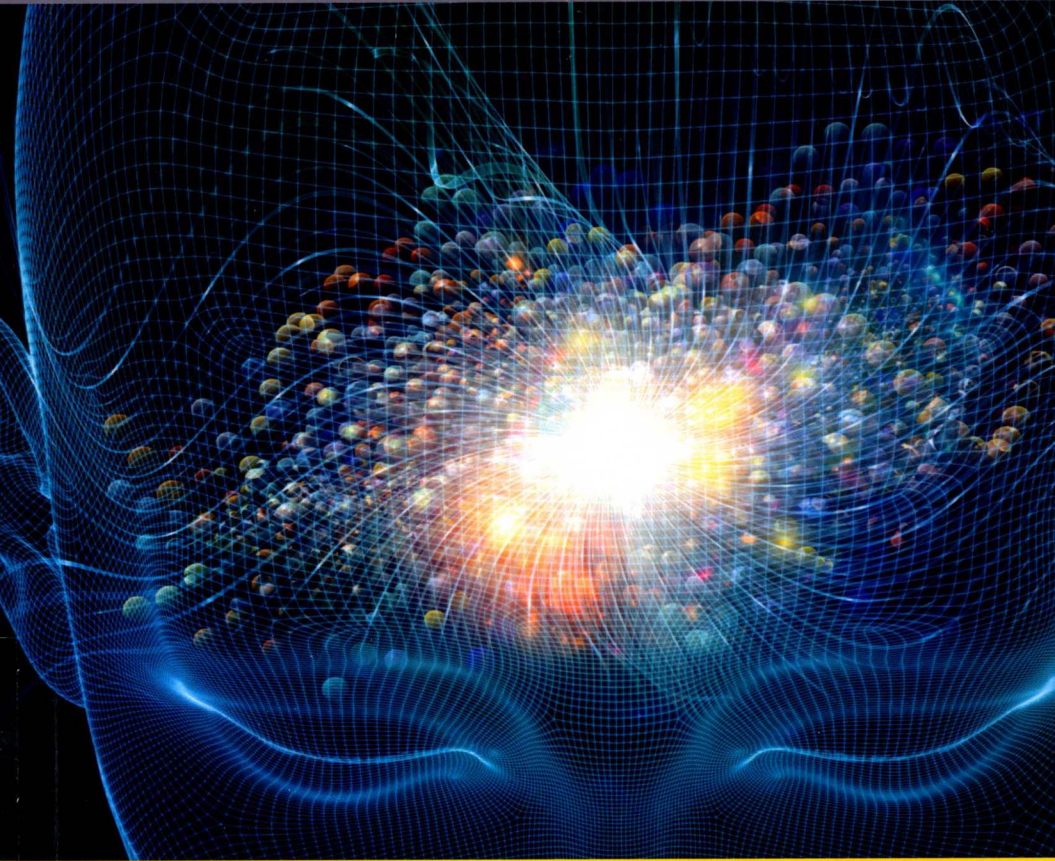


*Editor*

**S. R. Pandi-Perumal**

# Synopsis of **SLEEP MEDICINE**



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PRESS



**CRC Press**

Taylor & Francis Group

# SYNOPSIS OF SLEEP MEDICINE

*Edited by*  
**S. R. Pandi-Perumal**

**AAP** | APPLE  
ACADEMIC  
PRESS

Apple Academic Press Inc. | Apple Academic Press Inc.  
3333 Mistwell Crescent | 9 Spinnaker Way  
Oakville, ON L6L 0A2 | Waretown, NJ 08758  
Canada | USA

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*Exclusive worldwide distribution by CRC Press, a member of Taylor & Francis Group*

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Printed in the United States of America on acid-free paper

International Standard Book Number-13: 978-1-77188-346-7 (Hardcover)

International Standard Book Number-13: 978-1-77188-347-4 (eBook)

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### Library and Archives Canada Cataloguing in Publication

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Synopsis of sleep medicine / edited by S.R. Pandi-Perumal.

Includes bibliographical references and index.

Issued in print and electronic formats.

ISBN 978-1-77188-346-7 (hardcover).--ISBN 978-1-77188-347-4 (pdf)

1. Sleep disorders. 2. Sleep disorders--Diagnosis. 3. Sleep disorders--Treatment.

4. Sleep--Physiological aspects. I. Pandi-Perumal, S. R., author, editor

RC547.S95 2016

616.8'498

C2016-904679-6

C2016-904680-X

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### Library of Congress Cataloging-in-Publication Data

---

Names: Pandi-Perumal, S. R., editor.

Title: Synopsis of sleep medicine / editor, S.R. Pandi-Perumal.

Description: Toronto ; New Jersey : Apple Academic Press, 2016. | Includes bibliographical references and index.

Identifiers: LCCN 2016030185 (print) | LCCN 2016031120 (ebook) | ISBN 9781771883467 (hardcover : alk. paper) | ISBN 9781771883474 (eBook) | ISBN 9781771883474 ()

Subjects: | MESH: Sleep Wake Disorders | Sleep Disorders, Circadian Rhythm

Classification: LCC RC547 (print) | LCC RC547 (ebook) | NLM WL 108 | DDC 616.8/498--dc23

LC record available at <https://lcn.loc.gov/2016030185>

Apple Academic Press also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic format. For information about Apple Academic Press products, visit our website at [www.appleacademicpress.com](http://www.appleacademicpress.com) and the CRC Press website at [www.crcpress.com](http://www.crcpress.com)

# **SYNOPSIS OF SLEEP MEDICINE**

## ABOUT THE EDITOR

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### **S. R. Pandi-Perumal, MSc**

S. R. Pandi-Perumal is the President and Chief Executive Officer of Somnogen Canada Inc, a Canadian corporation. He holds a Master of Science from the Madurai Kamaraj University, Madurai, India. A well-recognized sleep researcher both nationally and internationally, he has authored over 100 publications in the field

of sleep and biological rhythms. His general area of research interest includes sleep and biological rhythms. He has edited nearly 25 volumes related to sleep and biological rhythms research. He had an honorable mention in the *New York Times* in 2004, and the India International Friendship Society awarded him the Bharat Gaurav Award on January 12, 2013. Further details about his academic credentials can be found at: <http://pandi-perumal.blogspot.com>.

# **Dedication**

*To my family....*

for their abundant support, for their patience and understanding, and for their everlasting love and affection.

# LIST OF CONTRIBUTORS

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## **K. L. Acosta**

University Sleep Disorders Center, College of Medicine, National Plan for Science and Technology, King Saud University, Riyadh, Saudi Arabia

## **I. M. Ahmed**

Department of Neurology, Sleep-Wake Disorders Center, Montefiore Medical Center, Albert Einstein College of Medicine, 3411 Wayne Avenue, Bronx, NY 10467, USA

## **R. G. Albuquerque**

Department of Psychobiology, Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, Vila Clementino, São Paulo, 04024-002, Brazil. E-mail: rac.albuquerque@gmail.com

## **A. Al-Harbi**

Department of Medicine, Pulmonary Division, Sleep Disorders Center, KAMC-KSUHS, Saudi Arabia. E-mail: HarbiA7@NGHA.MED.SA

## **H. Al-Jahdali**

Adjunct Professor - McGill University; Professor Pulmonary and Sleep Medicine, King Saud University for Health Sciences; Head of Pulmonary Division, Medical Director of Sleep Disorders Center, King Abdulaziz Medical City, Riyadh, PO Box 101830\*11665, Saudi Arabia. E-mail: Jahdali@yahoo.com

## **R. N. Al Ismaili**

University Sleep Disorders Center, College of Medicine, King Saud University, Riyadh, Saudi Arabia; The Strategic Technologies Program of the National Plan for Sciences and Technology and Innovation in the Kingdom of Saudi Arabia, Saudi Arabia

## **M. L. Andersen**

Department of Psychobiology, Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, Vila Clementino, São Paulo 04024-002, Brazil. E-mail: ml.andersen12@gmail.com

## **F. Armstrong**

Department of Neurology and Neuroscience, Center for Sleep Medicine, Weill Medical College of Cornell University, 525 East 68th Street, Room k-615, New York, NY 10065, USA. E-mail: armstrong.forrest@gmail.com

## **H. Attarian**

Department of Neurology, Circadian Rhythms and Sleep Research Lab, 710 N Lake Shore Drive, Suite 1111, Chicago, IL 60611, USA. E-mail: hattaria@nmff.org

## **R. Y. Baba**

Department of Neurology, Sleep-Wake Disorders Center, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, NY, USA. E-mail: rbaba@montefiore.org

## **A. S. BaHammam**

Sleep Disorders Center, College of Medicine, King Saud University, Box 225503, Riyadh 11324, Saudi Arabia. E-mail: ashammam2@gmail.com, ashammam@ksu.edu.sa

## **C. E. Bauer**

Center for Neuroscience, West Virginia University, 1 Medical Center Drive, Morgantown, WV 26505, USA. E-mail: cbauer5@mix.wvu.edu

## **G. M. Brown**

Centre for Addiction and Mental Health, University of Toronto, 100 Stokes St., Toronto, ON M6J 1H4, Canada. E-mail: gbrownpn@gmail.com

## **K. Buttoo**

601 Harwood Avenue South, Ajax, ON L1S 2J5, Canada. E-mail: kbuttoo@hotmail.com

## **D. P. Cardinali**

UCA-BIOMED-CONICET, Faculty of Medical Sciences, Pontificia Universidad Católica Argentina, 1107 Buenos Aires, Argentina. E-mail: danielcardinali@uca.edu.ar, danielcardinali@fibertel.com.ar

## **G. Copinschi**

Department of Endocrinology, Université Libre de Bruxelles, Brussels, Belgium. Formerly Chief, Division of Endocrinology, Hôpital Universitaire Saint-Pierre, Université Libre de Bruxelles, Brussels, Belgium. Formerly Chairman, Department of Medicine, Hôpital Universitaire Saint-Pierre, Université Libre de Bruxelles, Brussels, Belgium. E-mail: gcop@ulb.ac.be



**M. R. Ebben**

Department of Neurology and Neuroscience, Center for Sleep Medicine, Weill Medical College of Cornell University, 525 East 68th Street, Room k-615, New York, NY 10065, USA.

E-mail: Mae2001@med.cornell.edu

**S. H. Feinsilver**

Department of Medicine, Icahn School of Medicine at Mount Sinai, Division of Pulmonary, Critical Care and Sleep Medicine, 1 Gustave Levy Place, New York, NY 10029, USA.

E-mail: steven.feinsilver@mssm.edu

**D. E. Gacuan**

University Sleep Disorders Center, College of Medicine, National Plan for Science and Technology, King Saud University, Riyadh, Saudi Arabia

**S. George**

University Sleep Disorders Center, College of Medicine, National Plan for Science and Technology, King Saud University, Riyadh, Saudi Arabia

**C. Guilleminault**

Stanford Sleep Medicine Center, 450 Broadway St Pavilion C 2nd Fl MC 5704, Redwood City, CA94063, USA.

E-mail: cguil@stanford.edu

**R. Gupta**

Department of Psychiatry & Sleep Clinic, Himalayan Institute of Medical Sciences, Swami Ram Nagar, Doiwala, Dehradun, India. E-mail: sleepdoc.ravi@gmail.com

**S. F. Harris**

Department of Neurology, Sleep-Wake Disorders Center, Montefiore Medical Center, Albert Einstein College of Medicine, 3411 Wayne Avenue, Bronx, NY 10467, USA.

E-mail: slharris@montefiore.org

**A. B. Hernandez**

Department of Medicine, Icahn School of Medicine at Mount Sinai, Division of Pulmonary, Critical Care and Sleep Medicine, 1 Gustave Levy Place, New York, NY 10029, USA.

E-mail: adam.hernandez@mountsinai.org

**C. Hirotsu**

Department of Psychobiology, Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, Vila Clementino, São Paulo, 04024-002, Brazil. E-mail: milahirotsu@gmail.com

**A. Ivanenko**

Division of Child and Adolescent Psychiatry, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA. E-mail: aivanenko@sbcglobal.net

**L. R. Pinto Junior**

Department of Neurology and Sleep Medicine, Brazilian Academy of Neurology, Universidade Federal de São Paulo, Hospital Alemão Oswaldo Cruz, São Paulo (SP), Brazil. E-mail: lucianoribeiro48@gmail.com

**M. Khan**

Davison of Pulmonary, KAMC-KSUHS, Saudi Arabia. E-mail: iyazkhan@aol.com

**L. J. Kim**

Departamento de Psicobiologia, Universidade Federal de São Paulo

Rua Napoleão de Barros, 925, Vila Clementino, São Paulo, 04024-002, Brazil. E-mail: lenisekim@gmail.com

**M. H. Lader**

Department of Clinical Psychopharmacology, Institute of Psychiatry, King's College, London SE5 8AF, UK. E-mail: malcolm.lader@kcl.ac.uk

**A. Martin**

Universidade Federal do Rio Grande do Sul, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos, 2350, Porto Alegre, Brazil. E-mail: adriimartin@gmail.com

**E. Medina-Ferret**

EUTM, Hospital de Clínicas, Montevideo, Uruguay. E-mail: emedinaferret@gmail.com

**T. Mollayeva**

Toronto Rehabilitation Institute-University Health Network, 550 University Avenue, Rm 11120, Toronto, Ontario M5G 2A2, Canada. E-mail: tatyana.mollayeva@utoronto.ca

**H. E. Montgomery-Downs**

Department of Psychology, West Virginia University, Morgantown, WV, USA. E-mail: Hawley.Montgomery-Downs@mail.wvu.edu

**J. M. Monti**

Department of Pharmacology and Therapeutics, Department of Physiology, School of Medicine, Universidad de la República, Montevideo, Uruguay. E-mail: jmonti@mednet.org.uy

**D. N. Neubauer**

Department of Psychiatry and Behavioral Sciences, Johns Hopkins Bayview Medical Center, 4940 Eastern Avenue, Box # 151, Baltimore, MD 21120, USA. E-mail: neubauer@jhmi.edu

**J. F. Pagel**

Department of Family Practice, University of Colorado School of Medicine, Pueblo, CO, USA; Sleep Disorders Center of Southern Colorado affiliated with Parkview



Neurological Institute, Pueblo, CO, USA. E-mail: pueo34@juno.com

### **J. Palermo-Neto**

Neuroimmunomodulation Research Group, Department of Pathology, School of Veterinary Medicine, University of Sao Paulo (USP), Sao Paulo, Brazil. E-mail: jpalremo@usp.br

### **S. R. Pandi-Perumal**

Somnogen Canada Inc, College Street, Toronto, ON M6H 1C5, Canada. E-mail: pandiperumal2015@gmail.com

### **Marisa Pedemonte**

Facultad de Medicina CLAEH, Punta del Este, Uruguay. E-mail: marisa.pedemonte@gmail.com

### **S. O. Qasrawi**

University Sleep Disorders Center, College of Medicine, King Saud University, Riyadh, Saudi Arabia; The Strategic Technologies Program of the National Plan for Sciences and Technology and Innovation in the Kingdom of Saudi Arabia, Saudi Arabia

### **A. F. B. Rêgo**

Neurology and Sleep Medicine, Brazilian Academy of Neurology, Universidade Federal Do Estado do Rio de Janeiro, Carlos Bacelar Clinic, Rio de Janeiro (RJ), Brazil. E-mail: andreabacelar@uol.com.br

### **T. Rogula**

Bariatric and Metabolic Institute, Cleveland Clinic, 9500 Euclid Ave, M66-06, Cleveland, OH 44118, USA. E-mail: tomrogula@gmail.com

### **M. M. Schade**

Department of Psychology, West Virginia University, Morgantown, WV, USA. E-mail: mmgray@mix.wvu.edu

### **P. R. Schauer**

Bariatric and Metabolic Institute, Cleveland Clinic, 9500 Euclid Ave, M66-06, Cleveland, OH 44118, USA. E-mail: schauerp@ccf.org

### **L. Scrima**

Sleep Expert Consultants, LLC, 15011 E Arkansas Dr, Ste. B, Aurora CO 80012, USA. E-mail: scrimasleepdoc@msn.com

### **C. M. Shapiro**

Toronto Western Hospital, 399 Bathurst Street, Rm 7MP421, Toronto, Ontario M5T 2S8, Canada. E-mail: colinshapiro@rogers.com

### **N. Sherbini**

Head of Ethical Research Committee, Medina Region, Certified from Harvard Medical School in Practice of

Clinical Research; Department of Medicine, Pulmonary Division, Sleep Disorders Center, King Saud University for Health Sciences, Riyadh, Saudi Arabia. E-mail: drna-hed@yahoo.com

### **T. J. Swick**

American Academy of Neurology, Fellow, American Academy of Sleep Medicine; Department of Neurology, University of Texas Health Sciences Center-Houston; School of Medicine, and Medical Director: 1. Neurology and Sleep Medicine Consultants; 2. North Cypress Medical Center Sleep Disorders Center; 3. Apnix Sleep Diagnostics Laboratories, Neurology and Sleep Medicine Consultants, 7500 San Felipe, Ste. 525, Houston, TX 77063, USA. E-mail: tswick@houstonleepcenter.com

### **M. J. Thorpy**

Sleep-Wake Disorders Center, Montefiore Medical Center, Albert Einstein College of Medicine, 111 East 210th Street, Bronx, NY 10467, USA. E-mail: michael.thorpy@einstein.yu.edu, thorpy@aecom.yu.edu

### **P. Torterolo**

Departamento de Fisiología, Facultad de Medicina, Universidad de la República, General Flores 2125, 11800 Montevideo, Uruguay

### **I. Trosman**

Sleep Medicine Center, Division of Pulmonary Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago IL, USA. E-mail: itrosman@yahoo.com

### **S. Tufik**

Department of Psychobiology, Universidade Federal de São Paulo, Rua Napoleão de Barros, 925, Vila Clementino, São Paulo, 04024-002, Brazil. E-mail: sergio.tufik@unifesp.br

### **R. A. Velluti**

Centro de Medicina del Sueño, Facultad de Medicina CLAEH, Punta del Este, Uruguay. E-mail: ricardo.velluti@gmail.com

### **C. N. Warren**

Department of Psychology, West Virginia University, Morgantown, WV, USA. E-mail: cnwarren@mix.wvu.edu

### **A. Zager**

Neuroimmunomodulation Research Group, Department of Pathology, School of Veterinary Medicine, University of Sao Paulo (USP), Sao Paulo, Brazil. E-mail: adrianozager@gmail.com

# LIST OF ABBREVIATIONS

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AANAT	Arylalkylamine N-acetyl-transferase	APC	Antigen presenting cells
AAP	American Academy of Pediatrics	APPLES	Apnea positive pressure long-term efficacy study
AASM	American Academy of Sleep Medicine	AR	Allergic rhinitis
AB	Awake bruxism	ArI	Arousal index
ABG	Arterial blood gases	ASP	Advance sleep phase
AC	Alternate current	ASPD	Advance sleep phase disorder
ACTH	Adrenocorticotrophic hormone	ASPS	Advanced sleep phase syndrome
AD	Alzheimer's disease	ASV	Adaptive servo-ventilation
ADA	Americans with disabilities	ASWPD	Advanced sleep-wake phase disorder
ADCADN	Autosomal dominant cerebellar ataxia, deafness, and narcolepsy	AVAPS	Average volume-assured pressure-support
ADHD	Attention deficit hyperactivity disorder	A $\beta$	Amyloid-beta
ADNOD	Autosomal dominant narcolepsy, obesity, and type 2 diabetes	BAC	Blood alcohol concentration
AEs	Adverse experiences	BAEP	Brainstem auditory evoked potentials
AHI	Apnea-hypopnea index	BMI	Body mass index
AI	Apnea index	BPAP	Bi-level positive airway pressure
ALMA	Alternating leg muscle activation	BSMI	Benign sleep myoclonus of infancy
AMP	Adenosine monophosphate-activated protein	BZD	Benzodiazepines
AMPK	Adenosine monophosphate-activated protein kinase	BZRAs	Benzodiazepine receptor agonists
AN	Autonomic nervous	C4-M1	Central-mastoid1
APA	American Psychiatric Association	CAs	Confusional arousals
APAP	Auto-titrating positive airway pressure	CBT	Cognitive behavioral therapy
		CBT-I	Cognitive behavioral therapy for insomnia
		CCGs	Clock-controlled genes
		CD4+	Cluster of differentiation 4

CDC	Centers for Disease Control and Prevention	DHEA	Dehydroepiandrosterone
CH	Chloral hydrate	DISE	Drug-induced sleep endoscopy
CKD	Chronic kidney disease	DLB	Dementia with Lewy bodies
CKId	Casein kinase I delta	DLMO	Dim light melatonin onset
CKIe	Casein kinase I epsilon	DNA	Deoxyribonucleic acid
CNS	Central nervous system	DORA	Dual orexin (hypocretin) receptor antagonist
COPD	Chronic obstructive pulmonary disease	DRN	Dorsal raphe nucleus
CPAP	Continuous positive airway pressure	DSM-5	Diagnostic and statistical manual of mental disorders, 5th edition
CPS	Cycles per second	DSPS	Delayed sleep phase syndrome
CPSC	Consumer product safety commission	DSWPD	Delayed sleep-wake phase disorder
CRH	Corticotropin-releasing hormone	DZ	Dizygotic
CRSD	Circadian rhythm sleep disorder	ECG	Electrocardiography
CRSWD	Circadian rhythm sleep-wake disorders	ECG	Electrocardiogram
Cry1	Cryptochrome 1	EDS	Excessive daytime sleepiness
CSA	Central sleep apnea	EEG	Electroencephalogram
CSAHS	Central sleep apnea-hypopnea syndrome	EEG	Electroencephalography
CSAS	Central sleep apnea syndromes	EFM	Excessive fragmentary myoclonus
CSB	Cheyne-Stokes breathing	EFNS	European Federation of Neurological Societies
CSBS	Cheyne-Stokes breathing syndrome	EHS	Exploding head syndrome
CSF	Cerebrospinal fluid	EMA	European Medicines Agency
CSF	Colony-stimulating factor	EMG	Electromyography
CSNK-I	Casein kinase-I	EMG	Electromyogram
CSR	Cheyne-Stokes respiration	EOG	Electrooculogram
CT	Computed tomography	EOG	Electrooculography
DA	Disorders of arousal	EPAP	Expiratory positive airway pressure
DA	Dopamine	ESS	Epworth sleepiness scale
DAT	Dopamine transporter	E <sub>T</sub> CO <sub>2</sub>	End-tidal CO <sub>2</sub>
DC	Direct current	F4-M1	Frontal4-Mastoid1
DEA	Drug Enforcement Agency		
DEB	Dream-enactment behavior		

FDA	Food and Drug Administration	HPA	Hypothalamus-pituitary-adrenal
FFT	Fast Fourier transformation	hPer2	Human Period2
fMRI	Functional MRI	HRQL	Health-related quality of life
FP	Follicular phase	HRT	Hormone replacement therapy
FRC	Functional residual capacity	HTL	Hypothalamus
FSH	Follicle-stimulating hormone	Hz	Hertz
GABA	Gamma-amino butyric acid	ICAM	Intercellular adhesion molecule
GAD	Generalized anxiety disorder	ICD	International classification of diseases
G-CSF	Granulocyte colony-stimulating factor	ICSD	International classification of sleep disorders
GDM	Gestational diabetes mellitus	ICSD-3	International classification of sleep disorders, 3rd edition
GERD	Gastroesophageal reflux disorder	ICV	Intracerebroventricular
GH	Growth hormone	IDO	Indoleamine 2, 3-dioxygenase
GHB	Gamma-hydroxybutyrate	IFN	Interferon
GHRH	GH-releasing hormone	IH	Idiopathic hypersomnia
GHT	Geniculo-thalamic tract	IL	Interleukin
GI	Gastrointestinal	IL-1 $\beta$	Interleukin-1 beta
GINA	Global initiative for asthma	IPAP	Inspiratory positive airway pressure
GPCR	G protein-coupled receptors	IRT	Imagery rehearsal therapy
gRLS	Gestational restless leg syndrome	ISR	Intensive sleep retraining
H1N1	Hemagglutinin Type 1 and Neuraminidase Type 1	ISWR	Irregular sleep-wake rhythm
HAV	Hepatitis A vaccination	ISWRD	Irregular sleep-wake rhythm disorder
Hcrt	Hypocretin	IUGR	Intrauterine growth retardation
HDL	High-density lipoprotein	KLS	Kleine-Levin syndrome
HEENT	Head, eyes, ears, nose, and throat	LAEP	Late auditory evoked potentials
HF	Heart failure	LAUP	Laser-assisted uvulopalatoplasty
HFF	High frequency filter	LBW	Low birth weight
HFT	Hypnagogic foot tremor		
HIOMT	Hydroxyindole-O-methyltransferase		
HIV	Human immunodeficiency virus		
HLA	Human leukocyte antigen		

LC	Locus ceruleus	MWT	Maintenance of wakefulness test
LC-AN	Locus ceruleus autonomic nervous	MZ	Monozygotic
LD	Light-dark	NA	Nucleus of the amygdale
LDL	Low-density lipoprotein	NADP	Nicotinamide adenine dinucleotide phosphate
LDT-PPT	Laterodorsal and pedunculopontine tegmental nucleus	NADPH	Nicotinamide adenine dinucleotide phosphate
LFF	Low frequency filter	NASD	Non-apnea sleep disorders
LGN	Lateral geniculate nucleus	NES	Night eating syndrome
LH	Luteinizing hormone	NIH	National Institutes of Health
LM	Leg movement	NK	Natural killer
LP	Luteal phase	NOS	Not otherwise specified
LPS	Lipopolysaccharide	NREM	Non rapid eye movement
LSAT	Lowest oxygen desaturation indices	NSF	National Sleep Foundation
μV	Microvolt	NTSB	National Transportation Safety Board
MADs	Mandibular advancement devices	O2-M1	Occipital-mastoid1
MAO-B	Monoamine oxidase type B	OA	Oral appliances
MAOIs	Monoamine oxidase inhibitors	OCD	Obsessive-compulsive disorder
MBSR	Mindfulness-based stress reduction	OCST	Out-of-center sleep testing
MCH	Melanin-concentrating hormone	ODI	Oxygen desaturation index
MCI	Mild cognitive impairment	OHS	Obesity hypoventilation syndrome
MCP-1	Monocyte chemoattractant protein-1	OR	Odds ratio
MEG	Magnetoencephalography	OSA	Obstructive sleep apnea
MES-amphetamine	Mixed salts/mixed enantiomers amphetamine	OSAHS	Obstructive sleep apnea-hypopnea syndrome
MHC	Major histocompatibility	OTC	Over-the-counter
MMA	Maxillomandibular advancement	PaCO <sub>2</sub>	Pressure of carbon dioxide
MRI	Magnetic resonance imaging	PAP	Positive airway pressure
MS	Multiple sclerosis	PAS	p-aminosalicylic acid
MSA	Multiple-system atrophy	PCOS	Polycystic ovarian syndrome
MSLT	Multiple sleep latency test	PD	Parkinson's disease
MT <sub>1</sub>	Melatonin receptor1	PD	Panic disorder
		PDR	Posterior dominant rhythm
		PDSS	Parkinson's disease sleep scale

PET	Positron emission tomography	REMS	Risk evaluation and mitigation strategy
PFT	Pulmonary function tests	REMw/oA	REM sleep without atonia
PGO	Ponto-geniculo-occipital	RERAs	Respiratory effort-related arousals
PHOX2B	Paired like homeobox 2b	RF	Reticular formation
PLM	Periodic leg movement	RFA	Radiofrequency ablation
PLMD	Periodic limb movement disorder	RHT	Retinohypothalamic tract
PLMS	Periodic limb movements of sleep	RIP	Respiratory inductance plethysmography
PMDD	Premenstrual dysphoric disorder	RISP	Recurrent isolated sleep paralysis
PMR	Progressive muscle relaxation	RLS	Restless legs syndrome
POA	Preoptic area	RMD	Sleep-related rhythmic disorder
POMC	Pro-opiomelanocortin	RORA	Retinoic acid receptor related orphan receptor-A
PPD	Post partum depression	ROR $\alpha$	Retinoic acid receptor related orphan receptor- $\alpha$
PPN	Pedunculopontine nucleus	RR	Risk ratio
PS	Paradoxical sleep	RRE	Rev response element
PSG	Polysomnogram	RSWA	REM sleep without atonia
PSG	Polysomnography	RWA	REM sleep without atonia
PSM	Propriospinal myoclonus at sleep onset	SA	Sleep attacks
PSP	Progressive supranuclear palsy	SAD	Social anxiety disorder
PSQI	Pittsburgh sleep quality index	SB	Sleep bruxism
PTC	Pressor trigger of cataplexy	SCN	Suprachiasmatic nucleus
PTSD	Post-traumatic stress disorder	SCT	Stimulus control therapy
PTT	Pulse transit time	SD	Sleep disturbances
PVN	Paraventricular nucleus	SD	Standard deviation
QOL	Quality of life	SD	Sleep disordered breathing
RAAS	Reticular ascending activating system	S	Sleep efficiency
RBD	REM sleep behavior disorder	SEM	Slow eye movements
RDI	Respiratory disturbance index	SGA	Small for gestational age
REM	Rapid eye movement	SHVS	Sleep hypoventilation syndrome
REMOL	REM onset latency	SIDS	Sudden infant death syndrome
		SL	Sleep onset latency
		SLD	Sub lateral dorsal nucleus

SN	Substantia nigra pars com- pacta	TBI	Traumatic brain injury
SNRIs	Selective noradrenergic reuptake inhibitors	TCA's	Tricyclic antidepressants
SOREM	Sleep onset REM	Th cells	Thelper cells
SOREMP	Sleep onset REM period	TMN	Tuberomammillary nucleus
SRED	Sleep-related eating disor- der	TNF	Tumor necrosis factor
SRMDs	Sleep-related movement disorders	TRD	Tongue retaining devices
SRT	Sleep restriction therapy	TSH	Thyroid-stimulating hor- mone
SSRIs	Selective serotonin reup- take inhibitors	TST	Total sleep time
STs	Sleep terrors	UARS	Upper airway resistance syndrome
SUID	Sudden unexpected infant death syndrome	UPPP	Uvulopalatopharyngoplasty
SW	Sleepwalking	VCAM	Vascular cell adhesion mol- ecule
SWD	Shift work disorder	VEGF	Vascular endothelial growth factor
SWS	Slow wave sleep	VMS	Vasomotor symptoms
SXB	Sodium Oxybate	VTA	Ventral tegmental area
T cell	Thymocytes cell	W	Wakefulness
		WASO	Wake after sleep onset
		WED	Willis-Ekbom disease



# PREFACE

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If anyone were to ask, "why did you decide to edit this volume?", one would immediately think of two answers: First, that they genuinely believed there is a need for a volume of this sort, and, second, that, however pretentious it might sound, they believed that, because of their years of teaching and research experience, he/she is the right person to edit it.

However, I have a third answer. I have, since the beginning of my scientific career, despite my background in botany, been involved in the sleep field. Having edited over 20 volumes along with leading experts in the field of sleep and biological rhythms, I believe that I now have the requisite experience to edit an introductory sleep medicine volume on my own. This first edition of this volume is aimed at residents, fellows, house officers, and physicians of various specialties as well as clinical sleep researchers. The volume will give a basic grounding in sleep medicine to those who are established in related specialties as well as to younger professionals who are considering a future career in sleep medicine. This volume attempts to convey something of the fascinating complexity of the field as well as to separate figure from ground for those who are newcomers to the field and who are seeking guideposts for further research. Sleep medicine encompasses an unusually broad spectrum of contributions from biology, technology, and medicine. This volume seeks to summarize the consider-

able mass of knowledge that has now accumulated in the field and to impart its major findings in a manner that is both comprehensive but not overwhelming.

Inasmuch as sleep problems are frequently co-morbid with other medical conditions, the overt presenting symptoms of many patients may be driven by a number of other factors. Disruptions to circadian organization may have multiple effects of which sleep difficulties are simply the most visible. It is thus in the interest of clinicians to be alert to the ways in which sleep problems interconnect with other pathologies. It is often the case for instance that insomnia is not just insomnia, which is either a symptom or possibly a driver of correlated pathologies. It is thus in the interest of clinicians to be alert to this interconnectedness, and to recognize which difficulties are primary and which are not.

The literature on sleep and sleep medicine is enormous, and expanding rapidly. The objective of the editor has been to make this volume a useful tool for graduate students and newcomers who realistically do not always have time to check original publications. The authors have endeavored to give appropriate references to some of the more recent literature, and at the same time to quote the origins of some of the statements made.

There are often constraints to editing a volume, especially the first edition. For example, it is not always possible to address

all the topics that would be desirable for an introductory summary to cover. Additionally it is not always feasible to acquire the best experts in a special area. Nevertheless, for those who are interested in learning more about a specialized area of sleep medicine, the reference sections will represent a rich resource for this purpose. As with all major efforts of this kind we regard this introductory volume and those which will follow as "works in progress," and we anticipate that the content of future editions will evolve to respond to changes in the field as well as to the informational needs of our readers.

We have made every effort to ensure that the dosage recommendations are accurate and in agreement with the standards and collective opinion accepted at the time of publication. The formulations and usage described do not necessarily have specific

approval by the regulatory authorities of all countries. Since dosage regimens may be modified as new clinical research accumulates, readers are strongly advised to make note of the most recently recommended prescribing guidelines in their respective countries. Every effort leading up to the creation of this volume has been to make it into a practical and useful introduction to the sleep medicine field. However, as editor I remain responsible for any errors or mistakes which have occurred. This first edition will, I hope, stimulate in you as much excitement and satisfaction as it has in us. I sincerely hope that this volume will serve as a comprehensive guide for diagnostic problems in sleep medicine and it will find its way into the places where the battle against sleep dysfunctions is waged daily in clinics and hospitals around the world.

**S. R. Pandi-Perumal**  
*Toronto, Canada*