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临床神经病学

Clinical Neurology

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David A. Greenberg

4
fourth edition

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a LANGE medical book

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Preface

The fourth edition of *Clinical Neurology* retains its primary focus, arising from the authors' experience teaching in the clinics and wards of the University of California, San Francisco hospitals: an approach to neurology based on the patient's presenting symptoms or signs. Thus the chapters are organized according to problems such as headaches, seizures, stroke, and coma, rather than as a catalog of specific diseases. We believe this method has been a useful teaching tool and accordingly it is retained in the current volume.

A new edition of the textbook is required, however, because of the rapidly expanding knowledge of therapy for neurologic disease and of molecular, and especially genetic, disease mechanisms. A host of new and effective treatments for multiple sclerosis, Parkinson's disease, headache, epilepsy, and stroke has been incorporated into the therapy section of the text. Sections devoted to neurobiology have been extensively updated and expanded and summary tables of neurologic drugs and of genetic neurologic disorders have been added inside the covers for quick access. Because neuroimaging continues to evolve and improve, attention has been paid to new magnetic resonance (MR) and computed tomography (CT) images in the text. Finally, the appendix contains a new, extensive, step-by-step description of the neurologic examination.

In preparing this new edition, especially in the areas of therapeutics and genetics, we have again consulted our expert colleagues, who have been of great help. In this regard, we particularly thank Neil Raskin, Hill Panitch, Lowell Lubic, Kathy Gardner, Paula Clemens, James Corbett, Daryl Gress, Dawn McGuire, Allen Gelb, Howard Rowley, Mark Scheuer, Lydia Bayne, Megan Burns, and Joseph Guglielmo. The medical illustration office of the University Drive VA Hospital at the University of Pittsburgh has been especially helpful in providing patient photographs and reproductions of neuroimaging studies. The present and past staff at Appleton & Lange have, as always, been enormously helpful in moving this book through editing and production. We trust the final product will serve as a tool to demystify clinical neurology for students and practitioners, providing patients better and more focused diagnosis, which can increasingly be translated into therapy.

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Pittsburgh and San Francisco
December 1998

Contents

Disorders of Consciousness: Approach to Diagnosis & Acute Confusional States

1

Consciousness is awareness of the internal or external world, and disorders of consciousness can affect either the level of consciousness or the content of consciousness.

Disturbances of the Level of Consciousness

Abnormalities of the level of consciousness are characterized by impaired arousal or wakefulness, and they result from acute lesions of the ascending reticular activating system (Figure 1–1) or both cerebral hemispheres. The most severe degree of depressed consciousness is **coma**, in which the patient is unresponsive and unarousable. Less severe depression of consciousness results in **acute confusional states**, in which the patient responds to at least some stimuli in a purposeful manner but is sleepy, disoriented, and inattentive. In some acute confusional states, agitation rather than drowsiness predominates. This is the syndrome of **delirium**, which is often characterized by autonomic disturbances (fever, tachycardia, hypertension, sweating, pallor, or flushing), hallucinations, and motor abnormalities (tremor, asterixis, or myoclonus). Delirium frequently alternates with drowsiness.

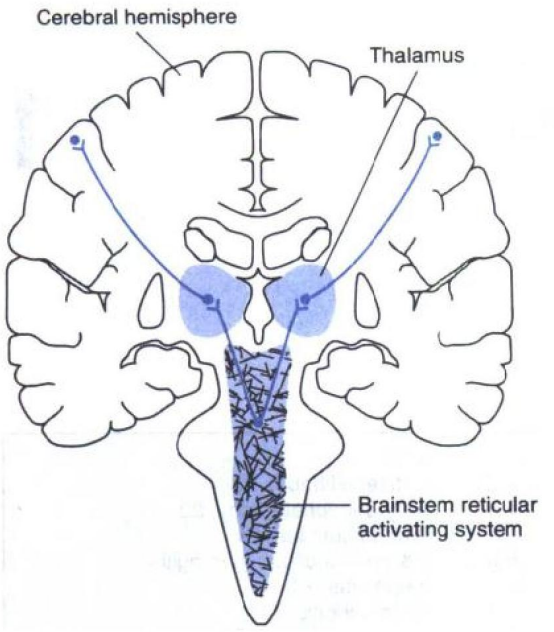


Figure 1–1. Brainstem reticular activating system and its ascending projections to the thalamus and cerebral hemispheres.

Disturbances of the Content of Consciousness

Many pathologic conditions can impair the content of consciousness without altering the level of consciousness. Examples include isolated disorders of language or memory due to focal brain lesions and widespread deterioration of mental function (dementia) from more diffuse, chronic pathologic processes. Dementia differs from acute confusional states in several respects (Table 1–1).

Confusional states are discussed in this chapter. Dementia and memory disorders are discussed in Chapter 2 and coma in Chapter 11.

I. APPROACH TO DIAGNOSIS

Evaluation of the patient with a suspected disorder of consciousness is aimed at determining the following:

(1) Whether such a disorder is present.

(2) Whether impairment of function is global or circumscribed.

(3) If global, whether the picture is that of a confusional state or dementia.

(4) Whether a treatable pathologic process exists.

The approach to diagnosis outlined below, which is designed to answer these questions, applies to any patient with a disorder of consciousness. Once the nature of the disorder is established, the specific cause can be investigated.

HISTORY

History of Present Illness

The history should establish the time course of the disorder and provide clues to its nature and cause. Confusional states are acute to subacute in onset, while dementias are chronic disorders. In an acute confusional state, the observations of police officers or ambulance attendants may be the only historical information available. When dementia is suspected, it is crucial to have a source of information other than the patient—usually a close relative—who can furnish details about the patient's previous level of functioning; the time when dysfunction became evident; and the nature of any changes in personality, behavior, mood, intellect, judgment, memory, or facility with language. Associated problems such as gait disorders, incontinence, and headaches should also be explored.

Prior Medical History

A. Cardiovascular System: A history of stroke, hypertension, vasculitis, or cardiac disease may suggest a vascular cause of a confusional state or multi-infarct dementia.

B. Diabetes: Cognitive disturbance in diabetic patients may relate to a hyperosmolar nonketotic state or to insulin-induced hypoglycemia.

C. Seizure Disorder: A history of epilepsy should suggest the possibility of ongoing seizures, a postictal state or head trauma in a confused patient.

D. Head Trauma: Recent head trauma suggests intracranial hemorrhage. Remote head trauma may

Table 1–1. Differences between acute confusional states and dementia.

	Acute Confusional State	Dementia
Level of consciousness	Impaired	Not impaired, except occasionally late in course
Course	Acute to subacute; fluctuating	Chronic; steadily progressive
Autonomic hyperactivity	Often present	Absent
Prognosis	Usually reversible	Usually irreversible

produce amnestic syndrome or chronic subdural hematoma with dementia.

E. Alcoholism: Alcoholism predisposes patients to acute confusional states from intoxication, withdrawal, postictal state, head trauma, hepatic encephalopathy, and Wernicke's encephalopathy. Chronic memory disturbance in an alcoholic is likely to be the result of Korsakoff's syndrome.

F. Drug History: A confusional state can result from intentional or accidental overdose with insulin, sedative-hypnotics, opioids, antidepressants, antipsychotic agents, or hallucinogens. The ability to tolerate such drugs often declines with age, and cognitive disturbances may result from doses that are well accepted by younger patients. Sedative drug withdrawal can also lead to a confusional state.

G. Psychiatric History: A history of psychiatric illness may suggest an accidental or intentional overdose with benzodiazepines, antidepressants, or antipsychotic agents; a previously undiagnosed medical disorder capable of producing organic psychosis (hypothyroidism, vitamin B_{12} deficiency); or a functional disorder masquerading as an acute confusional state or dementia.

H. Other: Homosexual or bisexual men, intravenous drug users, recipients of blood or clotting factor transfusions, the sexual partners of all these persons, and infants of infected mothers are at particular risk for developing acquired immunodeficiency syndrome (AIDS).

Family History

The family history can point to a heredodegenerative disorder as the cause of dementia.

GENERAL PHYSICAL EXAMINATION

A general physical examination helps to classify the disorder as either an acute confusional state or dementia and may suggest a systemic disease as its cause (Tables 1–2 and 1–3).

Vital Signs & General Appearance

Fever, tachycardia, hypertension, and sweating occur in many confusional states and should suggest such a state rather than dementia. Meningitis or systemic infection must receive early consideration in the febrile patient. Hypertension should alert the physician to the possibility of hypertensive encephalopathy, intracranial hemorrhage, renal disease, or Cushing's syndrome. Hypothermia occurs with exposure to cold, ethanol or sedative drug intoxica-

Table 1–2. Clinical features helpful in the differential diagnosis of acute confusional states.

Feature	Most Suggestive of
Headache	Head trauma, meningitis, subarachnoid hemorrhage
Vital signs	
Fever	Infectious meningitis, anticholinergic intoxication, withdrawal from ethanol or sedative drugs
Hypothermia	Intoxication with ethanol or sedative drugs, hepatic encephalopathy, hypoglycemia, hypothyroidism
Hypertension	Anticholinergic intoxication, withdrawal from ethanol or sedative drugs, hypertensive encephalopathy, subarachnoid hemorrhage, sympathomimetic intoxication
Tachycardia	Anticholinergic intoxication, withdrawal from ethanol or sedative drugs, thyrotoxicosis
Bradycardia	Hypothyroidism
Hyperventilation	Hepatic encephalopathy, hyperglycemia
Hypoventilation	Intoxication with ethanol or sedative drugs, opioid intoxication, pulmonary encephalopathy
General examination	
Meningismus	Meningitis, subarachnoid hemorrhage
Skin rash	Meningococcal meningitis
Tetany	Hypocalcemia
Cranial nerves	
Papilledema	Hypertensive encephalopathy, intracranial mass
Dilated pupils	Head trauma, anticholinergic intoxication, withdrawal from ethanol or sedative drugs, sympathomimetic intoxication
Constricted pupils	Opioid intoxication
Nystagmus/ ophthalmoplegia	Intoxication with ethanol or sedative drugs, vertebrobasilar ischemia, Wernicke's encephalopathy
Motor	
Tremor	Withdrawal from ethanol or sedative drugs, sympathomimetic intoxication, thyrotoxicosis
Asterixis	Metabolic encephalopathy
Hemiparesis	Cerebral infarction, head trauma, hyperglycemia, hypoglycemia
Other	
Seizures	Withdrawal from ethanol or sedative drugs, head trauma, hyperglycemia, hypoglycemia
Ataxia	Intoxication with ethanol or sedative drugs, Wernicke's encephalopathy

Table 1–3. Clinical features helpful in the differential diagnosis of dementia.

Feature	Most Suggestive of
History	
(Male) homosexuality, intravenous drug abuse, hemophilia, or blood transfusion	AIDS dementia complex
Family history	Huntington's disease, Wilson's disease
Headache	Brain tumor, chronic subdural hematoma
Vital signs	
Hypothermia	Hypothyroidism
Hypertension	Multi-infarct dementia
Hypotension	Hypothyroidism
Bradycardia	Hypothyroidism
General examination	
Meningismus	Chronic meningitis
Jaundice	Acquired hepatocerebral degeneration
Kayser-Fleischer rings	Wilson's disease
Cranial nerves	
Papilledema	Brain tumor, chronic subdural hematoma
Argyll Robertson pupils	Neurosyphilis
Ophthalmoplegia	Progressive supranuclear palsy
Pseudobulbar palsy	Multi-infarct dementia, progressive supranuclear palsy
Motor	
Tremor	Dementia with Lewy bodies, corticobasal ganglionic degeneration, acquired hepatocerebral degeneration, Wilson's disease, AIDS dementia complex
Asterixis	Acquired hepatocerebral degeneration
Myoclonus	Creutzfeldt-Jakob disease, AIDS dementia complex
Rigidity	Dementia with Lewy bodies, corticobasal ganglionic degeneration, acquired hepatocerebral degeneration, Creutzfeldt-Jakob disease, progressive supranuclear palsy, Wilson's disease
Chorea	Huntington's disease, Wilson's disease
Other	
Gait apraxia	Normal pressure hydrocephalus
Polyneuropathy with hyporeflexia	Neurosyphilis, vitamin B_{12} deficiency, AIDS dementia complex

tion, hypoglycemia, hepatic encephalopathy, Wernicke's encephalopathy, hypothyroidism, or shock. In most dementias, the patient does not appear acutely ill unless a systemic disorder is also present.

Skin & Mucous Membranes

Jaundice suggests hepatic disease, and lemon-yellow coloration of the skin may occur in vitamin B_{12} deficiency. Coarse dry skin, dry brittle hair, and subcutaneous edema are characteristic of hypothyroidism. Petechiae are seen in meningococcemia, and petechiae or ecchymoses may reflect coagulopathy caused by liver disease, disseminated intravascular coagulation, or thrombotic thrombocytopenia purpura. Hot, dry skin is characteristic of intoxication with anticholinergic drugs. Cushing's syndrome may be associated with acne. Hyperpigmentation of the skin may be evidence of Addison's disease. Needle tracks associated with intravenous drug use suggest drug overdose or infective endocarditis.

Head & Neck

Examination of the head may reveal evidence of recent trauma, such as scalp lacerations or contusions, postauricular hematoma (Battle's sign), periorbital hematoma (raccoon eyes), hemotympanum, or cerebrospinal fluid (CSF) otorrhea or rhinorrhea. Percussion of the skull over a subdural hematoma may cause pain or may be associated with a sound described as stony dullness.

Meningeal signs, such as neck stiffness on passive flexion, thigh flexion upon flexion of the neck (Brudzinski's sign), or resistance to passive extension of the knee with the hip flexed (Kernig's sign), are seen in meningitis and subarachnoid hemorrhage.

Chest & Abdomen

Cardiac murmurs may be associated with infective endocarditis and its neurologic sequelae. Abdominal examination may reveal a source of systemic infection or suggest liver disease. Rectal examination may provide evidence of gastrointestinal bleeding, which is often the precipitating factor in hepatic encephalopathy.

NEUROLOGIC EXAMINATION

Mental Status Examination

Evaluation of mental status (Table 1–4) helps to classify a cognitive disorder as a confusional state, dementia, a circumscribed cognitive disturbance (aphasia, amnesia), or a psychiatric illness. The mental status examination is most useful if performed in a standardized fashion—and with the understanding that complex functions can be adequately evaluated only when the basic processes upon which they depend are preserved. Functions such as memory, lan-

Table 1–4. Comprehensive mental status examination.

Level of consciousness
Attention and concentration
Language and speech
Comprehension
Repetition
Fluency
Naming
Reading
Writing
Calculation
Speech
Mood and behavior
Content of thought
Hallucinations
Delusions
Abstraction
Judgment
Memory
Immediate recall
Recent memory
Remote memory
Integrative sensory function
Astereognosis
Agraphesthesia
Two-point discrimination
Allesthesia
Extinction
Unilateral neglect and anosognosia
Disorders of spatial thought
Integrative motor function
Apraxia

guage, calculation, or abstraction cannot be reliably assessed in the patient who is barely arousable or extremely inattentive. The minimental status examination (Table 1–5) is often used as a rapid bedside screening test for dementia.

In performing the mental status examination, the level of consciousness and attention are evaluated first. If these are impaired, an acute confusional state exists, and it may be difficult or impossible to conduct the remainder of the mental status examination. If the level of consciousness and attention are adequate, more complex cortical functions are examined next to determine whether there is global cortical dysfunction, which indicates dementia.

A. Level of Consciousness: The level of consciousness is described in terms of the patient's apparent state of wakefulness and response to stimuli. Impairment of the level of consciousness should always be documented by a written description of the patient's responses to specific stimuli rather than by the use of such nonspecific and imprecise terms as "lethargy," "stupor," or "semicoma."

1. Normal–The patient with a normal level of consciousness appears awake and alert, with eyes open at rest. Unless there is deafness or a language disorder, verbal stimulation results in appropriate verbal responses.

2. Impaired–Mild impairment of consciousness may be manifested by sleepiness from which the patient is easily aroused when spoken to. As consciousness is further impaired, the intensity of stimulation required for arousal increases, the duration of arousal declines, and the responses elicited become less purposeful.

B. Attention: Attention is the ability to focus on a particular sensory stimulus to the exclusion of others; **concentration** is sustained attention. These

Table 1–5. Minimental status examination.

Item	Points[1]
Orientation	
Time (1 point each for year, season, month, date, and day of week)	5
Place (1 point each for state, county, city, building, and floor or room)	5
Registration	
Repeat names of three objects (1 point per object)	3
Attention and calculation	
Serial 7s or spell "world" backward (1 point per subtraction or letter)	5
Recall	
Recall names of three objects repeated previously (1 point per object)	3
Language	
Name pencil and watch (1 point each)	2
Repeat "no ifs, ands or buts"	1
Follow three-step command (1 point per step)	3
Read and follow: "close your eyes"	1
Write a complete sentence	1
Construction	
Copy two intersecting pentagons	1
Total	30

[1]A total score of <24 should generally lead to more detailed investigation of the possibility of dementia, although norms vary to some extent with age and education.

Adapted from Greenberg DA: Dementia. In: *Geriatrics*. Lonergan ET (editor). Appleton & Lange, 1996.

processes are grossly impaired in acute confusional states, usually less impaired in dementia, and unaffected by focal brain lesions. Attention can be tested by asking the patient to repeat a series of digits or to indicate when a given letter appears in a random series. A normal person can repeat five to seven digits correctly and identify a letter in a series without error.

C. Language and Speech: The essential elements of language are comprehension, repetition, fluency, naming, reading, and writing, all of which should be tested when a language disorder (**aphasia**) is suspected. Calculation disorders (**acalculia**) are probably closely related to aphasia. Speech, the motor activity that is the final step in the expression of language, is mediated by the lower cranial nerves and their supranuclear connections. **Dysarthria,** a disorder of articulation, is sometimes difficult to distinguish from aphasia but it always spares oral and written language comprehension and written expression.

Aphasia may be a feature of diffuse cortical disease, as it is in certain dementias, but language impairment with otherwise normal cognitive function should suggest a focal lesion in the dominant hemisphere. A disorder of comprehension (**receptive, or Wernicke's, aphasia**) commonly leads to a false impression of a confusional state or psychiatric disturbance.

There are a variety of aphasic syndromes, each characterized by a particular pattern of language impairment; several have fairly precise pathoanatomic correlations (Figure 1–2).

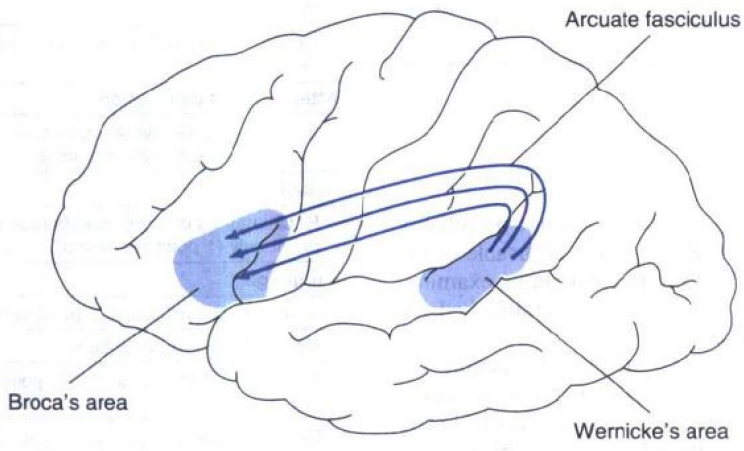
D. Mood and Behavior: Demented patients may be apathetic, inappropriately elated, or depressed, and their moods can fluctuate. If the examination is otherwise normal, early dementia can easily be confused with depression. Delirious patients are agitated, noisy, and easily provoked to anger.

E. Content of Thought: Abnormalities of thought content can help to distinguish between organic and psychiatric disease. **Visual hallucinations** are common in acute confusional states, while **auditory hallucinations** and **fixed delusions** are most common with psychiatric disorders. **Impairment of abstraction** may be revealed by the patient's concrete (literal) interpretation of proverbs or inability to recognize conceptual differences and similarities. **Judgment** is commonly tested by asking what the patient would do in a hypothetic situation, such as finding a stamped, addressed letter on the sidewalk.

F. Memory:

1. Functional components of memory– Memory is the ability to register, store, and ultimately retrieve information. Storage and retrieval of memories can be impaired by either diffuse cortical disease or focal bilateral dysfunction of the medial temporal lobes or their connections.

a. Registration–The ability to receive information through the various sensory modalities is largely a function of attention.



Pathologic Site	Type of Aphasia	Language Functions Preserved		
		Comprehension	Repetition	Fluency
Wernicke's area	Receptive	–	–	+
Arcuate fasciculus	Conductive	+	–	+
Broca's area	Expressive	+	–	–

Figure 1–2. Anatomic basis and clinical features of aphasias.

b. Storage–The process whereby selected new information is learned, or memorized, may be mediated by limbic structures, including the hippocampus. Stored memories are reinforced by repetition and by emotional significance; they are thought to be diffusely distributed in association areas of the cerebral cortex.

c. Retrieval–This is the ability to access previously learned information.

2. Amnesia–Memory disorder (amnesia) may be an isolated deficit or one feature of global cognitive dysfunction. In acute confusional states, attention is impaired, resulting in defective registration and an inability to learn new material. In dementia, attention is typically normal and problems with recent and—to a lesser extent—remote memory usually predominate.

In **psychogenic amnesia**, subjective and emotionally charged memories are more affected than is retention of objective facts and events; in **organic amnesia**, the reverse is true. Isolated loss of memory for personal identity (the inability to remember one's own name) in an awake and alert patient is virtually pathognomonic of a psychogenic disorder.

Additional terms sometimes used to denote aspects of acute-onset amnesia (eg, following head trauma) include **retrograde amnesia**, loss of memory for events immediately prior to the onset of the disorder, and **anterograde** or **posttraumatic amnesia**, impairment of memory in the period following the insult.

3. Testing of memory–Memory is assessed clinically by testing **immediate recall, recent memory**, and **remote memory**, which correspond roughly to registration, storage, and retrieval, respectively.

a. Immediate recall–Tests of immediate recall are similar to tests of attention and include having the patient repeat a random series of numbers or other information that has not been previously learned. The ability to repeat implies that the material has been registered. Most normal adults can repeat a series of seven numbers forward and five backward without difficulty.

b. Recent memory–Tests of recent memory assess the ability to learn new material. Typically, the patient is given three or four items to remember and asked to recall them three minutes later. Nonverbal tests requiring that an object previously shown to the patient be selected from a group of objects may be useful, especially for patients with expressive aphasia. Orientation to place and time, which requires newly learned information, is another important test of recent memory.

c. Remote memory–The practical distinction between recent and remote memory is that only the former requires an ongoing ability to learn new information. Remote memory is tested by asking the patient to recall material that someone of comparable cultural and educational background can be assumed to know. Common examples are personal, historical, or geographic data, but the questions selected must be appropriate for the patient, and personal items must be verifiable.

G. Integrative Sensory Function: Sensory integration disorders from parietal lobe lesions are manifested by misperception of or inattention to sensory stimuli on the contralateral side of the body, when the primary sensory modalities are intact.

Patients with parietal lesions may exhibit the following signs:

1. Astereognosis–The patient cannot identify, by touch, an object placed in the hand.

2. Agraphesthesia–The patient is unable to identify a number written on the hand.

3. Absence of two-point discrimination–This is an inability to differentiate between a single stimulus and two simultaneously applied adjacent, but separated, stimuli that can be distinguished by a normal person.

4. Allesthesia–This is misplaced localization of a tactile stimulus.

5. Extinction–A visual or tactile stimulus is perceived when applied alone to the side contralateral to the lesion but not when stimuli are applied bilaterally.

6. Unilateral neglect and anosognosia–Body image disorders caused by parietal lobe lesions take the form of unilateral neglect. The patient tends not to use the contralateral limbs, may deny that there is anything wrong with them (anosognosia), and may even fail to recognize them.

7. Disorders of spatial thought–These include **constructional apraxia, right/left disorientation, and neglect of external space** on the side opposite the affected parietal lobe. Tests for constructional apraxia include having the patient fill in the numbers on a clock face, copy geometric figures, or build figures with blocks.

H. Integrative Motor Function: Apraxia is the inability to perform previously learned tasks, such as finger snapping or clapping the hands together, despite intact motor and sensory function. Unilateral apraxias are commonly caused by contralateral premotor frontal cortex lesions. Bilateral apraxias, such as gait apraxia, may be seen with bifrontal or diffuse cerebral lesions.

Gait & Station

It is useful to observe the patient standing and walking early in the neurologic examination, since these activities may reveal additional neurologic abnormalities associated with disturbed cognitive function.

Cranial Nerves

In patients with impaired cognitive function, abnormalities associated with cranial nerves may suggest the underlying cause.

A. Lesions of the Eyes and Ears:

1. Papilledema suggests an intracranial mass,

hypertensive encephalopathy, or other process that increases intracranial pressure.

2. In the confused patient, **pupillary constriction** suggests opiate ingestion; **dilated pupils** are characteristic of anticholinergic intoxication but may also be a manifestation of generalized sympathetic hyperactivity. **Small, irregular pupils** that react poorly to light—but better to accommodation—can be seen in neurosyphilis.

3. Sedative drugs and Wernicke's encephalopathy produce **nystagmus** or **ophthalmoplegia.** Selective **impairment of vertical gaze (especially downward)** occurs early in progressive supranuclear palsy.

B. Pseudobulbar Palsy: This syndrome is characterized by dysarthria, dysphagia, hyperactive jaw jerk and gag reflexes, and uncontrollable laughing or crying unrelated to emotional state (**pseudobulbar affect**). It results from bilateral interruption of the corticobulbar and corticospinal tracts. Dementing processes that produce this syndrome include progressive supranuclear palsy and multi-infarct dementia.

C. Multiple Cranial Neuropathies: These can accompany infectious or noninfectious meningitis or AIDS dementia complex.

Motor Findings

A. Acute Confusional State: In the acutely confused patient, a variety of motor abnormalities may suggest the cause.

1. **Hemiparesis** is most apt to be due to an intracranial structural lesion, although focal neurologic signs may be present in such metabolic disorders as hypoglycemia and nonketotic hyperglycemia.

2. **Tremor** is common in sedative drug or ethanol withdrawal and other states accompanied by autonomic hyperactivity.

3. **Asterixis,** a flapping tremor of the outstretched hands or feet, is seen in hepatic, renal, and pulmonary encephalopathy and in drug intoxication.

4. **Myoclonus,** which consists of rapid shock-like muscle contractions, can occur with uremia, cerebral hypoxia, or hyperosmolar nonketotic states.

5. **Cerebellar signs** such as broad-based ataxic gait and, often, dysmetria on heel-knee-shin maneuver accompany Wernicke's encephalopathy and sedative drug intoxication.

B. Dementia: Motor signs are useful in the differential diagnosis of dementia.

1. **Chorea**–Huntington's disease, Wilson's disease.

2. **Tremor, rigidity, or bradykinesia**–Wilson's disease, acquired hepatocerebral degeneration.

3. **Myoclonus**–Creutzfeldt-Jakob disease, AIDS dementia complex.

4. **Ataxia**–Spinocerebellar degenerations, Wilson's disease, paraneoplastic syndromes, Creutzfeldt-Jakob disease, AIDS dementia complex.

5. **Paraparesis**–Vitamin B_{12} deficiency, hydrocephalus, AIDS dementia complex.

Abnormalities of Sensation & Tendon Reflexes

Dementias associated with prominent sensory abnormalities and loss of tendon reflexes include vitamin B_{12} deficiency, neurosyphilis, and AIDS dementia complex.

Primitive Reflexes

A number of reflexes that are present in infancy and subsequently disappear may be released by frontal lobe dysfunction in later life. It is presumed that such release results from loss of cortical inhibition of these primitive reflexes (frontal release signs), which include palmar and plantar grasps as well as palmomental, suck, snout, rooting, and glabellar reflexes. Although these responses are often seen in both acute confusional states and dementia, many can also occur in normal elderly adults. Their presence alone does not constitute evidence of cognitive dysfunction.

1. The **palmar grasp** reflex is elicited by stroking the skin of the patient's palm with the examiner's fingers. If the reflex is present, the patient's fingers close around those of the examiner. The force of the patient's grasp may increase when the examiner attempts to withdraw the fingers, and the patient may be unable to voluntarily release the grasp.

2. The **plantar grasp** reflex consists of flexion and adduction of the toes in response to stimulation of the sole of the foot.

3. The **palmomental reflex** is elicited by scratching along the length of the palm of the hand and results in contraction of ipsilateral chin (mentalis) and perioral (orbicularis oris) muscles.

4. The **suck reflex** consists of involuntary sucking movements following the stimulation of the lips.

5. The **snout reflex** is elicited by gently tapping the lips and results in their protrusion.

6. In the **rooting reflex**, stimulation of the lips causes them to deviate toward the stimulus.

7. The **glabellar reflex** is elicited by repetitive tapping on the forehead. Normal subjects blink only in response to the first several taps; persistent blinking is an abnormal response **(Myerson's sign).**

LABORATORY INVESTIGATIONS

Laboratory studies are critical in diagnosing disorders of cognitive function. Useful investigations are listed in Tables 1–6 and 1–7; those most likely to establish or support a diagnosis in acute confusional states are complete blood count, arterial blood gases

Table 1–6. Laboratory studies in acute confusional states.

Test	Most Useful in Diagnosis of
Blood	
WBC	Meningitis
PT and PTT	Hepatic encephalopathy
Arterial blood gas	Hepatic encephalopathy, pulmonary encephalopathy, uremia
Sodium	Hyponatremia
Serum urea nitrogen and creatinine	Uremia
Glucose	Hyperglycemia, hypoglycemia
Osmolality	Alcohol intoxication, hyperglycemia
Liver function tests, ammonia	Hepatic encephalopathy, Reye's syndrome
Thyroid function tests	Hyperthyroidism, hypothyroidism
Calcium	Hypercalcemia, hypocalcemia
Drug screen	Drug intoxications
Cultures	Meningitis
FTA or MHA-TP	Syphilitic meningitis
HIV antibody titer	AIDS and related disorders
Urine, gastric aspirate	
Drug screen	Drug intoxication
Stool	
Guaiac	Hepatic encephalopathy
ECG	Anticholinergic intoxication, vascular disorders
Cerebrospinal fluid	
WBC, RBC	Meningitis, encephalitis, subarachnoid hemorrhage
Gram's stain	Bacterial meningitis
AFB stain	Tuberculous meningitis
India ink preparation	Cryptococcal meningitis
Cultures	Infectious meningitis
Cytology	Leptomeningeal metastases
Glutamine	Hepatic encephalopathy
VDRL	Syphilitic meningitis
Cryptococcal antigen	Cryptococcal meningitis
Polymerase chain reaction	Bacterial meningitis, tuberculous meningitis, syphilitic meningitis, Lyme disease, viral meningitis and encephalitis, AIDS, leptomeningeal metastases
CT brain scan or MRI	Cerebral infarction, intracranial hemorrhage, head trauma, toxoplasmosis, herpes simplex encephalitis, subarachnoid hemorrhage
EEG	Complex partial seizures, herpes simplex encephalitis, nonconvulsive seizures

Table 1–7. Laboratory studies in dementia.

Test	Most Useful in Diagnosis of
Blood	
Hematocrit, mean corpuscular volume (MCV), peripheral blood smear, vitamin B_{12} level	Vitamin B_{12} deficiency
Thyroid function tests	Hypothyroidism
Liver function tests	Acquired hepatocerebral degeneration, Wilson's disease
Ceruloplasmin, copper	Wilson's disease
FTA or MHA-TP	Neurosyphilis
HIV antibody titer	AIDS dementia complex
Cerebrospinal fluid	
VDRL	Neurosyphilis
Cytology	Leptomeningeal metastases
CT scan or MRI	Brain tumor, chronic subdural hematoma, multi-infarct dementia, normal pressure hydrocephalus
EEG	Creutzfeldt-Jakob disease

and pH, serum sodium, serum glucose, serum urea nitrogen and creatinine, liver function tests, drug screens, stool test for occult blood, lumbar puncture, brain CT scan or MRI, and electroencephalogram (EEG).

Some of these studies can yield a specific diagnosis. Abnormal arterial blood gas or CSF profiles, for example, narrow the differential diagnosis to one or a few possibilities (Tables 1–8 and 1–9).

Reversible dementia may be diagnosed on the basis of laboratory studies (see Table 1–7). The most common reversible dementias are those due to intracranial masses, normal pressure hydrocephalus, thyroid dysfunction, and vitamin B_{12} deficiency.

Table 1–8. Arterial blood gases in acute confusional states.

Pattern	Differential Diagnosis
Metabolic acidosis (with increased anion gap)	Diabetic ketoacidosis, lactic acidosis (postictal, shock, sepsis), toxins (methanol, ethylene glycol, salicylates,[1] paraldehyde), uremia
Respiratory alkalosis	Hepatic encephalopathy, pulmonary insufficiency, salicylates,[1] sepsis
Respiratory acidosis	Pulmonary insufficiency, sedative drug overdose

[1]Salicylates produce a combined acid-base disorder.

Table 1–9. Cerebrospinal fluid profiles in acute confusional states.

	Appearance	Opening Pressure	Red Blood Cells	White Blood Cells	Glucose	Protein	Glutamine	Smears	Cultures
Normal	Clear, colorless	70–200 mm H_2O	0/μL	≤5 mononuclear/μL	≥45 mg/dL	≤45[1] mg/dL	<25 μg/dL	–	–
Bacterial meningitis	Cloudy	↑	Normal	↑↑ (PMN)[2]	↓↓	↑↑	Normal	Gram's stain +	+
Tuberculous meningitis	Normal or cloudy	↑	Normal	↑ (MN)[3,5]	↓	↑	Normal	AFB stain +	±
Fungal meningitis	Normal or cloudy	Normal or ↑	Normal	↑ (MN)	↓	↑	Normal	India ink prep + (*Cryptococcus*)	±
Viral meningitis/ encephalitis	Normal	Normal or ↑	Normal[4]	↑ (MN)[5]	Normal[6]	Normal or ↑	Normal	–	±
Parasitic meningitis/ encephalitis	Normal or cloudy	Normal or ↑	Normal	↑ (MN,E)[7]	Normal	Normal or ↑	Normal	Amebas may be seen on wet mount	±
Leptomeningeal metastases	Normal or cloudy	Normal or ↑	Normal	Normal or ↑ (MN)	↓↓	Normal or ↑	Normal	Cytology +	–
Subarachnoid hemorrhage	Pink-red (supernatant yellow)	↑	↑	Normal or ↑ (PMN)[8]	Normal or ↓[8]	↑	Normal	–	–
Hepatic encephalopathy	Normal	Normal	Normal	Normal	Normal	Normal	↑	–	–

[1]Lumbar cerebrospinal fluid.
[2]PMN, polymorphonuclear predominance.
[3]MN, mononuclear (lymphocytic or monocytic) predominance.
[4]Red blood cell count may be elevated in herpes simplex encephalitis.
[5]PMN predominance may be seen early in course.
[6]Glucose may be decreased in herpes or mumps infections.
[7]E, eosinophils often present.
[8]Pleocytosis and low glucose, sometimes seen several days after hemorrhage, reflect chemical meningitis caused by subarachnoid blood.
+, positive; –, negative; ±, can be positive or negative.

II. ACUTE CONFUSIONAL STATES

The common causes of acute confusional states are listed in Table 1–10.

DRUGS

Many drugs can cause acute confusional states, especially when taken in greater than customary doses, in combination with other drugs, by patients with altered drug metabolism from hepatic or renal failure, by the elderly, or in the setting of preexisting cognitive impairment. A partial list of drugs that can produce acute confusional states is provided in Table 1–11. Classes of drugs that are most commonly abused or employed in suicide attempts are discussed individually below.

ETHANOL INTOXICATION

Clinical Findings

Ethanol intoxication produces a confusional state that may be associated with nystagmus, dysarthria, and limb and gait ataxia. In nonalcoholics, although the severity and clinical features of encephalopathy correlate roughly with blood ethanol levels, clinical manifestations decline over hours despite a stable blood ethanol level. Chronic alcoholics, who have

Table 1–10. Common causes of acute confusional states.

Metabolic Disorders
Drugs[1]
Ethanol intoxication
Ethanol withdrawal
Sedative drug intoxication
Sedative drug withdrawal
Opioids
Anticholinergics
Sympathomimetics
Hallucinogens
Endocrine disorders
Hypothyroidism
Hyperthyroidism
Hypoglycemia
Hyperglycemia
Electrolyte disorders
Hyponatremia
Hypocalcemia
Hypercalcemia
Nutritional disorders
Wernicke's encephalopathy
Vitamin B_{12} deficiency
Organ system failure
Hepatic encephalopathy
Reye's syndrome
Uremia
Dialysis disequilibrium
Pulmonary encephalopathy
Organ transplantation
Infectious and Noninfectious Meningitis/Encephalitis
Bacterial meningitis
Tuberculous meningitis
Syphilitic meningitis
Viral meningoencephalitis
Herpes simplex virus encephalitis
AIDS
Fungal meningitis
Parasitic infections
Leptomeningeal metastases
Vascular Disorders
Hypertensive encephalopathy
Subarachnoid hemorrhage
Vertebrobasilar ischemia
Right (nondominant) hemisphere infarction
Systemic lupus erythematosus
Disseminated intravascular coagulation
Thrombotic thrombocytopenic purpura
Head Trauma
Concussion
Intracranial hemorrhage
Seizures
Postictal state
Complex partial seizure

[1]See also Table 1–11.

Table 1–11. Therapeutic drugs associated with acute confusional states.

Acyclovir	Disulfiram
Amantadine	Ergot alkaloids
Aminocaproic acid	Ethanol
Amphetamines	Ganciclovir
Anticholinergics	Hallucinogens
Anticonvulsants	Isoniazid
Antidepressants	Ketamine
Antihistamines (H_1 and H_2)	Levodopa
Antipsychotics	Lidocaine
L-Asparaginase	Methylphenidate
Baclofen	Methylxanthines
Barbiturates	Nonsteroidal antiinflammatory drugs
Benzodiazepines	Opioids
Beta-adrenergic receptor antagonists	Penicillin
Cephalosporins	Phenylpropanolamine
Chloroquine	Quinacrine
Clonidine	Quinidine
Cocaine	Quinine
Corticosteroids	Salicylates
Cycloserine	Selegiline
Cyclosporine	Thyroid hormones
Digitalis glycosides	

developed a tolerance to ethanol, may have very high levels without appearing intoxicated. Laboratory studies useful in confirming the diagnosis include blood alcohol levels and serum osmolality. In alcohol intoxication, serum osmolality determined by direct measurement exceeds the calculated osmolality (2 × serum sodium + 1/20 serum glucose + 1/3 serum urea nitrogen) by 22 mosm/L for every 100 mg/dL of ethanol present.

The clinical picture of ethanol intoxication is mimicked by intoxication with any sedative drug but can often be differentiated by the history, the odor of alcohol on the breath, or toxicologic blood and urine analysis. Moreover, sedative drugs do not increase serum osmolality.

Complications

Intoxicated patients are at high risk for head trauma. Alcohol ingestion may cause life-threatening hypoglycemia, and chronic alcoholism is associated with an increased incidence of bacterial meningitis. These possibilities must be investigated.

Treatment

Treatment is generally not required unless a withdrawal syndrome ensues (see below). Alcoholic patients should, however, receive thiamine to prevent Wernicke's encephalopathy (see below).

ETHANOL WITHDRAWAL

Three common withdrawal syndromes are recognized (Figure 1–3). Because of the associated risk of Wernicke's encephalopathy (discussed later), patients presenting with these syndromes should be given thiamine, 100 mg/d, intravenously or intramuscularly, until a normal diet can be ensured.

1. TREMULOUSNESS & HALLUCINATIONS

This benign, self-limited condition occurs within 2 days after cessation of drinking. It is characterized by