Nelson, Chairman; T. R. Price and E. Nelson, Editors

TWELFTH CONFERENCE, March 2–4, 1980

John Moossy and Oscar M. Reinmuth, Editors

Publisher's Note: Raven Press has taken over publication of the volumes in this series beginning with the Tenth Conference, based on the January 1976 Princeton meeting on cerebrovascular diseases. Those interested in purchasing earlier volumes in the series should write directly to the former publisher of the series, Grune & Stratton, Inc., 111 Fifth Avenue, New York, N.Y. 10011.

Preface

The history of the Princeton Conference now extends over three decades. In this time, significant progress has been made in our understanding of the pathogenesis of cerebrovascular disease and in the management of this group of disorders although much remains to be learned. The mortality from stroke has declined by 40% in the last 15 years. Stroke prevention is probably the most important factor in the declining stroke rate in the United States.

This conference represents a departure from those that preceded it in that the material presented on four selected topics was chosen on the basis of a critical review of submitted abstracts. This was done to ensure that the program contained the most up-to-date and exciting new work. Experts in these areas were then chosen to give an introductory statement summarizing the present state of the art for each topic while others were invited to discuss each of the presentations. A hallmark of these meetings is that almost 50% of the conference is devoted to discussion and exchange of ideas among all participants.

The four topics considered at this, the 13th Princeton Conference, were nuclear magnetic resonance (NMR) and positron emission tomography (PET), prognostic indicants in cerebrovascular disease, critical factors in prevention of irreversible ischemic damage, and intravascular factors in cerebrovascular disease.

The latest developments in brain imaging, using NMR and PET, are presented here by the most experienced researchers in these fields. Although still experimental, these new techniques promise fascinating and therapeutically useful insights into the physiologic and biochemical alterations of acute cerebrovascular disease.

The epidemiology of stroke has taught us much about the changing picture of cerebrovascular disease in the last 30 years. Population studies are essential to provide the "big picture" perspective that will help focus specific research on better prevention and management of stroke and further reduction in disability and mortality.

Specific methods of treating and reversing the neurologic deficits of acute stroke have been generally inadequate. A clear understanding of the complex pathophysiology of acute ischemic brain damage is perhaps the most important precursor to improved management of the acute stroke patient. This volume presents a lucid overview of the critical factors that influence the evolution of ischemia and dictate the range of therapeutic needs of stroke victims.

The delicate balance of forces that keep blood and its constituents in fluid suspension is offered as counterpoint to the disturbed interaction of sclerotic

blood vessel wall and activated clotting factors in vascular disease. A new look at old therapies and a futuristic assessment of other agents that might ameliorate abnormal clotting tendency and improve oxygen delivery is given.

Finally, a discussion of important intravascular mechanisms in cerebrovascular disease is presented.

This volume should be of interest not only to those actively engaged in research in these areas but to clinicians who deal on a day to day basis with patients affected by these disorders.

Martin Reivich, M.D.

Howard Hurtig, M.D.

Acknowledgments

The editors wish to thank those who have presented papers and the discussants for their lively responses and informative and stimulating presentations. We would particularly like to thank the chairmen who organized these sessions that generated such lively and enthusiastic interest. Special gratitude is also due to the Program Committee who put the program together, Drs. Moossy, Plum, Scheinberg, and Toole. Finally, our thanks go to Miss Marjorie Harper, our secretary, who labored long and hard over the administrative details of this meeting.

Participants: Thirteenth Research (Princeton) Conference on Cerebrovascular Diseases

Robert H. Ackerman

*Director, Carotid Evaluation and
Cerebral Blood Flow Laboratories
Massachusetts General Hospital
Fruit Street
Boston, Massachusetts 02114*

Ludwig M. Auer

*Univ. Doz. Dr.
Universitätsklinik für Neurochirurgie
Auenbruggerplatz, A-8036 Graz
Austria*

H. J. M. Barnett

*Professor and Chairman
Department of Clinical Neurological
Sciences
The University of Western Ontario
London, Ontario, Canada N6A 5A5*

Jean-Claude Baron

*Department of Biologie
Commissariat à l'Energie
Atomique Hôpital d'Orsay
Orsay, France*

Norman H. Bass

*Professor and Chairman
Albert B. Chandler Medical Center
University of Kentucky
Lexington, Kentucky 40506*

Caroline Becker

*Associate Professor of Epidemiology
University of North Carolina
UNC-207 Rosenau Hall—201H
Chapel Hill, North Carolina 27514*

Jose Biller

*Assistant Professor of Neurology
Loyola University Stritch School of
Medicine*

Anthony Breuer

*Professor of Neurology
Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, Ohio 44106*

Kenneth M. Brinkhous

*Alumni Distinguished Professor of
Pathology
University of North Carolina
Chapel Hill, North Carolina 27514*

Thomas Budinger

*Henry Miller Professor of Medicine
Research
Professor of Bioinstrumentation
Electrical Engineering and Computer
Sciences
Room 230, Donner Laboratory
University of California
Berkeley, California 94720*

Lou Caplan

*Chairman, Division of Neurology
Michael Reese Hospital
29th and Ellis Avenue
Chicago, Illinois 60616*

Robert Crowell

*Chief of Barrow Neurological Institute
Barrow Neurological Institute
St. Joseph's Hospital and Medical
Center
350 West Thomas Road
Phoenix, Arizona 85013*

James N. Davis

*Associate Professor of Pharmacology
Chief Neurologist, VA
Professor of Medicine and Neurology
Box 3850
Duke University Medical Center
Durham, North Carolina 27710*

Umberto DeGirolami

*Department of Pathology
(Neuropathology) and Neurology •
University of Massachusetts Medical
School*

*55 Lake Avenue North
Worcester, Massachusetts 01605*

N. H. Diemer

*Medical Physiology Institute-A
Copenhagen University
The Panum Institute
Blegdamsvej, DK-2200 Copenhagen
Denmark*

Charles Drake

*Chairman, Department of Surgery
University Hospital
London, Ontario N6A 5A5, Canada*

Thomas E. Duffy

*Professor of Biochemistry in
Neurology
Department of Neurology
Cornell University Medical College
New York, New York 10021*

Robert J. Duke

*Associate Clinical Professor
Department of Neurology
McMaster University
Hamilton, Ontario, Canada*

Manuel Dujovny

*Director, Neurosurgical Research
Laboratory
Henry Ford Hospital
Detroit, Michigan 48402*

Mark L. Dyken

*Professor and Chairman
Department of Neurology
Indiana University School of Medicine
Indianapolis, Indiana 46223*

J. Donald Easton

*Professor and Chairman
Department of Neurology
University of Missouri Medical Center
Columbia, Missouri 65212*

Sture Ericksson

*Department of Internal Medicine
Umea University
S-901 85 Umea, Sweden*

William S. Fields

*Professor and Chairman
Department of Neurology
University of Texas Health Science
Center
Medical School
P.O. Box 20708
Houston, Texas 77025*

Robert A. Fishman

*Chairman of Neurology
Neurology 794 M
University of California Medical
Center
San Francisco, California 94143*

Anthony Fletcher

*Associate Professor of Medicine
Washington University School of
Medicine
St. Louis, Missouri 63110*

Eric T. Fossel

*Assistant Professor of Biophysics
Harvard Medical School
Boston, Massachusetts 02115*

Julio H. Garcia

*Professor, Pathology and Neurology
University of Alabama in Birmingham
Birmingham, Alabama 35294*

Myron D. Ginsberg

*Professor of Neurology
Director, Cerebral Vascular Disease
Research Center
University of Miami School of
Medicine
Miami, Florida 33101*

Murray Goldstein

Acting Director
National Institute of Neurological
and Communicative Disorders
and Stroke
National Institutes of Health
Bethesda, Maryland 20205

Patricia A. Grady

Assistant Professor of Neurology
University of Maryland School
of Medicine
Baltimore, Maryland 21201

James Grotta

Assistant Professor of Neurology
University of Texas Medical School
P.O. Box 20708
Houston, Texas 77030

Vladimir Hachinski

Chairman, Division of
Cerebrovascular Research
P.O. Box 5339
Postal Station A
London, Ontario N6A 5A5, Canada

James H. Halsey, Jr.

Professor and Chairman
Department of Neurology
University of Alabama Medical Center
Birmingham, Alabama 35294

William K. Hass

Professor of Neurology
New York University School of
Medicine
New York, New York 10016

Wolf-Dieter Heiss

Professor
Max-Planck-Institut für Hirnforschung
Ostmerheimer Str. 200
5 Holn 91 (Merheim), Federal
Republic of Germany

John Hoak

Professor of Medicine
Director, Division of Hematology-
Oncology
University of Iowa, College of
Medicine
Iowa City, Iowa 52242

Konstantin-Alexander Hossmann

Professor of Experimental Neurology
Max-Planck-Institute for Brain
Research
Cologne-Merheim, Federal Republic
of Germany

Howard Hurtig

Chairman, Department of Neurology
Graduate Hospital
19th and Lombard Streets
Philadelphia, Pennsylvania 19146

Neal F. Kassell

Associate Professor
University of Iowa
Iowa City, Iowa 52242

Igor Klatzo

Chief, Lab of Neuropathology and
Neuroanatomical Sciences
National Institute of Neurological and
Communicative Disorders and
Stroke
National Institutes of Health
Bethesda, Maryland 20205

Arisztid G. B. Kovach

Department Chairman
Experimental Research Center
Semmelweis Medical University
Budapest, 1082-H, Hungary

David Kuhl

Chief, Nuclear Medicine
UCLA School of Medicine
Los Angeles, California 90024

Niels A. Lassen

Chief, Laboratory of Clinical
Physiology
Bispebjerg Hospital
Copenhagen, Denmark

Paul Lauterbur

Professor of Chemistry and Research
Professor of Radiology
Departments of Chemistry and
Radiology
State University of New York
at Stony Brook
Stony Brook, New York 11794

David E. Levy

*Associate Professor of Neurology
Cornell University Medical College
New York, New York 10021*

Fletcher H. McDowell

*Professor of Neurology
Cornell University Medical College
New York, New York 10021*

Gardner McMillan

*Associate Director
Arteriosclerosis Hypertension and
Lipid Metabolism Program
Division of Heart and Vascular
Disease*

*Federal Building
7550 Wisconsin Avenue
Bethesda, Maryland 20205*

John Stirling Meyer

*Chief, Cerebrovascular Research
VA Medical Center—Houston
Professor of Neurology
Baylor College of Medicine—Houston
Houston, Texas 77211*

Clark H. Millikan

*Professor of Neurology
Director, Cerebral Vascular Unit
University of Utah School of Medicine
Salt Lake City, Utah 84132*

J. P. Mohr

*Professor and Chairman
Department of Neurology
University of Southern Alabama
2151 Fillingim Street, 1100 MCFB
Mobile, Alabama 36617*

John Moossy

*Professor of Pathology and Neurology
University of Pittsburgh School of
Medicine
Pittsburgh, Pennsylvania 15261*

Michael A. Moskowitz

*Associate Professor of Neurology
Departments of Neurosurgery and
Neurology
Massachusetts General Hospital
Fruit Street
Boston, Massachusetts 02114*

Ronald E. Myers

*Associate Chief of Staff/Research
Res (151)
VA Medical Center
3200 Vine Street
Cincinnati, Ohio 45220*

Erland Nelson

*Chairman, Department of Neurology
Mt. Sinai Medical Center
California at 15th Street
Chicago, Illinois 60611*

Edwin M. Nemoto

*Associate Professor
University of Pittsburgh
Pittsburgh, Pennsylvania 15261*

John W. Norris

*Associate Professor of Medicine
(Neurology)
University of Toronto
Canada*

Fred Plum

*Neurologist-in-Chief
New York Hospital
Cornell Medical Center
525 East 68th Street
New York, New York 10021*

William J. Powers

*Instructor in Neurology and
Radiology
Departments of Neurology and
Radiology
Washington University School of
Medicine
St. Louis, Missouri 63110*

Thomas Price

*Professor of Neurology
University of Maryland Hospital
Baltimore, Maryland 21204*

William A. Pulsinelli

*Assistant Professor
Cornell University Medical College
New York, New York 10021*

Marcus Raichle

*Professor of Neurology and Radiology
Washington University School of
Medicine*

Box 8111

*660 South Euclid Avenue
St. Louis, Missouri 63110*

Oscar M. Reinmuth

*Professor and Chairman
Department of Neurology
University of Pittsburgh
Pittsburgh, Pennsylvania 15261*

Martin Reivich

*Professor of Neurology and Radiology
and Director*

*Cerebrovascular Research Center
Room 429, Johnson Pavilion/G2
36th and Hamilton Walk
University of Pennsylvania
Philadelphia, Pennsylvania 19104*

Jim Robertson

*Chairman and Professor
Department of Neurosurgery
University of Tennessee
Center for Health Sciences
858 Madison, Room 231
Memphis, Tennessee 38163*

William I. Rosenblum

*Professor and Vice Chairman
Department of Pathology
Director of Neuropathology
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298*

Robert G. Robinson

*Associate Professor of Psychiatry
Johns Hopkins University School of
Medicine
Baltimore, Maryland 21205*

Peritz Scheinberg

*Professor and Chairman
Department of Neurology
University of Miami School of
Medicine
Miami, Florida 33101*

Bruce S. Schoenberg

*Chief, Neuroepidemiology Section
National Institute of Neurological and
Communicative Disorders and
Stroke and
Clinical Professor of Neurology
Georgetown University School of
Medicine
Bethesda, Maryland 20205*

Bo K. Siesjö

*Professor
Laboratory of Experimental Brain
Research
University of Lund
S-221 85 Lund, Sweden*

Henry A. Sloviter

*Harrison Department of Surgical
Research
Professor of Surgical Research and
Professor of Biochemistry and
Biophysics
Departments of Neurosurgery and
Biochemistry
Hospital of the University of
Pennsylvania
Philadelphia, Pennsylvania 19104*

Anthony J. Strong

*Senior Lecturer in Neurosurgery
University of Newcastle upon Tyne
Newcastle upon Tyne, NEL 7RU
United Kingdom (England)*

Juan M. Taveras

Radiologist-in-Chief
 Massachusetts General Hospital
 Fruit Street
 Boston, Massachusetts 02114

James Toole

Professor and Chairman
 Department of Neurology
 Bowman Gray School of Medicine
 Wake Forest University
 300 S. Hawthorne Road
 Winston-Salem, North Carolina 27103

Michael Walker

Director, Extramural Programs
 National Institute of Neurological and
 Communicative Disorders and
 Stroke

National Institutes of Health
 Bethesda, Maryland 20205

Jesse Weinberger

Assistant Professor of Neurology
 The Mount Sinai School of Medicine
 1 Gustave Levy Place
 New York, New York 10029

Babette Weksler

Associate Professor of Medicine
 C-608 Neurology
 New York Hospital
 Cornell Medical Center
 525 East 68th Street
 New York, New York 10021

J. P. Whisnant

Professor of Neurology
 Department of Neurology
 Mayo Clinic
 Rochester, Minnesota 55901

Richard White

Professor of Pharmacology
 Department of Neurosurgery
 College of Medicine
 Coleman Building
 956 Court Avenue
 Memphis, Tennessee 38163

William E. Wilkinson

Assoc. Professor and Chief
 Division of Biometry
 Duke University Medical Center
 Durham, North Carolina 27710

William Williams

Professor of Medicine
 State University of New York
 School of Medicine
 750 East Adams Street
 Syracuse, New York 13210

Phil Wolf

Professor of Neurology
 Associate Research Professor of
 Medicine (Preventive Medicine in
 Epidemiology)
 Department of Neurology
 Boston University Medical Center
 80 East Concord Street
 Boston, Massachusetts 02118

Frank Wood

Associate Professor, Department of
 Neuropsychiatry
 Bowman Gray School of Medicine
 Winston-Salem, North Carolina 27103

George F. Wooten

Associate Professor of Neurology
 Washington University School of
 Medicine
 Box 8111
 660 South Euclid
 St. Louis, Missouri 63110

Frank M. Yatsu

Professor and Chairman
 Department of Neurology
 Oregon Health Sciences University
 Portland, Oregon 97201

Nicholas T. Zervas

Professor of Surgery
 Harvard Medical School
 Boston, Massachusetts 02114

Contents

Nuclear Magnetic Resonance and Positron Emission Tomography

- 1 Nuclear Magnetic Resonance and Positron Emission
Tomography
Paul C. Lauterbur
- 7 Nuclear Magnetic Resonance and Positron Emission
Tomography in Cerebral Vascular Disease
Thomas F. Budinger
- 15 Discussion
- 19 Effects of Aging and Stroke on Patterns of Local Cerebral
Glucose Utilization
David E. Kuhl
- 29 Evaluating Patients with Ischemic Cerebrovascular Disease
Using Positron Emission Tomography
M. E. Raichle
- 33 Discussion
- Prognostic Indicators in Cerebrovascular Disease**
- 41 Prognostic Indicators in Cerebrovascular Disease
Vladimir Hachinski
- 51 Changes in Stroke Mortality: Effects on Evaluating and
Predicting Outcome for Therapeutic Studies
Mark L. Dyken and Robert A. Calhoun
- 57 Discussion
- 63 Outcome of Patients with Asymptomatic Carotid Bruits
John W. Norris and Joseph G. D'Alton
- 73 Discussion
- 77 A Questionnaire for TIA Symptoms: A Predictor of
Subsequent Stroke
*William E. Wilkinson, Albert Heyman, Robert I. Pfeffer,
and J. Gordon Burch*

- 83 Discussion
- 93 Cardiovascular Disease Precursors of Completed Ischemic Stroke and Transient Ischemic Attacks
Bruce S. Schoenberg, Devera G. Schoenberg, David A. Pritchard, Abraham M. Lilienfeld, and Jack P. Whisnant
- 103 Discussion
- 109 The Significance of Clinical Deterioration in Acute Carotid Distribution Cerebral Infarction
James Grotta
- 117 Discussion
- 121 Clinical Predictors of Recovery from Ischemic Stroke
D. E. Levy, J. J. Caronna, R. H. Lapinski, P. G. Scherer, W. A. Pulsinelli, and F. Plum
- 129 Discussion
- 137 Poststroke Affective Disorders
Robert G. Robinson, Lyn Book Starr, Kenneth L. Kubos, and Thomas R. Price
- 147 Discussion
- 153 Has Prognosis Improved for Aneurysmal Subarachnoid Hemorrhage Patients?
James C. Torner, Neal F. Kassell, and Robert F. Woolson
- 161 Discussion
- Critical Factors in Prevention of Irreversible Ischemic Damage**
- 167 Discussion: Introduction
F. Plum
- 169 Brain Capillaries Expand and Rupture in Areas of Ischemia and Reperfusion
J. H. Garcia, S. L. Lowry, L. Briggs, H. L. Mitchem, R. Morawetz, J. H. Halsey, and K. A. Conger
- 181 Discussion
- 183 Influence of Tissue Osmolality on Intracerebral Fluid Shifts and the Development of Ischemic Brain Edema
K.-A. Hossmann and Y. Matsuoka

- 193 Discussion
- 195 Brain Glucose Levels as a Factor Influencing the Outcome of Ischemic Damage
F. Plum, W. A. Pulsinelli, and C. K. Petito
- 199 Discussion
- 213 Regional Vulnerability and Selective Necrosis in Experimental Focal Cerebral Ischemia
F. W. Marcoux, R. B. Morawetz, R. M. Crowell, Umberto DeGirolami, and James H. Halsey, Jr.
- 223 Discussion
- 225 Duration Versus Severity of Ischemia as Critical Factors of Cortical Cell Damage
W.-D. Heiss and G. Rosner
- 235 Discussion
- 237 Aspects of Tissue Injury in Cerebral Ischemia
Myron D. Ginsberg, Brant D. Watson, Shinichi Yoshida, Raul Busto, Kouichi Abe, William J. Goldberg, and Peritz Scheinberg
- 249 Discussion
- 251 Fatty Acid Metabolism and the Mechanisms of Ischemic Brain Damage
Bo K. Siesjö and Tadeusz Wieloch
- 269 Discussion
- 275 Are Neurotransmitter Uptake Mechanisms Selectively Damaged in the Ischemic Penumbra?
A. J. Strong, J. Hardy, G. S. Venables, G. Gibson, B. E. Tomlinson, L. Symon, N. M. Branston, and D. M. Bowen
- 287 Discussion
- 289 Ischemic Damage to Striatal GABAergic Neurons
W. A. Pulsinelli and A. J. Francis
- 297 Discussion