STATUS EPILEPTICUS
Practical Guidelines in Management
Dedication

This monograph, if one can call it a book, is the combined effort of several selfless, luminescent souls—my colleagues, my teachers, my students—who, through words and deeds, held my hand while working on this not too lucrative task. Through thick and thin, amidst all adversities, they stood with me, and supported me unflinchingly when I was about to lose my stance during the last few years. This is a humble endeavor, which took its shape as a memoir to the hundreds of thousands of persons whom we ceremoniously address as ‘patients,’ who drifted to another world on getting ‘seized’ continuously; among them were those who found another abode, perhaps a better one, and those many who came back to life to their near and dear ones after a long slumber.

I dedicate this effort to my father, Late Sri Radhakrishnan, who taught me everything; whose steadfast guidance and unwavering support in my formative years made me what I am, given all my likes and dislikes and, indeed, my whole persona, which bears glimpses of him still. Also, to my mother, Dr Thankom, who is always with me, a shadow merging into mine, with her enduring patience, stoicism and never-ending sacrifice that nurtured me to be a natural woman, who would readily lend a patient ear to others; I salute this mother who never insisted on or prescribed for me what I should do each day—a living example who taught me what life is, fostered me, and proved before my eyes how a woman can be silent and uncomplaining, and yet be independent and strong.

Also, a few people come into one’s life and create a lasting impression, which they themselves are quite oblivious of. One such great researcher, teacher and clinician, and above all, a compassionate human being whom I had the good fortune to know, is Professor Daniel H Lowenstein, whom I listened to as a student during my epilepsy training days in 2007, in Marysville, Melbourne, with my eyes wide-open and verily mesmerized. Later, I heard his hour-long oration named ‘The Last Lecture’, which surpassed Randy Pausch himself. His anecdotes and the lecture made me realize the real qualities of a teacher, who is a mentor besides. It changed my whole perception of life. I believe I reconstructed myself. He will positively remain a great influence and, I am sure, not only to me, but the likes of me and many others, in the years to come. I dedicate this endeavor to this doyen of epileptology, who often quotes Mahatma Gandhi’s words— “Live as if you were to die tomorrow; learn as if you were to live forever”.

These last lines of William Wordsworth’s Immortality Ode, are my motto:

Thanks to the human heart by which we live,
Thanks to its tenderness, its joys, and fears,
To me the meanest flower that blows can give
Thoughts that do often lie too deep for tears.
Contributors

Ashalatha Radhakrishnan  
Consultant Neurologist and Epileptologist  
R. Madhavan Nayar Center for Comprehensive Epilepsy Care  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Deepak Menon  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Gopalkrishna Dash  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Narayana Hrudayalaya Multispeciality Hospital  
Bengaluru, Karnataka, India

Haseeb Hassan  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Narayana Health (Rabindranath Tagore International Institute of Cardiac Sciences)  
Kolkata, West Bengal, India

Joseph Samuel P  
Consultant Neurologist  
R. Madhavan Nayar Center for Comprehensive Epilepsy Care  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Keni Ravish Rajiv  
Senior Resident  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Malcolm Jeyaraj K  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Stanley Medical College  
Chennai, Tamil Nadu, India

Pradeep P Nair  
Consultant Neurologist and Epileptologist  
Department of Neurology  
JIPMER  
Puducherry, India

Pramod Krishnan  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Manipal Hospital  
Bengaluru, Karnataka, India

Ragavendra S  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Vikram Hospital  
Bengaluru, Karnataka, India

Rajesh B Iyer  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Vikram Hospital  
Bengaluru, Karnataka, India

Ramshekar N Menon  
Consultant Neurologist and Epileptologist  
R. Madhavan Nayar Center for Comprehensive Epilepsy Care  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Sai Satish  
Consultant Neurologist and Post-doctoral Fellow in Epilepsy  
R. Madhavan Nayar Center for Comprehensive Epilepsy Care  
Department of Neurology  
Sree Chitra Tirunal Institute for Medical Sciences and Technology  
Thiruvananthapuram, Kerala, India

Shiva Kumar R  
Consultant Neurologist and Epileptologist  
Department of Neurology  
Sakra World Hospital  
Bengaluru, Karnataka, India
Foreword

The definition, diagnosis and management of status epilepticus have changed and advanced substantially over the past decade. Given that seizure disorders are very common, the recognition and management of status epilepticus has become a challenge over the past few years, especially with the advent of sophisticated neuroimaging techniques and diagnostic tests.

Dr Ashalatha Radhakrishnan, in this book on Status Epilepticus, has successfully brought out a very practical and systematic approach to the complexity inherent to the therapeutic armamentarium available to this syndrome. It is extremely well-rooted in the medical literature and conveys, what I think, is the ‘state-of-the-art’ in the care of the patients suffering from this condition.

The book contains 10 chapters and management protocols, contributed by 14 authors. Chapter 1 lucidly describes the progressive evolution of definition of status epilepticus, especially with reference to the time or duration. Chapters 2 to 5 touch open prehospital management, investigations, monitoring protocols and management guidelines in status epilepticus. Chapter 6 describes about anesthetic agents in status epilepticus. Chapter 7, on refractory and super-refractory status epilepticus, describes current approaches to treatment and reviews various aspects of prognosis. Chapters 9 and 10 on the ‘role of newer drugs’, and ‘altering the management strategies in persons with other comorbidities’ are also well compiled. Chapter 10, on nonconvulsive status epilepticus, needs special mention, since the author has supplemented the EEG tracings to it, for crispness and clarity. The book is capped at the end by the editor herself with a detailed but simplified algorithm, for diagnosing and managing status epilepticus.

This monograph would be a welcome addition to any medical/surgical intensive care unit or neurocritical care unit. Dr Ashalatha Radhakrishnan and her colleagues, need to be congratulated for bringing out this superb contribution to the medical literature; it will serve as a valuable reference manual in the lab coat of the trainees (and their teachers!) who care for patients with neurological disease for years to come.

Daniel H Lowenstein  MD
Executive Vice Chancellor and Provost
Dr Robert B and Mrs Ellinor Aird Professor of Neurology
University of California
San Francisco, California, USA
In order to produce the most practical and expedient modus operandi for tackling the increasingly complicated medical emergency called ‘status epilepticus’, my colleagues and I have undertaken the task of compiling and analyzing the available literature on this subject. By exploring the various facets of this neurological medical emergency, we hope to make the management of status epilepticus possible and productive to a vast majority of medical practitioners. From the various ‘definitions’ of this medical condition over the decades, and moving on to ‘prehospital management’ and ‘investigations’ leading finally to ‘signature EEGs’ and ‘management’, we have humbly attempted to produce a cartography of this condition—a map of the progress of this disorder along the medical terrain. Finally, for the ease of management in intensive care units, we have included a ‘flow chart’, and ‘protocol’, derived from evidences collated through all the chapters. We have pieced together all that we have read on this complex subject, augmented by our group discussions and brainstorming, in a simplified and comprehensive manner, a handbook is what we wanted to bring out, not a voluminous textbook. We hope that the younger professionals of posterity will be benefitted by our experience, the research we have unveiled, and its compilation.

Status epilepticus is a condition where new facets are added each day. The overused cliché ‘time is brain’ is not just a signature tune of stroke in neuroscience, but also of the shifting realities in status epilepticus, which warrants alert vigil and swift action. To miss the moment would be to miss the medical event itself! Hence, we have taken upon ourselves the task of reporting and recording the logistics of this emergency so that neither diagnosis nor therapy is out of reach of the practitioners.

Many people are on my thanks list for helping this venture crystallize. First, each of the authors on specific topics, who enriched the particular chapters with his/her experience and expertise. They deserve huge praise for taking time out of their hectic schedule to write for future diagnostic and therapeutic illumination on this subject and for coordinating scientific data to such a remarkable extent that they have enabled themselves for praise from, none other than, Professor Lowenstein, the ‘Master of Masters’ on status epilepticus. Next, my neurology trainees deserve thanks and approbation for purging the litany by framing a set of questions ’Test Yourself’, and best suited answers, at the end of each chapter. While engaging in self-brainstorming sessions, they were themselves getting enlightened in the process.

My special thanks go to my teachers, especially Professor Sanjeev V. Thomas, who remained a role model, a living example of how a teacher, a mentor and a superb human should be. He often appreciated his students even for every trivial and meagre achievement, and has always proved that a nondomineering mentor can do wonders for students and his junior colleagues, bringing the unbelievable worth out of them, specially so, in my case. I also thank Professor Abraham Kuruvilla and Professor MD Nair, who, directly and indirectly, motivated me towards my mission. My remarkable colleagues Dr Ramshekhar N Menon, Dr Raghavendra S, Dr Rajesh B Iyer, and Dr Gopalkrishna Dash, are remembered for always acknowledging my meaning and purpose in all my pursuits and giving me their share of selfless support. Last but not least, my family gets my momentous thanks for bearing with me when my being engrossed in my academic ventures took a portion off my family time.
I would like to offer a great deal of thanks to M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India, known for their fidelity to the medical fraternity, and have made this monograph a better reality than envisaged, for all their support and responsibility.

May the Almighty, who gave strength to our hands to join in this humble endeavor, illumine the path of many students of neuroscience and medicine, also show these beneficiaries of our efforts and pains, the way forward every time an unfortunate human gets ‘seized,’ so that he or she does not have to succumb prematurely and, thus, bring this handbook all its glory in its true sense!

Ashalatha Radhakrishnan
## Contents

1. Evolution of ‘Definitions’ of Status Epilepticus and Nonconvulsive Status Epilepticus  1
   Malcolm Jeyaraj K
   - History  1
   - Operational Definition  1
   - Mechanistic Definition  3
   - Nonconvulsive Status Epilepticus  3
   - Bedside Application of the Definition  4

2. Prehospital Management of Status Epilepticus  7
   Shiva Kumar R
   - “Time is Brain” in Status Epilepticus  7
   - Incidence of Seizures in the Prehospital Setting  7
   - Prehospital Diagnosis of Convulsive Status Epilepticus  8
   - Spectrum of Seizures Encountered in Prehospital Setting  8
   - Stages of Status Epilepticus  9
   - Prehospital Evaluation and Management of Status Epilepticus  10
   - Steps in Prehospital Management of Status Epilepticus  11
   - Epilepsy Identity Card  18

3. Investigations and Monitoring Protocol in Status Epilepticus  23
   Haseeb Hassan
   - Evaluation of Convulsive Status Epilepticus  23
   - Evaluation of Nonconvulsive Status Epilepticus  24
   - Role of Electroencephalography  25
   - Monitoring and General Management after Initial Control of Status Epilepticus  28

4. First-line Therapy in Status Epilepticus  32
   Keni Ravish Rajiv, Raghavendra S
   - First-line Therapy for Management of Status Epilepticus  33

5. Second-line Therapy in Status Epilepticus  39
   Pramod Krishnan
   - Phenobarbitone  40
   - Sodium Valproate  42
   - Levetiracetam  43
   - Lacosamide  44
   - Clobazam  45
   - Topiramate  45
   - Clonazepam  46

6. Anesthetic Agents in Status Epilepticus  50
   Gopalkrishna Dash
   - When to Consider Anesthetic Medications?  50
   - Anesthetic Medications  50
   - EEG Monitoring in Refractory Status Epilepticus  52
   - Choice of Anesthetic Medication  53
7. Refractory and Super-refractory Status Epilepticus
   Ramshekhar N Menon
   • Definitions 56
   • Importance of Defining Refractoriness 56
   • Epidemiology and Outcome of RSE and SRSE 57
   • New-onset Refractory Status Epilepticus 57
   • Do These Terminologies have a Pathophysiological Basis? 58
   • Clinical Presentations and Critical Insights into Management 59

8. Critical Appraisal of Alternative Therapies in Refractory and Super-refractory Status Epilepticus
   Deepak Menon, Rajesh B Iyer
   • Immunomodulatory Agents 63
   • Inhalational Anesthetic Agents 65
   • Repetitive Transcranial Magnetic Stimulation 65
   • Electroconvulsive Therapy 66
   • Emergency Surgery 66
   • Ketogenic Diet 66
   • Hypothermia 67
   • Magnesium 67
   • Pyridoxine 68
   • Calcium-channel Blockers 69

9. Status Epilepticus in Special Situations
   Pradeep P Nair
   • Management of Status Epilepticus in Elderly 72
   • Management of Status Epilepticus in Liver Diseases 73
   • Management of Status Epilepticus in Renal Diseases 74
   • Management of Status Epilepticus in Pregnant Women 75
   • Management of Poststroke Status Epilepticus 75

10 When to Suspect, How to Identify and Treat Nonconvulsive Status Epilepticus?
   Ramshekhar N Menon
   • Epidemiological Data Highlighting Importance of Recognizing Nonconvulsive Status Epilepticus 81
   • Pathophysiology and Neurological Sequelae 82
   • EEG Criteria for Diagnosis 82
   • Clinical Presentations and Classification 83
   • Management of Nonconvulsive Status Epilepticus 104

Management Protocol in Status Epilepticus–1
   Sai Satish, Joseph Samuel P

Management Protocol in Status Epilepticus–2
   Ashalatha Radhakrishnan

Index 115