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Monograph on EPILEPSY PRACTICE

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5 CHAPTER

Treatment

GENERAL PRINCIPLES AND DRUG SELECTION

- The treatment of epilepsy principally focuses on treatment of epilepsy in children and adolescents, as that is the age when most of the seizures have their onset, at <20 years of age.
- Treatment with medicines results in freedom from seizures in about 70%.
- It is debatable whether the antiseizure medication (ASM) should be started after the first seizure or could be delayed till the occurrence of the second seizure.
- The clinical diagnosis of epilepsy is established only when the person has had two or more unprovoked seizures or if the risk of another seizure is >60% after the first one.
- *The factors linked to an increased risk of recurrence are*:
  - Abnormalities on neurologic examination
  - An abnormal MRI of the brain
  - Abnormal EEG with epileptiform discharges
  - History of nocturnal seizures

The presence of any one of these factors increases the risk of recurrence twofold.

Some types of epilepsies are self-limited. In childhood focal epilepsy with centrotemporal or occipital spikes, long duration of treatment may not be required as eventually these children outgrow their seizures. Moreover, if the seizures are focal and if nocturnal, the parents are comfortable with not initiating ASM even if the seizures are recurrent. However, the decision for initiation could vary in those with daytime seizures, generalized tonic–clonic seizure (GTCS) type, and long duration of seizures.

The initiation of drug treatment could be delayed until the occurrence of a second seizure, as up to 40% may not have a recurrence, and treatment can be withheld, in those with self-limited focal epilepsies of childhood and based on the parents decision as mentioned earlier. Consideration of cognitive behavioral adverse effects could also influence the decision by the parents to initiate the drug treatment.

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There is no adequate data available at present on the impact of cognitive and behavioral effects of the newer antiseizure medicines. Their effects on an individual child is unpredictable, which is also a matter of concern to the parents, influencing their decision to initiate drug treatment.

CHOICE OF THE ANTISEIZURE MEDICATION

The three factors which decide the choice of the drug are:

1. The seizure type
2. The efficacy of the drug for that particular seizure type
3. The adverse effect of the drug

Going by the age of onset of seizures, the following treatment options can be followed:

- *Epileptic spasms*: Steroids and vigabatrin (VGB)
- *Absence seizures*: Ethosuximide, valproic acid, and lamotrigine (LTG)
- *Focal seizures*: Carbamazepine (CBZ), oxcarbazepine (OXC), LTG, and lacosamide (LCM)
- *Generalized seizures*: Valproic acid remains the most effective drug

There are >25 ASMs available in the market of which the newer ones have lesser adverse effects and drug interactions. The choice of the first drug to use would obviously depend on its efficacy and tolerability. The other factors influencing the choice of the drug include the epilepsy syndrome, the ASM pharmacology, and the patient's characteristics, including the socioeconomic and cultural factors.

The single most important factor would be the type, or types of seizures, and if there are multiple, which ones need to be targeted. This is where the description of the seizures, given by the patient and eyewitness, becomes important along with a video recording of the seizure.

The next major deciding factor would be the adverse effect profile of the drug chosen, and it would be preferable to choose the one, causing less drowsiness and cognitive dulling. It is worth noting the higher risk of Stevens–Johnson syndrome with HLA-B*1502 and a risk of liver failure in those with a POLG1 mutation, especially when choosing CBZ and valproate, respectively. This is where pharmacogenomics play a part in the choice of the medication.

Monotherapy is associated with better compliance and fewer side effects in comparison with combination therapy, and therefore serial monotherapy trials of two ASMs that are appropriate first-line treatment for the seizure type should be undertaken before combinations are tried. About 60% of patients with newly diagnosed epilepsy achieve seizure control with the first or second ASM. Attention should be given to choosing the most appropriate initial ASM taking into account the type of seizure and/or the epilepsy syndrome.

In general, the medication is started at a low dose with increments in weeks to establish an effective and tolerable dose. Valproate and levetiracetam (LEV) can be commenced at effective doses with rapid titration or no titration.

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Serum concentration of ASM measurement helps determine the compliance, assess the adverse effects, and decide on the most effective dose. Concentrations associated with optimal control vary with individuals and may occur below, within, or above the so-called "therapeutic" or "target" ranges for the drugs, especially in children and elderly. The ranges should be regarded purely as a guide to prescribing, and routine measurement of serum drug levels is not recommended particularly with regards the newer ASMs.

The commandments in the pharmacological treatment of epilepsy are:

- Choose the correct drug for the seizure type and/or epilepsy syndrome
- Start at a low dose and titrate up slowly
- Keep the regimen simple with twice-daily dosing at the most
- Try two suitable drugs as monotherapy before adding the second drug in combination
- If seizures persist, combine the best tolerated first-line drug with one of the newer drugs depending on seizure type and the mechanism of action
- Simplify the schedules and regimens in patients receiving polypharmacy

Reasons for "Pseudoresistance" to ASMs

- *Wrong diagnosis*: Syncope, cardiac arrhythmia, psychogenic non-epileptic seizures, and malingering
- Underlying brain neoplasm
- *Wrong drug*: Inappropriate medication for the seizure type
- Pharmacokinetic/pharmacodynamic drug interactions
- Wrong dose
- Adverse effects preventing dose increase
- Wrong lifestyle
- Poor compliance with medication
- Inappropriate choices (alcohol or drug abuse)

ANTISEIZURE MEDICATIONS

Established Antiseizure Medications

Many patients are still on one of the older ASMs (established drugs) and hence worthwhile to look at them and the newer ones.

Carbamazepine

- It has been a first-line treatment option for focal seizures and tonic–clonic seizures. It might exacerbate generalized absences and myoclonic seizures.
- Started in low doses of 200 mg a day and increased over 3–10 days depending on the urgency.
- Diplopia, headache, dizziness, nausea, and vomiting are the common side effects.

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- Idiosyncratic reactions with severe skin eruptions including erythema multiforme and Stevens–Johnson syndrome can occur in those who are HLA-B*1502 positive.
- Fluid retention could happen because of its antidiuretic hormone (ADH)-like action and cause hyponatremia. A dose-dependent major congenital malformation can occur in children exposed to the drug in utero.

Clobazam

- Clobazam (CLB) is a useful adjunct for drug-resistant focal and generalized seizures and in Lennox–Gastaut syndrome (LGS).
- Short-term administration of 10–20 mg daily is a good strategy for prevention of premenstrual seizures, and as "cover" in other stressful situations such as weddings and surgery.
- It is a useful prophylactic at onset of fever in children with regular febrile seizures and in those who have clusters of focal seizures with impaired awareness (FSIA) or secondary generalized seizures when given immediately after the first event.

Clonazepam

- Enhances gamma-aminobutyric acid (GABA) inhibition
- Clonazepam (CZP) is used as adjunctive treatment for generalized seizures such as absence, myoclonic, and atonic seizures

Phenobarbital

- Prolongs the chloride channel opening at the $GABA_A$ receptor, resulting in neuronal hyperpolarization.
- Earlier widely used for focal and tonic–clonic seizures but has become a second-line treatment because of sedation and behavioral problems.
- However, the drug is effective, well tolerated, and is inexpensive and hence continued to be in use.

Phenytoin

- Like CBZ, phenytoin blocks voltage-gated sodium channel.
- It has been the first-line medication for the prevention of focal and tonic–clonic seizures and also parenterally for acute treatment of seizures and status epilepticus.
- It is not efficient against myoclonic, atonic, and absence seizures.
- Administered as a single dose or two divided doses of 300 mg a day.
- Adverse effects can be neurotoxic such as ataxia, nystagmus, dysarthria, somnolence, asterixis, and dysmorphic effects with chronic use such as gingival hyperplasia, hirsutism, acne, and facial coarsening.

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- Uncommon long-term problems include folate deficiency, osteopenia, peripheral neuropathy, and cerebellar atrophy which can take years to develop.
- Rare idiosyncratic reactions include Stevens–Johnson syndrome, hepatitis, bone marrow suppression, lymphadenopathy, and lupus-like syndrome.
- It is a hepatic enzyme inducer and reduces serum concentrations of CBZ, valproate, LTG, and topiramate (TPM).

Fosphenytoin (FOS) is a parenterally used ester prodrug of phenytoin. It can be given intravenous (IV) or intramuscular (IM) as it is water soluble. It is the first ASM given IV at a loading dose of 20 mg/kg for status epilepticus and continued as a maintenance dose of 100 mg 8 hourly.

Sodium Valproate

- It acts as sodium channel blocker and also as a GABA facilitator.
- It is a broad-spectrum ASM effective for all seizure types and particularly for genetic generalized epilepsies.
- The starting dose would be 500 mg once or twice daily.
- Distressing adverse effects include tremor, weight gain, loss of hair, and menstrual irregularities including amenorrhea. Encephalopathy associated with hyperammonemia can rarely occur. Insidious development of parkinsonism has been noted to occur.
- There is an increased dose-dependent risk of major congenital malformation in offspring exposed to high doses of valproate during the first trimester of pregnancy.
- It would be prudent not to start women of childbearing age on sodium valproate (VPA) without neurological advice.

Lacosamide

- It acts by enhancing the slow inactivation of voltage-gated sodium channel.
- LCM has recently been approved as monotherapy for focal seizures and focal becoming generalized seizures and also in children of over 6 years of age.
- The initial dose is 50 mg twice daily increased to 100 mg twice daily after a week with a maximum of 200 mg twice daily.
- Parenteral preparation is also available for IV administration.
- Dizziness, headache, nausea, and double vision are common side effects and incoordination, nystagmus, tremor, and somnolence have also been reported.

Lamotrigine

- It blocks the slow inactivated state of the sodium channel preventing the release of excitatory neurotransmitters glutamate and aspartate.

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- It is another broad-spectrum anticonvulsant like valproate effective against all seizure types though it might exacerbate myoclonic seizures in some patients.
- Monotherapy in children has been approved and is favored in children with learning disabilities and multiple seizure types.
- LTG is administered as once daily dose and in those on enzyme inducers as twice daily doses.
- Low starting dose with slow titration is advisable, especially when used in combination with VPA when there is increased risk of occurrence of rashes.
- Started as 25 mg once daily increased by 25 mg every 2 weeks when used with VPA as a combination.
- It is a safe drug to use as monotherapy in pregnancy because of its low teratogenicity.
- As with other ASMs the common side effects include headache, nausea, vomiting, insomnia, diplopia, ataxia, and tremor.
- Spontaneously subsiding maculopapular rash can occur in a small proportion, <0%, in patients who are also on VPA.
- Rare occurrences of Stevens–Johnson syndrome and toxic epidermal necrolysis have been reported.
- LTG serum levels fall during pregnancy and in patients on estrogen containing oral contraceptives and also before menses and serum concentration levels help in adjusting the doses.

Levetiracetam

- It binds to synaptic vesicle protein 2A (SV2A), a protein involved in synaptic vesicle exocytosis and release of a range of neurotransmitters.
- It can be given for a variety of seizure types including myoclonic and can be used for focal-onset seizure in infants as young as 1 month of age and older as adjunctive therapy and for primary generalized tonic–clonic seizures from 6 years of age.
- Controlled release and IV formulations are available and IV LEV is frequently used for treatment of acute seizures and status epilepticus and has become the drug of first choice in this setting.
- Dose is initiated at 250–500 mg twice daily and titrated in 1,000 mg increments every 2 weeks as required and tolerated, to a maximum of 4,000 mg a day. Even 250 mg twice daily is sufficient in some for seizure remission.
- LEV is well tolerated and the common side effect is somnolence. Behavioral problems such as agitation, aggression, emotional lability, hostility, psychosis, anxiety, and depression are not uncommon, especially in adolescence.
- It has no clinically important drug interactions even with oral contraceptives.
- The half-life is 8–10 hours and steady state is reached in 2 days of twice daily dosing.

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Oxcarbazepine

- It is a prodrug of hydroxycarbamazepine and prevents burst firing of neurons by blocking the sodium channels and modulating the calcium and potassium currents
- The starting dose of OXC recommended is 150–600 mg/day titrated up to 3,000–4,000 mg/day depending on the need. It can be used in children over 3 years of age at a starting dose of 5 mg/kg daily increasing to 30 mg/kg daily.
- Patients can be immediately switched over to OXC from CBZ at 1.5 times the dose of CBZ.
- Central nervous system (CNS) side effects are common and include drowsiness, dizziness, diplopia, nausea, vomiting, and ataxia. Rash occurs less frequently than with CBZ but can cause Stevens–Johnson syndrome and toxic epidermal necrolysis. Hyponatremia is more common with OXC than CBZ due to the ADH-like effect.

Topiramate

- It has multiple pharmacological modes of actions including blocking of sodium channels and high voltage-activated calcium channels; attenuates kainate-induced responses; enhances GABAergic neurotransmission; and inhibits carbonic anhydrase.
- TPM is effective in partial and tonic–clonic seizures and myoclonic epilepsies. It is beneficial in treating infantile spasms and LGS. It is also recommended as monotherapy in newly diagnosed epilepsy.
- Started at an initial dose of 25–50 mg/day and increased by 25–50 mg every 1–2 weeks till a maximally effective and/or tolerated dose is achieved. In drug-resistant epilepsy (DRE) doses up to 200–400 mg twice daily is optimal while lower doses are adequate in those who are on nonenzyme-inducing ASMs. When used in combination with LTG, a low dose of 50–100 mg daily might be adequate.
- CNS side effects include ataxia, poor concentration, confusion, dysphasia, dizziness, paresthesia, word finding difficulty, and cognitive dulling. The risk of kidney stones is high in those with a history of renal stones and who are taking calcium stones and vitamin C and is to be avoided in them and those with glaucoma.
- Paresthesia is rather common in the first few days of commencing treatment and needs reassurance and reduction of dose for some time to get used to the medicine.

Zonisamide

- Zonisamide (ZNS) blocks voltage-dependent sodium and T-type calcium channels, inhibiting the release of excitatory neurotransmitters.
- ZNS is efficacious for drug-resistant focal seizures and a variety of generalized seizure types including tonic–clonic, tonic, atonic, and

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atypical absence seizures. It is also effective in juvenile myoclonic epilepsy (JME) and progressive myoclonic epilepsy (PME).
- Dose of ZNS recommended is 50–100 mg/day in two divided doses in adults and 2 mg/kg/day in two divided doses in children.
- Anorexia, dizziness, ataxia, somnolence, confusion, and impaired concentration are the common side effects.
- The half-life is 50–70 hours and hence a steady state is reached in about 15 days but the half-life is decreased by about 50% if used with enzyme-inducing ASMs.

Perampanel

- Perampanel (PMP) targets specific brain receptors to reduce excessive electrical activity that triggers seizures.
- It is used as an add-on treatment with other ASMs for focal-onset seizures in children aged 4 years of age and older.
- Primary generalized tonic–clonic seizures in children 7–12 years and older.
- It is being used as a first add-on or monotherapy for patients with difficult-to-control epilepsy.
- It is a selective and noncompetitive antagonist of the AMPA glutamate receptor and reduces the glutamate-induced neurotransmission inhibiting the seizure generation and spread.

Cenobamate

- Cenobamate (CNB) is a highly effective modern ASM approved as adjunctive treatment for adults with drug-resistant focal-onset seizures.
- It has a dual mode of action; preferentially inhibits the persistent component of voltage-gated sodium channels which reduces excessive neuronal excitation.
- It acts as a positive allosteric modulator of $GABA_A$ receptors which enhances the brain's natural inhibitory signals.
- These actions work to stabilize brain function and reduce seizure likelihood.
- Effective for patients with DRE, even those who have failed on other medications.
- It is taken orally once daily.
- Demonstrated significant seizure frequency reduction with high rates of patients achieving a 50% reduction in seizures.
- With CNB a "start-low and go-slow" titration schedule is advised to mitigate the risk of serious adverse reactions, specifically a severe allergic reaction called drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome.

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- The starting dose is 12.5 mg once daily, increased every 2 weeks in increments up to a target maintenance dose of 200 mg daily.
- CNS-related side effects are common and include somnolence, dizziness, headache, fatigue, and double vision.
- CNB is contraindicated in individuals with familial short QT syndrome.
- CNB interacts with other medications by inducing and inhibiting certain liver enzymes (CYP3A4, CYP2B6, and CYP2C19) which can decrease or increase concentrations of other drugs.
- It might reduce the effectiveness of hormonal contraceptives.

Vigabatrin

- It inhibits GABA transaminase, the enzyme responsible for the metabolic degradation of GABA.
- It is an effective add-on drug for focal seizures with or without generalization but can worsen myoclonic jerks and generalized absences.
- Visual field defects associated with it have curtailed its use. However, it is still the drug of choice for infantile spasms and is ideal for children with coexistent tuberous sclerosis.
- VGB is added to existent ASM at a dose of 500 mg once or twice a day to allow tolerance to sedation.
- Tiredness, weight gain, dizziness, and headache are common side effects.
- VGB does not interfere with hepatic metabolic enzymes.

CHOICE OF ASMS IN FOCAL AND GENERALIZED EPILEPSIES

- Well-conducted randomized controlled trials (RCTs) comparing the efficacy of a new drug with old established drugs are lacking for several ASMs. Head-to-head comparison studies of newer and older ASMs are not done frequently.
- The landmark study, SANAD trials A and B, showed superiority of LTG over CBZ for focal epilepsies; the established older valproic acid was the most effective medication for generalized seizures.
- Meta-analysis of several trials of various ASMs may provide more information on comparative efficacy. In 2017, a network meta-analysis of 10 ASMs was published.
- 10 ASMs CBZ, LTG, LEV, OXC, valproic acid, ZNS, TPM, phenytoin, phenobarbital, and gabapentin were used in both focal and generalized epilepsies as monotherapy and the efficacy compared.
- The results showed that LTG and LEV were significantly better than CBZ for focal seizures which was better than phenytoin and phenobarbital.

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- For generalized seizures, valproic acid was noted to be superior to phenobarbital, TPM, and CBZ.
- A similar network meta-analysis on pediatric patients with 22 different ASMs showed similar findings.
- CBZ and LTG were superior in new-onset focal epilepsies.
- LEV and PMP seemed to show advantage in the management of refractory focal epilepsies.
- Phenytoin and phenobarbital delayed seizure recurrence and established early seizure control. However, this was associated with lower retention rate in view of the adverse effects.

TREATMENT CHOICES IN SPECIFIC ELECTROCLINICAL SYNDROMES IN CHILDREN

Epileptic Spasms

Previously known as infantile spasms, these usually occur in infants though could occur later in childhood. The typical spasms are sudden brief stiffening of the whole body occurring in clusters which lasts several seconds to minutes and affects the axial muscles. Most often these spasms occur in the setting of an epileptic encephalopathy and early diagnosis and appropriate treatment are mandatory for good seizure and cognitive outcomes and the outcome is better with early initiation of treatment.

Oral steroids or IM ACTH and VGB are the drugs of choice. Steroids are preferred except when spasms are due to tuberose sclerosis where VGB is more efficacious. Retinal toxicity with irreversible peripheral visual field constriction is a risk with VGB use. Reversible hyperintense signal abnormalities are noted in the MRI, in a third of infants on VGB, in the basal ganglia, thalamus, brainstem, and the white matter.

Absence Seizures

These seizures are characterized by sudden, brief episodes of unresponsiveness which could be associated with flutter of eyelids, and nodding of head and other facial movements. The remarkable feature is that this type of seizures can be brought about by sustained hyperventilation which is considered a diagnostic test. Even though the child is unaware during the episode, it can continue the activity or conversation as though nothing has happened. These episodes could occur several times in a day and the EEG is diagnostic. The EEG shows the classical 3 Hz generalized spike and wave complexes as mentioned earlier. Ethosuximide and valproate are equally effective in controlling seizures though ethosuximide is a better choice given that the adverse effect is less in children. Other seizure types such as GTCS and myoclonic seizure could coexist when valproate would be the choice.

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Lennox–Gastaut Syndrome

Lennox–Gastaut syndrome is an electroclinical syndrome characterized by a drug-resistant epileptic encephalopathy, manifesting with multiple motor and nonmotor seizure types.

- *Motor*: Tonic, atonic, tonic–clonic, and tonic–atonic
- *Nonmotor*: Atypical absences and nonconvulsive status epilepticus

The characteristic EEG feature of this syndrome is mountainous slow waves with generalized slow-spike wave complexes at 1.5–2.5 Hz. The seizures in LGS occur before 5 years of age and up to a third of children with epileptic spasms progress to have LGS later. Though there could be multiple causes, structural brain lesions and genetic causes predominate, with the cause remaining unknown in up to 30%. Impaired cognition is associated and could occur before or after the onset of the seizures, depending on the etiology.

The seizures are frequent, occurring almost daily in many, which makes the management quite challenging, given the adverse effects of polypharmacy, and the need to prevent injuries resulting from the seizures. Valproic acid is the first-line choice as it is a broad-spectrum ASM being effective for multiple seizure types. A number of drugs have been tested in double-blind placebo-controlled trials as adjunct therapy, and finally a Cochrane review concluded that no one drug was superior to another. LTG, rufinamide, felbamate, CLB, TPM, and cannabidiol offer a >50% reduction in the overall occurrence in 30–60% of patients. High dose CLB was found to be particularly effective in reducing the drop seizure and its effect was sustained. Though valproic acid remains the mainstay of the treatment of LGS, no controlled trials have been done on it.

The nonpharmacologic treatments include ketogenic diet, vagus nerve stimulation (VNS), corpus callosotomy, and resective surgery. The focus of management in LGS is the overall quality of life (QOL) and not the number of seizures controlled. Rare or even regular break through seizures are preferred by the caregivers over cognitive and sedating drug side effects.

Electrical Status Epilepticus in Slow-wave Sleep

Continuous spikes in slow-wave sleep, as it is otherwise known, is an epileptic encephalopathy occurring between the ages of 4 and 8 years. This encephalopathy is characterized by regression of language or cognitive functions which could be associated with other neurobehavioral changes secondary to the continuous epileptiform discharges. These electrical discharges when associated with language regression and auditory agnosia are referred to as Landau–Kleffner syndrome. The etiology of this encephalopathy is multiple including structural and genetic causes. Children with the self-limited focal epilepsy could also show a similar EEG pattern as electrical status epilepticus in slow-wave sleep (ESES) without the accompanying cognitive dysfunction. There are few effective treatment

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options for this condition and the two commonly used treatment options are steroids and high dose benzodiazepines.

DISEASE-SPECIFIC TREATMENT CONSIDERATIONS

The treatment options would include supplementation with deficient cofactors or nutrients to reduce the frequency of seizures in some specific genetic or metabolic diseases.

Examples:

- *Pyridoxine for pyridoxine dependent seizures*: This is a rare genetic epilepsy due to mutations in the *ALDH7A1* gene. Leads to build up of toxic substances causing developmental delays, intellectual impairment, and severe difficulty to treat seizures. Treatment requires lifelong pyridoxine with dietary changes.
- *Ketogenic diet*: In glucose transporter deficiency (GLUT1), providing alternative fuel when glucose transport to the brain is defective. A rare genetic disorder due to faulty *SLC2A1* gene and causes infantile seizures, developmental delay, and movement disorder.
- *Biotin (B7 vitamin) supplementation*: In biotinidase deficiency, caused by mutations in the *BTD* gene, which produces the biotinidase enzyme which recycles biotin from proteins. Causes seizures, developmental delays, skin rashes, hair loss, and is inherited in an autosomal recessive pattern and is treated with biotin supplementation.

Epilepsy is worsened in certain disorders by certain specific medications.

Example: Phenytoin, CBZ, and LTG in Dravet syndrome, due to SCNA1 mutation.

Some ASMs may be selectively more effective in certain channelopathies.

Example: Phenytoin, CBZ, LTG, and other sodium channel blockers in channelopathies, such as SCN8A, SCN2A, and KCNQ2 mutations, as with high dose of phenytoin being effective in SCN8A epilepsy.

Targeting dysfunctional receptors and or channels and pathways, is another approach, using unconventional medications.

Examples:

- Use of quinidine in KCNT1 mutation
- Memantine in GRIN2A mutation
- Everolimus in mammalian target of rapamycin (mTOR) signaling

EPILEPSY SURGERY

Drug-resistant seizures cause progressive cognitive and psychosocial morbidities and increased mortality associated with uncontrolled seizures of many years duration. It is generally recommended that DRE patients be referred to specialty epilepsy surgery centers. Children with catastrophic

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epilepsy should be referred early because of the risk of severe developmental disability.

Types of Epilepsy Surgery Procedures and Their Indications

- *Anterior temporal lobectomy*: Mesial temporal sclerosis
- *Focal resection*: Focal-onset seizures arising from resectable cortex
- *Corpus callosotomy*: Tonic, atonic, or tonic–clonic seizures, with falls and injuries; large nonresectable lesions; secondary bilateral synchrony
- *Hemispherectomy*: Rasmussen's syndrome or other unilateral hemisphere pathology in association with functionally impaired contralateral hand
- *Subpial transections*: Focal-onset seizures arising from unresectable cortex

Vagus Nerve Stimulation

Vagus nerve stimulation provides a nonpharmacologic approach to treatment to epilepsy treatment. The system comprises of an implantable multiprogrammable pulse generator that delivers electrical current to the vagus nerve with the aim of reducing the frequency and/or the severity of seizures. The generator is implanted in the patient's left upper chest and a bipolar lead connects it to the left vagus nerve in the neck. Radiofrequency signals are communicated to the generator noninvasively by a programming wand and a handheld magnet operated by the patient or carer can turn the stimulator on or off. The mechanism of action is not known and is fairly well tolerated.

Adverse effects are mild and resolve with changes in settings and include hoarseness, throat pain, cough, and dyspnea. The advantage is it does not cause the CNS side effects associated with the ASMs and also no systemic effects on the liver, pulmonary, or gastric.

Direct Brain Stimulation

Direct brain stimulation (DBS) is an option for DRE patients who are not eligible for resective surgery. Bilateral stimulation of the anterior nucleus of the thalamus in the SANTE (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) trial showed significant reduction of seizures in the short term but has not been replicated.

Ketogenic Diet

This is a high fat, low protein, and very low carbohydrate diet given to children in the age group of 5–10 years DRE. It is very effective in children who have failed numerous drug trials and does not have the cumulative sedative effects of multiple ASMs. This is best done with the advice of an experienced nutritionist.

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Monograph on EPILEPSY PRACTICE

Salient Features

- This monograph comprehensively covers all aspects of epilepsy relevant to the management of an epileptic patient in practice.
- A clinical approach is maintained throughout this discussion making it easy to assimilate the material presented.
- Considerable weightage has been given to the elicitation of the history, as this is the most important aspect in the assessment of a person with seizures, leading to appropriate and efficient management.
- The types of epilepsy and the epileptic syndromes described provide insight into the evaluation and analysis of the possible ethology of the seizures.
- Advances in the evaluation of epilepsy, including presurgical evaluation, have been dealt with quite extensively. The various currently available antiseizure medications have been highlighted including the management of status epilepticus.
- The role of surgery, the procedures, and the indications have also been elucidated to familiarize the reader with the current surgical options.
- Added noteworthy features in this monograph are the discussions on breakthrough seizures, drug-resistant seizures, and epilepsy in special populations, including the novel New Onset Epilepsy in Adults (NOEA).
- The key points are highlighted after each discussion for a quick recap.

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