TABLE 328-1 DIFFERENTIAL DIAGNOSIS OF COMA

1. Diseases that cause no focal or lateralizing neurologic signs, usually with normal brainstem functions; CT scan and cellular content of the CSF are normal
   a. Intoxications: alcohol, sedative drugs, opiates, etc.
   b. Metabolic disturbances: anoxia, hyponatremia, hypernatremia, hypercalcemia, diabetic acidosis, nonketotic hyperosmolar hyperglycemia, hypoglycemia, uremia, hepatic coma, hypercarbia, Addisonian crisis, hypo- and hyperthyroid states, profound nutritional deficiency
   c. Severe systemic infections: pneumonia, septicemia, typhoid fever, malaria, Waterhouse-Friderichsen syndrome
   d. Shock from any cause
   e. Postseizure states, status epilepticus, nonconvulsive status epilepticus
   f. Hypertensive encephalopathy, eclampsia
   g. Severe hyperthermia, hypothermia
   h. Concussion
   i. Acute hydrocephalus
2. Diseases that cause meningeal irritation with or without fever, and with an excess of WBCs or RBCs in the CSF, usually without focal or lateralizing cerebral or brainstem signs; CT or MRI shows no mass lesion
   a. Subarachnoid hemorrhage from ruptured aneurysm, arteriovenous malformation, trauma
   b. Acute bacterial meningitis
   c. Viral encephalitis
   d. Miscellaneous: fat embolism, cholesterol embolism, carcinomatous and lymphomatous meningitis, etc.
3. Diseases that cause focal brainstem or lateralizing cerebral signs, with or without changes in the CSF; CT and MRI are abnormal
   a. Hemispheral hemorrhage (basal ganglionic, thalamic) or infarction (large middle cerebral artery territory) with secondary brainstem compression
   b. Brainstem infarction due to basilar artery thrombosis or embolism
   c. Brain abscess, subdural empyema
   d. Epidural and subdural hemorrhage, brain contusion
   e. Brain tumor with surrounding edema
   f. Cerebellar and pontine hemorrhage and infarction
   g. Widespread traumatic brain injury
   h. Metabolic coma (see above) with preexisting focal damage
   i. Miscellaneous: Cortical vein thrombosis, herpes simplex encephalitis, multiple cerebral emboli due to bacterial endocarditis, acute hemorrhagic leukoencephalitis, acute disseminated (postinfectious) encephalomyelitis, thrombotic thrombocytopenic purpura, cerebral vasculitis, gliomatosis cerebri, pituitary apoplexy, intravascular lymphoma, etc.

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; MRI, magnetic resonance imaging; RBCs, red blood cells; WBCs, white blood cells.

coma after sudden severe headache and vomiting). The most common stroke, infarction in the territory of the middle cerebral artery, does not cause coma, but edema surrounding large infarctions may expand over several days and cause coma from mass effect.

The syndrome of acute hydrocephalus accompanies many intracranial diseases, particularly subarachnoid hemorrhage. It is characterized by headache and sometimes vomiting that may progress quickly to coma with extensor posturing of the limbs, bilateral Babinski signs, small unreactive pupils, and impaired oculocephalic movements in the vertical direction.

The majority of medical causes of coma can be established without a neuroimaging study but if the history and examination do not indicate the cause of coma, CT or MRI is needed. Sometimes imaging results can be misleading such as when small subdural hematomas or old strokes are found, but the patient's coma is due to intoxication.

BRAIN DEATH

This is a state of irreversible cessation of all cerebral function with preservation of cardiac activity and maintenance of respiratory and somatic function by artificial means. It is the only type of brain damage recognized as equivalent to death. Criteria have been advanced for the diagnosis of brain death, and it is essential to adhere to standards endorsed by the local medical community. Ideal criteria are simple, can be assessed at the bedside, and allow no chance of diagnostic error. They contain three essential elements: (1) widespread cortical destruction that is reflected by deep coma and unresponsiveness to all forms of stimulation; (2) global brainstem damage demonstrated by absent pupillary light reaction and by the loss of oculovestibular and corneal reflexes; and (3) destruction of the medulla, manifested by complete and irreversible apnea. The heart rate is invariant and does not accelerate to atropine. Diabetes insipidus is usually present but may only develop hours or days after the other clinical signs of brain death. The pupils are usually midsized but may be enlarged; they should not, however, be small. Loss of deep tendon reflexes is not required because the spinal cord remains functional. Babinski signs are generally absent and the toe response is instead, often flexor.

Demonstration that apnea is due to structural medullary damage requires that the P_{CO_2} be high enough to stimulate respiration during a test of spontaneous breathing. Apnea testing can be done safely by the use of diffusion oxygenation prior to removing the ventilator. This is accomplished by preoxygenation with 100% oxygen, which is then sustained during the test by oxygen administered through a tracheal cannula. CO_2 tension increases ~0.3–0.4 kPa/min (2–3 mmHg/min) during apnea. At the end of a period of observation, typically several minutes, arterial P_{CO_2} should be at least >6.6–8.0 kPa (50–60 mmHg) for the test to be valid. Apnea is confirmed if no respiratory effort has been observed in the presence of a sufficiently elevated P_{CO_2}. Other techniques, including the administration of CO_2 to accelerate the test, are used in special circumstances. The apnea test is usually stopped if there is serious cardiovascular instability.

An isoelectric EEG may be used as a confirmatory test for total cerebral damage. Radionuclide brain scanning, cerebral angiography, or transcranial Doppler measurements may also be included to demonstrate the absence of CBF, but they have not been as extensively correlated with pathologic changes.

The possibility of profound drug-induced or hypothermic depression of the nervous system must be excluded, and some period of observation, usually 6–24 h, is desirable, during which the clinical signs of brain death are sustained. It is advisable to delay clinical testing for at least 24 h if a cardiac arrest has caused brain death or if the inciting disease is not known.

Although it is largely accepted in Western society that the respirator can be disconnected from a brain-dead patient and that organ donation is subsequently possible, problems frequently arise because of poor communication and inadequate preparation of the family by the physician. Reasonable medical practice, ideally with the agreement of the family, also allows the removal of support or transfer out of an intensive care unit of patients who are not brain dead but whose neurologic conditions are nonetheless hopeless.

TREATMENT COMA

The immediate goal in a comatose patient is prevention of further nervous system damage. Hypotension, hypoglycemia, hypercalcemia, hypoxia, hypercapnia, and hyperthermia should be corrected rapidly. An oropharyngeal airway is adequate to keep the pharynx open in a drowsy patient who is breathing normally. Tracheal intubation is indicated if there is apnea, upper airway obstruction, hypoventilation, or emesis, or if the patient is liable to aspirate because of coma. Mechanical ventilation is required if there is hypoventilation or a need to induce hypocapnia in order to lower ICP. IV access is established, and naloxone and dextrose are administered if narcotic overdose or hypoglycemia is a possibility; thiamine is given along with glucose to avoid provoking Wernicke's disease in malnourished patients. In cases of suspected basilar thrombosis with brainstem ischemia, IV heparin or a thrombolytic agent is often used, after cerebral hemorrhage has been excluded by a neuroimaging study. Physostigmine may awaken patients with anticholinergic-type drug overdose but should be used only with careful monitoring; many physicians believe that it should only be used to treat