Chapter 2
Coma

History

Coma is a state of eyes-closed unresponsiveness in which even the most vigorous stimulation fails to arouse the patient (Posner et al. 2007). Because comatose patients cannot communicate, the history must be assembled from family members, emergency service records, and hospital notes. Clues to the etiology of coma obtained from the history include the presence of trauma, evidence of intoxication, and history of cardiac, pulmonary, hepatic, and renal disease. The tempo of coma onset may also be helpful: sudden onset in the absence of trauma favors a cardio-genic source or intracranial hemorrhage, whereas gradual onset is more consistent with a metabolic cause or a slowly expanding mass lesion. In many cases the history contains few details beyond the patient being “found down” and the evaluation of the comatose patient quickly shifts to physical examination and diagnostic testing.

Examination

Mental Status Examination

The purpose of the mental status examination of the comatose patient is to verify that they are actually comatose rather than merely encephalopathic. Before beginning the examination, make sure to discontinue any short-acting sedatives such as midazolam or propofol. By definition, a comatose patient’s eyes should be closed and they should appear as if they are sleeping. If gently calling out their name does not produce any response, yell out their name or gently squeeze their hand. Attempt to awaken them with increasingly noxious stimuli: severely encephalopathic patients may respond to painful maneuvers such as rubbing the sternum, applying nail bed pressure, or pinching the areola whereas comatose patients will not. Document the reaction to each stimulus and also note what happens when it is withdrawn.

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Pupillary Reactions

Abnormal pupillary reactions may provide insight into structural causes of coma involving the thalamus and brainstem. Asymmetric pupils strongly suggest structural lesions. In most cases, symmetric pupils indicate a metabolic source of coma, but there are several important structural lesions that preserve pupillary symmetry and must not be missed. Preexisting pupillary irregularities, such as those which might be due to prior cataract surgery must be excluded before assigning too much weight to an abnormal pupillary examination. Chapter 7 contains a more detailed discussion of pupillary neuroanatomy and function. The following patterns of pupillary reactions are the most important in comatose patients:

1. Normal size pupils with normal reactions (Fig. 2.1a). This pattern suggests a toxic or metabolic disturbance.
2. Small, reactive pupils (Fig. 2.1b). Small, reactive pupils are more likely secondary to toxic or metabolic disturbances, though they may also be produced by thalamic lesions.
3. Unreactive midsize pupils (Fig. 2.1c). Midbrain lesions produce unreactive midsize pupils. More commonly, however, this pattern is the result of toxic or metabolic disturbances.

![Fig. 2.1 Pupillary reactions in coma. See text for details](image-url)
4. Unreactive pinpoint pupils (Fig. 2.1d). Pontine lesions classically produce pinpoint pupils. Opioid intoxication is another important source of pinpoint pupils, but trace reactivity may be maintained.

5. Asymmetric pupils, abnormal pupil is dilated (Fig. 2.1e). The most common causes of this pattern in comatose patients are uncal herniation and a ruptured posterior communicating artery aneurysm. Both conditions are true neurologic emergencies that require rapid evaluation and treatment.

6. Asymmetric pupils, abnormal pupil is constricted (Fig. 2.1f). Coma accompanied by Horner syndrome points to lateral brainstem damage.

7. Fixed and dilated pupils (Fig. 2.1g). This pattern suggests severe coma or brain death but is not helpful in defining the cause.

**Blink Reflexes**

The sensory arc of the blink reflex originates in the cornea and travels in the ophthalmic branch of the trigeminal nerve (Fig. 2.2). These trigeminal nerve fibers synapse in the ipsilateral principal sensory nucleus of the trigeminal nerve and the
nucleus of the spinal trigeminal tract in the pons and medulla. Neurons originating from these trigeminal nuclei send axons to both the ipsilateral and contralateral facial nuclei. The facial nucleus gives rise to the facial nerve which innervates the ipsilateral orbicularis oculi, contraction of which produces blinking.

To assess the corneal reflex, peel both eyelids open and gently stroke the sclera and cornea with a wisp of cotton or sterile gauze. Both eyes should blink in response to this stimulus. Dropping normal saline onto the sclera is an alternative to cotton or gauze that will reduce the chance of abrasion. Test the blink reflex in each eye in sequence, observing both the response in the ipsilateral and contralateral eye. The following are the important blink reflex patterns found in comatose patients (Fig. 2.3):

1. Normal responses in both eyes indicate preserved integrity of the blink reflex pathways in the pons and medulla (Fig. 2.3a).
2. Stimulation of the right eye produces no blink in either eye, while stimulation of the left eye produces normal blink responses in both eyes (Fig. 2.3b). This pattern points to dysfunction of the right trigeminal nerve or sensory nuclei in the pons and medulla.
3. Stimulation of either eye fails to produce a blink response in the right eye (Fig. 2.3c). The lesion in this case is in the right facial nucleus or nerve.
4. Stimulation of either eye produces a blink in the ipsilateral eye, but not in the contralateral eye (Fig. 2.3d). This pattern suggests disruption of the pathways connecting the trigeminal nuclei to the contralateral facial nucleus in the pons and medulla.
5. Bilaterally absent blink responses (Fig. 2.3e). This points to severe brainstem dysfunction, which may be due to structural or metabolic processes. Patients who wear contact lenses may also lose corneal sensitivity, and therefore, their blink responses.

![Fig. 2.3 Common patterns on blink reflex testing in patients in coma. See text for details](image-url)
Eye Position

Horizontal Eye Position

The frontal eye fields (FEF) in the frontal lobes are the most important structures in the supranuclear control of horizontal eye movements. Projections from the FEF synapse with the contralateral abducens nucleus. Thus, activation of the right FEF or left abducens nucleus produces leftward eye deviation. Supranuclear, nuclear, and infranuclear lesions may lead to abnormal eye positions which can help to localize the process responsible for coma. In all cases, it is helpful to interpret eye deviation with respect to a hemiparesis, if present (Fig. 2.4):

1. Destructive right frontal lesions such as strokes or tumors produce rightward deviation of the eyes accompanied by left hemiparesis (Fig. 2.4a).
2. Irritative right frontal lesions such as seizures produce leftward deviation of the eyes. There may or may not be a left hemiparesis (Fig. 2.4b).
3. Right thalamic lesions (particularly hemorrhages, which may irritate the thalamic intralaminar nuclei) produce “wrong-way eyes” which are deviated to the left and are accompanied by left hemiparesis (Fig. 2.4c) (Fisher 1967).
4. Right pontine lesions produce leftward eye deviation. Left hemiparesis may or may not be present (Fig. 2.4d).

Fig. 2.4 Patterns of horizontal eye deviation and hemiparesis in patients with coma
Horizontal *dysconjugate* (the eyes look in different directions) gaze abnormalities are often helpful in localizing coma. Common patterns include:

1. Exodeviation (outward deviation) of both eyes. This is the pattern seen in many patients with coma, and usually does not have localizing value.
2. Hypodeviation and exodeviation of one eye ("down and out") secondary to third nerve palsy.
3. Esodeviation (inward deviation) of one eye secondary to sixth nerve palsy or increased intracranial pressure.

**Vertical Eye Position**

The supranuclear control of vertical eye movements is more complex, and involves the bilateral frontal lobes and structures within the brainstem including the vestibular nuclei and interstitial nucleus of Cajal in the midbrain. The important abnormalities of vertical ocular eye position in coma include:

1. Downward deviation of the eyes ("the setting sun sign") suggesting a severe dorsal midbrain lesion (Baloh et al. 1985).
2. Vertical ocular misalignment pointing to skew deviation from a brainstem lesion or fourth nerve palsy.
3. Hypodeviation and exodeviation of one eye ("down and out") secondary to third nerve palsy.

**Spontaneous Eye Movements**

The spontaneous eye movements of comatose patients are usually slow and roving or absent altogether. Absent eye movements suggest a greater depth of coma, and possibly, brain death, but do not have particular localizing value. Ocular bobbing is characterized by quick downward eye movements which are followed by a slower return back to the primary position, and classically reflect pontine damage (Fisher 1964). Dipping refers to slow downward eye movements with a quicker upward return. Bobbing and dipping may also have inverse forms, in which the first movement is upwards rather than downwards.

**Oculocephalic Responses**

The oculocephalic response is assessed in comatose patients by the head thrust maneuver or by cold caloric testing. To test the oculocephalic response via the head thrust maneuver, grasp the head by the forehead and chin. Peel the eyelids open and turn the head briskly to one side. The eyes will turn in the direction opposite of head
rotation in patients with intact brainstem function. Dysconjugate eye movements may accompany structural brainstem lesions. Eye movements will be absent in patients who are deeply comatose or brain dead. Do not use the head thrust maneuver in patients with possible cervical spine instability, as neck manipulation may worsen motor deficits and even lead to paralysis.

Because the head thrust maneuver is only a weak stimulus to eye movement, many comatose patients require cold caloric testing. To test cold caloric responses, place the head of the bed at 30° above the horizontal, thereby aligning the horizontal semicircular canal parallel to the ground. Examine the auditory canal to ensure that excessive cerumen accumulation will not interfere with the test, and disimpact the ears as necessary. Fill a 60-mL syringe with ice water and attach the syringe to a short piece of intravenous tubing. Place the tubing into the ear and infuse the ice water slowly over 5 min. If brainstem function is intact then the eyes should deviate towards the side of the ice water infusion. After performing the test on one ear, wait approximately 5 min for the vestibular system to reset, and test the opposite ear. Important patterns of abnormal oculocephalic response testing are shown in Fig. 2.5:

1. Cold water placed in either ear produces ipsilateral eye deviation of both eyes (Fig. 2.5a). This is the expected response in a patient with a metabolic encephalopathy and an intact brainstem.

Fig. 2.5 Important patterns of cold caloric testing in patients with coma
2. Cold water placed in the right ear produces no response; cold water placed in the left ear produces tonic ipsilateral eye deviation (Fig. 2.5b). This is the pattern seen in patients with right vestibular nerve or lateral pontine damage.

3. Cold water placed in the right ear produces rightward eye deviation of the right eye only; cold water placed in the left ear produces leftward eye deviation of the left eye only (Fig. 2.5c). This is consistent with a midline lesion of the midbrain and pons producing bilateral internuclear ophthalmoplegia (Chap. 6).

4. Cold water placed in either ear produces no response (Fig. 2.5d). This occurs with severe coma or brain death.

Motor Examination

The motor examination helps to determine the presence and severity of coma and in some cases localizes the responsible lesion. Movements may be divided into the following four categories:

Spontaneous and Purposeful

Spontaneous, purposeful movements indicate that the patient is not comatose, and should prompt evaluation for encephalopathy as detailed in Chap. 1.

Spontaneous but Nonpurposeful

For comatose patients, the most important spontaneous, nonpurposeful movement is polymyoclonus caused by anoxic brain injury and characterized by brief muscle jerks followed by relaxation of the arms, legs, and face. Sometimes polymyoclonus may take the form of violent jaw closure and result in tongue laceration or even severing of a mechanical airway (Chap. 14).

Reflexive

Comatose patients may demonstrate one of several reflex movements. In most patients, these are limited, local, nonpurposeful movements. They may be differentiated from normal movements by their lack of habituation to repeatedly applied, painful stimuli. The most widely known reflex movements in coma are decorticate and decerebrate posturing. In decorticate posturing, a painful stimulus causes flexion at the elbows, wrists, and fingers, and adduction of the arms. In decerebrate posturing, a painful stimulus causes internal rotation of the arms with extension at the elbows and flexion-pronation at the wrists. In both decorticate and decerebrate posturing, there is extension at the hips, extension at the knees, and plantar flexion at the ankles. Classically, decorticate lesions arise from lesions above the red
nucleus in the midbrain while decerebrate lesions arise from lesions between the red nucleus and above the vestibular nuclei in the medulla. The anatomic basis of decorticate and decerebrate posturing is less well defined in humans than in laboratory animals, though, and both may result from nonstructural, metabolic processes or from brainstem pathology. Both forms of posturing are associated with a poor outcome, with decerebrate posturing portending a worse prognosis.

**Absent**

If the patient does not move spontaneously or in response to verbal command, compress the fingernail or toenail bed with the handle of a reflex hammer. Severely encephalopathic patients but not those in coma may move the hand or foot away from such a stimulus with purpose. In some patients, a painful stimulus may produce only a facial grimace or heart rate elevation with no visible motor response in the limbs. This lack of a motor response in the presence of a preserved autonomic response is due either to severe brain damage or to neuromuscular dysfunction (Chap. 12). Absent response to pain with no change in heart rate suggests severe coma or brain death.

**Respiratory Patterns**

Abnormal respiratory patterns may suggest specific anatomic localizations of coma (Posner et al. 2007). The classic patterns are not observable while the patient is intubated, sedated, and paralyzed, but may become obvious if mechanical ventilation is discontinued temporarily. Cheyne-Stokes breathing is characterized by hyperpneic phases which build to a crescendo and then taper to apneic periods lasting for 10–20 s. This pattern is common in congestive heart failure and usually indicates intact brainstem function. Hyperventilation is associated with toxic and metabolic encephalopathies, generally those which produce metabolic acidosis. Central neurogenic hyperventilation is rare, and is usually seen in the context of infiltrating brainstem glioma or lymphoma (Tarulli et al. 2005). Apneustic breathing is characterized by two- or three-second pauses which occur at the end of inspiration and expiration, and reflects pontine damage. Ataxic breathing has an irregular, gasping quality, and is secondary to lower pontine or upper medullary dysfunction.

**Investigation of Impaired Consciousness and Coma**

Approximately 2/3 of coma is due to medical conditions, such as metabolic abnormalities and toxins while the remaining 1/3 is due to structural causes such as trauma, brain hemorrhage or tumor (Posner et al. 2007). Because the number of potential causes of coma is quite large, it is helpful to divide the investigation into three phases based on the frequency of the responsible causes and the ease of obtaining diagnostic testing:
Phase 1—History, Examination, and Basic Studies

By the time a neurologist is consulted, a basic metabolic workup and CT scan of the brain are usually available. This information helps to establish one of the following diagnoses:

Trauma—Patients with head trauma sufficient to cause coma almost always have abnormal head CT scans. In addition to skull fractures, abnormalities following trauma include epidural, subdural, intraparenchymal, and subarachnoid hemorrhages. Some patients have no clear evidence of fracture or hemorrhage but CT shows evidence of diffuse axonal injury.

Intracranial mass lesion—Bilateral frontal or brainstem lesions including tumors, abscesses, and intracranial hemorrhages may all lead to coma.

Subarachnoid hemorrhage—Aneurysmal rupture leading to subarachnoid hemorrhage is an important cause of coma that may be detected with CT scan (Chap. 19).

Hypoxic-ischemic injury—Whether due to anoxia following cardiac arrest or to severe hypoxia secondary to pulmonary disease, irreversible brain damage occurs after minutes of global ischemia and is among the most serious causes of coma.

Toxic or metabolic disturbances with normal imaging studies—Comatose patients with normal CT scans usually have a toxic or metabolic disturbance, often more than one. Routine laboratory testing is generally sensitive to the conditions listed in Table 2.1.

Table 2.1  Medical causes of coma

| Hypoglycemia |
| Hyperglycemia |
| Renal failure |
| Hyponatremia |
| Hypernatremia |
| Hepatic failure |
| Hypothyroidism |
| Hyperthyroidism |
| Hypercalcemia |
| Systemic infection |
| Intoxication with: |
| Alcohol |
| Cocaine |
| Barbiturates |
| Opioids |
| Benzodiazepines |
| Amphetamines |
| Acetaminophen |
Phase 2—MRI, EEG, and Lumbar Puncture

Although history, CT scan, and basic laboratory studies often disclose the etiology of coma, further evaluation is necessary should these initial investigations fail to identify the responsible process.

MRI serves several purposes in patients with coma of unclear etiology. Diffusion-weighted MRI identifies hypoxic-ischemic changes several days before they are detectable by routine head CT. MRI may also disclose two specific infarctions which are poorly visualized by CT. The first is infarction in the paramedian thalamic artery, which supplies the intralaminar nuclei of the thalamus and rostral midbrain (Barth et al. 2001) (Fig. 2.6). The second is infarction of the base of the pons leading to the locked-in state. Other causes of coma which may be missed by CT but detected by MRI include occult encephalitis or posterior reversible encephalopathy syndrome (Chap. 1).

EEG helps to establish the presence of severe encephalopathy or brain death in unclear cases of coma. A more important application of EEG in comatose patients, however, lies in its ability to detect nonconvulsive status epilepticus.

Fig. 2.6 Axial FLAIR MRI in a patient with paramedian thalamic artery infarction. This is an uncommon cause of coma, but it is important to recognize because it is often overlooked. The bilateral thalamic hyperintensities are quite symmetric, and it is easy to misdiagnose this finding as an artifact.
(NCSE), a potentially reversible condition which often eludes clinical diagnosis (Chaps. 1 and 20). Continuous rather than a routine 30-min EEG should be employed if NCSE is suspected, as 20% of patients may have their first seizures only after more than 24 h of monitoring (Claassen et al. 2004).

Lumbar puncture should be performed to evaluate for central nervous system infections, particularly bacterial meningitis and herpes encephalitis (Chap. 1).

**Phase 3—Uncommon Etiologies and Coma Mimics**

If the diagnosis remains unclear after an initial panel of investigations, MRI, EEG, and lumbar puncture, then consider less common toxins, neuromuscular mimics of coma, and psychogenic unresponsiveness.

Some toxins which may not be detected by routine toxicology screens are listed in Table 2.2. Consultation with a toxicologist is often helpful when considering these less common agents.

Severe neuromuscular disorders may lead to a state of profound weakness that mimics coma. Conditions such as Guillain-Barre syndrome, myasthenia gravis, and botulism are usually diagnosed before weakness reaches this severity, but occasionally motor function declines so precipitously that the deterioration may go unrecognized. Rapidly progressive weakness and difficulty weaning from the ventilator due to neuromuscular disease acquired in the intensive care unit are discussed further in Chap. 12.

Psychogenic unresponsiveness secondary to conversion disorder, malingering, or catatonia may be profound to the point that it mimics a comatose state. Obviously, exhaustive medical evaluation must be conducted before these possibilities are even considered: review all imaging studies, EEG, lumbar puncture, blood tests, and toxicology screens. For patients with conversion disorders or malingering, cold caloric testing may cinch the diagnosis and cure the coma by inciting violent nausea and vomiting. Although patients with psychiatric disorders do not have an organic explanation for coma, they require attention and life support that is just as careful as that which is provided to patients with organic neurologic disorders.

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<tr>
<th>Table 2.2</th>
<th>Less common toxins which lead to coma</th>
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<td>Rohypnol</td>
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<td>Ketamine</td>
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<td>Phencyclidine</td>
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<td>Ethylene glycol</td>
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<td>Methanol</td>
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<td>Antidepressants</td>
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<td>Anticonvulsants</td>
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Prognostication in Coma

The ability to accurately predict the outcome of a comatose patient is essential, as it provides families with reasonable expectations about the potential for recovery and advisability of continuing life support. Prognostication is based on the proximate cause of coma, the neurologic examination, and in some instances, diagnostic test results.

The largest body of data concerning coma prognostication comes from patients with coma after cardiac arrest. Often, the goal in this patient population is to define which group of patients has no chance of a good neurologic outcome: if any reasonable chance of a good outcome remains, aggressive supportive care must be continued. The following examination and laboratory results predict against a meaningful neurological recovery in patients who have sustained a cardiac arrest, and should be applied only to patients with this specific etiology. Take note that persistent hypothermia and pharmacologic sedation must be excluded as alternate causes of coma (Levy et al. 1981; Wijdicks et al. 2006; Fugate et al. 2010):

- Absence of brainstem reflexes at any time
- Myoclonic status epilepticus at day 1 (24 h after cardiac arrest)
- Somatosensory evoked potentials showing absent N20 responses at days 1–3
- Neuron specific enolase level >33 μg/L
- Absent pupil or corneal response at day 3
- Extensor posturing or absent motor response at day 3

Note that elevated neuron-specific enolase and motor response criteria are not of sufficient specificity to predict a poor prognosis in patients treated with hypothermia (Fugate et al. 2010). In most cases, authoritative statement about coma prognosis should wait until at least 72 h after cardiac arrest and rewarming. Unless supplemental tests are available, be cautious about providing too much prognostic information before this time point and continue to provide maximal supportive care.

The Persistent Vegetative State

After several days to a few weeks of deep coma, patients may appear to awaken and enter a vegetative state, which is given the name persistent vegetative state (PVS) if it lasts for at least 1 month (Jennett and Plum 1972). This state is characterized by roving or tracking eye movements and what appears to be an irregular sleep–wake cycle. These patients, however, do not interact with their environment in a meaningful way. They may grunt or moan, but do not speak or comprehend. PVS is the result of bilateral cortical damage with relatively preserved diencephalic and brainstem function. Although it may seem that PVS is a better cognitive state than coma, its ultimate prognosis is still quite poor: at 1 year following onset, only 1% of non-traumatic and 7% of traumatic PVS had a good outcome (The Multi-Society Task Force on PVS 1994). PVS should be considered permanent if it persists for 3 months.
in patients with non-traumatic conditions and for 12 months in patients with traumatic brain injuries (Giacino 2004). News stories of patients recovering after years of coma or PVS are exceptional, and should not be used to give families false hope.

The Minimally Conscious State

Patients recovering from coma or a vegetative state, particularly those due to traumatic etiologies, may enter a minimally conscious state (MCS) that resembles PVS with several important differences. Patients are able to respond to external stimuli in a limited way by nodding their head yes or no, verbalizing in a very basic fashion, holding objects appropriately, and following simple commands (Giacino et al. 2002). While recovery to functional independence remains unlikely in MCS, the prognosis is better than it is for PVS (Lammi et al. 2005). Anecdotal reports and small case series have shown improvement in MCS patients treated with zolpidem, amantadine, levodopa, or transcranial magnetic stimulation (Oliveira and Fregni 2011).

Brain Death

Brain death is defined as the complete loss of brain function despite preserved cardiac function. It is particularly important to recognize brain death in order to allow decisions about withdrawing aggressive medical support and to plan for organ procurement. Before a patient is diagnosed with brain death, all potentially reversible causes of coma must be corrected. Sedatives such as midazolam and propofol must be discontinued and core temperature should be raised to at least 97 °F. Next, the patient must be carefully examined, typically by using an institution-specific brain death protocol. A patient who is brain dead must be unarousable to any stimulus, lack pupillary and corneal reflexes, have no cold caloric responses, and not gag or cough when suctioned. Deep tendon reflexes may be (and often are) preserved. Many institutions require reexamination several hours or a day later, though this repetition is unlikely to alter the clinical impression of brain death: in one study, a second examination reversed the diagnosis in zero of more than 1200 patients (Lustbader et al. 2011).

The apnea test is used to confirm brain death. Hypercarbia is a profound stimulus to breathe, and failure of hypercarbia to produce a respiratory effort indicates brain damage incompatible with life. Before performing the apnea test, obtain a baseline arterial blood gas sample and note the partial pressure of carbon dioxide (P_{CO2}). Next, preoxygenate the patient with 100 % oxygen for at least 10 min. Following preoxygenation, discontinue mechanical ventilation while continuing to provide oxygen via a face mask. The apnea test is positive if no respiratory efforts are visible after 10 min of ventilator discontinuation. Before reconnecting the patient to the
ventilator, draw a repeat arterial blood gas sample to confirm the adequacy of hypercarbia: the $P_{CO_2}$ level must reach an absolute level of 60 mmHg or a relative level 20 mm Hg higher than the baseline level.

In some patients, difficulties with interpreting the neurological examination or minor metabolic abnormalities prevent airtight confirmation of brain death. In such cases, supplementary diagnostic tests establish brain death by showing absence of cerebral electrical activity or cerebral blood flow. These include:

- EEG showing electrocerebral silence
- Somatosensory evoked potentials showing absent N20 responses
- Absent cerebral blood flow as determined by
  - Transcranial Doppler ultrasound
  - Cerebral angiography
  - Radionuclide cerebral perfusion scanning

**Increased Intracranial Pressure**

Expansion of intracranial contents is limited by the rigid confines of the skull. Blood, tumor, abscess, and edema are tolerated to a limited extent before symptoms and signs of increased intracranial pressure develop. In its earliest stage, increased intracranial pressure causes nonspecific headaches and visual blurring. Recognition of increased intracranial pressure at this stage may allow the responsible process to be diagnosed and reversed, thereby preventing additional neurologic deterioration. Funduscopic examination may show papilledema (Chap. 19, Fig. 2.2) Further increases in intracranial pressure lead to encephalopathy, seizures, and a variety of focal neurological findings. The most devastating consequences of increased intracranial pressure are the herniation syndromes in which brain tissues are displaced from their normal locations, compressing or damaging otherwise healthy structures. The most important of these syndromes are uncal and transtentorial herniation.

**Uncal Herniation**

A hemispheric mass or edema may cause expansion of one cerebral hemisphere relative to the other, leading to herniation of the uncus of the ipsilateral temporal lobe medially and inferiorly into the tentorial notch (Posner et al. 2007). The earliest signs of uncal herniation are ipsilateral pupillary dilatation produced by stretching or compression of the third nerve and a decrease in consciousness produced by compression of the upper brainstem. Pupillary dilatation in the presence of preserved consciousness, however, is never due to uncal herniation (Posner et al. 2007). As uncal herniation progresses, hemiparesis usually develops ipsilateral to the herniating mass as the contralateral cerebral peduncle is compressed, the so-called
Kernohan notch phenomenon. Less commonly, the ipsilateral cerebral peduncle is compressed leading to a contralateral hemiparesis. Thus, pupillary dilatation is more reliable than hemiparesis in lateralizing uncal herniation. Shearing or compression of the posterior cerebral arteries in the tentorial notch may lead to strokes and cortical blindness. Because uncal herniation may progress rapidly to a state of irreversible neurologic compromise or death, it must be identified as quickly as possible to allow treatment of the responsible source.

**Transtentorial Herniation**

An expanding midline lesion may cause herniation downwards through the tentorium, compressing the thalamus and brainstem (Posner et al. 2007). In early transtentorial herniation, the patient appears to be sleepy with small, minimally reactive pupils. It is very easy to misdiagnose the patient with a metabolic encephalopathy, and a high index of suspicion must be maintained in order to make the diagnosis at this stage, as further progression is generally associated with a poor outcome. As herniation continues, the midbrain is compressed, leading to paresis of upgaze, unresponsiveness, and decorticate posturing. Continued downward herniation compromises the pons, resulting in loss of lateral eye movements and decerebrate posturing or motor unresponsiveness. In the final stage of transtentorial herniation, medullary compression produces irregular breathing, flaccidity, and eventually death.

**Other Herniation Syndromes**

Subfalcine herniation is caused by a hemispheric mass causing medial displacement of ipsilateral cerebral contents inferior to the falx cerebri. Upward herniation occurs when a large cerebellar mass or infarct leads to expansion of the posterior fossa contents superiorly. Tonsillar herniation involves herniation of posterior fossa contents inferiorly with compression of the medulla or cervicomedullary junction by the cerebellar tonsils. Extracranial herniation is displacement of intracranial contents externally through a skull defect, either traumatic or iatrogenic.

**Management of Increased Intracranial Pressure**

The definitive treatment of increased intracranial pressure is removing the proximate cause, whether it is hemorrhage, edema, tumor, or abscess (see also Chaps. 21 and 23). In many cases, this is not possible and medical management becomes the focus of treatment.
Once neurological deterioration due to increased intracranial pressure is identified, the first step in management is to improve cerebral venous drainage by placing the head of the patient’s bed at a 45° angle. Next, intubate the patient and hyperventilate them to a carbon dioxide partial pressure ($P_{CO_2}$) of 26–30 mm H$_2$O. This decrease in $P_{CO_2}$ produces an alkaloic cerebral vasoconstriction and increases the volume available to the brain parenchyma. Reduction of the $P_{CO_2}$ to 25 mm H$_2$O or lower increases the risk for cerebral ischemia and should be avoided. The benefits of hyperventilation usually last for only a few hours, and sustained hyperventilation may increase the chance of cerebral ischemia. Sedation with propofol or fentanyl will prevent the patient from fighting the ventilator and reduce the chance of a gag or cough leading to a dangerous spike in intracranial pressure.

Placement of an intracranial pressure monitoring device can be considered for patients in whom the neurologic examination cannot be monitored reliably. Studies of the benefit of intracranial pressure monitoring on survival have created considerable controversy, however, and the benefit on tailoring treatments to intracranial pressure readings is not clear (Chestnut et al. 2012). For most patients, the goal is to avoid sustained intracranial pressure of >20 mm Hg. In patients without invasive intracranial pressure monitoring, frequent serial examinations and a daily head CT to look for progressive midline shift should be performed.

Osmotic diuretics are the mainstay of medical management of increased intracranial pressure. The two main treatment options are mannitol and hypertonic saline, and each has its advocates. The osmotic diuretic mannitol is initially administered as an intravenous bolus of 1 g/kg followed by smaller boluses of 0.25–0.5 g/kg every 6 h, as dictated by clinical response and intracranial pressure readings, if available. The serum osmolality should be measured with each dose of mannitol and be kept below 320 mOsm. Hypertonic saline is administered as a 30 mL bolus of a 23.4 % solution or a 150 mL bolus of 3 % solution, with a maintenance infusion of 3 % solution to keep the serum sodium concentration between 145 and 150 mEq/L, again monitoring for clinical response or a reduction in intracranial pressure readings.

In patients in whom the source of increased intracranial pressure cannot be addressed, consider craniotomy and temporal lobectomy to reduce rapidly increasing intracranial pressure. Because most patients who reach the stage at which this intervention is considered have a poor prognosis, decisions about neurosurgical intervention should be made very carefully. Other treatments including barbiturates, corticosteroids, and therapeutic hypothermia do not improve outcome in patients with increased intracranial pressure, and should be avoided.

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