Introduction

Stupor and coma are disturbances in consciousness resulting from dysfunction of both cerebral hemispheres or the reticular activating system. ***Stupor*** *is unresponsiveness from which the patient can be aroused only briefly by vigorous, repeated stimulation.* ***Coma*** *is unresponsiveness from which the patient generally cannot be aroused. Causes may be structural or global (often metabolic). Diagnosis is clinical; identification of cause usually requires laboratory tests and CNS imaging. Treatment is immediate stabilization and specific management of the cause. For long-term stupor or coma, adjunctive treatment includes passive range-of-motion exercises, enteral feedings, and prevention of pressure ulcers. Prognosis varies by cause.*

The alert state requires intact function of the cerebral hemispheres and preservation of arousal mechanisms in the reticular activating system (RAS)—an extensive network of nuclei and interconnecting fibers in the upper pons, midbrain, and posterior diencephalon.

Etiology and Pathophysiology

Various structural and global CNS disorders cause stupor or coma. A decrease in consciousness results from dysfunction of the RAS or both cerebral hemispheres; unilateral cerebral hemisphere disorders may produce severe neurologic deficits but not coma. With increasing injury, stupor progresses to coma, and coma to brain death. Other forms of altered consciousness include delirium (marked by agitation rather than lethargy), syncope, and seizures; in the last two, consciousness is briefly lost.

Structural disorders may cause stupor or coma through direct, mechanical disruption of the RAS or through the indirect influence of mass effect and edema. A unilateral massive hemispheric focal lesion (eg, left middle cerebral artery stroke) rarely disturbs consciousness unless the contralateral hemisphere is already compromised or becomes edematous. Infarcts of the upper brain stem cause various degrees of stupor or coma, depending on their extent.

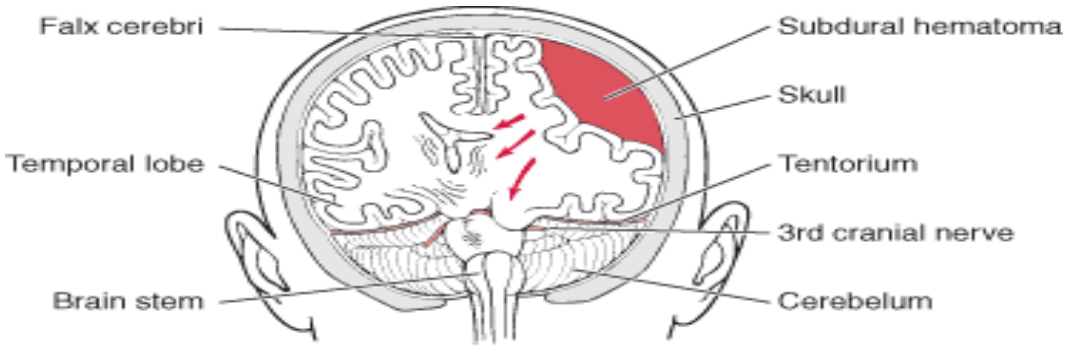
Global or systemic disorders that can cause stupor or coma often involve cerebral anoxia or ischemia. Psychiatric disorders (eg, psychogenic unresponsiveness) can mimic disturbed consciousness but are usually distinguished from true stupor or coma by a normal physical and neurologic examination.

Herniation syndromes

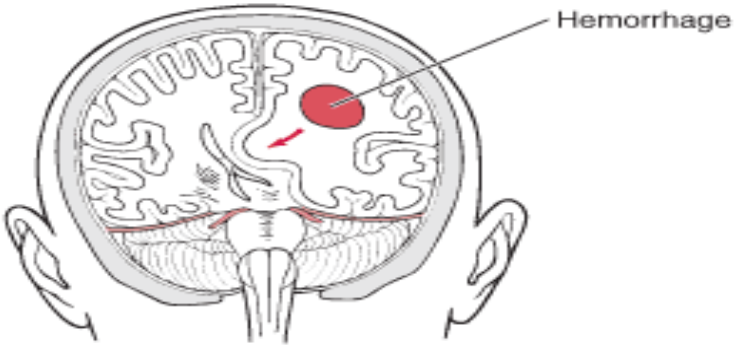
Because the skull is rigid (after infancy), intracranial masses or edema may increase intracranial pressure, which can cause brain tissue to herniate through a rigid intracranial barrier.

In transtentorial (uncal) herniation, the temporal lobe shifts across the edge of the tentorium cerebelli (a tentlike structure on which the temporal lobe normally rests). The uncus—the medial edge of the herniating lobe—crushes the diencephalon and upper brain stem, causing compression ischemia and infarction of the tissues containing the RAS (see Fig. 1: Stupor and Coma: Tentorial and subfalcine herniation.). Herniation of both temporal lobes (central herniation), usually because of bilateral masses or diffuse edema, causes bilateral compression of the midbrain and brain stem.

Tentorial and subfalcine herniation.



Tentorial Herniation



Subfalcine Herniation

Because the skull is rigid after infancy, intracranial masses or swelling may increase intracranial pressure, which can cause protrusion (herniation) of brain tissue through a rigid intracranial barrier: falx cerebri (subfalcine herniation of the cingulate gyrus), tentorial notch (tentorial herniation), or foramen magnum (tonsillar herniation). Transtentorial and tonsillar herniation are life threatening.

In tentorial herniation, one medial temporal lobe may herniate, usually because of a unilateral mass, and cause unilateral damage. The 1st structure compressed may be the ipsilateral 3rd cranial nerve, causing a unilateral dilated fixed pupil and oculomotor paresis; the posterior cerebral artery, causing a homonymous hemianopia; or the opposite cerebral peduncle, causing ipsilateral hemiparesis. Then, the midbrain and brain stem can be compressed, causing impaired consciousness, abnormal breathing patterns, pupils fixed in midposition, loss of oculocephalic and oculovestibular reflexes (the eyes do not move in response to head rotation or to caloric stimulation, respectively), bilateral motor paresis with decerebrate rigidity or flaccidity, and Cushing's reflex (hypertension, particularly systolic, and bradycardia). Herniation of both temporal lobes (central herniation), usually because of bilateral masses, causes bilateral, symmetric damage, compressing the midbrain and brain stem and producing many of the same symptoms as tentorial herniation.

Tonsillar herniation results from infratentorial masses (usually) or supratentorial masses. The cerebellar tonsils, forced through the foramen magnum, compress the brain stem and obstruct CSF flow, causing acute hydrocephalus. Symptoms include obtundation, headache, vomiting, meningismus, dysconjugate eye movements, and abrupt respiratory and cardiac arrest.

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In subfalcine herniation, the cingulate gyrus herniates under the falx cerebri.

Symptoms, Signs, and Diagnosis

Repeated noxious stimuli do not arouse comatose patients; stuporous patients are aroused only briefly. In comatose patients, stimulation may trigger primitive reflex movements (eg, decerebrate or decorticate posturing).

Diagnosis and initial stabilization should occur simultaneously. Airway, breathing, and circulation must first be ensured; patients with infrequent, shallow, or strenuous respirations or low O_2 saturation (by pulse oximetry or arterial blood gas measurements) require intubation. Hypotension must be corrected. Finger-stick glucose testing is required. Patients with low glucose levels should be given thiamin 100 mg IM (to prevent Wernicke's encephalopathy in susceptible patients) and 50 mL of 50% dextrose. If opioid overdose is suspected, naloxone 2 mg IV is given. If trauma is involved, the neck is stabilized with a hard collar until an x-ray can be taken to check for fractures.

History

Medical identification bracelets or the contents of a wallet or purse may provide clues (eg, hospital identification card, drugs). Relatives, paramedics, and police officers should be questioned about onset of the disturbance (eg, whether seizure, headache, vomiting, head trauma, or drug was involved). They should describe the environment in which the patient was found; containers that may have held food, alcohol, drugs, or poisons should be examined and saved for chemical analysis and possible legal evidence. Relatives should be asked about recent infections, psychiatric problems, and previous illnesses. Medical records should be reviewed if available.

Physical examination

Physical examination should be focused and efficient. Signs of head trauma include periorbital ecchymosis (raccoon eyes), ecchymosis behind the ear (Battle's sign), hemotympanum, instability of the maxilla, and CSF rhinorrhea and otorrhea. Scalp contusions and small bullet holes can be missed unless the head is carefully inspected. The fundi should be examined for papilledema, hemorrhages, and exudates. Passive neck flexion, possible in the absence of trauma, may detect stiffness, suggesting subarachnoid hemorrhage or meningitis. The cervical spine or neck should be immobilized until clinical history, physical examination, or imaging tests exclude fracture.

Fever or petechial rash suggests CNS infection. Needle marks may suggest drug overdose (eg, of opioids or insulin). A bitten tongue suggests seizure. Breath odor may indicate alcohol intoxication.

Neurologic examination

The neurologic examination determines whether the brain stem is intact and where the lesion is located within the CNS. State of consciousness, pupils, eye movements, respirations, and motor functions help determine the level of CNS dysfunction.

Arousal is evaluated by attempting to wake patients first with verbal commands, then with nonnoxious stimuli, and finally with noxious stimuli (eg, pressure to the supraorbital ridge, nail bed, or sternum). The Glasgow Coma Scale assigns points based on the responses to stimuli. Eye opening, facial grimacing, and purposeful withdrawal of limbs from the noxious stimulus indicates that the depth of unconsciousness is relatively light. Asymmetric motor responses to pain may indicate a focal hemispheric lesion.

As stupor deepens into coma, noxious stimuli may trigger stereotypic reflex posturing. Decorticate posturing (arm flexion and adduction with leg extension) indicates hemispheric damage to the corticospinal tract with preservation of the brain stem. Decerebrate rigidity (neck, back, and limb extension with clenched jaws) suggests upper brain stem damage and represents a deterioration in motor response. Flaccidity without movement suggests severe injury throughout the neuraxis and represents the worst possible motor response. Asterixis and multifocal myoclonus accompany

metabolic disorders such as uremia, hepatic failure, anoxia, and drug toxicity. In psychogenic unresponsiveness, motor response is typically absent, but muscle tone and reflexes remain normal.

In transtentorial herniation, the herniating temporal lobe may first compress the ipsilateral 3rd cranial nerve, causing a unilateral dilated fixed pupil and oculomotor paresis; the posterior cerebral artery, causing homonymous hemianopia; or the opposite cerebral peduncle, causing ipsilateral hemiparesis. Then, the midbrain and brain stem can be compressed, causing impaired consciousness, abnormal breathing patterns, pupils fixed in midposition, loss of oculocephalic and oculovestibular reflexes, bilateral motor paresis with decerebrate rigidity or flaccidity, and Cushing's reflex (hypertension, particularly systolic, and bradycardia); these midbrain findings also occur with central herniation.

In tonsillar herniation, symptoms include obtundation, headache, vomiting, meningismus, dysconjugate eye movements, and abrupt respiratory and cardiac arrest.

Ophthalmic examination

This examination provides information about brain stem function (see Table 3: Stupor and Coma: Interpretation of Pupillary Response and Eye Movements). It includes pupillary responses, extraocular movements, funduscopic examination (for papilledema or hemorrhage), and assessment of other neuro-ophthalmic reflexes. Pupils usually become fixed early if a structural lesion is present, but the pupil response is preserved until very late in metabolic coma.

When eye movements are absent, the oculocephalic reflex is tested by the doll's-eye maneuver: The eyes are observed while passively rotating the patient's head from side to side. This maneuver should not be attempted after trauma unless cervical spine fracture is excluded. If consciousness is normal and visual fixation is possible, the eyes follow head movement. If consciousness is depressed and brain stem is intact, gaze appears fixed on the ceiling as the head rotates. If brain stem function is destroyed, the eyes move with head movement as if they are fixed in their sockets.

If the oculocephalic reflex is absent, oculovestibular (cold caloric) testing is done. After integrity of the tympanic membrane is confirmed, a syringe connected to a flexible catheter is used to irrigate the external auditory canal with 10 to 40 mL of ice water over a 30-sec period. In conscious patients (eg, with psychogenic coma), this test causes deviation of the eyes toward the irrigated ear with nystagmus beating away from the irrigated ear. In comatose patients with preserved brain stem function, both eyes deviate toward the irrigated ear but without nystagmus. Responses are absent or dysconjugate when the brain stem is impaired by a structural lesion or by deepening metabolic coma.

Respiratory patterns

Dysfunction of both hemispheres or the diencephalon may cause periodic cycling of breathing (Cheyne-Stokes and Biot's respirations) midbrain or upper pontine dysfunction may cause central neurogenic hyperventilation, with respiratory rates of > 40 breaths/min. Pontine or medullary lesions typically cause an inspiratory gasp (apneustic breathing), which often progresses to respiratory arrest.

Tests

Initially, pulse oximetry, finger-stick blood glucose measurements, and cardiac monitoring are done. Blood tests include a comprehensive metabolic panel, CBC with differential and platelets, coagulation tests, and ammonia level. Arterial blood gases are measured, and if the diagnosis remains unclear, carboxyhemoglobin, sulfhemoglobin, and methemoglobin levels are checked. Blood and urine should be obtained for Gram stain, culture, and routine toxicology screening; alcohol levels are also measured. Testing for certain drugs (eg, salicylates, acetaminophen, tricyclic antidepressants) should be done when toxic ingestion is suspected because several drugs are often coingested. ECG (12-lead) should be done.

Unless a cause is immediately apparent, noncontrast head CT should be rapidly done to check for mass lesions, hemorrhage, edema, and hydrocephalus. If this test is not diagnostic, contrast CT or MRI may detect isodense subdural hematomas, multiple metastases, sagittal sinus thrombosis, herpes encephalitis, or another cause missed by routine CT. Chest x-rays should also be taken.

If infection is suspected, lumbar puncture is done to check opening pressure. CSF analysis includes cell and differential counts, protein, glucose, Gram stain, cultures, and sometimes, depending on the clinical context, specific tests (eg, cryptococcal antigen, Venereal Disease Research Laboratory [VDRL] tests, PCR for herpes simplex). In unconscious patients, CT must be done before lumbar puncture to exclude an intracranial mass or obstructive hydrocephalus because in such cases, suddenly lowering CSF pressure by lumbar puncture could trigger fatal herniation.

EEG may be done if diagnosis remains uncertain; in the rare patient with nonconvulsive status epilepticus, EEG shows spikes, sharp waves, or spike and slow complexes. However, in most comatose patients, EEG shows slowing and reductions in wave amplitude that are nonspecific and often occur in metabolic encephalopathy.

Prognosis and Treatment

Prognosis depends on the specific cause, duration, and depth of stupor or coma. After trauma, a Glasgow Coma Scale score of 3 to 5 may indicate fatal brain damage, especially if pupils are fixed or oculovestibular reflexes are absent. If pupils are unreactive or motor response to noxious stimuli is absent or reflex 3 days after cardiac arrest, patients have virtually no chance of a good neurologic recovery. If the cause is barbiturate overdose or a reversible metabolic disorder, patients may lose all brain stem reflexes and all motor response but may recover fully.

Immediate stabilization and support are provided during diagnosis. Most patients with stupor or coma require admission to an ICU for ventilatory support and for monitoring of neurologic state. Specific treatment depends on the cause (see elsewhere in the manual).

For herniation, treatment includes mannitol 25 to 100 g infused IV, endotracheal intubation, and controlled ventilation with a target P_{CO_2} of 25 to 30 mm Hg. For herniation due to tumors, a corticosteroid (eg, dexamethasone 16 mg IV, followed by dexamethasone 4 mg po or IV q 6 h) is also required. Mass lesions should be surgically decompressed as soon as possible.

Stuporous or comatose patients require meticulous long-term care. Stimulants and opioids should be avoided. Enteral feeding is started with precautions to avoid aspiration (eg, elevation of the head of the bed); a percutaneous endoscopic jejunostomy tube is placed if necessary. Early attention to skin breakdown and pressure points is required to prevent pressure ulcers. Topical agents to prevent desiccation of the eyes are beneficial. Passive range-of-motion exercises done by physical therapists may reduce deconditioning, and taping or dynamic flexion splitting of the extremities may prevent contractures.

Table 1

Common Causes of Stupor and Coma

Cause	Examples
Structural disorders	Aneurysm rupture and subarachnoid hemorrhage Brain abscess Brain tumor Cranial trauma (concussion, cerebral lacerations or contusions, epidural or subdural hematoma) Hydrocephalus (acute) Upper brain stem infarct or hemorrhage
Global disorders	CNS vasculitis Drugs and toxins (eg, barbiturates, carbon monoxide, ethyl alcohol, methyl alcohol, opioids) Hypothermia Infections (meningitis, encephalitis, sepsis) Metabolic disorders (eg, diabetic ketoacidosis, hepatic coma, hypoglycemia, hyponatremia, hypoxia, uremia)

Table 2

Glasgow Coma Scale*

Area Assessed	Response	Points
Eye opening	Open spontaneously; open with blinking at baseline	4
	Open to verbal command, speech, or shout	3
	Open in response to pain applied to the limbs or sternum	2
	None	1
Verbal	Oriented	5
	Confused conversation, but able to answer questions	4
	Inappropriate responses; words discernible	3
	Incomprehensible speech	2
	None	1
Motor	Obeys commands for movement	6
	Responds to pain with purposeful movement	5
	Withdraws from pain stimuli	4
	Responds to pain with abnormal (spastic) flexion (decorticate posture)	3
	Responds to pain with abnormal (rigid) extension (decerebrate posture)	2
	None	1