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Paediatric Epilepsy: A Comprehensive Overview of Diagnosis, Treatment and Surgery

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Abstract:
Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures due to abnormal electrical activity in the brain. In children, it represents one of the most common long-term neurological conditions. Epilepsy is one of the most common brain problems in children, and it happens most often in the first year of life. Epilepsy is a common brain condition that happens in about 0.5–1% of children around the world. Around 15% of patients do not achieve adequate seizure control with antiepileptic medications. These individuals are potential candidates for surgical intervention, and the majority belong to the pediatric age group (18 years or younger). Paediatric epilepsy surgery is a vital treatment option for children with drug-resistant epilepsy, offering the potential for seizure freedom and improved developmental outcomes. About 5 in every 1,000 children are affected by epilepsy in any given year. Each year, an average of 5 to 7 new cases occur per 10,000 children between the ages of one and fifteen. Risk factors linked to the onset of seizures in children include premature birth, neurological comorbidities, a positive family history, fever, infections, maternal alcohol use, pregnancy-related complications, and maternal smoking. Early detection and proper classification of epilepsy are crucial for choosing the right treatment. The main approach is the use of antiseizure medicines, but in difficult-to-control cases, dietary therapies, surgery, or brain stimulation may also be considered. Advances in neuroimaging, electroencephalography, and molecular genetics have significantly improved the understanding and classification of paediatric epilepsy syndromes.

Keyword: Seizure**,** Epilepsy, Premature birth, epilepsy surgery, paediatric epilepsy

Introduction
Epilepsy continues to be a leading neurological disorder on a global scale. Seizures are among the leading reasons for referral to paediatric neurology and constitute a significant contributor to childhood morbidity. Epilepsy represents one of the most prevalent neurological disorders in childhood, with an estimated incidence of 4–8 cases per 1,000 children. Since the etiology of epilepsy frequently cannot be established, the diagnostic process depends on obtaining an extensive patient history, reports from seizure observers, EEG recordings, and neuroimaging studies evaluating central nervous system function and anatomy. A key manifestation of epilepsy is the occurrence of epileptic seizures, which are brief episodes of abnormal bioelectrical activity within the brain's nerve cells. In simplified terms, seizures are classified as either generalized or focal (partial), depending primarily on the brain regions involved in the abnormal discharges. The identification of an epileptic syndrome—defined by the combination of seizure types, electroencephalographic patterns, and neuroimaging findings—represents the final step in establishing a diagnosis. Epilepsy surgery in children is an important therapeutic option for those whose seizures are not adequately controlled with antiepileptic drugs. Approximately 20–30% of paediatric patients with epilepsy develop drug-resistant forms of the disorder, leading to significant impairment in cognitive, behavioural, and psychosocial development. Close to 60% of individuals with epilepsy are affected by focal epilepsy syndromes. Among this group, around 15% continue to have seizures that do not respond

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to medication, making them suitable candidates for surgical approaches. Drug-resistant epilepsy (DRE), according to the International League Against Epilepsy (ILAE), refers to the condition where seizures persist despite appropriate trials of two well-tolerated and correctly dosed anti-seizure drugs. Globally, about 50 million individuals live with epilepsy, and nearly one-third of them continue to experience uncontrolled seizures even with medication.

Risk Factors

Risk factors refer to conditions that increase the likelihood of developing epilepsy, and these vary between childhood-onset and late-onset epilepsy. Commonly recognized factors include traumatic brain injury, prenatal or birth-related trauma, infections affecting the central nervous system, developmental abnormalities, tumors, and inherited predispositions. In many cases, epilepsy can be traced back to genetic influences. Prenatal exposures, such as maternal infections, alcohol consumption, or fetal distress, further increase the risk Genetic predisposition plays a major role, as several childhood epilepsy syndromes are linked to mutations in ion channel and neurotransmitter-related genes. Perinatal and neonatal complications, such as hypoxic–ischemic encephalopathy, low birth weight, prematurity, or birth trauma, are also strongly associated with later epilepsy. Infections of the central nervous system, including meningitis, encephalitis, and neurocysticercosis, are well-recognized contributors, especially in regions where these conditions are endemic. Even children whose birth weight falls within the normal range are at heightened risk for epilepsy due to intrauterine growth restriction. In reality, women may suffer hypoxia, which can increase the incidence of epilepsy and interfere with the unborn brain's normal growth. Head trauma, cord prolapse, and extended labor (> 6 hr) were correlated with a higher prevalence of epilepsy in newborns. In terms of postnatal variables, low birth weight (less than 2.5 kg), delivery difficulties, male young children are more likely to develop epilepsy due to variations in astrocyte structure and brain connection.

Etiology

Epilepsy in children is a heterogeneous disorder with multiple possible causes. Understanding the etiology is crucial for accurate diagnosis, prognosis, and management. Broadly, etiologies are classified into genetic, structural, metabolic, infectious, immune, and unknown causes as per the International League Against Epilepsy (ILAE) classification.

1. Genetic Causes : Some epilepsy syndromes are primarily genetic in origin, such as Dravet syndrome, childhood absence epilepsy, and benign familial neonatal seizures. Alterations in ion channel–related genes like SCN1A, KCNQ2, and CHD2 have been associated with these conditions.
2. Structural Causes : Acquired injuries to the brain, including hypoxic-ischemic damage around birth, cerebrovascular events in the neonatal period, or trauma to the head, are also significant causes.
3. Metabolic Causes : Metabolic disorders present from birth, such as pyridoxine-dependent epilepsy, glucose transporter type 1 (GLUT1) deficiency, and various mitochondrial conditions, can be responsible for epilepsy.
4. Infectious Causes : Infections affecting the central nervous system, including meningitis, encephalitis, neurocysticercosis, and congenital infections from the TORCH group, are important causes of epilepsy.

Pathophysiology

1.Neuronal hyperexcitability

Seizures result when the balance between excitation and inhibition favours runaway synchronous firing. Mechanisms include increased glutamatergic transmission, reduced GABAergic inhibition, alterations in intrinsic membrane properties (e.g., persistent sodium currents), impaired potassium buffering, and changes in network connectivity that promote hypersynchrony. These principles apply across ages but interact with developmental stage.

2.Ion channelopathies and genetic causes

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A large and growing fraction of early-onset epilepsies are attributable to single-gene defects affecting ion channels (e.g., SCN1A, KCNQ2, CACNA1A), synaptic proteins, or regulatory molecules. Channel mutations can produce gain- or loss-of-function effects that alter neuronal firing, burst propensity, and seizure susceptibility. Genetic architecture ranges from monogenic epileptic encephalopathies to oligogenic and complex inheritance; copy-number variants and de novo mutations are common in severe infantile epilepsies. Genetic diagnosis often explains pathophysiology and guides therapy (e.g., sodium-channel blockers contraindicated in SCN1A Dravet).

3.Structural and developmental lesions

Cortical malformations (e.g., focal cortical dysplasia, hemimegalencephaly), perinatal hypoxic-ischemic injury, stroke, and traumatic lesions disrupt normal cortical architecture, produce aberrant excitatory circuits, and frequently act as epileptogenic foci. In infants and young children, insults during critical periods of circuit formation can have disproportionately strong epileptogenic effects.

4.Glia, inflammation, and neuroimmune mechanisms

Astrocytes and microglia influence extracellular ion homeostasis, neurotransmitter clearance (notably glutamate), and blood–brain barrier function. Inflammatory cytokines, complement activation, and autoantibodies can lower seizure threshold, promote epileptogenesis, and contribute to epileptic encephalopathies. In paediatrics, infection-related and post-infectious inflammatory mechanisms are particularly relevant.

5.Metabolic and mitochondrial dysfunction

Inherited metabolic disorders (e.g., inborn errors of metabolism) and mitochondrial disease frequently present with early-onset seizures. Metabolic derangements (energy failure, lactate accumulation, impaired ATP generation) impair ionic pumps and synaptic transmission, facilitating seizures. Some metabolic epilepsies have specific treatments (dietary, cofactor therapy).

6.Network plasticity and epileptogenesis

Following an initial insult or ongoing seizures, processes such as aberrant synaptogenesis, axonal sprouting, loss of inhibitory interneurons, and altered receptor expression can transform a transiently hyperexcitable state into a chronic epileptic network. In the developing brain these processes can also impair cognitive and behavioral development, contributing to the concept of epileptic encephalopathy.

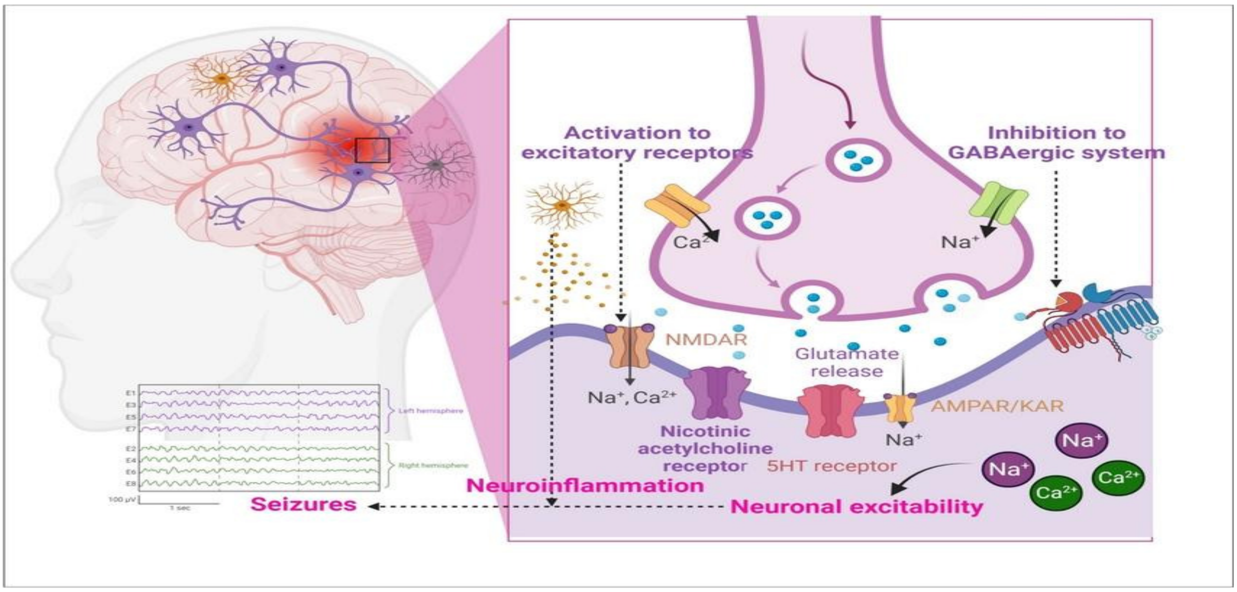

Figure: Pathophysiology Of Paediatric Epilepsy

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Diagnosis

The diagnosis of paediatric epilepsy is a complex and multifaceted process that requires integration of clinical, neurophysiological, and neuroimaging data. Accurate diagnosis is essential not only for confirming the presence of epilepsy but also for identifying the underlying aetiology and determining the most appropriate management strategy.

1. Clinical Evaluation

The diagnostic process begins with a thorough clinical history and detailed description of seizure events. Information regarding the onset age, seizure frequency, duration, and precipitating factors is crucial. Witness accounts or video recordings of episodes often assist in distinguishing epileptic seizures from non-epileptic paroxysmal events such as syncope, breath-holding spells, or movement disorders. Developmental history, perinatal events, and family history of epilepsy or neurological disorders also provide important diagnostic clues.

2. Seizure Classification

Accurate classification of seizures and epilepsy syndromes is fundamental for guiding treatment. The International League Against Epilepsy (ILAE) classifies seizures into focal, generalized, and unknown onset categories, based on clinical features and electroencephalographic findings. In children, seizure types may evolve over time, and age-specific epilepsy syndromes such as West syndrome, Lennox–Gastaut syndrome, and childhood absence epilepsy must be considered.

3. Electroencephalography (EEG)

EEG remains the cornerstone of epilepsy diagnosis. Interictal EEG helps detect epileptiform discharges, such as spikes, sharp waves, or spike-and-wave complexes, which provide evidence of cortical hyperexcitability. Ictal EEG recordings, when possible, confirm the epileptic nature of events and localize seizure onset zones. Long-term video EEG monitoring is particularly valuable in differentiating epileptic from non-epileptic events and in surgical evaluation.

4. Neuroimaging

Magnetic Resonance Imaging (MRI) is the imaging modality of choice for detecting structural brain abnormalities that may underlie epilepsy. High-resolution MRI with epilepsy-specific protocols can identify cortical dysplasias, hippocampal sclerosis, tumors, and vascular malformations. Functional imaging techniques—such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), and functional MRI—offer complementary information by revealing areas of altered metabolism or perfusion, aiding surgical planning.

5. Genetic and Metabolic Testing

Advancements in molecular genetics have revolutionized epilepsy diagnosis. Genetic testing is particularly important in early-onset or drug-resistant epilepsy, where monogenic causes are common. Next-generation sequencing panels and whole-exome sequencing help identify pathogenic variants, enabling syndrome-specific management and genetic counselling. Metabolic investigations, including serum and cerebrospinal fluid analyses, are indicated when inborn errors of metabolism are suspected.

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Pharmacological Treatment of Paediatric Epilepsy

Drug Class	Examples	Mechanism of Action (MOA)	Main Clinical Indications
1. Sodium Channel Blockers	Carbamazepine, Phenytoin, Lamotrigine, Oxcarbazepine, Lacosamide	Stabilize inactivated state of voltage-gated Na^+ channels → inhibit repetitive neuronal firing	Focal (partial) seizures, generalized tonic-clonic seizures
2. Calcium Channel Blockers (T-type)	Ethosuximide, Zonisamide, Valproate (partly)	Inhibit T-type Ca^{2+} channels in thalamic neurons → suppress abnormal thalamocortical activity	Absence seizures, mixed seizure types
3. GABAergic Enhancers (↑ inhibitory neurotransmission)	Valproate, Benzodiazepines (Clobazam, Clonazepam), Phenobarbital, Vigabatrin, Tiagabine, Topiramate	Enhance GABA-A receptor activity or increase GABA availability (via enzyme inhibition or reuptake blockade)	Myoclonic, atonic, generalized, and infantile spasms
4. SV2A Vesicle Protein Modulators	Levetiracetam, Brivaracetam	Bind to synaptic vesicle protein 2A → regulate neurotransmitter release and reduce excitatory transmission	Broad-spectrum use (focal and generalized seizures, myoclonic)
5. Glutamate (Excitatory) Receptor Antagonists	Perampanel (AMPA antagonist), Topiramate (AMPA/Kainate partial antagonist)	Inhibit glutamate-mediated excitatory neurotransmission	Adjunct therapy in refractory epilepsy, Lennox–Gastaut syndrome
6. Carbonic Anhydrase Inhibitors	Topiramate, Zonisamide, Acetazolamide	Inhibit carbonic anhydrase → mild acidosis stabilizes neuronal membranes and reduces excitability	Adjunct for refractory epilepsy, catamenial seizures
7. Multiple-Mechanism Drugs	Valproate, Topiramate, Zonisamide	Combine Na^+ and Ca^{2+} channel blockade with GABA enhancement and/or glutamate inhibition	Broad-spectrum (generalized, myoclonic, absence, focal)

Drug Class	Examples	Mechanism of Action (MOA)	Main Clinical Indications
8. GABA Transaminase Inhibitor	Vigabatrin	Irreversible inhibition of GABA transaminase → ↑ GABA concentration in CNS	Infantile spasms (esp. tuberous sclerosis), refractory focal seizures
9. GABA Reuptake Inhibitor	Tiagabine	Inhibits GABA transporter (GAT-1) → ↑ synaptic GABA	Adjunct for focal seizures
10. Hormonal / Corticosteroid Therapy	ACTH (Corticotropin), Prednisolone	Reduces corticotropin-releasing hormone (CRH) and suppresses neuronal excitability	Infantile spasms (West syndrome)
11. Barbiturates	Phenobarbital, Primidone	Potentiate GABA-A receptor → prolong Cl^- channel opening → hyperpolarization	Neonatal seizures, status epilepticus (if refractory)
12. Benzodiazepines	Diazepam, Lorazepam, Clobazam, , Midazolam	Enhance GABA-A receptor activity → increase Cl^- influx → neuronal	Status epilepticus (acute), adjunct for or seizures

History of surgery for pediatric epilepsy

Surgical management of epilepsy in children can be traced back to the late 19th century. Early pioneers such as Victor Horsley, William Macewen, and Fedor Krause highlighted the potential of neurosurgery in treating epilepsy. In 1886, Dr. Victor Horsley carried out a craniotomy on a 22-year-old patient with recurrent seizures, applying the principles of cerebral localization described by Jackson and Ferrier. Even earlier, in 1879, Dr. Macewen documented epilepsy surgery in the pediatric population. IN 1893, Fedor Krause reported the pioneering use of electrical stimulation in the operating room and broadened the scope of epilepsy surgery to encompass non-lesional cases. In the 1920s, Dr. Wilder Penfield built upon the contributions of leading neurologists by employing electroencephalography (EEG) and incorporating electrocorticography to guide surgical planning. In 1938, McKenzie performed the first hemispherectomy for epilepsy in a child with infantile hemiplegia. Several surgical methods have been reported, with the endoscope-assisted hemispherectomy being among the more recent innovations. In 1982, Wieser introduced the selective amygdalohippocampectomy technique specifically for mesial temporal lobe epilepsy. Later, in 1998, the International League Against Epilepsy (ILAE) established standardized guidelines for paediatric epilepsy and formally defined drug-resistant epilepsy (DRE).The earliest randomized controlled trial (RCT) on paediatric epilepsy surgery was carried out by Dwivedi and colleagues in South Asia. The study enrolled children and adolescents fulfilling the

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International League Against Epilepsy (ILAE) definition of drug-resistant epilepsy (DRE) who experienced focal or secondary generalized seizures. Their findings demonstrated that after one year, 77% of patients who underwent surgery achieved seizure freedom, in contrast to only 7% of those managed with medical therapy alone. A little over a decade later, Engel and his team released findings from the Early Randomized Surgical Epilepsy Trial, showing that 73% of patients who underwent surgery for temporal lobe epilepsy remained seizure-free two years afterward, compared with those who continued on medical therapy. By the late 20th and early 21st centuries, major developments in neuroimaging techniques (such as MRI, PET, and SPECT), electrophysiological studies, and microsurgical methods significantly expanded the scope and success of paediatric epilepsy surgery worldwide. Modern procedures such as lesionectomy, hemispherectomy, corpus callosotomy, and vagus nerve stimulation have become established therapeutic options for carefully selected children with drug-resistant epilepsy (Harvey et al., 2008; Jayakar et al., 2014).Today, paediatric epilepsy surgery is recognized as a safe and effective treatment for drug-resistant epilepsy, offering many children the potential for seizure freedom and improved neurodevelopmental outcomes.

Presurgical evaluation

The goals of presurgical evaluation are 1. To establish the diagnosis of epileptic seizure. 2. Define the electroclinical syndrome. 3. Delineate the lesion(s) responsible for the seizures. 4. Evaluate the past AED treatments and ensure that an adequate medical treatment had been provided. According to the ILAE, every child with drug-resistant epilepsy should be assessed at a specialized epilepsy center and considered for a surgical consultation. The evaluation begins with a careful clinical history and witness seizure description, detailed neurological and developmental assessment, and review of antiseizure medication history to establish drug-resistance according to established ILAE criteria. Conditions such as cortical dysplasia, tuberous sclerosis complex, polymicrogyria, hypothalamic hamartoma, hemispheric syndromes, Sturge-Weber syndrome, and Rasmussen syndrome are appropriate diagnoses for early surgical referral. The evaluation process begins with detailed clinical assessment, including seizure semiology, developmental history, comorbidities, and a thorough neurological examination. Seizure description and video recordings provide essential information for hypothesizing the potential seizure onset zone. A critical step is long-term video-EEG monitoring, which correlates clinical semiology with ictal and interictal electroencephalographic changes. In children, prolonged video-EEG is invaluable in distinguishing epileptic seizures from non-epileptic events and in defining electroclinical syndromes (Rosenow & Lüders, 2001).Neuroimaging is another essential component of evaluation. High-resolution 3T MRI with epilepsy-specific protocols is the gold standard for identifying structural lesions such as cortical dysplasia, hippocampal sclerosis, or low-grade tumors. In MRI-negative or discordant cases, adjunctive imaging modalities are employed. Interictal FDG-PET can identify areas of hypometabolism corresponding to the EZ, while ictal SPECT can highlight regions of hyperperfusion during seizure onset. Advanced post-processing techniques, such as SISCOM (subtraction ictal SPECT co-registered with MRI) and statistical parametric mapping (SPM), further improve localization accuracy (Jayakar et al., 2014). Functional MRI (fMRI) is increasingly used in pediatric patients for mapping eloquent cortex, particularly motor and language areas, reducing the need for invasive procedures.

Surgical Procedure

Epilepsy surgery in children aims to achieve seizure freedom or significant reduction while preserving neurological and cognitive functions. The choice of procedure depends on the epileptogenic zone (EZ) localization, underlying pathology, and developmental considerations. Surgical management for children with drug-

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resistant epilepsy aims to achieve seizure control, reduce medication burden, and improve neurodevelopmental outcome; careful candidate selection after a comprehensive presurgical work-up (history, prolonged video-EEG, high-resolution MRI with epilepsy protocols, functional imaging and, when indicated, intracranial EEG) is essential to define the epileptogenic zone and predict benefit from surgery. The principal operative strategies fall into two categories: resective (removal of the epileptogenic lesion or epileptogenic cortex) and disconnective/palliative procedures. Resective operations include lesionectomy for well-circumscribed lesions, tailored cortical resections or lobectomies (for example temporal lobectomy in mesial temporal epilepsy), and selective procedures such as selective amygdalohippocampectomy when preservation of surrounding cortex is required. Disconnective options — ranging from corpus callosotomy for drop attacks to hemispherotomy/functional hemispherectomy for unilateral, diffuse hemispheric pathology — are chosen when resection is not feasible but interruption of seizure spread can provide major clinical benefit. In recent years minimally invasive alternatives have expanded the armamentarium: laser interstitial thermal therapy (LITT), stereotactic radiofrequency thermocoagulation (including SEEG-guided thermocoagulation), and stereotactic radiosurgery are increasingly used for small, deep, or surgically challenging foci, offering shorter recovery times and lower immediate morbidity for selected patients. Intraoperative adjuncts (neuronavigation, awake or asleep functional mapping where feasible, intraoperative electrocorticography, and neuromonitoring) reduce risk and help tailor extent of resection; postoperative complications vary by procedure but overall surgical mortality in modern series is low while seizure-freedom rates and developmental gains are substantial when the epileptogenic zone is accurately localized and fully addressed. Long-term outcomes depend on pathology (lesional etiologies such as focal cortical dysplasia, low-grade tumours, and hippocampal sclerosis have higher seizure-freedom rates), completeness of resection, age at surgery (earlier surgery is often linked to better developmental outcomes in appropriately selected infants and young children), and multidisciplinary postoperative support that addresses neurodevelopment, cognition, and psychosocial needs.

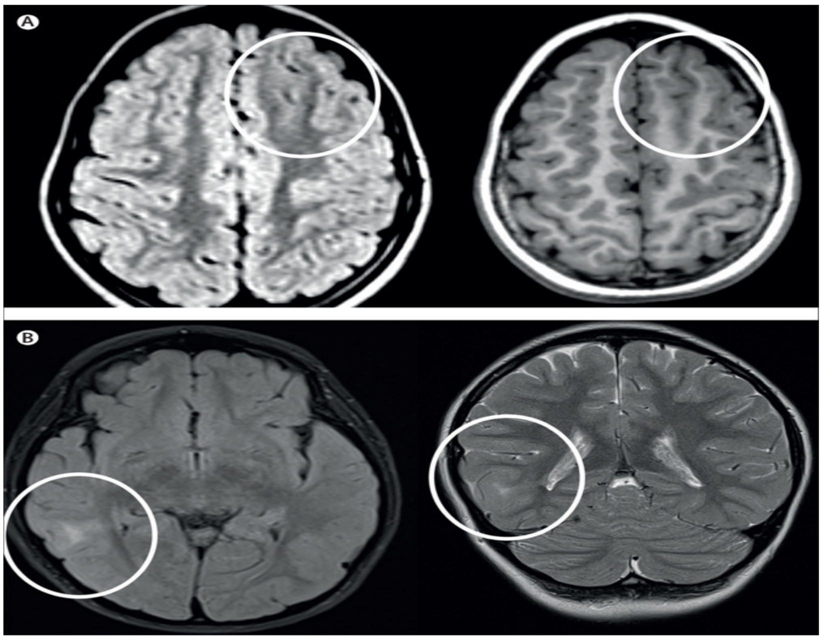

Figure: Paediatric Epilepsy Surgery

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Palliative Surgery

Corpus callosotomy (CCS) has been reported to provide improvement in about 70–80% of children experiencing drop attacks and in approximately 30% of those with generalized tonic-clonic seizures. Present guidelines suggest that the surgery should be tailored to the type of seizure rather than the overall epileptic syndrome. Total CCS resulted in a better outcome on drop attacks than the partial one. Total CCS is essentially indicated in children. In older children and adults, the degree of callosal section performed depends on the severity and distribution of EEG abnormalities. Vagus nerve stimulation (VNS) represents a palliative surgical option aimed at reducing seizure intensity and enhancing quality of life, even among children with drug-resistant epilepsy. It is typically considered when resective, potentially curative surgery is either not feasible or has previously failed. Most candidates for VNS lack clearly defined epileptogenic zones on EEG. A further challenge is that the implanted device limit the ability to perform standard MRI studies. In contrast, corpus callosotomy (CCS), which disrupts interhemispheric synchronization, may unmask previously hidden focal EEG abnormalities, thereby allowing identification of potential targets for subsequent curative resection. Palliative surgeries are an important alternative to improve seizure severity and development of cognition in childhood. Physicians can apply several therapeutic strategies to combine with palliative epilepsy surgeries to attain the fundamental goal of therapy.

Resective Surgery

Resective surgery aims to remove the epileptogenic tissue responsible for recurrent seizures and is the principal curative surgical strategy for children with drug-resistant epilepsy (DRE). Candidate selection relies on a multidisciplinary presurgical evaluation that integrates a detailed clinical history, seizure semiology, prolonged video-EEG, high-resolution 3T MRI with epilepsy protocols, and adjunctive functional imaging (interictal FDG-PET, ictal SPECT) and advanced post-processing when MRI is non-lesional. Invasive monitoring with stereotactic EEG (SEEG) or subdural grids may be required when noninvasive data are discordant or localization remains uncertain. Early referral and timely surgery after failure of appropriate antiseizure medication trials are associated with better seizure and developmental outcomes.

Conclusion

Paediatric epilepsy is a complex condition requiring early diagnosis and individualized management. While most children respond to medication, some need advanced treatments, including surgery. Advances in imaging, genetics, and surgical techniques have improved outcomes and quality of life. A multidisciplinary approach and continued research into precision medicine are vital for further progress in care and long-term prognosis.

Reference

1. Pratibha Singhi and Ajay Gupta; Epilepsy in Children-Important Facets https://doi.org/10.1007/s12098-021-03682-z. The Indian Journal of Paediatrics (October 2021) 88(10):991-2
2. Annegers JF. Epidemiology and genetics of epilepsy. Neurol Clin 1994; 12: 15-29.
3. Chen H, Koubeissi MZ. Electroencephalography in Epilepsy Evaluation. Continuum (Minneap Minn). 2019;25(2):431–453. doi:10.1212/CON.0000000000000705.3

4. Katyayan A, Diaz-Medina G. Epilepsy: Epileptic Syndromes and Treatment. Neurol Clin. 2021;39(3):779–795. doi:10.1016/j.ncl.2021.04.002
5. Bastos F, Cross JH. Epilepsy. Handb Clin Neurol. 2020;174:137–158. doi:10.1016/B978-0-444-64148-9.00011-9
6. Falco-Walter J. Epilepsy-Definition, Classification, Pathophysiology, and Epidemiology. Semin Neurol. 2020;40(6):617–623. doi:10.1055/s-0040-1718719
7. Jayalakshmi S, Nair A, Radhakrishnan K. Surgery for childhood epilepsy. J Pediatr Neurosci. 2011;6(Suppl 1):S86–S93. doi:10.4103/1817-1745.85718
8. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of
9. drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010;51:1069-77.
10. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314-9.
11. Asadi-Pooya AA, Hojabri K. Risk factors for childhood epilepsy: a case-control study. Epilepsy and Behavior. 2005;6(2):203-6.
12. Fisher RS, Acevedo C, Arzimanoglou A, et al. (2014). ILAE official report: a practical
13. clinical definition of epilepsy. Epilepsia, 55(4):475–482.
14. Camfield P, Camfield C. (2015). Incidence, prevalence and aetiology of seizures and epilepsy in children. Epileptic Disorders, 17(2):117–123.
15. Wirrell EC. (2016). Predicting pharmacoresistance in pediatric epilepsy. Epilepsia, 57(2):244–255.
16. Cross JH. (2019). Epilepsy in childhood: clinical presentation and diagnosis. The Lancet Child & Adolescent Health, 3(2):107–118.
17. Imen Ketata, Emna Ellouz, Rahil Mizouri. Impact of prenatal, neonatal, and postnatal factors on epilepsy risk in children and adolescents: a systematic review and meta-analysis. Acta Epileptologie. 2024;6(1).
18. Sun Y, Vestergaard M, Pedersen CB, Christensen J, Basso O, Olsen J. Gestational Age, Birth Weight, Intrauterine Growth, and the Risk of Epilepsy. American Journal of Epidemiology [Internet]. 2007 Nov 27 [cited 2022 Oct 18];167(3): 262-70. Available from: https://academic.oup.com/aje/article/167/3/262/132284
19. Sun Y, Vestergaard M, Pedersen CB, Christensen J, Olsen J. (2006). Gestational age, birth weight, intrauterine growth, and the risk of epilepsy. American Journal of Epidemiology, 163(7): 658–665.
20. Glass HC, Hong KJ, Rogers EE, Jeremy RJ, Bonifacio SL, Sullivan JE, Barkovich AJ, Ferriero DM. (2011). Risk factors for epilepsy in children with neonatal encephalopathy. Pediatric Research, 70(5): 535–540.
21. Lawn JE, Cousens S, Zupan J. (2005). 4 million neonatal deaths: When? Where? Why? The Lancet, 365(9462): 891–900.
22. Camfield P, Camfield C. (2015). Incidence, prevalence and aetiology of seizures and epilepsy in children. Epileptic Disorders, 17(2): 117–123.
23. Wirrell EC. (2016). Predicting pharmacoresistance in pediatric epilepsy. Epilepsia, 57(2): 244–255.
24. Scheffer IE, Berkovic S, Capovilla G, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for

Classification and Terminology. Epilepsia. 2017;58(4):512–521.
25. Wirrell EC, Grossardt BR, Wong-Kisiel LC, Nickels KC. Incidence and classification of new-onset epilepsy and epilepsy syndromes in children in Olmsted County, Minnesota from 1980–2004: A population-based study. Epilepsy Res. 2011;95(1–2):110–118.
26. Mercimek-Mahmutoglu S, Cordeiro D. Genetic and metabolic causes of epilepsy in children. Handb Clin Neurol. 2013;113:1811–1824.
27. Singhi P. Infectious causes of seizures and epilepsy in the developing world. Dev Med Child Neurol. 2011;53(7):600–609.
28. Quek AM, Britton JW, McKeon A, et al. Autoimmune epilepsy: clinical characteristics and response to immunotherapy. Arch Neurol. 2012;69(5):582–593.
29. Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S, Beckerman B. Defining early seizure outcomes in pediatric epilepsy: the good, the bad, and the in-between. Epilepsy Res. 2001;43(1):75–84
30. Shao LR, et al. Pediatric Epilepsy Mechanisms: Expanding the Paradigm. Children (Basel). 2019.
31. Scheffer IE, et al. ILAE Classification of the Epilepsies: Position Paper. Epilepsia. 2017.
32. Vera-González A, et al. Pathophysiological Mechanisms Underlying the Etiologies of Epilepsy. In: [book chapter]. 2022.
33. Sumadewi KT, et al. Biomolecular mechanisms of epileptic seizures and epilepsy. 2023.
34. Lolam V, et al. Developmental mechanisms underlying pediatric epilepsy. Front Neurol. 2025 (review).
35. Harvey AS, Cross JH, Shinnar S, Mathern GW. (2008). Defining the spectrum of international practice in pediatric epilepsy surgery patients. Epilepsia, 49(1), 146–155. doi:10.1111/j.1528-1167.2007.01421.x
36. Jayakar P, Gaillard WD, Tripathi M, Libenson MH, Mathern GW, Cross JH. (2014). Diagnostic test utilization in evaluation for resective epilepsy surgery in children. Epilepsia, 55(4), 507–518. doi:10.1111/epi.12544
37. Cross JH, Jayakar P, Nordli D, et al. (2006). Proposed criteria for referral and evaluation of children for epilepsy surgery: Recommendations of the Subcommission for Pediatric Epilepsy Surgery. Epilepsia, 47(6), 952–959.
38. Engel J Jr. (2011). A greater role for surgical treatment of epilepsy: Why and when? Epilepsy Currents, 11(6), 161–163.
39. Schijns OE, Hoogland G, Kubben PL, et al. The start and development of epilepsy surgery in Europe: a historical review. Neurosurg Rev 2015;38:447-61.
40. Horsley V. Remarks on Ten Consecutive Cases of Operations upon the Brain and Cranial Cavity to Illustrate Details and Safety of the Method Employed. Br Med J 1887;1:863-5.
41. McKenzie K. The present status of a patient who had right cerebral hemisphere removed. JAMA. 1938;111:168.
42. Engel J Jr, McDermott MP, Wiebe S, et al. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA 2012;307:922-30.
43. Dwivedi R, Ramanujam B, Chandra PS, et al. Surgery for Drug-Resistant Epilepsy in Children. N Engl J Med 2017;377:1639-47.
44. Rasmussen T. Hemispherectomy for seizures revisited. Can J Neurol Sci 1983;10:71-8.
45. Wieser HG, Yaşargil MG. Selective amygdalohippocampectomy as a surgical

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treatment of mesiobasal limbic epilepsy. Surg Neurol 1982;17:445-57.
46. Guidelines for neuroimaging evaluation of patients with uncontrolled epilepsy considered for surgery. Commission on Neuroimaging of the International League Against Epilepsy. Epilepsia 1998;39:1375-6.
47. Schijns OE, Hoogland G, Kubben PL, et al. The start and development of epilepsy surgery in Europe: a historical review. Neurosurg Rev 2015;38:447-61.
48. Radhakrishnan. K. Medically refractory epilepsy. In: Radhakrishnan K, editor. Medically refractory epilepsy. Trivandrum: Sree Chitra Tirunal Institute for Medical Sciences and Technology; 1999. p. 1-39.
49. Jayakar P, Gaillard WD, Tripathi M, et al. Diagnostic test utilization in evaluation for resective epilepsy surgery in children. Epilepsia 2014;55:507-18.
50. Engel J Jr. The current place of epilepsy surgery. Curr Opin Neurol 2018;31:192-7.
51. Jayakar P, Gaillard WD, Tripathi M, et al. Diagnostic test utilization in evaluation for resective epilepsy surgery in children. Epilepsia 2014;55:507-18.
52. Cross JH, Jayakar P, Nordli D, et al. Proposed criteria for referral and evaluation of children for epilepsy surgery: Recommendations of the ILAE Task Force. Epilepsia. 2014;55(4):618–625.
53. Wyllie E, et al. The treatment of epilepsy: principles and practice. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2015. (Textbook, comprehensive on pediatric presurgical evaluation).
54. Rosenow F, Lüders H. Presurgical evaluation of epilepsy. Brain. 2001;124(9):1683–1700.
55. Duncan JS. Imaging in the surgical treatment of epilepsy. Nat Rev Neurol. 2010;6(10):537–550.
56. Wellmer J, Quesada CM, Rothe L, et al. Proposal for a magnetic resonance imaging protocol for the detection of epileptogenic lesions at early outpatient stages.
57. Epilepsia. 2013;54(11):1977–1987.
58. Cascino GD. Structural neuroimaging in partial epilepsy: MRI, PET, and SPECT. Epilepsia. 2001;42(Suppl 4):3–12.
59. Jayakar P, Gotman J, Harvey AS, et al. Diagnostic utility of invasive EEG for epilepsy surgery: Indications, modalities, and techniques. Epilepsia. 2014;55(3):386–400.
60. Cross JH, et al. *Epilepsy surgery for children and adolescents: evidence—*The Lancet Child & Adolescent Health (Review). 2022.
61. Koutsouras GW, et al. Surgery for pediatric drug resistant epilepsy: a narrative review. Translational Pediatrics. 2023.
62.
63. Dallas J, et al. Indications, techniques, and outcomes of common surgical procedures in epilepsy. Seizure. 2020.
64. Sabzvari T, et al. A comprehensive review of recent trends in surgical approaches for epilepsy management. Cureus. 2024 (includes discussion of minimally invasive techniques).
65. StatPearls. Epilepsy Surgery. 2023 (concise overview of procedures, monitoring, and outcomes).
66. Maehara T, Shimizu H: Surgical outcome of corpus callosotomy in patients with drop attacks. Epilepsia42: 67–71, 2001
67. Sunaga S, Shimizu H, Sugano H: Long-term follow-up of seizure outcomes after corpus callosotomy. Seizure
68. 18: 124–128, 2009

69. Elliott RE, Rodgers SD, Bassani L, Morsi A, Geller EB, Carlson C, Devinsky O, Doyle WK: Vagus nerve stimulation for children with treatment-resistant epilepsy: a consecutive series of 141 cases. J Neuro-surg Pediatr 7: 491–500, 2011
70. Morris GL, Gloss D, Buchhalter J, Mack KJ, Nickels K, Harden C: Evidence-based guideline update: vagus nerve stimulation for the treatment of epilepsy: report of the guideline development subcommittee of the American academy of neurology. Epilepsy Curr 13: 297–303, 2013
71. Dwivedi R, Ramanujam B, Chandra PS, et al. Surgery for drug-resistant epilepsy in children. N Engl J Med. 2017;377(17):1639–1647. doi:10.1056/NEJMoa1615335
72. Jayakar P, Gotman J, Harvey AS, et al. Diagnostic utility of invasive EEG for epilepsy surgery: indications, modalities, and techniques. Epilepsia. 2016;57(11):1735–1747. doi:10.1111/epi.13515
73. Harvey AS, Cross JH, Shinnar S, Mathern GW. Defining the spectrum of international practice in pediatric epilepsy surgery patients. Epilepsia. 2008;49(1):146–155.
74. Gonzalez-Martinez J, Bulacio J, Thompson S, et al. Technique, results, and complications related to robot-assisted stereoelectroencephalography. Neurosurgery. 2016;78(2):169–180.
75. Cross JH, Jayakar P, Nordli D, et al. Proposed criteria for referral and evaluation of children for epilepsy surgery: recommendations of the Subcommission for Pediatric Epilepsy Surgery. Epilepsia. 2006;47(6):952–959.
76. Wilmshurst JM, Berg AT, Lagae L, et al. Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. Epilepsia. 2015;56(8):1185–1197.
77. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512–521.
78. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):522–530.

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