9

Neurologic Disorders

■ I. BRAIN DEATH

A. Definition. Traditionally, death has been defined as the absence of spontaneous respirations and spontaneous pulse. A more contemporary definition of death includes the concept of *brain death,* defined as the permanent cessation of all brain function. This concept has evolved coincident with the increasing use of transplantation and, thus, is an important concept for the critical care practitioner to master.

B. Legal Status of Brain Death. In the United States, the concept of brain death and criteria for its diagnosis has been codified in the vast majority of states. Physicians operating outside of areas with specific legislation on brain death often rely on common law for legal certification of death, but the judicial acceptance of the brain death concept is universal in the United States.

C. Determination of Brain Death. Specific requirements for determination of brain death vary from institution to institution. In most institutions, specific sets of criteria are established. The recognition of irreversibility in most instances requires that the cause of the coma be established and be sufficient to account for the loss of brain function observed. For example, when drugs or toxins have been implicated, blood levels of these agents must be absent or below therapeutic levels before the determination of brain death by clinical examination.
   1. Clinical Determination of Brain Death
      a. A common checklist for the diagnosis of brain death is depicted in Table 9.1.
      b. The specific brain stem functions tested vary from site to site, but every institutional protocol includes a number of simple bedside tests demonstrating the absence of brain stem function. One such example is the cold water caloric test (Table 9.2).
      c. In most institutions, two clinical observers must concur with diagnosis of brain death and so note in the patient's chart.
      d. The final component of the clinical evaluation of brain death is usually the apnea test (Table 9.3).

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Table 9.1. Clinical Determination of Brain Death

A. Coma of established cause
- Temperature ≥32°C
- Absence of significant central nervous system depressants or significant metabolic disturbances
- Patient not in shock

B. Absence of spontaneous movements, decerebrate or decorticate posturing

C. Absence of brain stem responses
- Pupils fixed
- Corneal reflex absent
- Unresponsiveness to pain in the distribution of the cranial nerves (i.e., supraorbital pressure)
- Absence of cough or gag reflex
- Absence of "doll's eyes"
- No eye movement with cold water (caloric test) bilaterally

D. Absence of respiratory activity for at least 3 min (See apnea test)

Table 9.2. Cold Water Caloric Test

A. Elevate patient's head at 30-degree angle

B. Inject 50 mL of ice water into each external ear canal using an IV catheter (after determination that the ear canal is free of cerumen). The patient should be observed for several minutes for the presence of eye movements

Table 9.3. The Apnea Test

1. Oxygenate with 100% FiO_2 for 5–10 min before the test
2. Keep O_2 at 4–8 L/min delivered through a cannula in the endotracheal tube while the patient is disconnected from the ventilator.* (If hypotension and/or dysrhythmias develop, immediately reconnect to the ventilator. Consider other confirmatory tests.)
3. Observe for spontaneous respirations
4. After 10 min, obtain ABG. Patient is apneic if PCO_2 ≥60 torr (mmHg) and there are no respiratory movements

* In patients with COPD, the PaO_2 must be <50 torr at the end of the apnea test.
Abbreviations: ABG, arterial blood gas; COPD, chronic obstructive pulmonary disease; FiO_2, fraction of inspired O_2; PaO_2, partial pressure of O_2 in arterial blood PCO_2, partial pressure of CO_2 in arterial blood.

e. Ancillary Tests for Brain Death: Other tests used in determining brain death include the following:
   (1). Electroencephalogram (EEG): An isoelectric EEG is not required as a criterion for brain death in most institutions. However, it may be used as a confirmatory test.

(2). Cerebral Angiography: In the presence of toxic substances or sedative agents, the irreversibility of coma may not be determined clinically. The four-vessel cerebral angiogram may be used to determine the absence of brain blood flow; and thus, the irreversible nature of coma, confirming the diagnosis of brain death.

(3). Cerebral Radionuclide Studies: Technetium 99 (T^{99}) nuclear imaging studies of the cerebral circulation have been used in some centers as corroborative tests in determination of brain death. This procedure is not as sensitive for cerebral blood flow as four-vessel arteriography in determination of brain death.

f. The patient who is brain dead is *DEAD*. The physician does not require any permission of the family or other individuals to remove a dead patient from mechanical ventilation or other life support maneuvers.

■ II. COMA

A. Definition. *Coma* is a term denoting neurologic unresponsiveness. It represents part of a continuum from normal functioning to the absence of neurologic functioning with intermediate states of drowsiness and stupor. Consciousness is separated into two components: level of arousal and the content of consciousness.

1. Level of Arousal
   Level of arousal depends upon the interaction between the reticular activating system of the brain stem and the cerebral hemispheres bilaterally.
2. Content of Consciousness Exists Within the Cerebrum. These two components—content and consciousness—may be affected individually. For example, *dyskinetic mutism* is a term applied to patients who appear awake (with open eyes, which, on occasion, may even track movements within the room) but have an absence of the content of consciousness. An individual who suffers basilar artery occlusion may develop the "locked-in" syndrome. In this syndrome, the content of consciousness is preserved, but the ability to communicate directly with the environment is absent.

B. Etiology. Coma is a frequent cause of hospital admission. Common causes of coma are depicted in Table 9.4.

Table 9.4. Common Causes of Coma

— Cerebrovascular accidents
— Central nervous system (CNS) trauma
— CNS infections
— Drug intoxication
— Metabolic
— Metastatic or primary CNS neoplasia
— Systemic infection (sepsis)
— Unknown

C. Diagnosis
1. Careful History and Physical Examination
History should include information leading up to the discovery of the comatose patient. Pertinent points in the physical examination include evidence of head trauma (e.g., hemotympanum), cerebrospinal fluid (CSF) rhinorrhea, contusions, or lacerations. A complete neurologic examination looking for focal signs should be recorded.
2. Toxic-Metabolic Phenomena
Toxic-metabolic phenomena are found eventually to be responsible for the majority of patients with coma without obvious cause, and thus, evaluation for hypo- or hyperglycemia, hypo- or hypernatremia, renal failure, liver dysfunction with subsequent hepatic encephalopathy, and toxin ingestions as the cause of coma should be sought.
3. Computed Tomography (CT) Scan of the Head
Mass lesions, supratentorial or in the posterior fossa, may be found unexpectedly at CT scan and account for unconsciousness. Thus, all patients with coma of unknown etiology should have neuroimaging studies completed.
4. Lumbar Puncture
Patients without evidence of mass lesion should undergo CSF examination primarily to rule out infection. Specific diagnostic studies are noted in Table 9.5.

Table 9.5. CSF Studies in Patients With Coma of Unknown Etiology

— Tube I	Cell count with differential
— Tube II	Glucose, protein
— Tube III	Gram's stain, acid fast bacilli (AFB) stain, routine cultures, India ink or cryptococcal antigen, pneumococcal antigen, meningococcal antigen, VDRL
— Tube IV	Special studies as indicated (lactic acid, rheumatoid factor, etc.)

D. Treatment. Always remember the ABCs (airway, breathing, and circulation).
1. Comatose patients with absent airway-protective reflexes should undergo endotracheal intubation (with assisted mechanical ventilation in those patients with inadequate spontaneous ventilations).
   a. Circulation: Assessment of blood pressure and pulse rate to determine the adequacy of cardiovascular function.
2. Specific management is dictated by the clinical condition of the patient.
   a. The patient with an infectious source should be treated aggressively with intravenous (IV) antibiotics. Patients with mass lesions should be considered for early surgical intervention.
   b. Patients with toxic-metabolic events should receive appropriate therapy with close monitoring of electrolytes and/or drug levels.

c. Many clinicians recommend empiric therapy of the comatose patient with naloxone, a narcotic antagonist (2–8 mg IV), and dextrose (50 g IV push). However, some data suggest that high levels of glucose may be deleterious to injured neurons, and thus, with the advent of bedside glucose testing, many would advocate the determination of blood glucose before the administration of dextrose.
d. Flumazenil: A specific benzodiazepine antagonist is also available; however, in the absence of specific knowledge of benzodiazepine overdose, we do not recommend its administration because of its potential for seizures in patients with tricyclic antidepressant overdose.

3. Nonspecific Management
   a. Intravenous access for the administration of medications.
   b. Nasogastric (NG) decompression should be considered through an NG tube.
   c. A urinary catheter should be placed for urine monitoring and ease of nursing care for the comatose patient.
   d. Deep venous thrombosis prophylaxis should be administered to all patients in whom no contraindications exist (i.e., heparin 5,000 U SQ q12 h or low molecular weight heparin 0.5 mg/kg).
   e. Stress ulcer prophylaxis should be administered in every comatose patient (H_2-blockers, sucralfate, proton-pump inhibitors, etc.).
   f. Care and comfort measures (including lubrication of conjunctival spaces and eye taping).
   g. Passive range of motion of upper and lower extremities, for the prevention of contractures.
   h. Skin care (including frequent turning and positioning).

■ III. INTRACRANIAL HYPERTENSION

A. Physiology
   1. The contents of the cranial vault include the brain, CSF, and the cerebral blood volume. These contents are constrained by the skull itself.
   2. The brain is a highly metabolic organ and very dependent on continued blood supply.
   3. Because of the closed nature of the cranial vault, cerebral blood flow is dependent upon the difference between mean arterial pressure and intracranial pressure (ICP).

B. Etiology. A large number of intracranial processes may result in a rise in ICP and impairment of cerebral blood flow (see Table 9.6). These specific entities may require individualized therapy, and they are discussed in other sections of this book.

C. Management
   1. ABCs
   2. Positioning of the Patient
      A 30-degree head-up tilt is recommended for those patients who do not have a contraindication (i.e., hypotension).
   3. Hyperventilation

Table 9.6. Causes of Intracranial Hypertension

— Brain tumors
— Fulminant hepatic failure
— Head injury
— Meningitis and/or encephalitis
— Subarachnoid hemorrhage
— Vasculitis
— Other

The fastest way to control intracranial pressure is hyperventilation. Acute reductions in arterial PCO_2 result in vasoconstriction and decrease in intracranial blood volume. Specific PCO_2 values of approximately 25–35 torr (mmHg) are commonly advocated, although to our knowledge, no controlled studies have demonstrated the utility of these specific target values.

4. Osmotic Agents
   Mannitol, at doses of 0.25 g–1 g/kg of ideal body weight (IBW) intravenously over 10–20 min pulls water from the brain and results in a decrease in ICP. Plasma osmolality should be maintained below 340 mOsm/L. *Note:* The initial administration of mannitol may result in paradoxical increases in ICP; thus, many authors recommend prior therapy with a loop-acting diuretic (i.e., furosemide).
5. Anesthetics and Sedatives
   Barbiturates at first were popular because of their capacity to decrease brain metabolism and cerebral blood flow, thus lowering ICP. The therapeutic value of barbiturates is controversial, as its side effects may outweigh benefits (severe hypotension requiring vasopressors). Patients requiring mechanical ventilation require sedation; a good agent to use is Propofol. It is easily titrated, has a short half-life, permitting a frequent neurologic assessment.
6. Corticosteroids
   The only clear role of corticosteroids in the management of intracranial hypertension is in cerebral edema secondary to certain neoplasms. Their use in trauma, cerebrovascular accidents (CVAs), and metabolic causes has not been demonstrated to improve outcome and therefore cannot be routinely recommended.
7. CSF Drainage and ICP monitoring
   An intraventricular catheter may be placed percutaneously at the bedside and permit simultaneous monitoring and therapy of ICP. Sustained elevations of ICP >20 cmH_2O can be managed by withdrawal of CSF through the intraventricular catheter.
8. Positive End-Expiratory Pressure (PEEP)
   Some authors have advocated *not* using PEEP; however, in conditions in which this therapy is required (i.e., low lung compliance), routinely used levels of PEEP (3–7 cmH_2O) are not expected to impair cerebral blood drainage.
9. Therapeutic Hypothermia
   Although still no universally accepted and certainly not the standard of care, therapeutic hypothermia has been used with success in cases of intracranial

hypertension refractory to medical management. For further details about this technique please see Chapter 15, "Special Techniques".

■ IV. CEREBROVASCULAR DISEASE

A. Epidemiology. Approximately 700,000 people have a new or recurrent cerebrovascular disease each year. Stroke is still the third leading cause of death and leading cause of disability in the United States.

B. Classification. A number of different syndromes comprise the disorders labeled *cerebral vascular accidents (CVAs).* These disorders can be broadly grouped into two large categories: (1) those that produce vascular insufficiency (secondary to thrombosis, embolism, or stenosis leading to focal areas of ischemia) and (2) those that produce ruptures of the vascular tree, causing intracranial hypertension and secondary cerebral ischemia.

1. Vascular Insufficiency
   a. Transient Ischemic Attacks (TIAs): TIAs are defined as the sudden or rapid onset of neurologic deficits secondary to cerebral ischemia that lasts from a few minutes to up to 24 h without residual signs or symptoms. Atherosclerosis is the most frequent cause.
   b. Stroke
      (1). Definition: Stroke is the rapid onset of neurologic deficits involving a set vascular territory with neurologic signs and symptoms lasting >24 h.
      (2). Risk Factors: Similar to those for TIA. An increasing frequency of stroke related to vasospasm secondary to cocaine abuse has been noted in the last decade in the United States.
      (3). Classification of Stroke: Both thrombosis and embolism may result in vascular insufficiency and the phenomena of stroke. Clinically, the differentiation of thrombosis and embolism is quite difficult. However, some clinical characteristics of each are noted in Table 9.7.
      (4). Embolic Stroke: The most common causes of embolic stroke include emboli secondary to atrial fibrillation, valvular heart disease, bacterial and nonbacterial endocarditis, trauma, secondary to myocardial infarction or ventricular aneurysm, atrial myxoma, and paradoxical embolism secondary to endocardial disease.

Table 9.7. Clinical Characteristics of Embolic and Thrombotic Strokes

	Embolism	*Thrombosis*
Predisposing Factors	Valvular heart disease Endocarditis Myocardial infarction Atrial fibrillation	Atherosclerosis Diabetes Hypertension Arteritis
History of prior TIA	Uncommon	Common
Onset of symptoms	Rapid onset	Progression over hours

(a). Thrombotic Stroke: Occurs when a clot develops in a cerebral vessel. Intrinsic or extrinsic diseases of the cerebral vessels may contribute to thrombotic strokes. These include
  i. Arteriosclerosis.
  ii. Fibromuscular dysplasia.
  iii. Extension of embolism or dissection into cerebral arteries because of arteritis (Takayasu's disease, giant cell arteritis, and other vascular diseases).
  iv. Increased viscosity secondary to proteins or increased cellular elements (i.e., Waldenstrom's macroglobulinemia, leukemias with elevated blast counts, and erythrocytosis of any cause).
  v. TIAs are a risk factor for completed stroke, with the highest risk being in the first 3 months immediately following the onset of TIAs.

(5). Initial evaluation and the management of cerebral ischemic syndromes.
  (a). ABCs: Secure the airway and assist with breathing and circulation as with any other patient presenting with a potentially critical illness.
  (b). Careful Examination of the Patient: Emphasis should be on the neurologic examination to localize the area of deficits and on other areas of the physical examination to rule in or rule out secondary causes for the ischemic syndrome.
  (c). Laboratory Evaluation: Complete blood count, prothrombin time (PT), partial thromboplastin time (PTT), glucose, electrolytes, serum urea nitrogen (BUN), and creatinine are routinely ordered. Chest radiograph, ECG, and CT scan of the head should be done without delay (to rule out hemorrhage, infarction, subdural hematoma, or intracranial masses).
  (d). In any patient with new neurologic abnormalities, lumbar puncture should be considered to rule out infectious causes and for the completion of the evaluation for subarachnoid hemorrhage (after head CT scan has ruled out increased intracranial pressure).
  (e). Echocardiography: For patients with a history or physical examination suggestive of cardiac abnormality, echocardiography should be ordered.
  (f). Other useful studies may include duplex ultrasonography and cerebral angiography.

(6). In patients with embolic CVAs with progressively worsening neurologic deficits (stroke in evolution), anticoagulation, beginning with heparin, is recommended. In addition, heparin is commonly prescribed for patients with recurrent TIAs despite antiplatelet therapy. *Note:* Anticoagulation should be started (with heparin) in patients with worsening neurologic deficits (stroke in evolution or suspected embolic source). Anticoagulation is contraindicated in patients with CT or LP evidence of hemorrhage, and it is relatively contraindicated in patients with gastrointestinal (GI) bleeding or coagulation disorders and in patients with hypertension.

(7). Blood Pressure Control: Therapy to maintain systemic blood pressure at approximately 150/100 mmHg is advocated. Caution must be exercised, as reductions in blood pressure may worsen the clinical condition by producing ischemia in poorly perfused regions of the central nervous system (CNS).

(a). Thrombolytic therapy for ischemic stroke is now the standard of care. Intravenous recombinant tissue plasminogen activator (rtPA) is the only FDA-approved medical therapy proven to reduce the effects of an ischemic stroke. The best results from rtPA are seen when given within 3 h of onset of symptoms.

2. Rupture of the Vascular Tree
   a. Subarachnoid hemorrhage (SAH) accounts for about 10% of all strokes and 16–20% of cerebral vascular deficits. The etiology of SAH includes ruptured aneurysms of cerebral vessels, bleeding from arteriovenous malformations of the CNS, and trauma.
      (1). Clinical Manifestations
         (a). Neurologic deficits may include focal neurologic signs as well as coma.
         (b). Generalized excruciating headache with neck stiffness is classically described.
      (2). Evaluation and Management
         (a). ABCs, as noted previously.
         (b). CT scan of the head demonstrating subarachnoid blood is seen in approximately 90% of the cases.
         (c). Lumbar puncture should be performed in those patients whose CT scan is negative and for whom clinical suspicion of SAH is still high.
         (d). The patient should be kept at bed rest. Cardiac monitoring and frequent (q1–2 h) neurologic assessments should be ordered.
         (e). Analgesia for headache should be prescribed (acetaminophen and codeine are commonly used).
         (f). Glycemic control is desired in patients with ICH; hyperglycemia may worsen brain injury. It is recommended to treat with insulin patients who reach blood sugar levels >145 mg/dL.
         (g). Stool softeners and mild laxatives should be prescribed to prevent constipation (and thus increased ICP).
         (h). Blood pressure control: Keep blood pressure in ranges that maintain CPP >60 mmHg (CPP = MAP–ICP). If needed, an antihypertensive agent may be used; intravenous labetalol, intravenous nicardipine, or intravenous clevidipine are the drugs of choice in this clinical setting.
         (i). Surgical management: With the evolution of microsurgical techniques the surgical management of cerebral aneurysms is an effective and safe procedure.
         (j). Endovascular therapy: Intraluminal approach (using platinum coils) is an effective alternative to surgical clipping. A coil is inserted into the lumen of the aneurysm, a local thrombus then forms around the coil, obliterating the aneurysmal sac.
   b. Intracerebral Hemorrhage: Intracerebral hemorrhage commonly occurs following trauma. When it occurs spontaneously, it is frequently accompanied by hypertension. Neurologic abnormalities, as seen in other types of strokes, are usually present, and the specific diagnosis requires neuroimaging studies.
      (1). Management
         (a). ABCs, as required for every critically ill patient.
         (b). Control severe hypertension: As noted above, cerebral ischemia may occur with reductions in blood pressure. However, control of hypertension may reduce cerebral edema and improve neurologic function.

(c). Additional management of intracranial hypertension as noted above may be required.
(d). Supportive therapy as required for all intensive care unit (ICU) patients should continue.
(e). Activated recombinant factor VIIa has been used by some centers for expanding hematomas. The data of large trials, however, has mixed results.

c. Surgical evacuation of the hematoma should occur in patients with accessible lesions, who have progressive signs of deterioration.

■ V. STATUS EPILEPTICUS

A. Definition. Status epilepticus is defined as seizure activity continuing for 5 or 10 min or frequent clinical seizures without an interictal return to the baseline clinical state. It is a condition that may lead to permanent neurologic damage or even death.

B. General Approach. The management of seizure disorders is based on clinical information.
1. Most seizures stop spontaneously within 30–90 s.
2. The diagnosis of status epilepticus is straightforward and can be determined through observation of the patient in most cases.
3. Generalized seizure disorders without motor findings may lead to changes in mental status or coma and may not be clinically apparent, and thus further diagnostic testing (i.e., EEG) may be required.
4. Continued seizure disorders may result in enzyme elevation (creatine kinase [CK]), making the diagnosis of other clinical conditions more difficult (i.e., myocardial infarction).

C. Specific Management
1. ABCs: As in all critically ill patients, airway, breathing, and circulation must be maintained. Patients should be positioned so they cannot harm themselves from their motor activity. Oxygen should be administered, and continuous observation of the patient should ensue.
2. Blood glucose, calcium, magnesium, and other electrolytes, as well as BUN, liver functions, anticonvulsant levels, complete blood count, and toxicologic screen should be obtained.
3. A normal saline infusion should be established, and 50 cc of 50% glucose and 100 mg of thiamine should be administered intravenously.
4. ECG and blood pressure monitoring should be established.
5. Diazepam (Valium) is the first-line agent, 5 mg over 1–2 min IV, repeated every 5–10 min, or lorazepam (Ativan) 2–4 q5 min can be administered in those patients continuing to seize.
6. Reoccurrence of seizures within 15–20 min following administration of benzodiazepines is quite frequent, and other antiepileptic agents should be instituted. Phenytoin is used because of its proven efficacy in preventing the frequency of seizures given IV, at a dose of 20 mg/kg and a rate of 50 mg/min, should be administered as a loading dose for patients not previously receiving phenytoin. If dysrhythmias and/or hypotension ensue, the infusion

should be stopped and resumed at a slower rate. Phosphenytoin is another alternative.

7. Persistent seizures following phenytoin administration should result in administration of phenobarbital IV at rates of 50–100 mg/min until the seizure stops or until a loading dose of 20 mg/kg IBW total has been given.
8. Continued seizures should prompt the administration of other medications: Intravenous propofol (5–30 cc/h) has been used in some cases of refractory seizures with success. Valproic acid has also been used with success, at a dose of 10 mg/kg at a rate of 20 mg/min. In some cases, therapeutic hypothermia has been used for intractable status epilepticus.
9. EEG monitoring is appropriate for patients receiving general anesthetic control of status epilepticus. Continuous EEG monitoring is also granted for patients in whom the initial EEG is not diagnostic.
10. Review of laboratory data and additional history and physical examination for underlying disorders that may have resulted in the status epilepticus should be undertaken. Mainstay of treatment is the identification and correction of predisposing factors.
    a. Antiepileptic drug non-compliance
    b. Withdrawal syndromes (alcohol, barbiturates, baclofen, benzodiazepines)
    c. Acute structural injury
    d. Metabolic abnormalities (hypoglycemia, hepatic encephalopathy, uremia, etc.)
    e. Use or overdose of drugs that lower seizure threshold (theophylline, imipenem, tricyclic antidepressants, lithium, clozapine, flumazenil, lidocaine)
11. Following control of the status epilepticus, careful physical and laboratory evaluation for underlying disease processes should ensue. Patients without a clear etiology should undergo head CT scan and lumbar puncture unless contraindicated.
12. Continuous motor seizures may lead to muscle breakdown and thus release of myoglobin and other intracellular components into the circulation. One must be concerned about maintenance of adequate hydration as well as protection from pigment-induced renal failure. (See Chapter 14, "Renal and Fluid-Electrolyte Disorders.")

■ VI. NEUROMUSCULAR DISORDERS

A. Guillain-Barré Syndrome (GBS)

1. Definition. GBS is an acute immune demyelinating disorder of the peripheral nervous system that results in motor and sensory symptoms with few sensory signs. In the vast majority of cases, it results in complete recovery. However, in up to 25% of patients, respiratory failure due to weakness of the respiratory muscles ensues and mechanical ventilation is required for a period of time. Peaks of occurrence are in the 15- to 35- and 50- to 75-year-old age groups.
2. Clinical Manifestations. GBS presents in a typical pattern. The usual history is that of a patient with a normal previous health status interrupted by a mild upper respiratory or GI illness followed by ascending weakness and numbness.

Table 9.8. Major Clinical Manifestations of Guillain-Barré Syndrome

— Distal paresthesias (initially lower extremities)
— Rapidly progressive motor weakness (ascending neuropathy)
— Symmetry is seldom absolute
— Facial weakness is common (one-third of cases)
— Recovery usually begins 2–4 weeks after progression stops
— Sinus tachycardia and labile blood pressure are common
— CSF protein elevation (after the first week)
— Nerve conduction abnormalities are detectable

Other factors include recent vaccination or surgery. Major clinical manifestations are depicted in Table 9.8. Atypical presentations may include a descending paralysis.

3. Diagnostic Evaluation
   a. Careful physical examination should be performed, attempting to rule out other causes of neuropathology (spinal cord lesions, infection, metabolic or toxic, etc.).
   b. Lumbar puncture usually reveals elevated protein. There are usually few mononuclear leukocytes in the CSF with lymphocyte counts <10/cc.
   c. Eighty percent of all patients show slow nerve conduction.
4. Management
   a. ABCs.
   b. Supportive measures; close monitoring of respiratory function with frequent measurements of the vital capacity and/or negative inspiratory force (NIF) are indicated.
   c. A vital capacity of <20 mL/kg is an indication to consider intubation and assisted mechanical ventilatory support.
   d. Active and passive range of motion of lower and upper extremities should be performed to prevent the formation of contractures.
   e. Bladder and bowel care should be done as many of these patients develop adynamic ileus and urinary retention.
   f. Decubitus ulcer prevention and care should be instituted.
   g. Prevention of thromboembolism with appropriate therapy (i.e., fractionated or unfractionated heparin and support stockings).
   h. Plasma exchange presumably removes or dilutes circulating factors implicated in the pathogenesis of GBS. It has been shown to decrease ventilatory dependence and earlier recovery in GBS.
   i. Intravenous immunoglobin (IVIG) is as effective as plasma exchange in GBS.
   j. Corticosteroids have not been proven to be of value in this syndrome.

B. Other Chronic Neurologic Disorders
   1. A number of chronic progressive neurologic disorders may result in patient admission to the ICU for physiologic support. These include amyotrophic lateral sclerosis, multiple sclerosis, severe Parkinson's disease, etc. Many of these patients are admitted because of their need for aggressive tracheobronchial toilet or mechanical ventilation.

2. Major concerns in managing these patients involve the decision to institute aggressive therapy. It is preferable that these decisions be addressed with the patient and their family before the need for these services, so that unwanted supportive measures are not forced upon them.

■ VII. DELIRIUM IN THE ICU

A. Epidemiology. Ten percent of medical and surgical patients become delirious during their hospitalization. These patients are at risk for harm to themselves (by the discontinuation of an IV line, arterial line, NG tubes, etc.) and others. Patients who develop delirium are at greater risk of mortality. Patients at high risk for the development of delirium are
   1. Those at the extremes of age (elderly and children)
   2. Patients with preexisting brain injury
   3. Drug-dependent patients or poly-pharmacy
   4. Postcardiotomy patients
   5. Patients with human immunodeficiency virus (HIV) disease

B. Clinical Features
   1. A prodromal state manifested by restlessness, irritability, anxiety, or sleep difficulty.
   2. A rapidly fluctuating course. Patients are intermittently clear thinking and coherent or grossly confused, disoriented, and disorganized.
   3. Reversed sleep-wake cycles and increased activity and confusion during the nighttime h.

C. Evaluation and Management
   1. ABCs, as required for all patients with a critical illness.
   2. Careful attention to metabolic problems that may produce CNS disturbances should be sought.
   3. Laboratories including blood glucose, electrolytes, calcium, BUN, and liver function tests should be obtained as well as arterial blood gases or pulse oximetry to rule out hypoxemia (a common cause of mental status change in the ICU).
   4. ECG should also be obtained to help rule out myocardial ischemia.
   5. For delirium assessment, the use of Confusion Assessment Method (CAM) is useful as a screening tool. The modified version CAM-ICU is helpful screening tool in patients that are mechanically ventilated and unable to communicate verbally.
   6. Patients with unexplained mental status changes should receive CT scanning or magnetic resonance imaging of the brain followed by lumbar puncture to rule out infectious or other causes.
   7. Careful review of the medications prescribed for the patient should be undertaken. Drugs commonly associated with delirium are depicted in Table 9.9.
   8. Whether or not the etiology is known, some simple interventions that may help control the patient's confusion and behavior are often missed. For example, if the patient normally wears eyeglasses or a hearing aid, return these items. The old practice of placing delirious patients together is not helpful, and indeed, it may increase the aggressive behavior of both patients, thus, making orientation

Table 9.9. Drugs Commonly Associated With Delirium

Analgesics (e.g., morphine)
Antibiotics (e.g., aminoglycosides)
Antivirals (e.g., amantadine, acyclovir)
Anticholinergics (e.g., atropine)
Anticonvulsants (e.g., phenytoin)
Anti-inflammatory agents (e.g., corticosteroids, nonsteroidal anti-inflammatory drugs)
Antineoplastic drugs
Cardiac drugs (e.g., beta-blockers, angiotensin-converting enzyme inhibitors)
Drug withdrawal (e.g., ethanol, benzodiazepines)
Sympathicomimetics (e.g., amphetamines, cocaine)
Miscellaneous (e.g., disulfiram, lithium)
Herbal preparations (e.g., *Atropa belladonna* extract, Jimson weed, St. John's wort, valerian)

almost impossible. Physical restraints should be used as a last resort, if at all; they frequently increase agitation and may cause physical harm to the patients.

9. Haloperidol (Haldol) is a highly potent antipsychotic agent that effectively calms agitation, sedates, and reduces hallucinations and paranoid thinking. For the patient with a mild level of delirium or agitation, a starting dose of 0.5–2 mg IV or IM is usually enough. However, for patients with severe agitation, a starting dose of 5–10 mg may be necessary. An interval of 20–30 min should be allowed between doses. After giving three doses of haloperidol with no improvement in symptomatology, give 1–2 mg IV lorazepam (Ativan) concurrently, or alternate with haloperidol every 30 min. Assuming the patient is calm, reduce the dose by 15% every 24 h. *Note:* Haloperidol is not approved for IV use despite its common use for this indication. Large IV doses have been used in critically ill patients without evident harm or side effects. Doses as high as 100 mg IV bolus have been given to medically ill patients without evidence of respiratory depression.
10. Delirium should prompt neuropsychiatric consultation for recommendations in evaluation and therapy.

■ VIII. USEFUL FACTS AND FORMULAS

A. **Cerebrospinal Fluid (CSF).** Normal pressures and volumes for human CSF are shown in Table 9.10.
The normal composition of the CSF is depicted in Table 9.11.
Additional normal values for CSF in humans are depicted in Table 9.12.

Table 9.10. Normal CSF Pressures and Volumes

CSF pressure	
Children	3.0–7.5 mmHg
Adults	3.5–13.5 mmHg
Volume	
Infants	40–60 mL
Young children	60–100 mL
Older children	80–120 mL
Adult	100–160 mL

Table 9.11. Normal Composition of the CSF

	CSF Concentration (mean)
Specific gravity	1.007
Osmolality (mOsm/kg H_2O)	289
PH	7.31
PCO_2 (mmHg)	50.5
Na^+ (mEq/L)	141
K^+ (mEq/L)	2.9
Ca^{++} (mEq/L)	2.5
Mg^{++} (mEq/L)	2.4
Cl_- (mEq/L)	124
Glucose (mg/dL)	61
Protein (mg/dL)	28

Table 9.12. Normal CSF Values

CSF parameter	*Newborns*	*Infants, older children, and adults*
Leukocyte count	<32/μL	<6/μL
Differential white cell count	<60% polymorphs	<1 polymorph
Proteins	<170 mg/dL	<45 mg/dL
Glucose	>30 mg/dL	>45 mg/dL
CSF: blood/glucose ratio	>0.44	>0.5

Table 9.13. CSF Abnormalities in Multiple Sclerosis

	Alb	*IgG/TP*	*IgG/Alb*	*IgG index*	*Oligoclonal banding of Ig*
Multiple sclerosis	25%	67%	60–73%	70–90%	85–95%
Normal subjects	3%	—	3–6%	3%	0–7%

Abbreviations: Alb, albumin; IgG/TP, IgG value/total protein; Ig, immunoglobulin.

When there are many red blood cells (RBCs) or white blood cells (WBCs) in the CSF, the total protein of the CSF may be *corrected* utilizing the following formula: Protein actual

$$= \text{Protein CSF} - \frac{\text{Protein}_{\text{serum}} \times (1 - \text{Hct}) \times \text{RBC}_{\text{CSF}}}{\text{RBC}_{\text{blood}}}$$

Common CSF abnormalities in patients with multiple sclerosis are depicted in Table 9.13.
The abnormalities in immunoglobulin G (IgG) production in these patients can be estimated by the *Ig G index:*

$$\text{Ig G index} = \frac{\text{CSF IgG/CSF albumin}}{\text{Serum IgG/serum albumin}} = \text{normal} < 0.66$$

B. **Cerebral Blood Flow**. The cerebral circulation follows the same physiological principles of other circulatory beds, such as *Ohm's law:*

$$F = \frac{P_i - P_o}{R}$$

where F = flow; P_i = input pressure; P_o = outflow pressure; R = resistance. The term "$P_i - P_o$" is referred to as the *cerebral perfusion pressure (CPP).*

The CPP can be estimated by the following formula:

$$\text{CPP} = \text{MAP} - \text{ICP}$$

where MAP = mean arterial pressure; ICP = intracranial pressure.

The *pressure-volume index (PVI)* can be calculated as follows:

$$\text{PVI} = \Delta V/[\log P_p/P_o]$$

where P_p = Peak CSF pressure (increase after volume injection and decrease after volume withdrawal).

The *cerebral blood flow (CQ)* is normally 50 mL/100 g/min and is determined by the *Hagen-Poiseuille equation* of flow through a tube:

$$CQ = \frac{(K \times Pr^4)}{(8L \times \eta)}$$

where P_p = cerebral perfusion pressure (CPP); r = the arterial radius; η = blood viscosity; L = arterial length; K = constant.

C. **Brain Metabolism**. *Oxygen availability to neural tissue (CDO_2)* is reflected in the formula:

$$CDO_2 = CQ \times PaO_2$$

where CQ = cerebral blood flow; PaO_2 = arterial oxygen concentration.

The *cerebral metabolic rate ($CMRO_2$)* can be calculated as follows:

$$CMRO_2 = CBF \times AVDO_2$$

where CBF = cerebral blood flow; $AVDO_2$ = arteriovenous oxygen content difference.

The *oxygen extraction ratio (OER)* can be utilized to assess the brain metabolism:

$$OER = SaO_2 - SjvO_2/SaO_2$$

where SaO_2 = arterial oxygen saturation; $SjvO_2$ = jugular venous oxygen saturation.

$$OER \times CaO_2 = CMRO_2/CBF$$

where

$$CaO_2 = (Hb \times 1.39 \times SaO_2) + [0.003 \times PO_2(mmHg)]$$

$$CMRO_2 = CBF \times (CaO_2 - CjvO_2)$$

The *arterial-jugular venous oxygen content difference ($AjvDO_2$)* is calculated as follows:

$$AjvDO_2 = CMRO_2/CBF$$