The term coma refers to a state in which a person is unaware of self and surroundings, even if stimulated from the outside. Between consciousness and deep coma, there is a continuum of possible levels of responsiveness and awareness. Encephalopathy is a broad term that may be used to indicate a decrease in awareness; a patient who develops confusion and decreased awareness can be said to be “encephalopathic.” Because many of the nuances of the neurologic examination are lost in the comatose patient, the EEG plays a special role in ascertaining the depth of coma. In patients who have been pharmacologically paralyzed, a common practice in intensive care units (ICUs), the neurologic examination yields limited information. In such patients the EEG may be the principle source of information regarding the patient’s neurologic state.

Broadly speaking, the EEG may contribute information in the setting of coma in three ways. First, the pattern seen on a single EEG “snapshot” may suggest the depth and severity of the coma. Second, trends seen in repeat or serial EEGs can be a useful indicator of improvement or deterioration in a patient’s status. The specific EEG parameters used to follow such trends and their implications are discussed in this chapter. Third, in a minority of cases the EEG pattern seen in coma can suggest its specific cause, such as the association of triphasic waves with hepatic and other metabolic encephalopathies or the unexpected discovery of continuous subclinical seizure activity.

**INDIVIDUAL PARAMETERS OF THE EEG IN COMA: Voltage, Frequency, Reactivity, and the Presence of Normal Sleep Elements**

There is a general correspondence between EEG coma patterns and the depth and severity of the coma. A variety of EEG attributes can be followed on serial testing to track a patient’s progress in the comatose state. In patients who have a deteriorating neurological status, a parallel deterioration in the EEG is expected. Likewise, in patients with progressive neurologic improvement, a concomitant improvement in the EEG is expected. Thus the EEG can serve as a useful adjunct to the clinical examination.

**Slow-Wave Voltage**

Low-voltage slow waves intermixed with the patient’s baseline background activity may be the first EEG sign of encephalopathic change (see Figure 12-1). An increase in the amount or amplitude of slow-wave activity suggests an increase in the severity of the encephalopathy. With deepening coma, slow-wave amplitude may continue to increase, and very high-voltage slow-wave patterns may be seen. Rather than intermixing with the background activity, the high-voltage slow-wave activity becomes the background. As cerebral function is increasingly affected, however, slow-wave amplitude can only increase to a certain point. With yet more severe cortical dysfunction, cortical rhythms begin to decrease in amplitude. With the most severe neurological processes cortical function becomes depressed and the brain becomes less able to maintain slow-wave voltages, resulting in diminished background activity and voltage. Thus, very low-voltage patterns in coma (voltage depression) are considered more ominous than high-voltage slow-wave patterns. The EEG patterns associated with the most severe degrees of cortical dysfunction show marked suppression of voltages or even electrocerebral inactivity.

Given this described sequence of initially increasing, then decreasing slow-wave amplitude with increasingly severe encephalopathy, a linear relationship between slow-wave amplitude and severity of encephalopathy cannot be assumed. When amplitudes are seen to decrease, this could represent either a trend toward normalization or signal a trend toward voltage depression and increasing dysfunction. In such cases, other EEG features (discussed later) such as frequency and reactivity of the background may help clarify the meaning of the change (see Figures 12-2 and 12-3).

The evolution of slow-wave activity during the improvement phase of a neurologic process may be less tightly linked to the patient’s neurologic status. The clearing of slow-wave activity often lags behind the patient’s clinical improvement. In a patient who is recovering from a dramatic encephalopathy, EEG slow-wave activity may still be present even as the patient wakes up, sits up, and begins talking. The persistence of slow-wave activity in the face of an improving neurologic picture is not necessarily a poor neurologic sign as long as there is a trend toward EEG improvement. Likewise, the slow-wave activity that follows a seizure
Low- to medium-voltage delta activity is seen superimposed on an otherwise unremarkable background in a stuporous 12-year-old boy with meningitis.

A typical slow-wave pattern in coma is shown with high-voltage semirhythmic delta waves. A small amount of intermixed theta activity is also seen, particularly near the vertex and in the occipital areas. Compare to Figure 12-3.
(postictal slowing) may persist well past the point that patients report feeling back to their preseizure baseline. Slow-wave activity may persist after a seizure for hours, commonly a few days, but occasionally for as long as 3 to 4 weeks depending on the type of seizure, the duration of the seizure, and the general neurologic health of the individual.

**Slow-Wave Frequency**

The relationship of slow-wave frequency to coma severity is more straightforward than it is for slow-wave amplitude. In general, decreasing slow-wave frequencies suggest increasing severity of encephalopathy. A decrease in slow-wave amplitude can be associated with either improvement or deterioration in neurologic status as described earlier. Counting wave frequency is a useful tool for distinguishing between the two possibilities. If background frequency is increasing, this is a good sign; slower slow waves suggest deterioration. A similar approach is taken when comparing two hemispheres with slow-wave activity—one with higher voltages than the other. Higher voltage slowing may mark the more affected hemisphere, but it may be that the opposite hemisphere manifests lower voltages because it is the more abnormal side. In such cases, comparing the frequencies generated by each side may clarify which is the relatively “healthier” hemisphere, identified by its higher frequency.

**Reactivity**

EEG reactivity is an additional useful feature in assessing the depth coma. The EEG is monitored for change when the patient is stimulated. The stimulus may be as simple as calling the patient’s name or could include purposeful noxious tactile stimulation. Intensive care unit procedures such as endotracheal tube suctioning or venipunctures also provide an opportunity to observe EEG reactivity. An unreactive EEG is one that shows no change in response to stimulation. Reactive EEGs show a change with stimulation, such as an increase in amplitude and rhythmicity in low-voltage tracings or a relative flattening of the background in higher voltage tracings.

**Presence of Normal Sleep Elements**

The presence of identifiable sleep elements in the EEG in coma is felt to be associated with a relatively better neurologic prognosis. The presence of sleep features implies that there is enough cerebral structure intact to generate these elements. Sleep spindles are the most commonly identified sleep feature in this setting. In rare cases, the higher centers that generate sleep elements are intact, but there has been a severe injury at lower levels of the central nervous system, resulting in a poor outcome despite the persistence of sleep elements.
**SPECIFIC EEG PATTERNS IN COMA AND NEUROLOGIC PROGNOSIS**

The prognostic impact of the EEG patterns discussed here must always be interpreted in the context of the coma’s underlying etiology. Although various coma patterns have different reputations in terms of the severity of the encephalopathic state that they imply, even the most severe patterns can have a good final outcome if the etiology of the coma is inherently reversible. A good example of a reversible process is drug overdose. Patients with drug overdose may show, at least for a period of time, otherwise ominous EEG patterns such as burst suppression, voltage depression, or even “flat” EEG patterns. After the drug effect has cleared, assuming no permanent brain injury, the patient (and the EEG) may recover completely. This stands in contrast to the patient who shows a burst-suppression pattern or voltage depression after a prolonged cardiac arrest, a type of injury that is less likely to be reversible. In this group of patients, these EEG patterns have a more ominous significance.

Some of the most useful studies that have examined the prognostic impact of different EEG patterns in coma have limited the study group to patients with anoxic insults, such as those caused by cardiac arrest. This approach has the advantage of excluding the important variable of coma etiology from long-term outcome; however, the conclusions of these studies should only be extrapolated outside this etiologic group studied with caution. It is no surprise that two patients with the same EEG pattern in coma, such as a drug overdose patient and a patient with a malignant brain tumor, may have very different neurologic outcomes but similar EEG findings. Because EEG patterns are dictated more by the function of the cerebrum than the brainstem, the minority of patients with devastating brainstem injuries but relative sparing of the cerebrum may have misleadingly benign EEG findings. The order that specific coma patterns are listed in the following subsections should not imply a strict ranking, although they are generally described in order of increasing severity.

**Intermittent Rhythmic Delta Activity**

Among EEG findings in encephalopathy, intermittent rhythmic delta activity (IRDA) is considered to lie at the milder end of the spectrum of encephalopathic EEG patterns. IRDA may appear in patients who are awake or who are mildly lethargic or stuporous; IRDA patterns are not associated with deeply comatose states. IRDA tends to occur in the frontal regions in adults (frontal intermittent rhythmic delta activity, or FIRDA) and in the occipital regions in younger children (occipital intermittent rhythmic delta activity, or OIRDA; see Figure 12-4). When encephalopathic states become more severe, IRDA patterns may be replaced by continuous slow-wave patterns. Various types of IRDA are discussed in more detail in Chapter 9, “The Abnormal EEG.”

![Figure 12-4](image-url) Occipital intermittent rhythmic delta activity (OIRDA) and excess fast activity are seen in a 9-year-old intensive care unit patient with postictal confusion (arrows). The increased fast activity is the result of treatment with lorazepam. Intermittent rhythmic delta activity is usually associated with mild encephalopathies.
Spindle Coma

Spindle coma may be indistinguishable from normal Stage II or III sleep (see Figure 12-5). The term may be applied to generalized slow-wave patterns obtained in comatose patients in which sleep spindles can be identified, although in most examples of spindle coma, the amount of spindle activity is exaggerated. Coma patterns that include normal sleep elements usually fall into better prognostic groups. This makes intuitive sense because the ability to generate normal sleep elements implies that the centers responsible for generating spindles, located in the diencephalon and above, are functionally intact. Some cases of spindle coma with poor outcome may be explained by patterns of damage that involve brainstem structures but have left higher cerebral structures relatively unaffected. Spindle coma can be distinguished from alpha coma (discussed later) in that, in spindle coma each spindle has a discrete duration and spindles should be maximally expressed in the frontocentral regions; alpha patterns in alpha coma (discussed later) are more diffuse and continuous.

Continuous Slow-Wave Patterns

Diffuse slow-wave patterns are among the most frequently encountered EEG patterns in coma. Just as there is a continuum among alert, stuporous, and comatose states, so is there a continuum between the normal EEG and EEG patterns with various degrees of diffuse slowing. Diffuse slow-wave patterns are usually comprised of delta frequencies, but theta frequencies may be seen as well. Slow-wave patterns in coma are usually nonrhythmic. Rhythmic slow-wave patterns are more often seen in the setting of metabolic encephalopathies.

As described in the previous section on slow-wave voltage in coma, higher slow-wave voltages are generally considered “more healthy” than lower voltages, but the relationship between voltage and depth of coma is complex, because declines in slow-wave voltage may potentially be associated with either clinical deterioration or improvement. EEGs that show reactivity to noxious stimulation are generally associated with a better neurologic prognosis than those that are unreactive, and those with higher frequencies are generally prognostically better than those with lower frequencies.

As with other coma patterns, the underlying cause of the coma is probably the strongest predictive factor in outcome, often more important than the specific EEG pattern itself. Outcome after an anoxic event associated with delta slowing may be quite different from the outcome seen after a generalized seizure that is followed by similar delta slowing in the postictal period; there is the expectation that the latter pattern may be completely reversible.

Asymmetric voltages in slow-wave patterns suggest that an asymmetric process is at work. Diffuse processes, such as metabolic derangements, are usually associated with symmetrical patterns. The exception to this rule is the case of a symmetrical process acting on an asymmetrical brain. For instance, although most patients with hyperosmolar coma would be expected to show a symmetrical slow-wave pattern, a patient with hyperosmolar coma who has suffered a previous stroke may...
show an asymmetric pattern in reaction to the metabolic derangement—healthy brain regions may react differently to the metabolic abnormality compared with previously injured regions. As discussed earlier, it may not always be clear which side is more severely affected when slow-wave patterns are asymmetrical (see Figure 12-6). Other findings superimposed on a slow-wave background such as periodic lateralized epileptiform discharges (see Chapter 9) or epileptiform activity may suggest additional diagnoses.

**Alpha Coma**

The alpha coma pattern consists of diffuse alpha activity in the range of 8 to 13 Hz (see Figure 12-7). Most reports have associated the alpha coma pattern after anoxic insult with a relatively pessimistic outcome, although with some exceptions. A similar pattern of diffuse alpha activity may be seen in toxic and metabolic encephalopathies, especially drug intoxications. In contrast to the postanoxic state, the alpha coma pattern after drug intoxication is felt to have a relatively more favorable prognosis.

Various theories have been put forward to explain the genesis of alpha rhythms in alpha coma. Some have suggested that the pattern is related to the spindle generator. Others have suggested that this alpha activity represents a paradoxically retained alpha-range activity related to the posterior rhythm. An additional possibility is that, because of diffuse cortical injury, the alpha activity of alpha coma represents a slowed version of the beta activity that is usually generated by the normal cortex. The dependence of neurological outcome on the cause of coma after alpha coma is a reminder of the general importance of considering etiology in assessing prognosis in coma.

**Triphasic Waves**

The appearance and significance of triphasic waves is discussed in more detail in Chapter 9, “The Abnormal EEG” and shown in Figure 9-34. The presence of triphasic waves is almost always associated with a state of depressed consciousness. Triphasic waves are usually caused by a metabolic derangement such as hepatic coma or renal failure but are occasionally seen after an anoxic insult. The prognosis of patients with triphasic waves depends on the course of the underlying process.

**Nonconvulsive Status Epilepticus**

Among EEG coma patterns, prompt diagnosis of nonconvulsive status epilepticus (NCSE) is important because it is a cause of coma that may be amenable to treatment.
with antiseizure medications. Both generalized and complex partial status epilepticus eventually evolve into states that resemble coma. Patients with continuous generalized seizures often begin by having repetitive, outwardly observable generalized convulsions. As the generalized seizure discharges repeat, however, the convulsive movements become less prominent, eventually culminating in a state in which the patient lies unresponsive and motionless even as the electrographic seizure discharges continue. Patients may transition to this nonconvulsive state within 30 minutes or less of seizure onset. Similarly, prolonged complex partial seizure activity (complex partial status epilepticus) will evolve to a stuporous or comatose state, sometimes with cyclical fluctuations in responsiveness (see Figures 12-8 and 12-9). Careful observation of patients with either generalized or complex partial status epilepticus may reveal intermittent, subtle rhythmic movements in the face or limbs, but absence of this finding cannot be relied on to exclude the diagnosis. Absence status epilepticus can present as a confusional state, although many patients retain the ability to walk and converse, albeit in a confused fashion, despite the presence of continuous discharges. Therefore, the different types of NCSE are important elements in the differential diagnosis of coma.

NCSE may have a variety of causes ranging from the patient with idiopathic epilepsy who experiences a seizure that fails to terminate to the patient in whom NCSE occurs as a terminal event following severe anoxic, metabolic, or neoplastic processes. When NCSE is caused by a severe, irreversible injury, the electrographic seizure pattern may evolve to a low-voltage pattern and eventually to a “flat” EEG.

**Burst-Suppression Patterns**

Burst-suppression patterns consist of periodic bursts of polymorphic activity, often containing sharp features, separated by periods of voltage suppression (see Figure 12-10). In a minority of patients, a myoclonic movement may accompany each burst. Burst-suppression patterns have been associated with anoxic injury and are generally associated with a poor prognosis for neurologic recovery. In infants and children, and especially in the minority of patients in whom the pattern improves promptly, outcome may be somewhat better. Burst-suppression patterns can also be caused by drugs, either by drug overdose or the purposeful use of drugs, such as barbiturates, to induce coma. The postanoxic and pharmacologic versions of burst suppression are usually easily distinguished by history and laboratory testing. Pharmacologic burst-suppression patterns have the potential for complete reversibility and are therefore in a separate prognostic group.

The purest form of burst-suppression is an unrelenting pattern that does not cycle to other patterns, is present on every page of the EEG, and is unaffected by outside stimuli. Lower voltage bursts and longer and flatter interburst intervals correlate with increasing severity. Transitional versions of burst suppression that
Figure 12-8  The EEG reveals that this patient's unresponsiveness is caused by continuing electrographic seizure activity or nonconvulsive status epilepticus.

Figure 12-9  This highly rhythmic pattern with sharp features in this comatose patient is also consistent with nonconvulsive status epilepticus.
change, or even pause, with outside stimuli (so-called reactive burst suppression) are probably associated with a better prognosis than the pure form of the pattern.

**Voltage Depression**

Low-voltage records or voltage depression in coma (tracings in which voltages persistently do not exceed 20 µV in any head region) are considered severely abnormal. The pattern suggests a degree of injury so severe that the cerebrum cannot generate significant voltages. Voltage depression may be seen after continued deterioration of a burst-suppression pattern in which the bursts have disappeared leaving only the periods of suppression. It may also be seen near the end of a sequence of continued voltage decline as described earlier.

Certain pitfalls in the diagnosis of voltage depression should be avoided (see Figures 12-11 and 12-12). The term implies a persisting pattern; some patients have a period of voltage depression after a seizure, but this period should be short-lived. Voltage depression also may occur transiently after anoxia. Therefore, very short tracings are inadequate to establish a diagnosis of voltage depression. Standard instrument settings may hide some features of a low-voltage EEG and may even suggest electrocerebral inactivity unless appropriate adjustments to amplifier gains are made. Finally, a small percentage of normal adults may have a low-voltage EEG pattern during wakefulness; the foregoing discussion of low-voltage patterns only applies to recordings obtained from patients in coma.

**EEG RECORDING IN SUSPECTED CEREBRAL DEATH**

The role of the EEG in the patient with suspected brain death is not straightforward. The original definition of death as the cessation of all vital signs became impractical with the advent of modern intensive care and mechanical ventilation. In response, an ad hoc committee was convened at Harvard Medical School in 1968 to establish a definition of irreversible coma or brain death that could replace the older definition when necessary in intensive care settings where mechanical ventilation may be in use. The guidelines attempted to identify individuals with “no discernible central nervous system activity” (“A definition of irreversibly coma,” 1968). The guidelines are designed to create a new legal definition of death such that when the criteria set forward for the diagnosis of brain death are met, the patient can be declared legally dead and removed from the ventilator.
This EEG of a comatose patient is displayed at a sensitivity of 7 $\mu$V/mm and appears flat. Especially when electrocerebral inactivity is suspected, sensitivities of 2 $\mu$V/mm should be used (see Figure 12-12).

When the same page of EEG as was shown in Figure 12-11 is displayed at a sensitivity of 2 $\mu$V/mm, a small amount of definite electrocerebral activity is seen over the right hemisphere (bottom eight EEG channels). No electrocerebral activity is seen over the left hemisphere and midline, however. Pulsation artifact is seen in the channels that include O1.
The specific guidelines for determination of brain death vary among countries, jurisdictions, and even among individual hospitals. Almost all official criteria require a complete lack of responsiveness, lack of patient movement, lack of respiratory effort when the patient is taken off the ventilator during a trial period, and absent brainstem reflexes. The role of EEG in diagnosing brain death varies by location; an EEG showing electrocerebral inactivity (ECI) is usually not required to make the determination of brain death but can serve as an adjunct to the diagnosis. Patients with true ECI recordings, especially when two such recordings are obtained 24 hours or more apart, rarely experience neurologic recovery. An ECI recording considered alone, i.e., apart from the context of the patient’s history and examination, should not be considered synonymous with brain death.

EEG recordings performed in the setting of suspected cerebral death are almost always carried out in ICUs. The large amount of electrical equipment in most ICUs makes this setting an electrically hostile environment and increases the challenge of obtaining clean EEG recordings at the high amplifier gains necessary for determination of ECI (see Figure 12-13). Nevertheless, with careful technique, satisfactory EEG tracings for this purpose are obtainable.

Because of the gravity of the question at hand, an EEG performed with the goal of establishing a complete lack of brain wave activity or ECI should meet certain minimal technical standards. The most recent guidelines from the American Clinical Neurophysiology Society were published in 2006 (“Guideline 3,” 2006) and are summarized in the following list.

Electrocerebral inactivity is defined as a complete lack of EEG activity over 2 µV when the following appropriate recording techniques are used.

1. A full set of electrodes should be used, including the midline electrodes, Fz, Cz, and Pz, with the exception of areas that may be inaccessible because of recent surgery or trauma.
2. Interelectrode impedances should be between 100 ohms and 10,000 ohms.
3. The integrity of the recording system should be verified to confirm that the apparent low-voltage tracing was not caused by a disconnection in the recording apparatus. This is done by tapping the individual electrodes and confirming the presence of the tapping artifact on the recording.
4. A double-distance montage with some interelectrode distances greater than 10 cm should be used during at least some portion of the recording. Greater interelectrode distances increase the chance of detecting low-voltage activity. An extracephalic electrode placed on a limb (e.g., the right hand) can help identify artifacts. An electrocardiogram (EKG) channel should also be applied to help identify EKG artifact.

Figure 12-13 This page of EEG is displayed at 2 µV/mm and shows electrocerebral activity (ECI); none of the waves seen are of cerebral origin. Tracings displayed at the amplifier gains necessary for determination of ECI are prone to large amounts of artifact. On this page, several channels show pulsation EKG artifact. Beyond the use of high amplifier gains, several other procedural requirements must be met, as described in the text, before the EEG diagnosis of ECI can be made.
5. The record should be recorded at a sensitivity of 2 μV/mm for at least 30 minutes to minimize the possibility of missing a 2 μV signal.

6. Appropriate filter settings should be used with a bandpass of 1 to 30 Hz or wider (low-frequency filter set at 1 Hz and high-frequency filter set at 30 Hz).

7. Additional monitoring techniques should be used to distinguish artifact from brain wave activity at the high amplifier gains used. This may include an EKG and a respiratory channel, if necessary, to monitor ventilator artifact.

8. There should be no EEG reactivity to intense tactile, auditory, or visual stimuli.

9. The recording should only be made by a qualified EEG technologist.

10. If the diagnosis of ECI is uncertain, the recording should be repeated.

REFERENCES


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