"Ocular bobbing" describes brisk downward and slow upward movements of the eyes associated with loss of horizontal eye movements and is diagnostic of bilateral pontine damage, usually from thrombosis of the basilar artery. "Ocular dipping" is a slower, arrhythmic downward movement followed by a faster upward movement in patients with normal reflex horizontal gaze; it usually indicates diffuse cortical anoxic damage.

The oculocephalic reflexes, elicited by moving the head from side to side or vertically and observing eye movements in the direction opposite to the head movement, depend on the integrity of the ocular motor nuclei and their interconnecting tracts that extend from the midbrain to the pons and medulla (Fig. 328-3). The movements, called somewhat inappropriately "doll's eyes" (which refers more accurately to the reflex elevation of the eyelids with flexion of the neck), are normally suppressed in the awake patient. The ability to elicit them therefore reflects both reduced cortical influence on the brainstem and intact brainstem pathways, indicating that coma is caused by a lesion or dysfunction in the cerebral hemispheres. The opposite, an absence of reflex eye movements, usually signifies damage within the brainstem but can result from overdoses of certain drugs. In this circumstance, normal pupillary size and light reaction distinguishes most drug-induced comas from structural brainstem damage.

Thermal, or "caloric," stimulation of the vestibular apparatus (oculovestibular response) provides a more intense stimulus for the oculocephalic reflex but provides essentially the same information. The test is performed by irrigating the external auditory canal with cool water in order to induce convection currents in the labyrinths. After a brief latency, the result is tonic deviation of both eyes to the side of cool-water irrigation and nystagmus in the opposite direction. (The acronym "COWS" has been used to remind generations of medical students of the direction of nystagmus—"cold water opposite, warm water same.") The loss of induced conjugate ocular movements indicates brainstem damage. The presence of corrective nystagmus indicates that the frontal lobes are functioning and connected to the brainstem; thus catatonia or hysterical coma is likely.

By touching the cornea with a wisp of cotton, a response consisting of brief bilateral lid closure is normally observed. The corneal reflex depends on the integrity of pontine pathways between the fifth (afferent) and both seventh (efferent) cranial nerves; in conjunction with reflex eye movements, it is a useful test of pontine function. CNS-depressant drugs diminish or eliminate the corneal responses soon after reflex eye movements are paralyzed but before the pupils become unreactive to light. The corneal (and pharyngeal) response may be lost for a time on the side of an acute hemiplegia.

Respiratory Patterns These are of less localizing value in comparison to other brainstem signs. Shallow, slow, but regular breathing suggests metabolic or drug depression. Cheyne-Stokes respiration in its typical cyclic form, ending with a brief apneic period, signifies bihemispheral damage or metabolic suppression and commonly accompanies light coma. Rapid, deep (Kussmaul) breathing usually implies metabolic acidosis but may also occur with pontomesencephalic lesions. Agonal gasps are the result of lower brainstem (medullary) damage and are recognized as the terminal respiratory pattern of severe brain damage. A number of other cyclic breathing variations have been described but are of lesser significance.

LABORATORY STUDIES AND IMAGING

The studies that are most useful in the diagnosis of coma are chemical-toxicologic analysis of blood and urine, cranial CT or MRI, EEG, and CSF examination. Arterial blood gas analysis is helpful in patients with lung disease and acid-base disorders. The metabolic aberrations commonly encountered in clinical practice are usually exposed by measurement of electrolytes, glucose, calcium, osmolarity, and renal (blood urea nitrogen) and hepatic (NH_3) function. Toxicologic analysis may be necessary in any case of acute coma where the diagnosis is not immediately clear. However, the presence of exogenous drugs or toxins, especially alcohol, does not exclude the possibility that other factors, particularly head trauma, are also contributing to the clinical state. An ethanol level of 43 mmol/L (0.2 g/dL) in nonhabituated patients generally causes impaired mental activity; a level of >65 mmol/L (0.3 g/dL) is associated with stupor. The development of tolerance may allow the chronic alcoholic to remain awake at levels >87 mmol/L (0.4 g/dL).

The availability of CT and MRI has focused attention on causes of coma that are detectable by imaging (e.g., hemorrhage, tumor, or hydrocephalus). Resorting primarily to this approach, although at times expedient, is imprudent because most cases of coma (and confusion) are metabolic or toxic in origin. Furthermore, the notion that a normal CT scan excludes an anatomic lesion as the cause of coma is erroneous. Bilateral hemisphere infarction, acute brainstem infarction, encephalitis, meningitis, mechanical shearing of axons as a result of closed head trauma, sagittal sinus thrombosis, and subdural hematoma isodense to adjacent brain are some of the disorders that may not be detected. Nevertheless, if the source of coma remains unknown, a scan should be obtained.

The EEG (Chap. 442e) is useful in metabolic or drug-induced states but is rarely diagnostic. However, it is the essential test to reveal coma that is due to clinically unrecognized, nonconvulsive seizures, and shows fairly characteristic patterns in herpesvirus encephalitis and prion (Creutzfeldt-Jakob) disease. The EEG may be further helpful in disclosing generalized slowing of the background activity, a reflection of the severity of an encephalopathy. Predominant high-voltage slowing (δ or triphasic waves) in the frontal regions is typical of metabolic coma, as from hepatic failure, and widespread fast (β) activity implicates sedative drugs (e.g., benzodiazepines). A special pattern of "alpha coma," defined by widespread, variable 8- to 12-Hz activity, superficially resembles the normal α rhythm of waking but, unlike normal α activity, is not altered by environmental stimuli. Alpha coma results from pontine or diffuse cortical damage and is associated with a poor prognosis. Normal α activity on the EEG, which is suppressed by stimulating the patient, also alerts the clinician to the locked-in syndrome or to hysteria or catatonia. Still, the most important use of EEG recordings in coma is to reveal clinically inapparent epileptic discharges.

Lumbar puncture is performed less frequently than in the past for coma diagnosis because neuroimaging effectively excludes intracerebral and extensive subarachnoid hemorrhage. However, examination of the CSF remains indispensable in the diagnosis of meningitis and encephalitis. For patients with an altered level of consciousness, it is generally recommended that an imaging study be performed prior to lumbar puncture to exclude a large intracranial mass lesion. Blood culture and antibiotic administration usually precede the imaging study if meningitis is suspected (Chap. 164).

DIFFERENTIAL DIAGNOSIS OF COMA

(Table 328-1) The causes of coma can be divided into three broad categories: those cases without focal neurologic signs (e.g., metabolic and toxic encephalopathies); meningitis syndromes, characterized by fever or stiff neck and an excess of cells in the spinal fluid (e.g., bacterial meningitis, subarachnoid hemorrhage, encephalitis); and diseases associated with prominent focal signs (e.g., stroke, cerebral hemorrhage). Conditions that cause sudden coma include drug ingestion, cerebral hemorrhage, trauma, cardiac arrest, epilepsy, and basilar artery occlusion from an embolism. Coma that appears subacutely is usually related to a preexisting medical or neurologic problem or, less often, to secondary brain swelling surrounding a mass such as tumor or cerebral infarction.

The diagnosis of coma due to cerebrovascular disease can be difficult (Chap. 446). The most common diseases are (1) basal ganglia and thalamic hemorrhage (acute but not instantaneous onset, vomiting, headache, hemiplegia, and characteristic eye signs); (2) pontine hemorrhage (sudden onset, pinpoint pupils, loss of reflex eye movements and corneal responses, ocular bobbing, posturing, and hyperventilation); (3) cerebellar hemorrhage (occipital headache, vomiting, gaze paresis, and inability to stand and walk); (4) basilar artery thrombosis (neurologic prodrome or warning spells, diplopia, dysarthria, vomiting, eye movement and corneal response abnormalities, and asymmetric limb paresis); and (5) subarachnoid hemorrhage (precipitous