

hippocampal hyperintensities on magnetic resonance imaging (MRI), suggests severe global damage and extensive ischemic injury and is highly indicative of poor outcome.

The use of therapeutic hypothermia quite likely influences the clinical examination and ancillary test findings. There is a scarcity of data about the utility of physical examination, EEG, and evoked potentials in predicting outcomes among cardiac arrest patients with induced hypothermia. It is well accepted that one should consider observation for longer than 72 hours before prognosticating outcome in patients treated with hypothermia.

COMA-LIKE STATES

Patients with *locked-in syndrome* have a lesion (usually a hemorrhage or an infarct) that transects the brainstem at a point below the reticular formation (thereby sparing consciousness) but above the ventilatory nuclei of the medulla (thereby maintaining cardiopulmonary function) (Table 105-4). Such patients are awake, with eye opening and sleep-wake cycles, but the descending pathways through the brainstem that are necessary for volitional vocalization or limb movement have been transected. Voluntary eye movement, especially vertically, is preserved, and patients can open and close their eyes or produce appropriate numbers of blinking movements in answer to questions. The EEG is usually normal, reflecting normal cortical function.

Psychogenic unresponsiveness is a diagnosis of exclusion. The neurologic examination shows reactive pupils and no reflex posturing in response to pain. Eye movements during the doll's eyes maneuver show volitional override rather than the smooth, uninhibited reflex lateral eye movements of coma. Ice water caloric testing either arouses the patient because of the discomfort produced or induces cortically mediated nystagmus rather than the tonic deviation typical of coma. The slow, conjugate roving eye movements of metabolic coma cannot be imitated and therefore rule out psychogenic unresponsiveness. Likewise, the slow, often asymmetrical, and incomplete eye closure seen after passive eye opening in a comatose patient cannot be feigned and also rules out psychogenic coma. In contrast, conscious patients usually exhibit some voluntary muscle tone in the eyelids during passive eye opening. The EEG in psychogenic unresponsiveness is that of normal wakefulness, with reactive posterior rhythms on eye opening and eye closing. In patients with catatonic stupor, lorazepam administration may produce awakening.

The vegetative state (VS), now also called *unresponsive wakefulness syndrome*, is exhibited by patients with eye opening and sleep-wake cycles. The reticular activating system of the brainstem is intact to produce wakefulness, but the connections to the cortical mantle are interrupted, precluding awareness.

A VS is termed *persistent* after 3 months if the brain injury was medical or after 12 months if the brain injury was traumatic. The determination as to when *persistent* equals *permanent* cannot be stated absolutely. Prediction early in VS of which patients will remain persistently vegetative is particularly difficult in cases of trauma. Lesions of the corpus callosum and dorsolateral brainstem seen on MRI 6 to 8 weeks after trauma correlated with persistence of VS at 1 year. A combined analysis of morphologic MRI studies and post-traumatic brainstem spectroscopy can be a predictor of persistent vegetative states (PVS) and minimally conscious states (MVS). In rare cases, patients show late improvement, but they do not return to normal. Bilateral absence of SSEPs in the first week predicts death or VS.

Patients in a PVS open their eyes diurnally and in response to loud sounds; blinking occurs with bright lights. Pupils react, and eye movements occur both spontaneously and with the doll's eyes maneuver. Yawning, chewing, swallowing, and, uncommonly, guttural vocalizations and lacrimation may be preserved. Spontaneous roving eye movements (very slow, with constant velocity) are particularly characteristic and distressing to the patient's visitors because the patient appears to be looking about the room. The brainstem origin of the eye movements is documented by their being readily redirected by the oculocephalic (doll's eyes) reflex. The limbs may move, but motor responses are only primitive; pain usually produces decorticate or decerebrate postures or fragments of these movements.

MCS is a newly described entity in which patients do not meet criteria for PVS. Both patients in PVS and those in MCS demonstrate severe alteration in consciousness. In contrast to PVS, subjects with MCS exhibit evidence of limited interaction with the environment by visually tracking, following simple commands, answering yes or no (not necessarily reliably), or having intelligible verbalization or restricted purposeful behavior. It is estimated that the rate of misdiagnosis between the VS and MCS is about 40%.

Novel applications of functional neuroimaging in patients with disorders of consciousness may aid in differential diagnosis, prognostic assessment, and identification of pathophysiologic mechanisms. In one study, authors prospectively evaluated cortical activation in response to a familiar voice in seven patients in VS and four subjects in MCS. All four of the MCS patients and only two of the VS patients showed activation that extended beyond the primary auditory cortex to hierarchically higher-order associative temporal areas. Over the course of 3 months, these two VS patients improved clinically to MCS.

Brain death characterizes the *irreversible cessation* of brain function. Therefore, death of the organism can be determined based on death of the brain. Although local laws may dictate some details, the standard definition permits a diagnosis of brain death based on documentation of irreversible cessation of all brain function, including function of the brainstem (Table 105-5). Documentation of *irreversibility* requires that the cause of the coma is known, that the cause is adequate to explain the clinical

TABLE 105-4 LOCKED-IN SYNDROME

Clinical features	Recovery possible
Eye opening	Onset over 1-12 wk (vascular)* or
Reactive pupils	Onset over 4-6 mo (nonvascular)*
Volitional vertical eye movements in response to command	Prognosis favorable
Muteness	Normal CT scan*
Quadriplegia	Early recovery of lateral eye movements*
Sleep-wake cycles	
Causes	
Pontine vascular lesions (common)	
Head injury, brainstem tumor, pontine myelinolysis (rare)	

CT, Computed tomography.

*Implications for care.