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Chapter 1

# Disorders of consciousness

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## Introduction

The assessment of the patient with acute impairment of consciousness requires an organized, systematic approach, beginning with the history (the diagnosis is suspected on the history alone in over 85% of cases), the physical examination, and basic laboratory testing. It is only after these steps that well-chosen neuroimaging is performed, always with a specific question in mind. This review synthesizes clinical, laboratory, and radiological approaches with a strategy that will provide useful diagnostic and prognostic information. We also provide a special focus on the potential future role of novel neurodiagnostics in the acute care setting.

Consciousness is composed of two principal components: alertness and awareness. Alertness is a function of the ascending reticular activating system (ARAS) in the rostral brainstem tegmentum (from the midpons through the midbrain) and then the thalamus and its projections through the cerebral white matter to the cerebral cortex. This allows for an eyes-open vigilant state, including arousability and spontaneous wake and sleep cycles. (This system and its various neurotransmitters will be discussed later.)

Awareness depends on the integrity of integrated cerebral gray-matter structures and their interconnecting fibers running through the white matter. Awareness has multiple inter-related functions, including sensation, perception, memory, attention (with selectivity), emotions, judgment, motivation, and planned action, with various interconnected anatomical loci.

Thus, consciousness is not a unitary phenomenon, but has multiple components. It is best to describe impairment of consciousness in terms of the type of impairment and its degree. Note also that a patient can be fully awake and aware, but may not be responsive due to central (including psychogenic) or peripheral nervous system causes. Thus, the absence of response is not necessarily proof of a disorder of consciousness (DOC).

## The approach

A patient with acutely altered consciousness is brought into the emergency room by the ambulance service. You are asked to consult on the patient to provide a diagnosis and, if necessary, a prognosis, and to recommend steps in management, including investigation and treatment.

The above is a common clinical problem and the clinician should have an approach that will maximize precision and effectiveness. Let us suppose that the initial ABC management (airway, breathing, and circulatory) has been performed and that initial blood work has been sent, so that we can concentrate on the diagnostic approach. The initial step is history-taking, followed by the neurological and relevant general examinations.

As in the clinical approach to all neurologic disorders, the initial step is to localize the problem, then to determine the etiology. In DOC, the issue of prognostic determination often follows.

A. **History**: The history can help localize the problem as well as provide a story of the tempo or course of the illness, thus addressing both where and what.

   A description of the acute behavioral change is usually available from the ambulance attendants and persons living with the patient. Was the problem a disturbance in alertness or a change in behavior? Was it a sudden collapse or a gradual and progressive or fluctuating change? Were there any preceding incidents or illness, e.g., head injury, drug ingestion, fever, or headache? Were there

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focal features, e.g., a hemiparesis or aphasia, which preceded the loss of consciousness? What chronic conditions were present, e.g., cancer, diabetes, epilepsy, or autoimmune diseases; or cardiac, pulmonary, hepatic, or renal impairment? What medications was the patient taking? Was there a history of drug or alcohol abuse? What were the details of the collapse – falling limply vs. like a tree? Were there convulsive movements? Did anyone feel for a pulse?

B. **The neurological examination**: The degree of obtundation, using the Glasgow Coma Scale (GCS) [1] or FOUR score if desired, is determined [2]. Observe spontaneous movements and response to stimulation. If the patient remains unresponsive one applies progressively increasing stimuli, starting with calling the patient's name then applying somatic stimulation. Cranial nerve examination can help localize the lesion to specific cranial nerves or the brainstem. Check for gaze preference or palsy (using oculocephalic or caloric testing), and pupillary reactivity and size. The corneal reflex if unilaterally absent can be localizing, but corneal reflexes being present or absent bilaterally can reflect the degree of ARAS depression from an overwhelming metabolic disorder or a drug overdose. The combination of intact pupillary and absent oculovestibular reflexes raises the possibility of Wernicke–Korsakoff's encephalopathy, but we have seen the same phenomenon with a wide variety of sedative and analgesic drugs as well as antihistamine overdoses. The presence of nystagmus with caloric testing is strongly supportive of psychogenic unresponsiveness. One should always check for vertical eye movements, as lesions of the thalamus or rostral brainstem can abolish vertical but not horizontal eye movements.

Motor tone is assessed by passively moving the patient's limbs and noting the resistance to movement. Patients with neuroleptic malignant syndrome, malignant hyperthermia, or serotonin syndrome typically have marked, persistent increased resistance to movement. Patients with other causes of encephalopathy, when comatose, may have flaccid tone, but encephalopathic patients with metabolic or septic causes often show a fluctuating, velocity-dependent increase in tone (the resistance increases with the speed of movement) known as *gegenhalten* or paratonic rigidity. In parkinsonian rigidity (commonly produced by neuroleptic medications or metoclopramide), the resistance is present throughout the range of movement and is not as velocity-dependent as in *gegenhalten*. In spasticity, there is a velocity-dependent increase in tone and then a release as the muscle spindles fire, causing flaccidity (clasp-knife effect). It is useful to note the motor responses to stimulation. The lack of movement on one side of the body, or hemiplegia, indicates a central cause for the paralysis. Purposeful movements in which the arm moves to the stimulus, often pushing it away or crossing the midline, indicate a lighter level of consciousness and an intact motor system on the side with movement. Decerebrate (upper- and lower-limb extension) or decorticate (upper limbs flexed at the elbows) were thought to indicate lesions below or above the red nucleus in the midbrain, respectively, but in humans both can occur with deep cerebral lesions, and the type of posturing can alternate over time.

In the less obtunded patient, the presence of postural-action tremor (with the upper limbs held up against gravity and/or moving to a target), asterixis (flapping tremor caused by the loss of postural tone as the patient holds the upper limbs out and extends the wrists), and multifocal myoclonus are strongly suggestive of a toxic or metabolic encephalopathy.

C. **Routine blood and urine testing**: Routine testing of serum glucose, electrolytes, magnesium, calcium, phosphate, urea, and creatinine and arterial or capillary blood gases are usually worthwhile. Urine is commonly sent for glucose, protein, and cell counts, but bacterial culture and drug screening (usually with specific drugs in mind) are commonly indicated. Serum drug concentrations, checking for alcohol or drug intoxications or for compliance of maintenance drugs, e.g., anticonvulsants, are often performed. Blood gas determination can help narrow the differential diagnosis (e.g. a metabolic acidosis is commonly due to increased lactate (as in sepsis or hypoperfusion), ketones or uremic toxins, or some exogenous agents such as methanol or propylene glycol). Point-of-care testing often obviates the need to administer glucose intravenously; if the latter is done it is wise to give thiamine simultaneously to prevent Wernicke–Korsakoff's encephalopathy.



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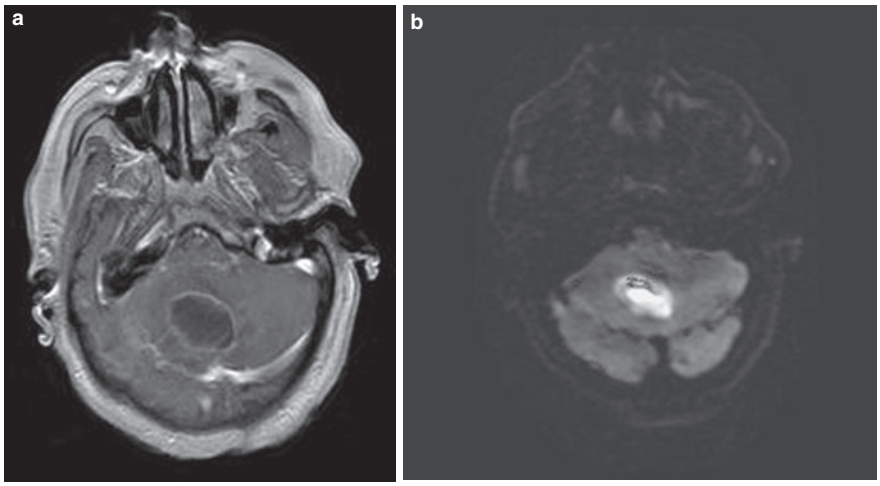


**Figure 1.1** (A) Axial T1-weighted post contrast-enhanced MRI shows a ring-enhancing cerebellar abscess that occurred with purulent meningitis. There is associated compression of the fourth ventricle. (B) A diffusion-weighted MRI scan shows diffusion restriction, a feature that can help differentiate abscess from tumor.

D. **Lumbar puncture (LP)**: In the acutely comatose patient LP is used to rule out central nervous system (CNS) infection or subarachnoid hemorrhage. Less commonly, meningeal carcinomatosis can present with loss of consciousness. A computer tomography (CT) imaging of the head before LP is usually done, as unexpected mass lesions, e.g., cerebral or cerebellar abscess, can coexist with bacterial meningitis (Figure 1.1), making the LP dangerous. Subarachnoid hemorrhage can be detected by CT in over 95% of cases (Figure 1.2). Other contraindications to LP include coagulopathy and infection near or over the proposed puncture site.

E. **Neuroimaging in the acute setting**: Neuroimaging is necessary in all cases of disorders of consciousness except for those in which a non-structural cause of coma is readily identified, e.g., hypoglycemia reversed by an infusion of glucose. Even in metabolic, toxic, or infectious cases, neuroimaging is often advisable to exclude cerebral edema, associated traumatic lesions, a cerebral abscess, or empyema. CT scanning is usually available and is usually sufficient to make decisions about the safety of doing an LP.

One of the most common indications for neuroimaging in the emergency room (ER) is for stroke. Hemorrhagic stroke is readily detected on CT. However, ischemic stroke may be missed in very acute infarction. Subtle loss of gray–white differentiation can be helpful in showing ischemic damage affecting the cortex, insula, and basal ganglia. This forms the basis of the ASPECT scoring system, which has a correlation of greater than 80% between observers [3]. Recently, the American Academy of Neurology recommended diffusion-weighted MRI over CT for the assessment of acute ischemic stroke [4]. This allows for clearer delineation of the infarcted vascular territory.

## A classification of DOCs

1. **Brain death**: This is the permanent cessation of all functions of the brain. Brain death is an unambiguous state when properly diagnosed but can be misidentified in situations where clinical history is unknown or the examination is limited by trauma or prior alterations of sensory-motor function. Recognition of such confounding variables is crucial for the accurate assessment of brain death [5].
2. **Coma**: An unarousable unconscious state, in which stimulation does not produce an arousal response, due to dysfunction of the ARAS. Coma can be graded dependent on motor responses. Two scales that are used to grade consciousness are the GCS [1] and the FOUR score [2]. These are listed in Tables 1.1 and 1.2. Coma is usually defined as a GCS score of 8 or less; with the FOUR score as the



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**Table 1.1** The Glasgow Coma Scale (GCS)

| | | |
|---|---|---|
| Best eye response | Spontaneous – open with blinking at baseline | 4 |
| | Opens to verbal command, speech or shouting | 3 |
| | Opens to pain (not applied to face) | 2 |
| | None | 1 |
| Best verbal response | Oriented | 5 |
| | Confused conversation, but able to answer questions | 4 |
| | Inappropriate responses, words discernible | 3 |
| | Incomprehensible speech | 2 |
| | None | 1 |
| Best motor response | Obeys command for movement | 6 |
| | Purposeful movement to painful stimulus | 5 |
| | Withdraws from pain | 4 |
| | Abnormal (spastic) flexion, decorticate posture | 3 |
| | Extensor (rigid ) response, decerebrate posture | 2 |
| | None | 1 |

**Table 1.2** The FOUR score scale

| | | |
|---|---|---|
| Eye response | Eyelids open or opened, tracking, or blinking to command | 4 |
| | Eyelids open but not tracking | 3 |
| | Eyelids closed but open to loud voice | 2 |
| | Eyelids remain closed to pain | 1 |
| | Eyelids closed but open to pain | 0 |
| | Eyelids closed but open to pain | 4 |
| Motor response | Thumbs up, fist or peace sign | 4 |
| | Localizing to pain | 3 |
| | Flexion response to pain | 2 |
| | Extension response to pain | 1 |
| | No response to pain or generalized myoclonus status | 0 |
| | Brainstem reflexes, pupil and corneal reflexes present | 4 |
| | One pupil wide and fixed | 3 |
| | Pupil or corneal reflexes absent | 2 |
| | Pupil and corneal reflexes absent | 1 |
| | Absent pupil, corneal, and cough reflex | 0 |
| | Respiration not intubated, regular breathing pattern | 4 |
| | Not intubated, Cheyne–Stokes breathing pattern | 3 |
| | Not intubated, irregular breathing | 2 |
| | Breathes above ventilator rate | 1 |
| | Breathes at ventilator rate or apnea | 0 |

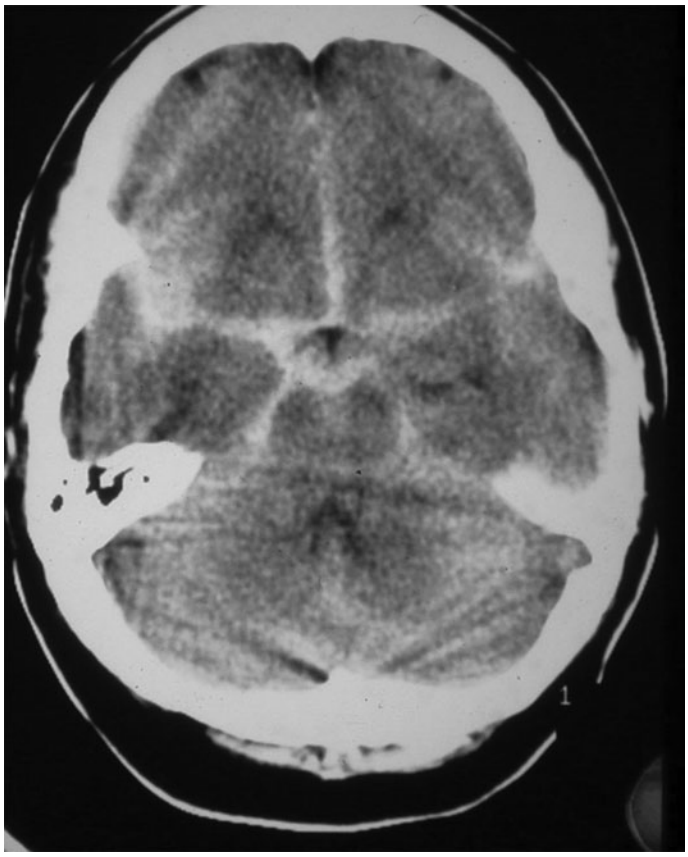

**Figure 1.2** Subarachnoid hemorrhage. An axial CT scan showing severe filling of the basal cisterns with blood in a case of spontaneous subarachnoid hemorrhage due to a ruptured berry aneurysm.



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failure of eye opening (0 for eye response) and a motor response of 3 or less. Coma is typically a transient state that gives way either to further recovery of brainstem function or deterioration and brain death.

3. **Stupor**: Brief arousal with eye opening or better, but the patient quickly lapses into a sleep-like state when not stimulated to waken. Stupor is, thus, also a disorder of the ARAS.
4. **Vegetative state** (**VS**): VS is a behaviorally defined state in which patients show no evidence of self or environmental awareness. VS patients, like comatose patients, may have spontaneous, or stimulus-induced, stereotyped movements, and retain brainstem regulation of visceral autonomic functions. The key difference from coma is that VS patients demonstrate cyclical variation of eyes-open and eyes-closed periods across 24-hour periods. VS patients, however, do not have normal sleep–wake cycles; typically, an electroencephalogram (EEG) in VS displays a monotonous slow pattern regardless of whether the eyes are open or closed, or fragmentary components of normal electroencephalographic sleep–wake phenomenology may appear [6]. VS may represent a transitional state on the way to recovery of consciousness or could be a chronic condition in cases of more severe brain injuries. The term persistent vegetative state (PVS) has gone somewhat into desuetude and carries a temporal connotation of duration of at least one month of VS clinical features [7, 8].

   VS patients typically show one of three main pathological findings if remaining in a prolonged VS following structural brain injury. Diffuse cortical and thalamic cell loss is most common and is present in the setting of global ischemia due to cardiac arrest. The second is widespread damage to axonal connections, mostly long-range fibers (as opposed to U fibers), labeled as diffuse axonal injury (DAI). The third and least-common pattern of injury is extensive damage to the upper brainstem and thalamus, which usually occurs due to basilar artery stroke [9]. The common link between these three injury types and VS is the loss of corticothalamic function, either from cell death, disconnection, or loss of brainstem activation. *In vivo* imaging studies demonstrate that VS reflects very diffuse corticothalamic dysfunction (reviewed by Laureys and Schiff [10]). Metabolic studies reveal that VS is associated with the reduction of global metabolic rates to 50% or less of healthy control values. Comparable reductions in cerebral metabolic rate arise during generalized anesthesia and slow-wave sleep in healthy controls, both considered unconscious brain states.
5. **Minimally conscious state** (**MCS**): The MCS was defined by the Aspen Workgroup as "a condition of severely altered consciousness in which there is minimal but definite behavioral evidence of conscious awareness." There is, thus, at least one aspect of awareness that is preserved [11]. Operationally, definition of MCS behaviors are often obtained from the Coma Recovery Scale Revised (CRS-R [12]) MCS patients show a wide range of behaviors from a low-level of non-reflexive behavior such as visual tracking of a mirror or localization of noxious stimuli, to high-level behavior such as consistent or inconsistent movements to command or inaccurate or inconsistent communication via gesture or even verbalization. Pathological studies indicate that MCS is typically associated with similar patterns of injury seen in VS but with considerably more preservation of cortical and particularly thalamic neuronal pools [13].
6. **Delirium** (**acute confusional state**): The essential component is a disorder of sustained attention, upon which various cognitive disorders are superimposed. This has varied localization, but is often a diffuse disorder of higher cortical function (see Chapter 3).

The various DOCs will be discussed in turn.

## Brain death

### Illustrative case

A 70-year-old man suffered a cardiac arrest at home. He was asystole in the ER. After resuscitation and the return of spontaneous circulation (ROSC) he was treated with hypothermia (temperature 33 °C) in the intensive care unit (ICU). His pupils remained at 3 mm and were unreactive during the 24-hour period of hypothermia. His temperature remained at 33 °C for another day and he was then slowly passively rewarmed. After all sedative drugs and



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neuromuscular relaxants were stopped and his temperature achieved 36 °C he was neurologically reassessed. Neuromuscular blockade was excluded by a positive "train of four" response with a nerve simulator. His pupils were 3 mm and unreactive; corneal, oculovestibular, gag, and cough reflexes were absent. There was no motor response to stimulation and he made no spontaneous movements and did not breathe above the ventilator. An attempt at reducing the ventilator rate was associated with a drop in his oxygen saturation (the patient had been a very heavy smoker and suffered from emphysema). He required inotropic support to maintain his blood pressure and desmopressin (DDAVP (1-desamino-8-D-arginine vasopressin)) to treat diabetes insipidus.

Brain death was considered, but the clinical criteria could not be applied because an apnea test was not feasible. He was, therefore, transported to the radiology suite for a CT angiogram (CTA), which showed normal enhancement of the major intracranial arteries including the internal carotid arteries and the proximal middle cerebral arteries (Figure 1.3). The patient's clinical features remained the same. Although the prognosis appeared to be hopeless, the family was not willing to withdraw life-supporting therapy (LST), for religious reasons. The following day the patient had a single-photon emission computed tomographic (SPECT) scan using technetium-labeled hexamethylpropyleneamine oxime (HMPAO-$Tc^{99m}$). This showed no perfusion of the brain (Figure 1.4) and the patient was declared brain dead. The family was informed that the patient was declared dead and that LST would be discontinued.

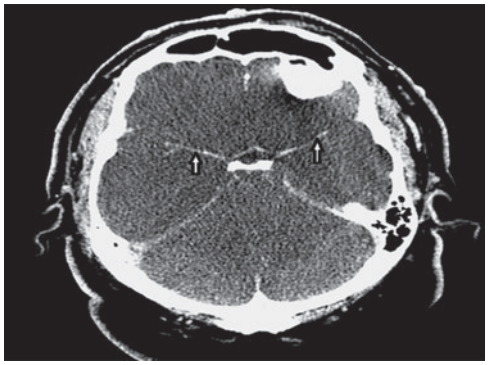

**Figure 1.3** False negative CT angiogram in brain-death evaluation. The CT angiogram shows normal enhancement of the proximal portions of the major intracranial arteries, including the middle cerebral arteries (arrows).

In this scenario the patient could not be declared "brain dead" on clinical grounds alone, as the apnea test could not be performed. Therefore, an ancillary test to confirm brain death was needed (over 20% of patients being considered for the neurological determination of brain death require such ancillary testing [14]). An ancillary test for the declaration of brain death should meet the following criteria: (1) There should be no "false positives", i.e., when the test is positive for brain death there should be no patients declared who have the potential for recovery of any brain function. (2) The test should be capable of "standing alone" as proof of brain death, the test should prove that the brain is not viable. (3) The test is standardized in technique, technology, and the classification of results. (4) The test should be available in centers with ICUs. The only tests that meet these criteria are tests of intracranial circulation. In Canada, only the following tests are acceptable: (1) Standard four-vessel cerebral angiography, (2) CTA, (3) magnetic resonance angiography (MRA), and (4) nuclear medicine flow studies or SPECT [15]. A problem with most of these tests is that there can be "false negatives" as any intracranial arterial filling is regarded as negating brain death. Indeed, in some cases, as in the case illustrated above, the proximal portions of intracranial arteries can sometimes fill with contrast without the parenchyma of the brain being *perfused*. This is most commonly seen in the context of brain swelling after a neurosurgical procedure or trauma. It follows that we need a refinement of the ancillary tests that indicates *lack of perfusion of the brain*, without which the brain cannot be viable. Suitable tests include: (1) CT perfusion studies as a component of CTA, (2) radionuclide tests such as SPECT that require the agent to penetrate into the brain parenchyma from the capillary bed, (3) MRI perfusion studies, and (4) filling of the deep cerebral veins (note that superior sagittal sinus filling can occur in brain death due to contributions from diploic veins of the skull).

## Coma

Two of the most common causes of acute onset coma for which outcome prediction is challenging are anoxic-ischemic encephalopathy from cardiac arrest and reperfusion and traumatic brain injury (TBI). We shall present cases of each with emphasis on prognostic determination. We shall also provide some cautionary information on acute hepatic encephalopathy.



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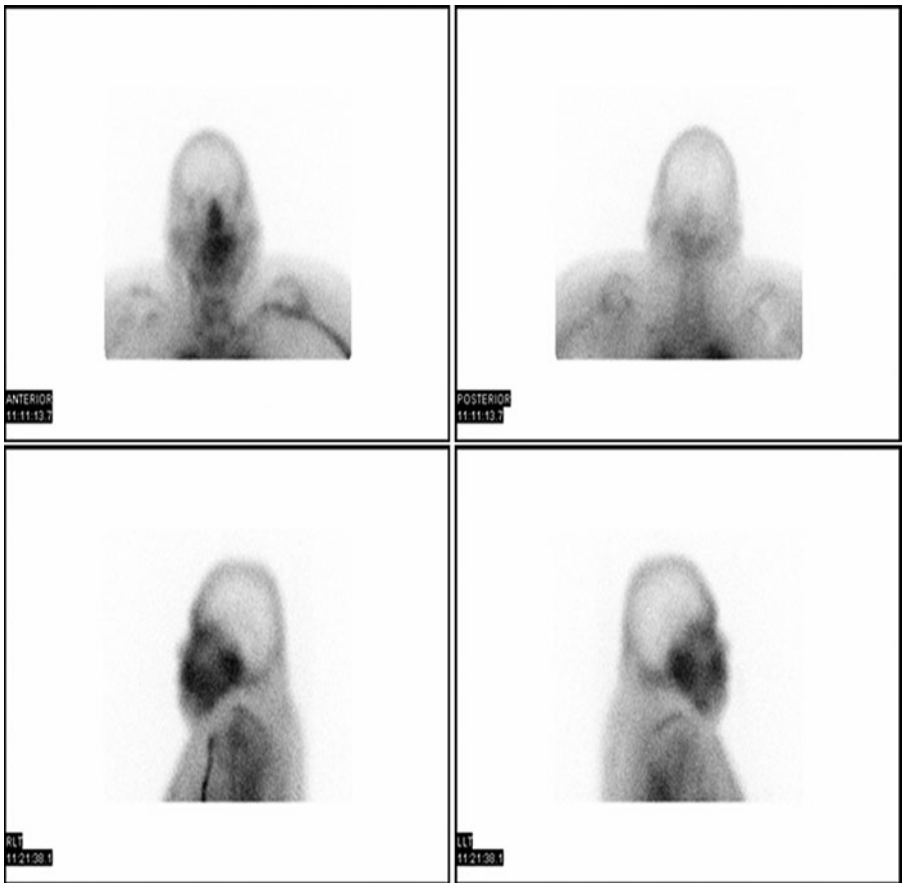


**Figure 1.4** A SPECT scan using HMPAO-$Tc^{99m}$ shows lack of brain uptake of the nucleide tracer. The other structures of the head did take up the tracer, producing the "hot nose" or "empty light bulb" sign, compatible with brain death.

## Anoxic-ischemic encephalopathy

Cardiac arrest and subsequent ROSC carries a multifactorial threat to the brain's neurons.

Different brain regions and specific neuronal populations appear more susceptible to hypoxic-ischemic injury (selective vulnerability). This is likely due to being located in a vascular border zone or due to higher metabolic rates requiring increased oxygen or to density of N-methyl-D-aspartate (NMDA) or α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors on neuronal membranes. The CA1 neurons of the hippocampus are the most sensitive to ischemia and injury can result in memory dysfunction. The Purkinje cells of the cerebellum, the large neurons in layers 3, 5, and 6 of the neocortex, and the reticular neurons of the thalamus, are commonly affected. Brainstem nuclei are relatively more resistant. In addition, three vascular border zones are susceptible to a reduction in blood flow due to the distance from the parent vessel, and these areas become clinically important in cases of severe hypotension and incomplete cardiopulmonary arrest. The cortical border zones are the anterior border zone between the anterior cerebral artery (ACA) and the middle cerebral artery (MCA), and the posterior border zone, between the MCA and posterior cerebral artery (PCA). The internal, or subcortical, border zone is found at the junctions between the branches of the anterior, middle, and posterior cerebral arteries with the deep perforating vessels, including lenticulostriate, Heubner, and anterior choroidal arteries. Infarction of the anterior border zone results in brachial diplegia, or "man-in-a-barrel" syndrome. Infarction of the posterior border zone results in visual deficits and in severe, bilateral cases may result in cortical blindness.



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## Prognostic determination in patients not treated with hypothermia

In 2006, the American Academy of Neurology published practice parameters that summarized the available literature and provided an algorithm to establish a prognosis [16]. These were based on literature that antedated the use of hypothermia. The criteria appeared valid with very low false-positive rates (FPRs) for predicting an outcome no better than total dependency in a nursing home after 24 hours (Figure 1.5).

If a patient has absence of all brainstem reflexes, motor responses, and apnea, ancillary testing can be used to confirm a diagnosis of brain death. It is wise to wait at least 24 hours from the time of the arrest as some initially lost brainstem reflexes and motor responses can recover within that time. In patients who remain comatose, but have a less severe neurological insult, clinical signs and electrophysiological tests can be used to establish a poor prognosis. The clinical signs that predicted poor neurological outcome were myoclonus status epilepticus on day 1, absence of the pupillary light reflex or corneal reflex on day 3, and best motor response of extension or worse on day 3. Somatosensory evoked potentials (SSEPs) completed on day 1 to 3 that demonstrate bilateral absent N20 responses also predicted poor outcome (Figure 1.6). Serum neuronal-specific enolase (NSE) greater than 33ug/L on day 1 to 3 was also a reliable indicator of poor outcome. The practice parameters allow a physician to identify a patient who will definitely have a poor neurological outcome, but it is important to note that many patients without any of these criteria will also have poor outcomes.

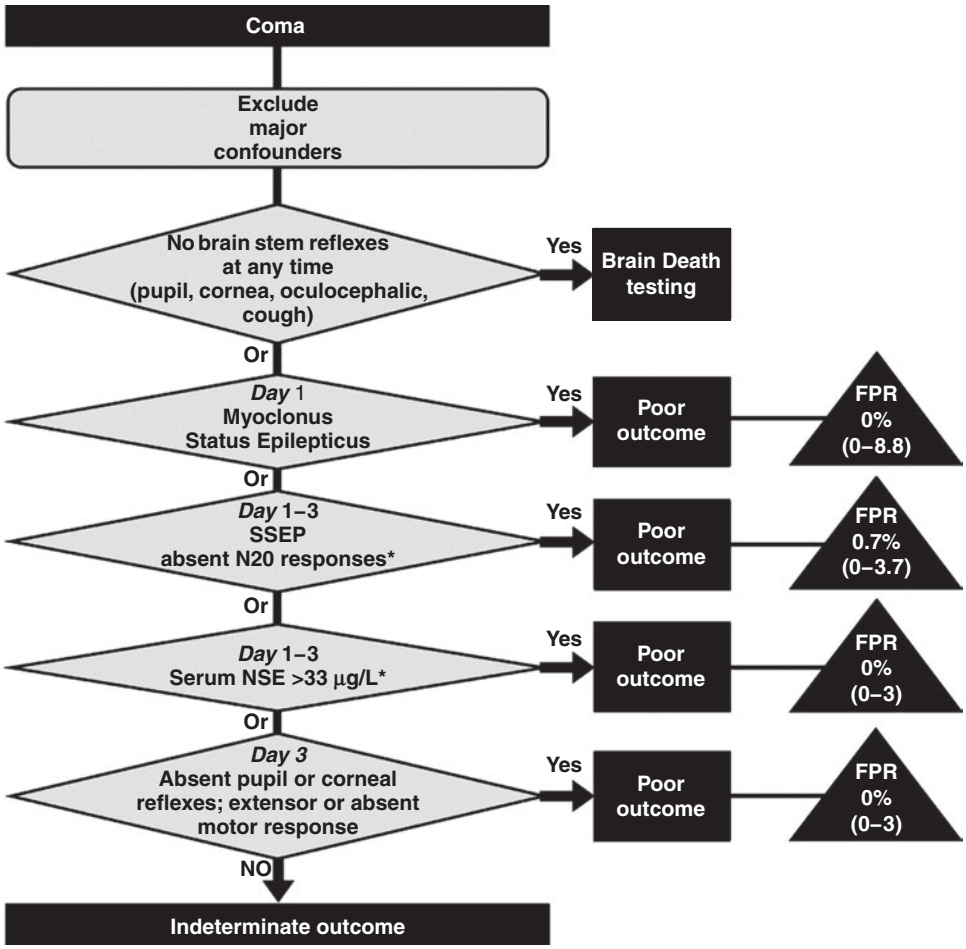


**Figure 1.5** Algorithm for neurological prognostication after cardiac arrest. Note this practice parameter algorithm antedated the literature for hypothermic protocols. (From [16] Wijdicks et al., 2006, with permission.)



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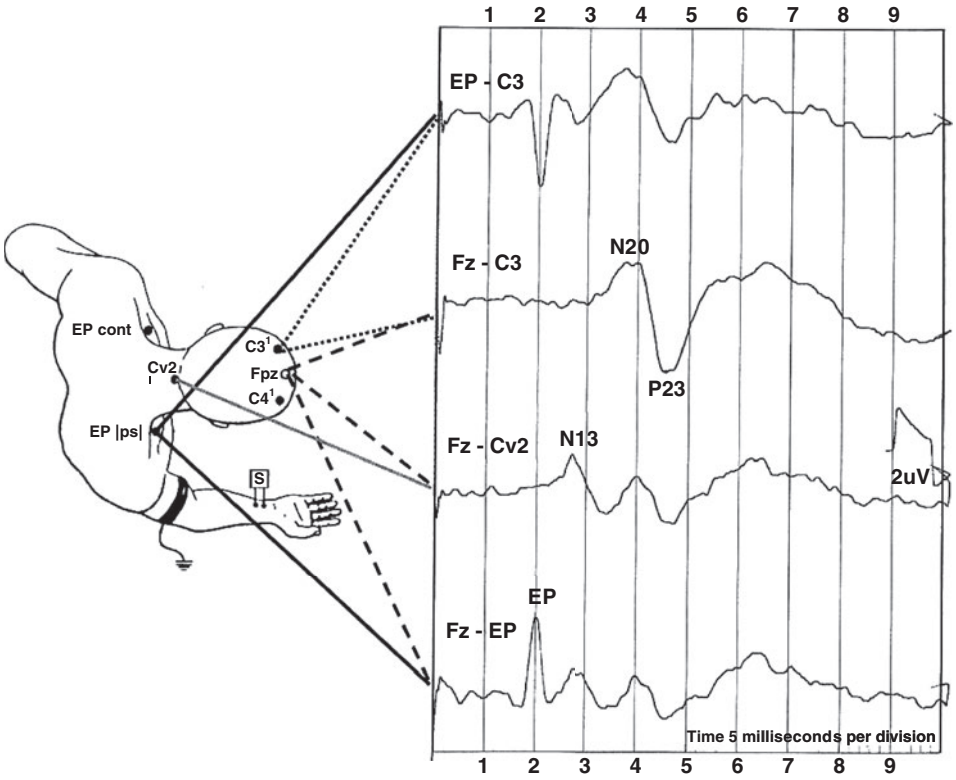


**Figure 1.6** Setup for testing somatosensory evoked potentials. Note the potentials recorded from Erb's point over the brachial plexus, the high cervical spinal cord and the contralateral primary somatosensory area.

Although neuroimaging and EEG were not thoroughly evaluated in the 2006 AAN (American Academy of Neurology) guidelines, these tests can have great predictive value, especially when combined with other testing modalities. CT scans of the brain are often normal in the first few hours after the arrest, but at least by day 3 they show swelling and inversion of the gray–white densities (Figure 1.7) in patients with a poor prognosis [17].

The EEG may be used to prognosticate in the post-arrest period, but one must be aware of its sensitivity to multiple confounders, including sedation, hypothermia, and multi-organ failure. The presence or absence of EEG reactivity has considerable prognostic value. EEG reactivity is defined as a change in frequency and/or amplitude that occurs in response to verbal or noxious stimuli. Al Thenayan and colleagues [18] retrospectively reviewed the EEG of 29 patients post-arrest and found that 17 out of 18 patients who lacked EEG reactivity did not regain conscious awareness. In a prospective series of 34 patients conducted by Rossetti and colleagues [19], a non-reactive

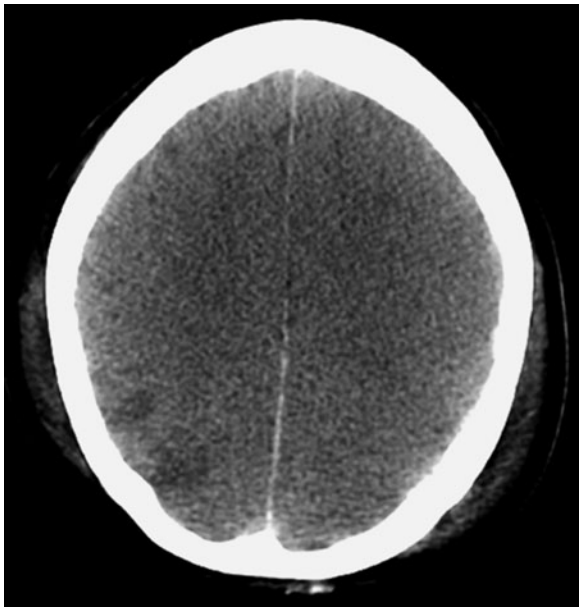

**Figure 1.7** CT showing cerebral edema with generalized loss of the usual gray–white matter differentiation in a case of severe AIE.



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background had a positive predictive value of 100%. In addition, all the survivors had EEG reactivity and 74% of these patients had a favorable neurological outcome. An additional series by Rossetti and colleagues [20] found that non-reactivity had an FPR of 7% for predicting mortality following cardiac arrest.

Up to 30% of post-arrest patients may develop status epilepticus. While often associated with poor outcomes [21], this same group found that epileptiform activity on the first EEG recording predicted poor outcome with an FPR of 9% [19]. Aggressive anti-epileptic treatment should be administered to these patients until other criteria suggest poor outcome. In summary, the EEG can aid in prognostication, both for favorable and unfavorable outcomes, but must be considered in context with other established prognostic indicators as the positive predictive value is insufficient to use in isolation.

## Illustrative case

A 45 year-old woman with multiple comorbidities, including diabetes mellitus and chronic renal failure, suffered an asystolic cardiac arrest 2 days after an aortic valve replacement. The resuscitation was prolonged (probably more than 20 minutes) before ROSC. Because of the recent surgery she was not treated with the hypothermic protocol (see later). She remained deeply comatose with a GCS of 3. On day 3, while off all sedation for more than 24 hours, her pupils showed slight reactivity, the corneal reflexes were bilaterally absent and there was no motor response to noxious stimuli. The CT scan (also done on day 3) showed marked swelling of the hemispheres with loss of sulci, basal cisterns, and loss of gray–white differentiation (Figure 1.7).

The EEG, also on day 3, was iso-electric (flat) without reactivity (Figure 1.8).

Since the 2006 AAN guidelines could be applied (no hypothermia), her clinical findings (absent corneal reflexes and no motor response on day 3) and the unfavorable CT scan and EEG indicated a poor prognosis. On discussion with the family, LST was withdrawn and she suffered a terminal cardiac arrest within 1 hour.

## Prognosis of cardiac-arrest patients treated with hypothermia

In 2002, two landmark studies published in the *New England Journal of Medicine* showed that therapeutic hypothermia (TH) (32–34 °C) significantly improved the mortality and morbidity post-arrest [22, 23].

Studies done on cardiac-arrest patients treated with hypothermia have shown that many of the 2006 AAN guideline features have reduced prognostic accuracy. Rossetti and colleagues [20] found higher FPRs for predicting mortality for absence of pupillary reactivity (FPR 4%), presence of axial myoclonus (FPR 3%), and best motor response of extensor or worse (FPR 24%). Al Thenayan and colleagues [24] found that motor response, specifically extension or worse, was not prognostically reliable at day 3 following TH. In their prospective review 14 patients had delayed return of the motor response as late as day 6 post-arrest and two of these patients had favorable

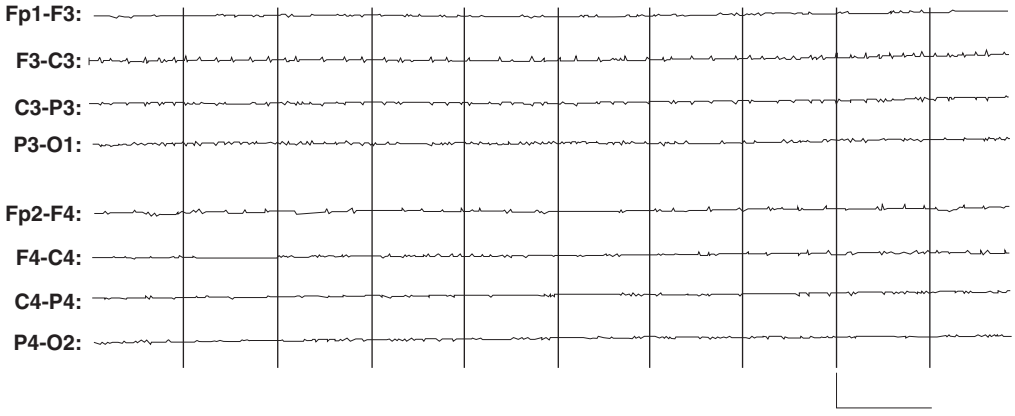


**Figure 1.8** Flat or iso-electric EEG.



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