



Introduction

Approach to the Diagnosis of Possible Seizures

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The patient with a “spell” of altered sensorimotor function, consciousness, or behavior presents a major diagnostic challenge, because the differential diagnosis is broad, the history is frequently sketchy, and the physical examination often is noncontributory (1,2). Under these conditions, the clinician must be able to recognize certain patterns from fragmentary clues. These patterns will point to a likely etiology for the episode and give a sensible structure to further evaluation.

Terminology in this area of medicine is confusing (3). In the following text, the word *seizure* is used to describe a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. The abnormal electrical activity may not be explicitly demonstrated, because electroencephalograms (EEGs) concurrent with the behaviors are usually lacking. If the etiology of a clinical episode is not epilepsy, then the word “seizure” should be avoided, and less specific terms should be employed. Imprecise terms also should be avoided during the evaluation of nonepileptic events. Patients sometimes refer to any event of catastrophic magnitude as a seizure or fit, such as “having a heart seizure” or “throwing a fit.” Physicians may tell patients that they have nonepileptic seizures as a face-saving device; unfortunately, use of the

word seizure may perpetuate the patient’s foggy understanding of the underlying condition. This term also has become synonymous for psychogenic nonepileptic events and, thus, should not be applied if an alternative physiologic etiology is suspected. The term “psychogenic seizure” literally connotes an epileptic seizure generated by psychologic factors—a rare entity indeed. The term “pseudoseizure” has, rightly, fallen out of favor because the modifier “pseudo” implies faking to some patients. The term “functional” is an entrenched synonym for psychologic and psychosomatic, even though patients with functional illness tend to be dysfunctional. Whenever possible, the suspected underlying physiologic etiology should be employed in the description of transient neurological events. Some episodes of altered consciousness result from seizures, but many do not.

Table I-1 lists the most important imitators of epilepsy. Perhaps the most common cause of transient alteration of consciousness is syncope, which broadly can be divided into cardiac and noncardiac etiologies. Causes of cardiac syncope can include arrhythmias, aortic stenosis, coronary syndromes, cardiomyopathy, pulmonary embolism, pulmonary hypertension, cardiac tamponade, aortic dissection, the long QT syndrome (LQTS), and the Brugada syndrome (4–6).

As a group, noncardiac causes of syncope are more common. This category includes neurally mediated

TABLE I-1
Imitators of Epilepsy

Syncope
Cardiovascular
Arrhythmias
Other cardiac and coronary syndromes
Circulatory obstruction
Noncardiogenic
Vasovagal syncope
Reflex syncope syndromes
Hypovolemic or hypotensive syncope
Transient ischemic attacks
Transient global amnesia
Atypical migraine
Vertigo
Toxic and metabolic
Hypoglycemia
Waxing and waning delirium
Alcohol or drug-related syndromes
Sleep disorders
Intermittent movement disorders
Breath-holding spells
Gastric reflux or esophageal spasm
Psychiatric causes
Nonepileptic events
Other conversion reactions
Panic attacks, anxiety, hyperventilation episodes
Depression
Malingering

reactive syncope syndromes, in which hypotension or bradycardia occur secondary to a precipitating stimulus. Examples include vasovagal syncope, carotid sinus hypersensitivity, and a variety of situational syncope syndromes including coughing, micturition, defecation, and swallowing (4–8).

Orthostatic hypotension is another important cause of syncope. It can be associated with autonomic dysfunction or be independent from it (8). Transient ischemic attacks (TIAs) in the anterior or posterior circulation can be confused with a seizure (9), as can transient global amnesia (10), drop attacks (11–13), and atypical migraine syndromes (14). A waxing-and-waning delirium can result from any of the many causes of metabolic encephalopathy, including hypoglycemia (15), as well as from a variety of toxic exposures, including alcohol (16) and the various drugs of abuse (17). Parasomnias, narcolepsy, and daytime hypersomnolence can all be associated with altered neurobehavioral function (18–20). Movement disorders associated with tics (21) or tremors and the paroxysmal kinesigenic dyskinesias (22) can all be confused with seizures.

TABLE I-2
Factors to Consider in Spell Diagnosis

Setting for precipitating factors
Prodrome
Time course
Stereotypy
Behavior during episode
Ameliorating factors
Nature of recovery

Dizziness and vertigo (23–25), if recurrent and transient, can raise the concern for the presence of a seizure disorder. In infants, relatively benign episodes such as breathholding spells (26) and gastroesophageal reflux (27) can precipitate an evaluation for seizures. Psychologic causes of altered neurobehavioral function include psychogenic nonepileptic events (28) and other conversion reactions, panic attacks, anxiety, and hyperventilation episodes (29–31), malingering, and depression. Each of these is considered in detail elsewhere in this volume.

EVALUATION OF THE PATIENT WITH SPELLS: HISTORY

The key features of a spell history include setting, prodrome, time course, stereotypy, precipitating and ameliorating factors, behavior during the episode, and the nature of recovery (Table I-2).

The history should be taken from the patient and from an observer, since an alteration of consciousness by definition impeaches a patient's capacity to fully describe the episode. With complex partial or absence seizures, and in some transient ischemic attacks, it is common for a patient to maintain that there was no loss of consciousness, whereas an observer will report a clear interval of partial or complete unresponsiveness. In spell diagnosis, a phone call to an observer is always a worthwhile effort.

Setting and Precipitants

The most useful diagnostic maneuver for the evaluation of patients with spells is an elicitation of a detailed description of the onset of symptoms. Information should be obtained regarding setting. Reactive syncope is characterized by hypotension or bradycardia occurring in the setting of a precipitating stimulus such as emotional upset, phlebotomy, coughing, urination, or defecation (7,8,32). Conversion reactions also can

be associated with altered neurobehavioral function. A few convulsive jerks in a setting suggestive of syncope simply may reflect convulsive syncope, secondary to transient hypoxia, rather than epilepsy (33–36). Even a new-onset generalized tonic-clonic convulsion can represent a cardiac etiology with prolonged ischemia (34). Confusion while fasting is likely to be from hypoglycemia. Loss of consciousness upon arising after prolonged bed rest probably is hypovolemic and hypotensive in origin. Breath-holding spells in children occur in a characteristic setting: the child works up to a temper tantrum, stops breathing, turns blue, and only then has a seizure (26). Individuals may, when asked, report anxieties or phobias leading up to the episodes, thereby suggesting functional etiologies, such as hyperventilation spells, panic attacks, or conversion syndromes. Vertigo may be precipitated by sudden changes of head position, for example, upon tilting the head back to change a light bulb in the ceiling. Rarely, loss of consciousness with head position change may be a consequence of sudden alteration of intracranial pressure, as with hydrocephalus (37), colloid cyst of the third ventricle (38), or Chiari malformation (39,40). Seizures sometimes imitate the catastrophic condition, brainstem herniation (41), and vice versa. Hypoglycemia occurs in a setting of fasting or reaction to a large carbohydrate load and should be considered when neurobehavioral disturbance occurs in this setting (15). Patients with diabetes or eating disorders are prone to hypoglycemia. Alcohol consumption may be difficult to ascertain by history, but heavy ethanol intake can predispose to alcoholic blackouts and spells from simple intoxication (16).

Seizures are notable for their spontaneous occurrence at unpredictable times, with the exception of a relation to the sleep–wake cycle or the menstrual cycle. Episodes that awake an individual from sleep are not likely to be functional. To apply this principle, the historian must be clear that the attack occurred during sleep, and not soon after arousal.

Patients and observers should be asked directly what was happening just before the attack occurred and whether they have an indication of what brought about the attack. As an illustration, consider a developmentally delayed young man who is seen for episodes of nondirected violence with lack of recall for the events. The question arises whether he is having seizures. Discussion with his counselors reveals that all his episodes occur at a time of frustration with his daily tasks or interactions with others; none occur spontaneously during peaceful times. This history would weigh against epilepsy as an etiology and argue strongly for a psychiatric-behavioral cause of the spells.

Hyperventilation spells are common (29–31,42). A history of heavy breathing in a setting of anxiety may point to hyperventilation as an etiology. Unfortunately, hyperventilation often goes unobserved, because the increase in respiratory rate can be subtle. Prodromes of lightheadedness and perioral or digital numbness should raise suspicion for underlying hyperventilation spells.

Experienced physicians maintain skepticism about reported precipitants of spells. Every seizure clinic is replete with patients whose attacks only occur when the moon is full, on a particular day of the week, when they are constipated, when the weather is hot (or cold), when their spouse is present, or when they are not in a physician's office. Functional episodes have variable onsets and precipitants, often highly idiosyncratic. Conversion symptoms and anxiety attacks, although related to levels of anxiety, often occur at quiet times. When informed that spells are "stress related," patients often argue that they take place at times when they are relaxed, cheerful, and engaged in mundane activities; watching TV appears to be a favorite. On the other hand, episodes that are consistently precipitated by stressful situations are likely to be nonepileptic, and they may be functional or migrainous. The relationship of stressful settings and immediate precipitation of physiologic seizures is weak.

Peculiar precipitants argue for functional etiologies. Syndromes of "reflex epilepsies" are exceptions to this rule (43). Approximately 3% of patients with epilepsy are likely to seize when exposed to flashing lights at photic frequencies of 5 to 20 per second (44). Unusual precipitants for reflex epilepsies have been documented: sounds (45), music (46,47), singing (48), reading passages of text (49,50), drawing (51), writing (52), eating (53–55), exposure to water (56) or a hot bath (57,58), blinking (59), eye convergence (60), talking on the telephone (61), or even certain stereotyped patterns of thought (62). In our experience, the majority of cases of unusual reflex precipitants are functional. Video-EEG documentation is required to characterize usual (nonphotic) reflex precipitants.

Factitious spells (malingering) usually occur in a setting of litigation, disability evaluations, avoidance of unpleasant duties, drug-seeking, or insurance disputes. The examiner should not be shy about eliciting a history of these factors. Nevertheless, physiologic illnesses, such as posttraumatic epilepsy (63) or posttraumatic migraines (64), may be present and call for an open-minded evaluation.

The ability to precipitate a spell by suggestion is a reliable indicator of a conversion syndrome. However, several subtleties are involved in the interpretation of

spell induction, and these are considered in a section below.

Prodrome

The nature of the start of an episode is most informative. Patients should be asked to describe the prodrome of their spells in detail. Certain auras are not only characteristic of complex partial seizures, but also can aid in localization. Such auras include gastrointestinal upset, body heat or tingling, perceptual distortions, *déjà vu*, and inappropriate emotionality (65–68). Vasovagal syncope usually is heralded by lightheadedness, anxiety, cold clammy skin, pallor, and slowing of the heartbeat (8). Cardiac arrhythmias may be associated with palpitations, but so can several other nonspecific conditions. Such symptoms can overlap with those seen at the start of a hypoglycemic episode (15), but hypoglycemia usually also carries a recognizable gnawing hunger. A narcoleptic attack is initiated by a sense of uncontrollable sleepiness. Vestibular disease presents a sense of spinning or tilting in space. The term “dizzy” requires elaboration in order to ascertain whether the patient means vertigo, connoting vestibular disorders, or lightheadedness, connoting presyncope, migraine, or functional episodes. Vertigo itself may derive from several conditions: most commonly, medication toxicity, alcohol, benign positional vertigo, vestibular neuronitis, Meniere’s syndrome, tumors or lesions of the vestibular nerve, brainstem or cerebellar disease, or vestibular migraine (24).

Complicated migraines present a wide variety of prodromes, but visual symptoms, such as shimmering lights, scotoma, or blurring of vision are common. Migrainous spells also can include more typical common migraine symptoms of headache, nausea, lightheadedness, or photophobia. The classic order of visual symptomatology followed by headache may not apply in practice; headache may precede, follow, or occur concurrently with other symptoms. Acephalgic migraine—migraine without headache—is a diagnostically difficult entity and probably more common than is generally recognized. The clinician should be aware of the ability of certain forms of complicated migraine to induce loss of consciousness (69,70).

Time Course

Epileptic seizures have a clear start and finish, usually lasting for a period of a few seconds to a few minutes. Episodes that fluctuate for hours either are exceptional cases of status epilepticus or, more likely, nonepileptic events. True status epilepticus, whether tonic-clonic or nonconvulsive, is a serious and disabling event. Patients

are slow to return to normal consciousness and function after status epilepticus. When in doubt, an EEG can be helpful in diagnosis. The EEG is always abnormal during status epilepticus, although tracings may reveal only nonspecific findings, such as slowing. The “reprise phenomenon,” by which a patient halts a spell, returns to relative normalcy, and then slips back into the episode, suggests a functional etiology. The famous artist Vincent van Gogh corresponded to his brother, Theo, about episodes of confusion, vertigo, distorted perceptions, and mood alterations lasting for days (71). Although van Gogh may well have had epilepsy, these particular episodes were much more likely generated by other causes, such as manic-depressive illness (72) or, less likely, vestibular disease (73). The time course was not consistent with seizures.

Unfortunately, many of the imitators of epilepsy exhibit time courses similar to seizures. Syncope, TIAs, confusional migraine, and sleep disorders can progress over an interval of seconds to minutes. In these instances, differential diagnosis must be based on other criteria.

Stereotypy

Stereotypy connotes similarity. Epileptic seizures in a given patient are fairly similar to each other. If there is an aura of heat and flushing prior to a seizure in some seizures, then this is likely to be the aura in all of those seizures exhibiting auras. Stated conversely, episodes with widely varying auras or behaviors are likely to be nonepileptic. An aura defines the site of seizure origin. Patients with true multifocal seizure origins are usually rather severely impaired, and diagnosis of epilepsy is not difficult. Exceptions do occur. The stereotypy of a true complex partial seizure will be altered by several factors: medication, environment, attentional state of the patient, and biologic variability.

Ameliorating Factors

Ameliorating factors consist of circumstances or activities employed by the patient to abort spells after they have begun. The clearest use of amelioration is paper-bag rebreathing to terminate a hyperventilation attack. Napping may terminate bouts of daytime hypersomnolence episodes or migraines, and food may shorten the duration of hypoglycemic episodes. The head-down position reverses symptoms of hypovolemic or vasovagal syncope. Lying still, perhaps in a specific posture (good ear down for benign positional vertigo), may reduce symptoms of vertigo. Anxiety attacks sometimes can be ended by relaxation exercises. Abstinence from alcohol consumption or from use of illicit drugs serve

for both diagnosis and treatment of spells related to substance abuse. Rare patients with epileptic seizures can inhibit their seizures with sensory stimulation (74). The experience of being in the hospital may in itself decrease seizure frequency (75).

Behavior during Episode

The appearance of an episode is one of the least reliable methods for diagnosing epilepsy. The entertainment industry has shown that actors convincingly can imitate seizures. Some patients are excellent actors. Additionally, the wide variety of behaviors seen during complex partial seizures grants great latitude to the appearance of a possible seizure. Chapter 3 lists a variety of behaviors observed in an epilepsy monitoring unit during seizures with documented concurrent EEG changes.

Although a variety of diagnostic strategies may be employed, beyond the history itself, video-EEG monitoring remains the most useful method for differentiating epileptic from nonepileptic events (76). Certain behaviors recognized since the days of Sir William Gowers (77) are unlikely to occur during an epileptic seizure. Video-EEG monitoring has been used extensively to catalog correlates of seizures with no EEG changes. Abrupt onset of unresponsiveness, thrashing and uncoordinated movements, rocking movements, and pelvic thrusting are particularly common in psychogenic seizures (28, 78–81).

Preservation of consciousness is impossible during a generalized tonic-clonic seizure. Patients who recall events or conversations transpiring during their generalized seizure are experiencing psychogenic or other nonepileptic episodes. This rule only applies to the period of diffusely generalized seizurelike activity, and it must be applied with caution. Many people with secondarily generalized epilepsy recall their auras or focal motor onsets. Rare cases exist in which preservation of awareness exists during bilateral tonic or clonic motor activity, presumably because of linked bilateral motor cortex seizure foci. Vague recollections of the postictal state also are physiologic. The definition of complex partial seizures requires only an alteration of consciousness, not its absence. Preservation of some awareness and (usually distorted) recall for events during a partial seizure does not rule out a diagnosis of epilepsy. Similarly, awareness and ability to recall is partially present at the start of absence seizures. Penry and associates (82) showed that stimuli presented within a few seconds after onset of EEG spike-wave discharges often were recalled; stimuli presented after more than 10 to 20 seconds of spike-waves were not.

Attention to Tasks during an Epileptic Seizure

Volitional behavior should not occur during a generalized seizure. A conversion syndrome is likely if a patient resists forcible eye opening during a generalized tonic-clonic epileptic seizure, avoids dropping limbs on the face, follows objects visually, turns repeatedly away from the examiner, preserves modesty, startles to a loud noise, or resists tickling. Conversely, failure to perform any of these actions does not rule out a conversion syndrome. Volition may be preserved in partial seizures, but it is usually of a rudimentary type.

Health care personnel inadvertently train patients in seizure behavior with leading questions. With little active intent on the part of the patient or physicians, conversion syndromes may be honed to a fine imitator of epilepsy. In such cases, even experienced clinicians may be incorrect about whether an observed episode was a seizure or conversion episode, with diagnostic errors in both directions.

Directed violence is not an expected component of epileptic seizures. Numerous defendants have employed the so-called “epilepsy defense” to explain a criminal act (83). The majority of such attempts have been unsuccessful, because most criminal acts involve complex behavior with considerable planning and cognition. A person cannot purchase a gun, drive to the victim’s house, aim, and shoot during an epileptic seizure. However, aggressive acts that require little thought, such as pushing, hitting, grabbing, or shouting, are possible during seizures or the stage of postictal delirium.

Automatic behaviors can be performed during complex partial seizures. A task such as dishwashing could be completed during a seizure, although the task might be carelessly performed. Patients with complex partial seizures have been known to drive or walk home during a seizure, or find themselves in an unfamiliar location after a seizure. Such instances probably occur because complex partial seizures can disrupt memory acquisition. Responsiveness and behaviors may be relatively normal; they are simply not recalled. Similar phenomena are observed in cases of transient global amnesia.

Seizures originating in the frontal lobes present special problems in diagnosis (67, 84, 85). Perhaps the best example of this difficulty is the case of autosomal dominant nocturnal frontal lobe epilepsy (86). Previously known as paroxysmal nocturnal dystonia, this familial epilepsy syndrome was also often mistaken for night terrors or psychogenic events, but ultimately was determined to be due to a mutation in the alpha-4 subunit of the neuronal nicotinic acetylcholine receptor (87). Frontal lobe seizures characteristically are brief, associated with minimal loss of consciousness and quick return to consciousness, and may show atypical

behaviors, such as unusual facial expressions, twisting or posturing (supplementary motor cortex seizures) (88), or odd vocalizations. Their frequency can exceed dozens per day. Ictal EEG recordings may be negative during brief seizures from deep frontal foci, and serum prolactin levels from such seizures do not necessarily rise (89,90). As such, frontal lobe seizures are particularly likely to be incorrectly labeled as conversion reactions. The most difficult diagnostic cases require video-EEG monitoring, with careful direct observation.

Nature of Recovery

Immediate recovery after an apparent generalized tonic-clonic seizure favors a functional etiology. But this rule does not hold for all conditions producing loss of consciousness. Rapid recovery is common after syncope or positional vertigo. Postictal dysfunction following epileptic seizures can be divided broadly into early, intermediate, and prolonged effects. Early postictal disturbance is common in the first hour, particularly after complex partial seizures, and may include somnolence, disorientation, memory impairment, headache, and focal deficits such as paresis (91,92). Intermediate duration postictal deficits may last hours or even a few days. Postictal paresis is referred to as a Todd's paresis (92,93). Prolonged postictal dysfunction can be seen after seizure clusters or status epilepticus, in patients with underlying encephalopathy, and in the elderly. Manifestations include postictal encephalopathy (94), prolonged postictal paresis (95), and postictal psychosis (96). Conversely, an extremely prolonged recovery of a focal deficit might suggest that an episode was ischemic rather than convulsive. The coexistence of cerebral ischemia and epilepsy is possible, because cerebrovascular disease may be the most common identifiable etiology of new-onset epilepsy in the elderly. Unfortunately, clinicians have no easy method to determine whether prolonged limb weakness is a consequence of ischemia or a Todd's paresis. Further complicating the issue are rare seizures presenting primarily as hemiparesis (97,98).

EVALUATION OF THE SPELLS PATIENT: EXAMINATION

The key to spell diagnosis usually is in the history. The physical examination is of relatively limited value in the diagnosis of epilepsy, unless the examiner is able to examine a patient during a spell. Astute examiners rarely may observe clues to a syndrome associated with epilepsy, such as multiple café au lait spots or adenoma sebaceum, suggestive of tuberous sclerosis (99), or papilledema, indicative of increased intracranial pressure. Physical findings are more useful in diagnosing

TABLE I-3
Useful Physical Exam Maneuvers
in Diagnosis of Spells

MANEUVER	CONDITION
Orthostatic blood pressures	Syncope
Listen for bruits	Cerebrovascular disease
Heart sounds	Arrhythmias, embolic sources
Check for nystagmus	Vestibular disease
Dix-Hallpike maneuver	Benign positional vertigo
Hyperventilation	Hyperventilation spells
Observe for sleepiness	Hypersomnia
Tics, tremors, chorea	Movement disorder
Mental status exam	Delirium
Nonphysiological findings	Functional disorder
Psychiatric screen	Affective or thought disorder

certain imitators of epilepsy. Table I-3 lists several potentially useful maneuvers and associated conditions. Predisposition to various forms of syncope can be detected by physical examination (4,8). Orthostatic blood pressures, allowing for at least 1 minute of standing, should be measured in patients thought to have hypovolemia or autonomic insufficiency. Cardiac auscultation may point to arrhythmias or valvular disease. Circulatory obstruction from such rare (in this setting) causes as tension pneumothorax, pericardial tamponade, or pulmonary embolus, can be detected by the cardiorespiratory examination. Transient ischemic attacks of the cerebral circulation are common. The presence of vascular bruits and abnormal peripheral pulses may provide indirect evidence for cerebrovascular disease. Abnormal sleepiness sometimes can be detected in clinic, once the clinician has calibrated the usual soporific potency of his or her clinic routine. Patients in a waxing-waning delirium show fluctuating alertness and cognition. Nystagmus and past-pointing with the eyes closed can be indicative of vestibular disease, mistaken for epilepsy.

Anticonvulsants produce nystagmus, even in therapeutic doses; however, anticonvulsant-induced nystagmus is usually direction-changing with gaze and relatively symmetric upon looking left or right. Nystagmus from vestibular disease is most often asymmetric with directions of gaze and often comprises a rotatory component (24,100). The Dix-Hallpike maneuver, with rapid head tilt posteriorly and laterally, may bring out subtle nystagmus in positional vertigo (100). Examination for nystagmus with the ophthalmoscope may also be useful (101). Caution is indicated, because vestibular

symptoms are a recognized aura for certain complex partial seizures. With complex partial seizures, however, consciousness is altered.

A neurologic examination is useful for detection of movement disorders that might be confused with seizures. The examiner may observe tics, tremors, abnormal postures, dystonia, chorea, athetosis, myoclonus, or ballismus, suggestive of basal ganglia or motor system disease. Movement disorders often are intermittent. The distinction between certain abnormal movements and simple partial motor seizures can be difficult.

Certain patients with conversion symptoms or malingering exhibit nonphysiologic physical findings. Such findings include exact splitting of the midline with a sensory exam; regional anesthesia with preserved coordination of the impaired body part; dense numbness not corresponding to dermatomes, nerve plexi, or peripheral nerves; cylindrical tunnel vision; blindness with preserved visual fixation; distractible paralysis; and a variety of other findings.

INDUCTION OF EPISODES

It is useful to attempt the induction of an episode. This process begins by asking the patient or observers what conditions were present at the onset of the attack. These conditions should then be replicated if possible. If an attack occurred upon assuming the upright position or tilting the head back and to the left, the patient should be asked to do so in clinic. A diagnosis of orthostasis or vertigo, respectively, may emerge. Anxiety attacks related to phobias occasionally can be precipitated by putting the patient in a stressful situation.

Hyperventilation is an essential diagnostic maneuver for presumed hyperventilation spells. The procedure should be explained in advance, in clear and honest terms. In our practice, patients are told that subtle increases in rate or depth of breathing can lower the carbon dioxide in the blood, and that this in turn can alter the brain's circulation and chemistry. Hyperventilation can precipitate seizures or episodes that imitate seizures, without awareness by the patient of alterations in breathing patterns. The patient is then asked to breathe rapidly and deeply through the mouth, for a continuous time of at least 4 minutes, or until they become too symptomatic to persist. Most people become lightheaded and develop perioral or digital paresthesias during vigorous hyperventilation. A positive hyperventilation study is one that replicates the sensations and symptoms of a spontaneous spell. If a hyperventilation test is positive, the test should be repeated with attempted spell abortion by paper-bag rebreathing. The paper (never plastic!) bag over the mouth and nose recirculates exhaled carbon dioxide

and rectifies hyperventilation-induced hypocarbia. Prolonged bag rebreathing does carry a potential risk for hypoxia (102) and, therefore, should be performed cautiously. Elimination of symptoms with bag rebreathing further supports a diagnosis of hyperventilation attacks and leads immediately to a therapeutic option for the spells. True absence seizures can be precipitated by hyperventilation. Precipitation of other seizure types is possible, but less common. To clarify ambiguous responses, hyperventilation can be performed with concurrent EEG monitoring.

Induction is a useful technique for the diagnosis of functional episodes (103,104). Patients with conversion symptoms may be very suggestible, allowing the induction of "psychogenic seizures" in clinic. The ability to precipitate and terminate a seizurelike episode by suggestion is strong evidence for a functional etiology. Several different methods for spells induction have been suggested. The precise method is not critical, but adherence to a few principles is very important. First, trickery and dishonesty should be avoided. We do not favor placebo injections. They may document conversion symptoms, but at the same time they can destroy the patient's trust of medical personnel. Such a loss of trust complicates subsequent medical care. Second, the patient should agree to allow a spell to be precipitated. Spell induction is a form of hypnosis (104), and like hypnosis, the patient must be guided rather than forced to an outcome. It is helpful to explain to the patient that observation of an attack is useful for diagnosis and therapy. Treatment must be directed to the right cause. On this occasion, perhaps the patient would be willing to allow an attack to occur in order to be able to choose the best treatment. A simplified list of possible etiologies can be presented in advance, including seizures, circulation problems, and subconscious psychologic (stress-related) causes. If the patient refuses to allow spell induction, we do not press the point, because failure is likely. On the other hand, induction often is successful in patients with psychogenic episodes who cooperate with induction.

In our clinic, induction is performed with a combination of hyperventilation and suggestion. The hyperventilation is used for dual purposes: testing for hyperventilation spells and as a general dissociative stimulus for the precipitation of any conversion symptom. The "dreamy-dizzy" state produced by hyperventilation provides a receptive condition for suggestion. Reassuring and positive statements are made during the hyperventilation: "You will soon be feeling dizzy"; "It will be difficult to feel your fingers"; "Soon you will start to feel strange." Such statements simply reflect the usual concomitants of hyperventilation, but they demonstrate to the patient that something is happening.

The patient is then told to nod his head as soon as he feels that his spell is coming on, so a notation can be made. The positive emphasis is on when he feels symptoms, not if he feels symptoms. Improvisation directed toward specific symptoms of the patient's reported attacks is useful. If attacks begin with left hand trembling, the examiner may comment that the left hand appears to be tremulous, or perhaps the examiner may even start it shaking to bring on the attack. Once an attack is sufficiently developed to allow characterization, suggestion is used to bring the patient back to baseline. An instruction is given to relax, breathe slowly, and let the spell pass. Encouragement is given that things are settling down. An alternative methodology uses guided imagery to produce an episode.

The next important principle of spell induction is that diagnosis occurs primarily in the "debriefing" session after an induction. It is not appropriate to induce peculiar behavior and conclude that a patient does not have seizures. The seizure may differ from the induced spell. When conversant, the patient should be asked how the episode that just took place was similar to and how it was unlike a typical spontaneous episode. A ranking of 0–10 on a scale of 0 (not at all like the spontaneous attack) to 10 (identical to the spontaneous attack) may be useful. Sometimes patients volunteer that the symptoms are stronger or weaker than a typical spell, but otherwise similar. Friends and relatives also may be asked to give opinions on similarity of an induced and spontaneous episode.

After an induction, immediate feedback should be given to the patient. If nothing resembling a typical spell occurred, we remark that hyperventilation does not seem to be a precipitating factor for the episodes. If the induction produced a psychogenic episode, then we inform the patient that the episode observed did not have the appearance of an epileptic seizure and that further evaluation is warranted. The possibility of psychologic etiologies is raised as an issue for further exploration. It is never possible to be certain that a patient does not have epilepsy, only that observed episodes are not seizures. This issue is discussed further in Chapter 4.

ROUTINE LABORATORY AND NEUROIMAGING TESTS

Most routine laboratory and neuroimaging studies contribute to the diagnosis of spells primarily by helping to rule out other etiologies. EKG, cardiac Holter monitoring, CXR, or ventilation-perfusion lung scans may be diagnostic of cardiac-induced episodes. Serum glucose can point to fasting hypoglycemia, or an abnormal glucose tolerance test may reveal reactive hypoglycemia. Glucose tolerance testing would be done only for a high

index of suspicion based on the clinical history. Spells thought to be related to alcohol or drug abuse can be investigated by toxic screens of blood or urine. An impression of vestibular disease can be investigated with quantitative calorics and nystagmography. No blood tests or special diagnostic studies are presently widely accepted for the diagnosis of complicated migraine, although provocative tests, such as the histamine challenge, have been advocated by some. In general, routine laboratory studies and neuroimaging should be performed selectively in diagnosis of spells, based on a suspicion for particular etiologies.

Serum Prolactin

The measurement of serum prolactin is a useful blood test in diagnosing seizure disorders. Prolactin is a polypeptide hormone produced by the anterior pituitary, involved in milk production and endocrine function. Unlike most pituitary hormones, prolactin is under negative hypothalamic control via prolactin inhibiting factor. When seizure activity influences the hypothalamic-pituitary axis, prolactin inhibiting factor is presumed to be inhibited itself, and prolactin is released into the circulation. Trimble (105) first showed that serum prolactin rises with generalized epileptic seizures, but not with psychogenic seizure-like episodes. Complex partial seizures can also raise serum prolactin. Sensitivity is approximately 90% for tonic-clonic seizures and 70% for complex partial seizures (106). Complex partial seizures originating in the frontal lobes rarely elevate serum prolactin (89,90), again emphasizing the difficulty in diagnosis of frontal lobe epilepsy. Several conditions can generate false-positive elevations of serum prolactin (see Chapter 5), including: stress, surgery, general anesthesia, strenuous exercise, sleep, orgasm, breast stimulation, estrogens, endometriosis, primary hypothyroidism, prolactin secreting pituitary adenomas, multiple sclerosis, phenothiazines and butyrophenones, opiates, L-DOPA, bromocriptine, other ergots, apomorphine, metoclopramide, and some antiepileptic drugs. Therefore, acute rises of two to three times the baseline levels are more specific for the diagnosis of a seizure than is an elevated single serum level (106).

Serum prolactin elevations reach a peak 10 to 20 minutes after a seizure and return to baseline by 60 minutes after a seizure (107). This imposes a practical limit on the use of prolactin to diagnose epilepsy, because most spells occur away from a medical setting. We have shown that prolactin accurately can be assayed by pricking the finger and applying capillary blood to filter paper (108). The specimen is stable at room temperature for a week and may be analyzed at leisure. This finding opens the possibility of using a suitable kit in the

home or work setting to determine if infrequently recurrent spells are seizures. One remaining limitation of prolactin for diagnosis is a lack of available data on prolactin levels after several of the imitators of epilepsy, including cerebrovascular ischemia or migraine.

Electrodiagnostic Monitoring

The routine EEG is useful for diagnosing spells, but the interpretation of the EEG must be cautious. Many normal variants, such as asymmetrical vertex waves, wicket spikes, small sharp spikes, 14- and 6-per second positive spikes, and rhythmical temporal theta bursts of drowsiness (formerly called psychomotor variant), can be mistaken for interictal spikes and sharp waves (109; and see Chapter 1). Additionally, a few percent of the normal American population exhibit interictal epileptiform discharges in a baseline EEG (110,111). The combination of an ambiguous history for a seizure and normal variants in the EEG can be an invitation to inappropriate treatment. Conversely, many individuals who have epilepsy lack abnormalities on an interictal EEG (112). Repeat EEGs to a total of about four EEGs may increase the yield (113). Other procedures useful for eliciting abnormalities in the EEG are activating procedures such as sleep deprivation or use of extra scalp (114) or sphenoidal electrodes (115). Prolonged digital EEG recordings may be performed in the ambulatory setting (116). Ambulatory EEGs are useful in capturing spells, but care must be taken in interpretation, because they are very subject to movement artifact.

As discussed in Chapter 16, sleep studies are of value when the history suggests hypersomnolence as a possible etiology of an episodic disorder of consciousness (18–19). A sleep disorder mimicking epilepsy should not be mistaken for a seizure disorder linked to the sleep cycle (117,118).

Inpatient video-EEG monitoring is one of the most powerful methods for diagnosis of spells with altered neurobehavioral function (119–121). Such monitoring extends the eyes and ears of the clinician. Depending on the question being asked, long-term epilepsy monitoring can be helpful in establishing a diagnosis, in seizure classification, in the localization of seizure foci in presurgical evaluations, and in quantification of seizure activity (121). However, in monitoring units, EEG changes rarely provide a diagnosis for the many imitators of epilepsy.

PITFALLS IN DIAGNOSIS OF EPILEPSY

When epilepsy presents in a classical fashion, with recurrent complex partial or tonic-clonic seizures, accompanied by interictal epileptiform EEG patterns,

TABLE I-4
Pitfalls in Diagnosis of Epilepsy

Obtaining an inadequate history
Overemphasizing the rare and obscure
Leading the patient to an inaccurate history
Mixed seizures and psychogenic seizures
Over-reading the EEG
Overinterpretation of a therapeutic trial
Incorrect attribution of causation

the diagnosis is easy. Unfortunately, the history may be incomplete, or other medical conditions may confound the clinical picture. In these circumstances, the diagnosis of epilepsy depends on the clinical judgment and experience of the practitioner. Several potential diagnostic pitfalls are to be avoided (Table I-4).

The cardinal error is obtaining an inadequate history. Observers of spells should be queried directly. “Dizzy spells” without loss of consciousness may be revealed by co-workers to be full tonic-clonic seizures. Diagnosticians should not train patients to give a textbook seizure history. By the time multiple physicians have asked a patient if they have ever experienced an odor “like burning rubber” at the start of their seizure, most patients have convinced themselves that they have.

The improper interpretation of an EEG can cause great harm. Many benign and normal variant patterns can be mistaken for epileptiform discharges (109). The combination of a shaky history and an overinterpreted EEG is especially pernicious. The diagnosis of epilepsy may suffer from incorrect attribution of causation. Focal seizures can cause a postictal transient hemiparesis (Todd’s paresis) (92,93), but cerebrovascular insufficiency can directly cause hemiparesis and a seizure (122). Bilateral carotid occlusive disease can cause brief loss of consciousness (123). Distinguishing primary epilepsy from epilepsy secondary to cerebrovascular disease can be difficult. A setting conducive to cerebrovascular disease is influential, as is rate of recovery (more rapid after seizures), a history of prior seizures, TIAs, or strokes. Similarly, seizures can induce cardiac arrhythmias (124), as well as result from them (125).

The novice diagnostician tends to overemphasize the rare. Most staring spells are simple daydreaming. Most explosive outbursts in children are temper tantrums. Most episodes of a previously well person losing consciousness and falling to the ground are syncope. The diagnostic probabilities are altered when it is known that an individual suffers from epilepsy. As an example, temporal lobe seizure (78,126) should be considered as an etiology of loss of consciousness in a per-

son with known complex partial epilepsy; however, it should be far down on the differential diagnosis of syncope in a person with no prior history of seizures. Primary pain is a rare symptom of epileptic seizures (127–129), and seizures should not be on the usual differential diagnosis of pain.

The most difficult diagnostic cases tend to be those with mixed disorders. A certain percentage of individuals with documented psychogenic seizures may, at other times, exhibit epileptic seizures. The incidence of mixed epileptic and nonepileptic events has been estimated, at times, to be as high as 37% (130) but is more likely 10% or less (131,132). In these cases, it may be that the epileptic seizures and their aftermath somehow became a “template” for subsequent nonepileptic spells. By documenting lack of EEG changes during a generalized seizurelike episode, video-EEG monitoring can show that the episode under observation is nonepileptic in etiology, but it can never prove the etiology of prior episodes. Inference by analogy is imprecise. Even after establishing a diagnosis of nonepileptic attacks, the experienced clinician remains vigilant for the possibility of a mixed disorder. As a practical matter in this circumstance, it often suffices to remove anticonvulsants with the understanding that epileptic seizures may emerge and require reevaluation.

The improvement of spells with anticonvulsants gives incomplete testimony as to the nature of the disorder. Placebo effects are significant in any medical disorder, and especially in those with psychogenic components. The efficacy of antiepileptic drugs is not limited to seizures. Carbamazepine and sodium valproate have long been recognized as useful mood stabilizers (133,134). Of the newer antiepileptic medications being used for mood stabilization, evidence is available for lamotrigine (135–137). Limited supportive information is available for topiramate, oxcarbazepine, zonisamide, and tiagabine (137), while gabapentin has mixed reviews (138,139) for mood stabilization. Phenobarbital and benzodiazepines are effective both as anticonvulsants and as tranquilizers. Phenytoin can suppress ventricular arrhythmias. When a positive response to an antiepileptic agent is encountered, the clinician should consider what else besides epilepsy might be under treatment. Conversely, some patients with presumed epilepsy worsen with increasing doses of antiepileptic drugs. This can be a clue to underlying psychogenic seizures (140).

CONCLUSION

The diagnosis of a patient with “spells” usually can be obtained with a careful review of the history, physical examination, and judicious use of testing (141). The key

is an awareness of the types of conditions that can imitate epilepsy and their presentations. The nature of precipitating factors and the detailed appearance of the episode narrow the differential diagnosis. Occasionally, physical findings and laboratory tests, such as routine or special EEG studies, are of value, but they should be employed selectively and in the clinical context. A careful ear, an observant eye, an open mind to multiple possibilities, patience, and good clinical judgment usually lead to the correct diagnosis.

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