Our understanding of the pathology of amyotrophic lateral sclerosis is a continuously changing field. New hypotheses are generated with each new discovery; they are abandoned to be reanalyzed after some time under the light of new observations. This book presents a series of reviews from experts in different aspects of the disease focus on these hypotheses. There are also a few review chapters providing clear examples of these new observations that make the field reanalyze previous conclusions.

Navigating Life with Amyotrophic Lateral Sclerosis provides accessible, comprehensive, and up-to-date information about the challenges patients, family members, and caregivers face when confronted by ALS, a disease that affects approximately 5,600 Americans every year, with as many as 30,000 people managing the disease at any given time. ALS is a difficult disease for the patient and is also challenging for the caregiver and family as there are many questions, issues relating to care, and problems to manage. This guide covers all aspects of managing ALS, from the onset of symptoms, diagnosis, treatments, and coping strategies, to the use
of home health care or hospice, and new research in the field. The book also sheds lights on difficult topics, such as end-of-life care and managing legal affairs. Navigating Life with Amyotrophic Lateral Sclerosis is unique because it covers two perspectives: one author is a neurologist with 30 years of experience treating ALS patients, and the other author experienced first-hand the issues in providing care for a parent with ALS. Formatted in a question-and-answer style, peppered throughout with patient stories, and with sections devoted to family members and caregivers, this compassionate resource provides guidance to those seeking to understand how to live with this disease.

Dedicated to our readers, we include novel information (not reported in IntechOpen’s books before) about new contributions of aberrant astrocytes to MND damage and death in the SOD1G93A rat experimental model of ALS; novel genetic studies on ALS; an update of the structural and functional consequences of the spinal muscular atrophy-linked mutations of the survival motor neuron protein; stem cell therapy for MND; and the novel treatment for SMA and ALS in the introductory chapter. This book contains selected peer-reviewed chapters written by international researchers. In this publication, the readers will find a compilation of state-of-the-art reviews about etiology, therapies, investigations, the molecular basis of disease progression and clinical manifestations, and the genetic familial ALS, as well as novel therapeutic modalities. We look forward with confidence and pride to the remarkable role that this book will play for a new vision and mission.
Amyotrophic Lateral Sclerosis (ALS) or Lou Gehrig’s disease is an adult-onset fatal neurodegenerative disease characterized by progressive apoptosis of upper and lower motor neurons in the brain, brainstem and spinal cord. This results in paralysis of bulbar, limb, thoracic and abdominal skeletal muscles, and death within 2-5 years of diagnosis. In this book, the authors present current research on the symptoms, treatment and prognosis of ALS. Topics include audiological profiles and hearing loss in ALS patients; the role of the lipid transcription factor and sterol regulatory element binding protein 1 (SREBP1) in ALS; molecular targeted therapy for ALS; physical and communication disabilities in ALS; psychological interventions for ALS patients and their caregivers; and a study of ALS progression and propagation.

SPECTRUMS OF AMYOTROPHIC LATERAL SCLEROSIS

Discover state-of-the-art research findings on ALS from leading authors and editors in the field. In Spectrums of Amyotrophic Lateral Sclerosis: Heterogeneity, Pathogenesis & Therapeutic Directions, distinguished researchers and editors Dr. Christopher A. Shaw and Jessica R. Morrice deliver a practical and powerful perspective on Amyotrophic Lateral Sclerosis (ALS) as a heterogeneous spectrum of disorders. This increasingly accepted point-of-view allows researchers and medical professionals to develop better targeted interventions and more precise therapies. In the book, readers will find chapters on a wide variety of critical issues facing ALS researchers and healthcare practitioners treating ALS sufferers, including animal...
models of ALS, neuronal support cells known to have a pivotal role in ALS, and current challenges in ALS clinical trials, among others. The authors describe pathologic features common to all cases of ALS and why animal models, though crucial, should be interpreted with caution. Finally, multiple genetic and environmental etiologies of the disease are discussed. Readers will also benefit from the inclusion of: A thorough introduction to ALS as a spectrum disease and the implications for models, therapeutic development and clinical trial design Explorations of the genetic basis of ALS, prospective sALS etiologies, and the involvement of microbiome in ALS Discussions of ALS-PDC and environmental risk factors, protein aggregation in ALS, defects in RNA metabolism in ALS, and the non-cell autonomous nature of ALS and the involvement of glial cells Examinations of animal models of ALS and perspectives on previously failed ALS therapeutics and current therapeutic strategies Perfect for clinical neurologists, healthcare providers and caretakers, clinicians, and researchers studying motor neuron disease, Spectrums of Amyotrophic Lateral Sclerosis: Heterogeneity, Pathogenesis & Therapeutic Directions is also an indispensable resource for the neurodegenerative research community, neurology residents, and graduate-level neuroscience students.

A flurry of recent research on the role of the RNA/DNA-binding proteins TDP-43 and FUS as well as a dozen other factors (e.g., C9ORF72 and profilin) has led to a new paradigm in our understanding of the pathobiology of the motor neuron disease, Amyotrophic Lateral Sclerosis (ALS).
How these factors trigger neuromuscular dysfunction is critical for developing more effective ALS therapeutics. The ‘gain-of-toxicity’ or ‘loss-of-function’ of these etiological factors is a key question. Recent studies on the imbalance in genome damage versus repair have opened avenues for potential DNA repair-based therapeutics. This book highlights emerging science in the area of ALS and discusses key approaches and mechanisms essential for developing a cure for ALS.

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder affecting motor neurons in the spinal cord, brainstem and motor cortex. The disease induces paralysis, and death results from respiratory failure. The pathogenesis of ALS begins before a diagnosis can be made in the clinic. Analyzing processes influencing disease progression is an important strategy to elucidate disease mechanisms. We investigated factors influencing ALS disease progression, using the framework that the interplay of a range of extrinsic and intrinsic factors determine phenotypes. Our analysis of intrinsic, genetic factors focused on the H63D polymorphism in the HFE iron regulatory gene. Our results suggest homozygosity for H63D HFE is correlated with approximately 2-year longer disease duration and decreased levels of soluble superoxide dismutase protein in patients with ALS. We propose H63D HFE causes mild endoplasmic reticulum stress, which increases the risk for ALS but also promotes adaptive mechanisms that prolong survival in those who develop ALS. Studies analyzing intermediate factors focused on protein biomarkers. We measured 35 biomarkers in cerebrospinal fluid and plasma of patients with ALS, and created models predicting ALS prognosis based on biomarkers panels comprised of inflammatory cytokines, growth factors, and iron metabolism markers. We then focused on ferritin, which correlated with
longer disease duration in our models. Our results suggest ferritin is elevated in the blood of patients with ALS versus healthy controls and those with non-ALS neurological diseases. We propose elevated ferritin in ALS patients is an adaptive response to oxidative damage. Studies analyzing extrinsic factors focused on pharmacotherapies. Our results suggest HMG-CoA reductase inhibitors (statins), which are commonly prescribed to manage cholesterol, adversely impact phenotype in ALS model mice. G93A SOD1 mice administered statins had accelerated disease progression and decreased survival, with double transgenic animals harboring both SOD1 G93A and H67D HFE, homologous to human H63D HFE, having the worst phenotype. This underscores the need for surveillance of disease progression in patients with ALS receiving statin therapy. Our results suggest strategies to stratify patients in clinical trials, enabling more precise evaluation of outcomes; as well as therapeutic approaches that may improve the clinical situation for patients with ALS.

ALS, also known as Lou Gehrig's Disease, is the most common of the motor neuron diseases that cause muscle atrophy. ALS is a chronic, progressively debilitating disease characterised by progressive muscle atrophy starting in the limbs and spreading to the rest of the body, often accompanied by overactive reflexes. It usually manifests itself after the age of 40. The exact cause of ALS is unknown and there is no cure at this time. ALS may be fatal in one year or continue for 10 or more years. This new book includes leading edge research from around the world and covers the aetiology, pathogenesis, symptoms, diagnosis, and treatment of amyotrophic lateral sclerosis (ALS).

The motor neuron diseases (or motor neuron diseases) (MND) are a group of progressive neurological disorders that destroy motor neurons, the cells that control voluntary muscle
activity such as speaking, walking, breathing, and swallowing. Neurological examination presents specific signs associated with upper and lower motor neuron degeneration. Signs of upper motor neuron damage include spasticity, brisk reflexes and the Babinski sign. Signs of lower motor neuron damage include weakness and muscle atrophy. Every muscle group in the body requires both upper and lower motor neurons to function. It is a common misconception that "upper" motor neurons control the arms, while "lower" motor neurons control the legs. The signs described above can occur in any muscle group, including the arms, legs, torso, and bulbar region. Symptoms usually present between the ages of 50-70, and include progressive weakness, muscle wasting, and muscle fasciculations; spasticity or stiffness in the arms and legs; and overactive tendon reflexes. Patients may present with symptoms as diverse as a dragging foot, unilateral muscle wasting in the hands, or slurred speech. This new book presents the latest research from around the globe.

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, devastating and fatal disease characterized by selective loss of upper and lower motor neurons of the cerebral cortex, brainstem, spinal cord and muscle atrophy. In spite of many years of research, the pathogenesis of ALS is still not well understood. ALS is a multifaceted genetic disease, in which genetic susceptibility to motor neuron death interacts with environmental factors and there is still no cure for this deleterious disease. At present, there is only one FDA approved drug, Riluzole which according to past studies only modestly slows the progression of the disease, and improves survival by up to three months. The suffering of the ALS patients, and their families is enormous and the economic burden is colossal. There is therefore a pressing need for new therapies. Different molecular pathways and pathological mechanisms have been implicated in ALS. According to past
studies, altered calcium homeostasis, abnormal mitochondrial function, protein misfolding, axonal transport defects, excessive production of extracellular superoxide radicals, glutamate-mediated excitotoxicity, inflammatory events, and activation of oxidative stress pathways within the mitochondria and endoplasmic reticulum can act as major contributor that eventually leads to loss of connection between muscle and nerve ultimately resulting to ALS. However, the detailed molecular and cellular pathophysiological mechanisms and origin and temporal progression of the disease still remained elusive. Ongoing research and future advances will likely advance our improve understanding about various involved pathological mechanism ultimately leading to discoveries of new therapeutic cures. Importantly, clinical biomarkers of disease onset and progression are thus also urgently needed to support the development of the new therapeutic agents and novel preventive and curative strategies. Effective translation from pre-clinical to clinical studies will further require extensive knowledge regarding drug activity, bioavailability and efficacy in both the pre-clinical and clinical setting, and proof of biological activity in the target tissue. During the last decades, the development of new therapeutic molecules, advance neuroimaging tools, patient derived induced stem cells and new precision medicine approaches to study ALS has significantly improved our understanding of disease. In particular, new genetic tools, neuroimaging methods, cellular probes, biomarker study and molecular techniques that achieve high spatiotemporal resolution have revealed new details about the disease onset and its progression. In our effort to provide the interested reader, clinician and researchers a comprehensive summaries and new findings in this field of ALS research, hereby we have created this electronic book which comprises of twenty seven chapters
having various reviews, perspective and original research articles. All these chapters and articles in this book not only summarize the cutting-edge techniques, approaches, cell and animal models to study ALS but also provide unprecedented coverage of the current developments and new hypothesis emerging in ALS research. Some examples are novel genetic and cell culture based models, mitochondria-mediated therapy, oxidative stress and ROS mechanism, development of stem cells and mechanism-based therapies as well as novel biomarkers for designing and testing effective therapeutic strategies that can benefit ALS patients who are at the earlier stages in the disease. I am extremely grateful to all the contributors to this book and want to thank them for their phenomenal efforts. Manoj Kumar Jaiswal, Ph.D.
February 5, 2017 New York, NY

ALS, also known as Lou Gehrig's disease, cannot be cured but it can be treated. A great deal can be done to treat the symptoms of ALS, to improve an individual's quality of life, and to help families, caregivers, and loved ones to cope with the disease. This extensively revised and rewritten new edition of the bestselling Amyotrophic Lateral Sclerosis: A Guide For Patients and Families addresses all of those needs, and brings up-to-date important information to those living with the reality of ALS. The book is completely revised throughout and contains NEW information on: Recently developed approaches to treating ALS symptoms Use of non-invasive ventilators Multidisciplinary team care New guidelines being developed by the American Academy of Neurology for patients with ALS The use of riluzole (Rilutek) to treat ALS Amyotrophic Lateral Sclerosis covers every aspect of the management of ALS, from
clinical features of the disease, to diagnosis, to an overview of symptom management. Major sections deal with medical and rehabilitative management, living with ALS, managing advanced disease, end-of-life issues, and resources that can provide support and assistance in this time of need.

Amyotrophic Lateral Sclerosis: A Patient Care Guide for Clinicians is a practical reference for clinicians caring for ALS patients that brings together the collective wisdom of those at the forefront of patient-oriented research and practice. The book compiles recent findings of both evidence-based and experience-based research to provide clinicians with tools that improve quality and length of life for people with ALS. To present a truly multidisciplinary approach to ALS, this book mirrors the organization of a large clinic with separate departments working collaboratively. It begins with a review of current understandings of ALS including diagnostic criteria, genetic and sporadic subtypes, epidemiology, co-morbidities, and prognosis. From there the book is divided into chapters that include neurological assessment, nursing care and coordination, speech and swallowing interventions, nutrition and nutrition therapy, physical therapy, occupational therapy, respiratory therapy, assistive technology, social work practice related to ALS, and web-based resources. Each chapter is led by experts from that discipline who review evidence- and experience-based care options. In addition, the entire North American ALS Research Group (ALSRG) has had a chance to weigh in as well, making this a unique and well-rounded resource. The book
addresses everything from breaking the news of an ALS diagnosis to end-of-life care and bereavement. By putting experts in conversation with each other, both within and across individual disciplines, Amyotrophic Lateral Sclerosis: A Patient Care Guide for Clinicians provides comprehensive, real-world care information that can’t be found anywhere else. Amyotrophic Lateral Sclerosis features: A practical reference for all members of the ALS care team, covering everything from breaking the news to end-of-life care and bereavement Chapters that mirror the organization of large multi-disciplinary ALS clinics and include pertinent information for each member of the care team Evidence- and experience-based findings provide current scientific and clinical consensus and a forum for real-world care options Nutritional Care in Amyotrophic Lateral Sclerosis: An Alternative for the Maximization of the Nutritional State. Hardbound. Rapid progress has been made in both the research and clinical aspects of amyotrophic lateral sclerosis (ALS). There are striking achievements in many areas of ALS research. The contents of this volume will allow the reader to easily understand this progress, finding exciting advances in every section that could not have been imagined several years ago. This volume will bring great benefits to all researchers and clinicians involved with amyotrophic lateral sclerosis. "Amyotrophic Lateral Sclerosis: From Diagnosis to Treatment focuses on two aspects of neuroimaging related to amyotrophic lateral sclerosis that have greatly evolved in the last decades: the development of optical tools in the biology field and advances in the field of
magnetic resonance imaging. Therapeutic writing and expressive disclosure interventions have been demonstrated to facilitate the emotional processing of thoughts and feelings about the amyotrophic lateral sclerosis experience, with relevant implications for illness adjustment. Based on these premises, the authors explore the linguistic patterns in the cognitive-affective processing of illness experience in people with amyotrophic lateral sclerosis. Following this, the authors discuss recent studies that offer a new perspective on sensory networks in motor neuron diseases to understand the true extent and pathophysiology of amyotrophic lateral sclerosis and suggest new potential biomarkers for the diagnosis of this tragic disease. The closing study focuses on the respiratory involvement of amyotrophic lateral sclerosis, which is the principal cause of death. Amyotrophic lateral sclerosis is characterized by respiratory failure consequent to respiratory muscles dysfunction, as well as bulbar muscles which support the upper airways, developing in dyspnoea and impaired sleep"--

Amyotrophic Lateral Sclerosis (ALS or motor neurone disease) is a progressive neurodegenerative disease that can cause profound suffering for both the patient and their family. Whilst new treatments for ALS are being developed, these are not curative and offer only the potential to slow its progression. Palliative care must therefore be integral to the clinical approach to the disease. Palliative Care in Amyotrophic Lateral Sclerosis: From diagnosis to bereavement reflects the wide scope of this care; it must cover not just the terminal phase, but support the patient and their family from the onset of the disease. Both the multidisciplinary palliative care team
and the neurology team are essential in providing a high standard of care and allowing quality of life (both patient and carer) to be maintained. Clear guidelines are provided to address care throughout the disease process. Control of symptoms is covered alongside the psychosocial care of patients and their families. Case studies are used to emphasise the complexity of the care needs and involvement of the patient and family, culminating in discussion of bereavement. Different models of care are explored, and this new edition utilizes the increase in both the evidence-base and available literature on the subject. New topics discussed include complementary therapies, personal and family experiences of ALS, new genetics research, and updated guidelines for patient care, to ensure this new edition remains the essential guide to palliative care in ALS.

Recently, the implication of biocompatible nanotechnologies has set the stage for an evolutionary leap in diagnostic imaging and therapy. In this scope, the book presents a comprehensive overview of the possible causes, diagnostic criteria, and treatment assessments of amyotrophic lateral sclerosis, and presents the recent findings using innovative ALS is not a curable disease, but it is a treatable one. Treatments are now available that can make a major difference in prolonging life and enhancing the quality of life for people with the disease, and there are treatments for many of the symptoms of ALS that can help ease its burden. Multidisciplinary teams in specialized ALS centers are providing top quality care and comprehensive rehabilitation for persons with ALS. In spite of the progressive nature of this disease and its clear tendency to shorten life, the momentum of research in this disease is expanding dramatically and numerous clinical trials are testing promising new therapies. Our understanding of the basic causes of ALS is expanding gradually. The substantial resources of patient advocacy
groups such as the Amyotrophic Lateral Sclerosis Association and Muscular Dystrophy Association provide tremendous help and support for people with ALS and their families. Although the diagnosis of ALS can initially be devastating, the vast majority of people discovering new courage from within to battle this disease and live life with vigor and enthusiasm. The information in this book will prove useful to people with ALS and their families both in managing the disease and living within its limitations."

A condition that causes the death of neurons which control the voluntary muscles of the body is known as amyotrophic lateral sclerosis (ALS). It is also referred to as Lou Gehrig's disease or motor neurone disease. Patients with ALS exhibit signs of muscle stiffness, muscle twitching and muscle wasting. The person may experience progressive difficulty in speaking or swallowing, and weakness in the arms or legs. The diagnosis of ALS is based on a study of the clinical signs and symptoms, full medical history and neurologic examinations. Blood tests and MRIs can rule out the likelihood of other diseases. ALS has no medical cure. Its management is focused on providing supportive care, treating symptoms and improving quality of life. Medicines like riluzole prolong survival by 2-3 months, while edaravone slows functional decline to some extent but at the cost of quality of life. Respiratory failure is managed with non-invasive ventilation. For patients with advanced ALS, invasive ventilation is an option that can prolong survival even as the disease continues to progress and body functions decline. The various studies that are constantly contributing towards advancing diagnosis and treatment of amyotrophic lateral sclerosis are examined in detail in this book. It presents researches and studies performed by experts across the globe. This book will prove to be immensely beneficial to students and researchers in the field of neuroscience.
Though considerable amount of research, both pre-clinical and clinical, has been conducted during recent years, Amyotrophic Lateral Sclerosis (ALS) remains one of the mysterious diseases of the 21st century. Great efforts have been made to develop pathophysiological models and to clarify the underlying pathology, and with novel instruments in genetics and transgenic techniques, the aim for finding a durable cure comes into scope. On the other hand, most pharmacological trials failed to show a benefit for ALS patients. In this book, the reader will find a compilation of state-of-the-art reviews about the etiology, epidemiology, and pathophysiology of ALS, the molecular basis of disease progression and clinical manifestations, the genetics familial ALS, as well as novel diagnostic criteria in the field of electrophysiology. An overview over all relevant pharmacological trials in ALS patients is also included, while the book concludes with a discussion on current advances and future trends in ALS research.

Amyotrophic lateral sclerosis (ALS), which was described since 1869 by Jean Martin Charcot, is a devastating neurodegenerative disease characterized by the selective and progressive loss of upper and lower motor neurons of the cerebral cortex, brainstem and the spinal cord. The cognitive process is not affected and is not merely the result of aging because may occur at young ages. The only known cause of the disease is associated with genetic mutations, mainly in the gene encoding superoxide dismutase 1 (familial ALS), whereas there is no known cause of the sporadic form of ALS (SALS), which comprises >90% of cases. Both ALS types develop similar histopathological and clinical characteristics, and there is no treatment or prevention of
the disease. Because effective treatments for ALS, as for other neurodegenerative diseases, can only result from the knowledge of their cellular and molecular pathophysiological mechanisms, research on such mechanisms is essential. Although progress in neurochemical, physiological and clinical investigations in the last decades has identified several mechanisms that seem to be involved in the cell death process, such as glutamate-mediated excitotoxicity, alterations of inhibitory circuits, inflammatory events, axonal transport deficits, oxidative stress, mitochondrial dysfunction and energy failure, the understanding of the origin and temporal progress of the disease is still incomplete and insufficient. Clearly, there is a need of further experimental models and approaches to discern the importance of such mechanisms and to discover the factors that determine the selective death of motor neurons characteristic of ALS, in contrast to other neurodegenerative diseases such as Parkinson’s and Alzheimer’s disease. Whereas studies in vitro in cell cultures, tissue slices or organotypic preparations can give useful information regarding cellular and molecular mechanisms, the experiments in living animal models obviously reflect more closely the situation in the human disease, provided that the symptoms and their development during time mimics as close as possible those of the human disease. It is necessary to correlate the experimental findings in vitro with those in vivo, as well as those obtained in genetic models with those in non-genetic models, aiming at designing and testing therapeutic strategies based on the results obtained.