PRACTICING NEUROLOGY

What You Need to Know, What You Need to Do

Second Edition

Rahman Pourmand, MD

HUMANA PRESS

Practicing Neurology

Current Clinical Neurology

Daniel Tarsy, MD, Series Editor

Stroke Recovery: *Cellular and Genetic Therapies,* edited by ***Daniel M. Rosenbaum and Sean I. Savitz, 2007***

Practicing Neurology: *What You Need to Know, What You Need to Do, Second Edition,* by ***Rahman Pourmand, 2007***

Sleep Disorders in Women: *From Menarche Through Pregnancy to Menopause,* edited by ***Hrayr P. Attarian,*** *2006*

Diagnostic Criteria in Neurology, edited by ***Alan J. Lerner,*** *2006*

Psychiatry for Neurologists, edited by ***Dilip V. Jeste and Joseph H. Friedman,*** *2006*

Status Epilepticus: *A Clinical Perspective,* edited by ***Frank W. Drislane,*** *2005*

Thrombolytic Therapy for Acute Stroke, Second Edition, edited by ***Patrick D. Lyden,*** *2005*

Parkinson's Disease and Nonmotor Dysfunction, edited by ***Ronald F. Pfeiffer and Ivan Bodis-Wollner,*** *2005*

Movement Disorder Emergencies: *Diagnosis and Treatment***,** edited by ***Steven J. Frucht and Stanley Fahn,*** *2005*

Inflammatory Disorders of the Nervous System: *Pathogenesis, Immunology, and Clinical Management***,** edited by ***Alireza Minagar and J. Steven Alexander,***

Practicing Neurology

What You Need to Know, What You Need to Do

Second Edition

By

Rahman Pourmand, MD

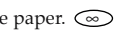
Department of Neurology, Stony Brook University Hospital, Stony Brook, NY

HUMANA PRESS
TOTOWA, NEW JERSEY

999 Riverview Drive, Suite 208
Totowa, New Jersey 07512

humanapress.com

Due diligence has been taken by the publishers, editors, and authors of this book to assure the accuracy of the information published and to describe generally accepted practices. The contributors herein have carefully checked to ensure that the drug selections and dosages set forth in this text are accurate and in accord with the standards accepted at the time of publication. Notwithstanding, as new research, changes in government regulations, and knowledge from clinical experience relating to drug therapy and drug reactions constantly occurs, the reader is advised to check the product information provided by the manufacturer of each drug for any change in dosages or for additional warnings and contraindications. This is of utmost importance when the recommended drug herein is a new or infrequently used drug. It is the responsibility of the treating physician to determine dosages and treatment strategies for individual patients. Further it is the responsibility of the health care provider to ascertain the Food and Drug Administration status of each drug or device used in their clinical practice. The publisher, editors, and authors are not responsible for errors or omissions or for any consequences from the application of the information presented in this book and make no warranty, express or implied, with respect to the contents in this publication.

This publication is printed on acid-free paper. 

ANSI Z39.48-1984 (American Standards Institute) Permanence of Paper for Printed Library Materials.

For additional copies, pricing for bulk purchases, and/or information about other Humana titles, contact Humana at the above address or at any of the following numbers: Tel.: 973-256-1699; Fax: 973-256-8314; E-mail: orders@humanapr.com, or visit our website: http://humanapress.com

Printed in the United States of America. 10 9 8 7 6 5 4 3 2 1

Library of Congress Cataloging in Publication Data

E-ISBN: 978-1-59745-297-7

Pourmand, Rahman.
Practicing neurology : what you need to know, what you need to do / by Rahman Pourmand. -- 2nd ed.
p. ; cm. -- (Current clinical neurology)
Includes index.
ISBN 1-58829-609-1 (alk. paper)
1. Neurology--Handbooks, manuals, etc. 2. Nervous system--Diseases--Handbooks, manuals, etc. I. Title. II. Series.
[DNLM: 1. Nervous System Diseases--diagnosis--Handbooks. 2. Nervous System Diseases--therapy--Handbooks. WL 39 P877p 2007]
RC346.P68 2007

Series Editor's Introduction

The neurological examination and neurologic differential diagnosis are all too often regarded as daunting because of their perceived complexity by physicians in training as well as by more mature practicing doctors. Neurological examinations as documented in hospital or office records often betray this perception by their frequent brevity and lack of significant and useful information. *Practicing Neurology*, now in its 2nd edition, is meant for the non-neurologist and seeks to demystify this traditional view of the neurological evaluation. As indicated by the author, medical students and non-neurology residents wish to learn how to carry out a good neurological examination, how to properly interpret abnormal neurological findings, how to formulate the clinical problem, what tests and procedures to consider, and how to begin to treat neurological disorders.

In order to achieve these goals, Dr. Pourmand takes as his jumping off point the fact that the experienced neurologist typically tailors his examination to the specific problem presented by the patient. Each examination is different and emphasizes what is important for that particular patient while taking care not to neglect other important parts of the evaluation. The 'focused' or 'directed' neurological examination is what often emerges. By contrast, the beginner usually commits himself to doing the full and comprehensive examination and elaborating all-inclusive differential diagnosis lest some important detail be inadvertently omitted. For the neophyte this is probably as it should be but at some point, with a bit of experience, it becomes possible and even necessary to plot a shorter road to correct diagnosis and management.

This volume helps to chart a path to that goal by outlining the essential but inclusive neurological examination including tips on what is important, what can sometimes be dispensed with, and the particular significance of many findings. This is followed by the diagnostic formulation which emphasizes the traditional '*where* and *what* is the lesion' and a list of traditional neurological signs and their significance. Brief but very useful primers concerning neurological localization and common neurological constructs let the non-neurologist in on many useful tricks of the trade which are second nature to the neurologist in many useful tricks of the

trade which are second to the neurologist but usually quite foreign to the non-neurologist. Useful focused sections on the approach to common neurological conditions and neurological urgencies and emergencies follow that provide additional invaluable lessons for the non-neurologist.

Daniel Tarsy, MD
Department of Neurology
Beth Israel Deaconess Medical Center
Harvard Medical School
Boston MA

Preface

When medical students and non-neurology residents rotating through the neurology service are asked about their expectations, their responses are uniform: They want to learn how to conduct effective neurologic examinations, they want to know the value and indications of neurologic procedures and testing, and they want to know how to evaluate and manage common neurologic conditions. This book addresses those topics.

After practicing neurology for more than 20 years in an academic setting, I believe I have met the expectations of my students, so I decided to put it in writing for others as well. In my opinion, knowing or reading thousands of pages of textbooks is not only impossible but also unnecessary to diagnose and treat the common neurologic conditions that physicians encounter in day-to-day practice, whether in the hospital, clinic, or emergency room. The second edition of this book again summarizes what and how much you need to know and do to confidently diagnose and manage most neurologic cases. You do not have to be a genius to figure out why a patient has footdrop. The bottom line is that neurology is not difficult; it just takes longer to do and requires mental exercises to reach the diagnosis. This handbook makes neurology easy, stimulating, and fun.

Rahman Pourmand, *MD*

A Viewpoint from a Medical Student

There is no doubt (at least in my mind) that the brain is the most mysterious and fascinating organ in the body. This one organ is essentially who we are and what makes each of us unique. As a fourth year medical student, I know that other medical students frequently view the subject of neurology as complicated and abstract. The great strength of this book rests with the author's clear and concise explanations of difficult neurological topics. This small, easy to carry book somehow manages to cover all of the essential topics that we are expected to know about in neurology and it does so in a fun way that invites you to keep reading. I had no problem completing the book during my clerkship in neurology.

The ability to perform a solid and thorough neurological exam is the core of what a medical student should master in their neurology rotation. This book accomplishes this task with its thorough explanation of all the components of the neurological examination.

Neurological disease notoriously encompasses some of the worst disease processes in medicine. The old edition of this book provided a comprehensive review of the essential neurological topics; however, new aspects of these diseases are being discovered by researchers every day. The new edition of this book includes the latest advancements in the diagnosis and treatment of neurological diseases.

Ultimately, this book makes neurology what it should be—easy to understand and intellectually stimulating. I will continue to use this book as a guide during my internship and residency. This book is an essential reference tool that every medical student should have during medical school and throughout the rest of their medical careers.

Clair Cascella, MS IV
Stony Brook University Medical Center
Stony Brook, NY

Contents

Series Editor's Introduction v
Preface vii
A Viewpoint from a Medical Student ix

Part I Evaluation

1 Highlights of Neurological History and Examination 3
2 Neurological Formulation 29
3 Some Neurological Signs of Interest 31
4 Approach to the Patient with Suspected Hysteric Conversion 35
5 Neuroanatomy of Localization 39
6 Some Common Neurological Constructs 41
7 Neurodiagnostic Tests and Procedures 47

Part II Common Neurological Conditions

8 Cerebrovascular Accidents 67
9 Seizure and Epilepsy 79
10 Central Nervous System Infections 85
11 Alteration of Mental Status 91
12 Demyelinating Disorders 97
13 Neurological Complications of Alcohol 107
14 Dizziness and Vertigo 111
15 Headaches and Facial Pain 115
16 Peripheral Neuropathy 129
17 Movement Disorders 137
18 Sleep Disorders 145
19 Neuromuscular Diseases 153
20 Back and Neck Pain 175

Part III Neurological Urgencies and Emergencies

21 Coma 181
22 Status Epilepticus 189

23 Brain Edema, Transtentorial Herniation, and Increased Intracranial Pressure 193
24 Metastatic Epidural Spinal Cord Compression 197
25 Acute Meningitis and Encephalitis 199
26 Delirium Tremens 201
27 Wernicke's Encephalopathy 203
28 Myasthenia Gravis Crisis 205
29 Guillain-Barré Syndrome 207
30 Temporal Arteritis 209

Index 211

I Evaluation

1

Highlights of Neurological History and Examination

GENERAL CONSIDERATIONS

A primary objective of medical students and residents rotating in the neurology service is to learn and to be able to perform a good neurological examination. They often think that the neurological examination is difficult and hard to remember. However, more importantly, I believe that many medical students and junior residents do not know what to look for, how to find neurological signs, and how to interpret their findings.

In this chapter, I will summarize and share my views of the neurological examination with the reader, which I have found to be useful, practical, meaningful, and easy to remember after practicing neurology for several years. Of course, by no means are these views complete and standard, and I understand that some are subject to disagreement by other neurologists.

First, despite several detailed textbooks on how to do a neurological examination, there is no standard neurological examination. Most neurologists, over years, develop the technique and formula with which they are comfortable. My advice to the medical students and residents is this: Try to perform the neurological examination systematically and practice a formula that you like. I start with the mental status examination, followed by cranial nerves, motor and sensory, reflexes, cerebellar, and then gait. The neurological examination may begin with the problem area, followed by the remaining parts.

Although a systematic examination is recommended, flexibility is also important, because a detailed neurological examination is not always possible in all patients, for example, in comatose or agitated patients or in infants. To make the neurological examination even easier, I do not routinely perform several neurological tests, for example, smell, Weber and Rinne tests, gag reflex, taste, corneal reflex, or temperature. I do these only if clinically indi-

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

cated. I do not see any reason to check anal wink reflex in a patient complaining of headaches, or perform corneal reflex in a patient presenting with weakness. However, students should perform a complete neurological examination to validate each sign and their variability, and to gain confidence. In a cooperative and uncomplicated patient, a complete neurological examination does not take longer than 20–25 minutes. The goal of the neurological examination and history is to hypothesize where and what type the lesion is, how to plan the investigation, and determine what therapy can be offered to the patient.

NEUROLOGICAL HISTORY

Take a thorough and detailed history; this is the most important part of the neurological evaluation, because your neurological examination is based on the history. Listen to the patient carefully, and show that you are interested and concerned. One good strategy is to consider that the history of the patient is indicative of an underlying neurological disorder, until proven otherwise. Remember that by history taking, you are checking most parts of the mental status examination. If you have taken a good history by asking the right questions, then you should be able to:

1. Hypothesize the most likely anatomical site(s) of the neurological problem, whether the lesion involves the central nervous system (CNS), peripheral nervous system, both, or neither: **Where is the lesion?**
2. List the most likely cause/causes of the neurological problem, whether vascular, neoplastic, infectious, and so on: **What is the lesion?**
3. Establish the onset of illness and the temporal profile as **acute**, **subacute**, **chronic**, **progressive**, or **paroxysmal**.

Remember: If you are not able to plan the hypothesis, do not pursue the neurological examination, go back and take more history.

NEUROLOGICAL EXAMINATION

Perform a focused neurological examination in detail, but do not forget to complete your examination. Having completed your neurological history and examination, then try to:

1. Formulate the pertinent findings and make a list of differential diagnoses regarding localization and etiologies. Exclude the unlikely ones and narrow down the differential as much as possible.
2. Plan your investigations and order tests systematically to confirm or support your impression or to exclude others.
3. Discuss the management and prognosis with the patient and establish your follow-up plan.

PERFORMING THE NEUROLOGICAL EXAMINATION

The neurological examination not only is different, complex, and takes longer than any other organ, but is also unfamiliar to the majority of patients. It is important to explain to the patient what you are going to do, what you are trying to accomplish, and how the examination helps address the patient's problem(s). Communication with the patient during examination is crucial. To gain trust and cooperation from your patient, pay more attention to the problem; you may want to examine this area first, and if you decided to check it later, inform the patient. The comfort of the patient should be considered during the examination. For example, if the patient is lying on the bed, start with the areas that can be tested in that position, such as the heel-to-shin test, abdominal reflexes, sensory testing, Babinski sign, and so on. Then, do as much as possible in the sitting position, and then check the patient walking.

MENTAL STATUS EXAMINATION AND HIGHER CORTICAL FUNCTION TESTS

Before pursuing formal testing of higher cortical function, you must establish that the patient is awake, alert, can hear, and is not aphasic. The formal higher cortical function test is not necessary in all patients; you can assess cognitive function for the most part when you are taking history. In this setting, I quickly check orientation, attention, short-term memory, judgment, and insight. I do formal higher cortical function testing if the patient complains of memory loss, is suspected of having dementia, has experienced a recent change in mental function, or if during the history taking I find a deficit or problem.

What to Do

The Mini-Mental State Exam is commonly used for bedside evaluation of cognitive function. This test, in contrast to more-detailed neuropsychometric testing, does not differentiate focal from diffuse CNS lesions. The total points for the test are 30; if the patient has a score less than 23, the patient has mental impairment.

	Test	Points
1.	Orientation	10
2.	Retention and recall	6
3.	Attention and calculation	5
4.	Naming	2
5.	Repetition	1
6.	Comprehension	3
7.	Reading and writing	2
8.	Construction block	1

As a part of the cognition test, I check for **agnosia** and **apraxia.** Before you check for abnormalities in these areas, you must be sure that the patient is able to see, touch, and has no motor weakness or hand incoordination. Agnosia and apraxia are generally indicative of an parietal occipital lobe lesion. Note the following abnormalities:

- Inability to draw a clock or cross (construction apraxia).
- Inability to comb hair or drink through a straw (ideational apraxia).
- Inability to name fingers (finger agnosia).
- Inability to recognize the objects by touch (astereognosis).
- Inability to recognize drawing number in hands (agraphesthesia).
- Inability to understand written language (alexia).
- Inability to write (agraphia).

How to Interpret the Findings

If the patient shows deficits in many areas of the Mini-Mental State Exam, the patient has either a diffuse or multifocal CNS disorder. If the process is chronic and slowly progressive, consider dementing illness caused by a degenerative disorder. If acute or subacute, consider confusional state caused by a toxic or metabolic derangement.

If the patient shows only one or a few deficits, consider focal CNS insult and then look for more focal signs: aphasia, visual field (VF) defect, and hemiparesis. If the patient has finger agnosia, check for dyscalculia, left–right disorientation, and dysgraphia, because the patient could have Gertsmann's syndrome, which is indicative of a dominant parietal lobe lesion (stroke).

***Caveat*:** The two most common causes of dementia are Alzheimer's disease and multiple strokes (<65 age, frontotemporal dementia is second to AD). Dementia can be easily mistaken for global confusion, depression (particularly in the elderly), aphasia, mental retardation, and psychiatric illness. Long-term memory loss with preserved short-term is clinically insignificant.

CRANIAL NERVE EXAMINATION

General

Anatomy

- All cranial nerves (CNs) originate from the brainstem, except CNs I and II.
- The location of CNs III and IV nuclei are in the midbrain; CNs V, VI, VII, and VIII are in the pons; and CNs IX, X, XI, and XII are in the medulla.
- CNs I, II, and VIII are purely sensory; CNs III, IV, VI, XI, and XII are purely motor; and the remainder are mixed.
- CNs III, VII, IX, and X have parasympathetic fibers.

Situations From Which Dysfunction of CNs Could Arise

- Supranuclear lesion.
- Brainstem lesions.
- Cranial nerve lesions.
- Neuromuscular junction.
- Surrounding structures, such as the cerebellum.

Some Clinical Hints

- The presence of CN dysfunction implies a lesion above the foramen magnum; therefore, a spinal cord lesion does not give rise to symptoms and signs of CN abnormalities.
- CN abnormalities plus ipsilateral appendicular motor or sensory deficits is consistent with a supranuclear lesion, for example, stroke.
- CN abnormalities plus contralateral, appendicular, motor, or sensory deficits imply a brainstem lesion, for example, stroke or tumor.
- Unilateral CNs V–VIII dysfunction plus contralateral appendicular motor or sensory deficit is indicative of a cerebellopontine angle lesion, such as a tumor.
- Unilateral CNs IX–XI dysfunction without appendicular deficit is seen in foramen jugular lesions, such as a tumor.
- Unilateral abnormality of CNs III, IV, V, and VI is suggestive of cavernous sinus lesion, for example, thrombosis.
- Unilateral abnormality of CNs IX, XI, and XII is indicative of bulbar palsy, for example, stroke.

Examining CN I: Olfactory Nerve—Sense of Smell

Is it necessary to screen CN I routinely? The answer is no. Most neurologists rarely test this nerve; it is typically only tested if the patient complains of a problem. I usually ask patients whether they have difficulty with smell or taste. When checking smell, do each nostril separately by closing the other. Any scent can be used to test this nerve, but the stimulus should be nonirritating.

Some Clinical Hints

- Anosmia is the inability to recognize scent, and *hyposmia* is diminishment of smell.
- The sense of smell diminishes with increasing age.
- The most common causes of bilateral anosmia/hyposmia are the common cold and trauma to the nose and head.
- Neurological diseases that are associated with hyposmia include Parkinson's disease, dementia, and vitamin B_{12} deficiency.
- Consider a subfrontal tumor in cases of unilateral anosmia.
- Hyposmia is commonly associated with a taste problem.
- The odor of ammonia is recognized through the trigeminal nerve (CN V); therefore, the patient who has no sense of smell, including to ammonia, should be considered to have a functional disorder (conversion).

Examination of the Eye: Examining CNs II–IV, VI

The examination includes the following checks:

- Eyelids.
- Pupils.
- Visual acuity (VA).
- VF.
- Eye movements.
- Fundi.

The examination of the eyes begins by sitting or standing in front of the patient (except when checking the pupils). Note any asymmetry of the eye globe or the presence of droopy eyelids (ptosis).

If Ptosis Is Found, What Does It Mean?

- Isolated, fixed, unilateral ptosis is usually congenital or because of old eye trauma.
- Elderly individuals may have droopy eyelids because of laxity of eyelid muscles.
- Ptosis with an abnormality of pupils is seen in patients with Horner's syndrome or CN III nerve palsy.
- Fluctuating, unilateral, or bilateral ptosis is suggestive of myasthenia gravis.
- Do not mistake ptosis from eye closure weakness in Bell's palsy.

Make the Following Observations When Checking Pupils

A. Any asymmetry of size or anisocoria.
B. Any asymmetry to the direct and consensual light reflex.
C. Any irregularity of pupillary border.
D. Check pupillary reaction to accommodation.
E. Do the swinging-flashlight test by shifting between two eyes rapidly and repeatedly to see if one pupil remains dilated as compared to the other.

Remember: The afferent pathway for pupillary light reflex is the optic nerve (CN II), and for the accommodation is the frontal lobes, but the efferent pathway for both are the parasympathetic fibers of the CN III. Examine the pupil in a semidark room and do not stand in front of the patient; have the patient fixate the eyes on a distant object while you shine the light obliquely at the pupils.

Common Pupillary Abnormalities

A. Anisocoria up to 2 mm in an awake and normal person is a normal variant. In an unconsciousness patient, it should be considered abnormal until proven otherwise.
B. Elderly individuals usually have smaller pupils.
C. **Marcus-Gunn (M-G)** pupil, or afferent pupillary defect, is when one pupil does not constrict as compared with the other eye when you swing the light. M-G

pupil is indicative of an optic nerve (CN II) lesion anterior to the chiasm such as optic neuritis. M-G pupil is always unilateral.

D. **Horner's syndrome** consists of miosis, ptosis, and anhydrosis. Horner's syndrome can arise from any lesion from the hypothalamus to the superior cervical ganglion in the neck, and is commonly seen in neck pathologies. Try to localize the lesion by doing a cocaine-and-amphetamine test to differentiate a first-order neuron from a third-order neuron.
E. **Adie's pupil** is a common finding and is seen in young, healthy women. One eye is dilated and has poor reaction to direct light but is better to accommodation. Some patients may have hyporeflexia (knee jerk) on the same side (Adie–Holmes syndrome).
F. **Argyll–Robertson pupils** are small and bilateral, with poor reaction to direct light but react to accommodation. Argyll–Robertson pupils are caused by a midbrain lesion, and are seen in syphilitic tabes and diabetes.

Visual Acuity

Check visual acuity (VA) in a well-lighted room. Always ask the patient whether he or she wears glasses; if so, test VA while patient wears their glasses (correction). I use a near vision chart 14 in. from the patient. Check VA of each eye separately. Decreased VA with correction is seen in any ocular pathology and CN II lesion.

Visual Field

There are different confrontation techniques when doing a visual field (VF) evaluation, and neurologists have strong opinions about their techniques. The important point is to sit about one arm length from the patient, and make sure the patient fixates the eyes. It is best to check each eye separately. Bilateral finger moving is good to detect **visual inattention**. Make sure your hands are apart, out of your field, and about 30 cm above eye level. Finger counting (one eye at a time) is probably the easiest and more accurate confrontation technique for a VF evaluation. It is difficult to perform a VF assessment in an uncooperative or lethargic patient. In this case, check blink reflex to brisk threat. VF is divided to nasal and temporal vertically from the patient's point of view. The VF defect is **homonymous** when the same part of the field is affected: If this exactly matches, it is called **congruous**, and if it does not match, it is called **incongruous**.

Some common VF defects include:

A. Tunnel vision is generally indicative of nonorganic disease.
B. Bitemporal hemianopia is caused by a chiasmatic lesion.
C. Homonymous quadrantopia is caused by a temporoparietal lobe lesion.
D. Homonymous hemianopia when **incongruous** is indicative of an optic tract lesion; when it is **congruous**, it is suggestive of a lesion behind the lateral geniculate body; and when there is **macular sparing**, this is suggestive of an occipital cortex lesion.

Caveat: If VF defect is limited to one eye, consider ocular, retinal, optic nerve lesion, or conversion disroder. If bilateral, the lesion is at or behind the chiasm or bilateral anterior to chiasm.

Fundi

Fundoscopic examination should be done in all patients presenting with neurological complaints. Dim the light and sit or stand in front of the patient. Check the right eye while holding the ophthalmoscope with the right hand, and check the left eye with the left hand. Ask the patient to fixate the eye on one spot on the wall, and then approach the eye from the side at about a 15° angle. During the fundoscopy, check the eye for retinal problems, blood vessel abnormalities, and the optic discs. You need to know some normal variants, for example, normal pigmentation on the disc edge or nasal blurriness and temporal pallor of the discs. From a neurological viewpoint, it is important to distinguish papilledema from optic neuritis.

Remember: If you look at the disc and see the disc margin well but the patient cannot see (decreased VA), the patient most likely has retrobulbar optic neuritis. If the patient cannot see (decreased VA) and you cannot see the disc margin, consider optic neuritis or papillitis. If you cannot see the disc margin, but the patient sees well, you are probably dealing with papilledema. Optic neuritis or retrobulbar optic neuritis is usually unilateral, and papilledema is usually bilateral.

Eye Movements: CNs III, IV, and VI

When checking eye movements or extraocular eye movements (EOMs), stay about one arm's length from the patient to avoid strain on convergence. Ask the patient to follow your finger or penlight with the eyes, without moving the head. You may hold the patient's chin gently with the other hand. Move your finger slowly upward, downward, to the left, and then to the right. A routine check for saccadic vs. pursirt vergence is necessary. In the unconscious patient and in the patient suspected of having supranuclear palsy or ocular myopathy (fixed ophthalmoplegia), EOMs can be assessed by oculocephalic ("doll's eyes") or oculovestibular (caloric) reflexes.

When You Are Checking EOMs, Note Whether:

A. Both eyes are aligned at rest or deviated (conjugated or dysconjugated).
B. There are any spontaneous movements of the eyes (nystagmus).
C. One or multiple cranial nerves are affected.
D. Patient complains of diplopia.
E. Existence of ptosis.
F. There is vergence near triad: convergence, accommodation, papillary constriction.

Situations From Which Eye Movement Abnormalities May Arise

A. From a lesion affecting supranuclear gaze centers, which includes the frontal lobes, occipital lobes, and cerebellovestibular pathway: **stroke**, **progressive supranuclear palsy**, **Parkinson's disease**.
B. From a brainstem lesion affecting CNs III, IV, and VI nuclei: **stroke**, **brainstem glioma**.
C. From a brainstem lesion affecting internuclear (CNs III, IV, and VI) connections by involving the medial longitudinal fasciculus, known as **internuclear ophthalmoplegia**: **multiple sclerosis**, **stroke**, **brainstem glioma**.
D. From a lesion affecting cranial nerves: **compressive CN III palsy**, **diabetic ophthalmoplegia**, **ophthalmoplegic migraine**.
E. From a neuromuscular disorder: **ocular myasthenia gravis**.
F. From primary eye muscle disease: **myotonic muscular dystrophy**, **oculopharyngeal muscular dystrophy**, **mitochondrial myopathies**.

Caveat: Diplopia is the prime symptom of many acquired EOM disorders. Supranuclear and internuclear lesions, and primary ocular myopathies, however, usually do not manifest as diplopia. Diplopia is maximum in the direction of paretic muscle. Horizontal diplopia is a result of CN III or VI nerve dysfunction and vertical is a result of CNs III and IV.

Some Points About Nystagmus

A. Nystagmus is classified according to the direction of the fast component.
B. A few beats of unsustained (transient) jerky eye movements on extreme horizontal gaze is not abnormal.
C. When you are checking for nystagmus, move your finger slowly, and briefly hold your finger in four directions, as you do for EOMs. Be sure the patient is able to see your finger with both eyes. Hold your finger at about a 45° angle from the eye.
D. Isolated (without any associated neurological signs), acquired vertical, or horizontal nystagmus is usually drug induced, as by antiepileptic drugs.
E. Nystagmus could be physiological or caused by an inner ear disorder (vestibulopathy), brainstem and cerebellar lesions, or retinal disease (inability to fixate).
F. Horizontal nystagmus is common. Vertical nystagmus, if not drug-induced, is the result of a brainstem or posterior fossa lesion.
G. Vestibular (peripheral) nystagmus is differentiated from brainstem (central) by being unsustained, fatigable, associated with vertigo and nausea, and reduced by fixation.
H. Multidirectional nystagmus could be caused by drugs, alcohol, or a posterior fossa lesion.
I. Dissociated or ataxic nystagmus is seen when there is palsy of adduction on one eye and nystagmus on abduction of the eye. This is often referred to as internuclear ophthalmoplegia. If bilateral and occurs in a young patient, multiple sclerosis is highly suspected.

Interpretation of Some Common EOM Abnormalities

A. Horizontal gaze palsy. The patient looks away from the paralyzed side but is looking toward the site of lesion. Gaze palsy is correctable by the doll's eye maneuver or caloric reflex. This is commonly seen in hemisphere stroke.
B. Disconjugate gaze palsy is seen in a brainstem (pontine) lesion, and the eye does not move by the doll's eye maneuver.
C. Upward or downward gaze palsy is usually a result of a pontomesencephalic lesion.
D. Supranuclear palsy as seen in progressive supranuclear palsy and Parkinson's disease. The eyes move with the caloric test (eyes move by reflex induction and not voluntarily).
E. Isolated cranial nerve palsy could be because of diabetes, migraine, vasculitis, neuritis, aneurysm, or trauma.
F. Bilateral internuclear ophthalmoplegia is because of a medial longitudinal fasciculus lesion. Consider multiple sclerosis or pontine glioma in a young patient and brainstem stroke in the elderly.

EXAMINING THE FACE: CNS V AND VII

Clinical Presentation: Facial Numbness and Drooping Face

CN V: Trigeminal Nerve

HOW TO EXAMINE

1. **Motor:** Muscles of mastication—resist to jaw opening or closing. Feel the contraction of the masseter and temporalis muscle while the patient is clenching the teeth.
2. **Jaw jerk:** Have the patient open the mouth slightly and relax the chin. Place your finger on the chin and tap your finger gently with a percussion hammer. Most normal individuals have no jaw jerk. Increased, or "brisk," jaw jerk is seen in an upper motor neuron lesion, with localization of the lesion above the foramen magnum.
3. **Corneal reflex (CR):** I do not routinely check this reflex. I do a CR check on patients with Bell's palsy, comatose patients, or in patients suspected to have brainstem or cavernous sinus lesion. The afferent limb of this reflex is supplied by CN V and the efferent limb by CN VII.

   How to do the corneal reflex. Do CR with a cotton wisp and not a Q-tip or paper. Explain to the patient what you are going to do; it is best to demonstrate by touching the patient's face with cotton. Touch the edge of the cornea while the patient is looking to the other side, or you can touch the bottom of the cornea while the patient is looking up. You can check CR by blowing air onto the eye (this is a particularly useful technique in comatose patients and/or

patients unable to keep their eyes open). Note an ipsilateral and contralateral eye blink, and ask the patient whether the sensations of both corneal touches were the same or different.

Remember: Do not touch the cornea too briskly because you will get a reflex blink response. It is important that you touch the cornea and not the sclera, because you may not get a response (common mistake by students). The corneal reflex is decreased or absent if the patient is wearing contact lenses.

Interpretation: When CR is absent bilaterally, consider a trigeminal nerve (CN V) or a pontine lesion; if it is absent unilaterally, a facial nerve or cerebellopontine lesion.

4. **Sensory:** Sensation of the face is by the trigeminal nerve (CN V) V1, V2, and V3 branches. Start by checking light touch first, then with pinprick, so the patient can become familiar. If there is a sensory loss, try to see if it follows any branch distribution. I check temperature if there is a definite defect in light touch and pinprick. Sensation at the angle of the jaw is not mediated by the trigeminal nerve.

   Interpretation:

   a. Sensory loss in the distribution of a single branch—V1: herpes, cavernous sinus thrombosis; V2: trauma; V3: basal tumor or meningitis.
   b. Sensory loss in the distribution of all branches: geniculate ganglion, sensory root or nucleus lesion, for example, basilar meningitis or pontine lesion.
   c. Sensory loss of light touch only: sensory root lesion.
   d. Sensory loss of pain and temperature: brainstem lesion.
   e. Sensory loss in the distribution of V2 or V3: metastasis.
   f. Sensory loss around the mouth: syringomyelia.

Facial Nerve: CN VII

You Need to Know That the Facial Nerve:

1. Controls the muscles of facial expression (you do not have to know their names).
2. Controls the tensor tympani and stapedius muscles.
3. Controls taste of the anterior two-thirds of the tongue.
4. Controls salivation and lacrimation.

How to Examine

a. Look at the patient's face and note if there is any asymmetry between the nasolabial folds, forehead wrinkles, blinking, or smiling.
b. Ask the patient to show the teeth, whistle, or wrinkle their forehead and again look for asymmetry.
c. Gently check eye resistance of closure muscles. Note if there is weakness of the lower face and forehead muscles on the same side. Bell's phenomenon is when the eyes roll up while the patient is trying to close the eyes. The sensory portion of the facial nerve supplies the external auditory canal up to the tragus of the ear.

d. Testing the sense of taste is not routinely performed. When the patient complains of lack of taste, check each side of the anterior two-thirds of the tongue and the posterior one-third separately with normal saline and sugar solution.

Some clinical hints: Slight facial asymmetry without facial weakness is insignificant; similarly, asymmetry that disappears on voluntary expression or smiling is also insignificant. A flat face in Parkinson's disease is not indicative of a facial nerve lesion. **Facial nerves pull down the eyelids and close the eyes; CN III, on the other hand, keeps the eyes open**. Therefore, ptosis is not because of a facial nerve lesion.

Interpretation

A. Lower facial and forehead muscle weakness is consistent with **lower motor neuron** (LMN) weakness:
   1. Isolated unilateral LMN facial weakness: Bell's palsy.
   2. Bilateral LMN weakness: sarcoidosis, Lyme disease neuropathy, Guillain-Barré syndrome.

B. Lower facial muscle weakness with relative preservation of the forehead muscles is consistent with **upper motor neuron** (UMN) weakness:
   1. UMN weakness plus ipsilateral, appendicular neurological deficit: supratentorial lesion, for example, stroke or tumor.
   2. UMN weakness plus contralateral appendicular neurological deficit: brainstem lesion, pontine.

C. Bilateral UMN weakness with dysarthria, dysphagia, inappropriate laughing and crying: corticobulbar tract lesion or pseudobulbar palsy, for example, bilateral strokes.

Examining Hearing and the Vestibular System: CN VIII

Examine Hearing

1. Examine the ear canals by otoscope.
2. Note if the patient has any hearing impairment or complains of hearing problems with normal conversation.
3. The most simple and quickest way to check hearing is rub your fingers at the front of each ear while covering the other ear.
4. If you find any hearing defect, then proceed with **Rinne's** and **Weber's** tests.
5. Rinne's test is done to compare bone conduction (BC) from air conduction (AC). Place the tuning fork (512 Hz) over the mastoid firmly until the vibration noise disappears, and then, place the tuning fork in front of the ear. Normally, the patient should still hear the humming.
6. Weber's test: Place the tuning fork over the head vertex and ask the patient if he or she hears humming equally in the two ears; normally, this is equal. In patients with conductive deafness, Weber is lateralized to the deaf ear.

INTERPRETATION

1. **Conductive hearing loss:** BC>AC, and Weber is lateralized to the deaf side. This is commonly seen in middle ear disease or with a buildup of ear wax.
2. **Sensorineural hearing loss:** AC>BC, but BC>AC in the other ear. This is seen in many conditions such as Ménière's disease, meningitis, cerebellopontine lesions, or brainstem disease.
3. When you find hearing loss for the first time, formal audiological testing is mandatory.

Examine the Vestibular System

1. Ask the patient whether he or she experiences dizziness while you are testing eye movements and note the presence of nystagmus.
2. If the patient presents with acute vertigo, you want to now whether the vertigo is because of inner ear (vestibulopathy) disease or a brainstem lesion, and then you may proceed with the head-tilt test (Nylen-Barany maneuver or Hallpike's test).

What to Do

a. Check eye movements for nystagmus when the patient is sitting on a table.
b. Then, have the patient lie down and hang the head from the table, then turn the head to the left, and then to the right, and later in a sitting position and look for nystagmus and vertigo in each position. If the patient develops vertigo and nystagmus immediately, consider a brainstem lesion. If vertigo and nystagmus develop after a delay and fatigue, consider an inner ear disorder.

Caveat: The caloric test in a conscious patient is best performed in a laboratory, because the patient may develop severe dizziness or nausea. In a conscious patient, you can irrigate the ear with room-temperature water (instead of ice-cold water). You are checking for fast component or nystagmus. With cold irrigation, it is directed to the opposite to the side of stimulation. Warm-water nystagmus is directed toward the side of stimulation. In an unconscious (comatose) patient, you are checking for slow tonic eye deviation, whereas ice-cold water irrigation moves the eyes toward the side of stimulation.

Examining the Mouth: CNs IX, X, and XII

In practice, the motor portion of CNs IX and X are usually tested. CN XII is purely motor. You are examining the tongue, pharynx, and larynx.

Examining the Tongue

1. Inspect the tongue for atrophy and fasciculation.
2. Then, ask the patient to protrude the tongue and note any tongue deviation.
3. Ask the patient to protrude the tongue and move it side to side and note for asymmetry of movement. Ask the patient to push the tongue into each cheek, one side at a time.

Common Mistakes

Small, tremor-like movements of the tongue on protrusion should not be mistaken for fasciculation. Fasciculation occurs when the tongue is resting in the mouth. In patients with unilateral facial muscle weakness, the tongue appears to be deviated. Do not mistake this for CN XII lesion. This can be corrected by lifting up the weak facial muscle.

Interpretation

A. In an LMN lesion, the tongue deviates toward the side of the lesion, and in a UMN lesion, the tongue deviates away from the side of the lesion and is often associated with hemiparesis.
B. Bilateral LMN lesions present with tongue weakness and are often associated with tongue atrophy and fasciculation.
C. Bilateral UMN lesions present with tongue weakness and are often associated with hyperactive gag reflex and labile affect (pseudobulbar palsy).

Examining the Pharynx

A. Ask the patient to open the mouth and note the position of the uvula spontaneously and/or by saying "ah" and note the movement of the soft palate and uvula.
B. I check the gag reflex when a patient has dysarthria or dysphagia. For the gag reflex, touch the pharyngeal wall with a cotton applicator and note symmetry of palate movements and movements of the uvula. Ask the patient about any difference of sensation between the sides. The afferent arm of the gag reflex is CN IX and efferent is CN X.

Interpretation

A. Uvula moves to one side: CN X lesion.
B. Absence of gag reflex is seen in LMN lesion.
C. Hyperactive gag reflex is seen in UMN lesions.

Examining the Larynx

A. Ask the patient to cough and drink a glass of water.
B. For direct vocal cord function, ear, nose, and throat consultation is required.

Interpretation

A. Poor cough is usually seen in vocal cord palsy.
B. Unilateral recurrent laryngeal nerve palsy (branch of vagus: CN X) presents with hoarseness and is commonly seen after thyroid surgery.
C. Dysphagia followed by cough (choking) is seen in CN X palsy.
D. Dysarthria, dysphagia, hoarseness, Horner's syndrome, and contralateral sensory loss with ipsilateral cerebellar dysfunction are indicative of brainstem lesion (lateral medullary syndrome).

Examining the Shoulders and Neck: CN XI

CN XI, or the spinal accessory nerve, has branches from the medulla and cervical spinal roots of C2–C4, and innervates the sternomastoid and the trapezius muscles.

Examination

1. Simply look at the neck for sternomastoid and trapezius muscle wasting and fasciculation or shoulder drops.
2. Ask the patient to shrug the shoulders: Check the resistance against your pushing down on the shoulders, and note any asymmetry. For the sternomastoid, ask the patient to hold his or her neck against your push to the right, and then the left jaw angles (temperomandibular joint). Note the strength and bulk of the sternomastoid muscles, and observe any asymmetry.

INTERPRETATION

- Ipsilateral weakness of the trapezius and sternomastoid muscles is indicative of peripheral CN XI palsy. If this is associated with ninth and tenth nerve palsy, consider foramen jugular lesion.
- Weakness of the sternomastoid on one side and trapezius on the other side is seen in ipsilateral UMN lesion.
- Unilateral inability to shrug is because of a contralateral UMN lesion.
- Bilateral weakness and atrophy of sternomastoid muscles is usually seen in myotonic muscular dystrophy, fascioscapulohumeral muscular dystrophy, or motor neuron disease.
- Ipsilateral weakness of the trapezius (inability to shrug) and hemiparesis is suggestive of internal capsule infarction in the distribution of the anterior cerebral artery.
- Unilateral sternomastoid weakness is rare and usually is posttraumatic.

Sensory Examination

SENSORY MODALITIES

- Pain and temperature (extroceptive).
- Vibration, joint position sense, light touch (proprioceptive).
- Stereognosis, graphesthesia, two-point discrimination, double-simultaneous stimulation (higher cortical sensory).

ANATOMY

Pain and temperature sense travel through the spinothalamic tract and cross at the spinal cord level, whereas proprioceptive signals travel through the posterior column and cross at the medulla. Higher cortical sensory is the primary function of the parietal lobes.

General Considerations

- The sensory system should be screened in all patients.
- The sensory examination needs concentration and patience by both the examiner and examinee.
- The sensory examination should be done in an organized manner.
- You need to educate and, if necessary, demonstrate to the patient what you are going to do and what response you are expecting from the patient.
- Start the sensory testing by doing light touch, vibration, and joint position sense first, because they are less disturbing and you are assessing the patient's reliability.
- Ensure that you are comparing the sensory function between left/right and distal/proximal.
- Start the sensory testing from an abnormal area, moving toward the normal area.
- Sensory examination is complementary to the motor system.
- By doing sensory testing, you need to establish whether the deficit is in the distribution of one nerve or multiple nerves or root; whether the sensory deficit is symmetric, or asymmetric or distal versus proximal; and, most importantly whether the deficit is segmental (level).
- Most often, the patient has mapped the sensory deficit for you. Your job, therefore, is to confirm the sensory loss or dispute it.

Examination

1. **Light touch.** Use a small piece of cotton or, alternatively, a fingertip. You must dab the skin and not rub the skin. Explain to the patient when an area of the body is touched to say "yes." Do this while the patient's eyes are closed. You can quantitate the test comparing between touch and nontouch. Give a few seconds between each touch. The area of abnormality can be mapped.
2. **Vibration.** Use a 128-Hz tuning fork. Demonstrate to the patient (by placing the fork over the chin or forehead) to be sure that the patient understands that the patient has to report "buzzing" or "humming" and not the sense of being touched by the fork. Ask the patient to close the eyes, and place the tuning fork over a bony prominence or over the ball of the large toe or fingers. Start distally and move proximally. However, if distally normal, you do not have to move proximally. Determine the threshold by perceiving vibration to the lowest intensity. Ask the patient to report to you when he or she no longer feels vibration and compare the patient's perceptions with your own. You can objectively test vibration by comparing buzzing to touch feeling.
3, **Joint position sense.** The joint position sense can be performed in several ways:
    a. Moving toes or fingers up and down. Demonstrate to the patient what you are doing while the patient's eyes are open. Ask the patient to close the eyes and hold the big toe between your fingers from the side, and stabilize the joint with the other hand. Start with large movements to small movements, until errors are made by the patient. The test can be objective by assessing the degree of joint movements.
    b. If joint movements are not possible, or difficult to assess, the easy way to test joint position is to ask the patient to extend the arms to the side and bring the index fingers of both hands together when the eyes are open or closed.

c. The fourth digit is the most sensitive joint to detect subtle joint position sense deficit.
d. **Romberg test.** This test is easier to do when you are testing the station and gait. Ask the patient to stand up, put the feet together, and place the arm in front of the face. Ask the patient to close the eyes; if the patient falls when the eyes are closed, the Romberg test is considered positive. The patient should not have significant weakness or vestibular dysfunction.

Remember: Stand by or behind the patient so you can catch the patient in case the patient falls. The Romberg test assesses posterior column function. You cannot perform the Romberg test if the patient cannot stand without assistance.

Hint: The easiest way to check posterior column function instead of standard vibration and joint position testing is to do **directional scratch test:** With tip of a blunt object (broken tongue blade) randomly stroke a 2-cm-long scratch over palm and midsole, and ask patient to tell you the direction of the scratch.

4. **Pinprick.** Use a safety pin. Explain to the patient and demonstrate what you are going to do (sharp versus dull, symmetry). Try to establish the threshold to the least-intensity stimulus. Start from an abnormal area and move toward a more normal area. Similarly, begin distally and move proximally to assess the distribution. You assess the difference between sharp and dull objectively. The pinprick examination can map out the sensory loss.
5. **Temperature.** Temperature testing is not done routinely. Most neurologists check temperature sensation when the patient reports an abnormality or in suspected special disease (syringomyelia). You can informally check coldness by using the metal part of your percussion hammer and compare it to the rubber head of the hammer (warmer). Formally, the temperature is tested with two tubes filled, one with cold and one with warm water. Dry the tubes before testing. **Some neurologists suggest doing the temperature test instead of pinprick, because it is painless and gives you the same information.**
6. **Double simultaneous stimulation.** Demonstrate to the patient what you are going to do and what answer you are expecting. Ask the patient to close the eyes and randomly touch different parts of the body with a cotton ball or the tip of your finger, one spot at a time or two different spots simultaneously. Abnormal double simultaneous stimulation is suggestive of a nondominant parietal lobe lesion. Other modalities of higher cortical sensory are covered on p. 6.

SOME CLINICAL HINTS:

1. Try to memorize sensory loss in the distribution of median, ulnar, radial, and axillary nerves in the upper extremity, and lateral femoral cutaneous, femoral, sciatic, and peroneal nerves in the lower extremities.
2. Try to memorize the following anatomical landmarks for segmental sensory level: shoulder pad = C4, nipple = T4, umbilicus = T10, groin = L1.
3. A sensory deficit can be seen in any lesion affecting a single peripheral nerve to the parietal lobe and even psychogenic (hyperventilation). To localize the site of the problem, combine the sensory abnormalities with the rest of the neurological findings.

EXAMINING THE MOTOR SYSTEM: STRENGTH, MUSCLE TONE, BULK, AND REFLEXES

Clinical Presentation: Muscle Weakness and Wasting

When approaching the patient with weakness you need to establish:

a. The muscles are weak objectively and not just fatigued.
b. The onset, course, and distribution of weakness.
c. Whether the weakness is because of a UMN or LMN lesion and/or nonorganic (functional).

   A. LMN weakness: normal or decreased muscle tone, hypo- or areflexia, atrophy, fasciculation, with or without sensory deficit.
   B. UMN weakness: extensors in the upper extremities and flexors in the lower extremities, hypo- or hypertonia, hyperreflexia, clonus, and the presence of pathological reflexes.
   C. Functional weakness: nonanatomical, erratic (give-away) weakness, discrepancy between voluntary use of muscles and when tested directly, normal reflexes, tone, and sensory examination.

The Medical Research Council Scale is commonly used to demonstrate the degree of weakness by manual muscle testing.

MRC Scale	
5	Normal
4	Moderate movement against resistance
3	Mild movement against resistance
2	Movement when gravity is eliminated
1	Trace of movement
0	No movement

Consider the Following Factors That Affect Strength Testing

- Limb pain because of soft tissue, bone, or joint disease.
- Position of the limb. Test the muscle when the limb is in the mid position and not when it is completely flexed or extended (locked position).

Interpretation

Muscle weakness should be interpreted in the context of muscle tone, bulk, and reflexes, as well as other associated neurological signs.

Muscle Tone

Tone is increased resistance by passive movements of the limb at the joint level. Tone examination is often neglected, and this is partly because of the fact that the patient does not complain of a tone problem.

Tone in the upper extremities is checked at the wrist and elbow joints, and for the lower extremities at the knee level. Try to relax the joint, and then check the tone.

Interpretation

A. Normal tone.
B. Decreased tone: mild = hypotonia; severe = flaccid.
C. Increased tone:
    1. **Spasticity:** increased tone throughout range of motion, and then there is a sudden release (catch). Seen in UMN lesion. Spasticity is velocity dependent (sudden release).
    2. **Rigidity:** increased tone throughout the range of motion. If intermittent and ratchet-like, is called cogwheel rigidity, which is seen in extrapyramidal diseases such as Parkinson's disease. Rigidity is not velocity dependent (continuous).
    3. **Paratonia or gegenhalten:** increased tone appears when the patient opposes the movement of a limb. Seen in a bifrontal lobe lesion and diffuse encephalopathy.
    4. **Myotonia:** delay in muscle relaxation after the muscle is activated, either spontaneously (e.g., handgrip myotonia) or induced by percussion (percussion myotonia). Seen typically in myotonic muscular dystrophy.
    5. **Dystonia:** contraction of agonist and antagonist muscle producing sustained abnormal limb posture. Seen in extrapyramidal disorders.

Muscle Atrophy and Fasciculation

Muscle atrophy and fasciculation (twitching of muscle fascicle) is commonly seen in a LMN lesion such as in motor neuron diseases, radiculopathy, or chronic polyneuropathies. Consider muscular dystrophy when there is generalized muscle wasting without fasciculations. Disuse atrophy is seen after stroke and when a limb is casted.

Caveat: Fasciculations without muscle atrophy or without association of other lower motor neuron signs may be benign (physiologic) or drug-induced (cholinergics). In obese individuals, fasciculation is difficult to detect. This is similar in newborns (check hands, pectoralis, or tongue muscles). Hands in the elderly (senile hands) may appear to have intrinsic muscles wasting, but strength (grip) is good when tested.

Clinical Hints

Subtle unilateral weakness because of an UMN lesion can be detected by the following testing:

- **Pronator drift sign:** Ask the patient to hold the arms out in front with the palms up and fingers open, and close the eyes. Downward drifting of the arms with pronation of the hand indicates weakness because of UMN.

- **Test strength of the wrist extensors.** Weakness of these muscles is seen early in the course of a UMN lesion.
- **Ask the patient to rapidly tap the fingers together.** Slowness or clumsiness is indicative of an early UMN lesion. This sign, however, should be interpreted within the context of the clinical history.
- **Foot-circling sign:** For subtle weakness of distal lower extremity because of UMN lesion, the patient is unable or does a clumsy job when asked to circle the foot.
- **Forearm-rolling test:** The affected forearm cannot roll around the other.

Reflexes

In practice, there are four groups of reflexes: muscle stretch reflexes, superficial reflexes, corticobulbar reflexes, and pathological reflexes.

Some General Rules When Testing Reflexes:

- The seated position is best for obtaining reflexes; abdominal reflexes, cremasteric, and Babinski's reflex are better done in the supine position.
- Feel the tendon for localization or tenderness before tapping.
- Relax the joint before tapping.
- Swing your hammerhead to tap, not just touch, the tendon. The speed of the hammerhead is important.
- The response to tapping may be jerking of the limb, twitching of corresponding muscles, or feeling the tendon twitch under your finger.
- Listen for the sound of the taps, because true absence of reflexes has a dull sound.
- Always check reflexes simultaneously between two sides to establish symmetry.
- Hyper- or hyporeflexia is clinically significant when either are associated with other neurological signs if they are asymmetric.
- Bilateral absence of brachioradialis or ankle jerks in an asymptomatic patient often has no clinical significance.
- Unilateral absence of ankle jerks is consistent with an S1 root lesion.
- Do "reinforcement" before concluding that the reflex is absent.
- Asymmetry of reflexes is significant when it is reproducible.
- Remember, absence of ankle jerks after age 60 can be normal.

Superficial Reflexes

Superficial reflexes are elicited by stroking the skin (abdominals, cremasteric, plantar) or mucous membranes (gag, corneal). The most important reflex in this group that has to be checked in all patients with a neurological presentation is the **plantar** response. The majority of superficial reflexes are polysynaptic and affected by a segmental (root, nerve) lesion, as well as suprasegmental (cortical, brainstem) lesions.

Plantar Reflexes

The plantar reflex is best obtained when the patient is supine. Hold the ankle with the other hand. Explain to the patient what you are going to do. Stroke the lateral border of the foot across to the pad of the foot with a blunt object such as a key or broken tongue blade and observe the following responses:

- All toes flex = flexor plantar response. This is normal.
- Extension of the big toe and spreading of the other toes = extensor plantar response or Babinski's sign. This is abnormal.
- Extension of the big toe only = "toe sign," in other words, upgoing toe. This is abnormal.
- Dorsiflexion of the foot, flexion at the knee, and flexion at the hip = triple-flexor response. This is abnormal.
- Nonstereotype flexion of the foot and knee = withdraw response. This is normal.
- No movement = no response

Interpretation

- Flexor plantar response is normal.
- No response is seen in some normal individuals or in patients with severe weakness or neuropathy.
- Babinski's sign, extensor toe sign, and stereotyped triple-flexor response are abnormal, and indicative of a UMN lesion involving the pyramidal tract from the L2 level of the spinal cord to the cerebral cortex.

Caveat: If the patient is sensitive (ticklish), you can reduce the withdrawal response by repeated plantar reflex (some patients will adapt). Use less pressure and stroke the lateral aspect of the sole without crossing the pad of the foot and note big toe movement. If you do not succeed, use an alternate stimuli such as stroking the lateral aspect of the foot or checking for Chaddock's sign, or gently prick the dorsum of the big toe (Bing's sign).

Clinical hints: Absence of Babinski's sign does not rule out a UMN lesion, particularly in the acute stage (stroke or acute spinal cord injury). Presence of Babinski's sign without any other UMN sign should be interpreted with caution. Extensor plantar response is not always seen in UMN conditions. If one side clearly is flexor and other side is equivocal or silent, the latter should be considered abnormal, if clinically relevant. Dystonic extensor toe posture seen without plantar stimulation, this seen in extrapyramidal disorders.

Corticobulbar Reflexes

These reflexes (jaw jerk, snout, rooting, sucking) are mediated through the corticobulbar tract. They are clinically significant when they are hyperactive,

indicating a bilateral UMN lesion. For example, in patients suspected of having a UMN lesion, a brisk jaw jerk indicates that the lesion is above the foramen magnum, most likely at or above the pontine level.

Common mistake: Tapping the chin or mouth too hard is not only disturbing but may produce a false positive hyperactive response. For the jaw jerk and the snout, place your index finger of the left hand on the chin and mouth, and tap gently.

Pathological Reflexes

These reflexes are commonly known as the frontal release signs (grasp, glabeller, or palmomental). These signs are primitive, and their presence is indicative of bifrontal lobe lesions or a diffuse CNS insult. Bilateral Hoffman's and Tromner's signs, however, are elicited in some normal individuals, but the asymmetry of the responses may be more significant. A positive glabellar (Meyerson's) reflex is commonly seen in Parkinson's disease. A galbellar reflex is induced by gently tapping (hammer or finger) the glabellar nerve. The reflex is positive when the patient continues to blink each time you tap.

Examination of Gait

When possible, gait should be tested in all patients, because the gait is a function of the motor sensory, vestibular, visual, and cerebellar systems.

For adequate gait testing, about 20 ft of walking distance is necessary. It is best that the patient be barefooted. You should be able to see the arms and legs (use a hospital gown, underwear, or pants rolled up to the knees) before asking the patient to walk. With females, appropriate clothing is essential.

Examination

1. Ask the patient to walk as usual. Note whether the gait is broad-based, symmetric/asymmetric, or if the patient's arms swing or not.
2. Ask the patient to walk on toes, heels, and, then, heel-to-toe (demonstrate). Heel-to-toe is also known as tandem gait.
3. You may examine the patient for Romberg's test as previously described when you are checking the gait.

Interpretation of Your Findings

- Patient has difficulty initiating walk—**gait apraxia:** consider normal pressure hydrocephalus.
- Patient has broad-based, uncoordinated gait and staggers—**ataxia:** cerebellar disease.

- Short-stepped gait, stooped posture, with little or no arm swing: Parkinson's disease, drug-induced Parkinsonism.
- Patient has short-stepped gait, erect posture, with arm swing—**marche à petit pas:** consider diffuse cerebrovascular disease.
- Legs crossed over—**scissoring:** bilateral UMN lesions, cerebral palsy.
- Marked pelvic and shoulder rotation—**waddling:** myopathy, muscular dystrophy.
- Bizarre, inconsistent, worse when watched—**functional:** psychogenic.
- Patient has pain and limping—**antalgic gait:** acute lumbar disc herniation.
- On leg swing out and adduction—**circumduction:** hemiparesis because of UMN lesion.
- Patient lifts one knee high and slaps the feet—**steppage:** foot drop, peroneal palsy, or L5 root lesion.
- Patient is unable to walk on heels—**foot drop:** same as above.
- Nonneurological gait difficulties: consider arthritis or orthopedic problems.

Testing Coordination and Cerebellar Function: How to Test and What It Means

Upper Extremity

Finger-to-nose. This is best done in the sitting position. Stay in front of the patient and hold your index finger about one arm's length from the patient. Ask the patient to touch your finger with his or her index finger, then to the tip of the nose. Make sure the patient's arm is extended. You may move your target finger in different directions. The task is to be done slowly at first, and then faster. Do one arm at a time.

1. Patient accurately performs the task: **normal**.
2. Patient develops tremor when approaching the target (your finger or his nose)—**intention tremor**: cerebellar disease.
3. Patient misses the target: past-pointing or **dysmetria**.

Rapid alternating movements. Demonstrate to the patient (finger tapping, hand tapping, etc.), first in slow motion, and then faster. Do one hand at a time.

> If the patient is able to do the task with normal rate and rhythm—**normal**.
> If movements are irregular, disorganized, dysrhythmic, uncoordinated—**dysdiadochokinesia**.

Rebound test. Ask the patient to flex at the elbow and resist you as you try to extend the arm. Place your other hand on the patients shoulder and turn the patient's head toward the other direction, to shield the patient's face and eyes. Let the arm go suddenly. Do one side at a time.

> Arm returns to steadying position—**normal**.
> Arm oscillates several time then stays—**abnormal rebound**.

Alternatively, you can do this test by asking the patient to straighten the arms in the air and resist as you push them down, and then you let the arms go. Again, if the arms bounce before they stop, it is abnormal.

LOWER EXTREMITY

Head-to-toe test. This is done when testing gait. You need about 20 ft of walking space. Ask the patient to walk heel-to-toe in a straight line.

If the patient falls to one side or becomes unsteady, this is abnormal—**ataxia**.

Heel-to-shin test. For best results, this test needs to be done in the supine position. Ask the patient to lift one leg up and place the heel on the shin of the other leg, and then smoothly rub it along the shin down toward the toes. The test is abnormal if movement is irregular or the heel falls off the leg. Make sure the patient rubs the heel on the shin, and not the pad of the foot. Repeat the test several times, if doubtful.

Foot or heel tapping test. Similar to fast alternating movements in the upper extremity.

TRUNK

Ask the patient to sit up from the supine position without using the hands.

If the patient falls to one side—**truncal ataxia**.

Ask the patient to stand on his feet.

If the patient becomes unsteady and has a tendency to fall—**truncal ataxia**.

In both tasks, the eyes should remain open.

Interpretation

- Unilateral or bilateral limb ataxia or incoordination is seen in a cerebellar hemisphere lesion.
- Truncal ataxia is indicative of midline or super vermis pathology.
- Other signs of cerebellar dysfunction include nystagmus, tremor, dysarthric speech, and, less frequently, hypotonia and pendular reflexes.

Caveats

- Severe loss of joint position sense can produce incoordination, commonly known as "sensory ataxia." The difference between cerebellar ataxia and sensory ataxia is that the latter is worse with eye closing. In sensory ataxia, the outstretched hand (when eyes are closed) may show abnormal, uncoordinated movement known as "pseudoathetosis."
- Patient with motor weakness in one side (e.g., stroke) may show clumsiness on finger-to-nose or heel-to-shin testing. This is not because of a cerebellar disorder;

the movement is slow, but not irregular. You can correct the coordination by holding the weak limb, and then ask the patient to do the task.

- Patients with Parkinson's disease or essential tremor may perform finger-to-nose poorly, and this is because of rigidity and tremor, respectively.
- A normal finger-to-nose test does not rule out a cerebellar lesion, because in a midline cerebellar lesion, this task can be preserved.

2
Neurological Formulation

Neurological formulation is simply your summary of findings from the patient's history and neurological examination. By gathering this information you should be able to formulate:

- What the most likely anatomic site is: *Where is the lesion?*
- What the most likely etiological cause is: *What is the lesion?*
- The differential diagnosis.
- What diagnostic tests to order to support your opinion or excluding other possibilities.
- What therapeutic measure(s) to be planned.

Formulation is best based on solid neurological history and findings. You always have the option to reformulate according to the patient's neurological evolution and/or when the laboratory data become available.

MODIFIED NEUROLOGICAL EXAMINATION

Obtaining a detailed neurological history and examination in all patients is not always possible, and at times impractical and unnecessary. The general rule is, however, you should complete the neurological examination and history as much as possible.

A. A *focused examination* is done primarily on return patients, unless the neurological history suggests a recent change. Selective examination should be based on choice and not negligence.
B. You may choose to begin with a focused history and examination with a new patient by addressing the chief complaint first, and then complete the rest of the examination later. The best example is a patient presenting with back pain radiating to the leg, when you may start by examining the back and lower extremities, and then explore other areas.
C. Comatose patients often require a limited, but specific neurologic examination.
D. Neurological examination in the pediatric age group differs from adults, and will not be discussed.
E. In agitated and uncooperative patients, neurological examination is sometimes best achieved by careful observation of the patient's behavior.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

3
Some Neurological Signs of Interest

MARCUS-GUNN PUPIL

Marcus-Gunn pupil, or relative afferent pupillary defect, is evident when one pupil paradoxically dilates to direct light when the flashlight swings between two eyes. Marcus-Gunn pupil is always unilateral and is seen in an optic nerve lesion anterior to the optic chiasm, such as retrobulbar optic neuritis or optic neuritis (papillitis), and rarely seen in compressive optic nerve lesions or retinal degeneration.

LHERMITTE'S SIGN

Lhermitte's sign, or "barber's chair sign," is an electrical shock or paresthesia-like feeling running down the back when the neck is flexed or extended. This sign is usually seen in a cervical cord lesion such as demyelinating disease (multiple sclerosis), cervical spondylotic myelopathy, or cervical spinal cord tumor.

BRUDZINSKI'S AND KERNIG'S SIGNS

To test for these two signs, it is best to have the patient lie supine. Brudzinski's sign is present when the knees and hips flex during passive neck flexion. Kernig's sign is present when there is resistance to straightening the flexed knee. The positivity of these signs is indicative of meningeal irritation (meningitis, subarachnoid hemorrhage). These signs are not evident if the neck stiffness is not caused by meningeal irritation such as cervical spondylosis, Parkinsonism, or cervical lymphadenopathy. Unilateral Kernig's sign may be seen in lumbar radiculopathy.

TINEL'S SIGN

This sign presents when a gentle percussion at the wrist produces paresthesias in the distribution of the sensory branches of the median nerve. This sign

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

is often elicited in carpal tunnel syndrome, but also seen in other entrapment neuropathies (cubital tunnel syndrome).

FROMENT'S SIGN

This sign is present when pulling a piece of paper (or index card) between the thumb and index finger. The sign is positive when thumb flexion is seen. This occurs because the adductor pollicis muscle is weak and the long flexor is compensating. Froment's sign can be detected in an early ulnar nerve lesion at the elbow, either unilaterally or bilaterally.

STRAIGHT LEG-RAISING TEST (LASEGUE)

With the patient in a supine position, lift the leg while holding the heel. Limitation of leg raise to 45–60°is suggestive of nerve root compression. Tightness of the hamstring muscles is not indicative of a radiculopathy.

PATRICK'S SIGN

This sign differentiates sacroiliac joint disease from lumbosacral radiculopathy. The sign is positive when placing the heel (symptomatic side) on the opposite knee and pressing the leg down and out causes pain in the hip region, indicating sacroiliac joint disease. The sign is negative in radiculopathy.

PRONATOR DRIFT SIGN

The patient's hands are outstretched in front of the face with the palms facing upward and eyes closed. Drift of the arm with pronation of the hand is indicative of motor weakness because of an upper motor neuron lesion. This sign is checked with the weakness is subtle.

HOOVER'S SIGN

With the patient in the supine position, place your hand under the heel of one leg, and ask the patient to raise the other leg against resistance. Normally, you feel pressure on your hand. Hoover's sign is positive when you do not feel pressure. This is a good sign to check when you suspect the weakness is because of hysteric conversion.

TODD'S PARALYSIS

Transient hemiparesis after focal motor seizure (postictal weakness). This sign is often mistaken for stroke or transient ischemic attack.

HALLPIKE'S TEST

Hallpike's sign, or head-tilt test, is done for evaluation of positional vertigo. Hang the head of the patient gently from the bed, and while supporting the head, move the head to the right and then to the left, and note the presence or absence of nystagmus. Normally there is no nystagmus. In inner ear disease, the patient develops vertigo and nystagmus after a few seconds, which is fatigable. In a central lesion, nystagmus occurs immediately and does not fatigue.

PUPILLARY SPARING

Pupillary sparing is retention of pupillary reaction to light in cases of third cranial nerve palsy (ptosis and eye movement abnormalities). Pupillary sparing is seen in ischemic third nerve palsy such as in diabetics and hypertensive patients. It is less likely seen in compressive third nerve palsies such as aneurysm or tumors.

FISHER'S SIGN

Repeatedly tapping the middle joint of thumb with the tip of index finger causes other fingers to move synchronously. The absence of movement of other fingers is indicative of a corticospinal tract lesion.

FOREARM-ROLLING TEST

This test involves rapidly rolling one arm around the other. With a subtle pyramidal tract lesion, one arm does not roll around the other.

FOOT TAPPING SIGN

This sign checks the speed of foot tapping. Slowness of foot tapping may be as useful or even more useful a sign as Babinski sign for upper motor neuron dysfunction.

PARADOXICAL PTOSIS

In patients with unilateral ptosis, the contralateral lid may droop when you're closing or lifting the ptotic lid with your finger. This phenomenon (Herring Phenomenon) is often seen in ocular myasthenia gravis.

4

Approach to the Patient with Suspected Hysteric Conversion

HYSTERIC CONVERSION

Definition: neurological symptoms (complaint) and signs (deficits) that are nonorganic, resulting from psychological factors.

When to Suspect

- Motor or sensory symptoms that are not accompanied by more objective deficit (e.g., reflex changes, muscle tone, or atrophy).
- The pattern of motor or sensory deficit is not anatomical.
- The patient is not concerned about the deficits.
- The patient has secondary gain motive.
- The patient has a history of personality disorder or multiple hospitalizations.

In Suspect Cases, Remember That:

- Bizarre, purely subjective complaints neither exclude an organic lesion nor support psychogenic (functional) disorder. The best example is multiple sclerosis, where presentation can be subjective and multifocal (non-anatomical) and appears to be bizarre.
- Ruling out of neurological disease is important, but this does not establish the diagnosis of hysteric conversion. The diagnosis should be based not only on exclusion of organic disorder, but also should be supported by **positive signs** of conversion.
- Avoid ordering extensive, expensive, and invasive tests in suspected cases, and do not subject the patient to unnecessary surgical procedures or drug therapy that cause harm or habit.
- When examining a patient with suspected hysteria, try not to embarrass or threaten the patient.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Even if the history and examination are strongly suggestive of hysteria, this does not mean that the patient does not have a superimposed organic neurological problem. The patient is asking for help but in an inappropriate way (exaggerating the deficit).

Common Mistakes

- Premature diagnosis of hysteria.
- Diagnosis of hysteria simply based on the patient's behavior and personality.
- Diagnosis of hysteria on the basis of inconsistency of sensory examination, which is a subjective test for both the patient and the examiner.
- Multiple sclerosis, transient ischemic attacks, small stroke, seizures, sleep and movement disorders, and myasthenia gravis are a few examples that are commonly mistaken as hysteria.

There are many cases in practice thought to be hysteria that later are diagnosed as multiple sclerosis by magnetic resonance imaging.

Common Positive Neurological Signs of Hysteric Conversion

- **Memory loss:** You find that all cognitive function tests are normal, except memory loss.
- **Unconsciousness:** You find the neurological examination to be normal; the patient does not strike the face when the arms are held up and dropped suddenly over the face.
- **Blindness:** You find a normal eye examination (pupils, visual field, discs, and optokinetic nystagmus).
- **Deafness:** You find the patient responds to loud noise and/or music.
- **Anosmia:** You find the patient is anosmic, even to ammonia and alcohol (these chemicals irritate the trigeminal nerve in the mucosa and not the olfactory nerve).
- **Gait:** You witness the patient staggering, reeling commonly known as astasia-abasia, but the patient does not fall, and holds the rail, furniture, wall, or examiner to prevent a fall and self-injury.
- **Sensory deficit:** You find inconsistent and patchy sensory loss; ipsilateral sensory loss to all modalities including special sense (vision, hearing, smell); midline sensory deficits (splitting the midline) to all modalities; vibration lateralized when you place a tuning fork over the forehead, chin, or sternal bone (vibration always transmits to both sides in these bones); and the patient responds to a yes-and-no test when you touch the patient each time (the patient is supposed to pause because the patient claims that he or she feels nothing).

- **Weakness:** In the patient presenting with upper extremity weakness, you find irregular or "give-away" weakness, where the patient gives you maximum strength briefly; the weakness often improves with the examiner's encouragement; you may find the patient contracts the antagonist muscle instead; you may find there is no significant asymmetry of strength when both arms are simultaneously checked; and for lower extremity weakness, you may find a positive Hoover's sign.

Hint: It may be most useful to indirectly test the patient (observe the patient's action when the patient believes he or she is not being tested) or misdirect the patient's attention (e.g., checking strength while you are talking with the patient about an unrelated subject).

5
Neuroanatomy of Localization

Localization in neurology requires knowledge of neuroanatomy, but for the most part, detailed neuroanatomy is not necessary. The following is a recommended outline of neuroanatomy that is helpful for most common neurological encounters.

You need to know:

- Blood supply and circulation of the cerebral cortex, internal capsule, basal ganglia, cerebellum, and brainstem (carotids and vertebrobasilar system).
- Function of different lobes of the cerebral cortex (left and right side).
- Anatomy of internal capsule.
- Brainstem nuclei and tracts.
- Eye movement control system.
- Pupillary control system.
- Visual field pathway.
- Autonomic control of the bladder.
- Common root innervation of cervical, lumbosacral, and sacral spinal cord.
- Anatomy of the motor unit (anterior horn cell, peripheral nerve, neuromuscular junction, and muscle).

Other Important Neuroanatomical Structures

Long Tracts

Long tracts are the prime structures of clinical neurology. These tracts cross; therefore, they lateralize neurological symptoms and signs. Remember the following tracts:

- **Corticospinal tract (descending).** This tract connects the cerebral cortex (precentral gyrus) to the spinal cord (lateral and ventral), and passes through the anterior third of the internal capsule and crosses at the lower medulla.
- **Corticobulbar tract (descending).** This tract connects the cerebral cortex (precentral gyrus) to the brainstem nuclei and passes through the genu of the

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

internal capsule. Crosses before connection to the nuclei.

- **Spinothalamic tract (ascending).** This tract connects the skin (conducting pain and temperature) to the cerebral cortex (postcentral gyrus) of the contralateral side by synapsing to the third-order neuron in the ventralis posterolateralis of the thalamus. This tract passes through the posterior limb of the internal capsule.
- **Dorsal column (lemniscal) tract (ascending).** This tract connects the skin, joint, and tendon sensation (proprioception) to the contralateral cerebral cortex (postcentral gyrus). This tract also travels through the posterior limb of the internal capsule and synapses in the ventralis posterolateralis of the thalamus before ending in the cortex.
- **Visual tract (straight).** This tract connects the retina to the occipital lobe and crosses at the optic chiasm.

Medial Longitudinal Fasciculus

This tract connects the nuclei of cranial nerves III, IV, and VI, functions as efferent to the lateral vestibular nuclei, and descends to the spinal cord. This structure has an important role in lateral eye movements.

Common Sensory Dermatomes

Shoulder pads = C4, nipple = T4, umblicus = T10, groin = L1, big toe = L5, thumb = C6, little finger = C8.

6
Some Common Neurological Constructs

1. **Subcortical (e.g., internal capsule) versus cortical lesion:**
   - Motor weakness (paresis) usually affects the face, arm, and leg equally.
   - Primary sensory deficits (paresthesia, numbness) are more prominent because of involvement of the posterior limb of the internal capsule. Cortical lesions affect higher cortical sensory, manifesting as agnosia, agraphesthesia, and impairment of double simultaneous stimulation.
   - Visual field defects are more common because visual tracts travel through the posterior limb of the internal capsule. Occipital lobe lesions produce visual field defect, but usually are not associated with motor or sensory deficit.
   - Speech dysarthria is more common. A dominant cortical lesion produces aphasia and apraxia.
2. **Gerstmann's syndrome.** This syndrome is commonly caused by a stroke affecting the left angular and supramarginal gyrus and clinically characterized by finger agnosia, left–right disorientation, agraphia, and dyscalculia.
3. **Watershed or border zone infarcts.** Watershed areas are end-artery zones between superficial branches of a major cortical blood supply such as between the anterior cerebral artery–middle cerebral artery and middle cerebral artery–posterior cerebral artery. Bilateral watershed infarcts occur in severe hypotension or hypoxia, and unilateral watershed infarcts occur when the affected artery is stenotic, and collateral circulation cannot compensate in a hypotensive episode.
4. **Internuclear ophthalmoplegia.** Internuclear ophthalmoplegia (INO) is characterized by weakness of the adducting eye (site of lesion) and monocular nystagmus (dissociated nystagmus) of the abducting eye. Although INO can be seen in many brainstem lesions, bilateral INO (medial longitudinal fasciculus lesion) in young adults is most consistent with multiple sclerosis, and in the elderly it is due to ischemic brainstem insults. Patients with INO usually do not complain of blurred or double vision.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

5. **Wallenberg's, or lateral medullary, syndrome.** This syndrome is caused by infarction of the medulla and cerebellum due to occlusion of the vertebral or posterior inferior cerebellar artery (PICA) and is characterized by:
   - Ipsilateral (to the site of the lesion) decreased pain and temperature of the face.
   - Dysarthria, dysphagia, and ipsilateral decrease of palatal, pharyngeal, and vocal cord movements.
   - Ipsilateral Horner's syndrome.
   - Ipsilateral dystaxia.
   - Hiccups, vertigo, nausea.
   - Contralateral body sensory loss (pain and temperature).
6. **Bilateral lower extremity paresis resulting from upper motor neuron lesion. This paresis could be caused by:**
   a. Spinal cord or brainstem lesion.
   b. Hemispheric lesion.
      - Bilateral frontal lobe infarction (occlusion of bilateral anterior cerebral arteries or watershed infarcts).
      - Hydrocephalus.
      - Parasagittal mass (falx meningioma).
      - Callosal lesion.
7. **The hallmarks of the brainstem lesions are:**
   - Cranial nerve dysfunction.
   - Contralateral body motor and sensory deficits (crossed deficits).
   - Cerebellar signs.
   - Gaze palsy.
   - Nystagmus.
   - Dysarthria.
   - Alteration of mental status and coma at the onset in of an acute severe brain stem lesion.
8. **Extra-axial versus intra-axial brainstem lesion.** Suspect extra-axial lesion (without compressing brainstem) when multiple cranial nerve dysfunction is not associated with motor sensory deficit or altered mental status. Acoustic neuroma, meningioma, epidermoid cyst, and aneurysm are few causes of extra-axial brainstem lesion.
9. **Pseudobulbar palsy.** Lesions involving bilateral corticobulbar tracts manifest as dysarthria, dysphagia, drooling of the mouth, and a labile affect (inappropriate laughing or crying). The bulbar muscles are weak, but they are not atrophied.

10. **Dysarthria: clumsy hand syndrome.** This condition is commonly due to a lacunar infarction in the base of the pons and sometimes the internal capsule, and is clinically characterized by dysarthria, dysphagia, hand clumsiness, and often extensor plantar response (Babinski's sign).
11. **Hallmarks of spinal cord lesions are:**
    - Sensory level deficit.
    - Bilateral or unilateral extremity weakness. Distal weakness is greater than proximal weakness.
    - Bowel or bladder dysfunction.
    - Absence of cranial nerve abnormalities.
12. **Brown-Séquard syndrome.** This syndrome is commonly due to an extramedullary lesion (spinal cord hemisection syndrome):
    - Ipsilateral (to the lesion) spastic paresis due to involvement of the lateral corticospinal tract.
    - Ipsilateral lower motor neuron weakness due to involvement of anterior horn cells or roots.
    - Ipsilateral loss of vibration and joint position sense due to involvement of the posterior column
    - Contralateral loss of pain and temperature sense due to involvement of spinothalamic tract.
13. **Conus medullaris and cauda equina syndromes.** These two syndromes are usually because of a compressive lesion (tumor, cyst) involving the spinal cord at the level of the **conus** (S3–C1), **epiconus** (L4–S2), or spinal roots at the level of the **cauda equina** (lumbosacral roots below L3):
    a. Occurrence of either syndrome in isolation is rare because of anatomical proximity.
    b. Clinically difficult to differentiate, but cauda equina has the following characteristics:
        - More gradual onset.
        - Predominantly unilateral (or bilateral but asymmetric) radicular pain.
        - More asymmetry of weakness (lower extremities).
        - More asymmetry of saddle distribution sensory loss.
        - Absence of knee and ankle jerks.
        - Sphincter or sexual dysfunction is usually less severe and occurs later.
    c. Suspect **conus medullaris** when the patient presents with bilateral lower extremity weakness, diminished or absent ankle reflexes, symmetrical saddle sensory loss, and early sphincter (bowel, bladder) or sexual dysfunction.

14. **The differences between upper and lower motor neuron weakness of the face.** The upper part of the face (forehead) has bilateral innervation from the corticobulbar tract, whereas the lower face has unilateral innervation from the contralateral corticobulbar tract. Therefore:
    - Lesions involving the facial nerve or nucleus cause ipsilateral upper (forehead) and lower facial muscle weakness (peripheral VII seventh nerve palsy).
    - Lesions involving the corticobulbar tract, above the facial nucleus, cause weakness of the contralateral lower face muscles (central VII seventh nerve palsy).
15. **Tongue deviation.** Lesion involving the nucleus of the axons of cranial nerve XII cause the tongue to deviate toward the site of the lesion. If the patient can move the tongue side to side but cannot protrude the tongue, this is because of an upper motor neuron lesion (corticobulbar tract involvement).
16. **Conditions with which cerebellar lesions are commonly associated with:**
    - Ataxia or clumsiness of the hands and legs (limb ataxia).
    - Brainstem symptoms and signs.
17. **Conditions with which lesions affecting anterior horn cells are usually associated with:**
    - Asymmetric muscle weakness, with greater involvement of distal muscle group.
    - Hypotonia.
    - Muscle atrophy and fasciculation (later stages).
    - Hyporeflexia.
    - Absence of sensory symptoms and/or deficit.
18. **Conditions which peripheral polyneuropathies present with:**
    - Predominantly symmetrical, other distal extremity symptoms (paresthesia, hyperesthesia, dysesthesia) and sensory deficit.
    - Predominantly distal muscle weakness and atrophy.
    - Hypo- or areflexia.
19. **Conditions which radiculopathies usually present with:**
    - Unilateral radicular pain or paresthesia.
    - Neck or back pain.
    - Muscle weakness and possibly atrophy in the distribution of the involved root.
    - Hypo- or areflexia.
20. **Conditions which plexopathies are associated with:**
    - Unilateral motor and sensory deficits in the distribution of more than one root and nerve.

- Muscle atrophy (later stages).
- Hypo- or areflexia.

21. **Conditions that could cause weakness and atrophy of the hand muscles could be due to:**
    - C8–-T1 radiculopathy.
    - Lower trunk brachial plexopathy.
    - Median and ulnar mononeuropathies (carpal and cubital tunnel syndromes).

For the first two conditions, always look for the presence of Horner's syndrome and sensory deficit in the medial aspect of the forearm; for the latter condition, the strength of flexor pollicis longus muscles is intact (innervated by anterior interosseus nerve).

22. **Wrist Drop**
    - Triceps and brachioradialis muscle strength are intact: **posterior interosseus mononeuropathy** with no sensory loss.
    - Wrist extensors are weak but only the triceps is spared: **radial nerve lesions** at or above the spiral groove.
    - Wrist extensors and triceps are weak: **radial nerve lesion at the axilla**.
    - Weakness of extensors, triceps and deltoid: posterior cord of the **brachial plexus**.
23. **Winging of scapula**

    A. **Because of serratus anterior weakness:**
    - Winging at rest.
    - Medically deviated scapula.
    - Winging is accentuated by flexion of the arm.

    B. **Because of trapezius weakness:**
    - Slight winging at rest.
    - Laterally deviated scapula.
    - Winging is accentuated by abduction of the arm.
    - Shoulder is lower on affected side.

24. **Foot drop.** Peroneal neuropathy versus L5 radiculopathy; weakness of ankle inversion; flexion of toes (flexor digitorum longus); and extension of great toe (extensor hallucis longus) are all suggestive of L5 radiculopathy. L5 radiculopathy is often associated with back pain, sensory loss, and absence of ankle jerk.
25. **Quadriceps weakness and atrophy.** Femoral neuropathy versus L2–L4 radiculopathy; thigh adductors are strong in pure femoral neuropathy and weak in L2–L4 radiculopathy.

26. **Postsynaptic neuromuscular junction disorder**
    - Fluctuating, asymmetric, oculobulbar, and proximal limb weakness.
    - Normal muscle tone, bulk, sensory, and reflexes.
27. **Presynaptic neuromuscular junction disorder**
    - Fluctuating, symmetric proximal limb weakness.
    - Decreased or absence of reflexes and autonomic dysfunction.
28. **Conditions with which primary muscle disease (myopathy) presents:**
    - Predominantly proximal, often symmetrical muscle weakness.
    - Normal or atrophied muscle.
    - Normal sensory examination and reflexes.

7
Neurodiagnostic Tests and Procedures

Remember the following general rules when you are ordering a diagnostic test or procedure on your patient:

1. Diagnostic procedures are a supplement or an extension of your history and physical examination, and are ordered to support your clinical impression or exclude other possibilities.
2. Diagnostic procedures should be considered on an individual basis and not routinely; not all patients with dementia need to have an electroencephalogram (EEG) or spinal tap. Each patient should be analyzed individually.
3. The clinician should be familiar with the test, knowing how it is done (explaining it to the patient), and the risks, limitations, contraindications and indications, sensitivity, and specificity.
4. Consider the potential risk(s) (invasiveness) and cost of the test. Explain these facts to the patient when necessary. For practical purposes, consider ordering the test that gives you the most information and is noninvasive. Consider ordering an invasive test when it has a high sensitivity, specificity, and is beneficial to the patient by influencing the treatment and/or outcome.
5. At times, it is necessary and justified to repeat a test. Some disease processes require time to establish their full clinical expression; repeating a test will increase its diagnostic yield, for example, repeating an EEG in the evaluation of a seizure disorder.
6. When ordering a test, provide adequate and pertinent information regarding the history and physical findings to the consultant. Be as specific as possible regarding what you are looking for.
7. It is important to be directly involved with reviewing the test. The best example is reviewing neuroimaging personally with the radiologist and discussing the case. This not only shares your knowledge, but also influences your management and enhances your communication with other services.
8. If the results of the test do not correlate with the patient's history and findings, go back, take more history, and repeat your examination; most often, you will find the answer (retrodiagnosis). Furthermore, not always does the

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

severity (or degree of abnormalities) in the test results correlate with the severity of disease (e.g., magnetic resonance imaging [MRI] findings with severity of multiple sclerosis). Incidental tests results should be handled individually (e.g., asymptomatic carotid stenosis).

9. Although diagnostic procedures influence the treatment plan, they should not be used as the sole indicator of the response to treatment (with few exceptions). Remember, you are treating the patient's problem and not the laboratory results. For example, when treating a patient with polymyositis or myasthenia gravis, the goal of therapy is to improve the patient's strength, not to address a falling serum creatine kinase level or acetylcholine receptor antibody titer. In certain clinical settings, however, the test can be used as an objective guide.
10. It is very important to discuss the results of the test and subsequent plan of action with the patient and the patient's relatives.
11. Neurological procedures are not only helpful when they are positive (abnormal), but also when they are negative (normal). For example, a negative head computed tomography (CT) scan or MRI in a patient presenting with stroke is suggestive of subcortical lacunar infarction, and a normal EEG in demented patients is suggestive of the possibility of pseudodementia.
12. The majority of neurodiagnostic procedures are performed by a technician, with few exceptions (spinal tap, needle electromyography, cerebral angiogram, myelogram, and pharmacological testing). Only the cerebral angiogram requires short-term hospital admission. Reliability of test results depends not only on the interpreter's qualifications (knowledge and experience), but also on techniques (personnel, equipment, patient's cooperation, etc.).

NEUROIMAGING TECHNIQUES

Plain X-Rays

Plain X-rays of the spine are ordered in an initial evaluation of patients presenting with spine injury, neck and back pain, or when spine metastasis is suspected. Skull films, on the other hand, are rarely performed.

CT Scan

- A CT scan is ordered to identify abnormal density, whether hypodense (dark) or hyperdense (white, bright), or isodense.
- CT scans are now available in almost all health care centers, and the CT scan is a good screening neuroimaging technique for the initial assessment of patients presenting with stroke, intracerebral and subarachnoid hemorrhage, head trauma, meningitis, dementia, hydrocephalus, and brain tumors.

- The CT scan is superior to MRI in the detection of intracerebral hemorrhage ("clotted"), particularly subarachnoid hemorrhage and calcified lesions.
- In most cases, a noncontrasted CT scan is sufficient. Consider iodinated contrast agents when an enhancing lesion (tumors, vascular malformation, metastasis, inflammatory diseases) is suspected.
- The CT scan is less sensitive and specific than an MRI is. Therefore, order an MRI if available in the following clinical situations: small central nervous system lesions (e.g., small stroke, lacune), multiple sclerosis, brain metastasis, primary brain tumors, inflammatory diseases (vasculitis, herpes encephalitis, AIDS encephalopathy), brainstem and posterior fossa lesions, pituitary tumors, temporal lobe lesions (e.g., patients with intractable complex partial seizures), spinal cord lesions, and compression.
- *CT angiography (CTA*) This technique involves rapid injection of intravenous contrast—the extracranial and intracranial cerebral arterial supplies are reconstructed three-dimensionally. This technique is useful for detecting aneurysms, dissections, and stenosis. Other contrast CT techniques include *CT perfusion imaging* and *CT angiography source images*. The latter studies show low densities in acute ischemic stroke.

Magnetic Resonance Imaging

- MRI is not only more sensitive and specific than the CT scan for detection of brain and spinal cord lesions, but it also has much higher resolution showing detailed anatomy.
- MRI is an ideal technique for assessing lesions involving the brainstem, posterior fossa, spinal cord, and sinus venous thrombosis.
- In T_1-weighted MRI, the cerebral spinal fluid has a dark appearance; in T_2-weighted MRI, the cerebral spinal fluid and eyeballs have a bright-white appearance. The T_1-weighted image shows the outline anatomy because it has better resolution, and the T_2-weighted image is good for detection of pathology.
- The contrast agent in MRI is safe and nonionic (commonly known as gadolinium). Contrast MRI is considered when an enhancing lesion is suspected or when there is disruption of the blood–brain barrier.
- MRI is rapidly replacing many neurodiagnostic tests: evoked potentials, myelogram, cisternogram, CT scan, and brain scan.
- *Perfusion MRI* is used to detect the dynamics of blood volume, and *diffusion MRI* to detect early areas of ischemia. *Diffusion-weighted MRI* can detect abnormalities caused by acute ischemia within 15–30 minutes of onset. Diffusion-weighted MRI shows hyperintense signal because of decreased water diffusion in infarcted area. All these three MRIs are now used in major stroke centers.

Some Disadvantages of MRI

- MRI is expensive and not readily available.
- The patient needs to be cooperative and lie still for the entire testing (45 minutes is average).
- Some MRI machines are not made for obese patients (>300 lb).
- Some patients require presedation because of claustrophobia.
- MRI cannot be done in patients requiring close monitoring such as comatose patients.
- MRI is contraindicated in patients with pacemakers, a metallic clip (cerebral aneurysm), cochlear implants, Harrington rods, or other metallic foreign bodies.
- Although most healthcare centers are equipped with MRI, only limited centers have 24-hour MRIs.

Myelography

Since the advancement of the CT scan and MRI, myelography is rarely utilized. A water-soluble contrast agent is injected into the subarachnoid space. A myelogram is an invasive procedure and carries some degree of risk including back pain, post-spinal tap headache, infection, and, occasionally, seizures. A myelogram is performed more in neurosurgery or orthopedic departments. In general, if an MRI is not available and you are looking for spinal root and cord compression, a myelogram followed by a CT scan is a reasonable approach.

Cerebral Arteriography

This is an invasive procedure to visualize extra- and intracranial blood vessels. Contrast agent is injected through a catheter into the femoral or brachial artery. Arteriograms have been estimated to cause approximately 1% morbidity and mortality. A cerebral angiogram is usually done in highly selected cases when CT scan or MRI provide no definite answers or a vascular lesion is suspected (vasculitis, arteriovenous malformation, etc.), arterial dissection, or when carotid endarterectomy is contemplated. An arteriogram is also used to treat or obliterate an arteriovenous malformation by injecting particles (interventional angiogram).

Magnetic Resonance Angiography

This is a noninvasive technique to visualize extra- or intracranial blood vessels. Stenosis or occlusion of blood vessels can be identified. Magnetic resonance angiography (MRA) is particularly useful for detection of arterial dissections and aneurysms larger than 3 mm in diameter. MRA is a quick, noninvasive screening test for arterial stenosis, but it is not as sensitive as a

conventional angiogram. MRA is an alternative to angiography in elderly individuals, in patients with renal failure, and in patients with an allergy to contrast agent.

For assessment of cerebral vein thrombosis, a magnetic resonance venogram is been used.

Carotid Doppler Duplex Ultrasonography

Carotid ultrasound measures the degree of carotid stenosis according to the velocity of blood flow through the blood vessel. It can differentiate between an occluded and open artery. The degree of stenosis is usually underestimated by this technique. Carotid Doppler is a very sensitive, noninvasive screen for the evaluation of carotid stenosis in patients presenting with stroke or transient ischemic attacks. Carotid Dopplers determine whether further studies are indicated (MRA or angiogram).

Transcranial Doppler

Transcranial Doppler (TCD) is an ultrasound technique that measures the blood flow and noninvasively images the velocity of cerebral circulation in the distribution of major intracranial arteries. In experienced hands, this procedure is safe, fast, and reliable. Combined duplex and TCD increases the sensitivity and specificity of the test when performed by skilled technician.

Indications

- To detect stenosis more than 65% in major intracranial arteries.
- To assess the collateral circulation of the intracranial arteries.
- To assess and monitor response to treatment of cerebral vasospasm following subarachnoid hemorrhage.
- To detect arteriovenous malformations, assess their arteries and flow, and evaluation of their obliteration following embolization (injecting particles into the arteriovenous malformation).

TCD may soon become the procedure of choice to assess suspected brain death and monitoring patients for increased intracranial pressure.

Positron Emission Tomography

Positron emission tomography (PET) is a technique that maps different anatomic regions of the brain according to their biochemical, physiological, or pharmacological characteristics. In other words, CT or MRI image the brain according to structural abnormalities, and PET images the brain according to the functional abnormalities (functional imaging). To obtain pictures by PET, radioisotopes (oxygen, carbon, etc.) are produced by a cyclotron, and then incorporated into a biological agent. Specific receptor ligands are labeled

to map specific receptor sites (cholinergic, adrenergic, serotonergic). In humans, the most commonly used agent is ^{18}F-fluoro-2-deoxy-D-glucose (commonly known as FDG). Although PET in many centers is used as a research tool, its clinical utility is increasing. FDG-PET is a safe and sensitive technique, but has limited use for the time being because of its cost, complexity of technique (requiring a cyclotron), and unavailability. The current clinical uses of PET are:

- Localization of epileptogenic focus in patients considered for surgical treatment of epilepsy (intractable).
- Differential diagnosis of dementia: differentiating Alzheimer's disease from multi-infarct dementia.
- Movement disorders: early diagnosis of Parkinson's disease, Huntington's disease, or differentiating Parkinson's disease from progressive supranuclear palsy.
- Grading primary brain tumors and choosing the sites for biopsy.
- Differentiating postirradiation brain necrosis (encephalopathy) from recurrent brain tumor (best test to differentiate these two conditions).

Single-Photon Emission CT

A single-photon emission CT (SPECT) scan measures regional cerebral blood flow, which correlates with regional cerebral metabolism. A radioisotope is tagged with a receptor-binding agent and injected intravenously. The common agent is ^{99m}Tc-hexamethylpropylene amine oxime (commonly known as HMPAO). This agent crosses the blood–brain barrier, metabolizes to a less lipophilic compound, and leaves the brain slowly; therefore, regional cerebral blood flow can be measured for the next several hours. SPECT does not need a cyclotron, and the radioisotope is commercially available. The cost of a SPECT scan is the same as a CT scan, and is more available than a PET scan. The indications for SPECT scan are the same as those of a PET scan.

Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy (MRS) provides chemical composition of abnormal tissue. It is used to differentiate a brain tumor from multiple sclerotic plaque or stroke, classify brain tumors.

ELECTROPHYSIOLOGICAL TESTS

Nerve Conduction Studies and Needle Electrode Electromyography

Although the term electromyography (EMG) is commonly used in practice, you should know that EMG actually has two components, one is **nerve conduction studies (NCS)**, and the other is **needle electrode EMG**.

You should also know that EMG is ordered to evaluate the integrity and dysfunction of the **motor unit**. The motor unit simply refers to a single motor nerve and all the muscle fibers it innervates. In broader terms, the motor unit consists of the anterior horn cell, root, plexus, peripheral nerves, neuromuscular junction, and muscle fibers (peripheral nervous system). EMG is the single most useful diagnostic test to assess diseases of the peripheral nervous system.

Methodology

A. Nerve Conduction Studies

NCS are performed either by a physician or a qualified and trained technician. Any accessible nerve can be stimulated. The NCS consist of **motor nerve conduction studies and sensory nerve conduction studies**.

For motor NCS, the nerve is stimulated by a surface electrode at different sites along the nerve (usually two sites), and the motor nerve action potential or compound motor action potential (CMAP) is recorded from a surface electrode placed over the motor point of the innervated muscle. Very rarely are needle electrodes used for stimulation or recording. The parameters that are measured are **latency** (time required for the nerve impulse from stimulation site to produce an action potential), **amplitude** (height of action potential), **morphology**, and **conduction velocity** (the velocity between the stimulating site).

The abnormalities include (same for sensory nerves) conduction block, absence of response, slowing of conduction velocity, delayed latencies, decreasing amplitude, or change in the morphology.

For **sensory nerve conduction** studies, the mixed or purely sensory nerves (sural, superficial radial) are stimulated, and sensory nerve action potentials are recorded from the nerve itself. The sensory nerve action potentials are particularly useful in evaluation of patients suspected of having peripheral polyneuropathies, focal neuropathies (e.g., carpal tunnel syndrome), plexopathy, and sensory neuronopathy (diseases affecting dorsal root ganglia).

B. Needle Electrode EMG

Methodology. The needle electrode EMG is performed only by a physician (neurologist or physiatrist). A disposable needle (commonly known as concentric) is inserted into the muscle; the muscle is evaluated during rest, and during minimal and maximal voluntary contraction. During rest, the normal muscle is quiet and does not produce any sound or waves (except when the needle is inserted at the end-plate region). Abnormal activities at rest include **fibrillation potentials** (a potential related to one single muscle fiber), **fasciculations** (potentials from several muscle fibers), **positive sharp waves** (a downward deflected waveform), and repetitive complex discharges. During

voluntary minimal contraction, the motor unit potentials (MUPs) are evaluated. The MUPs are produced by a group of muscle fibers that belong to one corresponding motor neuron. The **morphology**, **amplitude**, **duration**, **number** of phases, and **complexity** of the waveform are then assessed. Assessing of MUPs is to differentiate **neuropathic** from **myopathic** (muscle disease) disorders. Myopathic MUPs are small, short duration, and polyphasic. Neurogenic MUPs are large, long in duration, and polyphasic.

C. Other Techniques

- **Repetitive nerve stimulation.** This is a technique used when neuromuscular junction disorders such as **myasthenia gravis** or **Lambert-Eaton myasthenic syndrome** is suspected. The CMAP is recorded from distal or proximal muscle, and then the nerve is stimulated at the rate of 2 shocks per second. Gradual decrease of amplitude of CMAP is called decrement, which is considered abnormal if more than 10%. In presynaptic disorders such as myasthenic syndrome, there is significant increase of amplitude (increment) when the nerve is stimulated at a higher rate (>20 seconds) or after briefly exercising the muscle, followed by a single shock stimulation.
- **Single-fiber EMG.** This is a highly specialized technique, and time-consuming. It should be done by an experienced electromyographer. The main indication for this procedure is in myasthenia gravis when repetitive nerve stimulation and antibody measurement are inconclusive. In this technique, a pair of muscle fibers that belong to one anterior horn cell are isolated with minimal voluntary muscle contraction. The pair of muscle fibers usually fire at the same time, but in myasthenia gravis and myasthenic syndrome, they fire irregularly (known as jitter). Single-fiber EMG is highly sensitive and nonspecific. In neuromuscular diseases, neurogenic and myopathic conditions, the jitter is increased (when compared with normal).

Indications

In general, order NCS and needle electrode EMG when you suspect the patient as having motor neuron disease (amyotrophic lateral sclerosis), radiculopathy (neck and back pain), plexopathy, peripheral polyneuropathy, entrapment neuropathy (e.g., carpal tunnel syndrome, nerve injury gunshot wounds, etc.), neuromuscular junction disorders (myasthenia gravis and syndrome, botulism), or primary muscle disease (inflammatory myopathies, muscular dystrophy, metabolic myopathy, etc.).

To obtain the best results when ordering an EMG test, you should provide a pertinent history and physical findings to the electromyographer. Be as specific as possible regarding the area of concern (e.g., are you considering motor neuron disease or peripheral polyneuropathy?).

Complications and Limitations

Although needle EMG is considered to be invasive, it is a safe, relatively sensitive, and specific test and causes only minor discomfort for most patients. The majority of patients tolerate this procedure. Because disposable needles are used, the risk of infectious disease transmission is virtually nil. The sensitivity of the EMG depends on duration, stage, and severity of the suspected disease; extent of the study performed; and the knowledge and experience of the electromyographer.

Evoked Potentials

Overview

The evoked potentials (EPs) are used to assess the integrity of the sensory pathways in the central nervous system. The sensory nerve is stimulated repeatedly (100–2000 stimuli), and responses are recorded from surface electrodes placed on the spine or cerebral cortex. The computer averages the responses (averages out background noise and EEG). EPs are noninvasive and less ordered since the introduction of MRI. Abnormalities of EPs imply a lesion on the same side (side-to-side abnormalities are assessed). Specificity of EP abnormalities is less; therefore, the findings should be interpreted within the context of clinical features.

Visual EPs

Unilaterally, the retinas are stimulated by changing black-and-white checkerboard pattern (pattern-reversal stimuli), and recording electrodes are placed over the occipital head regions. The major positive wave (known as P100) occurs approximately after 100 milliseconds. Unilateral abnormality of P100 (prolonged latency) is indicative of optic nerve lesion anterior to the optic chiasm (e.g., optic neuritis). Bilateral abnormalities of P100 (delayed latency, decreased amplitude, or absence response) are suggestive of a lesion affecting the visual pathways from the retina, optic nerves anterior to the chiasm, or optic tracts behind the chiasm.

Indications

- Patients suspected of having multiple sclerosis.
- Functional visual loss.

Brainstem Auditory EPs

Unilaterally (monoaurally), auditory nerves are stimulated by constant click sound while the other ear is masked by white noise. Commonly, five waves are measured in the first 10 milliseconds (known as waves I, II, III, IV,

and V). The more reliable and stable waves are waves I, III, and V. The parameters are measured, including the absolute latencies of each wave and interpeak latencies of waves I–III, III–V, and I–V. The amplitude also is measured. Prolonged interpeak latency of III–V is suggestive of a pontomesencephalic lesion.

Indications

- Multiple sclerosis.
- Posterior fossa tumor, acoustic neuroma, cerebellopontine angle lesions.
- Confirmatory test for brain death.
- Evaluation of hearing in normal children or postmeningitis.

Somatosensory EPs

This is an extension of NCS. The peripheral nerve (median, ulnar, peroneal, or tibialis) is stimulated repeatedly, and responses are recorded from the spine (dorsal column) and somatosensory cortex (vertex head region). The responses are varied depending on the height of the patient and length of the limb.

Indications

- Multiple sclerosis.
- Subacute combined degeneration.
- Spinocerebellar degeneration, spinal cord trauma.
- Functional hemisensory loss.
- Spinal cord function monitoring during spine surgery (prime indication in recent years).

Electroencephalogram

EEG records spontaneous brain potentials by approximately 21 pairs of electrodes placed over the scalp. The electrodes are connected to each other in different ways, known as montages. The EEG is assessed during wake and resting stages as well as during activating procedures known as **hyperventilation**, **sleep**, and **photic stimulation**. The EEG is recorded as an analog on EEG paper or as digital on a disk. In special circumstances, an EEG can be recorded continuously as ambulatory cassette EEG recording and prolonged video/EEG monitoring.

You should know the normal EEG waveforms. The waveforms are separated from each other by their morphology, frequency (measured by Hertz), location, and reactivity:

- Alpha (8–13 Hz): located over parieto-occipital head regions, during wakefulness, and are enhanced by eye closing and disappear with eye opening.

- Beta (>13 Hz).
- Theta (4–7 Hz): normal during sleep, abnormal during awake.
- Delta (1–3 Hz): normal during deeper sleep, abnormal during awake.

Many EEG abnormalities are nonspecific with few exceptions. The main abnormal waves in EEG are slow waves (theta and delta during awake) and epileptiform discharges (spike and sharp waves).

Indications

A. Epilepsy

1. Differentiating epilepsy from nonepileptic events (syncope, transient ischemic attacks, etc.).
2. Help to differentiate partial from generalized epilepsy (classification).
3. Help to diagnosis specific epileptic syndrome.
   a. Hypsarrhythmia: infantile spasm.
   b. 3-Hz spike and wave discharge: absence.
   c. Generalized slow spike and wave: Lennox-Gastaut syndrome.
   d. Generalized multiple spike and wave: myoclonic epilepsy.
   e. Periodic lateralized epileptiform discharges: herpes simplex, encephalitis, acute infarct, metastasis, brain abscess.

Caveat: The most conclusive evidence of epilepsy is recording clinical seizure simultaneously with epileptic discharges in EEG (electroclinical seizure or ictal event). Most outpatient EEG recordings are recorded **interictally** (between the seizures); therefore, a normal EEG does not exclude epilepsy.

B. Status Epilepticus

In many centers, continuous EEG recording is done in patients with status epilepticus; however, EEG is particularly useful in the following:

- **Nonconvulsive status epilepticus:** absence or complex partial.
- Suspected ongoing **electrical status** (seizure): when clinical motor convulsions have stopped in patients with grand mal status.

C. Alteration of Mental State

Alteration of mental state usually produces generalized slow waves. Some metabolic encephalopathies may be associated with sharp or triphasic waves (hepatic).

Hint: If the patient is confused and disoriented, but the EEG shows only minimal slowing, suspect degenerative disorder. If the patient is less confused, but the EEG shows significant slowing and sharp waves, suspect metabolic encephalopathy (EEG is worse than patient).

D. Coma

In a comatose patient, an EEG is particularly useful in prognostication; alpha-coma, burst–suppression pattern, isoelectric, and periodic pattern are all indicative of a poor prognosis.

E. Infection

1. Herpes simplex encephalitis, periodic lateralized epileptiform discharges (sometimes need serial recordings).
2. Subacute sclerosing panencephalitis: periodic (5–8 seconds) bursts of 2–3 Hz, high-voltage slow and sharp waves, followed by a relatively flat background between them.
3. Creutzfeldt-Jakob disease: periodic, generalized, 1–2 Hz, sharp, and triphasic.
4. Waves over very low amplitude and slow background.

F. Pseudoepilepsy

In patients with suspected psychogenic seizures (pseudoepilepsy), the EEG is monitored during a clinical seizure, which can be achieved by induction of "seizure" by suggestion or by prolonged video/EEG monitoring. The latter is more reliable.

G. Epilepsy Surgery

Prolonged video/EEG monitoring is particularly useful when surgical intervention (e.g., temporal lobectomy) is considered for a patient with intractable seizures.

H. Brain Death

EEG is used as a confirmatory test for establishment of brain death. EEG is considered to be isoelectric when no activity more than 2 μV is recorded for 30 minutes. The recording should be performed according to an established protocol. Severe hypothermia, severe hypotension, and intoxication with sedative hypnotics should be excluded.

SLEEP STUDIES

Polysomnogram

A polysomnogram consists of the continuous recording of multiple biological variables (EEG, eye movements, electrocardiogram, submental and limb EMG, respiration, and finger oximetry) during nocturnal sleep. A polysomnogram is scored during awake, stage I–IV of non-rapid eye movement (nREM), and REM sleep.

Indications

- Insomnia.
- Sleep apnea.

- Narcolepsy.
- Periodic limb movements during sleep.
- Idiopathic hypersomnia.
- REM behavior sleep disorder.
- Parasomnias: sleepwalking, night terrors, nightmares.

Multiple Sleep Latency Test

The multiple sleep latency test (MSLT) is best done after an overnight polysomnogram. In this test, five 20-minute naps are measured for onset of stage one sleep every 2 hours. Sleep-onset REM also is measured. EEG, submental EMG, eye movements, electrocardiogram, and respirations are monitored. The average latency of five naps is about 10 minutes. The latency of 3–5 minutes is abnormal, and 7–8 is borderline. If one nap latency is 10 minutes or more, recording five naps are not done, and the test is terminated.

Indications

- Excessive daytime hypersomnolence.
- Narcolepsy (short multiple sleep latency test, or two or more sleep-onset REMs).

AUTONOMIC FUNCTION TESTS

Overview

Autonomic function tests are ordered to assess the integrity of unmyelinated or small myelinated peripheral nerve fibers, as these fibers are unmeasurable by conventional NCS. In some centers, autonomic function tests are done primarily for research purposes. The sympathetic nerve fibers can be stimulated by inserting a very thin needle into the peripheral nerve (e.g., peroneal). This technique is invasive and tedious, and impractical for clinical use (electroneurography). For clinical use, the ideal tests should be noninvasive, safe, reliable, simple, and reproducible.

Most autonomic laboratories (primarily academic-based) adopt batteries of tests with which they are familiar. The autonomic function tests are to evaluate the end-organ response to different maneuvers (reflex). Autonomic dysfunction generally presents with symptoms or signs related to **eyes**, **cardiovascular**, **gastrointestinal**, or **genitourinary systems**. These tests should not be ordered routinely, and only considered when there is strong indication for them. The clinician should make this judgment based on carefully undertaken history and physical examination. The following categories of tests are in use in practice:

A. **Cardiovagal heart rate response.** Beat-to-beat heart rate is monitored continuously (by Finapres or Collins monitor), and then the heart rate response to deep breathing, standing, and the Valsalva maneuver is measured.

B. **Adrenergic tests.** Beat-to-beat blood pressure is measured in response to standing, tilt, the Valsalva maneuver, sustained handgrip, or ice-cold water immersion test.
C. **Sudomotor tests.** This includes quantitative sudomotor axon reflex test, sympathetic skin response, thermoregulatory sweat test, and sweat imprint.
D. **Sympathetic skin response.** This is a simple technique, evoking unmyelimated fibers by electrical stimulation of median and peroneal nerves, and recorded from the palms and soles.

Complications and Limitations

Autonomic tests as mentioned above are safe and noninvasive. Occasionally there have been reports of syncope (during tilt) and minor local skin injuries (thermoregulatory sweat test). The Valsalva maneuver may carry some risks in elderly patients (glaucoma), and should not be performed in patients with chronic lung disease. Autonomic tests should be done as a battery (a single test is not adequate). Patients should not be dehydrated and or receiving medications that may affect the test results.

Indications

- Progressive autonomic neuropathy, diabetic neuropathy, amyloid neuropathy, immune-mediated neuropathy, pure autonomic neuropathy, porphyria, Fabry's disease, multiple-system atrophy.
- Distal small-fiber neuropathy.
- Postural tachycardia syndrome.
- Sympathetically mediated pain.
- Syncope.
- Evaluation of the response to therapy, such as in patients with diabetes, syncope, Lambert-Eaton myasthenic syndrome (response to 3,4-diaminopyridine).
- Disorders affecting sweat production.

LUMBAR PUNCTURE

Overview

Lumbar puncture (LP) is the insertion of a special needle ("atraumatic" Sprotte) into the subarachnoid space at the level of the L3–L4 or L4–L5 vertebrae for **diagnostic**, **therapeutic**, and **anesthetic** purposes. You should have established indication(s) for LP. Prior to LP, it is very important to explain the procedure to the patient and tell the patient what you are looking for. Most patients are nervous, and have heard that you are using a big needle, which may cause them to be paralyzed. Assure them the procedure is safe: you are using a long but thin needle, and it will not cause paralysis (the needle is not

going to touch the spinal cord). If you suspect the patient may have a problem with bleeding, obtain coagulation studies (prothrombin time, partial thromboplastin time, platelet count). If you suspect brain mass or increased intracranial pressure, obtain a head CT scan or MRI before LP.

Indications

A. Diagnostic

- Central nervous system infections (meningitis/encephalitis).
- Subarachnoid hemorrhage.
- Demyelinating disorders: multiple sclerosis.
- Inflammatory polyneuropathies: Guillain-Barré syndrome or chronic inflammatory demyelinating polyneuropathy.
- Paraneoplastic syndrome.
- Unexplained dementia with progressive course and acute onset.
- New onset of seizures in adults when infection is suspected.
- Vasculitis: stroke in young.
- Pseudotumor cerebri: to measure opening pressure.
- Normal pressure hydrocephalus: to predict the response to shunt.
- Myelography (with or without CT scan).

B. Therapeutic

- **Intrathecal administration:** antibiotic or antifungal agent, chemotherapy agent, antispasmatic agent, pain medication, relieving the pressure (pseudotumor).
- Blood patch: for treatment of post-LP headaches.

C. Anesthetic

- Epidural block for management of pain or during delivery.

Some technical points:

- Expose the lower back and hip so you can see and feel the area.
- Mark your anatomic landmark.
- Clean the area widely.
- Position the patient in fetal position on the left lateral decubitus.
- Position yourself comfortably and have a nurse to assist you.
- Insert the needle between the L3–L4 interspace; the needle plane should be vertical with bevel, facing up.
- Direct the needle toward the umbilicus.
- When you feel a "pop," draw the stylet and let one drop of fluid escape, and then measure pressures (always do so).
- Measure the pressure by extending the patient's legs and not while the patient is in the fetal position.

- If you are not getting fluid (dry tap), you have the following options:
  1. Insert the needle slightly deeper.
  2. Rotate the needle.
  3. Aspirate very slowly.
  4. Consider the sitting position.
  5. Ask your colleague to try.
  6. Consider fluoroscopy.
- Obtain adequate fluid and save, label, and freeze one tube (2 mL) for future reference.
- If you suspect traumatic bloody tap:
  1. Note gradual clearing from first tube to last.
  2. Bloody tap because of trauma does not clot.
  3. Centrifuge the fluid.
  4. The ratio of white blood cells to red blood cells in traumatic tap is about 1:700.
  5. Traumatic tap is not associated with high protein.

Contraindications

- Increased intracanial pressure, except in pseudotumor cerebri.
- Patients who are receiving anticoagulant or platelet count is less than 20,000/mL.
- Subcutaneous infection at the site of insertion.
- Complete spinal cord block because of mass (Froin's syndrome: extremely high cerebrospinal fluid protein).

Complications

- Iatrogenic post-LP meningitis.
- Post-LP headaches: headache on standing. Common in women. Occurs in about 10–15% of cases. The onset is usually three to five days after LP, and resolves spontaneously. In chronic post-LP headache, blood patch gives immediate and dramatic relief.
- Bleeding: spinal epidural, subdural, or subarachnoid.
- Transient unilateral sixth cranial nerve palsy.
- Backache.
- Occasionally, transient lower limb paresthesia.
- Brain herniation; in case of supra or subtentorial mass.

BIOPSIES

A. Brain Biopsy

Brain biopsy can be considered when all noninvasive methods fail to provide the diagnosis, and is particularly considered in younger patients when the

diagnosis not only may influence the treatment, but also helps in the prognosis. Most brain biopsies are done by stereotaxis technique. The complications include hemorrhage, infection, and neurological deficit.

Brain biopsy is indicated in the diagnosis of primary brain tumor and/or single metastasis, infections such as herpes simplex encephalitis, and degenerative disorders of the brain such as suspected cases of Creutzfeldt-Jakob disease.

The ideal site for brain biopsy is when the lesion can be localized by imaging techniques, is superficial and accessible, and does not involve a critical brain region (language zone) or the brainstem.

B. Leptomeningeal Biopsy

The leptomeningeal biopsy is performed in highly suspected cases of isolated central nervous system vasculitis or carcinomatous meningitis.

C. Temporal Artery Biopsy

A temporal artery biopsy is done for the diagnosis of suspected cases of temporal arteritis.

D. Muscle Biopsy

Muscle biopsy is done openly (by incision) or by a special needle (needle biopsy). The procedure is done in an outpatient setting under local anesthesia. Muscle biopsy has minimal risks such as infection, bruising, and discomfort. The muscle to be biopsied should be selected from weak, but not wasted, muscles. Muscle biopsy is generally indicated for any myogenic (myopathy) disease such as polymyositis, metabolic/mitochondrial myopathies, muscular dystrophies, or congenital myopathies.

E. Nerve Biopsy

A nerve biopsy is commonly performed from the sural nerve, behind the lateral malleolus. The procedure is done under local anesthesia. It is important to keep in mind that when considering a nerve biopsy, you must be certain that the specimen is going to be processed adequately in a reliable and experienced laboratory. A nerve biopsy is indicated in unexplained peripheral polyneuropathies when all diagnostic tests have been exhausted.

The main indications for a nerve biopsy are vasculitic neuropathies, amyloid neuropathy, inflammatory neuropathy, leprosy, and storage neuropathies (metachromatic leukodystrophy). The side effects of a nerve biopsy are hypersensitivity and discomfort at the site of the biopsy, which often resolves spontaneously after several weeks.

OTHER DIAGNOSTIC TESTS

A. Forearm Ischemic Exercise Test

This test is considered in patients presenting with postexertional myalgia, particularly when McArdle's disease (myophosphorylase deficiency) or deaminase deficiency is suspected. The baseline serum lactate and ammonia are measured. By placing a blood pressure cuff and raising the pressure above systolic level, ischemia is induced. The patient then exercises by continuously squeezing a handgrip ergometer for approximately 1–2 minutes. The blood pressure cuff is then released, and blood from the antecubital vein is dawn. The serum lactate and ammonia are measured 0, 3, 5, 10, and 15 minutes post-exercise. No rise in lactate or ammonia when compared with baseline and a control subject is considered abnormal. This test now can be done without ischemia, but with longer exercise (e.g., 5–10 min), which makes it more tolerated.

B. Pharmacological Tests

1. Edrophonium (Tensilon) Test

The edrophonium, or Tensilon, test is done for the diagnosis of suspected cases of myasthenia gravis. The test is usually done in an outpatient setting. For elderly patients and/or patients with history of chronic lung disease or cardiac history, it is recommended the test be done as an inpatient or in the emergency room with continuous monitoring of vital signs. The total dose of Tensilon is 10 mg/mL. A test dose of 2 mg is given, and then the rest (8 mg) as whole or in increments. Before doing a Tensilon test, it is crucial to establish a clear objective muscle weakness (e.g., ptosis, eye muscle weakness, dysarthria). False positive results occur when a clear objective deficit cannot be established (e.g., fatigue).

2. Cocaine Test

This test is done for localization of the site of a lesion in the case of Horner's syndrome. One drop of 10% cocaine is instilled into each eye, followed by another drop 1 minute later. Normally, both eyes should be dilated in about 45 minutes. The pupil with loss of sympathetic innervation (Horner's) will not dilate. To localize further, one drop of 1% hydroxyamphetamine (Paredrine test) is instilled. Normal pupils will not dilate; the side of Horner's dilates, which indicates first- or second-order neuron as the site of the lesion.

II Common Neurological Conditions

8
Cerebrovascular Accidents

STROKE

Initial Assessment on Arrival to Emergency Room

- Stabilize the vital signs and monitor the heart and blood pressure (BP).
- Start intravenous line and administer intravenous fluid (25% normal saline at a rate of 50–75 mL/hour).
- Draw blood and send to the lab for complete blood count, prothrombin time, partial thromboplastin time, platelet, chemistry profile, cardiac enzymes, and arterial blood gases.
- Obtain a 12-lead electrocardiogram.
- Obtain brief, but pertinent, medical and neurological history, and establish the onset and duration of stroke.
- Do a 5-minute neurological examination focusing on mental status, pupillary function, stiff neck, and focal neurological deficits.
- Consult the neurologist and stroke team at your hospital.
- Obtain head computed tomography (CT) scan without contrast to exclude hemorrhagic stroke or mass lesion.

Therapeutic Considerations

- Provide oxygen if patient is hypoxic.
- Keep patient's head flat in bed (0–15°) for first 24–48 hours, and 30° thereafter.
- Consider thrombolytic agent: tissue plasminogen activator or alteplase. Should be used in selected patients. Consult neurologist, stroke specialist, or emergency room physician if you have doubt. Remember, this agent should be given within 3 hours of ischemic stroke. Protocol guidelines should be followed strictly. Obtain consent. The dose is 0.9 mg/kg, 10% given over 1 minute, and remainder over 1 hour. Monitor vital signs. Repeat head CT in 24 hours.
- If seizure occurs, treat with antiepileptic drug.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Avoid glucose-containing fluid: If blood glucose is elevated, try to normalize in 6 hours, because high glucose is associated with poor outcome. Bring down the blood glucose between 200 and 250 mg/dL.

What You Should Do About Elevated BP

You should know that:

1. In acute stroke, systemic arterial BP is often elevated; most patients with stroke are known to be hypertensive or have newly discovered hypertension at the time of stroke. In the majority of cases, however, his elevation is transient and self-limited, and this is because of autonomic overactivity in the acute setting.
2. In acute stroke, there is partial or complete loss of autoregulation in the ischemic brain; therefore, regional cerebral blood flow is dependent on the arterial BP to maintain adequate perfusion.
3. In acute stroke, the peri-infarct "penumbra" zone is ischemic but has functional neural tissue, and rapid lowering BP causes further ischemia—"deteriorating stroke."

What to Do

- Generally, no treatment is necessary for mildly to moderately elevated BP.
- When you decide to treat increased BP, do it slowly while monitoring neurological function.
- In a known hypertensive patient with mild elevation of BP, you may consider holding antihypertensive drug temporarily.
- Check BP several times before treatment.

Consider treating hypertension in acute stroke in the following circumstances: hemorrhagic stroke, BP more than 220/120 mmHg or mean arterial BP more than 130 mmHg, patient with papilledema, patient with dissecting aneurysm, patient with end-organ dysfunction (cardiac ischemia or renal failure), or patient who is considered for tissue plasminogen activator treatment.

- The target reduction for BP for the severely hypertensive patient is 185/105–110 mmHg.
- Use an antihypertensive drug that is easy to titrate, can be used parenterally, does not lower the BP rapidly, and does not raise intracranial pressure.
- The two most commonly used agents are an angiotensin-converting enzyme inhibitor, enalapril, and a β-blocker (labetalol). The calcium antagonist (nifedipine) is not recommended. Labetalol is probably the drug of choice. Administer a loading dose of 10 mg intravenously, and double the dose every 20 minutes thereafter, for a total of 300 mg, twice a day, and then 10 mg every 8 hours if needed. This drug cannot be used in diabetics and asthmatics.

Further Assessment, Workup, and Management

What You Should Do After Initial Assessment

- Admit the patient to the ward or stroke unit if available, with close observation of vital signs and neurological function.
- Obtain more history: onset of stroke, duration, preceding symptoms (such as headache, transient ischemic attacks [TIAs], or transient visual loss), time of occurrence of stroke, evolution of stroke.
- Establish the medical history of risk factors: previous stroke or TIAs, hypertension, diabetes, heart disease, peripheral vascular disease, high cholesterol, history of drug abuse, or smoking.
- Complete your examination with special attention to:

a. **Neurovascular examination.**
   - Record BP: both arms on separate occasions.
   - Examine peripheral pulses.
   - Listen for presence of carotid and/or subclavicular bruits.
   - Listen to the heart for murmur or arrhythmia.
   - Examine the fundi for papilledema, retinopathy, or retinal emboli.

b. **Neurological examination.** Complete your neurological examination and try to answer the following questions:
   - **Where is the stroke?** Cortical versus subcortical, brainstem, or cerebellum.
   - **What blood supply to the brain is affected?** Anterior circulation versus posterior circulation, large blood vessel versus small, penetrating blood vessels.
   - **Is stroke ischemic or hemorrhagic?**
   - **Which part of brain is involved and which part is spared?**

Stroke Workup

- The following systems are checked in patients presenting with brain attack (stroke, Table 1):

1. **Brain:** This incude head non-contrast head CT scan and multimodality of MRIs. In selected patients you may consider ordering EEG (if seizure is suspected) or PET and SPECT (suspect other etiology).
2. **Heart:** This includes electrocardiogram, chest X-ray, 2D echocardiogram. In selected patients you may consider ordering trans-esophageal echocardiogram (TEE), cardiac scan, Holter monitoring.
3. **Blood vessel:** This includes carotid ultrasound, carotid duplex, and MRA. In selected patients you may consider ordering TCD, catheter angiography.
4. **Blood:** This includes CBC, chemistry, PT, PTT, lipid profile, ESR, RPR, B12, CRP, homocysteine level. In selected patients you may consider ordering proteins C and S, lupus anticoagulant, factor V Leiden.

Table 1
Stroke/Transient Ischemic Attacks Workup

Organ	Routine	Selective
Brain	CT	MRI, EEG, PET, SPECT
Heart	EKG, CXR, echocardiogram	Holter monitor, cardiac scan, thalium scan, transesophageal echocardiogram
Blood vessel	Carotid Doppler	MRA/cerebral angiogram
Blood	CBC, chemistry, PT, PTT, lipids, ESR, FTA, urine analysis	Protein C&S, ATIII, antiphospholipid antibodies, homocystein, other coagulation factors

ATIII, antithrombin III; CBC, complete blood count; C&S, culture and sensitivity; CXR, chest X-ray; CT, computed tomography; EEG, electroencephalogram; EKG, electrocardiogram; ESR, erythrocyte sedimentation rate; FTA, fluorescent treponemal antibody; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging; PET, positron emission tomography; PT, prothrombin time; PTT, partial prothrombin time; SPECT, single-photon emission computed tomography.

- **A few words about head CT scan in acute stroke:** In acute stroke or TIAs, non-contrast CT scan is ordered because you want to exclude hemorrhage. The sensitivity of CT scan to detect ischemia is higher after 24–72 hours. Within 6 hours of stroke following signs suggest of infarction:
- Low density in distribution of major blood vessel
- Loss of Sylvian fissure
- Hyperdense MCA sign
- Loss of gray-white matter differentiation in the basal ganglia
- Effacement of cortical sulci

Further Therapeutic Interventions

a. **Ischemic brain edema.** Cerebral edema after ischemic stroke peaks about 48–72 hours after the onset. Cerebral edema with raised intercranial pressure and transtentorial herniation is one of the common causes of acute mortality in the stroke patient. Ischemic brain edema begins as cytotoxic and changes to vasogenic. Management should include the following:

   - Supplement O_2.
   - Elevate the head of the bed to 30°.
   - Intubate and hyperventilate briefly (to a pO_2 of 25–30 mmHg, if necessary [Glasgow Coma Scale sore of <8]).
   - Use hyperosmolar agents: manitol (20%) 1 g/kg over 30 minutes, followed by 0.25 g/kg every 4–6 hours. Follow up with clinical response and serum osmolality. Hyportonic saline treatment is discussed in Chapter 15.

- Try furosemide intravenously, 40 mg, twice a day.
- Fluid restriction.
- Use of steroids has not been established.
- Surgical intervention such as hemicraniectomy and decompression in large cerebellar infarct, hemorrhage, or evacuating large clot in an accessible location can be life saving.

b. **Prevent and treat complications of stroke.** Stroke complications include aspiration pneumonia, urinary tract infection, deep venous thrombosis, decubiti, hyperglycemia, and cardiac arrhythmia.
c. **Modify risk factors.** Risk factors include hypertension, diabetes, cardiac disease, cardiac arrhythmia, high cholesterol, and cigarette smoking.
d. **Physical, occupational, and speech therapy**
e. **Prevent further strokes**

- **Medical**.

  Antiplatelets: aspirin (80–1300 mg/day), ticlopidine (Ticlid 250 mg, twice a day), clopidogrel (Plavix 75 mg/day), dipyridamole and aspirin (Aggrenox one cap twice a day).

  Anticoagulants: heparin/warfarin (Coumadin)—cardiogenic embolization, stroke in evolution, coagulopathy, carotid dissection.

- **Surgical:** carotid endarterectomy for high-grade stenosis (>70%), carotid stenting.

TRANSIENT ISCHEMIC ATTACKS

- A TIA is sudden neurological deficit (caused by focal or retinal ischemia) that resolves spontaneously and completely within 24 hours (usually 15–20 minutes), and without acute infarction.
- TIAs are a major risk factor for stroke and heart attack. The incidence of ischemic stroke is about 10%.
- Patients with recent TIAs (7–10 days), crescendo TIAs (series), or prolonged TIAs (lasting several hours) should be admitted to the hospital to expedite the workup and management.
- TIAs are usually due to embolization from artery to artery (e.g., carotid to middle cerebral artery) or cardiogenic (heart to artery). Other causes include vasculopathies, hematological diseases, and steal syndrome.
- Patients with lateralized and stereotyped (same distribution) repeat TIAs usually have artery-to-artery embolization.
- If hemispheric TIAs are associated with amaurosis fugax (transient monocular blindness), suspect an internal carotid source for embolization.
- Consider TIA when an elderly individual with stroke risk factor presents with transient neurological symptoms and signs.
- High-risk TIA patients are elderly males and those with frequent attacks, active heart disease, and peripheral vascular disease.

- TIAs should be differentiated from complicated migraine, partial seizure, syncope, lacunar infarct, multiple sclerosis, and even carpal tunnel syndrome.
- Workup for patients with TIAs is the same as patients with stroke (*see* Table 1). Patients presenting within 72 hours should be hospitalized. With patients presenting at 7 days or more, outpatient workup would be reasonable.
- Treatment of TIAs includes modifications of risk factors and preventive measures. Medical prevention measures include use of antiplatelets (aspirin, ticlopidine, clopidogrel) or anticoagulants (warfarin). Surgical preventive treatment includes carotid endarterectomy.

LACUNAR STROKES

Lacunar strokes are small, ischemic strokes in the distribution of small penetrating arteries of the circle of Willis (lenticulostriate, thalamoperforate) and paramedian branches of the basilar artery. The common locations of lacunes are internal capsule, basal ganglia, thalamus, and pons. They account for about 20% of all ischemic strokes.

When to Suspect Lacunar Stroke

- Arm and leg are equally affected (motor or sensory deficit).
- Motor and/or sensory deficit that is not associated with higher cortical function abnormalities: aphasia, apraxia, astereognosis, agraphesthesia.
- Dense neurological deficit associated with normal repeated head CT scan.

Major Risk Factors for Lacunar Infarcts

1. Hypertension.
2. Diabetes.
3. Hypercholesterolemia.
4. Aging.
5. Smoking.

Five Common Clinical Lacunar Syndromes

1. **Pure motor stroke:** posterior limb of internal capsule or pons infarct. The most common form. Weakness of ipsilateral face, arm, and leg.
2. **Pure sensory stroke:** thalamic infarct. Sensory deficit in face, arm, and leg.
3. **Sensorimotor:** posterior limb of internal capsul or thalamus. Weakness and numbness of face, arm and leg.
4. **Ataxic-hemiparesis:** pons or internal capsule infarct. Ipsilateral limb weakness and ataxia, disproportionate to the weakness.
5. **Dysarthria—clumsy hand**: pons or internal capsule infarct. Ipsilateral facial weakness, with mild arm weakness and dysarthric speech. The least common of these five.

Workup for lacunar stroke is same as stroke (*see* Table 1). Cerebral angiogram generally is not indicated unless carotid endarterectomy is considered. Prognosis of lacunar stroke is generally good. Treatment is same as other ischemic strokes with the exception of anticoagulation (heparin/warfarin), which is rarely indicated.

EMBOLIC STROKE

When to Suspect Embolic (as opposed to thrombotic) Stroke

- Patient presents with sudden and fixed neurological deficit, particularly during the daytime and activity.
- Rapid resolution of neurological deficit (sudden onset and offset).
- Stroke associated with headache, seizure, or altered mental status.
- Stroke occurs in young adult.
- Stroke occurs in the distribution of two or more major blood vessels of the brain (not in distribution of penetrating blood vessel).
- Hemorrhagic infarct on head CT scan.
- Patient presents with acute isolated neurological deficits such as aphasia or visual field defect.
- Stroke occurs in a patient who has strong **history of heart disease** but weak history of atherosclerosis (documented by history and diagnostic tests).

Strong history of heart disease includes: atrial fibrillation, valvular disease, myocardial infarction, cardiomyopathy, prosthetic valves, ventricular hypokinesia or dilatation, cardiac thrombus, atrial myxoma, and patent foramen ovale (paradoxical embolization).

CAUSES OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE

- Ruptured cerebral aneurysm or arteriovenous malformations.
- Hypertensive hemorrhage: pons, putamen basal ganglia, thalamic.
- Drugs: cocaine, amphetamines, phenylpropanolamine.
- Anticoagulant: warfarin.
- Thrombocytopenia or other coagulopathies.
- Cerebral amyloid angiopathy: an elderly patient presents with recurrent lobar hemorrhage (leading cause after hypertension).
- Central nervous system (CNS) vasculitis.
- Metastasis: melanoma, renal cell carcinoma, lung cancer, choriocarcinoma.

Caveat: The location of the hemorrhage is helpful in establishing the cause. Head CT scan is superior to magnetic resonance imaging in detecting an intracerebral hemorrhage. You must determine the cause of hemorrhage.

Consult a neurosurgeon because many hematomas can be evacuated; surgical evacuation of cerebellar hemorrhage can be life-saving. You may consider treating the elevated blood pressure more aggressively in hemorrhagic stroke. Stabilize airway and treat raised intracranial pressure. Prognosis depends on location and size of hemorrhage and age of the patient.

SUBARACHNOID HEMORRHAGE

- The two leading causes of spontaneous subarachnoid hemorrhage (SAH) are ruptured saccular aneurysm and arteriovenous malformation.
- The majority of cerebral aneurysms (saccular, berry) are in the anterior circulation distribution: anterior communicating artery (30%), posterior communicating artery (24%), and middle cerebral artery (13%).
- The incidence of aneurysmal SAH is about 10:100,000 per year.
- Head CT scan is the neuroimaging procedure of choice to document hemorrhage. If head CT scan is negative, perform lumbar puncture with attention to opening pressure, cerebral spinal fluid protein, and cell counts. Xanthochromia in cerebral spinal fluid is usually seen 3–4 hours after bleeding. If head CT and lumbar puncture are negative, doubt presence of SAH. If lumbar puncture or head CT scan positive for bleed, obtain a four-vessel cerebral angiogram.

Remember: The angiogram may not show aneurysm (clotted because of hematoma formation, vasospasm). In highly suspected cases, the angiogram needs to be repeated in 1–2 weeks. Complications of aneurysmal SAH are restart of bleeding, intracerebral hematoma, intraventricular hemorrhage, acute hydrocephalus, delayed ischemic stroke because of vasospasm, seizure, hyponatremia (syndrome of inappropriate antidiuretic hormone production), cardiac ischemia, and arrhythmia (because of autonomic hyperactivity).

Treatment of Aneurysmal SAH

1. Grade the clinical status.
2. Consult neurosurgeon as soon as you suspect SAH.
3. Medical treatment (your job as neurologist or attending physician): Admit the patient to the intensive care, monitor vitals and neurological status, order complete bed rest, elevate the head to 30°, and start intravenous fluid with normal saline. Control the blood pressure and cardiac arrhythmia, correct hyponatremia, and administer prophylactic antiepileptic drugs. Control pain and headache; prescribe stool softener; treat **vasospasm** (very important to recognize) with nimodipine, 60 mg, by mouth every 6 hours; and intravenous fluid.
4. Surgical treatments: evacuation of hematoma, ventriculoperitoneal shunt (acute hydrocephalus) and clipping or coiling of aneurysm to prevent

rebleeding. Most authorities recommend early clipping of aneurysm in patients with mild neurological dysfunction (grades 1 and 2). Coiling of aneurysm is gaining superiority over clipping.

Dissection of Extracranial Arteries

- Dissection of extracranial arteries is increasingly recognized as cause of stroke in young adults.
- Dissection of arteries usually is because of trauma in 50% of cases, and most often because of trivial trauma to neck such as head turn or neck twist.
- Carotid and vertebral arteries are two common sites of dissection.
- Stroke because of dissection is caused by acute arterial stenosis or embolization from the top of dissection or aneurysmal formation.
- A carotid dissection patient will present with neck or retro-orbital pain, followed by focal neurological sign and symptoms; look for presence of carotid bruit and Horner's syndrome on same side of neck or eye pain.
- Diagnosis of dissection is established by cerebral angiogram, but carotid Doppler, magnetic resonance imaging, and magnetic resonance angiopathy may provide useful information.
- Most authorities recommend anticoagulation (heparin and warfarin) if hemorrhagic stroke and/or large stroke does not exist. Anticoagulation may continue for 3 months, followed by repeating cerebral angiogram to assess opening of the artery and recanalization.

ISOLATED CNS VASCULITIS

- Isolated CNS vasculitis (or angiitis) affects small arteries and capillaries of the brain and spinal cord without systemic involvement.
- CNS vasculitis is an immune-mediated condition, although it is sometimes seen after drug abuse (cocaine).
- Clinical features include headache, mental confusion (encephalopathy), multifocal neurological signs, and seizure.
- Sedimentation rate is either normal or mildly elevated. Spinal fluid may show increased protein concentration and mild lymphocytic pleocytosis.
- Diagnosis is made by cerebral angiogram which shows "beading"; however, angiogram may be negative (lack of sensitivity), and furthermore, beading may be seen in nonvasculitic conditions such as infectious process, atherosclerosis, and neoplastic angioendotheliosis (lack of specificity). The role of angiogram in evaluation of vasculitis is unclear. In highly suspected cases, cortical brain and leptomeningeal biopsy is warranted. Brain biopsy, however, is hampered by sampling error (sensitivity is about 80–85%).

- When diagnosis of CNS vasculitis is established, the patient should be treated promptly with high doses of prednisone and cyclophosphamide. Cyclophosphamide should continue for at least 1 year. Some authorities recommend repeating angiogram before stopping cyclophosphamide.

SOME COMMON CLINICAL STROKE SCENARIOS

1. Causes of Stroke in Young Adults

- Dissection of extracranial vessels of carotid (carotid/vertebral).
- Cardiogenic embolization.
- CNS vasculitis.
- Atherosclerosis.
- Drugs (cocaine, phenylpropanolamine).
- Moyamoya disease.
- Coagulopathy: proteins C and S deficiencies, antithrombin III deficiency, antiphospholipid antibody syndrome.
- Sickle cell anemia.
- Cerebral venous thrombosis.

2. Anterior Circulation TIAs and Stroke

Anterior circulation consists of the internal carotid artery and its branches: middle cerebral artery, anterior cerebral artery, and penetrating branches of the middle and anterior cerebral arteries (lenticulostriates). Anterior circulation TIAs and stroke present with lateralizing signs (motor/sensory), speech difficulties, ipsilateral cranial nerve dysfunction, and occasional contralateral visual loss (amaurosis fugax).

3. Posterior Circulation TIAs and Stroke

Posterior circulation consists of the vertebrobasilar system, posterior cerebral arteries, and penetrating branches (paramedians) and thalamoperforates. Posterior circulation TIAs and stroke present with diffuse neurological symptoms and signs referable to the brain stem and cerebellum such as dizziness, bilateral blurred vision, diplopia, ataxia, multiple cranial nerve dysfunction, and unilateral or bilateral motor/sensory deficits. Isolated signs or symptoms rarely related to posterior circulation ischemic event.

4. Wallenberg Syndrome

There are many brain stem strokes, but remember Wallenberg syndrome, or lateral medullary syndrome. Wallenberg syndrome is stroke because of occlusion of a ventral artery or posterior inferior cerebellar artery, which causes ischemic infarct at the pontomedullary junction and clinically characterized by:

- Sudden onset of vertigo, nausea.
- Dysphagia, dysarthria.
- Ispilateral (toward site of lesion) facial numbness, weakness, and Horner's syndrome.
- Contralateral body sensory loss and motor weakness.
- Ipsilateral cerebellar dystaxia.
- Hiccups.

5. When and How to Use Anticoagulation in Stroke

Anticoagulants are given to stroke patients to prevent further stroke or TIAs and to prevent potentially devastating neurological deficit (locked-in syndrome or coma, as in cases of basilar artery thrombosis). Although not proven scientifically, the potential indications of anticoagulation in stroke are:

- Noninfectious cardiogenic embolic stroke or TIAs.
- Basilar artery thrombosis.
- Series of TIAs (crescendo TIAs).
- Dissection of extracranial vessels.

How to Use Anticoagulant:

- Establish the indication.
- Obtain noncontrast head CT scan; repeat in 24–48 hours if symptoms worsen.
- If head CT scan shows small ischemic stroke, administer anticoagulant immediately.
- If head CT scan shows large ischemic stroke with surrounding edema or hemorrhagic stroke, wait for 2–3 weeks, and then repeat head CT scan and consider anticoagulation, depending on the individual and clinical status.
- If patient is severely hypertensive, control blood pressure to reasonable degree before anticoagulant administration.
- Anticoagulation begins with continuous infusion of heparin and a switch to warfarin, maintaining international normalized ratio to 2–2.5 of control. With many clinical conditions you need to anticoagulant are temporary (weeks to months). Cardiogenic embolic events usually require chronic anticoagulation.

6. Aphasias

Aphasia is an acquired language disorder. Patient should be awake, alert, and can hear before you assess the aphasia. Aphasias are usually caused by stroke. Do 5–10 minutes of bedside testing and be able to recognize the four common aphasias.

1. Establish the **spontaneous (spoken) language** and whether is **fluent** or **nonfluent**.
2. **Check repetition**; give the patient a sentence to repeat.
3. **Check comprehension**.
   - If the patient has **nonfluent** spontaneous speech and has poor repetition and comprehension, the patient has **global aphasia**.
   - If the patient has *nonfluent* speech with poor repetition, but has relatively good comprehension, the patient has expressive *Broca's aphasia* (motor or anterior aphasia).

   Hint: the majority of nonfluent aphasias are global but either predominantly expressive or receptive. Nonfluent aphasias are usually associated with contralateral motor paresis and visual field defect. These patients are unable to write with either hand.

   - If the patient has **fluent** spontaneous speech but has difficulty in repetition and comprehension, the patient has receptive, *Wernicke's*, *posterior,* or *sensory, aphasia.*
   - If the patient has **fluent** speech with poor repetition but has relatively good comprehension, the patient has **conduction** aphasia.

Caveat: All of these common aphasias have poor repetition, and the lesion involves the perisylvian region of the dominant hemisphere, known as **language zone**, which is supplied by middle cerebral artery. If the patient has difficulty in reading (alexia), with or without difficulty in writing (agraphia), the lesion is in the distribution of the **posterior cerebral artery**.

9
Seizure and Epilepsy

- Seizures are transient abnormal neuronal discharges of the cerebral cortex that often result in stereotyped behavior.
- Seizure is often a manifestation or symptom of many medical conditions. Epilepsy is the occurrence of two or more unprovoked seizures. Epilepsy is a chronic disorder. In other words, a seizure is a sign, and epilepsy is a disorder.
- It has been estimated that approximately 10% of individuals reaching age 70 will have a seizure, but only 1–2% will be subject to recurrence and become epileptic. After a generalized tonic-clonic seizure, with normal exam, magnetic resonance imaging (MRI), and electroencephalogram (EEG), 15–30% have recurrence.
- Seizure should be differentiated from syncope, migraine, transient ischemic attack, multiple sclerosis, hypoglycemic attack, sleep disorder (narcolepsy/cataplexy/night terror, rapid eye movement behavior disorder), anxiety attacks, and pseudoseizure (psychogenic nonepileptic seizure).
- Routine workup for onset of unprovoked seizure in adults includes blood count, chemistry profile, EEG, and neuroimaging (computed tomography scan, MRI). Further workup depends on individual case (lumbar puncture).
- Late onset of seizures is usually because of vascular, degenerative, and neoplastic processes. However, more than half of the patients remain idiopathic, which is possibly genetically determined. Family history of seizure, previous history of head trauma, and prior history of seizure including febrile convulsion in childhood are important to establish.
- The most important part of evaluation of patients presenting for first time with a seizure is to take a good history. The history of the event and particularly postictal symptoms and signs are very important. Interviewing the witness is crucial.
- The EEG is the gold standard test for establishing the diagnosis of seizure and epilepsy. Most EEGs, however, are obtained between the seizure (interictal), which is positive in 50% of patients with partial epilepsies and about 60–65% in those with generalized epilepsy. Normal EEG does not rule out

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

the diagnosis of epilepsy. EEG when recorded during the seizure is called ictal, and if obtained immediately afterward is called postictal.

- For practical purposes in adults, most adult seizures can be classified into **partial (focal)** and **generalized**.
- Partial seizures arise from a specific area of the brain and the EEG may show focal spike and or sharp waves. Partial seizures are classified further into:

1. **Simple partial seizures**.
   - Motor manifestation (Jacksonian marsh).
   - Sensory manifestation.
   - Somatosensory.
   - Psychic.
2. **Complex partial seizures**.
   - Originating from temporal lobe.
   - Originating from frontal lobe.
   - Originating from parietal lobe.
   - Originating from occipital lobe.
3. **Partial seizure with secondarily generalized**.
   - The difference between simple and complex partial seizure is impairment of consciousness, which occurs in complex partial seizure. An aura is a simple partial seizure. Remember the "4As": aura, alteration of consciousness, automatism, and amnesia for complex partial seizures.
   - Generalized seizures arise from bilateral diffuse hemispheres and the EEG may show generalized, bilateral spike/wave discharge. Generalized seizures with onset in adulthood include:

Primary generalized seizures: absence (petit mal), generalized tonic-clonic (grand mal), myoclonic. Patients with primary generalized seizure generally have normal neurological exam and brain imaging. The seizures are genetically caused, have good prognosis, and are easily controlled with antiepileptic drugs.

Secondary generalized seizures: Patients present with variety of seizure types caused by organic brain damage; they are mentally slow with abnormal exam and brain imaging. Prognosis is poor and often requires multiple antiepileptic drugs. Lennox-Gasteux syndrome is an example of this category.

- Classification of seizures is important to know and memorize because it helps you to:
  1. Plan the workup.
  2. Choose the right drug therapy.
  3. Suspect etiology.
  4. Prognosticate.

- Mistaking absence seizures for complex partial seizures not only leads to inappropriate workup, but also to inappropriate therapy. Complex partial seizures last longer (30 seconds to 2–3 minutes), may be preceded by aura, and postictally, the patient is confused, disoriented, and amnestic. Absence seizures are common in childhood, presenting with brief starring episodes and if lasting longer, can be associated with eye blinking and minor motor activities.
- Establish diagnosis of epilepsy firmly before you begin your treatment. Starting medication is easier than discontinuing it.
- The goals of drug therapy in epilepsy are to prevent seizures and improve quality of life with the least side effects from the antiepileptic drug (AED).
- Discuss possible allergic reaction(s) and side effects of the AED with the patient and relatives. The family should be involved in care of the patients with epilepsy. Although you should always consider single-AED therapy (monotherapy), some individuals may need rational polypharmacy (e.g., status epilepticus, multiple seizure type, as in secondary generalized seizure). There are several new AEDs. Before prescribing them, know their indications and side effects, and it is best to refer such patients to a neurologist if the seizures are not controlled with conventional AEDs.
- Choose the AED based on seizure type, and always start with one medication (monotherapy). Check blood drug level when the level reaches its steady state (usually five times that of the drug's half-life).
- The frequency of drug administration is dependent on its half-life (the shorter the half-life, the more frequent the dosing). Unless patient has frequent seizures, start the AED at a low dose and increase slowly. A once- or twice-a-day regimen improves compliance.
- When the drug level reaches steady stage, increase the dose very slowly (e.g., increase phenytoin by 30 mg), because a full-dose increase (100 mg) may result in overdose. If seizure is controlled with subtherapeutic AED level, it is not necessary to increase the dose, with the exception of during pregnancy (see section headed "Epilepsy in Pregnancy").
- The drug level should not be checked routinely; it should be used as a guide when there is concern about compliance, drug toxicity, or drug interaction.
- Sedative AEDs such as phenobarbital and primidone are not recommended in adult patients.
- In **status epilepticus**, use a drug that can be given intravenously, acts quickly, reaches brain rapidly, has longer half-life, and causes less sedation.
- In "breakthrough of seizures," try to find the precipitating factors before increasing the dose or changing and/or adding another AED.
- Typical alcohol withdrawal seizures do not require maintenance AED therapy.
- Elderly onset of epilepsy should be evaluated by EEG and MRI of the head. In the elderly, use AED with low dose and gradually increase the dose. Use

AED that causes no significant sedation or drug interaction (elderly often taking several prescribed medications).

- Epileptic patients do not necessarily remain epileptic for the rest of their lives. Patients with absence seizure may outgrow their seizure. In general, discontinuation of AED is frequently considered in children. You may consider discontinuing the AED when the patient is free of seizures for 2–3 years. Most neurologists do not discontinue AEDs in patients with partial seizures or mentally retarded patients with multiple seizure types. Patients with juvenile myoclonic epilepsy should continue medication for life.
- Consider withdrawal of the AED if:

1. Patient has onset of epilepsy in childhood.
2. Seizures are the generalized type, particularly primary generalized.
3. EEG, neuroimaging, and neurological examination are normal.
4. Patient is free of seizure for 2–3 years.
5. Patient has had infrequent seizures in previous years.

- How to Discontinue AED:

a. Discuss the risks and benefits of stopping the AED with patient and relatives, document in the chart, and obtain consent.
b. Obtain an EEG and blood AED level.
c. If the patient is taking more than one AED, taper one drug at a time.
d. Discontinue very slowly (6–12 months).
e. Advise patient not to drive or work in high-risk jobs, and avoid sleep deprivation and alcohol consumption during withdrawal period.
f. If seizures recur, reinstitute the medication and continue indefinitely.

Current New AEDs

- **Felbamate** was introduced in 1993. Frequent laboratory monitoring (blood count and liver function tests) is recommended. Felbomate is indicated in patients with refractory seizure, particularly patients with Lennox-Gastaut syndrome. This agent is rarely used.
- **Gabapentin** (Neurontin): mechanism of action is not known. It is eliminated from the kidneys and has no drug interaction. It may be drug of choice for seizures in acute intermittent porphyria. The effective dose is 3600– 4800 mg in divided doses, beginning with the lower dose. Gabapentin is effective in patients with partial and secondarily generalized seizures. It is a good choice for elderly epileptics. This agent was recently Food and Drug Administration (FDA)-approved for treatment of postherpetic neuralgia.
- **Lamotrigine** (Lamictal) was released in 1995. It is thought to block sodium channels, and it is effective against absence, generalized tonic-clonic, and secondarily generalized seizures. It is also effective in Lennox-Gastaut syndrome. The most common side effects are dizziness, diplopia, and ataxia.

About 10% report skin rash, particularly children, and if the patient is receiving valproate and if the dose is increased at a faster rate. Slow titration is recommended. This agent now approved as monotherapy.

- **Topiramate** (Topomax) has been on the market since 1997. It is effective against partial and generalized seizures in adults and children. The most common side effects are sedation and weight loss. Kidney stones occur in 15% of patients. Slow titration is recommended. A dose of 25 to 50 mg/day, with weekly increases up to 200–400 mg/day, is recommended.
- **Tiagabine** (Gabitril) was approved in October 1997. It is effective against partial and secondarily generalized seizures. The average dose in adults 32–64 mg/day, with slow titration.
- **Oxcarbazepine** (Trileptal). Start at 300 mg twice a day, to max dose 1200 mg/day. Pediatric and intravenous forms are now available.
- **Levetiracetam** (Keppra). Start at 500 mg twice a day, to max dose 3000 mg/day. Pediatric and IV forms are now available.
- **Zonisamide** (Zonegram). Start at 100 mg/day, to max dose 600 mg/day.
- **Pregabaline** (Lyrica). Start at 50 mg, three times a day; titrate up to 600 mg/day. This drug is also FDA-approved for treatment of pain in postherpetic neuralgia and diabetic neuropathy.
- Newer AEDs are generally used as adjuncts. They have been advocated to have better safety and tolerability profile as compared with conventional drugs. Their serum level data for most part are not available, and their affects on the fetus are unknown.

Epilepsy in Pregnancy

- Do not change AED therapy during pregnancy; you may do so before or after pregnancy. Avoid polypharmacy in pregnancy.
- Pregnant epileptics need to be seen monthly in the clinic, and the AED should be checked.
- Try not to use valproate in pregnancy.
- There is no contraindication for breastfeeding for an epileptic mother.
- Pregnant epileptics should receive 4 mg folate each day.
- If a pregnant woman is taking valproate or carbamazepine, check α-fetoprotein and perform an ultrasound during the first trimester.
- The chance of fetal malformation in epileptics is generally three to four times greater than in nonepileptic women.

Other Considerations

- Patients with intractable seizure need to be reevaluated by MRI (which may show new lesion) and repeat EEG (changing of seizure type). Most importantly, these patients should be referred to epilepsy center for consideration

of surgical intervention to treat their seizure or they may consider AED drug trial studies.

- Consider pseudoseizure when patients report recurrent seizures, despite trial of several major AEDs. Although there are many ways to differentiate true seizure from pseudoseizure, the definite diagnosis often needs prolonged video/EEG monitoring. Pseudoseizures often occur in association with true seizures.
- The most common form of surgery for treatment of intractable seizure is temporal lobectomy. Another operation is corpus callosotomy (disconnection), which is done for intractable generalized seizure. Other procedures include hemispherectomy and vagal nerve stimulation. Surgical treatment of epilepsy is generally underutilized. Before temporal lobectomy, patients undergo intensive testing to localize the focus of epilepsy.
- Before labeling the patient having medically intractable seizure, be sure patient is not having pseudoepilepsy, is not receiving wrong drug or diagnosis, and has good compliance.
- Establish the seizure control, quality of life, and drug side effects in follow up visit of epileptic patients. Limited neurological examination should include cognition and cerebellar function. Repeat blood work, AED level, or other testing should not be done routinely and should be individualized according to type of seizure, symptoms, and signs. Consider blood work (complete blood count and chemistry profile) in asymptomatic patients twice a year. Mentally retarded patients may need more frequent blood work.
- Most neurologists do not treat single, unprovoked generalized tonic-clonic seizure, particularly if the EEG is normal and the patient has normal imaging and neurological examination. However, you may treat a single seizure if you think a recurrent seizure can lead to serious consequences (e.g., truck driver or high-risk job patients).
- The chance of recurrence of seizure after single generalized idiopathic seizure is about 20–50%.
- Head trauma is probably the most frequent preventable cause of epilepsy in the industrial countries.
- Epileptic patients are permitted to drive motor vehicles, but each state and country has its own law and regulations (know the laws of your state). Some states require physicians to report epileptics to the authorities. You should document in your note that you have discussed this issue with your patient and encourage the patient to report his or her seizure to state authorities.
- Non-convulsive status epilepticus (Complex partial or absence) present with confusion, behavior changes and automatism. Diagnosis is made by trial of short-acting intravenous anti-epileptic drug (e.g., Lorazepam) or an EEG.

10
Central Nervous System Infections

SOME CLINICAL TIPS

- Suspect central nervous system (CNS) infection when the patient presents with fever, headaches, nausea and vomiting, photophobia, alterations of mental state, or focal neurological deficit.
- The triad of meningitis—fever, headaches, and meningismus—are not always present in all patients, but fever and headaches are the most common occurrence.
- Jolt-accentuated headache, increased intensity of headache by side-to-side head movement, is another useful sign.
- Encephalitis can occur when a febrile patient presents with behavior, personality changes, mental dysfunction, and seizure, with or without focal neurological deficit. Meningitis and encephalitis often occur together (meningoencephalitis).
- All patients with suspected CNS infection should have blood cultures, brain imaging (computed tomography scan/magnetic resonance imaging [MRI]), and cerebrospinal fluid (CSF) examination.
- Because of a high rate of morbidity and mortality in bacterial meningitis and herpes simplex encephalitis, empiric broad-spectrum combined antibiotic and acyclovir therapy should begin promptly and not be delayed when performing imaging or spinal tap.
- Consult an infectious disease specialist when you are dealing with CNS infection.

BACTERIAL MENINGITIS

- Bacterial meningitis is a medical emergency.
- In suspected cases, after obtaining blood culture (which could be positive up to 40%), begin with a combination of broad-spectrum antibiotics.
- The choice of antibiotic is simply an educated guess (age of the patient, underlying risk factors help in decision making). In adults, one of the following combinations are recommended:

  a. Ceftriaxone (8–12 g/day), four times daily intravenously, and vancomycin (2 g/day), four times daily intravenously.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

b. Ceftriaxone and rifampin.
c. Ceftriaxone and chloramphenicol.
d. Dexamethasone (0.15 mg/kg intravenously, every 6 hours) shortly before or at the same time as the antibiotic(s), for 2–4 days, and taper when evaluation is completed.

- In pneumococcal meningitis, spinal fluid should be examined 48 hours after antimicrobial therapy and 48 hours after treatment course (usually 2 weeks).
- The two leading pathogens of bacterial meningitis in adults are *Streptococcus pneumoniae* (pneumococcus) and *Neisseria meningitidis*. The risk factors for developing bacterial meningitis are immunosuppression (AIDS, immunosuppressive drugs), alcoholism, intravenous drug use, congenital heart disease, sinusitis, cancer, basilar skull fracture, sepsis, pneumonia, and sickle-cell anemia.
- Recurrent bacterial meningitis (often pneumococcus) is seen in patients with basilar skull fracture (because of CSF leak), sinusitis, sickle-cell anemia, and splenectomized patients.
- Meningitis following head trauma, ventriculoperitoneal shunt, or intracranial surgeries usually is caused by *Staphylococcus aureus*.
- Complications of bacterial meningitis are increased intracranial pressure, cerebral edema, brain abscess, cortical venous thrombosis, epilepsy, subepidural and epidural abscess, hydrocephalus, mental retardation, hearing loss, and syndrome of inappropriate antidiuretic hormone production.
- Repeat CSF analysis in successfully treated bacterial meningitis is generally not warranted.
- Persistent fever or persistent predominantly neutrophilic pleocytosis signifies inadequate or wrong combination antibiotic therapy, resistant pathogen, parameningeal infection source, or brain abscess.

VIRAL (ASEPTIC) MENINGITIS

- Viral meningitis presents with low-grade fever, headaches, malaise, neck stiffness, or tenderness. Spinal fluid usually shows predominantly lymphocytic pleocytosis and mild elevation of protein concentration with normal glucose and cultures. Treatment is supportive.
- When you suspect herpes simplex encephalitis, obtain brain imaging, electroencephalogram, and send blood and spinal fluid for herpes simplex virus antibody and DNA (polymerase chain reaction [PCR]) testing, and begin acyclovir therapy (10 mg/kg, intravenously every 8 hours, for 2–3 weeks).

TUBERCULOUS MENINGITIS

- Tuberculous (TB) meningitis is increasingly prevalent, with 300–400 cases every year in the United States.

- Tuberculin skin test and chest X-ray could be negative, but do not exclude the diagnosis.
- Coinfection of TB/HIV is about 20%.
- CNS manifestations include meningitis, cranial neuritis, stroke, seizure, and hydrocephalus.
- Diagnosis is established by series CSF analysis for acid-fast bacillus smears, cultures, and PCR.
- Head computed tomography scan and MRI may reveal basilar meningeal enhancement and hydrocephalus or tuberculoma.
- Initiate empiric antituberculous drugs in patients presenting with meningitis and CSF shows low sugar, elevated protein, and lymphocytic pleocytosis, particularly in high-risk patients.
- Treatment of TB meningitis consists of a four-drug therapy:
  - Isoniazid: 10 mg/kg day orally, then 5 mg/kg.
  - Rifampin: 600 mg/day orally.
  - Pyrazinamide: 15–30 mg/kg day orally.
  - Ethambutol: 15–25 mg/kg day orally.
- The combination therapy should continue for two months, until sensitivity is known, then may decrease to two drugs, usually isoniazid and rifampin. Drug therapy should continue for 18–24 months, with periodic repeated spinal taps.
- Most authorities recommend adjunctive therapy with corticosteroids: 60 mg prednisone daily, with tapering over 6 weeks, or dexamethasone intravenously for the first 3 weeks.

NEUROSYPHILIS

- Positive serology for syphilis (e.g., fluorescent treponemal antibody-absorption test) in any patient with unclear history of nontreatment or partial treatment justifies spinal tap for spinal fluid examination.
- Active neurosyphilis is usually associated with increased cells, protein, immunoglobulin M, and increased Venereal Disease Research Laboratory (VDRL) titer in the CSF.
- All patients with HIV should be tested for syphilis.

Clinical Syndromes

a. **Asymptomatic:** a common clinical scenario where CSF is abnormal (increased cells, protein, and positive VDRL), but there are no neurological deficits or signs.
b. **Meningovascular:** stroke, aphasia, focal neurological deficits, seizure.
c. **Meningitis:** headache, fever, cranial nerve palsies, hydrocephalus.

d. **Tabes:** loss of proprioception, painless foot ulcers, joint destruction (Charcot's joint), abnormal pupillary reaction (Argyl-Robertson), sensory ataxia, and lightning pain
e. **General paresis:** slowly progressive, personality changes, dementia, myoclonic jerks, seizure, and focal neurological deficits.

Treatment of Neurosyphilis

Aqueous penicillin G, 2–4 million units, every 4 hours intravenously for 10–14 days, followed by 2.4 million units benzathine penicillin intramuscularly, every week for 3 weeks. In case of allergy to penicillin, doxycycline or chloramphenicol is given for 1 month. Repeat CSF analysis every 6 months for 2 years. Repeat treatment if CSF shows pleocytosis, VDRL titer was increased, or neurological condition worsens.

CREUTZFELDT-JAKOB DISEASE

Creutzfeldt-Jakob Disease (CJD), or spongiform encephalopathy, is a transmissible disorder related to bovine spongiform encephalopathy or "mad cow disease." The causative agent is a prion, which is a protein without DNA. CJD characteristically presents with rapidly progressive dementia, myoclonic jerks, ataxia, and upper and lower motor neuron signs. The electroencephalogram, when the disease is established, shows periodic, 1- to 2-Hz, generalized sharp and triphasic waves. Other supportive tests include MRI, which may show signal intensity in the basal ganglia and abnormal diffusion-weighted imaging; CSF 14-3-3 protein-γ isoform is elevated in about 53% of cases. The definite diagnosis is made by brain biopsy or at autopsy. CJD is the most frequent prion disease in humans. There are four types: sporadic, familial, iatrogenic, and variant. The variant CJD affects younger individuals, with longer duration, and presents with sensory complaints, depression, anxiety, and psychosis. Other prion diseases in humans include kuru, fatal familial insomnia, Gerstmann Straussler-Scheinke, and Alpers syndrome. Familial CJD, fatal familial insomnia, and Gerstmann Straussler-Scheinker are hereditary, and they show mutation in the *PRNP* gene on the short arm of chromosome 20. Hereditary forms are very rare. All prion diseases are fatal and share more or less similar brain pathology.

AIDS

- Neurological symptoms and signs can be the onset of AIDS in about 10–13% of cases.
- About 50% of patients with positive HIV antibody will develop a neurological disorder during the course of their illness, and up to 95% of patients with AIDS have neuropathological changes in the nervous system at autopsy.

- Neurological complications generally correlate with level of CD4 count in the blood (the lower the CD4 count, the more severe the neurological problem).

Neurological Complications

A. Central Nervous System

a. Direct effect of retrovirus (HIV).
   - Meningitis: subacute/chronic.
   - AIDS encephalopathy (dementia), HIV-D.
   - Myelopathy.
   - Sensory neuropathy.

b. Indirect effect.
   - Opportunistic infections.
   - Stroke.
   - Lymphoma.

B. Peripheral Nervous System

a. Peripheral neuropathies.
   - Acute demyelinating polyneuropathy (Guillain-Barré syndrome).
   - Chronic demyelinating polyneuropathy.
   - Mononeuritis multiplex.
   - Distal, symmetrical, sensory painful neuropathy.
   - Cytomegalovirus radiculopathy.
   - Diffuse infiltrative lymphocytic syndrome.

b. Myopathies.
   - Inflammatory myopathy (polymyositis).
   - Nemaline myopathy, vacuolar myopathy, inclusion body myopathy.

c. Drug-induced neuromyopathies.
   - Distal, sensory, painful neuropathy: caused by azidothymidine, dideoxyinosine, dideoxycytidine, and stavudine.
   - Mitochondrial myopathy: caused by azidothymidine, presents with proximal weakness, myalgia, and elevated serum creatine kinase.

AIDS Encephalopathy

AIDS encephalopathy, or dementia, is a subcortical dementia that presents with apathy, personality changes, tremor, myoclonia, seizure, ataxia, dementia, bradykinesia, and long tract signs. Highly active antiretroviral therapy (HAART) has reduced the incidence of dementia to half. Lifetime prevalence in homosexuals is about 15%. Diagnosis is supported by MRI of the brain that shows diffuse atrophy and hyperintense white matter lesions. CSF examina-

tion shows elevation of protein concentration and elevated level of β_2-microglobulin (>3.8 mg/L) and positive PCR (RNA).

AIDS MYELOPATHY

AIDS vacuolar myelopathy occurs in 10–15% of patients with AIDS, and clinically presents with proprioception loss, spastic paraparesis, and neurogenic bladder (similar to subacute combined degeneration of the cord because of vitamin B_{12} deficiency). This myelopathy can be seen at autopsy in about 50% of patients. CSF adenosyl methionine concentration may be reduced.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection affecting the CNS white matter caused by reactivation of JC virus in immunosuppressed and immunocompromised patients (AIDS, malignancy, immunosuppression). PML can present as the initial manifestation of HIV, and approximately 10% develop PML during their course of illness. Cerebellar hemisphere(s) and the brainstem may also be involved, but the spinal cord is rarely affected. The disease manifests as progressive mental dysfunction, aphasia, visual field defects, seizure, incoordination, and multifocal neurological deficits. PML should be suspected in any immunosuppressed patients presenting with focal or multifocal neurological dysfunction. Some patients have more prolonged and fluctuating course. Brain MRI shows T_2 signal intensity in white and gray matter. CSF protein is elevated, and positive PCR testing for JC virus DNA can help the diagnosis. Definite diagnosis is made by stereotaxic brain biopsy.

11
Alteration of Mental Status

Alteration or changing mental status is a common cause of hospital admission, and neurologists are often asked to evaluate these patients in consultation.

You need to establish:

- Onset of illness (acute, subacute, or chronic).
- Course (rapidly progressive, nonprogressive, slowly progressive, or fluctuating).
- Underlying medical diseases.
- Preexisting primary neurological problems: seizure, stroke, dementia.
- Use of medication(s) that may affect mental function or any new drug that is added to the patient's regimen, or as medication is changed.

DELIRIUM

Delirium is simply an *acute confusional state*. The hallmarks of delirium are disorientation, inattentiveness, and global impairment of cognitive function. Although in practice delirium is known to be associated with autonomic overactivity such as fever, tachycardia, hallucination, and tremor, the lethargic form of delirium is more common. Therefore, the clinical characteristic of delirium is a fluctuating state of the alertness.

What You Should Do

1. Take a detailed medical, psychological, and neurological history (often obtained indirectly from family members).
2. Perform a general physical (to assess underlying medical cause) and neurological examination (to assess particularly whether organic or focal brain lesions exist). (Beware: You may easily miss a subdural hematoma in a delirious patient.) Pay special attention to cognitive function; pupillary size, symmetry, and reactivity; whether the neck is stiff; and motor examination and presence of any involuntary movements (e.g., tremor, myoclonia, chorea, or asterixis).

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

3. **Try to identify the underlying cause (or causes):**
   a. **Toxic/metabolic encephalopathies.** Toxic/metabolic encephalopathies are the most common cause of delirium. Metabolic conditions include electrolyte imbalance; renal, hepatic, or pulmonary failure; endocrine disorders; and septicemia. Many environmental toxins can produce encephalopathy, but in practice, drug-induced encephalopathy is more common. Remember, adding new drugs or minor drug change in elderly patients might cause delirium. Drugs that are known to cause confusion include anticholinergics, antihistamines, antihypertensive, digitalis, antipsychotic, antiparkinsonians, steroids, antidepressants, cocaine, LSD, and alcohol.
   b. **Multifocal brain lesions.** Meningoencephalitis, vasculitis, and AIDS are few examples.
   c. **Focal brain lesion.** Any focal lesion involving limbic systems or memory regions can manifest as mental confusion.

Some hints: Acute mental confusion in elderly individuals with nonfocal neurological examination is most likely because of underlying infection (urological in females), drug regimen changes, or hypoxia (beclouded dementia). In young individuals with similar presentation, drug overdose or drug/alcohol withdrawal is the most likely cause.

DEMENTIA

You should know that:

- Dementia is an acquired brain disorder, characterized by decline of cognitive and intellectual function, leading to mental, physical, and social disability, and dependency. Before you consider the diagnosis of dementia, you should establish that the patient has intact sensorium (i.e., is alert, awake); sensorium is impaired in delirium.
- Suspect dementing illness when the patient:
  - Gets confused with minor distraction.
  - Exhibits slowness of movements.
  - Exhibits emotional lability or irritability.
  - Gets lost and/or misuses words.
- Distinguish the following conditions from dementia: senile forgetfulness, depression (pseudodementia), psychiatric illness (schizophrenia), aphasia, transient global amnesia, and nonconvulsive (absence/complex partial) status epilepticus.
- Approximately 4% of people over age 65 and up to 40% over age 85 are demented. In the elderly population, Alzheimer's disease (AD) is the leading cause (50–75%). Mild cognitive impairment (MCI) affects about 10% of people over age 65, and about 15% of them develop AD each year.

Causes of Dementia

The causes of dementia are generally either medical, neurological, or psychiatric. In the elderly population, AD is the leading cause, followed by vascular dementias and Parkinson's disease (PD). Approximately 10% of dementias are because of reversible causes (e.g., chronic meningitis, normal pressure hydrocephalus, chronic subdural hematoma, toxic/metabolic derangement, and vasculitis).

ALZHEIMER'S DISEASE

Definite diagnosis of AD can be made only by brain biopsy or at autopsy. The probable diagnosis of AD can be made when a patient presents with following symptoms and other causes have been excluded:

- Slowly progressive dementia.
- Prominent, progressive memory loss and at least one other cognitive dysfunction.
- Onset after age 60.
- No focal neurological deficit and no impairment of gait or motor tasks.

The leading risk factors for AD are age, family history, high homocysteine level, and stroke. Four gene proteins have been recognized to play a role in AD: apolipoprotein E4, amyloid precursor protein, and presenilins-1 and -2. Genetic testing has no practical clinical implication at this point. Familial AD (FAD) affects less than 10% of AD patients. No single gene has been identified in AD.

Treatment

The caregivers should be educated about the disease and provided with social support and community resources.

Depression

Depression occurs in 30–50% of AD patients. Selective serotonin reuptake inhibitors have fewer side effects than do tricyclic antidepressants. Paroxetine (Paxil), 10–40 mg/day, and sertraline (Zoloft), 25–100 mg/day, are the drugs of choice.

Sleep Disorders

Trazodone (Desyrel), 25–100 mg/day, is a good choice.

Improve Cognition

The following central anticholinesterase inhibitors (cholinergics) have been approved in patients with AD:

- Tacrine hydrochloride (Cognex). This agent is rarely used because it requires tight titration and has poor side effects profile.

- Donepezil (Aricept). This agent is commonly prescribed because of fewer side effects and it needs no titration. The target dose is 5–10 mg every day.
- Rivastigmine (Excellon). Needs titration. The target dose is 3–12 mg every day.
- Galantamine (Reminyl). Needs titration. The target dose is 16–24 mg every day.
- Memantine (Namenda). This agent is an *N*-methyl-D-aspartic acid (NMDA) antagonist and usually used as adjunctive therapy with cholinergics (donepezil) in moderate to severe AD. The target dose is 10–20 mg/day. Most cholinergic drugs are used in mild to moderate AD.

Disease Progression

Estrogen, vitamins C and E, prednisone, nonsteroidal anti-inflammatory drugs, selegiline, statins, and ginko biloba may slow the disease progression.

VASCULAR OR MULTI-INFARCT DEMENTIA

Vascular dementia is suspected when a patient has:

- Onset of mental function impairment with prominent executive dysfunction after stroke.
- Abrupt onset followed by stepwise worsening.
- Unilateral or bilateral corticospinal tracts findings.
- Pseudobulbar features.
- Strong risk factors for stroke.
- Cerebral infarcts (cortical or subcortical) or diffuse white matter changes on magnetic resonance imagine (MRI).

PARKINSONISM AND DEMENTIA

Parkinsonian features and dementia are seen in:

- Primary PD (up to 30–40%).
- Late-stage AD.
- Progressive supranuclear palsy.
- Diffuse Lewy body disease.
- Primary nigral degeneration.
- Corticobasal degeneration.
- Frontotemporal dementia.
- Multiple system atrophy.

DEMENTIA WITH LEWY BODIES

Dementia with Lewy bodies is the second most common neurodegenerative disease after AD causing dementia and is characterized by the following:

- Gradual and slowly progressive dementia.
- Prominent or persistent and progressive memory impairment.
- Fluctuating confusion, cognitive dysfunction, and alertness.

- Persistent visual hallucinations.
- Mild Parkinsonian features without tremor.
- Increased sensitivity to neuroleptic agents.
- Sleep disorders, autonomic dysfunction, frequent falls, syncope.

FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia (FTD) affects both men and women equally with age of onset earlier than AD. About 20–50% are familial; some may have mutation in the tau protein gene and some have abnormal accumulation of *TDP-43* protein. FTD is clinically characterized by:

- Behavioral and personality changes with impairment of executive function, and relative preservation of memory.
- Progressive nonfluent and fluent aphasia.
- Association of FTD with Parkinsonisms and motor neuron disease may occur.

WHAT YOU SHOULD DO WHEN EVALUATING A SUSPECTED DEMENTED PATIENT

1. Obtain a detailed history (medical, neurological, and psychiatric) from the patients, relatives, caregivers. Try to establish the onset and course of dementia.
2. Perform detailed medical and neurological examinations. When doing neurological examination, pay special attention to cognitive function: for most part, the Mini-Mental Status Examination (MMSE) is sufficient.

   Caveat: When doing the MMSE, try not to irritate patients; explain the purpose of your questions. Level of education, age of the patients, and whether they are taking sedative medications will affect the results of MMSE. Well-educated individuals can perform well on the MMSE, even when their cognitive function is impaired. In these cases, formal neuropsychological testing is necessary.
3. Establish whether a focal neurological deficit exists and whether patient has prominent gait or motor problem(s).
4. Observe for any involuntary movements: chorea, myoclonus, tremor dystonia.
5. Look for the following signs, which are commonly found in dementia patients:
   - Grasp, rooting, snout, and palmomental reflexes.
   - Glabellar sign (seen in PD).
   - Increased jaw jerk.
   - Paratonia (gegenhalten): resistance to all passive movements of the joints.
   - Motor perseveration: repeating a motor task.
   - Motor impersistence: inability to maintain a motor task—keeping eyes closed, keeping tongue out, maintaining handgrip, and so on.

Workup

The following tests are recommended in all demented patients: cell blood count, chemistry profile, chest film, electrocardiogram, thyroid function tests (T_4, thyroid-stimulating hormone), vitaminB_{12}/folate level, serology for syphilis, and head neuroimaging (computed tomography scan/MRI). The following tests are considered for selected patients with dementia: electroencephalogram, lumbar puncture, HIV testing, heavy metal screen, positron emission tomography/single-photon emission computed tomography scan, angiogram, neuropsychometric testing, or brain biopsy.

Some Points About Workup

- It is not uncommon to find low vitamin B_{12} levels in the elderly; therefore, significant deficiency should be further confirmed by determination of serum methylmalonic acid, homocysteine level, or trial of vitamin B_{12} therapy.
- In demented patients, electroencephalogram is recommended when clinical presentation suggests seizure disorder or Creutzfeldt-Jakob disease.
- Head neuroimaging (computed tomography/MRI) is particularly useful when:
  - —The patient has symptoms of dementia for less than 6 months.
  - —Onset in patients younger than 60 years of age.
  - —History of seizure.
  - —Existence of focal neurological signs.
  - —Gait abnormalities.
- Lumbar puncture is indicated when:
  - —Rapidly progressive dementia less than 1 month.
  - —Suspect chronic infection as a cause.
  - —Positive serum fluorescent treponemal antibody-absorption test.
  - —Suspect normal pressure hydrocephalus.
  - —Onset of dementia in patients younger than 50 years of age.
  - —Suspect central nervous system vasculitis or meningeal carcinomatosis.
- Single-photon emission computed tomography or positron emission tomography scans can be useful in differentiating AD from vascular dementia or dementia with Lewy bodies.
- Routine genetic testing for AD is not indicated. No genetic test can accurately predict at what age an individual might be affected by the disease. If a family requests genetic testing, they should be referred to the Alzheimer's Association (800-272-3900).

12
Demyelinating Disorders

Acquired central nervous system (CNS) demyelinating disorders that are commonly seen in adults include:

- Multiple sclerosis (MS).
- Acute disseminated encephalomyelitis (ADEM).
- Acute/subacute transverse myelitis.
- Isolated optic neuritis (ON).
- Clinically isolated syndrome (CIS).
- Cerebral pontine myelinolysis.

MULTIPLE SCLEROSIS

MS is the most common demyelinating disorder in young adults and a leading cause of disability in the same age group. The disease affects the CNS myelin, producing what is commonly known as plaque. The MS plaques characteristically are disseminated in the CNS, separated in time and space. The disease commonly affects young females between the ages of 20 and 40 and has a higher prevalence in the northern states. Most authorities believe it is an autoimmune disease, which is triggered by viruses such as human herpes virus-6, Epstein-Barr virus, or environmental factors in genetically predisposed individuals. The chances of an immediate family member developing MS are about 3–5%, and for monozygotic twins, about 30%.

Clinical Course

- Relapsing and remitting MS accounts for approximately 80–90% of patients at the onset.
- Secondary progressive MS: Up to 80% of cases with relapsing and remitting MS develop this form.
- Primary progressive MS accounts for approximately 10% of patients at the onset.
- Progressive relapsing MS: Progression continues between relapses.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

Initial Clinical Presentations

The most common symptoms of MS are sensory complaints (numbness, paresthesia), weakness, clumsiness, visual symptoms, and sphincter disturbances. The onset of MS is variable and different from patient to patient, and because the initial symptoms are often subjective and nonanatomical (multifocal), both over- and underdiagnosis of MS are common in clinical practice.

When to Doubt the Diagnosis of MS

Doubt the diagnosis of MS when the patient presents with the onset of:

- Dementia.
- Aphasia, apraxia.
- Convulsion.
- Progressive course.
- Movement disorders.
- Absence of relapse or visual symptoms.
- Age of onset younger than 10 or older than 70 years

Strong Symptoms and Signs of MS

- Onset of unilateral, painful optic neuritis (ON).
- Bilateral internuclear ophthalmoplegia.
- Multitude of sensory symptoms with or without pain.
- Unilateral intense itching in cervical dermatome, or band-like tight sensation around the trunk or limbs.
- Multifocal corticospinal tract signs.
- Vertigo and incoordination.
- Early bladder dysfunction (frequency, urgency).
- Lhermitte's phenomenon.
- Uhthoff's phenomenon: worsening of symptom and signs after exposure to heat or exertion. Heat causes conduction block in demyelinating fibers.
- Facial myokymia: spontaneous, undulating movements of the facial muscles.
- Fatigue, after minor exertion with prior adequate rest period.
- Charcot's triad: intention tremor, nystagmus, scanning speech.

Diagnosis of MS

MS should be suspected on the basis of **clinical history and neurological examination**. Although as listed here some signs and symptoms are highly suggestive of MS (e.g., bilateral internuclear ophthalmoplegia in a young woman), there is no unique finding for this disorder. Diagnostic criteria that were proposed in 1982 have undergone changes a few times since. The

changes include adding cerebrospinal fluid (CSF) and magnetic resonance imaging (MRI) features to the clinical presentation. Discussing the criteria is outside the scope of this book. Pediatric MS increasingly recognized and gaining ground. The following laboratory tests are suggested to support the diagnosis of MS.

Magnetic Resonance Imaging

MRI of the brain and spinal cord not only aids in the diagnosis of MS, but also helps to rule out other conditions and monitor the effect of drug therapy and the disease progression. On MRI, the MS plaques appear in the white matter, characteristically ovoid in appearance, and are arranged perpendicularly to the lateral ventricle or corpus callosum (Dawson's fingers). Plaques are hyperintense in T_2-weighted MRI. Three areas of increases signal intensity with association of perpendicular to ventricles and size larger than 6 mm, or one infratentorial location has sensitivity of 80%, and specificity of 96% with positive predictive value of 65% for MS.

Detecting plaques with spinal cord MRI is almost as common as with brain MRI. Doing spinal MRI will increase the sensitivity of brain MRI by demonstrating the likelihood of dissemination. The enhanced lesions are indicative of disease activity, which are further made clear by using a higher dose of contrast (gadolinium), thinner slices with delayed images, and/or using the newer technique of magnetization transfer imaging. Ring enhancement also indicates active or new plaque.

Black Holes

On T_1-weighted MRI, MS plaques are seen as isointense to white matter, but some appear darker, "black holes." These lesions are usually in supratentorial regions, and about half of them resolve in a few months. Persistent black holes are indicative of severe demyelination and axonal (Wallerian) degeneration, and therefore are useful in measuring disease progression.

Cortical Atrophy

Cortical atrophy may develop over the course of MS, which indicates that gray matter may also be involved in MS. Cortical atrophy is best demonstrated on fluid-attenuated inversion recovery MRI. Cortical atrophy may be clinically relevant to cognitive impairment in MS patients. Cognitive impairment is seen in 40–60% of patients during the course of disease.

Magnetic resonance spectroscopy and diffusion tensor imaging are additional techniques that provide further evidence of axonal loss and diffuse involvement of white matter in patients with primary progressive MS, where white matter could appear to be normal.

Caveat: Normal MRI of the brain with history and neurological findings consistent with MS does not rule out MS. Likewise, abnormal MRI of the brain without history and neurological findings consistent with MS cannot allow a diagnosis of MS to be made with certainty. Normal MRI of the brain without convincing history and physical make the diagnosis of MS unlikely. Numbers of plaques shown by MRI does not always correlate with severity of the disease or clinical presentations (because some plaques are considered silent) but might correlate with prognosis, long-term disability and response to therapy.

Cerebrospinal Fluid

CSF abnormalities in MS include:

- Mildly elevated or normal CSF protein concentration and cells.
- Elevation of immunoglobulin (Ig)G with oligoclonal band is found in 80–90% of clinically definite MS. The best assay is isoelectric focusing followed by immunoblotting.
- Increased IgG index (normal level ≤ 0.7) is indicative of breakdown in the blood–brain barrier, because albumin is not part of CSF protein. An abnormal index is found in 90% of clinically definite MS.
- Antimyelin antibodies. Myelin basic protein and myelin oligodendrocyte glycoprotein antibodies may help in diagnosis of suspected of MS or disease severity. Further studies are needed to recommend these for diagnosis or as a therapy guide.

Evoked Potentials

When an MRI cannot be performed or is unavailable, multimodality evoked potentials can be used to establish multifocal sites of the lesion in the CNS and optic nerve, which can prove dissemination in space and not time. Visual evoked potential is probably the most useful of the evoked potentials in identifying patients with clinically definite MS.

Few Possible Variants of MS

• *Neuromyelitis Optica (Devic's disease)*

Neuromyelitis optica (NMO) presents with bilateral optic neuropathy and cervical myelopathy. It is more common in non-Caucasian ethnicity, and in Japan may account for 20–40% of MS cases. Optic neuropathy and myelopathy occur together or separately. At the onset, brain MRI is normal, but cervical spinal MRI shows plaques that span three or more vertebral segments. CSF analysis may show neutrophilic pleocytosis, and positive myelin oligodendrocyte glycoprotein. Serum IgG antibody to aquaporin 4 (AQP4), or NMO-IgG, has been advocated as a marker for NMO. Treatment of NMO begins with immunosuppression.

• *Marburg Variant*

This is variant that presents with acute focal deficit and mass lesion on MRI. Biopsy is required for definite diagnosis.

Prognosis

a. **One-third rule:** Generally speaking, one third of patients do well, one third become disabled but continue their daily living activities independently, and one third become wheelchair-bound.
b. **Kurtzke 5-year rule:** "Absence of significant motor or cerebellar deficit at 5 years correlates with limited disability at 15 years."
c. **Good prognosis:** onset before age 40, female relapsing/remitting type, sensory complaints at the onset and infrequent exacerbation, and mild MRI disease burden at diagnosis

Therapy

Acute Exacerbation

Although oral corticosteroids are still in use with acute exacerbation, most treatment centers recommend intravenous methylprednisolone (Solu-Medrol) as follows:

- Check blood chemistry and urine.
- Treat infections first, if any exist.
- Administer Solu-Medrol intravenously at a rate of 1 g every 90 minutes in 5% dextrose solution and monitor blood pressure and pulse. The total dose is 500–1000 mg/day for 5 days, followed with or without oral prednisone taper.
- Side effects: headaches, dizziness, muscle cramps, confusion.

  Caveat: In a known case of MS, before considering Solu-Medrol, exclude and treat urinary tract infection or fever from any kind of infection and electrolyte imbalance if they exist, because these conditions exacerbate neurological deficit (pseudorelapse).

Disease-Modifying Agents

The disease-modifying agents (DMAs) are indicated in all forms of relapsing MS. DMAs are shown to reduce relapse rate, reduce progression and disability, and decrease number of MRI lesions. Currently, these agents are recommended early, when the diagnosis of MS has been established. They are to be continued indefinitely, unless patients fail to respond or develop undesirable side effects; and then, another agent can be tried. Patients should be advised that these drugs do not stop the disease or make them feel better.

Current Food and Drug Administration-Approved DMAs

There currently five Food and Drug Administration (FDA)-approved DMAs.

INTERFERON-β

- **Interferon (IFN) β-1b (Betaseron)**. Administered subcutaneously, 0.25 mg (1 mL), every other day. Neutralizing antibody (NAB) may develop up to 30% of patients.
- **IFNβ-1a (Avonex)**. Six million units (30 mcg), given intramuscularly, weekly. About 5% may develop NAB.
- **IFNβ-1a (Rebif)**. Given subcutaneously, 22–44 mcg, every other day. About 20% may develop NAB.

GLATIRAMER

Glatiramer acetate (Copaxone) is a mixture of amino acids similar to myelin basic protein. It is delivered subcutaneously daily at 20 mg. Occurrence of NAB is very low.

The most common undesirable side effect of IFNs is a flu-like syndrome with severe chills and profuse sweating, which can be controlled by anti-inflammatory drugs. It is recommended to check blood count, liver function tests every 3–6 months, and periodic thyroid profile. Glatiramer acetate is rarely associated with the flu-like syndrome and requires no laboratory monitoring. Lymphadenopathy has been reported.

MITOXANTRONE

Mitoxantrone (Novantrone) is a chemotherapeutic agent and given intravenously. Because of its potential cardiotoxicity, it is recommended only for rapidly progressive MS. This drug is given intravenously every 3 months. Besides cardiotoxicity, mitoxantrone is frequently associated with alopecia and amenorrhea. Heart function should be monitored very closely.

NATALIZUMAB

Natalizumab (Tysabri) is an α-4 integrin antibody, FDA-approved for relapsing MS, but was withdrawn voluntarily from the market because of the report of progressive multifocal leukoencephalopathy in two patients receiving natalizumab, one of whom died from the disease. The relationship to multifocal leukoencephalopathy, however, is unclear, and further data are needed. This agent is currently under consideration by FDA to be released for clinical use again.

OTHER AGENTS

There are many other agents in use for individual MS patients or special clinical circumstances that are beyond the scope of this book.

Symptomatic Therapy

Spasticity

- Baclofen, 10 mg, three times a day, up to 80 mg/day.
- Benzodiazepine.
- Dantrolene (dantrium): 75 mg/day.
- Tizanidine.
- Botulinum toxin.

Tremor

- β-Blocker, clonazepam, gabapentin, primidone.

Depression

- Tricyclic antidepressants, selective serotonin reuptake inhibitor.

Pain

- Tricyclic antidepressants, carbamazepine, gabapentin, topiramate, doxepin.

Fatigue

- Amantadine, pemoline, fluoxetine, modafinil.

Bladder dysfunction

- Oxybutynin, propantheline, tolterodine.

Cognitive dysfunction

- Donepezil.

Rehabilitation

Physical and occupational therapy is recommended for all MS patients.

ACUTE DISSEMINATED ENCEPHALOMYELITIS

- ADEM is an acute, monophasic encephalitis that occurs after a viral illness or vaccination (postinfection or parainfection). It is more common in children than adults, and is believed to be caused by an immune response to an antigen (virus or vaccine).
- Neurological manifestations include headache, malaise, confusion, lethargy, seizures, and multifocal neurological deficits. Optic neuritis, if occurring, tends to be bilateral, and myelitis tends to be complete.
- The prognosis is generally good, and recovery is often spontaneous.
- The **most distinguishing features from MS** are **monophasic** course and absence of true relapse. However a relapse can occur (multiphasic forms).
- Although CSF, MRI, and histopathological of ADEM and MS can be similar, the CSF IgG is rarely elevated, and oligoclonal bands are usually absent. CSF cell count in ADEM is usually more than 50 lymphocytes/mm^3.

- About 10–20% of patients with ADEM evolve to MS like syndrome overtime.
- MRI of the brain typically shows multiple high-signal intensity lesions involving white matter, with preservation of periventricular regions. The lesions usually are asymmetric, and occipital head regions are predominantly involved. The lesions can affect gray matter, basal ganglia, and thalamic sites as well. In contrast to MS plaques, the lesions are usually the same age (have more uniform enhancement) and tend to be larger and less demarcated than the MS plaques are.
- Treatment of ADEM is supportive and symptomatic, but many neurologists consider a 5-day pulse of methylprednisolone treatment (1000 mg/day).

ISOLATED, UNILATERAL ON (OPTIC NEURITIS)

- Acute onset of orbital pain, particularly eye pain on eye movement test.
- Central or paracentral scotoma.
- Progressive, often unilateral visual loss.
- Color desideration (red and green).

Examination

- Decreased visual activity.
- Impaired visual field.
- Impaired color perception.
- Relative afferent pupillary defect (Marcus-Gunn pupil).
- Swollen disc with blurred margin (pulpillitis) or normal disc appearance (retrobulbar ON).

Therapy

The natural history of ON is good; most cases revolve spontaneously. Intravenous methylprednisolone can speed the recovery but does not change the outcome at 6 months. Oral prednisone is no longer used because it can cause rebound flares of ON. Although scientifically unproven, the majority of neurologists prescribe a course of pulse methylprednisolone treatment. Some authorities advocate steroid therapy to the patients with abnormal MRI. The disease has a recurrence rate of 15–30%.

ACUTE/SUBACUTE TRANSVERSE MYELITIS

- Acute or subacute onset of leg paresthesia and back pain, followed by flaccid paraparesis.
- Sensory level deficit (commonly thoracic).
- Bowel or bladder dysfunction.

- About 40% have preceding febrile illness.
- Workup: blood count, chemistry profile, rapid plasma reagin test, erythrocyte sedimentation rate, vitamin B_{12}, HIV testing, CSF examination, and MRI of the brain and spinal cord.

Therapy: Therapy is supportive and symptomatic. Pulse intravenous methylprednisolone is recommended when brain MRI is abnormal or patient has dense deficit. Prognosis is generally good, with complete recovery occurs in about two thirds of the patients.

CLINICALLY ISOLATED SYNDROME (CIS)

CIS is defined as a single monosymptomatic attack that is highly suggestive of MS, such as isolated, painful ON, partial acute/subacute transverse myelitis, or other strong indicators as previously described. CIS poses a diagnostic and therapeutic challenge to the neurologists. It is recommended that all patients presenting with CIS should have contrast brain MRI. If brain MRI is abnormal, showing two or more white matter lesions consistent with demyelination, conversion to MS is about 60–80%, and if it is negative, the chance is about 20%. The individual with a positive brain MRI should begin DMAs. In a patient with a negative MRI, it is wise to repeat in 3–6 months. If the repeat MRI is positive, initiate DMA, and if it remains negative, a repeat MRI is warranted if the patient developed new symptoms in the interim. Although intravenous Ig also been used but most experts recommend INF, such as Avonex, if decided that the patient is to be treated.

CENTRAL PONTINE MYELINOLYSIS OR OSMOTIC CEREBRAL DEMYELINATION

Central pontine myelinolysis is a rare demyeliminating disease that is most commonly seen in alcoholics and malnourished patients. The cause is unknown, but has been related to rapid correction of serum osmolality or hyponatremia.

- Clinical manifestations include lethargy, mental confusion, flaccid quadriparesis, and pseudobulbar palsy.
- Diagnosis is suspected when an alcoholic patient with hyponatremia becomes quadriparetic after correction of hyponatremia.
- MRI of the brain frequently shows a midline demyelinating lesion in the basis pons; the lesions also can be seen in thalamus, basal ganglia, and subcortical white matter. There is no specific therapy, but slow correction of serum osmolality (12 mmol/L/day) and hyponatremia (130 mmol/L) will prevent the disease.

13
Neurological Complications of Alcohol

NEUROLOGICAL COMPLICATIONS OF ALCOHOL

1. Acute alcoholic intoxication: mild euphoria to coma (depends on the serum alcohol level).
2. Alcoholic blackout: transient amnesia after a binge.
3. Alcohol withdrawal syndromes: tremulousness, autonomic hyperactivity, hallucinosis.
4. Alcohol withdrawal seizures.
5. Delirium tremens: confusion, florid hallucination, and autonomic hyperactivity.
6. Nutritional deficiencies:
   - Wernicke-Korsakoff syndrome.
   - Alcoholic polyneuropathy.
   - Pellagra.
7. Neurological complication of uncertain etiology:
   - Alcoholic cerebellar degeneration.
   - Central pontine myelinolysis.
   - Marchiafava-Bignami disease: degeneration of corpus callosum.
   - Alcoholic myopathy.
   - Alcoholic amblyopia.
8. Encephalopathy:
   - Hepatic encephalopathy.
9. Trauma:
   - Subdural hematoma.
   - Posttraumatic epilepsy.
10. Other neurological association:
    - Stroke.
    - Movement disorders.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

ALCOHOL WITHDRAWAL SEIZURES

- Alcohol withdrawal seizure ("rum fit") occurs about 24–48 hours after cessation or reduction of drinking after chronic use.
- Seizures are brief, generalized tonic-clonic, and occur one to three in a row.
- The majority of patients have other signs of withdrawal, such as tremulousness, agitation, and hallucinosis.
- Seizures are self-limited.
- Approximately 3% may present as status epilepticus.
- Patients with uncomplicated cases usually have normal neurological examination and brain imaging.
- Neuroimaging and electroencephalogram (EEG) are warranted in all patients with withdrawal seizure when presenting for the first time, and should be repeated thereafter if neurological status has changed.
- EEG after seizure may show diffuse nonspecific slowing; photomyoclonic response, however, may be seen.
- Alcohol withdrawal seizure does not lead to chronic epilepsy if patient remains abstinent.
- Treatment includes hydration, administration of thiamine and benzodiazepine, and correcting underlying triggering factors such electrolyte imbalance or infection.
- Alcohol withdrawal seizures do not require maintenance such as with chronic antiepileptic (AED) drugs, because if the patient continues drinking, the patient will still have seizures and is unlikely to take the medication, and if the patient stops drinking, the patient does not need AEDs.
- Status epilepticus in alcoholics must be treated like any other status epilepticus.
- Consider maintenance AEDs in a patient with alcohol withdrawal seizure if:
  1. Seizures are focal.
  2. Patient has focal neurological deficit or focal structural insult demonstrated on brain imaging.
  3. Epileptiform discharges on EEG.
  4. Seizure after prolong duration of abstinence.

ALCOHOLIC NUTRITIONAL POLYNEUROPATHY

- Alcoholic nutritional polyneuropathy is a chronic, progressive, sensor/ motor axonal polyneuropathy.
- The disease causes a painful, burning sensation in the feet and decreased reflexes.
- Hyperhidrosis of the feet and hands is common.
- Treatment includes administration of thiamine and multivitamins and symptomatic treatment of pain.

ALCOHOLIC CEREBELLAR DEGENERATION

- Alcoholic cerebellar degeneration is a slowly progressive disorder with atrophy of cerebellar cortex and superior vermis.
- Its typical features include impairment of stance and gait (truncal ataxia), with minimal or no nystagmus, dysarthria, or upper extremities ataxia as seen with finger-to-nose testing.
- It is often associated with variable degree of polyneuropathy. Treatment is supportive with physical and occupational therapy. Thiamine and a multivitamin are commonly prescribed.

14
Dizziness and Vertigo

KEY POINTS OF HISTORY

- Differentiate dizziness from true vertigo (sensation of movement) and other terms that are used by the patient, because the description by the patients can be nonspecific, many times, for example, "lightheadedness," "faint," or "giddiness" is vertigo and vice versa.
- Sudden onset of vertigo is due to asymmetry of vestibular system dysfunction.
- Approximately half of patients presenting with dizziness have true vertigo.
- Establish the onset of problem, and whether it is acute, subacute, or chronic.
- Vertigo is usually paroxysmal. Constant vertigo suggests psychogenic and not vestibular dysfunction. Chronic conditions such as acoustic neuroma rarely present with vertigo.
- Aggravating factors can be head or body position.
- Benign positional vertigo accounts for about half of all cases of vertigo.
- Associated symptoms: nausea, vomiting, fullness of ears, hearing loss, tinnitus, all of which suggest otological etiologies; headaches, diplopia, blurred vision, ataxia, paresthesia, all suggestive of central nervous system (CNS) etiologies.
- History of recent ear or upper respiratory infection or head trauma.
- History of drug regimen or drug overdose.
- History of depression or other psychiatric problems.
- Vertigo that is provoked by exertion, loud noise, sneezing, or coughing (Tullio's phenomenon) is suggestive of perilymphatic fistula.

KEY POINTS OF PHYSICAL EXAMINATION

- Check cardiovascular system for cardiac arrhythmia, murmur, orthostatic hypotension, and carotid or subclavian bruits.
- Check ear for infection, trauma, or impacted wax.
- Do Nylen-Barany (Dix-Hallpike) test: Have the patient, from seating position on the table, quickly lie down supine with head positioned 45° over the

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

end of the table, and then rotate the head 45° side to side (for 30 seconds). Observe for vertigo, nausea, and nystagmus (onset, direction, and duration); presence of these symptoms/signs is suggestive of vestibulopathy if they have delayed onset, and are fatigable and unidirectional. Nystagmus in vestibulopathy is upbeat and torsional and resolves with eye fixation.

- Complete neurological examination, with special attention to brainstem, cranial nerves, and cerebellar function, stance, and gait.

CAUSES OF VERTIGO

Vertigo is a multifactorial condition. The neurologist is often consulted to differentiate whether vertigo is caused by inner ear disease (vestibulopathy) or CNS lesion. Keep in mind migraine as a possible cause of vertigo in a young adult.

SYMPTOMS AND SIGNS OF CNS CAUSES

1. The onset could be acute, subacute, or chronic.
2. When doing the head-tilt test or Nylen-Barany test, the onset of vertigo is sudden, without any latency or delay and it does not fatigue (decrease severity with repetition of tilt). Vertigo persists as long as head is kept tilted.
3. Nystagmus is often multidirectional.
4. Nausea/vomiting, generalized fatigue, and hearing loss is less severe.
5. Associated neurological symptoms and signs (brainstem/cerebellar dysfunction) are further supportive of CNS causes.

SOME CNS CAUSES OF VERTIGO

- Posterior circulation transient ischemic attacks or stroke.
- Brainstem stroke or tumor.
- Cerebellopontine angle tumors.
- Posterior fossa pathologies.
- Multiple sclerosis.
- Spinocerebellar degeneration.
- Migraine variant.

CAUSES OF DRUG-INDUCED DIZZINESS AND VERTIGO

- Aminoglycosides.
- Penicillin.
- Aspirin.
- Sulfonamide.
- Antiepileptic drugs.
- Antihistamines.

SOME COMMON OTOLOGICAL CAUSES OF VERTIGO

Benign Paroxysmal Positional Vertigo

- Benign paroxysmal positional vertigo is the most common cause of acute vertigo.
- Characteristically presents with recurrent episode of vertigo, lasting seconds to minutes, aggravated by head position, particularly rolling over in bed.
- Hearing is intact and rarely does tinnitus occur.
- It is thought to be caused by calcium deposit in the posterior semicircular canal (canalithiasis) after head trauma or repeated ear infection.
- Although generally self-limited, the condition is disabling at times.

Acute Labyrinthitis or Vestibular Neuronitis

- Acute vestibular neuronitis or labyrinthitis causes more severe and prolonged duration of vertigo, associated with nausea and vomiting and, occasionally, hearing impairment and tinnitus.
- Usually preceded by upper respiratory tract infection. It is usually self-limited.
- Some experts recommend a course of methylprednisolone to prevent hearing loss.

WORKUP OF DIZZY PATIENT

Workup depends upon the suspected etiology, after history and examination. If the patient has hearing loss and tinnitus, and is suspected of having otological disease, the patient should be evaluated by an ear, nose, and throat specialist for a formal audiogram and caloric testing. If CNS causes are suspected, magnetic resonance imaging of the head is indicated. Dizziness of undetermined etiology should be tested for complete blood count, erythrocyte sedimentation rate, chemistry profile, electrocardiogram, thyroid function test, and fluorescent treponemal antibody test. Electronystagmography and brainstem auditory evoked response have limited use.

SYMPTOMATIC DRUG THERAPY FOR DIZZINESS

1. Anticholinergic. Scopolamine disk (Transderm-Scop): 1.5 mg/disk behind the ear, or 0.5–1 mg, three times a day orally.
2. Antihistamines. Meclizine hydrochloride (Antivert): 25–100 mg/day in divided dose, or dimenhydrinate (Dramamine): 50 mg four times a day.
3. Antiemetics. Promethazine hydrochloride (Phenergan): 50–100 mg/day in divided dose, or metoclopramide.
4. Benzodiazepines. Diazepam or lorazepam.
5. Diuretics. Hydrochlorthiazide: 50 mg/day.

Caveat: All above medications except diuretics have sedation effects, and they should be used only when necessary, such as for frequent and severe symptoms. The response to pharmacotherapy is generally unrewarding. Vestibular exercise—inducing vertigo by repeating the position to produce adaptation—is effective in treating mild vertigo (Brandt-Daroff exercise). For benign paroxysmal positional vertigo, the most effective treatment is repositioning maneuvers such modified Epley and Semon maneuvers.

15
Headaches and Facial Pain

HEADACHES

Evaluation of the Patient With Headache

History: Obtaining a careful and thorough history of the headache is the most important part of the evaluation. You should establish the following as you are taking the history:

- Age at onset of headache.
- Onset of headache: whether it is acute, subacute, or chronic.
- Severity and frequency of the headache.
- Characteristics of the pain as described by the patient.
- Location and duration of the headache.
- Any associated symptoms or signs.
- What the aggravating or relieving factors are.
- Have there been any recent changes of headache type?
- Any relation to menstrual period or season?
- How often are medications used or how was the response to previous treatment?

Social history: occupation, marriage, history of alcohol or drug abuse.

Family history: Very important; about 50% of patients with migraine have a positive family history.

Medical history: history of hypertension, depression, glaucoma.

Medication history: contraceptives, diet control pills, or medications that have been used for headaches.

Physical and Neurological Examination

Examine the head and neck, record blood pressure, and check peripheral and temporal arteries pulses. With any new patient, a complete neurological examination is mandatory. Special attention is particularly given to the neck for stiffness, bruits, fundoscopy examination, pupillary size and reactions, visual field, cranial nerves, and any focal neurological signs.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

Laboratory Tests

With a thorough history taking that is supplemented by careful examination, the diagnosis of many headaches and facial pains can be made with a high degree of certainty. In a few clinical conditions, which will be discussed in this chapter, laboratory tests are warranted.

Tension-Type Headache

- The most common type of headache, affecting about 80% of patients presenting with headache. The onset is insidious and builds up as the day goes on. The pain is achy, dull, and often starts from the occipital head regions and spreads bifrontally or in a band-like pattern. Tightness of the neck muscles is common.
- The headaches may last from 30 minutes to several days and can occur daily or episodically.
- Some patients may give a history of migraine-type headaches in previous years.
- Pathophysiology is unknown, but stress or tension is a contributing factor. The trigeminal neurovascular system most likely is involved.
- The neurological examination is generally normal. In a typical case there is no need for laboratory studies.
- Tension-type headaches can occur episodically or chronically.

Treatment. Daily exercise, muscle relaxation, and avoidance of alcohol and caffeine. Aspirin, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and tricyclic antidepressants (TCAs) are effective drugs. Start TCA in a low dose and build up to the adequate dose. Avoid polypharmacy, and do not use narcotic medication.

Migraine Headaches

Migraine With Aura (Formerly Called Classic Migraine)

- Unilateral, intermittent, moderate to severe throbbing (pulsating, sharp) headache, particularly over the frontotemporal regions—"sickening headaches."
- A small percentage of patients may complain of irritability, mood changes, or food cravings (chocolate) a few days before the headaches—premonitory symptoms.
- Migraine is common in middle age and in educated women.
- Migraine is commonly associated with nausea/vomiting, photophobia, and phonophobia.
- The headache is aggravated by physical activity, menstrual period, contraceptives, alcohol, smoking, cheese, monosodium glutamate, and processed foods.

- The onset of headache is usually acute; duration is between 4 and 72 hours.
- A patient with a migraine headache prefers a dark, quiet room.
- Aura manifesting as visual symptoms such as hemianopia, flashing lights (photopsia), stars/spots, and more characteristically scintillating scotoma. Other less common auras include facial and arm paresthesia, numbness around mouth (chiro-oral), speech difficulties, and weakness. The aura could be present singly or in combination, and usually lasts 10–15 minutes.
- Migraine is now believed to be neuronal in origin, involving the brainstem, hypothalamus, and trigeminal system. An aura is due to neuronal suppression secondary to decreased cerebral blood flow originating from the occipital lobes, spreading anteriorly (cortical spreading depression of Lau).
- It has been shown that patients with migraine with aura have higher incidence of patent foramen ovale and atrial septal defects.
- Migraine is a chronic disease and comorbid, with many medical conditions.

Migraine Without Aura (Formerly Called Common Migraine)

This form of migraine is more common than migraine with aura, and has the same clinical presentation but headache is diffuse.

Forms of Migraine or Variant

Complicated migraine. Focal neurological signs persist up to 48–72 hours after the resolution of headaches. The most common forms of complicated migraine are ophthalmoplegic and hemiplegic migraine. Before the diagnosis of complicated migraine can be made, a structural lesion (e.g., arteriovenous malformation, aneurysm) should be excluded by a neuroimaging technique, unless the patient is known to you and has previously been investigated.

Migraine infarction. Migraine infarction is a neurological deficit that persists after the resolution of the headache. Stroke workup is required in these patients.

Basilar artery migraine. This form of migraine is commonly seen in young girls, manifesting as an occipital throbbing headache associated with dizziness, blurred vision and diplopia, vertigo, ataxia, paresthesias, and even syncopal episodes. An electroencephalogram (EEG) needs to be done to rule out a seizure, and a magnetic resonance imaging (MRI) of the head to rule out a posterior fossa and brainstem lesion.

Migraine aura without headache—acephalgic migraine

- Onset of typical migraine aura: scintillating scotoma without headaches.
- In young adults, this should be differentiated from a seizure (EEG).
- In the elderly, this should be differentiated from transient ischemic attacks (stroke workup).

Other variants

These include **retinal**, **vertiginous migraines**, and **familial hemiplegic migraine**.

Treatment of Migraine

Nonpharmacological

- Avoidance of aggravating factors.
- Biofeedback and relaxation techniques.
- Regular daily exercises, physical therapy.
- Establish a good relationship with the patient. Patients with migraines are generally sensitive and intelligent individuals. They want to know the cause of the headaches, the type of medications, and the outcome. Set aside time for questions.

Pharmacotherapy

a. **Symptomatic: nonspecific**

- NSAIDs. The only cyclooxygenase-2 inhibitor, rofecoxib, for migraine was withdrawn from market because of reported cardiovascular side effects.
- Aspirin.
- Acetaminophen, alone or in combination with caffeine (Excedrin).
- Minor narcotics; hydrocodone, buterphanol (Stadol) in special cases.

b. **Symptomatic: abortive**. These drugs are given during an aura, with a single effective dose, or before the peak of the headache. Abortive drugs should be given in moderate to severe migraines. The response is more predictable when given via the nonoral route. If headaches are frequent, preventive therapy should be used. Generally speaking, abortive therapy should not be used more than 10 days per month to prevent medication-induced headache.

Ergotamines. These can be given alone or in combination with caffeine (Cafergot, ergostat). Ergotamines can be given orally, parenterally, as a suppository, or as nasal spray. The maximum oral dose is 6 mg/day. Ergotamines are vasoconstrictors, and their antimigraine effects are mostly because of stimulation of the 5-hydroxytryptamine (5HT)-1-D or 5HT-B receptors. These drugs are habit forming and can produce withdrawal headaches. Ergotamines are contraindicated in pregnancy, complicated migraine, and in patients with hypertension, ischemic heart disease, and peptic ulcer disease. With the elderly patient, obtain an electrocardiogram before using ergotamines. Ergots are rarely used nowadays.

Dihydroergotamine (DHE-45). This is an agonist to 5HT-1-D and 5HT-1-B and other aminergics. This drug can be given intravenously, intramuscularly, or subcutaneously. This drug relieves headache in 80% of patients, and is a particularly good drug to use in severe migraine or intractable

migraine. The contraindications are the same as those for ergotamines, but the side effects are less, and it does not cause habituation. Intravenously, DHE-45 should be administered with an antiemetic agent (metoclopramide [Reglan]). DHE nasal spray (Migranal) is also available.

Serotonin receptor agonists (Triptans)

Sumatriptan (Imitrex). This is a specific 5HT-1-A and 5 HT-1-B receptor agonist. This medication can be given intramuscularly, subcutaneously, orally, or as a nasal spray. The maximum subcutaneous dose is 12 mg/day, and maximum oral dose is 200 mg/day. Side effects, contraindications, and precautions are the same as ergotamines.

Zolmitriptan (Zomig). This enters the brain faster and stays longer than sumatriptan does. The dose is 2.5 or 5 mg. The dose should not exceed 10 mg/day. Nasal spray and "fast-melt" forms are also available.

Naratriptan (Amerge). This drug is for prolonged and frequent attacks and is supplied as 1- and 2.5-mg tablets. The dose should not exceed 5 mg/day.

Rizatriptan (Maxalt). The dosage is a 5- or 10-mg tablet or dissolving wafer, and can be given up to 30 mg/day.

Almotriptan (Axert). The dosage is a 6.25 and 12.5-mg tablets, to max dose 25 mg/day.

Eletriptan (Relpax). Comes in 40- and 80-mg tablets. Start with 40 mg.

Frovatriptan (Frova). Comes in 5- and 7.5-mg tablets.

Triptans should not be used in combination. If a patient fails to respond to one, try another, with enough washing period. Triptans should not be used in uncontrolled hypertension, patients with unstable angina, Raynaud's, and patients with ischemic heart disease and impaired liver function. Triptans are also not recommended for males older than 50, pregnant women, during lactation, and for variants of migraine, such complicated migraine, basilar artery migraine, and familial hemiplegic migraine. Triptans should be used in early stage of headaches.

Isometheptene (Midrin). This is a combination of isometheptene, dichloralphenazone, and acetaminophen. The maximum dose is 6 capsules per day or 10 capsules per week. It has a bad taste and may elevate the blood pressure. This agent is rarely used now.

For severe nausea and vomiting associated with migraine, use intravenous metoclopramide (10 mg) or procholrperazine (10 mg).

Prophylactic treatment. Preventive therapy in migraine is indicated when:

- Headaches are frequent (more than three per month).
- Headaches are severe and disabling (interfere with work or household duties).

- Headaches have no warning.
- Headaches are not responding to abortive or symptomatic treatment.
- Preventive therapy should used more frequently to prevent medication-induced headache.

Start prophylactic drugs with a low dose, and titrate according to the patient's tolerance and response. These drugs should be given on a daily basis until an adequate response is achieved. Maintain at the lowest effective dose, and then the drugs may be discontinued after adequate headache-free period. Be sure to know their side effects and contraindications. These drugs include:

β-Blockers

- Propranolol and timolol have been approved.
- Others: metoprolol, nadolol, atenolol.
- Not to be used in asthma, diabetes, and cardiac dysfunction.

TCAs

- Amitriptyline: 25–150 mg/day.
- Doxepin: 25–300 mg/day.
- Nortriptyline.

Calcium-channel blockers

- Verapamil: 80–400 mg/day.

NSAIDs

- Naproxen: 500–1000 mg/day.

Antiserotonin

- Methysergide (Sansert): 2–8 mg/day. Rarely used now.

Antiepileptic drugs

- Valprox (Depakote): 500–2000 mg/day.
- Gabapentin.
- Topiramate: 25 mg/day. Increase up to 100 mg twice a day.

Most neurologists prefer antiepileptic drugs (e.g., topiramate) as first-line drugs for migraine prevention.

Other agents

Angiotensin-converting enzyme inhibitors, botulinum toxin, coenzyme Q10, riboflavin, butterbur. These agents been studied in small number of patients. Their use should be individualized.

Menstrual Migraine

Prophylaxis with naproxen, 550 mg, twice a day, or frovatriptan, 2.5 mg, twice a day for a week.

Status Migrainosus

These are repeated migraine headaches resulting in dehydration (nausea and vomiting). Most patients require a brief hospitalization for treatment:

- Discontinue analgesics, sedatives, and narcotics.
- Rehydration with intravenous fluids.
- DHE-45, 0.5–1 mg intravenously, every 8 hours, plus intravenous metoclopramide (Reglan), 10 mg.
- If the headache persists: dexamethasone, 4 mg intravenously, twice a day, or 5–10 mg intravenously with benzodiazepam or ketoralac, 30–60 mg intravenously.

Recommended Protocol for Repeated Dose of DHE-45

- Premedicate: 10 mg metoclopramide, intravenously over 30 minutes.
- DHE-45, 0.5 mg, over 1 minute, given intravenously.
- If headache improves: DHE-45, 0.5 mg, intravenously, every 8 hours as necessary.
- If headache improves, but severe nausea: metoclopramide or lower dose of DHE-45, 0.15 mg.
- If headaches persists, but no nausea: DHE-45, 0.5 mg intravenously, every 8 hours.

Cluster Headache

- Sudden onset of severe, intermittent, unilateral retro-orbital sharp pain—"suicide headaches."
- Frequently associated with lacrimation and rhinorrhea on same side of pain, with photophobia and phonophobia.
- Partial Horner's syndrome sometimes seen after headache on same side of pain.
- Male-to-female ratio is 2:1. In woman cluster headache should be differentiated from "hemicranial" headaches.
- The headache lasts between 30 minutes and up to 3 hours, and occurs as a cluster (several days to weeks, with interval(s) of no headache, or chronic daily).
- The patient prefers walking and pacing during the pain.
- The headache is precipitated by certain drugs (nitroglycerin), alcohol, smoking, and hot weather.
- Majority of patients are smokers.

Treatment

Nonspecific symptomatic. The treatment is the same as for migraine.

Specific: Abortive

- Oxygen (100% by mask), 20 L/minute for 20 minutes.
- Sumatriptan: same as migraine.

- Nasal lidocaine drops (10%): 1 mL in cotton swab in nostril for 5 minutes.
- Nasal sumatriptan.
- Nasal DHE and capsaicin.

Prophylactic

- Calcium-channel blocker (Verapamil).
- Corticosteroids (60 mg/day for 3 days).
- Chronic cluster headache may require lithium carbonate (300 mg, three times a day) to provide level of 0.7–1.2 mEq/L.
- Valproic acid, topiramate.
- Melatonin (10 mg at bedtime).
- For intractable cluster headache, consider glycerol injection or Gamma Knife lesion of trigeminal ganglion, or other techniques.

Some Common Headache Syndromes

Chronic Daily Headache (CDH)

Transformed migraine: Chronic, frequent migraine-like headache that does not respond to conventional antimigraine drugs. The patients often have mixed headaches (tension and migraine). This is probably the most common reason the patient is seeking a specialist. Risk factors for CDH include: Frequent headache, obesity, medication overuse, low education, snoring.

Analgesic-rebound headache: This is another form of mixed headaches and can occur when the patient overuses analgesics or medications that have butalbital (Fiorinal), benzodiazepines, or NSAIDs. Overnight, the patient develops withdrawal symptoms manifesting as a headache in the morning. These patients need to be detoxified again to respond to symptomatic or prophylactic medications.

Migraine and Pregnancy

Women with the onset of migraine during their menses or menarche usually improve when they become pregnant. In a small percentage of patients the headache worsens. A new onset of migraine-like headache during the postpartum period warrants further diagnostic workup to rule out sinus venous thrombosis, pseudotumor cerebri, and stroke.

TREATMENT

- Consult gynecologist.
- Try nonpharmacological remedies.
- Specific-abortive treatments: Ergotamines, serotonin agonists (Triptans), and Midrin should be avoided.
- Nonspecific symptomatic treatments: Acetaminophen, NSAIDs, and minor narcotics (hydrocodone) can be used for a more severe headache.
- Prophylactic: Propranolol, amitriptyline and fluoxetine are to be used in lower doses if deemed necessary.

Posttraumatic Headaches

- Tension or mixed-quality headaches.
- Often diffuse or bifrontal and occur after minor head trauma (concussion).
- Often associated with other symptoms of post-concussion syndrome (dizziness, fatigue, poor concentration).
- In uncomplicated cases (when there is no litigation), the headaches resolve spontaneously in a few months.

  Treatment: Nonspecific symptomatic: aspirin, acetaminophen, NSAIDs, amitriptyline, and propranolol. Assurance is also important.

Pseudotumor Cerebri

- Chronic, diffuse, dull, achy headache. Worse in the morning.
- Associated symptoms include visual obscuration, occasionally pulsatile tinnitus, and diplopia (transient sixth cranial nerve palsy).
- Very rarely, obvious papilledema is absent.
- The majority of patients are young, female, and overweight (especially recent change in weight).
- In uncomplicated cases, the neurological examination is normal, except for bilateral papilledema.

DIAGNOSIS

The pathophysiology is not clearly understood, but it is thought there is poor absorption of the cerebrospinal fluid.

- Neuroimaging: computed tomography (CT) scan/MRI to rule out space-occupying or sinus venous thrombosis.
- Spinal tap: to establish a high opening pressure (>28 mmHg) and normal cerebraospinal fluid composition.

TREATMENT

- Weight reduction: effective, but impractical most of the time.
- Nonspecific symptomatic: NSAIDs, acetaminophen, TCA.
- Specific: acetazolamide (Diamox), 250 mg, four times a day; furosemide, 80 mg/day; prednisone, 40 mg/day for several weeks.
- Spinal tap: Repeat lumbar puncture (LP) to reduce opening pressure.
- Lumboperitoneal shunt and optic nerve sheath fenestration (decompression) when visual acuity decreases or the patient develops visual field defect.

Caveat: Patients with pseudotumor cerebri should be followed closely by a neurologist and an ophthalmologist. The goal of therapy is to not only control the headache but, more importantly, to save optic nerve function.

Headaches That May Require Short-Term Hospitalization

- First or worst headache of the patient's life.
- Headache with a progressive course.
- Headache associated with unexplained fever.
- Headache associated with focal neurological symptoms and signs other than typical aura.
- Headache associated with the onset of seizures or prolonged mental confusion.
- Status migrainosus, when dehydration and pain need to be corrected intravenously.
- Headaches associated with neck stiffness.

Headaches Requiring Specific Diagnostic Tests

- **Pseudotumor cerebri:** MRI/CT scan of brain, lumbar puncture, complete blood count (CBC), erythrocyte sedimentation rate (ESR), thyroid-stimulating hormone, T_4.
- **Temporal arteritis:** CBC, chemistry profile, ESR, temporal artery biopsy.
- **Basilar artery migraine:** EEG, MRI of the brain (rule out posterior fossa lesion).
- **Migraine with infarction, migraine with atypical or prolonged aura, or migraine that is unresponsive:** CBC, chemistry, ESR, MRI/magnetic resonance angiography (MRA) or angiogram (when unruptured aneurysm, arteriovenous malformation, or vasculitis is suspected), carotid Doppler, echocardiogram. In pregnant women with new onset migraine or postpartum, additional testing such as antiphospholipid antibody, and proteins C and S might be warranted (rule out coagulopathy).
- **"First (or Worst) Headache of My Life":** For this type of headach, particularly if associated with neck stiffness; subarachnoid hemorrhage is always suspected.
- **Thunderclap headache:** Thunderclap headache is a severe headache that reaches the maximum within a minute or so. Consider unruptured aneurysm, and obtain at least an CTA. The same strategy is recommended for coital headaches, including LP.
- **Acute meningitis:** Neuroimaging followed by an LP.
- **Spontaneous internal carotid artery dissection:** severe, unilateral periorbital headache, carotid bruits, Horner's syndrome, or focal neurological symptoms and signs: MRI/MRA or angiogram.

Other Rare Headache Syndromes

There are a few rare headache syndromes that neurologists should know about. These include the following: short-lasting, unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT), chronic paroxys-

mal hemicrania, hypnic headache, nummular headache (patchy pain), ice-pick headache, and coital or exertional headache.

OPHTHALMOLOGY AND HEADACHES

In practice, several headache syndromes are often associated with eye symptoms and signs.

- **Local eye disorder:** glaucoma, uveitis, cataract.
- **Migraine headache:** photophobia, visual auras, ophthalmoplegia, retinal migraine.
- **Cluster headache:** ipsilateral (to pain) lacrimation, ipsilateral Horner's syndrome, photophobia.
- **Pseudotumor cerebri:** visual obscuration, diplopia, blurred vision, photophobia, papilledema, visual field defect or decreased acuity (untreated severe cases).
- **Temporal arteritis:** decreased visual acuity, visual field defect, ischemic optic neuritis.
- **Subarachnoid hemorrhage:** photophobia, diplopia, papilledema, subhyaloid hemorrhage (pathogonomic if present).
- **Meningitis/focal encephalitis:** photophobia, papilledema, visual field defect.
- **Cavernous sinus thrombosis:** ophthalmoplegia, proptosis, eye swelling.
- **Tolosa-Hunt syndrome:** ophthalmoplegia (cavernous sinus granuloma).

NEURALGIAS

Facial pain syndrome is caused by any pathology or condition arising from the face and mouth such as sinusitis, dental infections, gum disease, throat infection, and temporomandibular joint dysfunction (syndrome). When the description of the facial pain does not correlate with any known condition, by either history or examination, the term atypical facial pain is applied. In this segment, only primary neuralgias were chosen for discussion.

Trigeminal Neuralgia

- Severe, sudden, paroxysmal, short-duration (30–60 seconds), lancinating, unilateral facial pain in the distribution of one or two branches of the trigeminal nerve (commonly V2 and V3). The incidence is about 4–5 per 100,000.
- The pain is often triggered by touch, talking, swallowing or brushing teeth, and shaving.
- Pain does not awaken the patient at night.
- Immediately after the pain, transient facial numbness may occur.
- Trigeminal neuralgia is more common in middle age or in elderly women.
- The pain is sometimes so severe it may induce facial grimacing (tic).

- In younger individuals, the onset of trigeminal neuralgia may be seen with the onset of multiple sclerosis.
- The onset of trigeminal neuralgia in the young and a persistent motor or sensory deficit after pain warrants an MRI to exclude a brainstem lesion or multiple sclerosis.
- The cause is usually related to compression of nerve by an aberrant artery or vein (>80%).
- MRI/MRA of brain is considered if patient failed respond to medical therapy, younger patient (<40), bilateral presentation, more than one branch involved, persistent sensory loss, and pain in distribution of V1.

Treatment

Medical. The drug of choice is carbamazepine (Tegretol), starting with a lower dose and titrating according to the response, aiming for a level of 8–13 mg/dL (600–1200 mg/day). Other effective medications are:

- Phenytoin, 300–400 mg/day.
- Oxcarbzepine.
- Lamotrigine.
- Baclofen, 20–80 mg/day.
- Clonazepam, 12 mg/day.
- Amitriptyline, 50–100 mg/day.
- Divalproex (Depakote), 1000–1500 mg/day.
- Gabapentin (Neurontin), 2400–3600 mg/day.
- Topiramate.

Surgical. Before considering surgical options, you may want to treat the patient with combination of medication (rational polypharmacy). The surgical procedures include:

Ganglionalysis by radiofrequency or by infiltration of alcohol or glycerol. In selected cases, repositioning of the compressing artery to the trigeminal nerve through a posterior fossa craniotomy may be considered (*microvascular decompression—Jannetta procedure*). *Gamma Knife radiofrequency* (70–80% effective), and *CyberKnife radiofrequency,* with same effectiveness. Other techniques include *radiofrequency rhizotomy, balloon compression,* and *neurorectomy*. All surgical procedures have higher rate of pain recurrency and facial sensory loss except microvascular decompression.

Postherpetic Neuralgia

- Affects V1, and presents with pain after rash resolved. Pain may occur months after rash, and sometimes rash appears later. Pain is a burning ache associated with itching and allodynia.

- Elderly women are at risk. Other risk factors are severity of rash and pain at the onset.
- Pain may persist for many years.
- Treatment includes topical lidocaine, capsaicin cream, gabapentine, amytriptyline, opioids, and nerve bock.

Occipital Neuralgia

- Unilateral sharp, stabbing pain in distribution of greater or lesser occipital nerve.
- Pain may be triggered by tapping the nerve.
- Often is idiopathic but could be caused by trauma.
- Treatment is nerve block with mixture of corticosteroid and marcaine.

16
Peripheral Neuropathy

GENERAL CONSIDERATIONS

Peripheral neuropathy (PN) is a term applied to any condition affecting peripheral nerve function. The disorder can affect the peripheral nerve soma (motor or sensory neurons), which are referred to as neuronopathies, or peripheral nerve fibers, which are neuropathies. Most peripheral nerves are mixed, having sensory motor and autonomic nerves. The pure form of sensory or motor neuropathy occurs when the soma (dorsal root ganglion or anterior horn cells) are selectively involved.

When evaluating a patient with suspected PN, a systematic approach is the best way to reach the diagnosis. Evaluation begins with a careful history taking (history of neuropathy, past medical history, social history, family history, history of drugs, medications, or toxic exposure, and occupational history). Physical examination begins with an evaluation of possible systemic illness, skin, and deformities (bone, spine). Neurological examination must be complete, with special attention to motor and sensory function. When approaching the patients, you should ask yourself:

- **Does peripheral neuropathy exist?**
- **What is the cause of the neuropathy?**
- **What treatment can be offered to the patient?**

This chapter focuses on the answers to these questions. The reader is referred to more comprehensive textbooks for more detail of any particular neuropathies.

Does a Peripheral Neuropathy Exist?

Not all patients complaining of "pins and needles," numbness, weakness, atrophy, or reflex changes have PN; therefore, it is fruitful to establish the existence of PN first, before going any further.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

CLINICAL FEATURES OF PN

Symptoms

Sensory. The common symptoms of PN include "pins and needles" (paresthesia), numbness, hypesthesia, dysesthesia, or unpleasant sensations, pain, a burning feeling, and a decrease or insensitivity to cold and warm. These symptoms typically begin in the distal lower extremities (toes) and gradually progress to the upper extremities and proximally. At the onset, they can be asymptomatic or focal or symmetric. They can be intermittent or slowly progressive. Some patients may even present with imbalance (sensory ataxia as a result of proprioception involvement).

Motor. The motor symptoms include complaints of weakness, muscle cramps, and fasciculation. Again, these symptoms usually begin in the distal lower extremities and progress proximally and to upper extremities. The extensor muscles are more greatly affected than are the flexors. Some neuropathies may begin proximally or start from the upper extremities. The onset could be symmetric or asymmetric. Patients typically complain of difficulty with dexterity and fine movement of the hands (turning keys, unbuttoning a shirt, etc.).

Autonomic. Autonomic symptoms include orthostatic hypotension, dizziness, dry eyes or mouth, abnormal sweat pattern, persistent diarrhea, vomiting, and impotence.

Signs

Sensory. Sensory signs are those that you detect by your examination, and these include decreased or absent sensory modalities (pain, touch, vibration, joint position) and a positive Romberg sign. The typical sensory deficits in a chronic generalized neuropathy are of "stocking-glove" distribution. The sensory deficit, however, could be in the distribution of one nerve (mononeuropathy) or multiple nerves (polyneuropathy or mononeuropathy multiplex). Preservation of proprioception is suggestive of a small fiber neuropathy (small myelinated or unmyelinated fibers). Some neuropathies may not present with a sensory deficit (motor neuropathies).

Motor. These include muscle weakness (distal more so than proximal, extensors more so than flexors), muscle atrophy (later stage), decrease or absence of reflexes, normal or decreased muscle tone, fasciculation, and occasionally tremor (postural).

Autonomic. Orthostatic hypotension, absence of heart rate variability to standing, sluggish pupillary reactions to light, Horner's syndrome, and dry mouth or eyes.

Other important signs. Any patient who presents with a neuropathy should be examined for skin and bone deformities or other systemic manifestations (e.g., lupus, sarcoidosis, leprosy). The following manifestations have particular diagnostic importance:

Palpable, hypertrophic nerve (greater auricular, superficial peroneal): hereditary neuropathies, chronic demyelinating neuropathies, amyloid neuropathy, and leprosy.

Skin lesions: porphyria; sarcoidosis; lupus; Fabry's disease (angiokeratoma); Refsum's disease (ichthyosis); diabetic skin ulceration; and syndrome of polyneuropathy, organomegaly, endocrinopathy, M protein, and skin lesions (POEMS), which is associated with hyperpigmentation.

Nail beds: Mee's line (arsenic and thalium poisoning), white nail (POEMS).

Deformities: pes cavus, kyphoscoliosis (hereditary neuropathies).

Hypertrophic muscle: hereditary neuropathy, amyloidosis.

Enlarged tongue: amyloidosis.

Enlarged and yellow tonsils: Tangier's disease.

ELECTROPHYSIOLOGICAL DIAGNOSIS

Any patient with suspected PN should have electrophysiological testing, which includes nerve conduction studies (NCS) and needle electromyography (EMG). This test helps to establish the existence of PN and exclude other neuromuscular diseases affecting the motor unit. This test can also reveal the pathology, distribution, severity, and evaluation of PN. Normal NCS, however, do not rule out the presence of PN (small fiber neuropathy or early stage of PN).

CAUSES OF PN

There are more than 100 causes of PN. Finding the etiology of neuropathy (if underlying disease is unknown, e.g., diabetes, alcohol) is the most difficult task for the practitioner. There are two ways to find the cause.

Mnemonic Approach

The mnemonic DANG THERAPIST may be used to memorized some the causes of PN:

D = diabetes.
A = alcohol.
N = nutritional deficiency (B_{12}).

G = Guillain-Barré syndrome (the most common form of acute neuropathy in Western countries).
T = toxic (heavy metals/drugs), metabolic (thyroid, liver, kidney disease).
H = hereditary (hereditary motor sensory neuropathies [HMSN])—the most common types are:

- HMSN 1: Charcot-Marie-Tooth (CMT), demyelinating form.
- HMSN II: CMT, neuronal (axonal) form.
- HMSN III: Dejerine-Sottas disease.
- HMSN IV: Refsum's disease.
- HMSN V, VI, VII.

E = environmental.
R = recurrent acute intermittent porphyria (AIP), chronic inflammatory demyelinating polyneuropathy (CIDP).
A = amyloid.
P = porphyria.
I = inflammatory—Guillain Barré syndrome (GBS), CIDP, Lyme disease, HIV, vasculitis, paraproteinemia.
S = systemic diseases.
T = tumor—paraneoplastic neuropathy (remote affect of carcinoma).

Classification Approach

Peripheral neuropathies are classified in many ways. The following classification is probably the most useful and easy to memorize to identify the etiology and plan a logical workup.

Acute Neuropathies

Acute Mononeuropathies

Acute peroneal nerve palsy. Commonly presents with foot drop. On examination, there is weakness of foot dorsiflexors and evertors, with or without sensory deficit. Reflexes are usually preserved. Peroneal palsy must be differentiated from L5 radiculopathy or sciatic neuropathy. Underlying generalized neuropathy should also be excluded.

Acute radial nerve palsy. Acute radial nerve palsy presents with wrist drop without significant sensory deficit. The site of the lesion is either at the spinal groove of the humerus or at the forearm (dorsal interosseus nerve). In children, wrist drop raises the possibility of lead intoxication, and in adults is usually seen in alcoholics.

Acute seventh nerve palsy. Acute idiopathic peripheral seventh cranial nerve (Bell's) palsy is a common clinical entity. Decreased tearing and taste, and hypersensitivity to sound (hyperaccusis) usually implies proximal nerve

involvement and an unfavorable prognosis. Protect the cornea from dryness and ulceration. Corticosteroids may expedite the recovery if administered within the first week.

Acute third nerve palsy. This palsy presents with acute eye pain on movement, ptosis, and diplopia. Pupillary responses are typically preserved. The common causes are diabetes and atherosclerosis.

Acute generalized polyneuropathies

- Acute inflammatory demyelinating polyneuropathy or GBS (discussed in Chapter 29).
- Acute toxic/metabolic neuropathies.
- Acute intermittent porphyria.
- Infectious neuropathies: Lyme disease, HIV, diphtheria.

Subacute, Chronic, and Symmetric Sensorimotor Polyneuropathies

This category of neuropathies contains the most common forms and imposes diagnostic challenges to the clinician. It includes polyneuropathies associated with diabetes, alcohol use, nutritional deficiency (vitamin B_{12}), paraproteinemias, amyloids, and toxic/drug-induced paraneoplastic neuropathies.

Mononeuropathy Multiplex

These neuropathies present with involvement of different single nerves at different sites and at different times. The best example is the presentation of wrist drop followed by foot drop, and later, a median neuropathy. The common causes include diabetes, vasculitis, leprosy, HIV, and sarcoidosis.

Relapsing/Remitting Neuropathies

The best example of this group is CIDP.

Hereditary Polyneuropathies

- HMSN types I–VII.
- Hereditary neuropathy with liability to pressure palsy (HNPP).
- There are now more than 30 subtypes of hereditary neuropathy, based on their mode of inheritance and their genetic markers.

Entrapment Neuropathies

- **Carpal tunnel syndrome:** median nerve compression at the wrist.
- **Cubital tunnel syndrome:** ulnar nerve compression just below the elbow.
- **Tarsal tunnel syndrome:** tibialis nerve entrapment in the tarsal tunnel of the foot.

- **Meralgia paresthetica:** entrapment of the lateral femoral cutaneous nerve beneath the inguinal ligament or in pelvis. Presents with patchy paresthesias of the lateral aspect of the thigh.

NEUROPATHY EVALUATION

- **NCS and Needle EMG.** NCS and needle EMG should be done in all patients suspected of having neuropathies, not only to establish the existence of neuropathy, but also to help plan further workup.
- **Routine or Intial Evaluations.** These studies are done in all patients with neuropathies: complete blood count, sedimentation rate, chemistry profile, serum protein electrophoresis and immune fixation, and vitamin B_{12} level (serum methylmalonic acid, and homocysteine level are more specific than vitamin B_{12}, but they cost more).
- **Selective Workups.** More selective workup is best to plan according to the NCS/EMG and classification:

1. **Acute mononeuropathies.** Routine workup.
2. **Acute generalized polyneuropathies:**
   - GBS: NCS and spinal tap (show elevated protein without increase in cells).
   - Other acute neuropathies: heavy metal intoxication (urine/serum lead, mercury), porphyria (porphobilinogen deaminase level of red blood cells), HIV (cerebral spinal fluid, HIV antibody, CD4 count), Lyme disease (cerebral spinal fluid analysis, Lyme antibodies).
3. **Chronic, symmetric polyneuropathy.** Routine workups and a few selective studies in selected cases: anti-Hu antibody chest computed tomography scan for paraneoplastic neuropathy in men, anti-GM1 antibodies in cases of multifocal motor neuropathy (MMN), protein electrophoresis, and abdominal fate or nerve biopsy in case of amyloidosis
4. **Mononeuropathy multiplex.** Sedimentation rate, RA factor, antinuclear antibody, C-reactive protein, cryoglobulins, angiotensin-converting enzyme level, chest X-ray, hemoglobin A1C, muscle/nerve biopsy (superficial peroneal and peroneus brevis muscle), and skin/nerve biopsy (leprosy).
5. **Relapsing/remitting neuropathies.** Workups as with acute generalized neuropathies. Antinerve antibodies in selected cases, GM1 antibody in suspected MMN, and/or GQ1b antibody in suspected Miller-Fisher syndrome.
6. **Hereditary neuropathies:**
   - DNA analysis (CMT1A) for CMT and HNPP.
   - Sural nerve biopsy in selected cases.
   - Spinal tap, plasma phytanic acid level, and nerve biopsy in suspected Refsum's disease.

7. **Entrapment neuropathies.** Routine workups, thyroid function tests (thyroid-stimulating hormone, T_4), and imaging techniques (selected cases: elbows, pelvis).

TREATMENTS THAT CAN BE OFFERED TO THE PATIENT

Specific Therapies: a Few Examples

- Prednisone, immunosuppressive drugs: vasculitic neuropathies, CIDP.
- Plasma exchange, intravenous immunoglobulin: GBS, CIDP, paraprotein neuropathies.
- Intravenous immunoglobulin: GBS, CIDP, MMN.
- Antimicrobial: leprosy, Lyme disease, HIV.
- Low-phytanic acid diet: Refsum's disease.
- Correcting underlying metabolic/systemic disease: diabetes, thyroid, kidney.
- Chelating therapy, penicillamine: heavy metal neuropathies.
- High carbohydrate diet with 3 mg/kg/day of hematine (panhematine), for 4 days during attack: acute intermittent porphyria.
- One hundred micrograms of vitamin B_{12} (intramuscularly) twice weekly for 4 weeks, then weekly for 3 months, and then monthly thereafter: vitamin B_{12} deficiency.

Symptomatic Therapies

- Pain/paresthesia; sharp, lancinating pain (*epicretic pain*): gabapentin (Neurontin), pregabaline (Lyrica), carbamazepine, lamotrigine (Lamictal), or other antiepileptic drugs.
- Baclofen, prazosin, mexiletine, 200 mg/day for 3 days. Increase to 200–400 mg three times a day (assess the heart first).
- Burning, deep pain (*protopathic*): amitriptyline, desipramine (Norpramine), nortriptyline (Pamelor), duloxetine (Cymbalta), tramadol (Ultram), opiods, capsacin (Zostrix) ointment, three to four times a day (may mix with 5% eutectic mixture of local anesthetic cream).
- Occupational (bracing, etc.), physical therapy.
- Surgery: entrapment and compressive neuropathies.

CLINICAL CLUES TO SOME NEUROPATHIES

- CMT: pes cavus, hammertoes, reverse champagne-bottle appearance of legs (stork legs).
- Refsum's disease: scaly and dry skin (ichthyosis), retinitis pigmentosa, hearing loss, cataract, cardiac conduction defect.
- Fabry's disease: angiokeratomas—reddish maculopapular rash in the umbilical and groin areas, kidney failure.

- Arsenic poisoning: hyperkaratosis, pink hands, scaly skin of the soles and palms, Mee's lines on the fingernail beds.
- POEMS: hyperpigmentation of skin (S), white nails, clubbing, organomegaly (O), endocrinopathy (E)—gynecomastia, testicular atrophy

17
Movement Disorders

Movement disorders (MDs) typically result from abnormalities of the extrapyramidal system. The core structures of the extrapyramidal system include the caudate nucleus, globus pallidus, substantia nigra, red nucleus, thalamic nucleus, subthalamic nucleus and their connections to the cerebral cortex, brain stem, and cerebellum, with the final output being pyramidal tract. The main transmitter substances are dopamine, acetylcholine, GABA and glutamate. MDs can be hyperkinetic, hypokinetic, or dyskinetic. This chapter highlights the approach to common MDs.

EVALUATION

In history taking, you should determine the patient's age at onset, the course of illness, the family history, history of psychiatric illness, or use of neuroleptic drugs. In the neurological examination, pay attention to the type of abnormal (involuntary) movement and any associated neurological findings.

DIAGNOSIS

The most important aspect of evaluating an MD is recognizing the general category of abnormal movements (pattern recognition). Many times recognizing and differentiating types of MDs is challenging, even to an experienced neurologist; therefore, not infrequently a referral to a specialized center is necessary.

TERMINOLOGY

- **Tremor:** rhythmic involuntary oscillating of a body part. Usually involves distal extremities. Tremor is subclassified according to position of the limb (rest, action, intention, postural).
- **Chorea:** rapid, continuous, irregular, brief, purposeless movements, often involve distal limb.
- **Athetosis:** slow, irregular undulating, writhing-type movement, often associated with chorea.
- **Tics:** stereotyped, irregular simple or complex movements.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- **Dystonia:** sustained, abnormal contraction of a group of muscles, resulting in abnormal posture of the limb.
- **Ballismus:** violent, flinging movements often involving proximal limb, usually unilateral (hemiballismus), but can be bilateral lower or upper extremities because of contralateral subthalamic nucleus lesion.
- **Myoclonus:** sudden, irregular shock-like contraction of the muscle or group of muscles.
- **Tardive dyskinesia:** stereotyped movements often involving the facial and oral muscles, manifesting as tongue protrusion, chewing, lip smacking, and facial grimacing. The trunk and extremities are often also involved. This condition is seen after chronic use of dopamine-blocking antipsychotic or antiemetic drugs.
- **Rigidity:** increased muscle tone throughout the passive range of motion of the limb. When there is coexistence of tremor, the examiner detects a ratchet-like resistance, referred to as "cogwheel rigidity."

PARKINSON'S DISEASE

Parkinson's Disease (PD) is caused by slowly progressive degeneration of the dopaminergic neurons of the substantia nigra. Dopamine depletion accounts for most motor symptoms of PD. Approximately 50–60% of dopaminergic neuronal loss is required before clinical symptoms appear. The prevalence of PD is about 1–2% of individuals over age 70. The incidence is 4–21 cases per 100,000 people. The average age of onset is 55 years, but cases of patients in their 20s have also been reported. Most cases are sporadic. Genetic factors play role. At least nine genetic loci been identified in autosomal dominant and recessive forms (*PARK1–PARK11*). Several proteins that the gene encodes have also been discovered: α-synuclein, parkin, ubiquitin, DJ1, and others. Risk factors: increasing age, family history, male gender, caucasian, environmental.

Clinical Features

- **Resting tremor:** 4–7 Hz, coarse, pill-rolling tremor. The tremor usually starts either hand asymmetrically and sometimes involves the legs and chin. The tremor diminishes with action and is exacerbated at rest, during physical and mental activities, and walking. Tremor-dominant PD has been described. In this situation, micrographia might help in diagnosis.
- **Cogwheel rigidity:** usually presents in the affected limb and neck. The rigidity is increased by contralateral repeated movements (e.g., finger tapping).
- **Bradykinesia:** slowness of voluntary movements such as diminished arm swing during walking, masked face, diminished blinking, and micrographia. Limb bradykinesia is seen during finger tapping. The amplitude and speed of the movements will decrease the longer the movement is performed.

- **Postural instability:** stooped posture, short-stepped walking, shuffling, festination, and frequent falls.
- **Other symptoms and signs (nonmotor):** depression, personality changes, psychosis and dementia, variety of sleep disorders, sialorrhea, facial seborrhea, autonomic dysfunction, dysphagia, and constipation. Sometimes nonmotor manifestations are more prominent and disabling than are motor manifestations.

Differential Diagnosis

- Essential tremor.
- Drug-induced Parkinsonism.
- Parkinsonism because of environmental toxins.
- Other degenerative conditions: progressive supranuclear palsy and multiple system atrophy: includes striatonigral degeneration, Shy-Drager syndrome and olivopontocerebellar degeneration), corticobasal ganglionic degeneration, normal pressure hydrocephalus, and Wilson's disease.

Management

The management of PD is complex. Early and mild PD can be treated by general practitioners, but more advanced stages of the disease are best handled by a neurologist with special interest and expertise in PD. The following are general guidelines, and the reader is advised to refer to neurology textbooks for more detail.

What You Should Know

- Treatment of PD is threefold: pharmacological, surgical, and nonpharmacological.
- The goal of therapy is to improve the patient's quality of life and reduce disability as much as possible with the lowest effective dose of medication.
- PD is a chronic, progressive disease.
- Rational polypharmacy is justified and often necessary. Start with low doses and titrate slowly.
- Pharmacotherapy should be tailored individually according to the patient's symptoms, severity, age, and whether cognitive function is impaired. The age factor is the most important.
- Levodopa remains the most effective drug to treat all manifestations of PD, but its use should be delayed as long as possible in patients younger than age 65 years of age, to delay its adverse motor side effects (fluctuations and dyskinesias). If the patient does not respond to levodopa, consider other diagnoses.

- Nonmotor manifestations should be addressed and treated appropriately. Treating hallucinations in PD is challenging. Quetiapine (Seroquel) is probably first choice. Risperidone (Risperidal) also is effective but usually exacerbates parkinsonism. Acetylcholine inhibitors (e.g., donepezil, rivastigmine) are also effective for hallucinations. The diagnosis of PD is clinical. Modern imaging techniques, such as fluoro-dopa PET, can detect changes in caudate and putamen, which can be useful in atypical cases or early detection of disease.

Pharmacotherpy

- **Anticholinergics:** benzotropine mesylate (Cogentin), trihexiphenidyl mesylate (Artane). These agents are not used as often because of their poor tolerance and effectiveness. They may be used in younger patients when tremor is disabling.
- **Amantadine hydrochloride** (Symmetrel): This agent has mild dopaminergic and anticholinergic properties. It is indicated in mild and early PD. It has short-term benefit. The dose is 200–300 mg/day, as monotherapy. Watch for ankle edema, livedo reticularis, and confusion.
- **Monoamine oxidase B inhibitor:** selegiline (Deprenyl, Eldepryl). This agent is used in mild, early PD, and has modest effects on rigidity and akinesia. Its neuroprotective effect has been questioned. The dose is 5 mg, twice daily. Selegiline (Zydis) is absorbed readily from buccal mucosa. The new MAO-B inhibitor, azilect (Rasagiline) is now on the market as initial monotherapy for PD or as an addition to levodopa in more advanced patients. MAO-B inhibitors may increase the risk of skin cancer in PD (melanoma). Do not combine with cold medications or opiods.
- **Levodopa:** Levodopa remains the most effective drug for motor manifestations of PD, except for tremor. Levodopa is given in combination of peripheral decarboxylase inhibitor (Sinemet and Sinemet CR). Start with regular Sinemet with dose of 25/100 mg, three times a day, and titrate gradually. Most people respond to 400–600 mg of levodopa. A form of Sinemet (Parcopa), which dissolves under the tongue, is also available. Controlled-release Sinemet (Sinemet CR) may be used if necessary. Mental confusion, hallucinations, and motor fluctuations are more serious side effects of levodopa.
- **Dopamine agonists:** These agents directly stimulate dopamine receptors. They are used as monotherapy in early moderate PD or as adjunctive to levodopa to delay motor fluctuations. They should be started at a very low dose. If a patient does not respond to levodopa, the patient is very unlikely respond to agonists. Agonists include: **Ergot-derived:** bromocriptin (Parlodel), with a starting dose of 1.25 mg, twice a day, up to 40–90 mg/day. Pergolide (Permax), starting with 0.05 mg, twice a day, with a maximum dose of 3–5 mg/day. This drug is now removed from the US market because of reported development of restrictive valvular heart disease. **Nonergot-derived:** pramipexole (Mirapex),

with a starting dose of 0.125 mg, three times a day, with a maximum dose of 1.5–4.5 mg/day. Ropinirole (Requip) should begin with 0.25 mg, three times a day, with a maximum dose of 16–24 mg/day. Apomorphine (Apokyn) is used as rescue drug for freezing. The drug is given subcutaneously, 2 mg/day, up to a 20-mg maximum daily in divided dose. Rotigotine (Neupro): this is newest agonist, and available as skin patch (Transdermal).

- **Catechol-o-methyltransferase inhibitors:** These agents extend the effect of levodopa, and therefore are used as adjunctive drugs, particularly for end-of-dose akinesia. Tolcapone (Tasmar) is given, 100 mg, three times a day. Entacapone (Comtan) is given at a dose of 200 mg with each dose of Sinemet to a maximum of 800 mg/day. A combination of entacapone and Sinemet (Stalevo) is now available.

How to Start Drug Therapy

If the patient presents with prominent and disabling tremor without other manifestation of PD, and patient is younger than 60 years old, you may try anticholinergics. For mild and early PD, a short-term use of amantadine would be reasonable. If the patient's daily living activities are impaired and require more aggressive treatment, you may begin with agonist monotherapy for patients younger than 60 years old, and reserve levodopa for patients with more severe PD and older than 65 years old.

Surgical Treatment

Surgical treatments are considered in highly selected patients with advanced PD and patients who are dependent on levodopa but experiencing uncontrollable motor fluctuations. These procedures include deep brain stimulation (DBS), pallidotomy, and thalamotomy. DBS is most commonly used. Adrenal implant, fetal implant, and direct brain infusion of glial cell derived neurotrophic factor was used experimentally but have been abandoned. Surgical treatment should be performed in experienced centers.

Other Treatments

This includes patient and caregiver education, exercises, physical and occupational therapy, and nutritional evaluation.

ESSENTIAL TREMOR

- Essential tremor (ET) is usually a bilateral but asymmetric tremor affecting the hands, but may affect the neck, head, jaw, and sometimes the tongue.
- Tremor of neck and tongue may affect speech and swallowing.
- The tremor is worse when limb is in action (writing, reading, drawing, drinking) and postural (outstretched arms) or when goal-directed (finger-to-nose testing). Some patients may also have resting tremor or mild gait ataxia.

- There is strong family history (>50%).
- ET affects approximately 5% of the population.
- The onset could be middle age or after 65.
- The tremor should exist for at least 5 years and other causes excluded before the diagnosis of ET can be made.
- Characteristically, some patients show a favorable but brief response to a small amount of ethyl alcohol.
- Using the term "*benign* essential tremor" may not be appropriate because the tremor can be very disabling.

Pharmacotherapy

β-Blockers

- Propranolol (Inderal) is the drug of choice. Start at 60 mg/day. Long acting. If necessary, increase to 80 mg/day, or regular Inderal up to 320 mg/day. Not to be used in patients with asthma, heart block, and type 1 diabetes.

Other β-Blockers

These include atenolol, nadolol, metoprolol, and sotalol. There are limited studies and experience with these agents.

Antiepileptics

- Primidone (Mysoline) is used as second-line drug in patients who cannot take propranolol for any reason. The problem with this drug is that most patients cannot tolerate the sedative side effects. Start with a very low dose and increase when necessary. The starting dose is 25 mg at bedtime. The maximum effective dose is 500–750 mg.

Caveat: Before considering using other drugs, if the response to either propranolol or primidone is suboptimal, coadminstration of both agents is recommended. The effectiveness of either agent is about 50%.

Other Antiepileptics

Other antiepileptic drugs such as gabapentin, topiramate, or levetiracetam have shown some effect in treatment of ET.

Benzodiazepines

Alcohol

Although long-term use of alcohol should be discouraged, use of alcohol (e.g., red wine) before a meal in social events may be considered in some patients. Addiction to this form of therapy is possible but uncommon. Oral 1-octanol is also effective in some patients, although it is very expensive and not recommended.

Botulinum Toxin

This agent may be considered in severe forms of head or limb tremor.

Surgical Treatment

Stereotactic thalmic DBS are reserved for patients with severe disabling tremor not responding to medical treatment.

PROGRESSIVE SUPRANUCLEAR PALSY

The main features of progressive supranuclear palsy include:

- Onset of progressive axial rigidity and bradykinesia, with frequent falls.
- Onset at 40 years old or more, but younger than those with onset of PD.
- Poor vertical gaze with impaired saccadic eye movement.
- Poor response to levodopa drugs.

CORTICOBASAL GANGLIONIC DEGENERATION

This is rare disorder and characterized by:

- Bradykinesia and rigidity that is unresponsive to levodopa.
- Alien limb and cortical sensory signs (apraxia).
- Focal dystonia, tremor, or myoclonus.

Drug-Induced Extrapyramidal Syndromes

Suspect drug-induced MDs when a patient is receiving antipsychotic medications, particularly dopamine blockers, and when patients are living in a long-term psychiatric institution. Any form of abnormal involuntary movements can be induced by these agents.

Neuroleptics With High Incidence of Producing Extrapyramidal Syndromes

Haloperidol (Haldol).
Fluphenazine (Prolixin).
Trifluoperazine (Stelazine).

Neuroleptics With Low Incidence of Producing Extrapyramidal Syndrome

Clozapine (Clozaril).
Quetiapine (Seroquel).
Olanzapine (Zyprexa).
Thioridazine (Mellaril).
Resperidone (Resperadol).

Other Medications

Metoclopramide (Reglan).
Prochlorprazine (Compazine).
Promethazine (Phenergan).

ACUTE DRUG-INDUCED DYSTONIA

Acute drug-induced dystonia presents with abnormal tongue or jaw postures and neck dystonia, occurring within the first 3 days of starting a neuroleptic. The treatment is benzotropin (Cogentin), 2 mg intravenously or intramuscularly, or 50 mg diphentrydramine (Benadryl) intravenously.

TARDIVE DYSKINESIA

Tardive dyskinesia presents as abnormal oral, buccal, lingual, or truncal movements following chronic use (6 months or more) of dopamine blockers.

Treatment

- Gradual reduction of neuroleptics if possible.
- Reserpine (Serpasil): This drug depletes central nervous system biogenic amines. Begin with 0.25 mg/day and increase to 2–4 mg/day if necessary.
- Valproate (Depakote): 500–2500 mg/day.
- Clonazepam (Klonopin): 1–2 mg/day.
- Baclofen: 10–30 mg/day.
- Diazepam: 5–20 mg/day.
- Vitamin E: 400–800 mg/day.

MYOCLONUS

Myoclonus has many causes, but detailed discussion of the subject is beyond the scope of this handbook. Most myoclonus are treated with clonazepam and/or valproate (Depakote) or other antiepileptic drugs.

18
Sleep Disorders

RECOGNITION

Recognition of sleep disorders is important because:

- They are common, affecting approximately 10–15% of the US population.
- Many medical, neurological, and psychiatric disorders present with sleep problems.
- Sleep disorders can have a significant affect on a patient's physical, social, and occupational life.

SLEEP: THE BASICS

Non-Rapid Eye Movement Sleep

1. Electroencephalographic features:
   - Stage 1: drowsiness; disappearance of alpha wave, mild slowing of background.
   - Stage 2: light sleep; spindle wave, vertex sharp wave, K-complexes.
   - Stages 3 and 4: deep sleep, slow waves (theta and delta).
2. Decreased body temperature. Increased vagal tone.
3. Normal muscle tone.
4. Increased growth hormone secretion.

Rapid Eye Movement, or Active, Sleep

1. Electroencephalogram features: similar to stage 1 non-rapid eye movement (NREM), presence of rapid jerky eye movements, saw-tooth waves.
2. Decreased muscle tone except for extraocular muscles, diaphragm, and occasional limb jerks.
3. Increased autonomic activities: increased body temperature, increased basal metabolic rate, increased blood pressure, pupillary dilatation, sweating, irregular breathing, increased brain activity, and cerebral blood flow.
4. Penile erection.
5. Dreaming.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

Sleep Cycles

In adults, sleep begins with NREM. The first REM sleep occurs within 70–90 minutes; successive REMs occur every 90 minutes. Four to six REM cycles occur during 7–8 hours of sleep. In adults, REM constitutes about 20% of total sleep. After age 60, there are virtually no stages 3 and 4 of NREM.

Biological Rhythms

Circadian rhythm cycles about every 24 hours, but in most of us, the sleep–awake cycle is about 25 hours (ultradian).

Neuroanatomy

Raphe nuclei in the pons are the source of NREM, and the lateral geniculate nucleus of the pons are the source of REM. Serotonin is the major neurotransmitter for sleep.

SLEEP DISORDERS

Insomnias

Insomnia is a chronic lack of adequate sleep to maintain normal daytime function. Transient insomnia is common. Chronic insomnia could be caused by medical, neurological, psychiatric, and drug/alcohol problems, or it can be idiopathic. Most parasomnias are associated with insomnia. Treatment depends on the underlying cause. Low doses of sedative–hypnotic medications (benzodiazepines) are used for disabling insomnias.

EXCESSIVE DAYTIME SLEEPINESS

Narcolepsy

- Incidence: 1:1000–1:10,000.
- Onset: 20–40 years, equally affects men and women. Not only is the patient at risk for accidents, but there is also significant social affects.
- Highly associated with HLA-DR2, and HLA-DQ1 and HLA-DQB1 proteins.
- Excessive daytime sleepiness: sleep attack, last 10–15 minutes during sedentary situation, often leaves the patient feeling refreshed on awakening.
- Cataplexy: sudden onset of hypotonia after an exciting or emotional event (laugh, anger, etc.), lasting 1–2 minutes. Eye and respiratory muscles are usually spared. Recently, it has been shown that approximately 90% of narcoleptics with cataplexy have no detectable neuropeptide orexin or hypocretin in their cerebral spinal fluid. Orexin-producing neurons are located in the lateral hypothalamus (Orexin-A and -B).

- Sleep paralysis: generalized weakness, during falling asleep or on awakening, lasting a few minutes. Can be frightening.
- Hypnagogic hallucination: vivid (auditory or visual) hallucination during sleep or on awakening.

Diagnosis

Patients suspected of having narcolepsy syndrome should be referred to a sleep center. The diagnostic procedures include an overnight polysomnogram to assess the quality of sleep and rule out other possible associated sleep disorders, followed by a daytime multiple sleep latency test in which the latency of five naps is measured within 2 hours. Latency less than 5 minutes is abnormal. Narcolepsy is highly suggestive if patient had two or more stages of sleep-onset REM during this test. Measuring cerebral spinal fluid orexin (hypocretin) level is useful if cataplexy is present. The assay for this protein is now available in some sleep centers. Measurement of HLA-DQB1 might be considered in selected cases.

Treatment

The goal of treatment in patients presenting with sleep attacks (excessive daytime sleepiness) is to increase alertness during daytime, when the patient has to be awake (work, driving, etc.). Sleep hygiene and avoiding drugs causing insomnia are important.

- **Modafinil.** This agent is probably the drug of choice in men and in women who are not on contraceptives. It is not amphetamine-related. The dose is 200–400 mg, given in morning and mid-day.
- **Amphetamines.** These drugs include dextroamphetamine, methamphetamine, and methylphenidate. Methylphenidate (Ritalin) is commonly prescribed. The dose is 5–20 mg, twice during the daytime. Some patients may require higher doses.
- **Tricyclic antidepressants, clorimpramine, venlaflaxin, fluoxetin.** These compounds are generally used in patients with sleep paralysis and cataplexy.
- **Gamma hydroxybutyrate (Xyrem).** This agent is a metabolite of gamma-aminobutyric acid and is the only Food and Drug Administration-approved drug for treatment of cataplexy, sleep paralysis, and hypnagogic hallucination. The dose is 2–4.5 mg, at bedtime in a divided dose.

Sleep Apnea Syndrome

Sleep apnea syndrome (SAS) is periodic cessation of breathing ($\geq$10) during sleep, with periods of awaking, usually by loud snore. Occasional brief apnea is generally normal. There are three types of SAS: obstructive sleep apnea, central type, and mixed.

Obstructive Sleep Apnea

Obstructive sleep apnea is seen in obese, middle-aged (30–60 years) men and women with short necks. Thoracic movement is intact, but there is no airflow through the nose during sleep.

Symptoms and signs. The symptoms of obstructive sleep apnea are early-morning headache, excessive daytime sleepiness, fatigue, poor concentration, and decreased libido. Loud snoring after an apneic episode is observed by sleep partner. On examination, these individuals are obese, have short necks, and often they have neck collar sizes larger than $17^1/_2$. Enlarged tonsils, adenoids, or micrognathia are seen in some. About half of patients have hypertension, and there are a few with pulmonary hypertension, polycythemia, and cardiac arrhythmias.

Central Sleep Apnea

With central sleep apnea, there is cessation of chest and upper air flow during sleep. Symptoms are similar to those of obstructive sleep apnea. The etiology is unknown.

Mixed Sleep Apnea

Mixed sleep apnea is a combination of both obstructive and central apneas. It probably is more common than the other two.

Complications of SAS

Complications of SAS include cardiac arrhythmia, hypoxia, pulmonary hypertension, night heart failure, hypertension, stroke, polycythemia, and asystole.

Diagnosis

SAS is suspected in patients presenting with excessive daytime sleepiness or early morning headaches who are obese, have short and wide necks, and their bed partners report loud snoring, or apnea or choking during sleep. Many sleep labs do not do overnight polysomnograms, daytime multiple sleep latency tests, or maintenance of wakefulness test, because they are time-consuming and expensive. Other practical and easier tests include the Epworth Sleep Scale, which is an eight-question self-administered test. With this test, most SAS patients score more than 10 points. Some labs now recommend use of portable machines. The Eden-Trace recording system is a four-channel respiratory monitor that can measure respiratory flow and airflow.

Treatment

- Weight loss (which is often difficult to maintain).
- Avoidance of alcohol.

- Diuretic: acetazolamide (Diamox), 1000 mg/day.
- Antidepressants.
- Aminophylline.
- Continuous positive airway pressure or bilevel positive airway pressure. Continuous positive airway pressure is now the treatment of choice. It is important to educate the patient to maintain good compliance.
- Surgeries. Uvulopalatopharyngoplasty is now applied to patients with severe SAS who do not respond to conservative treatment. Other techniques include radiofrequency tissue ablation and tracheostomy. Removal of enlarged tonsils, adenoids, or masses is also helpful.

PARASOMNIAS

Parasomnias are abnormal behavior or physiological events that occur exclusively or are exacerbated during sleep.

NREM Parasomnias

Enuresis (bedwetting). Bedwetting beyond age 5 is abnormal; it occurs primarily during stages 3 and 4. Primary cases are usually because of neurological or maturational lag and often are familial. Secondary cases are because of urological, psychological, or medical (diabetes) problems.

Treatment: low-dose imipramine, tricyclic antidepressants, behavioral therapy.

Sleepwalking. Sleepwalking, or somnambulism, is a complex behavior, characterized by walking, climbing, running, or doing odd thing during stages 3 and 4. Sleepwalking occurs in 10% of adults and is often associated with sleep eating or sleep talking. The patient awakens confused. Usually, the onset is in childhood (17%) and disappears after adolescence. The individuals should be protected from self-injury. Benzodiazepines are given to prevent injury.

Sleep talking (somniloquy). This is a common problem, and many people experience it. It could be associated with sleepwalking.

Teeth-grinding (bruxism).

Night terror (pavor nocturnus). Night, or sleep, terror is characterized by sudden onset of a scream or cry, and is associated with autonomic hyperactivation: tachycardia, tachypnea, and sweating. If awakened, patient is confused and has no recollection of the night terror. Common in childhood, it disappears by adolescence. It could cause serious injury. It occurs in 3% of children and 1% of adults. Mothers should be given assurance that the condition is benign and temporary.

Sleep myoclonus (hypnic jerks). Sudden body jerks during stages 1 and 2. Treatment is low-dose clonazepam (0.5–1 mg) at bedtime.

Periodic limb movements. Stereotyped, rhythmic head or limb movements, seen most frequently in children. Benzodiazepines or antidepressants can be given for treatment.

Posttraumatic stress disorder. Subjective sleep complaints, flashbacks, or nightmares. Any emotional trauma may lead to posttraumatic stress disorder. PTSD is often associated with nightmare.

Restless-leg syndrome (RLS). RLS causes unpleasant, indescribable sensation of legs, resulting in the irresistible urge to move the limbs. RLS occurs as patients are beginning to rest or in transition of awake to sleep. Restless arm syndrome has rarely been reported. It is often associated with nocturnal myoclonus. RLS may be primary, with strong family history or secondary to medical (uremia, diabetes, iron deficiency), neurological (peripheral neuropathy), or psychiatric illnesses. Women are most affected. Peripheral neuropathy and iron deficiency should be ruled out. Iron replacement is recommended for most patients. The drug class of choice is the dopamine agonists: pramipexole (Mirapex) or ropinirole (Requip), starting with a low dose and slow titration. Other drugs include clonazepam, temazepam (Restoril), carbamazepine, Sinemet, and opioids.

REM Sleep Parasomnias

REM Sleep Behavior Disorder

REM sleep behavior disorder (RBD) is a recently described sleep disorder affecting about 0.5% of general population. It affects elderly men and is characterized by nondirected, violent behavior such as kicking, punching, yelling, and running, during REM sleep. Patients with RBD act upon their dream; in these individuals, hypotonia or atonia during REM does not occur. RBD is suspected when the patient or the patient's bed partner complains of injury during sleep. The patient has no control or recollection of the behavior during sleep. RBD is commonly associated with or precedes degenerative diseases of the central nervous system such as Parkinson's disease, Huntington's disease, olivopontocerebellar atrophy, dementias, multisystem atrophy, and spinocerebellar degeneration. The drug of choice is clonazepam, with a starting dose of 0.5–1 mg at night. If the patient does not respond to clonazepam, imipramine, carbamazepine, clonidine, Sinemet, or gabapentin may be tried.

Nightmares

Nightmares are frightening dreams that usually awaken individuals from REM sleep. This condition occurs at any age and may be associated with medical or psychological problems. Nightmares should be differentiated from complex partial seizures. Treatment involves behavioral therapy to correct the

underlying medical illness. Cyproheptadine (Periactin), 4–24 mg, at night, might be helpful.

REM Sleep Sinus Arrest

This condition is sinus cardiac arrest during REM sleep, recently described in the literature. Clinically, these individuals may present with early-morning lightheadedness, blurred vision, or chest pain. The condition could be related to autonomic hyperactivity during REM. With the severe form, the patient may require pacemaker.

Impaired or Painful Penile Erection

Impairment of penile erection or painful erection is a disorder occurring during REM sleep, affecting primarily middle aged men.

SLEEP–WAKE (CIRCADIAN) SLEEP DISORDERS

Jet lag is frequently seen in overseas travelers and best managed by continuation of daylight activities at the destination and trying to sleep according to local time. In severe cases, a trial of melatonin might be helpful (5 mg). Another disease is sleep-phase syndrome (nurses, police officers, i.e., people who do shift work), which often requires no specific treatment.

19
Neuromuscular Diseases

KNOW THE MOTOR UNIT

The **motor unit** is the anatomic core of the peripheral nervous system. It consists of motor neurons or **anterior horn cells**, and **muscle fibers** that are innervated their peripheral axons. Other parts of motor units are the nerve root, plexus, and neuromuscular junction. Knowing components of the motor unit helps you localize the site of pathology in the peripheral nervous system.

The number of motor units is different according to the size of the muscle being innervated. In eye muscles, one anterior horn cell innervates about 10 muscle fibers, whereas in thigh muscles there are up to 2000 fibers per anterior horn cell.

Peripheral nerve axons are either myelinated or unmyelinated. The majority of autonomic fibers are unmyelinated or lightly myelinated.

Muscle fibers consist of myofibrils and myofibrils have thousands of myofilaments. Myofilaments are contractile proteins (actin and myosin). Each muscle fiber has one neuromuscular junction structure (end-plate zone). You should know the structure and function of the neuromuscular junction.

- In a histochemistry study of the muscle biopsy specimen when stained with adenosine triphosphatase (preincubation pH = 9.4), two distinct muscle fiber types are recognized. Type 1 fibers stain light brown, and type 2 fibers stain dark brown. Type 1 fibers are red, aerobic, oxidative, and fatigue resistant. Type 2 fibers are white, anaerobic, glycolytic, and fatigable. Types 1 and 2 are equally distributed in a checkerboard pattern.

EVALUATION

The history is a very important part of evaluation of a patient with neuromuscular disease. Do not forget family history and a list of prescribed medications.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

Common Symptoms of Neuromuscular Disease

- Weakness, fatigue.
- Sensory complaints.
- Myalgia and cramps.
- Falling and difficulty walking.

Common Signs

- Weakness: can be focal, unilateral, or diffuse, predominantly proximal or distal, symmetric or asymmetric (pattern or distribution), progressive or fluctuating.
- Muscle bulk: normal, atrophied, or hypertrophied.
- Sensory deficit: normal, decreased, or increased.
- Muscle tone: normal, hypo-, or hypertonia.
- Reflex changes: normal, decreased, or increased.
- Spontaneous movements: fasciculation (muscle twitches), myokymia (undulating muscle contractions), cramps.

Commonly Performed Diagnostic Tests for Patients With Neuromuscular Disease

- **Blood work:** blood cell count, chemistry profile, serum creatine kinase (CK), sedimentation rate, thyroid function tests, serum autoantibodies, and DNA analysis if hereditary disorder is suspected. The blood tests chosen depend on the suspected cause.
- **Electrophysiological tests:** nerve conduction studies (NCS), needle electromyogram (EMG), repetitive nerve stimulation, single-fiber EMG (SFEMG).
- **Imaging:** chest X-rays, chest computed tomography (CT) scan and other imaging techniques (e.g., positron emission tomography scan, magnetic resonance spectroscopy, magnetic resonance imaging [MRI]) depending on suspected cause.
- **Diagnostic tests** should be tailored individually.
- **Spinal tap** in selected cases.
- **Muscle, nerve, or skin biopsy** in selected cases.

DIAGNOSIS

The best way to reach diagnosis or plan your workup is to try to localize the site of pathology along the **motor unit**. **Ask yourself**, Is the disorder because of anterior horn cell or plexus lesion, peripheral neuropathy, neuromuscular junction disease, or muscle disease (myopathy)?

Clinical Characteristics of Motor Neuron Disease

As an example, the clinical characteristics of amyotrophic lateral sclerosis (ALS) are:

- Weakness and muscle atrophy, more prominent in distal muscles and often asymmetric. Bulbar muscles are generally affected (manifesting as dysarthria,

dysphagia); ocular muscles are generally spared. The weakness is progressive ("creeping paralysis").
- Sensory complaints or deficit, usually absent or minimal.
- Muscle tone generally increased.
- Generalized persistent fasciculation (do not forget to look at the tongue for atrophy and fasciculation).
- Reflexes are hyperactive, but may diminish when there is severe muscle wasting. In a weak and atrophic limb, a 2+ reflex is considered hyperactive.
- Plantar responses are often extensor (Babinski's sign).
- Mental status, eye movements, sensory, autonomic, bladder, and sex functions are generally normal or less affected.

Clinical Characteristics of Nontraumatic, Adult-Onset Brachial Plexitis

- Onset of severe shoulder pain, made worse by movements.
- Weakness and sensory deficit, referable to the affected nerves.
- Often unilateral.
- Depressed reflexes.
- Muscle atrophy in later stages in the majority of patients.
- Usually upper trunk of plexus is affected.

Clinical Characteristics of Polyneuropathies

- Sensory symptoms and deficit, which usually begin at distal limbs and may progress proximally.
- Motor weakness and wasting. Distal muscles are greatly involved.
- Motor and sensory features, which could be symmetric or asymmetric in distribution.
- Reflexes are often diminished or absent.
- Muscle tone either normal or decreased.

Clinical Characteristics of Neuromuscular Junction Disorders (e.g., Myasthenia Gravis)

- Weakness and fatigue in distribution of oculobulbar or limb muscles.
- Weakness fluctuates: improves with rest, worsens with use.
- Muscle tone, sensory examination, and reflexes are generally normal.

Clinical Characteristics of Primary Muscle Disease (Myopathy)

- Weakness, which usually affects proximal muscles. Weakness is usually slowly progressive, but can be nonprogressive and asymmetric.
- Muscle atrophy may or may not be present.

- Weakness and atrophy are usually diffuse, particularly when the disease is established.
- Muscle tone generally is normal.
- Sensory and reflexes are generally normal.

MOTOR NEURON DISEASES

Amyotrophic Lateral Sclerosis

- ALS is a chronic, progressive neuromuscular disorder caused by degeneration or loss of motor neurons in the spinal cord, lower brainstem nuclei, and motor cortex.
- The etiology is unknown, but autoimmune factors, post-viral infection, environmental factors (free radicals), mitochondrial dysfunction, cytoskeletal abnormalities, apoptosis, and genetic predisposition have been proposed as possibilities.
- About 10% of cases are familial, and a defect in the superoxide dismutase gene has been recognized in 20% of familial cases.
- The incidence of ALS is approximately 2–3:100,000, with 7000 new cases reported annually in the United States.
- Males are affected more than females are, with peak age of onset of 40–50 years, with ALS equally affecting males and females after age 70.
- The onset is insidious, with weakness and atrophy of distal muscles (hand muscles usually first), which begins asymmetrically, presenting as hand clumsiness. The course is progressive, with variation among patients. Progression is usually horizontal between the extremities. Following involvement of limbs, bulbar muscle involvement manifests as dysarthria and dysphagia. Death occurs 3–5 years after the onset in most patients, usually because of pulmonary infection.

Clinical Pearls

- Suspect ALS when a patient has a combination of upper motor neuron (weakness, spasticity, hyperreflexia, extensor plantar response, pseudobulbar) and lower motor neuron (weakness, atrophy, fasciculation) signs in more than three limbs (bulbar and/or paraspinal muscle are considered as one limb).
- The onset of disease can be atypical, such as onset of foot drop, bulbar onset, hemiplegic variant, pseudobulbar onset, onset of head drop, and rarely, reported onset of respiratory muscles failure.
- Always look for tongue atrophy and fasciculation, particularly in patients presenting with dysarthria and dysphagia.
- The following symptoms and signs are generally **absent or less prominent** in ALS: extraocular-muscle dysfunction, sensory and autonomic dysfunction, bladder dysfunction, and decline of cognition. If the patient presents initially with these symptoms and signs, or if they constitute main features of the patient's problem, doubt diagnosis of ALS.

Diagnosis

The diagnosis of ALS is based on clinical presentation, course, and neurological findings. The most useful confirmatory test are NCS and needle EMG. NCS results are usually within normal range, but needle EMG results show active and chronic neurogenic changes, which should be present in at least three limbs (tongue or paraspinal muscles may be considered one limb). All patients with ALS should have NCS/EMG and MRI of the cervical region. Blood tests include cell count, sedimentation rate, serum protein electrophoresis, thyroid-stimulating hormone, vitamin B_{12} level, CK, Lyme disease titer, serum calcium, and rapid plasma reagin test. HIV testing is recommended for at-risk patients. MRI of brain, magnetic resonance spectroscopy, spinal tap, antiganglioside antibodies, muscle biopsy, and genetic testing are considered when other disorders are suspected. Although the diagnosis of ALS in typical cases is relatively straightforward, there are several neuromuscular diseases posing some diagnostic challenge, namely, multifocal motor neuropathy (MMN), progressive lower motor neuron syndrome, primary lateral sclerosis, post-polio syndrome, benign fasciculations, inclusion body myositis (IBM), Kennedy disease, and adult onset Tay-Sachs disease.

Management

- Establish diagnosis of ALS before you discuss your impression with the patient and relative.
- Provide adequate information to the patients and caregivers in timely fashion.
- Treatment for the most part is supportive and symptomatic (spasticity, cramps, depression, pseudobulbar features): physical and occupational therapy, speech, respiratory and nutritional assistance. Most ALS patients are best served by referral to ALS centers.
- So far, one drug has been approved by the Food and Drug Administration: riluzole (Rilutek) is given in a 50-mg dose twice a day by mouth, which may slow the progression for only a few months. Numerous drug trials are now underway.
- Dysphagia is best to be managed by gastric feeding tube placement and balanced nutrition.
- Respiratory failure may require mechanical support, depending on the patient's wishes.

PERIPHERAL NEUROPATHIES

The approach to evaluation of peripheral neuropathies is discussed in Chapter 16. This section discusses selected topics in neuropathy.

Common Mononeuropathies

Bell's Palsy

- Acute idiopathic peripheral seventh nerve palsy.

- Presentation is often unilateral, causing weakness of facial muscles (forehead and lower face), manifesting as difficulty in closing of the eyes, wrinkling forehead, and difficulty in smiling or drinking.
- The cause is unknown, but post-viral inflammation and autoimmune involvement has been proposed.
- The prognosis is worse when the weakness is severe or the proximal nerve is involved, manifesting as hyperacusis and decreased tearing or taste.
- Most neurologists obtain a complete blood count, erythrocyte sedimentation rate (ESR), glycosylated hemoglobin (Hb_{A1c}), thyroid function tests, Lyme disease titers, and angiotensin-converting enzyme level. NCS and EMG may help to prognosticate (decreasing amplitude of action potential and denervation potentials in the facial muscles: worse prognosis).

Differential diagnosis: The differential diagnosis of Bell's palsy includes central seventh nerve palsy, which is associated with ipsilateral appendicular motor or sensory deficit. Cerebellopontine angle lesions often associated with involvement of the fifth, sixth, and seventh cranial nerves.

Treatment: Most practicing neurologists administer a 7- to 10-day course of corticosteroids (starting with 60 mg/day) in the acute stage (within 5–7 days). Most neurologists use a combination of prednisone and acyclovir (1 g three times a day for 1 week), although studies have shown that combination treatment made no difference over prednisone alone. Protect against corneal dryness and subsequent infection by patching the eye and artificial tears. Prognosis of Bell's palsy is generally favorable, with excellent recovery in up to 70% of cases. The patients need to know this fact, and they need to know that facial paralysis is not because of stroke.

Carpal Tunnel Syndrome

- Carpal tunnel syndrome, or median neuropathy at the wrist, is the most common mononeuropathy. It presents with paresthesia and pain in the hand and arm, usually worse at night and relieved by rubbing or shaking the hand. In the chronic stage, weakness and atrophy of the thenar muscles may be seen. The leading risk factors are female gender and obesity, follow by occupation (workplace), and endocrine diseases such as diabetes, acromegaly, hypothyroidism (myxedema), and amyloidosis. Pregnancy, fibromyalgia, and dialysis are also risk factors. In younger patients without obvious risk factors associated with other entrapment neuropathy, consider conditions such as multifocal motor neuropathy (MMN) and hereditary neuropathy with liability to pressure palsy (HNPP).
- Carpal tunnel syndrome is probably the most common cause of numbness of the hand.
- Positive Tinel's and Phalen's signs, ischemic pressure, and flicker signs support the diagnosis.

Workup includes: complete blood count, ESR, thyroid function test, fasting blood sugar and serum protein electrophoresis, and rheumatoid factor. The diagnosis is established by NCS, which shows delayed distal motor and sensory latency of the median nerve, but relatively normal ulnar nerve latencies and conduction velocities. Other diagnostic procedures such MRI or ultrasound need more use in diagnosing carpal tunnel syndrome to prove their value.

Treatment: Treatment of carpal tunnel syndrome starts with conservative (cock-up wrist splint), which is best used on a full-time basis; treating aggravating factors; and pain control. Pyridoxin is generally ineffective. Hand exercises are helpful. Short-term oral corticosteroid therapy (60 mg/day, tapering over 10 days) has been advocated by some authorities. Local injection (wrist) of corticosteroids is usually helpful if performed by experienced specialist, but its effect is temporary. Other non-surgical techniques include magnetic stimulation (further studies need to be done), acupuncture, and ultrasound therapy. The most effective therapy is surgical decompression of the nerve, which can be done by open incision or noninvasive endoscopic approach.

Surgery is indicated when medical and conservative treatments are found to be ineffective or the patient develops hand weakness or thenar atrophy. Surgical procedures include the standard open endoscopic and small palmar incision approach. The outcome of open and endoscopic approaches is the same. The choice of procedure depends on the patient's choice and preference, and the experience of surgeon.

Cubital Tunnel Syndrome

- Cubital tunnel syndrome results from ulnar nerve compression at or distal to the elbow, which is the most common site of entrapment for this nerve. Like carpal tunnel syndrome, cubital tunnel syndrome has various causes. It can be bilateral.
- The patient experiences numbness and paresthesia of the fourth and fifth fingers, followed by weakness (check for Froment's sign), and atrophy of ulnar-innervated muscles of the hand. Pain is less common.
- NCS and electromyographic testing enables localization of the site of compression.
- Cubital tunnel syndrome must be differentiated from lower trunk plexus lesion (always look at a pupils for Horner's syndrome to rule out possibility of upper lobe tumor of the lung) and C7–C8 radiculopathy. Ulnar neuropathy could be a sign of generalized neuropathy or MMN. Treatment is conservative, followed by surgical release in selected cases.

Foot Drop: Peroneal Nerve Palsy

- Peroneal nerve palsy results from compression of the peroneal nerve at the fibular head.

- The onset of the disease is usually acute. Predisposing factors include generalized neuropathy, crossing of legs for a long time, general anesthesia, weight loss, coma, prolonged casting, prolonged hospital stay, prolonged surgery, and HNNP.
- On examination, there is weakness of the foot dorsiflexors and evertors. The patient is unable to stand or walk on heels, has steppage gait, and is tripping.
- Sensory complaints and deficits are minimal. There are no reflex changes.
- Peroneal palsy must be differentiated from L5 root lesion. With an L5 root lesion, often there is history of back and radicular pain, weakness of dorsiextensors and invertors of foot, and weakness of extensor hallucis longus. Knee-jerk reflex is diminished.
- L5 radiculopathy is further differentiated from peroneal palsy by NCS/EMG testing.
- Treatment is supportive: physical therapy, short leg brace to improve walking, and stabilizing the ankle joint. Surgical decompression rarely performed.

Diabetic Neuropathies

Diabetes is now the most common cause of polyneuropathy in the world. Its clinical presentations include:

- Distal, symmetric sensory motor polyneuropathy.
- Distal, symmetric sensory polyneuropathy.
- Autonomic neuropathy: postural hypotension, dizziness, impotence, dry eyes or mouth, persistent diarrhea or nausea, bladder dysfunction.
- Diabetic ophthalmoplegia: third nerve, often unilateral, pupillary response, and size is usually normal.
- Peripheral seventh nerve palsy.
- Entrapment neuropathies: carpal and cubital tunnel syndromes, femoral neuropathy.
- Mononeuropathy multiplex: asymmetric neuropathy superimposed with generalized polyneuropathy, which should be differentiated from vasculitis.
- Thoracolumbar polyradiculopathy: this must be differentiated from cardiopulmonary pathologies, acute abdominal pathology, or lumbar radiculopathy.
- Diabetic amyotrophy (Bruns-Garland syndrome): acute or subacute onset of thigh pain, followed by weakness and later wasting of thigh and hip muscles (pelvifemoral or L2, -3, or -4 root distribution). Prognosis is generally good, and most patients recover within few months. Use of intravenous Ig (IVIg) has been advocated on the basis of inflammation in the nerve biopsies in some series. Differential diagnosis includes lumbosacral polyradiculopathy, focal myositis, inclusion body myositis, and femoral neuropathy.

Chronic Inflammatory Demyelinating Polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired, chronic, autoimmune sensory motor polyneuropathy, affecting adults 40–70 years of age. The features of chronic inflammatory demyelinating polyneuropathy include:

- Onset of sensory motor neuropathy, which develops over period of months.
- The course could be monophasic, relapsing remitting, and or progressive.
- Approximately 30% of patients have history of febrile illness.
- The disease usually begins with onset of distal symmetric leg paresthesia, followed by symmetric distal and proximal hip and shoulder muscle weakness. Some patients have only weakness of lower extremities.
- Cranial and autonomic nerve fibers are less affected.
- On examination, the patients have predominantly distal proprioceptive sensory loss, muscle weakness, and depressed or absent reflexes.
- The diagnosis is supported by NCS, demonstrating demyelination (slowing nerve conduction velocities, delayed latencies and F-waves, and conduction block with dispersion of motor nerve action potential). Spinal fluid protein is elevated. In practice, cerebral spinal fluid analysis and nerve biopsy are not required for diagnosis.
- Treatment begins with IVIg monthly, with alternative options of plasmapheresis, corticosteroids, immunosuppressive drugs, or chemotherapy.
- Prognosis is good if the patient is diagnosed early and receives prompt treatment. Approximately 75% of patients recover to their independent life styles.

Multifocal Motor Neuropathy (MMN)

MMN is a chronic, rare immune-mediated neuropathy characterized by:

- Onset of asymmetric neuropathy affecting the arms, presenting as weakness in distribution of single or multiple peripheral nerve (ulnar, median, radial), with no or minimal sensory symptoms.
- Lower extremity may be affected later. Weakness if untreated, followed by atrophy and depressed reflexes. Many patients have cramps and fasciculation. Cranial nerves are less affected.
- The disease is more common in men aged 20–70 years.
- MMN is suspected if a middle-aged man presents with motor weakness and atrophy in distribution of nerve, with depressed reflexes and fasciculation, with absence of sensory deficits. Diagnosis is supported by NCS showing demyelination and conduction block, although axonal features can be seen. Antibody to GM1 ganglioside has been reported in 60–70% of cases; however, positive antibody is not required for the diagnosis.

- MMN can be mistaken for ALS. Absence of upper motor neuron signs, conduction block on NCS, and absence of diffuse denervation and reinnervation on needle examination will exclude ALS.
- Treatment of MMN begins with IVIg. In refractory cases, cyclophosphamide is considered. Corticosteroids are ineffective.

Hereditary Neuropathies

- Charcot-Marie-Tooth (CMT) is the most common inherited (autosomal dominant) polyneuropathy in humans, with an estimated prevalence of 1:2500.
- CMT-1 is referred to hereditary motor sensory neuropathy (HMSN) type I, which is demyelinating form, and CMT2 (HMSN type II), which is the neuronal form affecting dorsal root ganglion and lower motor neurons.
- CMT1 is characterized by peroneal muscle atrophy, producing stork legs, or inverted champagne bottle, appearance. The most unique foot deformity is pes cavus (high-arched feet and hammertoes). Hypertrophic nerves may also be seen or detected on palpation. NCS demonstrate marked, uniform slowing of conduction velocities, decreased amplitude, and prolonged distal latencies. Nerve biopsy shows characteristics of onion-bulb formation, which is proliferation of Schwann cells, with demylination and remyelination.
- CMT should be suspected in a patient who presents with an undetermined cause of neuropathy, and examination shows depressed reflexes and pes cavus deformity.
- With CMT2, NCS slow only slightly, and nerve biopsy shows axonal degeneration and regeneration.
- Other inherited neuropathies include: HMSN III, or Dejerine-Sottas or CMT-3, which starts in childhood and progresses to severe disability (wheelchair-bound by the teen years). NCS shows marked showing conduction velocities (<10 m/second).
- HNPP: autosomal dominant, presents with mononeuropathy multiplex, and multiple-pressure palsies (often because of minor pressure). NCS show demyelinating neuropathy with features of compression (delayed distal motor and sensory latencies). Nerve biopsy shows focal demyelination and remyelination, producing sausage-like "tomaculous" structures on teased nerve fiber preparation.
- DNA testing is now commercially available (CMT1A) for diagnosis of CMT1, CMT3, which shows duplication at chromosome 17 P11-2, and deletion in HNPP.
- Classification of hereditary neuropathies is not only based on clinical and electrophysiological features, but on their genetic markers. There are now at least 30 phenotypes/genotypes of CMT, which is beyond the scope of this book.

DISORDERS OF NEUROMUSCULAR JUNCTION

Acquired Autoimmune Myasthenia Gravis

- Myasthenia gravis (MG) is the most well-known autoimmune disease in humans.
- The disease is caused by an immune attack against the postsynaptic (endplate) membrane of the neuromuscular junction of the skeletal muscle.
- The onset is often acute or subacute and may be triggered by stress, infection, surgery, pregnancy, drugs, and other unknown environmental factors.
- The disease has two peak onsets: age 20–30 in women and 50–60 in men.
- The clinical hallmarks of MG are fluctuating muscle weakness and fatigue. The most typical presentation is weakness in distribution of ocular (ptosis, diplopia) and bulbar muscles (dysphasia, dysphonia, and dysarthria). The limb muscles are less affected. Onset of MG with proximal limb and respiratory muscle weakness is less common.
- Muscle tone, bulk, sensory, and reflexes are otherwise normal, unless patient has other medical and neurological diseases.

Diagnosis

The diagnosis of MG is made on the basis of the clinical features and is confirmed further by the following diagnostic tests.

Edrophonium (Tensilon) Test

The Tensilon test is an easy and quick test for diagnosis of MG. The Tensilon dose is 10 mg/mL, given intravenously. Before doing the Tensilon test, establish muscle weakness that can be measured objectively (ptosis, diplopia, dysarthria). If there is no good objective weakness the test is unreliable and not helpful. Administer 2 mg as a test dose and monitor heart rate (pulse), blood pressure and respiration; if no reaction is seen, give another 3 mg and if no response seen then, administer the remaining 5 mg. The response should be dramatic and objective (unequivocal) to be considered positive. Always have a vial of atropine available to overcome excessive muscarinic side effects. Tensilon acts quickly, and the response may last 10–15 minutes. Elderly patients with asthma or chronic obstructive pulmonary disease and cardiac disease are best to be monitored carefully in the hospital. Otherwise, the Tensilon test can be done in the office. In a typical presentation of MG, an unequivocal positive Tensilon test is diagnostic for MG. Remember, Tensilon may improve fatigue in many neuromuscular diseases, but the response is usually not as dramatic as is seen in MG.

If Tensilon is not available or cannot be used, do a **sleep** or **ice pack** test. In a patient with an objective weakness, have the patient close the eyes and rest for 15–20 minutes. In case of ptosis, place an ice pack on the eye for a

few minutes. The test is considered to be positive if ptosis or diplopia resolved temporarily.

Electrophysiological Tests

NCS and needle EMG results are usually normal in MG, but they need to be done to exclude other neuromuscular diseases. Two electrophysiological tests that are done for confirmation of neuromuscular junction disease are:

- **Repetitive nerve stimulation (Jolly test).** A gradual decreasing amplitude of motor nerve action potential (decremental response) of the muscle is seen, when the innervated nerve stimulated at a rate of 2 pulses a second (up to 10% decrement is normal). Sensitivity of this test is about 60%. Distal and proximal muscles (e.g., facial, trapezius) should be tested.
- **Single-fiber EMG.** This test is a more complex and highly sensitive test in which the time interval between two muscle fibers belonging to one anterior horn cell is measured by a special needle electrode. The two muscle fibers usually fire simultaneously, with minimal contraction of the muscle, but in MG they do not fire simultaneously (increased variability or jitter). SFEMG is highly sensitive (meaning in a weak muscle because of MG, the result is always abnormal), but is highly nonspecific (abnormal in many neuromuscular diseases).

Acetylcholine-Receptor Antibody

This test is highly specific for MG (very rarely reported in other conditions). In patients with moderately severe generalized MG, the antibody is positive in more than 90% of patients, but in purely ocular MG, it is positive in only about 50% of cases. About 10–15% of patients of generalized MG have negative antibody (seronegative MG). In the latter population of patients, between 40 and 70% have antibody against muscle specific tyrosine kinase (MUSK). Muscle specific tyrosine kinase-positive patients are usually women with predominantly bulbar and respiratory symptoms responding to plasmapheresis.

Other Autoantibodies

Anti-striate muscle, anti-citric acid, and anti-titin antibodies are useful in patients suspected having thymoma (elderly patients). Remember, not all patients with enlarged thymus glands on chest CT scan have positive anti-striate muscle antibody, and tests for the antibody are not always negative in patients with a small thymus gland. The value of this antibody test is that if the antibody and chest CT scan are both negative for thymoma, thymectomy is not necessary in an elderly patient, and antibody-positive thymectomy may be considered, if the patient is medically stable.

Blood Tests

These tests include ESR, anti-nuclear antibodies, serum CK, thyroid function tests, and rheumatoid arthritis factor.

Imaging

A routine chest X-ray is indicated in adult onset MG, but elderly patients need chest CT scans to rule out thymoma.

Treatment

Symptomatic

Anticholinesterase (AChE) inhibitors: The most commonly used drug is pyridostigmine (Mestinon), given orally (60-mg tablets). Start at a low dose and titrate according to response. You should know the side effects and explain them to the patients. Overmedicating with pyridostigmine may exacerbate weakness (cholinergic crisis).

Immunosuppressive therapy:

- Corticosteroids.
- Immunosuppressive drugs: azathioprine, cyclophosphamide, cyclosporine A, methotrexate, mycophenolate mofetil (CellCept).
- Thymectomy: trans-sternal or maximal (trans-sternal and transcervical).
- Plasmapheresis (plasma exchange): for acute worsening of MG (crisis, post-thymectomy, other).
- IVIg: for acute weakness, and exacerbation or intractable cases.

Guidelines Regarding Therapy

1. Establish diagnosis of MG before initiating therapy.
2. Individualize therapeutic options.
3. Explain the advantages and disadvantages of each therapeutic option to the patient.
4. The goal of therapy is to achieve clinical remission (no fatigable muscle or weakness without receiving any medications).
5. Titrate the dose of AChE inhibitors according to the patient's response to achieve optimal response. If patient does not respond to an adequate dose (290 mg/day for most patients), increasing the dose not only does not help, but also can cause side effects and exacerbating weakness. AChE inhibitors are good for symptomatic relief, but if they do not help strength, there is no point in using them or increasing the dose.
6. Thymectomy is indicated in all patients 15–60 years, with stable medical conditions. Patients with thymoma should have a thymectomy, regardless of age. Most neurologists do not recommend thymectomy for pure ocular MG.
7. Most centers do trans-sternal thymectomy. Thymectomies should be done in a center with experienced surgeons and team knowledgeable about the disease.
8. Thymectomy is an elective procedure and should not be done urgently. Patients should be stabilized and be as strong as possible before thymectomy. The response to thymectomy is often delayed (up to 2 years on average). The

rationale behind thymectomy is the long-term benefit and the chance that achieving long-lasting remission should be higher. In general, early thymectomy is recommended (after adequate stabilization).

- Corticosteroids are given to patients with a suboptimal response to AChE inhibitors or post-thymectomy worsening. In more severe MG, you may begin with a high daily dose of prednisone (e.g., 60 mg/day) and continue, to reach maximum response (usually takes 3–4 weeks). Then change to high alternate daily dose (e.g., 110 mg every other day) and continue for another 2–3 weeks before you begin slow tapering of the drug. If you decide on a high daily dose, it is advisable to hospitalize the patient (for possible worsening). In milder cases, you may begin with low alternate dose (20 mg every other day), with gradual incremental increases. This can be done on an outpatient basis. Some patients with ocular MG may require prednisone therapy.
- Immunosuppressive drugs (azathioprine and others). These medications are given when patients develop undesirable side effects to prednisone or cannot take corticosteroids, or suffer a relapse when you are tapering the prednisone. They act slowly. Their side effects need to be monitored closely. Most neurologists are now using mycophenolate mofetil as adjunctive immunosuppressive drug, between 1000 and 2000 mg/day.
- Plasma exchange (plasmapheresis). Plasma exchange is usually considered for acute exacerbation of MG (myasthenic crisis, post-thymectomy worsening), and some authorities use plasma exchange prior to thymectomy. Plasma exchange acts quickly (usually after the second or third exchange), but its effect is short lived (3 months at most). This is a quick booster. Exchange has morbidity, and is a costly procedure.
- IVIg. The indications and the cost are the same as exchange, but it is easier to use and is more available. Its therapeutic responses, however, are unpredictable.

Clinical Pearls

- Suspect MG in young adults presenting with onset of diplopia or ptosis. Doubt MG when the patient presents with generalized fatigue without fluctuation and absence of ocular/bulbar muscle dysfunction after 2–3 years.
- The hallmark of muscle weakness in MG is its fluctuation (variable, made worse by exertion and better by rest) and distribution of affected muscles (ocular/bulbar and extremities).
- Always obtain adequate history of prescribed medication, because some drugs can produce myasthenic features (antibiotics, antiepileptic drugs, antiarrhythmics, penicillamine).
- Establish objective muscle weakness prior to doing the Tensilon test.
- The sensitivity of tests for repetitive nerve stimulation will increase if several muscles are tested.

- The most specific and sensitive test for diagnosis of MG is ACh receptor antibody. It should be done by a reliable lab.
- Chest X-ray and CT scan are indicated in all myasthenic patients.
- The goal of therapy is to achieve remission without medication or with very low doses of medication.
- Individualize therapeutic options because not only are the myasthenics different individuals, but also their presentation is different, and even degree of muscle weakness is different from muscle to muscle in any given case.
- Thymectomy is an elective surgery and should not be done urgently when the patient is weak or unstable. Thymectomy should be done in a center with experienced surgeons, neurologists, and intensive care specialists.

Lambert-Eaton Myasthenic Syndrome

- Lambert-Eaton myasthenic syndrome (LEMS) is a slowly progressive, symmetric proximal muscle weakness (such as difficulty rising from a chair).
- Oculobulbar and respiratory muscles are spared or minimally affected.
- Majority of patients have autonomic symptoms such as dry mouth, constipation, and impotence.
- Approximately 30% of patients complain of distal paresthesia.
- On examination, patients have proximal hip muscle weakness and depressed or absence of reflexes, which may improve by exercise.
- Always consider LEMS in an elderly man or woman who presents with insidioius onset of proximal hip muscle weakness associated with dry mouth and areflexia.
- LEMS is associated with underlying malignancy in about 60–70% of cases (small cell lung cancer being the most common, even in nonsmokers)
- Antibody against P/Q type voltage-gated calcium channels is detected in approximately 98% of LEMS associated with cancer and 70% of LEMS without cancer. Incidence of lung cancer in seronegative LEMS is much less than in seropositive LEMS. Seronegative LEMS could have antibody against synaptagamine-1.
- Patients with LEMS should have antineuronal antibody (anti-Hu), chest CT scan, bronchoscopy, and other tests for detecting underlying carcinoma. If chest CT scan was negative, whole-body positron emission tomography scan is recommended. Many times, the occult cancer is detected after onset. Therefore, diagnostic tests for cancer detection should be continued periodically for 3–5 years.
- Diagnosis of LEMS is best confirmed by electrophysiological testing. The most characteristic is very low amplitude motor action potential at rest. Repetitive nerve stimulation at slow-rate stimulation (2 pulses per second) shows decremental response, but in contrast to MG, a higher rate of stimulation (e.g., 20 pulses per second) shows marked increased amplitude (incre-

mental responses) up to 200% from baseline. The easy and quick way to detect a marked increment is to exercise the muscle for 30 seconds and apply a single shock: If the amplitude increases by 200% or more from baseline, even in one muscle, the diagnosis of LEMS is certain. SFEMG as seen in MG shows significant increase of jitter value.

Treatment

- Detect and treat underlying carcinoma.
- AChE inhibitors (Mestinon) may help some patients.
- 3–4-Diaminopyridine is probably the most effective drug for symptomatic relief, but it has not been approved by the Food Drug Administration. This drug blocks outward potassium current from the cell, which prolongs the duration of activation of acetylcholine in the presynaptic membrane and increases calcium entry to preterminal and further release of acetylcholine. The drug also helps autonomic symptoms. The dose is between 15 and 60 mg/day, not to exceed 80 mg. Higher doses may result in cardiac arrhythmia and seizure.
- In more severe cases corticosteroids, immunosuppressive drugs, IVIg, and plasmapheresis should be considered.

Botulism

Botulism is caused by ingestion of a neurotoxin (types A, B, and E) produced by anaerobic, Gram-negative *Clostridium botulinum*, often from improperly canned foods (home-canned, home-processed, low-acid foods), through wounds, and possibly intravenous drug use.

Clinical Features

Botulism presents with sudden onset of blurred vision, diplopia, bulbar dysfunction (dysarthria, dysphagia), and symmetric descending limb weakness. Autonomic symptoms such as dry mouth, constipation, urinary retention, and dilated fixed pupils may be seen. Respiratory muscle weakness may occur later.

Diagnosis

The diagnosis is confirmed by doing repetitive nerve stimulation at a higher rate, which shows incremental responses, similar to LEMS, that last longer. The leading differential diagnoses are Guillain-Barré syndrome, MG, and Miller-Fisher syndrome. More specific tests for botulism are the mouse inoculation test for toxin and serum/stool/food cultures for detecting the organism. Detecting toxin in the blood is diagnostic.

Patients with botulism should be hospitalized and monitored closely and if necessary, intubated.

Treatment includes ventilatory support, AChE inhibitors, and trivalent equine antitoxin, which can be life-saving if used within 24 hours after diagnosis. Antitoxin can be obtained by calling the local state health department. The role of antibiotics is unproven despite their common use (penicillin, metronidazole).

MUSCLE DISEASES (MYOPATHIES)

Inflammatory Myopathies

There many types of inflammatory myopathies. Autoimmune (idiopathic) myopathies such polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM) are highlighted in this section.

Polymyositis

- The onset of PM can be acute or subacute, with symmetric proximal muscle weakness (e.g., difficulty rising from a chair, combing hair).
- Muscle tone and bulk are normal at the onset.
- Sensory examination and reflexes are normal.
- Muscle pain occurs only in one third of cases.
- PM rarely affects children younger than age 15. True PM in adults is not as common as once thought.
- Occult carcinoma may be seen in 8–10% of cases.
- The disease is caused by an autoimmune attack ($CD8^+$ and macrophages) against muscle fibers. PM can be associated with other autoimmune diseases (overlap syndrome).
- Serum CK often moderately elevated.
- NCS are normal, but needle EMG shows spontaneous potentials in the form of fibrillation, positive sharp wave, and small, polyphasic, short-duration, low-amplitude motor unit potentials.
- The diagnosis is confirmed by muscle biopsy, which shows muscle fiber necrosis, regeneration, and inflammatory cells infiltrate around and invading the muscle fibers, as well as detailed immunohistochemical studies. Because of sampling error, negative biopsy does not rule out the diagnosis. It is recommended that the muscle sample of patients suspected of having PM be tested for major histocompatibility antigen type 1.

Treatment is begun with corticosteroids, between 60 and 80 mg/day, and continued until steady improvement has been achieved, before starting taper. The goal of treatment is more improving the muscle strength and less the decline of serum CK. If the patient failed to respond to prednisone alone (after 3 months), combine prednisone with immunosuppressive drugs (azathioprine, methotrexate, mycophenolate mofetil). In more-resistant cases, trial of IVIg

and cyclosporine should be considered. Patients who do respond may be tried on tacrolimus, etanercept, or rituximab. In more-intractable cases, plasmapheresis and intravenous cyclophosphamide are to be considered.

Caveat: Because of the rarity of PM, it is advisable to repeat muscle biopsy (in which you may find IBM instead) in patients who failed to respond to an adequate trial of prednisone or combination with a first-line immunosuppressive drug. Beware of steroid myopathy in patients presenting with recurrent weakness while on chronic use of prednisone, where it uniquely presents with thigh muscle weakness and sparing neck flexors.

Dermatomyositis

- Onset of subacute mild proximal muscle weakness or no weakness (amyopathic DM). Unlike PM, DM affects children (childhood DM).
- Characteristic skin lesions: heliotropic rashes around the eye and cheeks, V- and shawl signs, and *Gottren's nodules* (scaly, violet rashes over the knuckles) are diagnostic. Nail bed telangiectasia and necrosis may be seen. In childhood DM, subcutaneous calcification may be seen.
- Serum CK may be mildly to moderately elevated.
- EMG shows myopathic features, such as in PM, but can be normal.
- DM is highly associated with other autoimmune diseases (overlap syndrome).
- Association with malignancy is between 15 and 25%. Late-onset DM (after age 40) should be investigated for malignancy in the lung, breast, ovary, and gastrointestinal (GI) system.
- Other autoantibodies: anti-PM-1, anti-Jo-1, and anti-RO—not only associated with overlap syndrome, but also indicative of cardiomyopathy or interstitial lung disease associated or DM or PM. Antisynthetase syndrome is present in patients with DM/PM with positive anti-Jo-1 antibody. These patients present with Raynaud's, interstitial lung disease, carditis, arthritis, and "mechanic's hands" (dry, cracked hands).
- Muscle biopsy, which may demonstrate inflammatory cells around blood vessel wall (vasculitis). Immune deposits can be demonstrated in the endothelial membrane. The hallmark muscle biopsy feature, however, is atrophy of muscle fibers at the periphery of muscle fascicle (*perifascicular atrophy*), which can be detected up to 90% of childhood DM.
- In DM, the immune attack ($CD4^+$) and complement (MAC-Cb9) is directed against intramuscular endothelium, causing microangiopathy and subsequent ischemia and necrosis of the muscle fibers. Therefore, DM is distinctly different from PM, sharing only few clinical similarities.
- Treatment options and strategies in DM are similar of those described in PM, except the use of IVIg as initial or second-line treatment. In relapse cases of DM that are unresponsive to initial drug therapy, beware of recurrency or development of underlying carcinoma.

Inclusion Body Myositis

- IBM is a disease of the elderly (sporadic form), with onset at age 50 and above. IBM is probably the most commonly acquired muscle disease after age 60. It has a slowly progressive course leading to moderate/severe disability.
- The onset of muscle weakness is insidious, affecting distal and proximal muscles with atrophy, and it is often asymmetric. The unique patterns of weakness and atrophy include fingers, wrist flexors, and inner forearm muscles in the upper extremities. In the lower extremities, quadriceps and foot dorsiflexors (foot drop) are generally affected. The hereditary form affects younger patients as well, but quadriceps muscles are spared. Dysphagia has been reported frequently.
- Serum CK is mildly elevated.
- IBM is usually not associated with malignancy or other autoimmune diseases, but association with amyloid cardiomyopathy, HIV, and post-polio syndrome has been reported.
- Pathogenesis of IBM is unknown. Amyloid-related degeneration because of the aging process and an immune dysregulation have been proposed.
- EMG shows mixed myopathic and neurogenic changes.
- The diagnosis is confirmed by muscle biopsy, which shows muscle necrosis and a mild to moderate inflammatory response. The most characteristic is presence of rimmed vacuoles that contain filamentous inclusions, demonstrated by electron microscopic examination. Remember, rimmed vacuoles are also seen in other myopathies. If clinical presentation is typical, presence of rimmed vacuoles can be diagnostic.

Caveat: In practice, IBM probably is more common than are PM or DM. Suspect IBM when an elderly patient presents with proximal and distal muscles weakness and in evaluation, you find mildly elevated serum CK and mixed neurogenic/myopathic EMG; in this case, consider muscle biopsy. Suspect IBM when the patient with a previous diagnosis of PM does not respond to corticosteroids or immune suppressive drugs; consider repeating muscle biopsy in these cases.

There is no effective treatment currently available for IBM, but most neurologists consider a 6-months-to-1-year trial of immunosuppressive drugs or corticosteroids if the patient insists. All treatment options as described for PM/DM have been tried. Use of oxandrolone and high-dose β-interferon-1a have shown some promising benefit. Patients should receive physical and occupational therapy.

Congenital Myopathies

- Congenital myopathies are a slowly progressive or nonprogressive (static) group of muscle diseases, with onset in childhood or late adulthood.

- Clinically may present with ocular or proximal weakness or respiratory failure, but their clinical phenotype is variable.
- Reflexes may be normal or depressed.
- Dysmorphic features (bone, joint) are common.
- NCS and needle EMG may be normal or show mixed myopathic/neurogenic pattern.
- Serum CK may be normal or mildly elevated.
- Diagnosis is confirmed by muscle biopsy that shows myopathic features and specific structural changes in the muscle fibers, from which the name of myopathy is given: type 1 fiber predominant, central core disease, nemaline (rod) myopathy, centronuclear (myotubular) myopathy, and congenital muscle fiber disproportion.
- Management is conservative and symptomatic.

Muscular Dystrophies

- Muscular dystrophies are hereditary, progressive myopathies, with onset of muscle weakness in early childhood or adulthood.
- Muscular dystrophies are classified by their clinical phenotype and genetic defect. The muscle biopsy shows dystrophic features, and often there are markedly elevated serum CK levels. The EMG shows myopathic motor unit potentials.
- The three leading X-linked muscular dystrophies (MDs) are Duchenne's (DMD), Becker's (BMD) and Emery-Dreifuss (EDMD). Defective protein (dystrophin) in DMD/BMD is absent in DMD and reduced or abnormal in BMD. DMD/BMD presents with onset weakness in early childhood, with a progressive course to patients being wheelchair-bound by their teen years in DMD. The diagnosis now can be established by blood polymerase chain reaction for deletion and if inconclusive, muscle biopsy for dystrophin assay. In patients with the DMD/BMD phenotype but negative polymerase chain reaction, limb–girdle MD2I should be considered as possibility. In EDMD, the defective protein is emerin. This dystrophy presents with distal muscle weakness and atrophy, with prominent joint contractors and cardiac conduction defects.
- Most experts use prednisone for patients with DMD after age 5. Gene therapy, stem cell therapy, and other treatments are under investigation.

Myotonic Muscular Dystrophy

- Myotonic muscular dystrophy (DM1) is the most common muscular dystrophy in adults, with a prevalence of 1:8000.
- It is of autosomal-dominant inheritance. The gene defect is located in the long arm of chromosome 19q13.3, and the severity of disease increases with successive generations (anticipation).

- The clinical manifestations vary from patient to patient, and even among siblings.
- DM is a multiple system disease affecting muscle, heart, GI and endocrine systems, skin, and brain.
- Muscle weakness and atrophy affecting more distal muscles than proximal. Typical features include temporalis muscle atrophy, bifacial diplegia, bilateral ptosis, weakness and atrophy of sternomastoid muscles, atrophy of forearm muscles, and weakness of wrist extensors and dorsiflexors of the feet.
- Reflexes are depressed or absent.
- Characteristic myotonia (delayed muscle relaxation) is seen by hand grip (grip myotonia—prolonged hand shake sign), percussion myotonia (myotonia induced by tapping the muscle).
- Dysarthria and dysphagia are seen in more advanced stages.
- Systemic signs include frontal baldness, cataract, cardiac conduction defect, GI dysfunction, testicular atrophy, diabetes, mental retardation, and sleep apnea syndrome.
- EMG reveals a typical "dive bomber" sound or myotonic discharge on needle examination and myopathic features.
- The diagnosis of DM is based on clinical features and confirmed by DNA analysis showing expansion of trinucleotide repeat (known as CTG) in the protein kinase gene. A normal repeat is 5–30 bp, and more than 50 bp is abnormal. The longer the repeat, the worse is the disease and cardiac dysfunction. All patients with DM should have yearly cardiac evaluation and slit-lamp eye examination.
- Recently, myotonic dystrophy type 2 (DM2) has been described. DM2 is caused by a CCTG repeat expansion in intron 1 of the zinc finger protein 9 gene. DM2 presents in adults only (there is no congenital DM2; this is an important distinction from DM1) with proximal muscle weakness, which commonly know as proximal myotonic myopathy (PROMM). Other phenotypic features of DM1 may be seen in proximal myotonic myopathy with variable degrees. Cognitive dysfunction is less prominent in DM2, and myotonia is seen on EMG.
- Therapy is supportive. Antimyotonic drugs include phenytoin, procainamide, mexiletine, acetazolamide, and dantrolene, which can be tried in selected cases. It is important that the patient also be followed up by a cardiologist.

Fascioscapulohumeral Muscular Dystrophy

- Fascioscapulohumeral muscular dystrophy is the second most common dystrophy in adults, with a prevalence of approximately 1:20,000.
- In adults, the onset is usually at 20–30 years of age, with weakness of facial muscles (difficulty drinking with a straw, whistling, and smiling) and later, weakness and atrophy of scapular fixator, neck extensors, biceps, triceps,

and foot dorsiflexors. Deltoids are generally spared. Prominent winging of scapula, "Popeye" appearance of the arm, and pectoralis muscles crease are unique clinical features. Hypertrophy of extensor digitorum brevis is also unique to this disease. Telangiectasia of retina (Coats' syndrome) and sensorineural hearing loss are also seen.

- The defect is at the 4q35 location in the chromosome 4.
- Muscle biopsy shows myopathic features and inflammatory response in 20–30% of cases. Muscle biopsy, however, is not necessary for diagnosis in typical cases. Genetic testing shows specific repeat DNA array (D4Z4) with short repeat (<10 bp).
- Serum CK is mildly elevated, and EMG shows myopathic features.
- Treatment is supportive and symptomatic. Most patients have a normal life span with some disability. Retinal telangiectasia is treated with periodic photocoagulation.

Metabolic Myopathies

Primary metabolic myopathies with adult onset include:

1. Disorders of carbohydrate metabolism:
   - McArdle's disease (myophosphorylase deficiency).
   - Phosphofructokinase deficiency.
   - Acid maltase deficiency.
2. Disorders of lipid metabolism:
   - Carnitine deficiency.
   - Carnitine palmitoyltransferases I and II deficiency (CPT1 and -2).
3. Mitochondrial myopathies.
4. Other myopathies:
   - Myoadenylate deaminase deficiency.

Secondary metabolic myopathies:

- Myopathies because of endocrine disorder or toxic/drug-induced myopathies.

Metabolic myopathies generally present with muscle pain, cramps, and weakness, with or without any relation to exercise, sometimes with episodes of myoglobinuria and lactic acidosis. Some are genetically determined. Diagnosis is made based on clinical presentation, serum CK, myoglobinuria, resting lactate and pyruvate, abnormal exercise-test response, muscle biopsy, and DNA analysis. Treatment is supportive and symptomatic, but enzyme replacement may help. Patients with mitochondrial myopathies can be helped by administration of vitamins C, K, and B complex, and coenzyme Q10. Patients should be advised to avoid triggering factors. Diet with sucrose may be helpful to McArdle's disease patients.

20
Back and Neck Pain

Back and neck pain are common complaints and are the main reasons for work-related injury and disability claims, with a major economic affect in industrial countries. Many conditions cause back and neck pain (spinal, non-spinal, psychological). Back pain is treated with many specialties: family practice, orthopedic, chiropractic, neurological surgery and neurologists.

MUSCLE SPRAIN

Muscle sprain or strain is a common clinical scenario that occurs after minor trauma, causing shearing of muscle and fascia. It presents clinically with localized constant, deep pain, without radiation to the limb. There are no neurological symptoms. Treatment is symptomatic, and no diagnostic testing is necessary.

RADICULOPATHIES

A spinal root can be compressed by any lesion; the two leading causes are herniated nucleus pulposus and spondylosis. Radiculopathy typically presents with back or neck pain, which radiates to the limb in distribution of the corresponding compressed nerve root. Pain is usually dull and achy, but can be sharp. The pain is aggravated by walking, standing, twisting, bending, sneezing, coughing, or straining. Pain may relieve by rest and knee or hip flexion. The onset of radiculopathy can be spontaneous and usually starts after minor trauma, lifting heavy objects, or repeated bending. Some patients may complain of sensory symptoms such as paresthesia and/or limb weakness (foot dragging, foot drop). The common root syndromes in the back are S1 root because of herniated L5–S1 intervertebral disc, and L5 root caused by disc herniation of L4–L5 interspace. In cervical regions, C6 and C7 root compression are the two most common root syndromes. Memorize the myotome and dermatome distribution of these four common root syndromes. Remember, the L5 root has no reflex level. The knee-jerk reflex is for the L4 root, and the ankle-jerk reflex is for the S1 root. Foot drop can be seen with a L5 root

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

lesion, but if tibialis anterior muscle is innervated by L4 (which is normally seen in some individuals), foot drop may not occur.

Caveat: Spontaneous onset of low back pain in an older individual, with or without root symptoms, should prompt consideration of spinal metastasis, until proven otherwise. In the lumbosacral region, disc herniation compresses the root laterally, but in the cervical region, the disc may compress the root laterally and spinal cord posteriorly (myelopathy). Central disc herniation or spondylosis can compress multiple lumbosacral roots and present with cauda equina or conus medullaris syndrome, which are neurological emergencies.

LUMBAR STENOSIS

Slowly progressive hypertrophy of the vertebral facets and degeneration of vertebrae and discs, causing narrowing of the nerve root foramina and spinal canal. This condition is common in elderly individuals and presents with symptoms and signs similar to bilateral lumbosacral polyradiculopathy. Most patients complain of dull, constant back pain and sometimes paresthesia of lower extremities that is aggravated by walking or standing (spinal or neurogenic claudication) and relieved by stooping or sitting down. Nonsteroidal anti-inflammatory drugs and physical therapy will help the pain in most cases.

EVALUATION

History

- Onset and location of pain.
- Aggravating and relieving factors.
- Cause of the pain, for example, accident, lifting, bending, or spontaneous.
- Any complaints about weakness or sensory symptoms.
- Any bowel or bladder dysfunction.
- History of claudication.
- Does position or movement of the limb affect the pain?

General Physical Examination

- Examine the spine for any deformity or curvature.
- Test the spine for range of motion.
- Check spine for focal tenderness and paraspinal muscle spasm.
- Examine the gait.
- Do straight-leg-raising test in lumbosacral radiculopathy.
- Do Patrick's test if sacroiliac osteoarthritis is suspected.
- Examine abdomen, pelvic, or peripheral pulses in atypical presentation.

Focused Neurological Examination

A focused neurological examination is to be performed to establish objective evidence of *spinal nerve root* or *spinal cord compression*.

- Examine strength and differentiate muscle weakness from weakness because of pain.
- Test for dermatomal sensory loss.
- Check for the presence or absence of reflexes.
- Check muscle tone.
- Assess gait.
- Assess for presence or absence of long tract signs (hyperreflexia, clonus, Babinski's sign).
- In a patient with suspected of cauda equina, check for saddle anesthesia, rectal tone, and anal wink reflex.

Clinical point: The history and examination of patients with back and neck pain should be directed toward finding an organic etiology known as "red flag," such as cancer, neurological diseases, infection, and disc herniation.

DIAGNOSTIC TESTS

Neuroimaging

Neuroimaging includes plain X-ray, computed tomography scan, magnetic resonance imaging, and bone scan. Imaging techniques should be utilized individually; not all patients with neck or back pain need imaging.

Nerve Conduction Studies, Electromyogram

Nerve conduction studies and electromyograms show electrophysiological changes of root compression. It is best to perform these tests 2–3 weeks after the onset of symptoms. Be specific when you are ordering the test. Most patients with radiculopathy who do not respond initially to treatment or develop motor or sensory deficit need an electromyogram. Again, this test is not indicated in all patients, only those with neurological deficits. Electromyograms assess the physiological changes in radiculopathy, and imaging provides anatomic information, and often these two test are complementary.

Blood Work

Erythrocyte sedimentation rate, serum protein electrophoresis, prostate-specific antigen, complete blood count, and chemistry profile are indicated with patients with spontaneous-onset pain.

TREATMENT

Medical/Conservative

- Bed rest (very short period in patients with severe pain), avoid lifting, weight reduction.
- Neck traction, cervical collar, back brace, corsets.
- Analgesics: nonsteroidal anti-inflammatory drugs, acetaminophen, tramadol, opioids, gabapentine.
- Muscle relaxants: cyclobenzaprine. Their use, however, is limited.
- Physical therapy and back exercises when acute pain has subsided.
- Spine manipulation would be helpful if performed by an experienced practitioner.
- With more chronic back pain, the patient may be referred to a pain management center for consideration of steroid injection, epidural injection, transcutaneous and percutaneous nerve stimulations, acupuncture, or Botox injection.

Surgical

Surgical procedures include laminectomy, fusion, discectomy, and spinal fusion. Minimally invasive surgical approaches are also in use in selected cases. Surgical referral is considered in the following:

- Patient failed to respond to medical/conservative therapy.
- Progressive neurological deficit.
- Cauda equina/conus medullaris syndromes.
- Signs of cord compression.
- Symptomatic spinal stenosis, when it is resistant to medical and conservative treatment.

Caveat: In acute lumbosacral radiculopathy, only a few days' rest is adequate, particularly if history is clear for acute radiculopathy (e.g., back pain following a heavy lift). No diagnostic test is necessary at the beginning. Only 10% of patients with radiculopathy need surgery. Pain alone is not a good reason for surgery.

III Neurological Urgencies and Emergencies

21
Coma

TERMINOLOGY

Coma: a state of unconsciousness and unresponsiveness to external stimuli. Coma is caused by dysfunction of either or both the reticular activating system and cerebral cortex.

Persistent vegetative state: occurs often after coma. Patients appear to be conscious and able to be aroused but are unaware of surroundings and self. Signs should persist at least 1 month before the diagnosis of persistent vegetative state can be made. Patients have sleep–awake cycles.

Locked-in syndrome: occurs commonly after surviving coma. Patients are quadriplegic with cranial nerves and speech deficits but can communicate with eye or head movements.

Brain death: comatose (due to irreversible cause), unresponsive to noxious stimuli. Cortical and brainstem reflexes are lost. May need further confirmation by absence of brain activity on electroencephalogram (EEG) or absence of cerebral blood flow on brain scan if clinical criteria are met in at least 6 hours. Ancillary tests also required in children younger than 1 year of age. Confirmatory test is not required if duration is between 12 and 24 hours, and clinical criteria are met. The examination should be performed by a physician other than the patient's family physician or physician involved in organ donation team. In most centers, the legal confirmation of brain death is based on the absence of cortical and brainstem responses (spinal reflex may present) and positive apnea test (no respiratory derive with pCO_2 >60 mmHg or >20 mmHg baseline). Prerequisites of brain death confirmation include no sedative drug intoxication, absence of severe electrolytes imbalance, core body temperature higher than 97°F, and systolic blood pressure higher than 90 mmHg.

WHAT TO DO

Coma is a medical emergency, requiring prompt diagnosis and management. The following steps should be taken:

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

1. Stabilize the patient first.
2. Obtain history and do a careful examination.
3. Do a quick neurological examination appropriate for the comatose patient and interpret your findings.
4. Locate the site of lesion according to your physical and neurological signs.
5. Try to discern the most likely cause(s) and remember, coma is a sign of underlying pathology. Remember, the most common causes of coma are toxic/metabolic derangements, which are potentially treatable and reversible. The "big three" are toxic/metabolic causes, trauma, and stroke.
6. All patients should have a head neuroimaging (computed tomography [CT] scan/ magnetic resonance imaging [MRI]).
7. Try to prognosticate the outcome of the patients.

STABILIZING THE PATIENT

- Clear the airway, intubate if necessary.
- Oxygenate.
- Maintain circulation.
- Establish intravenous line and draw blood for cell count, chemistry, toxic/drug screen, antiepileptic drug level, and arterial blood gases.
- Administer 100 mg thiamine intravenously, 50 mL of 50% dextrose (if finger stick glucose <80 mg), and 2 mg naloxone HCl (Narcan) if narcotic overdose is suspected. If bilateral small pupils do not dilate after 10 mg of Narcan, opiate intoxication can be ruled out.

Caveat: Patients with global ischemic/hypoxic (e.g., post-cardiac arrest) encephalopathy may not need glucose, because further elevation of glucose may cause further neuronal damage.

HISTORY AND PHYSICAL EXAMINATION

Obtain history from relatives, friends, police, and paramedics. Witnesses should not leave the hospital until questioned thoroughly. Obtain past medical, neurological, and psychiatric history. Establish the onset of coma (acute, subacute, or chronic).

Physical examination should begin with assessment of blood pressure, pulse, respirations, and temperature.

Inspect skin for needle tracks, jaundice, spider angiomata, petechiae, lacerations, hematoma, ecchymosis, bleeding, and fracture.

NEUROLOGICAL EXAMINATION

Doing a complete neurological examination in comatose patients is not only impractical, but unnecessary. However, most authorities recommend the following neurological examination in all comatose patients.

1. **Look at the patient.** Note the following:
   - Any movements.
   - Any abnormal movements: myoclonic, seizures, asterixis.
   - Any asymmetry of limb position: paralysis.
2. **Head and neck.**
   - Inspect head, neck, and face for signs of trauma, look for tongue lacerations (signs of seizures).
   - Meningismus: subarachnoid hemorrhage (SAH), meningitis.

   Caveat: In posttraumatic coma, do not manipulate the neck, unless spine fracture or dislocation have been excluded by X-ray.
3. **Look at the eyes.** In comatose patients, the eyes are closed because of tonic eyelid contraction. This also indicates that the upper pons is intact. Remember, in comatose patient there is no resistance to passive eye opening. In psychogenic coma, there is a resistance.
4. **Pupils:**
   - Check the size: small, pinpoint, dilated or normal.
   - Check for symmetry: equal or asymmetric (anisocoria).
   - Check reaction to direct light: normal, sluggish, unreactive:

     Bilateral small reactive: pontine lesion, toxic/metabolic cause.
     Small, midsize, reactive: metabolic/toxic cause.
     Bilateral, dilated, fixed (unreactive): severe anoxia, glutethimide and/or atropine poisoning, hypoxia, hypothermia.
     Midsize, unreactive: midbrain.
     Unequal dilated: third nerve palsy, uncal herniation.
     Unequal, small, fixed reactive: Horner's syndrome, midbrain, thalamic.

Caveats: Anisocoria in comatose patients should be considered pathological, until proven otherwise (trauma to the eye, glaucoma operation). Beware of eye drops, because these can affect pupillary responses. At times, it is necessary to use a magnifying glass to observe subtle pupillary responses. Spontaneous rhythmic pupillary contraction is called *hippus*. In general, reactive, symmetric pupils are indicative of a toxic/metabolic cause of coma, and unreactive and asymmetric pupils are indicative of a structural lesion.

5. **Eye movements: spontaneous.** Open the eyes and note:

   Roving eye movements: slow, horizontal, side-to-side eye movement, indicative of intact brainstem.
   Nystagmus: posterior fossa lesion, drug intoxication (antiepileptic drug), seizures.
   Ocular bobbing: slow upward and rapid downward movement; seen commonly in pontine hemorrhage.

Ocular dipping: slow downward and rapid upward movement, seen in pontine lesions.
Conjugate eye deviation away from paretic side: commonly seen in pontine lesion.
Conjugate eye deviation toward paretic side: indicative of supratentorial lesion.
Disconjugate eye deviation: brainstem lesion.
Skew deviation: one eye up and the other down, seen in brainstem, pontine tegmentum lesions.
Persistent downward gaze: tectal lesion.
Persistent upward gaze: probable nonconvulsive status epilepticus.

Eye movements: reflexive.

Oculocephalic (doll's eyes): in a comatose patient with intact brainstem, brisk lateral head movements cause the eyes to move contralaterally.

Caveats: Do not do this maneuver in post-traumatic coma, unless neck injury has been ruled out. Do not do this maneuver briskly in elderly patients.

Oculovestibular (caloric): First, check the ears to rule out bleeding or perforated tympanic membrane. The ear canal should be clean. Elevate the head 30°. Irrigate one ear at a time. In the comatose patient with an intact brainstem, ice-cold water (10–20°C) will make the eyes move slowly (tonically) toward the side of irrigation. Try more water if there is no response (sometimes 200 mL is necessary). Irrigate the other ear after 10 minutes. Cold caloric test checks the lateral eye movements.

To evaluate vertical eye movements, irrigate both ears simultaneously (cold water, downward; warm water, upward). Remember, in a conscious person unilateral ice-cold water irrigation moves the eyes toward the side of stimulation, but causes nystagmus to opposite direction; with warm water, the nystagmus is toward the side of stimulation.

MOTOR RESPONSE

Look for spontaneous limb movements; diminishment of movement on one side suggests a structural lesion. If there are no spontaneous limb movements, try to induce movements with noxious stimuli and note whether movement is purposeful, unilateral, or quadriplegic. If no response noted, beware of possibility of use of paralyzing agents, locked-in syndrome, cervical cord compression, and even acute polyneuropathy.

ABNORMAL POSTURES

1. **Decorticate** or flexor posture: bilateral hemispheric lesions, bilateral internal capsule insults, or thalamic.

2. **Decerebrate** or extensor posture: brainstem lesion or metabolic derangement.
3. **Diagonal** posture: decorticate one side and decerebrate the opposite. Supratentorial lesion or lesion at the level of vestibular nuclei.

RESPIRATORY PATTERNS

Note the respiratory pattern if the patient is not intubated and ventilated mechanically.

- **Normal pattern:** metabolic causes of coma.
- **Cheyne-Stokes respirations:** metabolic, hypoxic, diffuse bihemispheric.
- **Ataxic:** very irregular: brainstem lesion, particularly medullary lesion. Also seen in meningitis.
- **Apneustic:** prolonged inspiration or expiration. Midpons lesion.
- **Hypoventilation:** metabolic; increased intracranial pressure (ICP), drug overdose (sedative/hypnotic).
- **Hyperventilation:** metabolic; brainstem lesion.

  Caveat: If patient has ataxic respiration, use of sedative drug may cause respiratory arrest.

OTHER NEUROLOGICAL SIGNS

- Unilateral loss of corneal reflex indicates pontine lesion.
- Lower brainstem reflexes (gag, cough, hiccup, and respiration) are lost when severe neuronal necrosis has occurred (brain death).
- Muscle stretch reflexes are not helpful in evaluation of coma, because they may be preserved despite severe brain insult. Asymmetry of reflexes, however, can be useful.
- Long tract signs, such as spasticity and pathological reflexes (Babinski's sign), are commonly indicative of structural lesion.
- Bilateral papilledema is indicative of increased ICP, but may be seen a few days after onset of coma.
- Absence of venous pulsation is not always indicative of increased ICP.

DIFFERENTIAL DIAGNOSIS

Combine the history, physical, and neurological findings and note the following clues:

- Gradual onset of coma, without clear-cut focal or lateralizing signs and preserved pupillary reflex is seen commonly in toxic/metabolic disorders.
- Meningeal signs, with or without fever and with or without lateralizing signs, raise the possibility of SAH, meningitis, or encephalitis. In profound coma, neck stiffness however may be absent.

- Sudden onset of coma with focal or lateralizing neurological seizures, and abnormal pupillary responses or eye movements indicates subtentorial lesion (posterior fossa and brainstem).
- Gradual onset of coma with rostrocaudal deterioration, associated with lateralizing neurological deficit, with or without pupillary abnormalities and eye movement abnormalities, indicates supratentorial lesions, such as a massive stroke or hemorrhage.

NEURODIAGNOSTIC STUDIES

- CT or MRI of the head are indicated for all patients in coma without obvious etiology, to assess nature and severity of structural lesion.
- EEG also is recommended for all comatose patients to assess the etiology (toxic/metabolic encephalopathy), to assess seizures, and may help in determining prognosis.
- Cervical spine film is indicated in all cases of traumatic coma.
- Spinal tap is recommended when SAH or meningitis is suspected.

PROGNOSIS OF COMA

Generally speaking, the prognosis for the coma patient depends on age of the patient, cause and duration of coma, course of coma, neurological deficits, and underlying medical conditions of patient. EEG (burst–suppression patterns, periodic patterns, and alpha–theta patterns carry poor prognosis). Head CT/MRI are also helpful in determining the prognosis (showing structural causes). Glasgow Coma Scale (Table 1) is used in making the prognosis for postanoxic (postcardiac arrest) or posttraumatic coma. If the patient has been paralyzed by a muscle relaxant, then you cannot use this scale. Marked elevation of serum neuron-specific enolase and glial protein S-100 are reported to be associated with poor outcome in anoxic coma.

Table 1
Glasgow Coma Scale

Eye opening	Score
No response	1
To pain	2
To verbal stimuli	3
Spontaneously	4
Best verbal response	
No response	1
Incomprehensible response	2
Inappropriate words	3
Disoriented and conversant	4
Oriented and conversant	5
Best motor response	
No response	1
Extension (decerebrate)	2
Abnormal flexion	3
Flexion—withdrawal to pain	4
Localizes pain	5
Obeys commands	6
Total	**15**

About 90% of patients with a Glasgow Coma Scale score of 4 or less within first 48 hours die or remain in a persistent vegetative state. Nearly 90% of patients with a Glasgow Coma Scale score of 11 or more recover or will have minimal disability.

22
Status Epilepticus

In this chapter, only generalized convulsive status epilepticus (SE), is discussed.

WHAT YOU SHOULD KNOW

- Generalized convulsive SE is a medical emergency, requiring prompt assessment and treatment.
- At least 100,000–150,000 cases of SE occur each year in the United States.
- One-half of patients with SE have no history of seizures.
- SE is the initial presentation of an epileptic condition in 10% of patients. The mortality of adults presenting with SE for the first time may be as high as 20%.
- In about two-thirds of the cases of SE there is an underlying cause (or causes) such as systemic metabolic derangement, drugs, hypoxia, infection, alcohol or drug withdrawal, stroke, encephalitis, brain tumor, or discontinuation of antiepileptic drugs (in the epileptic population). Beware: some drugs will bring down the seizure threshold (e.g., theophylline, imipenem, isoniazid, clonazepam, cyclosporine).
- The longer seizures persist, the more difficult they are to control.
- The mortality of SE is about 30% if the seizure last longer than 1 hour. SE in adults due to or caused by hypoxia has higher mortality rate.

DIAGNOSIS

Generalized convulsive SE is the state of continuous seizures: whenever seizures persist for a sufficient length of time (in practice, longer than 5 minutes) or repeated frequently enough (in practice, more than twice) that full recovery of consciousness does not occur between the seizures. A common clinical situation would involve a patient brought to the emergency room because of seizures, with the duration and number of seizures unknown. If the patient remains unresponsive after 10 minutes of observation or has another seizure, you should treat patient as SE.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

Remember: It is also critical to evaluate and treat a generalized convulsive seizure quickly if it lasts longer than 5–10 minutes, because it likely represents more than a single seizure.

MANAGEMENT

Goals of Therapy

- Stop seizures (clinical and electrographical) as soon as possible (within 30–45 minutes).
- Diagnose and correct underlying cause(s).
- Prevent and treat systemic complications.

Guidelines for Management

In confronting a patient in SE, it is important to:

- Not panic.
- Secure the airway, circulation, and cardiac status first.
- Stop the seizures promptly with an organized approach.
- Be familiar with a treatment plan that you are comfortable with and that has been successful.
- Not wait for results, and not change your treatment plan on the basis of antiepileptic drug (AED) level (persistent seizure is more harmful than a high level of AED).
- Choose AED that can be given intravenously.

Steps of Therapy

- Establish and secure airway. Provide oxygen. Measure blood pressure and heart rate continuously and place pulse oximetry.
- Establish two intravenous accesses, one open with normal saline for intravenous drug administration, and another for drawing blood for glucose, electrolytes, blood cell count, toxic/drug screen, arterial blood gases, and AED level.
- Establish cardiac monitor and call for an electroencephalogram (EEG).
- Administer 100 mg thiamine intravenously. Unless you know the patient is not hypoglycemic, administer one ampule (50 mL) of 50% glucose intravenously. Glucometer reading is not reliable, and waiting for the results of the blood sugar may do more harm than giving glucose empirically (some authorities do not give glucose in the early stage of SE [e.g., the first 10–15 minutes] because there is release of catecholamine and secondary hyperglycemia). Hyperglycemia might cause further neuronal damage.

Terminate SE Clinical and Electrically

- Administer intravenously either lorazepam, 0.1–0.3 mg/kg at 2 mg/minute for a total of 8 mg, or diazepam, 0.2 mg/kg at 5 mg/minute up to a total dose of 20 mg. Most neurologists use lorazepam.

- Administer intravenous fosphenytoin (Cerebyx), a total dose of 20 mg/kg. Fosphenytoin is give at rate of 100–150 mg/minute. Blood pressure, respiration, and heart rate should be watched carefully during infusion. Slow down the rate if you see changes. Fosphenytoin is contraindicated if the patient is allergic or has an established history of heart block. More than 80% of SE is controlled at this stage.

IF SEIZURES PERSIST, THERE ARE TWO OPTIONS

- Give an additional 10 mg/kg of fosphenytoin, with consideration of another dose of 0.05 mg/kg of lorazepam. Most experts prefer this option.
- Consider intubation and give phenobarbital, 20 mg/kg, at rate of 50–100 mg/min.

IF SEIZURES PERSIST—REFRACTORY SE

In this setting, patients should be intubated and continuous EEG recording is recommended. Choose one of the following options:

- **Pentobarbital.** Administer a 10-mg/kg loading dose at rate of 100 mg/minute, and then 2 mg/kg/hour. Continue this rate for 24 hours, and then taper over the next 24 hours. Before considering tapering, be sure the phenytoin level is between 25–30. An adequate dose of pentobarbital is judged by the appearance of burst–suppression pattern on the EEG. If seizures recur while weaning or EEG showed frequent focal discharges, continue maintenance infusion longer. Pentobarbital may cause severe hypotension, requiring use of pressure agents. Pentobarbital is a good option if patient's blood pressure is stable; otherwise, use one of the following options.
- **Midazolam.** Administer a 0.2-mg/kg bolus slowly, followed by continuous 0.05–0.5 mg/kg per hour.
- **Propofol.** Administer a 1- to 2-mg/kg bolus, and then 5–10 mg/kg per hour. This agent is good choice in patients with chronic obstructive pulmonary disease. You may consult an anesthesiologist for assistance.
- **Intravenous valproate (Depacone).** Administer a 20- to 30-mg/kg loading dose, followed by 1 mg/kg per hour. Experience with this drug is limited at this time.

KEY POINTS ABOUT SE

- Prognosis of SE depends on the duration of seizures, promptness, adequacy of therapeutic measures, and the underlying cause. Treat associated acidosis, infections, and other metabolic problems.
- Simultaneous EEG recording is highly recommended if available
  To determine whether patient is simply in a postictal state or continuing to have electrographic seizures (subclinical SE).
  To direct therapy, e.g., burst–suppression pattern, while using pentobarbital, midazolam, or propofol.

To determine a focal abnormality, because clinically this may not be obvious.
To determine the degree of encephalopathy.

- Many times the patient stops having major convulsions but remains stuporous, and continues having subtle seizures such as facial muscle twitching, twitching of the jaw and limbs, subtle generalized and nystagmoid eye movements. This stage is commonly referred to as subtle generalized SE, and the EEG shows periodic electrical discharges (electroclinical dissociation). This condition now is considered another end of generalized SE, and is caused by a delay or inadequate therapeutic measures, or ongoing seizures and requires immediate and aggressive intervention.
- When the patient presents with SE but their AED level is therapeutic or a high level, it is often indicative of an underlying metabolic or organic cause.
- Routine administration of bicarbonate is unnecessary unless the patient is severely acidotic for a long time. Similarly, naloxone is given only when narcotic overdose is suspected.
- Brain imaging (MRI/CT scan) should be considered in all adults with SE.
- Lumbar puncture is indicated in febrile patients even if signs of meningitis are absent. Remember, cerebral spinal fluid pleocytosis can be seen in patients with SE.

FOLLOW-UP AND MAINTENANCE

1. If the patient presents with SE and a low level of AED, continue the same medication and improve compliance, before considering different agent.
2. If the patient had a high level of AED, consider switching to a different medication or add another AED.
3. If the AED level is still low after seizures are stopped, consider miniload (e.g., 500 mg of phenytoin by mouth), before discharging the patient.

23

Brain Edema, Transtentorial Herniation, and Increased Intracranial Pressure

BRAIN EDEMA

- Brain edema is defined as an increase in brain sodium and water content.
- Brain edema occurs in many neurological conditions such as stroke, trauma, tumors, infections, encephalopathies, and hydrocephaly.
- Brain edema is classified into three major types: vasogenic, cytotoxic, and interstitial:

  Vasogenic: seen primarily in the white matter. Common causes: brain tumor, abscess, infarction, and hemorrhage. Clinical presentation: focal neurological deficits, decreased level of consciousness, pupillary asymmetry, and increased intracranial pressure (ICP).

  Cytotoxic (cellular): seen in the white and gray matter. Common causes: ischemic/ hypoxic encephalopathies (e.g., post-cardiac arrest) and meningitis. Clinical presentation: stupor, coma, focal or generalized seizures, and myoclonic jerks.

  Interstitial: increased brain fluid due to blockage of cerebral spinal fluid absorption, seen primarily in periventricular white matter. Common causes: pseudotumor, obstructive hydrocephalus. Clinical presentation: headache, nausea, vomiting, mental alteration, papilledema, or gait difficulty.

  - Ischemic brain edema (after stroke) begins with cellular changes to vasogenic. In meningitis, the edema begins from the cellular, and then changes to vasogenic and may then to interstitial (hydrocephalus).

TRANSTENTORIAL HERNIATION

- Brain herniation is caused by mass or any cause that increases ICP; subsequently, the brain substance shifts from higher pressure to lower pressure.
- The most common forms of herniation are subfalcine, uncal, and cerebellar tonsilar herniation.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Clinical presentation of uncal herniation: dilation and ophthalmoplegia (third nerve compression) followed by ipsilateral (to site of lesion) hemiplegia and bilateral corticospinal tract signs (Kernohan's notch phenomenon), followed by irregular respiratory pattern, fixed and dilated pupils, coma, and cardiorespiratory collapse.

INCREASED ICP

- The signs of ICP are headache, vomiting, mental dysfunction, confusion, papilledema, bradycardia, decreased respiration (Cheyne-Stokes respirations), and increased blood pressure (Cushing's triad).
- In a patient suspected of having increased ICP, try to answer these questions:

1. Does a space-occupying lesion exist?
2. What part of the brain is involved?
3. What is most likely the cause?

Remember: Despite signs of increased IC a posterior fossa tumor may not have localizing signs.

WHAT TO DO

- Stabilize the patient, secure vitals.
- Keep head elevated (30–45° degrees).
- Keep patient moderately dehydrated.
- Obtain computed tomography scan or magnetic resonance image of head in all patients with symptoms of increased ICP.
- Eliminate or treat the underlying cause with the most effective mode of therapy. Increased ICP in many cases requires neurosurgical procedures.
- **Hyperventilation (HV):** Intubate and maintain pCO_2 to 25–30 mmHg; HV immediately reduces the blood flow (vasoconstriction) and decreases ICP. Prolonged use of HV causes further ischemia to the normal and damaged brain area, and therefore should be avoided. HV takes effect within 10 minutes. HV should be used less in acute stroke or acute head trauma because of vasoconstriction.
- **Hyperosmolar agents:** Mannitol is most commonly used; the dose is 1–2 g/kg (25%) given in 500 mL of 5% dextrose in water. May repeat 0.5 g/kg, every 4–6 hours. Serum osmolality is used as a treatment guide (maintain below 320 mOsm/L) or between 295 and 305 mOsm. Monitor serum sodium (maintain <150 mEq), serum osmolality, and kidney function.
- **Diuretics:** Furosemide (Lasix) and acetazolamide (Diamox) may be helpful in pseudotumor or ischemic brain edema. Furosemide is preferred, 20–40 mg intravenously, every 12 hours, usually given after mannitol.
- **Corticosteroids:** Dexamethasone is particularly useful in brain edema caused by primary or metastatic brain tumors or infections. The recom-

mended dose is 10 mg intravenous loading, followed by 6 mg every 6 hours. Use of steroids in ischemic brain edema or cellular brain edema (hypoxia) is less clear.

- **Barbiturates:** same dose as used in treatment of status epilepticus.
- **Hypothermia:** Decreasing core body temperature to 32–34°C has been used in traumatic coma.
- **Shunt:** in case of hydrocephalus to drain cerebral spinal fluid.
- **Hypertonic Saline:** hypertonic with 3 or 23%, with maintaining serum osmolality between 320 and 330 mOsm is gaining interest, but best to be managed by a neurointensivist.
- ICP monitoring is particularly useful in brain edema following head trauma.
- Neurosurgical procedures in the treatment of increased ICP and brain edema include hemispherectomy, ventricular drainage, and/or evacuation of mass lesion in selected cases. In recent years, decompressive craniectomy has been found to be useful in young patients with severe head injury.

24
Metastatic Epidural Spinal Cord Compression

Any patient with known cancer presenting with persistent, unexplained, and spontaneous back pain should be considered as having epidural spinal cord compression (ESCC) until proven otherwise.

- Suspect ESCC when an elderly patient who is a smoker presents with spontaneous back pain.
- Up to 90% of patients with metastatic ESCC have abnormal plain spine films: vertebral collapse, erosion, subluxation. Radiological evidence of thecal indentation should raise the possibility of ESCC.
- Magnetic resonance imaging with contrast remains the most sensitive and specific imaging technique.
- Neurological symptoms and signs of ESCC are back pain and tenderness, followed by paresthesias, sensory loss, weakness, reflex changes, and bowel and bladder dysfunction.
- In patients with suspected ESCC and minimal neurological signs, give a 10-mg intravenous bolus of dexamethasone, followed by 4 mg intravenously or orally, every 6 hours.
- In a patient with progressive neurological deficits, administer 100 mg intravenous bolus of dexamethasone, followed by 20 mg every 6 hours; taper off in 2 weeks, and follow with radiation therapy.

Surgical decompression is considered if: type of cancer is unknown, neurological deterioration occurs after radiation, radioresistant tumors, or intractable pain. Radiation therapy is often required after surgery.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

25
Acute Meningitis and Encephalitis

Acute meningitis and encephalitis are medical emergencies, because if undiagnosed and not treated promptly, they have high mortality and morbidity rates.

The clinical hallmarks of acute central nervous system infection are fever, headaches, and nuchal rigidity, except in neonates, which may present with irritability, and the elderly, presenting with changes in the mental state.

Encephalitis is considered when the patient presents with alteration of mental state, personality changes, confusion, and memory deficit, as well as focal and lateralizing neurological signs such as paresis, aphasia, visual field defect, or focal seizures.

ACUTE MENINGITIS

The general approach to suspected cases of acute meningitis is as follows:

- Perform a quick neurological examination; look particularly for meningeal signs, mental status abnormalities, focal neurological deficits, or papilledema.
- Obtain a set of blood cultures and routine admission labs.
- Start intravenous line and administer broad-spectrum combination antibiotics empirically. The choice of antibiotic depends on the age of the patient.
- Administer dexamethasone intravenously, 0.15 mg/kg every 6 hours for 4 days, to reduce complications.
- Treat existing seizures or electrolyte abnormalities.
- Do lumbar puncture (LP) as soon as possible.
- If the patient has focal neurological signs or signs of increased intracranial pressure, obtain head computed tomography scan or magnetic resonance imaging before LP.
- Record opening pressure of cerebrospinal fluid (CSF) and send CSF fluid for complete analysis and cultures. Save 2–3 mL of CSF for future evaluation.
- Spinal fluid analysis will differentiate bacterial from viral meningitis, and the laboratory will define the antibiotic sensitivities of the infecting organism.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- The antibiotic therapy should continue for at least 10 days.
- Repeat LP approximately 48 hours after antibiotic therapy particularly for pneumococcal meningitis, because its unpredictable course and clinical examination.

ACUTE ENCEPHALITIS

The leading cause of acute encephalitis is herpes simplex virus (HSV) type 1, which characteristically affects unilateral or occasionally bilateral frontotemporal lobe. HSV encephalitis is suspected when encephalitis is suspected particularly in immunocompromised patients.

- Begin intravenous antiviral therapy with acyclovir as soon as HSV is suspected. The dose is 10 mg/kg, three times a day, for 14–21 days. Monitor kidney function.
- Perform an LP; the CSF in herpes encephalitis shows high protein concentration, lymphocytic pleocytosis, and at times, xanthochromia.
- The most specific and sensitive test for HSV encephalitis CSF is measurement of the virus DNA by PCR, which is very useful in the early stage of the disease (within 1 week after the onset). The specificity and sensitivity of PCR is about 98% and is considered the diagnostic procedure of choice.
- Head imaging such as head computed tomography scan or magnetic resonance imaging may identify an abnormal signal (increased T_2) in the temporal lobe. The typical electroencephalographic feature is occurrence of periodic or quasiperiodic lateralized epileptiform discharges over the temporal lobe.
- Brain biopsy may be considered when neurological status deteriorates, despite acyclovir therapy and when PCR is negative, although it is rarely performed.
- Mortality is about 70% of untreated HSV encephalitis. About half of the survivors have variable degree of neurological disability.

RULE OF THUMB

In suspected cases of acute bacterial meningitis, initiate intravenous combination-antibiotic therapy and perform an LP as soon as possible. In case of encephalitis, initiate intravenous acyclovir.

26
Delirium Tremens

WHAT YOU SHOULD KNOW

- Delirium tremens (DTs) is a medical emergency.
- It occurs in approximately 5% of patients who present with alcohol withdrawal seizures.
- The onset of DTs is acute, manifesting as profound confusion, delusion, vivid visual hallucinations, tremor, agitation, insomnia, nausea and vomiting, and autonomic hyperactivity (dilated pupils, fever, tachycardia, profuse sweating, orthostatic hypotension).
- The onset of DTs is about 48–96 hours after cessation of alcohol intake (patients are often hospitalized for a different reason) and usually resolves in 3–4 days after treatment.
- Patients with DTs should be investigated for underlying medical conditions such as infection, pancreatitis, liver disease, or subdural hematoma.
- Mortality from DTs in untreated cases is about 5%; this is resulting from circulatory collapse, cardiac arrhythmia, hyperthermia, and infection.
- Although the diagnosis of DTs is clinical, all patients should have a complete blood count, coagulation studies, serum amylase, blood chemistry, chest X-ray, spinal tap, and head computed tomography scan.
- Although DTs is not due to thiamine deficiency, thiamine is given to prevent the development of Wernicke's encephalopathy.

WHAT TO DO

- Stabilize and monitor vitals.
- Hydrate the patient well (sometimes 6–8 L per day is needed); use more normal saline fluid.
- Add B-complex vitamins to each fluid bag.
- Restrain the patient, if necessary, to prevent injury.
- Calm the patient with short-acting sedatives such as diazepam or lorazepam. Diazepam is given 10 mg intravenously, followed by 5 mg every 10 minutes until the patient is calm, and then maintained with 5 mg every 1–4 hours as necessary. With a milder form of DTs, you can start with chlordiazepoxide

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

50–100 mg, every 6 hours, for the first day, followed by 50 mg, every 6 hours, for 2 days. Lorazepam and oxazepam are also effective. In refractory DTs, you may add phenobarbital or propofol to benzodiazepines with consideration of intubation if required.

- Administer intravenous thiamine, 200 mg, and then 100 mg/day for several days.
- Correct any electrolyte abnormalities (hypomagnesemia, hypokalemia, hypocalcemia, or hypoglycemia).
- Treat coexistent medical conditions such as infection and pancreatitis. Reduce hyperthermia (cooling blanket).
- β-Blocker agents (atenolol) or α-2 adrenergic agents (clonidine) may be used to reduce autonomic hyperactivities.

COMMON MISTAKE

Complete sedation of patients in DTs requires large doses of sedatives. Oversedation should be avoided since it suppresses mental alertness, and depresses cardiopulmonary function, and increases the risk of aspiration.

27
Wernicke's Encephalopathy

WHAT YOU NEED TO KNOW

- The cause of Wernicke's encephalopathy (WE) is thiamine deficiency, and it is commonly seen in chronic alcoholics, but it is also seen in any poor nutritional state (hypoalimentation, cancer, starvation, chronic gastrointestinal disease, AIDS, gastric bypass, and renal dialysis patients). Sometimes WE precipitated by administration of glucose, even without poor nutritional status.
- The onset of WE is acute or subacute. Typical clinical features include:
  1. **Global confusional state (encephalopathy): apathy, disorientation, confusion, lethargy.** Rarely, stupor and coma are reported. Remember that between 5 and 10% may have normal mental status.
  2. **Eye abnormalities:** nystagmus (horizontal or vertical), lateral rectus weakness (diplopia), gaze palsy, total external ophthalmoplegia, and rarely, ptosis and retinal changes. Abducens palsy is always bilateral.
  3. **Ataxia:** truncal. Difficulty in stance and gait.
- Isolated signs in an alcoholic do not exclude the diagnosis (e.g., ophthalmoplegia alone), because all features of triad are only seen in a third of patients. The Caine criteria use any of the three in malnourished patients suspected of having WE.
- The majority of patients with WE have signs and symptoms of peripheral neuropathy and vestibular dysfunction.
- The diagnosis of WE is primarily clinical, but an abnormality in cold caloric testing and reduced erythrocyte thiamine transketolase is seen. Magnetic resonance imaging of the brain may demonstrate increased T_2 signal intensity in aqueduct, periventricular regions, medial thalamus, and mamillary bodies. In the chronic stage, atrophy of mamillary bodies can be detected.
- Response to therapy (thiamine) is good and often complete in cases of ophthalmoplegia, but ataxia and mental confusion recovery may be slow and incomplete.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Untreated WE leads to Korsakoff psychosis or coma with fatal outcome.

WHAT TO DO

- Hospitalize the patient.
- Administer thiamine parenterally (200-mg loading dose), followed by 100 mg/day for 3–4 days, and then continue orally, 50 mg twice a day, with vitamin B complex.
- Improve the nutritional state of the patient.
- Search for and treat the underlying medical condition (infection, pancreatitis, electrolyte abnormalities).

COMMON MISTAKES

- Use of high-carbohydrate diet or high-glucose solution without adding adequate supplemental thiamine causes further depletion of thiamine reserve.
- Rapid correction of hyponatremia may lead to quadriplegia (central pontine myelinolysis).

28
Myasthenia Gravis Crisis

WHAT YOU SHOULD KNOW

- Crisis in myasthenia gravis is defined as rapidly progressively respiratory and bulbar muscle weakness.
- In crisis, do not spend too much time differentiating whether the patient is in **myasthenic** or **cholinergic** crisis. This differentiation not only is unnecessary, but also is often difficult. **Your main goal is to keep the patient alive**.
- It is important to recognize and treat **impending crisis**; impending crisis is suspected when the patient presents with sleeping difficulties, tachycardia, dyspnea, and dysphagia.
- The goal of therapy is to strengthen respiratory and bulbar muscles; less important are limb and eye muscles.
- Try to identify underlying causes for crisis: infection, electrolyte abnormalities, stress, excessive use of cholinesterase inhibitors, postoperative status. Some causes of crisis remain unknown.
- **Remember:** In crisis, treat the infection aggressively with the best available antibiotic. Do not be concerned that the antibiotic may affect neuromuscular transmission adversely.
- In crisis, it is best and most practical to stop all cholinesterase inhibitors (e.g., pyridostigmine [Mestinon]), because the patients at this point are in the intensive care unit and are resting, and second, these drugs causes excessive tracheal secretion and may cause cholinergic crisis.
- It is good practice to transfer stable patients to the nearest medical center that is equipped with a plasma exchange facility and ICU.

WHAT TO DO

1. Secure the airway and stabilize the patient.
2. Obtain chest X-ray, and forced vital capacity and arterial blood gases values.
3. Electively intubate the patient when forced vital capacity is less than 12 mL/kg.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

4. Stop all cholinesterase inhibitors (pyridostigmine).
5. Admit the patient to the intensive care unit.
6. Arrange for plasma exchange.
7. Identify and treat the underlying cause aggressively.
8. If plasma exchange is not available, you may consider use of intravenous immunoglobulin (the effectiveness of intravenous immunoglobulin in crisis is less clear), or increase corticosteroid (Solu-Medrol).
9. Cholinesterase inhibitors may be reinstituted after 48–72 hours, with lower dose and gradual titration.

AVOID A COMMON MISTAKE

You receive a call from your patient, who states that the cholinesterase inhibitor (**pyridostigmine**) is **no longer** helpful, and the patient is having difficulty sleeping and swallowing. Do not adjust or increase the pyridostigmine over the telephone. Assess the patient in your office and/or the emergency room for impending crisis.

29
Guillain-Barré Syndrome

WHAT YOU SHOULD KNOW

- Guillain-Barré syndrome (GBS) is the most common cause of acute, generalized motor paralysis in healthy individuals.
- It is also the most common cause of acute inflammatory demyelinating polyneuropathy caused by immune attack (cellular and humoral factors) against the myelin sheath.
- Weakness usually starts with the legs, with proximal distribution and minimal sensory loss. However occasionally weakness begin in upper limbs and or cranial nerves, distribution.
- Any patient who presents acutely with symmetric, proximal weakness associated with decreased or absent muscle stretch reflexes should be considered as having GBS, until proven otherwise.
- The weakness evolves within days to weeks, most commonly peaking in 2–3 weeks.
- Cranial nerve and respiratory muscle weakness usually occur later.
- Doubt the diagnosis of GBS if the patient has preserved reflexes despite significant weakness, has persistent segmental or unilateral sensory loss, has developed bowel and bladder dysfunction initially, or has atypical electrophysiological features and persistently elevated cerebral spinal fluid cell count.
- The most important diagnostic tests are spinal fluid examination, which typically shows high elevation of protein concentration but no rise or minimal rise of cell count (albuminocytological dissociation), and nerve conduction studies and needle electromyogram, which show demyelinating neuropathy. Remember, however, the nerve conduction and electromyogram studies may not show changes for the first week. In the early stages of the disease, F-waves and H-reflexes may be prolonged or absent. Reduced amplitude of motor response generally implies a poor prognosis. Sural nerve action potentials should be preserved.

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Prognosis of GBS is good, with complete recovery reported in 15% of cases. Significant disability is about 5–10%, minimal disability may be seen up to 65% of cases, and mortality is about 5% due to dysautonomia, cardiac arrest, sepsis, pulmonary embolism, or acute respiratory distress syndrome. The recurrence rate is 2–5% after complete recovery and 10% prior to complete recovery.
- GBS is an acute demyelinating polyneuropathy presenting predominantly with motor weakness. There are two additional autoimmune polyneuropathies that clinically present similarly to GBS, but the immune attack is against the axon. These include acute motor sensory axonal neuropathy (AMSAN) and acute motor axonal neuropathy (AMAN). Both conditions are often preceded by diarrhea related to *Campylobacter jejuni*. Differentiating GBS from AMAN and AMSAN is based on electrophysiological features. Treatment for axonal forms is similar to GBS, but prognosis of AMSAN in particular is much less favorable than GBS.

WHAT TO DO

1. Admit the patient to the intensive care unit.
2. Assure the patient regarding good chance of recovery with effective therapy despite progressive worsening.
3. Monitor respiratory function; if forced vital capacity is less than 20 mL/kg, consider elective intubation. Some use the 20/30/40 rule, where forced vital capacity less than 20 mL/kg, maximum inspiratory pressure less than 30 mL/kg, and maximum expiratory pressure less than 40 mL/kg.

   Bedside hint: Counting to 25 in one breath = 2 L, 10 = 1 L roughly measures FVC.
4. Arrange for plasmapheresis if the patient is rapidly worsening. Remove 200–250 mL/kg of plasma in 4–6 exchanges on alternate days and replace with 5% albumin or fresh frozen plasma. Rare complications of exchange include hypotension, bleeding tendency, cardiac arrhythmia. Hepatitis and AIDS are risks if plasma is used as replacement.
5. If plasmapheresis is unavailable, the patient is unstable hemodynamically, or weakness is not severe, intravenous immunoglobulin is as effective as plasmapheresis. Although you may choose IVIg as your first line treatment. The dose is 400 mg/kg, for five consecutive days, or 2 g/kg for 2 days. Combining plasmapheresis and intravenous immunoglobulin is not recommended. Corticosteroids are not indicated in GBS.
6. Further subacute and long-term therapeutic measures are nursing, management of autonomic dysfunction, prevention of infection, controlling bladder function, deep vein thrombosis and plasma exchange prophylaxis, and physical therapy.

30
Temporal Arteritis

WHAT YOU SHOULD KNOW

- Temporal arteritis (TA) is a medical emergency; if undiagnosed and untreated, it may cause permanent blindness, transient ischemic attacks, or stroke.
- In an elderly individual, if there is an onset of severe, unilateral or bilateral persistent headache or head pain, and temporal tenderness, TA should be considered until proven otherwise.
- Typical presentation of TA is unilateral or bilateral boring headaches, head pain, or scalp tenderness (when brushing hair, or wearing a hat). The temporal artery is usually but not always tender, nodular unpulsatile. Constitutional symptoms include anorexia, fatigue, weight loss, malaise, proximal myalgia (polymyalgia rheumatica), and visual symptoms. Temporal tenderness and jaw claudication are highly suggestive of TA.
- The most important diagnostic tests are markedly elevated (increase with patient's age) erythrocyte sedimentation rate (ESR), C-reactive protein, and granulomatous inflammation in temporal artery biopsy (TAB).
- Normal ESR occurs in about 10% of cases (biopsy proven). A normal TAB can be seen because of skip lesions. Onset before age 40 and the absence of headaches are very rare. There rare instances with biopsy-proven TA presented with visual loss, without headaches, scalp tenderness, and normal or mildly elevated ESR (called occult TA). TA, therefore should be considered in older patients presenting with unilateral or bilateral painless visual loss.
- TAB should not be considered negative unless both temporal arteries are biopsied and an adequate length (5 cm) is taken. Bilateral TAB at the outset is considered in selected cases.

WHAT TO DO

- In suspected cases of TA, order ESR and C-reactive protein (CRP). ESR should be measured as soon as blood is drawn (delay in measurement may falsely or show low level).

From: *Current Clinical Neurology:*
Practicing Neurology: What You Need to Know, What You Need to Do
By: R. Pourmand © Humana Press Inc., Totowa, NJ

- Begin corticosteroid (prednisone) orally, 60–80 mg/day, and schedule patient for TAB (of the more symptomatic side).
- Do not delay therapy waiting for biopsy results, because prednisone does not effect histological changes sometimes even up to 2 weeks. If frozen section is negative, consider biopsy from the other side.
- Patients who present with visual symptoms should be treated initially with intravenous steroid (e.g., methylprednisolone, 250 mg, four times a day for 3–5 days) followed by high-dose oral prednisone (e.g., 80 mg/day).
- High-dose oral prednisone should be continued until ESR is normalized (2–3 months), and then taper slowly to lowest effective dose (6–12 months). The majority of patients require prednisone therapy for 1–2 years. Alternate-day prednisone is not as effective. Monitor ESR, CRP, visual symptoms, and steroid complications. Patient should receive calcium and vitamin D supplements and bone density measurement. It is also important to do a chest X-ray yearly for several years to detect development of any thoracic aortic aneurysm.
- If patient develops undesirable side effects to prednisone, adding methotrexate is warranted.
- When visual loss has occurred in one eye, you should be aggressive with therapy to protect the other eye.

Index

A

Acetylcholine receptor autoantibody, myasthenia gravis diagnosis, 164
Acquired immunodeficiency syndrome (AIDS),
  encephalopathy, 89, 90
  myelopathy, 90
  neurological complications, 88, 89
Acute disseminated encephalomyelitis (ADEM), features, 103, 104
AD, *see* Alzheimer's disease
ADEM, *see* Acute disseminated encephalomyelitis
Adie's pupil, 9
AEDs, *see* Antiepileptic drugs
AIDS, *see* Acquired immunodeficiency syndrome
Alcohol,
  cerebellar degeneration, 109
  delirium tremens features and management, 201, 202
  essential tremor management, 142
  neurological complications, 107
  nutritional polyneuropathy, 108
  withdrawal seizures, 108
Almotriptan, migraine treatment, 119
ALS, *see* Amyotrophic lateral sclerosis
Alzheimer's disease (AD),
  diagnosis, 93
  treatment, 93, 94
Amantadine hydrochloride, Parkinson's disease management, 140
Amyotrophic lateral sclerosis (ALS),
  clinical features and pearls, 156
  diagnosis, 157
  management, 157
Anisocoria, 8
Anosmia, 7
Anterior horn cell,
  lesions, 44
  motor unit, 153
Anticoagulation, indications in stroke, 77
Antiepileptic drugs (AEDs), *see also specific drugs*,
  guidelines for use, 81, 82
  migraine treatment, 120
  novel drugs, 82, 83
  withdrawal, 82
Aphasia, stroke features, 77, 78
Apomorphine, Parkinson's disease management, 140
Argyll–Robertson pupil, 9
Athetosis, definition, 137
Autonomic function tests,
  complications and limitations, 60

indications, 60
overview, 59, 60

B

Back and neck pain,
diagnostic tests, 177
evaluation, 176, 177
lumbar stenosis, 176
muscle sprain, 175
radiculopathy, 175, 176
treatment, 178
Ballismus, definition, 138
Bell's palsy, features and management, 157, 158
Benign paroxysmal positional vertigo, features, 113
Benzotropine mesylate, Parkinson's disease management, 140
Beta-blockers,
essential tremor management, 142
migraine treatment, 120
Biopsy,
brain, 62, 63
leptomeningeal, 63
muscle, 63
nerve, 63
temporal artery, 63
Botulinum toxin, essential tremor management, 142
Botulism,
clinical features, 168
diagnosis, 168
treatment, 169
Brachial plexitis, clinical characteristics, 155
Brain,
biopsy, 62, 63
edema,
management after stroke, 70
types, 193
Brain death,
definition, 181
electroencephalogram, 58
Brainstem auditory evoked potentials, 55, 56
Brainstem lesions, features, 42
Brandt-Daroff exercise, 114
Bromocriptine, Parkinson's disease management, 140
Brown-Séquard syndrome, features, 43
Brudzinski's sign, 31

C

Caloric test, 15
Carotid artery, duplex Doppler ultrasonography, 51
Carpal tunnel syndrome, features and management, 158, 159
Cauda equina syndromes, features, 43
Central nervous system infection,
acquired immunodeficiency syndrome, 88–90
clinical tips, 85
Creutzfeldt-Jakob disease, 88
electroencephalogram, 58
meningitis,
bacterial, 85
tuberculous, 86, 87
viral, 86
progressive multifocal leukoencephalopathy, 90
syphilis, 87, 88
Central pontine myelinolysis, features, 105
Cerebellar degeneration, alcoholic, 109

Cerebellar lesions, features, 44
Cerebral arteriography, indications, 50
Cerebrovascular accident, *see* Stroke; Subarachnoid hemorrhage
Charcot-Marie-Tooth disease (CMT), features and management, 162
Chorea, definition, 137
Chronic inflammatory demyelinating polyneuropathy, features and management, 161
CIS, *see* Clinically isolated syndrome
CJD, *see* Creutzfeldt-Jakob disease
Clinically isolated syndrome (CIS), features, 105
Cluster headache, *see* Headache
CMT, *see* Charcot-Marie-Tooth disease
Cocaine test, 64
Coma,
  definition, 181
  differential diagnosis, 185, 186
  electroencephalogram, 58
  evaluation, 182–186
  Glasgow Coma Scale, 187
  prognosis, 186
  stabilization of patient, 182
Computed tomography (CT), indications, 48, 49
Conus medullaris, features, 43
Coordination, evaluation, 25–27
Cortical atrophy, multiple sclerosis, 99, 100
Corticobasal ganglionic degeneration, features, 143
Cranial nerves,
  anatomy, 6
  clinical hints of dysfunction, 7
  eye examination, 8–12
  olfactory nerve evaluation, 7
  pathology, 7
Creutzfeldt-Jakob disease (CJD), features, 88
CT, *see* Computed tomography
Cubital tunnel syndrome, features and management, 159

D

DBS, *see* Deep brain stimulation
Deep brain stimulation (DBS),
  essential tremor management, 142
  Parkinson's disease management, 141
Delirium, management, 91, 92
Delirium tremens (DTs), features and management, 201, 202
Dementia,
  Alzheimer's disease, 93, 94
  dementia with Lewy bodies, 94, 95
  evaluation and workup, 95, 96
  frontotemporal dementia, 95
  management, 92, 93
  Parkinsonism, 94
  vascular dementia, 94
Dermatomyositis,
  clinical features, 170
  treatment, 70
DHE-45, *see* Dihydroergotamine
Diabetic neuropathy, features and management, 160
Diazepam, dizziness treatment, 113
Dihydroergotamine (DHE-45), migraine treatment, 118, 119

Dissection, extracranial arteries, 75
Dizziness,
drug-induced dizziness, 112
history, 111
physical examination, 111, 112
treatment, 113, 114
workup, 113
DTs, *see* Delirium tremens
Dysarthria, features, 43
Dystonia,
definition, 138
drug-induced dystonia, 143, 144

E

Edrophonium test, 64, 163
EEG, *see* Electroencephalogram
Electroencephalogram (EEG),
indications, 57, 58
principles, 56, 57
Electromyography (EMG),
back and neck pain, 177
complications and limitations, 55
indications, 54, 55
myasthenia gravis diagnosis, 164
overview, 52, 53
single-fiber, 54
technique, 53, 54
Eletriptan, migraine treatment, 119
Embolic stroke, *see* Stroke
EMG, *see* Electromyography
Encephalitis, acute management, 200
Entacapone, Parkinson's disease management, 141
Epidural spinal cord compression (ESCC), features and management, 197
Epilepsy,
antiepileptic drugs,
guidelines for use, 81, 82
novel drugs, 82, 83
withdrawal, 82
definition, 79
electroencephalogram, 57, 79, 80
general considerations, 83, 84
pregnancy, 83
ESCC, *see* Epidural spinal cord compression
Essential tremor (ET),
clinical features, 141, 142
treatment, 142
ET, *see* Essential tremor
Evoked potentials,
brainstem auditory, 55, 56
multiple sclerosis, 100
overview, 55
somatosensory, 56
visual, 55
Eye movement,
coma patient evaluation, 183, 184
evaluation, 10–12

F

Facial nerve, evaluation, 13, 14
Felbamate, epilepsy management, 82
Fisher's sign, 33
Foot drop, etiology, 45
Forearm ischemic exercise test, 64
Forearm-rolling test, 33
Formulation, neurological, 29
Froment's sign, 32

Frontotemporal dementia, features, 95
Frovatriptan, migraine treatment, 119
Fundoscopy, 10

G

Gabapentin, epilepsy management, 82
Gait, examination, 24, 25
Galtiramer, multiple sclerosis management, 102
Gamma hydroxybutyrate, narcolepsy management, 147
GBS, *see* Guillain-Barré syndrome
Gerstmann's syndrome, features, 41
Glasgow Coma Scale, 187
Guillain-Barré syndrome (GBS), features and management, 207, 208

H

Hallpike's test, 33
Hand muscle atrophy, associated conditions, 45
Headache,
  chronic daily headache, 122
  cluster headache features and treatment, 121–122
  evaluation,
    history, 115
    laboratory tests, 116, 124
    neurological examination, 115
  eye disorders, 125
  hospital admission criteria, 124
  migraine,
    menstrual migraine, 120
    pregnancy, 122, 123
    status migrainosus, 121
    treatment, 118–120
    variants, 117, 118
    with aura, 116, 117
    without aura, 117
  occipital neuralgia, 127
  postherpetic neuralgia, 127
  posttraumatic, 123
  pseudotumor cerebri, *see* Pseudotumor cerebri
  rare headache syndromes, 124, 125
  tension-type headache features and management, 116
  trigeminal neuralgia, *see* Trigeminal neuralgia
Hearing, evaluation, 14, 15
History, *see* Neurological history
Hoover's sign, 32
Horner's syndrome, 9, 64
Hydrochlorothiazide, dizziness treatment, 113
Hysteric conversion,
  definition, 35
  diagnostic mistakes, 36
  neurological signs, 36, 37
  suspected cases, 35, 36

I

ICP, *see* Intracranial pressure
Inclusion body myositis,
  clinical features, 171
  treatment, 171
Insomnia, *see* Sleep disorders
Interferon-β, multiple sclerosis management, 102
Internuclear ophthalmoplegia, features, 41

Intracranial pressure (ICP), management of elevation, 194, 195
Intravenous immunoglobulin (IVIg), myasthenia gravis management, 166
Isometheptene, migraine treatment, 119
IVIg, *see* Intravenous immunoglobulin

K

Kernig's sign, 31

L

Lacunar stroke, *see* Stroke
Lambert-Eaton myasthenic syndrome (LEMS),
  clinical features, 167, 168
  treatment, 168
Lamotrigine, epilepsy management, 82, 83
LEMS, *see* Lambert-Eaton myasthenic syndrome
Leptomeningeal biopsy, 63
Levetiracetam, epilepsy management, 83
Levodopa, Parkinson's disease management, 140
Lhermitte's sign, 31
Localization, neuroanatomy,
  knowledge requirements, 39
  long tracts, 39, 40
  medial longitudinal fasciculus, 40
  sensory dermatomes, 40
Locked-in syndrome, definition, 181
Lorazepam, dizziness treatment, 113
LP, *see* Lumbar puncture
Lumbar puncture (LP),
  complications, 62
  contraindications, 62
  indications, 61, 62
  multiple sclerosis findings, 100
  overview, 60, 61

M

Magnetic resonance angiography, indications, 50, 51
Magnetic resonance imaging (MRI),
  disadvantages, 50
  indications, 49
  multiple sclerosis, 99, 100
Magnetic resonance spectroscopy, indications, 52
Marcus-Gunn pupil, 8, 9, 31
Meclixine hydrochloride, dizziness treatment, 113
Medical Research Council Scale, muscle strength, 20
Meningitis,
  acute meningitis management, 199, 200
  bacterial, 85
  tuberculous, 86, 87
  viral, 86
Methysergide, migraine treatment, 120
Midazolam, status epilepticus management, 191
Migraine, *see* Headache
Mini-Mental State Exam,
  interpretation, 6
  scoring, 5
Mitoxantrone, multiple sclerosis management, 102

MMN, *see* Multifocal motor neuropathy
Modafinil, narcolepsy management, 147
Motor unit,
  anatomy, 153
  disease clinical characteristics, 154, 155
Mouth, cranial nerve evaluation, 15, 16
Movement disorders, *see also specific disorders*,
  definitions, 137, 138
  diagnosis, 137
  drug-induced dystonia, 143, 144
  drug-induced extrapyramidal syndromes, 143
  evaluation, 137
MRI, *see* Magnetic resonance imaging
MS, *see* Multiple sclerosis
Multifocal motor neuropathy (MMN), features and management, 161, 162
Multiple sclerosis (MS),
  clinical presentation, 98
  course, 97, 98
  diagnosis, 98–100
  epidemiology, 97
  treatment, 101–103
  variants, 100, 101
Multiple sleep latency test,
  indications, 59
  principles, 59
Muscle,
  atrophy, 21, 22
  biopsy, 63
  fasciculations, 21, 22
  motor unit, 153
  sprain, 175
  strength testing, 20
  tone, 20, 21
Muscular dystrophy,
  classification, 172
  fascioscapulohumeral muscular dystrophy, 173, 174
  myotonic muscular dystrophy, 172, 173
Myasthenia gravis,
  clinical characteristics, 155, 163
  crisis features and management, 205, 206
  diagnosis, 163–165
  edrophonium test, 64, 163
  treatment, 165–167
Myelography, indications, 50
Myoclonus,
  definition, 138
  features and management, 144
Myopathy, *see also specific myopathies*,
  associated conditions, 46
  clinical characteristics, 155, 156
  congenital myopathies, 171, 172
  metabolic myopathies, 174

N

Naproxen, migraine treatment, 120
Naratriptan, migraine treatment, 119
Narcolepsy,
  clinical features, 146, 147
  diagnosis, 147
  treatment, 147

Natalizumab, multiple sclerosis management, 102
NCS, *see* Nerve conduction study
Neck,
  cranial nerve evaluation, 17—19
  pain, *see* Back and neck pain
Nerve biopsy, 63
Nerve conduction study (NCS),
  back and neck pain, 179
  complications and limitations, 55
  indications, 54, 55
  overview, 52, 53
  technique, 53
Neurological examination,
  back and neck pain, 176, 177
  coma patients, 182–185
  communication with patient, 5
  coordination and cerebellar function, 25–27
  cranial nerve examination, 6–19
  dizziness and vertigo, 111, 112
  gait examination, 24, 25
  general considerations, 3, 4
  headache, 115
  mental status examination, 5, 6
  modified examination, 29
  muscle and reflex evaluation, 20–24
  questions answered, 4, 5
  stroke, 69
Neurological history,
  back and neck pain, 176
  coma patients, 182
  dizziness and vertigo, 111
  general considerations, 3, 4
  headache, 115
  questions answered, 4
Neuromuscular disease, s*ee also specific diseases*,
  clinical characteristics,
    brachial plexitis, 155
    motor neuron disease, 154, 155
    myasthenia gravis, 155
    myopathy, 155, 156
    polyneuropathy, 155
  evaluation, 153, 154
  motor unit anatomy, 153
  signs and symptoms, 154
Nystagmus, 11

O

Occipital neuralgia, features, 127
Optic neuritis, isolated, 104
Oxcarbazepine, epilepsy management, 83

P

Parasomnia, *see* Sleep disorders
Parkinson's disease,
  clinical features, 138, 139
  dementia, 94
  differential diagnosis, 139
  epidemiology, 138
  management, 139–141
Patrick's sign, 32
Pentobarbital, status epilepticus management, 191
Peripheral neuropathy,
  associated conditions, 44, 135, 136
  causes, 131, 132
  classification, 132–134
  electrophysiological diagnosis, 131
  evaluation, 129, 134, 135
  mononeuropathies,

Bell's palsy, 157, 158
carpal tunnel syndrome, 158, 159
cubital tunnel syndrome, 159
peroneal nerve palsy, 159, 160
signs, 130, 131
symptoms, 130
treatment, 135
Peroneal nerve palsy, features and management, 159, 160
Persistent vegetative state, definition, 181
PET, *see* Positron emission tomography
Physical examination, *see* Neurological examination
Plasmapheresis, myasthenia gravis management, 166
Plexopathy, associated conditions, 44, 45
PML, *see* Progressive multifocal leukoencephalopathy
Polymyositis,
clinical features, 169
treatment, 169, 170
Polyneuropathy, clinical characteristics, 155
Polysomnography,
indications, 58, 59
principles, 58
Positron emission tomography (PET), indications, 51, 52
Postherpetic neuralgia, features, 127
Pramipexole, Parkinson's disease management, 140
Pregabaline, epilepsy management, 83
Pregnancy,
epilepsy, 83
migraine, 122, 123
Progressive multifocal leukoencephalopathy (PML), features, 90
Progressive supranuclear palsy, features, 143
Promethazine hydrochloride, dizziness treatment, 113
Pronator drift sign, 32
Propofol, status epilepticus management, 191
Pseudobulbar palsy, features, 42
Pseudoepilepsy, electroencephalogram, 58
Pseudotumor cerebri,
clinical features, 123
diagnosis, 123
treatment, 123
Ptosis, 8
Pupil, abnormalities, 8, 9
Pupillary sparing, 33
Pyridostigmine, myasthenia gravis management, 165, 206

Q

Quadriceps weakness, etiology, 45

R

Radiculopathy,
associated conditions, 44
back and neck pain, 175, 176
Radiosurgery, trigeminal neuralgia management, 126
Reflex,
corticobulbar reflexes, 23, 24
pathological reflexes, 24
plantar reflexes, 23

superficial reflexes, 22
testing, 22
Repetitive nerve stimulation, technique, 54
Respiration, coma patient evaluation, 185
Rigidity, definition, 138
Rinne's test, 14
Rizatriptan, migraine treatment, 119

S

SAH, *see* Subarachnoid hemorrhage
Scapula winging, etiology, 45
Scopolamine, dizziness treatment, 113
SE, *see* Status epilepticus
Seizure,
alcohol withdrawal seizures, 108
antiepileptic drugs,
guidelines for use, 81, 82
novel drugs, 82, 83
withdrawal, 82
definition, 79
electroencephalogram, 79, 80
general considerations, 83, 84
generalized, 80
partial, 80
Selegiline, Parkinson's disease management, 140
Shoulder, cranial nerve evaluation, 17–19
Single-photon emission computed tomography (SPECT), indications, 52
Sleep,
circadian rhythms, 146
cycles, 146
neuroanatomy, 146
non-rapid eye movement sleep, 145
rapid eye movement sleep, 145
Sleep disorders,
circadian sleep disorders, 151
insomnias, 146
narcolepsy, 146, 147
parasomnias,
non-rapid eye movement sleep, 149, 150
rapid eye movement sleep, 150, 141
recognition, 145
sleep apnea syndrome,
central sleep apnea, 148
diagnosis, 148
mixed sleep apnea, 148
obstructive sleep apnea, 148
treatment, 148, 149
Solu-Medrol, multiple sclerosis management, 101
Somatosensory evoked potentials, 56
SPECT, *see* Single-photon emission computed tomography
Spinal cord compression, *see* Epidural spinal cord compression
Spinal cord lesion, features, 43
Status epilepticus (SE),
clinical features, 189
diagnosis, 189, 190
electroencephalogram, 57
follow-up and maintenance, 192

management, 190–192
Straight leg-raising test, 32
Stroke,
blood pressure control, 68
clinical scenarios, 76—78
embolic stroke, 72, 73
initial management,
assessment in emergency department, 67
therapeutic considerations, 67, 68
ischemic brain edema management, 70
lacunar stroke, 71, 72
neurological examination, 69
neurovascular examination, 69
prevention of recurrence, 70
workup, 69, 70
Subarachnoid hemorrhage (SAH),
etiology, 74
treatment, 74
Subcortical lesions, features, 41
Sumatriptan, migraine treatment, 119
Syphilis, features and management, 87, 88

T

TA, *see* Temporal arteritis
Tardive dyskinesia,
definition, 138
features and management, 144
TCD, *see* Transcranial Doppler
Temporal arteritis (TA), features and management, 208, 209
Temporal artery, biopsy, 63
TIA, *see* Transient ischemic attack
Tiagabine, epilepsy management, 83
Tic, definition, 137
Tinel's sign, 31, 32
Todd's paralysis, 32
Tolcapone, Parkinson's disease management, 141
Tongue deviation, features, 44
Topiramate, epilepsy management, 83
Transcranial Doppler (TCD), indications, 51
Transient ischemic attack (TIA),
clinical scenarios, 76
workup and management, 69—71
Transtentorial herniation, features, 193, 194
Transverse myelitis, acute, 104, 105
Tremor, definition, 137
Tricyclic antidepressants,
migraine treatment, 120
narcolepsy management, 147
Trigeminal nerve, evaluation, 12, 13
Trigeminal neuralgia,
clinical features, 125, 126
treatment, 126
Trihexiphenidyl mesylate, Parkinson's disease management, 140

V

Valproate, status epilepticus management, 191

Vasculitis, central nervous system, 75
Verapamil, migraine treatment, 120
Vertigo,
  causes, 112, 113
  history, 111
  physical examination, 111, 112
  treatment, 113, 114
Vestibular neuritis, vertigo, 113
Vestibular system evaluation, 15
Visual acuity, evaluation, 9
Visual evoked potentials, 55
Visual field, evaluation, 9, 10

W

Wallenberg's syndrome, features, 42, 76, 77
Watershed infarcts, features, 41
Weber's test, 14
Wernicke's encephalopathy, features and management, 203, 204
Wrist drop, etiology, 45

X

X-ray, indications, 48

Z

Zolmitriptan, migraine treatment, 119
Zonisamide, epilepsy management, 83