SEIZURES IN CHILDHOOD
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Assistant prof: Basma Adel Ibrahim
Pediatric neurologist
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Seizures in Childhood

An epileptic seizure is a sudden, transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain.

The International League Against Epilepsy (ILAE) operational classification of seizure types divides epileptic seizures into four categories based on the presumed mode of seizure onset: focal, generalized, unknown onset, and unclassified

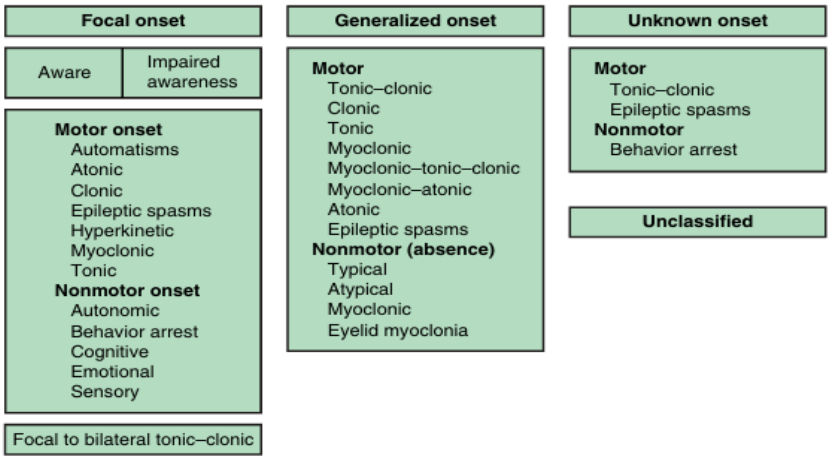

Fig. 633.1 International League Against Epilepsy classification of seizures. *(Modified from Katyayan A, Diaz-Medina G. Epilepsy: epileptic syndromes and treatment. Neurol Clon. 2021;39:779–794, Fig. 1, p. 780.)*

1. **IN FOCAL (FORMERLY KNOWN AS PARTIAL) SEIZURES**:
   The first clinical and electroencephalographic (EEG) changes suggest initial activation of a system of neurons limited to part of one cerebral hemisphere.
- Simple partial seizure is an outdated term that refers to a focal seizure with no alteration in consciousness or awareness; the current term is focal aware seizure.
- Complex partial seizure is also an outdated term that denotes focal seizures with altered consciousness or awareness of the surroundings; they are currently referred to as focal seizures with impaired awareness.

2. **IN GENERALIZED SEIZURES** t:
   The first clinical and EEG changes indicate synchronous involvement of both hemispheres.
3. A seizure may be labeled as being of **UNKNOWN ONSET** if there is not enough clinical information available to determine if the seizure is focal or generalized.
4. If the clinical characteristics of a seizure are unusual and a determination of onset cannot be made despite an adequate evaluation, the seizure may be labeled as **UNCLASSIFIED.**

Approximately 30% of patients who have a first afebrile seizure later develop epilepsy; the risk is approximately 20% if the neurologic exam, EEG, and neuroimaging are normal.

Some definition in seizure :

AN UNPROVOKED SEIZURE is one that is not an acute symptomatic seizure.

A REMOTE SYMPTOMATIC SEIZURE is one secondary to a distant brain injury, such as an old stroke.

REFLEX SEIZURES are a type of seizure precipitated by a sensory stimulus. These types of seizures can be caused by a variety of stimuli, including visual (flickering lights, patterns, reading), auditory (music), somatosensory, or proprioceptive stimuli; praxis; eating; bathing in hot water; or being startled

EPILEPSY

Definition :The clinical diagnosis of epilepsy usually requires the occurrence of at least one unprovoked epileptic seizure with either a second such seizure occur in a time frame of longer than 24 hours in between them. or enough EEG and clinical information to convincingly establish an enduring predisposition to develop recurrences.

Epeiomology:

- Approximately 4–10% of children experience at least one seizure (febrile or afebrile) in the first 16 years of life
- The cumulative lifetime incidence of epilepsy is 3%, and more than half of the disorders start in childhood.
- The annual prevalence is 0.5–1.0%.

Thus, the occurrence of a single seizure of afebrile seizures does not necessarily imply the diagnosis of epilepsy.

Seizure disorder is a general term that is usually used to include any one of several disorders, including epilepsy, febrile seizures, and, possibly, single seizures and symptomatic seizures secondary to metabolic, infectious, or other etiologies (e.g., hypocalcemia, meningitis).

An epileptic encephalopathy is an epilepsy syndrome in which there is a severe EEG abnormality that is thought to result in cognitive and other impairments.

Developmental encephalopathy denotes a disorder in which the underlying etiology (e.g., a specific gene variant) contributes to a developmental delay independently of the patient's seizure burden and/or EEG abnormalities.

The terms epileptic and developmental encephalopathy can be combined (i.e., developmental epileptic encephalopathy) in specific situations where both the EEG abnormalities and the underlying etiology contribute to the patient's developmental delay.

etiology of epilepsy:

i. Genetic epilepsy (previously also referred to as idiopathic epilepsy) implies that the epilepsy syndrome is the direct result of a known or presumed genetic defect(s) that is not causative of a brain structural or metabolic disorder other than the epilepsy. This category encompasses genetic generalized epilepsies (previously called idiopathic generalized epilepsies), such as childhood absence epilepsy, as well as epilepsies caused by a known gene defect

ii. Structural epilepsy (previously called symptomatic epilepsy) refers to an epilepsy syndrome caused by an underlying structural brain disorder that may or may not be genetic. This includes etiologies such as old stroke or hypoxic- ischemic injury, as well as epilepsy secondary to tuberous sclerosis (which is also genetic).

iii. Immune-mediated epilepsy is an important category that describes epilepsies occurring secondary to immune- mediated central nervous system (CNS) inflammation. This group of disorders warrants special attention because immunotherapies such as steroids and intravenous immunoglobulin(IVIG) may be the first- line treatments. Autoimmune encephalitidessuch as anti–N- methyl- d- aspartate (NMDA) receptor encephalitis and anti- LG1 limbic encephalitis are examples of immune- mediated epilepsies.

iv. Infectious epilepsy describes epilepsies secondary to chronic infectious conditions such as tuberculosis and HIV rather than acute infections such as bacterial meningitis or herpes simplex virus (HSV) encephalitis.

v. The older terms cryptogenic epilepsy and presumed symptomatic epilepsy refer to an epilepsy syndrome in which there is a presumed underlying brain disorder causing the epilepsy and affecting neurologic function, but the underlying disorder is not known; the disorder is now referred to as unknown epilepsy, designating that the underlying cause of the epilepsy is still unknown.

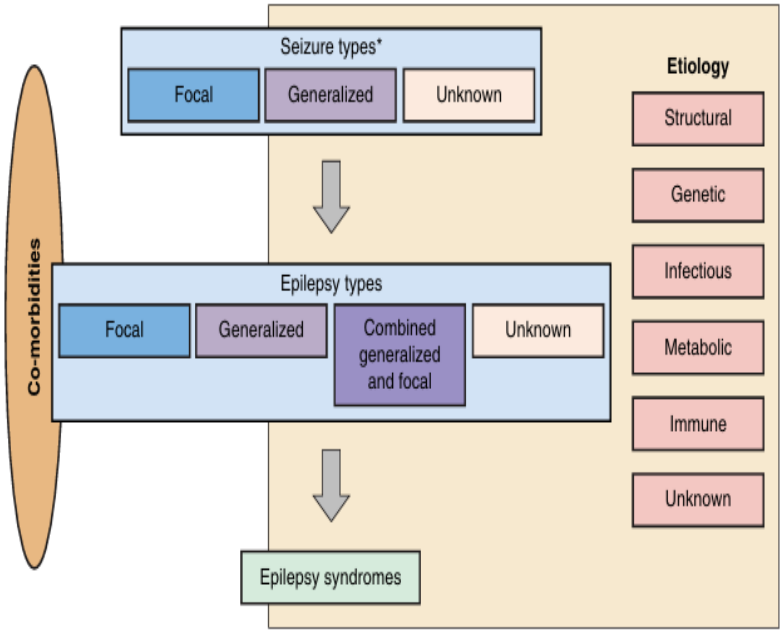

Fig. 633.2 ILAE classification of epilepsies. *Denotes onset of seizure. *(From Katyayan A, Diaz-Medina G. Epilepsy: epileptic syndromes and treatment. Neurol Clon. 2021;39:779–794, Fig. 2, p. 781.)*

EVALUATION OF THE FIRST SEIZURE

The initial evaluation of an infant or a child during or shortly after a suspected seizure should include an assessment of the adequacy of the airway, ventilation, and cardiac function, as well as measurement of temperature, blood pressure, and glucose concentration. For acute evaluation of the first seizure, the

physician should search for potentially life- threatening causes of seizures, such as meningitis, systemic sepsis, unintentional or intentional head trauma, and ingestion of drugs or medications or other toxins.

The history should aim to determine if the event was a seizure or not and to define factors that might have promoted the convulsion and to provide a detailed description of the seizure and the child's postictal state.

The subsequent step in an evaluation is to determine whether the seizure has a focal onset or is generalized. (clarifying the seizure semiology)

Focal seizures could include forceful turning of the head and eyes to one side, unilateral clonic movements beginning in the face or extremities, or a sensory disturbance, such as paresthesia or pain localized to a specific area. Focal seizures in an adolescent or adult usually indicate a localized lesion, whereas these seizures during childhood are often either secondary to a lesion or the result of a genetic epilepsy. Focal seizures in a neonate may be seen because of focal lesions such as perinatal stroke or because of a metabolic abnormality such as hypocalcemia that results in focal seizures that may not generalize because of immaturity of the brain connections.

Focal and generalized motor seizures may be tonic- clonic, tonic, clonic, myoclonic, or atonic.

i. Tonic seizures are characterized by increased tone or rigidity (usually lasting 2 seconds up to several minutes)
ii. Atonic seizures are characterized by flaccidity and lack of movement.
iii. Clonic seizures consist of rhythmic, fast muscle contractions and slightly longer relaxations;
iv. Myoclonus is a shocklike contraction of a muscle of <50 milliseconds that is often repeated.

The duration of the seizure and state of consciousness (retained or impaired) should be documented.

The history should determine whether an aura preceded the convulsion and the behavior the child was exhibiting immediately preceding the seizure. Auras can take the form of a number of sensations, including visual (e.g., flashing lights or seeing colors or complex visual hallucinations), somatosensory (tingling),olfactory, auditory, vestibular, or experiential (e.g., déjà vu, déjà vécu feelings) sensations, depending on the precise localization of the origin of the seizures. The most common aura experienced by children consists of epigastric discomfort or pain and a feeling of fear.

The posture of the patient, presence or absence and distribution of cyanosis, vocalizations, loss of sphincter control (more commonly of the urinary bladder), and postictal state (including sleep, headache, and hemiparesis) should be noted.

In addition to clarifying the seizure semiology, a detailed history is crucial in identifying an underlying cause for the seizure. Reported personality changes or symptoms of increased intracranial pressure can suggest an intracranial tumor. Similarly, a history of cognitive regression can suggest a degenerative or metabolic disease. A history of prenatal or perinatal distress or of developmental delay can suggest etiologic congenital or perinatal brain dysfunction. Acute to subacute personality changes, psychiatric symptoms,and/or associated movement abnormalities may suggest an autoimmune etiology.

The examination of a child with a seizure disorder should also be geared toward the search for an organic cause. The child's head circumference, length, and weight are plotted on a growth chart and compared with previous measurements. A careful general and neurologic examination should be performed. A funduscopic exam should be performed to evaluate for the presence of papilledema, optic neuritis, retinal hemorrhages.

The finding of unusual facial features or of associated physical findings such as hepatosplenomegaly may point to storage disease or inborn error of metabolism as the cause of the neurologic disorder. The presence of a neurocutaneous disorder may be indicated by the presence of vitiliginous ash leaf lesion , adenoma sebaceum, shagreen patches, or retinal phakomas (tuberous sclerosis);of multiple café- au- lait spots (neurofibromatosis); or of V1- or V2- distribution nevus flammeus (Sturge- Weber syndrome) .

Localizing neurologic signs, such as a subtle hemiparesis with hyperreflexia, an equivocal or positive Babinski sign, and pronator drifting of an extended arm with eyes closed, might suggest a contralateral hemispheric structural lesion, such as a slow-growing glioma, as the cause of the seizure disorder. Unilateral growth arrest of the thumbnail, hand, or extremity in a child with a focal seizure disorder suggests a chronic condition, such as a porencephalic cyst, arteriovenous malformation,or cortical atrophy of the opposite hemisphere.

Laboratory tests :In an acute setting such as the emergency department, the decision to pursue laboratory testing, including serum electrolytes, complete blood count, and/or urine toxicology tests, should be made on a case- by- case basis that considers the patient's clinical history and examination.

- ECG to rule out long QT or other cardiac dysrhythmias and other tests directed at disorders that could mimic seizures may be needed
- A lumbar puncture is usually of limited value in an acute workup of a nonfebrile seizure unless the history or examination is concerning for an infectious or inflammatory process or if there is clinical concern for intracranial bleeding despite normal brain imaging.
- A routine EEG should be performed in all cases of a first unprovoked nonfebrile seizure to help predict the risk of seizure recurrence. If the patient's neurologic status has returned to baseline, the EEG can often be done on an outpatient basis even though the yield may be slightly lower because the EEG has been delayed beyond the first 12hours.
- Emergent brain imaging with a head CT or brain MRI is usually performed if the seizure was focal, if there are postictal focal deficits on neurologic exam, or if the patient's status is not returning to baseline; in patients with trauma preceding the seizure; and in patients with a high risk medical history. Brain MRI is preferred over a CT scan on non-emergent basis should be considered in most patients. CT is useful if a rapid study is needed to look for trauma, a mass, or signs of increased intracranial pressure.

FEBRILE SEIZURES

Febrile seizures are seizures that occur between the ages of 6 and 60 months of life (peak 12- 18 months old) with a temperature of 38°C (100.4°F) or higher, that are not the result of CNS infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures.

Types of febrile seizures :

- A simple febrile seizure is a primary generalized, usually tonic- clonic, attack associated with fever, lasting for a maximum of 15 minutes, and not recurrent within a 24- hour period.
- A complex febrile seizure is more prolonged (>15 minutes), and/or is focal, and/or recurs within 24 hours.

Febrile status epilepticus is a febrile seizure lasting longer than 30 minutes. Most patients with simple febrile seizures have a very short postictal state and usually return to their baseline normal behavior and consciousness within minutes of the seizure.

Between 2% and 5% of neurologically healthy infants and children experience at least one, usually simple, febrile seizure.

Simple febrile seizures do not have an increased risk of mortality even though they are concerning to the parents.

Complex febrile seizures may have an approximately twofold long- term increase in mortality rates as compared with the general population over the subsequent 2 years, probably secondary to a coexisting pathology.

There are no long- term adverse effects of having one or more simple febrile seizures. Compared with age-matched controls, patients with febrile seizures do not have any increase in the incidence of abnormalities of behavior, scholastic performance, neurocognitive function, or attention. Children who develop later epilepsy, however, might experience such difficulties.

Several factors affect the recurrence risk ,Although approximately 15% of children with epilepsy have had febrile seizures, only 5% (range 1–33%,dependent on risk factors) of children who experience febrile seizures proceed to develop epilepsy later in life. There are several predictors of epilepsy after febrile seizures .

Risk Factors for Recurrence of Febrile Seizures*
MAJOR :Age <1 yr
Duration of fever <24 hr
Fever 38–39°C (100.4–102.2°F)
MINOR:Family history of febrile seizures
Family history of epilepsy
Complex febrile seizure
Daycare
Male gender
Lower serum sodium at time of presentation

*Having no risk factors carries a recurrence risk of approximately 12%; one risk factor, 25–50%; two risk factors, 50–59%; three or more risk factors, 73–100%

Risk Factors for Occurrence of Subsequent Epilepsy After a Febrile Seizure
Simple febrile seizure 1%
Recurrent febrile seizures 4%
Complex febrile seizures (>15 min in duration or recurrent within 24 hr) 6%
Fever <1 hr before febrile seizure 11%
Family history of epilepsy 18%
Complex febrile seizures (focal) 29%
Neurodevelopmental abnormalities 33%

Having more than one risk factor is at least in part additive.

GENETIC AND OTHER FACTORS LEADING TO FEBRILE SEIZURES

The genetic contribution to the incidence of febrile seizures is manifested by a positive family history for febrile seizures in many patients. In some families, the disorder is inherited as an autosomal dominant trait, and multiple single genes that cause the disorder have been identified in such families. However, in most cases the disorder appears to be polygenic, and many genes predisposing to it remain to be identified. Genes associated with febrile seizures include SCN1A, SCN1B, SCN9A, and CPA6.

GENERAL APPROACH TO THE PATIENT WITH FEBRILE SEIZURES.

Each child who presents with a febrile seizure requires a detailed history and a thorough general and neurologic examination.

Febrile seizures often occur in the context of otitis media; roseola and human herpesvirus (HHV) 6 infections; and infections with norovirus, parechovirus, enteroviruses, Shigella, or similar agents, making the evaluation more demanding. In patients with febrile status epilepticus,HHV- 6B (more frequently) and HHV- 7 infections may account for 30% of the cases.

Lumbar Puncture

- ✓ Meningitis should be considered in the differential diagnosis, and lumbar puncture should be performed for all infants younger than 6 months of age who present with fever and seizure, if the child is ill-appearing, or at any age if there are clinical signs or symptoms of concern.
- ✓ A lumbar puncture is an option in a child 6- 12 months of age who is deficient in Haemophilus influenzae type b and Streptococcus pneumoniae immunizations or for whom the immunization status is unknown.
- ✓ A lumbar puncture is an option in children who have been pretreated with antibiotics.

Electroencephalogram

If the child is presenting with the first simple febrile seizure and is otherwise neurologically healthy, an EEG need not be performed as part of the evaluation. An EEG would not predict the future recurrence of febrile seizures or epilepsy even if the result is abnormal. Spikes during drowsiness are often seen in children with febrile seizures, particularly those older than age 4 years, and these do not predict later epilepsy.

EEGs performed within 2 weeks of a febrile seizure often have non specific slowing, usually posteriorly. Thus in many cases, if an EEG is indicated, it is delayed until or repeated after more than 2 weeks have passed. An EEG should therefore generally be restricted to special cases in which epilepsy is highly suspected and, generally, it should be used to delineate the type of epilepsy rather than to predict its occurrence. If an EEG is done, it should be performed for at least 20 minutes in wakefulness and in sleep according to international guide-lines to avoid misinterpretation and drawing of erroneous conclusions.At times, if the patient does not recover immediately from a seizure, an EEG can help distinguish between ongoing seizure activity and a prolonged postictal stateBlood Studies

Blood studies (serum electrolytes, calcium, phosphorus, magnesium,and a complete blood count) are not routinely recommended in the workup of a child with a first simple febrile seizure. Blood glucose should be measured initially and with prolonged postictal obtundation or with poor oral intake (prolonged fasting). Serum electrolyte values may be abnormal in children after a febrile seizure, but this should be suggested by precipitating or predisposing conditions elicited in the history and reflected in the physical examination. If clinically indicated (e.g., dehydration), these tests should be performed. A low sodium level is associated with a higher risk of recurrence of the febrile seizure within the following 24 hours.

Neuroimaging :A CT or MRI is not recommended in evaluating the child after a first simple febrile seizure. The workup of children with complex febrile seizures needs to be individualized. This can include an EEG and neuroimaging, particularly if the child is neurologically abnormal.

TREATMENT

i. In general, antiepileptic therapy, continuous or intermittent, is not recommended for children with one or more simple febrile seizures.
ii. Parents should be counseled about the relative risks of recurrence of febrile seizures and recurrence of epilepsy, educated on how to handle a seizure acutely, and given emotional support.
iii. If the seizure lasts for longer than 5 minutes, acute treatment with lorazepam, midazolam, or diazepam is needed . Rectal diazepam is often prescribed to families to be used at home as a rescue medication if a febrile seizure lasts longer than 5 minutes . Alternatively, buccal or intranasal midazolam or diazepam may be used.
iv. In cases of frequently recurring febrile seizures, intermittent oral clonazepam (0.01 mg/kg every 8-12 hours up to a maximum dose of 1.5 mg/day) or oral diazepam (0.33 mg/kg every 8 hours) can be given during febrile illnesses. Such therapies help reduce, but do not eliminate, the risks of recurrence of febrile seizures.
v. Historically, continuous therapy with the antiepileptic drugs (AEDs) phenobarbital or valproic acid was occasionally used to prevent febrile seizures. However, in the vast majority of cases, use of continuous therapy is not justified because of the risk of side effects and lack of demonstrated long-term benefits, even if the recurrence rate of febrile seizures is expected to be decreased by these drugs.
vi. Antipyretics can decrease the discomfort of the child but do not reduce the risk of having a recurrent febrile seizure.
vii. Chronic antiepileptic therapy may be considered for children with a high risk for later epilepsy. The possibility of future epilepsy does not change with or without antiepileptic therapy.
viii. Iron deficiency is associated with an increased risk of febrile seizures, and thus screening for that problem and treating it appear appropriate.

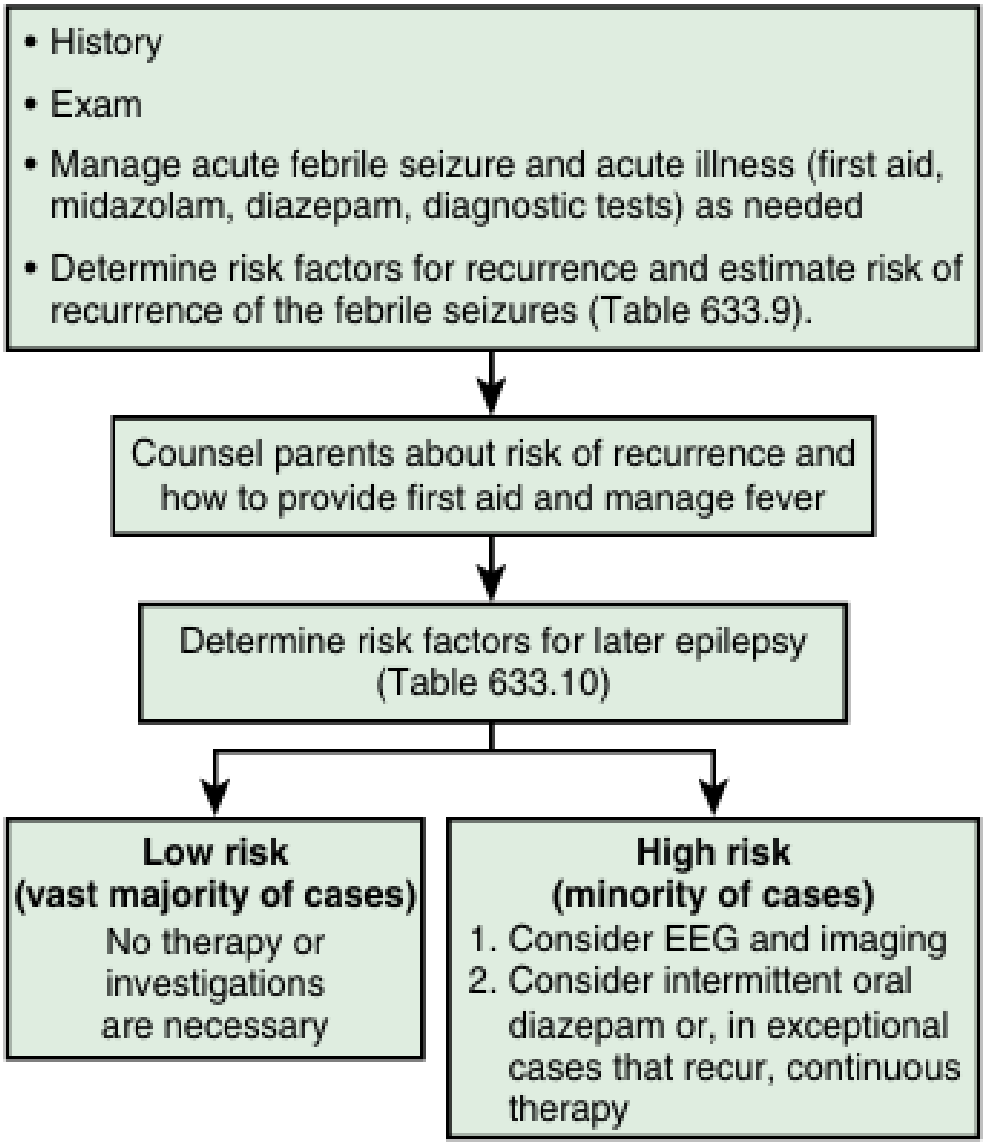

Fig. 633.5 Treatment algorithm for the management of febrile seizures. *(Modified from Mikati MA, Rahi A. Febrile seizures: from molecular biology to clinical practice. Neurosciences [Riyadh]. 2004;10:14–22.)*

Unprovoked Seizures:

Focal Seizures and Related Epilepsy

Focal seizures account for approximately 40% of seizures in children and can be divided into focal seizures with preserved awareness, in which consciousness is not impaired, and focal seizures with impaired awareness, in which consciousness is affected.

Focal seizures with preserved or impaired awareness can each occur in isolation, one can temporally lead to the other (usually from preserved to impaired awareness), and/or each can progress into secondary generalized seizures, called focal to bilateral tonic- clonic seizures, although less commonly, the secondary generalized seizure may also be tonic, clonic, or atonic.

- **FOCAL SEIZURES WITH PRESERVED AWARENESS:** These can take the form of sensory seizures (auras, called focal aware seizures) or brief motor seizures, the specific nature of which gives clues as to the location of the seizure focus. Brief motor seizures are the most common and include focal tonic, clonic, or atonic seizures. Often there is a motor (Jacksonian) march from face to arm to leg, adversive head and eye movements to the contralateral side, or postictal (Todd) paralysis that can last minutes or hours, and sometimes longer.
- **FOCAL SEIZURES WITH IMPAIRED AWARENESS**: These seizures usually last 1- 2 minutes and are often preceded by an aura, such as a rising abdominal feeling, déjà vu or déjà vécu, a sense of fear, complex visual hallucinations, micropsia or macropsia (temporal lobe), generalized difficult- to-characterize sensations (frontal lobe), focal sensations (parietal lobe), or simple visual experiences (occipital lobe). Subsequent manifestations consist of decreased responsiveness, staring, looking around seemingly purposelessly, and automatisms. Automatisms are automatic semipurposeful movements of the mouth (oral, alimentary such as chewing) or of the extremities (manual, such as manipulating the sheets; leg automatisms such as shuffling, walking, or bicycling movements).
  The patient might appear to react to some of the stimulation around him or her, but does not later recall the epileptic event.
- **FOCAL TO BILATERAL TONIC-CLONIC SEIZURES:** These can either start with generalized clinical phenomena (from rapid spread of the discharge from the initial focus) or as focal seizures with subsequent clinical generalization.

  EEG in patients with focal/partial seizures usually shows focal spikes or sharp waves in the lobe where the seizure originates.

  Brain imaging is critical in patients with focal seizures. MRI is preferable to CT, which misses subtle but, occasionally, potentially clinically significant lesions.

BENIGN EPILEPSY SYNDROMES WITH FOCAL SEIZURES

The most common such syndrome is benign childhood epilepsy with centrotemporal spikes (BECTS), which typically starts during childhood (ages 3- 10 years) and is outgrown by adolescence. The child typically wakes up at night because of a focal seizure with preserved awareness causing buccal and throat tingling and tonic or clonic contractions of one side of the face, with drooling and inability to speak but with preserved consciousness and comprehension. Focal seizures with impaired awareness and secondary generalized seizures can also occur. EEG shows typical wide- based centrotemporal spikes . MRI is normal. Patients respond very well to AEDs such as oxcarbazepine and carbamazepine

Generalized Seizures and Related Epilepsy Syndromes

ABSENCE SEIZURES: Typical absence seizures usually start at 5- 8 years of age and are often, because of their brevity, overlooked by parents for many months even though they can occur up to hundreds of times per day. Unlike focal seizures with impaired awareness, they do not have an aura, usually last for only a few seconds, and are sometimes accompanied by eyelid flutter or upward rolling of the eyes but typically not by the usually more florid automatisms seen in focal seizures with impaired awareness (absence seizures can have simple automatisms such as lip smacking or picking at clothing, and the head can very minimally fall forward).

Absence seizures do not have a postictal period and are characterized by immediate resumption of what the patient was doing before the seizure. Hyperventilation for 3- 5 minutes can precipitate the seizures and the accompanying 3- Hz spike–and–slow- wave discharges.

Absence seizures are most often initially treated with ethosuximide,which is as effective as, but less toxic than, valproate; both are more effective than lamotrigine (which has fewer side effects than valproate). Alternative drugs of first choice are lamotrigine and valproate,especially if generalized tonic- clonic seizures coexist with absence seizures. Other medications that could be used for absence seizures include acetazolamide, zonisamide, or clonazepam.

SEVERE GENERALIZED EPILEPSIES

West syndrome :starts between the ages of 2 and 12 months and consists of a triad of infantile epileptic spasms that usually occur in clusters (particularly in drowsiness or upon arousal), developmental regression, and a typical EEG picture called hypsarrhythmia. Hypsarrhythmia is a high- voltage, slow, chaotic background with multifocal spikes. Patients with cryptogenic/idiopathic (referred to as unknown etiology) West syndrome have normal development before onset, whereas patients with symptomatic west syndrome have preceding developmental delay owing to perinatal encephalopathies, malformations, underlying metabolic disorders, infections like with congenital Zika virus, or other etiologies like genetics .

West syndrome, especially in cases where the etiology is unknown (i.e., cases that are not explained by the presence of a gene variant or a structural brain anomaly), is a medical emergency because a delay in diagnosis of 3 weeks or longer can affect the long- term prognosis. The spasms are often overlooked by parents and by physicians, being mistaken for startles caused by colic or other benign paroxysmal syndromes

1. West syndrome is best treated with hormonal therapy in the form of either ACTH injections or, possibly, oral steroids. Side effects, more common with the higher doses, include hypertension, electrolyte imbalance, infections, hyperglycemia and/or glycosuria, and gastric ulcers. Prophylactic therapy for ulcers with an H2 blocker or protein pump inhibitor is desirable while the patient is receiving hormonal therapy. Also, live vaccines are contraindicated, and other vaccines are not effective during ACTH and steroid therapy because of the immune- suppressive effects of these hormonal agents. Thus all vaccines are not given during hormonal therapy and in the period after it (usually ≤3 months after the last dose).
2. Vigabatrin can be used as a first- line agent to treat infantile spasms in patients with tuberous sclerosis and is the second- line choice if hormonal therapy was unsuccessful in other cases of infantile spasms.
3. The ketogenic diet is probably the third- line therapy. Subsequent alternative treatment options for spasms include valproate, benzodiazepines such as nitrazepam and clonazepam, topiramate, lamotrigine, zonisamide, pyridoxine, and IVIG. None of these alternative drugs offers uniformly satisfactory results.

- APPROACH TO EPILEPSY SURGERY: If a patient has failed three drugs, the chance of achieving seizure freedom using AEDs is <10%. Therefore proper evaluation for surgery is necessary when a patient fails two or three AEDs, usually within 2 years of the onset of epilepsy and often sooner than 2 years.
- In infants who do not respond immediately to antiepileptic therapy, vitamin B6 (100 mg intravenously) is given as a therapeutic trial to help diagnose pyridoxine-responsive seizures, with precautions to guard against possible apnea.

STATUS EPILEPTICUS

Status epilepticus (SE) is a medical emergency that should be anticipated in any patient who presents with an acute seizure. The ILAE has refined the definition of SE to reflect the time at which treatment should be initiated (t1) and time at which continuous seizure activity leads to long- term sequelae (t2) such as neuronal injury, depending on the type of SE.

For generalized tonic- clonic seizures, SE is defined as continuous convulsive activity or recurrent generalized convulsive seizure activity without regaining consciousness (t1 = 5 minutes, t2 ≥30 minutes).

The definition differs for SE consisting of focal seizures with impaired awareness (t1 = 10 minutes, t2 = 30 minutes) and absence SE (t1 = 10- 15minutes, t2 = unknown).

The most common type of SE is convulsive status epilepticus (generalized tonic, clonic, or tonic- clonic), but other types do occur, including nonconvulsive status (focal with impaired awareness, absence), myoclonic status, epilepsia partialis continua, and neonatal SE.

Approximately 30% of patients presenting with SE are having their first seizure, and approximately 40% of these later develop epilepsy.

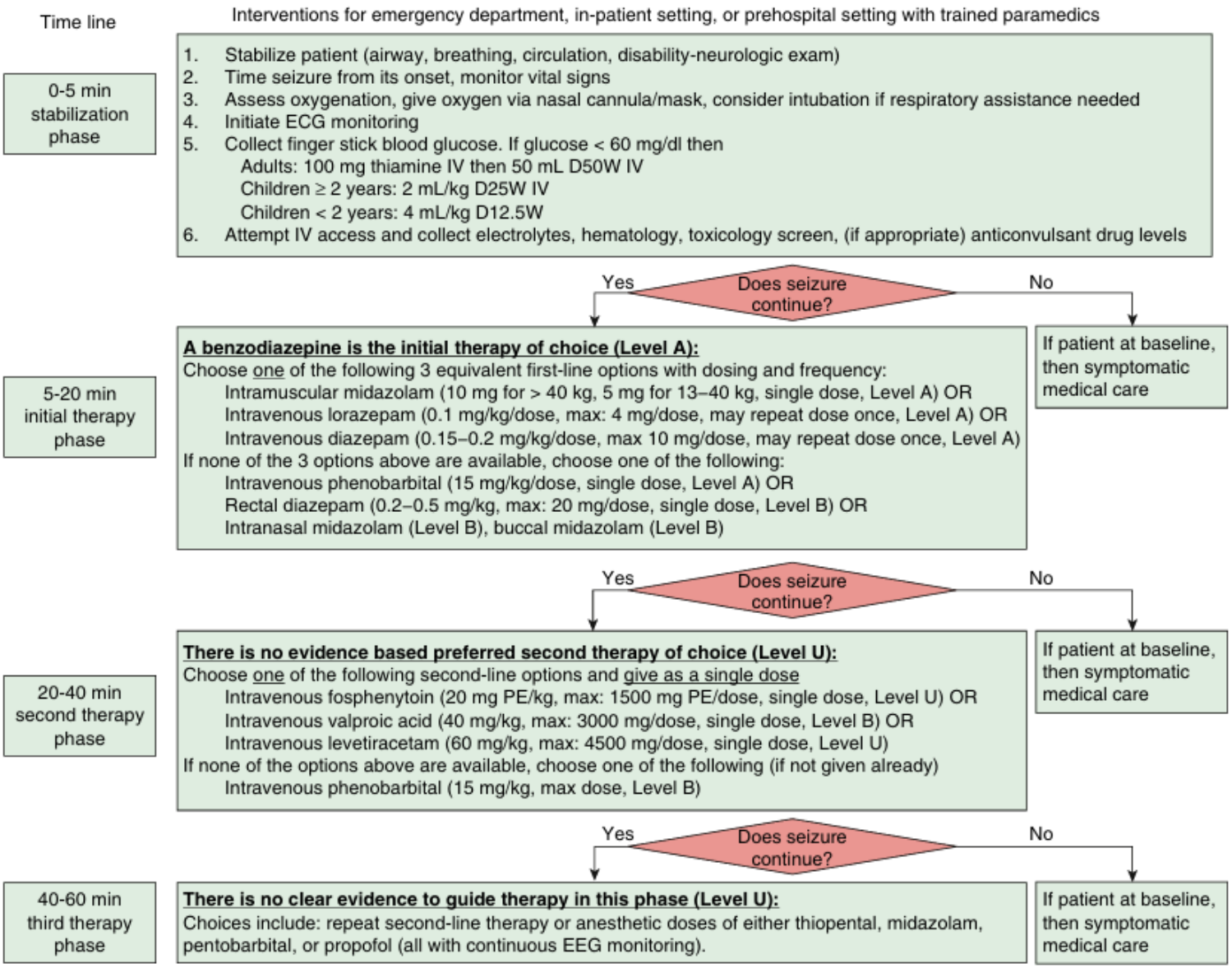

Fig. 633.16 Proposed treatment algorithm for status epilepticus. Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytic framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate. *(From Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline committee of the American Epilepsy Society. Epilepsy Curr. 2016;16[1]:48–61, Fig.1.)*

Table 633.23	Doses of Commonly Used Antiepileptic Drugs in Status Epilepticus	
DRUG*	**ROUTE**	**DOSAGE**
Lorazepam	Intravenous Intranasal	0.1 mg/kg up to maximum of 4 mg, may repeat in 5-10 min 0.1 mg/kg up to maximum of 5 mg
Midazolam	Intravenous Intramuscular Intranasal Buccal	0.2 mg/kg up to 10 mg total dose, may repeat in 5-10 min Continuous infusion maintenance: 0.05-2 mg/kg/hr 0.2 mg/kg 0.2 mg/kg 0.5 mg/kg
Diazepam	Intravenous	0.15 mg/kg up to a maximum total dose of 10 mg; may repeat in 5-10 min
	Rectal	2-5 yr: 0.5 mg/kg 6-11 yr: 0.3 mg/kg ≥12 yr: 0.2 mg/kg
Fosphenytoin	Intravenous	Loading: 20 mg/kg PE, infusion rate maximum 50 mg PE/min Maintenance: 4-8 mg/kg/24 hr divided tid
Ketamine	Intravenous	Loading: 1 mg/kg Maintenance: 0.5-2 mg/kg/hr
Phenobarbital	Intravenous	Loading: 15-20 mg/kg (maximum 1,000 mg) Maintenance: 3-5 mg/kg/24 hr divided bid
Pentobarbital coma	Intravenous	Loading: 5-15 mg/kg Maintenance: 1-5 mg/kg/hr
Propofol	Intravenous	Loading: 1-2 mg/kg Maintenance infusion: 1.2 -3.9 mg/kg/hr
Thiopental	Intravenous	Loading: 2-7 mg/kg, infusion rate maximum 50 mg/min Maintenance infusion: 0.5-5 mg/kg/hr
Valproate	Intravenous	Loading: 20-40 mg/kg Maintenance: 30-60 mg/kg/24 hr divided bid
Lacosamide†	Intravenous	Loading: 4-8 mg/kg (maximum 400 mg) Maintenance: 4-12 mg/kg/day divided bid (maximum 400 mg/day)
Levetiracetam	Intravenous	Loading: 30-60 mg/kg (maximum 4,500 mg) Maintenance: 30-60 mg/kg/24 hr divided bid (maximum 3,000 mg/day)
Topiramate	Enterally	Loading: 5-10 mg/kg Maintenance: 5-12 mg/kg/day divided bid (maximum 400 mg/day)

*Reflects current trends in use that may not be FDA approved. For FDA indications, see Table 633.13.
†May cause PR prolongation.
PE, Phenytoin sodium equivalents.

Neonatal Seizures

Seizures are possibly the most important and common indicator of significant neurologic dysfunction in the neonatal period. Seizure incidence is higher during this period than in any other period of life: seizures occur in 57.5 per 1,000 in infants with birthweights <1,500 g and 2.8 per 1,000 in infants weighing between 2,500 and 3,999 g. The etiology of neonatal seizures depends on postnatal age of onset as well as EEG and clinical features

Causes of Neonatal Seizures According to common Age of Presentation

AGES 1- 4 DAYS
Hypoxic- ischemic encephalopathy
Drug withdrawal, maternal drug use of opiate or barbiturates
Drug toxicity: lidocaine, penicillin
Intraventricular hemorrhage
Sepsis
Acute metabolic disorders •Hypocalcemia :Maternal hyperthyroidism, or hypoparathyroidism •Hypoglycemia: Maternaldiabetes, Hyperinsulinemic hypoglycemia Hypomagnesemia Hyponatremia or hypernatremia:Iatrogenic or inappropriate antidiuretic hormone secretion.
Inborn errors of metabolism Galactosemia,Hyperglycinemia ,Urea cycle disorders, Pyridoxine dependency and pyridoxal- 5- phosphate dependency (must be considered at any age)
AGES 4- 14 DAYS
Infection Meningitis (bacterial),Encephalitis (enteroviral, herpes simplex)
Metabolic disorders Hypocalcemia related to diet, milk formula Hypoglycemia, Galactosemia,Fructosemia Beckwith syndrome
Drug withdrawal, maternal drug use of narcotics or barbiturates
Benign neonatal convulsions, familial and nonfamilial
Kernicterus, hyperbilirubinemia
Developmental delay, epilepsy, neonatal diabetes syndrome
AGES 2- 8 WK
Infection Herpes simplex or enteroviral encephalitis,Bacterial meningitis
Head injury Subdural hematoma,Child abuse
Inherited disorders of metabolism Aminoacidurias, Urea cycle defects, Organic acidurias, Neonatal adrenoleukodystrophy
Malformations of cortical development Lissencephaly, Focal cortical dysplasia Tuberous sclerosis Sturge- Weber syndrome

Hypoxic- Ischemic Encephalopathy: This is the most common cause of neonatal seizures, accounting for 50–60% of patients. Seizures secondary to this encephalopathy occur within 24 hours of birth.

Vascular Events: These include intracranial bleeds and ischemic strokes, and account for 10–20% of patients. Three types of hemorrhage can be distinguished: primary subarachnoid hemorrhage, germinal matrix–intraventricular hemorrhage, and subdural hemorrhage. Patients with arterial strokes or venous sinus thrombosis can present with seizure, and these can be diagnosed by neuroimaging

Intracranial Infections: Bacterial and nonbacterial infections account for 5–10% of the cases of neonatal seizures and include bacterial meningitis, TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus, herpes simplex virus) infections, and, particularly, herpes simplex encephalitis.

Brain Malformations: Brain malformations account for 5–10% of neonatal seizure cases.

Metabolic Disturbances: include disturbances in glucose, calcium, magnesium, other electrolytes, amino acids, or organic acids and pyridoxine dependency. Hypoglycemia can cause neurologic disturbances and is common in small neonates and neonates whose mothers are diabetic or prediabetic. Hypocalcemia occurs with two peaks. The first peak corresponds to low birthweight infants and is evident in the first 2- 3 days of life. The second peak occurs later in neonatal life and often involves large, full- term babies who consume milk that has an unfavorable ratio of phosphorus to calcium and phosphorus to magnesium. Hypomagnesemia is often associated with hypocalcemia. Hyponatremia can cause seizures and is often secondary to inappropriate antidiuretic hormone secretion or water intoxication.

Local anesthetic intoxication: seizures can result from neonatal intoxication with local anesthetics that are inadvertently administered into the infant's scalp.

Inborn errors of metabolism : Neonatal seizures can also result from disturbances in the amino acid ,or organic acid metabolism. These are usually associated with acidosis and/or hyperammonemia.

Drug Withdrawal: Seizures can rarely be caused by the neonate's passive addiction and then drug withdrawal after birth. Such drugs include narcotic analgesics, sedative- hypnotics, and others. The associated seizures appear during the first 3 days of life.

Neonatal Seizure Genetic Syndromes: Seizure syndromes include benign neonatal convulsions (fifth- day fits), which are usually focal motor seizures that start around the fifth day of life . Autosomal dominant benign familial neonatal seizures have an onset at 2- 4 days of age and usually remit at 2- 15 weeks of age.

TYPES OF NEONATAL SEIZURES

seizures can be categorized as motor,nonmotor

Motor Seizures

1. Automatisms: include transient eye deviations, nystagmus, blinking, mouthing, and abnormal extremity movements (rowing, swimming, bicycling, pedaling, and stepping). Automatisms occur more commonly in premature than in full- term infants.
2. Clonic Seizures: can be focal or multifocal. Multifocal clonic seizures incorporate several body parts and are migratory in nature. The migration follows a non- Jacksonian trend; for example, jerking of the left arm can be associated with jerking of the right leg. Generalized clonic seizures that are bilateral,

symmetric, and synchronous are uncommon in the neonatal period, presumably because of incomplete myelination at this age.

3. Epileptic Spasms: are sudden generalized jerks lasting 1- 2 seconds that are distinguished from generalized tonic spells by their shorter duration and by the fact that spasms are usually associated with a single,very brief, generalized discharge.
4. Myoclonic Seizures: Myoclonic seizures are divided into focal, multifocal, and generalized types. Myoclonic seizures can be distinguished from clonic seizures by the rapidity of the jerks (<50 milliseconds) and by their lack of rhythmicity.
5. Tonic Seizures: can be focal or generalized (generalized are more common).

Nonmotor Seizures

1. Autonomic: involve fluctuations in autonomic system function, including alterations in the cardiovascular, vasomotor, pupillary, and thermoregulatory function. These seizures may include heart rate changes, hypertension episodes, and apnea. Autonomic seizures typically accompany additional seizure types and are rarely seen in isolation.
2. Behavioral Arrest: seizures include cessation of activity or immobilization. This seizure type is rarely seen in isolation and can be seen as a component of sequential seizures.

Seizures Versus Jitteriness

Jitteriness can be defined as rapid motor activities, such as a tremor or shake, that can be ended by flexion or holding the limb. Seizures generally do not end with tactile or motor suppression. Jitteriness, unlike most seizures, is usually induced by a stimulus. Unlike jitteriness, seizures often involve eye deviation and autonomic changes.

DIAGNOSIS

Detailed prenatal and postnatal history and performing an adequate physical examination, Continuous bedside EEG monitoring in the neonatal intensive care unit is the preferred

Blood should be obtained for determinations of glucose, calcium,magnesium, electrolytes, and blood urea nitrogen.

A lumbar puncture may be indicated in neonates with seizures, unless the cause is obviously related to a metabolic disorder (such as hypoglycemia or hypocalcemia) or attributable to a structural etiology such as hypoxic- ischemic injury or intracranial hemorrhage. The CSF findings can indicate a bacterial meningitis or aseptic encephalitis. Prompt diagnosis and appropriate therapy improve the outcome for these infants. Bloody CSF indicates a traumatic tap or a subarachnoid or intraventricular bleed. Immediate centrifugation of the specimen can assist in differentiating the two disorders. A clear supernatant suggests a traumatic tap, and a xanthochromic color suggests a subarachnoid bleed.

Infants with focal seizures, suspected stroke or intracranial hemorrhage, and severe cytoarchitectural abnormalities of the brain (including lissencephaly and schizencephaly) who clinically may appear normal or microcephalic should undergo MRI or CT scan.

PROGNOSIS

The prognosis of neonatal seizures has improved owing to advancements in obstetric and intensive neonatal care but depends on the etiology and other organ system injury. Prematurity and high seizure burden have been shown to be associated with early death. The correlation between EEG findings and prognosis is clear. An abnormal EEG background is a powerful predictor of a less favorable later outcome.

TREATMENT

A mainstay in the therapy of neonatal seizures is the diagnosis and treatment of the underlying etiology (e.g., HIE, hypoglycemia, hypocalcemia, meningitis, drug withdrawal, trauma) whenever one can be identified.

Lorazepam and Other Benzodiazepines

Lorazepam is often used in the acute treatment of neonatal seizures; The dose is 0.1 mg/kg when used for acute treatment of seizures, and 0.05 mg/kg .Diazepam has also been used, and midazolam is often started as a continuous infusion for refractory cases of neonatal seizures.

Phenobarbital

Consensus guidelines and existing data support the use of phenobarbital as the first-choice treatment of neonatal seizures. The usual loading dose is 20 mg/kg. If this dosage is not effective, then additional doses of 10-20 mg/kg can be given until a cumulative dose of 40 mg/kg is reached. Twenty- four hours after starting the loading dose, maintenance dosing can be started at 3- 6 mg/kg/day, usually administered in two separate doses.

Phenytoin and Fosphenytoin

Consensus guidelines support the use of fosphenytoin as a second line anti-seizure medication in neonatal seizures. . Phenytoin is given at a loading dose of 20 mg/kg slowly , so as to prevent cardiac problems; The heart rate should be monitored while the drug is administered.

Other Medications

Approximately 45% of neonates respond to the first drug used if it is phenobarbital or phenytoin, and an additional 15% respond to the second agent. Levetiracetam (which can be given intravenously with a later convenient conversion to oral solution) is commonly used as a second- or third- line agent (40- 60 mg/kg). Topiramate, a possible third line agent.

- Avoid Valproate, as it is more likely to be toxic in children younger than 2 years of age than in older children.

Duration of Therapy

The duration of therapy is related to the risk of epilepsy developing later in infants suffering from neonatal seizures, a risk that ranges from 10% to 30% and depends on the individual neurologic examination and the etiology of the seizures.