Intracerebral Hemorrhage

Edited by

J. R. Carhuapoma
Johns Hopkins University Hospital, Baltimore, MD, USA

S. A. Mayer
Columbia University Medical Center, New York, NY, USA

D. F. Hanley
Johns Hopkins University Hospital, Baltimore, MD, USA
To my son Ethan and my family for their unconditional support JRC
To Catherine, Philip and Elizabeth SAM
To my wife and family who have supported my career DFH
# Contents

[List of contributors] ix

*Foreword by Thomas Brott* xii

## Section 1 – Epidemiology

1. **The epidemiology of intracerebral hemorrhage** 1  
Matthew L. Flaherty, Daniel Woo, and Joseph P. Broderick

## Section 2 – Etiology of non-traumatic intracerebral hemorrhage

2. **Acute hypertensive response in intracerebral hemorrhage** 17  
Ameer E. Hassan, Haralabos Zacharatos, and Adnan I. Qureshi

3. **Etiology of tumor-related intracranial hemorrhage** 31  
Andreas F. Hottinger and Lisa M. DeAngelis

4. **Cerebral amyloid angiopathy** 41  
Steven M. Greenberg

5. **Coagulopathy-related intracerebral hemorrhage** 58  
Hagen B. Huttner and Thorsten Steiner

6. **Vascular malformations of the brain** 71  
Christian Stapf and J. P. Mohr

7. **Cerebral venous thrombosis and intracerebral hemorrhage** 84  
Isabelle Crassard and Marie-Germaine Bousser

## Section 3 – Clinical presentation

8. **Clinical presentation of intracerebral hemorrhage** 101  
Carlos S. Kase

## Section 4 – Diagnostic investigations

9. **Computerized tomography and CT angiography in intracerebral hemorrhage** 121  
Rush H. Chewning and Kieran P. Murphy

10. **MRI of intracerebral hemorrhage** 125  
Ken Butcher and Stephen M. Davis

11. **Cerebral angiography** 139  
Rush H. Chewning and Kieran P. Murphy

12. **Laboratory and other ancillary testing in intracerebral hemorrhage: an algorithmic approach** 149  
Michael Chen and Louis R. Caplan

## Section 5 – Management and critical care

13. **Medical management of intracerebral hemorrhage** 159  
Neeraj S. Naval, Paul A. Nyquist, and J. Ricardo Carhuapoma

14. **Surgical management of intracerebral hemorrhage** 165  
A. David Mendelow

15. **Future therapy in intracerebral hemorrhage and intraventricular hemorrhage: aspiration and thrombolysis** 176  
Paul A. Nyquist, Neeraj S. Naval, and J. Ricardo Carhuapoma
### Contents

**Section 6 – Prognosis and outcome**

16. **Mathematical models of intracerebral hemorrhage and intraventricular hemorrhage outcomes prediction: their comparison, advantages, and limitations** 187  
   Stanley Tuhrim

**Section 7 – Advances in pathogenesis and treatment of intracerebral hemorrhage: experimental**

17. **Animal models and experimental treatments of intracerebral hemorrhage** 193  
   Kenneth R. Wagner and Mario Zuccarello

18. **Thrombin and secondary brain damage following intracerebral hemorrhage** 206  
   Guohua Xi, Richard F. Keep, and Julian T. Hoff

19. **Cytoprotection strategies for experimental intracerebral hemorrhage** 217  
   Crystal MacLellan, James Peeling, and Frederick Colbourne

**Section 8 – Advances in pathogenesis and treatment of intracerebral hemorrhage: clinical**

20. **Natural history of perihematomal brain edema** 229  
   Manuel Rodríguez-Yáñez, Antoni Dávalos, and José Castillo

21. **Hemostatic therapy for intracerebral hemorrhage** 238  
   Wendy C. Ziai and Stephan A. Mayer

*Index* 254

*Color plate section between pp. 158 and 159.*
Contributors

Marie-Germaine Bousser MD
Department of Neurology,
Lariboisière Hospital, Paris, France

Joseph P. Broderick MD
Department of Neurology,
University of Cincinnati,
Cincinnati, OH, USA

Ken Butcher MD PhD FRCPC
Division of Neurology,
University of Alberta,
Edmonton, Alberta, Canada

Louis R. Caplan MD
Department of Neurology,
Beth Israel Deaconess Medical Center,
Boston, MA, USA

J. Ricardo Carhuapoma MD FAHA
Departments of Neurology, Neurosurgery,
and Anesthesiology & Critical Care Medicine,
Division of Neurosciences Critical Care,
The Johns Hopkins Medical Institutions,
Baltimore, MD, USA

José Castillo MD PhD
Department of Neurology,
Hospital Clínico Universitario,
University of Santiago de Compostela,
Santiago de Compostela, Spain

Michael Chen MD
Departments of Neurology and Radiology,
Rush University Medical Center,
Chicago, IL, USA

Rush H. Chewning BA
Department of Radiology,
The Johns Hopkins Hospital,
Baltimore, MD, USA

Frederick Colbourne PhD
Department of Psychology,
University of Alberta, Edmonton, Alberta,
Canada

Isabelle Crassard MD
Department of Neurology,
Lariboisière Hospital, Paris, France

Antoni Dávalos MD PhD
Department of Neurosciences,
Hospital Germans Trias i Pujol,
Barcelona, Spain

Stephen M. Davis MD FRACP
Department of Neurology,
Royal Melbourne Hospital,
Melbourne, Victoria, Australia

Lisa M. DeAngelis MD
Department of Neurology,
University of Cincinnati, Cincinnati, OH, USA

Matthew L. Flaherty MD
Department of Neurology,
Memorial Sloan-Kettering Cancer Center,
New York, NY, USA

Daniel F. Hanley MD
Departments of Neurology, Neurosurgery,
and Anesthesiology & Critical Care Medicine,
Division of Brain Injury Outcomes Research,
The Johns Hopkins Hospital,
Baltimore, MD, USA

Ameer E. Hassan DO
Department of Neurology,
<table>
<thead>
<tr>
<th>List of contributors</th>
</tr>
</thead>
</table>

**University of Minnesota Medical Center, Minneapolis, MN, USA**

**Julian T. Hoff MD**  
Formerly Department of Neurosurgery, University of Michigan, Ann Arbor, MI, USA

**Andreas F. Hottinger**  
Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

**Hagen B. Huttner MD**  
Department of Neurology, University of Heidelberg, Heidelberg, Germany

**Carlos S. Kase MD**  
Department of Neurology, Boston Medical Center, Boston, MA, USA

**Richard F. Keep PhD**  
Department of Neurosurgery, University of Michigan, Ann Arbor, MI, USA

**Crystal MacLellan PhD**  
Department of Psychology, University of Alberta, Edmonton, Alberta, Canada

**Stephan A. Mayer MD**  
Department of Neurology, Columbia University Medical Center, New York, NY, USA

**A. David Mendelow PhD FRCSEd**  
Department of Neurosurgery, Newcastle General Hospital, Newcastle upon Tyne, UK

**J. P. Mohr MD PhD**  
Department of Neurology, Columbia University Medical Center, New York, NY, USA

**Kieran P. Murphy MD**  
Department of Radiology, The Johns Hopkins Hospital, Baltimore, MD, USA

**Neeraj S. Naval MD**  
Department of Neurology, Neurosurgery, and Anesthesiology Critical Care Medicine, Neurosciences Critical Care Division, Oregon Health Sciences University School of Medicine, Oregon, USA

**Paul A. Nyquist MD**  
Department of Neurology, Neurosurgery, and Anesthesiology & Critical Care Medicine, Division of Neurosciences Critical Care, Johns Hopkins Medical Institutions, Baltimore, MD, USA

**James Peeling PhD**  
Department of Chemistry, University of Manitoba, Winnipeg, Manitoba, Canada

**Adnan I. Qureshi MD**  
Department of Neurology, University of Minnesota Medical Center, Minneapolis, MN, USA

**Manuel Rodriguez-Yáñez MD**  
Department of Neurology, Hospital Clínico Universitario, University of Santiago de Compostela, Santiago de Compostela, Spain

**Christian Stapf MD**  
Department of Neurology, Lariboisière Hospital, Paris, France

**Thorsten Steiner MD**  
Department of Neurology, University of Heidelberg, Heidelberg, Germany

**Stanley Tuhrim MD**  
Department of Neurology, Mt Sinai Medical Center, New York, NY, USA

**Kenneth R. Wagner PhD**  
Department of Neurology, University of Cincinnati, Cincinnati, OH, USA

**Daniel Woo MD**  
Department of Neurology, University of Cincinnati, Cincinnati, OH, USA
List of contributors

Guohua Xi MD
Department of Neurosurgery,
University of Michigan,
Ann Arbor, MI, USA

Haralabos Zacharatos DO
Department of Neurology,
University of Minnesota Medical Center,
Minneapolis, MN, USA

Wendy C. Ziai MD
Department of Neurology,
The Johns Hopkins Hospital,
Baltimore, MD, USA

Mario Zuccarello MD
Department of Neurology,
University of Cincinnati, Cincinnati,
OH, USA
Foreword

Intracerebral Hemorrhage is the first major text devoted to non-traumatic intracerebral hemorrhage (ICH) to appear in almost 20 years. The 21 chapters detail a generation of progress since the introduction of brain computerized tomography (CT) in 1973. At that time, and for the first time, the phenotype of non-traumatic ICH could be clarified. The Polaroid-print images of ICH pasted into patient medical records were understandable in all languages. The distinction between ICH and territorial cerebral infarction was no longer fuzzy, to await the final verdict at the autopsy table. Testable hypotheses replaced speculation.

During the next two decades, faster and more accurate CT scanning and then magnetic resonance imaging (MRI) allowed rigorous clinical-radiographic studies (Chapters 8–10). Publications related to ICH sky-rocketed in number. In 1991, the National Institutes of Health funded the first investigator-initiated R01 research grant to study ICH in emergency departments. The US federal funding of additional studies of ICH surged. Worldwide, CT-based clinical studies described the dynamic profile of ICH. The pivotal role of ICH volume growth in clinical deterioration during the first minutes and hours after symptom onset was established. In parallel with the studies of ICH in the emergency department setting, experimental (Chapters 17, 18) and clinical studies proceeded (Chapters 1–8). Subtypes of ICH were identified with greater precision, facilitating epidemiological studies, mechanistic experimental studies, and, more recently, genetic studies by subtype.

Outcomes research has clearly shown that survival and recovery after ICH is improved when patients are cared for in specialized neurological intensive care units, with a focus on aggressive medical support and best medical practices. The search for a “magic bullet” has been more elusive. In 1995, recombinant tissue plasminogen activator (rt-PA) was shown to be safe and effective as treatment for ischemic stroke, if administered intravenously within 3 hours of symptom onset. Medical centers engaged in administration of rt-PA as urgent treatment geared-up for a similar emergency approach to ICH. Complex multi-departmental systems for urgent patient transport, diagnosis, and treatment were already in place at these centers. Active bleeding during the first minutes and hours after ICH onset provides a logical therapeutic target. The 40%-plus major morbidity and mortality following ICH has provided opportunity for firm clinical end points to evaluate treatment outcomes. Accordingly, attempts at very early surgery via craniotomy or endoscopic techniques were initiated (Section 5). Thrombolytic agents including instillation of rt-PA were utilized in several trials. Unfortunately, these attempts at treatment within 3–12 hours suffered from slow enrollment and from disappointing therapeutic results. Surgical evacuation of ICH within 90 minutes, or even 3 hours, was not an achievable goal, and complete surgical evacuation has been difficult to achieve. Fortunately, encouraging technical results were observed following catheter-based techniques for clot removal in the setting of intraventricular hemorrhage, particularly when employed in combination with locally instilled thrombolytic drugs. Controlled studies of these techniques for parenchymal and intraventricular hemorrhage are currently underway (Chapter 15).

In 2005, the long-awaited results of the International Surgical Trial in Intracerebral Haemorrhage (STICH) were published, the results of which are discussed in Chapter 14 by the principal investigator, David Mendelow. The STICH trial was a major accomplishment as 1033 patients were randomized at 83 centers from 27 countries. Overall, the operated patients did not benefit, though subgroup analysis suggested that early surgery may improve outcomes for patients with lobar ICH. The STICH II trial, designed to answer that question, is also described by Dr. Mendelow in Chapter 14.
Medical treatments for ICH are detailed in Sections 5, 6, and 7. General supportive treatments in intensive care units and rehabilitation treatments in dedicated units have improved outcomes. For specific medical treatment, ongoing bleeding following onset of ICH is the logical target for intervention. Optimal management of blood pressure, and perhaps even acute lowering of blood pressure, may be shown to influence outcome (Chapter 13). Of particular interest, the recent randomized trials of procoagulant therapy have shown promise in slowing bleeding (Chapter 21). Both the phase II and phase III studies of recombinant factor VIIa as very early treatment for ICH demonstrated lower ICH volumes in the actively treated patients compared to those treated with placebo. Clinical outcomes were improved in the phase II trial but not in the phase III trial. In the future, initiation of procoagulant treatment even earlier and with improved patient selection may be shown to enhance clinical outcomes after ICH.

Perhaps most importantly, the biggest transformation over the past 20 years has been widespread acceptance of the concept that ICH is a treatable medical illness. Historically ICH was viewed as a hopeless, life-negating event for which caregivers had nothing to offer other than prayers and compassion. What has become dramatically clear, however, is that many ICH patients die as a result of self-fulfilling prophecies of doom. As caregivers have been more aggressive with their interventions and persistent with their support, the biggest surprise has been how often functional recovery far exceeds what we once thought was possible. This is the key insight that has served as the ultimate motivation for the contributors to this book, who have devoted their careers to finding effective treatments for this devastating disease.

Thomas Brott, MD
Mayo Clinic
Jacksonville, FL