

Coma and Brain Death (Dr. Merchut)

Coma

1. Clinical features of coma

Coma is defined as a **sleep-like, unarousable, unresponsive state**. Other patients with impaired consciousness but some limited degree of responding are described as obtunded or stuporous. In coma, only brain stem reflexes are clinically testable, since cortical function is absent. Any restoration of cortical function depends on finding and effectively treating the cause of coma. Thus, comatose patients may fully recover, partly improve or progress to brain death. After days to weeks, a patient with nonprogressive cortical damage, such as anoxic encephalopathy after cardiac arrest, may transition from coma to the **persistent vegetative state**. Here, the eyes periodically open or move, sleep and wake cycles occur, and pain responsiveness may return, but meaningful interaction remains absent since severe cortical impairment persists.

2. Pathogenesis of coma

Severe metabolic or systemic conditions that diffusely depress cortical function may cause coma. Hypoxia, inadequate cerebral blood flow, hypoglycemia, and drug intoxication or overdose can directly impair neuronal function, while systemic infection, metabolic disturbances, and hepatic or renal failure can indirectly affect cerebral cortex. Timely correction of these conditions is critical, since failure to do so may cause permanent cortical deficits, particularly for the "hypo's" of severe hypotension, hypoxia, and hypoglycemia.

Various disorders or diseases may produce coma from bilateral lesions in the cerebral hemispheres, such as ischemic infarction, hemorrhage, head trauma, tumor, or infection. However, **a solitary, unilateral cerebral lesion does not produce coma unless it adversely affects the opposite hemisphere via brain edema or herniation**. Coma may be produced by a brain stem lesion if it disrupts the reticular formation. The tegmental brain stem **reticular formation**, projecting to thalamic and subcortical nuclei, is important for wakefulness and arousal.

3. Examination of the unresponsive patient

Although the bedside neurological examination is limited in an unresponsive patient, it may still provide important clues for localizing the problem to various levels of brain or brain stem. Serial, repeated observations of the patient may show a progressive loss of neurological function and brain stem reflexes, often indicative of a rostral to caudal deterioration due to edema or inflammation. This limited examination includes evaluation of motor responses, breathing patterns, pupil size and reactivity, and reflexive ocular movements. In general, **asymmetrical neurological signs strongly suggest a structural lesion**, such as an ischemic infarction, hemorrhage, or tumor, while **symmetrical abnormalities usually are due to a more diffuse or toxic-metabolic process**, such as anoxia.

Strictly speaking, **motor responses** to command or withdrawal to painful stimuli do not occur in coma, since an appropriate, localizing response to a noxious stimulus requires some cortical function. For example, when the examiner rubs the sternum, the patient grabs the examiner's hand and pushes it away. However, comatose patients may show certain stereotyped or automatic movements spontaneously or after painful stimuli. **Decorticate posturing** is flexion of the upper limbs with extension of the lower limbs, associated with a lesion at the level of the cerebral cortex or hemisphere. **Decerebrate posturing** is extension of the upper and lower limbs, associated with a lesion at the level of the midbrain (red nucleus).

Abnormal **breathing patterns** in coma should be noted, although they do not always localize to the brain or brain stem levels classically associated with them. **Cheyne-Stokes respiration** is a very distinctive pattern of alternating tachypnea and apnea (crescendo-decrescendo respiration). The patient is observed to take progressively deeper, often faster, breaths, followed by slower and shallower breathing leading to a period of apnea, after which the cycle repeats. In a comatose patient, this pattern is produced from **bilateral cortical involvement** due to metabolic encephalopathy, such as renal failure, a unilateral lesion with severe brain edema, or from bilateral structural lesions in cerebral cortex. On occasion, Cheyne-Stokes breathing may be seen in noncomatose patients with congestive heart failure, where slowed circulation time creates delayed feedback to the carotid chemoreceptors influencing the respiratory rate. Elderly, otherwise healthy subjects also may have Cheyne-Stokes breathing while they sleep.

An increased respiratory rate, or hyperventilation, may be related to anxiety or fear, or may be a reflexive response to pulmonary congestion. Rarely, **central neurogenic hyperventilation** may result from a lesion or edema in the **low midbrain to upper pons**. An **ataxic respiration pattern** consists of variable breaths at an irregular rate from a lesion or edema in the **medulla**, involving the cardiorespiratory control centers there. This is an ominous sign, signaling impending respiratory arrest and the emergent need to intubate and mechanically ventilate the patient.

The size of the pupils and the pupillary light reflex is important in the examination of the unconscious patient (Fig. 1). Often **in coma from metabolic causes the pupillary light reflex is preserved** despite loss of other brain stem or cranial nerve reflexes. Sympathetic (pupillodilator) fibers travel down the entire brain stem, while parasympathetic (pupilloconstrictor, third cranial nerve) fibers are a "circuit" at the midbrain level. A tectal (dorsal) **midbrain lesion** selectively involves the parasympathetic fibers, causing **large, fixed pupils** (unopposed sympathetic fibers). The presence of a **larger, "blown," fixed pupil** which is unresponsive consensually or directly to light often is due to compression of the ipsilateral oculomotor nerve (CN III) from a swollen temporal lobe (**uncal herniation**). This is a neurological emergency since progressive edema and herniation of the brain stem is fatal. A **pontine lesion** selectively involves the sympathetic fibers, causing **small, pinpoint pupils** (unopposed parasympathetic fibers). In the absence of a pontine lesion, small, unreactive pupils may also occur from high doses of narcotics or cholinergic eyedrops used to treat glaucoma. Neurologically intact elderly subjects tend to have such tiny pupils that the pupillary light reflex is difficult to assess.

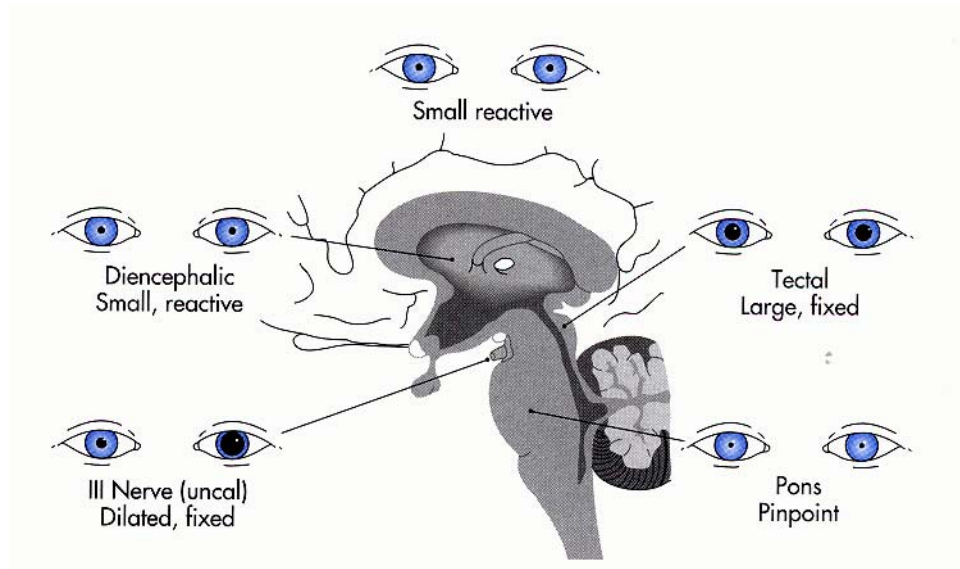


Fig. 1 Pupillary abnormalities in coma

(from Plum F, Posner JB. *The Diagnosis of Stupor and Coma*, ed 3, Philadelphia: FA Davis, 1980)

Reflexive eye movements are also important to check in every unresponsive patient. In trauma cases, a cervical fracture must first be excluded before the patient's neck is moved during this part of the examination. Again, whenever there are **asymmetric** abnormalities of eye movements (or pupils) a **structural lesion** is the more likely cause of coma than a toximetabolic condition. It should also be noted that reflexive eye movements may be suppressed by vestibulotoxic drugs, such as benzodiazepines, in the absence of a brain stem lesion. The **oculocephalic reflex** (Fig. 2) is also called the "doll's eyes reflex" since the eyes in an antique china doll would roll when rotating the doll's head. This is a brain stem mediated reflex which can be tested in comatose patients, since cortical control or suppression of eye movements is absent. The **eyes should normally move in the direction opposite to the lateral turn of the head** by the examiner. In fully conscious or mildly drowsy patients, functional cerebral cortex can fixate or "command" the eyes into varied positions regardless of how the head is passively moved. The **oculovestibular (cold caloric) reflex** (Fig. 2) is another brain stem mediated reflex which can be tested in unconscious patients. Before testing the patient, the examiner must use an otoscope to exclude blockage of the ear canal or a ruptured tympanic membrane. The patient's head is then elevated about 30 degrees above horizontal and one ear canal is irrigated with up to 100 cc of ice water. The induced convection movement of cooled endolymph creates reduced vestibular activity from that ipsilateral semicircular canal, causing the **eyes to normally move slowly toward the cold (irrigated) ear**. A conscious patient would have the same response, plus cortically-mediated nystagmus, with the eyes beating toward the opposite, non-irrigated ear. Ice water irrigation of the ear canal is very noxious, however, and is not performed in awake

patients. While examining the eyes of comatose patients, it is also helpful to check for the corneal and palpebral reflexes.

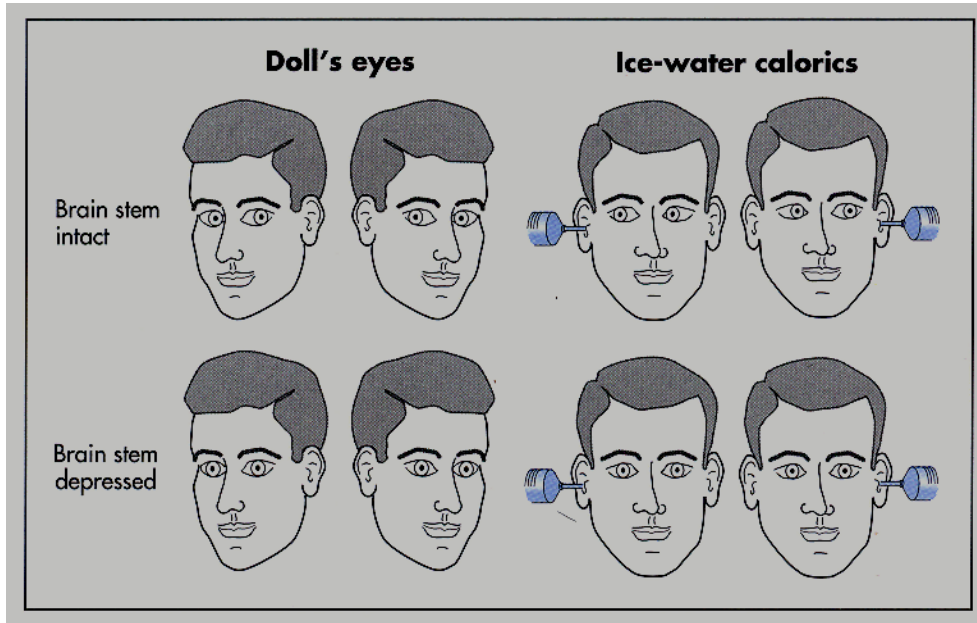


Fig. 2

Reflexive ocular movements. With preserved brain stem function, the eyes normally roll opposite to the turn of the head (doll's eyes, or oculocephalic reflex), and the eyes slowly turn toward the ear irrigated with ice water (cold caloric or oculovestibular reflex). (Modified from Collins RC: *Neurology*, Philadelphia 1997, WB Saunders.)

4. Emergency treatment of the comatose patient

Always establish adequate respiration, oxygenation, and circulation emergently even while the cause of coma is unknown. Emergent care of coma involves the "**ABC's**" of **Airway, Breathing, and Circulation**. Immediately rule out **hypoglycemia** with a fingerstick testing device, or empirically give 50% dextrose intravenously. Hypoxia and hypoglycemia cause neuronal death if not promptly corrected, so these basic measures are critical.

A **structural cause of coma**, such as a hemorrhage, ischemic infarction, or mass lesion, is more likely in the presence of **asymmetrical** neurological signs. A comatose trauma patient is suspected to have intracranial bleeding unless it is ruled out. In these cases, a brain CT or MRI scan is readily performed while basic resuscitative measures are carried out. Treatment of brain edema and surgical removal of the hematoma may be needed.

General measures to reduce increased intracranial pressure (ICP) in comatose patients include mechanical **hyperventilation and osmotic diuretics** like mannitol. With hyperventilation, intracranial blood volume is reduced since hypocarbia causes arterial vasoconstriction. Cerebral water volume is reduced by the effect of osmotic diuretics on the intact blood-brain barrier in normal brain tissue. Intravenous corticosteroids such as **dexamethasone** can counteract the edema produced by a cerebral tumor, abscess or encephalitis, although specific treatments for these lesions must soon follow. Brain edema from ischemic infarction or hemorrhage is unaffected by corticosteroids, but these patients may survive after decompressive craniectomy or hematoma removal.

Toximetabolic causes of coma usually produce symmetrical neurological signs, and these patients should be evaluated for electrolyte abnormalities, hypothermia, hepatic or renal failure, carbon monoxide poisoning, or drug intoxication or overdose. While waiting for the results of urine or serum drug screens, narcotic or benzodiazepine antagonists could be given to see if the patient briefly awakens, if drug intoxication is strongly suspected. Coma can be also caused by subarachnoid hemorrhage or meningoencephalitis, where a brain CT or MRI scan and lumbar puncture would be indicated if these conditions are suspected. In general, brain scans are also performed on unresponsive patients who fail to wake up and have no detectable metabolic cause of coma.

Brain Death

1. Significance and pathology of brain death

In brain death there is irreversible loss of function for both cerebrum and brain stem, leading to the inevitable failure of other vital organs, including the heart. Brain death effectively is death of the entire body, and can be diagnosed while the heart is still beating. The declaration of brain death prevents inappropriate use of costly, high-technology medical care and allows harvesting of viable donor organs. Although any experienced physician can make this declaration, it is usually relegated to a neurologist or neurosurgeon.

Brain death may be the consequence of hemorrhage from trauma, uncontrolled hypertension, or a ruptured berry aneurysm. Other causes include large or multiple ischemic infarctions, meningoencephalitis, and anoxia from cardiac arrest. Extensive areas of the brain become ischemic with shifting or herniation of vital areas due to edema.

In the case of cerebral anoxia after cardiac arrest, the gross brain is fragile and easily disintegrates when removed at autopsy. It appears swollen, and hardens poorly in fixative. Evidence of herniation caused by edema may be found at the temporal lobes and foramen magnum. Necrosis is most severe in the cerebral cortex and cerebellar folia. Characteristic ischemic "red neurons" are found in the cerebral cortex and appear eosinophilic and shrunken, while in the cerebellum Purkinje cells are ischemic or absent. Ischemic infarction or hemorrhage may be seen in other areas of the brain.

2. Diagnosis of brain death

In order to declare brain death, **the apparent cause should be known**, such as traumatic head injury or a witnessed cardiopulmonary arrest, **and must be of sufficient severity to account for the irreversible coma**. A brain CT scan may help show extensive hemorrhage, edema or ischemic changes. If the cause of coma is unknown or uncertain, the patient requires continued life support measures while longer periods of observation and further diagnostic testing are undertaken. In brain death, there is **no neurological improvement despite adequate treatment of any reversible causes of coma, such as drug intoxication, circulatory shock, or hypothermia (core temperature below 32°C)**. Severe metabolic or endocrine abnormalities should be corrected as well, and the effect of anesthetics and neuromuscular blocking drugs should be allowed to dissipate if coma occurs in the postoperative period. When the etiology of coma is known and no reversible causes require treatment, the generally accepted observation period is 6 hours; an "absolute" time period has not been established. The brains of infants or children tend to withstand anoxia better than the adult brain, and occasionally undergo remarkable recovery. For this reason, longer observation periods are suggested for those 7 days to 2 months old (48 hours), 2 months to 1 year old (24 hours), and over 1 year old (12 to 24 hours).

The bedside neurological examination should **not show any hint or suggestion of cerebral function in a comatose patient unresponsive to painful stimuli**. Thus, there should be no decorticate or decerebrate posturing, seizures, swallowing, yawning, or vocalizations. However, some spinal cord mediated movements may still persist, such as muscle stretch reflexes or the Babinski sign. **All cranial nerve or brain stem reflexes must be absent without any spontaneous respirations**. The pupils do not react to light and the corneal, oculocephalic (doll's eyes), oculovestibular (cold caloric) and gag reflexes are absent. These findings should be noted initially and at the end of the observation period. **Apnea can be verified by specific testing** methods if the patient remains hemodynamically stable. The ventilated patient is given 100% oxygen for 10 minutes to create an oxygen reserve in the lungs, and a baseline arterial blood gas is tested. The ventilator is then discontinued while 100% oxygen is still supplied through the tubing. If the ensuing hypercarbia induces respiratory movements, apnea is ruled out. If no respiratory movements occur after 10 minutes, another arterial blood gas is tested. Apnea is confirmed if no breathing is observed despite reaching a pCO₂ of 60 mm Hg or greater (or perhaps a pCO₂ 20 mm Hg above baseline value). The mechanical ventilator is restarted at the end of the test, or earlier if hypotension or arrhythmias occur during the apnea test.

Confirmatory tests of brain death are not required, but are used in situations where bedside examination of cranial nerve and brain stem reflexes is equivocal or impossible to do, as in the setting of severe facial and ocular trauma or edema. Confirmatory testing should also be done in comatose children under 1 year of age. A "flat line" or isoelectric EEG after 30 minutes of recording with a special protocol was the "classical" way of confirming the clinical diagnosis of brain death, but recording artifacts or minimal electrical activity may hamper interpretation. Another "classical" confirmatory test of brain death was cerebral angiography, which showed failure of any

intracranial blood flow over a 10 minute period, due to fatal brain edema. This would be particularly helpful in comatose patients with absent cerebral responsiveness and brain stem reflexes, but no clearly discernible cause of brain death. A **radioisotope brain scan** is often the currently preferred confirmatory test, since it also demonstrates absence of cerebral blood flow over a 10 minute period, but it can be performed at the bedside instead of the angiography suite.

3. References

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