TABLE 105-1 MULTIFOCAL DISORDERS INDICATING METABOLIC COMA

Disseminated intravascular coagulopathy	Thrombotic thrombocytopenic purpura
Sepsis	Fat emboli
Pancreatitis	Hypertensive encephalopathy
Vasculitis	Diffuse micrometastases

reticular activating system, impairment of reflex eye movements is often the critical element of diagnosis of a brainstem lesion. A comatose patient without impaired reflex lateral eye movements does not have a mass lesion compromising brainstem structures in the posterior fossa. CT is not able to show some lesions in this region. Posterior fossa lesions may block the flow of cerebrospinal fluid from the lateral ventricles, resulting in the dangerous situation of *noncommunicating hydrocephalus.*

Metabolic abnormalities are caused by deficiency states (e.g., thiamine, glucose), by derangements of metabolism (e.g., hyponatremia), or by the presence of *exogenous toxins* (e.g., drugs) or *endogenous toxins* (e.g., organ system failure). Metabolic abnormalities result in diffuse dysfunction of the nervous system; therefore, with rare exceptions, they produce no localized signs such as hemiparesis or unilateral papillary dilation. The diagnosis of *metabolic encephalopathy* means that the examiner has found no focal anatomic features on examination or neuroimaging studies to explain coma but that a specific metabolic cause has not been established. Drugs have a predilection for affecting the reticular formation in the brainstem and for producing paralysis of reflex eye movement on examination. *Multifocal structural disorders* may simulate metabolic coma (Table 105-1).

In the late stages of status epilepticus, motor movements may be subtle even though *seizure activity* is continuing throughout the brain (nonconvulsive status epilepticus). Once seizures stop, the so-called *postictal state* can also cause unexplained coma.

DIAGNOSTIC APPROACH

The history and examination are essential in the diagnosis and are not replaced by brain imaging (Table 105-2). A history of a premonitory headache supports a diagnosis of meningitis, encephalitis, or intracerebral or subarachnoid hemorrhage. A preceding period of intoxication, confusion, or delirium points to a diffuse process such as meningitis or endogenous or exogenous toxins. The sudden apoplectic onset of coma is particularly suggestive of ischemic or hemorrhagic stroke affecting the brainstem or of subarachnoid hemorrhage or intracerebral hemorrhage with intraventricular rupture. Lateralized symptoms of hemiparesis or aphasia before coma occur in patients with hemispheric masses or infarctions.

The physical examination is critical, quickly accomplished, and diagnostic. The issues are three: (1) Does the patient have meningitis? (2) Are signs of a mass lesion present? and (3) Is this condition a diffuse syndrome of exogenous or endogenous metabolic etiology? Emergency management should then be instituted accordingly (Table 105-3).

Identification of Meningitis

Signs of meningeal irritation are not invariably present and have differing sensitivities depending on the cause: They are extremely common with acute pyogenic meningitis and subarachnoid hemorrhage and less common with indolent, fungal meningitis. Nevertheless, the presence of these signs on examination is the central clue to the diagnosis. Missing these signs results in time-consuming additional tests such as brain imaging and the potential loss of a narrow window of opportunity for directed therapy.

Passive neck flexion should be carried out (Fig. 105-2) in all comatose patients unless a history of head trauma exists. When the neck is passively flexed by attempting to bring the chin within

TABLE 105-2 CAUSES OF COMA WITH NORMAL COMPUTED TOMOGRAPHY SCAN

Meningeal disorders Subarachnoid hemorrhage (uncommon) Bacterial meningitis Encephalitis Subdural empyema	Endogenous toxins, deficiencies, derangements Hypoxia and ischemia Hypoglycemia Hypercalcemia
Exogenous toxins Sedative drugs and barbiturates Anesthetics and γ-hydroxybutyrate* Alcohols Stimulants Phencyclidine† Cocaine and amphetamine‡ Psychotropic drugs Cyclic antidepressants Phenothiazines Lithium Anticonvulsants Opioids Clonidine§ Penicillins Salicylates Anticholinergics Carbon monoxide, cyanide, and methemoglobinemia	Osmolar causes Hyperglycemia Hyponatremia Hypernatremia Organ system failure Hepatic encephalopathy Uremic encephalopathy Pulmonary insufficiency (carbon dioxide narcosis) Seizures Prolonged postictal state Spike-wave stupor Hypothermia or hyperthermia Brainstem ischemia Basilar artery stroke Pituitary apoplexy Conversion or malingering

*General anesthetic, similar to γ-aminobutyric acid; used as a recreational drug and body building aid. It has a rapid onset and rapid recovery, often with myoclonic jerking and confusion. It causes deep coma lasting 2 to 3 hours (Glasgow Coma Scale score = 3) with maintenance of vital signs.

†Coma associated with cholinergic signs: lacrimation, salivation, bronchorrhea, and hyperthermia.

‡Coma after seizures or status epilepticus (i.e., a prolonged postictal state).

§An antihypertensive agent that is active through the opiate receptor system; overdose is frequent when used to treat narcotic withdrawal.

TABLE 105-3 EMERGENCY MANAGEMENT

1. Ensure airway adequacy.
2. Support ventilation and circulation.
3. Obtain blood for glucose, electrolytes, hepatic and renal function, prothrombin and partial thromboplastin times, complete blood count, and drug screen.
4. Administer 100 mg of thiamine intravenously (IV).
5. Administer 25 g of dextrose IV (typically 50 mL of 50% dextrose) to treat possible hypoglycemic coma.*
6. Treat opiate overdose with naloxone (0.4-2 mg IV repeated every 2-3 minutes as needed).
7. The specific benzodiazepine antagonist flumazenil (0.2 mg IV every 1 min, x1-5 doses; max is 1 mg) should be given for reversal of benzodiazepine-induced coma or conscious sedation.†

*The glucose level is poorly correlated with the level of consciousness in hypoglycemia; stupor, coma, and confusion are reported with blood glucose concentrations ranging from 2 to 60 mg/dL.

†Not recommended in coma of unknown origin because seizures may be precipitated in patients with polydrug overdoses that include benzodiazepines with tricyclic antidepressants or cocaine.