A. THE CLINICAL RECOGNITION OF SEIZURES

This is the most difficult aspect of seizure management, clearly the most critical, and yet it receives relatively little attention. Despite the sophistication of electrophysiologic methods for the diagnosis of seizures, the majority of patients will be assessed without the benefit of any technology beyond the routine scalp recording. Unfortunately, physicians are generally quite reluctant to make a clinical diagnosis of seizures. This reluctance arises from a lack of confidence. The current emphasis on elaborate monitoring techniques had made the reluctant clinician even more reluctant to make a clinical judgement, not because he has been confronted repeatedly with errors in his clinical judgement but because of the discomfort he feels in making the diagnosis in the first place; as a result, the possibility of deferring that judgement to a laboratory result becomes the more comfortable choice. Often the patient has so many symptoms that the physician contemplating seizures as the etiology is confronted with an overriding fear of overdiagnosis. In actuality, this fear is unjustified and the diagnostic error is, by far, in the direction of under diagnosis as evidenced by the number of behaviors which respond to the anticonvulsant treatment of “the seizures”.

For the most part, the diagnostic difficulty is over the recognition of non-convulsive seizures. However, even episodes involving motor activity can be confusing. In a rare case, the diagnostic error is over the significance attached to a normal EEG in a patient with clear-cut convulsive seizures. The clinical diagnosis of seizures in the mentally retarded represents even more of a challenge. Firstly, their level of function may be low enough that it is difficult to assess fluctuations. Secondly, the vast majority of clinicians are totally unfamiliar with what is normal behavior for the mentally retarded. The parents of mentally retarded children often don’t know either, because their complaints about their child’s behavior have so often been met by the he’s-retarded-what-do-you-expect attitude. Finally, and of major importance in some patients, the effect of seizures against the backdrop of an abnormal brain can produce some very bizarre behavior. Most of the time, however, seizures in the mentally retarded look much like those in the non-retarded.

Despite the intellectual awareness on the part of most clinicians of the manifestations of partial complex seizures, the most common obstacles to the diagnosis of seizures in clinical practice are the inability to apply this knowledge with confidence resulting in the following diagnostic dogmas.

1. If the patient doesn’t jerk all over, it’s not a seizure.
2. If the patient isn’t unconscious, it’s not a seizure.
3. If the patient can walk or talk, it’s not a seizure.
4. If the EEG is normal, it’s not a seizure.
5. If the patient doesn’t respond to an anticonvulsant, it’s not a seizure.

1. THE CHARACTERISTIC PROFILE OF SEIZURES

*Single Seizures* - The key to the clinical recognition of seizures is a constant awareness of the characteristic time course of seizures and freedom from preconceived notions about what behaviors can or cannot be seizures. The profile for a single seizure is a step function, which consists of three phases. The initial phase is the patient’s normal level of function, which is then abruptly impaired during the ictus (second phase), and the final phase is the abrupt return to the patient’s normal state of function. The recognition of behavior as episodic or paroxysmal depends on the severity of the impairment and its duration. Obviously, brief mild alterations in function will be difficult to detect with confidence even though they may significantly impair cognitive function. Invariably, however, the patient has episodes of varying duration and severity such that the clinician is able to develop confidence in the diagnosis on the basis of multiple long episodes. This is facilitated by the increase in physical signs such as alterations in facial and axial tone, pupillary size and responsiveness, which occur with the lengthening of the episodes. Briefer episodes can then be classified as...
probably seizures, possible seizures, and probably not. It is important not to worry excessively about labeling every event as seizures or not seizures. This is not possible nor is it necessary for treatment until the end point in seizure control is near. In fact, it is often counter-productive; if a physician feels obligated to make a decision about every single incident, rather than make an error in questionable episodes, he will not make a commitment about any of the episodes. My experience has been that so many of these doubtful episodes are the consequence of seizures that I feel more comfortable saying that something is not a seizure than I do in raising it as a possibility. In fact, so many things in the “not seizures” decision category have gone away with control of “the seizures”, that I will now rarely say something can’t be seizures in a patient with known seizures.

Frequent Seizures - The usual step function signature of a seizure is obscured when the patient has seizures in clusters. Typically, the first seizures are brief and mild, and become more severe before they again taper off or terminate abruptly. Consequently, individuals having frequent seizures often appear to “tail in and tail out” over hours, days and even weeks. This phenomenon is why affective disorders enter the differential diagnosis. In some patients the seizures become so frequent that the result is a change in state (psychomotor stupor). In the mentally retarded, this state is more difficult to appreciate because the patient simply looks more retarded than he really is. The diagnosis of seizures in these patients is often dependent on an appreciation of the significance of brief periods of much improved functioning, although it is often suggested by the dazed or dopey appearance of such patients. This dazed look will only be appreciated if one can remember that being mentally retarded (M.A. > 2 months) does not alter alertness and vigilance (see below).

Identifying the Seizure Profile in a Patient - The recognition of seizures particularly the partial complex variety is dependent on the ability to detect with confidence “subtle” deteriorations in the abilities and behavior of the patient. Partial complex seizures are the most difficult recognition problem for physicians, resulting in no or partial treatment of these seizures. This is particularly unfortunate for the patient, since these seizures can seriously compromise cognitive function and behavior and therefore care. Partial complex seizures follow a stereotypic sequence in each patient and can be recognized by the recurrence of this rote pattern. However, recognition of these seizures depends heavily on an awareness of what is normal for the individual. This is not a problem in adults, but it is a substantial problem in the mentally retarded of all ages and in children particularly if behavior and disposition are the issues. For this reason, it is helpful to organize clinical observations in the following way. Unless the physician is able to spend a large amount of time with the patient, then these observations will be based on history from the parent and the parent’s inquiries of the teachers. To obtain this information from the parent, it is necessary to ask the parent to observe the child (including a review of class work sheets) for these symptoms for 2 weeks. Parents who have not attached any significance to this behavior will often return with documentation of many such episodes per week.

1. Level of Alertness or Responsiveness

a. Visual awareness of the environment Visual attentiveness is one of the most subtle cues to the patient’s alertness and it is independent of IQ and verbal abilities. The ability to fix and follow, to observe what is going on in one’s surroundings, and to be attracted to new sounds are the components of visual attentiveness; with subtle alterations in consciousness, it is the quality of these behaviors which is diminished so that responses to visual and auditory stimuli are delayed and slowed, i.e. the patient looks “dopey” or “dazed”. I often call this “the lights are on but the house is empty” appearance. This patient is looking around but very slowly, clearly lagging behind the busy world. To be aware of this state, the clinician must develop a conscious awareness of the patient’s visual alertness by “watching the watcher”. Beware of the tendency to attribute “poor watching” or diminished alertness to mental retardation. Mental retardation does not impair level of consciousness, unless the patient has skills below that of the 4-6 month old. Developmental delay or mental retardation is not an explanation for alterations in level of consciousness.

b. Characteristics of verbal interchange - This involves an assessment of the patient’s comprehension of conversation, the content of their answer and their articulation. Once again the emphasis is on deviation from the patient’s usual performance which is an issue in and of itself in the mentally retarded or developmentally delayed child. Except for articulation, these linguistic abilities are entirely voluntary and depend on the
willingness of the patient to interact with the examiner. For this reason, these judgments are more dependent on the amount of time spent with the patient, since many children are reticent to talk to an unfamiliar adult. Even teenagers enter a “deep freeze” act when dealing with adults.

To assess variations in this area, it is important to develop an awareness of how quickly the patient catches on to your line of questioning and of the quality of his answers including the organization of his thoughts and ability to pursue the point of the conversation. Notice also his articulation. The effect of seizures on these abilities will be subtle to the casual observer but more obvious to the parent or teacher who knows the child well. When partial complex seizures are present, you will notice that the patient doesn’t respond to a question in his or her usual way; this can range from a poorly organized answer that is just slightly off target to no response at all. In the latter case, the tendency is to think that the patient did not hear or understand the question and so the examiner repeats the question in a louder voice. With less incapacitating seizures, the answer is brief and may be correct or incorrect. Finally, in the mildest cases, the patient appears periodically disorganized. Finally, notice if the patient’s articulation of words is fluctuating. These fluctuations in the patient’s conversation often produce the impression in the mentally retarded or young child that the patient’s level of intelligence is fluctuating or that he is taking some kind of drug. Teachers may comment on the occurrence of nonsense errors or scribbles in the middle of a problem set or be confounded by the child’s ability to do a task at one time and not another.

2. **Fine motor dexterity** - Fine motor dexterity may be noticeably impaired during partial complex seizures, so it is helpful to note the patient’s ability to manipulate small objects with his hands as well as his handwriting. The most common observation is probably a total cessation of fine motor activity during seizures, but teachers will sometimes complain of intermittent deteriorations in handwriting.

3. **Gross motor dexterity and balance** - Overall coordination may be impaired during seizures causing the patient some difficulty with walking. The most common finding is a slight broadening of the base, i.e., the feet are slightly wider apart. Other common complaints are clumsiness particularly as it affects performance in some physical activity. In young children, actual falling may be seen. Surprisingly enough, compromise in gross motor skills is not very common except in patients with existing deficits such as the child at the toddler stage of walking, the clumsy child, or the child with the frank hemiparesis. If a child has a frank hemiparesis, the severity of the deficit is likely to fluctuate with seizure activity and should therefore be monitored.

4. **Muscle tone** - It is common to see some alteration in tone during partial complex seizures. This will be manifest as a flattening of the facies, opening of the mouth, and a drooping of the head; these changes in tone result in the so-called “drugged”, “dopey”, or “dazed” appearance of patients with seizures. On formal examination, fluctuations in muscle tone and in deep tendon reflexes may be seen during seizures; such alterations are probably most prominent in the infant. If a patient on anticonvulsants has an increase in partial seizure activity, this is the reason that most teachers think the child is intoxicated from the anticonvulsant; if the anticonvulsant is lowered, the child will get worse.

5. **Mood or behavior** - In many patients, alterations in mood and personality and behavior problems are quite prominent during seizures. The most common complaint is irritability, meanness, and, in children, hyperactivity and aggressiveness. Parents will complain that the child is mean, cruel and foul-mouthed during these times. One of the most incomprehensible aspects of this bad behavior to the parent is its on-off quality. The child can deliver a diatribe of vile curses, walk out of the room, and return in 5 minutes as though absolutely nothing had happened. This is the Dr.-Jekyll-Mr.-Hyde phenomenon. In reality, the child has very little memory for his, which is not appreciated until the parents begin questioning the child about the events. Because the child makes everyone painfully aware of his presence, it rarely occurs to anyone that the child is not aware of what has gone on. This does not mean that the child is not aware that everyone is now angry with him and that he did something bad; in fact, the child is often remorseful or apologetic. Finally, some children with seizures will have sudden attacks of fatigue or tiredness. Beware of this complaint if it is not appropriate for age or for the child; many children outgrow naps at 18 months to 2 years. The “sleeping child” who is really fitting is noticeable for his absolute immobility—none of the usual restlessness seen in sleep.
Other Clues to the Recognition of Seizures

Probably the greatest value of “provokers” is that they add confidence to the epileptic origin of abnormal behavior. The behavior may “look like seizures” as above but if it “acts like” seizures, then diagnostic confidence increases.

1. **Provocations** - Seizures are often worse during periods of drowsiness, such as at wake-up time in the morning, after lunch and late in the day when the individual is becoming tired from the day's activities. In children, the worse times are often first thing in the morning and after school, which may initially be interpreted as a problem with parenting. Staying up late at night, a poor night’s sleep, and overwork leading to fatigue have the same effect on seizure frequency. Illness, particularly during the prodromal phase, is probably the most potent and most common precipitant of seizures in previously well-controlled children.

2. **Good days and bad days** - Patients often tail into out of bad spells. The spell, which is a cluster of seizures, may last a few hours to a few days or weeks which as mentioned earlier is the reason that mania or depression enter the differential in some children. The bad day may be heralded by a gradual increase in staring spells followed by awakening in a bad mood on the second or third day. At these bad times, all of the seizure symptoms are usually at their worst. In some patients the staring spells seem to have a slightly different “clock” than the irritability and meanness. This difference is probably most apparent in the difference between seizures when the medication is too low and too high. When too high, the problems are usually the staring spells and fluctuation in cognitive performance but not the irritability and meanness; when too low, all of the symptoms recur.

Much of the above information is obtained by history from a parent or spouse. It is often helpful to review with the observer the kinds of information that are helpful and have them return after two weeks of watching. Negative answers are often replaced by “now that you mention it, he does this often”.

**IN SUMMARY, THE DIAGNOSIS OF SEIZURES DEPENDS ON THE RECOGNITION OF A RECURRENT, STEROTYPIC PATTERN OF DETERIORATION IN LEVEL OF FUNCTION AND BEHAVIOR WHICH IS ABRUPT IN ONSET AND TRANSIENT.** The diagnosis is not dependent on a single symptom, but a constellation of symptoms. It is not dependent on a single instance; these patients have multiple such episodes to report. Nor is it dependent on the opinion of a single observer. Except for the rare instances in which the physician is the primary observer, the diagnosis is really made by the parents and the teachers. The physician’s role is to train the parents in what to look for and then to interpret the significance of the observations. My final advice to all clinicians is: do not make the diagnosis until you are absolutely confident of its correctness and do not start anticonvulsants until you have made a diagnosis of seizures.

**THE CLASSIFICATION OF SEIZURES**

The classification system for seizures was developed by the International League Against Epilepsy or I.L.A.E. The current revision was published in the journal *Epilepsia* and is part of your handout. In general, physicians are provided with the outline of the classification system, but not the text of the article, which explains the terms used. I have provided you with the entire article so that you can review the most common symptoms and their classification. The most important distinction is between partial seizures and primary generalized seizures, because the etiologic concerns and anticonvulsant choice vary with these two categories. The most useful note is your chart will not be the exact I.L.A.E. category, but a precise clinical description of the seizure.

**THE ROLE OF THE EEG IN THE DIAGNOSIS OF SEIZURES**

*The diagnosis of seizures is a clinical diagnosis.* It is not dependent upon the EEG findings or the response to anticonvulsant medication. For most clinicians, the EEG becomes a no-win trap. The clinician who will not make a diagnosis of seizures in the absence of an epileptiform abnormality on the routine EEG finds the situation no clearer when the EEG is abnormal because there is no clinical correlation. If that clinician then resorts to prolonged monitoring with scalp electrodes to establish a clinical correlation, the issue will often
not be any clearer, since many foci are out of the range of scalp electrodes. Ultimately, electrical disturbances in the absence of clinical correlation dies not resolve the diagnostic problem. If depth electrodes are not appropriate, which they aren’t in most seizure patients, then the physician is left in the uncomfortable position of entertaining a diagnosis of seizures, going to elaborate and expensive methods to investigate this possibility, only to be left with no resolution and no treatment for a lot of patients who have significant problems.

A scalp EEG is only helpful in confirming the diagnosis of a symptom as a seizure if the tracing is positive at the time that the behavior occurs and if the electrographic abnormality occurs in a neuroanatomic area that could produce the symptoms under consideration. It is not sufficient for the EEG to be read “as epileptic discharge observed”. This is meaningless for the clinical problem. What does the seizure look like and how often does it occur? These are very important questions for the clinical management of the patient. When thinking about EEGs, keep in mind that scalp recordings only monitor the top two to three millimeters of the cortex and only that part of the cortex under the array used; this leaves large portions of the brain unsurveyed. Frontal lobes and temporal lobes are very important generators of seizures and yet they are either not accessed at all or incompletely by the conventional scalp montage. I would like to refer you to tow articles that make these points very clearly. The first article is on partial complex seizures of frontal lobe origin. Note that most of these patients were diagnosed as hysterics prior to the implantation of cortical electrodes, which confirmed the correlation of cortical discharges with the clinical behaviors. Note that the surface EEG tracings were negative or non-diagnostic in these patients. Finally, note the description of the clinical seizures; the ictal behavior deviates significantly from the conventional dogma of what seizures look like. The second article discusses seizures (clinical with electrographic confirmation) in an atelencephalic infant emphasizing the contributions to seizures that can be made by sub-cortical structures and once again therefore the limited role for the scalp EEG in the diagnosis of epilepsy.

THE ROLE OF ANTICONVULSANTS IN THE DIAGNOSIS OF SEIZURES

Once again, I want to emphasize that the diagnosis of seizures is a clinical diagnosis and that the diagnosis should be firm prior to starting anticonvulsants. The response to anticonvulsants should not be used as a diagnostic tool. There are two reasons for this prohibition: the first is that not every patient responds to anticonvulsant; in fact Matson’s study would suggest a response rate below 50% in the majority of cases; in addition some patients require high levels of anticonvulsants for a response which is often excellent. Secondly, an anticonvulsant may make some patients worse; adverse behavioral effects are well known with Phenobarbital and Tegretol. In some instances, an anticonvulsant will control generalized seizures but will actually exacerbate partial seizures resulting in a worsening of the patient. The worsening in both these situations would be a poor basis on which to rule out seizures.

APPROPRIATE USES OF THE ROUTINE SCALP EEG

In general, an EEG should be done in all newly diagnosed cases of seizures for several specific reasons:

1. to look for evidence of a focal abnormality such as a tumor or AVM;
2. to look for patterns with diagnostic implications (such as the burst suppression pattern in SSPE or Jacob-Creutzfeld disease) or with prognostic implications (such as hypsarhythmia or slow spike and wave);
3. to differentiate between absences due to partial complex seizures and those due to true petit mal; the drug of choice for the first entity is Tegretol whereas the drug of choice for petit mal is Zarontin or Depakene. True petit mal is, however, quite rare, so this is more of a theoretical issue than a practical issue;
4. to provide a baseline EEG in the event the patient has any deterioration and the question of a degenerative disease is raised.

INDICATIONS FOR REPEAT EEGS

The indications for obtaining repeat EEGs after the initial evaluation are a matter of common sense.
1. the seizure pattern changes (increased frequency or a new type of seizure develops);
2. new neurologic signs or symptoms develop;
3. the seizures have not responded to the proper use of anticonvulsants and the possibility of a degenerative disease must be considered. In this context, the initial EEG provides a very important baseline.
4. when the original EEG displayed a pattern which is known to change over time such as hypsarrhythmia, another EEG is indicated;
5. similarly, if the original EEG displayed a spike focus, it is probably important to see if the activity of that focus has subsided. It is unclear if ongoing spike activity will alter the outcome, i.e. in terms of continuation of the seizure disorder, or effect brain development.

Finally, the most common question is “How often should an EEG be repeated in a patient who has seizures but is doing well?” this depends on the underlying etiology of the seizures, but usually this means every two to five years.

B. TREATMENT OF SEIZURES WITH ANTICONVULSANTS

The principles of anticonvulsant treatment are quite simple and, if followed, will lead to very successful care for most of the patients that you will encounter. Physicians vary in the way they rank order anticonvulsants; this variability often reflects differences in their patient population and past experience. The most important policy is to periodically reassess these choices. If your first choice has become everyone else’s fourth choice, then there is some information you are overlooking. Secondly, use only one or two anticonvulsants at a time in a given patient. Drug interactions can be a serious problem for many reasons and the use of two or more anticonvulsants simultaneously results in an exponential number of interactions. For this reason, it’s unlikely that there is any gain from having patients on three or more medications as compared to one or two medications. If you have the choice between a more complicated dosing schedule with one anticonvulsant and the addition of a second drug, I’d advise you to work very hard to stay with a single drug. The second rule of anticonvulsant management is to discard a drug if it’s not helping; keep a drug only if it’s working. One of the most common errors is to add drugs and never stop them, even though they have not helped. The beneficial effect of a drug can be assessed both on the way up and on the way down; sometimes the efficacy of a drug is underestimated, because “you’ve forgotten how bad things were”.

Anticonvulsant Levels - Remember that the “therapeutic range” is based on population statistics. The lower limit of the therapeutic range is that level at which some subjects began to respond and the upper limit is the level at which some subjects began to have side effects. Every individual is different and can experience a therapeutic effect at a level below “therapeutic” or above the upper limits. Similarly, the levels at which an individual experiences side effects may be lower or higher than the average. The best guideline is the patient: use the drug at the level that works. Try to get out of the habit of saying that the anticonvulsant was in/below/above the therapeutic range, because this does not have meaning for seizure control or side effects in the individual; speak instead of the specific level and the patient’s response. It is also a better policy to use trough rather than non-trough levels, especially if the dosing frequency is less than one half life. A non-trough Tegretol level of 9-10 may be 4-5 at trough times, especially in young children. Many drug failures or partial successes might well be converted to complete successes if trough levels are used as a guideline.

Age-Dependent Metabolism of Anticonvulsant Drugs - There are three transitions in the metabolism of anticonvulsants—infancy, early childhood (about 4 years of age) and pubescence. Some of these transitions can be relatively abrupt resulting in a substantial rise in levels over a few weeks time. The presents another problem in children and that is the inability to obtain therapeutic drug levels with increasing doses. This is by in large a problem prior to 5 years of age in children who need levels in the high therapeutic range to achieve success. However, at older ages, the use of two drugs may so induce metabolism as to prohibit combinations. The shorter half life anticonvulsants (Tegretol and Depakene) present the greatest problem. If excessive metabolism becomes a problem, the contingencies are to increase dosing frequency, increase dose, and switch to a longer half life drug. Unfortunately, as in adults, Dilantin is not as effective in the treatment of partial complex seizures as Tegretol. One strategy we have tried in such cases is to use low dose Erthromycin with
Tegretol to inhibit the metabolism of the anticonvulsant. This has been quite successful and is often only necessary for a year or two.

**Monitoring Blood Work During Anticonvulsant Use** - No anticonvulsant is without side effects. Phenobarbital, Dilantin, and Tegretol all have serious side effects and regular monitoring of CBC and liver functions should be carried out with all anticonvulsants. I obtain this blood work immediately prior to starting an anticonvulsant or adding an anticonvulsant. During hospitalization, when I am making frequent changes in doses and using high doses, I repeat these studies every two weeks. On an outpatient basis, I follow the same schedule for about six weeks, which coincides with the frequency that I need blood levels of the anticonvulsants.

The issue that concerns us the most is the subacute onset of serious blood or hepatic toxicity. The best monitoring system is the patient or parent who monitors closely for clinical signs of problems. Periodic blood work has a statistically poor chance of catching a subacute side effect in the early stages of its development. There is therefore no logical schedule for monitoring after the first two to three months of therapy. I do not have a solution for that problem. I do advise each patient of the risks of anticonvulsants; my summary to them is that “one of my patients will pay for all of the benefits that the others have enjoyed. The payment is far less than the benefits enjoyed or anticonvulsants would not be on the market or be in such frequent use.” This is analogous to the situation with DPT immunizations. Without immunization, the morbidity and mortality from the disease is much higher. With immunization, a rare individual will suffer serious immunization-induced neurologic sequelae.