Conventional EEG

Professor Yasser Metwally
Professor of neurology, Ain Shams University, Cairo, Egypt

The 3 C/S spike wave charge

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Thank you for using my publication. This publication covers the clinical aspect of conventional EEG. It simply reflects thing the way I understand, deals with and interpret a conventional EEG tracing.

Conventional EEG has fallen short of expectation not because of its limited value, but rather because it is rarely ordered by a Knowledgeable clinician and interpreted by an electroencephalographer in a way most useful to the patient.

Another reason why Conventional EEG have fallen short of expectation, is its impressionistic, qualitative nature and this strongly reflects the needs for quantitative EEG. Quantitative EEG (Also called brainmapping, EEG cartography, Brain electrical activity mapping, BEAM) is a wonderful way of reflects the brain function in real time and in a totally non-invasive way. A short notice is given to brainmapping at the end of this textbook.

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Professor Yasser Metwally
Cairo, Egypt
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INTRODUCTION

Electroencephalography is the technique by which the electrical activity generated by the brain is amplified and displayed, resulting in an electroencephalogram (EEG). This method enables one to assess brain function noninvasively over a given period. Although many abnormalities on the EEG are nonspecific, several clinical presentations have associated EEG findings that are diagnostic of a specific condition or lesion in the central nervous system.
system. Before the advent of modern neuroimaging, the EEG was one of the most important noninvasive diagnostic tools available to the neurologist and neurosurgeon. It provided information on cerebral function when anatomic detail could not be accurately obtained. Current neuroimaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) of the brain now yield excellent neuroanatomic detail. Despite these advances, the EEG remains a valuable tool in the clinical evaluation of many disorders of the central nervous system, as it is readily available and safe and provides information on brain function that is still unique.

When an EEG is requested, it is important that the referring physician state the clinical question that is to be answered by the EEG. Common reasons for obtaining an EEG include a history of a clinical seizure and the need to rule out epileptiform activity; acute encephalopathy or coma of undetermined etiology; or a prolonged seizure with the need to rule out ongoing electrographic seizure activity (i.e., status epilepticus). When the EEG is completed, the findings are summarized in a report using accepted EEG terminology, with the most significant findings listed first. The EEG is also interpreted in the context of the clinical presentation and question, thus providing the clinician with a clinical correlation to the findings noted in the EEG.

- **History**

The early evaluations of the central nervous system by physiologists in the late 1700s and early 1800s consisted of stimulating the brain electrically rather than measuring the electrical currents it generates. Not until the latter half of the nineteenth century did the British physiologist Richard Caton describe the electrical activity of the brain in experimental animals. Caton obtained cortical EEG recordings, and he also noted that 'feeble currents of varying direction pass through the multiplier when the electrodes are placed on two points of the external surface of the skull. Early in the twentieth century, the Russian physiologist V.V. Pravdich-Neminsky used the term "electrocerebrogram," and he defined the predominant frequency bands of the cerebral electrical activity in animals, labeling them alpha and beta. In 1929 Hans Berger published the initial findings on the EEG in humans, calling it the "Elektrenkephalogramm," from which electroencephalogram has been derived. Previous investigators had noted the reactivity of the EEG in animals to peripheral somatic electrical stimulation. Berger showed that the human EEG is reactive to opening and closing of the eyes: such potential changes from the occipital region were later termed the Berger, or alpha, rhythm.

In 1934, Berger's findings were confirmed by Adrian and Matthews. The application of EEG in a neuropathologic condition was initially described by Walter when he demonstrated focal EEG slowing in patients with brain tumors, which he called delta waves. During the subsequent two decades, clinical investigators evaluated the use of the EEG in normal and neuropathologic conditions. Over the past six decades, standards have also been developed for the application and nomenclature of electrode placement and montage representation. The clinical significance of most EEG patterns has been well described. Advances in electronics and computers have been applied to electroencephalography, providing improved definition of both cerebral and extracerebral
activity (such as artifacts). The EEG now is "paperless," with a digitized EEG displayed in real time on a video monitor. Frequency spectral analysis (brain mapping) is being actively investigated, and it proved to be an additional tool in the evaluation of brain function.

- **Technical Aspects**

The electrical activity of the brain has an amplitude in the microvolt range, typically ranging from 10 to 150 µV. In a routine EEG, the brain's electrical activity is measured at the scalp using a surface electrode. The electrical signal is then conducted by wire to the EEG machine, where it is amplified, filtered, and displayed. This process is briefly summarized below.

  - **Electrodes**

Since the discovery of the EEG, several types of electrodes have been used. Subdermal needle electrodes were the first to be applied. However, owing to the variability of impedance and the potential for morbidity and transmission of infectious disease, this type of electrode is no longer routinely used. The most common electrode currently in use is a gold-plated disc 10 mm in diameter. Twenty-one electrode sites on the scalp are defined according to the International 10-20 System, which is based on skull landmarks (inion, nasion and left and right preauricular points) whose distances are then subdivided in a specified manner. A typical interelectrode distance is 6 cm. Scalp electrodes are identified by a letter and number (Fig-1). Most of the letters specify an approximate brain region, as follows: Fp: frontopolar; F: frontal; C: central; T: temporal; P: parietal; and O: occipital. The ear electrode is denoted by the letter A. Electrodes with odd numbers are on the left side of the head (Fp1, F3, C3, P3, O1, F7, T3, T5, and A1), and electrodes with even numbers are on the right side (Fp2, F4, C4, P4, 02, F8, T4, T6, and A2). Midline electrodes are designated by the letter "z" (Fpz, Fz, Cz, Pz, and Oz).

After marking the scalp according to the International 10-20 System, the technologist prepares each site by using a mild abrasive to lower and equalize the scalp impedance. An electrode is placed at each site using either a conductive paste or a collodion-soaked gauze patch through which conductive gel is injected into the disc. Properly prepared electrodes have impedances between 1000 and 5000 Ω.

Scalp electrodes provide adequate measurement of the cerebral electrical activity arising from the superior and lateral aspects of the brain. The anterolateral temporal lobe can be sampled by using a pair of "true" temporal electrodes (T1 and T2), in addition to the 10-20 System electrodes. However, the midline and basal aspects of the brain cannot be sampled well by electrodes on the scalp. In the past the nasopharyngeal electrode was used in an attempt to measure the electrocerebral activity of the anteromesial aspect of the temporal lobe. It consisted of a silver rod that was advanced through the naris until it came in contact with the posterior wall of the nasopharynx. However, it was subject to significant artifacts caused by breathing and swallowing. The sphenoidal electrode is an alternative that can be used to semiinvasively sample the anteromesial temporal lobe. It consists of a thin, Teflon-coated platinum or chlorided silver wire that is placed near the foramen ovale.
Using sterile technique, the sphenoidal electrode is inserted with a 20 or 22 gauge spinal needle, 1cm anterior to the tragus, beneath the zygomatic arch and toward the foramen ovale, approximately 3 to 4 cm deep to the skin.

Invasive monitoring of cortical electrical activity is performed using depth electrodes or subdural strip or grid array electrodes. The depth electrode is a thin, flexible Teflon sheath having 6 or 8 concentric stainless steel or platinum contacts along it with interelectrode distances of 5 or 10 mm. It is placed stereotactically using a rigid introducer, which is removed after electrode placement. Subdural strip or grid array electrodes consist of stainless steel or platinum discs embedded in a Silastic or Teflon sheet. The electrode contacts are separated by distances typically measuring 1 cm. Subdural electrodes are placed through a craniotomy site, the size of which is determined by the size of the electrode strip or array. These invasive electrodes may be used either extraoperatively during video-EEG monitoring or intraoperatively during surgical excision. Their primary use is to more accurately define an epileptic focus. In addition, the cortical surface electrodes can be used to stimulate the surface of the brain to determine the function of a specific area of cortex, such as speech, language comprehension, or motor control.

Figure 1. Scalp electrodes are identified by a letter and number

- EEG Machine

The cerebral electrical activity is conducted by wires from the scalp and/or invasive electrodes to the jackbox of the EEG machine. The inputs to the jackbox are then used to compose a montage, which is a specific arrangement or array of electrodes that display the EEG. The EEG machines currently available use 16, 18, or 21 channels. Each channel consists of a differential amplifier, which compares the input of two electrodes and amplifies the output to the pen-writing system or video display screen.

An upward pen deflection is defined as negative, and occurs when input 1 is negative with respect to input 2 or when input 2 is positive with respect to input 1. A downward pen deflection is defined as positive, and occurs when input 1 is positive with respect to input 2 or when input 2 is negative with respect to input 1. These two conditions are illustrated in
Fig-2, where there is a downward deflection in channel 1 because input 2 is more negative than input 1, and an upward deflection in channel 2 because input 1 is more negative than input 2. This example demonstrates a surfacenegative phase reversal in a bipolar montage, which localizes maximal surface electronegativity. Depending on the polarity of each input, or electrode, there may be summation, no change, or cancellation of the cerebral EEG activity between the two inputs. Cancellation indicates a region of isoelectricity, and the result is no change in the output of the amplifier and no pen deflection.

Before being displayed, the amplifier outputs are filtered, typically using a low-frequency filter setting of 1 Hz and a high frequency filter setting of 70 Hz. A 60-Hz "notch" filter may be used in a recording environment with excessive electrical interference, such as an intensive care unit. The amplitude of each channel can be adjusted by changing the amplifier gain, or sensitivity. The amplified, filtered outputs are then displayed either with an analog pen writing system or digitally on a video monitor. The routine paper speed is 30 cm/s, so that each page of EEG displays 10 s of electrical cerebral activity. A paper speed of 15 cm/s is often used in neonatal EEGs in order to compress the EEG and accentuate focal slowing. A faster paper speed such as 60 cm/sec can be used to expand the time scale in an attempt to see if two potentials or events occur synchronously or to better define high-frequency activity.

![Figure 2. Pen deflection based on inputs G1 and G2 into channels 1 and 2.](image)

- **Montages**

The brain's electrical activity is logically displayed using different montages, which are specific arrangements of electrodes. Each montage provides the electroencephalographer with a different view, to delineate both normal and abnormal activity. The objective of any montage is to display the electrical field potentials generated by cortical neurons. The output from each channel in a montage represents the voltage difference of the inputs from each pair of electrodes into the differential amplifier.
Current standards specify that each montage attempt to maintain a linear arrangement of electrodes having equal interelectrode distances. The display is oriented from anterior to posterior and from left to right. A bipolar montage is constructed by linking successive electrodes into sequential channels. In a referential montage, each electrode is 'referred' to a reference electrode, such as the ipsilateral ear or the vertex (Cz). The most commonly used montages are the longitudinal (anterior to posterior, or AP) bipolar montage, the transverse (left to right) bipolar montage, and the referential (to the ipsilateral ear) montage.

Typically, bipolar montages are used to localize the region of an abnormality. This is often seen as a phase reversal between two or more electrodes in a given region. Referential montages are useful to define the field or distribution of the abnormality by the amplitude of electrocerebral activity at the electrodes in the region of interest. Both types of montage have their disadvantages. Bipolar montages are susceptible to field cancellation because adjacent electrodes may be isoelectric in potential. Also, if the region of interest lies at the end of the linear chain of electrodes, no phase reversal will be apparent. In referential montages, it is important to be aware that if the reference is located in the field of the cerebral electrical signal of interest (called an active reference), cancellation or reverse polarity may be seen in the channels to which uninvolved electrodes are referenced. Finding an uninvolved or inactive reference may be difficult.

- **Obtaining the EEG**

Including the patient setup time, a routine EEG takes approximately 60 to 90 min and produces a 30-min recording. Electroencephalography on patients in the intensive care unit (ICU) or on neonates often takes longer, both because setting up takes longer and because a longer recording is made. The ICU is often a hostile environment for electroencephalography, owing to the abundance of electrical monitoring equipment, which may result in an excessive 60-Hz noise artifact on the EEG recording.

While placing the electrodes, the technologist obtains the patient's clinical history and past medical history, and a family history for epilepsy or clinical problems similar to those of the patient. Medications currently being taken are listed, especially ones that may affect the EEG, such as barbiturates, benzodiazepines, tricyclic antidepressants, or neuroleptic medications. Medication for sedation or sleep induction is also noted. If there is a skull defect from previous trauma or intracranial surgery, it is depicted diagrammatically on the front sheet of the EEG. At the beginning of the EEG recording, electrical and biological calibrations are performed. The sensitivity, high-frequency filter, time constant, or low-frequency filter, and the use of any other special filters (e.g., a 60-Hz notch filter) are also noted on the first page of each montage, as well as the level of consciousness and the mental state of the patient. Approximately 10 min of uninterrupted recording are performed for each montage. Longitudinal bipolar, transverse bipolar, and referential montages are obtained, and the technologist may also obtain additional montages to better display a suspected abnormality. The patient is allowed to fall asleep, and, later in the recording, attempts are made to fully alert the patient by testing memory or calculations. Also, during the recording, photic stimulation is performed to evaluate for photosensitive seizures. Last,
the patient is asked to hyperventilate for 3 to 5 min in an attempt to accentuate focal slowing or focal or generalized epileptiform activity.

**EEG Terminology**

A standard terminology is used to consistently describe each EEG. These terms summarize the electrocerebral activity as well as any abnormal waveform or transient in each region of the brain during the EEG. These terms are frequency, amplitude, polarity, morphology, distribution, rhythmicity, synchrony, reactivity, and persistence. Each term will be briefly discussed below.

Frequency refers to the repetition rate or number of cycles per second (Hz) of a given waveform. The frequency of a single waveform can be calculated from the inverse of the peak-to-peak duration of the waveform (1/time). During periods when the EEG is relatively sinusoidal, the frequency can be estimated by counting the number of cycles per 1 second epoch. Four frequency bands appear in EEGs and have been named delta (0.5 to 3.5 Hz), theta (4.0 to 7.5 Hz), alpha (8.0 to 12.5 Hz), and beta (13 Hz and greater).

Amplitude is the magnitude of the EEG activity in microvolts (µV). It is determined by measuring the pen deflection in millimeters (mm) at a specified machine sensitivity (µV /mm). Most EEGs are performed at a sensitivity of 7 µV /mm, such that a 10 mm pen deflection signifies an amplitude of 70 µV. In describing the EEG, quantitative measures may be used (i.e., 50 to 70 µV), or a qualitative scale may be used, in which low amplitude is defined as less than 20 µV, medium amplitude as 25 to 95 µV, and high amplitude as greater than 100 µV.

Polarity is the sign of the EEG activity and may be negative, positive, or isoelectric (i.e., zero). By convention, upward pen deflection signifies negative polarity, and downward pen deflection signifies positive polarity.

Morphology refers to the shape of the EEG waveform. It may be regular (i.e., sinusoidal) or irregular, monophasic, or polyphasic (e.g., a triphasic wave). The morphology of a transient is essential to determining whether the transient is normal or abnormal, nonepileptiform or epileptiform.

![Figure 3. Triphasic waves](www.yassermetwally.com)
Distribution of EEG activity may be focal or generalized. If focal, the activity should be defined by side and region involved (i.e., frontal, temporal, central, parietal, occipital, or midline). Generalized activity is widespread, involving both hemispheres equally. Although widespread, generalized activity is often either anteriorly or posteriorly predominant.

Rhythmicity: The EEG is rhythmic when it has a sinusoidal pattern at a relatively constant frequency. Arrhythmic activity is a mix of frequencies and morphologies.

Synchrony: EEG activity that occurs at the same time in different regions of the brain is called synchronous. Activity that occurs at the same time and same location on both sides of the scalp is bilaterally synchronous or bisynchronous. Conversely, activity that occurs at different times is asynchronous.

Reactivity refers to alteration in the EEG activity caused by stimulation of the patient. This is accomplished by visual stimulation (opening and closing the eyes), noxious stimulation (pinching the patient), auditory stimulation (a loud noise), or cognitive stimulation (simple arithmetic calculations). An unreactive EEG is one that shows no variation in activity over all scalp leads despite vigorous attempts at stimulation.

Persistence: A specific EEG activity appearing in a given region of the brain can be either intermittent or persistent. A persistent activity is present in the region for at least 70 to 80 percent of the record, despite stimulation and state change. EEG activity that is present in the region for less than 70 to 80 percent of the record is called intermittent, and may be further designated as rare, occasional, or frequent, depending on its total amount in the record.

• Normal EEG

The age of the patient and the level of consciousness (i.e., awake or asleep) are critical parameters in describing the normal EEG, as both factors determine the frequency, amplitude, polarity, morphology, distribution, rhythmicity, synchrony, reactivity and persistence of the activities that are recorded. The EEG of the neonate is significantly different from that of the infant of 3 months or older, and it will be discussed below.

In the normal awake EEG, the most notable feature is a posteriorly dominant, rhythmic activity that is symmetric, bisynchronous, and reactive. This activity has been called the alpha rhythm, which must be distinguished from the previously described alpha frequency range of 8 to 12.5 Hz. At approximately 3 months of age, a posteriorly dominant background alpha rhythm can be seen, which is high-amplitude, 3 to 4-Hz activity. From infancy through the early teenage years, the mean frequency of the background alpha rhythm increases gradually to 10 Hz, and the amplitude decreases to moderate voltage (Fig-4). These values then persist throughout adulthood and old age. Subharmonics (one-half normal frequency) and harmonics (twice normal frequency) of the alpha rhythm occur in a small percentage of normal individuals. These variants are reactive to various stimuli. A pattern of low amplitude, mixed fast frequencies can also be seen in normal adults, which may be due in part to subjects' inability to relax adequately during the EEG. In the central
head regions of adult subjects, the EEG consists of moderate to low-amplitude alpha and theta-range frequencies, whereas in the frontal head regions, low-amplitude beta-range frequencies are generally seen. These activities should be bisynchronous and symmetric. In 10 to 20 percent of young adults, either or both central head regions may show rhythmic, arciform alpha-frequency activity that is reactive to the patient performing mental arithmetic operations or moving the contralateral hand. This is called mu rhythm.

Figure 4. Background alpha rhythm and age relation.

Sleep has been divided into non-rapid-eye movement (NREM) and rapid-eye-movement (REM) phases. NREM has four stages: stage I (drowsy), stage II, stage III and stage IV. As the patient becomes drowsy, the background alpha rhythm becomes arrhythmic, with intermixed theta and beta frequencies that spread into the central head regions. A slow lateral eye movement artifact may be visualized on the EEG in the anterolateral head regions, because the retina is electronegative with respect to the cornea, resulting in an electrical dipole whose field changes with eye movement. Two additional features of stage I sleep are sharply contoured, surfacepositive theta transients of moderate amplitude that appear synchronously or asynchronously in the posterior head regions (positive occipital sharp transients of sleep or POSTS) and moderate to high-amplitude, sharply contoured, biphasic theta or alpha transients that phase-reverse at the vertex (vertex sharp waves). Stage II of sleep is defined by the presence of K complexes and sleep spindles. The K complex is a high-amplitude, biphasic slow wave of 0.5 to 1 s duration that has a distribution similar to that of the vertex sharp wave. The sleep spindle consists of rhythmic, moderate-amplitude alpha frequency activity lasting 0.5 to 1 s which is bisynchronous in the central head regions. In deeper stage I and stage II sleep, the remaining background consists of moderate to low-amplitude mixed theta, alpha, and beta frequencies. In stages III and IV of sleep, there is increasing delta activity having high amplitude and anterior predominance. In REM sleep, the EEG consists of diffusely distributed, moderate to low-amplitude mixed frequencies with rapid eye movement artifacts seen in the anterolateral head regions. The features of NREM sleep are absent during REM sleep (i.e., vertex sharp waves, sleep spindles, and K complexes).
Benign Variants and Artifacts

One of the major goals of EEG is to accurately define which EEG patterns are consistent with the diagnosis of seizures, and which patterns may be of no clinical significance (that is, normal). The "epileptiform" patterns and "seizure-like" discharges that are not significantly associated with seizures are called benign EEG variants and, in general, are considered normal findings on the EEG when it is properly obtained. For each of these patterns, the interpretation depends critically on the age and clinical state of the patient and the distribution, frequency, amplitude, and morphology of the waveform(s). The benign epileptiform patterns include benign epileptiform transients of sleep (BETS), 14 and 6-Hz positive bursts, 6-Hz spike and wave (phantom spike and wave), and wicket spikes. The benign seizure-like discharges include rhythmic midtemporal discharges (RMTD or psychomotor variant), midline theta rhythm, frontal arousal rhythm (FAR), and subclinical rhythmic electrographic discharges in adults (SREDA).

An EEG activity that does not originate from the brain is called an artifact. Artifacts can be divided into two major groups, physiologic and nonphysiologic. The accurate identification of artifacts can be crucial to the correct interpretation of both normal and abnormal EEGs. An electrically hostile environment such as an ICU often proves to be a significant challenge to the EEG technologist, who must recognize and, if possible, eliminate all artifacts. Any source in the body that has an electrical dipole or generates an electrical field is capable of producing a physiologic artifact. These include the heart (electrocardiogram and ballistocardiogram or pulse artifact), eyes (oculomotor artifact), muscles (myogenic artifact), and tongue (glossokinetic artifact). Sweating may alter the impedance at the electrode-scalp interface and produce an artifact. In the region of a skull defect, there may be accentuation of amplitude with very sharp morphology, which is called breach rhythm. Examples of nonphysiologic artifacts include 60-Hz interference from nearby electrical equipment, kinesiogenic artifacts caused by patient or electrode movement, IV drip artifact caused by a charged saline solution, and mechanical ventilator artifacts caused by patient movement or fluid movement in the ventilator tubing.

Abnormal EEG

Most abnormal EEG findings are defined by localizing the region of maximal electrode negativity associated with the abnormality. Models of radially oriented neurons have been proposed to define the origin of cortical electronegativity. However, much of the brain's cortical surface lies along the base and walls of sulci. Using scalp and cortical electrodes, Cooper and colleagues estimated that approximately 6 cm² of cortical surface was necessary to generate scalp-recorded electrical potentials. Abraham and Ajmone-Marsan have demonstrated that only 20 to 70 percent of spike discharges seen using electrocorticography are seen on scalp EEG. Significant abnormalities on the EEG consist of slowing, lack of reactivity, interictal epileptiform activity, periodic patterns, and ictal patterns. The clinical and pathologic importance of each finding depends on whether it is focal or generalized, intermittent or persistent. Although an amplitude asymmetry of greater than 50 percent is also considered abnormal, it must be demonstrated on multiple montages, including a referential montage, preferably to a common reference. Amplitude
asymmetries are often the result of normal anatomic variations (e.g., in skull thickness) or technical factors (interelectrode distances, electrode impedances, etc.).

As noted above, the normal frequency range for the background alpha rhythm is from 8 to 12.5 Hz. Therefore, in a maximally alerted adult patient, a background alpha rhythm of less than 8 Hz is considered abnormal. Intermittent, generalized delta slowing may appear as isolated diffuse polymorphic delta transients or as rhythmic delta activity. Intermittent rhythmic delta activity (IRDA) may be seen having frontal predominance (FIRDA) in adults or occipital predominance (OIRDA) in children. These findings are nonspecific in etiology. However, each abnormality noted above is consistent with diffuse bihemispheric cerebral dysfunction. In adult patients, the severity of the cerebral dysfunction is related to the degree of theta or delta slowing of the posterior background frequencies or to the total amount of generalized delta slowing that occurs during the EEG record.

Persistent frequency asymmetries of greater than 1 Hz between corresponding scalp regions are abnormal. Focal slow transients in the delta range often have variable morphology (are polymorphic) and are considered abnormal in all fully alerted, adult patients, with the exception of rare dominant-hemisphere temporal delta slowing in the elderly. When focal delta slowing is present for 70 to 80 percent of the record, it is called persistent polymorphic delta activity, or PPDA. Although not specific in etiology, focal PPDA is consistent with a structural lesion in the absence of a recent transient neurologic event such as a seizure, transient ischemic attack, or complicated migraine headache. If focal polymorphic delta activity appears in less than 70 percent of the record, it is noted as intermittent and qualified as rare, occasional, or frequent, depending on the total amount seen during the EEG. Intermittent focal delta slowing is nonspecific in etiology and clinical significance and is thought to be consistent with focal neuronal or cerebral dysfunction in the region of the slowing.

Generalized loss of reactivity is evidence of severe diffuse bihemispheric cerebral dysfunction, regardless of the dominant frequency. This finding is commonly seen in coma and will be discussed in more detail below. Focal loss of reactivity may be seen in the setting of an intracerebral structural abnormality, such as a cerebral infarct, abscess, or tumor. Focal unreactivity of the posterior background rhythm with eye opening is called Bancaud's phenomenon, because of its location, it is the most readily recognized form of focal unreactivity.
Two transients of special interest are the sharp wave and the spike discharge. These transients are important because of their high correlation with seizures, and they are often referred to as epileptiform discharges. They are defined by their morphology and duration, with sharp waves having a duration of 70 to 200 ms and spike discharges having a duration of 40 to 200 ms.
of 20 to 70 ms. When accompanied by an after-going slow wave, they are referred to as a sharp or spike and slow wave complex. If an epileptiform discharge appears focally, it is localized by finding a region with a phase reversal on the bipolar montages (Fig-5). Using a referential montage with an uninvolved reference, a focal epileptiform discharge is localized by defining the region of greatest electronegativity. The generalized epileptiform transient is most commonly a spike discharge, which may appear as an isolated spike, a spike-wave complex, or a polyspike and wave complex. Although they are called generalized, these discharges are often anteriorly predominant and may have shifting left or right sided emphasis, which averages out during the EEG. Spike-wave and polyspike-wave complexes often appear as repetitive discharges having a predominant frequency based on the repetition rate of the discharges (Fig-6).

Figure 7. The 3 c/s spike/wave discharge.
Figure 8. The Frontally predominant 3 c/s spike/wave discharge.

Table 1. Electroclinical criteria of the 3 c/s spike/wave discharge

- It is bilateral fairly symmetrical and synchronous.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset.
- Readily activated by hyperventilation.
- It might be proceeded by intermittent, rhythmic, bisynchronous monomorphic slow waves in the occipital regions (occipital intermittent rhythmic delta activity OIRDA).
- The 3 c/s SWD is usually associated with an ictal absence episode when it lasts over 5 seconds.
- The 3 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 3.5 years and disappear at the age of 16 years.
- This discharge pattern is markedly enhanced during nonREM sleep, usually during stage II. However the morphological features of this discharge pattern are altered during sleep with the discharge occurring in a more fragmented and atypical fashion, occurring in bursts of spikes, polyspikes and atypical spike/wave complexes. This discharge pattern usually occurs in conjunction with sleep spindles and has an invariable frontal midline maximum.
- Background activity is within normal before and after termination of the paroxysmal discharge.
Figure 9. The Frontally predominant 3 c/s spike/wave discharge.

Figure 10. Occipitally intermittent rhythmic delta activity proceeding typical 3 c/s spike/wave discharge in a patient with typical absence.
Figure 11. The 3 c/s spike/wave discharge in two different patients, notice that the waveform morphology is different in different patients.

The clinical significance of the epileptiform discharge will be discussed in more detail later. It must be properly recognized and distinguished from benign variants, artifacts, and normal EEG activity. Focal delta slowing in the same region as a suspected epileptiform discharge is additional evidence for focal neuronal dysfunction in the region of the presumed epileptic focus.

Sharp waves and spikes generally occur intermittently. In certain clinical settings, such as acute hemispheric cerebral infarction, sharp waves appear in a periodic fashion, and they are then referred to as periodic lateralized epileptiform discharges (PLEDs). PLEDs are most often seen in acute structural brain lesions. Generalized periodic sharp wave activity is classified on the basis of its morphology and frequency along with the specific clinical presentation. Examples include triphasic waves, generalized periodic epileptiform discharges (GPEDs), and the burst suppression pattern. Each of these patterns indicates that there is severe diffuse cerebral dysfunction.

An epileptic seizure rarely occurs during an EEG. The hallmark features of an ictal pattern are an evolution in frequency and field of the EEG activity during the event. Evolution in frequency refers to an increase or decrease from the initial frequency; evolution in field refers to spread of the activity into adjoining regions. The amplitude of the activity may increase, decrease, or remain the same during the ictal pattern or discharge. When there is an accompanying change in the clinical state of the patient, these findings are diagnostic of a seizure disorder. Ictal patterns that are not accompanied by a clinical change in the patient are called subclinical seizures. If the ictal discharge is focal in onset, then the seizure disorder is said to be partial in origin. However, if the discharge is generalized at onset, the seizure disorder may be either generalized or partial in origin, as a focal midline seizure focus may project equally to both hemispheres with a wide field. The morphology of the discharges, age of the patient, and ictal semiology are important factors in defining the type of seizure.

Activation procedures are used to enhance or increase abnormalities on the EEG. Although focal slowing is the abnormality most likely to be "activated," these procedures may also
accentuate epileptiform activity or induce a seizure. Activation procedures currently in use consist of hyperventilation (HV), intermittent photic stimulation (IPS), spontaneous and medication-induced sleep, and sleep after sleep deprivation. In the past, injections of seizure-inducing drugs such as pentylenetetrazol were used during the EEG to activate spike foci and induce seizures. However, these techniques are no longer used owing to the risk to the patient and the difficulty of discriminating spontaneous from drug-induced interictal and ictal discharges.

Hyperventilation should be performed for 3 to 5 min by any cooperative patient at least once during the EEG, provided there are no medical contraindications (cardiopulmonary disease, unstable cerebrovascular disease, etc.). Focal delta slowing that has been noted during wakefulness or drowsiness is often accentuated during hyperventilation. The induction of typical 3-Hz generalized spike and wave discharges and absence seizures by hyperventilation is well known. Hyperventilation has also been found to activate focal epileptiform discharges much less often than generalized epileptiform discharges. If hyperventilation provokes an absence seizure in a patient with an idiopathic generalized epilepsy, clinical unresponsiveness should be confirmed during the ictal discharge. Similar testing should also be performed in patients suspected of having nonepileptic seizures, or pseudoseizures, because hyperventilation may provoke a nonepileptic seizure in such patients.

Stimulus frequencies used during intermittent photic stimulation range from 1 to 20 Hz in increments of 2 to 3 Hz. In most subjects, a posteriorly predominant, bisynchronous and time-locked "driving response" is seen normally. The responses are best seen in the lower range flash frequencies in the very young and in the midrange frequencies in the adult. The absence of a driving response is also normal. In some subjects, the driving response may appear "spiky." Other normal findings during intermittent photic stimulation include the electroretinogram (ERG), which is seen in the frontopolar leads, and the photomyoclonic response (PMR), which is a synchronous myoclonic response involving the patient's facial and neck musculature, resulting in myogenic and kinesiogenic artifacts on the EEG. The artifacts generated by the PMR may appear as generalized spike or spike and wave activity. The PMR must be differentiated from the photoparoxysmal response (PPR), which is a burst of generalized epileptiform activity that is evoked synchronously by the intermittent photic stimulation, typically in the midrange frequency in susceptible patients, PPR may be seen in patients with an idiopathic generalized epilepsy, such as juvenile myoclonic epilepsy or absence epilepsy.

The process of becoming drowsy (stage I sleep) and falling into deeper stages of sleep has been shown to activate interictal epileptiform discharges of both focal and generalized types. This is accomplished in the EEG laboratory by recording during spontaneous sleep or sleep induced by medications (e.g., chloral hydrate). Typically, the epileptiform discharges appear more frequently on a scalp EEG during the lighter stages of sleep (stages I and II), and they appear less frequently during deeper stages of NREM sleep (stages III and IV) and during REM sleep. However, by using depth electrodes in patients with intractable partial seizure disorders, Rossi and colleagues demonstrated that interictal epileptiform discharges increase in frequency with increasing depth of NREM sleep.
The effect of sleep deprivation is less well established. Although it is often used as an activating method in patients with suspected seizures after a routine EEG without epileptiform features, it is not clear whether it causes any activation of the interictal epileptiform activity beyond that caused by falling asleep. Nevertheless, many EEG laboratories continue to recommend sleep deprivation with sleep as a follow-up EEG after a nondiagnostic routine EEG.

**SPECIFIC CLINICAL APPLICATIONS**

Although EEG is used most often as an ancillary test in clinical epilepsy, it also is an invaluable tool in other neurological conditions, such as encephalopathy, focal central nervous system (CNS) lesions, and clinical brain death, as well as for electrocorticography, and in neonatal medicine. The following sections discuss the usefulness of EEG in each of these situations.

- **Epilepsy**

Epilepsy is defined as "paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system. A seizure, or ictus epilepticus, is an epileptic attack or recurrence. The classification of epilepsies used by International League Against Epilepsy (ILAE) includes two major categories: partial epilepsies and generalized epilepsies. A partial seizure disorder is considered to have a focal region of onset in the brain, and awareness may be either preserved (simple partial seizure) or lost (complex partial seizure). A generalized seizure disorder is considered to involve most, if not all, of the brain at onset. The generalized seizure types may involve cessation of activity with loss of awareness (absence seizure) or generalized tonic-clonic activity (generalized tonic-clonic seizure). Both partial and generalized seizure disorders are further subdivided into idiopathic and symptomatic types, previously called primary and secondary, respectively. Idiopathic epilepsies are thought to be genetically heritable, are associated with normal intelligence, and occur during specific age periods. The symptomatic epilepsies are likely the result of a CNS injury, which in a symptomatic partial epilepsy consists of a focal lesion and in a symptomatic generalized epilepsy consists of diffuse cerebral abnormality. Symptomatic epilepsies are typically lifelong conditions.

It cannot be overemphasized that the diagnosis of epilepsy is based primarily on the clinical history. As noted above, a clinical seizure rarely occurs during an EEG, and thus the EEG is rarely diagnostic of a seizure disorder or epilepsy. In a large, population-based EEG study by Zivin and Ajmone-Marsan involving subjects without a history of seizures, approximately 2 percent of the subjects had EEGs with epileptiform discharges. Of the individuals in this subgroup, only 15 percent subsequently developed a seizure disorder. Therefore, epileptiform discharges seen on an EEG should not be referred to as interictal discharges unless it is known that the patient has a clinically defined seizure disorder. Focal or generalized epileptiform discharges should be noted as consistent with the interictal expression of either a partial or a generalized epilepsy, respectively. When applied in the
appropriate clinical setting, the EEG is useful in classifying the seizure type, predicting the long-term outcome, and choosing the appropriate antiepileptic medication.

Overall, symptomatic partial seizure disorders are the most common type of epilepsy. The clinical semiology of the partial seizure generally depends on the site of onset. In children, focal epileptiform discharges arising from the temporal region have the greatest incidence of clinical seizures, ranging from 85 to 95 percent. The next highest incidence (70 to 75 percent) is associated with frontal discharges. The central, parietal and occipital regions have the lowest incidence of seizures related to epileptiform discharges, estimated at 40 to 70 percent. In addition to the characteristics of recorded epileptiform activity, the age of the patient and the presence or absence of neurological deficits on examination are important factors that are helpful in determining the clinical significance of epileptiform discharges and in classifying the partial seizure disorder as either symptomatic or idiopathic. The occurrence of a clinical seizure with a focal electrographic correlate is diagnostic of a partial epilepsy. Blume and colleagues presented several types of scalp EEG correlates for partial seizures, most of which began with rhythmic sinusoidal activity or repetitive sharp wave activity that subsequently evolved in frequency. Most patients with complex partial seizures were noted to have a scalp correlate on the EEG. Patients with simple partial seizures were less likely to have a scalp correlate.

The best-defined idiopathic partial epilepsy is benign rolandic epilepsy. The classic EEG finding in this childhood seizure disorder is a characteristic monomorphic centrotemporal sharp wave. The sharp waves are often seen independently in the centrotemporal and adjacent regions, and they are accentuated by light sleep. The waking background rhythm is generally normal.

Of the idiopathic generalized epilepsies, the absence seizure is the most common type. The interictal EEG feature of this type of seizure disorder consists of generalized, high-amplitude, anteriorly predominant 3-Hz spike and wave discharges, called typical 3-Hz spike and wave. When the spike and wave discharges occur repetitively, they are called bursts. Although these discharges are called "3-Hz," the initial frequency of the burst is 3 to 4 Hz, and the frequency may slow to 2.5 Hz during more prolonged bursts. The discharges are reactive to alerting maneuvers and may become fragmented in deeper stages of sleep. Juvenile myoclonic epilepsy (JME) is another type of idiopathic generalized epilepsy. The spike and wave discharges of this seizure disorder are also generalized and anteriorly predominant, but they have an initial frequency of 4 to 6 Hz and may begin with a polyspike discharge. The EEG of a patient with an idiopathic generalized epilepsy who is maximally alerted is generally normal. During photic stimulation, there may be a photoparoxysmal response in both absence epilepsy and JME, which may be helpful in classifying recognized epileptiform discharges as consistent with an idiopathic generalized epilepsy rather than a symptomatic partial or generalized epilepsy.

Epileptiform patterns in symptomatic generalized epilepsies are of three types. A slow spike and wave pattern at approximately 2 Hz is seen in patients with mental retardation having multiple seizure types (atypical absence, tonic, atonic, or tonic-clonic seizures), which is known as the Lennox-Gastaut syndrome. A second type of interictal or ictal EEG
pattern seen in patients with symptomatic generalized epilepsy is generalized paroxysmal fast activity (GPFA), which consists of bursts of rhythmic, generalized beta activity. When the bursts are seen during wakefulness, they are commonly accompanied by a tonic seizure. During sleep, bursts of GPFA not accompanied by clinical changes are considered an interictal pattern. The third pattern of epileptiform activity in secondary generalized epilepsy is an atypical generalized spike and wave pattern, consisting of generalized 3 to 6-Hz spike or polyspike and wave activity. The waking background in patients with secondary generalized epilepsies is abnormally slow, including slowing of the posterior background rhythm and generalized slowing.

In patients suspected of having a seizure disorder, a normal routine, awake EEG should be followed with either a natural or medication-induced sleep EEG or a sleep-deprived EEG. Before the advent of long-term video-EEG monitoring for the diagnosis of possible seizures, three or more EEGs were often obtained to confidently conclude normality and absence of epileptiform activity. Because antiepileptic medications have been shown not to affect the frequency of focal interictal epileptiform discharges, the decision to treat a patient for a suspected partial seizure disorder should not be based solely on the initial EEG findings. Conversely, the EEG has not proven to be a reliable tool in predicting whether a patient's antiepileptic medication can be discontinued. In patients with an idiopathic generalized epilepsy, treatment with appropriate antiepileptic medication may eliminate all interictal epileptiform activity on the EEG. Therefore, the decision to discontinue an antiepileptic medication in a patient with a seizure disorder should be based on the type, etiology and response to medications of the seizures and not on interictal EEG findings.
Interictal epileptic activity

The interictal marker of a seizure focus is the spike or sharp wave. The distinction between these two patterns has no etiologic significance, the only difference being one of EEG pattern morphology. A spike is defined as being less than 70 milliseconds in duration, and a sharp wave has a duration of 70-200 milliseconds. The terms spike or sharp wave, while having particular meaning to the electroencephalographer, are often used interchangeably. Spikes and sharp waves are almost always of negative polarity at the scalp surface. These epileptiform discharges may arise from any region of the cerebral hemispheres but most commonly are manifested in the anterior temporal, frontal, or centrottemporal regions.

An anterior temporal spike or sharp wave is highly associated with the occurrence of clinical focal-onset seizures. When this pattern is seen on the EEG, the likelihood of the individual manifesting clinical seizures is over 90%. However, the converse is not necessarily true. While the EEG of most patients with temporal lobe seizures demonstrates anterior temporal spikes, an EEG negative for this finding does not exclude a diagnosis of epilepsy. Often, repeated EEG recordings or prolonged EEG monitoring is required to demonstrate the epileptiform pattern.

Frontal spikes and sharp waves also are highly associated with clinical seizures but not to the same degree as temporal discharges. Approximately 70-80% of individuals whose EEG demonstrates frontal spikes have clinical seizures. Frontal spikes or sharp waves are more likely to be associated with mass lesions such as neoplasms, traumatic lesions, or congenital cerebral malformations.

Centrottemporal or rolandic sharp waves are often a marker for a particular epilepsy syndrome of childhood known as benign rolandic epilepsy or benign focal epilepsy of childhood with centrotemporal spikes. This is a disorder in which a child, typically aged 4-12 years, develops focal seizures with sensory or motor seizures in the mouth or face region. These children also may have generalized seizures; typically, these seizures are nocturnal. The EEG pattern is unusual in that there is often a simultaneous negative waveform in the centrottemporal region and a positive one in the frontal region. This pattern of EEG polarity is virtually diagnostic of benign rolandic epilepsy.

Epileptiform EEG patterns are seen less commonly in the occipital, central, or parietal regions. Occipital spikes typically are seen in young children and may or may not be associated with clinical seizures. Discharges in any of these regions may indicate the presence of partial epilepsy.

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Table 2. Electroclinical criteria of spike/sharp wave discharge

- A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG.
- A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.
- Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.
- The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.
- Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.
- The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. Low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.
Encephalopathy and coma result from conditions that affect both cerebral hemispheres or the reticular activating system in the midbrain. The differential diagnosis is broad, including metabolic, toxic, anoxic/ischemic, infectious, endocrinologic, degenerative, and inflammatory processes. These processes affect the brain diffusely, and, consequently, changes in the EEG often appear generalized. While most EEG findings in encephalopathy and coma are nonspecific with regard to etiology, information relevant to the clinical course and prognosis can be obtained using the EEG.

In cases of mild encephalopathy, theta and delta activity is intermixed with the background alpha rhythm. Occasional generalized delta transients are also seen. As the encephalopathy worsens, there is loss of background alpha-range frequencies and an increased amount of generalized theta and delta activity. Intermittent-rhythm delta activity (IRDA) may appear, which in adults generally is frontally predominant (FIRDA), and is consistent with moderate diffuse bihemispheric cerebral dysfunction (Fig-13). In severe encephalopathy, there is generalized delta activity. Loss of reactivity in anyone of these stages implies greater severity, and, in specific clinical settings, a worse prognosis. In the clinical setting of severe anoxia (e.g., after cardiac arrest) or severe closed head injury, invariant patterns of persistent, generalized alpha activity (alpha coma), generalized periodic epileptiform discharges, or the burst suppression pattern (Fig-14) are associated with very poor outcome.

Figure 13. Frontal intermittent rhythmic delta delta activity (FIRDA)
Figure 14. Burst suppression pattern, consisting of bursts with an initial delta transient and superimposed theta activity lasting 2 s. During the burst intervals, there is no EEG activity. Ventilator artifacts are seen.

In the early reports of the EEG findings in hepatic coma, triphasic waves were noted which were initially thought to be pathognomonic for this condition. These three-phased generalized discharges consist of high-amplitude, sharp wave complexes that are repetitive, have an average frequency of 2 Hz, and show initial surface positivity and anterior predominance (Fig-17).
Figure 16. The intermittent rhythmic delta activity [left image] and the polymorphic slow wave activity [right image]

Table 3. Electrical criteria of The intermittent rhythmic delta activity.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]).
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.
Figure 17. Periodic triphasic waves at 1-Hz frequency

Triphasic waves may be intermittent and reactive, or they may be persistent and unreactive. There is no normal background rhythm. Although present on the EEG in most patients with hepatic failure, triphasic waves may also be seen in cases of other metabolic, toxic, anoxic, degenerative and inflammatory encephalopathies. In patients whose EEGs demonstrate triphasic waves, overall mortality is high, and there are few normal survivors. Periodic sharp waves having a morphology similar to that of triphasic waves may be seen in patients with Creutzfeldt-Jakob disease (CJD), but the frequency of the discharges typically averages 1 Hz. In early CJD, the periodic complexes are superimposed on a background that may have only mild slowing. As the disease progresses, the background rhythm is lost, resulting in a pattern of periodic 1-Hz discharges on a flat background. The clinical history of subacute dementia, seizures, and myoclonus in conjunction with this periodic pattern is strongly suggestive of CJD. To confirm this progression, sequential EEGs may need to be performed during the course of CJD.
Polymorphic delta activity (PDA) consists of arrhythmic slow waves that vary in frequency, amplitude, and morphology. PDA can occur in either a focal or generalized distribution. Continuous PDA is indicative of abnormalities involving subcortical white matter. One of the shortcomings of standard scalp EEG recordings is their limited spatial resolution. This holds true for the relationship of PDA to an underlying structural abnormality. Not only is the inherent localizing ability of the scalp EEG limited, but also the PDA of a structural lesion is referable not to the lesion itself but to the surrounding brain tissue. Because of this limitation, the area of a lesion is indicated not by the maximal amplitude of PDA but rather by a region of relatively low-amplitude slowing. Continuous, rather than intermittent, PDA is associated with large lesions, mass effect, and impairment of consciousness.

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.

Figure 18. Polymorphic slow wave activity in a patient with subcortical glioma, notice the marked variability in wave shape morphology, frequency and amplitude.
Table 4. Electrical criteria of the Polymorphic slow wave activity.

- Quite variable in wave shape morphology, frequency and amplitude.
- Commonly lateralized over a wide area of the scalp, persistent in eye closed, eye open state, during all sleep stages, with no visual reactivity. Polymorphic Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology.
- Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
- Commonly due to a subcortical white matter lesion inducing deafferentation of the cerebral cortex.
- A purely cortical lesion does not induce polymorphic slow wave activity.

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<th>Rhythmic delta activity</th>
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<td>consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized. In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]). Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies. FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy. In cases of encephalopathy with FIRDA, the pathophysiologic processes are believed to involve cortical and subcortical gray matter. OIRDA is associated with absence epilepsy in children aged 6-10 years</td>
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Figure 19. The intermittent rhythmic delta activity [left image] and the polymorphic slow wave activity [right image]
Table 5. Electrical criteria of The intermittent rhythmic delta activity.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
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- OIRDA is associated with absence epilepsy in children aged 6-10 years.

**Focal theta activity**

Is less likely to reflect a macroscopic structural lesion than is focal delta. Theta is commonly, however, associated with a functional disturbance, such as epileptogenic cortex, especially postictally, after amplitude suppression and focal delta have resolved. In addition, localized theta is usually superimposed on focal delta to some degree; the relative proportion of delta and theta reflects the size and/or severity of the underlying structural or functional cerebral abnormality.

Epileptiform activity may be seen on the EEG in some degenerative encephalopathies that have associated seizures. Multifocal, independent epileptiform spike discharges may be seen in Tay-Sachs disease, in several of the progressive myoclonic epilepsies (neuronal ceroid lipofuscinosis, Lafora body disease, and some mitochondrial encephalomyopathies), and in Rett syndrome. Atypical generalized spike and wave activity is present in Unverricht-Lundborg disease, which is another type of progressive myoclonic epilepsy.

Of the inflammatory encephalopathies, distinctive EEG findings are seen in subacute sclerosing panencephalitis (SSPE) and herpes simplex encephalitis. The clinical presentation of SSPE includes myoclonus with progressive encephalopathy. The EEG shows periodic, polyphasic sharp and slow wave complexes that have an interburst interval of 4 to 10 s. As SSPE progresses, there is gradual loss of the intermixed background frequencies, resulting in a pattern similar to burst suppression. Herpes simplex encephalitis is the most common sporadic viral encephalitis, typically presenting with fever, encephalopathy, and secondarily generalized seizures. The EEG commonly shows periodic lateralized epileptiform discharges (PLEDS), which are lateralized to the side of the herpes infection. Should both temporal lobes be involved, bilateral independent periodic epileptiform discharges (BIPLEDs) may be seen on the EEG. Other forms of inflammatory
encephalopathy typically result in nonspecific slowing of the EEG, the severity of which is often correlated with the severity of the encephalopathy.

Lastly, nonconvulsive status epilepticus should be considered in patients with a known seizure disorder or recently witnessed seizure who present with prolonged encephalopathy. Patients presenting in nonconvulsive status epilepticus may have subtle clinical findings of ongoing seizures, and electroencephalography is crucial in confirming response to therapy with cessation of electrographic seizure activity. The EEG in nonconvulsive status epilepticus generally shows widespread, repetitive sharp and slow wave complexes at 1 to 2 Hz. Administration of low-dose intravenous benzodiazepine therapy during the EEG usually results in rapid resolution of the ictal pattern and clinical encephalopathy. Should convulsive seizure activity not respond to conventional therapeutic intervention, then barbiturate coma or general anesthesia with concurrent EEG monitoring is needed to demonstrate a burst suppression pattern and lack of electrographic seizure activity.

- **Focal Lesions of the Central Nervous System**

The EEG findings in focal cerebral lesions are generally nonspecific. Serial EEGs may be necessary to fully appreciate the electrographic changes in conditions where there may be significant change in neurological status, such as acute stroke or progressive brain tumor. If only the cortical gray matter is involved, there is amplitude suppression of the surrounding EEG activity. However, many focal cerebral lesions involve both the cortical gray matter and the underlying white matter, resulting in slowing of the EEG activity with intermittent focal delta activity. Midline and infratentorial lesions may not produce any changes in the EEG, or they may result in generalized slowing.

When focal delta activity is intermittent, it is consistent with focal cerebral dysfunction of a nonspecific etiology. Focal delta activity that is nonreactive and is present for 70 to 80 percent of the record (Fig-20) is called persistent polymorphic delta activity (PPDA). PPDA is a specific finding in structural lesions of the brain, often seen in patients with a supratentorial high-grade cerebral neoplasm, a large cerebral abscess, or a stroke involving subcortical and cortical regions. Transient PPDA may be seen after a complicated migraine headache or a partial seizure. emphasizing the need for serial EEGs in certain cases.
As discussed above, intermittent rhythmic delta activity (IRDA) is generally a finding consistent with diffuse bihemispheric cerebral dysfunction. However, in a large series of patients with IRDA, brain tumor was seen in 30 percent and cerebrovascular disease in 19 percent. Although reported before the advent of computed tomography (CT), the diagnoses in this study were based on neuropathologic confirmation. The frontal lobe is the most common location for brain tumors associated with IRDA on the EEG.

Sharp waves or spike discharges are occasionally seen on the EEGs of patients with focal cerebral lesions. The epileptiform discharges are rarely the sole abnormality on the EEG, and they are most often associated with focal delta slowing. Periodic lateralized epileptiform discharges (PLEDs) may be seen in acute cerebral lesions such as stroke or herpes simplex encephalitis. PLEDs may be unilateral or bilaterally independent, termed BIPLEDs (Fig-21). PLEDs are generally self-limited, lasting 1 to 2 weeks during the acute phase of illness. There is a high incidence of seizures in patients whose EEG demonstrates PLEDs or BIPLEDs (Fig-22). Last, patients with a focal cerebral lesion may present in partial or generalized status epilepticus.

Figure 20. Persistent polymorphic delta activity (PPDA) in the right temporal region.
Figure 21. Bilateral independent periodic lateralized epileptiform discharges (BIPLEDs) due to right ICH and IVH.
Brain Death

Brain death has been defined as the "irreversible cessation of all functions of the entire brain, including the brainstem." The determination of brain death is important in clinical situations such as potential organ donation and withdrawal of life support. The clinical criteria for brain death in adult patients can be summarized as follows:

1. There is no known reversible etiology. Reversible factors that may cause coma or apparent coma must be ruled out, including sedative medications and paralytics (e.g., barbiturates, benzodiazepines, neuromuscular blocking agents), hypothermia (i.e., the core temperature must be greater than 32.2°C), a potentially reversible medical illness (e.g., hepatic failure, renal failure), and shock.

2. Coma and the absence of brain stem function (e.g., cranial nerve function and respiratory control) are demonstrated by a neurologist or neurosurgeon on two successive neurological examinations separated by an appropriate period. In adult patients, 12 h is generally an adequate period between examinations. However, in adults with anoxic/ischemic encephalopathy and in children, this interval may extend to 24 h or longer, depending on the circumstances. Criteria for newborns are not well established.
3. Confirmatory tests (e.g., EEG, cerebral angiogram or nuclear cerebral blood flow scan) may be used if the period of observation is less than that recommended above, as in the setting of organ donation. In all other circumstances, these tests are considered optional and are used at the discretion of the attending physician.

An EEG recording to determine brain death should not be considered until the clinical criteria are met. The EEG then be ordered to confirm electrocerebral inactivity or silence. (ECI and ECS. respectively). ECI is defined as lack of EEG activity greater than 2 µV. The following guidelines for performing an EEG to confirm ECI have been recommended by the American Electroencephalographic Society:

1. At least 8 scalp electrodes should be used, covering the frontal, central, temporal, and occipital regions of both hemispheres.

2. Interelectrode impedances should be between 100 and 1000 Ω.

3. The integrity of the recording system should be confirmed at the beginning of the recording. This is generally done by touching each electrode in succession and documenting the resulting electrode artifact.

4. Interelectrode distances should be 10 cm or greater.

5. Sensitivities must be increased from 7 µV/mm to 2 µV/mm during the recording, the duration of which should be at least 30 min, excluding time for EEG machine preparation (i.e., machine calibration at all sensitivities).

6. Filter settings should be 1 Hz for the low-frequency filter and 30 Hz or greater for the high-frequency filter.

7. Monitoring of additional cerebral and noncerebral sites should be done as needed. This is done to confirm the source of suspected artifacts, such as electrocardiogram, respiration, electromyogram. etc.

8. Unreactivity of the EEG should be documented using visual stimulation, auditory stimulation and somatosensory stimulation below and above the neck.

9. The EEG recording during ECI should be performed by a qualified technologist.

10. The EEG should be repeated if there is any doubt regarding the diagnosis of ECI.

It is crucial to remember that the EEG is only a confirmatory test for the presence of cerebral death and that the primary criteria are clinical. As the EEG is subject to artifacts whose source may not be determined, the utility of this test for confirmation of ECI may be limited in settings where factors which cause EEG artifacts are prevalent.
Electrocorticography (ECoG) is the technique by which the brain's electrocerebral activity is directly measured using either depth electrodes, cortical surface contact electrodes, or subdural electrode strips or arrays. Although ECoG is not a routine procedure, it has become widely used in the presurgical evaluation of patients with medically intractable partial epilepsy where the site of seizure onset cannot be adequately localized using noninvasive methods. ECoG has also proved to be an important technique for functional brain mapping of eloquent cortex during the neurosurgical resection of lesions such as brain tumors or vascular malformations.

In patients undergoing invasive monitoring with depth or subdural electrodes for epilepsy surgery evaluation, the decision of where to place the electrodes is based on several factors, including ictal semiology, interictal epileptiform activity and neuroimaging findings. Electodes should be placed to cover the region of suspected seizure onset. Often the corresponding contralateral cortex is also covered, for reference and to confirm that there is a single zone of epileptogenesis. A sufficient number of seizures are recorded with video-EEG monitoring using the invasive electrodes, and the behavioral onset of seizures is timed to confirm that it follows the electrographic onset. Interictal epileptiform activity is much more often recorded when invasive electrodes are used, and it is often multifocal. Upon completion of monitoring, depth electrodes may be removed at the patient's bedside. Removal of subdural electrodes is generally performed in the operating room.

The primary use of cortical stimulation is to identify areas of essential cortex, such as those subserving motor, sensory or language function. Brain mapping using cortical stimulation may be performed during epilepsy surgery or other neurosurgical procedures such as the resection of tumors or vascular malformations. It may be conducted intraoperatively with the patient awake in the operating room, or extraoperatively in the patient's room, where testing may be performed over several days in sessions lasting 1 to 3 h as needed. At most centers, stimulation consists of 0.3 to 1 ms biphasic square wave pulses at 50 Hz, lasting from 2 to 5 s each. The stimulation intensity starts at 0.5 to 1 mA and is raised in increments of 0.5 to 1 mA until a neurological deficit is produced or afterdischarges occur or a maximum 15 mA stimulus intensity is reached. During dominant temporal lobe surgery, object naming alone may be used if the zone of resection is more than 2 cm distal to the defined language cortex. However, when the zone of resection must border on language cortex, more extensive testing is performed, including reading, repetition, naming and comprehension. Motor and sensory areas may be similarly mapped by evoking either muscle contraction when stimulating areas of the precentral gyrus or regions of paresthesia when stimulating the postcentral gyrus. In all cases, the lowest stimulation intensity that evokes a response should be used, to limit the current field to the region of interest.

Clinical seizures provoked by cortical stimulation are in general not predictive of the zone of epileptogenesis in patients with intractable partial seizures. Afterdischarge potentials are brief, self-limited electrographic seizures that may be produced by cortical stimulation. Afterdischarges may evolve into a clinical seizure, and for this reason, anticonvulsant levels in patients with partial seizures are maintained in the therapeutic range when cortical
stimulation is being performed. At some medical centers, cortical stimulation is performed in an attempt to induce typical auras that the patient may experience. Temporal lobe epilepsy has been reported to have the highest concordance between spontaneous seizures and induced auras or seizures.

- Neonatal EEG

The neonatal period extends from birth (including premature birth) to age 2 months. The conceptual age (CA), or age since conception, is an important factor in interpreting the neonatal EEG, because it defines the level of maturation of the CNS. As the premature brain matures, well-defined patterns are seen that help to differentiate normal from abnormal EEGs at specific ages. Owing to the small size of the neonatal head, the International 10-20 System of electrode placements is modified to allow for coverage of the frontal, central, temporal, and occipital regions. Physiologic parameters such as heart rate, respirations, eye movements and limb myogenic activity are also monitored to help differentiate active sleep (rapid eye movements, variable heart rate and respiration) from quiet sleep (no movement with regular heart rate and respirations), and wakefulness from sleep. The EEG is performed at a paper speed of 15 mm/s (one-half the adult paper speed). This is done to allow a longer sampling time (generally 1 h) and to compress the EEG, as it consists predominantly of theta and delta range frequencies. Above a CA of 48 weeks, the standard EEG is performed.

Before 22 weeks CA there is no discernible electrocerebral activity. As the neonatal brain matures, a discontinuous, invariant pattern is seen initially, which is gradually replaced by more continuous, variant patterns as term gestation is reached. At 26 weeks CA, a discontinuous pattern is seen, with bursts of high-amplitude, sharply contoured theta activity, which is maximal in the temporal regions. During the interburst periods, there is no discernible EEG activity. The EEG is unreactive and remains so until 34 weeks CA. By 30 weeks CA, active sleep can be distinguished from quiet sleep by a reduction in amplitude and the amount of delta activity. At this age, beta-delta complexes (delta brushes) are seen in both stages of sleep; they gradually become less frequent and disappear by term. By 35 weeks CA, the EEG is reactive. Independent frontal sharp transients are seen, as well as occasional equally distributed independent sharp transients in both hemispheres, which may be seen until term. Wakefulness can be distinguished from sleep at 36 weeks CA, demonstrating continuous, low-amplitude mixed frequencies. At term, the EEG should be synchronous and reactive and should demonstrate both active and quiet sleep and wakefulness.

The most common abnormality in a neonatal EEG is the absence or delayed appearance of normal patterns. A low-amplitude EEG may be due either to cerebral dysfunction or to an extracerebral fluid collection such as scalp edema or a subdural hematoma. An increased number of multifocal independent sharp transients indicates diffuse cerebral dysfunction, which is maximal in the region of the most frequent transients. These sharp transients are not called sharp waves or spikes, as they do not indicate a seizure disorder in the neonate.
The clinical and EEG findings of a seizure in the neonate vary in semiology and pattern, and some are controversial. Seizures in a neonate may not be accompanied by an electrographic correlate. Conversely, electrographic seizures may have no clinical correlate, or they may have subtle correlates such as apnea or heart rate changes. The EEG diagnosis of a seizure is based on the evolution of frequency of focal rhythmic activity, which may be limited to a single electrode. Generalized tonic clonic seizures very rarely are seen, likely because the myelination and dendritic arborization of the CNS is limited at this age.

Obtaining an EEG should be considered in all premature or term neonates who have evidence of significant neurological dysfunction on clinical examination. In addition to providing information regarding CNS maturation, the neonatal EEG is often helpful in guiding neuroimaging assessment by cranial ultrasound, CT, or MRI. As neonatal seizures may have subtle or no clinical manifestations, the EEG is an invaluable tool in the clinical evaluation of the neonate.

References

INTRODUCTION

Despite advances in neuroimaging techniques over the past three decades that have helped in identifying structural lesions of the central nervous system, electroencephalography (EEG) continues to provide valuable insight into brain function by demonstrating focal or diffuse background abnormalities and epileptiform abnormalities. It is an extremely valuable test in patients suspected of epilepsy and in patients with altered mental status and coma. Patterns in the EEG make it possible to clarify the seizure type; it is
indispensable for the diagnosis of nonconvulsive status epilepticus and for separating epileptic from other paroxysmal (nonepileptic) episodes. There are EEG patterns predictive of the cause of the encephalopathy (i.e., triphasic waves in metabolic encephalopathy) or the location of the lesion (i.e., focal polymorphic delta activity in lesions of the subcortical white matter). The various EEG characteristics of infantile, childhood, and adult epilepsies are described as well as the EEG patterns that are morphologically similar to interictal/ictal epileptiform discharges but unrelated to epilepsy. An EEG is most helpful in determining the severity and, hence, the prognosis of cerebral dysfunction. Lastly, EEG is extremely helpful in assessing normal or abnormal brain functioning in a newborn because of the serious limitation in performing an adequate neurologic examination on the neonate who is intubated or paralyzed for ventilatory control. Under such circumstances, the EEG may be the only available tool to detect an encephalopathic process or the occurrence of epileptic seizures.

Electroencephalography (EEG) is the technique of recording from the scalp the spontaneous electrical activity of the brain and correlating it to the underlying brain function. Since the first recording of a human EEG in 1929 by Hans Berger, improvement in electronics and technology has made EEG one of the most widely used laboratory tests for clinical evaluation of neurologic disorders. However, in the past three decades with continuing advances in neuroimaging, particularly magnetic resonance imaging (MRI), the role of clinical EEG has become restricted and progressively more focused. Its major utility at present is in the evaluation of focal and diffuse encephalopathies, comatose conditions, epileptic disorders, and cerebral disorders affecting neonates and infants. The present article is not an attempt to describe EEG comprehensively in normal subjects and in different disease processes but to highlight its usefulness/limitation and emphasize precautions/care needed in its optimal utility. The subject will be discussed under seven sections: EEG in normal subjects, EEG in patients with altered mental status or diffuse encephalopathies, EEG in focal or lateralized cerebral hemispheric lesions, EEG in paroxysmal disorders, EEG in generalized epilepsies, EEG in neonates, and EEG in status epilepticus.

- **EEG In Normal Subjects**

The EEG in the normal awake child and adult is well known and needs no detailed description. The following are points of emphasis:

1. Alpha rhythm in the two hemispheres is very similar in frequency. A consistent difference of even 0.5 to 1.0 cps on the two sides is significant; the side showing a slower frequency may have a hemispheric dysfunction. Amplitude asymmetry is of relatively less significance, unless the asymmetry is prominent. In general, the alpha rhythm is higher in amplitude over the right hemisphere. If the amplitude of the alpha rhythm on the right side is more than 1 1/2 times that on the left side, the asymmetry is usually regarded as significant. When the alpha rhythm is over 25% higher in amplitude on the left side than the right side, this constitutes a significant asymmetry.[1]
2. Significant theta activity (4 to 7 Hz) is present in the EEG of children and adolescents. Delta activity in the awake tracing is rarely seen after the age of 5 years. A common EEG pattern in adolescents is the presence of intermittent delta waves intermixed with alpha rhythm over the posterior head regions, the so-called "slow waves of youth."

3. The EEG during non-rapid eye movement (NREM) sleep in children shows very prominent spikelike vertex sharp transients, which are often mistaken for epileptiform activity by EEG interpreters inexperienced with children's EEGs (Fig. 1). Similarly, positive occipital sharp transients (POSTs), when high in amplitude and sharp in configuration, can be easily misinterpreted as abnormal spikes, especially in linkages where occipital electrodes are connected to input terminal 2 (grid 2) of the amplifier (e.g., "double banana run").

4. In a small proportion of normal adult subjects, clearly identifiable and countable alpha rhythm may be entirely absent. The background may consist of irregular mixtures of low amplitude (<20 µV) activities, mostly from 5.0 to 30.0 cps without a dominant frequency. Such low-voltage EEGs have been studied in detail.[2] The EEG is reactive to various physiologic stimuli such as sleep, drugs, and pathologic processes. In over half of the patients with low-voltage EEGs, hyperventilation may bring out an alpha rhythm. During sleep, normal activities such as vertex sharp transients and sleep spindles may be generated. It is essential that low-voltage tracings be clearly distinguished from EEGs showing electrocerebral inactivity, which have a grave prognosis. These EEGs lack reactivity and lability, and with increased instrumental sensitivities show no electrical activity of cerebral origin. Low-voltage EEGs are generally considered to be a normal variant occurring in 7 to 10% of normal subjects over the age of 20 years. The low-voltage EEG does not correlate with neurologic or psychiatric disease.

5. Changes in the EEG during normal senescence has been described in detail.[3-5] The most frequent change is the slowing of the alpha frequency. By the age of 70 years, the mean alpha frequency decreases to 9.0 to 9.5 cps and decreases further to 8.5 to 9.0 cps beyond the age of 80 years. In healthy elderly subjects, even at or over the age of 100 years, the frequency of the alpha rhythm remains well above 8.0 cps.[6,7] Therefore, an average alpha frequency of less than 8.0 cps measured with the patient fully alert must be considered abnormal in elderly patients at all ages.

6. Another EEG finding is the presence of isolated transients of irregular focal slowing in the theta-delta frequency range over the anterior temporal region, reported in 40% of healthy elderly subjects.[4,5,8] They are most frequent over the left temporal area particularly during drowsiness (Fig. 2). Sometimes poorly defined sharp waves are interspersed with focal slow components. The left-sided accentuation of this activity remains unexplained. Such intermittent slow activity, with or without sharp components over the temporal region, has no correlation with intellectual or cognitive functioning or presence of a seizure disorder. More recent investigations suggest that the temporal slowing in the awake tracing may, in fact, not be the inevitable consequence of advancing age. In neurologically and psychologically normal septuagenarians, Katz and Horowitz[9] found that the focal slow activity was seen in only 17% of records and when present occupied less than 1% of the tracing. Hence, intermittent temporal theta-delta activity occupying only
a small proportion of the wake tracing should be considered as a normal aging phenomena. When the temporal slow activity comprises more delta than theta slow waves, which either recur frequently or occur in long runs and are widespread in distribution, a dementing process or focal lesion has to be seriously considered. Diffuse theta-delta activity in elderly subjects are likely to occur in those with intellectual impairment.[5]

Figure 1. EEG of a 2-year-old child with very prominent spikelike vertex sharp transients.
The term encephalopathy is usually applied to patients displaying altered mental status as a result of a diffuse disturbance of brain function. Common encephalopathies are divided into metabolic, toxic, inflammatory (encephalitis), anoxic, and degenerative types. The EEG in most encephalopathies shows an alteration of background activities and emergence of varying degrees of theta-delta slowing. Remember that the EEG findings are generally nonspecific from a differential standpoint. The EEG is unable to distinguish between different etiologies. The main contribution of the EEG is in providing an objective measure of severity of encephalopathy, prognosis, and effectiveness of therapy.[10]

There is a good correlation between the severity of the EEG changes, the severity of the encephalopathy, and the clinical state of the patient. In mild encephalopathy associated with mild clouding of consciousness and confusion, there is at first slowing of the posterior dominant rhythm, which decreases from a higher to a lower alpha frequency and then into the theta frequency range. More severe encephalopathy is associated with deeper levels of coma, and the background consists mainly of high-amplitude irregular delta activity. With further deterioration in the encephalopathy, the amplitude of all activities drop below 20 µV and the EEG may consist of relatively low-amplitude, invariant delta activity. Some tracings reveal suppression-burst pattern where there is regular alternation of very-low-amplitude EEG with relatively higher-amplitude EEG segments. The most extreme type of abnormality is, of course, lack of any cerebral activity (i.e., electrocerebral inactivity). Presence of the later three types of EEG patterns (invariant low-amplitude delta, suppression-burst, and electrocerebral inactivity) carry a grave prognosis, if drug intoxication can be excluded as the cause of encephalopathy. If due to drug intoxication,
these severely abnormal patterns are quite reversible with treatment, with a high potential for complete recovery of neurologic functioning.

Besides the degree of background slowing, there are two other features in the EEG that must be evaluated to determine the severity of encephalopathy. These are spontaneous variability of the EEG over several seconds to minutes, and reactivity to painful stimulation. In milder encephalopathies, the EEG shows spontaneous variability during the recording period and evidence of EEG reactivity to painful stimulation. When the EEG shows reactivity, painful stimulation commonly results in reduction of the amplitude, increase in frequency of the background activity, and reduction in the slow activity. There is often a "paradoxical activation," which is a period of more severe delta slowing following painful stimulation (Fig. 3). The presence of any type of reactivity (reduction in slow activity or increase in the degree of slowing) on painful stimulation suggests a lower grade of encephalopathy, whereas the EEG lacking spontaneous variability (invariant EEG) and total lack of any reactivity to intense and prolonged stimulation suggests a severe degree of encephalopathy.

![Figure 3. EEG of an 8-year-old child with hemolytic anemia and uremia, showing paradoxical activation characterized by increased delta slowing induced by painful stimulation.](image)

A grading system of EEG abnormalities in adults is shown in Table 1, similar to other rating systems.[11,12] It is helpful in prognosis, evaluation of effectiveness of therapy, and comparing serial EEG studies. The slow activities associated with an encephalopathy are usually widespread and symmetrical over the two hemispheres. In children, the slowing
may predominate over the posterior hemisphere, and in adults, usually over the frontal areas. These are simply maturation-related spatial EEG features, which do not signify that the encephalopathy is more severe posteriorly in children and anteriorly in adults.

Table 1. Grading of EEG Abnormalities in Diffuse Encephalopathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>Grade I</td>
<td>(almost normal) Dominant activity is alpha rhythm with minimal theta activity</td>
</tr>
<tr>
<td>Grade II</td>
<td>(mildly abnormal) Dominant theta background with some alpha and delta activities</td>
</tr>
<tr>
<td>Grade III</td>
<td>(moderately abnormal) Continuous delta activity predominates, little activity of faster frequency</td>
</tr>
<tr>
<td>Grade IV</td>
<td>(severely abnormal) Low-amplitude delta activity or suppression-burst pattern</td>
</tr>
<tr>
<td>Grade V</td>
<td>(extremely abnormal) Nearly “flat” tracing or electrocerebral inactivity</td>
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It is unusual to see prominent focal or lateralized EEG findings with a diffuse encephalopathy unless there is an associated focal process, such as an old infarct or tumor. An exception is nonketotic hyperosmolar coma, a form of metabolic encephalopathy, which is very often associated with focal clinical (e.g., focal seizures) and focal EEG findings. Herpes simplex encephalitis and Creutzfeldt-Jakob disease (in the early stages) may also produce lateralized EEG slowing related to unilateral emphasis of the associated pathologic process (see below).

Another EEG pattern associated with a mild form of encephalopathy is the presence of bursts of intermittent rhythmic delta activity (IRDA) superimposed on a more or less normal background activity. Depending on the area of predominance, the IRDA is further divided into frontal or occipital types. IRDA has been traditionally considered a "projected rhythm" and a hallmark of EEG findings in patients with deep midline lesions of diencephalic, upper brain stem, or posterior fossa locations.[13] Critical evaluations subsequently have cast serious doubts on this classic concept because this EEG pattern has been found in a large variety of pathological conditions and is often absent in deep midline lesions. As a matter of fact, the most common etiology of IRDA is a mild to moderate encephalopathy associated with some disturbance in consciousness (Fig. 4).[14]
Are there any unique or specific EEG features that help narrow the differential diagnosis of diffuse encephalopathy and point toward a more specific etiology? There are a few EEG patterns (e.g., triphasic waves, positive spikes, and periodic complexes) that, although not commonly encountered in encephalopathic patients, when present suggest a specific etiology for the encephalopathy. Periodic patterns are specifically encountered in anoxic encephalopathy and certain encephalitides, whereas triphasic waves and positive spikes characteristically occur in metabolic encephalopathies.

- **Metabolic Encephalopathy**

An EEG showing diffuse slowing of the background and presence of triphasic waves is highly suggestive of a metabolic encephalopathy. Triphasic waves are high amplitude (200 to 300 µV), usually bilaterally synchronous, symmetrical, and maximum in amplitude over the frontocentral regions (Fig. 5). The most prominent component is a positive sharp wave that is preceded by a short-duration negative sharp wave and followed by a long-duration negative slow wave.[15] However, variations are quite common and the waveform may be monophasic or biphasic.
Figure 5. EEG of a 69-year-old patient with hepatic encephalopathy, showing triphasic waves.

Although earlier authors[15] emphasized that the triphasic waves were highly specific for hepatic encephalopathy, this EEG pattern has been found to correlate best with any metabolic type of encephalopathy; hepatic, renal, and anoxic etiologies account for over 75% of EEGs with triphasic waves.[16-18] A feature of triphasic waves often stressed is the progressive time lag (25 to 140 milliseconds) of the positive component of the triphasic wave from the anterior to the posterior region. This feature was considered to be most specific for hepatic etiology.[17,19] Recent studies[18] demonstrated that the time lag is neither a consistent feature of triphasic waves, nor has any specificity with regard to the type of metabolic encephalopathy. The "peril" is that no single feature or group of features regarding triphasic waves distinguish hepatic from nonhepatic cases.
There are a few other "pearls" regarding triphasic waves. Patients with metabolic encephalopathies showing prominent triphasic wave activity in their EEG have an overall poor prognosis; in one series, over two thirds died in a matter of a few months.[20] Furthermore, triphasic waves occur essentially in adults; this pattern has been rarely reported below the age of 20 years.[21] This is particularly true with Reyes disease, an acute childhood encephalopathy with hepatic fatty infiltration, where triphasic waves are absent.[22] The EEG pattern of 14 to 6 per second, positive spikes are a well-known maturational EEG pattern normally seen in children in adolescence during NREM sleep. The presence of positive spike bursts in comatose patients with continuous delta activity is a unique, albeit rare, EEG pattern associated with hepatic or anoxic encephalopathy in children (Fig. 6).[23,24]

![Figure 6. EEG of a 16-year-old comatose patient with Reye's syndrome, showing 14 cps positive spikes.](www.yassermetwally.com)

- **Toxic Encephalopathy**

Overdose of hypnotic-sedative drugs is a common cause of coma encountered in the emergency room; excessive beta activity is a prominent feature in the EEG over the anterior head regions. What is less well recognized is that with more severe intoxication, the fast activity assumes a slower frequency (usually 10 to 13 Hz), which is widespread but with anterior predominance. The presence of generalized theta-delta activity with superimposed alpha frequency activity is a unique encephalographic pattern highly characteristic of sedative drug intoxication (Fig. 7). In the absence of prominent slow
activity, the anterior dominant generalized fast activity produces alpha or spindle coma pattern in the EEG indistinguishable from that seen with severe anoxic encephalopathy.[25,26]

Figure 7. EEG of an 18-year-old patient with phenobarbital intoxication, showing generalized theta-delta activity with superimposed beta frequencies (A) followed in 3 days by normalization of the EEG (B).

Very severe drug intoxication results in suppression-burst pattern or electrocerebral inactivity. Even though these patterns signify advanced intoxication, they do not carry as ominous a prognosis as when they occur in the setting of cardiopulmonary arrest. It has been repeatedly demonstrated that patients with drug-induced coma may have electrocerebral inactivity lasting over a day and may still make a full neurologic recovery.

Phencyclidine hydrochloride ("angel dust," "PCP pills") is associated with a distinctive EEG pattern similar to that of subacute sclerosing panencephalitis (SSPE). The EEG shows generalized sinusoidal 6.0 cps theta activity that is interrupted approximately every 4 seconds by generalized slow wave discharges.[27] A similar periodic EEG pattern is described transiently during ketamine (a phencyclidine derivative) anesthesia.
Anoxic Encephalopathy

EEG is commonly performed in patients with anoxic encephalopathy due to cardiopulmonary arrest for assessing the severity of cerebral insult and for prognosis. Patients with normal or almost normal EEG tracings (grade I encephalopathy) following an episode of cerebral anoxia have an excellent prognosis for full neurologic recovery. On the other hand, patients with grade IV or V EEG abnormalities have a uniformly fatal prognosis; most of these patients die without regaining consciousness. An EEG should be obtained at least 5 or 6 hours after successful resuscitation since it takes an hour or more for the EEG to stabilize after an anoxic episode.[12]

Besides electrocerebral inactivity, there are three other unique EEG patterns, encountered in association with anoxic encephalopathy, that carry a poor prognosis for neurologic recovery.

Periodic discharges in anoxic encephalopathy may be either bilaterally synchronous periodic epileptiform discharges (BiPLEDs)[28] or independently occurring periodic lateralized epileptiform discharges (bilateral PLEDs).[29] Both periodic EEG patterns are often associated with myoclonic seizures (or even myoclonic status) and carry an extremely poor prognosis and uniform mortality (Fig. 8). Vigorous antiepileptic medication treatment of myoclonic seizures related to the two EEG patterns do not affect the ultimate prognosis.

Suppression-burst EEG pattern due to anoxic encephalopathy is at times associated with interesting clinical phenomena; during periods of activity both eyes may open or there are other brief body movements (Fig. 9).[30,31] Whether this is an epileptic event (a brief myoclonic seizure) or a brain stem release phenomena remains unknown. At times these movements may cause confusion in the minds of relatives and even treating physicians about the patient's state of consciousness, as they may mimic volitional motor activity.

A rare EEG pattern seen in severe anoxic encephalopathy is the alpha coma pattern, denoting the conjunction of clinical coma associated with alpha frequency activity.[32-34] Because in such tracings the dominant frequency is alpha frequency activity without significant slower frequencies, the EEG superficially resembles that of an "awake" person, but there are major differences. The alpha frequency activity in alpha pattern coma is widespread in distribution and is often prominent over the anterior head regions (Fig. 10). Reactivity to any type of sensory stimulation is usually absent. The prognosis of alpha pattern coma is extremely poor; all patients have either died or survived in chronic vegetative state.
Figure 8. EEG of a 49-year-old comatose patient following severe anoxic encephalopathy, showing bisynchronous periodic epileptiform discharges synchronous with jerks of the left lower extremity monitored on a separate channel.
Figure 9. EEG of a 75-year-old patient with severe anoxic encephalopathy, showing suppression-burst pattern. During the burst activity there is opening of the eyes; eye movements monitored in the last channel.
Figure 10. EEG of a 77-year-old comatose patient following cardiopulmonary arrest 4 days previously, showing "alpha coma pattern." Patient died after 2 days.

Remember that EEG findings of alpha pattern coma are also seen in the setting of sedative/hypnotic drug intoxication[25,35] and in association with intrinsic brain stem lesions[36] with a much more favorable prognosis.

- Cerebral Death

The EEG is being employed with increasing frequency for the determination of cerebral death in patients with irreversible coma, particularly when organs have to be salvaged for transplantation. It cannot be overemphasized that the absence of cerebral activity on the EEG is only one of the criteria, and should always be considered along with the clinical findings and blood flow studies for brain death. To properly identify very-low-voltage cerebral activity, to distinguish physiological or instrumental artifacts, and to eliminate the possibility of errors through malfunctioning equipment or inadequate techniques, the American EEG Society[37] has a number of recommendations that must be followed during EEG recordings in all cases of suspected brain death. In such "flat" tracings, EEG activity may be obscured by very-low-amplitude fast activity due to sustained contraction of scalp muscles, which can be eliminated by giving a short-acting neuromuscular blocking agent (succinylcholine, 20 to 40 mg IV). This step, which is very easy to undertake, is often overlooked to obtain a satisfactory recording in such patients.

A single EEG and a 6- to 12-hour clinical observation after an unequivocal acute cerebral insult are minimum requirements for brain death evaluation in an adult. In young children, the guidelines are slightly different because of the more difficult task of
confirming brain death in this age group. A special task force[38] recommended the following:

1. Brain death should not be determined until at least 7 days of age.
2. Seven days to 2 months: two examinations and two EEGs separated by at least 48 hours are required.
3. Two months to 1 year: two examinations and two EEGs separated by at least 24 hours are required.
4. Older than 1 year: similar criteria as an adult (i.e., one EEG and at least 12 hours of observation).

- Encephalitides

In viral encephalitis the severity of the EEG abnormalities generally parallel the clinical picture, but at times the EEG may be more disorganized and slow than the mental state of the patient may suggest. With a few exceptions, the EEG changes in different viral encephalitides are generally nonspecific and not helpful to distinguish one etiologic agent from another.[39]

The EEG pattern and its evolution in herpes simplex encephalitis are rather characteristic so that the diagnosis can often be suspected by EEG findings when considered in the proper clinical setting. The EEG in herpes simplex encephalitis may show a prominent focal abnormality, usually a focus of polymorphic delta activity over a temporal region, corresponding to the initial localization of pathology to the temporal lobe of the brain.[40-42] The most characteristic EEG feature of herpes simplex encephalitis is the occurrence of pseudo-periodic, focal or unilateral, large amplitude, sharp wave complexes that repeat at regular intervals of 1 to 3 seconds.[40-43] These periodic lateralized epileptiform discharges are usually expressed maximally over the involved temporal lobe (Fig. 11). This characteristic periodic pattern is usually seen between 2 and 15 days after the onset of illness. As the disease progresses and the other hemisphere becomes involved, the periodic complexes may disappear on the side of initial involvement before appearing on the side more recently involved. With bilateral involvement of the brain, periodic complexes may occur over both hemispheres; they may then occur either synchronously or independently over the two sides.
The presence of unilateral or focal periodic complexes (PLEDs) is not unique for herpes simplex encephalitis. PLEDs may occur with acute focal cerebral hemispheric processes (e.g., infarction, brain abscess, or neoplasm). Nevertheless, the presence of unilateral periodic complexes in association with an acute febrile illness, focal seizures, and spinal fluid pleocytosis is strongly suggestive of herpes simplex encephalitis.

SSPE, a childhood disorder that is a slow virus infection of the central nervous system due to measles, has virtually disappeared from the United States since the introduction of measles vaccination. The EEG in SSPE is highly specific and characterized by the presence of high-amplitude periodic complexes that are bilateral, usually synchronous, and symmetrical. They are remarkably stereotyped and consist of two or more delta waves with or without sharp wave components intermixed with them. The periodic complexes repeat with a fair regularity every 4 to 10 seconds and there is a 1:1 relationship of the EEG periodic complexes to the clinical myoclonic jerks, when present (Fig. 12). In the early stages of the disease, the periodic complexes may occur at irregular and long intervals, and sleep may activate them. A sleep recording, therefore, is recommended in a suspected case of SSPE in which the awake tracing has failed to reveal periodic complexes. Also, in the early stages there is asymmetry of the periodic complexes, which may be associated with asymmetry of the myoclonic jerks that occur contralateral to the periodic complexes. Later in the disease, the periodic complexes are bilaterally symmetrical and synchronous.
Figure 12. EEG of a 16-year-old patient with subacute sclerosing panencephalitis, showing high-amplitude generalized periodic complexes repeating at intervals of 8 to 10 seconds and accompanied by eye jerks and myoclonic jerks of the upper extremities monitored on the last two channels.

Creutzfeldt-Jakob disease, a prion disorder of the central nervous system (CNS), is also characterized by a very specific EEG pattern, which consists of periodic, bilaterally synchronous wave forms.[49] The periodic discharges take the form of diphasic or triphasic sharp waves, which repeat regularly at a frequency close to one per second. There is a fairly close relationship between the periodic complexes and myoclonic jerks; the latter may occur a few milliseconds before or after the electrical event.

What is less well known is the fact that in the early stages of Creutzfeldt-Jakob disease, focal or lateralized periodic sharp waves (PLEDs) may occur,[50,51] which later evolve into bilaterally symmetrical and synchronous periodic discharges superimposed on a "flat" background (Fig. 13). Although the periodic EEG pattern is not pathognomonic, the presence of periodic sharp waves occurring regularly around one per second, in association with clinical findings of progressive dementia and myoclonus in elderly individuals, provides strong support to the diagnosis of Creutzfeldt-Jakob disease. This characteristic periodic pattern is reported in more than 75% of patients with histologically verified Creutzfeldt-Jakob disease, and the pattern becomes fully established within the first 3 months of the onset of symptoms.[52,53]
Figure 13. Serial EEGs of a 62-year-old patient with Creutzfeldt-Jakob disease. The first EEG (A), obtained 2 months after the onset of dementia and progressive right hemiparesis, shows left-sided delta activity. EEG 2 weeks later (B) shows periodic lateralized epileptiform discharges over the left hemisphere, and an EEG taken 5 months after the onset of illness (C) shows typical bisynchronous high-amplitude periodic complexes superimposed on "flat" background. Myoclonic jerks monitored on the last channel are synchronous to the periodic complexes.

- Degenerative Encephalopathies

In degenerative encephalopathies, a common denominator is a disturbance in the regulation and frequency of the background activity, but the EEG features do differ with regard to whether the pathologic process involves predominantly cortical and/or subcortical gray matter or cerebral white matter.[54] In disorders that primarily involve the cerebral white matter, the EEG is characterized predominantly by the presence of high-amplitude continuous generalized polymorphic delta activity associated with a markedly disordered background and virtual absence of epileptiform activity or paroxysmal discharges. Such changes are characteristically seen in all types of leukodystrophies, Schilder’s disease, and multifocal leukoencephalopathy. In diffuse cortical gray matter encephalopathies, the EEG is characterized by abnormal background activity that is slow, irregular, and low in amplitude. There is minimal continuous generalized polymorphic delta activity, and paroxysmal findings are usually absent or

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minimal. Examples include Alzheimer's or Pick's disease. In diffuse cortical and subcortical gray matter encephalopathies, the EEG shows generalized bilaterally synchronous paroxysmal discharges in the form of bursts of monorhythmic delta waves or paroxysms of slow spike wave activity superimposed on an abnormal background. Pathological conditions include cerebromacular degeneration (e.g., Batten's disease).

Degenerative disorders with lesions predominantly below the cerebrum produce only minimal alterations in the EEG. This is usually the case in spinocerebellar degeneration, Parkinson's disease, progressive supranuclear palsy, and so on, where the EEG either remains normal or shows mild nonspecific slowing of the background activity. There are virtually no other EEG features associated with degenerative encephalopathies that have a high correlation to a specific etiologic process. The exception is the occurrence of large-amplitude spikes in response to single flashes or at flickering rates below three per second, which is a highly characteristic feature of Batten's disease.[55] These large potentials may reach 50 to 500 µV, maximum over the occipital region, and sometimes associated with myoclonic jerks of the limbs and face (Fig. 14). With advancing retinal disease and blindness, the characteristic photic response is lost.

In patients with senile or presenile dementia, the EEG background shows varying degrees of slowing and disorganization[56-58] but may remain within normal limits in individuals with obvious intellectual impairment. A slowing of the alpha rhythm from 11 to 12 Hz to 8 to 9 Hz may represent a significant deterioration of the EEG, but in the absence of serial studies this would remain unrecognized. Furthermore, the rate of progression of dementia is important because patients with very slowly progressing dementia are likely to show minimal EEG changes. Epileptiform discharges are rare in the Alzheimer's type of presenile or senile dementia except in very advanced disease. Sharp or triphasic waves over the posterior head regions in severely demented patients have been reported.[59] At times these EEG waveforms may raise a suspicion of Creutzfeldt-Jakob disease; however, unlike Creutzfeldt-Jakob disease, these discharges occur irregularly with little or no tendency toward periodic occurrence.

Huntington's disease has a very characteristic clinical picture, and the diagnosis is confirmed by genetic testing. There is a high incidence of abnormal EEG tracing in Huntington's disease; the characteristic feature is the presence of a "flat tracing" with virtual absence of rhythmic activity. Such features are reported in as high as two thirds of
the patients with Huntington's disease.[60] There is absence of any EEG activity in excess of 10 µV. In addition, the EEG is practically devoid of any rhythmic activity, not merely a paucity of recognizable rhythms. Such "flat" EEGs in Huntington's disease need to be differentiated from a normal variant, low-amplitude tracings in adults, which have activity less than 20 µV and a paucity of recognizable rhythms. Hyperventilation would increase the amount and amplitude of rhythmic activity with normal variant, whereas in patients with Huntington's disease hyperventilation remains ineffective.[2]

- **EEG in Focal or Lateralized Cerebral Hemispheric Lesions**

Since the advent of computerized tomography and MRI, the EEG has been utilized less for localizing focal cerebral lesions, including brain tumors. Nevertheless, the EEG is still extensively used to evaluate the epileptogenic potential of a focal cerebral process demonstrated on imaging studies. The EEG shows focal or lateralizing findings in localized lesions that involve a superficial assessable portion of a cerebral hemisphere.[61] There is slowing and decreased amplitude of the alpha rhythm on the side of the focal cerebral lesion. With extensive processes, the alpha rhythm disappears and is replaced by slower-frequency activity (theta/delta). Comparable changes can occur in the anterior beta activity and can be spontaneous or drug-induced. During NREM sleep, spindles may be less persistent and of lower amplitude as may vertex sharp transients. In massive or rapidly progressive hemispheric lesions such as a major hemispheric stroke or large glioblastoma, there may be severe depression of all EEG activities in that cerebral hemisphere.

Since Walters' observation[62] a focus (localized activity) of delta activity has become the sign "par excellence" of focal structural lesions. The delta activity is called polymorphic or arrhythmic (PDA) because it consists of waves of irregular shape that change in duration, shape, and amplitude (Fig. 15) and fall in the frequency range of 0.5 to 3.0 Hz. Focal PDA indicates a lesion that involves subcortical white matter. Greater variability in the waveform (irregularity), longer duration of waves (slower frequency), and greater persistence indicate a more severe and acute focal process. A fact less often appreciated is that in a large area of PDA the focal process is best localized to the area showing the lowest-amplitude or "flat" PDA, rather than the area showing high-amplitude PDA.[63] Destructive lesions most frequently associated with focal PDA include neoplasm, abscess, infarct, hematoma, and contusion. However, focal PDA can appear transiently after a complex migraine attack or focal epileptic seizure. Hence, in a patient with prominent focal PDA with a history of a recent epileptic seizure, a repeat recording in a few days is indicated to assess the persistence or transient occurrence of this focal abnormality. Rapid disappearance of focal PDA would suggest a postictal change but would also lend support to a focal epileptic process. Static lesions such as infantile hemiplegia or Sturge-Weber syndrome[64] are associated with marked attenuation and often total absence of rhythmic activities (alpha or beta activity) over the entire affected hemisphere (Fig. 16). In contrast to progressive hemispheric lesions, such as cerebral tumor, there is very little, if any, slow activity over the involved hemisphere in such lateralized static focal processes.
Figure 15. EEG of a 43-year-old patient with right temporal glioma, showing polymorphic delta activity and low-amplitude spike discharges (*) over the right temporal region.

Figure 16. EEG of a 16-year-old patient with Sturge-Weber syndrome of the right hemisphere, showing total absence of rhythmic activities over the entire affected hemisphere.
Certainly, attenuation, disorganization, and slowing of the background activity on the side of the focal cerebral lesion and presence of PDA are EEG hallmarks of a focal cerebral process. Less often, the amplitude of the background activity may be higher on the side of the focal cerebral lesion,[65] which may lead to an erroneous interpretation of the side of the lesion. Such increase in the amplitude of the background activity is encountered with cerebral infarcts that have "healed," with skull defect related to previous craniotomy or in patients with slowly progressive tumors (Fig. 17). Often the enhanced background activity (such as alpha rhythm) over the side of the focal cerebral process is slightly slower in frequency as well as less reactive to eye opening,[63] which should alert the interpreter to the abnormality. Breach rhythms[66] associated with skull defects are focal "mu-like" rhythms in Rolandic or temporal region with sporadic slow waves and spiky or sharp transients (Fig. 18). These rhythms are unrelated to epilepsy and do not indicate recurrence of a tumor. The "spiky" grapho-elements should not be overinterpreted as epileptogenic discharges. For proper assessment of EEG asymmetries, it is therefore essential to know if the patient has had a craniotomy or skull defect, which may enhance background activities on the side of the breach of the skull.

Figure 17. EEG of a 47-year-old patient with a low-grade glioma of the left temporal lobe, showing slightly slow but higher amplitude alpha on the left side.
Figure 18. EEG of a 47-year-old patient with history of previous left craniotomy, showing breach rhythm in the left temporocentral region.

Epileptiform activity, such as focal spikes, sharp waves, or spike wave discharges, also occur in localized hemispheric lesions usually of an indolent or static nature. With acute hemispheric lesions, epileptiform discharges are less common but when seen often have a periodic character. PLEDs consist of sharp waves, repeating more or less regularly at one per second over a relatively large area of the hemicranium during most of the EEG study (Fig. 19). This distinctive focal periodic pattern usually occurs in patients with acute hemispheric strokes, brain abscess, primary (usually glioblastoma) or metastatic neoplasms, and herpes simplex encephalitis.[44,67]
An EEG is the most common and most useful test performed in evaluating patients suspected of epilepsy. There are many areas where an EEG has unique contributions. The value of an EEG lies in the fact that it not only shows specific ictal discharges during a clinical seizure but also characteristic epileptiform abnormalities in a high proportion of epileptic patients even in the interictal period. Furthermore, an EEG may be the only test demonstrating focal abnormalities responsible for the patient's epileptic seizures. Specific patterns in the EEG make it possible to classify the seizure type, which is an essential prerequisite to institute proper antiepileptic medication. An EEG is indispensable for the diagnosis of nonconvulsive epileptic status presenting a prolonged "twilight" state or a prolonged episode of abnormal behavior. In a patient with bizarre motor activity, the recording of an EEG during such an episode may be the only way to establish whether the abnormal behavior is due to an epileptic seizure or a nonepileptic event, physiologic or nonphysiologic. Finally, the EEG is indispensable to localize the epileptogenic (seizure producing) zone before resective surgery (excision of the epileptogenic zone) is undertaken in a patient with medically refractory focal epilepsy.

- EEG In Paroxysmal Disorders

Paroxysmal EEG activities, whether focal or generalized, are often termed "epileptiform activities." They are the EEG hallmark of epilepsy as they are highly correlated with the occurrence of clinical seizures. Epileptiform abnormalities are usually divided into "interictal" discharges, which appear in the interval between clinical seizures, and "ictal"
discharges, which accompany clinical seizures. The distinction is arbitrary because the designation "ictal" or "interictal" often depends on how closely the patient was clinically observed because minimal behavioral alterations associated with the EEG paroxysms can be easily missed. Morphologically, interictal epileptiform abnormalities consist of spikes and polyspikes, sharp waves, spike-slow wave complexes, multiple (poly) spike wave complexes, and sharp-slow wave complexes. Spike is defined as an EEG transient clearly distinguished from the background, with a pointed peak at conventional paper speed and a duration of 20 to 70 milliseconds. Sharp waves are transients of similar character as spikes but have a duration of longer than 70 milliseconds and less than 200 milliseconds. Spike-slow waves and sharp-slow wave complexes are constituted by spikes or sharp waves followed by a high-amplitude slow wave.

Morphologic characteristics of epileptiform discharges have little correlation with different types of epileptic seizures. The topographic distribution of these discharges are more important in the classification of epilepsies. Generalized discharges that are bilaterally synchronous and symmetrical are associated with generalized epilepsies, whereas focal or lateralized discharges constitute the EEG "signature" of partial (focal) epilepsies. Most patients do not have their epileptic seizures during the brief period of routine EEG; hence, the interictal epileptiform abnormalities are the ones heavily relied on for the diagnosis of epilepsy. Although the interictal epileptiform abnormalities have a high correlation with the occurrence of clinical seizures, they do not themselves mean that the patient has epilepsy. The irrefutable evidence of epileptic seizure is a clinical seizure associated simultaneously with ictal discharges in the EEG, although such evidence is often difficult to obtain except during prolonged video EEG monitoring.

"Ictal" or an electrographic seizure pattern is characterized by repetitive EEG discharges with relatively abrupt onset and termination, and characteristic pattern of evolution lasting at least several seconds. The commonest waves or complexes vary in form, frequency, and topography. The ictal pattern is generally rhythmic and frequently displays increasing amplitude, decreasing frequency, and spatial spread during the seizure. The three EEG characteristics of a focal "ictal" pattern, therefore, consist of sudden onset/termination, occurrence of a rhythmic pattern of activity during the epileptic seizure, and its characteristic evolution with respect to amplitude, frequency, and spatial distribution.

- **Proper Identification of Diagnostic Epileptiform Abnormalities in the EEG**

In the evaluation of abnormalities in the EEG, one needs to be constantly aware that there are many EEG transients that morphologically resemble epileptiform discharges and that need to be distinguished from diagnostically crucial epileptiform abnormalities to avoid overdiagnosis or misdiagnosis. These include:

Artifacts: for example, electrode pop, muscle potentials, eye movements, electrocardiogram (EKG), etc.
Normal components of ongoing background activity: for example, vertex sharp transients of sleep, POSTs, mu rhythm, lambda waves, drowsy activity during sleep in children that may often be associated with sharp components, etc.

Epileptiform variants of dubious clinical significance: there are a large number of benign epileptiform variants that must be recognized, lest they be misinterpreted. Although morphologically similar, they are nonepileptogenic as they have no established relationship with the process responsible for generating epileptic seizures. Such sharp transients include 14 to 6 per second positive spikes, small sharp spikes or benign epileptiform transients of sleep, 6 Hz spike wave or phantom spike wave, wicket spikes, psychomotor variant pattern or rhythmic midtemporal discharges, breach rhythm, etc. Sleep not only activates diagnostically useful epileptiform EEG patterns, but also unmask several types of nonepileptogenic sharp transients.

It is critical that the EEG interpreter has clear criteria for distinguishing diagnostically relevant epileptiform discharges from sharply contoured background activity or benign variants. Useful criteria have been formulated for identification of epileptiform events[68,69]:

Epileptiform discharges (spikes, sharp waves, and spike wave complexes) should be unarguably discrete events, not just accentuation of part of an ongoing sequence of waves. They should be clearly separable from ongoing background activity, not only by their higher amplitude but also by their morphology and duration.

Most epileptiform discharges have a bi- or triphasic waveform and they have a more complex morphology than even high-voltage background rhythms.

The epileptiform events are not sinusoidal but rather show asymmetric, rising and falling phases.

Most spikes and sharp waves are followed by a slow wave.

Finally, they should have a physiological potential field involving more than one electrode that helps to distinguish them from electrode-related artifacts or muscle potentials.

- **Specificity of Interictal Epileptiform Abnormalities**

Are "hard-core" epileptiform abnormalities encountered in normal children and adults who do not have a history of epileptic seizures? Different studies, some in children[70,71] and others in all age groups,[72-74] found an incidence of less than 2 to 4% of epileptiform abnormalities in the EEG of nonepileptic subjects. In an interesting study on EEG findings in 13,658 males ages 17 to 25 without a previous history of significant illness who were medically screened for training in the Royal Air Force of England, 69 (0.5%) had unequivocal epileptiform discharges.[75] Hence, the incidence of epileptiform abnormalities in the healthy population was significantly lower than the 2 to 4% noted in the nonepileptic patients referred to hospital EEG laboratories.
One can certainly conclude that if an individual has a "blackout spell" or episodic loss of consciousness, it is very likely to be an epileptic seizure if there are unequivocal epileptiform discharges recorded in the EEG. To reemphasize, interictal epileptiform discharges in the EEG are never diagnostic of epilepsy by themselves, but in the appropriate clinical setting, they provide important circumstantial evidence for the diagnosis of epilepsy.

- **Sensitivity of EEG and Techniques to Improve the Yield of Interictal and Ictal EEG Abnormalities in Patients with Epileptic Disorders**

Some patients with unequivocal epilepsy, especially focal epilepsy, may have repeatedly normal or nonspecific EEG studies. A single routine EEG consisting of half an hour recording during wakefulness, hyperventilation, and intermittent photic stimulation (IPS) provides diagnostic findings in approximately half of the patients with epilepsy.[76] The following describes a few ways to increase the yield of epileptiform abnormalities in an interictal EEG study.

Serial EEG Studies. EEGs recorded on more than one occasion will increase the chance for recording a specific epileptiform abnormality. Research[76] has demonstrated that serial EEG studies increase the yield for epileptiform abnormalities from 50% in the first record to 84% by the third EEG, and in 92% by the fourth EEG. There was little additional yield to serial EEGs beyond this point.[76] Thus, four or five EEG studies spread over a few years provide diagnostic abnormalities in over 90% patients with epilepsy. An opposite corollary is also true; serial negative EEG studies in a patient with continuing paroxysmal events should raise suspicion of nonepileptic episodes. It is also well known that interictal epileptiform discharges markedly increase after a clinical seizure[77]; hence, obtaining an EEG promptly after a clinical seizure will increase the chances of capturing interictal epileptiform discharges.

Activating Procedures. Activating procedures (e.g., hyperventilation, IPS), recording during sleep, are very well known to activate epileptiform discharges not recorded in the awake tracing. Hyperventilation and IPS are potent activators of generalized spike wave discharges associated with primary generalized epilepsies. On the other hand, sleep tends to bring out focal epileptiform abnormalities in patients experiencing focal epileptic seizures. Sleep activates virtually all focal epileptiform abnormalities; therefore, every patient suspected of epilepsy should have a sleep recording unless there is an unequivocal and specific abnormality displayed optimally during wakefulness. One of the best ways to ensure a sleep EEG is to instruct the patient to come for the EEG test after remaining awake during the entire or at least a major part of the previous night. Sleep deprivation appears to have a further activating effect that is additive to natural sleep itself, particularly in patients with complex partial seizures and in patients with juvenile myoclonic epilepsy.

Normal response to IPS includes photic driving (photic following) at flash rate or at harmonics. In about 5% of patients, asymmetric photic driving response (>50% difference in amplitude) may occur, which by itself (without asymmetric awake and/or sleep
activities) has no clinical significance. IPS is especially helpful in patients with primary generalized epilepsy in eliciting abnormal paroxysmal discharges. Photoparoxysmal response (PPR) has a high correlation with clinical epilepsy. It is characterized by the occurrence of generalized bilaterally synchronous spike wave or multiple spike wave discharges occurring with IPS. The most effective frequency is around 15 flashes per second but other frequencies may be equally effective. Reilly and Peters distinguished two types of PPR: prolonged (self-sustained), which continues for a short period after the stimulus has been withdrawn (Fig. 20), and self-limited, which cease before the flashes stop.[78] There is a much higher incidence of epilepsy in patients with prolonged (93%) compared with the self-limited (52%) PPR. A 1992 meta-analysis of the studies on PPR concluded: (1) PPR, prolonged or self-limited, had a significantly higher incidence of seizures than controls; (2) a prolonged PPR was associated with a much higher incidence of seizures (85%) than the self-limited group (50%); (3) patients with prolonged PPR more often had other epileptiform abnormalities in their resting EEG than the self-limited group; (4) the risk of epilepsy increased if the PPR was associated with epileptiform abnormalities in the resting EEG; (5) the seizure incidence associated with self-limited PPR without other epileptiform abnormalities was lower (30%) but still significantly higher than patients without PPR.[79]

Figure 20. An EEG of a 15-year-old patient with primary generalized epilepsy, showing prolonged (self-sustained) photoparoxysmal response.

Another photic-induced response that may superficially resemble PPR but has no significant correlation with epilepsy is a photo-myoclonic response (PMR). It consists of frontally dominant polyspikes synchronous with the flash rate and accompanied by rhythmic jerking of the muscles of the forehead, eyelids, and face. The response is blocked
when the eyes are opened and it promptly stops with withdrawal of photic stimulation. PMR is generally considered to be a muscular response without cerebral participation but some regard it to be an expression of cortical response within the spectrum of photic cortical reflex myoclonus. It is seen in some nervous or tense individuals or in patients with psychiatric troubles or elderly subjects. Its presence in an individual case has no diagnostic significance.

- **Besides photic driving, PPR, and PMR, other less common IPS-induced EEG responses include:**

Posterior hemispheric stimulus-dependent response: an anomalous steady state flash visual evoked potential (VEP) of unusually sharp waveform or high amplitude. This has no clinical correlation except when it represents very-high-amplitude and spiky VEPs in association with Batten’s disease or neuronal ceroid lipofuscinosis.

Rarely, IPS may activate a focal epileptiform discharge, usually an occipital spike focus.

Less often IPS may induce a frank seizure with clinical correlates (e.g., an absence, absence with eyelid myoclonus, single random generalized myoclonic jerks, repeated myoclonic jerks, occipital onset focal seizure, and rarely even a generalized tonic-clonic seizure).

Remember than 10% of patients with all forms of primary generalized epilepsy show PPR, with the highest incidence (30 to 35%) in juvenile myoclonic epilepsy.[80] The incidence of PPR is about 15% in childhood absence epilepsy, <10% in juvenile absence epilepsy, and 10 to 15% in epilepsy with generalized tonic-clonic seizures on awakening. PPR is also common in infantile and childhood epilepsies with myoclonic seizures such as benign and severe myoclonic epilepsies of infancy and myoclonic-astatic epilepsy of childhood. PPR is rare in focal epilepsies and secondary generalized epilepsies (e.g., Lennox-Gastaut syndrome).

It must be emphasized that PPR can be detected, although rarely, among individuals with headaches or other complaints, during evaluation for aviation jobs, or as a genetic marker in a susceptible individual with a family history of idiopathic generalized epilepsy. PPR in nonepileptic subjects has a prevalence of 1 to 4%; the response then is usually brief and less prominent.

IPS is not a totally benign activating procedure. One can induce a generalized tonic-clonic convulsion (often the first one) if photic stimulation is continued over a long duration in a patient who shows prominent PPR. It is recommended that the photic stimulation be limited to short periods (1 to 5 seconds) and terminated promptly as soon as generalized spike wave activity is recorded (Fig. 20).

Special Electrodes. Although the standard 10 to 20 international system of electrode placement provides reasonable coverage of the whole head, certain areas that have high epileptogenicity, such as the mesial temporal lobes in patients with mesial temporal sclerosis, are not fully explored by conventional placement and may require additional
electrodes. Nasopharyngeal electrodes have been widely used in the past in patients suspected to have with temporal lobe epilepsy. They are associated with variable degrees of discomfort and may prevent the patient from attaining sleep during the EEG recording. They have now been largely replaced by the use of anterior temporal electrodes, which are placed 1 cm above and one third the distance along the line from the external auditory meatus to the external canthus of the eye.[81]

In a comparison of the percentages of spikes detected by standard scalp electrodes, anterior temporal, mini-sphenoidal, surface sphenoidal, and nasopharyngeal electrodes in patients with suspected complex partial seizures, the anterior temporal electrodes provided significant improvement in detecting epileptiform abnormalities.[82] Recordings from standard scalp electrodes detected 58% of the discharges. Anterior temporal electrodes were the best; they detected 70% of all the discharges by themselves, and 81% in combination with standard scalp electrodes. It can be concluded that recordings from anterior temporal electrodes must be done to improve the detection of interictal epileptiform abnormalities in patients suspected of having temporal lobe epilepsy. Sphenoidal electrodes are almost invariably employed during video EEG monitoring as a part of the presurgical evaluation of patients with medically intractable complex partial seizures. The yield of abnormality from sphenoidal recordings is certainly greater than that with nasopharyngeal or anterior temporal electrodes, but it is difficult to justify the use of invasive electrode placement in routine EEG study for paroxysmal disorders.

Activation of an Actual Seizure During Routine EEG Study. All efforts must be made to capture the patient’s habitual episode during a routine EEG. If precipitating factors are known, these are appropriately exploited. Hyperventilation, a potent precipitator of an absence seizure in a child with primary generalized epilepsy, must always be utilized for at least 5 minutes, once in the beginning and again at the end of a routine EEG study. In rare patients with reflex epilepsy, playing specific music in musicogenic epilepsy, asking a patient to read from a book in reading epilepsy, bathing the patient in bathing epilepsy, asking the patient to eat his meals (eating epilepsy), smelling gasoline, and so on, may all be carried out to promote an ictal event.

In patients with possible pseudoseizures, suggestion protocols are often useful in precipitating episodes and demonstrating EEG changes.[83] It is important to emphasize that induced seizures must be clinically typical of a patient's habitual episodes before the diagnosis of pseudoseizures is strongly considered.

- **Some Interpretive Challenges of EEG Findings During Paroxysmal Events**

Some of the pitfalls regarding ictal EEG changes during an actual seizure need to be stressed. All epileptic seizures are not associated with distinctive concomitant surface EEG changes. Seizures that remain very localized, including epilepsia partialis continua and simple partial seizures (focal seizures with preserved consciousness), may not have changes in the scalp EEG because the diagnostic discharge may be deep-seated or involve only a small pool of neuronal tissue. However, epileptic seizures manifested by loss of consciousness, on the other hand, are accompanied by demonstrable changes in the scalp
EEG. Therefore, absence of such changes during a clinical episode of "unconsciousness" or bilateral widespread motor activity (resembling grand mal seizure) can be particularly important in making the diagnosis of nonepileptic events or pseudoseizures. Ten to 20% of patients with pseudoseizures do have epileptic seizures as well. The most one can say is that at least some of the clinical episodes appear to be functional, and this must be considered within the context of the entire clinical picture.

In evaluating patients with muscle jerks or other brief motor events, it needs to be established whether these represent epileptic phenomena. Simultaneous recording by placing two electrodes over the involved muscle may be very helpful in establishing the relationship of, or lack of, the EEG and the motor recordings. In patients with myoclonic seizures, it is not always easy to establish whether an electrical event synchronous with the motor jerk is indeed a cerebral discharge or simply a movement artifact. The presence of morphologically similar EEG discharges in other portions of the tracing but unassociated with obvious motor activity will establish that they represent a genuine cortical discharge rather than an artifact generated by sudden movement.

- EEG in Generalized Epilepsies

The epileptic process in generalized epilepsies involves large areas of the brain at the outset of the seizure, and the EEG is characterized by bilaterally synchronous generalized paroxysms of spikes and spike wave discharges. Generalized epilepsies are subcategorized as primary (idiopathic) and secondary (symptomatic).

A patient with primary generalized epilepsy (PGE) has no identifiable etiology, normal brain imaging, and normal neurocognitive functioning. The epilepsy has a strong genetic basis and is highly responsive to antiepileptic medication. The patient may suffer from absence (petit mal), myoclonic, and tonic-clonic seizures, among other generalized seizures. Many different syndromes of PGE have been recognized depending upon the predominant seizure type and the age of onset. Classically, the presence of rhythmic, anterior-dominant generalized bisynchronous 3 Hz spike wave discharges superimposed on a normal background are considered to be the EEG hallmark of PGE.

However, the most common EEG abnormality associated with PGE is the so-called "irregular" or "atypical" or "rapid spike" wave activity. This is characterized by generalized paroxysms of spikes or spike wave complexes occurring with an irregular frequency of about 3 to 5 Hz. Although some spike wave complexes will approximate 3 Hz, the overall impression is that the EEG abnormality is much less regular than the classic 3 Hz spike wave discharges (Fig. 21). Transient asymmetry of the bisynchronous spike wave activity and isolated "focal" spikes are common. Atypical generalized spike waves are not only seen in PGE but also in secondary generalized epilepsies such as progressive myoclonus epilepsies of different etiologies.
Besides the presence of brief (1 to 3 seconds) generalized spike wave discharges, there are no interictal epileptiform abnormalities that are specific for individual syndromes included under PGE (childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, epilepsy with myoclonic absences, and generalized tonic-clonic seizures on awakening). There are a few EEG features that are more common with certain syndromes: (1) polyspike wave discharges are more common with myoclonic epilepsies; (2) paroxysms of occipital-dominant rhythmic delta activity in the EEG is a feature most commonly encountered with childhood absence epilepsy; (3) short paroxysms of spike wave discharges of higher frequency (4.0 to 4.5 Hz) are more common with PGE manifesting primarily with generalized tonic-clonic seizures; and (4) PPR is most common with juvenile myoclonic epilepsy.

In patients with PGE, a routine EEG may capture one or more absence seizures or epileptic myoclonic jerks. In children an absence seizure may be induced during the EEG study by hyperventilation with characteristic generalized 3 Hz spike wave discharge, which is sustained for more than 3 seconds in duration. Epileptic myoclonic jerks are associated in the EEG with high-amplitude generalized polyspike wave discharges in association with myoclonic jerks. Not well recognized is the fact that the EEG in patients with PGE may record focal or lateralized spikes in addition to the overwhelming generalized bisynchronous spike wave activity.[84,85] Similarly, spike or spike wave activity occurring bilaterally but restricted to the frontal areas (where the generalized paroxysms are usually maximum) is also common. Such discharges are often called "abortive" spike wave complexes. Roughly one quarter of patients with 3 Hz spike wave activity in their EEG may show such focal or lateralized discharges,[84] which should generally be viewed as isolated fragments or limited expression of what is fundamentally a generalized epileptic
abnormality. Such focal epileptiform discharges often shift from one electrode to the other and from one side to the other.

Secondary generalized epilepsy (SGE) is a more serious disorder, secondary to known diffuse cerebral hemispheric insult. Patients are children who have frequent seizures of generalized type, usually medically refractory. Many have significant developmental delay and neurocognitive deficits. In contrast to PGE, the background activity of the EEG in SGE syndrome is disorganized and there are variable degrees of slowing. In addition, there are several paroxysmal EEG patterns associated with SGE syndrome: (1) irregular bisynchronous spike wave activity described above, which can occur both with PGE or SGE; (2) slow spike wave (2.5 Hz or slower in frequency) discharges; (3) hypsarrhythmia; (4) independent multifocal spike discharges (IMSD); and (4) generalized paroxysmal fast activity (GPFA). These EEG patterns are largely nonspecific for etiology but are expressions of severe neocortical insult. Many of these EEG patterns are also age-dependent.

West's syndrome (infantile epileptic encephalopathy) is characterized clinically by infantile spasms (jackknife seizures). The EEG usually shows a distinctive interictal pattern called hypsarrhythmia. It consists of very-high-amplitude, asynchronous slow activity superimposed on frequent multifocal spikes, polyspikes, or sharp waves or generalized spike wave complexes. The abundance of epileptiform activity, the entire absence of any organization ("chaotic" appearance), and absence of normal activities (e.g., alpha rhythm or sleep spindles) are constant features of a typical hypsarrhythmia pattern (Fig. 22). When some of the characteristic features are lacking or are less prominent, some would interpret the EEG as showing "modified hypsarrhythmia." Often the classical hypsarrhythmic pattern occurs only during NREM sleep, and the awake tracing showing diffuse slowing with minimal epileptiform activity. During an actual infantile spasm, there is an abrupt generalized attenuation of the background (i.e., an electrocremental response) (Fig. 23). This may be preceded by a high-voltage, usually generalized biphasic slow wave complex. During the electrocrement there may be low-amplitude beta activity with varying spatial distribution. These electrocremental events occur often during sleep but without behavioral accompaniment.
Figure 22. EEG of a 6-month-old infant with developmental delay and infantile spasms, showing typical hypsarrhythmic pattern.

Figure 23. EEG of a 5-month-old infant, showing electrodecremental response during an infantile spasm monitored on the last channel.
Hypsarrhythmia, which is an EEG pattern, and infantile spasms do not have an absolutely constant relationship and are not interchangeable terms. Typical and modified hypsarrhythmia occurs in two thirds of the EEGs of infants with infantile spasms, whereas the remaining one third show generalized slow spike wave discharges (described below).[86] Besides various pathologic conditions associated with a severe cortical insult, hypsarrhythmic pattern is often encountered in infants suffering from tuberous sclerosis or genetically determined metabolic conditions such as non-ketotic hyperglycemia.[87] Children with Aicardi's syndrome (agenesis of corpus callosum, mental retardation, infantile spasms, choreoretinal lesions) show a markedly asymmetric hypsarrhythmic pattern with virtually complete interhemispheric asynchrony of a suppression-burst-like background.[88]

The hypsarrhythmic pattern is a maturational pattern most commonly expressed between the ages of 4 and 12 months. As the infant grows older, beyond the age of 2 years, it is rare to encounter typical hypsarrhythmia, although infantile spasms may still continue. Hypsarrhythmia is replaced by different EEG patterns such as a diffusely slow tracing, slow spike wave discharges as seen with Lennox-Gastaut syndrome, IMSD, and, rarely, a normal tracing.

Adrenocorticotropic hormone therapy often has a dramatic effect on infantile spasms as well as the hypsarrhythmic EEG pattern, which may virtually disappear in a matter of a few days to a few weeks after initiation of therapy. However, despite these clinical and EEG improvements, the long-term neurocognitive development remains subnormal.

Lennox-Gastaut syndrome (childhood epileptic encephalopathy) is another common form of SGE manifesting in early childhood with developmental delay, neurocognitive deficits, and frequent generalized seizures including tonic seizures. The EEG shows generalized, slow spike wave discharges (1.5 to 2.5 Hz) superimposed on abnormally slow background activity (Fig. 24).[89,90] It is important to distinguish these EEG findings from those seen with primary generalized epilepsy where the background activity is normal for age and the generalized spike wave discharges are usually of faster frequency (3 to 5 Hz). Although appearing widespread and bilaterally synchronous, the slow spike wave activity is usually higher in amplitude over the anterior head regions (in 90% of patients); less commonly the amplitude is highest over the occipital areas. The duration of the paroxysms varies widely from isolated complexes to almost continuous slow spike wave activity, commonly without an identified behavioral or awareness change. Hence, the slow spike wave activity in Lennox-Gastaut syndrome is considered an interictal pattern, although it must be understood that subtle changes of behavior in retarded and uncooperative children are hard to recognize.
Figure 24. EEG of a 16-year-old child with mental retardation and tonic seizures, showing slow spike wave activity superimposed on a slow background.

When one encounters prolonged episodes of slow spike wave activity lasting several seconds to minutes, the interpretative challenge is to decide if these electrographic events represent an ictal pattern (atypical absences or nonconvulsive status) or they simply represent more pronounced interictal pattern. A history of similar long episodes of slow spike wave activity in one or more previous EEGs would support an interictal finding. Also, giving a small dose of lorazepam intravenously will have no affect on an interictal pattern but will usually abort an ictal pattern, at least temporarily.

If a tonic seizure is recorded during the EEG of a patient with Lennox-Gastaut syndrome, the characteristic finding is an electrodecrement or "flattening" lasting several seconds. In addition, high-frequency rhythmic activity in the alpha-beta frequency range commonly occurs during the electrodecrement.

Another distinctive EEG pattern of a symptomatic generalized epilepsy syndrome is IMSD characterized by the presence of three or more independent and noncontiguous foci of spike or spike wave activity with at least one focus in one hemisphere (Fig. 25).[91,92] As expected, the background activity is invariably disorganized and slow in frequency.
There is a close correlation between the three EEG patterns of hypsarrhythmia, slow spike wave, and IMSD associated with SGE. All of them are associated with diffuse or multifocal cerebral abnormalities and have similar clinical correlates of mental retardation, multiple and medically intractable seizure types, and a high incidence of neurologic deficits. Furthermore, serial studies over time may show a change of one pattern to the other in the same patient. Also, in the same EEG study, more than one of these patterns may coexist (e.g., IMSD during wakefulness and slow spike wave activity during sleep). It is very well known that at least 20% of infants with hypsarrhythmia may show slow spike wave usually by the second to fourth year of life. Both of these patterns may further change to IMSD in early childhood. Thus, these three EEG patterns have a common physiopathologic basis and are probably dependent more on cerebral maturation than on a particular kind of cerebral pathologic process. Hypsarrhythmia is usually seen in the later half of the first year of life in response to a cerebral insult prenatally, perinatally, or in the immediate postnatal period. It rarely results from cerebral insults after the second year of life. The slow spike wave pattern associated with Lennox-Gastaut syndrome is commonly observed between the ages of 2 and 5 years. The IMSD pattern is seen commonly throughout the first decade of life.

A unique EEG pattern of GPFA is seen predominantly during sleep consisting of high-frequency, 12 to 25 Hz repetitive spike discharges occurring synchronously over both hemispheres (Fig. 26). It is associated most commonly with SGE (usually Lennox-Gastaut syndrome) but it may rarely occur also with PGE or in patients with focal seizures,
particularly with a frontal lobe focus. This EEG pattern is usually not associated with an obvious clinical change, although subtle tonic seizures (opening of eyes and jaw, eye deviation upward) may be missed. In rare patients with PGE and 3 Hz generalized spike wave, the awake EEG may appear rather benign but the presence of GPFA during sleep is a warning that more severe encephalopathy may be present. In such patients, motor seizures are common and the disorder is likely to persist in adulthood.[94]

Figure 26. EEG of an 11-year-old patient with Lennox-Gastaut syndrome, showing generalized paroxysmal fast activity (B).

- **EEG in Focal or Localization-Related Epilepsies**

Focal epilepsies are usually categorized into two subgroups: (1) asymptomatic (secondary) localization-related epilepsies due to acquired focal cortical processes; and (2) idiopathic (primary) localization-related epilepsies, which are largely age-dependent and genetically based disorders, the best-known being benign Rolandic epilepsy (BRE).

The hallmark of focal epilepsy in the interictal EEG is the presence of a focus of epileptiform activity (i.e., spikes, spike waves, or spike wave complexes). The interictal
Paroxysmal activity is characteristically random, occurring at inconstant intervals. Intuitively, the positive correlation of an abundance of epileptiform discharges with a more frequent occurrence of clinical seizures would be expected. This is, however, not true. Abundance and rate of repetition of epileptiform discharges correlate very poorly with the frequency of clinical seizures. It is not uncommon to see rare interictal spikes in a patient who has frequent complex partial seizures. The reverse is also true, as in BRE where the child may have only rare clinical seizures but very abundant epileptiform discharges, particularly during sleep. An important fact regarding interictal epileptiform discharges is that they become much more frequent in the EEG immediately after a clinical focal seizure.[77]

Another characteristic of the interictal EEG is the presence of a focal abnormality of the background activity. This may take the form of intermittent low-voltage slow waves and attenuation of faster rhythm with the same localization as that of the epileptiform discharges. In general, when the focal epileptiform activity occurs along with abnormal focal organization, the possibility of a structural lesion is more likely and the focal epilepsy is most likely to be symptomatic. On the other hand, occurrence of random focal spikes without any accompanying features of focal disorganization of the background activity is usual with idiopathic or primary localization-related epilepsies such as BRE or benign occipital epilepsy.

The majority (85%) of patients with complex partial seizures have temporal lobe onset, whereas a small proportion (15%) have frontal lobe onset partial epilepsy. Temporal lobe epilepsy, which is the most common type of focal epilepsy in adults, is associated with interictal epileptiform discharges over one or both anterior temporal regions (Fig. 27). The peak of the potential field involves inferior frontal (F7 or F8), midtemporal (T3 or T4), and the ear lobe electrodes (A1 or A2). The F7 and F8 electrodes of the 10 to 20 electrode placement system more commonly record activity originating in the anterior temporal lobe rather than in the frontal areas. In suspected patients with temporal lobe epilepsy, recording from additional TI and T2 electrodes must be performed to optimally elicit epileptiform abnormalities of temporal lobe origin. In patients undergoing presurgical evaluation, anterior sphenoidal electrodes are commonly inserted, which markedly increase the yield of demonstrating temporal epileptiform abnormalities. In frontal lobe epilepsy, interictal epileptiform discharges are recorded over the frontal region but often the EEGs, even on several occasions, may remain normal.[95,96] Special attention must be paid to the midline electrodes (FZ and CZ), which can demonstrate low-amplitude epileptiform discharges. Also, additional supraorbital and midfrontopolar (FPZ) electrodes may be helpful in demonstrating epileptiform abnormalities in frontal lobe epilepsy.
Figure 27. EEG of a 68-year-old patient with a long history of complex partial seizures, showing a focus of sharp waves and low-amplitude slow activity over the right anterior temporal region.

BRE constitutes the most common primary (idiopathic) localization-related partial epilepsy with onset between the ages of 4 and 10 years. Virtually all recover by the age of 15 or 16 years when the patients become seizure-free and their EEGs revert to normal. The background EEG activity in wakefulness and sleep is normal. There are epileptiform discharges over the central or centrotemporal region, which are markedly activated during sleep (Fig. 28).[97] In some children, epileptiform discharges are restricted to sleep recording only.
Figure 28. EEG of a 9-year-old child with benign Rolandic epilepsy, showing a focus of right centrotemporal spike discharges. The right half of the figure shows a spike discharge with horizontal dipole distribution.

A horizontal dipole field is a highly characteristic feature of the centrotemporal epileptiform discharges associated with BRE.[98] The negative end of the dipole is located at the centrotemporal area, and the positive end toward the frontal regions bilaterally (see right half of Fig. 28). In 10 to 15% of patients with BRE, additional EEG abnormalities are seen. Independent spike foci may occur over the occipital and less commonly over the frontal regions. Interestingly, bisynchronous spike wave discharges also occur in approximately 10% of patients with BRE during routine EEG recordings.[99]

Centrotemporal or Rolandic spikes are not specific for BRE. Children with acquired brain insults involving fronto-centro-temporal regions (who may also have neurologic deficits, e.g., cerebral palsy) may show epileptiform activity over one or both central areas. In contrast to BRE such "lesional" patients usually have abnormal background activity, either focally or diffusely, and have secondary (symptomatic) partial epilepsy.

Many studies[100-102] have stressed that a small proportion of epileptics have midline spike foci; the epileptiform abnormalities are localized at the midline electrodes with some spread to parasagittal electrodes on both sides. They are best demonstrated in the coronal montage, which includes midline (FZ, CZ, and PZ) electrodes; the amplitude may be
somewhat asymmetric in parasagittal electrodes. The midline spike foci have highest amplitude at the CZ electrode in most of the patients. Such foci are common in children, and at least half of the patients show these discharges only during sleep. Certainly, caution must be exercised in distinguishing midline CZ spikes from normal sleep potentials such as vertex sharp transients. Midline spike foci have a high correlation with clinical seizures of focal or generalized type, and a significant proportion show evidence of cognitive or neurologic deficits.

Rarely, a focal seizure is recorded in a routine EEG in a patient with focal epilepsy. As mentioned before, the hallmark of an ictal EEG pattern associated with a focal seizure is the sudden appearance of focal rhythmic activity that evolves during a short period with a progressive change in the amplitude and frequency with a topographic spread. Postictally, there may be a period of "flattening" followed by variable degrees of slow wave activity, which may be generalized initially but usually becomes lateralized or focal later in the postictal period before the preictal EEG pattern becomes reestablished. A transient delta focus after the seizure is a very reliable sign of a localized lesion or at least a focal origin of the previous epileptic seizure. The postictal focal slowing may persist for a few seconds to a few hours or even a few days, depending upon such factors as the age of the patient, size of the lesion, duration, and number of seizures.

The ictal EEG pattern of complex partial seizures of temporal lobe onset usually starts with a focal rhythmic 4 to 7 Hz theta activity over one temporal region, which then spreads bilaterally, becoming higher in amplitude, slower in frequency, and often interspersed with sharp wave components.

Complex partial seizures of frontal lobe onset have a unique semiology compared with the complex partial seizures of temporal lobe onset.[95,96] The former are brief (less than 1 minute), commonly nocturnal, often occurring in clusters with many per day, have complex motor automatisms with kicking and thrashing, sexual automatism, vocalization, and with very short or no postictal period of confusion after the seizure. The frantic and often bizarre motor thrashing and kicking behavior and rapid return of awareness at the end of the seizure frequently leads to an erroneous diagnosis of pseudoseizures. Diagnostic difficulty is further compounded by the fact that routine EEG, even on many occasions, may be nonrevealing in patients with frontal lobe seizures.[95,96] Interictal abnormalities, when present, are often seen near the vertex bifrontally so that localization is not easy. Furthermore, the ictal EEG during a frontal lobe complex partial seizure often fails to provide diagnostic information because of marked contamination with ongoing movement artifacts during the seizure. Careful evaluation of the ictal EEG using coronal montage and high-frequency filtering may reveal rhythmic ictal patterns in frontal/central electrodes near the midline, spreading bilaterally to the parasagittal region. The frontal lobe complex partial seizures not only resemble pseudoseizures clinically but also lack diagnostic interictal and ictal EEG findings. Their brief duration, emergence out of sleep, and stereotypic semiology are highly characteristic features that help distinguish them from pseudoseizures.
• Certain EEG Patterns Morphologically Similar to Interictal/ictal Epileptiform Discharges But Unrelated to Epilepsy

There are some EEG patterns that, by virtue of having spike or sharp wave components or being rhythmic, closely resemble diagnostically important epileptiform discharges. Although they share some of the same electrographic features, their presence in the EEG has no correlation with epileptic seizures. These patterns have been reviewed in detail.[103]

The 14 and 6 Hz positive spikes are brief paroxysms, usually less than 1 second, of positive spikes with a frequency of 6 Hz at some times and 14 Hz at others. They are distributed over the posterior hemispheric regions, occurring usually unilaterally. If enough of them are recorded in a tracing, they are expressed on both sides of the head. They are most commonly seen in children and adolescents during drowsiness and light sleep. This pattern has been the subject of many reviews and long-drawn controversy but it is now held to be a normal sleep activity or a normal variant.

Small sharp spikes or benign epileptiform transients of sleep are spike potentials that are recorded in adults during drowsiness and light sleep. They are sporadic and shift from one side to the other, and have widespread distribution over the scalp despite low amplitude. The spikes are usually low amplitude (less than 50 µV), very short duration (less than 50 milliseconds), and mono- or diphasic potentials with no or minimal slow wave component following the spikes (Fig. 29). They are never associated with focal slowing or other abnormalities of the background activities. Their special distribution on the scalp may suggest a horizontally oriented dipole generator extending across the sagittal midline with opposite polarity on the two sides of the head. They are especially frequent in the EEG performed after a period of sleep deprivation and are considered to have no correlation with epileptic seizure disorder.[104]

The 6 Hz spike wave or phantom spike wave consists of bilaterally synchronous, short (less than 1 second) paroxysms of 5 to 7 Hz spike wave activity.[105] Although widespread in distribution, they are usually best developed over the posterior hemispheric region (Fig. 30). The spike component is usually low in amplitude, whereas the slow wave following it is more prominent; hence, the term "phantom spike wave." It occurs in young adults and is best expressed during drowsiness. There is still some controversy regarding their clinical significance, especially the ones that are anteriorly dominant. It has been suggested[106] that the 6 Hz spike wave activity that occurs with high amplitude and predominance over the anterior hemisphere and is recorded during wakefulness may have a high correlation with seizures, whereas predominantly occipital, low-amplitude, spike wave discharges occurring in drowsiness have no correlation with epileptic seizures.

"Psychomotor variant" or rhythmic midtemporal discharges is a rare EEG finding observed in less than 1% of the patient population coming to an EEG lab. It is characterized by long (several seconds to a minute) paroxysms of 5 to 7 Hz rhythmic activity with an admixture of sharp components occurring over the midtemporal (T3/T4) regions (Fig. 31).[107] The paroxysms are unilateral or bilateral. Bilateral paroxysms may appear independently on the two sides or simultaneously with variable asymmetry. The
pattern is invariant and without evolution from beginning to end. This EEG finding occurs during drowsiness or light sleep and has no correlation with epileptic seizure disorder.

The wicket temporal pattern is characterized by negative sharp transients that occur in runs and have a wicket shape. The repetition rate varies between 6 and 11 Hz in different and even in the same bursts. They are best seen in T3/T4 or F7/F8 electrodes with variable spread to A1/A2. They are usually bitemporal, occurring independently on the two sides. The pattern occurs exclusively in adults and is seen in both wakefulness and sleep.[108]

Subclinical rhythmic EEG discharges of adults is a rare EEG pattern[109,110] that closely resembles an ictal pattern, but there is no evidence that it represents an epileptic seizure. It occurs mainly in elderly subjects and may extend beyond 1 minute but without any clinical change. It is predominant over the posterior head regions and usually bilateral but may be asymmetric. In the most characteristic form the pattern begins with a series of rhythmic sharp-contoured waves that gradually merge into a sustained theta frequency. It may subside abruptly or gradually.[103]

There are many normal activities, particularly during sleep in children that, being sharp in configuration, are often mistaken for epileptiform discharges. These include vertex sharp transients and positive occipital sharp transients. In children, the vertex sharp transients may be quite high in amplitude and spiky in configuration, very closely resembling epileptiform discharges. One has to be very careful in interpreting sharp waves or spikes in children of Rolandic location expressed only during sleep. Normal mu rhythm in central leads and breach rhythm recorded in patients with iatrogenic or acquired skull defect may also consist of sharp components that may be mistaken for epileptiform discharges. Lambda waves, which are sharply contoured activity in the occipital region seen when a person has eyes open and scans the surrounding environment, need to be differentiated from posterior hemispheric epileptiform discharges.
Figure 29. EEG of a 72-year-old patient, showing benign epileptiform transients of sleep (small sharp spikes).
Figure 30. EEG of a 26-year-old patient, showing 6 Hz spike wave paroxysms (phantom spike wave).

Figure 31. EEG of an 11-year-old patient, showing rhythmic midtemporal discharges during drowsiness.
• **EEG in Neonates**

In recent years there has been much interest in using EEG to evaluate full-term or premature neonates\[111,112\] due to the serious limitations in performing an adequate neurologic examination. The neonate may be confined to an isolette, may be intubated, or may be paralyzed for ventilatory control. Under such circumstances, EEG is a very important tool to assess an encephalopathic process or occurrence of epileptic seizures. In addition, the background abnormalities have been classified in neonates and used to predict neurologic outcome.

The EEG of a neonate shows distinctive patterns related to the conceptional age (CA) and the behavioral state (awake, active sleep, quiet sleep). Space does not permit a description of EEG patterns associated with different conceptional ages, but this is summarized in Table 2. It is important to emphasize that the EEG maturation runs parallel in utero and in incubator; only minimal or no differences have been found between babies of the same CA born after different periods in utero.

**Table 2. EEG Maturation in Preterm Neonates**

<table>
<thead>
<tr>
<th>EEG Features</th>
<th>24-27 Weeks CA</th>
<th>28-31 Weeks CA</th>
<th>32-35 Weeks CA</th>
<th>36-38 Weeks CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuity</td>
<td>Discontinuous, long flat periods or tracé discontinua</td>
<td>Discontinuous or tracé discontinua</td>
<td>Discontinuous 50% of time, more or less continuous 50%</td>
<td>Continuous during awake and AS; during QS Good</td>
</tr>
<tr>
<td>Differentiation of awake and sleep</td>
<td>No differentiation</td>
<td>No differentiation</td>
<td>Wake/sleep diff. seen; also AS/AS diff. later in this period</td>
<td></td>
</tr>
<tr>
<td>Temporal theta</td>
<td>Present</td>
<td>Prominent</td>
<td>Decreasing</td>
<td>Absent</td>
</tr>
<tr>
<td>Occipital theta</td>
<td>Prominent</td>
<td>Decreasing</td>
<td>Decreasing</td>
<td>Absent</td>
</tr>
<tr>
<td>Delta brushes</td>
<td>None or minimal</td>
<td>Prominent, AS &gt; QS</td>
<td>Present, mainly in QS, less or none in AS</td>
<td>Rare in QS</td>
</tr>
<tr>
<td>Trace alternant (TA)</td>
<td>None</td>
<td>None</td>
<td>Prominent during QS (tracé discontinua)</td>
<td>Present in QS</td>
</tr>
<tr>
<td>Interhemispheric synchrony</td>
<td>Short bursts of synchronous EEG activity</td>
<td>Prominent asynchrony</td>
<td>Progressively more synchrony</td>
<td>Minor asynchrony may still persist</td>
</tr>
<tr>
<td>Sharp wave transients</td>
<td>Some (temporal) sharp activity during bursts</td>
<td>Some scattered sharp activity</td>
<td>Often prominent multi/local sharp waves</td>
<td>Sharp waves less prominent, see over frontal/temporal duin</td>
</tr>
</tbody>
</table>

**AS, active sleep; QS, quiet sleep; CA, conceptional age; diff., difference.**

In a full-term neonate four EEG patterns are observed related to the wakefulness/sleep cycle: (1) low-voltage irregular (LVI) is characterized by the presence of continuous low-amplitude (<50 µV), mainly widespread theta activity; (2) mixed pattern is characterized by continuous moderate amplitude (usually <100 µV) theta and delta activities; (3) high-voltage slow (HVS) consists of continuous high-amplitude semirhythmic, mostly delta activity (0.5 to 3.0 cps) in all regions with an amplitude of 50 to 150 µV; and (4) tracé

[www.yassermetwally.com](http://www.yassermetwally.com)
alternant (TA) pattern is characterized by the occurrence of 3 to 5 second bursts of high amplitude (50 to 100 µV) slow activity (0.5 to 3.0 Hz), which occur at intervals of 3 to 10 seconds when the background is relatively low amplitude (10 to 25 µV) consisting of theta waves. In other words, there is an alteration of bursts of large-amplitude slow activity separated by quiescent or "flat" periods of low-voltage activity.

These four EEG patterns are recorded in different states. The LVI EEG is usually recorded in wakefulness and in active sleep. The mixed pattern can also be recorded in active sleep and relaxed wakefulness. The TA and HVS patterns are characteristic of quiet sleep. A unique characteristic of neonate sleep is that as the neonate falls asleep, he usually enters a period of active (REM) sleep. This differs from older infants, children, and adults who never begin their sleep with a period of active (REM) sleep. It is only by 10 to 12 weeks postterm that sleep onset changes from active to quiet (NREM) sleep.

A couple of perils and pitfalls need emphasized in interpreting the neonatal EEG. The TA pattern of quiet sleep in a normal full-term neonate and tracé discontinua pattern in a normal premature neonate during quiet sleep have a superficial resemblance to the suppression-burst pattern that carries a poor prognosis. Differentiation between normal and abnormal discontinuous patterns becomes an important challenge in interpreting the neonatal EEG. The suppression-burst pattern is invariant and nonreactive to stimulation. It usually signifies a severe encephalopathy (usually ischemic/hypoxic), although it may occur transiently due to recent intravenous sedative/hypnotic medication. On the other hand, the TA and tracé discontinua pattern associated with quiet sleep in full-term and premature neonates, respectively, are state dependent and react to stimulation. In addition, long recordings would demonstrate activities characteristic of wakefulness and active sleep in normal full-term and premature (over 32 weeks CA) neonates. The TA pattern gradually disappears over 6 weeks postterm when the HVS pattern becomes the sole EEG accompaniment of quiet sleep.[113]

Another striking feature of the neonatal EEG is the frequent occurrence of multifocal sharp transients during indeterminate and quiet sleep. These start appearing at 35 weeks CA and constitute a normal finding in full-term neonates. The clinical significance of these sharp transients remains controversial. It is difficult to clearly separate abnormal (pathologic) sharp waves from normal sharp transients of the neonate. In general, the normal sharp transients are infrequent in occurrence, usually blunt in morphology (rather than assuming spiky configuration), arise from any scalp location but are common over frontal and temporal regions, are truly random in occurrence, without persistent focality, and largely confined to the burst phase of the TA pattern. However, no universal criteria have been established to separate normal sharp transients of the newborn from the abnormal sharp wave activity. Unless the sharp wave discharges are repetitive, periodic, or localized over one region, an epileptogenic significance must not be assigned to them. When the multifocal sharp transients are very frequent and occur even during active sleep and wakefulness, the EEG is considered to be abnormal but suggestive merely of a nonspecific encephalopathic process.
A unique EEG pattern of pathologic significance is the presence of positive Rolandic sharp waves (PRS). PRS may be confined to one hemisphere; if they are bilateral they may be consistently more abundant over one hemisphere. They are usually maximum at CZ but may be lateralized to C3 or C4 electrodes (Fig. 32). Their positive polarity is a distinctive feature in addition to their localization. Although initially described as the EEG correlates of the intraventricular hemorrhage, PRS waves may be seen in other conditions, including periventricular leukomalacia, parenchymal hemorrhage, hydrocephalus, hypoxic/ischemic insult, and other conditions. Presently, the view is that PRS waves represent a marker of different white matter lesions rather than being specific for periventricular/intraventricular hemorrhage. Positive polarity sharp waves at other locations (especially in the temporal region) have no distinctive significance and may just be a part of multifocal sharp transients in the neonates.

Abnormalities of the background activity in full-term neonates are usually classified as either severe or mild and are summarized in Table 3. The severe EEG abnormalities indicate severe impairment of brain function and carry a poor prognosis for survival and/or neurologic development. Severely abnormal EEG patterns consist of: (1) isoelectric EEG showing activity consistently below 5 µV; (2) persistent low-voltage tracing, EEG showing activity between 5 and 15 µV with very little variability or sleep/wake
differentiation; (3) paroxysmal tracing or suppression-burst pattern (discontinuous, invariant, and nonreactive pattern characterized by 1 to 10 second paroxysms of polymorphic activities such as sharp waves, spikes, and theta-delta activities interspersed with long quiescent periods as long as > 20 seconds); (4) invariant high-amplitude delta activity (persistent and nonchanging high-amplitude 0.5 to 3.0 Hz generalized activity); and (5) the presence of gross asynchrony and asymmetry of the EEG activity over the two sides of the head. Studies have established that the presence of these EEG abnormalities in a full-term neonate, particularly if the abnormalities have been persistent in serial EEGs, carry a very poor prognosis for survival or future neurologic development; over 90% of neonates with such severe abnormalities have an unfavorable outcome.[118,119]

Table 3. Classification of EEG Abnormalities in Neonates

<table>
<thead>
<tr>
<th>1. Grossly abnormal background activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Inactive (isoelectric) EEG</td>
</tr>
<tr>
<td>b. Low-voltage EEG</td>
</tr>
<tr>
<td>c. Trace paroxystique (suppression-burst)</td>
</tr>
<tr>
<td>d. Invariant delta activity</td>
</tr>
<tr>
<td>e. Gross interhemispheric asynchrony/asymmetry</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Mild abnormalities of background activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Immature for CA</td>
</tr>
<tr>
<td>b. Excessive asynchrony/asymmetry</td>
</tr>
<tr>
<td>c. Lack of sleep states</td>
</tr>
<tr>
<td>d. Excessive discontinuity</td>
</tr>
<tr>
<td>e. Focal abnormalities</td>
</tr>
<tr>
<td>f. Miscellaneous, e.g., excessive frontal slowing, excessive frontal or multifocal sharp for CA, excessive rhythmic activities, etc.</td>
</tr>
</tbody>
</table>

| 3. Positive Rolandic sharp waves              |
| 4. Ictal EEG patterns associated with neonatal seizures |

Mild abnormalities of the background activities include more than the usual asynchrony and/or asymmetry; EEG being immature for the conceptional age; lack of recognizable sleep states; excessive discontinuity ("flat" periods longer than 30 seconds); abnormal monorhythmic activities; and excessive multifocal sharp transients. The presence of more than one mild abnormality may suggest an underlying encephalopathic process of varying severity, particularly if the EEG shows persistent abnormality on serial studies. Several of the above mild abnormalities do occur in neonates who are heavily sedated; hence, iatrogenic causes need to be excluded before ascribing them to permanent neurologic insult.

- **Neonatal Seizures**

One of the major reasons an EEG is performed is if a neonate is suspected of having epileptic seizures. In neonates, epileptic seizures are often characterized clinically by subtle
motor behavior such as elevation of a limb, eye deviation, eyelid flutter, tonic posturing, bicycling movements of the legs, apnea, and so on. The EEG is indispensable in establishing the epileptic nature of the motor activity by demonstrating an associated ictal pattern. There are many unique features of neonatal seizures that are different from the seizures encountered in older children and adults. The International Classification of Epileptic Seizures is obviously inappropriate for neonates. The immature brain at this age is unable to initiate and sustain generalized epileptic discharges as in older children; hence, typical tonic-clonic seizures do not occur. Many of the neonatal seizures are subtle seizures as described above. At least some of these do not show a close relationship to an EEG change. The significance of such stereotypic motor events with no concomitant EEG changes becomes a controversial issue regarding diagnosis and management. Whether these events represent "epileptic" dysfunction (not "picked up" by scalp electrodes) or whether these stereotypic behaviors signify episodes of brain stem release phenomena has yet to be resolved.

The opposite situation is also common. An electrographic ictal pattern may occur without an obvious clinical change. Such "subclinical" seizures are common with a pharmacologic neuromuscular blockade, stupor and coma following severe hypoxic/ischemic encephalopathy, multifocal status epilepticus, and following apparently successful treatment of status epilepticus using antiepileptic drugs.

The EEG ictal pattern is highly variable but consists of rhythmic activity of some sort, which is well localized to a relatively small area of the brain. With rare exception, the ictal pattern in neonates is focal, unifocal, or multifocal. When multifocal, the ictal pattern may occur over two different regions at the same time but the discharges have different waveforms and different repetition rates. Multifocal seizures simultaneously occurring on the two sides is a unique feature of neonatal epileptogenesis.

Interictal epileptiform abnormalities are rarely present to aid in the diagnosis of neonatal seizures. Multifocal sharp transients over the frontal and temporal regions are common even in healthy neonates and, as mentioned above, do not correlate with present or future occurrence of epileptic seizures. It appears that in neonates the epileptic process exhibits "all or none" features: either a seizure manifests overtly with appropriate electrographic features or has no interictal epileptiform markers.

- **Ictal EEG patterns associated with neonatal seizures are of four basic types[111]:**

Focal spikes or spike wave discharges superimposed on a more or less normal background is an ictal pattern most commonly located over the Rolandic region (C3 or C4), and the frequency of the ictal discharge is usually over two per second (Fig. 33). In neonates, focal EEG discharges and clinical seizures do not necessarily imply focal brain lesions. Common etiologies include metabolic disturbances, such as hypocalcemia or hypoglycemia, and subarachnoid hemorrhage. Such an ictal pattern, when associated with normal a EEG background, is prognostically favorable.
Another focal ictal pattern consists of slow-frequency sharp waves or complex waveforms repeating approximately one per second, never recruiting at a faster rate (Fig. 34). This pattern is similar to PLEDs. The background activity is almost always low in amplitude. This pattern, called "depressed" brain discharges,[121] is associated with a severe cerebral insult (e.g., hypoxic/ischemic encephalopathy, encephalitis, cerebrovascular accident, etc.). The accompanying clinical seizures are usually subtle or the EEG discharges are entirely subclinical.

Focal monorhythmic pattern in the beta, theta, and delta frequency is a unique ictal pattern in neonates. It may start with low-amplitude focal 8 to 14 Hz activity that slows down to 4 to 7 Hz and then to 0.5 to 3.0 Hz rhythmic pattern. All types of combinations of the frequency band are possible but some ictal discharges may remain essentially monorhythmic ("alpha band" seizures) during a given seizure (Fig. 35). The background is always abnormal and usually low in amplitude. This type of pattern has been referred to as pseudo-beta-alpha-theta-delta ictal pattern[111] and is usually associated with subtle seizures, tonic or myoclonic seizures, or no behavioral clinical change. This ictal pattern is associated with severe CNS dysfunction and correlates with a poor outcome.

Multifocal ictal pattern is characterized by an abnormal background activity and the development of an ictal pattern independently or, rarely, simultaneously over two or more areas of one or both hemispheres. Two or more focal seizures may appear concomitantly in the same or, more commonly, the opposite hemisphere and appear to progress independently. This ictal EEG pattern is usually associated with subtle seizures; the underlying pathology consists of severe encephalopathy due to infection, congenital anomalies, birth trauma, or anoxia. This pattern carries a poor prognosis for normal neurologic development.
Figure 33. EEG of a 5-day-old neonate, showing focal ictal pattern characterized by rhythmic sharp waves in the left Rolandic region.
Figure 34. EEG of a 5-day-old neonate on ventilator, showing "depressed brain seizure" characterized by less than one per second, low-amplitude sharp waves over the right hemisphere.
Figure 35. EEG of a 3-day-old comatose neonate with history of seizures, showing an electrographic "alpha band" seizure pattern without clinical accompaniment.

- **Technical Aspects**

Several technical points are of crucial importance to optimize neonatal EEG recording. The study should be long enough to include active and quiet sleep; the total duration of the recording may exceed the usual 30 minutes recommended in adults. In most neonates it may be necessary to record the EEG for 45 to 60 minutes. The presence of sleep differentiation is an important maturational feature for EEG interpretation. Some abnormal patterns such as the degree of discontinuity, asynchrony and asymmetry, presence of multifocal sharp transients, or delta brushes can be evaluated only in quiet sleep. Additionally, polygraphic variables must be routinely recorded in addition to several channels of scalp EEG. These include respiration, extraocular movements, EKG, and chin activity. These non-EEG variables are critical in identifying different states (awake, active sleep, or quiet sleep) and recognition of various artifacts. A neonatal EEG lacking such polygraphic variables is difficult to interpret unless it is grossly abnormal.

- **EEG in Status Epilepticus**

Status epilepticus (SE) is usually defined as continuous seizure activity persisting for more than 30 minutes or more than one sequential seizure without full recovery of consciousness between seizures. A very common reason for ordering an emergency EEG is for the diagnosis and management of SE. A simplified classification of SE includes: (1) generalized convulsive status, characterized by motor seizures with loss of consciousness; (2) simple partial or focal status, characterized by focal motor seizures repeating frequently or
epilepsia partialis continua with the patient remaining fully conscious; and (3) nonconvulsive status (NCSE) characterized by a variable alteration of consciousness with minimal or no motor activity.

NCSE poses many challenging nosologic, diagnostic, and therapeutic problems. NCSE includes: (1) absence status, occurring in the setting of generalized epilepsy (idiopathic or symptomatic) and (2) complex partial status associated with focal or partial epilepsy of frontal or temporal onset. In both types, the patient may present with mental status alteration (e.g., slowness in behavior and mentation, confusion, and, rarely, stupor or coma). Then, there are patients who after treatment of generalized convulsive status continue to be obtunded or comatose and show epileptiform discharges in their EEG. These patients are often designated as having "subtle" SE or lumped under NCSE.

It is relatively easy to diagnose NCSE associated with focal epilepsy when there are frequent electrographic focal seizures with an ictal EEG pattern that evolves over time with change in the amplitude, frequency, and spatial distribution. However, it is quite common for the ictal EEG pattern associated with complex partial status associated with focal epilepsy to be generalized spikes or sharp waves repeating at 1 to 6 Hz frequency. Such a generalized EEG pattern is similar to that seen in typical absence status associated with idiopathic generalized epilepsy (absence epilepsy) and atypical absence status in children with secondary generalized epilepsy of the Lennox-Gastaut type. To complicate the situation even further, patients with Lennox-Gastaut syndrome interictally have generalized 1.0 to 3.0 cps spike wave discharges that may be very frequent, and one needs to decide if they represent an ictal pattern (hence atypical absence status) or simply represent a prominent interictal pattern. Some waxing or waning of such generalized epileptiform discharges may not help in the distinction because this may be simply related to state changes.

Some helpful criteria are proposed by Young et al[122] in patients who show almost continuously occurring generalized, nonevolving epileptiform discharges in their EEGs, including repetitive generalized or focal epileptiform discharges (spikes, sharp waves, and spike waves) that repeat at a rate faster than three per second, very likely represent an ictal pattern. Such repetitive discharges at a frequency slower than three per second are likely to be ictal if significant clinical and/or EEG improvement is demonstrated following small doses of intravenous lorazepam or diazepam. Rhythmic sinusoidal waves of any frequency (ranging from to frequency) may represent an ictal pattern if there is an evolving pattern at the onset (increasing amplitude and/or decreasing frequency) or a decrement pattern at the termination (decremental amplitude or frequency) or postdischarge slowing or voltage attenuation.

In a patient with obtundation or mental status change of recent onset, an EEG is indicated to rule out NCSE. If repetitive generalized epileptiform discharges are recorded in the EEG, 1 to 2 mg of lorazepam or 5 to 10 mg of diazepam are injected intravenously while the EEG is running. A marked clinical improvement of obtundation and disappearance of generalized paroxysmal activity in the EEG would strongly support the diagnosis of NCSE
(Figs. 36 and 37). Such a rewarding experience is most common in typical absence status and less common in other forms of NCSE.

Figure 36. EEG of a 53-year-old man with one day history of acute confusion and slowness of motor responses, showing almost continuous generalized spike wave activity.
Figure 37. EEG of the same patient seen in Figure 36 following 4 mg of intravenous lorazepam, showing disappearance of all paroxysmal activity and mental clearing, highly suggestive of nonconvulsive status epilepticus.

Reviewing the previous EEG and obtaining follow-up EEG studies also provide a helpful distinction between ictal and interictal basis for the repetitive generalized spike wave discharges seen in children with Lennox-Gastaut syndrome. A period of frequent repetitive generalized spike wave discharges associated with clinical deterioration of mental status is more likely an episode of atypical absence status, particularly if the previous EEGs or follow-up EEGs display dramatically fewer epileptiform abnormalities.

"Subtle" SE commonly includes patients who had a known episode of convulsive or generalized tonic-clonic status, brought under control by intravenous antiepileptic therapy (e.g., phenytoin, lorazepam, and barbiturates), but continue to remain obtunded or comatose without significant motor activity. EEG of such patients often show repetitive discharges, which may include lateralized periodic discharges (e.g., PLEDs or BiPLEDS) or generalized periodic discharges (PEDs). Some epileptologists[123] are of the opinion that progressive sequential EEG changes occur during generalized convulsive SE with an
"intermediary" pattern of PEDs and PLEDs (unilateral or bilateral) before disappearance of all paroxysmal EEG activities, and that the presence of these "intermediary" EEG patterns necessitate further aggressive therapeutic measures (e.g., inducing pentobarbital coma, etc.). Such views are not universal. Many, on the other hand, consider PED and PLED patterns observed during the course of convulsive status not an ictal pattern but suggestive of a severe epileptic encephalopathy reflective of a neuronal dysfunction from underlying brain damage.[124]

Refractory SE is usually treated by continuous intravenous anesthesia maintained by pentobarbital, propofol, or medazolam. The dose is regulated such as to control all clear-cut clinical or electrographic seizures and to maintain a suppression-burst pattern in the EEG. Therefore, continuous bedside EEG is monitored. There is no consensus as to the duration of "burst" and "flat" periods for optimal dosing. Most consider that establishing and maintaining any degree of suppression-burst pattern is adequate.

One final note of caution is that focal motor seizures including epilepsia partialis continua may not show ictal changes in the EEG because of the limited size of neuronal tissue involved during the epileptic seizure or because the ictal pattern in the EEG may be obscured by artifacts. Careful review of the EEG using different montages (especially a transverse bipolar montage going through the midline electrodes) and use of appropriate muscle filters may reveal a low-amplitude ictal pattern.

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INTRODUCTION

The occurrence of focal or generalized paroxysmal discharges in apparently healthy individuals is a puzzling and even annoying finding which requires some discussion. These findings may be quickly termed as false positives, but the EEG abnormalities are real and their irrelevance in view of the individual's good health is more apparent than real. Such spikes give testimony of certain cerebral dysfunctions which may or may not become manifest in the further course of events. These findings do not discredit the method of
Electroencephalography, which, after artifacts are ruled out, can only show facts. These disturbing facts are in need of a reasonable interpretation. Let us contemplate the indubitable fact that a complete medical evaluation will yield certain physical shortcomings and organic abnormalities in practically every healthy individual; even acne pimples are cutaneous lesions and hence abnormalities. What the electroencephalographer needs in such cases is a common sense philosophy as a basis for a wise interpretation. General medicine is full of examples of seemingly irrelevant and yet unmistakably present abnormalities which the prudent, seasoned physician will integrate into a holistic view of the individual. Seen from this angle, electroencephalography does not differ from the rest of medicine.

![Figure 1. Examples of sharp waves (left) and spike (right)](image)

Table 1. Electroclinical criteria of spike/sharp wave discharge

- A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG.
- A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.
- Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.
- The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.
Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.

The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. Low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.

The EEG evaluation of comparatively large healthy populations usually shows a certain percentage of abnormalities such as spike, sharp wave or paroxysmal discharge. One should thoughtfully contemplated the clinical significance of spikes in healthy persons. Above all, the interpretation must take into consideration age. In childhood, the occurrence of central-midtemporal (also parietal) spikes is associated with overt seizures in only 50-70% of the cases; this pertains mainly to the age from 3-12 yr. In occipital spikes (mainly age 3-5 yr), the epileptogenicity is even lower. In general, "benign" focal spikes (such as seen in benign Rolandic epilepsy) is seen, in healthy individual, much more often than generalized synchronous bursts of spikes or spike waves. In most children, the abnormalities disappear on follow up EEG studies and the minority develop overt clinical symptomatology.

Table 2. Interictal epileptic activity

<table>
<thead>
<tr>
<th>Interictal epileptic activity</th>
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<td>The interictal marker of a seizure focus is the spike or sharp wave. The distinction between these two patterns has no etiologic significance, the only difference being one of EEG pattern morphology. A spike is defined as being less than 70 milliseconds in duration, and a sharp wave has a duration of 70-200 milliseconds. The terms spike or sharp wave, while having particular meaning to the electroencephalographer, are often used interchangeably. Spikes and sharp waves are almost always of negative polarity at the scalp surface. These epileptiform discharges may arise from any region of the cerebral hemispheres but most commonly are manifested in the anterior temporal, frontal, or centrotemporal regions.</td>
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<tr>
<td>An anterior temporal spike or sharp wave is highly associated with the occurrence of clinical focal-onset seizures. When this pattern is seen on the EEG, the likelihood of the individual manifesting clinical seizures is over 90%. However, the converse is not necessarily true. While the EEG of most patients with temporal lobe seizures demonstrates anterior temporal spikes, an EEG negative for this finding does not exclude a diagnosis of epilepsy. Often, repeated EEG recordings or prolonged EEG monitoring is required to</td>
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demonstrate the epileptiform pattern.

**Frontal spikes and sharp waves** also are highly associated with clinical seizures but not to the same degree as temporal discharges. Approximately 70-80% of individuals whose EEG demonstrates frontal spikes have clinical seizures. Frontal spikes or sharp waves are more likely to be associated with mass lesions such as neoplasms, traumatic lesions, or congenital cerebral malformations.

**Centrotemporal or rolandic sharp waves** are often a marker for a particular epilepsy syndrome of childhood known as benign rolandic epilepsy or benign focal epilepsy of childhood with centrotemporal spikes. This is a disorder in which a child, typically aged 4-12 years, develops focal seizures with sensory or motor seizures in the mouth or face region. These children also may have generalized seizures; typically, these seizures are nocturnal. The EEG pattern is unusual in that there is often a simultaneous negative waveform in the centrotemporal region and a positive one in the frontal region. This pattern of EEG polarity is virtually diagnostic of benign rolandic epilepsy.

Epileptiform EEG patterns are seen less commonly in the occipital, central, or parietal regions. Occipital spikes typically are seen in young children and may or may not be associated with clinical seizures. Discharges in any of these regions may indicate the presence of partial epilepsy.

Both generalized synchronous (spike wave, polyspike wave) and Rolandoic (centroparieto-midtemporal) spikes in nonepileptic children suggest a genetic predisposition if no neurological deficit and no history of insult to the CNS are present. In children with a history of cerebral palsy and with no seizures but prominent spiking, the spike activity may herald future epileptic seizures. Even in perfectly healthy children with spikes, the possibility of future seizures cannot be completely ruled out, although the chances are slim.

In healthy children and especially in healthy adults with spikes, stress must be laid on certain personality disorders which are not incompatible with normal functioning. Psychological and mild psychiatric deviations include poor impulse control, proneness to hysterical conversion reactions, and schizoid manifestations. In such individuals, the presence of a cerebral dysfunction with paroxysmal EEG changes may hamper the natural process of psychological maturation. In some of these cases, head injuries or infections of moderate severity might have prompted or facilitated the EEG changes as well as the psychological deviations.

The high incidence of anterior temporal-midtemporal sharp transients in older patients with no clinical epileptic fits has no significance. These patients may even have overt sharp waves; others show small sharp spikes. Unless there is evidence of epileptic seizures, these discharges only indicate some degree of temporal lobe dysfunction, often compatible with good health.

This section must be capped by a strong plea to refrain from rash and ill-advised statements that a seizure-free person has epilepsy and must be treated because of spikes in
the EEG. These persons need further medical attention and repeat EEG should be done at reasonable intervals, such as every 2 yr in a child or adolescent and every 5 yr in an adult. Anticonvulsive treatment is not needed, but should not necessarily be denied to extremely apprehensive, introspective, and hypochondria-prone individuals.

Table 3. Pearls for practice

- In childhood, the occurrence of central-midtemporal (also parietal) spikes is associated with overt seizures in only 50-70% of the cases; this pertains mainly to the age from 3-12 yr. In occipital spikes (mainly age 3-5 yr), the epileptogenicity is even lower.
- In general, "benign" focal spikes (such as seen in benign Rolandic epilepsy) is seen, in healthy individual, much more often than generalized synchronous bursts of spikes or spike waves. In most children, the abnormalities disappear on follow up EEG studies and the minority develop overt clinical symptomatology.
- Both generalized synchronous (spike wave, polyspike wave) and Rolandic (centroparieto-midtemporal) spikes in nonepileptic children suggest a genetic predisposition if no neurological deficit and no history of insult to the CNS are present.
- In children, focal epileptiform discharges arising from the temporal region have the greatest incidence of clinical seizures, ranging from 85 to 95 percent. The next highest incidence (70 to 75 percent) is associated with frontal discharges. The central, parietal and occipital regions have the lowest incidence of seizures related to epileptiform discharges. estimated at 40 to 70 percent.
- When applied in the appropriate clinical setting, the EEG is useful in classifying the seizure type, predicting the long-term outcome, and choosing the appropriate antiepileptic medication.
- EEG has not proven to be a reliable tool in predicting whether a patient's antiepileptic medication can be discontinued. The decision to discontinue an antiepileptic medication in a patient with a seizure disorder should be based on the type, etiology and response to medications of the seizures and not on interictal EEG findings.

- Epileptic EEG sharp activity

Epilepsy is defined as "paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system. A seizure, or ictus epilepticus, is an epileptic attack or recurrence. The classification of epilepsies used by International League Against Epilepsy (ILAE) includes two major categories: partial epilepsies and generalized epilepsies. A partial seizure disorder is considered to have a focal region of onset in the brain, and awareness may be either preserved (simple partial seizure) or lost (complex partial seizure). A generalized seizure disorder is considered to involve most, if not all, of the brain at onset. The generalized seizure types may involve cessation of activity with loss of awareness (absence seizure) or generalized tonic-clonic activity (generalized tonic-clonic seizure). Both partial and generalized seizure disorders are further subdivided into idiopathic and symptomatic
types, previously called primary and secondary, respectively. Idiopathic epilepsies are thought to be genetically heritable, are associated with normal intelligence, and occur during specific age periods. The symptomatic epilepsies are likely the result of a CNS injury, which in a symptomatic partial epilepsy consists of a focal lesion and in a symptomatic generalized epilepsy consists of diffuse cerebral abnormality. Symptomatic epilepsies are typically lifelong conditions.

It cannot be overemphasized that the diagnosis of epilepsy is based primarily on the clinical history. As noted above, a clinical seizure rarely occurs during an EEG, and thus the EEG is rarely diagnostic of a seizure disorder or epilepsy. In a large, population-based EEG study by Zivin and Ajmone-Marsan [1] involving subjects without a history of seizures, approximately 2 percent of the subjects had EEGs with epileptiform discharges. Of the individuals in this subgroup, only 15 percent subsequently developed a seizure disorder. Therefore, epileptiform discharges seen on an EEG should not be referred to as interictal discharges unless it is known that the patient has a clinically defined seizure disorder. Focal or generalized epileptiform discharges should be noted as consistent with the interictal expression of either a partial or a generalized epilepsy, respectively. When applied in the appropriate clinical setting, the EEG is useful in classifying the seizure type, predicting the long-term outcome, and choosing the appropriate antiepileptic medication.

Overall, symptomatic partial seizure disorders are the most common type of epilepsy. The clinical semiology of the partial seizure generally depends on the site of onset. In children, focal epileptiform discharges arising from the temporal region have the greatest incidence of clinical seizures, ranging from 85 to 95 percent. The next highest incidence (70 to 75 percent) is associated with frontal discharges. The central, parietal and occipital regions have the lowest incidence of seizures related to epileptiform discharges, estimated at 40 to 70 percent. In addition to the characteristics of recorded epileptiform activity, the age of the patient and the presence or absence of neurological deficits on examination are important factors that are helpful in determining the clinical significance of epileptiform discharges and in classifying the partial seizure disorder as either symptomatic or idiopathic. The occurrence of a clinical seizure with a focal electrographic correlate is diagnostic of a partial epilepsy. Blume and colleagues [2] presented several types of scalp EEG correlates for partial seizures, most of which began with rhythmic sinusoidal activity or repetitive sharp wave activity that subsequently evolved in frequency. Most patients with complex partial seizures were noted to have a scalp correlate on the EEG. Patients with simple partial seizures were less likely to have a scalp correlate.

The best-defined idiopathic partial epilepsy is benign rolandic epilepsy. The classic EEG finding in this childhood seizure disorder is a characteristic monomorphic centrotemporal sharp wave. The sharp waves are often seen independently in the centrotemporal and adjacent regions, and they are accentuated by light sleep. The waking background rhythm is generally normal.

Of the idiopathic generalized epilepsies, the absence seizure is the most common type. The interictal EEG feature of this type of seizure disorder consists of generalized, high-amplitude, anteriorly predominant 3-Hz spike and wave discharges, called typical 3-Hz
spike and wave. When the spike and wave discharges occur repetitively, they are called bursts. Although these discharges are called "3-Hz." the initial frequency of the burst is 3 to 4 Hz, and the frequency may slow to 2.5 Hz during more prolonged bursts. The discharges are reactive to alerting maneuvers and may become fragmented in deeper stages of sleep. Juvenile myoclonic epilepsy (JME) is another type of idiopathic generalized epilepsy. The spike and wave discharges of this seizure disorder are also generalized and anteriorly predominant, but they have an initial frequency of 4 to 6 Hz and may begin with a polyspike discharge. The EEG of a patient with an idiopathic generalized epilepsy who is maximally alerted is generally normal. During photic stimulation, there may be a photoparoxysmal response in both absence epilepsy and JME, which may be helpful in classifying recognized epileptiform discharges as consistent with an idiopathic generalized epilepsy rather than a symptomatic partial or generalized epilepsy.

Figure 2. The 3 c/s spike/wave discharge.
Epileptiform patterns in symptomatic generalized epilepsies are of three types. A slow spike and wave pattern at approximately 2 Hz is seen in patients with mental retardation having multiple seizure types (atypical absence, tonic, atonic, or tonic-clonic seizures), which is known as the Lennox-Gastaut syndrome. A second type of interictal or ictal EEG pattern seen in patients with symptomatic generalized epilepsy is generalized paroxysmal fast activity (GPFA), which consists of bursts of rhythmic, generalized beta activity. When the bursts are seen during wakefulness, they are commonly accompanied by a tonic seizure. During sleep, bursts of GPFA not accompanied by clinical changes are considered an interictal pattern. The third pattern of epileptiform activity in secondary generalized epilepsy is an atypical generalized spike and wave pattern, consisting of generalized 3 to 6-Hz spike or polyspike and wave activity. The waking background in patients with secondary generalized epilepsies is abnormally slow, including slowing of the posterior background rhythm and generalized slowing.
In patients suspected of having a seizure disorder, a normal routine, awake EEG should be followed with either a natural or medication-induced sleep EEG or a sleep-deprived EEG. Before the advent of long-term video-EEG monitoring for the diagnosis of possible seizures, three or more EEGs were often obtained to confidently conclude normality and absence of epileptiform activity. Because antiepileptic medications have been shown not to affect the frequency of focal interictal epileptiform discharges, the decision to treat a patient for a suspected partial seizure disorder should not be based solely on the initial EEG findings. Conversely, the EEG has not proven to be a reliable tool in predicting whether a patient's antiepileptic medication can be discontinued. In patients with an idiopathic generalized epilepsy, treatment with appropriate antiepileptic medication may eliminate all interictal epileptiform activity on the EEG. Therefore, the decision to discontinue an antiepileptic medication in a patient with a seizure disorder should be based on the type, etiology and response to medications of the seizures and not on interictal EEG findings.

**References**


EEG EVALUATION OF FOCAL CEREBRAL LESIONS

- **Role of Electroencephalography in the Era of Computed Tomography**

The role of electroencephalography (EEG) in detecting focal cerebral disturbances has undergone a significant change in the last decade owing to the development and availability of computerized imaging techniques. EEG is generally complementary to these as, with the exception of positron emission tomography (PET) and single photon emission tomography (SPECT), only EEG evaluates changes in brain physiology. Furthermore, EEG provides the only continuous measure of cerebral function over time. Computerized transaxial tomography (CT) and magnetic resonance imaging (MRI) scanning are clearly the procedures of choice for delineating structural lesions. However, they do not currently reveal abnormalities unless anatomic alterations in brain tissue have occurred.

In this article, we will review the major electroencephalographic changes that occur with focal cerebral lesions, describe how they relate to CT findings, and indicate the relevance of focal physiologic dysfunction in the absence of structural pathology. Although this article deals with conventional electroencephalographic techniques, newer developments such as topographic EEG mapping and magnetoencephalography suggest that the monitoring of spontaneous and evoked electrical brain activity will continue to play an important role in neurologic diagnosis.
ELECTROENCEPHALOGRAPHIC ABNORMALITIES INDICATING FOCAL DYSFUNCTION

- **Focal Delta Activity**

Focal delta activity is the classic electroencephalographic sign of a local disturbance in cerebral function. A structural lesion is most strongly suggested if the delta activity is continuously present, shows variability in waveform amplitude, duration, and morphology (so-called "polymorphic" or "arrhythmic" activity), and persists during changes in physiologic state. Delta waves that attenuate with eye opening (or other alerting maneuvers), or fail to persist into sleep, are less indicative of structural pathology.

![Figure 1. A, Continuous left parietal-occipital polymorphic delta activity. Note associated loss of alpha rhythm and attenuation of faster frequencies over the occipital region. The responsible lesion was a malignant glioma of the left parietal lobe (B).](image)

The localizing value of focal delta is increased when it is topographically discrete or associated with depression of superimposed faster background frequencies. 3,19,34 Superficial lesions tend to produce more restricted EEG changes, whereas deep cerebral lesions may result in hemispheric, or even bilateral, delta. Lesions involving the central and parietal areas are less likely to present with a circumscribed delta focus, and are also correspondingly more apt to produce delta activity falsely localized to the temporal areas.

Focal delta is often, but by no means always, maximal over the actual lesion. If sufficient destruction of cortex has occurred, the voltage of delta activity may actually be reduced over the area of maximal cortical involvement and thus be higher in the areas bordering the lesion. 19 If two or more delta foci are present, the one that is most persistent and least rhythmic indicates the site of the major lesion, regardless of voltage.

Few studies have correlated focal delta with CT abnormalities. Gilmore and Brenner, 17 examined 100 consecutive EEGs containing focal polymorphic delta activity and reviewed the CT findings in these patients. Sixty-eight patients had focal CT lesions, 10 had nonfocal abnormalities, and 22 had normal scans. Although peak delta voltage was not always directly over the lesion, laterality was invariably correct. Normal CT scans occurred in...
patients with seizure disorders (12), concussion or contusion (5), ischemic strokes (3), viral encephalitis (1), and a progressive undiagnosed neurologic syndrome (1). Twelve patients with focal neurologic examinations had normal CT scans.

Weisberg and associated 57 studied 50 consecutive patients with a unilateral temporal delta pattern and neurologic signs. CT in these patients showed tumor (40 per cent), vascular lesions (20 per cent), diffuse atrophy (16 per cent), or hydrocephalus (4 per cent). Twenty per cent had normal CT scans, a figure similar to that of Gilmore and Brenner. 17 Half of the patients with normal CT had probable epilepsy; the remainder had no further evolution of their neurologic findings over a 4-year follow-up.

In another study, Weisberg and colleagues, 57 reviewed CT findings in 20 patients who had a "unilateral delta pattern" but normal neurologic examination, cerebrospinal fluid (CSF), and isotope brain scan. Six had abnormal CT scans: three showing diffuse atrophy and three with infarcts. The three patients with atrophy developed Alzheimer's disease within 1 year. The authors did not indicate why the remaining 14 patients with normal CT had been referred to the EEG laboratory.

Reports such as these demonstrate that although focal polymorphic delta is strongly correlated with localized anatomic pathology, EEG findings may occur in the absence of a demonstrable CT lesion. When focal delta is found without a corresponding CT abnormality, it is usually in the setting of seizures, nonhemorrhagic infarction, or trauma. 17, 57

Clinical, 46 and experimental, 18 observations indicate that polymorphic delta results primarily from lesions affecting cerebral white matter. Involvement of superficial cortex is not essential, and, indeed, lesions restricted to the cortical mantle do not generally produce significant focal delta. 18,46 It is likely that functional deafferentation of cortex, rather than a change in cortical metabolic rate, is critical. 18 Cerebral edema does not appear to make a substantial contribution to the production of delta waves. 16,18,46

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (white matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.

Because the likelihood of a demonstrable structural change is strongly correlated with the degree of slowing, the clinical associations of focal theta activity are less striking, especially for acute or subacute lesions. Focal theta may be seen in the early stages of a slowly growing neoplasm or in the resolution of acute lesions caused by stroke or trauma.
Figure 2. Polymorphic slow wave activity in a patient with subcortical glioma, notice the marked variability in wave shape morphology, frequency and amplitude.

Table 1. Electrical criteria of the Polymorphic slow wave activity.

- Quite variable in wave shape morphology, frequency and amplitude.
- Commonly lateralized over a wide area of the scalp, persistent in eye closed, eye open state, during all sleep stages, with no visual reactivity. Polymorphic Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology.
- Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (white matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
- Commonly due to a subcortical white matter lesion inducing deafferentation of the cerebral cortex.
- A purely cortical lesion does not induce polymorphic slow wave activity.

- Beta Activity

Abnormalities in beta activity are usually limited to voltage asymmetries. To be considered unequivocally abnormal, there should be a persistent amplitude difference of 35 per cent or greater (expressed as a percentage of the higher voltage). 32

Diminished beta activity results either from cortical dysfunction or from an increase in resistance of the medium separating cortex from scalp recording electrodes. Thus, local attenuation of beta may occur with a cortical infarction, for example, or in the presence of a subdural or epidural fluid collection. A beta asymmetry may also result from localized
scalp edema caused by head injury or infiltration from an intravenous line. Similar considerations apply as well to the localized absence or attenuation of background rhythms other than beta.

Focally increased beta activity is usually associated with a skull defect. Occasionally, localized enhancement of beta may occur over a tumor or as the manifestation of an epileptogenic focus.

- **Epileptiform Activity**

Focal epileptiform activity (spikes or sharp waves) may antedate the appearance of focal EEG-slowing or other clues to a tumor by months or years. In a multicenter study of 1396 patients with epilepsy, 10 per cent had tumors detected by CT. However, the incidence of tumor rose to 22 per cent when only patients with partial seizures were considered. Brain tumor did not occur in patients with primary generalized epilepsy and was found in only 5 per cent of those with secondary generalized seizures.

Periodic lateralized epileptiform discharges (PLEDS) usually occur in the setting of an acute or subacute destructive process. Impaired consciousness is virtually always present, and seizures are evident nearly 80 per cent of the time. The complexes are most often composed of di- or triphasic spikes or sharp waves recurring at approximately regular 1 to 2-second intervals. However, the distribution, morphology, voltage, and rate of repetition vary substantially among patients. Schwartz and coworkers studied 52 patients and found a typical electrographic evolution for PLEDS. Gradual simplification in morphology and progressive prolongation of the interval between discharges usually occurred within 4 weeks. In a few patients, however, clinical relapses were accompanied by reappearance of PLEDS.

![Image of EEG and CT scan](www.yassermetwally.com)

**Figure 3.** A, Left-sided PLEDS, maximally involving the left parietal-occipital region. Background rhythms are slowed bilaterally, and there is a slight reduction in faster frequencies on the left. The patient had an intracerebral tuberculoma on that side.
PLEDs may also occur independently over both hemispheres, a situation referred to as BIPLEDs. In patients exhibiting BIPLEDs, diffuse diseases, rather than focal lesions, are the rule. Thus, BIPLEDs are most often seen with infections (particularly herpes simplex encephalitis), anoxic encephalopathy, epilepsy, and sickle cell anemia.

Table 2. Major Diagnosis in Patients with PLEDs

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<th></th>
<th>NUMBER OF PATIENTS</th>
<th>STROKE</th>
<th>NEOPLASM</th>
<th>EPILEPSY</th>
<th>OTHERS*</th>
<th>ASSOCIATED SEIZURES</th>
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<tr>
<td>de la Paz and Brenner, 29</td>
<td>45</td>
<td>15</td>
<td>5</td>
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<td>Schwartz et al, 54</td>
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<td>Chatrian et al, 48</td>
<td>33</td>
<td>13</td>
<td>8</td>
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<tr>
<td>TOTAL</td>
<td>170</td>
<td>64 (38%)</td>
<td>35 (20%)</td>
<td>30 (17%)</td>
<td>41 (34%)</td>
<td>131 (77%)</td>
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*The majority of etiologies included unknown disorders, unspecified infections, herpes simplex encephalitis, electrolyte imbalance, hypoglycemia, bacterial meningitis, subdural hematomas and sickle cell disease.

LATERALIZED ELECTROENCEPHALOGRAPHIC FINDINGS

The character and distribution of the electroencephalographic changes produced by a focal lesion depend on size of lesion, its distance from the cortical surface, and the specific structures involved. A small lesion critically located in the thalamus, for example, may produce widespread hemispheric slowing and alteration in sleep spindles and alpha rhythm regulation. The same discrete lesion, however, located at the cortical surface, may produce few, if any, electroencephalographic findings. Indeed, cortical lesions must involve relatively large areas to produce attenuation of background rhythms in the relative absence of slowing. Examples include subdural hematomas and meningiomas. Large infarcts (due to middle cerebral or carotid artery occlusions, for instance) involve extensive areas of cortex as well as adjacent white matter, thus producing both hemispheric polymorphic delta and loss of overriding faster frequencies. Lesions that produce hemispheric depression of background rhythms affect both normal and abnormal patterns, as illustrated by the case of a subdural hematoma causing an interhemispheric asymmetry of triphasic waves in an alcoholic with hepatic failure.

Focal lesions may slow or attenuate the alpha rhythm unilaterally. A particularly striking abnormality of the alpha rhythm is unilateral failure to attenuate normally with eye opening (Bancaud’s phenomenon) or other alerting maneuvers. These changes are reliable
indicators of an ipsilateral, usually posterior, cerebral lesion, but they do not provide more specific localizing information.

![Image of EEG waves and brain scan]

**Figure 4.** A, Failure of alpha rhythm to attenuate normally with eye-opening on the left. The patient had a giant aneurysm of the left internal carotid-middle cerebral artery bifurcation with compression of the frontal and temporal lobes from below (B).

The photic driving response to repetitive flash stimulation may be consistently lateralized in normal individuals. 9 When it is the only finding in an otherwise normal record, an asymmetry of photic driving may usually be ignored. It is clear that a cortical lesion may depress the photic response unilaterally, but under these circumstances, the asymmetric photic response occurs in conjunction with other indications of focal dysfunction. Occasionally, focal lesions (especially subcortical or epileptogenic ones) may enhance the photic response on one side. 9

Hyperventilation will often enhance localized, low-amplitude polymorphic delta or convert intermittent slowing into a continuous focal abnormality. Focal spikes, or even seizures, sometimes appear only during hyperventilation. 42 A consistently asymmetric response to hyperventilation is always abnormal.

**GENERALIZED ELECTROENCEPHALOGRAPHIC CHANGES**

Generalized electroencephalographic abnormalities do not contribute to localization of a focal lesion or by themselves even suggest the presence of localized structural pathology. They do, however, provide information about the extent of dysfunction resulting from a focal lesion or about a coexisting abnormality (metabolic encephalopathy, for example).

Subfrontal, diencephalic, or infratentorial lesions may produce generalized electroencephalographic changes, usually a combination of intermittent bursts of rhythmic delta waves and continuous, widespread polymorphic theta and delta slowing. In the absence of obstructive hydrocephalus, electroencephalographic abnormalities are more frequent with rostral than caudal brain-stem lesions. Schaul and coworkers, 51 reviewed

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the EEGs of 154 patients with diencephalic or posterior fossa lesions. Only 12 per cent of patients with diencephalic lesions had normal EEGS, whereas 60 per cent and 73 per cent of patients with lower brain-stem or cerebellar pathology respectively had normal EEGS. If the EEG abnormality was clearly lateralized, an infratentorial lesion was unlikely.

Paroxysmal bursts of rhythmic delta waves with frontal or occipital predominance (the latter especially common in children) have been associated with subfrontal, deep midline, or posterior fossa lesions. In fact, however, intermittent rhythmic delta activity (IRDA) is nonspecific and is seen much more often in the setting of metabolic disorders or other encephalopathies affecting the brain diffusely than with focal lesions, regardless of location.

IRDA may appear against an otherwise normal background. In contrast to polymorphic delta, IRDA is usually reactive to alerting maneuvers, disappears in sleep, and is augmented by hyperventilation or drowsiness. Correlative studies using CT and PET have failed to demonstrate a particular anatomic structure responsible for generating IRDA. Physiologic investigations implicate dysfunction of thalamocortical interactions.

Rhythmic delta activity consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized. In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]). Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies. FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy. In cases of encephalopathy with FIRDA, the pathophysiologic processes are believed to involve cortical and subcortical gray matter. OIRDA is associated with absence epilepsy in children aged 6-10 years.

Figure 6. The intermittent rhythmic delta activity [left image] and the polymorphic slow wave activity [right image]
Table 3. Electrical criteria of The intermittent rhythmic delta activity.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA])
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.

CLINICAL APPLICATIONS

- The EEG as a Screen for Further Investigation

Patients with focal findings on neurologic examination require CT or MRI. When the clinical data do not strongly implicate a localized disease process, however, some clinicians have advocated using EEG as a cost-effective screen for more extensive, especially radiologic, investigation. Rosenberg and associated, 49 retrospectively reviewed 136 patients with abnormal neurologic examinations but whose findings and histories did not suggest focal pathology. Clinically, the patients could be divided into six groups: headache, first seizure, recurrent seizure, confusion or dementia, transient ischemic attacks, and miscellaneous disorders. Electroencephalographic findings could be assigned to one of three groups. Twenty-one patients had focal abnormalities (slowing, spikes, or attenuation). Four of these (20 per cent of this group) had CT scans showing stroke, tumor, or porencephaly; the remainder had normal CT scans. Sixty-four patients had generalized electroencephalographic abnormalities. in this group only two patients had abnormal CT scans: one showing multiple metastases and the other cerebral hemiatrophy. Fifty-one patients with normal EEGs had normal CT scans. Rosenberg and coworkers, 49 concluded that careful neurologic examination and EEG may obviate CT in many patients.

Weisberg and colleagues reviewed the results of CT in several hundred patients with chronic recurrent headaches, normal physical examinations, and normal EEGS. CT abnormalities occurred in under 0.5 per cent, and some of these were considered incidental. On the other hand, in patients with chronic headache and abnormal EEGs (9 per cent of their headache group), a focal EEG abnormality correctly predicted focal CT lesions. CT abnormalities did not occur in patients with diffuse or bilateral electroencephalographic

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findings. These authors also concluded that the combination of EEG and clinical neurologic evaluation were adequate screening procedures in selected patients.

- **Cerebrovascular Disease**

Single lacunes or other discrete, small subcortical vascular lesions usually produce little or no change in the EEG. Similarly, transient ischemic attacks not associated with chronic cerebral hypoperfusion or imminent occlusion of a major vessel do not significantly affect the EEG outside the symptomatic period. Superficial cortical or large, deep hemispheric infarctions characteristically result in acute, localized electroencephalographic abnormalities. If the infarction is nonhemorrhagic, CT may be normal at a time that the EEG clearly demonstrates a functional disturbance. Gilmore and Brenner, 17 reported 32 cases of acute ischemic stroke with appropriate electroencephalographic changes (focal polymorphic delta). CT scans were normal in six (19 per cent). Masdeu and colleagues, 40 selected 20 patients with hemispheric strokes, presumably involving a substantial amount of brain tissue. Eighteen (90 per cent) had focal EEG changes on presentation, and 80 per cent developed CT lesions within 2 weeks. In three patients (16 per cent), CT was initially negative at a time that EEG demonstrated a focal finding. Thus, in patients with ischemic, nonhemorrhagic strokes, the EEG may be sensitive to functional changes in the acute period before anatomic abnormalities have appeared.

In addition to demonstrating the functional effects of acute infarction, EEG may occasionally show bilateral focal abnormalities in a patient with stroke, suggesting more extensive disease or possible emboli. Cortical laminar necrosis rarely produces CT abnormalities but often results in focal or more widespread electroencephalographic changes. 59

EEG, regional cerebral blood flow (rCBF), and cerebral metabolic rate for oxygen (CMR02) may vary independently depending on the physiologic or pathophysiologic state. For instance, diffuse slow activity occurs normally during sleep, but RCBF and CMR02 remain normal or may even increase. 47 With cerebrovascular disease, slow-wave electroencephalographic abnormalities are usually coupled to the CMR., and RCBF. Occasionally, despite a decrease in metabolic rate in the area of infarction, the RCBF is increased ("luxury perfusion"). 37 Marginal regional perfusion and possible impending infarction may be suggested by EEG and confirmed by RCBF studies in the absence of CT changes. Yanagihara and coworkers, 59 described three patients with severe occlusive disease of one or both internal carotid arteries. Two had evidence of a recent stroke and one had TIAS. Electroencephalographic findings were restricted to the involved hemisphere and ranged from continuous polymorphic delta to moderately severe intermittent delta activity. Both EEG and clinical findings improved substantially following superficial temporal-middle cerebral artery anastomosis.

Moyamoya disease (progressive occlusive disease of the internal carotid arteries and its main branches with telangiectatic perfusion of the basal ganglia) is a rare disorder, mainly affecting children, that causes progressive neurologic deficits developing in an episodic or stuttering fashion. Sunder and associates, 54 reported three children with moyamoya
Of all infectious disorders affecting the brain, EEG is most important in the initial assessment of patients with possible herpes simplex encephalitis. Because the response to treatment with adenosine arabinoside (ARA-A) worsens as the interval between onset of
symptoms and initiation of antiviral therapy increases, early and accurate diagnosis is important. Although a definitive diagnosis can still be made only by brain biopsy, characteristic electroencephalographic changes in the clinical setting of encephalitis help select patients for early treatment and biopsy. The EEG is usually abnormal before CT lesions, suggesting herpes encephalitis, has appeared. Indeed, by the time CT lesions are recognized, most patients will have an unfavorable outcome.

The electroencephalographic changes in viral encephalitis generally consist of diffuse polymorphic slow activity, usually interrupted by bursts of more rhythmic, synchronous delta waves. A normal EEG should always raise doubt about the diagnosis. When herpes simplex is the infective agent, the majority of patients will show focal temporal or frontotemporal slowing that may be unilateral, or if bilateral, asymmetric. Periodic sharp wave complexes over one or both frontotemporal regions (occasionally in other locations and sometimes generalized) add additional specificity to the electroencephalographic findings. These usually occur between the second and fifteenth day of illness, but have been seen as early as the first day and as late as 2 months after the first symptoms appeared. The presence of periodic complexes does not seem to affect prognosis. If brain biopsy is undertaken, this should preferably be done in the region of maximal electroencephalographic abnormality.

Mizrahi and Tharp described characteristic focal or multifocal periodic electroencephalographic patterns in five of six neonates with herpes simplex encephalitis. They concluded that a periodic EEG in a neonate with focal seizures and CSF lymphocyte pleocytosis was virtually diagnostic of herpes infection. Awareness of this clinicoelectrographic correlation is especially important, as this condition may be overlooked, and focal CT abnormalities typical of adult herpes encephalitis are usually absent.

Although over 90 per cent of patients with supratentorial brain abscesses will show continuous ipsilateral focal or hemispheric polymorphic delta activity, CT has largely replaced EEG in the evaluation of patients with suspected brain abscess. Nonetheless, focal electroencephalographic changes may be seen in the early stage of cerebritis, before an encapsulated lesion is demonstrable on CT. Seizures are frequent following treatment of a cerebral abscess, and interictal epileptiform discharges in the convalescent or recovery period have been associated with a relatively increased risk of occurrence of seizures.

**Brain Tumors**

Electroencephalographic changes seen with tumors result mainly from disturbances in bordering brain parenchyma, as tumor tissue itself is electrically silent. In an attempt to understand the basis of electroencephalographic changes in patients with gliomas, Newmark and colleagues compared EEG findings with information obtained by PET and CT. Metabolic rates of cortical tissue overlying isolated gliomas mainly affecting white matter were unrelated to focal delta activity. They were also unable to find a consistent relationship between cortical metabolic rate and local EEG attenuation. Thus, neither focal delta nor local depression of background rhythms seem dependent simply on cortical...
metabolic rate. Rather, focal effects are probably due to modification of synaptic activity onto cortical neurons, destruction or alterations of the cortical neurons themselves, and relative metabolic effects caused by changes in blood flow, cellular metabolism, or the microenvironment. More diffuse electroencephalographic changes may be the consequence of increased intracranial pressure, shift of midline structures, or hydrocephalus.

It is important to remember that focal epileptiform activity may precede the appearance of delta activity or an unequivocal CT lesion. In descending order of prevalence, epileptiform discharges occur in oligodendrogliomas, astrocytomases, meningiomas, metastases, and glioblastomas. 35 Tumors located near the rolandic fissure are statistically most likely, and those of the occipital lobe least likely, to cause seizures. 33 Apparent generalized epileptiform discharges may occur with mesial parasagittal lesions, especially those of the anterior and inferior frontal lobe. 55

There can be no question that CT/MRI are the procedure of choice for detecting a cerebral tumor. In individual cases, however, EEG may provide important complementary information about the physiologic state of the brain. It can, for example, give some indication of the extent of cerebral dysfunction and permit fluctuations over time to be followed. This capability is especially promising as quantitative methodology (for example, power spectral analysis) becomes more widely available and begins to be applied routinely. Another role for EEG in patients with brain tumor is to help distinguish between direct effects of the neoplasm and superimposed metabolic or toxic encephalopathies. Finally, patients with brain tumors may have episodic symptoms, and EEG will often assist in differentiating among possible epileptic, ischemic, or noncerebral etiologies.

- **Trauma**

EEG plays a limited role in the management of patients with head injuries. Transient generalized slowing of variable degree is common following concussion. Although there may be intermittent or shifting frequency and voltage asymmetries, a persistent area of continuous polymorphic delta activity should raise the suspicion of a cerebral contusion, even in the absence of a focal clinical or CT abnormality. In children, bilateral occipital slowing may persist for days after even minor trauma. Focal or diffuse electroencephalographic abnormalities during convalescence or after the acute effects of the injury have subsided may help to separate neurologic from psychologic dysfunction. There is no evidence that EEG is predictive of post-traumatic seizures, at least within the first 3 months following injury. 1,27

**SUMMARY**

We have reviewed the principal electroencephalographic findings in focal cerebral lesions and indicated practical applications for EEG in the era of CT. CT has restricted the use of EEG for detecting and localizing brain lesions, but it has also allowed EEG to focus appropriately on physiologic rather than anatomic issues. Clinically important focal electroencephalographic abnormalities may occur in the absence of CT lesions, and clinicians must understand the implications of such dissociations.
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INTRODUCTION

The electroencephalogram (EEG) is a mainstay of diagnosis for patients with epilepsy, suspected seizures, or impaired consciousness. Prior to the availability of cerebral imaging techniques, such as computed tomography (CT) scanning and magnetic resonance imaging (MRI), the EEG was critical for the diagnosis of mass lesions in the cerebral hemispheres. For example, a comatose patient whose EEG manifested decreased amplitude over one cerebral hemisphere was strongly suspected of having a subdural hematoma. Such EEG diagnosis of cerebral lesions is no longer necessary. Nonetheless, EEG is a critical tool for
defining the physiology of focal abnormalities of the cerebrum; such physiologic foci may have no neuroimaging correlates. EEG can further define the clinical significance of regions with subtle or undetected changes on CT scan or MRI.

Focal EEG abnormalities may either be transient or continuous. Transient EEG abnormalities include epileptiform patterns, such as spikes or sharp waves; these must be distinguished from other transient patterns representing benign variants that may be mistaken for pathologic findings. Continuous focal abnormalities include alterations of ongoing EEG background activity (either attenuation or enhancement), focal slow-wave abnormalities, or periodic EEG patterns that consist of rhythmic and repetitive sharp wave or spike patterns. Each of these types of abnormalities typically is associated with underlying focal pathology. More widespread central nervous system (CNS) physiologic derangements, such as those due to metabolic disturbances, can also occasionally produce such focal EEG abnormalities; most often, these are superimposed on a structural abnormality, though the lesion may not be visualized on brain imaging.

- **Epileptiform discharge**

  The interictal marker of a seizure focus is the spike or sharp wave. The distinction between these two patterns has no etiologic significance, the only difference being one of EEG pattern morphology. A spike is defined as being less than 70 milliseconds in duration, and a sharp wave has a duration of 70-200 milliseconds. The terms spike or sharp wave, while having particular meaning to the electroencephalographer, are often used interchangeably. Spikes and sharp waves are almost always of negative polarity at the scalp surface. These epileptiform discharges may arise from any region of the cerebral hemispheres but most commonly are manifested in the anterior temporal, frontal, or centrotemporal regions.

  **An anterior temporal spike** or sharp wave is highly associated with the occurrence of clinical focal-onset seizures. When this pattern is seen on the EEG, the likelihood of the individual manifesting clinical seizures is over 90%. However, the converse is not necessarily true. While the EEG of most patients with temporal lobe seizures demonstrates anterior temporal spikes, an EEG negative for this finding does not exclude a diagnosis of epilepsy. Often, repeated EEG recordings or prolonged EEG monitoring is required to demonstrate the epileptiform pattern.

  **Frontal spikes and sharp waves** also are highly associated with clinical seizures but not to the same degree as temporal discharges. Approximately 70-80% of individuals whose EEG demonstrates frontal spikes have clinical seizures. Frontal spikes or sharp waves are more likely to be associated with mass lesions such as neoplasms, traumatic lesions, or congenital cerebral malformations.

  **Centrotemporal or rolandic sharp waves** are often a marker for a particular epilepsy syndrome of childhood known as benign rolandic epilepsy or benign focal epilepsy of childhood with centrotemporal spikes. This is a disorder in which a child, typically aged 4-12 years, develops focal seizures with sensory or motor seizures in the mouth or face region. These children also may have generalized seizures; typically, these seizures are
nocturnal. The EEG pattern is unusual in that there is often a simultaneous negative waveform in the centrotemporal region and a positive one in the frontal region. This pattern of EEG polarity is virtually diagnostic of benign rolandic epilepsy.

Epileptiform EEG patterns are seen less commonly in the occipital, central, or parietal regions. Occipital spikes typically are seen in young children and may or may not be associated with clinical seizures. Discharges in any of these regions may indicate the presence of partial epilepsy.

Table 1. Electroclinical criteria of spike/ sharp wave discharge

- A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG.
- A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.
- Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.
- The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.
- Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an
epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.

- The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. Low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.

- **Focal alteration in EEG background activity**

Visual analysis of the EEG includes evaluation of certain background rhythms, particularly the posterior predominant alpha rhythm, in terms of amplitude, frequency, reactivity, and symmetry. Any of these may be affected by regional alterations in brain function, usually due to focal intracranial lesions.

**Amplitude abnormalities**

Amplitude differences need to be interpreted with caution since isolated differences in amplitude may occur as a normal finding. The alpha rhythm may be increased in amplitude on one side, most often the right, by up to a 2:1 ratio. Less commonly, the alpha rhythm of the left hemisphere is increased by as much as a 3:2 ratio. More pronounced differences in background amplitude are abnormal.

Markedly diminished background amplitude on one side of the EEG, compared to homologous channels of the contralateral hemisphere, is found with abnormalities of cortical gray matter, or with excess fluid between the cortex and recording electrodes. This finding is characteristic of ischemic stroke with gray matter involvement or subdural hematoma. In patients with gray matter involvement, there is typically concurrent white matter involvement causing polymorphic delta activity. Decreased background amplitude also may occur with congenital lesions, such as porencephalic cysts, or with Sturge-Weber syndrome. Transient background attenuation also is characteristic of the postictal EEG of patients with focal-onset seizures. Less commonly, ipsilateral to cerebral lesions, enhancement of the alpha rhythm, sleep spindles, beta activity, or mu rhythm can be seen.

Amplitude abnormalities seen in the presence of skull defects should also be mentioned in the context of focal EEG disturbances. The breach rhythm is an accentuation of EEG amplitude in the region of a skull defect. This results from decrease in the filtering effect of the skull, and affects primarily faster frequencies, so that theta, alpha, and especially beta are accentuated more than delta, and waveforms appear unusually sharp.
Alterations in EEG background frequency typically are most useful in the assessment of diffuse rather than focal cerebral disturbances. The EEG background frequency of the two hemispheres in the adult EEG should be within 1 Hertz (Hz). Any greater difference is indicative of a lateralized EEG abnormality on the side with the slower background.

**Reactivity**

In focal cerebral lesions, the posterior predominant frequency may show unilateral impairment of reactivity to eye opening (Bancaud phenomenon) or alerting. Lesions do not need to be in the occipital lobes to produce these abnormalities of EEG reactivity.

- **Focal slowing**

**Polymorphic delta activity (PDA)** consists of arrhythmic slow waves that vary in frequency, amplitude, and morphology. PDA can occur in either a focal or generalized distribution. Continuous PDA is indicative of abnormalities involving subcortical white matter. One of the shortcomings of standard scalp EEG recordings is their limited spatial resolution. This holds true for the relationship of PDA to an underlying structural abnormality. Not only is the inherent localizing ability of the scalp EEG limited, but also the PDA of a structural lesion is referable not to the lesion itself but to the surrounding brain tissue. Because of this limitation, the area of a lesion is indicated not by the maximal amplitude of PDA but rather by a region of relatively low-amplitude slowing. Continuous, rather than intermittent, PDA is associated with large lesions, mass effect, and impairment of consciousness.

Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (white matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
Figure 2. Polymorphic slow wave activity in a patient with subcortical glioma, notice the marked variability in wave shape morphology, frequency and amplitude.

Table 2. Electrical criteria of the Polymorphic slow wave activity.

- Quite variable in wave shape morphology, frequency and amplitude.
- Commonly lateralized over a wide area of the scalp, persistent in eye closed, eye open state, during all sleep stages, with no visual reactivity. Polymorphic Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology.
- Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
- Commonly due to a subcortical white matter lesion inducing deafferentation of the cerebral cortex.
- A purely cortical lesion does not induce polymorphic slow wave activity.

Rhythmic delta activity consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized. In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]). Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies. FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy. In cases of encephalopathy with FIRDA, the pathophysiologic processes are believed to involve cortical and subcortical gray matter. OIRDA is associated with absence epilepsy in children aged 6-10 years.
The intermittent rhythmic delta activity and the polymorphic slow wave activity

**Table 3. Electrical criteria of The intermittent rhythmic delta activity.**

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA]).
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.

**Focal theta activity** is less likely to reflect a macroscopic structural lesion than is focal delta. Theta is commonly, however, associated with a functional disturbance, such as epileptogenic cortex, especially postictally, after amplitude suppression and focal delta have resolved. In addition, localized theta is usually superimposed on focal delta to some degree; the relative proportion of delta and theta reflects the size and/or severity of the underlying structural or functional cerebral abnormality.

- **Periodic EEG patterns**

**Periodic lateralized epileptiform discharges (PLEDs)** are EEG abnormalities consisting of repetitive spike or sharp wave discharges, which are focal or lateralized over one hemisphere, recur at intervals of 0.5-5 seconds, and continue through most of the duration.
of the EEG study. They are seen most frequently in the setting of acute unilateral lesions such as cerebral infarctions. They also may occur in other cerebral diseases, such as encephalitis or tumors, or in the setting of chronic lesions or long-standing epileptic disorders. PLEDs are usually self-limited and resolve after the acute phase of a cerebral insult. Rarely, they may persist on a chronic basis. Seizures often occur when PLEDs are seen on the EEG, but clinical and electrographic seizure manifestations typically differ from the baseline (PLEDs) condition. Certain paroxysmal neurologic symptoms, such as epilepsy partialis continua or transient confusional states, may be associated with PLEDs.

Bilateral independent PLEDs (BIPLEDs) are periodic complexes over both hemispheres. BIPLEDs are not synchronous and may differ in morphology and site of maximal expression on each side. This is an uncommon EEG finding. In a series of 18 patients, the most common etiologies were anoxic brain injury (28%) and CNS infection (28%). While BIPLEDs have been associated with herpes simplex encephalitis, the pattern can occur in other CNS infections as well.

The clinical correlates of BIPLEDs differ somewhat from that of PLEDs. With BIPLEDs, there is a higher incidence of coma (72% vs 24%), higher mortality rate (61% vs 29%), and less likelihood of focal seizures or focal neurologic deficits.

Brenner and Schaul have reviewed the classification of periodic EEG patterns based on the interval between the discharges, topographic distribution, and synchrony between hemispheres.

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INTRODUCTION

Before the advent of modern neuroimaging, EEG was the best noninvasive tool to use in searching for focal lesions. In the last few decades, with progress in imaging techniques, the role of EEG is changing; its use for localization of a brain lesion is being superseded by neuroimaging. The utilization of EEG outside of epilepsy has declined markedly.

The use of EEG in monitoring brain activity in the operating room and also in intensive care settings needs to be redefined and its utility reassessed. In clinical situations in which the primary question is the electrical functioning of the brain and not primarily localization, EEG will remain a necessary test. EEGs are performed routinely in various
clinical situations; therefore the neurophysiologist is expected to be familiar with the EEG findings even in situations in which they are of relatively limited value.

Like most neurophysiologic tests, EEG is a test of cerebral function; hence for the most part it will be nonspecific as to etiology. Although at one time authors discussed the application of EEG in differentiating various types of lesions, this clearly has not been clinically useful in the modern era. The exercise of describing EEG abnormalities by pathology (eg, stroke, abscess, tumor, even various types of tumors!), which was common in old EEG texts, is therefore not followed here. Instead, the different patterns of focal (nonepileptic) disturbances of brain function and their clinical significance are reviewed.

- **Waveform description**

**Slow activity**

Abnormal slow activity is by far the most common EEG manifestation of focal brain dysfunction. The abnormality that correlates best with the presence of a structural lesion is polymorphic or arrhythmic (as opposed to monomorphic or rhythmic) delta (ie, 1-3 Hz) slowing. This is all the more reliable when it is continuous, unreactive (ie, characterized by lack of change between states, such as wake or sleep, or in response to external stimuli), of high amplitude, polymorphic, and unilateral. The localization of slow potentials follows the same rules as that of epileptiform discharges. Thus, “phase reversals” are useful to localize slow potentials and do not imply abnormality or epileptogenicity.

**Amplitude asymmetry**

In the classification used here, the term asymmetry refers to asymmetry of amplitude and to normal rhythms. By contrast, a focal frequency asymmetry would be classified as focal slow (Lüders and Noachtar). Finally, readers should keep in mind that amplitude asymmetries should be evaluated on referential montages, since amplitude is highly dependent on interelectrode distances.

**Periodic lateralized epileptiform discharges**

Described in 1964 by Chatrian et al, periodic lateralized epileptiform discharges (PLEDS) are a special type of focal abnormality. As implied by their name, they are periodic, lateralized, and epileptiform. Periodicity is the most characteristic feature, and the one that sets PLEDs apart from other focal abnormalities. Periodicity refers to a relatively constant interval between discharges, which varies between 0.5 and 3 seconds and most often is around 1 second. The epileptiform morphology of the discharges is not invariable, as PLEDs are often closer to slow waves than to sharp waves in morphology.
Clinical correlation

Slow activity

Continuous focal slow activity is the only nonepileptiform focal abnormality that can be interpreted unequivocally as abnormal when it is an isolated finding. Other focal abnormalities are quite frequent but are of such low specificity that they almost never constitute an abnormality in themselves. To be interpreted as abnormal, these usually require the coexistence of a more definite abnormality such as slowing or epileptiform discharges.

As already outlined, focal slowing is nonspecific as to etiology, and in the era of neuroimaging the EEG has no role in diagnosing the nature of a lesion. Focal slowing is the most common abnormality associated with focal lesions of any type, including (but not limited to) neoplastic, vascular, subdural collections, traumatic, and infectious. It occasionally may be seen even in more subtle structural abnormalities such as mesiotemporal sclerosis or focal malformations of cortical development.

The physiologic basis for focal polymorphic delta activity caused by focal cortical lesions is not fully understood. It is probably due to abnormalities in the underlying white matter rather than the cortex itself. When present, focal slow activity correlates highly with the side of the lesion, but it is not reliable for lobar localization. The likelihood of a structural lesion (ie, specificity) diminishes when the slow activity lacks these characteristics and is intermittent, in the theta rather than the delta range, and of low amplitude. This type of slowing may be normal (eg, temporal slowing of the elderly). This is essentially the difference between focal “continuous slow” and “intermittent slow” (Lüders and Noachtar).

In a few situations in clinical neurology, the EEG may show clear evidence of focal dysfunction (ie, focal slow) while no structural abnormality is found. The typical cases in point are the focal epilepsies. A readily demonstrable structural lesion usually is not found on neuroimaging, typically MRI.

Focal brain dysfunction without structural abnormalities has been observed in transient ischemic attacks (TIA), migraine, and postictal states. Polymorphic delta activity in these cases may be indistinguishable from that caused by a structural lesion, except that it is short-lived (ie, it disappears over time). The postictal state is the most common cause of nonstructural polymorphic delta activity, but the activity disappears within minutes to hours after the ictal event. Patients with ongoing TIAs or migraine rarely undergo an EEG during the symptomatic period, so clinical data are scarce.

Amplitude asymmetry

Destructive lesions clearly can attenuate the amplitude of normal rhythms. However, normal rhythms are never perfectly symmetric in amplitude, therefore which asymmetries
to consider significant is not always clear. (Some have proposed a greater than 50% side-to-side difference as abnormal.)

A good rule of thumb is that, with very few exceptions, significant focal asymmetries are associated with slowing. The authors recommend that any amplitude asymmetry associated with slowing of frequency be considered significant.

Amplitude asymmetry or suppression of normal rhythms is somewhat more likely to be seen in structural abnormalities that increase the distance or interfere with the conduction of the electrical signal between the cortex and the recording scalp electrodes. Examples include subdural collections (eg, hematoma, empyema), epidural collections (eg, hematoma, abscess), subgaleal collections, and calcifications such as those seen in Sturge-Weber syndrome.

Amplitude asymmetry also may be more common than slowing in subdural hematomas. However, caution must be exercised before considering isolated nonepileptiform focal findings other than slowing as abnormal. In general, as with other types of focal EEG abnormalities such as slowing, amplitude asymmetry is nonspecific as to etiology.

Although asymmetry in amplitude is usually indicative of dysfunction on the side of depressed amplitude, one notable exception to this rule is the so-called breach rhythm. This is caused by a skull defect, which attenuates the high-frequency filter function of the intact skull. As a result, faster frequencies (eg, alpha, spindles, beta) are of higher amplitude on the side of the defect. Since morphology often is sharply contoured, determining the epileptogenicity of these discharges can be extremely difficult, and in this situation erring on the conservative side, by not interpreting them as epileptiform, is clearly preferable. Because of a cancellation effect between frontopolar (Fp1/Fp2) and frontal (F3/F4), eye movements often are not increased on the side of a skull defect and may indeed be of lesser amplitude on that side.

**Periodic lateralized epileptiform discharges**

PLEDS are caused by acute destructive focal lesions and are a transitory phenomenon: they tend to disappear in weeks, even if the causal lesion persists. Over time, the record takes on a less specific focal slow appearance, which is more likely to persist. By far the most common etiology is an acute cerebrovascular event; second most common is focal encephalitis such as that caused by herpes. In a clinical context suggestive of viral encephalitis, the EEG can be of great value for diagnosis and can guide tissue biopsy. Though most often associated with an acute destructive lesion, PLEDS, like other EEG findings, are not specific as to etiology and have been described in almost all types of structural lesions, including subdural hematoma and chronic lesions, especially in the presence of a superimposed systemic disturbance.

In keeping with their epileptiform morphology, PLEDS have a close association with clinical seizures, and on average about 80% of patients with PLEDS have clinical seizures. The transition between PLEDS and a clear ictal seizure pattern is very gradual, illustrating
the hypothesis that PLEDS may represent a subclinical ictal pattern. In clinical practice, however, PLEDS usually are managed as interictal discharges (ie, spikes or sharp waves). They indicate a high risk for focal seizures, but usually are not treated with antiepileptic drugs unless clinical evidence for seizures is noted. This position is endorsed by the authors and others. This is somewhat controversial, however, and some advocate antiepileptic treatment in all patients with PLEDS.

Periodic patterns in Creutzfeldt-Jakob disease usually are generalized and bisynchronous (see articles on encephalopathies) but occasionally, especially early in the course, they may be unilateral or markedly asymmetric, and thus take on the appearance of PLEDS.

Other less common focal patterns

An abnormal response to photic stimulation can be seen in focal lesions. Normal photic driving has long been known to be potentially reduced on the side of a lesion. Posterior destructive lesions are particularly likely to attenuate the driving response, but some reports have described an enhanced photic response on the side of dysfunction. However, since the normal driving response can be quite asymmetric, such a finding should be accompanied by a more reliable abnormality such as slowing of the waveform frequency in order to be interpreted as abnormal.

The Bancaud phenomenon refers to the unilateral loss of reactivity of a normal rhythm and initially was described in the context of the alpha rhythm. It should be considered a pathological finding only when associated with other more definite abnormalities, such as slowing.

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INTRODUCTION

Generalized EEG abnormalities typically signify dysfunction of the entire brain, although such dysfunction may not be symmetric in distribution. Generalized patterns thus may be described further as maximal in one region of the cerebrum (e.g., frontal) or in one hemisphere compared to the other. Identification of an abnormality as generalized may require analysis of the EEG by several montages to determine lack of focality. Careful elimination of external and bioelectric artifact is important to avoid misinterpretation of noncerebral activity (e.g., ECG), which can contaminate multiple channels, appearing as generalized abnormalities.

This chapter discusses EEG patterns that usually are generalized and are not considered primarily ictal. Many of these patterns occur in encephalopathic states, which themselves
can lower a patient’s threshold for seizures. Some patterns can be considered "epileptiform" since they contain spikes, sharp transients, or rhythmic paroxysmal patterns. Remember that the term "epileptiform" is descriptive of an EEG’s appearance only and does not necessarily imply that the pattern is "epileptogenic."

**SLOW ACTIVITY**

- **Alpha coma**

Unremitting 8- to 13-Hz EEG activity that is unresponsive to eye opening or other stimulation has been termed alpha coma. This activity differs in appearance from alpha rhythm (normal background activity) in its lack of reactivity and its spatial distribution. It is monorhythmic, diffuse, or may have anterior accentuation. Only minor fluctuations in amplitude occur, and no reactivity to external stimulation can be elicited. Spindle coma is similar in appearance and implications but consists of monorhythmic 13- to 15-Hz activities without reactivity. This pattern must be distinguished from normal alpha rhythm in the locked-in state and from slower segments of 10- to 18-Hz rhythms observed in various intoxications.

Alpha coma can be found in comatose patients with brainstem lesions and in severe posttraumatic and anoxic encephalopathies. Although this pattern indicates a poor prognosis, instances of recovery have been reported occasionally.

- **Diffuse slowing**

Generalized continuous theta and delta patterns occur in comatose and encephalopathic states of multiple potential etiologies. Patterns that fail to respond, either in amplitude or frequency, to noxious, auditory, or visual stimuli carry a poor prognosis for meaningful neurologic recovery. Similar patterns with preserved reproducible reactivity imply potential for some recovery and should be compared to recordings repeated several days later. These patterns must be distinguished from those of normal drowsiness and sleep.

- **Intermittent delta**

Intermittent rhythmic delta activity (IRDA) usually occurs at frequencies of 2-2.5 Hz with relatively sinusoidal, stereotypic, bilaterally synchronous waveforms appearing in short bursts. The ascending phase is sloped more steeply than the descent, and waves are typically bilateral and widespread with peak amplitude frontally in older individuals (FIRDA) and occipitally in children (OIRDA). These patterns attenuate with alerting or eye opening. Eye closure, drowsiness, and hyperventilation accentuate IRDA. Although IRDA disappears in stage 2 and deeper non–rapid eye movement (REM) sleep, it may reappear in REM sleep.

Multiple etiologies can result in IRDA, including metabolic, toxic, hypoxic, or various diffuse or focal intracranial diseases. Even when IRDA occurs unilaterally in association with a focal cerebral lesion, the lateralization of IRDA may be ipsilateral or contralateral.
to the lesion. Thus IRDA is a nonspecific nonlocalizing EEG pattern, unless associated with other focal findings on the EEG. Although the mechanisms for production of IRDA are understood incompletely, studies correlating with pathologic specimens suggest that IRDA is associated primarily with diffuse gray matter disease.

The degree of encephalopathy manifested appears to correspond to the proportion of IRDA on the EEG. This pattern must be distinguished from the frequently encountered frontally maximal intermittent delta that can be seen in drowsy elderly patients.

Figure 1. The intermittent rhythmic delta activity [left image] and the the polymorphic slow wave activity [right image]

Table 1. Electrical criteria of The intermittent rhythmic delta activity.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA])
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.
PERIODIC ABNORMALITIES

- **Burst suppression**

High-voltage bursts of slow, sharp, and spiking activity alternating with a suppressed background have been termed burst suppression. The duration of bursts or suppressed epochs is highly variable. Myoclonic jerking can occur concomitantly with the bursts and may be ictal. Chemical paralysis in the intubated ventilated patient is required to determine if the patterns of ictal potential persist after elimination of motion artifact. The endogenous pattern of burst suppression needs to be distinguished from pharmacologically induced patterns (eg, with etomidate, barbiturates, benzodiazepines). This pattern is encountered in deep coma and has been suggested as the final pattern in deterioration of generalized status epilepticus.

- **Subacute sclerosing panencephalitis**

Subacute sclerosing panencephalitis (SSPE) is an inflammatory disease of children and adolescents caused by chronic infection with the measles virus. The characteristic EEG pattern, initially described by Radermecker and Cobb and Hill, consists of high-voltage (300-1500 mV), repetitive, polyphasic sharp and slow wave complexes of 0.5- to 2-second duration that recur every 4-15 seconds. Rarely, the complexes can occur at intervals of 1-5 minutes. The interval between complexes may shorten as the disease progresses.

  The morphology of the waveforms tends to be consistent in a single recording but may be strikingly variable with disease progression. Although the complexes are usually symmetric and synchronous, they may be asymmetric with a time lag between hemispheres or lobes. The EEG usually is not changed by stimuli except in the earliest stages of the disease or in remission, when the EEG pattern tends to be more inconstant. The EEG background is slow and progressively more disorganized as the disease advances. The stages of sleep eventually become difficult to distinguish.

  Abnormal movements, cognitive deterioration, and the diagnostic EEG characterize the clinical disease. Stereotypic jerking or other movement abnormalities occur with the periodic complexes. Rarely, the periodic complexes become apparent before the movements manifest. The movements often disappear in sleep, even though the complexes persist.

**JAKOB-CREUTZFELDT DISEASE**

This disease is a long-latency infection caused by a prion. The characteristic EEG shows biphasic or triphasic discharges that are initially sporadic and may even be asymmetric. As the disease advances, the pattern becomes generalized and synchronous with continuous periodic stereotypic 200- to 400-millisecond sharp waves occurring at intervals of 0.5-1.0 seconds. Myoclonic jerks often occur in association with the sharp waveforms, but the relationship is not constant. Late in the illness and during sleep, myoclonic jerks disappear, despite the persistence of the periodic EEG. The sharp waves typically react to external stimuli. Early in the disease, alerting the patient may elicit the periodic pattern; later, when
the periodic pattern is readily apparent, rhythmic photic or other stimuli can "drive" the periodic frequency. Benzodiazepines or barbiturates can temporarily eliminate both myoclonic jerks and periodic patterns.

**ELECTROCEREBRAL INACTIVITY**

EEGs are performed occasionally to provide supportive evidence of brain death. Although brain death is defined by clinical criteria, some situations preclude complete or definitive examination findings (such as severe open head or eye trauma). In such situations, a confirmatory test is often helpful. Cerebral angiography demonstrating no blood flow is the most sensitive and specific confirmatory test, but it also is time and labor intensive and may be refused by the family as it is highly invasive. An EEG may be a reasonable alternative, but it needs to be performed according to strict criteria for clinical as well as medical-legal determinations.

Electrocerebral inactivity (ECI), or electrocerebral silence (ECS), is defined as no cerebral activity over 2 mV using a montage that uses electrode pairs at least 10 cm apart with interelectrode impedances <10,000 ohms and >100 ohms.

According to guidelines of the American Clinical Neurophysiology Society, the following are minimum technical standards for EEG recording in suspected brain death:

- A minimum of 8 scalp electrodes
- Impedances between 100 and 10,000 ohms
- Integrity of entire recording system tested by touching each electrode individually to obtain appropriately located artifact potential
- Interelectrode distances of at least 10 cm
- Sensitivity of at least 2 mV for 30 minutes of the recording, with appropriate calibrations documented
- High-frequency filter (HFF) not set below 30 Hz and low-frequency filter (LFF) not set above 1 Hz
- Additional monitoring techniques used as necessary to eliminate or prove waveforms are artifactual
- No EEG reactivity to strong and thorough tactile, auditory, or visual stimulation
- Recording performed by a qualified technologist working under the direction of a qualified electroencephalographer
- If ECI in doubt, EEG repeated after an interval (suggested 6 h)

**REFERENCES**

Electroencephalogram (EEG) abnormalities can be divided into three descriptive categories:

a) Distortion and disappearance of normal patterns,

b) Appearance and increase of abnormal patterns, and

c) Disappearance of all patterns.

The description of the above EEG abnormalities can be further expanded by identifying their spatial extent (local or widespread, unilateral or bilateral) and their temporal persistence (brief and intermittent or prolonged and persistent). The intermittent abnormalities characterized by the sudden appearance and disappearance of a pattern are called "paroxysmal."

The above classification of EEG abnormalities is purely descriptive. In addition to descriptive categorization, EEG abnormalities can be subdivided on the basis of their usual clinical correlations. Most abnormal patterns, whether persistent or intermittent, are...
nonspecific because they are not associated with a specific pathological condition or etiology. However, some patterns usually occurring paroxysmally with distinctive wave forms (such as spike, spike and wave, sharp wave, seizure pattern, or periodic complexes) are specific in that they are frequently associated with specific pathophysiological reactions (such as epilepsy) or a specific disease process (such as SSPE or Jakob- Creutzfeldt). This chapter will deal with the nonspecific abnormalities.

In spite of the fact that nonspecific abnormalities are not related to a specific pathophysiologic reaction or a specific disease process, they nonetheless can be divided into three basic categories based on their usual association with different types of cerebral disturbances. These three basic categories are:

1. Widespread intermittent slow abnormalities, often associated with an active (improving, worsening, or fluctuating) cerebral disturbance;

2. Bilateral persistent EEG findings, usually associated with impaired conscious purposeful responsiveness; and

3. Focal persistent EEG findings, usually associated with focal cerebral disturbance.

The above divisions are based on the usual clinical correlates, but it is important to realize that these correlations are statistical and not absolute. The best intuitive grasp of the somewhat variable relationship between EEG abnormalities and clinical or other laboratory evidence of central nervous system (CNS) disturbance is obtained when the EEG is viewed as an extension of the neurologic examination. When viewed from this perspective, the EEG studies electrical signs of neurologic function, whereas the neurologic examination studies physical signs. In any one patient, depending on the nature and location of the pathology, abnormalities may be found in both EEG and clinical examination, in only one examination, or in neither, just as abnormalities may be found in one, both, or neither of two subsets on the clinical examination (such as reflex and sensory examination). Furthermore, the results of both EEG and clinical evaluation may be normal although the patient has anatomic abnormalities detectable by contrast studies or computerized tomography. The opposite also holds, in that both the EEG and clinical examination may show distinct abnormalities when radiographic studies are normal. An intelligent integration of the results of functional tests (such as the EEG and clinical examination) with radiographic tests which study anatomy (such as contrast studies or computerized tomography) requires an understanding of the value and limitation of each test, as well as the overall clinical field of neurology. With this conceptual background, nonspecific EEG abnormalities will be discussed based on the three general categories of clinical correlation.
WIDESPREAD INTERMITTENT SLOW ACTIVITY ASSOCIATED WITH AN ACTIVE CEREBRAL DISTURBANCE

- Description

Morphologically, this type of abnormality is characterized by intermittent rhythmic slow activity often in the delta frequency range, thus accounting for its descriptive acronym, IRDA (intermittent rhythmic delta activity). When in the delta frequency range, it is often composed of runs of sinusoidal or sawtoothed waves with more rapid ascending than descending phases with mean frequencies close to 2.5 Hz. The waves are relatively stereotyped in form and frequency and occur in short bursts. This pattern usually demonstrates reactivity; it is attenuated by alerting and eye opening and accentuated with eye closure, hyperventilation, or drowsiness (stage 1, nonREM sleep). With the onset of stage 2 and deeper levels of nonREM sleep, the abnormal IRDA disappears. However, in REM sleep the abnormal IRDA may again become apparent.

Intermittent rhythmic delta activity is usually bilateral and widespread in distribution, with peak localization strongly influenced by age. In adults, the peak amplitude of the pattern is usually localized over the frontal area, thus giving rise to the acronym, FIRDA (frontal IRDA), whereas in children the peak amplitude frequently develops over the occipital or posterior head regions, giving the acronym, OIRDA (occipital IRDA). This difference in location from adults to children is not related to difference in pathological processes, but simply reflects an age-determined variation in what is an otherwise similar, nonspecific reaction to a wide variety of changing pathological processes.

Figure 1. Frontal intermittent rhythmic delta activity (FIRDA) associated with widespread polymorphic delta activity produced by drug intoxication.
Figure 2. Occipital intermittent rhythmic delta activity (OIRDA) associated with right cerebellar astrocytoma, the posterior maximum of the OIRDA is age-dependant and not related to the location of the pathology.

- **Etiologic Nonspecificity of IRDA**

IRDA is not specific for a single etiology and can occur in response to systemic toxic or metabolic disturbances as well as diffuse or focal intracranial diseases. This may be due to diverse etiologies, such as infectious, inflammatory, degenerative, traumatic, vascular, or neoplastic disorders.

Figure 3. Frontal intermittent rhythmic delta activity (FIRDA) associated with disorganized background after subarachnoid haemorrhage.

IRDA is also the nonspecific type of slowing that occurs in normal individuals in response to hyperventilation. In such cases, it should not be interpreted as an abnormality, but rather as the response of a normal CNS to the stress of an acutely changing pCO.
Nonlocalizing Nature of IRDA

Since IRDA may occur in response to systemic toxic or metabolic disturbances, diffuse intracranial pathology, or focal intracranial pathology, its localizing value obviously is limited. Even when it is due to a focal expanding lesion, the peak localization of the IRDA tends to be age-dependent (maximal frontal in adults and maximal posterior in children). It is independent of the localization of the lesion, which may be at some distance, either in the supra- or infratentorial space, from the maximum expression of the IRDA. The recognition that IRDA is a nonlocalizing rhythm, even when associated with an intracranial lesion, led to its earlier designation as a "projected" or "distant" rhythm. Such a designation, however, can be misleading because it encourages the misconception that the IRDA, associated with a "distant" lesion, is morphologically distinct from IRDA due to diffuse intracranial disease or a systemic toxic or metabolic disturbance.

Although frequently bilateral, IRDA may occur predominantly unilaterally. Even when it occurs unilaterally in association with a lateralized supratentorial lesion, the lateralization of the IRDA, although usually ipsilateral, may even be contralateral to the focal lesion. Therefore, when IRDA is present, determining whether it is due to a focal lesion (and if so, the location of the focal lesion) is best based on persistent localizing signs discussed later and not on the morphology or even the laterality of IRDA.

Mechanisms Responsible for IRDA

The mechanisms responsible for the genesis of IRDA are only partially understood. Earlier studies investigated the mechanisms of IRDA-associated lesions producing increased intracranial pressure. It was recognized early that with benign intracranial hypertension (pseudotumor cerebri), IRDA was not present. However, in increased intracranial pressure with tumor or aqueductal stenosis, IRDA is frequently present. Based on this, earlier workers related the appearance of IRDA to increased intraventricular pressure within the third ventricle tending to produce an acute or subacute dilatation of the third ventricle. Later studies investigated the appearance of IRDA in diffuse encephalopathies with documented post mortem histopathological changes. Based on these studies, it was concluded that the main correlate of IRDA was diffuse gray matter disease, both in cortical and subcortical locations. Finally, any comprehensive theory about the origin of IRDA must not only take into account that IRDA is found in diverse systemic and intracranial processes, but must also take into consideration that IRDA is more likely to appear during the course of an active (fluctuating, progressing, or resolving) cerebral disturbance and less likely to be associated with a chronic, stable, cerebral disturbance. Clinically, the earliest correlate of the appearance of IRDA, especially in an otherwise normal EEG, is a subtle, fluctuating impairment of attention and arousal. As the condition progresses, often leading to more persistent, bilateral abnormalities, frank alteration in consciousness appropriate to the degree of persistent, bilateral abnormalities usually appear.

In summary, IRDA is nonspecific in that it can be seen in association with a wide variety of pathological processes varying from systemic toxic or metabolic disturbances to focal intracranial lesions. Even when associated with a focal lesion, IRDA by itself is
nonlocalizing. The common denominator in the wide variety of pathological processes producing IRDA is that, when such an abnormality appears, it is likely to be associated with the development of widespread CNS dysfunction; the earliest clinical correlates are fluctuating levels of alertness and attention. With focal lesions, one mechanism may be an increased transventricular pressure with secondary disturbances at both the subcortical and cortical levels. With primary intracranial encephalopathies, it appears to be due to widespread involvement of the gray matter at subcortical and cortical levels.

Figure 4. The intermittent rhythmic delta activity [left image] and the the polymorphic slow wave activity [right image]

Table 1. Electrical criteria of The intermittent rhythmic delta activity.

- Consists of sinusoidal waveforms of approximately 2.5 Hz that occur intermittently in the EEG recording. It is most often symmetric but can be lateralized.
- In adults, the delta activity has a frontal predominance (frontal intermittent rhythmic delta activity [FIRDA]). In children, it is maximal posteriorly (occipital intermittent rhythmic delta activity [OIRDA])
- The intermittent rhythmic delta activity shows visual reactivity and is commonly suppressed in the eye open state unless the patient is comatose.
- Intermittent rhythmic delta activity is associated with structural lesions, most commonly diencephalic, infratentorial or intraventricular tumors, or with diffuse encephalopathies.
- FIRDA occurring in patients with a normal EEG background suggests that the pattern is due to a structural lesion; when associated with EEG background abnormalities, it is likely to be due to encephalopathy.
- OIRDA is associated with absence epilepsy in children aged 6-10 years.
FOCAL PERSISTENT EEG FINDINGS ASSOCIATED WITH FOCAL CEREBRAL LESIONS

As was done in the preceding section on bilateral persistent EEG findings, focal persistent EEG abnormalities can be divided into the following general descriptive types. These are a) distortion and disappearance of normal patterns, b) appearance and increase of abnormal patterns, and c) disappearance of all patterns.

There is some overlap in the first two types of abnormalities, since abnormal rhythms may be related to the distortion of previously recognized normal rhythms. Disappearance of all rhythms in a focal area can seldom be seen at the cerebral cortex, although they may be detected with electrocorticography.

The focal distortion of normal rhythms may produce an asymmetry of amplitude, frequency, or reactivity of the rhythm. Amplitude asymmetries alone, unless extreme, are the least reliable finding. Amplitude may be increased or decreased on the side of focal abnormality. However, if there is focal slowing of physiologic rhythms (for example, the alpha rhythm) by 1 Hz or more, this usually identifies reliably the side of focal abnormality, whether or not the amplitude of the rhythm is increased or decreased. The unilateral loss of reactivity of a physiologic rhythm, such as the loss of reactivity of the alpha rhythm to eye opening or to mental alerting, also reliably identifies the focal side of abnormality. Because of shifting asynchronies and asymmetries of the mu rhythm, the exact limits of normal asymmetry become more difficult to define; however, the asymmetrical slowing of the central mu rhythm by 1 Hz or more, usually associated with an increase in amplitude, is a reliable sign of focal abnormality often of a chronic nature.

In addition to the waking rhythms discussed above, the normal activity of sleep inducing spindles and vertex waves may be distorted or lost by a focal lesion in the appropriate distribution.
Figure 5. Frontal intermittent rhythmic delta activity (FIRDA) associated with widespread polymorphic delta activity in a patient with encephalitis.

As normal rhythms are distorted, focal abnormalities may produce focal persistent polymorphic delta activity (PPDA), one of the most reliable findings of a focal cerebral disturbance. The more persistent, the less reactive, and the more polymorphic such focal slowing, the more reliable an indicator it becomes for the presence of a focal cerebral disturbance.

Intermittent rhythmic delta activity (IRDA) may be seen with a focal cerebral disturbance but, as mentioned earlier, it is both nonspecific as far as etiology and nonlocalizing. When present in association with a focal cerebral lesion, it usually implies that the pathological process is beginning to produce an active cerebral disturbance of the type that is likely to become associated with changing (fluctuating or progressive) impairment of attention and alertness.

Focal epileptiform abnormality may occur in association with focal cerebral abnormalities, but since they have a relatively specific association with additional symptomatology such as epilepsy.

- **Etiologic Nonspecificity**

The above abnormalities do not reflect the underlying etiology but simply reflect that a pathological process is present. Similar abnormalities may occur, whether they result from focal inflammation, trauma, vascular disease, brain tumor, or almost any other cause of focal cortical disturbance, including an asymmetrical onset of CNS degenerative diseases.

- **Persistent Focal Abnormalities and Other Evidence of Focal Cerebral Disease**

In general, no matter what the etiology, there is a rough correlation between the EEG evidence of focal cerebral disturbance and clinical as well as radiographic evidence of focal
cerebral disturbance. However, in spite of this rough relationship, there are striking examples of lack of correlation in both directions. Some of this lack of correlation is understandable. For instance, a small infarct in the internal capsule is likely to be missed both by radiographic studies and EEG studies, in spite of the fact that its presence may be readily detected by significant abnormalities on clinical examination. On the other hand, both the clinical examination and the EEG may be strikingly normal in spite of the fact that the computed tomography (CT, MRI) scan shows evidence of a well-described cystic or calcified lesion in the silent area of the brain, which may have been present in a relatively nonprogressive form for a long period of time. Finally, the EEG may show major abnormalities in spite of a normal clinical examination with positive CT findings, provided the lesion is in a clinically silent area, such as one temporal or frontal lobe. With a transient ischemic attack, it is common for the clinical examination, the radiographic studies, and the EEG to be normal within attacks.

Nonetheless, in our experience, there are a small percentage of patients who have transient ischemic attacks likely on a hemodynamic basis, rather than on the more common embolic basis, who retain a major EEG abnormality in spite of the fact that their CT scan/MRI are normal and their neurologic examination has returned to normal after the transient attack. The exact mechanism responsible for this is uncertain, but it is interesting to note that another apparent hemodynamic cause of transient neurologic deficit in complicated migraine also may be associated with a marked residual EEG abnormality even when the neurologic examination has returned to normal and even when the CT scan is normal. Finally, it is not uncommon for the EEG to show clear-cut abnormalities and focal lesions without neurologic deficit without CT abnormalities when there is an associated epileptogenic process.

Chronic widespread hemispheric disease, such as Sturge-Weber syndrome or infantile hemiplegia, characteristically produces widespread voltage attenuation over the abnormal hemisphere. In one study, this electrographic accompaniment was seen in every patient with Sturge-Weber disease even when there was no associated focal neurologic deficit. These asymmetries were noted even in young children prior to the development of the characteristic intracranial calcifications. Finally, local contusion or inflammatory disease may produce a dramatic and marked EEG change without CT accompaniment and with or without accompanying focal clinical deficit, depending on the location and intensity of the abnormality. However, even when the EEG picks up subclinical abnormalities not associated with roentgenographic changes, the abnormalities in general are quite nonspecific and require close correlation with the clinical history and other information before arriving at a specific diagnosis.
Figure 6. Polymorphic slow wave activity in a patient with subcortical glioma, notice the marked variability in wave shape morphology, frequency and amplitude.

Table 2. Electrical criteria of the Polymorphic slow wave activity.

- Quite variable in wave shape morphology, frequency and amplitude.
- Commonly lateralized over a wide area of the scalp, persistent in eye closed, eye open state, during all sleep stages, with no visual reactivity. Polymorphic Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology.
- Persistent polymorphic delta activity may not precisely match the true location of the lesion, particularly since it presumably arises from physiological deranged neurons often lying on the margin of the destructive lesion. Persistent polymorphic delta activity is aetiologically nonspecific and is seen in a variety of subcortical (while matter) destructive lesions including neoplasms, infarctions, abscesses, trauma, and haemorrhage. It can also be seen in reversible processes such as focal ischemia in transient ischemic attacks or focal depression from a recent seizure.
- Commonly due to a subcortical white matter lesion inducing deafferentation of the cerebral cortex.
- A purely cortical lesion does not induce polymorphic slow wave activity.

Mechanisms Responsible for EEG Findings Associated With Focal Cerebral Disturbance

In the absence of a clear-cut understanding of the mechanisms responsible for the generation of normal EEG activity, an accurate explanation of how focal cerebral disturbances result in distortion in the amplitude, frequency, and reactivity of normal scalp-recorded rhythms is not possible. However, in general, these distortions occur because focal abnormalities may alter the interconnections, number, frequency, synchrony, voltage output, and axis orientation of individual neuronal generators, as well as the size
and location and integrity of the cortical area containing the individual generators giving rise to the total signal ultimately detected on the scalp.

There is general agreement among various workers that focal pathology in the underlying white matter is commonly associated with PPDA. In these cases, it is postulated that the white matter lesions produce PPDA by deafferenting the overlying cortex from its underlying white matter input.

If so, this theory could also be extended to explain focal PPDA occurring post-ictally. Although it would not be reasonable to explain post-ictal focal PPDA on the basis of a primary white matter disturbance, it is reasonable to assume that the postictal state, either by exhaustion or inhibition, may functionally deafferent the cortex from its underlying white matter input. Finally, even if deafferentation of the cerebral cortex from its underlying white matter is the primary mechanism responsible for PPDA, whether focal or generalized, additional factors such as the acuteness or changing nature of the deafferentation would have to be postulated as an additional important factor, inasmuch as PPDA is more commonly associated with acute, active disturbances and less commonly seen in chronic, stable disturbances.

**SUMMARY**

The nonspecific EEG abnormalities discussed in the preceding sections can be best thought of as electrical signs of cerebral dysfunction which may add new or confirmatory information about the patient's clinical condition. Although none of the findings in themselves are specific for a single etiology, taken in context with the clinical history they may be helpful in deciding between one of several possibilities (for example, functional versus organic), as well as in following the evolution of abnormality and giving prognostic information, especially in unconscious patients. In addition, EEG findings may suggest that additional studies and follow-up evaluation are needed. The nonspecific EEG findings were discussed under their usual clinical correlations, which are:

1. **IRDA**, usually associated with an active cerebral disturbance;

2. **Bilateral persistent abnormalities**, usually associated with impaired conscious purposeful responsiveness; and

3. **Focal abnormalities**, usually associated with focal cerebral disturbance.

Identification and categorization of these signs allows the EEG to be used as a dynamic tool to investigate function, especially if applied during the acute and evolving stages of various neurologic conditions and if correlated with other available information.
References


THE ELECTROENCEPHALOGRAPHY IN PATIENTS WITH EPILEPSY

The electroencephalogram (EEG) is the single most important test in the evaluation of patients with epilepsy, as it demonstrates the presence of various types of epileptiform activity that are associated with seizures. Epileptiform activity consists of paroxysmal waveforms of cerebral origin that have a distinctive morphologic appearance that is clearly distinguishable from the ongoing background activity and that have a high correlation with the presence of a seizure disorder.6,29,34,43 The main types of epileptiform discharges are spikes, sharp waves, and spike and wave discharges. Spikes are brief potentials having a steep ascending and descending limb with a duration of less than 70 msec.6 Sharp waves are broader potentials with pointed peaks, having a duration that usually ranges between 70 and 200 msec.6 A spike and wave discharge consists of a spike followed by a slow wave. Most of the discharges seen in the EEG represent interictal...
activity. When an ictal (seizure) discharge occurs, the electrographic manifestation consists of repetitive or rhythmic waveforms that have an abrupt onset, a characteristic pattern of evolution, and an abrupt termination. Epileptiform activity may be generalized or focal.

**GENERALIZED EPILEPTIFORM PATTERNS**

The main types of generalized epileptiform discharges are (1) 3-Hz spike and wave, (2) slow spike and wave (or generalized sharp and slow wave complexes), (3) atypical spike and wave discharges, (4) paroxysmal rhythmic fast activity, and (5) hypsarrhythmia.

- **3-Hz Spike and Wave Discharges**

The typical pattern consists of repetitive, stereotyped, generalized, bisynchronous, and symmetric spike and wave bursts occurring at a rate of 3 per second. The discharges, although generalized, often have a maximal amplitude over the frontal regions. There may be some variability in the typical pattern. Although the frequency is usually 3 Hz, the rate may be faster (4 Hz) at the beginning of a discharge and slower (2.5 Hz) at the end of the discharges. At times, double spikes may be associated with the slow wave complexes. The interictal record is usually normal. Some patients with the 3-Hz spike and wave pattern, however, may demonstrate rhythmic bisynchronous delta slow waves over the posterior head regions. The 3-Hz spike and wave discharges often occur in serial trains. If the burst lasts longer than 3 or 4 seconds, there is often a clinical accompaniment such as impaired consciousness, staring, motor arrest, or brief automatic or clonic movements associated with the burst.

Hyperventilation is a potent activator of the 3-Hz spike and wave patterns. Hypoglycemia also can potentiate 3-Hz spike and wave bursts, whereas eye opening or alerting the patient attenuates the epileptiform activity. During sleep, the morphologic appearance of the spike and wave discharges is altered, with the discharges occurring in a more fragmented fashion as atypical spike and wave or multiple spike and wave bursts.

The 3-Hz spike and wave pattern is the classic EEG pattern that is associated with absence (petit mal) seizures and is most often seen in children and adolescents between 3 and 20 years of age. The EEG pattern and the clinical seizures often resolve after adolescence. Usually, children with a 3-Hz spike and wave pattern and absence seizures are otherwise normal, mentally and neurologically, and do not have any underlying organic disease.
Figure 1. The 3 c/s spike/wave discharge.

Figure 2. The Frontally predominant 3 c/s spike/wave discharge.
Table 1. Electroclinical criteria of the 3 c/s spike/wave discharge

- It is bilateral fairly symmetrical and synchronous.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset.
- Readily activated by hyperventilation.
- It might be proceeded by intermittent, rhythmic, bisynchronous monomorphic slow waves in the occipital regions.
- The 3 c/s SWD is usually associated with an ictal absence episode when it lasts over 5 seconds.
- The 3 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 3.5 years and disappear at the age of 16 years.
- This discharge pattern is markedly enhanced during nonREM sleep, usually during stage II. However the morphological features of this discharge pattern are altered during sleep with the discharge occurring in a more fragmented and atypical fashion, occurring in bursts of spikes, polyspikes and atypical spike/wave complexes. This discharge pattern usually occurs in conjunction with sleep spindles and has an invariable frontal midline maximum.
- Background activity is within normal before and after termination of the paroxysmal discharge.

Figure 3. The Frontally predominant 3 c/s spike/wave discharge.
Slow Spike and Wave (Generalized Sharp and Slow Wave Complexes)

The slow spike and wave pattern consists of spike and wave discharges occurring with a frequency of 1.5 to 2.5 Hz. This pattern also has been termed "generalized sharp and slow wave complexes," as the duration of the spike component falls within the range of a sharp wave, that is, 100 to 200 msec, whereas the slow wave component has a duration of 300 to 500 msec. This has also been referred to as the "petit mal variant" pattern. 12, 13

Slow spike and wave discharges occur in a diffuse and bisynchronous manner but may be asymmetric with a shifting, lateralized, or focal. 5, 9, 32 The spike and wave discharges may occur singly or in serial trains lasting 10 to 15 seconds or longer. Although the trains of slow spike and wave discharges may be prolonged, there is often no apparent associated clinical accompaniment. The interictal background is often abnormal, showing generalized or focal slow wave abnormalities, asymmetry of the background, or various other types of focal or generalized epileptiform abnormalities. 12 The slow spike and wave discharges are
not usually influenced by hyperventilation, hypoglycemia, or photic stimulation. Drowsiness, however, tends to enhance the occurrence of the slow spike and wave pattern, and sleep greatly activates the EEG. 5, 9 During sleep, the EEG often shows generalized spikes and multiple spike and wave discharges or bursts of generalized paroxysmal fast activity. 5, 9, 13, 32

The slow spike and wave pattern is seen maximally between the ages of 1 and 6 years but may persist through adolescence and rarely into adulthood. 5, 9, 27, 32 The pattern is significant in that it usually occurs in children with some type of organic condition or diffuse encephalopathy who have signs of cerebral damage. 5, 12, 27 Many patients with this type of pattern have a severe seizure disorder, with an onset during the first 2 or 3 years of life. The seizures are usually generalized, consisting of tonic, tonic-clonic, clonic, atypical absence, akinetic, atonic or myoclonic (or both) seizures, and are often difficult to control. 5, 12, 27 In addition, a high percentage of the patients have signs of mental retardation and motor dysfunction. 5, 12 The triad of severe convulsive disorder, mental retardation, and slow spike and wave pattern has been referred to as the Lennox-Gastaut syndrome. 12

Figure 6. The 2 c/s slow spike/wave complexes of Lennox-Gastaut syndrome, notice the slow background.
Figure 7. The 2 c/s slow spike/wave complexes of Lennox-Gastaut syndrome, notice the slow background.

Table 2. Electroclinical criteria of the slow 1-2.5 c/s spike/wave discharge

- This EEG pattern is bilateral but asymmetrical and asynchronous with frequent lateralization and focalization.
- It has a frontal midline maximum.
- It is frequently continuous without any definite onset or offset and might extend through the whole record and is not associated with any clinical accompaniment.
- The discharge is not activated by hyperventilation.
- The 1-2.5 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 6 months (earlier than the 3 c/s SWD) and disappear at the age of 16 years and is replaced by anterior temporal sharp activity and the clinical seizure manifestations merge into the main stream of temporal lobe epilepsies.
- Background activity is often disorganized with frequent slow wave activity.
- The clinical correlate of this discharge is Lennox-Gastaut syndrome with multiseizure clinical presentation (grand mal fits, atonic fits, akinetic fits, atypical absence attacks, absence status). The occurrence of two or more than two types of seizures is almost the rule, mental retardation is very common.
- This discharge pattern could be idiopathic of genetic origin, cryptogenic with no overt cause, or symptomatic to a variety of brain diseases that include CNS infection, birth trauma, lipidosis, tuberous sclerosis, etc.
Figure 8. The 2 c/s slow spike/wave complexes of Lennox-Gastaut syndrome, notice the slow background and the frontal predominance of the discharge.

- Fast Spike/Wave Complex (4-5/Sec)

This pattern is closely related to the classical 3/sec spike wave complex; both discharge types are most commonly lumped together. A differentiation, however, is justified on clinical grounds.

The fast spike wave burst is usually of shorter duration (1 to 3 sec), it occurs in patients older than 15 yr, the bursts are always subclinical, and the associated seizure disorder is usually characterized by myoclonic jerking, grand mal attacks, or a combination of both seizure types (juvenile myoclonic epilepsy), whereas petit mal absences are quite uncommon. Paroxysmal flicker responses are common in such patients. A positive family history of epileptic seizure disorder is frequently found in this group of patients.

The 4/sec spike wave discharge is spatially distributed in the same manner as the 3/sec spike wave discharge; the frontal midline maximum is quite prominent.

Figure 9. The fast polyspike/wave complexes
The fast spike/wave complexes of juvenile myoclonic epilepsy has a strong genetic background. The gene locus was mapped on the short arm of chromosome 6.

Table 3. Electroclinical criteria of the fast 4-6 c/s spike/wave discharge

- This discharge occurs in patients older than 16 years.
- It is bilateral but less symmetrical and synchronous compared with the 3 c/s SWD and usually takes the morphological feature of polyspike wave discharge.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset and lasts for a very short periods (usually less than 3 seconds).
- This discharge pattern is not activated hyperventilation, however phobic stimulation is a potent activator of this discharge pattern.
- The clinical correlate of this discharge pattern is myoclonus and grand mal fits (juvenile myoclonic epilepsy).
- Studies using video monitoring combined with EEG recording revealed that the spike components of this discharge coincide with the myoclonic jerks and the slow waves coincide with periods of relaxation between the myoclonic fits, accordingly the number of spikes in this polyspike/wave complexes were found to be proportional to the severity of the myoclonic fits.
- The fast spike/wave complexes of juvenile myoclonic epilepsy has a strong genetic background. The gene locus was mapped on the short arm of chromosome 6.

- Generalized Atypical or Irregular Spike and Wave

Atypical spike and wave discharges are discharges that do not have the regular repetition rate or stereotyped appearance of the 3-Hz spike and wave or the slow spike and wave pattern. The spike and wave complexes occur with varying frequencies, usually ranging between 2.5 and 5 Hz. There may be admixed multiple spike (polyspike) components. The spike and wave discharges may have a variable expression; sometimes they can occur in an asymmetric fashion over homologous regions of the head; at other times they occur in a more localized fashion, as a forme fruste of the generalized discharges. Usually, the spike and wave bursts are brief, lasting 1 to 3 seconds. Hyperventilation is usually not very effective in activating the atypical discharge; however, sleep often potentiates the presence of spike and wave bursts. The interictal background may be normal or abnormal, depending on the underlying cause of the seizure disorder. The background is usually normal or minimally abnormal in patients with an idiopathic seizure disorder, whereas slow wave abnormalities may be present in patients with an underlying neurologic disorder. Atypical spike and wave can be seen in any age group and is often seen as an interictal abnormality in patients with various types of generalized seizures, or as the ictal accompaniment of myoclonic jerks.
Generalized paroxysmal fast activity consists of repetitive serial spike discharges or fast activity in the range of 10 to 20 Hz. This pattern also has been termed the "grand mal pattern" because of its frequent association with grand mal seizures; however, the use of a clinical term to describe an EEG pattern is to be discouraged. This pattern is seen at the onset of generalized tonic, tonic-clonic, or akinetic seizures. Fast paroxysmal rhythmic activity also can be seen during sleep recordings of patients with generalized seizures and patients with the slow spike and wave pattern.

The EEG accompaniment of a generalized tonic-clonic seizure reflects the various phases of the seizure. With the onset of the generalized tonic contraction of the body, the EEG shows generalized paroxysmal fast activity in the range of 20 to 40 Hz. This is followed by rhythmic activity in the range of 10 Hz, which increases in amplitude as it slows down in frequency. During this period, there is some generalized trembling of the body. This is followed by the clonic phase of the seizure. During this phase, the EEG shows bilaterally synchronous spike and slow wave discharges, with the spikes coinciding with the clonic jerks and the slow waves coinciding with the period of relaxation in between the clonic movements. As the clonic jerks slow down, the spike and wave complexes decrease in frequency, with increasing intervals between the spike and wave complexes. Finally, there is an abrupt cessation of the spike and wave discharges, which is followed by a generalized attenuation or slowing of the EEG during the postictal period, at which time the patient is limp and unresponsive. The slowing then gradually decreases and is replaced by more normal background activity as the patient recovers from the seizure.

Hypsarrhythmia

The term hypsarrhythmia was introduced by Gibbs and Gibbs and refers to a high-voltage arrhythmic and disorganized EEG pattern that consists of a chaotic admixture of continuous, multifocal, high-amplitude spike and sharp wave discharges and arrhythmic slow waves. The hypsarrhythmic pattern is seen in children between the ages of 4 months and 4 years and is predominantly found in infants and children with infantile spasms (West syndrome). The syndrome is not a specific disease entity but occurs in response to a severe cerebral insult or a diffuse or multifocal disease process occurring at an early age, usually before 1 year of age. In half the patients, the cause is unknown. In the other half, the syndrome may occur as a result of prenatal, perinatal, or postnatal insult, encephalitis, congenital defects, tuberous sclerosis, or various other dysgenetic, biochemical, or metabolic derangements that can occur in the young child.

The patients often have frequent infantile spasms or myoclonic jerks. Infantile spasms consist of tonic flexion or extension (or both) movements of the neck, body, and legs, usually lasting 3 to 10 seconds. The EEG accompaniment consists of an initial, high-voltage spike and sharp wave discharge, followed by an abrupt decrement or flattening of the EEG, which lasts for several seconds. Myoclonic jerks are very brief, lasting less
than a second, and are associated with a generalized, high-voltage spike or spike and wave discharge in the EEG. Infantile spasms and hypsarrhythmia are an age-related syndrome seen in early infancy and childhood and resolve after therapy or spontaneously after 4 or 5 years of age. 21

Figure 10. The Hypsarrhythmia pattern.
Table 4. Electroclinical criteria of Hypsarrhythmia discharge

- The word Hypsarrhythmia is originally derived from the Greek word hypsolos which means high and it refers to high voltage arrhythmia with a disorganized EEG pattern that consists of chaotic admixture of continuous, multifocal, high amplitude spikes, polyspikes, sharp waves and arrhythmic slow waves. This EEG pattern is dynamic and highly variable from one patient to another and between one study and another study for a single patient. Background activity is often disorganized with frequent slow wave activity.
- Marked change in the Hypsarrhythmia pattern also occurs during sleep. In REM sleep there is marked reduction to total disappearance of this EEG pattern. There is also normalization of this discharge pattern immediately following awakening from sleep.
- This discharge pattern is seen in children between the age of 4 months to 4 years and after the age of 4 years this pattern of discharge usually merges into the slow spike/slow wave complexes.
- Hypsarrhythmia pattern is frequently equated with infantile spasm (West syndrome), (characterized by massive flexion myoclonus of the head and neck called jack-knifing or Salaam attacks), however this pattern is not specific to any disease entity and is seen in response to any severe cerebral insult or severe multifocal disease process that occurs below the age of 1 year.
- Five different types of Hypsarrhythmia are present:
  - Hypsarrhythmia with increased interhemispheric synchronization.
  - Asymmetrical Hypsarrhythmia.
  - Hypsarrhythmia with a constant focus.
  - Hypsarrhythmia with episodes of voltage attenuation.
  - Hypsarrhythmia composed only of high voltage slow waves without spikes or sharp waves.

FOCAL EPILEPTIFORM DISCHARGES

The preferential localization of focal epileptiform discharges is related to a number of factors that include (1) an age-related distribution of spike discharges (there is a tendency for discharges to be localized to certain areas, depending on the state of maturation or the age of the patient); (2) the site of pathologic lesion producing the seizures; and (3) the degree of epileptogenicity of various areas of the brain. There is a difference in the threshold and susceptibility of various regions of the brain for developing an epileptogenic focus. The areas with the lowest threshold are the temporal lobe and the sensorimotor strip area. The frontal lobe also has a low threshold, whereas the parietal and occipital lobes have the highest thresholds.

The main types of focal discharges are occipital spikes, centroparietal spikes, centromidtemporal spikes, anterior temporal sharp waves, frontal spikes, midline spikes, and periodic lateral epileptiform discharges (PLEDs).
• **Occipital Spikes**

An occipital spike focus is seen most often in young children between 2 and 5 years of age, with a peak incidence at 4 years and a progressive decline afterward. The spikes occur as single or multiple spike discharges in a unilateral or bilateral fashion over the occipital head regions. Occipital spikes are not a highly epileptogenic spike in children, as only 40 to 50 per cent of children have seizures; however, a number of the children with occipital spikes may have visual difficulty, such as strabismus, cataracts, amblyopia, or various types of visual perceptive defects. A particularly rapid spike discharge, referred to as "needle sharp spikes," has been seen in congenitally blind children without a seizure disorder.

Although occipital spikes may be a benign phenomenon in younger children, the presence of occipital spikes in older children and adults is often related to some underlying lesion such as an infarct, a vascular malformation, a tumor, or trauma. The seizures that occur in patients with an occipital seizure discharge are often associated with visual symptoms in the contralateral field. If the focus is restricted to the occipital lobe, the symptoms usually consist of unformed visual hallucinations such as scintillating scotomata, flashing light or stars, or, rarely, a homonymous dimming of vision.

• **Centroparietal Spikes (Rolandic Spikes)**

Centroparietal spike discharges occur in children between 4 and 10 years of age. On occasion, the spike may be maximal over the vertex region. This is not a highly epileptogenic spike in children, as only 38 to 50 per cent of children with this type of spike discharge have seizures. The seizures usually consist of focal motor or sensory seizures that may become secondarily generalized. A number of patients with this type of spike discharge have cerebral palsy or some type of motor dysfunction or mental retardation with or without an associated seizure disorder.

• **Centromidtemporal (Sylvian) Spike Discharge of Childhood**

Centromidtemporal spikes are seen in children and adolescents between the ages of 4 and 13 years. The spike discharges are seen predominantly in the central and midtemporal leads, hence the name centromid-temporal spike. The site of origin appears to be the lower Rolandic or motor strip area, and if an extra electrode is placed midway between the central and midtemporal electrodes, the discharge is often maximal at this electrode. The discharges have a rather characteristic appearance: they consist of high-voltage, diphasic or polyphasic blunt spikes or sharp waves, followed by an aftercoming slow wave with a duration of 200 to 300 msec. On occasion, they can occur as very low-amplitude discharges. The spikes can be frequent and very prominent and may occur in brief clusters or in serial trains. The discharges may occur unilaterally or bilaterally or may shift from one site to another on subsequent recordings. At times, laterality of the spike discharges may not correspond to the hemisphere giving rise to the ictal symptoms.
frequency of the discharges is usually increased during drowsiness and sleep, and, occasionally, the discharges are seen only during sleep. 19

Approximately 60 to 85 per cent of children with centrotemporal spikes will have seizures. 3, 13, 25 The seizures, which have been called sylvian seizures, benign rolandic epilepsy, or benign seizures of childhood with centrotemporal spikes, are one of the most common types seen in childhood. 19, 25, 32 The seizures often have a focal sensory or motor onset with paresthesias of the side of the mouth, tongue, or cheek, or focal twitching of one side of the face or hand, which would be consistent with a focus of origin in the lower rolandic area (that is, the face, hand, and laryngopharyngeal region). During the seizure, the patient is unable to speak because of a motor speech arrest and may have excessive salivation or drooling because of difficulty or inability to swallow. The seizure may progress with hemiconic or tonic movements of the body and then become secondarily generalized. The seizures often occur during sleep or as the child awakens from sleep. Most of the patients are otherwise healthy and show no evidence of cerebral pathology, and the seizures and spikes usually disappear spontaneously in the second decade of life. On occasion, centrotemporal spike discharges can be seen as an incidental finding in the EEG in asymptomatic children who do not have seizures.

Figure 11. Trains of spikes/sharp waves recorded in a quasirhythrical pattern in a child with benign Rolandic epilepsy.

- **Anterior Temporal Spikes**

In contrast to the centro-midtemporal spike of childhood, which is primarily a suprasylvian spike, the true anterior temporal spike is an infrasylvian spike with a maximum in the anterior temporal or inferior frontal electrodes and prominent involvement of the midtemporal and ear leads. The anterior temporal spike is more commonly seen in the adolescent and adult age group and often appears after 12 or 13 years of age. Drowsiness and sleep markedly potentiate the presence of temporal discharges, which occur more than twice as frequently during sleep as in the awake tracing. 13, 24 The EEG evaluation of a patient with suspected temporal lobe seizures, therefore, would be considered incomplete unless a sleep recording is also performed.

The anterior temporal spike discharge is one of the most epileptogenic of all spike discharges; more than 90 per cent of patients with this spike discharge have seizures. 13
Various ictal patterns may be present during a seizure, 11, 20, 24 with the most common type of electrographic discharge consisting of incrementing sharp waves, spikes, or sinusoidal rhythms. The clinical seizures consist of various manifestations of complex partial seizures.

![Figure 12. Typical anterior temporal spikes in a patient with temporal lobe epilepsy](image)

- **Frontal Spike Discharges**

  Frontal spikes may be seen in persons of any age. These spikes also are highly epileptogenic, with approximately 80 per cent of patients who have a frontal spike discharge suffering seizures. 13 There is often some underlying pathology such as head trauma, tumor, vascular lesion, scarring, or the residual effects of encephalitis causing the epileptogenic focus. Various types of seizures can occur, including versive seizures, focal motor seizures, atypical absence seizures, complex partial seizures, and secondarily generalized seizures. 10, 36

- **Midline Epileptiform Discharges**

  These are discharges that arise from the midline or central vertex region and which may not be apparent unless midline leads are employed. The main type of seizure arising from the midline area is the supplementary motor seizure (mesial frontal seizure), which is characterized by posturing of the arm with elevation and abduction of the arm on one side, deviation of the head and eyes to the elevated arm, rhythmic movements, arrest of voluntary movements, vocalization or guttural sounds, or a motor speech arrest sometimes associated with generalized body sensation such as an epigastric sensation or a sense of fullness. 33, 36

- **Periodic Lateralized Epileptiform Discharges**

  Periodic lateralized epileptiform discharges (PLEDS) consist of focal, unilateral sharp waves, that occur in a periodic or quasiperiodic fashion of 1 per second to 1 every 3 seconds.
The sharp wave complexes have a variable morphologic appearance and vary in duration (100 to 200 msec) and in amplitude (100 to 300 uV). 2, 9, 32 PLEDs may occur with a widespread distribution over one hemisphere or in a more focal fashion. 7 The epileptiform discharges also may vary in morphologic appearance and shift in area of maximal emphasis in the same tracing and have a reflection to homologous regions over the opposite hemisphere. There is usually an attenuation or slowing of the background on the side of the PLEDs. Also occurring may be electrographic seizure discharges, which consist of repetitive trains of spikes or sharp waves over the involved area or hemisphere that may or may not be associated with clinical manifestations of seizures.

PLEDs usually occur as a result of an acute or subacute disturbance of cerebral function such as a vascular insult, herpes simplex encephalitis, a rapidly growing tumor, abscess, head trauma, or subdural hematoma or after intracranial surgery. 7, 9, 28 PLEDs thus are not specific for a single process but, when present, indicate the presence of some acute or subacute cerebral lesion. Bilateral PLEDs are most commonly seen with herpes simplex encephalitis or multifocal vascular disease. 9 In herpes simplex encephalitis, the discharges are usually maximal over the temporofrontal region, whereas with vascular lesions, the discharges are usually maximal over the parieto-posterior temporal region (that is, the watershed area).

The clinical features of a patient with PLEDs usually consist of the abrupt onset of recurrent seizures, obtundation, and a neurologic deficit. 7, 28 The seizures often consist of focal motor seizures that may become secondarily generalized. They may persist for several days and be difficult to control with anticonvulsants. At times, the seizures may take the form of epilepsia partialis continua. The neurologic deficit usually is related to the area of the brain from which the PLEDs are arising. PLEDs are a transient phenomenon and usually resolve over a period of 1 to 3 weeks. 7,9

Usually the patient's neurologic deficit, altered mentation, and seizures resolve in association with the disappearance of PLEDs, although there may be a discordance between the resolution of the EEG and the clinical findings. 7 In summary, PLEDs are not specific for a single etiologic process, but (1) they usually indicate the presence of an acute or subacute lesion; (2) they are often accompanied by seizures, obtundation, and neurologic dysfunction; and (3) they usually are a transient phenomenon and, depending on the underlying process, evolve into other types of EEG abnormalities or resolve with neurologic recovery.

**STATUS EPILEPTICUS**

Status epilepticus is a condition of recurrent or continuous seizure activity without recovery between the seizures.

Absence status (also termed spike-wave stupor, petit mal status, or nonconvulsive status) consists of prolonged episodes, during which there is disturbance of mental function in
association with continuous or repetitive, generalized spike and wave discharges on the EEG. 1, 42 Patients with absence status may have clouding of consciousness, confusion, an apparent psychiatric or cognitive disturbance, automatic behavior, lethargy, somnolence or amnesia, or combinations of these. There may be some associated myoclonic jerks or blinking of the eyes. Absence status can be seen in both children and adults, including patients more than 60 years of age. 1, 42

Partial complex status (psychomotor status or temporal lobe status) is an uncommon type of status epilepticus that can present as prolonged or repeated episodes of confusion with apparent psychiatric symptoms, automatic behavior, or amnesia. These episodes are associated with continuous or recurrent episodes of focal seizure activity on the EEG, usually over the temporal or frontal regions. 2, 31

Generalized tonic-clonic status (also called grand mal or convulsive status) is characterized by repeated generalized tonic-clonic seizures without recovery of consciousness between the seizures. The EEG shows repeated electrographic manifestations of tonic-clonic seizure activity or continuous, repetitive, generalized and bisynchronous spike and spike and wave discharges.

Focal status consists of repetitive or continuous focal motor or sensory seizures involving a localized area of the body. It is also associated with continuous or recurrent focal spike or sharp wave discharges on the EEG over the involved area. 41

**BENIGN EPILEPTIFORM PATTERNS**

The benign patterns consist of activity that has an epileptiform appearance but is not epileptogenic, that is, is not associated with seizures. This includes 14- and 6-Hz positive spike bursts, small sharp spikes, 6-Hz spike and wave pattern, rhythmic temporal theta activity of drowsiness (psychomotor variant pattern), and wicket spikes. 14, 30, 17-39 These benign wave forms can be seen in asymptomatic or normal persons and should not be interpreted as being indicative of a seizure disorder.

**SUMMARY**

The EEG is useful in evaluating seizure disorders by establishing or confirming the diagnosis of a seizure disorder, determining the type and focus of origin of the seizure, and helping make the distinction between an epileptic attack and a nonepileptic condition. The EEG also may show other abnormalities, such as focal slowing, that give a clue about the underlying disease process. A negative EEG does not exclude the diagnosis of epilepsy. Activating procedures such as hyperventilation, photic stimulation, and recording during sleep may help bring out epileptiform activity. 9, 13, 24 Occasionally, repeated or more prolonged recordings are necessary to demonstrate the epileptiform abnormalities. On the other hand, epileptiform-like activity may be present in the EEG without being associated with a seizure disorder. As the diagnosis of epilepsy is a clinical one, the EEG, like any test,
should not be used independently in making the diagnosis of epilepsy but should be interpreted in the context of the whole clinical setting.

REFERENCES


INTRODUCTION

It is often difficult of impossible to differentiate between ictal clinical, ictal subclinical and interictal EEG discharge. In fact we must acknowledge that there is a gray zone between ictal and interictal paroxysmal EEG discharge, the following point help to differentiate between ictal and interictal EEG discharge.

- **Sudden Change of Frequency**

There are, however, some valid guidelines for the detection of truly ictal events. The onset of a clinical seizure may be characterized by a sudden change of frequency. A new type of
rhythm appears, hesitantly, then more distinctly; soon it boldly dominates the tracing. This rhythm may be in alpha frequency or it may be faster or slower; it clearly demonstrates a new element of the tracing, indicative of a completely new electrophysiological event. The abnormal rhythm may or may not show spiky character. It tends to become slower with increasing amplitudes and more distinct spiky phases of the rhythmical waves.

- **Sudden Loss of Voltage**

  Sudden "desynchronization" of electrical activity is found in electrodecremental seizures. The onset of these attacks may look almost flat locally and/or diffusely, but extremely fast very low voltage activity may gradually increase in voltage with decreasing frequencies. Ictal rhythmical activity may soon become preponderant, similar to that found in the sudden change of frequency.

- **Sudden Increase of Voltage**

  The classical example is the sudden steep rise of amplitude in a classical petit mal absence with 3/sec spike waves. There is hence considerable variability in the ictal EEG events. This has been quite discouraging for those concentrating on automatic devices for seizure detection. Even the eye of the experienced electroencephalographer may have difficulties in the determination of ictal episodes.

**PROBLEMS OF TERMINOLOGY**

Definitions of EEG events are indispensable but quite difficult and often unsatisfactory. Attempts to re-assess the EEG terminology have been made from time to time; they often result in neologistic construction of terms which fail to receive general acceptance. The EEG terminology is filled with widely used, popular, and, alas, often quite sloppy and inaccurate terms. Nevertheless, most electroencephalographers know what is meant by such expressions in our professional jargon.

**INTERICTAL PAROXYSMAL PATTERNS**

- **Spike (Single or Random Spike)**

  A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable.

  The distinction from the background activity is based on wave morphology and amplitude. In many cases, spikes stand out against the background because of their high voltage. If the voltage of spikes and background activity is approximately equal, the faster character (i.e., the shorter duration) of the spike is its distinctive feature. It is possible that a spike of 50 msec duration and moderate amplitude may be imbedded in 20/sec activity (50 msec wave duration), for instance in an epileptic with considerable drug-induced fast activity. Under these circumstances, the spike activity may be undetectable. In such a case, fast paper
speed could demonstrate the morphological features of the spike (multiphasic and more pointed character with a dominant negative phase) in contrast with the more monotonous appearance of the fast waves.

The multiphasic character of a single spike deserves particular emphasis. A sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. A slow negative component may trail the spike discharge and often attain about the same amplitude as the negative main component of the spike. This trailing slow component of a single spike should not be regarded as evidence of a spike wave complex.

The electroencephalographer will very seldom find single spikes on the scalp with predominant positive component. Positive single spikes are more common in electrocorticographic and depth recordings; on the scalp, predominant positivity of single spikes raises the question of defective superficial cortical laminae. Following surgery of cortical A-V malformations, such positive spikes may be present occasionally.

Spikes represent the basic element of paroxysmal activity in the EEG. A unitarian view that all spikes mean a hidden or overt paroxysmal event would be erroneous. The fine semiology of spikes is extremely important and the EEG interpreter ought to consider the following questions:

a) What is the precise wave morphology?

b) Where do the spikes occur?

C) What is the age?

d) What is the state of awareness?

e) Is there any possibility of an artifact of similar appearance?

f) Is there any possibility of a physiological potential of similar appearance?

  o Wave Morphology

The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. Low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves.
Spatial Distribution

In childhood, occipital spikes are, in general, the most benign spike discharges, with less than 50% having clinical seizures; Rolandic central-midtemporal-parietal spikes are also quite benign, while frontal spikes or multi-focal spikes are more epileptogenic.

Age

The significance of the age factor is enormous. From the spikes of an epileptic newborn to a seizure focus of old age, age-determined varieties of spikes can be distinguished.

Level of Awareness

Random spikes may occur at any state of the waking-sleeping cycle and occur even in REM sleep when bilateral synchronous bursts of spikes or spike waves are usually suppressed.

Distinction from Similar Physiological Patterns

This differentiation is particularly important in the case of vertex sharp waves during deep drowsiness and stage 2 of light nonREM sleep. In childhood (after age 4), these waves may have a particularly spiky appearance and may be misinterpreted as paroxysmal spikes.

Physiological sharp or spiky vertex waves are usually quite easily distinguished from Rolandic spikes in sleep. Even in the more uncommon case of paroxysmal spike discharges over the vertex, the differentiation from physiological vertex sharp waves is not difficult.

The physiological nature of occipital lambda waves and "lambdoid" activity (positive occipital transients of sleep) must also be considered. The main component of this pattern is positive.

Distinction from Artifacts of Similar Appearance

This distinction depends on the electroencephalographer's experience and is usually an easy one. The interpretation of the clinical significance of spikes can be extremely difficult and depends on the electroencephalographer's experience in the art of reading the EEG tracing and also on his clinical understanding of epileptological problems. Extensive personal laboratory experience is just as essential as scientific knowledge in interpreting the EEG.

- Sharp Waves

A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.
The rising phase of the sharp wave is of the same order of magnitude as in spikes, but the descending phase is prolonged. This configuration with a steeper ascending phase, however, is not always present. A very unusual type of repetitive slow sharp wave activity has been reported in prematurely born infants with intraventricular hemorrhage; these discharges show predominantly positive polarity and are recorded mainly over the Rolandic region. The maximum of this activity is sometimes found over the vertex.

Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.

Sharp waves are usually found as random focal discharges; most anterior temporal spikes are, in a strict sense, sharp waves. This is also true for most benign Rolandic spikes of childhood. Sharp waves are more seldom found in generalized synchronous bursts where single spikes, spike waves, and polyspikes predominate. It has been contemplated that sharp waves on the scalp correspond with spikes in the depth or on the cortex. Combined depth and scalp recording clearly refutes this view. One can detect spikes as well as sharp waves in depth recordings; a deep sharp wave usually corresponds with a sharp wave on the scalp if there is any corresponding scalp activity at all.

The long duration of a sharp wave permits better insight into the multiphasic character of this potential. A small preceding positive component may be very fast and qualify as a spike; even a small biphasic spike discharge may precede the much larger sharp wave. Some sharp waves even exceed the maximum length of 200 msec. Others become very complex. They consist of a constantly varying number of components; such compounded sharp waves may occur as periodic discharges (periodic lateralized epileptiform discharges). It is certainly not incorrect to use the term "spikes" and "sharp waves" synonymously when a local paroxysmal event is discussed, although purists of nomenclature would regard this as a breach of etiquette.

The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.

- Polyspikes or Multiple Spikes

This discharge type represents a complex of spikes and may also be called polypike complex. In modern terminology, the term "multiple spike complex" is preferred on the grounds of linguistic considerations, because "polyspikes" is an etymological hybrid. It has
been defined as a complex paroxysmal EEG pattern with close association of two or more diphasic spikes occurring more or less rhythmically in bursts of variable duration, generally with large amplitudes.

Polyspike bursts are readily elicited by electrical stimulation of single depth leads, especially in limbic regions. On the scalp, however, polyspikes occur mostly as bilateral or generalized synchronous discharges. Exceptional focal polyspikes are occasionally encountered; these usually have a frontal maximum, except for occipital accentuation in hypsarrhythmia. Polyspikes and also polyspike-wave complexes are sometimes associated with concomitant myoclonus, especially in primary generalized epilepsy and in photosensitive individuals with this type of seizure disorder. Children with Lennox-Gastaut syndrome may also show the association of polyspikes and myoclonus.

- **Runs of Rapid Spikes**

This pattern has been described as "grand mal discharge", "fast paroxysmal rhythms", and "rhythmic spikes". It is seen only in sleep and occurs in older children, adolescents, and younger adults. It consists of bursts of spike discharges at a rate from 10-25/sec, usually generalized but with a well defined maximum over frontal regions; it may even be confined to the frontal leads. The voltage is in the medium to high range, often exceeding 100 or even 200 iL. The discharge rate is in most cases somewhat irregular. The bursts last for about 2 to 10 sec; bursts of more than 5 sec duration are usually associated with tonic seizures and thus represent an ictal pattern.

The obvious misnomer, grand mal discharges, is based on certain similarities with the ictal EEG of a grand mal seizure. In a patient population with grand mal seizures, runs of rapid spikes as an interictal pattern are a very rare finding. This pattern occurs in patients with secondary generalized epilepsy who suffer from more than one type of seizure and especially from akinetic seizures. This discharge is very typical in patients with Lennox-Gastaut syndrome; it is hardly ever found outside this clinical entity.

![Figure 1. Examples of sharp waves (left) and spike (right)](www.yassermetwally.com)
Table 1. Electroclinical criteria of spike/ sharp wave discharge

- A spike is a transient, clearly distinguished from the background activity, with pointed peak at conventional paper speeds and a duration from 20 to under 70 msec; the main component is generally negative. Amplitude is variable. Spikes represent the basic element of paroxysmal activity in the EEG.
- A sharp wave is a transient, clearly distinguished from background activity, with pointed peak at conventional paper speeds and duration of 70 to 200 msec. The main component is generally negative relative to other areas.
- Both spikes and sharp waves have multiphasic characters, being composed of a sequence of a minor positive, a major negative, and a second minor positive component is typical in most instances. The long duration of a sharp wave permits better insight into the multiphasic character of this potential.
- The spike/sharp wave potentials are reliable indicators of a potential seizure focus because they result from the characteristic neurophysiological event "the paroxysmal depolarization shift" (PDS). This phenomenon consists of thousands of neurons simultaneously undergoing large depolarization with superimposed action potentials. Both synaptic events and intrinsic cellular currents have been implicated in this process. EEG spikes/sharp waves are due to the slow depolarization currents in the PDS. Neurons surrounding the focus are inhibited during the paroxysmal depolarization shift, and within the focus the the paroxysmal depolarization shift is followed by a hyperpolarization potential. Both an increase in depolarizing events and a loss of inhibitory mechanisms can lead to persistence and propagation of the discharge as a seizure.
- Spikes and sharp waves are neurophysiologically closely related phenomena; both of them are typical paroxysmal discharges and highly suggestive of an epileptic seizure disorder, although both phenomena may occur in patients without a history of seizure disorder.
- The largest and most pronounced spikes are not necessarily associated with more serious epileptic seizure disorders. On the contrary, Rolandic spikes in a child age 4 to 10 yr are very prominent; however, the seizure disorder is usually quite benign or there may be no clinical seizures at all. low voltage spiking in the frontal or anterior temporal regions is highly epileptogenic even though its amplitude can be so low to the point that these spikes might be completely drowned within the background waves and subsequently can not be easily detected.

- **Spike Wave Complex (Classical 3/Sec)**

Classical 3/sec spike wave complexes are widely known even outside the community of electroencephalographers. It is officially termed "spike and slow wave complex"; this term comprises all types of spike wave complexes, which we will list separately because of markedly differing associated clinical-epileptological conditions. The official definition is quite simple: "A pattern consisting of a spike followed by a slow wave." Older terms such as "spike-and-dome complex," "wave-and-spike complex," and "dart-and-dome complex"
are seldom used these days and should be discouraged. The abridged term "3/sec spike wave" is certainly acceptable, since the omitted word "complex" is automatically implied. Spike wave complexes of the classical variety (3/sec) have been described as the EEG pattern of petit mal absences.

From this physiological point of view, the spike/wave discharge apparently represents an alternating succession of excitation and inhibition, with the spike representing excitation and the slow wave representing inhibition. The clinical ictal activities are thus constantly curbed by intervening inhibitory impulses which prevent the attack from progressing into massive downward discharges with motor effects (polyspikes with massive myoclonus) or to a full-blown grand mal attack. For this reason, motor manifestations of ictal episodes characterized by spike waves are almost always inconspicuous or modest. Furthermore, spike wave bursts rarely proceed into grand mal convulsions.

The distinction between classical (3/sec), slow (2-2.5/sec), and fast (4/sec) spike wave complexes and the smaller 6/sec spike wave discharge is justified on the basis of different clinical-epileptological correlates of each spike wave type; it is not an example of electroencephalographic hair-splitting. The classical 3/sec spike wave discharge is most typical and most pronounced in children with petit mal absences. Clinical absences are usually present when the burst lasts for longer than 5 sec. Thus, shorter bursts are usually subclinical, but numerous psychophysiological attempts have been made to demonstrate certain fluctuations of level of awareness even in apparently subclinical spike wave bursts. The classical spike wave complex is, in most cases, easily activated by hyperventilation, whereas the slow and the fast forms of this discharge show little or no enhancement.

A classical 3/sec spike wave burst does not run exactly at a rate of 3/sec. The complexes are faster at the onset of the burst (mostly around 4/sec), then slow down to 3.5 and 3/sec for the main portion, and eventually slow to 2.5/sec at the end of the burst. During a burst, the
spike discharges become gradually smaller, often shrinking to insignificance as well as in drowsiness and sleep.

The spatial distribution of the bursts is very typical; the maximum practically always lies over the frontal midline region, while a minimum is found over temporal and occipital areas. The understanding of this distribution type is highly conducive to a better comprehension of the underlying mechanisms. Practically all spike wave bursts are bilateral synchronous or generalized synchronous; the synchrony, however, is not perfect. The age of distribution is markedly in the range from 4 to 16 yr.

Figure 3. Frontally predominant 3 c/s spike/wave discharge in a patient complaining of typical absence episodes
The 3 c/s spike/wave discharge is Frontally predominant being much well formed anteriorly and poorly formed posteriorly.

Table 2. Electroclinical criteria of the 3 c/s spike/wave discharge

- It is bilateral fairly symmetrical and synchronous.
- It has a frontal midline maximum.
- It has a sudden onset and sudden offset.
- Readily activated by hyperventilation.
- It might be proceeded by intermittent, rhythmic, bisynchronous monomorphic slow waves in the occipital regions.
- The 3 c/s SWD is usually associated with an ictal absence episode when it lasts over 5 seconds.
- The 3 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 3.5 years and disappear at the age of 16 years.
- This discharge pattern is markedly enhanced during nonREM sleep, usually during stage II. However the morphological features of this discharge pattern are altered during sleep with the discharge occurring in a more fragmented and atypical fashion, occurring in bursts of spikes, polyspikes and atypical spike/wave complexes. This discharge pattern usually occurs in conjunction with sleep spindles and has an invariable frontal midline maximum.
- Background activity is within normal before and after termination of the paroxysmal discharge.

The 3 c/s spike wave discharge very rarely occurs below the age of 3.5 years and usually disappears at the age of 16 years. The 3 Hz SWD is inherited as an autosomal dominant
trait and is considered as an expression of an autosomal dominant gene with an unusual characteristic of low penetrance at birth, rises rapidly to complete penetrance at the age of 3.5 years - 16 years then decline gradually to almost zero penetrance at the age of 40 years.

Figure 5. Occipitally intermittent rhythmic delta activity proceeding typical 3 c/s spike/wave discharge in a patient with typical absence.

The 3 c/s spike wave discharge is seen in an unusually high proportion of normal non-epileptic siblings of patients with this discharge pattern, also the occipitally intermittent slow wave activity seen in those patients is also seen in normal siblings. Accordingly this discharge pattern should be regarded as an expression of a dominant genetic EEG trait which is not necessarily associated with any clinical seizure disorder. In fact the occurrence of this discharge pattern in non-epileptic children should only suggest a genetic predisposition rather than a clinical disease entity. The gene locus responsible for the 3 c/s spike wave discharge and the occipitally intermittent rhythmic slow wave activity has not been mapped to any specific chromosome.

Figure 6. The 3 c/s spike/wave discharge in two different patients, notice that the waveform morphology is different in different patients.

Past history of febrile convulsion is regarded as a risk factors for the future development of the 3 c/s spike wave discharge and its clinical accompaniment. The relationship between
febrile convulsion and the 3 c/s spike wave discharge is non causal relation and febrile convulsions are simply the first clinical expression of a genetic predisposition in children who will later develop the 3 c/s spike wave discharge and its clinical accompaniment. Failure to demonstrate the 3 c/s spike wave discharge at the time of the initial evaluation of febrile convulsion should not be surprising since the mean age of febrile convulsion patients is 16 months and the 3 c/s spike wave discharge is seldom seen below the age of 3.5 years.

- Slow Spike Wave Complex (1-2.5/Sec)

Following the demonstration of the 3/sec spike wave complex and its relationship to the petit mal absence the occurrence of slow-spike-wave complexes in a much different type of patients with seizures other than the petit mal absence was appreciated. The classical 3/sec spike wave complex was named "petit mal discharge." Consequently, the slow spike wave complex was termed "petit mal variant discharge."

The wave morphology of this pattern varies considerably. In the majority of the cases, the complex consists of a rather slow spike (according to the definition, a sharp wave, lasting 70 msec or longer) and a slow wave. In a sizeable number of cases, true spikes (60 msec or less duration) are followed by a slow wave.

The spatial distribution is, in most instances, quite similar to that of the 3/sec spike wave complex. In the vast majority of the cases, the bursts are bilateral or generalized synchronous (with imperfect synchrony); a frontal midline maximum is the rule in these discharges. Lateralization or occasional focal occurrence is sometimes observed, usually in children with severe residual brain damage in certain areas where parenchymatous destruction abolishes the spike wave discharge.

Generalized slow spike wave discharges are often quite prolonged. In some children or adolescents, the entire sleep portion (light and moderately deep nonREM sleep) consists of unabated generalized slow spike wave activity. The diagnosis of an "electrical status epilepticus" is not justified in such cases; there are no behavioral or polygraphic characteristics to suggest an ongoing ictal event. In some cases, the slow spike wave activity is found only in nonREM sleep.

While the classical 3/sec spike wave complex is seldom seen before the age of 4 and almost never before 3.5 yr, its slow counterpart (slow spike/ wave complexes) appears much earlier, sometimes before the age of 6 months. At this early age, the frontal maximum may not be readily demonstrable.

The slow spike wave complex is almost always associated with a severe and often uncontrollable type of childhood epilepsy (seldom with onset between ages 11 and 20 yr) called Lennox-Gastaut syndrome. Most of these children show a variety of minor attacks and evidence of mental retardation.
Thus, the distinction between slow (1-2.5/sec) and classical (3/sec) spike waves is of great clinical significance. One has to keep in mind, however, that many children or adolescents with slow spike waves also show series of 3/sec or even 4/sec spike wave complexes; the presence of these spike wave types is obviously of no significance in such cases and what counts is the slow type. On the other hand, patients with classical 3/sec spike wave complexes and a usually benign type of epileptic seizure disorder, almost never show slow spike waves except when a 3/sec or 4/sec spike wave burst may slow down to 2.5/sec at the end.
Table 3. Electroclinical criteria of the slow 1-2.5c/s spike/wave discharge

- This EEG pattern is bilateral but asymmetrical and asynchronous with frequent lateralization and focalization.
- It has a frontal midline maximum.
- It is frequently continuous without any definite onset or offset and might extend through the whole record and is not associated with any clinical accompaniment.
- The discharge is not activated by hyperventilation.
- The 1-2.5 c/s SWD is an age specific electrophysiological phenomenon. It usually start at the age of 6 months (earlier than the 3 c/s SWD) and disappear at the age of 16 years and is replaced by anterior temporal sharp activity and the clinical seizure manifestations merge into the main stream of temporal lobe epilepsies.
- Background activity is often disorganized with frequent slow wave activity.
- The clinical correlate of this discharge is Lennox-Gastaut syndrome with multiseizure clinical presentation (grand mal fits, atonic fits, akinetic fits, atypical absence attacks, absence status). The occurrence of two or more than two types of seizures is almost the rule, mental retardation is very common.
- This discharge pattern could be idiopathic of genetic origin, cryptogenic with no overt cause, or symptomatic to a variety of brain diseases that include CNS infection, birth trauma, lipidosis, tuberous sclerosis, etc.

- Fast Spike Wave Complex (4-5/Sec)

This pattern is closely related to the classical 3/sec spike wave complex; both discharge types are most commonly lumped together. A differentiation, however, is justified on clinical grounds.

The fast spike wave burst is usually of shorter duration (1 to 3 see), it occurs in patients older than 15 yr, the bursts are always subclinical, and the associated seizure disorder is usually characterized by myoclonic jerking, grand mal attacks, or a combination of both seizure types (juvenile myoclonic epilepsy), whereas petit mal absences are quite uncommon. Paroxysmal flicker responses are common in such patients. A positive family history of epileptic seizure disorder is frequently found in this group of patients.

The 4/sec spike wave discharge is spatially distributed in the same manner as the 3/sec spike wave discharge; the frontal midline maximum is quite prominent.
The fast spike/wave complexes of juvenile myoclonic epilepsy has a strong genetic background. The gene locus was mapped on the short arm of chromosome 6.

Table 4. Electroclinical criteria of the fast 4-6 c/s spike/wave discharge

- This discharge occurs in patients older than 16 years.
- It is bilateral but less symmetrical and synchronous compared with the 3 c/s SWD and usually takes the morphological feature of polyspike wave discharge.
- It has a frontal midline maximum
- It has a sudden onset and sudden offset and lasts for a very short periods (usually less than 3 seconds)
- This discharge pattern is not activated hyperventilation, however phobic stimulation is a potent activator of this discharge pattern.
- The clinical correlate of this discharge pattern is myoclonus and grand mal fits (juvenile myoclonic epilepsy).
- Studies using video monitoring combined with EEG recording revealed that the spike components of this discharge coincide with the myoclonic jerks and the slow waves coincide with periods of relaxation between the myoclonic fits, accordingly the number of spikes in this polyspike/wave complexes were found to be proportional to the severity of the myoclonic fits.
- The fast spike/wave complexes of juvenile myoclonic epilepsy has a strong genetic background. The gene locus was mapped on the short arm of chromosome 6.

- Hypsarrhythmia

The word Hypsarrhythmia is originally derived from the Greek word hypsolos which means high and it refers to high voltage arrhythmia with a disorganized EEG pattern that consists of chaotic admixture of continuous, multifocal, high amplitude spikes, polyspikes, sharp waves and arrhythmic slow waves. This EEG pattern is dynamic and highly variable from one patient to another and between one study and another study for a single patient. Background activity is often disorganized with frequent slow wave activity.
Marked change in the Hypsarrhythmia pattern also occurs during sleep. In REM sleep there is marked reduction to total disappearance of this EEG pattern. There is also normalization of this discharge pattern immediately following awakening from sleep.

![Hypsarrhythmia pattern](image)

**Figure 10. The Hypsarrhythmia pattern.**

This discharge pattern is seen in children between the age of 4 months to 4 years and after the age of 4 years this pattern of discharge usually merges into the slow spike/slow wave complexes.

Hypsarrhythmia pattern is frequently equated with infantile spasm ([West syndrome](https://www.yassermetwally.com)), characterized by massive flexion myoclonus of the head and neck called jack-knifing or Salaam attacks), however this pattern is not specific to any disease entity and is seen in response to any severe cerebral insult or severe multifocal disease process that occurs below the age of 1 year.

**Five different types of Hypsarrhythmia are present**

1- Hypsarrhythmia with increased interhemispheric synchronization.

2- Asymmetrical Hypsarrhythmia.

3- Hypsarrhythmia with a constant focus.

4- Hypsarrhythmia with episodes of voltage attenuation.

5- Hypsarrhythmia composed only of high voltage slow waves without spikes or sharp waves.
Table 5. Comparison between the classical generalized epileptic EEG discharge.

<table>
<thead>
<tr>
<th>EEG TYPE</th>
<th>AGE</th>
<th>CLINICAL CORRELATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical 3 c/s SWD</td>
<td>3.5 years -16 years</td>
<td>Petit mal epilepsy</td>
</tr>
<tr>
<td>Slow SWD (1-2.5 c/s)</td>
<td>6 months-16 years</td>
<td>Lennox-Gastaut syndrome</td>
</tr>
<tr>
<td>Fast SWD (4-6 c/s)</td>
<td>over 16 years</td>
<td>Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Hypsarrhythmia</td>
<td>4 months -4 years</td>
<td>West syndrome</td>
</tr>
</tbody>
</table>

- The 6/Sec Spike Wave Complex (Wave and Spike Phantom, Miniature Spike and Wave)

It is usually a pattern of adulthood but may also occur in adolescents and children. About 50 to 60% of the patients suffer from indubitable epileptic seizures (mostly grand mal), while the remainder shows a history of syncopal attacks, post-traumatic states, or psychiatric problems. The 6/sec spike wave complex is an uncommon but not rare pattern (about 0.5-1% in a central EEG laboratory). The discharge may be recorded in waking state, drowsiness, and light nonREM sleep; light drowsiness appears to be the optimal recording condition.

Regarding the spatial distribution of this discharge, two types are present. Type I with frontal accentuation, and Type I with occipital accentuation. We are evidently dealing with two different types of discharge; the frontal type is most commonly associated with epileptic seizure disorders and sometimes found in combination with other paroxysmal discharge types. The occipital types are found predominantly in patients with no evidence of epileptic seizure disorder.

- Rudimentary Spike Wave Complex ("Pseudo Petit Mal Discharge")

This pattern is most prominent over parietal areas. It is found only in infancy and early childhood when marked hypnagogic rhythmical theta activity is paramount in the drowsy state. In some of these children, the theta activity occurs in generalized bursts rather than in prolonged stretches; such bursts, sometimes as slow as 3-4/sec, may contain small spike elements which could justify a term like rudimentary spike waves. That this pattern denotes a mild abnormality; transition into a classical or other spike wave pattern does not occur. It has been shown that a history of febrile illness is very often found in children with rudimentary spike waves; a history of febrile convulsions is also quite common in such children.

- Small Sharp Spikes

It is the most inconspicuous paroxysmal discharge and hence is easily overlooked. (Only the occipital type of the 6/sec spike wave complex is equally small and unimpressive.) The main negative and positive components are of about equally spiky character. The discharge is fairly widespread and is seen chiefly over temporal and frontal areas, either shifting.
from side to side or synchronously firing. The pattern is almost exclusively found in drowsiness and/or light nonREM sleep. It is essentially a pattern of adulthood with a peak between age 30 to 60 yr; occurrence in adolescence and old age is somewhat less common. It is virtually absent in the first 10 yr of life. Small sharp spikes sometimes are precursors of typical anterior temporal spikes or sharp waves which, in such patients, simply occur somewhat later in drowsiness or sleep. Among nonepileptics, the discharges may occur in patients with cerebrovascular disorder, syncopal attacks, and psychiatric problems especially in patients with manic-depressive illness. A rather high prevalence of small sharp spikes is seen in presumed normal adult control subjects, reaching 7.9% in the range from 40 to 49 years and it must be stressed that this pattern is nonspecific should not be regarded as an abnormality.

- Needle-like Occipital Spikes of the Blind

Spike discharges of a particularly fast and needle-like character develop over the occipital region in most congenitally blind children. These spikes are completely innocuous, unrelated to epileptic seizure disorder, and probably due to a state of functional deaferentation. The discharges disappear during childhood or adolescence. Congenitally blind children with a history of retrolental fibroplasia often show evidence of accompanying cerebral impairment. Such children may show abundant and widespread but chiefly occipital spike activity; concomitant clinical epileptic seizures are fairly common in this condition. This type of spike activity must be differentiated from transient occipital spiking in nonepileptic congenitally blind children.

- The 14 and 6/Sec Positive Spike Discharge (Fourteen and Six Positive Bursts)

This pattern consists of "Bursts of arch shaped waves at 13-17 Hz and/or 5-7 Hz, most commonly at 14 and/or 6 Hz, seen generally over the posterior temporal and adjacent areas of one or both sides of the head during sleep. The sharp peaks of its component are positive with respect to other regions." The amplitudes are generally below 75 liv, that the pattern is best demonstrated by referential recording using contralateral ear lobes or other remote reference leads, and that the clinical significance is controversial.

The pattern occurs most commonly in children after age 4 and adolescents and declines in adulthood. Its occurrence in the waking state is exceptional; deep drowsiness and very light nonREM sleep are usually the ideal states for the documentation of the pattern, while deep sleep might be more conducive in very young children.

Children with attacks of abdominal pain, older children with severe nonmigrainous headaches, certain forms of mental retardation, and adolescent or young adult aggressive sociopathic individuals have been presumed to show the 14 and 6/sec positive spike pattern more often than other patients and normal control subjects, but this is still shrouded in doubt and controversy. Proven cases of epileptic seizure disorder very seldom show 14 and 6/sec positive spikes as the only significant finding. The demonstration of 14 and 6/sec positive spikes in advanced states of metabolic encephalopathies, especially in hepatic coma.
is an interesting exception. For completely unknown reasons, this essentially innocuous discharge may appear when slow activity becomes extremely pronounced in such patients.

- **Psychomotor Variant (Rhythmical Temporal Theta Bursts, Rhythmic Midtemporal Discharges)**

The pattern consists of long runs of rhythmical activity in the range of 5 to 6.5/sec with a maximum over the midtemporal region, often with considerable spread into posterior temporal, anterior temporal, and occipital areas. The theta activity shows a well defined negative sharp component which apparently stresses the paroxysmal character of the discharge. These trains of sharp theta waves may occur in a unilateral, bilateral shifting, or synchronous distribution type. The duration of a single run usually exceeds 10 see and may reach 1 min or more. Very often, the first run is noted in early drowsiness; in deep drowsiness and light sleep, the pattern tends to disappear. Patients with rhythmical theta bursts show shortened periods of REM sleep and also, to a lesser degree, of slow sleep in nocturnal sleep studies at the expense of long drowsy periods with the rhythmic theta pattern. The pattern occurs mainly in younger or middle-aged adults; it is also seen in adolescents, but it is exceptional in children. The clinical significance is not clear. Despite its strongly paroxysmal appearance, its epileptogenic properties seem to be very low; most patients have no history of clinical seizures.

- **Temporal Minor Sharp Transients of Old Age. Wicket Spikes**

Runs of mixed activity (with delta, theta, and alpha frequency) over anterior temporal and midtemporal regions are often interspersed with sharp transients and sometimes with frank spikes and sharp waves. These runs may be recorded in the waking state, in drowsiness (most commonly), and in light sleep. In the latter, spike activity may become fairly rhythmical in brief bursts known as "wicket spikes". Despite an occasional sharp and spiky appearance, this pattern is in the overwhelming majority of the cases unassociated with epileptic seizure disorder. It is usually found in patients with some degree of cerebrovascular disorder and therefore is a pattern of older or sometimes middle-aged individuals.

**ICTAL PAROXYSMAL PATTERNS**

- **Introductory Remarks**

Ictal EEG patterns may be a) a prolongation of a well defined interictal pattern which becomes ictal by virtue of its long duration (thus augmenting impact on neuronal function) or b) completely different from preceding interictal discharges. A typical example for the former case is the **petit mal absences** with short 3/sec spike wave bursts as interictal and prolonged 3/sec spike wave bursts as ictal phenomena. The emergence of a completely different ictal pattern is exemplified by partial forms of seizures (for instance, by cases of temporal lobe epilepsy with typical anterior temporal sharp waves in the interval and the sudden appearance of completely different patterns during a seizure.
Ictal patterns may be clinical with the typical motor and behavioral changes of a seizure of whatever category or subclinical with no demonstrable motor or behavioral changes. In such clinically silent ictal episodes, neuropsychological studies may demonstrate some changes.

- **Grand Mal (Tonic-clonic Seizures)**

The ictal EEG is invariably obscured by muscle artifact; it is demonstrable only in patients treated with curare or other strong muscle relaxants with artificial respiration. Fast rhythmic spikes are present in all leads, with some accentuation in upper frontal leads. This fast spike activity characterizes the tonic stage and becomes discontinuous in the clonic stage. Rhythmic slow waves alternate with bursts of polyspikes synchronously with clonic jerks (polyspikes) and brief relaxation (slow bursts). A period of post-ictal electrical silence is usually fairly brief; a phase of very irregular slow activity follows during the ensuing minutes.

- **Petit mal absences**

Typified by the generalized synchronous 3/sec spike wave complex occurring in more prolonged bursts

- **Psychomotor Seizures (Complex Partial Seizures, Temporal Lobe Seizures)**

The ictal EEG activity of psychomotor seizures was described as a special type of seizure discharge characterized by bursts of serrated slow waves, flat-topped 4/sec waves, and high voltage 6/sec waves ("seizure discharge of the psychomotor type").

- **Focal Motor and Other Focal Seizures (Partial Seizures with Simple Symptomatology)**

Cortical focal (partial) seizures are expected to be associated with a local discharge consisting of a sequence of repetitive spikes over the area contralateral to the motor or sensory (visual, auditory) clinical manifestations. In cases with a well documented EEG correlate of the seizure, the attack is often initiated by local desynchronization, i.e., very fast and very low voltage spiky activity which gradually rises in amplitude with diminishing frequency.

- **Myoclonic Seizures**

Myoclonus is a very complex phenomenon; a considerable number of disorders with myoclonus do not fall into the epileptic category. Epileptic myoclonus is classically characterized by concomitant polyspikes or polyspike wave discharges in the EEG, of bilateral or generalized synchronous character, usually with maximum over the frontal regions.
• **Tonic Seizures**

The relationship between tonic seizures and massive fast spike activity was discussed in the section on inter-ictal paroxysmal patterns and runs of rapid spikes. This pattern is the typical correlate of tonic attacks occurring in patients with the Lennox-Gastaut syndrome.

Some tonic seizures are characterized by simple flattening or desynchronization of all activity during the attack. Rhythmical activity around 10/sec and a very rare diffuse slow wave pattern (mainly delta frequency) are also described as EEG concomitants of tonic seizures.

• **Atonic Seizures**

These seizures are customarily divided into a short form, such as simple drop attack, lasting only seconds, and a longer form, lasting minutes and described as "inhibitory." The EEG shows a few polyspike waves or spike waves of generalized distribution followed by large slow waves (short forms). More rhythmical spike activity around 10/sec and intermixed slow activity in all leads constitute the EEG correlate of the longer lasting attacks; rhythmical slow spike wave activity (1.5-2/sec) may also occur.

• **Akinetic Seizures**

These attacks are characterized by arrest of all motion, which, however, is not caused by sudden loss of tone as in atonic seizures. The patients, usually children, are in an absence-like state; the EEG correlate is a slow (mostly 1-2/sec) spike wave discharge, generalized synchronous and often with clock-like rhythmicity. This type of seizure is rather poorly understood.

• **jacknife Seizures (Salaam Attacks)**

The EEG correlates of this common type of seizure in children with hypsarrhythmia (infantile spasms, West syndrome) are divided into a) sudden generalized flattening desynchronization, b) rapid spike discharges of high voltage in all leads, or c) no ictal alteration of the ongoing EEG activity.

**PERIODIC OR QUASIPERIODIC EEG DISCHARGE**

• **Introductory Remarks**

These rhythmically (or nearly rhythmically or "quasi-rhythmically") recurring discharges or patterns are of paroxysmal character, but they are usually not associated with epileptic seizure disorders characterized by chronically recurrent seizures. Periodic discharges or periodic activities are most commonly an important EEG feature of a severe ongoing CNS disease with certain paroxysmal or even overt epileptogenic properties. They are hence disease-suggestive and sometimes virtually disease-specific, rather than suggestive of epileptic seizure disorder in general.
The periodic character of these patterns in the presence of severe CNS involvement remains enigmatic; such rhythmical firing is markedly different from the predominantly random character of inter-ictal seizure discharges (spikes, sharp wave, etc.). There is no satisfactory model to explain the periodicity of the discharges.

Periodic discharges are always of large amplitude, mostly in the range of 100 to 300 ILv. These may be simple sharp waves, but of a duration which usually exceeds 150 msec. Other periodic discharges are compounded and polymorphic. Periodic discharges may be focal, widely scattered, or generalized synchronous.

- **Periodic Complexes in Subacute Sclerosing Panencephalitis (SSPE)**

The periodic complexes dominate the second stage of this disease; this is a prolonged phase in which the clinical diagnosis is usually made. This type of complex discharge practically does not occur in other clinical conditions and is hence almost disease-specific. It is a very reliable and highly contributory diagnostic finding in this disease. The discharges show a duration from 0.5 to 3 sec and are formed by two or more waves with mean amplitude of 500 liv (100 to 1000 liv). In some cases, the voltage may even reach 1400 Irv. The enormous height of this discharge may impress the inexperienced as a movement artifact; this idea is supported by frequent associated motor events such as myoclonus or sudden loss of tone.

The periodicity becomes manifest as the disease progresses; in its earlier stages, which are usually dominated by diffuse 1-3/sec activity of fairly rhythmical character, the compounded discharge may be aperiodic. Sometimes, the periodic discharge is present in the earliest stage of the disease and may persist to the fatal outcome; more often, this pattern disappears in the terminal or third stage. The elements of the discharge are variable; a giant slow wave is usually mixed with several sharp waves. The discharge is generalized, with a maximum over the frontocentral areas and vertex. The frequency of the complexes ranges from 4 to 16/min. The discharge is more impressive in the waking state.

Accompanying myoclonus is fairly synchronous with the discharge; the motor activity may precede or trail the discharge in a range of 200 to 800 msec. Minor interhemispheric asynchronous (15 msec) and an earlier appearance in parieto-occipital areas, than in frontal-central areas where the discharge shows its most impressive voltage, is also described.

The background activity between the complexes is quite variable. The background may be normal with posterior alpha rhythm; however, this is exceptional; severely disordered background activity is most commonly found. Slow activity prevails and numerous spikes are sometimes recorded, especially over anterior areas. Spike wave complexes may also be present; even clinical petit mal absences with classical 3/sec spike wave complexes have been observed.
• **Periodic Complexes in Herpes Simplex Encephalitis**

In an earlier stage, local mostly unilateral temporal polymorphic delta waves are the most striking feature, but soon large sharp waves emerge over the most affected region. These discharges usually fire at intervals from 2 to 4 sec. The discharge may be quite slow and exceed 1000 msec; consider that a sharp wave is defined as having a duration from 70 to 150 msec. The amplitudes are in the range from 100 to about 500 μV. Similar periodic sharp discharges have been demonstrated in neonatal herpes simplex encephalitis. In the course of the disease, the originally regional discharge tends to become generalized synchronous; asynchronous bilateral discharges may also occur.

In contrast with the complexes found in SSPE, the periodic discharge of herpes simplex encephalitis is of short periodicity, with the greatest intervals of 4 sec or less; this criterion is always met in the herpes simplex discharge. In some cases, the periodic discharge can be detected only when almost daily repeat records are carried out. This explains the fact that periodic discharges are not reported in all cases of herpes simplex encephalitis.

• **Periodic Discharges in Jakob-Creutzfeldt Encephalopathy**

The periodic discharge consists of a sharp wave or a sharp triphasic complex of 100 to 300 msec duration with a repetition rate of 0.5 to 2/sec or intervals of 500 to 2000 msec. The discharges occur against a severely disordered background of activity, mostly in generalized synchrony. Some cases show unilateral onset with discharges over one hemisphere or lateralized to one hemisphere for several days or weeks.

The periodic activity usually shows a maximum over the anterior region, except for the Heidenhain form which has a posterior maximum; in this special form, cortical blindness is a common feature. In sleep, the periodic discharges tend to disappear. The absence of periodic discharges after 10 wk of illness militates against Jakob-Creutzfeldt disease. Myoclonus is a typical clinical feature of this encephalopathy. The periodic patterns may or may not be associated with myoclonus.

• **Periodic Lateralized Epileptiform Discharges (PLED)**

Periodic Lateralized Epileptiform Discharges (PLED) may occur in a variety of acute neurological conditions. This pattern is most often associated with acute cerebral infarctions but may also occur in neoplastic and inflammatory pathology. As to acute vascular pathology, watershed-type infarctions are the most common structural substratum in patients with PLED.

PLED may be simple and large sharp waves or complex (compounded) discharges with mixed spiky and slower elements. The amplitudes usually lie around 100 to 300 μV, but may be occasionally much higher. The firing rate may be as fast as 3/sec or as slow as 12/sec. The discharge is found over the maximally involved area and the local background activity is almost always severely disordered. The focal maximum is customarily located over the boundary zone between middle and posterior cerebral arteries and thus over the
posterior temporal region and its immediate vicinity. More seldom are watershed infarctions found between the territories of middle and anterior cerebral arteries, with a maximum of PLED activity over the superior frontal region.

PLED are often associated with simultaneous focal motor twitching in contralateral face or fingers, hand, arm, leg, foot, etc. This underscores the paroxysmal character of the pattern. It is usually a temporary pattern which changes into other abnormalities within 1 to 2 days. Patients with PLED are in most cases acutely ill and often show a history of a variety of mixed problems, such as cerebral arteriosclerosis plus renal insufficiency or chronic alcoholism or diabetes mellitus. With all this emphasis on the vascular genesis of this pattern, the possibility of an underlying neoplasm must not be ignored. Patients with PLED are most commonly older adults; this pattern occasionally occurs in young adults and children.

- **Periodic Discharges in Acute Cerebral Anoxia**

Repetitive simple or compounded sharp waves in generalized synchrony may occur against a flat (or at least seemingly flat) background of activity in patients with acute cerebral anoxia. Myoclonus is often found in association with this type of activity. In most cases, these discharges are probably aborted bursts in a suppression burst pattern. True periodic discharges, however, may also occur.

**THE OCCURRENCE OF EPILEPTIC DISCHARGE IN HEALTHY NONEPILEPTIC PERSONS**

The occurrence of focal or generalized paroxysmal discharges in apparently healthy individuals is a puzzling and even annoying finding which requires some discussion. These findings may be quickly termed as false positives, but the EEG abnormalities are real and their irrelevance in view of the individual's good health is more apparent than real. Such spikes give testimony of certain cerebral dysfunctions which may or may not become manifest in the further course of events. These findings do not discredit the method of electroencephalography, which, after artifacts are ruled out, can only show facts. These disturbing facts are in need of a reasonable interpretation. Let us contemplate the indubitable fact that a complete medical evaluation will yield certain physical shortcomings and organic abnormalities in practically every healthy individual; even acne pimples are cutaneous lesions and hence abnormalities. What the electroencephalographer needs in such cases is a common sense philosophy as a basis for a wise interpretation. General medicine is full of examples of seemingly irrelevant and yet unmistakably present abnormalities which the prudent, seasoned physician will integrate into a holistic view of the individual. Seen from this angle, electroencephalography does not differ from the rest of medicine.

The EEG evaluation of comparatively large healthy populations usually shows a certain percentage of abnormalities such as spike, sharp wave or paroxysmal discharge. One should thoughtfully contemplated the clinical significance of spikes in healthy persons. Above all, the interpretation must take into consideration age. In childhood, the occurrence
of central-midtemporal (also parietal) spikes is associated with overt seizures in only 50-70% of the cases; this pertains mainly to the age from 3-12 yr. In occipital spikes (mainly age 3-5 yr), the epileptogenicity is even lower. In general, "benign" focal spikes (such as seen in benign Rolandic epilepsy) is seen, in healthy individual, much more often than generalized synchronous bursts of spikes or spike waves. In most children, the abnormalities disappear on follow up EGG studies and the minority develop overt clinical symptomatology.

Both generalized synchronous (spike wave, polyspike wave) and Rolandic (centroparieto-midtemporal) spikes in nonepileptic children suggest a genetic predisposition if no neurological deficit and no history of insult to the CNS are present. In children with a history of cerebral palsy and with no seizures but prominent spiking, the spike activity may herald future epileptic seizures. Even in perfectly healthy children with spikes, the possibility of future seizures cannot be completely ruled out, although the chances are slim.

In healthy children and especially in healthy adults with spikes, stress must be laid on certain personality disorders which are not incompatible with normal functioning. Psychological and mild psychiatric deviations include poor impulse control, proneness to hysterical conversion reactions, and schizoid manifestations. In such individuals, the presence of a cerebral dysfunction with paroxysmal EEG changes may hamper the natural process of psychological maturation. In some of these cases, head injuries or infections of moderate severity might have prompted or facilitated the EEG changes as well as the psychological deviations.

The high incidence of anterior temporal-midtemporal sharp transients in older patients with no clinical epileptic fits has no significance. These patients may even have overt sharp waves; others show small sharp spikes. Unless there is evidence of epileptic seizures, these discharges only indicate some degree of temporal lobe dysfunction, often compatible with good health.

This section must be capped by a strong plea to refrain from rash and ill-advised statements that a seizure-free person has epilepsy and must be treated because of spikes in the EEG. These persons need further medical attention and repeat EEG should be done at reasonable intervals, such as every 2 yr in a child or adolescent and every 5 yr in an adult. Anticonvulsive treatment is not needed, but should not necessarily be denied to extremely apprehensive, introspective, and hypochondria-prone individuals.

CONCLUSION

Paroxysmal discharges in the EEG are indicators of deviant neuronal behavior which may or may not amount to clinical epileptic seizures. Solid experience in clinical EEG and familiarity with the multitude of epileptic seizures disorders are the indispensable prerequisites for a truthful and clinically useful interpretation of paroxysmal EEG events.
REFERENCES

INTRODUCTION

It was stated that a spike focus does not necessarily denote a stable epileptogenic focus; benign Rolandic epilepsy stands as the epitome of the truth of this statement. Zones of cortical hyperexcitability (hyperirritability) may behave like a focus in the EEG, but these dysfunctions may burn themselves out with advancing age. Not so an epileptogenic focus which is based on cerebral pathology. Most of this pathology is residual, while the possibility of a space-occupying lesion must always be kept in mind. But are residual epileptogenic lesions quiet residues of a bygone active disease? Modern electromicroscopic work has shown that "residual" gliosis is a very active process, which provides a better understanding for the epileptic irritation of neurons. In this chapter we will discuss the electroclinical criteria of some focal epilepsies.

TEMPORAL LOBE EPILEPSY

- Introductory Remarks

The temporal lobe is far more often than any other areas the seat of an epileptogenic focus. What renders the temporal lobe so prone to harbor epileptogenic foci? The answer probably lies in 1) special anatomo-physiological properties of the limbic (arche- and
palocortical) portion of the temporal lobe, and 2) a certain vulnerability of neocortical and limbic parts of the temporal lobe to some forms of pathology.

Seizures arising from the temporal lobe have captivated the interest of epileptologists, electroencephalographers, neurologists, neurosurgeons, and even psychiatrists during the past decades. The impressive multitude of temporal lobe functions in the human are reflected by the enormous variety of seizure patterns. Temporal lobe functions are in part higher cortical functions; they are also functions of the limbic system with its crossroads of autonomic nervous system regulations and emotionality.

- **Terminology**

   The term "temporal lobe epilepsy" is correct as far as "seizures arising from the temporal lobe" are concerned. It should not be used as a synonym for psychomotor (complex partial) seizures, since 1) not all seizure manifestations of the temporal lobe fall into this category (many patients also have grand mal seizures and a few have grand mal only) and 2) psychomotor (complex partial) seizures may occasionally originate from the vicinity of the temporal lobe, usually as extensions of the limbic system into the fronto-orbital region. The reader will find more information and details on the historical development in the section on types of psychomotor seizures.

- **Clinical Ictal Manifestations**

   The wide variety of seizure manifestations is presented in the section on types of psychomotor seizures.

- **Ictal EEG Manifestations**

   See the section on types of psychomotor seizures.

- **Interictal EEG Manifestations**

   The anterior temporal spike or, more often, sharp wave discharge, randomly firing, is the classical EEG finding in the interseizure interval. With the use of the International Electrode System, this discharge is recorded from the F7, or F8, electrode, which is essentially frontobasal and slightly in front of the tip of the temporal lobe. Sleep EEG studies are highly important in demonstrating anterior temporal spiking otherwise anterior temporal spiking might be missed in a tracing obtained solely in the waking state.
The spike (sharp wave) discharge is bilateral in about 25 to 35% of the cases. Patients with bilateral anterior temporal spikes (sharp waves) are more likely to have both psychomotor and grand mal seizures. Sleep has an important role in the facilitation of temporal spikes.

Bilateral anterior temporal spiking may be bilateral independent or synchronous. Bilateral synchrony has been divided into real synchrony and discharges transmitted from one side to the other. The spike discharge occurs over one temporal lobe only in 34%, while transmission from side to side is noted in 24%, synchrony in 19%, and bilateral independence in 23%.

Brain tumor is rarely discovered in patients with bilateral independent temporal spikes. Patients with unilateral spikes often prove to have mesial temporal sclerosis; the superior aspects of the temporal lobe showed a maximum of corticographic spike activity. Patients with lesions of the basomesial surface and the tip of the temporal lobe revealed spikes transmitted secondarily to the opposite side or bilateral synchronous spiking. These patients may show less prominent or even equivocal scalp EEG findings.

The paroxysmal EEG abnormalities may exceed the boundaries of the temporal lobe. Psychomotor or complex partial seizures are more likely to occur when focal EEG abnormalities are limited to the temporal lobe.

In some patients, anterior temporal spikes are scanty, while consistent focal slowing is present over this area. This pattern is usually not good evidence for a space-occupying lesion unless progression of the focal slow (mainly polymorphic delta) activity is demonstrable.

Children and young adolescents with temporal lobe epilepsy and unequivocal complex partial seizures often have inconclusive EEG findings. Spikes or sharp waves may be over midtemporal or central regions (thus falsely suggestive of benign Rolandic epilepsy) or diffuse. Even generalized spike wave discharges may occur and slow spike wave complexes
may overshadow all other abnormalities when one deals with a case of Lennox-Gastaut syndrome giving rise to psychomotor seizures.

It evidently takes a while until the classical anterior temporal spike (sharp wave) focus is fully developed. Very rarely, the opposite happens with anterior temporal spiking being just a form of benign midtemporal spiking (even without any seizures and with full EEG normalization at age 11 yr). With advancing age, the anterior temporal spike focus increasingly becomes the impressive hallmark of temporal epilepsy, until an overabundance of this discharge occurs. Above age 50-60 yr, the anterior temporal spike or sharp wave is, in most cases, a simple exaggeration of temporal minor sharp activity, which is extremely common in elderly patients with mild or moderate degrees of cerebrovascular disorder and no seizure disorder whatsoever. In epileptics above age 50, temporal lobe spiking is a very common finding, but this does not necessarily mean that one is dealing with a temporal lobe epileptic; on the contrary, grand mal seizures outnumber psychomotor seizures by a wide margin.

The combination of total absence of paroxysmal discharges, marked unilateral temporal polymorphic delta activity, and recent onset of psychomotor seizures is very suggestive of a rapidly growing temporal lobe tumor. Very slowly growing tumors such as certain astrocytomas may show EEG patterns undistinguishable from those of temporal lobe epileptics with mesial temporal sclerosis. Meningiomas of the medial sphenoid wing position and psychomotor seizures may have very little or no EEG abnormality.

Small sharp spikes may appear over the temporal region and its neighborhood in early sleep as forerunners of typical large anterior temporal sharp waves, giving support to the diagnosis of temporal lobe epilepsy. The occurrence of small sharp spikes alone, however, contributes nothing to this diagnosis. These small discharges arise from a wide region, including deep structures and might indicate only some degree of neuronal hyperexcitability.

An unusual EEG pattern in temporal lobe epileptics might take the form frontal midline theta activity with an average frequency of 5.78/sec in 36% of these patients.
Table 1 Electroclinical characteristic of temporal lobe epilepsy.

- Anterior temporal spikes (or sharp waves) are the EEG cornerstone for the diagnosis of temporal lobe epilepsy (commonly recorded at F7, F8 electrodes). Anterior temporal or frontal midline theta activity is occasionally the EEG correlate of temporal lobe epilepsy. Marked unilateral temporal polymorphic delta activity is very suggestive of a rapidly growing temporal lobe tumor.
- The spike (sharp wave) discharge is bilateral in about 25 to 35% of the cases. Patients with bilateral anterior temporal spikes (sharp waves) are more likely to have both psychomotor and grand mal seizures. Sleep has an important role in the facilitation of temporal spikes.
- Brain tumor is rarely discovered in patients with bilateral independent temporal spikes. Patients with unilateral spikes often prove to have mesial temporal sclerosis.
- Above age 50-60 yr, the anterior temporal spike or sharp wave is, in most cases, a simple exaggeration of temporal minor sharp activity, which is extremely common in elderly patients with mild or moderate degrees of cerebrovascular disorder and no seizure disorder whatsoever.
- Children and young adolescents with temporal lobe epilepsy and unequivocal complex partial seizures often have inconclusive EEG findings. Spikes or sharp waves may be over midtemporal or central regions (thus falsely suggestive of benign Rolandic epilepsy) or diffuse. Even generalized spike wave discharges may occur and slow spike wave complexes may overshadow all other abnormalities when one deals with a case of Lennox-Gastaut syndrome giving rise to psychomotor seizures.
- Temporal lobe epilepsy (as an electroclinical syndrome) is usually found in older adolescents and in young and middle-aged adults; childhood and senium tend to dilute the clinical and EEG semiology. In particular the anterior temporal spikes or sharp wave focus is not well developed in young children as it takes a while to develop. In older age the anterior temporal spike or sharp wave is, in most cases, a simple exaggeration of temporal minor sharp activity, which is extremely common in elderly patients with mild or moderate degrees of cerebrovascular disorder and no seizure disorder whatsoever.

Unfortunately, it must be conceded that a fair number of patients with unequivocal psychomotor (complex partial) seizures show normal EEG tracings awake, asleep, and with activations, not only once but repeatedly. The availability of a CT scan, MRI is particularly important, since certain deep seated tumors impinging on the medial portions of the temporal lobe may give rise to seizures without inter-ictal EEG abnormalities. Sleep deprivation may occasionally bring the EEG abnormalities into the open. A sharp reduction of anticonvulsants usually has a remarkable effect, but, as a conscientious physician, one uses this form of activation with great reservation and reluctance. The epileptic rebound may lead to more widespread or even generalized seizure discharges, thus masking the focal character of the seizure disorder, or, much worse, the patient will have numerous seizures; worst of all, a dreadful status epilepticus grand mal may develop.
The addition of nasopharyngeal leads improves very slightly the chances of demonstrating a temporal lobe epileptogenic focus. In addition to the artifact-proneness of these leads, the electrodes may easily cross over to the side contralateral to the nostril of insertion. Sphenoidal leads are more likely to yield valuable additional information from the anterior portion of the temporal lobe; the invasive character of their insertion has discouraged most electroencephalographers from using these electrodes.

- **Age and Prevalence**

Temporal lobe epilepsy spans a period from early childhood to senility but, as was pointed out, classical cases are usually found in older adolescents and in young and middle-aged adults; childhood and senium tend to dilute the clinical and EEG semiology.

- **Psychological and Psychiatric Features**

A review of the copious literature on this subject could fill a monograph; in this context, we have to confine ourselves to a few basic statements. According to personal impression, the most common psychological features are irritability and hyposexuality; these data were derived from patients considered candidates for temporal lobectomy because of the severity of their seizure disorder.

A constant state of irritability renders these patients more volatile; some of them exhibit hostility and are prone to aggressive acts, but it must be stated very clearly that these cases are exceptional and not the rule. In recent decades, the conjunction of acts of violence or crime and temporal lobe epilepsy has been widely accepted without sufficient support from clinical data. Single observations of aggressive acts must be considered exceptional. Studies of large patient groups have clearly shown the rarity of aggressive acts in patients with temporal lobe epilepsy. Hyposexuality has been confirmed in these patients.

Patients with major psychomotor epilepsy are subject to an increased risk of psychiatric disturbance but that, except the immediate postictal psychotic state, the risk appears to reflect the site and extent of brain damage and the individual's psychosocial history and opportunities more than a diagnosis of epilepsy. This author also feels that... temporal lobe epilepsy makes a very small contribution to the pool of psychiatric disturbances, including violence.

Relationships to the schizoid personality have been frequently reported and combination with overt schizophrenia is well known, though not common.

The electroencephalographer will occasionally find that patients with temporal lobe epilepsy and schizophrenia show marked EEG improvement or completely normal tracings when the psychiatric condition is at its worst, while the patient is practically seizure-free, and vice versa (enhanced seizure disorder, massive spiking and psychiatric improvement). This "seesaw phenomenon" has been observed ("forced normalization").
A comparison of left- and right-sided temporal epilepsies (dominant versus nondominant temporal lobe) has shown some psychological-psychiatric differences. Epileptogenic foci in the temporal lobe in the dominant hemisphere are more likely to be associated with aggressive behavior.

The causes of temporal lobe epilepsy are as follows (in order of frequency)

- No histopathological abnormality, the most common
- Unspecified minor abnormalities
- Cortical neuronal loss and gliosis
- Gliomas and ganglioglioma
- Cortical neuronal loss, gliosis and hippocampal sclerosis
- Meningo-cerebral cicatrix and remote contusion
- Vascular formation of brain and/or pia
- Hamartomas
- Tumors other than gliomas
- Residuum of brain abscess
- Post-meningitic cerebral atrophy
- Tuberous sclerosis and formes frustes
- Subacute and chronic encephalitides
- Ulegyria
- Anomalous cases
- Residuum of old infarct

The higher incidence of tumors deserves special attention when one considers their progressive and eventually life threatening nature. A sizeable portion of these tumors, however, are of very mildly progressive nature and almost behave like a nontumoral lesion. Small tumors as the cause of seizures are found mainly in the mesio-inferior areas such as an uncus and amygdaloid region. Temporal lobe seizures may also be caused by a pituitary tumor with a large supradiaphragmatic portion and, furthermore, by lipomas of the corpus callosum.

- **Neurophysiological Mechanisms**

Limbic and neocortical portions of the temporal lobe (and, not seldom, of the adjacent fronto-orbital region) are actively involved in the ictal and inter-ictal epileptic phenomena of temporal lobe epilepsy. The uncinate region, comprising the amygdaloid complex, uncinate gyrus, and anterior-insular and peninsular portions of the temporal lobe, appears to be mostly involved in typical psychomotor automatisms, whereas the lateral temporal neocortex appears to be most active in experienced psychomotor seizures.

The role of the hippocampus remains enigmatic. Hippocampic electrical stimulation in man almost never results in afterdischarges or seizures this structure is more likely to be secondarily involved. Its role ..... "to consolidate memory traces", is often jeopardized in ictal activity. It must be added that the left and right hippocampus apparently serve special memory functions, with verbal memory on the dominant and nonverbal visual memory on
the nondominant side. Amygdalo-hypothalamic connections are likely to account for emotional responses, in normal physiology as well as, in a morbid and exaggerated form, during ictal activity. Connections between amygdala and basal ganglia (putamen, globus pallidus, putamen) might serve the behavioral-motor component of temporal lobe seizures. Autonomic manifestations are probably served by the amygdala through the hypothalamus or originate from the insular cortex. Bilateral temporal lobe involvement is very common.

- **Course and Therapy**

Until a few years ago, 4 principal medications were used for partial seizures: phenytoin, carbamazepine, valproate, and phenobarbital. In recent years, a number of newer medications have been approved by the FDA. These newer AEDs have not been evaluated in double-blind trials as monotherapy, so how they compare to the older AEDs is not known. The initial choice of medication depends on side-effect profile, cost considerations, and dosage schedule. The major VA trials did not show any significant difference in seizure control among the 4 older AEDs. Adverse effects were greater with phenobarbital and with valproate.

Single-drug therapy is the goal, and the dosage of each medication prescribed should be increased until either seizures are controlled or adverse effects occur.

**Drug Category: Anticonvulsants** - These agents prevent seizure recurrence and terminate clinical and electrical seizure activity.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Carbamazepine (Tegretol, Carbatrol, Epitol) - Affects sodium channels during sustained rapid repetitive firing. Extended release form preferred (Tegretol XR or Carbatrol) because of bid dosing, which improves compliance and leads to more stable blood levels. No IV formulation available.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>600-2000 mg/d PO</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>5 mg/kg/d initially, followed by maintenance dose of 15-20 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; concurrent MAOIs</td>
</tr>
<tr>
<td>Interactions</td>
<td>Danazol may increase serum levels significantly within 30 days (avoid whenever possible); do not coadminister with MAOIs; cimetidine may increase toxicity, especially if taken in first 4 wk of therapy; may decrease primidone and phenobarbital levels (their coadministration may increase carbamazepine levels)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>Do not use to relieve minor aches or pains;</td>
</tr>
</tbody>
</table>
### Drug Name

**Phenytoin** (Dilantin)- One of oldest drugs known for treatment of seizures; extremely cost-effective. In young women, can coarsen facial features, cause hirsutism and gingival hyperplasia. In addition, requires frequent blood levels because of nonlinear pharmacokinetics. Long-term use associated with peripheral neuropathy and osteopenia. Can be mixed only with isotonic saline since D5W causes phenytoin to precipitate. Fosphenytoin (prodrug of phenytoin) measured in units of phenytoin equivalents (PE). Fosphenytoin can be diluted with either saline or D5W.

### Adult Dose

- **Loading dose:** 15-20 mg/kg/d PO/IV at rate no faster than 50 mg/min
- **Maintenance:** 3-5 mg/kg/d PO/IV
- **Fosphenytoin loading dose:** 20 mg PE/kg infused at maximal rate of 150 mg/min

### Pediatric Dose

- **Initial dose:** 5-7 mg/kg/d PO/IV
- **Maintenance:** 5-7 mg/kg/d PO/IV

### Contraindications

Documented hypersensitivity

### Interactions

- Amiodarone, benzodiazepines, chloramphenicol, cimetidine, fluconazole, isoniazid, metronidazole, miconazole, phenylbutazone, succinimides, sulfonamides, omeprazole, phenacemide, disulfiram, ethanol (acute ingestion), trimethoprim, and valproic acid may increase toxicity
- Barbiturates, diazoxide, ethanol (chronic ingestion), rifampin, antacids, charcoal, carbamazepine, theophylline, and sucralfate may decrease effects
- May decrease effects of acetaminophen, corticosteroids, dicumarol, disopyramide, doxycycline, estrogens, haloperidol, amiodarone, carbamazepine, cardiac glycosides, quinidine, theophylline, methadone, metyrapone, mexiletine, oral contraceptives, valproic acid
<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>C - Safety for use during pregnancy has not been established.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precautions</td>
<td>Perform blood counts and urinalyses when therapy is begun and at monthly intervals for several months thereafter to monitor for blood dyscrasias; discontinue use if skin rash appears and do not resume use if rash is exfoliative, bullous, or purpuric; rapid IV infusion may result in death from cardiac arrest, marked by QRS widening; caution in acute intermittent porphyria and diabetes (may elevate blood glucose); discontinue use if hepatic dysfunction occurs.</td>
</tr>
<tr>
<td>Drug Name</td>
<td><strong>Valproate</strong> (Depacon, Depakene, Depakote)-Anticonvulsant effective for most seizure types, believed to exert anticonvulsant effect by increasing GABA levels in brain. Approved for monotherapy or adjunctive therapy for partial seizures and generalized tonic-clonic seizures. Depakene capsule or syrup, Depakote tablet or sprinkle.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>10-15 mg/kg/d IV initially at rate of 20 mg/min; increase by 5-20 mg/kg/wk to maximum 60 mg/kg/d or as tolerated</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>20 mg/kg/d initially followed by maintenance dose of 20-40 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; hepatic disease/dysfunction</td>
</tr>
<tr>
<td>Interactions</td>
<td>Cimetidine, salicylates, felbamate, and erythromycin may increase toxicity; rifampin may significantly reduce levels; in children, salicylates decrease protein binding and metabolism; may result in variable changes of carbamazepine concentration with possible loss of seizure control; may increase diazepam and ethosuximide toxicity (monitor closely); may increase phenobarbital and phenytoin levels, while either may decrease valproate levels; may displace warfarin from protein-binding sites (monitor coagulation tests); may increase zidovudine levels in HIV-seropositive patients</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>Thrombocytopenia and abnormal coagulation parameters have occurred; risk of</td>
</tr>
</tbody>
</table>
Thrombocytopenia increases significantly at total trough valproate plasma concentrations 110 mcg/mL in females and 135 mcg/mL in males; at periodic intervals and prior to surgery, determine platelet counts and bleeding time before initiating therapy; reduce dose or discontinue therapy if hemorrhage, bruising, or hemostasis/coagulation disorder occurs; hyperammonemia may occur, resulting in hepatotoxicity; monitor patients closely for appearance of malaise, weakness, facial edema, anorexia, jaundice, and vomiting; may cause drowsiness.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Phenobarbital (Barbita, Luminal, Solfoton) - One of first major AEDs, introduced in 1919. FDA approved for initial or adjunctive therapy for partial-onset seizures. Has major cognitive adverse effects, which has limited its use in favor of newer AEDs that have better side-effect profiles.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>90 mg PO qd initially; increase by 30 mg/d every mo to usual maintenance dose of 90-120 mg/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>3-5 mg/kg/d PO initially, followed by maintenance dose of 3-5 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>May decrease effects of chloramphenicol, digoxin, corticosteroids, carbamazepine, theophylline, verapamil, metronidazole, and anticoagulants (patients stabilized on anticoagulants may require dosage adjustments if added to or withdrawn from their regimen); alcohol may produce additive CNS effects and death; chloramphenicol, valproic acid, and MAOIs may increase toxicity; rifampin may decrease effects; induction of microsomal enzymes may result in decreased effects of oral contraceptives in women (must use additional contraceptive methods to prevent unwanted pregnancy; menstrual irregularities may also occur)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>In prolonged therapy, evaluate hematopoietic, renal, hepatic, and other organ systems; caution in fever, hyperthyroidism, diabetes mellitus, and</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Lamotrigine (Lamictal)- Newer AED approved as adjunctive therapy and cross-over monotherapy for partial seizures. Also blocks sodium channels during sustained rapid repetitive neuronal firing. FDA approved for children younger than 16 years only for Lennox-Gastaut syndrome; not FDA approved for children with partial seizures because of increased incidence of rash.</th>
</tr>
</thead>
</table>
| Adult Dose | Weeks 1 and 2: 50 mg/d PO; if given as adjunctive therapy with valproic acid, then 25 mg qod
Weeks 3 and 4: 100 mg/d PO in divided doses; if given as adjunctive therapy with valproic acid, then 25 mg/d, increase by 100 mg/d PO every wk; if coadministered with valproic acid, increase by 25-50 mg PO every other wk
Maintenance dose: 300-500 mg/d PO in divided doses; if coadministered with valproic acid, 100-200 mg/d |
| Pediatric Dose | Initial dose: 1-2 mg/kg PO
Maintenance dose: 5-10 mg/kg PO |
| Contraindications | Documented hypersensitivity |
| Interactions | Acetaminophen increases renal clearance, decreasing effects; similarly, phenobarbital and phenytoin increase metabolism, decreasing levels; valproic acid increases half-life |
| Pregnancy | C - Safety for use during pregnancy has not been established. |
| Precautions | Incidence of severe rash is 1% in pediatric and 0.3% in adult patients; almost all cases occur within 2-8 wk of treatment
Incidence of rashes of all types is 3.3% in monotherapy and with adjunctive therapy with enzyme-inducing AEDs (eg, phenytoin, carbamazepine); with enzyme-inhibiting AEDS (eg, valproate), incidence of rash is 10%; risk of rash reduced with slow titration |
| Drug Name | Gabapentin (Neurontin)- Approved by FDA as adjunctive therapy for partial seizures. Structurally related to GABA; however, |
### Drug Name

**Topiramate** (Topamax)- Approved by FDA as adjunctive therapy for partial seizures. Exerts action by 4 mechanisms: sodium channel blockade, enhancement of GABA activity, antagonism of AMPA/kainate-type glutamate excitatory receptors, and weak inhibition of carbonic anhydrase.

### Adult Dose

<table>
<thead>
<tr>
<th>Dose</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>400 mg PO qd in 2 divided doses; initial starting dose 25 mg/d with gradual increase of 25 mg/wk</td>
<td>Therapeutic response may be observed at dose of 200 mg/d; if renal CrCl &lt;70 mL/min, then reduce dose by half &gt;</td>
</tr>
</tbody>
</table>

### Pediatric Dose

<table>
<thead>
<tr>
<th>Dose</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-9 mg/kg/d PO</td>
<td></td>
</tr>
</tbody>
</table>

### Contraindications

Documented hypersensitivity

### Interactions

- Phenytoin, carbamazepine, and valproic acid can significantly decrease levels; reduces digoxin and norethindrone levels; carbonic anhydrase inhibitors may increase risk of renal stone formation and should be avoided; use with extreme caution when administering concurrently with CNS depressants since may have additive

### Adult Dose

Start at 300 or 400 mg PO tid and increase prn not to exceed 4800 mg/d

Usual minimum effective dose for partial seizures as an adjunct is 1200 mg; if CrCl 30-60 mL/min, 300 mg PO bid; if CrCl 15-30 mL/min, 300 mg PO qd

Hemodialysis patients: 200-300 mg after every hemodialysis

### Pediatric Dose

4-13 mg/kg/d PO initially

Maintenance: 10-50 mg/kg/d PO

### Contraindications

Documented hypersensitivity

### Interactions

Antacids may reduce bioavailability significantly (administer at least 2 h following antacids); may increase norethindrone levels significantly

### Pregnancy

C - Safety for use during pregnancy has not been established.

### Precautions

Caution in severe renal disease; dizziness or somnolence may occur when starting therapy, so patients should be warned not to drive or operate heavy machinery during initial phase of treatment
<table>
<thead>
<tr>
<th><strong>Effect in CNS depression, as well as other cognitive or neuropsychiatric adverse events</strong></th>
<th><strong>Pregnancy</strong></th>
<th>C - Safety for use during pregnancy has not been established.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Precautions</strong></td>
<td>1.5% of patients develop kidney stones, because it is weak carbonic anhydrase inhibitor and reduces urinary citrate excretion while increasing urine pH (more common in males)</td>
<td><strong>Drug Name</strong></td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>4 mg PO qd to start, increase by 4-8 mg/d every wk to maintenance dose of 32-56 mg in 2-4 divided doses</td>
<td><strong>Precautions</strong></td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Not established</td>
<td><strong>Drug Name</strong></td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>100 mg PO qd initially for 2 wk, then increase by 100 mg/d every wk to every 2 wk to maintenance dose of 100-300 mg bid</td>
<td><strong>Pediatric Dose</strong></td>
</tr>
</tbody>
</table>

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| **Interactions** | May increase serum carbamazepine levels; carbamazepine may increase concentrations; phenobarbital may decrease levels |
| **Pregnancy** | C - Safety for use during pregnancy has not been established. |
| **Precautions** | Administration associated with 2-3.5% risk of urolithiasis; anorexia, nausea, ataxia, impaired concentration, and other cognitive side effects have been reported; cleared by hepatic conjugation and oxidation; therefore, dose should be reduced in patients with hepatic insufficiency |
| **Drug Name** | Oxcarbazepine (Trileptal)- Approved by FDA as monotherapy and adjunctive therapy for partial epilepsy in adults and children aged 4-16 years. Blocks sodium-activated channels during sustained rapid repetitive firing. Has no antiepileptic activity itself; its 10-monohydroxy metabolite is active compound. |
| **Adult Dose** | 300 mg PO initially bid; increase by 300 mg bid every wk to maintenance of 600-1200 mg bid |
| **Pediatric Dose** | Not established |
| **Contraindications** | Documented hypersensitivity; hypersensitivity to carbamazepine (25-30% have cross-sensitivity) |
| **Interactions** | May decrease levels of dihydropyridine calcium antagonists and oral contraceptives; can reduce serum concentrations of carbamazepine, phenobarbital, phenytoin, and valproic acid; when given in doses 1200 mg/d, may increase phenytoin and phenobarbital serum concentrations significantly; can reduce serum concentrations of oral contraceptives and make oral contraceptives ineffective; can increase clearance of felodipine |
| **Pregnancy** | C - Safety for use during pregnancy has not been established. |
| **Precautions** | Among persons with hypersensitivity to carbamazepine, 25-30% will have hypersensitivity to oxcarbazepine; can cause cognitive adverse effects such as psychomotor slowing, impaired concentration, impaired speech and impaired language; in persons with impaired renal function (CrCl <30 mL/min), dose should |
begin at half usual starting dose, and dose increments should be made more slowly; can cause hyponatremia (sodium\textless{}125 mmol/L); rapid withdrawal can cause exacerbation of seizures; observe for adverse effects and monitor plasma levels of concomitant anticonvulsants during dose titration>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Levetiracetam (Keppra) - Approved by FDA in 1999 as add-on therapy for partial seizures. Mechanism of action unknown. Has favorable adverse-effect profile, with no life-threatening toxicity reported to this date.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>500 mg PO bid initially; increase by 500 mg PO bid every 2 wk; not to exceed 1500 mg PO bid in adults; lower doses recommended in elderly (start at 250 mg PO bid) and in patients with renal impairment</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Not established</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Renally excreted (67%) and, thus, dose should be lowered in renal impairment; major side effects include somnolence, asthenia, incoordination, mild leukopenia (3%), and behavioral changes such as anxiety, hostility, emotional lability, depression and psychosis (1-2%), and depersonalization</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Felbamate (Felbatol) - Approved for medically refractory partial seizures and Lennox-Gastaut syndrome. Has multiple mechanisms of action, including blockade of glycine site of NMDA receptor, potentiation of GABAergic activity, and inhibition of voltage-sensitive sodium channels.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>600 mg PO tid initially; increase by 600-1200 mg/d every wk; not to exceed 1200-1600 mg PO tid</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Not established</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; blood dyscrasias; hepatic dysfunction</td>
</tr>
<tr>
<td>Interactions</td>
<td>May increase steady-state phenytoin levels—40%</td>
</tr>
</tbody>
</table>
Temporal lobe epilepsy is a serious seizure disorder. Good therapeutic responses to first line medications are the exception rather than the rule.

It is saddening to see a large number of patients remain unresponsive to any medication. These patients are candidates for surgical treatment by temporal lobectomy. The facilities for seizure surgery are limited and the selection of patients is beset with psychological problems. Not every suitable candidate is sufficiently motivated to give his consent for this operation. In well screened material, about 40% of the patients will become seizure-free after temporal lobectomy.

The electroencephalographer is often amazed at the minor effects of temporal lobectomy on the EEG as such; such changes are often limited to local voltage depression corresponding to the cortical removal. The excision of this sizeable portion of brain tissue usually produces less EEG effect than a diagnostic cortical biopsy, which is often followed by marked local delta activity for a period of time. Persisting seizure discharges are likely to change their spatial distribution to some extent; previous anterior temporal spike activity may move to the midtemporal region.

FRONTAL LOBE EPILEPSY

- Introduction

Frontal lobe epilepsy is much less common than temporal lobe epilepsy. Moreover, frontal lobe epilepsy is less significant as an epileptological entity. Frontal lobe seizures often
consist of immediate grand mal attacks, thus obscuring any focal initiation, has been widely confirmed.

- Seven different clinical seizure patterns are distinguished:

1. Immediate unconsciousness followed by a grand mal with minimal or no lateralizing signs.

2. Immediate unconsciousness associated with initial turning of the head and eyes (sometimes of the body) to the opposite side, promptly followed by a grand mal, probably originating from the anterior third or fourth of the frontal lobe contralateral to the adersive movement.

3. Initial adversion of head and eyes to the opposite side, preserved consciousness, and conscious adersive (contraversive) attack which, after 5 to 20 sec may or may not be followed by a grand mal. The origin usually lies in the convexity of the intermediate frontal region.

4. Posturing movement of the body with tonic elevation of the contralateral arm, downward extension of the ipsilateral arm, and turning of head away from the side of the lesion as if looking at the raised hand. This type of seizure arises from the medial aspect of the intermediate frontal region in the vicinity of the supplementary motor region. This type of seizure has also been described as "mesiofrontal epilepsy" and was attributed to the supplementary motor region within the interhemispheric fissure.

5. Brief attacks of "dizziness," a "flush," or "weak" feeling. This vague sensation may stop after a few seconds or it may be followed by brief arrest of activity, confusion, and staring. This attack imitates the petit mal absence clinically and even electroencephalographically. In contrast with true petit mal absences, these attacks may be followed by a grand mal.

6. Sudden alteration of thought processes, such as "forced thinking" ("my thoughts suddenly became fixed"). This may be followed by a petit mal-like absence or by a grand mal.

7. Seizures arising from the fronto-orbital cortex are practically undistinguishable from temporal lobe epilepsy. Petit mal absence status-like ictal symptomatology due to a left frontal epileptogenic focus is occasionally demonstrated.
More frequently occurring seizure manifestations are listed in the following table.

Table 2. **Subdivision of Frontal Lobe Seizures.**

<table>
<thead>
<tr>
<th>More Frequent</th>
<th>Less Frequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deviation of head and eyes</td>
<td>Simple motor automatisms</td>
</tr>
<tr>
<td>Clonic and/or tonic manifestations</td>
<td>Autonomic manifestations</td>
</tr>
<tr>
<td>Falls</td>
<td>Subjective sensations</td>
</tr>
<tr>
<td>Breaking off of contact</td>
<td>Disturbances in normal motor behavior</td>
</tr>
<tr>
<td>Phonatory manifestations</td>
<td>Complex motor automatisms</td>
</tr>
<tr>
<td>Immobility</td>
<td>Visual sensations</td>
</tr>
<tr>
<td>Memory disturbances</td>
<td>Laughter</td>
</tr>
</tbody>
</table>

**EEG Observations**

Frontal lobe spiking may be found in various forms. Spike activity is particularly scarce and the search for an EEG focus often elusive in mesiofrontal (interhemispheric) foci. If demonstrable at all, spikes are found over the superior frontal or frontal midline region; their size is small.

Large and somewhat blunted sharp waves are found in cases of presumed fronto-orbital epilepsy. Generalized synchronous spike wave bursts are found in patients with bilateral synchrony. In some of the cases, only depth EEG can demonstrate the primary focus. The ictal patterns of frontal lobe epilepsy are not basically different from other forms of neocortical focal seizure disorders.

**Course and Therapy**

Anticonvulsants indicated for use in partial seizures are the medical treatment of choice. Patients will generally require many years of treatment, so consideration of side effects is important. While most of the anticonvulsants are in pregnancy category C or D, the risk of medication to the fetus must be weighed against the risk of maternal seizures to the fetus. Due to the risk of level fluctuations, patients should not switch between brand and generic anticonvulsants, and if a generic is used, patients should receive the same generic formulation consistently.
**Drug Category:** Anticonvulsants - Prevent seizure recurrence and terminate clinical and electrical seizure activity.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Carbamazepine (Tegretol, Tegretol XR, Carbatrol)- First-line agent for partial seizures with or without secondary generalization; particularly effective in the treatment of nocturnal motor/dystonic frontal lobe seizures; potential hematologic and other adverse effects; blood monitoring is recommended. Available as tablets, extended release tablets, extended release capsules, and suspension. Patients who are not using extended release form often require tid dosing.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>200 mg PO qd or bid, initially; increase by 200 mg weekly as needed; maximal recommended dose is 1200 mg/d in divided doses; although higher doses may be required in patients on other enzyme-inducing drugs</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Small children frequently require suspension &lt;6 years: 10-20 mg/kg/d bid or tid for tab, qid for suspension; increase as needed up to 35 mg/kg/d in divided doses 6-12 years: 100 mg bid or half tsp qid; increase as needed by 100 mg/d, up to a maximum of 1000 mg/d in divided doses</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; history of bone marrow depression; administration of MAO inhibitors within last 14 d</td>
</tr>
<tr>
<td>Interactions</td>
<td>Serum levels may increase significantly within 30 days of danazol coadministration (avoid whenever possible); do not coadminister with monoamine oxidase (MAO) inhibitors; cimetidine may increase toxicity especially if taken in first 4 wk of therapy; carbamazepine may decrease primidone, and phenobarbital levels (their coadministration may increase carbamazepine levels)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>Do not use to relief minor aches or pains; caution with increased intraocular pressure; obtain CBCs and serum-iron baseline prior to treatment, during first 2 months, and yearly or every other year thereafter; can cause drowsiness, dizziness, and</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Phenytoin (Dilantin Kapseals, Dilantin Infatabs)- Available as tablets, capsules, infatabs, and suspension. A first-line agent for partial seizures; advantage of phenytoin -- quickly achieves therapeutic level and the possibility of once daily dosing (Dilantin Kapseals), which increases compliance.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>Some patients will require oral loading, in order to obtain a therapeutic level quickly. Phenytoin can be loaded as 1 g divided in 3 doses (400-300-300) at 2 hour intervals; maintenance dose of 300 mg/d should be started 24 h after loading; if patients are not to be loaded, initiate dosing at 300 mg/d, either as tid, bid, or qd; further dosage increase should be based on response to treatment; due to zero order kinetics, increase by 30 mg or 50 mg IV administration should be reserved for situations such as status epilepticus or for patients with IV access only; IV loading dose is 15-20 mg/kg; fosphenytoin is more expensive than IV phenytoin, but does not cause tissue necrosis or irritation when extravasated, and may be given IM</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>&lt;6 years: Initiate at 5 mg/kg/d in 2-3 divided doses; maintenance is 4-8 mg/kg &gt;6 years: May require adult dosing</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; sino-atrial block, second and third degree AV block, sinus bradycardia, or Adams-Stokes syndrome</td>
</tr>
<tr>
<td>Interactions</td>
<td>Amiodarone, benzodiazepines, chloramphenicol, cimetidine, fluconazole, isoniazid, metronidazole, miconazole, phenylbutazone, succinimides, sulfonamides, omeprazole, phenacemide, disulfiram, ethanol (acute ingestion), trimethoprim, and valproic acid may increase phenytoin toxicity Phenytoin effects may decrease when taken concurrently with barbiturates, diazoxide, ethanol (chronic ingestion), rifampin, antacids, charcoal, carbamazepine, theophylline, and sucralfate Phenytoin may decrease effects of acetaminophen, corticosteroids, dicumarol,</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Valproic acid, divalproex sodium (Depakote, Depakene, Depacon)- Available as tablets, capsules, syrup, sprinkles, injection. Although valproate is considered a first-line agent for the treatment of primary generalized epilepsy, it is indicated for partial seizures as well, particularly for patients with secondary generalization. Must be used cautiously in women of childbearing age; has limited use in young children due to the risk of hepatic failure, which may be fatal.</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>Adult Dose</td>
<td>10-15 mg/kg/d PO in divided doses, and increase by 5-10 mg/kg/wk; usual maximum dose is 60 mg/kg/d Alternatively, 20 mg/min IV 60-min infusion; faster rates have been used</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>&lt;2 years: Not established; risk of hepatic failure &gt;2 years: Administer as in adults</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; hepatic disease/dysfunction</td>
</tr>
<tr>
<td>Interactions</td>
<td>Coadministration with cimetidine, salicylates, felbamate, and erythromycin may increase toxicity; rifampin may significantly reduce valproate levels; in pediatric patients, protein binding and metabolism of valproate decrease when taken concomitantly with salicylates; coadministration with carbamazepine may result in variable changes of carbamazepine</td>
</tr>
</tbody>
</table>

**Pregnancy**

| D - Unsafe in pregnancy |

**Precautions**

Perform blood counts and urinalyses when therapy is begun and at monthly intervals for several months thereafter to monitor for blood dyscrasias; discontinue use if a skin rash appears and do not resume use if rash is exfoliative, bullous or purpuric; rapid IV infusion may result in death from cardiac arrest, marked by QRS widening; caution in acute intermittent porphyria and diabetes (may elevate blood sugars; discontinue use if hepatic dysfunction occurs |
concentrations with possible loss of seizure control; valproate may increase diazepam and ethosuximide toxicity (monitor closely); valproate may increase phenobarbital and phenytoin levels while either one may decrease valproate levels; valproate may displace warfarin from protein binding sites (monitor coagulation tests); may increase zidovudine levels in HIV seropositive patients

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>D - Unsafe in pregnancy</th>
</tr>
</thead>
</table>

Thrombocytopenia and abnormal coagulation parameters have occurred; the risk of thrombocytopenia increases significantly at total trough valproate plasma concentrations > 110 mcg/mL in females and 135 mcg/mL in males; at periodic intervals and prior to surgery determine platelet counts and bleeding time before initiating therapy; reduce dose or discontinue therapy if hemorrhage, bruising or a hemostasis/coagulation disorder occur; hyperammonemia may occur, resulting in hepatotoxicity; monitor patients closely for appearance of malaise, weakness, facial edema, anorexia, jaundice, and vomiting; may cause drowsiness

<table>
<thead>
<tr>
<th>Precautions</th>
</tr>
</thead>
</table>

- **Drug Name**: Gabapentin (Neurontin)- Indicated for use in partial seizures with and without secondary generalization; has relatively few drug interactions and side effects.

- **Adult Dose**: 300 mg bid or tid; may be increased weekly up to 1800-2400 mg/d in divided doses; some patients require doses up to 3600 mg/d or higher; renally excreted, dosage adjustment necessary for patients with renal dysfunction

- **Pediatric Dose**:
  - <12 years: Not established
  - >12 years: Administer as in adults

- **Contraindications**: Documented hypersensitivity

- **Interactions**: Antacids may significantly reduce bioavailability of gabapentin (administer at least 2 h following antacids); may increase norethindrone levels significantly

- **Pregnancy**: C - Safety for use during pregnancy has not been established.
<table>
<thead>
<tr>
<th>Precautions</th>
<th>Caution in severe renal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Name</strong></td>
<td>Lamotrigine (Lamictal)- Newer agent, effective for partial seizures with or without secondary generalization. Main side effect of concern is rash, which may be severe.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>Dosing depends on coadministration of other anticonvulsants, specifically valproate; see dosing instructions for specific guidelines; slow titration is recommended to prevent the occurrence of rash</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Not established</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>Acetaminophen increases renal clearance of medication, decreasing effects; similarly, phenobarbital and phenytoin increase lamotrigine metabolism causing a decrease in lamotrigine levels; administration of valproic acid with lamotrigine increases half-life</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Serious or life-threatening rash, more likely in pediatric patients and patients on valproate. While many other side effects reported, all are infrequent or rare</td>
</tr>
</tbody>
</table>

<p>| <strong>Drug Name</strong> | Levetiracetam (Keppra)- Newer agent, effective for partial seizures with or without secondary generalization. Few side effects, no drug-drug interactions. Does not require blood monitoring, although there are reports of slight decreases in red and white blood cell counts. |
|Adult Dose | 500 mg bid increase an additional 1000 mg/d in divided dosing every two weeks to a maximum recommended daily dosage of 3000 mg; slower titration may be better tolerated by some patients; no IV form available; requires adjustment for impaired renal function |
| Pediatric Dose | Not established |
| Contraindications | Documented hypersensitivity |
| Interactions | None reported |
| Pregnancy | C - Safety for use during pregnancy has not been established. |</p>
<table>
<thead>
<tr>
<th>Precautions</th>
<th>Somnolence, coordination abnormalities, and behavioral abnormalities may occur; requires adjustment for impaired renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Name</td>
<td><strong>Oxcarbazepine</strong> (Trileptal)- Indicated as monotherapy or adjunctive therapy in the treatment of partial seizures with or without secondary generalization. Mechanism of action similar to carbamazepine, without metabolism to an epoxide. Active metabolite MHD (monohydroxy derivative). If patient is being converted from carbamazepine to oxcarbazepine, the inducing effect of carbamazepine on cytochrome P450 enzymes will be reduced, and other AEDs may need adjustment. No IV form available. If added to phenytoin, may elevate phenytoin levels by up to 20%.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>Monotherapy: 150 mg or 300 mg bid initially; dose may be increased by 300 mg/d q3d; maximum recommended daily dose of 1200-2400 mg in divided dosing; elderly patients may require slower titrations</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Approved for use as adjunctive therapy in pediatric patients age 4-16. Initiate at 8-10 mg/kg, generally not to exceed 600 mg/d in divided dosing; target dose is based on weight: 20-29 kg: 900 mg/d 29-39 kg: 1200 mg/d &gt;39 kg: 1800 mg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>Increases phenytoin level; may interact with oral contraceptives, calcium channel blockers</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Hyponatremia may be clinically significant with Na &lt;125; serum sodium measurement recommended; somnolence, concentration difficulty, ataxia</td>
</tr>
<tr>
<td>Drug Name</td>
<td><strong>Topiramate</strong> (Topamax)- Indicated for adjunctive treatment of partial seizures with or without secondary generalization, and for tonic-clonic seizures. Approved for adults and for children</td>
</tr>
</tbody>
</table>
**Topiramate**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Zonisamide (Zonegran) - Indicated for adjunctive treatment of partial seizures with or without secondary generalization. There is evidence that it is effective in myoclonic and other generalized seizure types as well.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>25-50 mg/d for 1 wk, then increase by 25-50 mg/d/wk in bid dosing to therapeutic dose of 200-400 mg/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>1-3 mg/kg/d for 1 wk, then increase by 1-3 mg/kg/d every 1-2 wks to target dose of 5-9 mg/kg/d taken bid</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>Phenytoin, carbamazepine and valproic acid can significantly decrease topiramate levels; topiramate reduces digoxin and norethindrone levels, when administered concomitantly; concomitant use with carbonic anhydrase inhibitors may increase risk of renal stone formation and should be avoided; use topiramate with extreme caution when administering concurrently with CNS depressants since may have an additive effect in CNS depression, as well as other cognitive or neuropsychiatric adverse events</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Risk of developing a kidney stone formation is increased 2-4 times that of untreated population; risk may be reduced by increasing fluid intake; caution in renal or hepatic impairment</td>
</tr>
</tbody>
</table>

**Zonisamide**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Zonisamide (Zonegran) - Indicated for adjunctive treatment of partial seizures with or without secondary generalization. There is evidence that it is effective in myoclonic and other generalized seizure types as well.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>100 mg/d for 2-wk, then increase by 100 mg/d q2wk to maximum of 400 mg/d; may be given qd or bid</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Not established</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>May increase serum carbamazepine levels; carbamazepine may increase zonisamide concentrations; phenobarbital may decrease zonisamide levels</td>
</tr>
</tbody>
</table>
| Pregnancy | C - Safety for use during pregnancy has not been
established.

Precautions
May cause drowsiness, weight loss, ataxia, nausea, and slowing of mental activity

Drug Name
Tiagabine (Gabitril)- Indicated for adjunctive treatment of partial seizures with or without secondary generalization. Mechanism of action in antiseizure unknown. Believed to be related to ability to enhance activity of gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS.

Adult Dose
Begin at 4 mg/d for 1 wk, increase by 4-8 mg/d per week to maximum of 56 mg/d in 2-4 daily doses

Pediatric Dose
Not established

Contraindications
Documented hypersensitivity

Interactions
Cleared more rapidly in patients treated with carbamazepine, phenytoin, primidone, and phenobarbital than in patients who have not received these drugs

Pregnancy
C - Safety for use during pregnancy has not been established.

Precautions
Patients receiving valproate monotherapy may require lower doses or a slower dose titration of tiagabine for clinical response; moderately severe to incapacitating generalized weakness has been reported following administration of tiagabine in up to 1% of patients with epilepsy; weakness may resolve after a reduction in dose or discontinuation of tiagabine; tiagabine should be withdrawn slowly to reduce potential for increased seizure frequency

ROLANDIC (SENSORIMOTOR) EPILEPSY

- Introductory Remarks

This subsection essentially pertains to Rolandic epilepsies of adult life; benign Rolandic epilepsy of childhood and rare cases of progressive Rolandic epilepsy in children have been presented in the chapter on age-determined epileptic conditions.

Focal motor seizures arising from the pre-central motor region have been well known. These seizures beautifully reflect the somatotopic arrangement of the motor cortex.
Jackson (1870) made a clear distinction between seizures starting with twitching of facial and glossal muscles and those starting with finger, hand, or foot movements of the opposite side.

The somatotopic arrangement of the motor cortex must not be conceived of as a mosaic in which the smallest focus of epileptic irritation will give rise to contralateral twitching of extremely small corresponding muscular segments. In other words, there does not seem to be full equality among the cortical segments. Areas with a large cortical-Rolandic representation also have low thresholds for electrical stimulation (index finger, thumb, then face and foot). This is probably also true for the less commonly focal sensory seizures arising from the post-central gyrus.

- **Clinical-ictal Manifestations**

Clonic twitching of contralateral muscle segments with preserved consciousness is the principal manifestation of Cortical motor Rolandic epilepsy. This clonic activity may a) remain localized, b) spread over the rest of the contralateral half of the body, and c) eventually culminate in a grand mal seizure. The spread of clonic activity from one body region to another is widely known as "Jacksonian march".

Focal Rolandic motor seizures usually last from 10 see to several minutes. Attacks exceeding a duration of 30 min must be regarded as a focal motor status or even as epilepsia partialis continua or Koshevnikov syndrome. Most attacks started in the hand, followed by mouth, arm, fingers, foot, face, and leg. Involvement of trunk muscles was uncommon.

As to epileptic manifestations of the sensory Rolandic cortex (post-central gurus), a variety of paresthesias or dysesthesias have been observed. "Formication," or the sensation of running ants, is the most common symptom, followed by numbness, pain, and sensations of heat or cold. Pain as a sensoricortical ictal symptom is more common than one would expect from experimental data concerning pain perception and the post-central gyrus.

Focal motor or sensory attacks can stop at any stage. Sensory focal attacks are usually quickly associated with focal motor activity. Uncontaminated sensory cortical seizures are so rare that one should thoroughly rule out possibilities such as ischemic cerebral attacks or peripheral neuritic pain.

Bilateral focal motor seizures are extremely rare. In such cases, the clonic motions spread from one side gradually to the other half of the body.

Post-epileptic paralysis (Todd's paralysis) has been known since the original observations of Todd (1856). Post-ictal paresis of the ictally involved muscle segments has been thought to be caused by metabolic exhaustion but, in recent years, the concept of active inhibition has prevailed. Postictal motor deficits are more common in active pathology such as vascular lesions, AV malformations, or tumors. In general, these motor deficits are more common in children and last for minutes, hours, or a few days.
EEG Findings

The ictal EEG shows astounding variations. Lack of ictal EEG changes is a well known weakness of electroencephalography, probably due to the smallness of the cortical spiking. In the majority of the cases, ictal repetitive spiking is present over the affected motor cortex. Interictal spike activity also shows variations ranging from absence to pronounced focal spiking, which, incidentally, is most common in children with benign Rolandic epilepsy. In patients with acute watershed-type infarctions, focal motor seizures are often accompanied by PLED.

Neurophysiological Considerations

Focal motor seizures are usually strictly cortical, but the structural lesion causing the seizures may not be precisely located in the Rolandic region. Neighboring lesions may cause the pre-central cortex to erupt in epileptic discharges due to its low threshold.

Etiology

Onset of focal motor or focal sensory seizures in adult life must always raise the suspicion of a tumor involving or in the vicinity of the Rolandic cortex. Arteriovenous malformations should also be considered one of the more common causes of focal motor seizures. Post-traumatic epilepsy and cerebral arteriosclerosis are also common causes; neurosyphilis and tuberculoma previously ranked high in the list of causes.

Prevalence

Prevalence is probably between 3 and 10% of a population of epileptics, depending on the sampling.

Therapy and Course

Therapy and course depend strongly on the type of underlying pathology. In general, focal motor and sensory seizures show a good to very good response to first line anticonvulsants. Surgical interventions are limited by the threat of subsequent catastrophic motor deficits. Removal of parasagittal meningiomas is usually followed by excellent results.

PARIETAL LOBE EPILEPSY

Epileptic phenomena of parietal origin do not form a well defined epileptological entity. Parietal lobe functions are complex; functional differences between the dominant and the nondominant parietal lobe compound the problems of parietal lobe function.

There is, therefore, no typical parietal lobe seizure symptomatology. In most cases, the seizures affect visual functions and a variety of complex visual disturbances may be found, such as scintillation or oscillopsia. Short attacks of extremely severe vertigo may occur.
Automatisms and ictal tonic postural changes of the upper limbs is reported as parietal lobe phenomena.

Trauma is the most common cause of these seizures. Post-traumatic epilepsy caused by lacerating wounds from high velocity projectiles and shell fragments most often affects the centroparietal region.

**OCCIPITAL LOBE EPILEPSY**

Epileptic phenomena of the occipital lobe are not common. When the attacks originate from the calcarine fissure, elementary visual sensations such as bright light, sparks, or a ball of fire are experienced. The sensations may move across the visual field or remain stationary for the duration of the seizure. Spread from a temporal lobe focus into the occipital region with elementary visual ictal sensations has been reported.

Attacks of blindness may be accompanied by generalized spike wave activity. Bilateral synchronous occipital spike wave activity has been reported during visual hallucinations. Epileptic nystagmus, also called oculocionic seizures, may occur during occipital lobe seizures. It is interesting to note that occipital lobe epilepsy tends to occur in acute or subacute cerebral disorders. Occipital lobe epilepsy must be carefully distinguished from migrainous or ischemic disturbances.

**REFERENCES**

INTRODUCTION

The age of the patients has great influence on the ictal, clinical and EEG characteristics of the epileptic seizures disorders and it also determines the course and prognosis of epilepsy in general. This is particularly true in the first two decades of life, especially for infancy and early childhood. There are certain age- determined epileptological entities or epileptic conditions which appear to be monolithic, in spite of a wide variety of etiologies and probably also despite variations in the localization of cerebral involvement. The role of age in epileptic seizure disorder has been substantiated by experimental work and clinical electroencephalographic investigations. We find in age-determined epileptic conditions a)
certain condition-related types of seizures, b) certain condition-related EEG patterns, and c) certain condition-related characteristics of course and prognosis.

In the past, this aspect of epileptic seizure disorder had been neglected; too much emphasis was universally placed on locus and cause of the seizure. From the historical viewpoint, the description of infantile spasm and the discovery of a specific EEG pattern called hypsarrhythmia mark the first individualization of an age-determined polyetiologic epileptic condition with certain clinical-electroencephalographic criteria. There is a long historical evolution of the very common condition known as febrile convulsions. The clinical picture of benign Rolandoic epilepsy became clear due to the efforts of numerous authors. Neonatal convulsions, which are a particularly heterogeneous group, must also be listed in this context and the thought-provoking notion of primary generalized epilepsy also belongs in this category.

**Figure 1.** The course of various age-dependent epileptic seizure disorders in a longitudinal view.

<table>
<thead>
<tr>
<th></th>
<th>0-3 months</th>
<th>4-24 months</th>
<th>2-5 years</th>
<th>6-10 years</th>
<th>11-15 years</th>
<th>16-20 years</th>
<th>21-30 years</th>
<th>Above 30 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNCB</td>
<td>Often seizure free</td>
<td>Conversion to (IS) and/or (LGS)</td>
<td>Conversion to (LGS)</td>
<td>Conversion to (LGS)</td>
<td>Often seizure free</td>
<td>TLE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNCS</td>
<td>0-24 months</td>
<td>4 months-5 years</td>
<td>4 months-5 years</td>
<td>4 months-30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td>4 months-5 years</td>
<td>Conversion to (LGS)</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FC</td>
<td>4 months-30 years</td>
<td>TLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGS</td>
<td>4 months-30 years</td>
<td>TLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGE 1</td>
<td>Often febrile convulsion</td>
<td>2 years-20 years</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGE 2</td>
<td>2 years-10 years</td>
<td>11 years-30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRE</td>
<td>Often seizure free</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NNCB**=neonatal convulsion, benign; **NNCS**= neonatal convulsion severe; **IS**= infantile spasm; **FC**=febrile convulsion; **LGS**= Lennox-Gastaut syndrome; **PGE 1**= primary generalized epilepsy with absence attacks; **PGE2**= primary generalized epilepsy with myoclonic attacks; **BRE**= benign Rolandoic epilepsy, TLE = temporal lobe epilepsy.
Table 1. Comparison between the classical age-dependant generalized epileptic EEG discharge.

<table>
<thead>
<tr>
<th>EEG TYPE</th>
<th>AGE</th>
<th>CLINICAL CORRELATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical 3 c/s SWD</td>
<td>3.5 years -16 years</td>
<td>Petit mal epilepsy</td>
</tr>
<tr>
<td>Slow SWD (1-2.5 c/s)</td>
<td>6 months-16 years</td>
<td>Lennox-Gastaut syndrome</td>
</tr>
<tr>
<td>Fast SWD (4-6 c/s)</td>
<td>Over 16 years</td>
<td>Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Hypsarrhythmia</td>
<td>4 months -4 years</td>
<td>West syndrome</td>
</tr>
</tbody>
</table>

NEONATAL CONVULSION

- Introductory Remarks

In the neonatal period of life, epileptic seizures are fairly common and may be caused by a wide variety of etiologies. There is some reason to presume that neonatal convulsions play a greater role in the lives of full-term infants than in premature infants, notwithstanding the high risk of brain damage caused by prematurity. The neonatal period may be extended to the first 3 mos of life by some, while holders of a stricter view limit this period to the first 3 wk. Neonatal convulsions are common; their prevalence may range from 0.2% to 1.2% of all live births.

Tonic seizures are also quite common; they consist of opisthotonus, extension or elevation of limbs, and, often, rotation of head and eyes. "odd movements" of the limbs (swimming or rowing movements), chewing, eye blinking, opening of eyes, nystagmus, and an abnormal cry are also among the clinical manifestation of neonatal seizures. Episodes of apnea may be ictal or nonictal. Neonatal seizures are divided into a) tonic, b) clonic, c) atonic, d) autonomic, and e) automatism-like seizures.

- Clinical Ictal Manifestations of Neonatal Seizures

At this early age, convulsive movements are not easily distinguished from physiological motor activity, this is particularly true for seizures in premature infants with barely recognizable convulsive movements. Combined video recording and tele-encephalographic documentation has been helpful in the distinction of physiological and convulsive motions.

Organized tonic-clonic sequences of the grand mal type do not occur in the first 4 to 6 mos of patient's life and are precluded by the lack of cerebral maturation in terms of myelination. Poorly organized tonic-clonic attacks may occasionally occur in neonates. Clonic seizures may begin in any part of the body and progress from one region to another in an irregular fashion. Spread often remains ipsilateral although full-blown hemiconvulsions are not encountered. Clonic movements may remain localized throughout the seizure.
Seizures Versus Status Epilepticus in the Neonate

Neonatal seizures are often unusually prolonged or consist of a seemingly endless succession of seizures with brief inter-ictal interval. For this reason, the term "neonatal status epilepticus" has been used frequently. It simply appears to be the nature of severe neonatal convulsions to show status-like character. The convulsions themselves do not reach the degree of severity found in status epilepticus of a more mature age, especially grand mal status. The severity of the clinical condition lies in the disorder which causes the seizures rather than in the seizure as such.

EEG Findings

In milder forms of neonatal convulsions (benign forms), chances are that the recording is obtained in the interictal state and the record shows no significant abnormalities.

In severe forms, ictal EEG abnormalities are the rule. Two types of ictal EEG changes ought to be distinguished. These are 1) repetitive long stretches of rhythmical spiking, often in the disguise of rhythmical slow activity with a disguised spike component often varying the frequency of ictal firing, ranging from alpha frequency down to the low delta range, and 2) a very irregular pattern with widespread nearly flat stretches and irregularly mixed bursts of high voltage slow activity, with waves in the medium and fast range, and massive spikes or sharp waves.

The first pattern described is more often noted. Its character is essentially multifocal. The onset of an attack is practically always focal. The occipital and central areas are the most common sites of focal ictal spiking, whereas the frontal and temporal areas are less often involved. The temporal region is the most frequent site, followed by the occipital region. The ictal discharge in the newborn generally remains localized to one hemisphere, it may spread slowly to involve the entire hemisphere or the entire contralateral hemisphere rather than spreading to the opposite side as it is often observed in adult seizures.

There are no firm electro-clinical correlations, although it has been thought that clonic movements more often occur with spikes and tonic phenomena, with delta discharges. Swimming or rowing movements or tonic spasms are sometimes associated with artifact-disturbed stretches of low voltage.

For the novice in neonatal EEG recording, the rhythmical slow or spike activity in an ictal episode appears to be "unreal" and hence artifactual, since the type of discharge is hardly ever seen at other periods of life.

As to the second pattern described above, no rhythmical spiking is noted; irregular bursts, often asynchronous, and interspersed nearly flat stretches dominate the picture. Generalized synchronous bursts are essentially alien to neonatal convulsions and only faint suggestions of such bursts may materialize. The accompanying ictal clinical manifestations are usually short tonic spasms or short myoclonic jerks. The entire pattern represents a foretaste of hypsarrhythmia; it is present with little or no interruption for weeks and tends
to convert into full-blown hypsarrhythmia. This occurs usually between the ages of 4 and 6 (or 3 and 5) mos when the voltage output reaches the typical high amplitudes of hypsarrhythmia.

In very severe forms of neonatal seizure disorder, the newborn shows an almost flat record in spite of numerous convulsive activities. This may be observed in neonatal herpes simplex encephalitis; the nearly flat character is prognostically ominous, although the infant will gradually show increasing voltage output and a more customary EEG type of neonatal convulsion.

The interictal EEG depends heavily on the general state of the body, especially on the level of consciousness. Preserved consciousness with an "alert look" was found in 30% of the infants despite repetitive convulsions. The EEG may show ictal-subclinical patterns. Otherwise, the record usually lacks the typical interictal finding of random spikes or shows such spikes in an attenuated form only. There is no evidence that a particular state of sleep facilitates or depresses seizures; a low percentage of active REM sleep, 22-30% compared with 40-60% in normal newborns, has been reported.

- **Aetiological Considerations**

The prognosis of neonatal convulsions depends heavily on its cause and the type of underlying pathology. This sets neonatal convulsions apart from other age-determined epileptic conditions, in which the etiology is usually less important that the epileptic condition as such. Causes ranges between extracranial infection (mainly gastroenteritis with dehydration and pneumonia), structural noninfectious brain damage (asphyxia for example) and metabolic disorder. It has to be kept in mind that structural brain damage from cerebral malformations, asphyxia, or birth injury manifests itself in the first few days of life, as opposed to seizures due to infections, which are more apt to occur after the first week.

Hypocalcemia in the first week of life is usually a more serious cause of convulsions than hypocalcemia of the second week, which is due to alimentary problems. Idiopathic infantile hypoglycemia has a very poor prognosis. In this EEG-oriented presentation, the multitude of causes can not be presented in detail.

- **Therapy and Prognosis**

Anticonvulsant treatment is essentially based on phenobarbital (im or orally, 2 mg/kg within 24 hr); the use of adjuvants cannot be discussed in this context.

The immediate or short-range mortality of neonatal convulsions is considerable and may reach 54%. The long-range prognosis is good only for the benign forms of neonatal convulsions, usually caused by extracranial infections and milder forms of metabolic disturbances. Mild to moderate infections with meningeal more than encephalitic involvement also suggest a good prognosis. Next come the more serious CNS infections, while cerebral malformations, very severe and very early CNS infection, and some very
damaging metabolic disturbances are most likely to result in "malignant" forms of neonatal convulsions, followed by either fatal outcome or severe CNS residues with mental retardation.

The EEG in the acute convulsive state has proved to be very helpful. 86% of the infants with normal neonatal EEG were normal at a mean age of 4 yr, whereas 69% of those with unifocal EEG abnormalities and 11.8% of those with multifocal EEG abnormalities were normal at a mean age of 4 yr.

**INFANTILE SPASM (HYPSARRHYTHMIA)**

- **Historical Remarks**

Infantile spasms consist of sudden tonic and myoclonic phenomena. The term "infantile spasms" is quite satisfactory from the clinical viewpoint and should be preserved. "Hypsarrhythmia" is an EEG term which denotes the EEG correlate of the condition and has found surprisingly wide acceptance with clinicians; a clinical term such as infantile spasms is certainly preferable as far as the clinical condition as such is concerned.

- **Age**

Infantile spasms are found in the age range from 4 to 30 mos; earlier and later occurrences of the condition are exceptional. This age range is particularly valid when one looks upon this condition from the combined clinical-electroencephalographic viewpoint. Then it becomes clear that a truly hypsarrhythmic EEG pattern does not develop before age 4 mos, although at 3 mos a very similar EEG picture may be present already. From a purely clinical viewpoint, one could define infantile spasms as beginning right after birth. The hypsarrhythmic pattern tends to develop out of the irregular pattern with bursts and flat stretches in neonatal convulsions as mentioned in the preceding section.

The end of the period of infantile spasms essentially parallels the disappearance of the hypsarrhythmic pattern; this usually occurs in the second half of the third year of life. In exceptional cases, the pattern may linger on for a year or even longer (up to 8 yr).

- **Clinical ictal Manifestations**

Both clonic and tonic phenomena may occur in infantile spasms. The most common type is a massive flexion myoclonus of head, trunk, and extremities, known as "jackknifing." The lightning-like character of this sequence of movements permits an exact analysis only with the use of videotape documentation. The tonic phenomena are slower and may last 2 to 5 see with accompanying autonomic changes such as flushing or lacrimation.

The clonic spasm may show some variation. Instead of abduction of the extremities, adduction may occur to such a degree that the infant appears to be embracing himself, whereas the abduction pattern seems to simulate the Moro reflex. Extensor spasms are also observed; there is sudden extension of neck and trunk with symmetrical forward extension.
and extension of lower extremities at the hips and knees ("cheerleader spasm"). Head nodding may also occur.

The ictal manifestations of infantile spasms are short but tend to repeat themselves in rapid succession. Unilateral spasms have been described. Up to several hundred or even several thousand spasms per day may occur.

- **Clinical Signs of Nonictal Character**

The general clinical picture of the baby depends on the degree of accompanying brain damage. A sizable number of infants with infantile spasms and hypsarrhythmia (about one-third) are brain damaged from birth; many of them have passed through a period of severe neonatal convulsions. Severe cerebral malformations or CNS infections are common causes in such cases. Signs of cerebral palsy in its various forms may be demonstrable.

In many other cases, infantile spasms suddenly start in a previously healthy baby and, at that time, the hypsarrhythmic EEG pattern is already present. When untreated, the psychomotor development of the infant shows signs of retardation starting with the onset of attacks.

- **EEG Findings**

The EEG findings are quite unique and essentially unmistakable, although there is a certain gray zone of questionable or borderline cases. The term hypsarrhythmia is derived from the Greek word "hypselos," which means "high," thus indicating the high voltage which generally predominates. No hypsarrhythmic recording can be appropriately obtained with the standard sensitivity of the EEG apparatus; lowering the sensitivity is required. Bursts of very high voltage slow waves occur in irregular fashion with a varying degree of bilateral synchrony which usually increases in sleep. The stages of early nonREM sleep are particularly conducive to a typical hypsarrhythmic recording. Long stretches of high voltage slow and intermixed spike activity may suddenly be interrupted by a brief stretch of near flatness in all leads, or less commonly near flatness in a few leads or over one hemisphere; these flat stretches are practically limited to sleep tracings.

The spike activity shows single spikes and sharp waves, as well as very brief sequences of polyspikes which are usually of smaller amplitude. The spike activity is almost always of posterior accentuation. **The posterior maximum of spike activity is quite helpful in differentiation from the Lennox-Gastaut syndrome**, which sometimes starts exceptionally early (i.e., between the ages of 6 and 12 mos), when one usually sees the onset and evolution of infantile spasms with hypsarrhythmia. Large slow spike waves of frontal accentuation are found in babies with the Lennox-Gastaut syndrome. This unfortunately barely known distinction helps clarify the differentiation of these two conditions.

The ictal EEG, the concomitant of infantile spasms, is quite variable. Fast activity and high voltage spikes may accompany the attacks, polyspikes and slow waves may be present, no change of the hypsarrhythmic interval EEG may occur, but, most commonly, a sudden
suppression of the EEG activity may be seen for several seconds. A sleep recording is a necessity since, in some cases, the waking record may be unreadable while hypsarrhythmia is confined to the sleep portion.

Hypsarrhythmia is almost but not always a reliable EEG correlate of infantile spasms. There are clinically convincing cases with no hypsarrhythmia, but in these rare exceptions the voltage output is unusually high. Unless there is a rapid response to treatment, the hypsarrhythmic pattern is likely to appear in the further course of such infants.

On the other hand, the clinician could be the one to be blamed when the expected hypsarrhythmia is not found; his presumptive diagnosis may be wrong. The clinical differential diagnosis of infantile spasms or hypsarrhythmia includes a variety of conditions:

- **Spasmus nutans:** EEG normal
- **Jactatio capitis nocturna:** EEG normal
- **Salaam tic or "salutatory" spasms (Moro):** Nonspecific EEG abnormalities sometimes with spikes in combination with epileptic seizures, but no hypsarrhythmia
- **Myoclonic encephalopathy (Kinsbourne, 1962):** EEG normal

**Aetiological and Neuropathological Considerations**

The etiologies are divided into the idiopathic group and the symptomatic group. There is general consensus among investigators that the symptomatic group with known neurological disease or evidence of any kind of brain damage is the larger one. The ratio is approximately one-third of cases with idiopathic forms to two-thirds with symptomatic forms. Computerized tomography can detect structural anomalies in cases which might have been diagnosed as idiopathic in earlier years.

The number of etiological factors is enormous. Traumatic or asphyxic perinatal brain damage may lead to cerebral palsy associated with hypsarrhythmia; many developmental and congenital CNS anomalies may lead to this condition, with tuberous sclerosis as a more common cause. Inborn errors of metabolism and post-infectious states must also be mentioned. The idiopathic form with no evidence of structural brain damage remains an enigma. This form was conceived as a nosological entity ("infantile myoclonic encephalopathy"), but this concept has not found general approval. Familial occurrence is not common, but certainly not negligible; it ranges from 3 to 6%.

**The Aicardi Syndrome as a Special Form of Infantile Spasm**

This syndrome consists of infantile spasms (flexor spasms), agenesis of the corpus callosum, and chorioretinal anomalies. The cause has remained obscure and the nature of this syndrome is poorly understood. The EEG shows hypsarrhythmia in some of these patients. Some of the hypsarrhythmic records showed remarkable asymmetries. Even the flexor spasms were often asymmetrical or limited to one-half of the body.
Pathogenetic Concepts

Infantile spasms with hypsarrhythmia (West syndrome) are now listed as "secondary generalized epilepsy," in company with the Lennox-Gastaut syndrome and specific epileptogenic encephalopathies, such as essential, hereditary myoclonus epilepsy or Tay-Sachs disease. This implies that there must be a primary focus which is eventually superseded by generalization of the EEG phenomena as well as the clinical manifestations, which are void of any specific focal character.

This basic concept of secondary generalization is not proven, although many of these cases show focal structural lesions. One could speculate, however, that a special genetic component predisposes certain infants to this type of epileptic reaction. Thus, a case of cerebral palsy may be accompanied by any type of epileptic seizure or infantile spasms-hypsarrhythmia if a special genetic predisposition is present.

Therapy and Prognosis

The goals of pharmacotherapy are to reduce morbidity and prevent complications.

Drug Category: Adrenocorticotropic agents - Cause profound and varied metabolic effects. Corticosteroids modify the body's immune response to diverse stimuli.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Corticotropin (Acthar, ACTH)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated efficacy (percentage of infants with West syndrome reaching seizure freedom) is 50-67%. Associated with serious, potentially life-threatening adverse effects. Must be administered IM, which is painful to the infant and unpleasant for the parent to perform. Daily dosages are expressed either as U/d (most common), U/m²/d, or U/kg/d. A prospective single-blind study demonstrated no difference in the effectiveness of high-dose, long-duration corticotropin (150 U/m²/d for 3 wk, tapering over 9 wk) versus low-dose, short-duration corticotropin (20-30 U/d for 2-6 wk, tapering over 1 wk). With respect to spasm cessation and improvement in the patient's EEG; hypertension was more common with larger doses.</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Not established; 5-40 U/d IM for 1-6 wk to 40-160 U/d IM for 3-12 mo suggested; some authors recommend 150 U/m²/d IM for 6 wk or 5-8 U/kg/d IM in divided doses for 2-3 wk</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; porcine protein</td>
</tr>
</tbody>
</table>

www.yassermetwally.com
<p>| Hypersensitivity, scleroderma, recent surgery, congestive heart failure, primary adrenal insufficiency, hypercortisolism, active herpes infection, active tuberculosis, herpes simplex ocular infection, thromboembolic disease, or active serious bacterial, viral, or fungal infection; avoid vaccines and immunizations during therapy |
| Amphotericin B can decrease response; acetazolamide or other carbonic anhydrase inhibitors can cause hypernatremia, hypocalcemia, hypokalemia, and edema; diuretics can reduce natriuretic and diuretic effects; potassium-depleting diuretics can cause hypokalemia; phenytoin, barbiturates, and rifampin can decrease corticosteroid effects; estrogens can potentiate effects; salicylates or NSAIDs can cause GI ulceration; growth hormone (somatropin) can reduce growth response to somatropin; warfarin can decrease anticoagulation response |
| C - Safety for use during pregnancy has not been established. |
| Because of increased risk of infection, hypertension, hypertrophic cardiomyopathy, and electrolyte disturbances, careful and frequent clinical and laboratory monitoring of the patient is essential. Caution in Cushing disease, hypertension, hypokalemia, hypernatremia, diverticulitis, ulcerative colitis or intestinal anastomosis, renal disease, diabetes mellitus, hypothyroidism, hepatic disease |
| Prednisone (Deltasone, Orasone, Meticorten)- Few comparative studies between ACTH and prednisone have been performed; one double-blind, placebo-controlled, crossover study demonstrated no difference between low-dose ACTH (20-30 U/d) and prednisone (2 mg/kg/d) while a second prospective, randomized, single-blinded study demonstrated high-dose ACTH at 150 U/m²/d was superior to prednisone (2 mg/kg/d) in suppressing clinical spasms and hypsarrhythmic EEG in infants with infantile spasms. |</p>
<table>
<thead>
<tr>
<th><strong>Pediatric Dose</strong></th>
<th>2 mg/kg/d PO for 2-4 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; viral infection, peptic ulcer disease, hepatic dysfunction, connective tissue infections, and fungal or tubercular skin infections; GI disease</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Barbiturates, phenytoin, rifabutin, and rifampin can increase metabolism of prednisone; hyperthyroidism can increase metabolism of prednisone; hypothyroidism can decrease metabolism of prednisone; isoproterenol in patients with asthma can increase risk of cardiac toxicity, clinical deterioration, myocardial infarction, congestive heart failure, and death</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>B - Usually safe but benefits must outweigh the risks.</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Prolonged therapy can affect metabolic, GI, neurologic/behavioral, dermatologic, and endocrine systems; metabolic adverse events can include (but are not limited to) fluid retention and electrolyte disturbances (eg, hypernatremia, hypokalemia, hypokalemic metabolic alkalosis, hypocalcemia), edema, hypertension, and hyperglycemia; GI adverse events can include nausea, vomiting, abdominal pain, anorexia, diarrhea, constipation, gastritis, esophageal ulceration, weight loss, and delayed growth; neurologic and behavioral adverse events reported during prolonged administration can include headache, insomnia, restlessness, mood lability, anxiety, personality changes, and psychosis; visual adverse events may include exophthalmos, retinopathy, posterior subcapsular cataracts, and ocular hypertension; dermatologic adverse events reported during therapy can include skin atrophy, diaphoresis, impaired wound healing, facial erythema, hirsutism, ecchymosis, and easy bruising; endocrinologic adverse events from prolonged use include hypercorticism and physiologic dependence; idiosyncratic reactions include pancreatitis and dermatologic hypersensitivity reactions (allergic dermatitis, angioedema, urticaria); avoid vaccination with live-virus vaccines; avoid abrupt discontinuation if the patient has been on long-term therapy; caution in congestive heart failure, hypertension,</td>
</tr>
</tbody>
</table>
glaucoma, GI disease, diverticulitis, intestinal anastomosis, hepatic disease, hypoalbuminemia, peptic ulcer disease, renal disease, osteoporosis, diabetes mellitus, hypothyroidism, coagulopathy or thromboembolic disease, or potential impending GI perforation

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Vigabatrin- Not approved by the FDA in the US but is available in many countries worldwide. Multiple studies (both open label and double blind) have demonstrated effectiveness in stopping seizures in infants with West syndrome, especially when caused by tuberous sclerosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Dose</td>
<td>Initial dose: 40 mg/kg/d in 2 divided doses Maintenance doses: 40-150 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Precautions</td>
<td>Dose-dependent adverse effects include hyperactivity, agitation, sedation, depression, psychosis, drowsiness, insomnia, facial edema, ataxia, nausea and/or vomiting, stupor, and somnolence; idiosyncratic reactions include visual field constriction; may exacerbate myoclonic and absence seizures in some patients; long-term reactions (cumulative adverse effects) include weight gain; lower doses in patients with renal dysfunction</td>
</tr>
</tbody>
</table>

**Drug Category: Benzodiazepines** - By binding to specific receptor-sites these agents appear to potentiate the effects of gamma-aminobutyrate (GABA) and facilitate inhibitory GABA neurotransmission and other inhibitory transmitters.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Clonazepam (Klonopin)- Considered second-line AED therapy against spasms associated with West syndrome. Adverse effects and the development of tolerance limit usefulness over time. Nitrazepam and clobazam are not approved by the FDA in the US but are available in many countries worldwide.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Dose</td>
<td>Maintenance dose: 0.01-0.2 mg/kg/d PO</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity, significant liver disease, and acute narrow-angle glaucoma</td>
</tr>
<tr>
<td>Interactions</td>
<td>Decrease plasma levels of phenytoin,</td>
</tr>
</tbody>
</table>
phenobarbital, and carbamazepine; potentiate CNS depression induced by other anticonvulsants and alcohol; may reduce renal clearance of digoxin; cimetidine and erythromycin decrease clearance

**Pregnancy**
D - Unsafe in pregnancy

**Precautions**
Dose-dependent adverse effects of clonazepam include hyperactivity, sedation, drooling, incoordination, drowsiness, ataxia, fatigue, confusion, vertigo, dizziness, amnesic effect, and encephalopathy; clobazam is considered the least sedating benzodiazepine; long-term (cumulative) adverse effects include tolerance and dependence; clobazam is considered to have the longest time to the development of tolerance; adjust dose or discontinue therapy in presence of renal or liver function impairment, since metabolism occurs in the liver and metabolites are excreted in urine

**Drug Category:** *Anticonvulsants* - Prevent seizure recurrence and terminate clinical and electrical seizure activity.

<table>
<thead>
<tr>
<th><strong>Drug Name</strong></th>
<th><strong>Valproic acid</strong> (Depakote, Depakene, Depacon)- Considered an effective second-line AED therapy against spasms associated with West syndrome.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Initial dose: 10-15 mg/kg/d PO in divided doses bid/tid Titrination: 5-10 mg/kg/d increments at weekly intervals until therapeutic effect is achieved or toxicity occurs Maintenance dose: 15-60 mg/kg/d PO</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; history of hepatotoxicity or pancreatitis (patients at high risk for hepatotoxicity include &lt;2 y, multiple concomitant AEDs including phenobarbital, underlying metabolic disease, such as, defect in fatty acid oxidation, and developmental delay)</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Coadministration with cimetidine, salicylates, felbamate, and erythromycin may increase toxicity; rifampin may significantly reduce valproate levels; in pediatric patients, protein binding and metabolism of valproate decrease when taken concomitantly with salicylates; coadministration with carbamazepine may result</td>
</tr>
</tbody>
</table>
in variable changes of carbamazepine concentrations with possible loss of seizure control; valproate may increase diazepam and ethosuximide toxicity (monitor closely); valproate may increase phenobarbital and phenytoin levels while either one may decrease valproate levels; valproate may displace warfarin from protein binding sites (monitor coagulation tests); may increase zidovudine levels in HIV seropositive patients

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>D - Unsafe in pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precautions</td>
<td>Dose-dependent adverse effects include asthenia, nausea, vomiting, somnolence, tremor, and dizziness; less common adverse effects include thrombocytopenia and parotid swelling; idiosyncratic reactions include hepatotoxicity and pancreatitis; long-term (cumulative) adverse effects include hair loss and weight gain</td>
</tr>
</tbody>
</table>

**Drug Name**

| Lamotrigine (Lamictal)- Inhibits release of glutamate and inhibits voltage-sensitive sodium channels, leading to stabilization of neuronal membrane. Effectiveness in West syndrome has been investigated in open-label studies with promising results. Initial dose, maintenance dose, titration intervals, and titration increments depend on concomitant medications. |

**Pediatric Dose**

<p>| Combination with AEDs that induce hepatic CYP-450 enzyme system WITHOUT valproate: Initial starting dose: 0.6 mg/kg/d PO for 2 wk; 1.2 mg/kg/d for wk 3-4; 5-15 mg/kg/d thereafter; after week 4, dosage increment not to exceed 1.2 mg/kg/d q1-2wk until maintenance dose achieved; maximum daily dose is 400 mg/d |
| Combination WITH valproate with or without other AEDs that induce hepatic CYP-450 enzyme system: Initial starting dose: 0.15 mg/kg/d PO for 2 wk; 0.3 mg/kg/d for weeks 3-4; 1-5 mg/kg/d thereafter; after week 4, dosage increment not to exceed 0.3 mg/kg/d q1-2wk until maintenance dose achieved; usual maximum daily dose is 200 mg/d |</p>
<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Documented hypersensitivity; history of erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis; erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interactions</td>
<td>Affected by concomitant AEDs; when used in conjunction with medications that induce hepatic CYP-450 microsomal enzymes (phenobarbital, carbamazepine, phenytoin), clearance is enhanced; conversely, when used in conjunction with medications that inhibit hepatic CYP-450 microsomal enzymes (valproate), clearance is diminished; lower starting doses, a slow titration rate (ie, 2 or more wk intervals between dosage increases), and smaller increments are needed</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Dose-dependent adverse effects include ataxia, diplopia, dizziness, headache, nausea, and somnolence; idiosyncratic reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis; no long-term (cumulative) adverse effects noted to date. Risk factors for associated severe dermatologic reactions include younger age (children more than adults), co-medication with valproic acid, rapid rate of titration, and high starting dose; give careful attention to initial starting dose, titration rate, and co-medications; prompt evaluation of any rash is prudent and imperative; approximately 10-12% of patients develop a non–life-threatening rash that usually resolves rapidly upon withdrawal and occasionally without changing the dosage</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Topiramate (Topamax)- Sulfamate-substituted monosaccharide with broad spectrum of antiepileptic activity that may have a state-dependent sodium channel blocking action, potentiates the inhibitory activity of the neurotransmitter gamma-aminobutyrate (GABA). May block glutamate activity. Effectiveness in West syndrome has been investigated in one open-label study with promising results.</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Initial starting dose: 2-3 mg/kg/d PO; increment of 2-3 mg/kg q3-4d&lt;br&gt;Maintenance dose: 15-20 mg/kg/d PO</td>
</tr>
<tr>
<td>----------------</td>
<td>------------------------------------------------------------------</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>May increase phenytoin plasma levels; may decrease valproate plasma levels; phenytoin and carbamazepine decrease levels</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Dose-dependent adverse effects include irritability, ataxia, dizziness, fatigue, nausea, somnolence, psychomotor slowing, concentration, constipation, and speech problems; if CNS adverse effects occur, reduce concomitant AEDs, slow titration, or reduce dose; no idiosyncratic reactions noted; oligohidrosis and nephrolithiasis are reported</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Zonisamide (Zonegran)- Effectiveness in West syndrome has been investigated in 5 open-label studies with promising results.</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Initial dose: 1-2 mg/kg/d; increase 1-2 mg/kg/d q2wk&lt;br&gt;Maintenance dose: 8-12 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>Phenytoin, phenobarbital, carbamazepine, and valproate decrease half life; no effect on steady-state plasma concentrations of other AEDs</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Dose-dependent adverse effects include headache, anorexia, nausea, dizziness, ataxia, paresthesia, difficulty concentrating, irritability, and somnolence; idiosyncratic reactions include severe rash (Stevens-Johnson syndrome, toxic epidermal necrolysis) with a reporting rate of 46 per million patient-years of exposure; oligohidrosis and nephrolithiasis are reported</td>
</tr>
</tbody>
</table>

**Drug Category:** *Vitamins* - Essential for normal metabolic processes

| Drug Name | Pyridoxine (Vitamin B-6)- Two distinct treatment |
situations exist where pyridoxine is used in patients with West syndrome:
(1) IV administration during diagnostic EEG to assess if patient's seizures and EEG abnormalities are related to pyridoxine dependency. In this approach, administer 50-100 mg IV during the diagnostic EEG; if a dramatic improvement is noted in the EEG, the patient is believed to have pyridoxine-dependent seizures.
(2) Long-term oral administration: Effectiveness of chronic oral high-dose pyridoxine in West syndrome has been investigated in multiple open-label studies with promising results; most patients who respond to chronic oral high-dose pyridoxine do so within 1-2 wk of initiation.

| Pediatric Dose | Initial dose: 10-20 mg/kg/d PO  
| Titration: 10 mg/kg q3d  
| Maintenance dose: 15-50 mg/kg/d PO (approximately 100-400 mg/d) |
| Contraindications | Documented hypersensitivity; do not administer IV to infants with cardiac disease |
| Interactions | Can decrease phenobarbital and phenytoin serum concentrations |
| Pregnancy | C - Safety for use during pregnancy has not been established. |
| Precautions | Usually well tolerated; adverse events include decreased appetite, nausea, vomiting, paresthesias, diarrhea, somnolence, and headache; abnormal liver function tests and low serum folic acid levels have been noted in some patients; long-term (cumulative) adverse effects can include severe sensory peripheral neuropathy, movement disorders, and ataxia |

Infantile spasms used to be regarded as therapeutically hopeless in view of the poor response to the classical anticonvulsants, such as phenobarbital and diphenylhydantoin. The observation of an excellent response to ACTH represents one of the most important steps forward in the history of modern anticonvulsive therapy.

The EEG shows almost immediate improvement under effective therapy. This does not necessarily reflect clinical improvement. Complete normalization may occur, but such responses are mostly temporary; return of spike activity, mostly over posterior regions, is a common event. In many cases with poor therapeutic response and especially in those with
preexisting brain damage and history of neonatal convulsions, transition into the Lennox-Gastaut syndrome is common.

**FEBRILE CONVULSIONS**

- **Introductory Remarks, Age and Definition**

This condition is probably the most common epileptic seizure disorder; about 3--4% of all children have at least one febrile seizure in infancy or early childhood. The attacks tend to occur between the ages of 6 mos and 5 yr, especially between 6 mos and 3 yr. The onset falls into the range of 6 to 24 mos. It is unwise to call fever-induced convulsions after the age of 4 yr "simple febrile convulsions."

Febrile convulsions must be strictly separated from epileptic seizures in infants or children with an acute severe febrile disease giving rise to structural lesions. The differences are indicated in Table 2. Lumping together both groups would tarnish the predominantly excellent diagnosis of simple febrile convulsions.
Table 2. Differences between Febrile convulsion and Seizures during febrile brain disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Febrile convulsion</th>
<th>Seizures during febrile brain disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical age</td>
<td>6 months- 3 years</td>
<td>0-3 years</td>
</tr>
<tr>
<td>Genetic</td>
<td>strong</td>
<td>None</td>
</tr>
<tr>
<td>Type of seizure</td>
<td>tonic-clonic</td>
<td>Tonic-clonic or hemiconvulsion</td>
</tr>
<tr>
<td>Duration of seizure</td>
<td>1-3 minutes</td>
<td>Prolonged, 10 minutes to hours or status epilepticus</td>
</tr>
<tr>
<td>Clinical setting</td>
<td>At the onset of fever, mostly due to upper respiratory tract infection, often coinciding with the first sharp rise of temperature</td>
<td>Mostly due to CNS infection or cerebrovascular accident of infancy</td>
</tr>
<tr>
<td>Cerebral pathology</td>
<td>None</td>
<td>Common</td>
</tr>
<tr>
<td>Post-ictal deficit</td>
<td>None</td>
<td>Common</td>
</tr>
<tr>
<td>EEG</td>
<td>Rapidly normalize after convulsion, with normal interictal pattern in over 90% of cases</td>
<td>Abnormal during convulsion and interictally</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Not necessary (neither during the acute convulsion nor for prevention of future convulsion)</td>
<td>Often needed</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Good, occasionally progress to primary generalized epilepsies</td>
<td>Guarded, non febrile seizures are common, occasionally progress to temporal lobe epilepsy</td>
</tr>
</tbody>
</table>

The simple febrile convulsion occurs in an infant during the steep rise of temperature at the beginning of a trivial infection involving mainly the upper respiratory tract. The mother may not even know that the child is running a fever when the convulsion occurs. The academic physician hardly ever has a chance to see these convulsions, which do not necessitate hospitalization but are usually followed by a visit to the doctor's office and subsequent clinical evaluation.

- **Clinical Manifestations**

Simple febrile convulsions represent a tonic-clonic seizure, essentially an infantile version of a grand mal attack. Some degree of lateralization may be present, but a strict hemiconvulsion or focal-motor type of seizure would militate against the assumption of a febrile convulsion. Most of these infants and children have two attacks; many have one or more seizures in the course of a few years.
• **EEG Findings**

Ictal EEG tracings are hard to obtain in a truly simple febrile convolution; grand mal-like EEG changes are most likely to occur. Tracings obtained in the hospital in the acute febrile state with convulsions show severe lateralized EEG changes, but these cases are most likely to fall into the category of epileptic seizures in infants with acute structural lesions.

In the interictal stage, the records are usually normalized and one seldom encounters abnormal tracings. When sedation is used, one is very often surprised to see the very large amount of sedation-induced fast activity, even using chloral hydrate. Short spike wave-like bursts in drowsiness and sleep may occur ("pseudo petit mal discharge"). The most common site was the occipital lobe and, in 88%, the spike focus disappeared within 3 yr. This was often followed by the appearance of a spike wave focus.

Abnormal interictal tracings are likely to indicate underlying cerebral impairment with paroxysmal properties; these infants might be candidates for a febrile epileptic manifestation (i.e., for a chronic epileptic seizure disorder) in the future. The prognosis for these children is mostly favorable.

• **Etiological and Pathophysiological Considerations**

A genetic predisposition to febrile convulsions is indubitable. The seizure-precipitating action of hyperthermia is not yet fully understood. The limitation of this action to infancy and early childhood is particularly enigmatic. Brisk changes of the water and electrolyte balance may play an important part.

In addition to trivial upper respiratory tract infections, there are some diseases of infancy of potentially epileptogenic character. The mild and short-lasting roseola infantum (exanthema subitum) is quite often associated with convulsions of infancy and early childhood. The question remains as to whether this represents a true febrile convolution or a mild or larval encephalitic component. A seizure at the beginning of the first steep rise of fever would support the diagnosis of a simple febrile convolution, while a seizure at the height of the hyperthermia would militate against it.

• **Therapy and Prognosis**

On the basis of risk/benefit analysis, neither long-term nor intermittent anticonvulsant therapy is indicated for children who have experienced 1 or more simple febrile seizures. In unusual circumstances, oral diazepam can be given with each fever.
**Drug Category: Benzodiazepines** - These agents have antiseizure activity and act rapidly in acute seizures.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Diazepam- Can decrease number of subsequent febrile seizures when given with each febrile episode. By increasing activity of GABA, a major inhibitory neurotransmitter, depresses all levels of CNS, including limbic and reticular formation. A study reported in New England Journal of Medicine continued therapy until child was afebrile for 24 h. However, this seems excessive.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Dose</td>
<td>0.33 mg/kg PO at the onset of fever; continue q8h until child is afebrile</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity, narrow-angle glaucoma</td>
</tr>
<tr>
<td>Interactions</td>
<td>Toxicity in CNS increased by phenothiazines, barbiturates, alcohols, MAOIs, and other sedative medications; cisapride can increase levels significantly</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>About two thirds of children who receive diazepam for this indication have ataxia, sleepiness, or similar adverse effects; use caution in patients who receive other CNS depressants; be careful with patients who have low albumin levels or hepatic failure, which may increase toxicity</td>
</tr>
</tbody>
</table>

The vast majority of febrile convulsions have an excellent prognosis. The question of whether or not to treat will not be discussed in this context.

**THE LENNOX-GASTAUT SYNDROME**

- **Introductory Remarks**

This epileptological entity has been recognized as such over the past five decades, following earlier EEG observations and presumptive electro-clinical correlations. The severity and poor prognosis of the seizure disorder in patients with slow spike wave complexes was quite evident, by contrast to the classical 3-4/sec spike wave complexes in patients with petit mal absences and the prognostically more favorable "primary generalized epilepsy."

The diagnosis of this syndrome is based on the occurrence of certain types of seizures, some of them practically syndrome-specific, and typical EEG changes; furthermore, the poor treatment response (with few exceptions) accompanying mental retardation, and frequently
demonstrable neurological deficits, lend strong support to the diagnosis. A multitude of etiologies may cause this condition and, in any case, the cause remains unknown.

- **Age**

This condition usually starts between the ages of I and 10 yr; onset in the second decade of life is much less common. Onset at age 6 to 12 mos has been observed and requires solid EEG documentation for differentiation from hypsarrhythmia-infantile spasms. About 10 to 20% of the cases have passed through a period of infantile spasms-hypsarrhythmia before the Lennox-Gastaut syndrome becomes evident.

- **Ictal Manifestations**

The types of seizure occurring in the Lennox-Gastaut syndrome are best divided into the following two groups.

  - **Seizures also occurring in other epileptic conditions.**

In this group, we find grand mal, playing a major role only at the onset of the seizure disorder, often completely absent, psychomotor automatisms, in some cases dominating the picture, quite commonly myoclonus, focal (partial elementary) seizures such as adversive, and Rolandic focal motor attacks.

  - **Seizures which are virtually specific for the Lennox-Gastaut syndrome.**

This group is composed of atonic seizures (drop attacks of particular diagnostic significance), akinetic seizures, purely tonic seizures, purely clonic seizures, a modified form of petit mal absence, and, as far as prolonged states are concerned, a variant of petit mal absence status.

The occurrence of more than one type of seizure is almost the rule in the Lennox-Gastaut syndrome; many children have more than two different types of seizures. Seizures also occurring in other epileptic conditions are described in the section on types of epileptic seizures. The more specific seizures, however, need a detailed presentation.

Atonic seizures are divided into a brief and more prolonged type. The attacks usually occur without provocation. In the brief atonic seizure, there is sudden more or less intense muscular hypotonia which may be preceded by a brief myoclonic jerk. Generalized severe hypotonia leads to an abrupt, almost lightning-like fall; the knees buckle, the torso and head slump forward, and the head may hit the floor or an object in a traumatizing manner. There may be, instead, a fall on the buttocks or a rudimentary seizure with sudden head drop on the chest.

Preceding myoclonus is usually associated with generalized spikes or polyspikes; the atonia (best recorded in a supine patient) is accompanied by spikes, a few spike-waves, and a
succession of slow waves. The attack usually lasts only 1 to 2 sec; the patient probably does not lose consciousness.

More prolonged atonic seizures are also called atonic absence or atonic epileptic seizures. Sudden atonia results in a fall, but the patient may remain lying on the floor, flaccid and immobile.

Generalized spikes, sharp waves, slow waves, and activity in the 10/sec range are found in these prolonged atonic seizures, which may last from 30 sec to a few minutes. The EEG changes and the traumatizing abruptness of fall distinguish this attack from the cataplectic attack, which is strictly nonepileptic. These children need to wear protective headgear.

Akinetic seizures are characterized by complete lack of mobility in spite of preserved muscle tone; there is impairment or loss of consciousness. There is no fall. In the supine child, the evaluation of muscle tone will tell the difference between this type and the atonic seizure. The attacks last from 30 sec to more than 1 min.

These attacks are not uncommon in children with Lennox-Gastaut syndrome, although they are not as frequently observed as atonic seizures. The ictal EEG findings are not absolutely conclusive. A very rhythmic slow spike wave discharge (1-2/sec) may be present in generalized synchrony for the duration of the attack. The occurrence of polyspike wave complexes are occasionally present in these attacks.

Tonic seizures show a variety of manifestations and their subdivision into axial, axorhizomic, and global tonic seizures. Such purely tonic attacks of bilateral character are limited to children with the Lennox-Gastaut syndrome when properly differentiated from lateralized tonic attacks due to mesiofrontal epileptogenic foci and a variety of nonepileptic attacks (tetanic, decerebration, etc.).

The attacks are short and last from about 5 to 20 sec. There is extension of the axial musculature with some opisthotonus; moderate flexion of the arms is noted and this may be followed by extension. Tracheobronchial hypersecretion occurs with repeated attacks and a fairly dangerous status may evolve. These attacks or very short rudiments are quite common in nonREM sleep and often are observed in a routine sleep tracing. Bilateral synchronous fast or moderately fast spike activity of about 10 to 25/sec of medium to high voltage and frontal accentuation is the EEG concomitant of these attacks ("runs of rapid spikes;"). Simple flattening or desynchronization may also occur. A diffuse slow ictal pattern has been mentioned. Generalized synchronous 3/sec spike waves are also seen in frequent axial tonic seizures.

Clonic seizures consist of prolonged myoclonic activity bilaterally; these jerks occur in very rapid succession; asymmetries are not uncommon. The clonic motions are of small amplitude and may involve the entire body or certain (sometimes even distant) parts. There is loss of consciousness. The attacks occur mainly in nonREM sleep and are seen chiefly in childhood. The ictal EEG shows much generalized activity in the 10/i sec range, mixed with spike wave-like discharges, slower and faster frequencies. The duration lies around 1 min.
Seizures resembling petit mal absences are uncommon and usually show tonic and clonic elements. Episodes of petit mal absence status in the Lennox-Gastaut syndrome are quite common.

- **Clinical Signs of Nonictal Character**

  About half of the infants, children, or adolescents with Lennox-Gastaut syndrome show no neurological deficit and no evidence of structural brain disease. This is supported by normal findings in computerized tomography in approximately 50% of the cases. The rest shows a wide variety of residual infantile brain lesions, which are often associated with neurological deficits such as forms of cerebral palsy.

  Mental retardation ranges from the most profound to the slightest degree, essentially depending on the age at onset; the earlier the seizures start, the more serious the intellectual deficit appears to be. In patients with onset after age 10, no mental deficit may be present.

- **EEG**

  EEG findings have been crucial in the individualization of the Lennox-Gastaut syndrome as a clinical entity. The outstanding feature is the slow spike wave complex ranging from 1 to 2.5/sec. It is more often an interictal rather than an ictal discharge and is most often of generalized synchronous character, although lateralization is also fairly common; local slow spike wave activity is quite rare. A maximum over the frontal midline is the rule.

  This discharge is enhanced in nonREM sleep and may become almost continuous. The spike component shows considerable variation; it may be slow ("blunted") or quite fast with true spike character. The slow spike wave discharge may be present in early infancy between the ages of 6 to 12 mos. Classical 3/sec or 3-4/sec spike wave complexes may also be discernible.

  Another important pattern is "runs of rapid spikes," which are seen in nonREM sleep only. This pattern is more common in older children, adolescents, or adults. More information can be found in the chapter on abnormal paroxysmal discharges.

  The EEG as such ("background EEG") is often disorganized and excessively slow, but a sizeable number of patients show a normal frequency spectrum with unremarkable posterior alpha rhythm, the basic rhythm. The degree of general slowing and disorganization usually underscores the severity or advanced stage of the case. These children are often seen in a state of overtreatment with anticonvulsants, resulting in toxic anticonvulsant levels. Interestingly, high and toxic levels of phenobarbital may be completely unassociated with fast EEG activity; this absence of barbiturate-induced fast frequencies is quite characteristic in advanced cases with considerable cerebral impairment.
• **Etiological and Neuropathological Considerations**

The aforementioned normal computed tomography (CT) scan findings in 50% of the cases further support the view that about half of the cases are idiopathic and hence without structural cerebral changes. The nature of idiopathic forms is completely unclear. Genetic predisposition is certainly more than just a hypothesis.

Acquired pathology of residual character is present in a considerable number of cases; with CNS infection and birth trauma/asphyxia as the leading problems. One could argue that such pathology alone can hardly account for this severe form of epileptic seizure disorder and that a genetic predisposition is a prerequisite. Even progressive pathology such as intracranial tumors may be associated occasionally with Lennox-Gastaut syndrome. Phenylketonuria, forms of lipidosis, **tuberous sclerosis**, lead encephalopathy, and toxoplasmosis have been specifically mentioned as etiological factors. In essence, we are dealing with the same dichotomy of idiopathic and symptomatic forms as in infantile spasms-hypsarrhythmia.

• **Pathogenetic Concepts**

The debatable concept of secondary generalized epilepsy was discussed earlier in the section on infantile spasms. All that was said there also applies to the Lennox-Gastaut syndrome.

• **Therapy and Prognosis**

**Medical Care:**

• The goals of treatment for patients with LGS are the same as for all epilepsy patients: the best quality of life with the fewest seizures (hopefully none), the fewest treatment side effects, and the least number of medications.

• Antiepileptic medications (AEDs) are the mainstay of therapy for patients with LGS. Unfortunately, no one medical treatment gives satisfactory relief for all or even most patients with LGS. A combination of medical treatment modalities frequently is required.

• The various medical treatment options for patients with LGS can be divided into the following 3 major groups:
  o First-line treatments based on clinical experience or conventional wisdom (eg, valproic acid, benzodiazepines [specifically clonazepam, nitrazepam, clobazam])
  o Suspected effective treatments based on open-label uncontrolled studies (eg, vigabatrin, zonisamide)
  o Proven effective treatments based on double-blind placebo-controlled studies (eg, lamotrigine, topiramate, felbamate)
Surgical Care:

- Corpus callosotomy: Corpus callosotomy is effective in reducing drop attacks but typically is not helpful for other seizure types and is considered palliative rather than curative. Seizure freedom following corpus callosotomy is rare but can occur.
- Vagus nerve stimulation: In 3 published small studies, approximately three fourths of LGS patients experienced greater than 50% reduction in seizure frequency with a follow-up period as long as 5 years.
- Focal cortical resection: In rare cases, resection of a localized lesion (eg, vascular lesion, tumor) can improve seizure control.

The goal of pharmacotherapy is to reduce morbidity and prevent complications.

Drug Category: Anticonvulsant - Prevent seizure recurrence and terminate clinical and electrical seizure activity.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Valproate (Depakote, Depakene, Depacon) - Considered a first-line treatment option for children with LGS for 2 decades; reported to be more effective in patients with cryptogenic LGS than in those with symptomatic LGS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>10-15 mg/kg/d PO divided bid/tid initially; titrate with 5-10 mg/kg/d increments qwk until therapeutic effect achieved or toxicity occurs; average maintenance dose is 15-60 mg/kg/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Administer as in adults</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; history of pancreatitis or hepatotoxicity; multiple concomitant antiepileptic medications (eg, phenobarbital), underlying metabolic disease (eg, defect in fatty acid oxidation), developmental delay</td>
</tr>
<tr>
<td>Interactions</td>
<td>Coadministration with cimetidine, salicylates, felbamate, and erythromycin may increase toxicity; rifampin may significantly reduce valproate levels; in pediatric patients, protein binding and metabolism of valproate decrease when taken concomitantly with salicylates; coadministration with carbamazepine may result in variable changes of carbamazepine concentrations with possible loss of seizure control; valproate may increase diazepam and ethosuximide toxicity (monitor closely); valproate may increase phenobarbital and phenytoin levels while either one may decrease valproate levels;</td>
</tr>
</tbody>
</table>
Valproate may displace warfarin from protein binding sites (monitor coagulation tests); may increase zidovudine levels in HIV seropositive patients.

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>D - Unsafe in pregnancy</th>
</tr>
</thead>
</table>

**Precautions**

Dose-dependent adverse effects include asthenia, nausea, vomiting, somnolence, tremor, and dizziness; less common adverse effects include thrombocytopenia and parotid swelling; idiosyncratic reactions include hepatotoxicity and pancreatitis; long-term (cumulative) adverse effects include hair loss, polycystic ovary disease, and weight gain.

**Drug Category: Benzodiazepine**

Clonazepam (Klonopin)- Considered effective first-line AED therapy against seizures associated with LGS; adverse effects and development of tolerance limit usefulness over time; nitrazepam (Mogadon) and clobazam (Frisium) are not approved by the FDA in the US but are available in many countries; a combination of valproic acid and benzodiazepine may be better than either drug alone; dosing on an every-other-day schedule or alternating two benzo diazepines daily may slow the development of tolerance.

**Drug Name**

Clonazepam (Klonopin)

**Adult Dose**

1.5 mg/d PO divided tid; titrate with 0.5-1 mg increments q3d; maintenance dose is <20 mg/d

**Pediatric Dose**

Maintenance dose: 0.01-0.2 mg/kg/d PO

**Contraindications**

Documented hypersensitivity; significant liver disease; acute narrow-angle glaucoma

**Interactions**

Decreases plasma levels of phenytoin, phenobarbital and carbamazepine; potentiates CNS depression induced by other anticonvulsants and alcohol; may reduce renal clearance of digoxin; may decrease control of parkinsonian symptoms by levodopa; disulfiram, cimetidine, and erythromycin decrease clearance.

**Pregnancy**

D - Unsafe in pregnancy

**Precautions**

Dose-dependent adverse effects include hyperactivity, sedation, drooling, incoordination, drowsiness, ataxia, fatigue, confusion, vertigo, dizziness, amnesic effect, and encephalopathy; clobazam is considered the least

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sedating benzodiazepine. Long-term (cumulative) adverse effects include tolerance, dependence; clobazam is considered to have the longest time to the development of tolerance. Adjust dose or discontinue if renal or liver function is impaired, since metabolism occurs in liver and metabolites are excreted in urine; caution in history of previous substance dependence; association with development of tolerance and psychologic and physical dependence exists.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Lamotrigine (Lamictal)- Efficacy as adjunctive therapy against seizures associated with LGS was demonstrated in two controlled trials and multiple open-label studies. Valuable for patients with LGS despite risk of dermatologic idiosyncratic reactions. Consider for use as soon as diagnosis of LGS made. Proper attention to concomitant medications, a low starting dose, and a very slow titration can minimize risk of dermatologic idiosyncratic reactions. Initial dose, maintenance dose, titration intervals, and titration increments depend on concomitant medications.</th>
</tr>
</thead>
</table>
| Adult Dose | If used in combination with AEDs that induce the hepatic CYP-450 enzyme system WITHOUT valproate:
Starting dose: 50 mg/d for 2 wk; 100 mg/d in weeks 3-4; increase by 100 mg/d q1-2wk until maintenance dosage is achieved
Maintenance dose: 300-500 mg/d given in 2 divided doses
If used in combination WITH valproate (with or without other AEDs that induce the hepatic CYP-450 enzyme system):
Initial starting dose: 25 mg every other d for 2 wk; 25 mg daily in weeks 3-4; increase by 25-50 mg/d q1-2wk until maintenance dosage achieved
Maintenance dose: 100-400 mg/d; if added to valproic acid alone, usual maintenance dose is 100-200 mg/d |
| Pediatric Dose | If used with AEDs that induce the hepatic CYP-450 enzyme system WITHOUT valproate:
Initial starting dose: 0.6 mg/kg/d for 2 wk; 1.2 mg/kg/d in weeks 3-4; 5-15 mg/kg/d thereafter; after week 4, dosage increment is not to exceed 1.2 mg/kg/d every 1-2 wk until maintenance dose is |
| **Contraindications** | Documented hypersensitivity; history of erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis; risk of potentially life-threatening rash (erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis) in adults is 0.3% and approximately 1% in children <16 y; risk factors for severe dermatologic reactions include younger age (children more than adults), co-medication with valproic acid, rapid rate of titration, and high starting dose; give careful attention to initial starting dose, titration rate, and co-medications; prompt evaluation of any rash is prudent and imperative; approximately 10-12% of patients develop a non–life-threatening rash that usually resolves rapidly upon withdrawal and sometimes without changing dosage |
| **Interactions** | Affected by concomitant AEDs; when used with medications that induce hepatic CYP-450 microsomal enzymes (phenobarbital, carbamazepine, phenytoin), clearance is enhanced; conversely, when used with medications that inhibit hepatic CYP-450 microsomal enzymes (valproate), clearance is diminished; lower starting doses, a very slow titration rate (ie, every 2 or more wk), and smaller increments are needed |
| **Pregnancy** | C - Safety for use during pregnancy has not been established. |
| **Precautions** | Dose-dependent adverse effects include ataxia, diplopia, dizziness, headache, nausea, and somnolence; idiosyncratic reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis; no long-term (cumulative) adverse effects are noted to date |
| **Drug Name** | Topiramate (Topamax)- Found to be safe and effective as adjunctive therapy (target dose 6 mg/kg/d) for patients with LGS in a multicenter, |
double-blind, placebo-controlled trial. In long-term open-label extension portion of this trial (mean TPM dosage 10 mg/kg/d), drop attacks were reduced by >1/2 in 55% of patients, and 15% of patients were free of drop attacks for >6 mo at the last visit.

<table>
<thead>
<tr>
<th>Adult Dose</th>
<th>25-50 PO mg/d PO initially; titrate with increments of 25-50 mg/d PO q1-2wk; maintenance dose is 250-500 mg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Dose</td>
<td>0.5-1 mg/kg/d PO initially followed by increments of 0.5-1 mg/kg q1-2wk; maintenance dose is 6-10 mg/kg/d</td>
</tr>
</tbody>
</table>

**Contraindications**

Documented hypersensitivity

**Interactions**

May increase phenytoin plasma levels; may decrease valproate plasma levels; may decrease digoxin levels; phenytoin, phenobarbital, and carbamazepine decrease levels; efficacy of oral contraceptives may be compromised with concomitant use

**Pregnancy**

C - Safety for use during pregnancy has not been established.

**Precautions**

Dose-dependent adverse effects include ataxia, dizziness, fatigue, nausea, somnolence, psychomotor slowing, and concentration and speech problems; if CNS adverse effects occur, reduce concomitant AEDs, slow titration, or reduce TPM dose; no idiosyncratic reactions are noted; caution in patients with history of renal stones since nephrolithiasis occurred in 1.5% of patients in controlled trials; oligohidrosis is reported

**Drug Name**

Felbamate (Felbatol)- Found to be safe and effective in patients with LGS in a randomized, double-blind, placebo-controlled adjunctive therapy trial; a 12-month follow-up study in patients who completed the controlled part of the study confirmed long-term efficacy; although effective, the significant risk of idiosyncratic reactions associated with use make it a third-line or fourth-line drug for LGS.

**Adult Dose**

1200 mg/d PO in 3-4 divided doses initially; reduce dosage of concomitant AEDs by 20-30%; titrate with increments of 1200 mg/d qwk to 3600
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Zonisamide (Zonegran)- Effectiveness in LGS has been investigated in 3 small open-label studies with promising results.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>100 mg/d PO initially; titrate with increments of 100 mg q2wk; maintenance dose is 400-600 mg/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>1-2 mg/kg/d PO initially; titrate with increments of 1-2 mg/kg/d q2wk; maintenance dose is 8-12 mg/kg/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>Phenytoin, phenobarbital, carbamazepine, and valproate decrease half life; does not effect steady-state plasma concentrations of other AEDs</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
</tbody>
</table>
Dose-dependent adverse effects include headache, anorexia, nausea, dizziness, ataxia, paresthesia, difficulty concentrating, irritability, and somnolence; idiosyncratic reactions include severe rash (Stevens-Johnson syndrome, toxic epidermal necrolysis) with a reporting rate of 46 per million patient-years of exposure; oligohidrosis is reported

Drug Name
Vigabatrin (Sabril)- Not approved by the FDA in the US but is available in many countries; in 6 open-label studies involving 78 LGS patients, 15% became completely seizure-free and 44% had >50% reduction in seizure frequency.

Adult Dose
1-2 g/d PO in 2 divided doses initially; titrate with increments of 500 mg/d; maintenance dose is 2-4 g/d

Pediatric Dose
40 mg/kg/d PO initially in 2 divided doses; maintenance dose is 40-100 mg/kg/d

Contraindications
Documented hypersensitivity

Interactions
None reported

Precautions
Dose-dependent adverse effects include hyperactivity, agitation, sedation, depression, psychosis, drowsiness, insomnia, facial edema, ataxia, nausea and/or vomiting, stupor, and somnolence; idiosyncratic reactions include visual field constriction; may exacerbate myoclonic and absence seizures in some patients; long-term reactions include weight gain; not approved by the FDA in the US but is available in many countries worldwide; lower doses in patients with renal dysfunction

Most cases of Lennox-Gastaut syndrome are not responsive to therapy. This is a gloomy picture; the course quite often leads to institutionalization, especially in patients with very early onset. The course of the disease, however, should not be conceived as a linear progression of deterioration. Observation of adult patients shows certain interesting trends.

In adulthood, the EEG may gradually lose the characteristics of the Lennox-Gastaut syndrome. The slow spike wave complex may disappear after age 20 or 15. and, instead, runs of rapid spikes in sleep only may become more prominent. This pattern, too, may gradually vanish and spikes or sharp waves of temporal and especially anterior temporal localization may then become predominant. Interestingly, this change may be associated with the appearance of psychomotor (complex partial) seizures as a new phenomenon or
enhancement of pre-existing seizures of this type. Thus, the patient seems to merge into the mainstream of temporal lobe epilepsy but will remain a deteriorated case with mental deficit or behavioral changes, often fostered by years of institutionalization. This process has been described as "secondary temporalization". It is doubtful whether all patients take this course.

**PRIMARY GENERALIZED EPILEPSY**

- **Introduction**

The entire concept of a primary generalized epilepsy has its foundation in the EEG. Who would have thought that a simple petit mal absence with its rather subtle clinical symptomatology could be the result of massive generalized synchronous epileptic discharges? The first observation of the ictal EEG pattern of petit mal has been the starting point for numerous attempts to explain the phenomenon of primary generalized seizure discharges.

- **Terminology**

The term "primary generalized epilepsy" has been introduced by the International League against Epilepsy. This term deserves general acceptance. It implies that the clinical and electroencephalographic phenomena of the seizures occurring in this epileptic condition are generalized from the start. This term has superseded older terms such as "centrencephalic epilepsy", "cortico-reticular epilepsy", and "common generalized epilepsy". Its weakness lies in the fact that it seems to burn all bridges for a retreat if a truly focal cortical onset with extremely rapid generalization should ever be convincingly demonstrated in the future.

- **Age and Prevalence**

The age depends on the type of seizure. Classical petit mal absences mostly start at age 4 to 6 yr; a special group starts at age 9 to 15 yr. Myoclonus and grand mal attacks usually start at age 11 to 14 yr. Improvement or full seizure control after age 20-25 yr is very common. A special manifestation is the petit mal absence status, which may occur in older children, adolescents, adults, and even the elderly.

Primary generalized epilepsy is sometimes preceded by a period of febrile convulsions in infancy and early childhood. It is never preceded by severe conditions such as infantile spasms or the Lennox-Gastaut syndrome.

- **Ictal Manifestations**

The petit mal absence was discussed in detail in the section dealing with types of seizures. The two different forms are 1) simple petit mal absences, starting at age 4 or shortly thereafter, with a large number of absences/day (sometimes exceeding 100/day); and 2)
"juvenile" petit mal absences with an onset at age 9 up to 15 yr, more prolonged or mixed with more motor activity.

Petit mal absences show a wide variety of mild to moderate motor accompaniment; rhythmical eye blinking in synchrony with the spike waves is the most common motor component. Retropulsion of the head is quite common ("retropulsive petit mal); adersive movements and some rhythmically repetitive oral motions may also occur.

Children with petit mal absences often start having grand mal seizures in early adolescence. Figures range from 31% to 54%. In most of these cases, the grand mal seizures do not pose a major problem and are readily brought under control.

Grand mal attacks in patients with primary generalized epilepsy are very often preceded by sudden bilateral myoclonus. These myoclonic jerks may also occur as isolated events, especially in the morning hours after a night of insufficient sleep. Many patients with this combination of grand mal and myoclonus may never have experienced any petit mal absences earlier in childhood. This petit mal-free form is a special variant of primary generalized epilepsy which also shows slightly different inter-ictal bursts in the EEG. These bursts are relatively short and dominated by 4/sec or 4-5/sec spike wave complexes which are, contrary to the classical 3/sec or 3-4/sec spike waves, not readily activated by hyperventilation. Many of these patients are flicker-sensitive (photoconvulsive response) and positive family histories are more often obtained in this group. Myoclonus may also be associated with brief petit mal absences.

Very prolonged absence-like stages, attacks of petit mal-like stupor, or petit mal automatisms have been termed "Petit mal status", whereas the modern terminology recommends the term "absence status." These states will be discussed in the section on status epilepticus. While all of the ictal manifestations of primary generalized epilepsy tend to occur in children and adolescents, the absence status not only occurs in elderlies but may even have its onset in old age.

- EEG

The 3/sec or 3-4 c/s spike wave pattern is the EEG correlate of the classical petit mal absence and also occurs, often abundantly, in the interval, sometimes in drowsiness and sleep. These generalized bursts, with or without clinical absence, are readily triggered by hyperventilation and may materialize after a few deep breaths in untreated patients. Intermittent photic stimulation may occasionally trigger petit mal absences with 3/sec spike waves; more often, it is associated with generalized polyspikes of frontal accentuation, with or without clinical myoclonic jerking, most often at frequencies of 14-18 flashes/sec. As was pointed out above, photosensitivity is more often noted in patients with 4/sec or 4-5/sec spike wave bursts and a history of grand mal and/or myoclonus.
The phenomenon of myoclonus is almost invariably linked with polyspike discharges as far as patients with primary generalized epilepsy are concerned. Polyspikes also contaminate the spike wave sequences in children with massive myoclonus as a variant of petit mal. In the majority of patients with primary generalized epilepsy, the EEG frequency spectrum appears to be normal aside from the generalized paroxysmal bursts, the so-called background activity. A remarkable exception is the occurrence of prolonged stretches of rhythmic high voltage 3/sec waves in occipital leads with moderate spread into the vicinity; these bursts occur in a significant number of children with petit mal absences. This rhythm is found in 55% of the patients with petit mal absences and persists in 60% of the cases following seizure control. Hyperventilation almost invariably activates this rhythm. In some cases, a very small spike component is discernible between the large rhythmic delta waves. The rhythmic posterior activity may be enhanced under treatment with ethosuximide (Zarontin), while the 3/sec spike wave complex disappears. Children with petit mal absences and rhythmic occipital delta trains fall into a special epileptological category. The occipital rhythmic slow activity is a very favorable prognostic sign.
The sleep records of patients with primary generalized epilepsy show frequent bursts of spikes, polyspikes, and spike waves; with common association between the K complex and the frontal midline maximum of the spike discharges. This maximum over the frontal midline is almost invariably present, not only in sleep but also in the waking state. This indicates that arousal plays an important role in the generation of these discharges. REM sleep is associated with an attenuation or total suppression of bilateral synchronous paroxysmal bursts. In exceptional cases, the maximum of the 3/sec spike wave bursts lies in the vertex region rather than in frontal midline; these children also show Rolandic spikes.

It goes without saying that genetic factors are particularly important in the field of primary generalized epilepsy. Generalized synchronous seizure discharges follow an autosomal-dominant pattern of genetic transmission, with variable penetrance regardless of presence or absence of seizures with an unusual characteristic of a very low penetrance at birth which rises to nearly complete penetrance (close to 50%) for age 4.5 to 16.5 years” with a gradual decline to almost no penetrance at age 40 yr. These figures are in excellent agreement with the incidence of generalized synchronous seizure discharges of the 3-4/sec spike-wave type as well as the clinical seizure manifestations of primary generalized epilepsy.

- The Presence of Focal Spikes in Patients with Primary Generalized Epilepsy

A certain type of focal spikes in childhood ("benign Rolandic spikes") may be occasionally present in children who, suffer from petit mal absences, especially after suppression of the absences and the spike waves with medication. This view would shed more light on the demonstration of genetic factors in children with midtemporal spikes.

- Concluding Remarks

The challenging problem of primary generalized epilepsy remains unsolved. Genetic predisposition and age (chiefly 4-20 yr) are significant factors. It is a specifically human disorder; for this reason, animal models can provide only partial insight into pathogenetic
mechanisms. In the human, the generalized synchronous seizure discharge originates from the interhemispheric frontal portion bilaterally. Arousing stimuli play a crucial role in the detonation of these discharges. In some patients, however, the mechanism of photosensitivity is paramount.

**BENIGN ROLANDIC EPILEPSY**

- **Introduction**

In children with spikes over the central region and/or adjacent midtemporal and parietal areas, a benign and readily controllable type of epileptic seizure disorder with focal motor seizures and/or grand mal is the rule. An increasing number of reports over the past 40 yr gives testimony to growing awareness of this special form of childhood epilepsy.

This form of childhood epilepsy is occasionally listed among the primary generalized epilepsies despite its prominent focal features in the ictal and electroencephalographic semiology. Such a classification certainly appears to be provocative. There are indeed certain relationships between benign Rolandic epilepsy and primary generalized epilepsies and conversion from one form to the other may occur. There is certainly good reason to separate benign Rolandic epilepsies from the bulk of focal (partial) epileptic seizure disorders which will be presented somewhat later.

- **Age and Prevalence**

Benign Rolandic epilepsy occurs at age 3 to 12 yr. The majority of these children are in the range from 6 to 10 yr. Disappearance of the seizures during adolescence (or even prior to puberty) is the rule. The seizures may occasionally recur much later in life, probably due to seizure-facilitating factors such as severe illness or toxic-metabolic factors.

The sex distribution shows that boys are more often affected. The prevalence is not quite clear and might be somewhere between 5 and 10% in a population of epileptics below age 15 yr.

- **Ictal Manifestations**

The seizures, regardless of focal or grand mal character, tend to occur during nocturnal sleep, mostly during the last hour of sleep or in the first 2 hr. About 80% of the attacks occur in sleep and, of the remaining 20%, about 10% take place shortly after awakening. (Note the similarities with primary generalized epilepsy.) Nocturnal seizures may awaken the child afterward. Preservation of consciousness and hence the ability to describe the experienced seizure was found in 58%; this indicates the predominance of focal seizures. Grand mal (tonic-clonic) seizures were noted in 26%.

The seizures are hardly ever seen by the physician, even by the epileptologist who sees sizeable numbers of these children. One therefore depends heavily on descriptions by the patient or his family; nocturnal video-tape or biotelemetry recordings are quite helpful.
Focal seizures often involve the face. The midtemporal spike localization has been thought to be related to paroxysmal activity in the very closely located lower portion of the motor strip (facio-laryngo-pharyngeal muscles). Hemifacial twitching is definitely more common than clonic motions in the contralateral arm; least common is clonic activity in the leg. In some cases, the entire half of the body participates, but a typical Jacksonian march does not seem to occur. Speech arrest is quite common (39% of the seizures). This is apparently an ictal anarthria with preserved internal speech.

Oropharyngeal involvement is very often reported, with sounds described as "guttural," "gargling," "throaty," "wheezing," or "as if going to vomit." Feelings of suffocation are reported as coming from the mouth but not from the chest. These patients also have focal seizures which are not Rolandic, with blindness, vertigo, and torsion of the body as ictal signs. This underscores the complexity of the underlying neurophysiological mechanisms.

- **EEG**

Spiking over central-midtemporal area in children is of limited epileptogenicity. It is reasonable to presume that 50-70% of these children have seizures and the remaining 50-30% are seizure-free. These latter patients are referred to the EEG laboratory because of a variety of symptoms such as behavior disorder, headaches, and other complaints or derivations.

The spatial distribution of the spike activity requires an appropriate number of electrodes; the International Electrode System is particularly suitable. Otherwise, the Rolandic cortex may lie between a frontal and a parietal electrode and strictly local spiking may escape detection, especially when the midtemporal region is not explored ideally. In my personal experience, a central maximum of spike discharge is slightly more often noted than a midtemporal maximum.

The spikes themselves are large and may be either spikes in the strict sense or sharp waves (see chapter on abnormal paroxysmal patterns). Spiking is usually enhanced in light nonREM sleep, during which the discharges may become extremely abundant. Their random character may give way to quasirhythmic or periodical spiking at intervals of less than 1 sec; previously unilateral spikes become bilateral synchronous or asynchronous. In many children, Rolandic spikes are found in the sleep portion only. REM sleep restores the unilateral character of the spiking. Bilateral parieto-occipital 4/sec spike wave-like discharges of moderate voltage is occasionally seen in the waking patient.
Figure 4. Trains of spikes/sharp waves recorded in a quasirhythmical pattern in a child with benign Rolandic epilepsy.

The rest of the tracing is usually normal in these patients and the frequency spectrum corresponds to age. Central mu rhythm is sometimes present and there is reason to presume that central spikes of childhood may be gradually replaced by mu rhythm, at least in some of the patients. There is indubitable evidence that, in a limited number of patients, the central spike activity can be blocked by contralateral fist clenching or, even better, by alternate clenching and opening of the fist. This provides further evidence for the functional character of the spikes.

In a small number of cases, the spike activity shows a consistent maximum over the vertex or over the centroparietal midline region, which may be the sole region of spiking, so that omission of midline leads would result in missing the abnormality. Some of these patients show focal motor or sensory ictal activity of leg predominance but, more often, the ictal symptoms do not correspond with the spike localization.

Clinical Signs of Nonictal Character

Neurological deficits are not compatible with benign Rolandic epilepsy. This condition is based on dysfunction rather than structural pathology. It is worthwhile, however, to search carefully for a true intracranial lesion. Arteriovenous malformation occasionally may be the cause of the discharges and associated seizure.

Central, midtemporal, or parietal spikes or spikes over the midline may also occur in children with evidence of cerebral palsy, in mostly diplegic, quadriplegic, or choreoathetoid forms. In these children, Rolandic spikes have a different connotation and do not herald a good prognosis for the seizure disorder. The reader will find more extensive discussion in the section on cerebral palsy.

Behavior disorders are very common in children with true Rolandic spikes; they may range from hyperkinetic behavior and signs of minimal cerebral dysfunction to severe anxiety neurosis. Various types of headaches may occur. The intelligence is normal in true benign Rolandic epilepsy.
Course

The seizures are easily controlled with routine anticonvulsive treatment. Treatment may even be withheld unless seizures repeat themselves.

Freedom from seizures in adolescence is the rule. The return of a single major convulsion may occasionally occur under the influence of infections, stress, or toxic substances. These cases show no resurgence of the central spike focus, which renders the EEG diagnosis very difficult. The presence of central mu rhythm may serve as a hint that the patient has had central spikes in the past, but such conclusions can be made only with reservations.

Etiological Considerations

This form of epilepsy is due to dysfunction rather than pathology. A genetic basis is the most logical thought.

Problem of Differential Diagnosis

Benign Rolandic epilepsy must be differentiated from:

1. Children with Rolandic spikes and no seizures whatsoever (these children are certainly not epileptics; about 30 to 50% of the children with Rolandic spikes have no overt clinical seizures).

2. Children with Rolandic spikes and a history of antecedent brain damage or cerebral palsy.

3. Children who have typical psychomotor seizures and evidence of temporal lobe epilepsy which may gradually progress in severity; these children may have atypical spike localization (central, midtemporal), while the classical anterior temporal sharp wave focus does not materialize before adolescence.

4. Children with midtemporal spikes, marked tendency to generalization and spike wave formation, clinically with aphasia, probably a temporary inflammatory condition which gradually subsides.

5. Children with frequent focal motor seizures which become progressively worse: "malignant" Rolandic epilepsy of childhood.

6. Children with centroparietal spikes elicited by tactile stimulation of corresponding cutaneous areas of the body (see under benign parietal epilepsy). The differentiation of these conditions rests on a careful combined clinical-electroencephalographic assessment of each case. The EEG shows considerable slowing. There is evidence of constant muscle activity, but no authentic cerebral spikes are demonstrable.
Spike Foci Outside the Rolandic Region in Children

Occipital spike foci are usually found between the ages of 2 to 5 yr. These children show no neurological or ophthalmological deficit; about 40% of them have clinical seizures, mostly grand mal, with good prognosis.

Frontal spike foci in children are associated with epileptogenicity, with about 80% having overt seizures, and a guarded prognosis. Multiple spike foci (two or more areas of independent spiking) are also highly epileptogenic; the prognosis is guarded and probably fairly good if Rolandic spikes predominate.

Considerations of Basic Mechanisms

True benign Rolandic epilepsy is likely to be based on temporary paroxysmal hyperirritability of the motor cortex, which naturally has a lower threshold of epileptic excitability. This is merely a working hypothesis in need of further substantiating evidence.

"Malignant" Rolandic Epilepsy

Cases of progressively worsening focal motor seizures and prolonged episodes of epilepsia partialis continua are quite rare but probably constitute a special epileptological entity. Motor deficits and mental decline are associated with the seizure disorder. Their etiology is poorly defined; chronic localized encephalitis may be one of the causes (Rasmussen syndrome). Hemispherectomy seems to be the only effective treatment; limited cortical excisions or lobectomies are ineffective.

The EEG shows endless sequences of ictal spike discharges during focal motor attacks but becomes uninformative in states of epilepsia partialis continua, which probably originate from deep structures or possibly from lamina V of the motor cortex without participation of the superficial layers.

Benign Parietal Epilepsy

The vast majority of these patients were children between the ages of 4 and 8 yr. The occurrence of spikes over the parietal region (parasagittal zone) following contralateral tactile stimuli characteristic of this condition. The paroxysmal response to tactile stimuli was found to be enhanced in nonREM sleep. Only 20% of children had clinical seizures; the remaining children were referred because of behavior problems.

Children with Midtemporal Spikes, Progressive Aphasia and Seizures

This syndrome of childhood epilepsy with progressive aphasia has stimulated much interest over the past 40 yr and may be regarded as an epileptological entity unless the discovery of a consistently present pathogenic agent such as a virus turns this condition into a specific disease entity.
This condition is found in children around ages 4 to 6 yr. Speech becomes less intelligible and eventually is limited to a few words. Myoclonic jerking and other forms of brief seizures (akinetic, etc.) are reported. The EEG shows marked spiking, mainly over the left midtemporal region, but there are numerous generalized spike wave-like bursts, first 3-4/sec and later in the 1.5-3/sec range, suggestive of a Lennox-Gastaut syndrome. Cortical biopsy may show inflammatory changes and gliosis with mildly appearance of the meninges over left temporal region. In the course of years, the speech function starts to improve, the seizure frequency diminishes, and the EEG abnormalities gradually vanish.

- Considerations of "Functional" Versus "Autochthonous" Seizure Discharges

The presentation of age-determined epileptic conditions clearly shows benign and vicious forms. It was mentioned before that generalized synchronous spikes and spike waves in primary generalized epilepsy and focal spikes in benign Rolandic epilepsy can be easily suppressed for a limited period with small doses of iv diazepam, whereas many cases of chronic epileptogenic foci are not touched by such small amounts.

This dichotomy of responses of human epileptogenic EEG discharges reminds us of a similar dichotomy which has been widely discussed among neurophysiologists and basic science workers in the field of epileptology. Are we dealing with basically normal neurons which fire excessively due to hypersynchronous synaptic input? Such an epileptogenic focus would consist of a hyperexcitable "neuronal aggregate". On the other hand, one could view the epileptogenic focus as composed of intrinsically abnormal neurons.

There is accumulating evidence that epileptic seizure disorders based upon neuronal hyperexcitability do exist. The key areas of predisposition to epileptic neuronal hyperexcitability may be summarized as follows.

1. Frontal lobe-supplementary motor area in interhemispheric fissure

   **Presumed trigger:** arousing stimuli in a state of reduced vigilance. Generalization: very common and very pronounced, exemplified by 3/sec spike waves, with or without petit mal absence (perhaps via cingulate and thalamocortical connections).

2. Occipital lobe Trigger: flickering light and other visual stimuli. Generalization: common, exemplified by polyspikes with or without myoclonus, occasionally by spike waves with or without petit mal absence, via occipito-frontocentral connections and/or geniculate-thalamocortical fiber systems.

3. Rolandic region Trigger: unclear; possibly sensorimotor idling. Generalization: is not quite as common; seizures, if occurring, are most often of focal motor character.

Hyperexcitability of all three key areas may occasionally exist in certain patients with primary generalized epilepsy. Such cases epitomize the significance of predisposition (i.e., genetic factors). The hyperexcitability of the sensory-parietal cortex with local spike responses to contralateral tactile stimuli seems to be a related phenomenon.
REFERENCES

INTRODUCTION

The first description of what might have been a case of status epilepticus (SE) can be found in the 25th and 26th tablets of the Sakikku cuneiform dating from 718-612 BC. The SE described in this classical period usually consisted of grand mal or generalized tonic-clonic convulsions (i.e., generalized convulsive SE, or GCSE). Sporadic descriptions of other forms of SE appeared, but not until the advent of EEG were these other forms systematically described. GCSE was recognized quickly as a medical emergency, and the other forms...
usually grouped together as nonconvulsive SE (NCSE) were not considered emergencies. This gave rise to a first practical classification of SE into GCSE and NCSE.

This classification soon was found to be inadequate. It grouped together SE consisting of absence or petit mal seizures (ie, absence SE, or ASE) and SE consisting of complex partial seizures (ie, complex partial SE, or CPSE), both of which could lead to clinically similar twilight states. At the 10th Marseille Colloquium in 1962, the traditional definition of SE was extended to consist of epileptic seizures that were so prolonged or repeated as to constitute a fixed and durable epileptic state. This definition implied that there were as many types of SE as there were seizures and that SE classifications should be similar to a seizure classification. The World Health Organization (WHO) dictionary defines SE as "a condition characterized by epileptic seizures that are sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition." This was modified in the 1981 version of the international classification to a condition in which "a seizure persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur."

Currently, some controversy exists with regard to the exact definition of SE. Gastaut (according to Shorvon) suggested that the episode should last at least 30-60 minutes to be considered SE. Most current studies accept a cutoff of 30 minutes. DeLorenzo and coworkers compared patients with seizures that lasted 10-29 minutes to patients whose seizures lasted 30 minutes or more. Shorter seizures were much more likely to stop without antiepileptic drugs (AEDs); they also had a much lower mortality rate. Shinnar and coworkers identified a subpopulation of children predisposed to prolonged (30 minutes) seizures and concluded that their data supported starting treatment of any seizure that lasts for 5-10 minutes and retaining the 30 minute cutoff in the definition of status epilepticus. Lowenstein, Bleck, and MacDonald argued that basing a definition on the onset of neuronal injury is questionable. Because isolated seizures rarely last longer than a few minutes, they proposed a revised operational cutoff of 5 minutes for GCSE in the adult.

However, many recognize that the best definition would be based on the physiology of SE and that such a definition should include failure of normal seizure-terminating mechanisms. Although some biochemical changes that take place during SE (eg, loss of GABA-A receptor sensitivity) are known, sufficient experimental data are lacking to formulate such a definition, which might need to encompass many different mechanisms. Fountain and Lothman suggested a pathophysiological classification based largely on manifestations found on EEG. First, he differentiated between isolated seizures (transient neuronal dysfunction) and SE (enduring neuronal dysfunction). SE then was subdivided, based upon the presence or absence of typical spike-wave (SW) complexes on the EEG, into SW SE and non-SW SE.
A 9-yr-old patient with a history of petit mal absences starting at age 6 yr and grand mal since age 8. Patient in petit mal absence status. There are generalized synchronous spikes of frontal accentuation, often forming double and triple spikes, as well as rudimentary spike wave complexes.

Pathophysiology of non-SW SE is thought to be impairment of GABA-ergic (primarily GABA-A) inhibition and accentuation of glutamatergic excitation. Adenosine is speculated to play a role in termination of SE. In SW SE, GABA-ergic (primarily GABA-B) inhibition is enhanced first, hyperpolarizing thalamic neurons and causing the wave. This then "de-inactivates" excitatory (speculatively, T-type calcium) channels, depolarizing the neuron, causing the spike and resulting in more GABA-ergic hyperpolarization. This process perpetuates the cycle.

**EPIDEMIOLOGY**

Extrapolating from their data from Richmond, VA, and empirically correcting for underreporting, DeLorenzo et al estimated that in 1 year, 152,000 patients in the US experience SE (incidence 61 per 100,000) for a total of 195,000 episodes (incidence 78 per 100,000).

They found that SE occurred most frequently in infants in their first year of life and adults older than 60 years. In children, etiology was a systemic, non-CNS infection in over half of cases. Low AED levels and remote causes (including congenital malformations) also explained a significant number of cases. In adults, distribution of etiologies was more even, low AED levels, stroke, and remote causes being the 3 major etiologic classes. In adults aged 60 years or older, acute or remote strokes caused 61% of cases.
Shorvon estimated the incidence of SE as 44.1-64.6 cases per 100,000 per year. Of these, 18-28 are GCSE, 3.5 CPSE, and 0.1 typical ASE. He also estimated that 8 cases per 100,000 are newly diagnosed epilepsies presenting with SE.

**MORBIDITY AND MORTALITY**

- **Determinants**

Determinants of mortality and morbidity include type of SE, etiology, age of patient, and duration of SE. Mortality rates in children are lower than in adults. Low-mortality causes include low AED levels and systemic infections. High-mortality causes include hypoxia and anoxia, cerebrovascular disease, metabolic disturbances, and tumors.

Waterhouse et al recently showed that SE consisting of intermittent seizures has a lower mortality rate than SE consisting of a continuous seizure; this finding was statistically significant in adults but not children.

DeGiorgio et al showed that serum neuron-specific enolase (a marker of acute brain damage) is elevated in GCSE, CPSE, and subclinical or subtle GCSE. The levels were lowest in GCSE, higher after CPSE, and highest after subclinical or subtle GCSE. This finding suggests that all of those forms of SE can cause neuronal damage. The authors concluded that the high levels after subtle GCSE are related to the poor outcome generally associated with that presentation. The intermediate levels after CPSE reflect long duration and potential for brain damage.

Krumholz believes that GCSE and CPSE have been well documented to cause brain damage and that, although ASE has not been documented definitively to cause brain damage, it does pose a significant problem of recurrence. Drislane has countered that the various forms of human NCSE have not yet been shown to cause permanent brain damage, at least sufficiently unequivocally to justify urgent treatment.

Jordan believes that when NCSE occurs in the setting of brain injury, the 2 conditions act synergistically to increase brain damage.

- **Generalized convulsive status epilepticus**

The greatest mortality and morbidity rates in SE occur in patients with GCSE. Recent estimates of mortality in patients with GCSE range from 8-32%. In the past, rates have been as high as 50%. Effects of GCSE can be subdivided into systemic effects and CNS effects, which can be further subdivided into those resulting from systemic physiologic changes and those resulting from neuronal activity (excitotoxicity).

Hauser and Hesdorffer believed that the deaths from SE in patients with acute CNS insult did not appear to be due to the SE but to systemic complications such as aspiration, compression fracture, acute tubular necrosis, hypotension, and the effect of the underlying pathology, of the progressive lesion in the CNS.
Early in GCSE, physiologic changes are characteristic of sympathetic overdrive, probably related to increased circulating catecholamines. In this early (or compensated) stage, the body changes to meet the demands of the neurons in the brain for increased oxygen and glucose and removal of metabolic waste products. Cerebral blood flow increases 200-600%.

Thirty to 60 minutes later, the patient passes into stage II or decompensated SE. Blood pressure falls, metabolic needs of the cerebral neurons are no longer met by homeostatic mechanisms, and cell death occurs. Fountain and Lothman stated that supply/demand mismatch does not occur until SE has continued for hours. High-energy phosphates continue to be available into late stages of SE. They conclude that the causes of histopathologic changes can be independent of cerebral physiology.

One of the cellular events that may lead to GCSE is release of glutamate, an excitatory neurotransmitter. Glutamate is toxic to neurons (ie, an excitotoxin). Elaboration of glutamate triggers a sequence of intracellular events that begins with increased intracellular calcium, which then proceeds to dysfunction of multiple intracellular systems, finally resulting in cell death.

- **Complex partial status epilepticus**

Morbidity rates in CPSE are much lower than in GCSE. CPSE is not a medical emergency. Krumholz described several patients with persistent neurological deficits thought to be secondary to CPSE. The patient does not experience the violent motor manifestations seen in GCSE. Therefore, systemic physiologic changes do not occur in CPSE.

The mechanism of CNS damage is thought to be similar to the excitotoxic neuronal death seen in GCSE. The long-term prognosis of CPSE is dependent on the underlying disease process.

- **Absence status epilepticus**

No definite examples of long-term sequelae of ASE have been reported. This would be consistent with the fact that different cellular mechanisms underlie the different types of SE. Snead et al separated typical and atypical ASE. Typical ASE occurs in the context of primary generalized epilepsy and may be very different clinically in children and adults. Prognosis of typical ASE usually is good. Distinction between typical and atypical ASE is made more on etiologic than on clinical grounds. Typical ASE is observed most commonly in patients with the Lennox-Gastaut syndrome. EEG may be (but is not always) useful in distinguishing typical and atypical ASE, however.

During prolonged seizures, the 3-Hz SW pattern characteristic of typical absence seizures often slows to 1.5-2.5 Hz, resembling the slow SW pattern characteristic of epileptic encephalopathies. Prognosis of atypical ASE is poor, which probably reflects the severity of the underlying disease.
ELECTROENCEPHALOGRAPHY (EEG)

EEG frequently is obscured by muscle and movement artifact during an episode of GCSE, and thus its usefulness may be limited. In diagnosis, EEG can distinguish SE from other causes of altered mental status. EEG also is useful in classifying SE into SW and non-SW forms, in choosing and monitoring therapy, and in formulating prognosis.

Animals with experimentally induced GCSE progress through a sequence of EEG stages according to Treiman's classification. These include discrete generalized seizures with interictal slowing, merged discrete seizures with waxing and waning of frequency and amplitude, continuous seizure discharge, almost continuous seizure discharge interrupted by flat periods, and periodic epileptiform discharges (PEDs) on a flat background (ie, periodic lateralized epileptiform discharges [PLEDs]).

Disagreement exists regarding the number of stages and the descriptions of individual stages, but enough independent descriptions indicate some sort of progression, at least in experimental animals, to support this proposal. Treiman believes that most cases of human GCSE are actually secondarily GCSE. Whether a similar sequence of changes occurs in primarily GCSE is uncertain. The full sequence has not been reported in humans. Although all stages have been reported in various individuals (sometimes several in a single individual), some investigators believe that humans, unlike experimental animals, do not always progress through a predictable sequence of EEG changes during SE. Whether PEDs comprise an ictal pattern or a marker of severe cortical dysfunction is still a subject of disagreement.

Nowack and Shaikh have reported fragments of Treiman's sequence in human patients with CPSE. Such a sequence may occur in cases of partial-onset (probably non-SW) human SE. In partial status epilepticus, Grand'Maison et al. have described a somewhat different set of stages than Treiman. Granner and Lee studied EEGs from 85 episodes of NCSE. They speculate that many cases with generalized-appearing ictal discharge (especially those with focal predominance) may actually have focal onset of the SE and that diazepam can be a useful tool for distinguishing between generalized and focal onset in this heterogenous group.

A patient who displays the violent motor manifestations of GCSE usually presents no diagnostic difficulty. However, Walker et al. reported that almost half of patients referred to a specialized center for "refractory SE" had nonepileptic conditions that mimic SE. Howell et al. discussed the difficulties of differentiating SE from pseudostatus epilepticus. Kaplan described 25 patients with NCSE in whom diagnosis was delayed up to 5 days because of presentations that suggested other entities. EEG can be helpful in making the correct diagnosis. Privitera et al. reported that 74 of 198 patients with altered levels of consciousness but no clinical convulsions had EEG evidence of definite or probable non–tonic-clonic SE. They believed that correct diagnosis could not be made on clinical signs alone. Their conclusion was that an emergency EEG should be obtained in all patients with altered levels of consciousness.
Experimental evidence suggests that patients with EEG patterns in late stages of SE respond better to phenobarbital than to more standard AEDs. However, Treiman found that the later the EEG stage of the SE, the harder it is to control. Whether to treat PEDs and, by extrapolation, any NCSE in critically ill patients is disputed. Husain et al used a combination of EEG and clinical findings to identify patients in whom PEDs should be treated. Patients whose EEGs showed higher voltage between PEDs responded more frequently to treatment.

Treiman described subtle GCSE, in which SE persists after partial treatment has eliminated convulsive movements of overt GCSE. EEG may be necessary to differentiate between partial and adequate treatment of GCSE. DeLorenzo found that NCSE can follow partial treatment of CSE and also felt that EEG can be useful in detecting such incomplete treatment. He also found that most NCSE following partial treatment of convulsive SE (CSE) was CPSE. EEG monitoring following treatment of CSE can guide treatment plans.

Jaitly et al evaluated EEGs performed after treatment of SE. They found that the presence of burst suppression or posttreatment ictal discharges was strongly (statistically) associated with mortality. The presence of PLEDs was also highly correlated (but not as strongly) with mortality and poor outcome. Drislane did a retrospective study of patients with focal SE and found no difference with regard to outcome or response to medications between the groups with continuous focal epileptiform discharge and the group with discrete electrographic seizures. He excluded patients with PLEDs with longer intervals (ie, those that recurred with a frequency of less than 1.5 Hz). Normalization of EEG correlated with good outcome. Using a somewhat different set of EEG features, Nei et al found that only the presence (at any time) of PEDs in the EEG predicted poorer outcome.

**DIFFERENTIAL DIAGNOSIS**

Usually, initial diagnosis of GCSE is not difficult. GCSE is a medical emergency. Treatment should not be delayed waiting for results of laboratory tests. Myoclonus that accompanies hypoxic or toxic insults may be confused with GCSE. Keep in mind that Treiman considers some cases of toxic or hypoxic myoclonus to be a subtle form of GCSE. Psychogenic SE is uncommon but may be a source of confusion. If differentiating the type of seizure is not possible on clinical grounds, EEG usually makes the distinction. Well-modulated alpha rhythm during or immediately after a spell suggests a psychogenic etiology. Presence of postictal slowing, especially focal, suggests an epileptic etiology.

Differential diagnosis of other forms of SE is more complicated because of polymorphic presentations. Nonconvulsive forms of SE (eg, CPSE, ASE) can be confused with psychiatric syndromes or toxic, metabolic, or other encephalopathies. Differential diagnosis of 1 form of NCSE should always include the other; CPSE and ASE cannot be distinguished on clinical grounds. Finally, always consider CPSE and ASE in differential diagnoses of patients with altered mental status.

Towne and coworkers have found that, of comatose patients without clinical convulsive activity who have EEG evidence of SE, 8% have NCSE.
TREATMENT OF STATUS EPILEPTICUS

- Generalized convulsive status epilepticus

GCSE is a medical emergency; provide therapy immediately without waiting for EEG results or other laboratory tests. Several protocols exist, none of which has been proven significantly superior. Given our current knowledge, having a clear plan of approach is more important than recommending one of the protocols over another.

Stabilize coexisting medical problems, treat metabolic abnormalities, and assure airway and oxygenation. Many medications employed to treat SE depress respiration, so intubation and ventilation may be necessary. Adequate facilities for this procedure must be available. Venous access must be obtained; treatment should be given intravenously. Test for hypoglycemia and treat if present. In adults, provide supplementary thiamine with glucose. Lumbar puncture is indicated if CNS infection is suspected.

Walker and Shorvon recommend dividing SE into premonitory, early, established, and refractory stages. The premonitory stage often occurs before the patient arrives at the hospital. At this point, rectal diazepam may abort SE. The early stage can be treated with intravenous benzodiazepines. Lorazepam (0.1 mg/kg) is the benzodiazepine of choice because of its long duration of action. Treiman et al have evaluated initial treatment of SE, comparing outcomes of patients given phenobarbital, phenytoin, diazepam plus phenytoin, or lorazepam. In patients with verified diagnosis of overt GCSE, response rates were as follows: lorazepam 64.9%, phenobarbital 58.2%, diazepam and phenytoin 55.8%, and phenytoin alone 43.6%. In statistical comparison of the pairs, only the difference between lorazepam and phenytoin alone was significant.

Suggested treatment in the established phase of SE is a combination of intravenous phenytoin (20 mg/kg) and lorazepam (if not already given) or intravenous phenobarbital alone (15-20 mg/kg). Fosphenytoin, a water-soluble phenytoin precursor, is an alternative when stability of intravenous access is questionable, since it does not have the tissue toxicity of extravasated phenytoin. It also can be given intramuscularly, but absorption by this route is not fast enough to treat SE adequately.

Other medical treatments are available, but in refractory SE (ie, that which does not respond to either regimen above), use of general anesthesia is reasonable. A commonly employed protocol for treatment of refractory SE is intravenous pentobarbital. A loading dose of 5 mg/kg is followed by 0.5-3 mg/kg/h titrated to cessation of seizures or a burst-suppression pattern on EEG. In a recent study of patients with refractory SE, Krishnamurthy and Drislane concluded that survival rate was better in patients whose EEG was more suppressed. Hypotension is a risk of pentobarbital infusion. In patients who cannot tolerate pentobarbital, alternatives include continuous infusion of benzodiazepines (eg, midazolam or propofol).

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• **Complex partial status epilepticus**

Favorable neurologic outcomes of CPSE have been reported regardless of whether medical treatment was successful. Reports of serious sequelae complicating CPSE are few. Thus, the question of how aggressively to treat CPSE remains controversial. In general, pending a good, randomized trial, CPSE should be treated similarly to GCSE, except that treatment should stop before the use of general anesthesia (eg, pentobarbital coma).

In acute stages and for diagnosis, treatment with an intravenous benzodiazepine may be helpful. Often, out-of-hospital treatment with rectal or oral benzodiazepines aborts an episode. Williamson believes that, since most patients with CPSE have a history of epilepsy, concomitant AED therapy should be optimized.

Walker and Shorvon reported that, although most episodes of CPSE are self-terminating, recurrent episodes are encountered, and medical treatment is often disappointing. Patients who have medically refractory localization-related epilepsy should be evaluated for surgical therapy.

• **Absence status epilepticus**

Walker and Shorvon reported that ASE responds rapidly to intravenous benzodiazepines. D'Agostino and coworkers believe that valproate is the medication of choice for ASE. Although effective, this treatment may result in complications such as sedation and respiratory depression. Kaplan summarized a case of a female with known absence epilepsy in which hospitalization was avoided by treating ASE with intravenous valproate. Snead et al stated that the more atypical the SE, the more difficult it is to control with benzodiazepines and other forms of therapy. Patients with primary generalized epilepsy should have optimized valproate or ethosuximide therapy to prevent recurrent episodes of ASE. Thomas et al reported that long-term anticonvulsant therapy may not be necessary in adults who are middle-aged or older at the onset of de novo ASE.

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INTRODUCTION

Until the past 4 decades, localization of brain tumors and other focal lesions was difficult. Neuroimaging techniques consisted of skull x-rays, which were usually negative, and pneumoencephalograms, which were invasive, painful, and often uninformative. In 1936, Walter, who introduced the term “delta waves,” first identified the association between localized slow waves on EEG and tumors of the cerebral hemispheres. This established EEG as an important tool for localizing brain tumors. For the next 4 decades electroencephalographers mounted an enormous effort to improve accuracy of localization and to seek clues to underlying pathologic processes.
Experience has shown EEG to be somewhat reliable in localizing lesions involving superficial accessible portions of the cerebral hemispheres, though it is of limited value in deep-seated lesions, especially posterior fossa tumors. The role of EEG in detecting focal cerebral disturbances has undergone a significant change since the development of CT scan and MRI. Today EEG is primarily complementary to these studies and is used mainly for evaluating functional changes in the patient’s condition. It demonstrates aspects of brain physiology that are not reflected in structural neuroimaging. Functional neuroimaging techniques, such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), and functional MRI (fMRI), can exhibit physiologic changes but not with the temporal resolution of EEG. Furthermore, EEG provides the only continuous measure of cerebral function over time.

This chapter reviews the major EEG changes that occur with different brain tumors, as determined by location, histologic type, associated complications, and surgical and nonsurgical treatments.

**BACKGROUND**

- **Classification**

Intracranial tumors have been classified by location and histology.

Classification by location, modified from Merritt, 1991, is as follows:

I. **Tumors of the skull**
   - A. Metastatic tumors
   - B. Eosinophilic granuloma

II. **Tumors of the meninges**
   - A. Meningioma
   - B. Meningeal carcinomatosis

III. **Tumors of the cranial nerves**
   - A. Acoustic neuromas
   - B. Trigeminal neuromas

IV. **Neuroectodermal tumors**
   - A. Cerebral
     1. Astrocytoma
     2. Oligodendroglioma
     3. Glioblastoma
B. Cerebellar
   1. Medulloblastoma
   2. Astrocytoma

C. Brainstem
   1. Glioma
   2. Ependymoma

V. Other primary tumors
   A. Pituitary adenoma
   B. Pinealoma
   C. Congenital tumors
      1. Craniopharyngioma
   D. Granulomas

VI. Metastatic
   A. Parenchymal tumors

The 1993 World Health Organization classification is based on histology. A simplified version is as follows:

I. Tumors of neuroepithelial origin
   A. Astrocytic tumors
      1. Astrocytoma
      2. Anaplastic (malignant) astrocytoma
      3. Glioblastoma
   B. Oligodendrogial tumors
   C. Ependymal tumors
   D. Mixed gliomas
   E. Choroid plexus tumors
   F. Neop epithelial tumors of uncertain origin
   G. Neuronal and mixed neuronal-glial tumors
      1. Dysembryoplastic neuroepithelial tumor
      2. Ganglioglioma
   H. Pineal parenchymal tumors

II. Embryonal tumors

III. Tumors of cranial and spinal nerves

IV. Tumors of the meninges

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A. Meningioma and its variants
B. Malignant neoplasms (eg, chondrosarcoma)

V. Lymphomas and hemopoietic neoplasms

VI. Germ cell tumors

VII. Cysts and tumorlike lesions
   A. Colloid cyst of the third ventricle
   B. Hypothalamic hamartoma

VIII. Tumors of the sellar region
   A. Pituitary adenoma
   B. Craniopharyngioma

IX. Local extension from regional tumors

X. Metastatic tumors

XI. Unclassified tumors

• Epidemiology

One estimate states that in the United States in 1990, approximately 20,500 new cases of primary brain tumors and 20,700 new cases of metastatic brain tumors occurred. Based on the 1989 US population of 249,000,000, these numbers signify an incidence rate of 8.2 per 100,000 for primary brain tumors and 8.3 per 100,000 for metastatic brain tumors.

The following characteristics apply to primary brain tumors:

• Second most common cause of cancer death in children and adults aged 34 years and younger
• Third most common cause of cancer death in men aged 35-54 years
• In 1990, represented approximately 1.5% of all cancers diagnosed and 2% of cancer deaths

The various types of brain tumors occur with different frequency in children and in adults. The most common childhood tumors are astrocytoma, medulloblastoma, and ependymoma. The most common adult tumors are metastatic brain tumors (from lung, breast, melanoma, and other primary tumors), glioblastoma, and anaplastic astrocytoma.

brain tumors presenting with seizures
Seizures occur in 40-60% of patients with supratentorial tumors and are the presenting symptom in 10-40%. When seizures start in adulthood, neoplasms are the cause in 2-20% of patients. In general, the more slowly a tumor grows, the more likely it is to present with a seizure. For example, as many as 92% of oligodendrogliomas are associated with seizures, and in most patients they are the presenting symptom. Location is also important in determining the likelihood of seizures. Perirolandic cortex is believed to be most epileptogenic, although this impression may reflect in part the ease of diagnosing seizures in the presence of prominent motor activity. Medial temporal structures are probably the next most epileptogenic, followed by other areas of frontal, temporal, and parietal lobes, with occipital lobe the least likely to produce seizures. Subcortical tumors, such as those in the thalamus and particularly the posterior fossa, rarely cause seizures.

**TYPES OF EEG ABNORMALITIES ASSOCIATED WITH BRAIN TUMORS**

EEG abnormalities in brain tumors depend on the stage at which the patient presents for evaluation. EEG changes observed with tumors result mainly from disturbances in bordering brain parenchyma, since tumor tissue is electrically silent (with the possible exception of tumors containing neuronal elements, such as gangliogliomas). For this reason, EEG localization often is misleading, although lateralization is generally reliable.

The following are common findings:

- Polymorphic delta activity (PDA)
- Intermittent rhythmic delta activity (IRDA)
- Diffuse or localized theta activity
- Localized loss of activity over the area of the tumor
- Asymmetric beta activity
- Disturbance of the alpha rhythm
- Spikes, sharp waves, or spike-wave discharges

Activation procedures are usually of limited value in patients with tumors, although hyperventilation occasionally can accentuate focal slowing. Asymmetries of photic driving can be useful at times, although they also can be misleading.

- **Slow Wave Activity**

Focal delta activity is the classic electrographic sign of a local disturbance in cerebral function. A structural lesion is strongly suggested if the delta activity is continuously present; shows variability in waveform amplitude, duration, and morphology (polymorphic); and persists during changes in physiologic states, such as sleep or alerting procedures. When focal delta is found without a corresponding imaging abnormality, it is usually in the setting of acute seizures (especially postictally), nonhemorrhagic infarction, or trauma.

Clinical and experimental observations indicate that PDA results primarily from lesions affecting cerebral white matter; involvement of superficial cortex is not essential, and
lesions restricted to the cortical mantle generally do not produce significant delta activity. Functional deafferentation of cortex likely is critical.

Delta activity that fails to persist into sleep or attenuates significantly with arousal or eye opening is less indicative of structural pathology, as is rhythmic or sinusoidal delta. The latter usually occurs intermittently and is termed IRDA. It is usually bilateral and of high amplitude and is typically maximal occipitally (OIRDA) in children and frontally (FIRDA) in adults. Unlike PDA, IRDA increases in drowsiness and attenuates with arousal. IRDA often is observed without structural pathology, as in metabolic encephalopathies, but it also can occur with diencephalic or other deep lesions; in this situation, an amplitude asymmetry can be present, with higher amplitude ipsilateral to the lesion.

As in other clinical settings, theta activity is indicative of less severe localized or diffuse dysfunction than delta activity and is observed more commonly with functional disturbances than with structural disturbances. When unaccompanied by delta activity, theta is less likely to indicate a lesion that produces a focal neurologic deficit or seizures.

- **Localized Loss and Asymmetries of Background Activity**

Since tumor tissue probably does not generate electrical activity detectable with conventional recording techniques, electrical silence is the best localizing sign of a cerebral tumor. However, it is a rare finding, occurring only when the tumor involves significant cortical areas with minimal subcortical disruption. Incomplete loss of activity, especially faster normal rhythms, is observed more commonly and is diagnostically helpful.

- **Alpha rhythm**

By the time the patient presents with focal or diffuse neurologic symptoms and signs, disturbance of the alpha rhythm may be present. Slowing of the alpha rhythm ipsilateral to a tumor is more common and significant than asymmetry of amplitude. However, disturbance of alpha rhythm depends on the site of the tumor. The more posterior the location, the more the alpha tends to be slowed, impersistent, or disturbed by admixed theta waves. The alpha rhythm also may fail to block to eye opening on the side of the neoplasm (ie, Bancaud phenomenon).

- **Beta activity**

Abnormalities of beta activity usually are limited to voltage asymmetries. To be considered unequivocally abnormal, a persistent amplitude difference of one third or greater (expressed as a fraction of the higher voltage) should be present. Diminished beta activity results either from cortical dysfunction, as in parenchymal tumors, or from an increase in resistance of the medium-separating cortex from scalp-recording electrodes, as in meningiomas or subdural collections. Focally increased beta activity usually is associated with a skull defect.
Interictal Epileptiform Discharges

- **Isolated discharges**

  Spikes, sharp waves, or spike-wave complexes occurring with consistent localization are observed uncommonly early in the course of brain tumors. In one study predating the CT scan era, such discharges appeared with only 3% of gliomas and metastatic tumors at the time of craniotomy. However, they were more common either as early findings of slowly growing neoplasms associated with seizures or later after focal slowing had developed.

- **Periodic lateralized epileptiform discharges**

  Patients with tumors may exhibit periodic lateralized epileptiform discharges (PLEDs) at times, particularly after a series of seizures. In a study of 282 patients with typical PLEDs, tumor was present in 18%. Most patients with this EEG finding have had or will have seizures, if they are observed sufficiently closely and persistently; the pattern likely represents a transitional state between ictal and interictal epileptiform discharges. Aggressiveness of treatment depends in part on whether the discharges are resolving (becoming less sharp, more localized, and further apart) or the opposite.

- **Seizure patterns**

  When electrographic seizures are recorded during a routine EEG, suspect status epilepticus. Clinical accompaniments may be subtle, as in aphasic or other forms of nonconvulsive status, particularly when the patient’s baseline condition has been compromised by the tumor, its treatment, or complications.

**EEG CHANGES IN TUMORS BY LOCATION**

Since EEG reflects activity of cortical neurons, hemispheric tumors affect EEG most consistently and prominently. In older studies, a normal EEG occurred in approximately 5% of hemispheric, 25% of deep or basal, and 25% of infratentorial tumors. The overall figure now may be 50% or higher, given the earlier diagnosis allowed by modern neuroimaging. Location is an important determinant of the likelihood and nature of EEG abnormalities.

**Frontal Lobe Tumors**

- Frontal lobe tumors characteristically cause focal PDA, which accurately localizes the lesion.
- In approximately one third of patients, slow waves are bilateral and may be IRDA rather than PDA. This occurs most often when deep structures such as the corpus callosum are involved (butterfly glioma).
- IRDA is more frequent with frontal tumors than with tumors in other hemispheric locations, even in children in whom the IRDA is often maximal occipitally (OIRDA).
The slow wave abnormality may be only in the theta range, particularly in small, slowly growing tumors.
The alpha rhythm usually is preserved, although it may be disrupted with large lesions.
Parasagittal tumors, particularly meningiomas, may cause decreased beta activity on the side of the tumor or runs of ipsilateral alpha and theta activity.
Sharp waves and spikes are most likely in slow-growing neoplasms and may be bilateral; occasionally, frontally predominant spike-wave complexes mimicking those of idiopathic epilepsies may be produced.

**Temporal Lobe Tumors**

Temporal gliomas are generally the easiest to localize on EEG, since PDA occurs over the tumor site in more than 80% of patients. Tumors in other locations, such as the thalamus, also may produce temporal delta; however, focal delta is more reliably localizing when background rhythms also are attenuated.

**Anterior temporal**

- When tumors are in this location, a well-preserved alpha rhythm occurs.
- PDA is well localized.
- EEG from the contralateral hemisphere is often virtually normal.
- Since these tumors often are associated with seizures, they may demonstrate interictal epileptiform discharges. These may be identical to those associated with nonneoplastic lesions such as mesial temporal sclerosis, especially when the tumor is located medially, as is often the case with very slow-growing tumors, such as gangliogliomas and dysembryoplastic neuroepithelial tumors.

**Posterior temporal**

- Tumors in this location are characterized by PDA and usually disturbance of the ipsilateral alpha rhythm.
- Slowing or disorganization of the alpha rhythm with intermixed theta is present.
- Occasionally, alpha amplitude is decreased markedly rather than slowed.

**Parietal Lobe Tumors**

- Tumors in this region less often produce localized slowing; PDA usually is lateralized but often not clearly localized. When phase reversals are present, they may be temporal or frontal rather than parietal.
- PDA is often slow (<2 Hz), but it is usually of lower amplitude than with frontal or temporal tumors.
- The alpha background generally is disturbed either ipsilaterally or bilaterally.
- Theta rather than delta activity may occur in meningiomas, low-grade gliomas, and small metastases.

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- In centroparietal tumors, mu rhythms may be attenuated ipsilaterally but occasionally may be more persistent and of higher amplitude.
- Since seizures are common in patients with tumors in perirolandic areas, ipsilateral epileptiform discharges may be present; at times they may be difficult to distinguish from mu, especially after craniotomy.

**Occipital Lobe Tumors**

- Most occipital gliomas produce focal changes, especially PDA, which spreads variably to more anterior and contralateral locations. Occipital meningiomas, mainly of the tentorium, can cause more focal EEG changes.
- The background alpha rhythm is rarely normal and may be impaired either ipsilaterally or bilaterally.
- Interictal epileptiform discharges are rare.

**Deep Hemispheric Tumors**

Deep hemispheric tumors include tumors impinging on the lateral and third ventricle and surrounding structures, including the diencephalon, basal ganglia, and corpus callosum. Neuroimaging has led to earlier diagnosis of smaller tumors that may be associated with normal EEGs. When abnormalities are observed, the following apply:

- The typical EEG finding is IRDA. This finding classically has been associated with hydrocephalus or increased intracranial pressure, but this assumption may be incorrect, since IRDA is uncommon in hydrocephalus of nonneoplastic origin and is not present in benign intracranial hypertension.
- PDA typically does not occur, although asymmetric IRDA is relatively common.
- Especially in older patients, rhythmic delta may be more continuous than intermittent.
- Alpha rhythm and sleep spindles may be disrupted ipsilateral to the lesion.
- Epileptiform discharges are very rare.

**Intraventricular and Sellar Tumors**

**Lateral ventricle (ependymoma, meningioma)**

- EEG may exhibit PDA over the ipsilateral temporal lobe.
- Theta and sharp waves may be present temporally.

**Third ventricle (colloid cyst, epidermoid, craniopharyngioma)**

- EEG is usually normal unless the lesion is large.
- Slowing may be bifrontal or diffuse.
- Runs of theta may be observed.

**Sellar region**
• EEG is usually normal
• If present, slowing is usually bitemporal.

Infratentorial tumors

Brain stem and cerebellum

• EEG is more often abnormal in children.
• If present, slowing is most often posterior and bilateral.
• IRDA may be observed, especially if hydrocephalus is present.

Cerebellopontine angle (acoustic neuroma)

• EEG is usually normal, especially with small tumors.
• When present, slowing is usually temporal or temporal occipital.
• Slowing is often intermittent and usually but not always ipsilateral; it may be bilateral or even predominantly contralateral.

TUMOR TYPE AND EEG

EEG patterns are not specific for tumor pathology, but some general correlations exist.

• Slowly growing extra-axial tumors, such as meningiomas, produce the mildest EEG disturbances, whereas rapidly growing intraaxial tumors, such as glioblastomas, cause the most marked abnormalities.
• Benign intraaxial tumors, such as astrocytomas or oligodendrogliomas, are intermediate in their effects on the EEG.
• Interictal discharges most commonly are observed initially in slowly growing tumors and often are observed later in the course of higher grade lesions.

Meningiomas

Being extraaxial, meningiomas compress the brain but cause little destruction of brain tissue. Therefore, meningiomas of the anterior or middle cranial fossa, unless large, infrequently alter EEGs. Convexity meningiomas are more likely to cause EEG changes. With rolandic or parasagittal meningiomas, common EEG changes include the following:

• Focal theta activity
• FIRDA
• Diminished, or less often, augmented beta activity
• Focal PDA that is usually low in amplitude (50-60 mV), intermittent, and misleadingly prominent in temporal derivations
• Epileptiform discharges observed in as many as 45% of patients
Gliomas

Slowly growing gliomas such as oligodendrogliomas and fibrillary astrocytomas (excluding tumors of deep structures) often can be distinguished from the more rapidly growing anaplastic astrocytoma and glioblastoma multiforme.

- With the more benign tumors, which comparatively are circumscribed, the abnormalities tend to be localized and within the theta range.
- In the rapidly growing tumors, relatively more overall abnormality is present, and the background (particularly the alpha rhythm) is more impaired and disorganized.
- Glioblastomas produce the most widespread, slowest (often 1 Hz or less), and largest (100-200 mV) delta waves. These tumors cause prominent PDA, with marked alteration of background rhythms. Also, the high incidence of necrosis makes “flat PDA” (low-amplitude slow delta with diminished fast activity) more likely.
- Indolent gliomas commonly cause seizures, and epileptiform activity may appear before significant slowing occurs. Later, delta appears, often intermittently and at 2-3 Hz. Still later, focal PDA becomes persistent.

Metastases

Metastatic tumors to the brain occur commonly with carcinomas of lung, kidney, and breast and with melanomas and chorionic carcinomas. When metastases are present bilaterally, slowing often appears diffuse, although it is often asymmetric; slowing from multiple bilateral lesions is often difficult to distinguish from a toxic-metabolic disturbance. Meningeal carcinomatosis usually causes changes that correlate with the clinical situation; when deposits are widespread and cause an encephalopathy, slowing is usually diffuse.

Isolated metastases usually cause less prominent abnormalities than gliomas of similar size and location. Slow waves show higher frequency, lower amplitude, and less persistence than with high-grade gliomas, and normal background rhythms are more likely to be preserved.

EEG CHANGES OVER TIME

Because of improvements in neuroimaging and neurosurgery and recognition of the benefits of early resection, serial EEG studies now rarely are performed prior to surgery. Older studies suggest that EEG evolution during tumor growth is characterized mainly by increased slowing—lower frequency, higher amplitude, more persistence, and wider distribution—with rate of change depending mainly on rate of tumor growth. Also, epileptiform discharges are more likely to occur as the tumor grows.

Occasionally, successful treatment with steroids or chemotherapy can cause reduction in slowing and epileptiform activity.

Following resection, dramatic changes may occur in the EEG; these usually stabilize over periods of weeks to months. Since screening for tumor recurrence now depends on
neuroimaging, serial EEGs usually are reserved for patients with clinical changes that are not explained by imaging, particularly when seizures are suspected.

**EEG changes after neurosurgery**

EEG changes after neurosurgery usually exhibit the following features:

- In the immediate postoperative period, the EEG frequently deteriorates, with prominent focal and sometimes generalized slowing. Localized PDA can occur if, for example, the temporal or frontal lobe was retracted to provide access to a deep tumor.
- After a week or so, EEG abnormalities improve, and slow waves diminish, although much individual variation exists.
- In most patients, the residual EEG abnormality becomes stable 3-4 months after craniotomy.
- Abnormalities seldom resolve completely; residual abnormality depends largely on completeness of tumor excision.
- Subsequent localized or generalized increase in slowing or loss of background activity strongly suggests tumor recurrence.
- With further progression, delta activity increases in voltage while frequency becomes slower and distribution wider.
- Emergence of epileptiform activity without changes in focal or generalized slowing is common but typically does not imply tumor recurrence.
- Appearance of a postoperative breach rhythm is almost universal. This consists of a localized increase in theta and faster frequency activity, usually 6-11 Hz, which shows a sharp, often arciform contour. Decrease in the filtering effect of the intact skull on higher frequency activity after a breach (break) in the cranium is the major cause of these changes, which generally persist despite replacement of the bone flap and healing of the craniotomy. Preoperative and postoperative recordings on a patient with an oligodendroglioma (see Picture 1, Picture 2) illustrate these changes. At times, such rhythmic activity can suggest a seizure pattern, but it does not have the characteristic evolution of frequency, amplitude, and distribution of an ictal discharge.

**Use of EEG to predict postoperative seizures**

Because of the tendency of focally increased high-frequency activity after craniotomy to sharpen the contour of background waves, identification of interictal epileptiform discharges is difficult. A distribution other than the breach rhythm, asymmetric up-slope and down-slope, extremely sharp peak, and prominent after-coming slow wave suggests epileptogenicity. However, in a preliminary study, degree of slowing (predominantly delta rather than theta) was associated more closely with seizures than with amount of sharp activity.

**Complications of brain tumors and their treatment**
The possibility of perioperative stroke has been mentioned. Sizable ischemic infarcts typically exhibit increased slowing in the region of the stroke, with loss of fast activity if cortex is involved. Hemorrhagic stroke or hemorrhage into the tumor bed also is accompanied by increased slowing, which may be bilateral if deep structures are affected.

If chemotherapy or radiation is effective, slowing can diminish even without surgery. Conversely, late effects of radiation can result in increased slowing, as well as new epileptiform activity and clinical seizures in the case of radiation necrosis. EEG probably does not help in distinguishing recurrent tumor from radiation necrosis. In radiation-induced or chemotherapy-induced encephalopathies, including methotrexate leukoencephalopathy, slowing of the EEG usually parallels the clinical situation.

The clinician and electroencephalographer also must remember that patients with brain tumors can develop additional diseases, particularly when immunosuppressed, such as progressive multifocal leukoencephalopathy or herpes simplex encephalitis. In these patients, EEG changes such as focal slowing or periodic discharges reflect the new condition.

CONCLUSIONS

The character and distribution of EEG changes produced by tumors depend primarily on lesion size, rate of growth, distance from the cortical surface, and specific structures involved.

In general, the following are true:

- PDA is the hallmark of tumor localization.
- Both metastatic tumors and gliomas commonly cause delta activity, often localized to the tumor site and neighboring zone, although bilateral slowing may occur. Changes are more marked with aggressive gliomas.
- Deep tumors are more likely to cause widespread hemispheric or bilateral slowing, often rhythmic (IRDA). Small deep tumors may cause no abnormalities, especially if the thalamus is not involved.
- When the tumor is growing rapidly and involves cortex, localized loss of background activity may occur.
- Slowing of the alpha rhythm is frequent in posterior supratentorial tumors.
- Spikes, sharp waves, or spike-wave discharges often are observed at the time of diagnosis in slowly growing tumors that are most likely to present with seizures. With more malignant neoplasms, both seizures and epileptiform discharges occur later.
- Craniotomies and other interventions alter the EEG in usually predictable ways. Breach rhythm can complicate the interpretation of interictal epileptiform activity.

Despite advances in neuroimaging, EEG still offers a unique view of physiologic changes over time in patients with brain tumors.
REFERENCES

MENINGITIS

The EEG in meningitis shows various degrees of slow-wave abnormalities, depending on the type of meningitis and the degree of involvement of the central nervous system.

Moderate to severe diffuse slow-wave abnormalities are often present in acute purulent meningitis, and paroxysmal epileptiform activity may be present in those patients who have seizures.

The electroencephalographic findings in tuberculous meningitis vary according to the location of the inflammatory process. In basal meningitis, the EEG may be normal and
show only mild nonspecific slowing. When the inflammatory process involves the cortical meninges, moderate to severe slowing occurs, depending on the degree of cortical involvement, the rate of progression of the disease process, the level of consciousness, the presence of metabolic or systemic factors, the pulmonary state of the patient, and the effects of medication. As with purulent meningitis, more severe slow-wave abnormalities are present in children, with the slowing often being maximal over the posterior head regions.

In aseptic meningitis, the EEG may be normal or show only mild slowing; the electroencephalographic findings may not necessarily correlate with the clinical severity of the inflammatory process or the development or degree of post-infectious sequelae.

Patients in whom meningoencephalitis develops in association with infectious mononucleosis may have mild to moderate diffuse or focal slow-wave abnormalities that may or may not coincide with the area of maximal neurologic dysfunction. On occasion, focal epileptiform abnormalities have been observed in patients who experience seizures.

The rate and degree of the improvement in the electroencephalographic abnormalities after treatment have some diagnostic and prognostic value. One of the characteristic features of meningococcal meningitis is the rapid improvement in the electroencephalographic findings, with the findings often returning to normal within 1 or 2 wk after treatment. In other types of purulent meningitis and tuberculous meningitis, the electroencephalographic abnormalities often require several weeks to resolve.

The EEG usually returns to normal in patients with uncomplicated meningitis; however, persistent electroencephalographic abnormalities or evidence of deterioration in the EEG suggests an unfavorable course, the development of a complication such as an abscess or hydrocephalus, or the presence of residual brain damage.

Although the electroencephalographic findings are not essential for making the specific diagnosis of meningitis, the EEG and particularly serial recordings are helpful in following the course of the disease, detecting the development of complications or relapse, and indicating the presence of sequelae or residual brain damage.

ENCEPHALITIS

The electroencephalographic findings in encephalitis are similar to those in meningitis, although the abnormalities are often more severe; this may be a helpful point in the differential diagnosis.

The EEG is almost always abnormal during the acute phase of encephalitis, with the most frequent finding being the presence of diffuse high-voltage, arrhythmic and/or rhythmic delta slowing. Diffuse polymorphic arrhythmic delta activity is more likely to occur when the white matter is involved, whereas paroxysmal, bisynchronous slow-wave activity is more likely to be present when the disease process involves the subcortical gray matter. The degree of slowing depends on the severity of the infection, the amount of cerebral
involvement, the level of consciousness, and other associated systemic or metabolic factors. In general, the leukoencephalitides, which primarily involve the white matter and which are caused by the group B non-neurotropic viruses (measles, rubella, variola) and the post-vaccinal states, are associated with more severe electroencephalographic abnormalities than are those caused by the group A neurotropic viruses (mumps, St. Louis and equine encephalitis). Children often show more severe electroencephalographic abnormalities than do adults. Epileptiform abnormalities also may be present, particularly if the patient is having seizures.

![Figure 1. EEG showing generalized slowing in an 11-mos-old boy with tuberculous meningitis.](image)

Slow-wave abnormalities have also been observed during the acute stages of uncomplicated childhood infections, such is measles, mumps, rubella, chickenpox, and scarlet fever, in which there is no overt evidence of nervous system involvement. The electroencephalographic abnormalities occur most frequently with measles infection, in which moderate to severe slow-wave abnormalities may be present as early as 1 to 4 days before the rash appears, reaching a maximum on the first day of the rash and then subsiding during the next 8 to 10 days. Transient slow-wave abnormalities also have been observed over the posterior head regions after measles vaccination.

The electroencephalographic abnormalities usually diminish in association with clinical improvement, but on occasion the electroencephalographic changes lag behind the clinical findings. However, persistent or increased abnormalities, particularly if they are focal, are associated with an increased likelihood of brain damage or post-encephalitic epilepsy. A return to a normal electroencephalographic pattern does not preclude residual brain damage.

Diffuse slow-wave abnormalities with, at times, more focal features and epileptiform activity may be seen in California encephalitis and there is a fairly good correlation
between the EEG and clinical findings, both during the acute stages of the disease and on follow-up examinations.

The entero-encephalitides caused by Coxsackie and ECHO viruses, which predominantly affect infants and young children, are accompanied by varying degrees of diffuse slow-wave abnormalities in the EEG. Western equine, Eastern equine, St. Louis, and Japanese encephalitis are also associated with variable slow-wave abnormalities in the EEG, which may or may not show a correlation with the clinical picture.

In tick-borne viral encephalitis (spring-summer encephalitis), slow-wave abnormalities may be present prior to the onset of symptoms. The abnormalities do not necessarily correspond with the clinical symptoms and severity of the infection; slow-wave abnormalities, however, may continue to be present in those patients with post-encephalitic symptoms. EEG recordings have only rarely been done in rabies. They have been described as showing a depression or "extreme desynchronization" in one case, and nonspecific findings in two other cases (Gastaut and Miletto, 1955; Radermecker, 1977). Diffuse slow-wave abnormalities similar to those seen in other post-vaccinal states may be present following rabies vaccination.

The EEG recordings in the rickettsbial infections (Eurasian typhus or spotted fever, Rocky Mountain spotted fever, tsutsugamushi fever) range from normal to those showing diffuse or focal slow-wave abnormalities, with epileptiform activity being present in those patients who develop seizures. The degree of EEG abnormality usually reflects the degree of encephalitic involvement.

Encephalitis or meningitis caused by fungal diseases (histoplasmosis, blastomycosis, and coccidioidomycosis) are associated with diffuse slow-wave abnormalities in the EEG. These changes are similar to those produced by bacterial and viral agents. More focal EEG abnormalities may be present if there is focal cerebral involvement by mycotic abscesses. As fungal infections tend to recur, the EEG may be helpful in following the clinical course of the patient and alerting one to a recurrence of the infection or the development of complications. As a rule, most of the different types of encephalitis do not give rise to specific types of EEG patterns. Instead, the EEG abnormalities are most often expressed as diffuse or focal slow-wave abnormalities, with the degree and extent of the slowing reflecting the intensity of parenchymal involvement.

**CHRONIC ENCEPHALITIS OF RASMUSSEN AND AGUILAR**

There is an entity of chronic smoldering encephalitis which occurs in children and young adults which is characterized by progressive neurologic and intellectual deterioration and recurrent episodes of intractable seizures. The seizures are variable; one type of seizure may be present at one point in time, to be replaced by a different type of seizure arising in a different location at another stage of the disease process. The EEG shows various types of epileptiform and slow-wave abnormalities, which migrate or spread to different areas of the brain during the disease process.
Widespread pathologic changes are present, with active areas of an inflammatory process being present in some regions of the brain, while other regions show scarring or evidence of a "burned out" encephalitis. The cause of the entity is unknown, however, the pathologic changes are similar to those of other viral encephalitides. The current thinking is that this represents a chronic, smoldering viral infection that flares up intermittently, with an exacerbation of seizures and neurologic and mental deficit.

**HERPES SIMPLEX ENCEPHALITIS**

The EEG often shows a characteristic pattern and temporal evolution which can be of great value in making the diagnosis of herpes simplex encephalitis, especially when serial recordings are obtained. During the earlier stages of the disease process, the background activity is disorganized and polymorphic delta activity develops in a focal or lateralized fashion, with a predominance over the involved temporal region. Soon after this, focal or lateralized sharp or slow-wave complexes appear, usually having a maximal expression over the involved temporal region. These complexes rapidly evolve into a periodic pattern, with the sharp waves having a stereotyped appearance and recurring every 1 to 3 sec. The periodic pattern is usually seen between 2 and 5 days after the onset of the illness but, on occasion, has been observed up to 24 and 30 days after the onset of the illness. If there is bilateral involvement of the brain, bilateral periodic complexes may be present, occurring synchronously or independently over the two hemispheres but often having a time locked relationship with one another. Focal or lateralized electrographic seizure discharges, consisting of repetitive sharp or slow waves or spike or polyspike bursts, may be present over the involved area or hemisphere.
During this time, there is a transient obliteration of the periodic discharges on the side of the seizure discharges. In the later stages of a fatal herpes simplex infection, the electrographic seizure discharges may occur in association with the periodic discharges without altering them. Additionally, during the later stages of the disease process, the periodic complexes often have a more broad slow-wave appearance and a longer interburst interval. During the final stages of a fatal infection, the EEG assumes an almost isoelectric appearance.

In nonfatal herpes simplex encephalitis, the periodic complexes disappear as the disease process resolves and are replaced by focal or lateralized slow-wave abnormalities or attenuation of activity over the involved area. The resolution of the electroencephalographic abnormalities often lags behind the improvement in the clinical state; the EEG frequently continues to show residual slow-wave abnormalities and focal epileptiform activity over the involved area.

As in adults, the presence of periodic complexes is a prominent feature in the EEG of infants with herpes simplex encephalitis, although the periodic discharges may show more of a shifting emphasis from area to area. After the resolution of the infection, the EEG frequently continues to show focal epileptiform discharges, as well as localized areas of attenuation of activity overlying residual cystic areas of the brain.
Although the findings in herpes simplex encephalitis are not pathognomonic for the disease, the presence of unilateral or bilateral periodic complexes in association with a febrile illness and a rapid evolution of neurologic signs is strongly suggestive of herpes simplex encephalitis.

**JAKOP-CREUTZFELDT**

Jakob-Creutzfeldt disease is a diffuse disorder of the central nervous system which occurs in the middle-age group. The disease is characterized by progressive dementia, motor dysfunction, myoclonus, and a characteristic periodic electroencephalographic pattern that is valuable in making or confirming the diagnosis.

The earliest electroencephalographic changes consist of a disorganization and decrease of normal background activity and the development of progressive slow-wave abnormalities. The slow-wave abnormalities are usually generalized, but at times they occur in a more focal or lateralized fashion. As the disease progresses, diphasic or triphasic sharp-wave discharges appear. initially, these discharges occur in a sporadic or intermittent fashion and may be asymmetric or predominate over one region, but eventually they evolve into the characteristic pattern, consisting of generalized and bisynchronous continuous periodic stereotyped sharp waves, recurring at intervals of 0.5 to 1 sec and having a duration of 200 to 400 msec. On a few occasions, the discharges have appeared as periodic lateralized discharges (PLEDS). Myoclonic jerks often occur in association with the periodic sharp waves; however, there is not always a constant relationship between the myoclonic jerks and periodic sharp waves; one can occur without the other. This is particularly true during sleep or late in the course of the disease, when the myoclonic jerks decrease or disappear, but the periodic sharp waves persist.

One characteristic feature of the periodic discharges in Jakob-Creutzfeldt disease is the reactivity of the sharp waves to alerting or afferent stimuli. Prior to the time when the periodic pattern has been established or when the sharp waves occur in a more intermittent or sporadic fashion, alerting the patient or arousing the patient out of sleep may bring out the periodic pattern. When the periodic pattern is present, rhythmic photic, auditory, or somatosensory stimuli can pace or set the rhythm of the sharp waves if the frequency of the stimuli falls near the range of the frequency of the spontaneous periodic pattern. However, loud noises and certain types of drugs, such as diazepam and the barbiturates, can temporarily abolish the periodic sharp waves and myoclonic jerks.

As the disease progresses, the interburst interval increases and the amplitude of the periodic sharp waves decreases. In the final stages of the disease, the EEG becomes almost isoelectric, with intermittent bursts of sharp or slow waveforms.

Although the electroencephalographic findings are not pathognomonic for Jakob-Creutzfeldt disease, the presence of the periodic electroencephalographic pattern in association with the clinical findings of progressive dementia and myoclonus is a strong indication of Jakob- Creutzfeldt disease.
SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)

SSPE is an inflammatory disease occurring in children and adolescents, believed to be caused by the measles virus and which is characterized by abnormal movements, a progressive intellectual deterioration, and a diagnostic electroencephalographic pattern. The characteristic electroencephalographic pattern consists of high-voltage (300 to 1500 mv) repetitive polyphasic and sharp- and slow-wave complexes ranging from 0.5 to 2 sec in duration, usually recurring every 4 to 15 sec. On rare occasions, these complexes may occur at intervals ranging up to 1 to 5 min. The periodic complexes may be present at any stage of the disease, but they usually are seen during the intermediate stages. Although the form and appearance of the periodic complexes is fairly constant and stereotyped in a single recording, the shape of the complexes varies in different patients and can change from time to time in the same patient at different stages of the disease process. The complexes are usually generalized and bisynchronous, but at times they may be asymmetric, have a time lag from side to side or front to back, or occur in a more lateralized or focal fashion, particularly in the earlier stages of the disease.

Initially, the complexes may occur at irregular intervals, but, once established, the complexes recur at regular intervals, although the repetition rate may vary during the course of the disease. Afferent stimuli do not usually affect the periodic complexes; however, on rare occasions, the complexes can be evoked by external stimuli. This occurs when the complexes are present in an inconstant manner, either when they first make their appearance or toward the end of the period of remission. Once the regular pattern of the complexes has been established, however, the complexes are no longer influenced by external stimuli. Drugs usually have little effect on the periodic complexes, although one report described the occurrence of periodic pattern after an intravenous injection of diazepam.

A prominent feature of SSPE is the stereotyped motor jerks or spasms occurring with the periodic complexes. The movements are often described as myoclonic jerks; however, they do not have the momentary lightning-quick nature of true myoclonus; instead, the movements consist of an initial "shock-like abruptness," followed by a momentary arrest of the movement, and then a gradually melting away to the position of rest. On less frequent occasions, the periodic complexes may be associated with an inhibitory phenomenon such as an arrest of movement, loss of tone, or drop attacks. The abnormal movements usually become evident about the same time that the periodic complexes appear on the EEG, however, on occasion, and particularly in the early stages of the disease, the periodic complexes may be present without the associated motor movements. On the other hand, the presence of the MOTOR jerks in the absence of the periodic complexes is uncommon. The motor movements often disappear during sleep, despite a persistence of the periodic complexes. Certain drugs, such as diazepam, may reduce or abolish the motor movements without altering the electroencephalographic complexes.

The resting EEG may be relatively normal when the complexes first appear. As the disease evolves, however, the EEG shows various changes, consisting of slowing and disorganization of the background, an asymmetry of the background activity, or both.
These changes are followed by an increase in the slow-wave abnormalities, usually occurring in a diffuse manner but at times having a focal or lateralized emphasis and coinciding with the area of maximal neurologic involvement. In the later stages of the disease, polymorphic delta activity or intermittent frontal dominant monorhythmic slow-wave activity may be present. On occasion, there may be a transient flattening or attenuation of activity after the periodic complexes. Various types of epileptiform discharges, spikes, sharp waves, or spike-and-wave complexes occurring in a focal or generalized fashion also may be present. Patients who have a remission or an improvement in the clinical state show a corresponding improvement on the EEG.

The typical stages of sleep become less recognizable as the disease progresses, and identifiable sleep stages become limited to two main types. These are a low-voltage fast pattern with or without spindle activity and a high-voltage slow-wave pattern. In the later stages of the disease, sleep spindles, V waves, and K complexes disappear and the electroencephalographic differentiation of the various stages of sleep is no longer possible. The periodic complexes often persist during sleep, although their shape and frequency may be modified. On rare occasions, periodic complexes may be activated or occur predominantly during the sleep recording.

In the final stages of the disease, there is often a reduction in amplitude and abundance of the electroencephalographic activity and the recording may become almost isoelectric. In some instances, however, alpha activity may still be present shortly before death.

Figure 3. Typical EEG pattern of periodic complexes in 11-yr-old girl with subacute sclerosing panencephalitis.

Although other entities may be associated with a periodic pattern, the stereotyped electroencephalographic complexes occurring in a regular and periodic fashion and having a constant relationship to motor movements make this pattern one of the most
characteristic and specific of all electroencephalographic patterns. Close attention to the EEG and clinical features aid in the diagnosis of SSPE and distinguish it from other types of encephalopathies or disease entities.

**BRAIN ABSCESS**

Brain abscesses may occur as a result of meningitis, septicemia, or septic emboli or as an extension of an infectious process involving the ears, mastoids, and sinuses.

In the early stages of an acute supratentorial abscess, the EEG may show diffuse slowing with a poorly defined focus. This pattern is more likely to occur with meningo-encephalitis, if the patient is obtunded, and when the more focal abnormalities are obscured by more generalized slow-wave abnormalities. Focal slowing becomes more apparent as the suppurrative process becomes localized; marked focal polymorphic delta slowing can develop overlying the site of the abscess, particularly if the lesion is located close to the surface of the brain. If there are multiple abscesses, multiple electroencephalographic foci may be present. More generalized, intermittent, or shifting bursts of rhythmic slow waves (that is, a projected rhythm) also may be present; these bursts may be seen with a disturbance of the frontal lobe or as a secondary effect of the mass lesion on midline structures. On infrequent occasions, focal or lateralized periodic sharp- or slow-wave complexes (periodic lateralized epileptiform discharges) may be present over the involved area of the brain.

![Figure 4. EEG showing focal delta slowing over the right frontal region in a 9-yr-old boy with a right frontal abscess.](image)

In general, the degree of the electroencephalographic abnormalities reflects the severity of the inflammatory process. The electroencephalographic changes seen with an acute focal supratentorial abscess are often more pronounced than those seen with other focal cerebral lesions; this difference can be helpful in suggesting or confirming the presence of an abscess. It has been stated that between 90 and 95% of all patients with a supratentorial abscess will have some type of electroencephalographic abnormality and that the EEG is helpful in localizing the site of the abscess in 70%.
Infratentorial abscesses produce less severe slow-wave abnormalities, and at times there may be little or no change on the EEG. When present, the slow-wave abnormalities usually consist of bilaterally synchronous or shifting groups of intermittent rhythmic slow waves.

Chronic abscesses develop more slowly and insidiously and often without overt clinical signs of the infectious process. These are usually well-encapsulated abscesses that develop after the initial infection has been cured. A chronic abscess behaves like a progressive mass lesion and shows the same type of electroencephalographic findings as a tumor (that is, focal slow-wave abnormalities, asymmetry, or attenuation of the background activity) and, if there is increased intraventricular pressure, a projected rhythm. If the abscess develops very slowly, only minor or subtle electroencephalographic changes may be present.

After treatment, the slow-wave abnormalities improve; however, the EEG rarely returns to normal. If surgical intervention is employed, the post-operative electroencephalograms show a rapid decrease in the degree of slow-wave abnormalities within the first few days after surgery; however, some slowing and asymmetry of activity often continue to be present over the surgical area. Epileptiform abnormalities are not very common in the acute stages of the abscess, however, about 75% of patients with cerebral abscesses subsequently suffer seizures, and those patients in whom the amount of epileptiform activity increases within the first 1 to 5 yr have a greater tendency of developing subsequent seizures.

**EMPYEMA**

An empyema is a localized focus of infection in the subdural space which usually develops from a local propagated infection and which can easily spread, making it an even more serious infectious process than an abscess. The EEG in the early stages may show a poorly defined focus. Later, more distinct focal slow-wave abnormalities develop, together with focal epileptiform discharges, indicating an irritative cortical focus. As with a subdural hematoma, there is often an attenuation or suppression of background activity over the side of the empyema.

**RHEUMATIC CHOREA**

Sydenham's chorea is a movement disorder occurring in patients with acute rheumatic fever. Sydenham's chorea occurs mainly in children and adolescents; it has been reported that more than half of the patients with Sydenham's chorea will have abnormal electroencephalographic findings during the disease process. The electroencephalographic findings consist of slow-wave abnormalities varying from a mild slowing of the background to generalized delta slowing, with the degree of slowing being proportional to the severity of the movement disorder. The slowing is usually diffuse, but often has a maximal expression over the posterior head regions. In addition, brief trains of rhythmic 2- to 3-Hz bilaterally synchronous slow waves may be present over the posterior head regions immediately after eye closure. More lateralized slow-wave abnormalities may be present in hemichorea. On a few occasions, epileptiform abnormalities have been observed. In general, the improvement on the EEG corresponds to the improvement in the clinical state,
although on occasion the electroencephalographic abnormalities may lag behind the clinical state.

REYE'S DISEASE

Reye's disease is a neurologic disorder of children and adolescents which is characterized by a rapid, progressive encephalopathy and fatty infiltration of the viscera. The cause is unknown, but a viral cause is suspected. The EEG shows various types of abnormalities which reflect the severity of the clinical state. In describing the prognostic value of the EEG in Reye's disease, patients whose electroencephalograms showed mild to moderate degrees of theta and delta slowing often survived, while patients with severe EEG abnormalities consisting of very low-voltage delta slowing or a burst suppression pattern usually died. A third group of patients had an intermediate degree of abnormalities consisting of moderate to high-voltage arrhythmic or semirhythmic delta slowing. These patients may either survive or die; serial recordings were helpful in determining whether the patient had a potential for improvement or would progress to an irreversible brain dysfunction.

Triphasic waves, which are seen in hepatic coma and hyperammonemia, are uncommon in Reye's disease. Epileptiform abnormalities consisting of focal or multifocal sharp-wave discharges or electrographic seizure activity may be present, usually occurring in the later stages of the disease when the patient has deteriorated to a comatose state. It is not uncommon to see lack of clinical-electroencephalographic correlation (that is, seizures without an electroencephalographic abnormality or vice versa. This is usually a poor prognostic sign.

MULTIPLE SCLEROSIS

The incidence of electroencephalographic abnormalities in multiple sclerosis as reported in the literature varies from 20 to 50%, depending on the location of the central nervous system involvement, the stage of the disease, and the criteria used. The electroencephalographic abnormalities, when present, usually consist of varying degrees of nonspecific slowing, which may occur in a focal or diffuse manner. The abnormalities are more likely to be seen during periods of exacerbation and often resolve during periods of remission. Patients with mental dysfunction may show moderate degrees of slow-wave abnormalities. At times, focal electroencephalographic abnormalities may be present and show some correlation with the area of maximal cerebral involvement; more often, however, there is little correlation between the electroencephalographic findings and the clinical findings. In rare instances, epileptiform abnormalities have been seen, however, in general, seizures are uncommon in patients with multiple sclerosis.

SUMMARY

Although the EEG shows a variety of patterns in association with various inflammatory processes, the EEG can help 1) confirm and indicate the degree and extent of central nervous system involvement by the inflammatory process; 2) make the diagnosis of herpes simplex encephalitis, Jakob-Creutzfeldt disease, and SSPE when the characteristic
electroencephalographic pattern of these diseases is present; 3) indicate the presence of a focal lesion; 4) monitor the course of the disease process; and 5) detect the development of complications or sequelae.

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ENCEPHALOPATHIC PATTERN I (GENERALIZED SLOWING)

Since the EEG is a test of cerebral function, diffuse (generalized) abnormal patterns are by definition indicative of diffuse brain dysfunction (ie, diffuse encephalopathy). This article discusses generalized slowing, which is the most common finding in diffuse encephalopathies. Generalized slowing can be divided in a clinically useful way into 3 patterns: background slowing, intermittent slowing, and generalized slowing.
• **Waveform description**
  
  o **Background slowing:** A posterior dominant and reactive background is present, but its frequency is too slow for age. The lower limit of normal generally is considered to be 8 Hz beginning at age 8 years. A guideline to remember the lower limits of normal is as follows: 1-3-5-8 Hz at ages 5-6-7-8 years, respectively.
  
  o **Intermittent slowing:** This involves bursts of generalized slowing, usually polymorphic delta. More rarely, the intermittent bursts are in the theta frequency range, and occasionally they can be rhythmic rather than polymorphic. When rhythmic, this pattern sometimes is referred to as frontal intermittent rhythmic delta activity (FIRDA). The EEG is still reactive to external stimulation and, for example, may have evidence of state changes such as drowsiness or sleep. A posterior dominant background is usually present, and it may be normal or slow in frequency.
  
  o **Continuous slowing:** Polymorphic delta activity (PDA) occupies more than 80% of the record. This is usually unreactive, and a posterior dominant background is usually absent.

• **Clinical correlation**

Essentially, the 3 levels of slowing described above represent 3 degrees of severity (ie, mild, moderate, and severe diffuse encephalopathy). As usual, this is completely nonspecific as to etiology and most commonly is observed in metabolic and toxic (including medication-induced) encephalopathies. It also can be observed in diffuse structural or degenerative processes. However, most slowly progressive neurodegenerative diseases (eg, dementias of the Alzheimer type) go along with a normal EEG until the very late stages.

**ENCEPHALOPATHIC PATTERN II**

Since EEG is a test of cerebral function, diffuse (generalized) abnormal patterns are by definition indicative of diffuse brain dysfunction (ie, diffuse encephalopathy).

This article reviews patterns that generally are considered the next level of severity beyond generalized slowing. These patterns include periodic patterns, including burst-suppression, background suppression, and electrocerebral inactivity (ECI).

• **Waveform description**
  
  o **Periodic patterns:** Discharges occur at regular intervals (periodicity). The discharges are typically complex and multiphasic and often are epileptiform in morphology. Thus they are like periodic lateralizing epileptiform discharges (PLEDs) except that instead of being lateralized, they are generalized. They sometimes are referred to as generalized periodic epileptiform discharges (GPEDs). Rather than their morphology, their periodicity sets them apart as a unique and clinically useful entity (as is true for PLEDs). By contrast, the term bi-PLEDs usually refers to periodic discharges that are asynchronous (ie, independent) between the 2 hemispheres.
Burst-suppression pattern: This subtype of periodic pattern has bursts of activity (mixture of sharp and slow waves) periodically interrupted by episodes of suppression (activity mV). Typically, the episodes of suppression are longer (typically 5-10 s) than the bursts of activity (typically 1-3 s).

Background suppression: This is a “nearly flat” EEG, with very low voltage activity (mV) and no reactivity, but the activity is still too large to meet criteria for ECI.

Electrocerebral inactivity: ECI is defined by no activity greater than 2 mV, and to support a diagnosis of brain death, ECI must be recorded according to strict guidelines to avoid “overcalling” brain death. These requirements include recording time, double interelectrode distances, testing reactivity, and the integrity of the system.

Clinical correlation

As usual, these severe encephalopathic patterns are completely nonspecific as to etiology but represent extremely severe degrees of diffuse encephalopathy. Because sedative medications can cause or aggravate these abnormalities careful interpretation is warranted when reading these patterns. It is important to emphasize that these patterns are indicative of very severe brain dysfunction if sedative medications can safely be excluded in their causation.

Periodic patterns, including burst-suppression patterns, are somewhat more common in anoxic injuries than in other systemic disturbances. Periodic patterns can be induced by high-dose sedatives such as barbiturates, benzodiazepines, or propofol. In fact, burst-suppression pattern is typically the goal and the method used to titrate doses of anesthetics for the treatment of refractory status epilepticus.

In the appropriate clinical context, certain periodic patterns can suggest and support the diagnoses of Jakob-Creutzfeldt disease (JCD) and subacute sclerosing panencephalitis (SSPE). Classically, the periodicity for JCD is approximately 1-2 seconds, whereas in SSPE it is much longer (approximately 4-10 s).

Rhythmicity or periodicity is one of the hallmarks of electrographic seizures, thus periodic patterns quite often are observed in the context of nonconvulsive status epilepticus. Often the decision whether to consider a periodic pattern ictal must rely on the clinical information or the response to anticonvulsant treatment.

ECI is supportive of a clinical diagnosis of brain death. Remembering and emphasizing that brain death is a clinical diagnosis is important. Contrary to a common misconception, EEG is not required for the diagnosis of brain death and is only considered as a supportive test.

ENCEPHALOPATHIC PATTERN III

Since EEG is a test of cerebral function, diffuse (generalized) abnormal patterns are by definition indicative of diffuse brain dysfunction (i.e., diffuse encephalopathy). This article
reviews less common encephalopathic patterns, including alpha coma, beta coma, spindle coma, and triphasic waves.

- **Waveform description**
  - Unusual special patterns observed in comatose patients include alpha coma, beta coma, and spindle coma. These patterns are characterized by electrical activity that morphologically resembles and sometimes appears nearly identical to normal waveforms (ie, alpha rhythm, beta activity, spindles).
  - To be classified into one of these patterns, the activity should be frankly excessive in amplitude, excessive in spatial distribution (widespread), appear in unusual spatial distribution, or appear in excessive in amount (ie, near continuous). Although some investigators classify these patterns abnormal even if the pattern is reactive, unreactive activity is preferred. The most important criterion is patient coma at the time of the clinical recording.
  - Triphasic waves are frontally positive sharp transients usually of greater than 70 microvolts amplitude. The positive phase is usually preceded and followed by a smaller negative waveform. As a rule the first negative wave is of higher amplitude than the second. They are bilateral and occur in bursts of repetitive waves at 1-3 Hz. No reactivity is the rule, and often an anterior-posterior temporal lag can be observed. The largest deflection is usually frontal and in ear referential montage the time lag is usually not present. The usual clinical correlate of triphasic waves is a metabolic or other diffuse encephalopathy. Thus, a triphasic morphology (while necessary) is not sufficient to classify a record as "triphasic waves."

- **Clinical correlation**
  - Alpha coma, beta coma, and spindle coma are infrequent. They are, as usual, nonspecific in regard to etiology, although anoxia often is associated with alpha coma and drugs with beta coma. They are generally indicative of a severe degree of encephalopathy. Reactivity is a good prognostic factor. In fact, some investigators, including the author, do not classify a record as alpha or spindle coma if it is reactive.
  - Triphasic waves classically are associated with hepatic encephalopathy. However, they are not specific and can be observed in uremic encephalopathy and even other types of metabolic derangements. Many other patterns can have a triphasic morphology. Like periodic patterns, triphasic waves quite often are observed in the context of nonconvulsive status epilepticus. Often the decision whether to consider triphasic waves ictal must rely on the clinical information or the response to anticonvulsant treatment.

**REFERENCES**


INTRODUCTION

EEG has been employed clinically for some time as a measure of brain function in the hope of determining and differentiating certain functional conditions of the brain. It is used in patients who suffer from cognitive dysfunction, either a general decline of overall brain function or a localized or lateralized deficit. This article addresses primarily the clinical use of EEG in evaluation of dementias and encephalopathies.

- Definition of dementia

Criteria from Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) should be used in the diagnosis of dementia. Clinical dementia is a fairly broad-based
decline of brain function; most definitions center on the patient’s intellectual decline and memory dysfunction. This is, however, a fairly simplistic approach; dementia is much more than these fundamental deficits. Some of the dementias have distinguishing features. The process that constitutes normal aging is still an ongoing debate. As our understanding and testing procedures develop, more people are being classified as suffering from some type of dementia.

In 1998, Widagdo et al performed a quantitative EEG (QEEG) study of age-related changes during cognitive tasks. This study revealed no conclusive differences between the young and the elderly. Cognitive decline, unlike normal aging, is associated with alterations in the temporospatial characteristics of EEG. The diagnosis of the initial stages of dementia is based mainly on neuropsychological testing and clinical suspicion. The EEG findings are nonspecific.

- **EEG findings in dementia**

In early dementia, the resting alpha frequency declines. Most authors agree that the lower limit of normal alpha frequency is 8.5 cycles per second. Medications can slow the posterior dominant rhythm; therefore, medication effect should always be excluded. In assessing the frequency of the alpha rhythm, alerting maneuvers are essential in order to ensure that the patient is in the best awake state and not drowsy. Computerized methods, such as EEG spectral analysis, coherence, and complexity (ie, correlation dimension), have been demonstrated to correspond to cognitive function.

Stevens et al recorded EEGs during 2 resting conditions (eyes closed and eyes opened) and 2 tasks (mental arithmetic and a lexical decision). The goal of the study was to evaluate which temporal and spatial EEG descriptors change with cognitive decline and normal aging. The EEGs were analyzed by using EEG microstates. The primary findings were a significant increase in the number of ultrashort EEG microstates and a reduction in the average duration of EEG microstates in cognitively impaired and demented patients. Cognitive impairment was associated with a reduction or loss of EEG reactivity. In contrast, no alterations in temporal or spatial EEG descriptors were found in normal aging. Cognitive tasks did not add to the information already obtained during the resting states. The reduction in EEG microstate duration correlated with loss of cognitive function.

Therefore, temporospatial analysis of the EEG record is a useful indicator of cortical dysfunction in dementia and correlates with degree of cognitive impairment. Apparently, temporospatial analysis may be useful in distinguishing patients with dementia from those experiencing normal aging. These data are largely preliminary; whether they contribute additional information to the clinical data in evaluating dementia is unclear.

- **Definition of encephalopathy**

Encephalopathy represents a brain state in which normal functioning of the brain is disturbed temporarily or permanently. Encephalopathy encompasses a number of conditions that lead to cognitive dysfunction. Some of these conditions are multifactorial...
and some have an established cause, such as hepatic or uremic encephalopathy. Because
the EEG patterns in most dementias and encephalopathies demonstrate few specific
features, they are discussed together. Some notable exceptions include Creutzfeldt-Jakob
disease (CJD) and subacute sclerosing panencephalitis (SSPE); however, no specific
patterns exist for most dementias and encephalopathies. Other conditions, such as hepatic
and renal encephalopathies, carry distinguishing features; nevertheless, similar patterns
may be seen in a fairly wide range of illnesses under certain conditions.

- EEG findings in encephalopathy

In general, the most prominent feature of the EEG record in encephalopathies (if there is a
change) is slowing of the normal background frequency. A gradual and progressive decline
over the course of the disease may be noted if serial EEGs are performed. Disorganization
of the record may develop gradually. Reactivity to photic or other type of external
stimulation may be altered. If a QEEG is done, it may show a frequency shift or decreased
interhemispheric coherence of background frequencies. Some conditions are associated
with an increase in seizure frequency, and in such cases, epileptic activity may be recorded.

In a given context, the EEG can play a clinically useful role, especially since functional
MRI, positron emission tomography (PET), and single-photon emission computed
tomography (SPECT) are either still in an experimental stage or require special settings
not widely available.

- Use of digital EEG data

Although in the following sections digital EEG data are cited frequently, these data
represent primarily digital analysis of clinical EEG recording. The referenced data are
presumed to be based on an EEG recording that is read by a clinician; presently, it is
recorded by using computerized technology for ease and also for availability for further
analysis. A variety of mathematical transforms are available after the initial clinical
interpretation—for example, coherence, Fourier transform, wavelets, and microstates (see
Digital EEG). These allow for further comparisons with norms and control groups but
should be interpreted in conjunction with the primary EEG reading.

DEMENTIA

- Alzheimer disease

EEG is the only clinical diagnostic instrument directly reflecting cortical neuronal
functioning. Although the EEG may be normal or minimally disturbed in a number of
patients in the initial stages of Alzheimer disease (AD), an abnormal EEG usually is
recorded later in the course. A large percentage of patients with moderately severe to
severe AD exhibit abnormal EEGs.

In 1981, Stigsby reported diffuse increases of delta and theta frequencies, as well as
decreases in the alpha and beta frequency ranges in AD. Frontal slowing was more
prominent. The slowing was more prominent anterior to the sylvian fissure, while the blood flow was more decreased posterior to the sylvian fissure. These findings may be explained by the fact that the EEG reflects the functional decline of the anterior structures, while the flow decrease correlates more with the structural damage of the parietal lobe. The frontal slowing probably reflects the loss of functioning of the frontal cholinergic system.

Wada et al showed that EEG coherence provides a measure of functional correlation between 2 EEG signals. They examined intrahemispheric EEG coherence at rest and during photic stimulation in 10 patients with dementia of the Alzheimer type. In the resting EEG, patients with AD had significantly lower coherence than gender- and age-matched healthy control subjects in the alpha-1, alpha-2, and beta-1 frequency bands. EEG analysis during photic stimulation demonstrated that the patients had significantly lower coherence, irrespective of the stimulus frequency. The changes in coherence from the resting state to the stimulus condition showed significant group differences in the region of the brain primarily involved in visual functioning. The patients had significantly lower coherence of their EEG reactivity to photic stimulation at 5 and 15 Hz over the posterior head regions.

These findings suggest that patients with AD may have an impairment of interhemispheric functional connectivity in both nonstimulus and stimulus conditions. This suggests a failure of normal stimulation-related brain activation in AD. Jelic et al found a positive correlation between levels of tau protein in the cerebrospinal fluid (CSF) and EEG alpha/delta ratio. In a subgroup with high CSF tau levels, a strong relationship between EEG alpha/theta and alpha/delta power was found. No such correlation was found in healthy controls and mildly cognitively impaired individuals with elevated CSF tau levels.

Locatelli et al used EEG coherence to evaluate the functionality of cortical connections and to get information about the synchronization of the regional cortical activity. They studied EEG coherence in patients with suspected AD. Alpha coherence was decreased significantly in 6 patients. Significant delta coherence increase was found in a few patients between frontal and posterior regions. The group with AD demonstrated a significant decrease of alpha-band coherence in the temporo-parieto-occipital areas. This was expressed to a greater extent in patients with more severe cognitive impairment. They theorized that these abnormalities could reflect 2 different pathophysiological changes: (1) the alpha coherence decrease could be related to alterations in corticocortical connections, whereas (2) the delta coherence increase suggests lack of influence of subcortical cholinergic structures on cortical electrical activity.

Strik et al studied EEG microstates in AD. The microstates of the resting EEG of patients presenting with mild or moderately severe dementia of the Alzheimer type demonstrated a significant anteriorization of the microstate fields, and the duration of sustained microstates was reduced. These differences were more important than the diffuse slowing. The measurements of microstates may be useful in the early diagnosis of AD. Muller et al conducted a study comparing SPECT and QEEG. They concluded that QEEG may be as useful as SPECT brain scanning in staging the disease; however, the correlation with clinical status was weak.
Siennicki-Lantz et al studied the relation of cerebral white matter lesions to AD. Cerebral blood flow (CBF) in white matter correlated with systolic blood pressure and multichannel EEG in senile dementia of the Alzheimer type. The presence and functional significance of white matter lesions in the aging brain or in dementia and their relation to blood pressure is an unsettled issue. White matter lesions occur in both cerebrovascular disease and AD. Probably, the white matter lesions in hypertensive patients are not related to but simply are coexistent with the AD. Their influence on overall expression of the degree of dementia is unclear; intuitively, however, the lesions should be causing additional cognitive dysfunction.

They observed significantly lower CBF in the white matter (WMCBF) in patients with AD than in controls. This was more obvious in the posterior cerebral region (ie, parieto-temporo-occipital area). QEEG from the posterior cerebral regions correlated with WMCBF. Systolic blood pressure was significantly lower in the AD group and was correlated positively with WMCBF in the posterior and anterior brain regions.

Epileptiform activity may occur more frequently in patients with AD than in the general population; clinical tonic-clonic seizures can occur. Bilateral synchronous periodic epileptiform discharges (BiPEDs), such as triphasic waves (TWs), may be recorded in AD, usually in the late stages (for more information on TWs, see Triphasic Waveforms). These findings are not specific for AD because they most often are observed in metabolic disorders, particularly hepatic encephalopathy and other degenerative diseases, such as CJD. While good correlation exists between severity of EEG abnormalities and cognitive impairment, epileptiform discharges or TWs are not predictive factors for seizures. EEG often can be useful in evaluating dementia in order to exclude a superimposed reversible metabolic etiology, and to confirm CJD when the dementia is rapidly progressive.

To investigate the relationship between QEEG band powers and CBF, Rodriguez et al studied 42 patients with suspected AD and 18 healthy controls who were elderly. They tried to differentiate patients with AD from the controls by QEEG and CBF measurements. Regional CBF and QEEG were correlated with one another, especially in the right hemisphere. Significant correlations were found between Mini Mental State Examination (MMSE) scores and relative power of the 2- to 6-Hz and the 6.5- to 12-Hz bands on either side and between MMSE scores and left regional CBF, while the correlation between MMSE scores and right regional CBF was less strong.

Employed together, QEEG and regional CBF sensitivity was 88% and specificity 89%, with a total accuracy of 88.3%. QEEG alone showed an accuracy of 77% in the whole group and of 69% in those with mild AD, and regional CBF alone an accuracy of 75% in the whole group and of 71% in those with mild AD. This study suggests that QEEG and regional CBF measurements used together are reasonably accurate in differentiating AD from healthy aging.

Lehtovirta et al studied the relation of apolipoprotein E (ApoE) to EEG changes. ApoE sigma-4 allele is a risk factor for late-onset AD and is proposed to have an impact on cholinergic function in AD. Because the cholinergic system has an important role in
modulating EEG, an impairment of the cholinergic system may have a relation to the EEG slowing that is characteristic of AD progression. The QEEG of 31 patients with AD was recorded at the early stage of the disease and after a 3-year follow-up. Patients with AD were divided into several subgroups according to the ApoE sigma-4 allele (ie, 2 sigma-4, 1 sigma-4, and 0 sigma-4). These subgroups did not differ in clinical severity or duration of dementia. The AD patients carrying the sigma-4 allele had more pronounced slow-wave activity than AD patients without the sigma-4 allele, although the disease progression rate did not change. These differences in EEG may suggest differences in the degree of the cholinergic deficit in these subgroups.

The typical electrophysiological correlates of myoclonus in AD are similar to those of cortical reflex myoclonus, with a focal, contralateral negativity in the EEG preceding the myoclonic jerk. The electrophysiological correlate of polymyoclonus that can be seen in AD and other pathological states is a bifrontal negativity in the EEG that precedes the myoclonic jerk. This new type of electrophysiological correlate of myoclonus may reflect activity of a subcortical generator.

- **Pick disease**

Pick disease, which is a frontotemporal dementia, is much less common than AD. The age of onset is earlier than that of AD. The EEG is less abnormal than in AD, especially in the early stages. Posterior alpha rhythm is more preserved. Theta and delta are increased. Frequency analysis may demonstrate a difference at a time when simple visual reading may not pick up a clear abnormality. The major feature of Pick disease is a decline in judgment and insight with relative early preservation of memory. Because EEG correlates poorly with the clinical symptoms, impressive EEG changes are not observed in this condition. Blood flow measurements correlate with thinking processes; Ingvar demonstrated these changes in 1977. Stigsby demonstrated a decrease in anterior blood flow in patients with Pick disease. Because the anterior cholinergic system is relatively preserved in Pick disease, the EEG changes are not prominent frontally.

- **Huntington chorea**

Huntington chorea is a combination of a movement disorder and a dementia, which is dominated by cognitive impairment, psychotic features, and memory impairment. The EEG changes show gradual and progressive slowing over time. The amplitude also attenuates as the disease progresses. About 30% of the patients have very-low-voltage EEGs with amplitudes below 10 microvolts. Hyperventilation as a rule does not increase the background voltage as it usually does in healthy subjects. About 3% of the patients show epileptiform activity; they tend to be juvenile cases. The EEG has not been proven to be of any predictive value in identifying future affected family members. Genetic testing is far more useful.
• **Progressive supranuclear palsy**

In progressive supranuclear palsy (PSP), usually the degree of dementia is not severe. The EEG may be normal initially but eventually shows increasing delta and theta activity. The delta may be rhythmic with frontal accentuation. Gross et al showed a decrease in background frequency down to 6-7/s and delta activity over the temporal regions. Sleep may show poor spindle development. Rapid eye movement (REM) sleep may be reduced or absent. These changes probably reflect the involvement of the locus ceruleus and the pontine raphe nuclei.

• **Parkinson disease**

The EEG is frequently normal. In advanced cases, however, marked slowing is noted. Sleep may be markedly abnormal with frequent awakenings, prolonged sleep latency, reduced REM sleep, periodic leg movements, etc. Wszolek et al studied patients with rapidly progressive familial parkinsonism and dementia with pallidopontonigral degeneration (PPND). The patients had PPND linked to chromosome 17q21-22; 11 EEGs of 9 patients were studied. EEGs revealed normal findings early in the disease and diffuse slowing that became more prominent with disease progression. Electromyograms (EMGs) and nerve conduction studies (NCSs) showed no abnormalities. Visual evoked potentials (VEPs) and sensory evoked potentials (SEPs) were normal. The clinical neurophysiologic study findings were consistent with a cortical and subcortical degenerative process.

With clinical deterioration, progressive decline is seen in the mean parietal frequency and background rhythms. Theta and theta-delta mixture may be recorded bilaterally in the posterior head regions. After stereotactic surgery, focal theta or delta slowing may be observed.

**VASCULAR DEMENTIA**

• **Binswanger disease**

Binswanger disease usually demonstrates slowing of background and a nonspecific pattern; however, Kuroda et al reported some other patterns. They described a 72-year-old patient with von Recklinghausen disease exhibiting akinesian mutism within 6 months of the onset of dementia. The EEG demonstrated periodic synchronous discharges (PSDs) suggesting CJD. The CT brain scan findings represented diffuse cerebral atrophy. Autopsy findings revealed diffuse subcortical white matter disease and marked arteriosclerotic changes of the subcortical arterioles.

The cortex was relatively spared, and the pathologic diagnosis confirmed Binswanger disease. Binswanger disease, therefore, can present with PSD and should be included in the differential diagnosis of dementia. On the other hand, Dziaiek et al described a group of 15 patients with Binswanger subcortical atherosclerotic encephalopathy who showed different EEG appearance. The EEG records were pathological in most cases, with varying degrees of slow activity that was distributed symmetrically.
**Circulatory encephalopathy**

- **Atherosclerosis**

Plachinda et al studied the correlations of cognitive disorders and the EEGs of elderly patients with circulatory encephalopathy. They explored the possibilities of using EEG for evaluating intellectual-mnemonic disorders in elderly patients with cerebral atherosclerosis. Ninety-five patients (aged 60-74 years) with atherosclerotic encephalopathy but without stroke were included in the study. Statistical analysis of the data demonstrated a correlation between psychological test results and EEG readings and computerized EEG data. In cerebrovascular disease, focal slowing is far more frequent than in nonvascular dementia; therefore, EEG can be useful in distinguishing the 2 conditions.

- **Multi-infarct dementia**

No specific EEG pattern is associated with multi-infarct dementia. Some background slowing may be observed, especially in advanced disease. These changes are less prominent and do not show the progressive course observed in AD. Research is very scanty. Edman et al found a significant relationship between the increase in EEG slow-wave activity and increases in severity of the parietal brain syndrome. A somewhat lower significance was found for the relation between the increase in slow-wave activity and increases in the degree of dementia. These results suggest that the EEG deterioration mainly reflects the progressive and gradual decline of parietal brain function.

Iznak et al used QEEG to reveal the specific features of and study amplitude-frequency parameters in patients with mild dementia of different origins compared to healthy elderly individuals. They found that alpha rhythm was suppressed in AD and vascular dementia and that alpha rhythm was slower and theta activity higher in AD. Patients with AD were characterized by desynchronized EEG.

- **Transient global amnesia**

A variety of records have been reported from normal to even epileptiform potentials in transient global amnesia (TGA). Nonepileptiform activity, such as bitemporal delta or bioccipital theta, has been reported. Kushner described patients with normal activity, one with occasional epileptic activity, and one with asymmetric alpha depression, while 2 patients had intermittent rhythmic slowing. TGA caused by a seizure is uncommon, and is believed to be caused by a vascular etiology or spreading depression. Patients with Korsakoff syndrome often have abnormal EEGs with theta-delta slowing.

**HEREDITARY ENCEPHALOPATHIES**

- **Action myoclonus**

Action myoclonus consists of arrhythmic muscular jerking induced by voluntary movement. It can be made worse by attempts at precise or coordinated movement (ie, intention myoclonus) and may be elicited by sensory stimuli. The effective stimulus for
Action myoclonus is thought to be feedback from muscle afferents, although it may be related to activity in the motor cortex relayed to the reticular formation preceding or coinciding with voluntary movement. The condition usually is associated with diffuse neuronal diseases, such as posthypoxic encephalopathy, uremia, and the various forms of peripheral neuroepithelioma, although action myoclonus may be limited to one limb in some cases of focal cerebral damage. It is caused by hyperexcitability of the sensorimotor cortex (ie, cortical reflex myoclonus) or reticular formation (ie, reticular reflex myoclonus), or both.

Autopsied cases have failed to reveal a clear pathology. Theories include loss of inhibitory mechanisms involving serotonin and possibly GABA transmitters. Myoclonus may be seen in degenerative disorders of the nervous system. It may be associated with tonic-clonic seizures or dementia. Myoclonus has been described in cases with Lafora inclusion bodies and cerebral storage diseases, as well as system degenerations: cerebellodentatorubral, pyramidal, extrapyramidal, optic, auditory, posterior columns and gracile and cuneate nuclei, spinocerebellar pathways, motor neurons of cranial nerves and anterior horns, and muscle fibers.

Action myoclonus usually responds to sodium valproate or clonazepam, and some patients with posthypoxic action myoclonus may improve with serotonin precursors.

- **Ramsay-Hunt and Unverricht-Lundborg syndromes**

The clinical distinction between Ramsay-Hunt syndrome and Unverricht-Lundborg syndrome (ie, Baltic myoclonus) is unclear because cerebellar signs are found in patients described under both syndromes. Some have proposed that the names could be joined and referred to as Unverricht-Lundborg-Hunt disease. Some authors have suggested that the condition be known as systems degeneration type of progressive myoclonus epilepsy. Presently, the cause of the condition (or spectrum of conditions) is not known.

- **Mitochondrial encephalopathy with lactic acidosis and stroke (MELAS) and myoclonus, epilepsy with ragged red fibers (MERRF)**

Isozumi et al described a 50-year-old woman with subacute dementia and myoclonus whose CT scan revealed brain atrophy and EEG revealed PSDs. She initially was thought be suffering from CJD but dramatically recovered over 5 months. Based on further investigations, the final diagnosis was mitochondrial encephalomyopathy. In general, the EEG changes were described as background slowing, multifocal epileptiform discharges, and photosensitivity.

- **Poststereotactic surgery**

Patients developed EEG slowing of different degrees about 50% of the time.
Alpers disease

This clinicopathological entity, consisting of progressive neuronal degeneration (ie, Alpers disease) of childhood with liver disease, has been studied by Boyd et al. The onset is in early childhood and consists of intractable fits and progressive dementia. EEG studies have been carried out in 12 children with this condition. The EEGs were similar and demonstrated abnormal patterns with high-amplitude, slow activity, as well as smaller polyspikes. The flash VEP was usually abnormal and often asymmetrical. In the appropriate clinical setting, the neurophysiologic features may aid the clinician in diagnosis of this autosomal recessive inherited disorder.

Adrenoleukodystrophy

Multifocal paroxysmal discharges, hypsarrhythmic pattern, and prominent arrhythmic delta are present in temporo-occipital areas. Epileptic discharges usually do not occur in adrenoleukodystrophy.

Zellweger syndrome

This is characterized by diffuse slowing.

Infantile neuroaxonal dystrophy

This condition is characterized by a high-voltage, 14- to 22-Hz activity that is not reactive to environmental stimuli.

Hallevorden-Spatz disease

In this disease the EEG is normal to slow.

Neuronal ceroid lipofuscinosis

In the infantile form, the EEG is slow and early, and posterior spikes may be present. Photic response is excessive and evokes high-voltage spikes that are polyphasic. The EEG abnormalities in the juvenile form are not as marked.

Gaucher disease

In patients with type III disease, posterior spikes and sharp waves, diffuse spike and waves, and photomyoclonic and photoparoxysmal responses may be present.

Metachromatic leukodystrophy

Diffuse slowing progresses to high-voltage generalized delta activity. Epileptic activity is rare; however, hypsarrhythmia may be observed.
• **Tay-Sachs disease**

EEG is generally slow. Generalized or multifocal spikes accompany the seizures.

• **Rett syndrome**

This is a progressive encephalopathy observed in girls. AI-Mateen et al reported 15 cases of Rett syndrome. The course is slowly progressive; it occurs only in girls and is characterized by early deterioration of higher brain function with dementia, autistic behavior, loss of purposeful use of the hands, and deceleration of head growth. When affected girls are aged 2-4 years, epilepsy may develop with minor motor seizures. Additional features may include an extrapyramidal disorder with dystonia and choreoathetosis, and lactic acidemia. A precise biochemical marker of this disorder has not been identified.

According to McIntosh et al, Rett syndrome consists of a progressive encephalopathy and psychomotor deterioration in young girls who have appeared clinically normal until age 6-18 months. The incidence is similar to phenylketonuria and autism in females. When the child is at least 6 months old, head growth decelerates in association with severe dementia, autism, apraxia, stereotypic "hand washing" movements, and loss of previously acquired skills. Other signs include breathing dysfunction, seizures, EEG abnormalities, and growth retardation. It appears to be sporadic in occurrence.

The EEG may demonstrate slowing, a variety of nonspecific patterns, and epileptiform discharges. The epileptic activity may include multifocal spikes, slow-wave spikes, and paroxysmal delta slowing with spikes that may appear in sleep; in certain cases, however, sleep may attenuate the EEG abnormalities. Background flattening occurs to some degree, corresponding with the stage of dementia and cognitive decline. Rolandic spikes may be elicited by noise.

**INFECTIOUS ENCEPHALOPATHIES**

• **Creutzfeldt-Jakob disease**

The EEG shows a fairly typical repetitive pattern of BiPEDs such as TWs, approximately 1-1.5 seconds apart. These usually are present during wakefulness and disappear during sleep. PSDs seem to be the EEG hallmark of the disease; however, a number of atypical EEG presentations have been reported without these waveforms. Aoki et al reported giant spikes with photic stimulation. These photic-stimulated giant spikes simultaneously suppressed PSDs. Necropsy exhibited extensive gray and white matter lesions. Both lateral geniculate bodies and pregeniculate bodies were involved preferentially. The superior colliculus, optic nerve, and optic tracts were not affected. The cortices of the occipital lobes were damaged severely. The Gennari line was spared. The lesion of the lateral geniculate body appeared to be associated with the unusual EEG feature.

Their findings indicate that the visual pathway may be involved in the generation of PSD in CJD. The EEG findings and the evolution of clinical signs were investigated by Hansen et
al in 7 patients with CJD who underwent serial EEG recordings. At the onset (mean 8.7 weeks) of periodic slow-wave complexes (PSWC), 5 patients already had progressed to akinetic mutism characterized by loss of verbal contact and movement disorder (ie, myoclonus, exaggerated startle reaction, or focal dyskinesia started in 5 patients). When akinetic mutism commenced (average 7.5 weeks), runs of frontal intermittent rhythmic delta activity (FIRDA) were found in all cases. These were later replaced by PSWC in 6 patients. Occurrence of PSWC often related negatively to external stimuli and sedative medication.

These data help in the selection of EEG recording dates to detect PSWC in patients in whom CJD is suspected. The survival time is short after the onset of PSWC (average 8 weeks). In earlier disease stages, FIRDA-like EEG activities should be regarded as compatible with the diagnosis of CJD and should encourage further EEG studies for the demonstration of PSWC in a more advanced stage of CJD.

EEG characteristics of CJD and its differential diagnosis were studied by Steinhoff et al. They found some nonspecific EEG findings and also typical PSWC in the course of the disease. They obtained a sensitivity of 67% and a specificity of 86%. With the exception of one familial variant of CJD, PSWC are usually absent in all other human prion diseases. They presented a pathophysiologic hypothesis on the development of PSWC based on the assumption that the specific periodicity of PSWC results from a still functionally active but greatly impaired subcortical-cortical circuit of neuronal excitability. They stressed the use of clinical signs, laboratory data, and EEG correlation and suggested that the clinical diagnosis of CJD should be reconsidered if repeated EEG recordings fail to reveal PSWC under technically adequate conditions. Some patients with CJD presented with visual blurring, diplopia, and visual loss—ie, the Heidenhain 5 variant.

Focal EEG abnormalities as described in the Heidenhain variant of CJD are uncommon. Lee et al reported a 73-year-old man presenting with visual symptoms, right hemianopia, and rapidly progressive dementia. Myoclonus was synchronous with generalized periodic epileptiform discharges on EEG. In addition, periodic focal sharp waves were present at the left occipital region. Diffusion-weighted MRI of the brain showed slightly increased signal intensity in the occipital parasagittal area, left more than right. The 14-3-3 protein was detected in the CSF. The patient died within 5 months of presentation.

- **Subacute spongiform encephalopathy**

Aguglia et al described 20 patients with subacute spongiform encephalopathy and periodic paroxysmal activities in the EEG. Evolution of clinical and EEG abnormalities were analyzed in all 20 (16 pathologically confirmed). Illness duration was less than 4 months in 65% and greater than 17 months in 10%. The early clinical stage was characterized by gradual gait disturbances, mental deterioration, and sensory or autonomic changes. In 10 EEG recordings from 7 patients examined in the early clinical stage, no periodic discharges were present.
Early periodic paroxysmal activity appeared within 12 weeks of the onset of the disease in 88% of the patients who underwent EEG recordings. This early periodic paroxysmal activity usually occurred at an intermediary EEG stage, when the patients demonstrated marked worsening of the clinical picture. Focal, segmental, and/or generalized myoclonic jerks were observed in 15%, 53%, and 100% of cases at prodromal, intermediary, and terminal stages, respectively. Different kinds of periodic paroxysmal activity were observed: (1) biphasic or triphasic periodic complexes, (2) periodic complexes with multiphasic configuration, and (3) periodic polyspiking discharges. Abnormal "pacing" by slowly repeated flashes was found in 4 patients presenting with visual hallucinations or cortical blindness. Burst-suppression activity was observed frequently in the terminal stage in decorticate patients.

- **AIDS dementia**

EEG abnormalities usually precede brain atrophy on CT brain scan. Generalized or multifocal slowing may be observed. Computerized EEG is abnormal in most cases. About one half of patients who have normal neurologic findings on physical examination exhibit abnormal EEGs. Thomas et al described a 40-year-old HIV-positive, right-handed homosexual man who was admitted for progressive mental deterioration coexisting with permanent, segmental, middle-amplitude, arrhythmic, asynchronous, and asymmetrical myoclonic jerks. EEG demonstrated frontocentral bursts of rhythmic triphasic 1.5- to 2-Hz sharp waves similar to the characteristic periodic pattern of CJD. Biological investigations were negative, thus ruling out a metabolic encephalopathy.

Dramatic neurological improvement occurred shortly after initiation of intravenous and then oral zidovudine, which produced absolute EEG normalization. This unusual electroclinical presentation of the AIDS dementia complex underlines the fact that this condition presents a diagnostic challenge, particularly in individuals in whom HIV infection has not been diagnosed previously.

- **Chronic rubella encephalitis**

This condition is characterized by myoclonus, mental deterioration, ataxia, and chorea, with diffuse slowing on EEG. Intermittent rhythmic delta activity (IRDA) has been described. Periodic activity with spikes and slow-wave spikes may occur.

- **Viral encephalitis**

Viral encephalitis always produces abnormal EEGs. If the cortical gray matter involvement is predominant, a more polymorphic delta activity is observed, while with subcortical involvement, a rhythmic pattern (ie, IRDA) is more common. In herpes simplex encephalitis, temporal and frontotemporal slowing is characteristic; a periodic pattern may develop as the disease evolves. Serial EEGs usually capture periodic lateralizing epileptic discharges (PLEDs). In late stages, the EEG may revert to normal.
• **Subacute sclerosing panencephalitis**

SSPE is a progressive, neurodegenerative disorder caused by defective measles virus replication in the brain as a consequence of measles immunization. The EEG may provide an important clue regarding SSPE and demonstrates bilaterally synchronous, high-amplitude spike or slow-wave bursts that often correlate with clinical myoclonus. As SSPE progresses, the background activity becomes suppressed, resulting in a burst-suppression pattern. Neuroimaging studies demonstrate nonspecific abnormalities or diffuse atrophy, although T-2 prolongation can be detected by MRI symmetrically in the cerebral white matter or multifocally in the subcortical white matter or cortex.

Flaherty et al described a 17-year-old boy with SSPE discovered when he presented with confusion after a mild head injury. The EEG strongly suggested the diagnosis. Repeated CT scans of the head were normal. The boy had a 3-year history of decreased vision, associated with a focal pigmentary retinopathy. On assessment, the patient demonstrated visual agnosia and early dementia. MRI scan demonstrated symmetrical demyelination of the white matter, particularly of the occipital lobes. The typical EEG findings and the presence of measles antibodies in the CSF confirmed the diagnosis of SSPE.

SSPE should be considered in young patients who have persisting cognitive dysfunction that is not proportional to the severity of the initial trauma. A focal pigmentary retinopathy, especially with macular involvement, should raise the possibility of SSPE, even if neurological symptoms are absent initially. The longest interval (till date) between the visual symptoms and onset of neurological signs of SSPE was reported by the author.

Koppel et al reported on the relation of SSPE and HIV. SSPE had largely disappeared from the United States because of nearly universal measles vaccination; however, it has re-emerged in children infected with HIV. Two children with SSPE were described. The first was HIV positive and presented with seizures and encephalopathy at the age of 21 months. The second developed myoclonus and dementia at 4 years of age; she was not infected with HIV but her mother had AIDS. MRI findings of the brain were nonspecific. EEG was characteristic of SSPE, showing high-voltage PSWCs and background slowing. Brain biopsy and high measles antibody titers in the CSF confirmed the diagnosis of SSPE.

**METABOLIC ENCEPHALOPATHIES**

• **Metabolic disorders**
  ○ Anoxic encephalopathy

Hypoxia causes diffuse slowing in the EEG. The acute and prolonged anoxia of cardiac arrest exhibits no changes initially. In 7-10 seconds, slow waves appear. This is followed by rhythmic, high-voltage delta activity; subsequently, attenuation and EEG flattening occurs. As a rule, irreversible brain damage results in 4-8 minutes. In some cases, establishing the completeness and duration of anoxia is difficult. Certain patterns carry a poor outcome: flat EEG and burst-suppression pattern nearly always carry a poor prognosis. Postanoxic...
EEGs may exhibit a variety of abnormal patterns: triphasic activity, alpha coma pattern, repetitive complexes, and bilateral PLEDs.

Takahashi et al reported a 47-year-old man admitted to the hospital for depression, who suddenly developed cardiopulmonary arrest of unknown etiology and entered a chronic vegetative state as a result of anoxic encephalopathy. PSDs were present for as long as 5 months. The wave pattern, periodicity, and duration of appearance of PSDs were similar to those of PSDs seen in CJD. The PSDs were prolonged gradually, with a course similar to that of the discharges observed in CJD. The mechanism of occurrence is considered to be similar to that of PSDs in CJD.

- **Hyponatremic encephalopathy**

Usually, nonspecific slowing is observed in hyponatremic encephalopathy. A variety of other patterns have been described: TWs; burst of high-voltage rhythmic delta; central, high-voltage, 5- to 7-Hz rhythm; and sensory stimulation-induced, high-voltage delta activity. Epileptic activity is very rare, even in cases of clinical seizure. Kameda et al reported a case of FIRDA in the EEG of a patient with pituitary adenoma, hyponatremic encephalopathy, and major depression. The pituitary adenoma is thought to be a major factor for FIRDA in this case. Complicating factors included diffuse encephalopathy and use of antipsychotic drugs; FIRDA remained in the EEG after these factors diminished. The size of the pituitary adenoma that was proposed to be associated with FIRDA in the EEG recording was not noted. FIRDA may be associated with a small pituitary adenoma less than 10 mm in size.

- **Hypocalcemia, hypercalcemia**

Paresthesias, tetany, muscle spasm and, rarely, seizures may occur in hypocalcemia. EEG findings include theta and polymorphic delta slowing, polyspikes, sharp waves, and paroxysmal activity. Hypercalcemia is associated with renal failure, neoplasms, bone destruction, parathormone releasing tumors, and hypervitaminosis D. Muscle weakness, polydipsia, polyuria, nausea, anorexia, and coma may develop. EEG changes appear when serum calcium level is approximately 13 mg/dL; slowing and intermittent rhythmic delta activity is seen. Photic driving may be prominent, and TWs may be recorded. When serum calcium is normalized, the EEG usually improves but not immediately. A hypercalcemic condition can be observed in association with hyperthyroidism. Confusional state and EEG alterations, among which diffuse monomorphic delta rhythms were remarkable, were shown by Juvarra. As soon as normalization of calcium serum level was achieved, rapid clinical and EEG improvement ensued.

- **Endocrine conditions**
  - **Adrenal disease**

EEG pattern is nonspecific.
- **Cushing disease**

EEG changes are uncommon.

- **Addison disease**

Nonspecific slowing and diffuse theta and delta may be seen in a disorganized manner.

- **Pheochromocytoma**

No particular EEG pattern has been noted.

- **Hypoglycemia**

The EEG resembles changes described with hypoxia; hyperventilation response is exaggerated and FIRDA may be observed. If prolonged coma ensues, the EEG changes persist and may become permanent. In most cases of hypoglycemia, a generalized disorganization of record occurs; in patients with long-term diabetes, the EEG is usually mildly to moderately diffusely disorganized and slow.

- **Hyperglycemia**

Similar slowing is the rule; however, epileptic activity may be observed with clinical seizure.

- **Hyperthyroidism**

This has a nonspecific pattern, but thyroid storm spikes may be observed.

- **Hypothyroidism**

Low-voltage theta is the rule with reduced photic driving response.

- **Nutritional deficiency syndromes**

Pyridoxine deficiency causes severe, and at times, fatal convulsion in infants. The underlying metabolic problem has been suggested to be insufficient GABA synthesis. Thiamine deficiency causes diffuse slowing in Wernicke encephalopathy. Malnutrition results in EEG slowing, proportional and corresponding to the clinical alertness of the patient.

- **Toxic agents**
  - **Carmofur**

Carmofur, an antineoplastic derivative of 5-fluorouracil, has been reported to cause subacute leukoencephalopathy. Kuzuhara described 3 individuals who developed subacute
leukoencephalopathy after carmofur (1-hexylcarbamoyl-5-fluorouracil) administration. Initial symptoms were unsteady gait and dementia, developing several weeks or months after administration of carmofur. Symptoms increased gradually even after stopping the drug. Severe encephalopathy with confusion, delirium, or coma developed. Symptoms were usually reversible but occasionally resulted in death. The EEG demonstrated marked slowing. CT scan of the brains of severely intoxicated patients showed marked hypodensity of the entire cerebral white matter. Carmofur must be discontinued immediately if any psychomotor symptoms develop.

- **Aluminum toxicity**

Platen et al reported a wide range of toxic effects of aluminum. This element has been demonstrated in plants and aquatic animals in nature, in experimental animals by several routes of exposure, and under different clinical conditions in humans. Aluminum toxicity is a major problem in agriculture, affecting perhaps as much as 40% of arable soil in the world. In fresh waters acidified by acid rain, aluminum toxicity has led to fish extinction. Aluminum is a very potent neurotoxin. Subtle neurocognitive and psychomotor effects and EEG abnormalities have been reported at plasma aluminum levels as low as 50 mcg/L.

Infants and patients with impaired renal function could be particularly susceptible to aluminum accumulation and toxicity. Evidence exists to suggest that aluminum may be the causative agent in the development of dementia in patients with chronic renal failure who are on dialysis (ie, dialysis dementia). The EEG may become abnormal months before the full-blown dementia develops. Aluminum also is associated with dialysis encephalopathy, which often is accompanied by osteomalacia and anemia. Such effects also have been reported in certain patient groups without renal failure.

Aluminum accumulation occurs in the tissues of workers with long-term occupational exposure to aluminum dusts or fumes. Such exposure may cause neurological effects.

In dialysis dementia, the EEG abnormalities usually are diffuse slowing, although TWs may occur. When seizure develops, high-voltage spike and slow-wave complexes and paroxysmal bursts with a frequency of 2-4 Hz have been observed. Polymorphic frontally dominant delta often is observed. The background slowing usually correlates with severity of mental status impairment. Subcortical dysfunction may be present with FIRDA.

- **Liver transplantation**

The EEG in hepatic encephalopathy may consist of slow waves and TWs; epileptic activity may be observed. Adams et al studied patients after liver transplantation. Seventeen (33%) of 52 patients who underwent 56 consecutive orthotopic liver transplants had serious postoperative neurological complications. Seizures were described in 13 (25%) patients; of these, 50% had onset of seizures within the first week. In 3 patients, the seizures were associated with postoperative metabolic encephalopathy and fatal progressive neurological deterioration. Cyclosporin was thought to be causing the seizures in some of these patients.
In others, electrolyte disturbances, steroid treatment for graft rejection, and cerebral infarction could have contributed to the occurrence of seizures.

- **Scleroderma**

CNS involvement and psychiatric manifestations can occur in systemic sclerosis (ie, scleroderma). Hietaharju et al evaluated CNS and psychiatric involvement in 32 patients. Severe CNS or psychiatric symptoms were present in 5 patients (16%), including encephalopathy, psychosis, anxiety disorder, grand mal seizures, and transient ischemic attack. In addition, abnormal VEPs were recorded in 5 of 32 patients (16%), suggesting optic neuropathy. EEGs were mainly normal or showed only slight nonspecific changes.

- **Hashimoto myoclonic encephalopathy**

Ghika-Schmid et al reported 2 patients with subacute diffuse encephalopathy characterized by confusion, myoclonic encephalopathy, and mild akineto-rigid extrapyramidal signs in one case and by apathy, memory deficit, and partial complex seizures in the other. Hashimoto thyroiditis with high titers of antithyroglobulin antibodies was diagnosed in both patients, who were not responsive to anticonvulsant medication but exhibited rapid neurological improvement following steroid treatment. On neuropsychological examination, predominant frontotemporal dysfunction was noted.

EEG activity was remarkable for its rhythmic delta activity, which was unresponsive to, or even paradoxically increased by, anticonvulsant treatment. Atrophy with temporal predominance was observed on MRI. These observations support the idea that this potentially treatable dementia and movement disorder should be classified as a separate clinical entity.

Kothbauer-Margreiter et al reported 6 patients with Hashimoto thyroiditis and associated encephalopathy and compared with 14 well-documented cases identified in the literature. Encephalopathy typically affects patients when they are euthyroid and in an appropriate clinical situation; antithyroid autoantibodies are the main indicators of the encephalopathy. Since clinical features of Hashimoto encephalopathy are nonspecific, other etiologies such as infectious, metabolic, toxic, vascular, neoplastic, and paraneoplastic causes need to be considered.

Two types of initial clinical presentation can be differentiated: (1) a vasculitic type with stroke-like episodes and mild cognitive impairment and (2) a diffuse progressive type with dementia, seizures, psychotic episodes, or altered consciousness. These types may overlap, particularly over the long-term course in untreated patients. A strong female predominance existed in this study; 18 of the 20 patients were women. The EEG was abnormal in 90% of cases; it showed nonspecific changes. The condition is steroid responsive.
TRIPHASIC WAVEFORMS

TWs initially were described by Foley et al in hepatic encephalopathy. They later were described in other metabolic states and brain tumors. Most electroencephalographers now agree that TWs are a relatively nonspecific pattern observed in a number of metabolic conditions, degenerative dementias, and anoxia. In a bipolar montage, TWs usually comprise a high-voltage, positive wave followed by a smaller negative deflection; they usually are bilaterally synchronous and maximal frontally. A fronto-occipital (anteroposterior) phase lag varies from 25-140 ms. This is expressed less in referential montages.

TWs have not been reported in children. Generally, the TW pattern carries a poor prognosis with a high mortality rate if it occurs in association with rapid neurological and clinical deterioration. However, TWs in a psychiatric population described by Blatt and Brenner carried a different prognosis. In a large retrospective study consisting of 15,326 EEGs performed from 1983-1992 in a psychiatric institute, 83 EEGs (62 patients—13 men and 49 women aged 59-90 years, with a mean age of 74 years) had TWs. All 62 patients were awake, though they often were confused. Most (n=56) had dementia, usually severe; 15 also had delirium. Six patients had no dementia. Infrequent etiologies included neuroleptic malignant syndrome (n=1) and hepatic encephalopathy (n=1); in 4, the cause was uncertain, although all were receiving lithium.

EEG features analyzed included frequency of background rhythms, distribution of the TWs, periodicity, and epileptiform abnormalities. Background rhythms were slow in all but 7 patients (mean 6.2 +1-1.7 [SD] Hz). TWs were maximal posteriorly in 47 patients and anteriorly in 6 patients and were diffuse in 9 patients. Neuroimaging studies demonstrated prominent posterior abnormalities in only 1 individual. Periodicity was prominent in 4 patients; in 2, the TWs were maximal anteriorly. Interictal epileptiform activity was present in 6 patients, a history of seizures in 8, and myoclonus in 4. TWs are uncommon in psychiatric populations; they occur primarily in elderly and severely demented patients.

Agugila et al discussed nonmetabolic causes of TWs and described 2 patients with TWs on their EEGs in the absence of metabolic disturbances. One patient had coma associated with cerebellar hematoma, the other had mild dementia associated with idiopathic calcifications.
of the basal ganglia and healthy auditory brainstem responses and subcortical and cortical SEPs. Neurologic examination revealed no asterixis in either patient.

The literature on nonmetabolic causes of TWs also was reviewed, and the clinical and anatomic reports of 10 patients were analyzed. Seven patients had focal brainstem-diencephalic lesions (craniopharyngioma [2], thalamic gliomas [3], pontine stroke [2]). Three patients suffered from diffuse subcortical or multifocal encephalopathies (Binswanger encephalopathy [1], cerebral carcinomatosis [1], multifocal cerebral lymphoma [1]).

From the clinical point of view, patients with nonmetabolic diseases causing TWs presented with either disturbance of higher cerebral functions with no asterixis or sudden onset of coma. Agugila et al concluded that TWs may result from focal brainstem/diencephalic lesions or from diffuse subcortical or multifocal encephalopathies in the absence of concomitant metabolic abnormalities. Nonmetabolic causes of TW should be suspected in patients presenting with neurological disturbances not associated with asterixis.

TWs also were evaluated by Sundaram et al, and their clinical correlates and morphology were assessed. Twenty-six (41%) of 63 consecutive patients with TWs had various types of metabolic encephalopathies, while 37 patients (59%) had nonmetabolic encephalopathies, usually senile dementia. TWs were not found to be specific for any single type of metabolic encephalopathy. Etiology was linked more closely to level of consciousness at recording than any morphologic or distributional feature of the TWs themselves. Thus, all 31 alert patients had nonmetabolic encephalopathies, while all 13 comatose patients had metabolic encephalopathies.

The second, positive component (wave II) most often had the highest voltage, while equally maximal waves I and II occurred next most commonly. In these patients, TWs most often were expressed maximally anteriorly. Among patients with metabolic encephalopathies, a posterior-anterior delay or lag of the wave II peak occurred more commonly than did the better known anterior-posterior lag. Lags occurred with both metabolic and nonmetabolic conditions but were more common with the former. No difference in quantity or mode of appearance existed between the metabolic and nonmetabolic groups when matched for consciousness level.

Prognosis for patients with either metabolic or nonmetabolic encephalopathies was unfavorable. Only 4 of 24 patients with metabolic encephalopathy and 1 of 35 patients with nonmetabolic encephalopathy were well at follow-up more than 2 years later. Forty percent of EEGs with sharp and slow-wave complexes (slow spike waves) had sporadically appearing TWs. The relative amplitudes of the 3 components differed from those of TWs in other conditions; equally maximal waves II and III were the most usual form.

**DIGITAL EEG**

As stated in the assessment report of the American Academy of Neurology and the American Clinical Neurophysiology Society, digital EEG is an established substitute for
recording, reviewing, and storing a paper EEG record. In this sense, digital EEG simply replaces and improves the paper record in ways similar to the way a word processor has improved letter writing by hand or even by a typewriter. However, routine digital recording of the clinical EEG by digital means does not add new information that was not present in the paper record.

Once the paper recording is made, a number of options become available for further analysis. Some processing methods, such as different montage displays and digital filtering, simply enhance the visibility of the record. Some other methods, such as calculating the mean band frequencies and different band-energy spectra, may bring into the forefront information that was already there in the paper record but is too tedious and time-consuming to calculate without use of a computer. Spike recognition is an important enhancement and a great time saver but needs careful review by the interpreting physician. Lately, technologic developments have enabled the authors to record long-term monitoring on small storage devices, making the diagnosis of syncope, seizures, and sleep disorders much easier.

EEG brain mapping visualizes some selected electrical event in the brain and maps its geographic distribution. Attempts have been made to standardize some aspects of brain mapping; however, no clear uniform recommendation has yet emerged. Although frequency bands are fairly well standardized, different ways to calculate the data exist. Normative values are being developed; however, most brain maps are not time locked to an event or brain state; therefore, comparisons of frequency bands are difficult to accomplish across groups or disease states. A clear definition for the clinical correlation of the brain maps is still needed; therefore, EEG brain mapping and other advanced QEEG techniques should be used only by physicians highly skilled in clinical EEG and only as an adjunct to traditional EEG interpretation.

These tests may be clinically useful only for patients well selected on the basis of their clinical presentation. Certain QEEG techniques are considered established as an addition to the digital EEG and include screening for possible epileptic spikes or seizures, long-term EEG monitoring or ambulatory recording, and operating room (OR) and ICU monitoring.

Continuous EEG monitoring by frequency trending helps to detect early intracranial processes in the OR or ICU (eg, screening for possible epileptic seizures in high-risk patients in the ICU). QEEG frequency analysis may be a useful adjunct to interpretation of the routine EEG. In a number of conditions, such as postconcussion syndrome, head injury, learning disability, attention disorders, schizophrenia, depression, alcoholism, and drug abuse, the use of QEEG remains investigational. On the basis of available clinical and scientific evidence and expert opinions, QEEG is not currently useful in civil or criminal cases.

QEEG is a derivative of regular EEG. The original data must be evaluated before proceeding to further mathematical translation of this same data set. A thorough understanding and firm knowledge base in clinical EEG diagnosis may help prevent erroneous interpretations of digitally displayed mathematical constructs (eg, brain map,
coherence map). Ideally, only physicians properly trained in EEG and, in addition, sufficiently well trained in mathematics and computing science should use these new technologies. A substantial risk of erroneous interpretations exists if any of the elements required is missing. Clinical use of any of the EEG brain mapping or other QEEG techniques by practitioners who are not physicians highly skilled and properly trained in clinical EEG interpretation or without reviewing the original record should be unacceptable.

- **Concluding remarks**

The EEG is regarded as a fairly nonspecific measure of clinical states, as detailed in this article. A limited number of abnormalities that can be recognized in widely varied disease states exist. On the other hand, an abnormal EEG is a sensitive measure of brain function. When the patient has clinically symptomatic encephalopathy or moderate dementia, the EEG is almost always abnormal. Clinical utility of EEG needs to be appreciated in a different way than some other diagnostic procedures. In medicine, clear correlations and specific answers are desired; however, based on the modality and the underlying principle of measurement, this goal cannot always be achieved.

Besides EEG, the MRI scan is very sensitive in showing various lesions in the brain. But knowing exactly what these lesions represent is difficult on the basis of mere appearance. While interpreting MRI images, the clinician relies to a large extent on other relevant clinical information. EEG measures electrical field variations, and a number of clinical conditions can disturb the normal electrical field of the brain. Simple state or electrolyte changes may alter the appearance and time variation of the brain-generated electrical fields; hence, a large number of conditions cause the EEG to appear abnormal. In EEG practice, the clinician has to rely to a large extent on the clinical history and the neurologic examination findings to make a clinically meaningful conclusion.

In most instances, the correct question may be whether the EEG is normal or abnormal. The next step is to decide how an abnormal EEG would help the clinical diagnosis; therefore, the EEG can be used to confirm clinical observation or suspicion, or to determine the extent of the abnormality for prognostic purposes (ie, attempting to predict outcome of the clinical condition). Sometimes, EEGs serve as a "proof" to families that indeed the brain function is disturbed so greatly that recovery is doubtful. In such cases, the EEG helps resolve anxiety and supports a more correct ethical decision.

The newer EEG techniques offer a number of conveniences and also enhance communication between the electroencephalographer and other clinical specialists; however, they may not make the record more specific but merely easier to understand. Computer analysis on the other hand may offer features that, although present in the regular record, are difficult or time-consuming to extract and display. EEG has a definite role in evaluating changes in mental states. It can confirm or refute nonconvulsive status epilepticus. EEG changes are usually proportional to the degree of metabolic, hepatic, or renal encephalopathy. EEG often is abnormal in subdural hematoma, normal pressure hydrocephalus (NPH), and CJD.
Computer analysis of the EEG may help reveal subtle changes in AD. This is promising and hopefully will soon become clinically useful and available. In cases of clinical dementia, a normal EEG with preserved alpha might help establish the diagnosis of Pick disease, while a slowed and shifted alpha frequency is seen in AD and PSP. Low-voltage, flat EEG and the appropriate clinical presentation may raise the suspicion of Huntington disease. While the EEG is nonspecific, in most cases it is abnormal in altered mental states.

EEG study should be requested if clear clinical indications are present or if the clinician has a reasonable presumption that it may give clinically relevant information. This information is expected to alter the clinical decision-making process. It should help the referring source in diagnosis and treatment. Another role is to help the patient or family to understand the ongoing disease process. EEG frequently is ordered to evaluate patients with different degrees of mental and behavioral changes and encephalopathy or coma. Usually, nonspecific abnormalities are present that do not give definite information about the cause of the underlying process but do provide information on its location and severity; therefore, unless epileptic seizures are a consideration, the EEG does not give direct unequivocal information on the cause of the patient's condition.

Nevertheless, the study may differentiate between a generalized and a focal abnormality. This may guide the clinician to further appropriate imaging studies. On the other hand, if the abnormality is generalized, the EEG can be used to characterize and monitor the disease process. With coma, the EEG may help in predicting the neurological prognosis. EEG is an important diagnostic tool in dementias in which specific morphological lesions are not apparent on imaging studies.

- **Personal perspective**

EEG often is compared with MRI; when this comparison is made, it usually refers to clinical MRI and not functional MRI studies. This comparison is puzzling, since a primarily anatomical test is being compared with a functional one. MRI is good at telling us where the lesion is, while the EEG is pretty good at separating normal and abnormal primarily cortical function. Topological usefulness of EEG is limited, although with computerization it may be improved. The purpose of MRI is to provide precise localization of a lesion, usually one that has passed a certain stage of evolution. The EEG, on the other hand, captures the changing electrical characteristics of a functioning brain, primarily those of the cortex.

Conditions can be identified with EEG that as a rule cannot be seen on the MRI; therefore, the use of these studies is not exclusive but complementary. The EEG may be used for the following:

- To exclude nonconvulsive status epilepticus
- To identify focal interictal epileptiform activity to confirm clinical suspicion that seizures may contribute to the condition in question
To attempt to record functional disturbance in individuals whose brain MRI is "normal" but brain dysfunction is evident clinically (eg, metabolic encephalopathies)

To attempt to record disease-specific patterns in the proper clinical setting, such as progressive myoclonic epilepsies, CJD, SSPE

To help a psychiatrist with the multitude of complex disorders masking as potential epilepsy or encephalopathy (eg, lithium intoxication may present with BiPEDs)

To identify focal or lateralized changes that suggest a structural cause to the encephalopathy

The truth often is stated that EEG is nonspecific and cannot diagnose etiology or localization well (eg, the cause of coma). However, nonspecificity is often not the question in general medical practice because most of the referrals in general neurology are individuals in whom the cause is pretty well clear, or reasonably suspected, on the basis of clinical history and laboratory chemistry. The question from the clinician is whether the brain is involved and the extent of brain damage, if any. To answer these questions, presently no clinical tool is more useful than the EEG.

REFERENCES


THE ELECTROENCEPHALOGRAM IN ALTERED STATE OF CONSCIOUSNESS

The electroencephalogram (EEG) is often of great value in the evaluation of patients with alterations of consciousness. In addition to the artifacts routinely encountered in the EEG laboratory, however, recordings made in the intensive care unit (ICU) are often contaminated by artifacts arising from monitoring equipment, life support systems, and personnel. The use of additional electrodes, the monitoring of the electrocardiogram (ECG), movements (for example, body, tongue, and eye) respiration, and the temporary disconnection of other equipment may be needed to identify the noncerebral origin of such activity. Klem, 34 has reviewed many of the problems encountered in performing bedside EEGs.

When recording the EEG of comatose patients, it is important to test for reactivity, 3 which is defined as a change in electrocerebral activity following stimulation. The recording should be continued for sufficient time without stimulation that the ongoing EEG activity can be studied and the presence or absence of spontaneous variability determined. Painful or auditory stimuli should be applied when both the patient and surroundings are relatively quiet. If reactivity is present, the EEG may show an attenuation of ongoing activity or an increase in amplitude, which is usually accompanied by the appearance of slower frequency activity. Reactivity usually indicates a lighter level of coma, and as the prognosis in most cases of coma is related to severity more than

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etiology, 43 this is generally a good sign. However, with patients in coma secondary to a drug intoxication in whom recovery will usually occur if appropriate treatment is instituted, the presence or absence of reactivity on the EEG is of less value regarding prognosis.

There are several pathophysiologic mechanisms that can result in alteration of consciousness and ultimately coma. 43 They are as follows: (1) supratentorial mass lesions compressing the diencephalic and mesencephalic reticular formation; (2) infratentorial mass or destructive lesions; and (3) metabolic encephalopathy.

The EEG may indicate that this alteration of consciousness is due to one of the followings (1) a diffuse. encephalopathy, particularly hepatic or some drug intoxications; (2) a focal brain lesion; or (3) continual epileptic activity without motor manifestations (nonconvulsive status).

Unfortunately, one of the limitations of the EEG is its lack of specificity. For example, focal continuous polymorphic delta activity (PDA) is usually indicative of a focal structural cerebral lesion. However, the variety of pathologic disturbances capable of producing this EEG abnormality is diverse and includes an infarct, hemorrhage, tumor, abscess and other focal lesions. Similarly, diffuse slowing of background rhythms is seen in various encephalopathies regardless of etiology.

The EEG may be of prognostic value if the etiology of the coma is known. if not, then serial EEGs are needed to indicate the progression of the encephalopathy.

**METABOLIC ENCEPHALOPATHY**

Diffuse processes affecting cerebral function are often metabolic in nature. In a series of 500 patients initially diagnosed as "coma of unknown etiology" the leading cause was diffuse or metabolic brain dysfunction. 43 In general, with progression from lethargy to coma, there is a diffuse slowing of background rhythms from alpha to theta and subsequently delta activity. The degree of slowing usually parallels the degree of alteration of consciousness and indicates its severity, although there are exceptions. The EEG may also show intermittent bursts of rhythmic delta activity in a generalized distribution. In adults, this is usually maximal anteriorly and is referred to as frontal intermittent rhythmic delta activity (FIRDA), whereas in children, it is often maximal posteriorly and has been named OIRDA (occipital intermittent rhythmic delta activity).

As noted previously, although a diffusely slow record indicates cerebral dysfunction, it is not specific for a single etiology. Possibilities would include a host of metabolic-toxic disturbances, inflammatory processes, and head trauma. Several of these entities are discussed in further detail in the following sections.
There are some patterns in metabolic encephalopathies that, although not pathognomonic, are often suggestive of a specific etiology. Foley and colleagues, 18 described blunt spike and slow wave complexes in patients with liver disease. These waveforms were subsequently termed triphasic waves by Bickford and Butt, 6 and consist of bursts of moderate to high amplitude (100 to 300 μV) activity usually of 1.5 to 2.5 Hz and often occurring in clusters. Although frequently predominant in the frontal regions, occasionally they are maximal posteriorly. A fronto-occipital lag may be present. The initial negative component is the sharpest, whereas the following positive portion of the complex is the largest and is subsequently followed by another negative wave. 38 They are bisynchronous but may show shifting asymmetries. A persistent asymmetry (not related to technical factors or a skull defect) would suggest an underlying structural lesion on the side of the lower amplitude. 38

Figure 1. Triphasic waves

Figure 2. Triphasic waves, occurring in clusters, in a 44-year-old man with hepatic encephalopathy.

Triphasic waves were initially believed to be highly specific for hepatic dysfunction. However, in a study reported by Simsarian and Harner, 51 triphasic waves were found in 42 patients with diverse metabolic encephalopathies; of these, one-half were hepatic in origin, whereas a variety of disorders constituted the remainder. More recently, Karnaze
and Bickford, 32 studied 50 patients whose EEGs showed triphasic waves. Etiologies were hepatic (28), azotemia (10), anoxia (9), hyperosmolarity (2), and hypoglycemia (1). Clearly, the frequency of this electroencephalographic pattern in any large series will depend on the patient population at the institution where the study is performed.

Simsarian and Harner, 51 believed that the presence of triphasic waves in metabolic encephalopathies did not accurately reflect the level of consciousness. It is generally held, however, that triphasic waves in hepatic disease tend to be seen in light coma and disappear with deepening levels. 6,38 Aside from metabolic encephalopathies, triphasic waves can be seen in patients with degenerative disorders such as Creutzfeldt-jakob disease.

Reye's syndrome, an encephalopathy seen primarily in children and associated with hepatic dysfunction, produces a variety of electroencephalographic abnormalities, but triphasic waves are uncommon. Aoki and Lombroso, 2 proposed a rating system of the EEG for prognostic purposes in this disorder, but Gottschalk and associates, 20 regard the clinical status (level of consciousness) on admission as the most accurate predictor of outcome. The EEG correlates well with the level of consciousness but not with the usual biochemical abnormalities seen in this syndrome. 20

An unusual finding in several cases of Reye's syndrome has been the presence of 14- and 6-Hz positive spikes. This pattern is commonly present in young children and adolescents in drowsiness and light sleep but not in deep coma. Yamada and coworkers, 62 have seen these waveforms in over 50 per cent of their patients with Reye's syndrome who were comatose and whose EEGs were markedly abnormal, showing diffuse delta activity. This high incidence of 14- and 6-Hz positive spikes contrasts with the scarcity of similar findings in other comatose patients. Yamada and colleagues, 62 cite several reports of this same pattern in comatose patients secondary to hepatic encephalopathy but whether this finding in coma is specific for hepatic dysfunction is uncertain.

- Renal

Renal disease shows abnormalities similar to other metabolic encephalopathies with progressive slowing of background rhythms and superimposed bursts of slow activity. Triphasic waves, are also seen, the incidence being similar to that in hepatic disease (approximately 20 per cent). 21 Seizures are more common in uremic than hepatic encephalopathy, and with renal disease, paroxysmal epileptiform abnormalities may be found in the EEG. Occasionally, with photic stimulation, there may be a photoparoxysmal or photomyogenic response.

Hughes, 28 reviewed the correlation between multiple EEGs (362) and chemical changes in 23 uremic patients undergoing chronic hemodialysis over long periods of time (up to 18 months). Seventy percent of patients had at least one abnormal EEG. The one single serum
index that correlated best with the EEG was the BUN, especially if the record showed a worsening.

Other syndromes described in patients with renal disease undergoing dialysis include the dialysis dysequilibrium syndrome (DDS) and progressive dialysis encephalopathy (DE). In patients who develop DDS, there is a worsening of the clinical state and EEG following dialysis. Kennedy and colleagues, 33 performed continuous EEG monitoring in 13 uremic patients undergoing dialysis. In all, the EEG either became abnormal during dialysis or EEG abnormalities present prior to dialysis became more marked. Characteristic findings were bursts of high-voltage rhythmic delta waves. In the DE syndrome, Hughes and Schreeder, 29 found bilateral spike and wave complexes in 77 per cent of patients with DE compared with only 2 per cent in chronic renal patients without DE. Bursts of diffuse slow waves usually maximal in the frontal area were also more frequent in DE patients, although common in both groups.

- Drug Intoxication

The presence of generalized fast activity on an EEG of a comatose patient should arouse the suspicion of a drug intoxication, particularly with drugs that are known to increase beta activity on the EEG, such as barbiturates or benzodiazepines. Usually, this activity is somewhat slower (10 to 16Hz) than the 20 to 25 Hz beta activity seen in patients who are awake and taking these medications, and it is superimposed on a diffusely slow background. With deeper levels of coma, intermittent episodes of suppression, a burst suppression pattern, and ultimately electrocerebral silence (ECS) can be seen. 23 An unusual pattern consisting of sinusoidal theta activity interrupted every few seconds by periodic slow wave complexes has been described in phencyclidine ("angel dust", "PCP") intoxication. 54 Drug intoxication can also result in other interesting EEG patterns, such as alpha coma and spindle coma, which are described in subsequent sections.

![Figure 3](www.yassermetwally.com)

**Figure 3.** Widespread fast activity maximal anteriorly, superimposed on slow activity, most marked posteriorly, in a 15-year-old girl in coma caused by a drug intoxication.
In delirium due to drug withdrawal, such as from barbiturates or alcohol, spontaneous epileptiform abnormalities may occur, and there may be a photomyogenic or photoparoxysmal response. The background rhythms are often normal or may contain excessive low amplitude fast activity.

**HYPOXIA**

Hypoxia, like drugs, can produce a wide variety of abnormal EEG patterns. Any type of generalized periodic pattern following a cardiorespiratory arrest carries a poor prognosis. Kuroiwa and Celesia, 35 reviewed 11 cases of their own and previously published reports of 105 other patients with a burst suppression pattern who were comatose after a cardiorespiratory arrest and not under the effects of CNS depressants. Of the 116 patients, Ill (96 per cent) died. Following an arrest, some patients are comatose with repetitive myoclonic jerks, and the EEG usually shows the jerks to be associated with repetitive spikes or sharp waves occurring at approximately 1-second intervals; again, this is often associated with a fatal outcome. Triphasic waves can occur in anoxia. These generally are seen in deeper levels of coma than when due to hepatic disease and are associated with a poorer prognosis. 32, 50

Several authors, 27,46,5 have devised systems of grading the EEG to aid in prognosis. The ratings are similar, with EEGs showing normal or near normal frequency activity being assigned low grades, whereas those with predominantly delta activity, intermittent suppression, and ultimately ECS having higher grades that reflect a poorer prognosis. However, some EEGs may be difficult to classify, particularly those showing monorhythmic nonreactive faster frequencies, periodicity, or focal features.

An alpha pattern coma has been described following hypoxia 22, 30, 53, 60 as well as with drug intoxications. 10, 22 Although the frequency of the activity is in the alpha range, it is widespread, often of greatest amplitude anteriorly and does not show the usual reactivity to passive eye opening and eye closure. Thus, it does not represent the normal physiologic alpha rhythm but rather is an abnormal pattern. The prognosis of alpha coma has generally been considered as poor but its prognostic significance has been recently reappraised by Iragui and McCutchen, 30 who reviewed the outcome in 94 reported posthypoxic cases. When the pattern was secondary to cardiopulmonary arrest (86 patients), only 10 survived. In contrast, when due to a respiratory arrest (8 patients), 7 survived. Moreover, recovery has been reported among patients in whom the pattern was secondary to a drug intoxications, 10,22 Although there have been relatively few cases of alpha pattern coma reported in pediatric patients, the prognosis in children, as in adults, is variable and appears to be related to etiology. 36

Unfortunately there have been few studies comparing the outcome of patients with coma associated with alpha frequency activity in the EEG with a clinically similar group of individuals who have other EEG findings after cerebral anoxia from cardiac arrest. One such study reported by Sorensen and coworkers, 53 suggested that the prognosis in
patients with alpha pattern coma was no worse than in other patients who had been comatose for more than 24 hours after cardiac arrest. Another type of alpha pattern coma has been described in patients with brain-stem lesions and is discussed in the section on subtentorial lesions.

SUPRATENTORIAL LESIONS

The EEG is usually markedly abnormal when coma is due to a supratentorial lesion. The abnormalities are greater with acute and rapidly expanding lesions rather than with chronic slow growing processes. The EEG, however, is of limited value in the precise localization of the lesion within the affected hemisphere. Several types of abnormalities may be seen. Often there is continual focal PDA over the involved side. With disturbances of deeper structures, FIRDA usually appears. Other EEG abnormalities may include focal attenuation of activity, a decrease of faster frequencies over the affected side, and focal epileptiform abnormalities. Such findings are not specific for any single etiology.

A pattern often seen with acute or subacute unilateral lesions is periodic lateralized epileptiform discharges (PLEDS). These were described by Chatrian and associates and are periodic complexes usually recurring every 1 to 2 seconds. They consist of spikes or sharp waves, often followed by a slow wave. PLEDs occur in a variety of disorders, most often acute unilateral lesions such as infarcts or tumors. They may also be seen in patients with chronic seizure disorders or old static lesions, especially when associated with recent seizures, alcohol withdrawal, or a toxic metabolic disorder. In a study of 45 patients whose EEGs showed this pattern, de la Paz and Brenner, found a recent stroke to be the most common cause (15 cases). Patients with chronic seizure disorders who had had recent seizures, but did not have a new structural lesion, accounted for 10 cases, whereas tumors were the third most common cause (5 cases). PLEDs also occurred with disorders that more often produce diffuse disturbances, such as hypoxia (3 cases).

Figure 4. Right sided PLEDs in a 52-year-old man following craniotomy for right subdural hematoma. The discharges were not ictal.
The clinical picture associated with PLEDs is usually obtundation, focal seizures, and focal neurologic signs. Although the majority of patients with PLEDs will have seizures during the acute stage of illness, PLEDs are usually an interictal pattern. If, during the recording, the patient has a seizure, a new pattern (often consisting of faster rhythmic activity) will appear. Regardless of etiology, PLEDs are a transient phenomenon. With time, the discharges usually decrease in amplitude, the repetition rate decreases, and ultimately the discharges cease.

The majority of patients with herpes simplex encephalitis (HSE) have PLEDS, particularly when serial recordings are obtained. At present, the EEG has been found to be the most useful neurodiagnostic aid in this disorder, followed by technetium and computerized tomographic (CT) scans. Although the presence of PLEDs in the EEG in a patient with a suspected viral encephalitis should raise the suspicion of HSE, there are other causes. Greenberg and coworkers, reported periodic complexes in a 17-year-old patient with a neurologic illness manifested by lymphocytic meningitis, coma, seizures, aphasia, hemiparesis, and hemianopsia who ultimately was found to have infectious mononucleosis encephalitis.

Although PLEDs are lateralized, they may be reflected synchronously to a lesser degree over homologous areas in the contralateral hemisphere. In contrast, with bilateral independent periodic lateralized epileptiform discharges (BIPLEDs), the complexes are asynchronous and usually differ in morphology, amplitude, rate of repetition, and site of maximal involvement. De la Paz and Brenner reported clinical findings in 18 patients whose EEGs showed this pattern. The most common causes of BIPLEDs were anoxic encephalopathy (five), CNS infection (encephalitis or meningitis) (five) and chronic seizure disorders (four). When compared with patients with PLEDS, those with BIPLEDs were more likely to be comatose (72 per cent versus 24 per cent) and had a higher mortality rate (61 per cent versus 29 per cent), but focal neurologic deficits and focal seizures were less common. Smith and colleagues, believed that BIPLEDS, although not pathognomonic, were suggestive of HSE, particularly when associated with an acute encephalitic process. In our series, although there were two patients with BIPLEDs due to HSE, three other patients had a CNS infection other than HSE that also produced this EEG picture.
Mizrahi and Tharp, 41 described a characteristic EEG pattern consisting of multifocal periodic or quasiperiodic complexes in neonatal herpes encephalitis. They concluded that a periodic EEG in a young infant with partial motor seizures and CSF lymphocytic pleocytosis is virtually diagnostic of HSE. More recently, the EEGs of 21 newborns with HSE were described by Sainio and associates. 47 Their patients had considerably shorter focal or unilateral periodic episodes than those described by Mizrahi and Tharp, 41 and the discharges were usually not associated with clinical seizures. Among 20 other babies with similar EEG findings but not having HSE, meningoencephalitis of uncertain etiology was the leading cause (11 cases).

SUBTENTORIAL LESIONS

The EEG is of less value in the evaluation and prognosis of patients with altered states of consciousness when the lesion is subtentorial rather than supratentorial or due to a diffuse metabolic process. The EEG is better in assessing hemispheric function, which determines quality of survival, rather than brain-stem function, which is needed for survival. However, the EEG may still be of value, particularly when the lesion is at or below the pontomesencephalic junction. As indicated earlier, alpha pattern coma has been described in patients with involvement of the upper pons and caudal midbrain, usually secondary to a vascular insult. With bilateral involvement of the pontine tegmentum, the patient is comatose with an EEG showing alpha activity. 11 In contrast to the posthypoxic alpha pattern coma, the alpha frequency activity seen with a brain-stem lesion is more posterior and shows more variability. In addition, there may be reactivity with sensory stimulation such as passive eye opening and eye closure or painful stimuli. 60 Although the EEG resembles normal wakefulness, few patients survive.

Patients with this type of alpha pattern coma need to be distinguished clinically from patients with a "locked-in" syndrome. 39 The latter are conscious, although paralyzed and mute, and can often communicate with eye blinks. Here the lesion affects the ventral pons
but does not involve the pontine tegmentum, and consciousness is not affected. Higher involvement of the midbrain and diencephalon result in coma and produce generalized slow (delta) waves that may be continuous or intermittent. 31, 37

Another condition that may simulate coma is psychogenic unresponsiveness. The EEG is often normal and the alpha rhythm, if present, shows reactivity to passive eye opening and eye closure. Neurologic findings, particularly the presence of nystagmus with oculovestibular testing, will help identify the cause of this apparently altered state of consciousness. 43

An EEG pattern that may be seen with subtentorial lesions, 9 as well as supratentorial lesions or diffuse encephalopathies, is spindle coma. This pattern is thought to be due to altered function caudal to the thalamus but rostral to the pontomesencephalic junction. 8 The spindle coma pattern was described by Chatrian and colleagues 13 in a study of 11 patients with head injury. They concluded that the presence of slow wave sleep activity, such as spindles, indicated a good prognosis. Britt and coworkers, reported 36 patients with nontraumatic alteration of consciousness of diverse etiologies, whose EEG activity resembled slow wave sleep. In those patients who were comatose (21), only four survived, whereas the prognosis was good in patients who were stuporous or semicomatose (14 of 15 patients survived). Hansotia and associates, 24 studied 370 comatose patients, among whom 5.9 per cent (22 patients) showed a spindle coma pattern. Approximately one third was due to head injury, whereas another third was secondary to cerebral hemorrhage or cerebral anoxia after myocardial infarction. They concluded that EEGs with spindle patterns are of dubious value in indicating the prognosis of coma, as the outcome for patients with this EEG pattern was no better than that without it. Thus, like other EEG patterns, spindle coma is not specific for a single etiology, and the prognosis is dependent on severity of insult, neurologic findings, and underlying cause.

NONCONVULSIVE STATUS EPILEPTICUS

The EEG is extremely useful in the identification of nonconvulsive status epilepticus, particularly when the cause of this acute confusional state is not clinically apparent. There are two major categories of nonconvulsive status: generalized and complex partial. Numerous terms have been used to describe the former including petit mal and absence status. 1,17

Absence status occurs in children and adults and is characterized by an impairment of consciousness ranging from minimal clouding to stupor and often lasting from hours to days. The EEG shows more or less continuous generalized, bilaterally synchronous, symmetric epileptic activity, usually maximal anteriorly. A variety of patterns have been described. 19 Most commonly (40 per cent), there are continuous spike and wave or polyspike and wave discharges with a frequency at about 3 Hz, usually ranging from 1 to 3 Hz. In approximately 30 per cent of cases, bursts of rhythmic 3 Hz spike and wave are superimposed on a normal or slow background. The majority of the remaining cases show
either arrhythmic spike and wave or polyspike and wave discharges or bursts of fast activity (10 to 20 Hz) with occasional spike and wave or polyspike and wave complexes and a diffusely slow background.

The behavioral alterations in absence status have sometimes resulted in an incorrect initial diagnosis of a primary psychiatric disorder, such as depression, psychosis, or hysteria. There are often clues to help identify the underlying epileptic nature of this acute disturbance. Most commonly, the episodes occur in known epileptic patients (90 to 95 per cent), although they can occur although a previous history of seizures, particularly in the elderly. The presence of associated myoclonic movements, such as eyelid flutter and rhythmic facial or upper extremity movements, is also suggestive of absence status. However, an EEG is the only laboratory means of verifying the diagnosis.

Other entities in the differential diagnosis include the postictal state, drug intoxication, transient global amnesia, and complex partial status epilepticus (CPSE). In adults, complex partial seizures are more frequent than absence seizures, but they rarely present as a prolonged confusional state. Nevertheless, there have recently been several reports of CPSE in both adults and children. In contrast to absence status, in CPSE, the EEG abnormalities usually are focal, most often affecting the temporal area, although they can become generalized.

Figure 6. Continuous generalized spike and polyspike and wave activity, maximal anteriorly, in a 60-year-old woman in absence status.

At times, however, these conditions can be difficult to distinguish even with EEG monitoring. Niedermeyer and colleagues described two patients with absence status...
whose ictal EEGs showed paroxysmal (spikes or rhythmical spike waves) activity that was consistently accentuated unilaterally over the superior frontal regions. They believed that the lack of symmetric, bilaterally synchronous paroxysmal discharges seen in their two cases did not negate the diagnosis of absence status but perhaps represented a variant or atypical form. Ballenger and coworkers 5 however, believed these cases showed a considerable overlap with those of continuous partial complex status.

Porter and Penry 45 believed that the clinical differences between absence status and complex partial status could help to differentiate these two disorders. The former ends abruptly without postictal abnormality, whereas the latter is associated with postictal confusion, depression, or general malaise. Treiman and Delgado-Escueta 55 have emphasized cyclic clinical phases in patients with CPSE, alternating between total unresponsiveness with stereotyped automatisms and partial responsiveness with reactive automatisms.

**ELECTROCEREBRAL SILENCE**

The end stage of coma is ECS, which is defined as "no cerebral activity over 2 mv when recording from scalp or referential electrode pairs, 10 or more cm apart with interelectrode resistances under 10,000 ohms (or impedances under 6000 ohms), but over 100 ohms. 25 The American EEG Society Guidelines", 25 discuss in detail technical standards to be used in recording patients with suspected cerebral death. These include considerations such as recording time, number of electrodes, interelectrode impedances, appropriate sensitivity and time constant, tests of reactivity and monitoring techniques. For further discussion of these recommendations and the rationale for each, the guidelines should be consulted.

In cases in which ECS is present and the patient is being evaluated for brain death, both hypothermia and drug intoxication must be excluded. 25 Regarding the former, Walker and associates, 57 state that unless the temperature is less than 32°C, it does not seem to depress the EEG appreciably, whereas arterial hypotension (at or below shock levels) is a more potent depressor of EEG activity and should be considered when interpreting the EEG. They also thought that the record usually should not be performed until clinical evidence of brain death has been present for 12 hours, although this time might be shortened if the cause of coma is well established as irreversible. In practice, 6 hours is often the minimum.

ECS, however, is not synonymous with brain death, as it may be due to intoxication with a CNS depressant drug, which is potentially reversible. It can occasionally be seen in patients with a persistent vegetative state 744 although the majority of such patients do show EEG activity.

As mentioned in the American EEG Society Guidelines, 25 there is still a need for systemic study of ECS in children under 3 years of age, as apparent ECS can be associated with
serious metabolic derangements or bilateral subdural hematoma. In addition, Ashwal and Schneider, 4 reported 5 children less than 3 years of age, all of whom demonstrated persistent diffuse 2 to 4 mV delta or theta activity, yet met the clinical criteria of brain death. None had evidence of cerebral blood flow by either an isotope bolus technique (five patients) or cerebral angiography (four patients).

**SUMMARY**

The EEG can be very helpful in the evaluation of patients with altered states of consciousness. Diffuse slowing of background rhythms and the presence of triphasic waves suggests metabolic dysfunction, particularly hepatic. Generalized fast activity may be seen in patients with a drug intoxication. Abnormalities, such as PLEDs or focal continual PDA, support a diagnosis of supratentorial lesion, whereas a normal appearing EEG in a comatose patient suggests a brain-stem lesion. In addition, the EEG may reveal that the alteration in consciousness is due to continual epileptic activity without motor manifestations (nonconvulsive status) that had not been suspected.

As indicated, certain patterns have prognostic implications. However, as these patterns are not specific for a single etiology, the EEG is of most help when the cause is known. For example, burst suppression or a diffuse alpha pattern coma can be seen in either hypoxia or a drug intoxication. With hypoxia, these patterns carry an extremely poor prognosis for useful recovery, whereas complete recovery is often seen in cases secondary to drug ingestion. As a more extreme example, a patient whose EEG shows ECS secondary to drug intoxication may recover but will not if the ECS is due to hypoxia or severe head trauma. If the etiology of the encephalopathy is unknown, then sequential records are needed for prognosis.

**REFERENCES**


INTRODUCTION

Electrical activity of each brain region is homeostatically regulated, resulting in predictable frequency composition of the background EEG. Replicated normative databases have established that the EEG power spectrum is independent of ethnic background. Artifact-free EEG evaluated relative to such norms displays few deviant values in healthy, normally functioning individuals. In subjects with psychiatric disorders, high proportions of abnormal findings have been reported with good concordance and high specificity and sensitivity across numerous studies, distinctive within a wide variety of disorders and often contributing to differential diagnosis and selection of treatment. New three-dimensional QEEG imaging methods offer an economical alternative to other functional brain imaging modalities.
Brain imaging technologies are yielding information about structural or functional abnormalities in patients with various psychiatric and neurological disorders. These imaging modalities include magnetic resonance imaging; positron emission tomography of regional cerebral metabolic rate, regional cerebral blood flow, and radioligand binding to receptors of neurotransmitters; single-photon emission computed tomography; functional magnetic resonance imaging; magnetoencephalography; quantitative electroencephalography (QEEG) and event-related potentials (ERP); topographic QEEG and statistical probability mapping; and low-resolution electromagnetic tomography. Evidence from these brain imaging methods has unequivocally established that "mental illness" has definite correlates with brain dysfunction. QEEG and ERP methods afford the psychiatric practitioner a set of noninvasive tools that are capable of quantitatively assessing resting and evoked activity of the brain with sensitivity and temporal resolution superior to those of any other imaging method.

Conditions such as anxiety disorder, depression, dementia, obsessive-compulsive disorder, schizophrenia, learning disabilities, and attention deficit disorder with and without hyperactivity are now understood to involve interactions between brain dysfunctions or altered neuroanatomical structure and environmental influences. Medications that profoundly alter the availability of neurotransmitters and affect a hypothesized pathophysiology are routinely prescribed by psychiatric practitioners. Nonetheless, little or no attempt is made in most cases, even in the treatment-resistant patient, to use biological assessment methods to select a treatment, to evaluate its physiological effect, and to demonstrate its efficacy objectively. Relevant biological measurements may become invaluable adjuncts for the selection and evaluation of treatment and may minimize false starts, decrease severity and shorten duration of symptoms, and markedly reduce costs. In this era, it will become increasingly essential to demonstrate the need for treatment and to substantiate its efficacy.

**EEG AND QEEG**

Of all the imaging modalities, the greatest body of replicated evidence regarding pathophysiological concomitants of psychiatric and developmental disorders has been provided by EEG and QEEG studies. Electrophysiological assessment is also the most practical of these methods, using relatively simple, inexpensive, compact equipment readily accommodated by clinics, hospitals, or private offices. QEEG analytical algorithms are widely available from commercial sources, and workshops with continuing medical education accreditation in collection, analysis, and interpretation of data are now regularly presented by professional societies as well as equipment manufacturers. However, despite extensive evidence of sensitivity and specificity, the adoption of QEEG by the psychiatric community has been slow. Two major factors may account for this.

First, the numerous reports of abnormalities found in psychiatric patients by visual inspection of the conventional EEG have been regarded as too nonspecific and are usually not included in increasingly compressed curricula. Further, the great majority of recent papers reporting the results of EEG, QEEG, and ERP studies of psychiatric patients have
appeared not in psychiatric journals, but rather in specialized electrophysiological or brain research publications.

Second, there has been considerable controversy about the clinical utility of QEEG in position papers published by various professional organizations over the past decade, concluding, in the words of one such statement, that "the clinical application of Quantitative EEG is considered to be limited and adjunctive...clinical use...must be an extension of routine EEG." These statements cited only a very few published findings in psychiatric disorders, which were frequently grouped with "other disorders" (including tumors, multiple sclerosis, migraine, solvent exposure, and radiation exposure).

During the last decade, more than 500 EEG and QEEG papers have reported well-designed studies, concurring that EEG and QEEG abnormalities are found in a high proportion of psychiatric patients. Individual studies usually include a substantial number of psychiatric patients and normal control subjects, and across all studies within any particular disorder, the overall sample size is very large. An overview of the findings reveals numerous consistent and concordant conventional EEG and QEEG findings among studies within the same DSM diagnoses. Many of these studies have been on never-medicated or unmedicated patients who have been medication free for substantial periods. Statistical significance, specificity, and sensitivity have been high. No comprehensive review of this large body of psychiatrically relevant literature has yet appeared.

This article provides a comprehensive, updated review of how conventional EEG and QEEG can be useful in present clinical psychiatric practice. Other relevant reviews have appeared.

- Basic QEEG Definitions

In QEEG, multichannel recording (usually 19 electrodes at standardized positions) of eyes-closed, resting or "background" EEG are visually edited and a sample of artifact-free data, usually 1 to 2 minutes, is analyzed, using the Fast Fourier Transform (FFT) to quantify the power at each frequency of the EEG averaged across the entire sample, known as the power spectrum. The test-retest replicability of power spectra thus computed has been shown to be highly reproducible in works cited below. The power spectrum of clinical interest is usually considered to extend from about 1 Hz to 20 Hz.

This frequency range has traditionally been separated into 4 wide frequency bands, typically defined as delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz), and beta (12.5–20 Hz). Results from each electrode can be represented as absolute power in each band (total µV2), relative power in each band (percentage of total power in each channel), coherence (a measure of synchronization between activity in two channels), or symmetry (the ratio of power in each band between a symmetrical pair of electrodes).
Neurophysiological Basis of EEG

Research on the origins of rhythmic brain electrical activity in the various frequency bands indicates that anatomically complex homeostatic systems regulate the EEG power spectrum. Brainstem, thalamic, and cortical processes involving large neuronal populations mediate this regulation, using all the major neurotransmitters.9–12

Pacemaker neurons distributed throughout the thalamus normally oscillate synchronously in the 7.5–12.5-Hz frequency range. Efferent projections globally distributed across the cortex produce the rhythmic electrical activity known as the alpha rhythm, which dominates the EEG of an alert healthy person at rest. Nucleus reticularis can hyperpolarize the cell membranes of thalamic neurons by gamma-aminobutyric acid (GABA) release, slowing the dominant alpha rhythm into the lower theta range (3.5–7.5 Hz) and diminishing sensory throughput to the cortex. Slow delta activity (1.5–3.5 Hz) is believed to originate in oscillator neurons in deep cortical layers and in the thalamus, normally inhibited by input from the ascending reticular activating system in the midbrain. The faster activity in the beta band (12.5–20 Hz) is believed to reflect corticocortical and thalamocortical transactions related to specific information processing.

The changes characteristically seen in the disorders reviewed in this paper may be understood by referring to Figure 1. Activation of the mesencephalic reticular formation (MRF) causes inhibition of the nucleus reticularis by cholinergic and serotonergic mediation, which releases the thalamic cells from inhibition by the n. reticularis. The dominant activity of the EEG power spectrum becomes more rapid, with the return of alpha activity and the higher frequency beta activity, and the flow of information through the thalamus to the cortex is facilitated.
Figure 1. Neurophysiological changes characteristically seen in the disorders reviewed in this paper may reflect disturbances of regulation in this homeostatic system. See text for a description of this model.

The cortex can activate n. reticularis directly by glutamatergic pathways to suppress the arrival of information to the cortical level and, by striatal projections, dopamine can inhibit the MRF. Such inhibition of the MRF enables inhibition of thalamic neurons to occur and blocks the flow of sensory information through the thalamus to the cortex.

This model suggests that deficiencies or excesses of any of the neurotransmitters should produce marked departure from the homeostatically regulated normative EEG spectrum. Such neurotransmitter perturbations are widely believed to make decisive contributions to much psychiatric pathophysiology.

The EEG power spectrum can be reasonably expected to be stable and characteristic for healthy human beings, as a result of homeostatic regulation by these processes, with high specificity probably reflecting our common genetic heritage. It is also reasonable to expect sensitivity in these measures to many dysfunctions believed to be abnormal in some psychiatric disorders. The data support these expectations.
Stability and Specificity of the EEG Power Spectrum as the Basis of QEEG

During the period when the origins of the EEG were being illuminated by studies such as those cited above, the resting EEG power spectra of large samples of healthy, functioning individuals across a wide age range were being studied quantitatively. Initial studies of this sort, using analog methods, showed systematic changes from ages 17 to 64,13 and then from ages 1 to 21,14 in the average power in the delta, theta, alpha, and beta frequency bands. These normative data were soon replicated by use of general-purpose digital computing equipment. Age regression is necessary to correct for maturational effects. Not only were the systematic changes with age confirmed, but no significant differences were found between the EEGs of normally functioning Swedish children and white or black U.S. children.15 Soon thereafter, normally functioning black children in Barbados were found to display the same values of the EEG power spectrum as the U.S. and Swedish groups.

Since then, numerous studies have confirmed the high specificity of normative distributions of power in the delta, theta, alpha, and beta bands. Positive findings different from the normative database in healthy, normally functioning individuals have repeatedly been shown to be within the chance levels, with very high test-retest reliability.16,17 Normative data have been extended to cover the age range from 1 to 95 years for each electrode in the standardized International 10-20 System and have been broadened to include measures of absolute power, relative power, mean frequency, coherence, and symmetry, as well as covariance matrices that quantify normal brain relationships.18–20 These multivariate composite measures are unique to QEEG; psychiatric disorders rarely entail focal abnormalities.

The independence of the normative QEEG descriptors from cultural and ethnic factors enables objective assessment of brain integrity in persons of any age, origin, or background. This independence and specificity, as well as high replicability, has been established in studies from Barbados, China, Cuba, Germany, Holland, Japan, Korea, Mexico, Netherlands, Sweden, the United States, and Venezuela.17,21–33 If normative distributions of QEEG measures are made gaussian,15,22 then the incidence of false positive QEEG findings obtained from visually edited, artifact-free resting EEG recordings is at or below the level expected by chance. If one were to require that the QEEG evaluation be performed on two separate samples and that any significant finding deviant at the P0.05 level be replicated in each of these two samples, the probability that this would occur by chance would be approximately PxP, or 0.05x0.05, or 0.0025. If such a replication were required, false positives would seem rather unlikely. Such a high level of specificity is beyond the confidence level achieved by many routinely used clinical tests, such as mammograms, cervical screenings, or CT brain scans.34

Why Should Psychiatric Patients Have EEG Studies?

In psychiatric diagnostics, physical or neurological conditions must be ruled out before a psychiatric disorder can be diagnosed.35 As many as 64% to 68%2,3 of EEGs in psychiatric patients provide evidence of pathophysiology, and these results have additional utility beyond simply ruling out "organic brain lesions."3 Such electroencephalographic
studies may also aid in differential diagnosis, treatment selection, and evaluation. Some longitudinal studies show that initial quantitative EEG profiles may distinguish among patients with the same DSM diagnosis who will respond preferentially to different medications or who will display different evolution of illness.

CONVENTIONAL AND QUANTITATIVE EEG STUDIES

A voluminous literature attests to the robustness of conventional EEG studies and their clinical utility in disorders of brain function. This approach has contributed valuable information for the clinical psychiatrist. This method is essentially based on visual pattern recognition. Over the past 20 years, algorithms for computer pattern recognition, the computer's unsurpassed capacity to measure and calculate, and the availability of normative databases across the human life span have enhanced electroencephalography, supplementing the electroencephalographer's trained eye with a quantitative and objective description of a patient's EEG record (QEEG). Even more powerful are statistical comparisons between numerous measures from the individual patient and those of age-matched normal subjects or of patient subjects having different diagnoses.

These two EEG approaches complement each other: conventional EEG provides reliable diagnostic information, especially sensitive to "organic" or neurological disorders, detecting features of waveshapes, frequency relationships, and transitions of state seldom encountered in the healthy individual. QEEG enables precise comparison of the individual patient's record with normative and psychopathologic patient databases. Across both EEG and QEEG studies, a broad consensus exists on the high proportion of abnormalities found in different psychiatric disorders and often on their electrophysiological profiles. In most of these studies, patients were without psychotropic medication, except for some of the reports evaluating patients with mood disorders or schizophrenia. Most of the chronic patients in those studies had been drug free for some period before evaluation.

- Dementias

Electroencephalography is particularly effective but generally underutilized in the evaluation of the confused or delirious patient. The hallmark of delirium usually is the slowing of the background EEG rhythm, to an extent that is positively correlated with the degree of severity of the condition. The one exception is in delirium tremens (DT), which usually shows a normal EEG record with fast rhythms. If abnormal slow activity is found in the DT condition, consideration should be given to a Wernicke encephalopathy or to a hepatic disorder. In the delirium accompanying the neuroleptic malignant syndrome, only a mild diffuse slow wave usually appears. When delusional manifestations are prominent, as in organic delusional states, one typically finds increased slow-wave activity over both temporal lobes. Delirium can be differentiated from dementia, and the significant factors are an increased theta activity and increase in delta relative power.

In organic syndromes showing cognitive deficits such as memory dysfunction, the prevalence of EEG abnormalities is directly related to the degree of cognitive impairment.
If clinical impairment is equivocal, the incidence of EEG abnormalities is usually slightly over 40%; with a mild-to-moderate impairment, a 65% incidence is expected. The EEG is a moderately sensitive, nonspecific indication of brain dysfunction, clearly useful in the diagnosis of Alzheimer's disease and also AIDS dementia, with general agreement in the literature that increased slow activity and decreased mean frequency are correlated with cognitive impairment and measures of clinical severity of Alzheimer's dementia.

EEG frequency analysis allows confident detection of excessive slowing, more readily measured and quantified than conventional EEG. QEEG studies in dementia patients are in agreement with conventional EEG findings, reporting increased delta and/or theta power, decreased mean frequency, decreased beta power, and decreased occipital dominant frequency. Many workers regard increased slow activity prior to reduction of alpha power as the earliest electrophysiological indicator appearing in Alzheimer's disease. The amount of theta activity shows the best correlation with cognitive deterioration and with clinical outcome in longitudinal follow-up, although one report found no predictive utility. Increased delta appears to be a correlate of severe advanced dementia, occurring subsequent to increased theta.

In cerebrovascular disease, several EEG frequency parameters are highly correlated with regional blood flow or metabolism. Sensitivity and specificity are high for detection of ischemia-related diffuse or focal impairment. These studies show sensitivity generally greater than 80%, false-positive rates below 5% to 10%, and correlations of $r>0.7$ between EEG and blood flow in ischemic and nonischemic regions. EEG slowing is highly correlated with decreased regional cerebral blood flow or metabolism. QEEG can detect reliable focal features that are missed in the routine EEG and can be quite abnormal even when the CT is still normal, such as in the first 1 to 3 days after stroke or when the degree of ischemia is mild enough to cause dysfunction without infarction.

Alzheimer's dementia and multi-infarct dementia (MID) have been differentiated by evaluating asymmetry of slow activity and coherence. Multiple studies report accurate discrimination of Alzheimer patients from depressed patients or from normal subjects by use of EEG or QEEG measures of slow activity. Accurate separation of Alzheimer's from frontotemporal dementia (Pick's disease) by use of QEEG has been reported.

**Conclusion**

Routine EEG has long been used to evaluate dementia and encephalopathy unresolved after initial clinical evaluation. There is excellent agreement between conventional and quantitative EEG studies of the dementias. QEEG may be useful in evaluating dementia or encephalopathy if routine EEG studies are not conclusive or if neuroimaging studies are
inconclusive or unavailable, as well as in differentiating between Alzheimer's dementia, multi-infarct dementia, depression, and normal aging.

A broad consensus exists across a very large number of EEG and QEEG studies of dementia patients: Both kinds of studies report a diffuse increased delta and/or theta power, with decreased beta power and mean frequency. These features are absent in depression and are focal in multi-infarct dementia, enabling these disorders to be differentiated from Alzheimer's dementia. A good correlation exists between severity of cognitive impairment, clinical outcome, and amount of EEG slowing.

- Schizophrenia

Numerous qualitative studies indicate abnormal conventional EEG findings in 20% to 60% of schizophrenic patients. A more specific finding in schizophrenia is a relatively low mean alpha frequency, although some patients may show a fast alpha rhythm. Catatonic patients often present with paroxysmal activity.

Numerous EEG and QEEG studies of background activity have been performed on carefully evaluated groups of unmedicated as well as medicated schizophrenic patients. Substantial agreement emerges from this body of literature. Deficient alpha power is consistently reported as well as altered alpha mean frequency or diminished alpha responsiveness. Numerous studies have reported increased beta activity in schizophrenia. Neuroleptics typically increase alpha power and reduce beta power, suggesting possible normalization of deviant features by medication.

Increased delta and/or theta activity has also been reported in a large number of studies. Increased slow activity can apparently result from neuroleptic treatment, although there are reports of increased delta in patients off medication for several weeks and reduction of delta or theta when medication is resumed. In the elderly schizophrenic patient, an increase in fast theta activity (7–7.5 Hz) is seen. A decrease in fast alpha (10–12 Hz) noted on the frontal areas has been called "hypofrontality."

Clinical relationships reported include 1) correlation between negative symptoms and delta waves in the temporal areas; 2) positive correlation between degree of QEEG abnormality and degree of clinical improvement, raising the question of whether this "degradation" of the EEG is a necessary condition for a clinical improvement with clozapine; and 3) correlation between blink rates, alpha power, and smoking. In sleep, a decrease has been found in stages III, IV, and REM, and also in REM latency and sleep continuity.

Results from a small number of studies are inconsistent with this consensus of a QEEG profile, showing increased delta or theta, decreased alpha, and increased beta in schizophrenia. For example, increased slow activity has not been found by some workers, and increased alpha and decreased beta have occasionally been reported. Not all of the studies reporting the increased slow activity/decreased beta power and mean frequency. These features are absent in depression and are focal in multi-infarct dementia, enabling these disorders to be differentiated from Alzheimer's dementia. A good correlation exists between severity of cognitive impairment, clinical outcome, and amount of EEG slowing.
alpha/increased beta profile found all of the indicated deviations. This inconsistency plausibly might arise from the coexistence of several subtypes with different QEEG profiles within the population of schizophrenic patients. Observations might depend on the mixture of subtypes within the relatively small samples collected for a particular study.

This heterogeneity has been recently documented in a large sample of medicated, nonmedicated, and never-medicated schizophrenic patients, using cluster analysis based on QEEG variables. Five subtypes were detected, with their QEEG profiles characterized by delta plus theta excess, theta excess, theta plus alpha excess with beta deficit, theta excess, and alpha excess with beta excess. Never-medicated patients were classified into three of these subtypes. Schizophrenic patients with QEEG profiles corresponding to some of the groups identified by this cluster analysis have been reported to display differential responses to treatment with haloperidol or risperidone. Additional evidence of heterogeneity in the schizophrenic population has been provided in QEEG studies by other groups.

Findings of asymmetry in schizophrenia have been inconsistent. However, these findings depend upon whether measurements were made over anterior or posterior regions. When the electrode array covered both regions, power was highest over the right hemisphere in anterior regions, but over the left hemisphere in posterior regions. This conclusion was supported by the cluster analysis just cited, in which this asymmetry pattern was found in every frequency band for all five subtypes. However, increased amounts of delta activity in the left anterior temporal area have been reported to discriminate schizophrenic patients from control subjects.

Increased interhemispheric coherence in anterior regions has been consistently found. In view of the decreased frontal coherence in depressive illness cited below, QEEG separation of schizophrenic patients from bipolar depressed patients may be possible.

**Conclusion**

Evaluation of EEG and QEEG literature on schizophrenia is complicated by the evident heterogeneity of the illness and the diversity of medication histories and dosage levels at the time of examination. In spite of these potential sources of difference among findings, considerable agreement nonetheless appears.

Across a large number of EEG and QEEG studies, there is a broad consensus that schizophrenia shows a high incidence of EEG and QEEG abnormalities. Most often, the reported abnormalities have been delta and/or theta excesses in frontal areas, a decreased mean frequency and lower power in the alpha band, and increased beta power. Increased anterior coherence also has often been reported. Coherence measures may contribute to distinguishing bipolar disorder from schizophrenia.

- **Mood Disorders: Unipolar and Bipolar Depression**
The incidence of abnormal conventional EEG findings in mood disorders appears to be substantial, ranging from 20% to 40%2,97,146–148 higher in 1) manic than depressed patients, 2) female than male bipolar patients, and 3) nonfamilial cases with late-age onset. Whether an "abnormal" EEG is a necessary correlate of a clinically effective series of ECT treatment is controversial. This suggestion, like that made above regarding clozapine in schizophrenia, will require further study.

Specific patterns noted in mood-disordered patients include the controversial small sharp spikes (SSS), 6/s spike and wave complexes, and positive spikes, seen especially in patients with suicidal ideation.2,149,150 The SSS pattern appears often in bipolar patients and also in their first-degree relatives.151

Numerous QEEG studies have found increased alpha and/or theta power in a high percentage of depressed patients.8,19,152–157 Antidepressants reduce alpha activity,153,158–161 suggesting normalization of these deviant QEEG features (in contrast to the increased alpha caused by neuroleptics).113–115 Interhemispheric asymmetry, especially in anterior regions, has been reported repeatedly,162–166 as has decreased coherence.19,121,167 In bipolar illness, in contrast to unipolar depression, alpha activity is reduced155,168 and beta activity increased.5,19 This difference may serve to separate unipolar from bipolar patients presenting in a state of depression without prior history of mania.5,167

Current treatment of bipolar disorder often includes the use of the anticonvulsant medications carbamazepine and sodium valproate. The successful use of these agents suggests overlap between convulsive disorders and bipolar illness. Ruling out convulsive illness with EEG studies prior to initiation of anticonvulsant treatment in bipolar patients may be prudent.

- Conclusion

Both EEG and QEEG studies report that a high proportion of patients with mood disorders display abnormal brain electrical activity. EEG studies report that small sharp spikes and paroxysmal events are often found, especially on the right hemisphere, and that abnormal sleep studies are common.

There is broad consensus in QEEG studies that increases in alpha or theta power, as well as asymmetry and hypocoherence in anterior regions, appear most often in unipolar depressed patients. Bipolar patients often display decreased alpha but increased beta activity.

Mood Disorders: Anxiety, Panic, Obsessive-Compulsive, and Eating Disorders

Several studies suggest a high incidence of EEG abnormalities in patients with anxiety disorders, panic disorders, and obsessive-compulsive disorder (OCD).2,169–172 Diminished alpha activity has been found in anxiety disorder by using QEEG,173,174 and increased theta activity has been reported in OCD.175,176 Two subtypes of OCD patients
have been described. One, with increased alpha relative power, responded positively (82%) to serotonergic antidepressants, while the second, with increased theta relative power, failed to improve (80%). Epileptiform activity can occasionally be found in patients with tics (or stuttering), in addition to nonspecific diffuse slow activity. In patients with panic disorder, paroxysmal activity was four times more common than in depressed patients. Temporal lobe abnormalities, in particular, have been emphasized in QEEG studies in this type of patient.

In anorexia nervosa, abnormal background activity in the EEG can be seen in nearly 60% of patients, possibly related to the effect of starvation on cerebral metabolism. Paroxysmal abnormalities are seen in about 12% of these patients. In intractable binge eating, "soft" neurological and EEG signs can appear. Both anticonvulsant and antidepressant drugs have been helpful in some of these patients. Patients with eating disorders frequently give a history of physical or sexual abuse as children, so the increase in EEG abnormalities in this group may be related to their abuse history. Alternatively, dietary and nutritional deficiencies may contribute to altered brain function.

**Conclusion**

Although abnormalities have been reported repeatedly in EEG and QEEG studies of patients in the above categories, consistent patterns have not yet been discerned.

- **Developmental Learning Disorders, Attention Deficit Disorders, and Autism**

Specific developmental learning disorders (SDLD) are estimated to affect 4% to 6% of all school-age children. Attention deficit disorders with or without hyperactivity (ADHD or ADD) have a prevalence of 6% to 9% in school-age children. Although ADD/ADHD and SDLD are believed to be distinct neuropsychiatric entities, there is considerable comorbidity between the two disorders. Precise and accurate determination of the presence of ADD/ADHD versus SDLD can be of critical importance in avoiding the potentially devastating impact of these disorders on children and their families. EEG and QEEG can contribute usefully to this distinction as well as to separating children with social or motivational factors underlying school problems from those with organic dysfunction.

The conventional EEG has been reported to be abnormal in 30% to 60% of children with ADHD or with specific learning disability (SDLD or LD), as reviewed by several authors. Reported abnormalities have often included diffuse slowing and decreased alpha activity.

In QEEG studies, a high incidence of excess theta or decreased alpha and/or beta activity has been reported in SDLD children, with theta or alpha excess often seen in children with ADD or ADHD. The types of QEEG abnormality found in SDLD children are related to academic performance. A large percentage of children with attention deficit problems (more than 90%) show QEEG signs of cortical dysfunction, the majority displaying frontal theta or alpha excess, hypercoherence, and a high incidence
of abnormal interhemispheric asymmetry. Using QEEG measures, it has been possible to discriminate replicably ADD/ADHD versus normal children, with a specificity of 88% and a sensitivity of 94%, and ADD versus SDLD children, with a sensitivity of 97% and a specificity of 84.2%

The EEG is frequently abnormal in autism. In 14 studies encompassing approximately 800 patients, the mean incidence of abnormal EEGs was 50% (median 47%), but the range of values for the incidence of abnormalities was considerable (10%–83%). This large range undoubtedly arose from differences both in the populations under study and, more important, the criteria used for abnormality. EEG abnormality can help predict a poorer outcome with regard to intelligence, speech, and educational achievement. Although clinical seizures are uncommon in autism, epileptiform activity sometimes occurs.

- Conclusion:

Numerous EEG as well as QEEG reports agree that a high proportion of children with developmental disorders—among which learning disabilities and attention-deficit hyperactivity have received the most attention—display abnormal brain electrical activity.

There is a wide consensus that delta or theta excess and alpha and beta deficits are commonly encountered in children with learning disorders and that theta or alpha excesses are often seen in children with ADD/ADHD.

- Alcohol and Substance Abuse

The changes during acute alcoholic intoxication include the slowing of the EEG, seen in the form of decreased alpha frequency and abundance, an increased amount of theta, and even some generalized delta rhythms. These slow waves have a relationship with the degree of intoxication. The extent of the disturbance of consciousness is related to the amount of slow activity.

For chronic alcoholism, as in the acute stage, an increase in slow activity is often seen. This change appears as a decrease in alpha frequency and abundance, related to the typical blood alcohol level of a given patient, and also an increase in the theta rhythm, especially on the temporal areas. Temporal and frontal areas may also display an increase in fast activity related to the neuropsychological impairment, which must be distinguished from muscle artifact and often characterizes these records. Family history of alcoholism plays a prominent role in the risk of the disease. In the subacute encephalopathy associated with alcoholism, not only are slow waves noted, but epileptiform activity can also be seen, even as periodic lateralized epileptiform discharges (PLEDS).

Recent studies of substance abuse have largely relied on QEEG. Replicated reports have appeared of an increased beta (relative power) in alcohol dependence. Increased alpha power, especially in anterior regions, has been reported in withdrawal, as well as after acute exposure to cannabis. Increased alpha and decreased delta and theta have been reported in crack cocaine users in withdrawal.
Conclusion

There is a broad consensus that both EEG and QEEG reveal marked abnormalities in alcoholics and substance abusers. The effects vary depending on the drug. Either increased slow activity with lower alpha and beta or the converse have been reported; this reflects the diversity of substances or states focused upon.

However, among numerous QEEG studies, there is a consensus of increased beta relative power in alcoholism and increased alpha in cannabis or crack cocaine users.

- **Mild Head Injury or Postconcussion Syndrome**

Patients with complaints of cognitive memory or attentional deficit after mild head injury without loss of consciousness frequently present for psychiatric evaluation for worker's compensation and disability benefits. Objective evidence of brain dysfunction in such cases is critical in the endeavor to separate the truly dysfunctional patient from the malingerer. EEG/QEEG evidence can play a critical role in such cases. Although the absence of abnormal brain electrical activity cannot definitively exclude the possibility of brain dysfunction, the presence of abnormalities, especially those most frequently associated with unequivocal traumatic brain insult, must be considered supportive of such claims.

There is a high incidence of diffuse axonal injury, about 50%, in the 50,000 patients per year with head injury who recover; these patients characteristically do not display structural lesions on CT or even on MRI scans early after injury. Among those who recover after moderate head injury, 90% have cognitive or neuropsychological deficits. Among such patients, studies involving many hundreds of cases have reported normal neurologic examinations but abnormal EEG. Numerous EEG and QEEG studies of severe head injury (Glasgow Coma Scale [GCS] 4–8) and moderate injury (GCS 9–12), using samples of 50 to 200 patients, have agreed that increased theta and decreased alpha power and/or decreased coherence and asymmetry often characterize such patients. Changes in these measures provide the best predictors of long-term outcome.

The studies cited above generally concur that the most characteristic QEEG or EEG abnormalities persisting after mild or moderate head injury are similar in type to those found after severe head injury, namely increased power in the theta band, decreased alpha, low coherence, and increased asymmetry. It is noteworthy that similar EEG abnormalities have been reported in boxers, correlated with the numbers of bouts or knockouts, and in professional soccer players who were "headers." These observations lend further credibility to the multiple reports of discriminant functions based on QEEG variables that successfully separated normal individuals from patients with a history of mild to moderate head injury years after apparent clinical recovery.
Conclusion

The consistency of these EEG and QEEG findings is high across the range from mild to moderate head injury as well as in sports-related head impacts, and similar types of abnormalities are observed in patients with severe head injury as they recover.

There is a broad consensus that increased focal or diffuse theta, decreased alpha, decreased coherence, and increased asymmetry are common EEG indicators of the postconcussion syndrome.

- Three-Dimensional Statistical Probability Images: Source Localization and QEEG Tomography

In the last decade, the problem of three-dimensional localization of the sources of voltage fields detected on the scalp has been energetically attacked by mathematicians and physicists as well as neurophysiologists. Basic early approaches have been reviewed by Lütkenhöner et al.234 and Buckner et al.235

The initial success in applying these new source localization techniques to electrophysiological signals was achieved by brain electrical source analysis, or BESA.236–238 This method has received widespread acceptance for the separation and identification of highly localized dipole generators, such as focal epileptic discharges or spikes, and some neurosurgical centers have begun to use the method to pinpoint surgical targets in patients with intractable seizures.

Attention was directed next to localization of multiple sources, and then to the related problem of distributed sources, by the use of deblurring techniques.239,240 Approaches to the localization of distributed sources have been explored in simulations, in patients with space-occupying lesions, and in psychiatric patients. These approaches have included localization of the centroids of FFT power maps,241 frequency domain localization,234 linearly constrained minimum variance spatial filtering,242,243 recursive minimum norms,244 optimal resolution kernels and the resolution field,245,246 a Bayesian approach using anatomofunctional constraints,247 and combinatorial optimization applied to finite element models.235 Maximum likelihood procedures have been used to search for equivalent dipoles in 36 patients with space-occupying lesions. In 75% of these cases, the origin of deviant delta activity was localized near the center of the lesion volume, even in deep subcortical regions.248

Perhaps the most promising approach to the inverse solution of distributed sources is low-resolution electromagnetic tomography (LORETA),249 a generalized minimum norm technique that has been analytically compared with several different solutions to the inverse problem and shown to be optimal.250 It has been applied to the localization of intracranial epileptiform activity, using subdural electrodes to confirm inferences from scalp,251 and to localizing space-occupying lesions with known positions based on CT scans.248,252 Locations defined by LORETA were found to correspond well to the actual position of the abnormalities.
Using LORETA, a group of 9 never-medicated first-break acute schizophrenic patients was compared voxel by voxel with a group of 36 normal control subjects, indicating stronger activity in the right frontal regions but weaker activity in posterior regions in the schizophrenic patients than in the normal subjects.253 These findings were in agreement with reports of hyperfrontality in some schizophrenic patients.

Topographic mapping of quantitative electrophysiologic data has recently been extended to quantitative electroencephalographic tomography, or QEEG-T, by Valdes-Sosa.254 A standard probabilistic brain atlas in Talairach space, constructed from more than 300 MRIs of normal individuals,255 was evaluated, voxel by voxel, to constrain the hypothetical generators of the distributed inverse solution to gray matter. Regression equations were then computed for the log spectra of sources in every voxel of gray matter (3,500 voxels). These voxel-normative data spanned the age range 5 to 97 years and were calculated over spectra ranging from 0.39 to 19 Hz, in 0.39 Hz increments. Statistical probability tomographic images (SPTI) were then obtained by Z-transformation of each voxel of the raw LORETA image obtained from an individual with respect to the corresponding voxel-normative data. Spatial statistical methods evaluated deviations from the norms of regions of interest, and results were displayed on slices from the probabilistic atlas with each voxel color coded for statistical significance.

QEEG-T has been used to seek CNS signs of HIV infection.256 Observed changes were of particular interest because of similarity to those found with increasing cognitive deterioration in aging. When LORETA was used to study 319 elderly patients staged by scores on the Global Deterioration Scale, systematic changes in certain brain regions were found with increasing cognitive impairment.257

Positive findings with different anatomical distributions were also found among five subtypes of schizophrenic patients identified by cluster analysis,138 OCD patients who were responders or nonresponders to selective serotonin reuptake inhibitors,77 and children with ADHD who were or were not clinical responders to stimulant therapy.200

○ Conclusion

The combination of QEEG with the distributed inverse solution technology of LORETA, along with the projection of statistically evaluated voxel source values on a probabilistic MRI atlas, may extend the clinical relevance of QEEG, yield valuable insights into the pathophysiology underlying some psychiatric disorders, and provide clues useful for the rationalization of pharmacotherapy.

SUMMARY

- Both conventional EEG and QEEG studies provide valuable information to the psychiatrist regarding diagnosis and treatment responsiveness.
- Conventional EEG is most useful in the following:
  1. Identifying paroxysmal activity.
  2. Identifying gross alterations in the background frequencies of the EEG.
3. Identifying intermixed slow activity that may be related to delirium or dementia.
4. Evaluating sleep disorders.

- Conventional EEG assessments should be included in the diagnostic workup for the following:
  1. An acute confusional state.
  2. The first presentation of schizophrenia.
  3. A major mood disorder or mania.
  4. Refractory behavioral problems such as obsessions, violence, or panic.
- Quantitative EEG studies are particularly well suited to identifying subtle changes in the topographic distribution of background activity. They can aid difficult differential diagnoses, such as:
  1. Distinguishing between delirium or dementia and depression.
  2. Distinguishing between schizophrenia and mood disorders.
  3. Assessing cognitive, attentional, or developmental disorders.
  4. Distinguishing between environmentally induced and endogenously mediated behavioral disorders.
  5. Evaluating alcohol or substance abuse.
- In dementia, multiple articles appearing within the last 5 years strongly suggest that QEEG may enable early detection and prognosis of future cognitive impairment. Such information might aid in development of prophylactic rather than remedial pharmacotherapeutic interventions, intended to prevent or slow further progress of the illness.
- Some QEEG studies show promise of predicting the likelihood of response to a particular pharmacologic treatment and of monitoring responsiveness to treatment. The potential clinical value of QEEG procedures for analytic selection of the treatment most likely to be efficacious would be enormous in learning and attentional disorders and in schizophrenia.
- Considerable attention is currently being given to the correlation of EEG or QEEG brain mapping with other brain functional mapping methods such as PET, SPECT, and MRI. Methods have been developed for the estimation of three-dimensional electrical source distributions in the brain computed from scalp recordings. If these source localization methods can be validated by more direct brain imaging using functional and structural MRI, PET, and SPECT, low-resolution electrical tomography offers the possibility of readily available, low-cost functional 3D brain images computed from QEEG recordings.

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