Seizures constitute the commonest neurological problem in children with significant epilepsy having its onset in childhood. Appropriate diagnosis and management of childhood epilepsy is essential to improve quality of life in these children. Evidence-based clinical practice guidelines, modified to the Indian setting by a panel of experts, are not available.

Process: The Indian Academy of Pediatrics organized a consensus meeting on the diagnosis and management of childhood epilepsy on 22-23 of July 2006 at Mumbai. An expert committee was formed consisting of pediatricians, pediatric epileptologists, pediatric and adult neurologists, electrophysiologists, neuroradiologists, neurosurgeons and intensivists. A consensus was reached during the discussion that followed presentation by each of these experts. The process of updating these recommendations and arriving at consensus continued till 2009.

Objectives: To develop practice guidelines for diagnosis and management of childhood epilepsy.

Recommendations: Recommendations for diagnosis and management of following childhood seizures and epilepsies are given: neonatal seizures, acute symptomatic seizures, neurocysticercosis, febrile seizures, idiopathic partial and generalized epilepsies, first unprovoked seizure, newly diagnosed epilepsy, catastrophic epilepsies of infancy, refractory epilepsies of older children and adolescents, epilepsy with cognitive deterioration and status epilepticus.

Key words: Childhood Epilepsy, Diagnosis, India, Management, Refractory epilepsy.

Seizures constitute the commonest neurological problem in children with significant epilepsy having its onset in childhood. A considerable treatment gap exists in developing countries due to poverty, stigmatization, and lack of trained manpower. Evidence-based clinical practice guidelines can improve the quality of care.

An expert consensus meeting was held at the PD Hinduja National Hospital, Mumbai on July 22-23rd 2006 under the IAP 2006 action plan. The aim was to produce a practice parameter for diagnosis and management of epilepsy in the Indian context. All 22 experts (Annexure I) had several years of experience and publications in epilepsy. Epilepsy subtopics were assigned to each expert with a format of five common questions faced by a practicing pediatrician. A manuscript and presentation were prepared by each expert, using evidence from the medical literature. Emphasis was placed on the resource-poor Indian context, which often makes guidelines from developed countries difficult to apply. The consensus statement was prepared and updated on a continuous basis till 2009.

Objectives

To provide easy, quick and practical guidelines for diagnosis and management of acute symptomatic seizures; and newly diagnosed and refractory childhood epilepsy to the practicing pediatrician.

Recommendations

1. Neonatal Seizures

Neonatal seizures are often acute symptomatic due to underlying brain insults. Focal clonic, multifocal
Clonic, and focal tonic seizures are usually accompanied by ictal EEG activity while subtle, generalized tonic and myoclonic episodes may be non-epileptic as they are not associated with electrographic ictal activity(3). True seizures are often accompanied by open eyes(4). Non-epileptic phenomena like jitteriness and benign sleep myoclonus should be differentiated. Serum glucose, electrolytes, calcium and magnesium must be done in all(5,6). CSF studies and culture must be done in all except when the diagnosis is definite e.g. hypoxic ischemic encephalopathy. A portable 60 minute EEG by a trained technician and interpreter is useful in recognizing subclinical seizures, epileptic encephalopathies and prognosis(6). A cranial ultrasound is the minimum imaging required, but an in-house MRI with diffusion tensor imaging is the modality of choice, done immediately for aetiology and at 3-6 months for prognosis(6). Management should be done as per Fig.1(5-7).

Oral phenobarbitone should be continued till discharge or up to 3 months (especially in those with an abnormal neurologic examination).

2. Acute Symptomatic Seizures

A seizure occurring within a week of an acute brain insult (trauma, infection, toxic, metabolic or vascular insult) is called an acute symptomatic seizure(8). Future risk of unprovoked seizures is only 3-10%.

Serum calcium, magnesium, electrolytes and glucose should be estimated for all children. Lumbar puncture should be done in febrile infants and in those with suspected meningoencephalitis. A plain CT scan is indicated in traumatic brain injury and a contrast enhanced CT scan is indicated in children above 2 years, especially those presenting with convulsive seizures, focal seizures, cluster of seizure (9), or focal neurological deficits to rule out granuloma.

In a hypocalcemic breastfed infant, an underlying vitamin D deficiency state in the child and the feeding mothers should be corrected(10). Anti-epileptic drugs (AED) are required in the acute phase and can be withdrawn in a week in acute traumatic brain injury(11) or in 3 months in illnesses with parenchymal involvement (e.g. CNS tuberculosis or pyogenic meningitis with parenchymal involvement).

3. Febrile Seizures

A simple febrile seizure occurs between the age of 6 months to 5 years. Complex febrile seizures are characterized by partial onset, duration ≥15 minutes, or multiple episodes in the same illness(12). Late onset febrile seizures, persistent febrile seizures, generalized epilepsy and febrile seizure plus (GEFS+) and febrile status epilepticus (FSE) are part of the spectrum of febrile seizures(13).

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**Fig 1. Algorithm for management of neonatal seizure.**
Lumbar puncture should be done in children with a suspected meningitis, especially in infants(13). EEG and neuroimaging have no role in simple febrile seizures(12).

Management includes definitive diagnosis, restraint in investigations, treatment of an acute episode, prophylaxis for future episodes and family counseling(12). Role of defervescence in preventing febrile seizures is questionable(13). Parents can be taught to use rectal liquid diazepam (0.5 mg/kg) or buccal or nasal(12,15) midazolam (0.3 mg/kg) for acute termination of seizures that last for two minutes or more.

Any prophylaxis of febrile seizures reduces the recurrence of seizures but does not reduce the risk of future epilepsy. Intermittent prophylaxis with oral clobazam in a dose of 0.75 mg/kg for 2-3 days in 2 divided doses during fever is useful to prevent recurrence. Febrile status, complex and recurrent febrile seizures (>6/year in spite of intermittent prophylaxis) may need EEG, neuroimaging and continuous prophylaxis with AED. Phenobarbitone and valproate may be used in infants and older children respectively, for 1-2 years(12). Carbamazepine and phenytoin are not useful.

4. Granuloma in Children

New-onset partial or generalized convulsive seizures occurring in clusters in an otherwise normal child is the commonest presentation of single small contrast enhancing CT lesion (SSECTL); necessitating neuroimaging, except when an idiopathic epilepsy syndrome is established with EEG(16). The commonest etiology is neurocysticercosis (NCC) followed by tuberculomas. Parenchymal NCC cysts should be classified as an active vesicular form (cystic, without enhancement or edema), a transitional colloidal/granular-nodular form (ring/disc enhancement with edema) or an inactive form (non-enhancing calcified lesions without edema). Active lesions when accompanied by edema often produce a focal background asymmetry on the EEG(17).

NCC vs. tuberculosis: On neuroimaging the presence of an eccentric scolex in a cystic lesion is pathognomonic of a NCC. Large (>2cm), often multiple, isodense lesions with shaggy borders and location in the posterior fossa are likely to be tuberculomas(18). MR Spectroscopy may help differentiate the two(19).

Cysticidal treatment is beneficial and recommended strongly in live NCC cysts and transitional NCC granulomas(20). Albendazole for a period of 7(20,21) or 28(20) days in a dose of 15 mg/kg in 2 divided doses is the treatment of choice. Prednisone should be used at 1mg/kg/day, 3 days before starting albendazole and continued for a total of 7 days to reduce the risk of cerebral edema at the time of cyst breakdown. A fundal examination should be performed before use of cysticidal drugs as ophthalmic lesions are an absolute contraindication for medical therapy.

AEDs are given in acute symptomatic seizures due to active lesions (cystic lesions, granulomas) till such time that they disappear or become inactive (no edema, no enhancement, calcified) – usually for a period of 6 months(22). Inactive calcified lesions presenting with seizures either de novo or as relapses should be considered remote symptomatic and should be treated till a 2 year seizure free period is achieved. Repeat imaging should be done to check the resolution of lesion after 6 month, if the child is clinically well or earlier, if the initial diagnosis was insecure or if the child is symptomatic.

5. Idiopathic Partial Epilepsies in Childhood

Benign epilepsy with centro-temporal spikes (Benign rolandic epilepsy, BECT)

This should be considered when a normal school aged child presents with brief and infrequent, partial, nocturnal, hemi-facial, sensory or motor seizures. An awake-cum-sleep EEG is necessary, as it displays a characteristic pattern of sleep activated runs of centro-temporal spikes or sharp waves. The syndrome has an excellent prognosis with remission in most cases by the age of 15-16 years(23, 24).

Panayiotopoulos syndrome (Early-onset childhood epilepsy with occipital paroxysms, CEOPs)

CEOP should be considered when a normal preschool (3-5 yrs) child presents with severe nocturnal vomiting, followed by eye deviation and status epilepticus, usually hemioliconic. This syndrome has
an excellent outcome(25). A later-age Gastaut variant of CEOPS is usually characterized by diurnal simple partial seizures with visual hallucinations or amaurosis and migraine like headaches. This has a variable prognosis and can persist into adult life. Neuroimaging is considered in cases with an abnormal perinatal history or examination, atypical EEG, or poorly controlled seizures.

Treatment with AED is not required when seizures are infrequent, but parental counseling is a must. In long term therapy, carbamazepine or valproate are preferred. The syndrome may evolve atypically with frequent refractory seizures, scholastic deterioration and/or behavioral changes; more often with the use of carbamazepine, emphasizing the need of clinical monitoring (26).

6. Idiopathic Generalized Epilepsies

**Childhood absence epilepsy (Petit-mal, CAE)**

This should be suspected in a normal school age child with frequent absence seizures often up to a hundred a day. These occur in the awake state with sudden staring, unresponsiveness and minor brief automatisms, leading to interruption of ongoing activity and unassociated with any post ictal abnormality(23). GTC seizures are unusual. Precipitation of seizure by hyperventilation is a simple clinical diagnostic test. Atypical absence seizures are prolonged, seen usually in catastrophic pediatric syndromes with neurocognitive deterioration.

An EEG showing a typical pattern characterized by frontally predominant generalized bursts of 3 Hz spike wave complexes with abrupt onset is diagnostic. There is no role for routine neuroimaging.

Valproate and ethosuximide (presently unavailable) followed by lamotrigine(27) and the benzodiazepines are the drugs of choice. Response to AEDs should be confirmed by repeat EEG with hyperventilation to check the disappearance of typical EEG pattern. Treatment is for a minimum seizure free period of 2 years with a normal EEG at discontinuation.

**Idiopathic generalized epilepsies of adolescent**

When a child presents with absence, myoclonic or generalized tonic, clonic seizures for the first time after 10 years, a diagnosis of idiopathic generalized epilepsies of adolescent onset is considered. EEG shows generalized paroxysms of spike or polyspikes wave discharges. Photosensitivity is common. Juvenile myoclonic epilepsy (JME), juvenile absence epilepsy (JAE) and epilepsies with only GTC seizures should also be considered in diagnosis(28).

JME presents in adolescents with history of early morning predominant upper limb myoclonic jerks leading to the patient dropping objects. This occurs often in sleep-deprived individuals, especially if suddenly awakened. JAE is similar to CAE, though the numbers of absences are much less and the onset is usually later. GTC seizures typically occur on awakening or in the evening(23).

Sodium valproate is the most effective drug in most cases of idiopathic generalized epilepsies(29), but it may cause weight gain, hair loss, and menstrual irregularities and has a higher incidence of fetal teratogenicity. Therefore, lamotrigine may be preferable in adolescent girls. Due to its lower cost, phenobarbitone may be used in poor patients with resource constraints, with only generalized tonic clonic seizures, but will not control myoclonic or absence seizures. Carbamazepine and phenytoin may worsen the syndromes. Lifestyle adjustments include avoiding precipitating factors like sleep deprivation and alcohol consumption.

Seizure control is achieved in 80% with monotherapy. Withdrawal of AEDs results in relapse in more than 90%, especially in JME and JAE, and often need low dose lifetime medication. In cases of epilepsies with only generalized tonic clonic seizures, a single trial of AED withdrawal after a 2 years of seizure free interval may be tried, but risk of recurrence is high and lifetime AED may be needed.

7. Investigations for Epilepsy

**Electroencephalography (EEG)**

*When should an EEG be done?*

EEG is recommended as a part of initial evaluation in all children presenting with an episodic event. Epileptiform abnormalities support a clinical
diagnosis of seizure, help in the diagnosis of specific syndromes and predict seizure recurrence(30); however, a normal EEG does not rule out epilepsy. The EEG interpretation is reliable only when it is well recorded and interpreted by an experienced EEG reader with at least one year of training in the same.

In the child with uncontrolled epilepsy, a repeat EEG helps in reclassifying the syndrome. Before AED discontinuation, an EEG aids in predicting the risk of recurrence in most syndromes barring a few e.g. BECTS.

In children with unexplained cognitive, neurobehavioral or scholastic deterioration; an EEG may help in diagnosis of specific disorders like SSPE, or epileptic encephalopathies like electrical status in slow wave sleep (ESES), and non-convulsive status epilepticus. There is no place for routine follow-up EEGs in patients who are doing well.

*How should an EEG be done(31)?*

- EEG should be recorded 3-4 days after the last seizure to avoid post-ictal slowing from interfering with the interpretation.
- A sleep EEG after deprivation should be part of all routine recordings in children above the age of three years.
- Minimum activation procedures like hyperventilation and photic stimulation should be used.
- Omission of AED prior to EEG recording is not recommended.
- Simultaneous video-EEG is useful in differentiating non-epileptic events from true seizures and for pre-surgical evaluation.

**EEG in status epilepticus (SE):**

A portable EEG can be done in children with convulsive SE who do not regain consciousness as expected, so as to exclude an ongoing nonconvulsive status epilepticus (NCSE). Continuous EEG monitoring is desirable in refractory SE when pentothal or propofol are being used for dose titration.

**Neuroimaging**

MRI is more sensitive than CT and is the modality of choice. CT retains a role in detecting calcification and in acute situations like head trauma, status epilepticus, and epilepsy, where granulomas are a possibility. MRI protocol should be adapted to the age of the child and the type of epilepsy syndrome(32). Neuroimaging is not recommended in benign epilepsies. High resolution MRI with special techniques is recommended for delineating the epileptogenic zone and the eloquent cortex in pre-surgical evaluation. The preferred sequences are T1W (preferably, inversion recovery), T2W and PD fast spin echo, Fluid-Attenuated Inversion Recovery (FLAIR), 3D T1 acquisitions with 1-2 mm partitions (better anatomy and morphometry).

**8. Management of First Unprovoked Seizure**

A good history is most important for diagnosis of a seizure. Open eyes, eye and head deviation, incontinence, tongue-bite are fairly specific for a seizure, whereas unresponsiveness, confusion, clonic/tonic movements are suggestive, though these may be prominent in non-epileptic events as well(33). If the child is less than 6 months, admission for observation and evaluation is recommended.

- EEG preferably 3-4 days after the seizure is recommended in all cases(34).
- Neuroimaging would be needed when there are seizure cluster, focal deficits, altered sensorium, focal EEG background change, etc(34).
- In the first seizure, AED should not be recommended, but a detailed discussion with the parents is necessary. Exceptions are status epilepticus due to high rate of recurrence(35) or severe parental anxiety. Home management of seizures includes use of rectal diazepam/buccal or nasal midazolam(36) in seizures lasting for more than 2 minutes.

**9. Management of Newly Diagnosed Epilepsy**

- Long term AED treatment should be started after second seizure(37). The aim of treatment is complete seizure control without significant adverse effects. AED is based on the predominant
seizure type or syndrome type with possible adverse effects and co-morbidities taken into account(37,38).

- All drugs are started in low doses and increased gradually up to a maximum dose till seizure control is achieved or side effects appear.
- Dosage needs to be adjusted to the child's daily activity. Extended release formulations in twice a day dosing are preferable(39).
- If no control is obtained with maximum doses of the first drug, then a second first line drug is initiated and the first drug tapered(38). If partial control is achieved(37), then a second AED should be added. All efforts should be made to use only rational polytherapy.
- There are no significant differences in the efficacy or tolerability of the four major first line anticonvulsants (phenobarbitone, phenytoin, valproate and carbamazepine) and any one can be used first(40), based on side effect profile. Carbamazepine and valproate appear to be better tolerated than phenobarbitone and phenytoin.
- A seizure diary should be kept by the parents.
- Therapeutic drug monitoring is useful in only few situations, including breakthrough or refractory seizures, to assess compliance, for diagnosis of clinical toxicity or with use of phenytoin, which has dose dependent pharmacokinetics(41).
- In most epilepsy, AED is withdrawn after 2 year of seizure freedom. Adolescent onset, remote symptomatic epilepsy and abnormal EEG after 2 years are predictors of relapse(42), warranting drug withdrawal after 4 years(43). Drug withdrawal is over 3-6 months(44,45) and one drug at a time in cases of polytherapy.

10. Conventional Antiepileptic Drugs

**Phenobarbitone**

Phenobarbitone could be used as a first line AED in neonatal seizures(46), in the first two years of life for partial/GTC seizures(47) and in neonatal and early infantile status epilepticus(SE). The dosage varies between 3-6 mg/kg/day given as a single night-time dose for routine use and 20 mg/kg given as loading for SE. Since deleterious cognitive and behavioral side effects remain a concern, it should be avoided in schoolgoing children.

**Phenytoin**

Though effective, should not be preferred as a primary AED in newly diagnosed epilepsy, especially in infancy, as levels fluctuate frequently in infants, making monitoring of drug levels imperative(41), and in adolescent girls as cosmetic side effects may be unacceptable(48). Maintenance dosages in older children are between 5-6 mg/kg given in one or two divided doses, but infants may need upto 15-18 mg/kg in 3-4 divided doses.

**Valproate**

As a result of its broad spectrum of efficacy, valproate could be the drug of choice for most children with newly diagnosed epilepsy, like idiopathic generalized epilepsy (CAE, JAE, BMEI, and JME), epilepsies with prominent myoclonic seizures or with multiple seizure types, and photosensitive epilepsies(49). However, in adolescent girls or obese patients, one may not use it as first line agent due to concerns of weight gain, hair loss and aggravation of polycystic ovarian disease (PCOD), which should be specifically looked for(50). Hair loss may be reduced by use of supplemental biotin(51). It could be used in partial epilepsies in infants where carbamazepine might precipitate generalized seizures and in refractory status epilepticus. The dose averages between 10-40 mg/kg/day. Twice-a-day dosing is preferred with extended release preparations(39), except in syrup (3 times a day). Parents should be counseled regarding danger symptoms and signs of hepatitis, like nausea, vomiting, drowsiness etc, especially in children below the age of 2 years, those on polytherapy and those with associated IEM, necessitating routine monitoring of LFT. Enzyme elevation upto twice normal or borderline elevation of ammonia can be disregarded when asymptomatic. The drug must be stopped immediately in all symptomatic patients irrespective of enzyme levels. In case the cause of the hepatitis becomes clear e.g. hepatitis A confirmed by serology, then valproate could be restarted after the hepatitis has resolved. In cryptogenic hepatitis it is best avoided. Carnitine supplements are not routinely recommended(52).
Carbamazepine

It is the drug of first choice for all newly diagnosed partial epilepsies(53), after the age of 2 years. The dose varies between 10-30 mg/kg in the form of twice a day dosing and preferably given as slow release preparations(54,55), if syrups are used they should be given three times a day. Carbamazepine may induce or exacerbate generalized seizures like infantile spasms, myoclonic, tonic and absence seizures in the younger child(56). Paradoxically, it may exacerbate partial seizures as well, in benign partial epilepsies. It may worsen the EEG with deterioration in cognition, behavior and language & can rarely precipitate electrical status in slow wave sleep (ESES)(57). Parents should be informed about the common side effects like appearance of new seizures, deterioration of school performance or appearance of rash (Steven’s) and Drug Rash Eosinophilia and Systemic Symptoms- DRESS syndrome shared with phenytoin and pheno-barbitone) which should be reported immediately. A routine hematological monitoring is not recommended.

11. Newer Antiepileptic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monotherapy Use</th>
<th>Add-on Use</th>
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<tr>
<td>Clobazam</td>
<td>Intermittent use (a) Febrile seizure prophylaxis to prevent acute seizure recurrence(57,58). (b) Reflex epilepsy e.g. hot water epilepsy (just before a hot water bath). (c) Catamenial epilepsy (Straddling the menstrual period). (d) During seizure clusters.</td>
<td>Add-on in refractory generalized epilepsies like absence, tonic and tonic-clonic and syndromes like LGS and in refractory partial epilepsies also(64).</td>
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Oxcarbazepine

Can be used as monotherapy in newly diagnosed partial epilepsy for children above 4 years of age(63), if affordable and available. It can be used for add-on therapy in refractory partial and secondary generalized epilepsy(64,65). Start with a dose of 10 mg/kg; titrated upwards weekly, guided by seizure control, to a maximum of 40 mg/kg. Though once daily preparations are marketed, it is prudent to give this drug in two divided doses. An abrupt switchover from CBZ to OXZ can be done in a dose ratio of 2:3(66). No routine monitoring of drug levels, blood counts or sodium is recommended, unless symptomatic (vomiting, drowsiness or increased seizures).

Lamotrigine

Monotherapy in newly diagnosed generalized epilepsy (absence and myoclonic)(67) and in other partial(68)/generalized epilepsies, and in specific epilepsy syndromes like idiopathic generalized epilepsy in teenage years, especially girls (as first choice)(29). Occasionally, myoclonic jerks maybe paradoxically worsened by lamotrigine, especially in JME.

Add-on in refractory generalized epilepsies like absence, tonic and tonic-clonic and syndromes like LGS and in refractory partial epilepsies also(64).
The dose should initially be 0.5 mg/kg (alone), 0.2 mg/kg (with VPA), and 0.6 mg/kg (with phenobarbitone, phenytoin, carbamazepine); it should be doubled every 2 weeks to a maximum of 15mg/kg (alone) and 5mg/kg/day (with VPA) and higher when used with enzyme inducers. LTG has to be titrated slowly to prevent rashes and Stevens Johnson syndrome.

**Topiramate**

It can be used as a second line add-on agent in refractory partial and generalized epilepsies as well as Lennox Gastaut syndrome(64). It maybe particularly useful in certain syndromes like infantile spasms(69,70) and Dravet’s syndrome(71). At present, its use as first line monotherapy in newly diagnosed epilepsy is not recommended because of a significant adverse effect profile.

It should be started at a dose of 0.5-1 mg/kg in bid doses, escalated weekly or biweekly, up to maximum of 5-10mg/kg (72); Higher doses (10-30 mg/kg) and rapid escalation (every 3 days) are considered in special situations (infantile spasms, status epilepticus); however, there could be a higher incidence of adverse events with high doses.
Clinical monitoring for adverse effects like weight loss, eye symptoms like blurring, redness, watering and eye pain (glaucoma/myopia), metabolic acidosis(73) and oligohydrosis(74) is necessary in all cases. Decreased appetite and weight loss are expected and should be communicated to the caregivers. Cognitive adverse effects can be minimized by converting to topiramate monotherapy, if possible.

Hydration should be maintained and calcium supplements should be avoided to minimize risk of renal stones.

**Levatiracetam**

It should be used only as an add-on drug to refractory partial(75,76) and some generalized epilepsies like, refractory absence or progressive myoclonic epilepsies(77). It is not recommended to be used as a first-line agent in newly diagnosed epilepsies, though recent data support a role in the idiopathic generalized epilepsies of adolescents (JME etc). Behavioral adverse effects like aggression are the most common adverse effects, rarely a paradoxical increase in seizure frequency may occur and this should be monitored carefully.

The usual effective dose is between 20-60 mg kg / day. One can start at 20 mg/kg in two doses and increase every 1-2 weeks till 60 mg/kg/day.

**Tiagabine**

As add-on in refractory partial seizures(78). It is not recommended as monotherapy in children with newly diagnosed epilepsy. NCSE (non convulsive status epilepticus) can occur in about 8% of patients and should be carefully excluded in children whose seizures/mental status deteriorate on treatment(79).

It is used in an initial daily dose 0.1 mg/kg TID; increased weekly by 0.1 mg/kg; maximum daily dose 0.4 and 0.7 mg/kg (uninduced and induced, respectively). In children over 12 years, it can be initiated at 4 mg/day; total daily dose increased by 4 mg in week 2 (divided doses); then increased by 4 to 8 mg/day (divided doses) each week until clinical response is achieved or to a maximum daily dose of 32 mg/d is reached.

### 12. Ketogenic Diet in Epilepsy

The ketogenic diet (KD) is a stringently controlled high fat and low protein/carbohydrate diet given with/without a restricted fluid intake to maintain ketosis on a long term basis(80). It has been shown that it is more efficacious than newer AEDs in controlling refractory seizures(81) and is more cost effective. It can be used with both non-vegetarian and vegetarian diets at any age and for all types of seizures. It has significant improvements in hyperactivity and aggression in almost all patients(80,81). Hence, it should be tried in all children above the age of 1 year with drug-resistant epilepsy, especially those who are not a surgical candidates or where surgery cannot be performed due to availability/affordability issues. Referral to centers providing the KD should be considered once adequate trials of three AEDs have failed, suggestive of pharmacoresistant epilepsy(82). Adverse effects(83) include GI disturbances, acidosis, increased susceptibility to infections, drowsiness, weight loss, nutritional deficiencies and rarely, renal calculi and pancreatitis. Most of these occur early in the diet and should be carefully monitored. The diet should be considered a failure if there is no benefit in 3-6 months and it should be discontinued after this time. In responders, it should be continued for 2-3 year after which it is gradually tapered.

### 13. Surgically Remediable Syndromes

All infants and children with refractory partial or generalized epilepsy should be referred as early as possible to a comprehensive epilepsy center for possible surgical evaluation. This process should be expedited if there is an imaging documented unilateral lesion or if the epilepsy is having significant effects on the child’s development.

Ideal surgically remediable syndromes(84) include:

- Hemispheric epilepsies with pre-existing contralateral hemiplegias/visual field defects caused by large unilateral gliotic lesions/atrophy, Rasmussen’s encephalitis, hemispheric dysplasias etc, where hemispherectomy/hemispherotomies could offer a possible surgical cure.
• Discrete lesions without involvement of functional motor, visual and language cortex, where a lesionectomy will often result in a complete cure. Common lesions would include developmental tumors, cortical dyslasias, AVMs etc. Sometimes lesions like large dyslasias/infarcts may need lobectomies/multi-lobar resections.

• Mesial temporal lobe epilepsy caused often by hippocampal sclerosis is not uncommon in teenagers and is amenable to an anterior temporal lobectomy.

• Drop attacks with injuries respond well to corpus callosotomy and should be offered as a palliative procedure.

14. Refractory Epilepsy

Refractory epilepsy in childhood can be defined as epilepsy which is uncontrolled despite adequate trials of three first line AEDs(82) and when it disrupts developmental progress or normal childhood activity(85). When faced with a child with uncontrolled epilepsy, always try and confirm whether the diagnosis is correct. Often non-epileptic conditions may be confused as seizures (see above). Also the type of seizure and if possible, a correct diagnosis of the specific epilepsy syndrome may facilitate correct choice of drug.

Errors in management must be looked for as pseudo-intractability often results from an inadequate dose, irrational polytherapy or wrong choice of AED e.g. carbamazepine for absence seizures(86). Every effort should be made to keep a seizure diary and see if a specific AED is actually helping or in some cases worsening the seizures e.g. carbamazepine/oxcarbazine may worsen and sometimes even induce absence/myoclonic seizures(87,88).

It is best to refer intractable epilepsy early to a tertiary center for appropriate evaluation (including high-end MRI using standardized epilepsy protocols, video EEG etc) as well as to get guidance on management options like newer AEDs, the ketogenic diet and surgery.

15. Catastrophic Epilepsies in Infancy and Early Childhood

West syndrome, symptomatic generalized epilepsies like the Lennox-Gastaut syndrome and many other lesional partial epilepsies starting in infancy, which may have fairly rapid effects on the developing brain with high risk are appropriately labeled as the catastrophic epilepsies. These often require fairly detailed knowledge and expertise in both evaluation and management and are best referred to a specialized center where pediatric neurologist or epileptologist is available for specialized care.

West syndrome (WS)

Early recognition needs taking a detailed history of the jerks with an emphasis on when they occur (usually on awakening in clusters lasting few minutes)(89). Typically, they are described as “jhatka” in Hindi, “dachakte” in Marathi and “chamke” in Gujarathi. There is often loss of eye contact and social smile, which should be carefully looked for. This may sometimes precede spasm onset by days or weeks.

A detailed history of preceding perinatal events (hypoxic-ischemic encephalopathy, neonatal hypoglycemia etc), developmental milestones, examination of the skin for stigmata of tuberous sclerosis, head circumference measurement and careful neurologic/developmental examination looking for deficits/delays will help to differentiate cryptogenic vs. symptomatic spasms.

An EEG should be done to confirm the diagnosis, though the characteristic pattern of hypsarrhythmia is not mandatory for diagnosis(89,90). Moreover, an experienced electroencephalographer should be available for interpretation.

If the history and examination do not reveal an obvious etiology, an MRI preferably with special techniques to look for malformations of cortical development should be undertaken. Metabolic tests are usually unhelpful and should be done only in selected infants(90), where there is a high suspicion for a neurometabolic condition e.g. consanguinity, positive family history, etc.
Steroids are the drugs of first choice in all cases of West syndrome (90,91), especially so in cryptogenic WS, except in tuberous sclerosis. ACTH is preferred over oral steroids (90,91). Oral prednisolone is given in doses of 2-4 mg/kg (91) or natural ACTH in 30-40 units/day (3-6 U/kg) for 2 weeks, with rapid taper over the next 2 weeks. Rapid control of the spasms within 1 month of onset is associated with rapid developmental gains (VPA could be continued after steroids in symptomatic West syndrome).

Vigabatrin is preferred in TS as first choice (90,91) and in steroid failures in the others (taking into account availability/affordability issues). It should be used for a period of 3-6 months only, due to the fear of visual field defects.

Nitrazepam/high dose VPA/Topiramate can be used as alternatives. The ketogenic diet and surgery in selected lesional cases are other alternatives.

**Lennox Gastaut syndrome**

Any toddler, who has epileptic drop attacks and is delayed or has arrest in development, should be considered to have LGS (89). Usually other types of seizures are also present (like atypical absence and brief tonic seizures in sleep).

An MRI is essential in case no obvious cause is identified on history and examination. An EEG should be performed to confirm the diagnosis though the typical slow spike-wave paroxysms are not mandatory for diagnosis (89). It is mandatory for diagnosis of non-convulsive status epilepticus, which often occurs in LGS and manifests as decreased responsiveness, drooling and regression of milestones lasting hours to days (89).

VPA and CLB should be used initially. LTG (92) or TPM (71) should be added in case of continuing seizures. CBZ and OXZ should be avoided.

The ketogenic diet should be used early, if available. Helmets should be worn to prevent head injury. It is best to refer such children to a tertiary epilepsy center to manage these complicated patients.

**Dravet’s syndrome (Severe myoclonic epilepsy of infancy)**

One should think of this syndrome in normal infants with onset of refractory febrile/afebrile, focal/generalized seizures in the first year of life (94). They often present as refractory febrile or afebrile status epilepticus (SE) (94) which often lasts several hours. Over the next 2-3 years, delayed language development, autistic features and later, gait difficulties become evident. Myoclonic and absence seizures, often photosensitive usually become prominent after the first year, though they are not mandatory for diagnosis (93). VPA, CLB and TPM (71) are drugs most likely to help prevent SE, though a full remission is unlikely to occur. LTG and CBZ regularly worsen these seizures and therefore should be avoided in all febrile seizures in infancy, even those which are clinically focal. Once this condition is considered, it is best to refer to a tertiary care center for further evaluation and management.

**16. Refractory Epilepsies in Older Children and Adolescents**

**Mesial Temporal Lobe Epilepsy**

Clinical recognition of mesial temporal lobe epilepsy (MTLE) is important as it is the most common refractory epilepsy syndrome in the older child/teenager. It is often caused by hippocampal sclerosis, though other etiologies like cortical dysplasia, tumors and vascular malformations may also underlie it. It presents as complex partial seizures with an aura of fear or epigastric sensation followed by unresponsiveness, automatisms and later secondary generalization. The patients have often had febrile seizures (often febrile status epilepticus) in the past. The complex partial seizures present several years later and over time become refractory.

Sleep deprived EEGs with special electrodes are often needed in these cases and should be also done in specialized centers. High quality MRIs need to be done to diagnose hippocampal sclerosis and where MTLE is suspected, it is better to refer the child for an MRI through a specialized center to avoid dual costs. In many children, conventional AEDs like CBZ, PHT and newer AEDs like OXZ and TPM are effective for a while in controlling seizures.
However a large number become resistant to AEDs and there is a progressive cognitive, behavioural and memory impairment, if the epilepsy remains uncontrolled. Early surgery in the form of anterior temporal lobectomy is significantly more effective than best medical treatment in adults(95).

**Epilepsia Partialis Continua**

Epilepsia partialis continua should be suspected when focal, fairly constant myoclonic/clonic jerks involve one or more parts of the body (face/limb/tongue) only unilaterally(96). In most children, progressive, presumably immune-mediated encephalitis, Rasmussen’s encephalitis underlies this disorder. Over time, a progressive hemiplegia with deterioration in cognition and behaviour is usual, as the epilepsy is resistant to all AEDs(96).

Investigation should include a MRI which is initially often normal but shows progressive hemiatrophy and unilateral signal changes. EEGs are also helpful though they may be deceptively show absence of abnormalities. Only focal background disturbances may be seen. Till a hemiplegia develops immune therapies like steroids and IVIG can be used.

Treatment is again primarily surgical(96) and a hemispheric resection/disconnection are the procedure that seems to benefit a large number. The only drawback is that a permanent motor/visual field defect is invariant after a hemispherectomy. Hence, this procedure becomes difficult in children who still have good function of the limbs.

17. Epilepsies and Cognition

Cognitive deterioration, academic underachievement and behavioral problems are common co-morbidities in children with chronic epilepsy(97-99). Uncontrolled seizures and worsening of the EEG with increasing epileptiform abnormalities are more likely to be responsible for cognitive deterioration, than any AED(100).

All children with epilepsy should be screened with a simple child behavior checklist(101) consisting of questions directed towards mood, behavior and school performance. Some children merit a more formal neuropsychological examination.

Sensitization of parents and teachers regarding associated co-morbidities and early referral for psycho-educational evaluation and special education is useful.

All attempts to switch to monotherapy should be done to reduce AED induced behaviour / cognitive effects.

It is important to recognize rare but important syndromes like the Landau-Kleffner syndrome (LKS) and Continuous Spike-Wave in Slow-Wave Sleep (CSWS)(102,103). LKS presents as predominant language deterioration in a previously normal child who may or may not have clinical seizures. Initially the child may stop responding when called and may appear to be deaf; there may be school performance as well as behavior deterioration. CSWS is a more global disturbance with a frank dementia and autism. Both these syndromes are presumably causally associated with a continuous epileptic discharges in non-REM sleep – electrical status in slow wave sleep (ESES). Hence, any child with or without epilepsy, who has cognitive, language and behavioural deterioration should have an awake and more importantly sleep EEG to establish the diagnosis. Evaluation and management of these complex syndromes need referral to specialized epilepsy centers.

18. Status Epilepticus

Children with seizure clusters are at increased risk of SE. Use of oral CLB or DZP for 2 days may be beneficial in decreasing this risk. A child who is brought to the physician from an extramural setting still convulsing should be considered to be in SE; the minimum time for this definition of SE is regarded as >5 minutes(104). There is an increased risk of irreversible neuronal injury after 30 minutes of convulsive status(105). A management algorithm(106-110) is provided for status epilepticus in Fig 2.

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Establish ABCs: Establish IV access, draw blood for laboratory investigations
IV glucose, calcium, or pyridoxine (in neonates and infants)

↓

IV Lorazepam 0.1 mg/kg
OR

IV diazepam 0.2 mg/kg followed by IV phenytoin/fosphenytoin
(If no IV access use PR diazepam 0.5 mg/kg or buccal/nasal/IM midazolam 0.2 mg/kg; intraosseous access could be considered as a next step if IV still not available.)

↓

Repeat Lorazepam/ Diazepam once more SOS (5-10 mins)

↓

IV fosphenytoin 20 PE (phenytoin equivalent)/kg/phenytoin 20 mg/kg(30 mins)
(Consider transfer to PICU facilities as child at risk of refractory status)

↓

IV valproate (1:1 diluted NS 20-40 mg /kg over 1-5 minutes; given as continuous infusion at a rate of 5mg/kg/hr, if required.
OR

IV phenobarbital 15-20 mg/kg
(Re-assess airway again; consider tracheal intubation, if the
airway is compromised or the patient develops respiratory depression)(45-60 min)

↓

Transfer to a PICU set-up is mandatory as the child has refractory SE and will need intensive monitoring in
a tertiary PICU set up.

↓

Midazolam infusion (loading dose of 0.2 mg/kg, followed by 0.1 mg/kg/h titrate every 15 mins upwards by
0.05 mg/kg/h till control; maximum dose 2 mg/kg/h)
OR

Propofol infusion/ Pentothal infusion
(Propofol should not be routinely recommended in view of significant morbidity and mortality in children)

↓

General anesthesia if above steps fail
(Tertiary hospital set-up essential)

In refractory status epilepticus needing coma producing therapies (Pentothal etc)
EEG monitoring preferably continuous should be used, if available. It should also be used if coma persists
despite control of convulsive status epilepticus (to exclude non convulsive status epilepticus)

**Fig. 2 Management algorithm for status epilepticus.**

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ANNEXURE

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