Personal Practice

Approach to the Management of a Child with Epilepsy

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Epilepsy is conventionally defined as two or more unprovoked seizures. Even though epilepsy is the most common neurologic problem encountered in pediatric practice, there are still no well defined guidelines about management which can be applied to every child with epilepsy and which are acceptable to all physicians dealing with childhood epilepsy. In this communication we have presented an approach to the management of children with epilepsy, based on current knowledge and personal experience. Some of the common questions and issues that arise during management have also been addressed.

At the outset, clarification of certain definitions(l) is essential to avoid confusion in terminology: *(i) Epileptic seizure* is a paroxysmal clinical manifestation presumed to result from an abnormal and excessive discharge of a set of neurons in the brain; *(ii) Epilepsy* is a condition characterized by two or more epileptic seizures unprovoked by any immediate cause. (Multiple seizures within 24 hours, and an episode of status epilepticus are considered single events. Febrile convulsions and neonatal seizures are excluded); *(iii) Epileptic syndromes(2)* are certain epileptic disorders with a common cluster of signs and symptoms such as age of onset, seizure type(s), EEG characteristics and sometimes prognosis.

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Approach to a child with epilepsy should focus on establishing a correct diagnosis, deciding about the need for antiepileptic drugs, choice of most suitable drug and proper followup of the patient. This can be achieved by following a systematic approach to address the following questions.

Is this an epileptic seizure or a non-epileptic event (NEE)?

This is the first question that needs to be answered when a child is brought with a history of a paroxysmal seizure like event. An understanding of NEEs that mimic epilepsy is important to avoid a mistaken diagnosis of epilepsy. NEE may be categorized as either psychogenic or physiologic. The latter are more common in infancy and childhood(3). Psychogenic seizures occur in both non-epileptic as well as epileptic children. Some of the common NEEs are listed in *Table I*. Inattention and day dreaming in school children may also be mistaken for absence seizures. Repetitive rhythmic movements and startling episodes in children with mental deficiency are often misinterpreted as seizures.

A detailed history of the exact sequence of events and circumstances, along with physical examination is essential for differ-

entiating NEEs from true seizures. At times however, this may be extremely difficult. Although an EEG is of help, it may not always be decisive. One must be aware that the EEG may be normal in 30-50% of children with epilepsy; and also that epileptiform activity *(viz.,* spikes or sharp waves) can be seen in EEG(s) of some normal children and therefore a diagnosis of epilepsy should not be made only on the basis of such changes. Children with pure physiologic or pure psychogenic NEE may show EEG abnormality and even focal abnormalities on CT or MRI scan(3). In such cases, neurodiagnostic EEG-video recording is needed for making a correct diagnosis. A possibility of NEE should also be considered in all children with a history suggestive of refractory seizures or multiple seizure types.

TABLE I—*Some Common Non Epileptic Events in Infants and Children*

* Breath-holding spells
* Syncopal attacks
* Shuddering attacks
* Tics
* Benign paroxysmal vertigo
* Complicated migraine
* Night terrors
* Somnambulism
* Narcolepsy
* Gastro-esophageal reflux with laryngospasm and apena

What is the type of seizure(s)?

Having confirmed that the child has true epileptiform seizure, it is essential to find out the type of seizures. The International League Against Epilepsy (ILAE) classification of seizures(4) summarized in *Table II* is important for proper choice of medication. It is based on clinical as well as EEG criteria. For communities where an EEG may not be easily available, a predom-

TABLE II–*Summary of International Classification of Seizures*

Partial (local, focal)
Simple partial–no loss of consciousness
Complex partial (formerly temporal lobe or psychomotor)
With impairment of consciousness at onset
Simple partial onset followed by impairment of consciousness
Partial evolving to generalized tonic-clonic convulsions
Simple
Complex (including those with simple partial onset)
Generalized (convulsive or nonconvulsive) seizures
Typical absence (formerly petit mal) and atypical absence
Myoclonic
Tonic
Clonic
Tonic-clonic (formerly grand mal)
Atonic
Unclassified epileptic seizures

inantly clinical simple classification has been proposed(1). At times, classification of the types of seizures alone may not be totally satisfactory. Classification of epilepsies and epileptic syndromes (5) may be more useful for proper diagnosis, treatment and prognosis. Although these classifications are in evolution and are difficult for the nonspecialist, they have established unanimity in terminology and should therefore be adopted whenever possible. It may be worthwhile understanding that: *(i) Idiopathic epilepsies* are those with no underlying cause, except a possible hereditary predisposition; *(ii) Symptomatic epilepsies* are considered the consequence of a known or suspected CNS disorder; and *(iii) Cryptogenic epilepsies* are presumed to be symptomatic but the etiology is not known.

Precise details in the history of the event(s) and its circumstances are the corner stone of accurate diagnosis of seizures and their type. The first clinical signs of a seizure, designated by the misleading term of 'aura' have a highly localizing value(1) and should therefore be asked about. As a doctor rarely witnesses a seizure, classification depends almost entirely on the description given by a witness, usually a parent or a school teacher. A disturbed parent of a child with the first seizure episode may not be able to narrate events sequentially, may be utterly confused about the side of origin, if any, and also may overestimate the duration of seizures. In children with recurrent seizures over a long time, a correct recall of events is even more unlikely. Hence it is important to take the history very patiently and it is often helpful to get the witness to enact the event.

A complete clinical and neurological examination should be done in all children with epilepsy particularly to ensure that there is no underlying neurological abnormality. Although in primary generalized epilepsies, the clinical examination may not add much information, but it is particularly valuable in certain epileptic syndromes. It is important to know that there is a definite age predilection in some of the epilepsies *(Table III)*. In infants and young children, a developmental assessment should also be done as a part of the initial assessment as well as follow up to exclude developmental delay or regression.

A combination of the age of onset, clinical description of seizures, neurodevelopmental assessment and EEG helps in classifying the epilepsy/epileptic syndrome. A CT or MR scan may be needed in some cases.

To treat or not to treat?

After classification comes the crucial question of whether antiepileptic medication should be started or not. This decision should be guided by the risk of seizure recurrence, and the potential morbidity of anti-epileptic drug (AED) therapy. The risk of recurrence after a first unprovoked seizure varies from 23% - 80% depending on risk factors(6,7). The risk is higher in patients with a neurologic insult. Seizure etiology and EEG are the strongest predictors of recurrence(8) - the risk being low (24%) in idiopathic epilepsy and normal EEG, and high (65%) in symptomatic epilepsy and abnormal EEG(8). Routine treatment

TABLE III–*Age Predilection of Some Epilepsies*

	Type of Epilepsy	Usual age
*	Infantile spasm	3-12 mo
*	Benign/severe myoclonic epilepsy of infancy	6 mo-2yrs
*	Lennox-Gastaut syndrome	2-8 yrs
*	Absence seizures	3-8 yrs
*	Benign rolandic epilepsy	3-13 yrs
*	Juvenile myoclonic epilepsy	13-16 yrs

after a first unprovoked seizure is not indicated. The decision to treat should be individualized. In a neurologically normal child, with idiopathic generalized tonic clonic seizure, there is no need to start treatment. Initiation of AED after a first unprovoked seizure may at times be considered in children with a constellation of risk factors, namely, remote symptomatic seizure, children with partial seizure (except Rolandic), prior acute symptomatic seizure, sibling with epilepsy, Todd's palsy, and first seizure during sleep (9).

It may be pertinent to mention here that status epilepticus may present as a first seizure in children who are otherwise neurologically normal. While some consider this as an indication for starting AED(9), recent studies in both children and adults have shown that risk of seizure recurrence following status epilepticus as a first unprovoked seizure is not different from seizure recurrence following a brief first unprovoked seizure(10). Prolonged treatment with AEDs has not been recommended(ll). It may be re-emphasized that even in the presence of some risk factors of recurrence, majority of children are not treated after the first unprovoked seizure(9).

Most children with recurrent seizures require treatment except those who have provoked seizures and those in whom episodes of seizures are separated by years(12). For occasional provoked seizures, the provoking factor (metabolic, toxic, trauma, acute cerebral anoxia, *etc.)* should be identified and treated. Since such conditions have no reason for continuing liability to recurrent seizures, prolonged treatment is not needed unless the seizures were of such severity that epileptogenic brain damage may have resulted(12). When two or more unprovoked seizures have occurred, treatment has to be started.

Which drug to use ?

Having decided that treatment is to be started, the doctor has to think about the choice of the most suitable AED. Before embarking on drug therapy, it is imperative for the doctor to be familiar with the basic pharmacokinetics of the commonly used AED *(Table IV).* It may be worthwhile understanding some of the properties that influence drug administration and monitoring.

(a) Time in peak concentration (T max);

TABLE IV–*Pharmacokinetics and Dosages of Some Commonly Used AED(s)*

Drug	T max (hours)	Elimination half-life (h)	Starting dose (mg/kg/day)	Maintenance dose (mg/kg/day)	Number of doses/day	Time for SSC(days)	Therapeutic range (µg/ml)
CBZ	5-10	10-30	5	10-30	2-4	10	4-12
PHT	8-12	3-60	5	5-12	1-2	7-21	10-20
PB	6- 8	30-150	3	3-5	1-2	14-21	15-40
ESM	1- 4	30-60	10	15-30	1-2	7-14	30-60
CZP	1- 4	30-40	0.01-0.03	0.1-0.3	2-3	14	20-80
VPA	1- 4	4-15	10	15-60	2-3	3-5	50-150

CBZ = Carbamazepine; PHT = Phenytoin; VPA = Valproic Acid; PB = Phenobarbitone;
ESM = Ethosuximide; CZP = Clonazepam; SSC = Steady state concentration.

i.e., the time taken to achieve maximum serum level after a single dose.

(b) *Half life*—time taken to reduce the concentration of a drug by half. Drugs with a long half life need to be given less often than those with a short half life.

(c) *Steady state concentration (SSC)*—time taken for serum levels to reach a steady state. This requires about five half lives with maintenance doses. It is important to understand that steady therapeutic levels of a particular AED can be achieved only after a given time, *i.e.*, after its five half lives and therefore drugs with long half lives like phenobarbitone will take longer time to reach SSC.

(d) *Tlierapeutic* range—The range of serum drug level within which most patients respond satisfactorily. These are good guidelines but not 'absolute' because there are interindividual variations in response to AED(s).

The choice of the initial AED is mainly based on the efficacy of a drug for a particular seizure type/syndrome, and the ratio of its efficacy to side effects. In our country, cost may also be a consideration. *Table V* indicates the choice of drugs according to seizure types and epileptic syndrome. It may be mentioned here that myoclonic seizures and drop attacks in children may be exacerbated by CBZ and no significant difference in efficacy has been found between prednisolone and ACTH for treatment of infantile spasms. Considering the high cost of ACTH, and less severe side effects of prednisolone(9), it may be advisable to use prednisolone as first choice for treatment of infantile spasms in **our** country.

How many drugs to use? Mono or polytherapy?

Unlike many other issues in the management of epilepsy, this is perhaps an aspect where there is no controversy today. The goal of therapy is restoration of a normal life through complete control of seizures using a single drug with least side effects. A single drug is capable of providing satisfactory seizure control in 40-75% of patients with epilepsy(14). Advantages of monotherapy are: *(a)* less adverse effects *(b)* no problem of drug interactions; (c) lower cost, and *(d)* better compliance.

How to initiate and adjust AEDS?

Generally treatment should be started with a small dose of the proper drug to minimize side effects, and then gradually increased to the anticipated maintenance dose over a few weeks. One may give half the proposed maintenance dose for the first 1-2 weeks and then give the full dose(15). Phenytoin, however, can be started with maintenance dose right away(16). If drug

TABLE V-- *Choice of Antiepileptic Drug According to Seizure Type and Epilepsy Syndrome*

Type of seizures/ epileptic syndrome	*First choice AED*	*Second choice AED*
Partial seizures with/ without genralization	CBZ, PHT	VPA, PB
Generalized tonic-clonic seizures	VPA, PHT, CBZ	PB
Childhood absence epilepsy	VPA, ESM	CZP, ACM
Juvenile myoclonic epilepsy	VPA	PB, CZP
Progressive myoclonic epilepsy	VPA	PVA+ CZP
Lennox Gastaut sydrome	VPA	CZP
Infantile spasms	Oral steroids or ACTH	VPA
Rolandic epilepsy	CBZ, VPA	PHT

monitoring facilities are readily available, drug level may be checked after an optimal time (5 times the half life) to see if steady-state concentration (SSC) has been reached. If the level is still low, the dose should be increased, keeping a watch for side effects. In certain situation, namely, *(a)* very frequent seizures or *(b)* a relatively prolonged seizure or (c) major seizures few hours before presentation, wherein a rapid rise in serum level is desired, a loading dose (2-3 times the presumed maintenance dose) may be given orally, or parenterally in case of PHT or PB. With CBZ and VPA, dose may be increased every third day up to required maintenance. *Table IV* summarizes these details.

Should liquid preparations be used?

Liquid preparations of AED(s) may be needed for infants and young children. It must then be ensured that correct amounts are dispensed using either a calibrated syringe or a measure spoon. Liquid preparations require frequent renewal owing to short shelf-life, may contain potentially damaging ingredients like sucrose and at times may be more rapidly absorbed, leading to transient side-effects. Also, the higher cost of liquid AEDs is an important consideration in our country. Hence tablets are preferable whenever possible.

What should be the frequency of dosing? What is the relation to mealtime?

Fluctuation in serum level of AED should be kept as small as possible. Doses should, therefore, be evenly spaced and their frequency adjusted depending on formulation, bioavailability and half-life. While phenobarbitone and phenytoin can be given in daily or twice a day schedules, drugs like valproate and carbamazepine should be given in multiple doses. Children are liable to forget the afternoon dose at school times; timing should, therefore be appropriately adjusted and compliance ensured. Slow release tablets are useful if infrequent dosing schedule needs to be adopted. It is advisable to give valproate after meals as absorption is delayed and the smoothing effect on plasma level is enhanced. Also, gastric irritation is ameliorated. Some drugs like phenytoin do not require any attention to the time of day or relation to meals.

How frequently should a patient be called for follow up?

During the phase of initiating therapy, it is advisable to call the patient for two **or** three visits if feasible. Dose adjustments, baseline investigations, explanation of the problem and its management, and answering the patient's/parents' questions are done during these visits. Parents should be informed about possible side effects of the AED being used and should be advised to report if they notice any side effects or if there is seizure recurrence. In a well controlled child, a three-six monthly follow up is generally sufficient. If however the seizures are not well controlled, the followup will depend on seizure frequency and time required for drug to reach SSC after each manipulation of dose.

What to check at follow up visits?

The following should be carefully checked at every visit:

(a) Seizure frequency- reduction or elimination: appearance of new seizure type-it is preferable to maintain a seizure diary if there are frequent seizures.

(b) Dosage and compliance

(c) Formulation and trade name of AED being used.

(d) Relevant side effects of AED being used.

(e) De teriora tion in school performance, behavioral altera tion.

It is advisable that patients adhere to a specific brand of AED as absorption may differ between similar formulations from various manufacturers. Significant increase in serum phenytoin concentrations has been observed when the same maintenance doses of medication are taken from different sources. Significant changes in blood level also occur when formulations are changed from tablet to syrup or from fast to slow release preparations(17).

Should dose be adjusted with increasing weight?

It is not necessary to increase dose of AED in well stablilized patients even if the drug levels are sub-therapeutic(18).

How to manage a seizure recurrence while a child is on AED?

If recurrence of seizures occurs soon after starting anticonvulsants, one can wait for the SSC to build up. If however, seizures occur after that time period, then one has to look for two important factors; namely, adequate compliance and provoking factors. If there is a good compliance and no obvious precipitating factors, *e.g.,* fever, intercurrent illness, co-medication, change in formulation, *etc.,* then the dose of anticonvulsant has to be increased. Ideally a drug level should be obtained in such circumstances.

How to monitor for adverse side effects? Which ones are an indication to stop therapy?

AEDs cause four distinct types of toxicity: actue dose related, acute idiosyncratic, chronic, and teratogenic. Side effects occur in 50% of treated patients and are more common with polytherapy(17). The most frequent adverse effects are dose related and are mild and reversible. Idiosyncratic effects are potentially lethal but are fortunately rare: they warrant immediate discontinuation of drug. One should rely on clinical changes rather than laboratory tests which are done at arbitrary points; for example, nausea, vomiting, abdominal pain in a child on valproate should alert the physician about impending liver cell failure. Similarly, recognizing dermatologic signs is also important.

Some baseline investigations before starting AED have been recommended (18), *e.g.,* liver function tests before valproate. Periodic routine laboratory tests (hematology, serum chemistries, urine, *etc.)* are **of** doubtful value as life threatening reactions are rarely predicted by such tests. *Table VI* summarizes the major adverse effects of AEDs.

What are the causes of poor response to therapy?

When a child fails to respond to therapy, the following need to be done: (/) Reconfirm the diagnosis of epilepsy and carefully exclude non-epileptic events; *(ii)* Recheck that the appropriate drug for the seizure type is being used in adequate doses and that there has been no arbitrary modification of dose or change of formulations by parents; *(iii)* Ensure compliance; *(iv)* Exclude underlying progressive brain damage; *(v)* If child is on polytherapy, exclude drug interaction; and *(vi)* Check that child is not getting overdosage since certain AED's (PHT, CBZ, CLP) may themselves cause seizures with overdosage. It may at times be extremely difficult or impossible to get complete seizure control in certain situations, *viz.,* severe brain damage, Lennox Gastaut syndrome, *etc.*

What is the management protocol of refractory seizures?

The initial drug of choice should be in-

TABLE VI–*Side Effects of Commonly Used Anticonvulsants*

Drug	Side Effects		
	Acute		Chronic
	Dose related	Idiosyncratic	
CBZ	Diplopia Enchephalopathy Exacerbation of seizures	Morbiliform rash Steven Johnson syndrome Aplastic anemia	Psychic disturbance Hormonal imbalance
PHT	Cerebellar signs Encephalopathy Dyskinesias	Rash Hepatitis Lymphadenopathy	Gingivial hypertrophy Acne, Chloasma Hirsuitism Megaloblastic anemia Rickets, Coarse facies, Peripheral neuropathy
PB	Sedation	Rash Exfoliation Toxic epidermal necrolysis Hepatotoxicity	Hyperkinesia, Insomnia Distractability, Paradoxical insomnia, Memory and cognitive impairment, Connective tissue disorder
VPA	Gastroinstestinal problems Peripheral edema	Acute hepatotoxicity Acute pancreatitis	Alopecia, Tremor Weight gain
ESM	Gastrointestinal problems Encephalopathy	Rash	Lupus, Extra pyramidal signs, Myelosupression
CZP	Encephalopathy Ataxia Hypersalivation	Rash	Thrombocytopenia, Hyperkinesia, Aggression Increased seizures

creased to the maximum dose that is tolerated without clinical toxicity (even if the drug level goes above therapeutic range). If still there is no control, a second drug is added and similarly increased. Only when seizures are well controlled, or maximum dose/toxicity is reached, the first drug may be slowly withdrawn.

If both drugs are ineffective in maximally tolerated doses, only then polytherapy with two drugs should be initiated. Using more drugs normally does not help: on the other hand, toxicities increase. When two drugs are being used it is well worth gradually reducing the dose of these since this approach often reduces seizures frequency.

The possibility of pyridoxine dependency should be considered in every child with refractory seizures upto the age of two years, including those with infantile spasms(19). This diagnosis can be confirmed by giving 50-100 mg of intravenous pyridoxine under EEG control, during clinical seizure activity. A positive response is seen within minutes to hours and should be followed by an oral maintenance dose of 50-100 mg/day.

Steroids and ketogenic diet are sometimes used in refractory seizures particularly in Lennox Gastaut syndrome. The other drugs that may be tried are adjunctive drugs, namely, acetazolamide and newer AEDs. Some children with refractory seizures may benefit from surgery which is available only in specialized epilepsy surgery units.

In general, if there is no satisfactory response within three months, it is advisable to refer the patient to an expert.

How should the drugs for combination therapy be selected?

The principles of combination therapy are as follows: *(i)* AEDs with different mechanisms of action and with few or no drug interactions should be prescribed together; and *(ii)* AEDs with large therapeutic index and with the fewest side effects should be selected. Newer AEDs may also be used in combination, for example, lamotrigine vigabatrin and gabapentine have been used as add on therapy for partial and secondarily generalized seizures. Felbamate has been found useful in partial epilepsy and some cases of Lennox Gastaut Syndrome. However the role of newer AEDs still needs to be established and these should not be used indiscriminately.

What are the indications of hospitalization in epileptics?

Normally children with epilepsy are managed on an outpatient basis. Only occasionally hospitalization may be needed for: *(i)* Management of status epilepticus; *(ii)* Careful observation of seizure type; *(iii)* Distinguishing between seizures and NEE; *(iv)* Frequently occurring or refractory seizures, particularly where there is no access to medical help; *(v)* Serious adverse reactions of AED(s); and *(vi)* Ensuring compliance in poor responders.

What is the role of EEG in childhood epilepsy?

EEG is the single most valuable investigation in patients with known or suspected seizures. At the same time, it is one of the most abused diagnostic investigation. It is, therefore, important for physicians to use it rationally, with a clear objective. In this context it is worth remembering that **a** number of normal phenomena may simulate epileptiform discharges and a careful examination of the EEG can prevent pitfalls in interpretation. Moreover, epileptiform discharges including 3 Hz spike and slow wave have been seen in about 3% of normal children(20) and also in siblings of some epileptic children. The possibility of evolving changes in EEG with age, with brain maturation, should be entertained. The interpretation of pediatric EEG(s) should, therefore, be done by a person well versed in the subject. Routine interictal scalp EEG demonstrates features of epilepsy in 50-60% cases(21)-the yield may be increased to 90% using various activation procedures, especially sleep. Temporal and frontal lobe onset seizures may sometimes be diagnosed only on sleep EEGs. Hence sleep EEG(s) should always be asked for. Ictal records are rarely possible except in absence seizures.

EEG is useful for:

(a) Diagnosis: Epileptiform activity supports a diagnosis of epilepsy, a normal EEG however, does not exclude it.

(b) Classification of seizures: The EEG can be very useful in making precise diagnosis of the type of epilepsy, namely, generalized versus partial. It is particularly useful in distinguishing typical 3 Hz spike wave absences from complex partial seizures and in patients with tonic-clonic seizures without an aura to differentiate between primary generalized seizures and those with a focal onset.

(c) *Classification into syndromes:* The EEG is valuable for indentifying specific epileptic syndromes like West syndrome (hypsarrhythmia), Lennox Gastaut syndrome (slow bi- or triphasic spikes with 1-2 Hz slow waves), Rolandic epilepsy (paroxysmal spikes from the centrotemporal region), juvenile myoclonic epilepsy (generalized clusters of spikes of high frequency on a normal background), *etc.*

(d) Establishing etiology: Specific EEG patterns have been described in subacute sclerosing panencephalitis, Batten's disease, lissencephaly and Angelman's syndrome in all of which clinical epilepsy may occur(21).

(e) Extent of brain damage is indicated by the diffuse abnormality of background rhythm. Focal slowing often indicates an underlying focal structural damage.

(f) Deciding drugs: To a limited extent the EEG may assist in choice of drugs, for example, use of valproate/ethosuximide in childhood absence epilepsy. Spike wave patterns in children with other types of absence seizures may prohibit the use of carbamazepine which can cause an exacerbation of epilepsy in these seizure disorders.

(g) Assessing response to therapy: The widespread misconception that the EEG will provide information about the state of the patient's epilepsy leads to unnecessary EEG examinations. Periodic EEGs are not required; patient management should remain essentially clinical. In certain situations (West syndrome, absence epilepsy, photosensitive epilepsy and pyridoxine deficiency seizures), the EEG returns to normal soon after instituting appropriate therapy and may therefore, be helpful in assessing response to treatment.

(h) Withdrawal of therapy: This decision is essentially clinical and should not be dictated by the EEG. The EEG may be normal but the child may require prolonged treatment, for example, in juvenile myoclonic epilepsy. Conversely, the EEG may remain abnormal long after clinical remission in certain syndromes (benign partial epilepsy with centrotemporal spikes). However, the EEG may occasionally be helpful in deciding withdrawal of treatment in some difficult cass(21). In general, the chances of relapse are least likely if the child is neurologically normal, has had limited number of seizures and the EEG is normal or only mildly abnormal.

(i) Contemplating epilepsy surgery: Simultaneous EEG and video monitoring and invasive depth EEG(s) are of invaluable assitance in preoperative assessment.

To summarize therefore, during management of childhood epilepsy, an EEG is needed: *(i)* during initiation of treatment, *(ii)* rarely after starting therapy to assess response in specific epileptic syndromes, and *(iii)* very rarely to help decide withdrawal of therapy in difficult cases.

Routine EEG(s) during treatment are not indicated. If however, there is a recent deterioration in clinical state, or change in the type of seizures, an EEG should be asked for and the patient re-evaluated.

What are the indications of brain imaging?

Early CT head done in children with all types of seizures, in a study revealed abnormality in one third of the cases(22). The yield is much higher in children with neurological abnormalities. In our experience, more than half of children with partial seizures have lesions on CT scan(23). Indications of neuroimaging in a child with epilepsy include." (a) Partial seizures-in all children (except rolandic and occipital epilepsy). This is particularly important in our country as unlike the West, neurocysti-

cercosis and tuberculomas are the most important causes of partial seizures in children(24) and both of these are medically treatable; *(b)* Abnormal neurological signs and phakomatoses; (c) EEG indicating structural lesion, for example, persistent localized slow wave changes (delta focus) and/or spike or sharp wave focus; *(d)* Refractory seizures; (e) Sudden change in seizure pattern, neurological examination or EEG; *(f)* Recent worsening in epileptics previously well controlled on the same medication; *(g)* Children with developmental delay or regression; *(h)* Seizures in early infancy (except febrile seizures); and *(i)* When surgery is contemplated. Generally a CT Scan is enough. However, MRI is superior to CT in identifying neuronal migration defects, gliomas and vascular malformations and in visualizing temporal lobe structures. Localization of such lesions and hippocampal sclerosis may be important in complex partial seizures. However, in a long standing well controlled case with prior normal CT, MRI is rarely necessary(21).

Newer imaging techniques are now being increasingly used to delineate functional anatomy. These are very sensitive in detecting the region of metabolic dysfunction corresponding to the EEG focus, and are helpful when surgery is being contemplated. They are not required in usual practice.

What are the indications of antiepileptic drug monitoring?

The judicious use of drug monitoring can improve the control of seizures. Logic and clinical judgement must be used in deciding when AED levels are to be done and how to apply the information obtained. Drug dosage should be determined clinically by the degree of seizure control and the appearance of side effects. It should never be adjusted up and down to keep blood level in the therapeutic range. Therapeutic ranges are more useful for phenytoin, carbamazepine and phenobarbitone, and less useful for valproate. Indications(25,26) for getting drug levels include: *(i)* If seizures are not controlled in spite of using maximum dose of appropriate AED (look for trough levels); *(ii)* If seizures recur in a well controlled child where compliance is ensured; *(iii)* Symptoms **or** signs of AED toxicity (look for peak level); *(iv)* In polytherapy when an AED is being added or discontinued; *(v)* When it is not clear if clinical deterioration is related to disease or drug; *(vi)* Change in AED regimen (dose, drug or other medication); *(vii)* Significant systemic diseases that may alter drug metabolism, for example, renal or hepatic failure; and *(viii)* Detection of noncompliance.

Some people like to ensure a therapeutic range after starting AED and thus get blood levels after the AED has reached steady state. However, this is not mandatory particularly if seizures are controlled.

Drug levels in this context, have some established pitfalls which include: *(a)* There is no strict correlation of efficacy and/or toxicity with drug level; *(b)* Optimum blood level for patients is very individual; *(c)* A single sample may be misleading since there is a lot of diurnal variation; and *(d)* faults with the methods of assay.

When and how to discontinue AED? What is the outcome?

Discontinuation of AED(s) must be based on knowledge about natural history of the particular epilepsy and the possibility of remission. There is a strong correlation between individual epileptic syndromes and the success or failure of therapy. The prognosis is best with primary generalized epilepsy whereas it is not so good with secondary partial seizures, particularly complex partial seizures; children with

multiple seizure fare w orst. In gene ral, 70% of children with seizures, who are seizure free for 2 or more years while on AED will remain so after withdrawal(21,25). Usually therefore withdrawal of AED therapy is recom mend ed after a two years seizure free interval. If a child has multiple risk factors for seizure recurre nce, particularly underly ing neurolog ic abnormali ty, grossl y abnormal EEG, multiple seizure types, *etc.* withdraw al has to be indiv idualized after weighing benefits versus risks of prolonged AED therapy. The benefit risk ratio is often more in the direction of withdrawing AED.

The standard practic e in most epilepsy centers is to taper off AED(s) over a period of 3-6 months. However, no correlation has been found between seizure recurrence and the taper period(26). Advanta ges of relatively quicker tapering include less cost and that the outcome of discontinuin g treatment may be known sooner. So periods as short as 6 weeks have been recommended by some for tapering AED to a stop(26). Among those children in whom seizures relapse, 60-70% occur either during the reduction of therapy or within one year after stopping AED(s); nearly 100% of relapses occur with in 2 yrs of withdrawa l of AEDs. So to look for relapse, patient should be followed up for 3-5 yrs.

Should a recurrence after withdrawal of AED be re-treated?

If AED discontinuation has been attempted, and the first relapse is charac terized by frequent attacks (simi lar in type to the previous seizures0 in a 24 hours period, and there is persistent EEG abnormalit y, AED should be restarted(27). When a seizure recurre nce is treated with AED, more than 80% children become sei zure free; the risk of a second relapse has been found to be associated with so me clinical aspects preceding drug withdrawa l (presence of etiologica l factors, seizure free period < 4 yrs before discontinuation, multiple AEDs) and with the characteristi cs of the first relapse (more than one seizure during a 24 hour period, no change in seizure type, presence of EEG abnormalities before first relapse(27).

Cognitive, behavior and other problems

The physician dealing with children with epilepsy should be aware of the fact that these children can have a number of cognitive and beh avior probl ems whi ch also need attention. These may be because of the epilepsy itself or because of AED(s).

Nearly half of children with epilepsy have schooling difficulties(28). The question regarding intelligence of children with epilepsy has remained controversial; while some believe that most of these children are of normal overall intelligence(29), others have shown that the intelligence scores of these children tend to cluster towards the lower side of norm al(30). We found that children with idiopathic generali zed epilepsy have significantly lower 10 scores than those of controls(31).

All AED(s) have the potenti al for adverse effects on cognition or behavior. Although most AED(s) in therapeutic doses have not shown such signif icant adver se effects, there is considerable individual variability. Phenobar bitone has greater adverse effects than other AED(s) (particularly restlessness, irritab ility, hyperac tivity, efc.)-sometimes severe enough to warrant discont inua tion of drug. Recent studies have not found significant differences between the effects of phenytoin and those of CBZ or VPA.

The lack of understan ding and miscon ceptions about epilepsy(32,33) form another issue th at needs to be ta ckled by the

physician. Explanation about the illness and helping parents clear their doubts, goes a long way in developing positive attitudes towards the child with epilepsy.

In summary therefore, the proper approach towards a child with epilepsy requires an understanding by the physician particularly regarding the type of epilepsy, choice of appropriate AED and its pharmacokinetics, judicious use of investigative facilities, and a proper rapport with the family to ensure compliance, regular follow up and management of associated problems. Although we have tried to outline a rantional approach which is applicable to most children with epilepsy, the decisions in a particular child have to be individualized by the treating physician.

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