International Encyclopedia of Rehabilitation

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Coma

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Definition

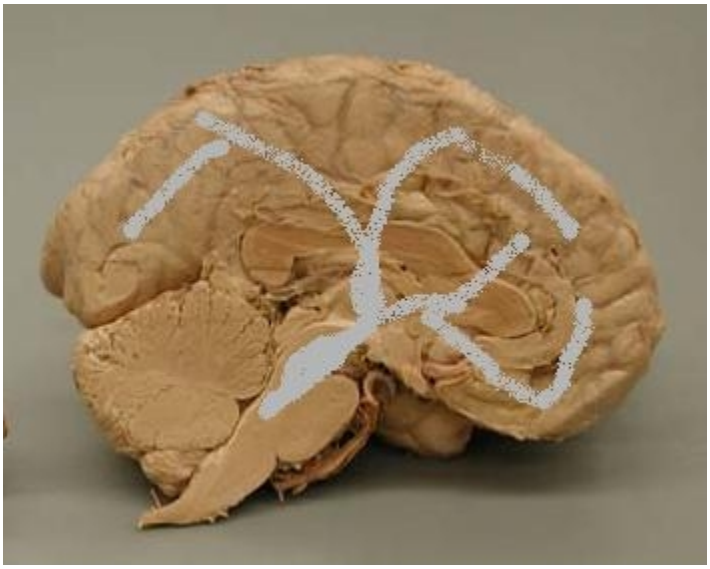
Coma is a state of unarousable unconsciousness. The patient cannot be made to "awaken", even though he/she may have some motor response to a stimulus.

Pathophysiology of Coma

Consciousness consists of two principal components: wakefulness or arousability and awareness. Awareness or the "content of consciousness" consists of higher functions, including attention, perception and memory with links to language systems, motivational and emotional centres and executive functions that provide selection and direction of responses. Awareness requires the person to be awake. Hence coma involves the "arousal system" of the brain. This arousal system requires some description.

In the 1940s Moruzzi and Magoun (1949) conducted a series of stimulating and destructive experiments on the brains of cats and monkeys and concluded that arousal and wakefulness required the functional integrity of the "ascending reticular activating system" (ARAS). This arousal network was found to comprise the reticular formation in the dorsal part of the midbrain and pons, with projections to the thalamus and hypothalamus and thence in a widespread manner to the cerebral cortex.

Figure 1: The ascending reticular activating system.



The concept of the key role of the ARAS has been validated and further refined. In the thalamus the medial and intralaminar nuclei are the main targets of the brainstem projection. The output from the thalamus is "gated" by the reticular nucleus of the thalamus, a sheet of gray matter overlying the main body of the thalamus. A number of neurotransmitters are important in the ARAS projection system: norepinephrine, dopamine, acetylcholine and serotonin are involved in "projections" from brainstem and hypothalamic centers. The neurotransmitter that plays a local role in the ARAS is glutamate, acting on various receptors. Inhibition of the ARAS, required for "tailoring" responses and selection of which pathways to be allowed to influence the cortex, uses gamma-amino butyric acid (GABA) acting at various levels. The hypothalamus is the major "pacemaker" for circadian rhythms and the wake-sleep cycle. Various neurotransmitters are operative there, including histamine, orexin-hypocretin in addition to GABA, glutamine and dopamine. As can be seen in Figure 1, there are multiple projections (with varied and multiple neurotransmitters), allowing for redundancy in the arousal system. This probably accounts for why coma is rarely a long-lasting condition, as some pathways are usually spared unless the damage or dysfunction is extremely extensive.

Clinical Assessment of the Comatose Patient

As in other aspects of medicine, the history can be of great assistance in narrowing the differential diagnosis. Had the patient been previously ill, e.g., with a brain tumor, cancer, or a recent febrile illness or was the event sudden and unexpected? Was the patient depressed or have there been previous suicidal attempts? What medications was the patient taking? What active illnesses did he/she have, e.g., diabetes, epilepsy, hypertension, conditions associated with impaired immunity, hepatic failure, renal impairment, cardiac problems? Was the loss of consciousness gradual or abrupt? Had there been fluctuations in conscious level? Have there been other episodes of reversible coma? Were there focal features, e.g., lateralized weakness or aphasia preceding the loss of consciousness? Any recent changes in behavior or mental functioning are recorded. Positive responses can help guide the evaluation and diagnostic tests. Remember that the telephone is part of the doctor's armamentarium and that there may be historical clues on the patient, e.g., Medic-Alert bracelet, card in wallet with a list of drugs or conditions.

The assessment should be systematic, addressing the issues in turn:

Is the patient really comatose?

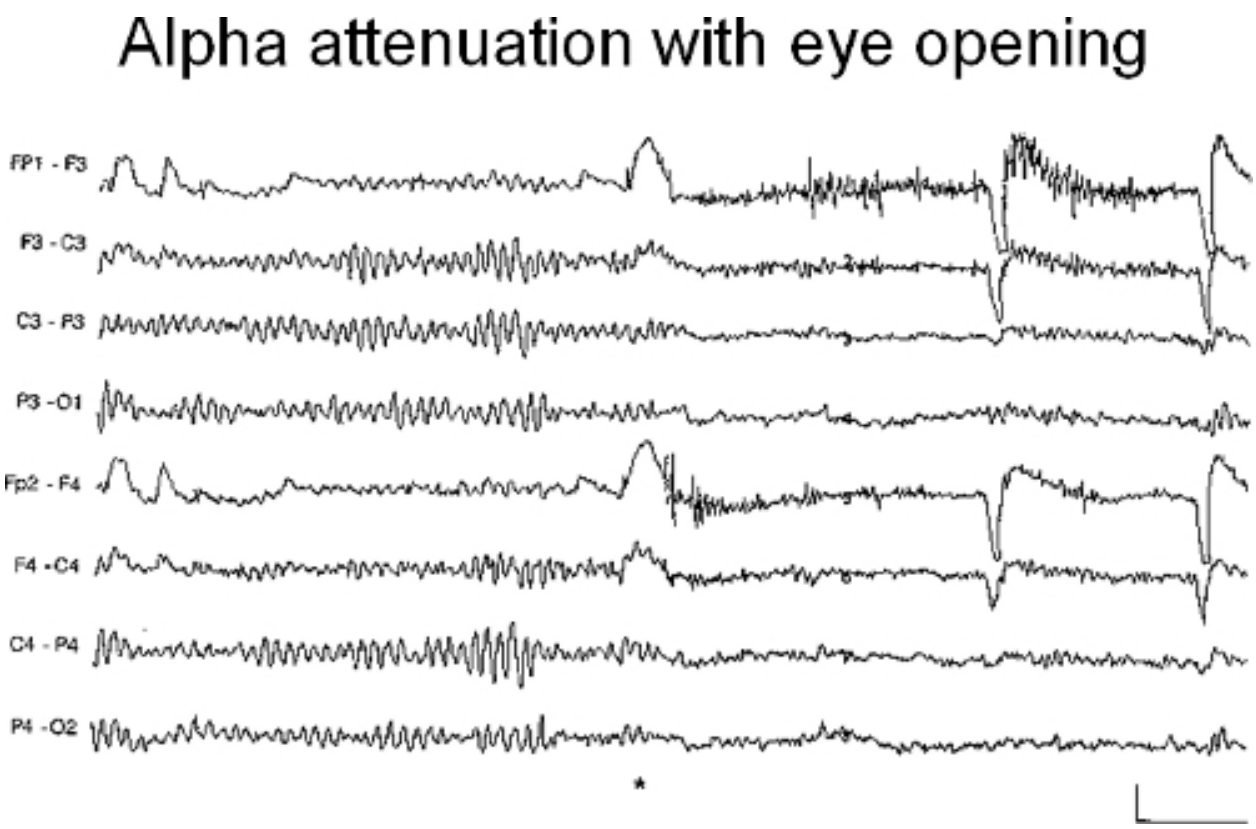
A patient who is unresponsive with eyes closed is not necessarily in coma. Two conditions can mimic coma:

Psychogenic unresponsiveness

The patient may, because of malingering or a conversion reaction, not respond, but yet the ARAS is working well and the patient is truly awake. This can be shown to be the case when there are findings that defy our knowledge of physiology. A clue that unresponsiveness is psychogenic is the presence of nystagmus when ice water is injected into the ear canal. The fast phase of nystagmus requires wakefulness (the slow tonic shift of the eyes towards the irrigated ear can be found in a comatose patient whose brainstem connections are working normally.) In addition, the patient may resist eye opening or move to avoid being tickled. If the patient is

rolled from side to side, the eyes sometimes tend to deviate towards the dependent side (Trimble 2001). Some patients may show bizarre phenomena that superficially resemble epileptic seizures (Trimble 2001). If an electroencephalogram (EEG) is done, the recording will be that of normal wakefulness with blocking of the background activity with passive eye opening (Figure 2.)

Figure 2: A normal, awake EEG with blocking of the alpha rhythm by eye opening.



Locked-in syndrome

The patient may be awake but unable to move because he/she is paralyzed. This commonly occurs with lesions of the basis pontis, causing paralysis of the voluntary motor pathways to the mid-lower brainstem and spinal cord. Such patients usually can open their eyes and make vertical but not horizontal eye movements. Their lower face and bulbar musculature and motor control of the limbs are lost, however. Thus they can swallow and breathe automatically from local reflexes and circuits in the caudal brainstem, but they cannot control these functions voluntarily. Basilar artery thrombosis (Schonewille et al, 2005) and central pontine myelinolysis (a demyelinating condition often due to rapid shifts in serum osmolality) (Karp et al., 1993) are the most common causes. Patients can also be globally paralyzed with severe, acute polyneuropathies or the prolonged action of neuromuscular blocking agents. When the paralysis is this marked, the EEG can offer proof that the patient is conscious or has the capacity for consciousness (see Figure 2).

Establish the level of consciousness

Coma can be graded and the grading system can be used to follow the course of the patient. The Glasgow Coma Scale (GCS) is almost universally used (Teasdale and Jennett, 1974).

Table 1

Item	Factor	Score
Best motor response	Obeys	6
	Localizes	5
	Withdraws	4
	Abnormal flexion	3
	Extensor response	2
	None	1
Verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Eye opening	Spontaneous (not in a seizure or with myoclonus)	4
	To speech	3
	To pain	2
	None	1

The maximum score is 15. In general, we consider a GCS score of 8 or less as indicating coma. Other coma scales that have some advantages over the GCS have been developed, e.g., the Reaction Level Scale (Starmark et al., 1988) and the FOUR Score (Wijdicks et al., 2005), but none has been widely adopted.

Where is the lesion/region of dysfunction?

As in real estate, location is of major importance. The presence of intact brainstem function (using the papillary, corneal, vestibulo-ocular and pharyngeal reflexes) indicates that the problem is either metabolic in nature or that there are bilateral structural lesions involving the thalamus or both cerebral hemispheres or, if the lesion is lateralized that there is enough horizontal shift of midline structures to render the thalamus dysfunctional. There are a some caveats:

Wernicke's encephalopathy

In destructive or compressive lesions of the brainstem causing coma, the papillary light reflex is almost invariably spared. However, because of the topography of lesions in Wernicke's encephalopathy, affecting the floor of the 4th ventricle, the vestibulo-ocular reflex is abolished, even with caloric testing.

Pupillary light reflex

The pupillary light reflex can be absent in cases of overdose of drugs with parasympatholytic side effects, e.g., amitriptyline or in massive overdoses of sedative drugs or in marked hypothermia (mimicking brain death).

The general assessment

Always check the vital signs: fever or hypothermia can point to an infectious or inflammatory condition, heat stroke if severe hyperthermia, thyroid storm, Wernicke's encephalopathy or myxedema coma (hypothermia). Severe hypertension, e.g., 200/140 can indicate hypertensive encephalopathy. Signs of head injury include bruising about the head, raccoon eyes (bruising limited by the margins of the orbit) indicating an orbital fracture, Battle's sign or bruising over the mastoid or blood behind the ear drum indicating a basal skull fracture. A tongue bitten on the lateral aspect could indicate a recent convulsive seizure. A petechial rash might indicate meningococcal sepsis or thrombotic thrombocytopenic purpura. Jaundice and ascites point to liver failure. Needle marks suggest intravenous drug abuse. Bacterial endocarditis is often accompanied by Janeway lesions (small erythematous or hemorrhagic lesions on the palms or soles), splinter hemorrhages, Osler's nodes or Roth spots (hemorrhagic lesions with white centres in the retina). A subhyaloid hemorrhage in the fundus almost always indicates a ruptured berry aneurysm.

An analysis of the respiratory pattern coupled with blood gas assessment can narrow the diagnosis considerably, especially in cases of hyperventilation ($PaCO_2$ usually <30 mm Hg). If there is a respiratory alkalosis (pH> 7.45) early sepsis or salicylate poisoning, hepatic failure, cardiopulmonary disease or psychogenic unresponsiveness are main considerations. If the $PaCO_2$ is <30 mm Hg and the pH is < 7.35 consider lactic acidosis, advanced salicylate poisoning, uremia, diabetic ketoacidosis or intoxication with methanol or ethylene glycol (especially if there is an osmolar and anion gap). Apneustic breathing with an inspiratory cramp often relates to a lesion in the pons, but there are often other signs.

Investigations

The choice of investigations is guided by the history, examination and preliminary basic laboratory tests.

The presence of lateralized neurological signs or of compromise of brainstem function is a strong indication for neuro-imaging of the brain. MRI scanning is more sensitive than CT for acute ischemic lesions, acute infections (e.g., herpes simplex encephalitis) and any posterior fossa structural abnormality. Most conditions associated with raised intracranial pressure will be revealed with CT scanning, which is quicker and more accessible. CT scanning is usually advisable before a lumbar puncture (LP) is done.

Multifocal or diffuse processes are usually either metabolic, septic, toxic, due to multifocal brain lesions, or conditions associated with abnormal cerebrospinal fluid (CSF). The following screening is usually done, unless the cause is obvious: complete blood count, serum urea, creatinine, glucose, calcium, magnesium, phosphate, electrolytes (sodium, potassium, chloride, and bicarbonate), hepatic function tests (transaminases, bilirubin, ammonia, INR), urinalysis, arterial blood gases (pH, PaO_2, $PaCO_2$ and bicarbonate). Blood cultures, drug screens and screens for coagulation problems (platelet count, blood smear, serum lactic acid dehydrogenase, and fibrinogen concentration), thyroid and adrenal function tests are sometimes needed. LP is done for suspected meningitis, encephalitis or subarachnoid hemorrhage).

Electroencephalography (EEG) is helpful in ruling out nonconvulsive status epilepticus (often present when patients are slow to recover from convulsive seizures or in patients with acute structural brain lesions or encephalitis) and to broadly classify disorders into metabolic or structural causes and in helping with prognostic determination after cardiac arrest.

Management of the Comatose Patient

The acutely comatose patient requires support while investigations are taking place. These include airway protection (often an endotracheal tube is required), ventilation support if spontaneous breathing is inadequate, maintenance of an adequate blood pressure and organ perfusion with inotropic drugs and intravenous fluids if necessary. Management of body temperature is also important. Severe hypothermia needs to be corrected and hyperthermia should be avoided.

It is important to do a serum glucose determination at point of care to ensure the patient does not have untreated hypoglycaemia. Thiamine (50-100 mg) should be given intravenously to prevent Wernicke's encephalopathy if there is any possibility of malnutrition. If narcotic or benzodiazepine overdose is suspected, intravenous naloxone or flumazenil, respectively, should be given.

Definitive therapy of the underlying condition awaits a precise diagnosis. However, seizures sometimes accompany some coma-producing conditions (e.g., encephalitis, cortical vein thrombosis, and alcohol or drug withdrawal) and may require emergency therapy for this complication. Usually lorazepam 2-4 mg is given intravenously followed by a loading dose (15-20 mg/kg) of phenytoin or phenytoin equivalent or 30-60 mg/kg of valproate. If ongoing, continuous seizures fail to respond to these medications, the patient is considered to have refractory status epilepticus and anesthetic agents (with endotracheal intubation and assisted ventilation) are often used (Rosetti 2009).

Prognostic Determination

As physicians we are trained to treat the treatable promptly and effectively to assure optimal results. However, some comatose patients have suffered widespread, irreversible brain damage that compromises quality of life. Such prognostic determination is as important as achieving a diagnosis. Very often when brain damage would lead to the vegetative or minimally conscious states, a severely incapacitated condition or profound dementia, the patient would not want to survive. Advance directives from the patient or instructions from substitute decision makers often dictate withdrawal of life support measures, letting the patient die with palliative measures in place. These wishes need to be respected under the principle of autonomy of the patient.

Prognostic determination is challenging, but this can be achieved in many cases of coma after cardiac arrest (Young 2009). Prognostication is still problematic but improving for severe traumatic brain injury (Petroni et al., 2010). Cases of severe brain damage from multiple strokes, hypoglycaemic encephalopathy, and encephalitis are best assessed individually, taking into consideration age, exam features and neuro-imaging results. Physicians should realize that prediction can almost never achieve 100% accuracy, but circumstances and families look to physicians to provide informed prognostic information to help with decision-making. We need to do our part in a responsible manner (Koch 2009).

Rehabilitation

The early prognostication of patients in coma helps in deciding their level of care. Determination of patients with the potential for favourable outcomes allows for better allocation of resources. For example, the early assessment and institution of rehabilitation can allow for better outcomes, shorter acute hospital length of stay and earlier integration into communities (Granger et al, 2010).

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