Neurological Disorders due to Systemic Disease

How do you identify which neurologic syndromes occur due to systemic disease?

Neurological problems commonly occur in the context of underlying systemic disease, and may even be the presenting symptom of a medical condition that has not yet been diagnosed. Consequently neurologists need to be aware when a neurological presentation might indicate an underlying systemic disorder.

Neurological Disorders due to Systemic Disease provides the tools you need to make these connections. The unique neurologic presentation-based approach relates to the common clinical situations you encounter, including:

- Headache
- Stroke
- Movement disorders
- Neuromuscular disorders
- Encephalopathies, seizures, myelopathies, neuro-ophthalmologic and neuro-otologic disorders, sleep disorders, and others

Major categories of systemic illness are explored for each presentation to guide you towards a likely cause. These include:

- Endocrine, electrolyte, and metabolic disorders
- Systemic autoimmune disorders
- Organ dysfunction and failure, and critical medical illness
- Systemic cancer and paraneoplastic disorders
- Systemic infectious disease
- Complications due to drugs and alcohol
- Vitamin and mineral deficiencies

Written by a leading cast of experts, with a practical approach including “things to remember” for each presentation, Neurological Disorders due to Systemic Disease should be on every neurologist’s desk.
Neurological Disorders due to Systemic Disease
To my sons David, Michael, Adam, and Elliot, who teach me so much.
Neurological Disorders due to Systemic Disease

Edited by

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Preface

The aim of this book is to provide an overview of the clinical presentation, pathophysiology, diagnosis, and management of the various neurological syndromes that occur in the clinical context of an underlying systemic disease or its treatment.

Although written primarily with the neurologist (generalist neurologist, subspecialist neurologist, or neurologic trainee) in mind, the material in this book should also be accessible and of interest to internal medicine and other primary care physicians, internal medicine subspecialists, and medical students. It is my hope that both neurologist and non-neurologist readers of this text will find that the unique neurologic-syndrome-based approach in the following pages will provide clinically useful insight into the wide variety of neurological disorders that occur due to systemic disease, and provide practical clinical clues to the neurological, and the underlying systemic, diagnosis and management of these patients.

I would like to thank the neurology residents and my general neurology attending colleagues at Rush University Medical Center for creating a stimulating clinical and academic milieu in our daily “work” in the inpatient and outpatient diagnosis and management of the many patients with neurologic disorders from systemic disease. Special gratitude goes to our patients with these disorders for entrusting their care to us.

I would also like to thank my publishers at Wiley-Blackwell, in particular Martin Sugden, PhD, for getting this book off the ground, and to Julie Elliott and Rebecca Huxley, for their expertise in seeing the project through to completion. Finally, a very special thank you to my wife, Julie, for all of her support.

Steven L. Lewis, M.D.
Chicago, Illinois
September, 2012
Neurological problems commonly occur in the context of an underlying systemic disease, and these neurologic presentations are a frequent source of inpatient and outpatient neurological consultation. In many patients, the neurological disorder is a manifestation of a previously diagnosed systemic illness or its treatment, but in still many others the neurological disorder is the presenting manifestation of a medical condition that has not yet been diagnosed. The aim of this book is to provide the physician with an overview of the clinical presentation, pathophysiology, diagnosis, and treatment of the various neurological syndromes that occur in the setting of systemic illnesses.

In this book, “systemic disease” and “medical disease” are used interchangeably, and refer to the kind of disease or syndrome in which the primary dysfunction involves an organ or system other than the nervous system, with the nervous system disorder occurring as a secondary—though in many cases, a potentially major—consequence. This book, therefore, focuses mostly on the neurological illnesses that occur in the setting of those primary illnesses that are typically considered to be under the purview of general internal medicine or its subspecialties. In addition, this book discusses the neurological complications that occur due to medications and other therapies typically used to treat these systemic illnesses. Conversely, this book does not focus on diseases—such as many genetic disorders—with multisystem manifestations that include both neurological and systemic complications, but where the neurological disease is not considered a complication of the systemic disease.

Unlike most books on this subject, the chapters of this book are organized and defined by neurological clinical scenarios, rather than by medical diseases. Specifically, each chapter focuses on a particular category of neurological presentation (e.g., movement disorders) and discusses the various systemic illnesses, or their treatment, that can cause dysfunction within that category of neurologic disorders. This organizational scheme, I propose, especially parallels the very common clinical scenario where the medical illness underlying the neurological syndrome is unknown; in these scenarios, the clinician needs to have some knowledge and understanding of the various systemic illnesses that can lead to these neurologic presentations.

The following major neurologic presentations define the chapters of this book: headache, encephalopathy, dementia, stroke, seizures, neuroophthalmologic disorders, neurootologic disorders, movement disorders, spinal cord disorders, peripheral nerve disorders, neuromuscular junction disorders, disorders of skeletal muscle, autonomic nervous system disorders, and sleep disorders. Each chapter, in turn, is subdivided into major categories of systemic illness that can lead to neurologic dysfunction: endocrine disorders; electrolyte and other metabolic disorders; systemic autoimmune disorders; organ dysfunction and failure; systemic cancer and paraneoplastic disorders; systemic infectious diseases; complications due to transplantation, complications of critical medical illness; drugs, alcohol, and toxins; and vitamin and mineral deficiencies. In individual chapters, some of these subheadings are excluded when they are not particularly relevant to that chapter’s neurologic topic.

The book begins with the chapter on headache (Chapter 2) by Kevin Kahn, MD, from the Carolina Headache Institute, who discusses secondary headache syndromes that can be associated with systemic
disease, as well as the interface between systemic
illness and primary headache syndromes. Chapter 3,
written by Allison Weathers, MD, from Rush Uni-
versity Medical Center provides an overview of the
diffuse encephalopathy (delirium) syndromes that
(by definition, arguably) occur within the setting of
systemic dysfunction. In contrast, in Chapter 4,
Jennifer Molano, MD, and Brendan Kelley, MD,
from the University of Cincinnati tackle the interaction
of systemic dysfunction and neurologic syndromes that
more resemble dementia than typical toxic-metabolic
encephalopathies; these authors also provide additional
insights into the interface between the primary degen-
erative dementias and systemic illnesses.

In Chapter 5, Sarkis Morales-Vidal, MD, and José
Biller, MD, from Loyola University Medical Center
review the many systemic disorders that can be asso-
ciated with, and potentially cause, cerebrovascular
disease and stroke that the clinician should keep in
mind in addition to the usual and well-known medical
stroke risk factors. In Chapter 6, Matthew Hoerth,
MD, and Joseph I. Sirven, MD, from the Mayo Clinic,
Scottsdale, discuss the many medical problems that
can lead to seizures; typically, recognition of these
systemic causes of seizures can avoid unnecessary, or
prolonged, antiepileptic drug therapy in these patients.

In Chapter 7, Matthew Thurtell, MBBS, from the
University of Iowa and Janet Rucker, MD, from the
Mount Sinai School of Medicine review and illustrate
the many neuroophthalmological signs and symptoms
that occur due to, and give clue to, the presence of an
underlying potentially serious and sometimes vision-
threatening systemic illness. In Chapter 8, Terry Fife,
MD, from the Barrow Neurological Institute in
Arizona discusses the many—and probably underre-
cognized by many neurologists—auditory or vestibu-
lar neurootologic syndromes that can occur due to
medical illness.

In Chapter 9, Brandon Barton, MD, and Chris-
topher Goetz, MD, from Rush University Medical Cen-
ter review the many movement disorders (including
dystonia, tremor, chorea, myoclonus, ataxia, and tics)
that can occur due to systemic disease or its treatment. In Chapter 10, Sital Patel, MD, and I,
also from Rush, discuss myelopathies (whether from
extrinsic compression of the spinal cord or intrinsic
noncompressive spinal cord dysfunction) that can
coccur as a complication of an underlying medical
disorder.

In Chapter 11, Michelle Mauermann, MD, from the
Mayo Clinic Rochester and Ted Burns, MD, from the
University of Virginia review the many neuropathic
syndromes, and their characteristic clinical patterns,
that can occur due to systemic disorders. Extending
the discussion further, in Chapter 12, Jaffar Khan,
MD, from the Emory University School of Medicine
discusses presynaptic and postsynaptic neuromuscular
junction disorders and their association with under-
lying systemic illness. In Chapter 13, Hannah
Briemberg, MD, FRCPC, from the University of Brit-
ish Columbia reviews the many myopathic disorders
that can occur as a consequence of medical illness and
certain medications.

In Chapter 14, Brent Goodman, MD, and Eduardo
Benarroch, MD, from the Mayo Clinic, Rochester,
review autonomic nervous system manifestations that
can occur—with or without other signs of neurologic
dysfunction—in the setting of systemic disease; the
authors also review how to assess for these autonomic
disorders. Finally, in Chapter 15, Erik St. Louis from
the Mayo Clinic, Rochester, discusses the association
of disorders of sleep, including the parasomnias, and
underlying systemic illness.

Each chapter concludes with a list of the authors’
suggestion of “Five things to remember about” that
particular neurologic topic and its relation to systemic
disease; these can be construed as suggested minimum
“take home” points that provide some additional
overall clinical perspective for the reader.

Although written primarily with the neurologist
(generalist neurologist, subspecialist neurologist, or
neurologic trainee) in mind, the material in this book
should also be of interest and accessible to internal
medicine physicians, other primary care providers,
internal medicine subspecialists, and even interested
medical students. It is my hope that the reader of this
text will find that the unique neurologic syndrome-
based approach in the following pages will provide
clinically useful insight into the wide variety of
neurological disorders that occur in the context of
systemic disease, and provide practical clinical clues
to both the neurological diagnosis and the under-
lying medical diagnosis and management of these
patients.
The chief complaint of headache must always be considered to have an origin in medical illness before primary headache entities may be considered. The accepted criteria for migraine and other primary headache disorders by the International Headache Society (IHS) have at their core the mandate that secondary headaches must be excluded [1]. This chapter will review the potential secondary headaches that can occur as a consequence of medical illness.

An understanding of the mechanisms through which head pain is generated is critical to appreciating how systemic illness can generate headache. Sensation within the head depends upon afferent nerves from the anterior aspect of the head and the posterior aspect of the head that converge upon the trigeminal nucleus caudalis in the pons. This nucleus then sends further input to the thalamus and higher cortical structures to process new sensory information. During primary headache disorders such as migraine, this system is activated by either peripheral or central triggers to send electrical impulses efferently to peripheral structures. The depolarization of nerves ending in the periphery results in a release of inflammatory substances causing swelling, inflammation, and pain within peripheral structures. Such structures include meningeal arteries, sinuses, skin, and musculature within the head and neck. In addition to activation of peripheral structures, there is an increase of excitatory input or lack of inhibitory control centrally that results in increased sensitivity of all senses as well as activation of brainstem emesis/nausea centers. Thus, pain generated within the head is mediated through trigeminally innervated structures. The associated features of pain are generated by trigeminally related central activation and disinhibition. The pain from other primary headache disorders such as cluster headache, tension-type headache, and the trigeminal autonomic cephalgias all generate pain via these same trigeminal pathways. The manifestation of pain is often pulsatile or throbbing but can present as burning, stinging, aching, sharp, dull, pressure, squeezing, and so on. Associated features are typically sensitivity to light (photophobia) and noise (phonophobia), nausea, and vomiting, but can also present as sensitivity to smell (osmophobia) or touch, sinus congestion, lacrimation, rhinorrhea, scleral erythema, ptosis, neck pain/tension/stiffness, and worsening with position or activity.

Since the final common pathway of head pain is trigeminally mediated, many secondary headaches seem to have features in common with the primary headaches. For instance, meningitis, an infection of trigeminally innervated membranes around the brain, can present with light/sound sensitivity, nausea, throbbing pain, and stiff neck. It is the presence of other systemic features such as fever, in addition to guidance from the patient history, that help separate the primary from secondary headaches. Thus, it is important to remember that headaches that are new to an individual or are associated with abnormal signs on exam or are a dramatic change from preexisting headaches are red flags that mandate consideration of secondary headaches. The secondary headaches can often mimic migraine since anything that can irritate central or peripheral trigeminally innervated structures will affect the same pain mechanisms as the primary headaches.