Acute Seizure Problems

CARY SUTER, M.D.

Professor and Chairman, Department of Neurology, Medical College of Virginia, Health Sciences Division of Virginia Commonwealth University, Richmond, Virginia

Seizures are a symptom and not a disease. A seizure is the result of an abnormal electrical discharge of a collection or group of living but damaged or abnormal neurons. When the group of neurons is in the cerebral cortex, a focal or partial seizure occurs, producing abnormal activity related to that part of the brain. The victim may experience a focal jerking or focal numbness, or flashing lights if the lesion is in the occipital lobe; or he or she may be subject to peculiar automatic behavior if the lesion is in the temporal lobe. When the activity spreads to the central portions of the brain in the thalamus and upper brain stem, neurons in this area discharge, producing unconsciousness and a generalized convulsive or generalized nonconvulsive seizure. Abnormality of neurons in the central part of the brain (centrencephalic system) will, of course, produce generalized seizures without a focal beginning. Despite the fact that a seizure is only a symptom, many persons, including physicians, find seizures frightening and there is almost a reflex reaction to stop the seizure at all costs. For this reason, individual episodes of seizures are often over-treated with sedative and anticonvulsive drugs without due regard to the underlying disease, and without an orderly plan of drug therapy.

Acute seizure problems include a variety of conditions that demand immediate attention to obtain the most accurate diagnosis and treatment. These include:

1. Convulsive Status Epilepticus
   a. Motor status (Jacksonian status)
   b. Epilepsia partialis continua
   c. Status myoclonus
   d. Status with secondary generalization
   e. Focal motor with secondary generalization
   f. Focal adversive with secondary generalization

2. Generalized
   a. Primary generalized
      a. Tonic-clonic status (grand mal status)
      b. Status myoclonus
      c. Status with secondary generalization
      d. Focal motor with secondary generalization
      e. Focal adversive with secondary generalization

II. Nonconvulsive or Stupor Status Epilepticus
1. Absence status (petit mal status)
2. Psychomotor status

III. Other Types of Seizures
1. Seizures in the newborn
2. Febrile seizures
3. First or single seizure
   a. Childhood
   b. Teens
   c. Adults
   d. Elderly
4. Withdrawal seizures
5. Hysterical attacks

These conditions will be discussed with special emphasis on drug therapy and diagnosis of underlying disease in convulsive status epilepticus.

I. Convulsive Status Epilepticus
The most serious acute seizure problem is that of status epilepticus, particularly generalized convulsive status epilepticus. This condition has been defined as the occurrence of repeated generalized convulsive seizures without the patient regaining consciousness between attacks and with the seizures and unconsciousness lasting longer than thirty minutes. Though such continued seizures may cause additional brain...
damage, the major concern actually has to do with the primary cause of the unconsciousness. Acute disease states such as poisoning, encephalitis, drug withdrawal, hypoglycemia, or hypocalcemia may all produce repeated convulsive seizures without the patient regaining consciousness. When confronted with such a problem the physician should quickly observe the patient's attacks to see if there is any evidence for focal beginning or any indication that the attack might be hysterical. The physician should examine the patient quickly to see if there are any clear focal or lateralizing signs such as a dilated pupil or a unilateral Babinski sign; the presence of fever should be noted. Most important of all, the physician should not panic and should not immediately treat the patient with a large injection of medication.

First, blood should be drawn for chemical analysis. A tube of blood should be saved for toxicology study and also blood for serum determination of anticonvulsant drugs. Next, an intravenous infusion should be started and the patient should be given intravenous glucose up to 1 gm/kg of weight as a 25% or 50% solution; for infants, calcium gluconate is often given. The patient may become cyanotic during the tonic phase of the convolution, but respiratory assistance is seldom necessary. An oral airway may be inserted and mechanical respirator support should be available if required, particularly after giving anticonvulsant medicine. Only after these measures are taken should drug therapy begin. Except in unusual cases, the drug therapy will be nonspecific and symptomatic and aimed solely at reducing the frequency and severity of the convulsive seizures as attempts are made to diagnose the underlying cause.

**Drug Therapy.**

At the present time in the United States there are three main drugs available for the treatment of status epilepticus. These are phenobarbital, diazepam (Valium), and phenytoin (Dilantin).

**Phenobarbital:** Phenobarbital is the oldest, safest, and most commonly used anticonvulsant for control of status epilepticus. It does produce some respiratory depression and also some sedation, but it has a relatively long-lasting anticonvulsant effect. Maximum concentration in the brain is not achieved until nearly one hour after administration. The most common mistake in giving phenobarbital for status epilepticus is to give it in doses that are too small and do not represent an adequate loading dose. The intravenous dose should be a total of 5 to 15 mg/kg; in an adult this should be given in single doses of at least 240 mg to 360 mg at a time, and repeated in 30 to 60 minutes. In infants it can be administered as a slow intravenous infusion until a total of 10 to 15 mg/kg has been given. In many respects phenobarbital remains the most universally useful, safest drug for status epilepticus and is usually the best drug for use in the neonate and infant. At any age, if phenobarbital in adequate doses is not effective, then it should be followed either with phenytoin, paraldehyde, or some short-acting anesthesia with respiratory support of the patient. An injection of diazepam after the patient has already been given phenobarbital carries considerable danger of respiratory arrest.

**Diazepam (Valium):** Since its introduction by Gastaut in 1965, diazepam has become very popular as a treatment for status epilepticus. It is a rapidly acting drug and the speed with which it stops the seizures has a reassuring effect upon the physician. Unfortunately, the fact that the seizure stops so quickly may lull the physician into an unrealistic sense of security and keep him from pursuing the underlying cause of the status epilepticus with sufficient diligence. Diazepam can be given in a total dose of 0.25 to 0.5 mg/kg. A starting dose of 10 mg given intravenously at the rate of 1 mg/min is often sufficient to stop the clinical seizures, at least temporarily. This dose may then be repeated if the seizures recur.

Respiratory arrest is often a side effect of diazepam injection, particularly if the patient has previously received barbiturates. Hypotension also occurs at times. For this reason diazepam should be given with respiratory assistance at hand. To maintain long-term control of the seizures, drugs such as phenytoin often have to be added.

**Phenytoin (Dilantin):** Until recently, phenytoin was not considered a first-line drug in the treatment of status epilepticus. Recently, however, a number of physicians have used phenytoin as the first and only drug in the treatment of status epilepticus and reported excellent results. To be effective, phenytoin needs to be given intravenously in a so-called loading dose which is between 10 and 15 mg/kg. The danger of intravenous phenytoin injections is that of cardiac arrhythmia and occasional cardiac arrest. It is best to give phenytoin with a cardiac monitor and to stop the injection if any evidence of arrhythmia develops. There are reports of giving a single loading dose of 700 to 1,000 mg of phenytoin without complication, but we have had a personal experience with a fatal
cardiac arrest giving this amount as a single injection. It is probably safer to figure the total loading dose and give it in either two or three separate intravenous infusions, perhaps 30 to 60 minutes apart. In adults a total dose of 400 to 500 mg can be given at once (at 50 mg/min), and later an additional amount to bring the total up to the calculated loading dose.

The advantage of phenytoin is the fact that it has a relatively long duration of action when given in a loading dose and also that it does not produce the amount of sedation produced by a larger dose of either diazepam or phenobarbital.

**Other Drugs Used in Status Epilepticus:** Paraldehyde is a very effective anticonvulsant given rectally or intravenously. It can be given intravenously in a diluted solution in normal saline with the usual dose being 4 to 6 cc of paraldehyde. It should not be given to adults in the emergency room due to the possibility of giving the drug to a patient with alcohol still in the bloodstream and producing a breakdown to formaldehyde with consequent toxic effects. When paraldehyde is given it should be in fresh solution and should be in a tube or syringe specified as inert.

In alcohol withdrawal seizures which do not usually present as status epilepticus, chlordiazepoxide (Librium) is effective, though phenobarbital is also.

A number of other drugs have been used in status epilepticus, particularly sodium amytal, which have considerable danger of producing respiratory arrest. Drugs such as clonazepam are not commonly available for intravenous use, though they may be effective in certain types of status epilepticus, particularly myoclonus. Sodium valproate has been reported effective in status epilepticus, but it is not available in the United States.

It has been recently recognized that a severe status epilepticus may be produced by overdoses of tricyclic antidepressants—amitriptyline (Elavil), imipramine (Tofranil), and others. In addition, it has been recognized that physostigmine represents a direct treatment for this type of convulsion and may be lifesaving.

Other treatments such as intravenous urea and intracarotid sodium amytal have been reported, but are not in common use.

**Diagnosis of Underlying Disease.**

The symptomatic treatment of generalized convulsions should not retard investigation to determine the underlying cause of the seizures. A great variety of diagnostic aids are available. In addition to the blood chemistries mentioned previously, screening for toxic substances is available in most hospitals. In the absence of any evidence of increased intracranial pressure, a lumbar puncture and cerebrospinal fluid (CSF) examination is indicated; this is especially true in a neonate and also in children, particularly if they have fever or stiff neck. However, examination of spinal fluid is indicated at any age since it may give some clue to the underlying disease.

Strange as it may seem, the use of an electroencephalogram (EEG) in monitoring the treatment of status epilepticus has not been common. Only recently have 24-hour bedside or emergency room EEGs been available. The use of the EEG in both the diagnosis and monitoring of treatment of status epilepticus is ideal; it is particularly useful in showing focal or asymmetrical abnormality, and in showing response to anticonvulsant drugs. In a few patients with repeated attacks which are thought to be convulsive seizures, an EEG is normal and the diagnosis of hysterical attacks can be made. The EEG is also of value in consideration of the problem of coma so that the type of EEG may give some indication as to the underlying cause of the unconsciousness in addition to showing the repeated seizure activity.

The recent widespread use of computerized tomography (CT) scan makes the screening of patients for intracranial lesions much easier. This is especially indicated if the seizures have a focal beginning or result in focal postictal findings. Obviously, the patient's actual convulsive seizures must be controlled before the tests can be adequately carried out.

The EEG is useful even if it cannot be obtained immediately during the convulsive seizure. During the postconvulsive state it may give information concerning postictal slowing, focal abnormality, or even continuous electrographic seizure activity, which will be useful in diagnosis. Since the seizure is a symptom of the brain and since it is manifested primarily by electrical abnormality, it is only reasonable that an EEG should be used to monitor its diagnosis and treatment whenever possible.

**Other Types of Status Epilepticus.**

Focal or partial status epilepticus of a motor variety occurs in both acute and chronic central nervous system diseases. Patients with old areas of damage in the central nervous system and with a history of repeated focal and secondary generalized convulsive seizures may present with primarily focal motor status epilepticus. Such patients will usually be
conscious. This condition may continue after the generalized status epilepticus has been controlled. In such patients control of the focal motor status epilepticus, though desirable, does not justify the use of massive doses of sedative drugs. Diazepam is often successful and when it is not, a loading dose of phenytoin is reasonable treatment.

So-called epilepsy partialis continua is more often an acute condition, secondary to a cerebral embolus, cerebral hemorrhage, or a brain tumor; it may also occur in encephalitis. In this condition the patient may be confused or unconscious, secondary to the underlying disease, and the motor movements may be relatively weak, though repeating continuously in an irregular though somewhat rhythmic fashion. This condition is often associated with cerebrovascular lesions in patients with additional toxic or metabolic disease. The EEG in such cases often shows a pattern which has been described as periodic, lateralized epileptiform discharges (PLED). Treatment of this type of focal status epilepticus with anticonvulsant drugs has been relatively unsuccessful. The condition usually runs a self-limited course, coming to an end in two to four days, often without recurrence. In this instance treatment to correct any underlying metabolic or toxic situation is as important as treatment with anticonvulsant drugs, and any treatment with anticonvulsant drugs should not be overdone.

A particular type of status epilepticus consisting of repeated myoclonic jerks is seen in patients who have suffered severe anoxic damage to the brain. These attacks often occur 12 to 24 hours after cardiopulmonary arrest and continue for one or two days; they are frequently associated with an otherwise isoelectric EEG and generally their occurrence suggests a very poor prognosis. Useful treatment for this condition has not been clearly defined. Large doses of phenobarbital or phenytoin may produce some decrease in the myoclonic jerks, but this may also happen spontaneously. When such patients are treated with large doses of drugs and then otherwise meet the criteria for brain death, problems arise due to the presence of such medications in their blood. In some patients with these myoclonic attacks drugs such as clonazepam and sodium valproate may be most effective.

II. Nonconvulsive or Stupor Status Epilepticus

A rare but interesting group of patients are those with nonconvulsive status epilepticus. These comprise a group of so-called petit mal status epilepticus or spike-and-wave status epilepticus. Such patients may simply be confused yet able to walk around and carry on some kind of conversation but may be very forgetful; they often give the appearance of being severely toxic with medication and as a result may be withdrawn from medication and have a generalized convulsive seizure. In such patients observation of rhythmic twitching of the eyebrows or facial muscles is often a tip-off that this is actually a status epilepticus. In these patients the EEG is, of course, diagnostic. Treatment with diazepam or clonazepam intravenously or orally may be useful.

More rare is the small group of patients with so-called psychomotor status epilepticus. In these patients peculiar behavior may go on for hours or days, associated either with a temporal lobe discharge or with a diffused theta discharge in the EEG. Here, again, the EEG is the essential diagnostic test.

III. Other Types of Seizures that Present an Acute Problem

1. Seizures in the newborn. These are common and represent an acute problem primarily in terms of diagnosis, and to some degree, of control of the attacks. The neonate is particularly subject to seizures secondary to metabolic derangements, such as hypoglycemia, hypocalcemia, and hypomagnesemia. Of course seizures are frequently secondary to congenital abnormalities or birth injuries. The possibility of infection, particularly meningitis, is always present and as a result, unless the infant responds quickly and definitely to treatment for metabolic derangement, a CSF examination is always indicated. Certainly in seizures of the newborn a search for the underlying cause is most important. As far as drug treatment is concerned phenobarbital is the drug of choice, but phenytoin also may be used and must be given intravenously since oral medication is not absorbed. In the neonate, phenytoin has a long half-life (up to 100 hours), so a single loading dose (10 to 20 mg/kg) may be sufficient. Since seizures in the newborn are often accompanied by changes in respiration and in cardiac function, the electroencephalographic recording really must be a polygraphic recording, including EKG, respiration, eye movement, and motor tone. Such polygraphic recording for diagnosis and during the treatment of continued seizures in the newborn should be used if available.

2. Febrile seizures. The problem of seizures with fever in children, particularly between the ages of six
months and three years, occurs frequently in the practice of pediatricians and family physicians. There is extensive literature on this condition and considerable disagreement about the diagnosis and management. Misunderstanding arises from the fact that careful neurological examination and electroencephalographic recordings have not been used to make a differential diagnosis in the matter of febrile seizures. In any case, when a seizure occurs in an infant with fever, it is important to know that the child does indeed have a fever and if possible what the underlying cause of the fever might be. It is also important to observe the child as soon as possible for evidence of any central nervous system lesion or focal neurological abnormality. In this regard an EEG in the acute state can be useful but often shows only diffuse slowing while an EEG a week or ten days after the seizure, especially with a child on no medication, is a much more valuable test. If such an EEG is completely normal, it is very likely that the child falls into a classification of so-called “benign febrile seizures.”

The predisposition to such seizures seems at times to run in families, and the condition is almost always limited to a few seizures, with sudden rising fever, between the ages of six months and three years and is almost never followed by recurrent focal or generalized seizures in adulthood. If, however, the EEG is abnormal, it may indicate preexisting brain damage and thus a prognosis of possible future seizures without fever. Children with such EEGs often have retarded development and some neurological findings, either postictally or between the seizures. A few children with fever or seizures show a so-called centrencephalic type of EEG. In the families of such children adults often have a history of inherited epilepsy of typical petit mal and grand mal syndrome. When febrile seizures are separated in this fashion, those children with an abnormal EEG as well as those with focal seizures or focal neurological findings have a distinct likelihood of having epilepsy later in life. Those with no focal findings, no abnormal EEGs, and only brief generalized seizures, have an excellent chance of never having difficulty later in life.

Treatment of truly “benign febrile seizures” may only require aspirin and phenobarbital when the child has fever, or regular use of phenobarbital for one or two years. Children with abnormal EEG and neurological findings may need prolonged anticonvulsant treatment.

A particular syndrome of fever associated with repeated convulsions (often one-sided) and then with hemiplegia has been described as being associated with the occurrence of focal motor or psychomotor seizures later in life. This has been called the hemiconvulsion, hemiplegia, epilepsy (HHE) syndrome and apparently represents an acute illness, either of a vascular or infective nature. In this situation CT studies as well as cerebral arteriograms are useful in making an etiological diagnosis.

3. The first or single seizure. The first or single seizure at any age represents an acute problem. In the past such attacks have often not been observed closely and persons having single seizures have not been studied sufficiently to arrive at a diagnosis. If the seizure is actually a generalized convulsive attack, patients are often started on anticonvulsant drugs without any type of neurological study other than a brief examination. Once on anticonvulsant drugs EEGs may be normal and the dilemma exists as to what the underlying diagnosis might be. As a rule the first or single seizure should not be treated with anticonvulsant drugs unless it represents a status epilepticus. One or two seizures occurring and then stopping should not be treated until the patient has been studied neurologically and with the EEG, and if indicated, with CT scans, CSF examination, and other tests. A firm diagnosis as to the cause of the seizure is very important in planning future management. Again, the immediate use of the EEG is often very helpful; in any case an EEG is advisable before putting the patient on treatment even if this takes two or three days.

In childhood the first or single seizure, though it may appear to be a generalized convulsive attack, is most commonly secondary to a focal or partial derangement in the brain. In addition to a great number of focal lesions remaining from birth and infancy a number of children have so-called benign central temporal epilepsy. These children often have sharp waves in the central temporal region associated with focal and secondary generalized convulsive seizures. Their EEG abnormalities are often banished easily with anticonvulsant drugs and are usually seen only if a sleep-deprivation record is obtained. Petit mal seizures also usually begin in childhood but do not present as an acute problem.

It is well known that any prior existing condition such as cerebral palsy, birth injury, or the so-called HHE syndrome may first cause clinical seizures during the teens. There is some element related to growth and sexual development which seems to increase the tendency to seizures at this time. During the teens
persons who have only had petit mal type seizures in childhood often have their first generalized convulsive seizure. For this reason, the great number of seizures beginning in the teens are actually caused by hereditary conditions, or to damage to the brain before, during, or after birth. Obviously, a few seizures begin during the teens from acute causes, such as encephalitis, brain tumors, and toxic metabolic causes, but these are rare. Careful electroencephalographic recording, including a wake and sleep-deprivation record, are useful; depending on the findings other tests can be made. At times a careful history brings out the fact that the teen-ager actually had a seizure early in life.

Adult-onset seizures have characteristically been considered more likely to represent the occurrence of a new central nervous system disease, such as an infection, brain tumor, or vascular abnormality. This is indeed true, though a number of persons have their first seizure in early adulthood based on preexisting hereditary or other lesions. In any case, the occurrence, particularly of a focal and secondary generalized seizure in adulthood, demands a complete neurological study; in addition to the EEG and plain skull x-rays this must include, if possible, a CT scan and an isotope brain scan. If all of these tests are negative except for a focal EEG, then cerebral arteriography should be considered. Again, it is important to make a diagnosis, if at all possible, before committing the patient to anticonvulsant medication.

The occurrence of seizures in the elderly, though having all the implications of seizures in younger adults, are more likely to be related to metastatic brain tumor and to cerebrovascular disease. For this reason, again, CT scans, isotope brain scans, and cerebral arteriography are indicated. The diagnosis of the cause rather than simple symptomatic treatment of the seizure is of utmost importance.

4. Withdrawal seizures. Many patients who present at an emergency room with the occurrence of a recent generalized convulsive seizure, and occasionally a repeated generalized convulsive seizure in the emergency room, are suffering from withdrawal syndrome. The most common withdrawal syndrome is alcohol withdrawal, but patients also have withdrawal seizures from barbiturates, diazepam, and a number of other medications. Such patients are usually not in status epilepticus and do not have focal neurological findings. They may have some mental derangement or confusion and with alcoholism they may have true delirium tremens; in many of these patients the history of previous alcohol intake is clear. The patient presenting with the first withdrawal seizure deserves hospitalization and limited diagnostic study. Certainly a complete neurological examination should be made and an EEG should be obtained on the first or second day; CSF examination and a plain skull x-ray are also indicated. If these tests are normal and the history is clear, further studies may not be needed. If there is any doubt, a CT scan should be obtained. In the patient who presents repeatedly with withdrawal seizures such elaborate study may not be indicated, but care should be taken not to miss the occurrence of a recent subdural hematoma, or development of some other intracerebral lesion. Since withdrawal seizures are essentially self-limited, the drug treatment is not vitally important. Most withdrawal seizures respond well to diazepam, phenobarbital, or phenytoin. Alcohol withdrawal seizures can also be treated with chlordiazepoxide. If the attacks are clearly withdrawal seizures, continuous anticonvulsant medication is not indicated.

5. Hysterical attacks. Some of the most dramatic attacks, both in their severity and repeated frequency, are not cerebral seizures at all but are behavioral in origin and represent a variety of hysterical attacks. The patient often shakes violently, usually from side to side rather than in a true tonic or clonic fashion. Patients may begin with focal manifestations and may seem to have a typical postictal state; in addition to shaking from side to side they may stiffen or arch their backs without much movement. Such attacks are frequent, never occur while the patient is asleep, and are usually viewed with much concern by relatives and friends. The neurological examination is, of course, normal and the EEG, if it can be seen free of movement or artifact, is also normal. Repetition of such attacks can often be produced by suggestion during EEG monitoring. One such patient who presented at our emergency room, and others in our vicinity, imitates such a perfect focal and secondary generalized convulsive seizure that he has on at least one occasion experienced respiratory arrest due to an injection of 40 mg of diazepam. Other patients with hysterical attacks have been rushed or flown into the medical center, receiving large doses of phenobarbital or phenytoin. A considerable amount of skepticism about repeated severe attacks in the patient who is neurologically normal is indicated.

In summary, the EEG is the ideal instrument for monitoring seizure activity in acute seizure problems. Increased use of the EEG in the diagnosis and monitoring of treatment of the seizure is one of the major
changes that has come about in management of this condition. The availability of CT scanning is also changing our ability to diagnose underlying disease.

When presented with an acute seizure problem the physician must always remember that the seizure is a symptom and must not consider it any different from any other symptom, such as cough due to pulmonary disease or vomiting or diarrhea due to gastrointestinal disease. Just as with symptoms such as cough, vomiting or diarrhea, the physician should strive to diagnose the underlying illness.

REFERENCES


