



# PROGRESS IN STROKE RESEARCH: 1

Edited by

Roger M Greenhalgh  
*Senior Lecturer in Surgery*  
*Honorary Consultant Surgeon*  
*Charing Cross Hospital, London*

F Clifford Rose  
*Consultant Neurologist*  
*Charing Cross Hospital;*  
*Medical Ophthalmology Unit*  
*St Thomas' Hospital, London*



A PITMAN MEDICAL PUBLICATION

Distributed by

YEAR BOOK MEDICAL PUBLISHERS, INC.

35 E. Wacker Drive, Chicago

*First published 1979*

© Pitman Medical Publishing Co Ltd, 1979

*This book is copyrighted in England and may not be reproduced by any means in whole or in part. Application with regard to reproduction should be directed to the Copyright owner.*

*Distributed in Continental North, South and Central America, Hawaii, Puerto Rico and The Philippines by*  
YEAR BOOK MEDICAL PUBLISHERS, INC.

*by arrangement with*  
PITMAN MEDICAL PUBLISHING CO LTD

Library of Congress Cataloging in Publication Data  
Main entry under title:

Progress in stroke research.

“A Pitman medical publication.”

Includes index.

1. Cerebral vascular disease. 2. Cerebrovascular disease — Research. I. Greenhalgh, Roger Malcolm. II. Rose, Frank Clifford.

RC388.5P73 1979 616.8'1 79-14019  
ISBN 0-8151-3937-3

Text set in 10 pt IBM Press Roman, printed and bound  
in Great Britain at The Pitman Press, Bath

# Foreword

*Professor A. J. Harding Rains*

In terms of benefit to the patient, the centre of our medical universe, much has taken place with regard to strokes in the past 25 years. Progress has been possible through development in scientific effort through measurement, technological advances and a continued and high standard of the clinical art. Especially significant is the coming together in academic and clinical linkages of those in the different disciplines of medicine who are devoted to a subject such as this. What is particularly encouraging also is the coming together of pure scientists with clinicians and those in professions allied to medicine. Furthermore it is realised that progress is also being made through an international effort.

It is right that we should question any progress claimed in terms of gain versus risk. Does progress offer gain in understanding of causes, gain in knowledge of pathology and physiology, gain in assessment techniques especially those which are non-invasive, gain in methods of treatment and rehabilitation, and does it offer reduction of risks inherent in such progress?

I welcome this opportunity of publicising the contribution of this book to a wider international audience, relating as it does the progress that is being made for the patient's sake and stimulating continuing effort towards progress in the future.

A. J. Harding Rains, MS, FRCS  
Professor of Surgery, University of London  
at Charing Cross Hospital Medical School

# Contributors

- N Angelides, Department of Surgery, St Mary's Hospital, London W9
- J J Bergan, Magerstadt Professor of Surgery, Chief, Division of Vascular Surgery, Northwestern University, Chicago, Illinois, USA
- W Blackwood, Hon Visiting Consultant, Department of Pathology, Charing Cross Hospital, London W6; Emeritus Professor of Neuropathology, Institute of Neurology, Queen Square, London WC1
- K E Britton, Consultant in Charge of Nuclear Medicine and Radioisotopes, St Bartholomew's Hospital, London EC1
- R Capildeo, Senior Registrar, Department of Neurology, Charing Cross Hospital, London W6
- R N Chakravarty, Associate Professor, Department of Experimental Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India
- J S Chopra, Associate Professor and Head, Department of Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India
- M Collard, Service de Neurologie, Hopital Civil de Charleroi, France
- L T Cotton, Consultant Surgeon, King's College Hospital, London SE5
- Christine Court, Department of Social Medicine, Charing Cross Hospital, London W6
- J C W Crawley, Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex
- K C Das, Professor, Department of Haematology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India
- W J Dekoninck, Service de Neurologie, Hopital Civil de Charleroi, France
- G Dorf, Section of Clinical Pharmacology, Academic Department of Medicine, Royal Free Hospital, London NW3
- G H Du Boulay, Professor of Neuroradiology, Institute of Neurology, Queen Square, London WC1
- H H G Eastcott, Consultant Surgeon, St Mary's Hospital, London W9
- J F Fernandes e Fernandes, Department of Surgery, St Mary's Hospital, London W9
- W S Fields, Professor and Head of Department, The University of Texas Health Science Center at Houston Medical School, Houston, Texas
- C D Forbes, University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G4 0SF
- J-C Gautier, Professor of Neurology, Hopital de la Salpêtrière, 47 Boulevard de l'Hopital, 75013 Paris, France

- M J Gawel, Lecturer, Department of Neurology, Charing Cross Hospital, London W6
- A Gerebtzoff, Service de Neurologie, Hopital Civil de Charleroi, France
- R G Gosling, Reader in Physics, Guy's Hospital, London SE1
- M Granowska, Research Senior Registrar, St Bartholomew's Hospital, London EC1
- R M Greenhalgh, Senior Lecturer and Hon. Consultant Surgeon, Charing Cross Hospital, London W6
- D N W Griffith, Section of Clinical Pharmacology, Academic Department of Medicine, Royal Free Hospital, London NW3
- S Haberman, Lecturer, Department of Actuarial Sciences, City University, London EC1
- A Herxheimer, Senior Lecturer, Department of Pharmacology, Charing Cross Hospital Medical School, London W6
- M Horrocks, Biomedical Engineering Department, King's College Hospital Medical School, London SE5
- K Howlett, Consultant Neuroradiologist, Charing Cross Hospital, London W6
- R D Illingworth, Consultant Neurosurgeon, Charing Cross Hospital, London W6; Central Middlesex Hospital, London NW10
- J Jacquy, Service de Neurologie, Hopital Civil de Charleroi, France
- I M James, Section of Clinical Pharmacology, Academic Department of Medicine, Royal Free Hospital, London NW3
- R F Jewkes, Consultant in Nuclear Medicine, Charing Cross Hospital, London W6
- R V Johnston, University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G40 5F
- T Jones, MRC Cyclotron Unit, Hammersmith Hospital, London W12
- B E Kendall, Consultant Neuroradiologist, National Hospital, Queen Square, London WC1
- P A Lamis, Department of Vascular Surgery, Baptist Medical Center, Atlanta, Georgia
- T Y Lee, Research Physicist, St Bartholomew's Hospital, London EC1
- R R Lewis, Consultant Physician, Guy's Hospital, London SE1
- G D O Lowe, University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G40 5F
- J S P Lumley, Senior Lecturer and Hon. Consultant Surgeon, St Bartholomew's Hospital, London EC1
- David A McClusky, Department of Vascular Surgery, Baptist Medical Center, Atlanta, Georgia
- John McFie, Consultant Neuropsychologist, Charing Cross Hospital, London W6
- K D MacRae, Senior Lecturer in Statistics, Charing Cross Hospital Medical School, London W6
- Susan P Mills, Research Assistant, Department of Surgery, Charing Cross Hospital, London W6

- D L Mitchelson, Research Fellow, Department of Human Sciences, University of Technology, Loughborough, Leicester
- T Needham, Department of Surgery, St Mary's Hospital, London W9
- A N Nicolaides, Senior Lecturer and Hon. Consultant Surgeon, St Mary's Hospital, London W9
- C C Nimmon, Senior Physicist, St Bartholomew's Hospital, London EC1
- G D Perkin, Consultant Neurologist, Charing Cross Hospital, London W6
- I Petrosino, Research Fellow, St Bartholomew's Hospital, London EC1
- S K Prabhakar, Senior Resident, Department of Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India
- C R M Prentice, University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G40 5F
- E W Radü, Research Fellow, Lyshoema Radiological Department, National Hospital, Queen Square, London WC1
- D L Rail, Registrar in Neurology, Charing Cross Hospital, London W6
- A J Harding Rains, Professor of Surgery, Charing Cross Hospital, London W6
- M M Reavey, University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G40 5F
- V C Roberts, Biomedical Engineering Department, King's College Hospital Medical School, London SE5
- F Clifford Rose, Physician in Charge, Department of Neurology, Charing Cross Hospital; Consultant Neurologist, Medical Ophthalmology Unit, St Thomas' Hospital, London SE1
- R W Ross Russell, Consultant Physician, National Hospital, Queen Square, London WC1; Moorfields Eye Hospital, London EC1; Consultant Neurologist, St Thomas' Hospital, London SE1
- M Rutland, Research Senior Registrar, St Bartholomew's Hospital, London EC1
- J S Sodhi, Professor, Department of Radiology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India
- P E Stanton, Department of Medical Surgery, Georgia Baptist Medical Center, Atlanta, Georgia
- L Symon, Professor of Neurological Surgery, Institute of Neurology, The National Hospital, Queen Square, London WC1
- C W Taylor, Professor of Surgery, St Bartholomew's Hospital, London
- D J Thomas, Consultant Neurologist, St Mary's Hospital, London W2
- J E Thompson, Professor of Surgery, Baylor University, Medical Center, Dallas, Texas
- Rita Twiston-Davis, Research Speech Therapist, Charing Cross Hospital, London W6
- M J Verta, Vascular Fellow, Northwestern University, Chicago, Illinois
- P L Wahi, Professor and Head, Department of Cardiology, Postgraduate Institute of Education and Research, Chandigarh 160012, India

M L Woollard, Section of Clinical Pharmacology, Academic Department of  
Medicine, Royal Free Hospital, London NW3

J S T Yao, Associate Professor of Surgery, Northwestern University, Chicago,  
Illinois

M G Yasargil, Director, Neurochirurgische, Universitätsklinik, Kantonsspital  
Zürich

Y Yonekawa, Oberarzt, Neurochirurgische, Universitätsklinik, Kantonsspital,  
Zürich

B Zumstein, Oberarzt, Neurochirurgische, Universitätsklinik, Kantonsspital,  
Zürich



## CONTENTS

Foreword by A J Harding Rains	iii
List of Contributors	ix

### PART I PATHOPHYSIOLOGY OF STROKE

1	Epidemiological aspects of stroke	S Haberman, R Capildeo and F Clifford Rose	3
2	Risk factors in carotid artery stenosis and intracranial aneurysms	R M Greenhalgh, S P Mills and G W Taylor	15
3	Arterial pathology in cerebral ischaemia and infarction	J C Gautier	28
4	Atheroembolism and cerebral ischaemia	R W Ross Russell	40
5	Pathological aspects of emboli in the brain	W Blackwood	44
6	The influence of blood viscosity on cerebral blood flow and symptoms	D J Thomas	47
7	The outcome of asymptomatic bruit	J E Thompson	56
8	Hemodynamic assessment and surgical correction of kinking of the internal carotid artery	P E Stanton, D A McClusky and P A Lamis	65
9	Experimental cerebral infarction	L Symon	79

### PART II RESIDUAL ISCHAEMIC NEUROLOGICAL DEFICIT AND ASSESSMENT

10	The significance of the pathology of extracranial arteries for the neurologist and the surgeon	J C Gautier	93
----	--	-------------	----

11	The assessment of neurological disability	R Capildeo and F Clifford Rose	106
12	Bioengineering in motor function assessment and therapy	D L Mitchelson	117
13	The assessment of communication deficit	R Twiston-Davis	125
14	The place of angiography	K Howlett	133
15	The value of CAT scanning in assessing the degree of infarction in the brain	G H Du Boulay, E W Radü, D J Thomas and B E Kendall	140
16	The functional brain scan: neuropsychological assessment	J McFie	144

### PART III MEDICAL MANAGEMENT OF STROKE AND PRESTROKE

17	Towards a computer-based data bank for stroke patients	R Capildeo, S Haberman and F Clifford Rose	153
18	Should strokes be investigated?	M J Gawel	159
19	Stratification for the management of prestroke conditions	D L Rail and R M Greenhalgh	167
20	A pharmacologist's view of drug trials for stroke and prestroke	A Herxheimer	172
21	Statistical aspects of clinical trials	K D MacRae	176
22	Anticoagulants in transient ischaemic attacks	G D Perkin	181
23	Platelet-suppressive therapy in cerebral ischaemia	W S Fields	204
24	The effect of ornithine alpha-ketoglutarate in stroke	D N W Griffith, G Dorf, I M James and M L Woollard	207
25	Platelet aggregates in cerebrovascular disease — correlation with fibrinogen	R V Johnston, M M Reavey, G D O Lowe, C D Forbes and C R M Prentice	212
26	Stroke in the young in North-West India	J S Chopra, S K Prabhakar, K C Das, R N Chakarvarty, J S Sodhi and P L Wahi	217
27	Medico-social aspects of stroke: a domiciliary follow-up study	Christine Court, R Capildeo and F Clifford Rose	237

## PART IV NON-INVASIVE ASSESSMENT OF CAROTID ARTERY DISEASE

28	Carotid artery assessment and imaging by spectrally analysed Doppler ultrasound	R G Gosling and R R Lewis	247
29	The use of fluid-filled oculoplethysmography and carotid phonoangiography in the diagnosis of extracranial carotid artery occlusive disease	J S T Yao, M J Verta and J J Bergan	270
30	The value of carotid phonoangiography and Doppler ultrasound in the diagnosis of internal carotid stenosis	A N Nicolaides, T Needham, J Fernandes and N Angelides	281
31	Doppler ultrasound in the evaluation of carotid artery stenosis — a comparative study	M Horrocks, V C Roberts and L T Cotton	287

## PART V ASSESSMENT OF REGIONAL CEREBRAL BLOOD FLOW

32	Assessment of cerebral blood flow by the electrical impedance method	J Jacquy, A Gerebtzoff, M Collard and W J Dekoninck	301
33	Non-invasive measurement of regional cerebral flow before and after microvascular surgery	K E Britton, M Granowska, M Rutland, T Y Lee, C C Nimmon, I Petrosino and J S P Lumley	307
34	Recent technical developments in the xenon-133 inhalation technique for cerebral blood flow measurement	J C W Crawley	319
35	The combined use of the intravenous xenon-133 technique and the $^{15}\text{O}_2$ inhalation method	D J Thomas and T Jones	330
36	Comparison of practical aspects of radioisotope methods for regional cerebral blood flow	R F Jewkes	340

## PART VI EXTRACRANIAL SURGERY FOR STROKE

37	Evolution of carotid and vertebral arterial surgery	H H G Eastcott	347
38	Selecting stroke patients for extracranial surgery	W S Fields	356

39	Results of carotid surgery using an intraluminal shunt	J E Thompson	360
40	Selective cerebral protection during carotid endarterectomy	J S T Yao and J J Bergan	367
PART VII INTRACRANIAL SURGERY FOR STROKE			
41	Surgical management of subarachnoid haemorrhage due to ruptured intracranial aneurysm	R D Illingworth	377
42	Selection for extracranial to intracranial bypass	J S P Lumley	387
43	Surgical technique for extracranial to intracranial bypass	R M Greenhalgh and R D Illingworth	393
44	Results of superficial temporal to middle cerebral artery bypass — review of 90 cases	B Zumstein, M G Yasargil and Y Yonekawa	404
45	Medical and surgical cooperation in stroke presentation and management	W S Fields	410
	Index		413

# **Part I Pathophysiology of Stroke**



## Chapter 1

### EPIDEMIOLOGICAL ASPECTS OF STROKE

*S Haberman, R Capildeo and F Clifford Rose*

#### Introduction

One in three persons will develop cerebrovascular disease. It is the third most frequent cause of death in England and Wales, and the probability of ultimate death from it is 1 in 8 [1].

We shall discuss the trends in mortality rates for England and Wales since 1958 (when the Seventh Revision of the WHO International Cause of Death Classification was introduced), with a view to answering the following questions:

- (a) Have the mortality rates for cerebrovascular disease, overall and subdivided by age, sex and pathology, changed, and if so to what extent?
- (b) What are the possible explanations for such changes, and, in particular, is there any relationship with the corresponding trends for hypertensive disease and ischaemic heart disease?

#### Method

The main source of data in this review is the officially published mortality statistics for England and Wales, for the years 1958 to 1975 [2,3]. Where possible, information from OPCS Quarterly Monitors [4] was used to provide information relating to 1976. The official 'cause of death' statistics are derived from the underlying causes as stated on the death certificate by the certifying physician.

When comparing the mortality rates for any two years by a single-figure index, the effect of the difference in the age and sex structures of the two populations must be eliminated. This is achieved by calculating age- and sex-adjusted mortality rates, rather than crude rates. The England and Wales population for 1973 has been used as the standard (the male population to standardize the male rates, and the female population for the female rates). The 1973 population has been used so that reference can be made to results recently published [5].

For measuring the significance of time trends in mortality rates, Kendall's rank correlation coefficient,  $T$ , between the rate and the year of occurrence has been calculated. Allowance was made for tied ranks by using the tables published by Sillitto [6].

An alternative approach to estimating the significance of trends in age- and sex-specific mortality rates is to fit a straight line of the form:

$$\log_e(\text{mortality rate}) = \alpha + \beta t \text{ where } t = \text{calendar year.}$$

The fit was made using a least-squares approach. Tests may then be performed to ascertain whether the estimate of a particular slope,  $\beta$ , is significantly different from zero, and whether the difference between the estimate of two slopes,  $\hat{\beta}$ , is significantly different from zero (in particular, this second test may be applied to corresponding male and female trends).

### Accuracy of the Data

The official mortality statistics for England and Wales are well presented, but the accuracy of the data cannot be accepted without reservation. Thus, in a study of the accuracy of death certification, the diagnoses before and after autopsy for a group of cerebrovascular disease deaths in England and Wales showed wide disagreement [7].

There are at least six potential sources of bias impeding the use of mortality statistics for epidemiological analysis [8,9], viz:

- (a) Diagnostic difficulty  
Since cerebrovascular disease involves an interference with neurological function, a diagnosis of stroke is usually straightforward.
- (b) Lethality of the disease  
When the case fatality rate is less than 100% (as with cerebrovascular disease), the question arises of how the survivors compare with those who die. If cerebrovascular disease were an illness of short duration with an inevitably fatal outcome, then the diagnosis of cerebrovascular disease would invariably appear on the death certificate. But most stroke patients do not die within a short period [10], survivors dying from myocardial infarction, pneumonia or other unrelated illnesses. For this reason, cerebrovascular disease may not appear on the death certificate. This feature depends to some extent on the severity and persistence of residual signs.
- (c) Contributing causes  
Possible errors in estimating the numbers of deaths attributable to a particular cause arise because that cause may frequently be listed on the death certificate as a *contributory* cause rather than an *underlying* cause of death. This was found in the US study of multiple causes of death – in 1955, cerebrovascular disease was stated as an underlying cause of death in only 57.1% of the cases where it was mentioned on the certificate [11].  
The source of this error is the variability between certifying doctors in choosing cerebrovascular disease as an underlying cause of death when there are multiple pathologies present.
- (d) Statistical processing  
The problems of statistical processing include:
  - (i) changes in the rules and procedures for the classification of causes of death;
  - (ii) changes in the classification code of causes of death, and their misinterpretation.

To avoid such heterogeneity, we have considered a period that spans only one revision of the WHO International Cause of Death Classification (1967).



The effect of the 1967 Revision on numbers of cerebrovascular disease deaths has been estimated by the Registrar General [12] as decreasing the numbers of deaths by 0.2% for both sexes. Clearly, this is not an important effect.

For the major pathological types of cerebrovascular disease, the Registrar General does not produce revised estimates of the numbers of deaths before 1968, so that it is only possible to discuss the trends for these subgroups from 1968.

(e) Reporting of age at death

This is not thought to be significant. The use of age-groups eliminates any potential error from this factor.

(f) Calculation of total population numbers

The computation of mortality rates involves using for the denominator census totals or estimates of the population total in non-censal years. Errors arise in making such intercensal estimates, but they are not thought to be significant for England and Wales, which has an accurate and complete system of vital registration. Thus, Cox [13] reports a 0.008% error in the estimate of the 1931 population, when compared with the census total.

Of these six potential errors, two, (b) and (c), are thought to be important for cerebrovascular disease. If the errors are constant in magnitude between years, and the subgroups of the population under consideration are homogeneous, then mortality data may furnish valuable epidemiological information. The epidemiological value of mortality statistics depends on how clearly they estimate the underlying incidence of disease in the population. The most important consideration is not whether the mortality rates tend to underestimate the actual disease frequency, but whether the differences in mortality by various population characteristics (e.g., age, sex, race) tend to reflect similar differences in the frequency of the disease.

Despite the limitations listed above, the analysis of mortality statistics provides for many purposes an inexpensive and convenient means of obtaining clues to aetiological hypotheses, determining consistency between hypotheses and indicating the frequency of specific diseases in the population [9].

With this justification, many studies have used mortality statistics as a means of approaching the epidemiology of cerebrovascular diseases in England and Wales, US and elsewhere [5,8,14–24]. We propose to apply such an analysis to the statistics for a recent period for England and Wales.

## Results

Under the latest revision of the International Cause of Death Classification deaths from cerebrovascular disease are assigned to rubrics 430–438. Each rubric in this group corresponds to a different diagnostic type of cerebrovascular disease. Table I shows the frequency distribution of deaths from cerebrovascular disease between these diagnostic types for 1974 and 1975 [3]; the figures have been rounded to the nearest integer. It is clear that certifying physicians allocate about 50% of cerebrovascular disease deaths to cerebral haemorrhage and cerebral thrombosis, and about 40% to the ill-defined rubrics 436, 437 and 438. Cerebral embolism and transient cerebral ischaemia are rarely used as a cause of death. In view of this concentration of the numbers of deaths and the statistical unreliability