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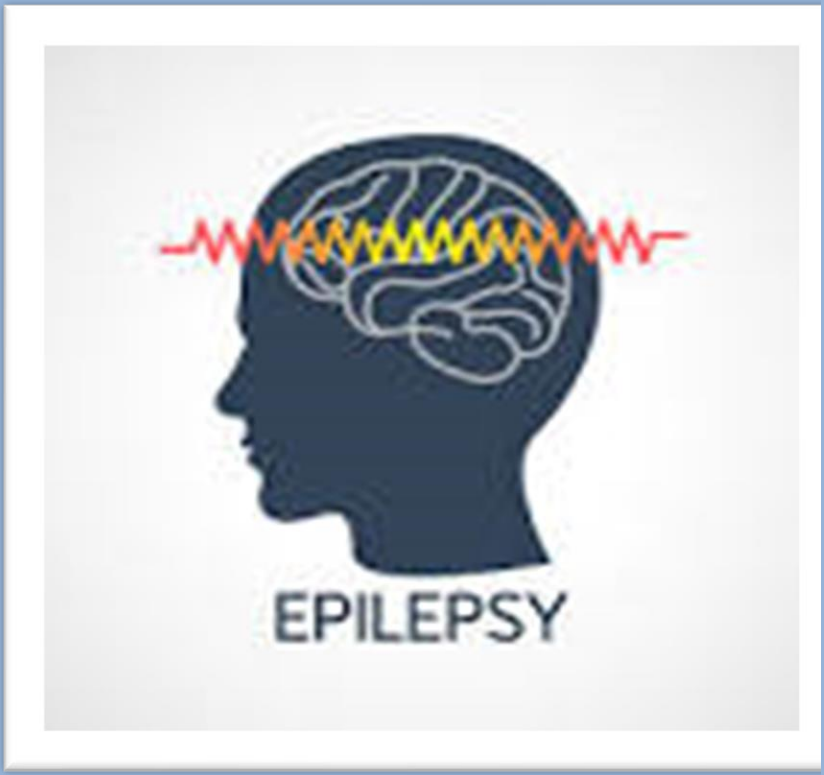

SEIZURES IN CHILDHOOD

Lectures 1+2

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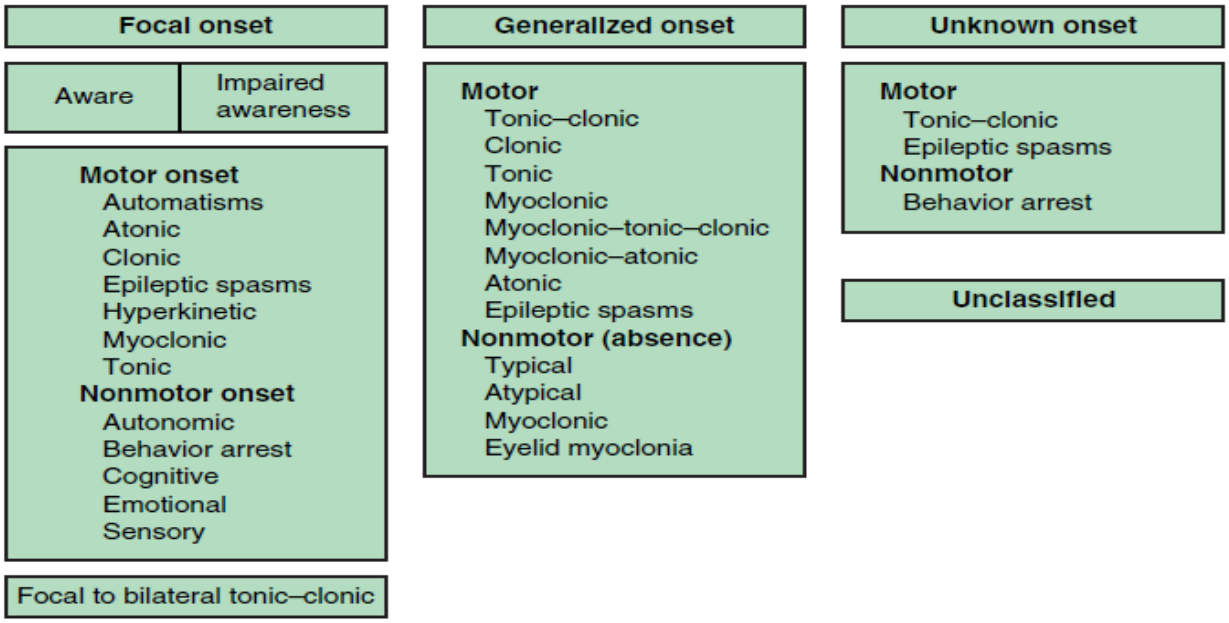
INTRODUCTION

DEFINITION OF SEIZURE:

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.



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.)*

- **Focal** (formerly known as *partial*) **seizures**, the first clinical and EEG changes suggest initial activation of a system of neurons limited to part of one cerebral hemisphere.
  Focal seizures can be described as motor or non-motor and are further characterized by preserved or impaired consciousness, which is used synonymously with the term **awareness**. Simple partial seizure is an outdated term that refers to a focal seizure with no alteration in consciousness or awareness; the current term is **focal aware seizure**. Complex partial seizure is also an outdated term that denotes focal seizures with altered consciousness or awareness of the surroundings; they are currently referred to as **focal seizures with impaired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**.
- **Generalized seizures**, the first clinical and EEG changes indicate synchronous involvement of both hemispheres.
- **Unknown onset** if there is not enough clinical information available to determine if the seizure is focal or generalized.
- **Unclassified:** If the clinical characteristics of a seizure are unusual and a determination of onset cannot be made despite an adequate evaluation.

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 is normal.

Q/ WHAT DOES THE TERM PROVOKED VS UNPROVOKED SEIZURES MEAN?

Provoked seizures OR Acute symptomatic: occur secondary to an acute problem affecting brain excitability, such as an electrolyte imbalance, or major structural, inflammatory, or metabolic disorders of the brain, such as meningitis, encephalitis, acute stroke, or brain tumor. Consequently, the prognosis depends on the underlying disorder, including its reversibility or treatability and the likelihood of developing epilepsy from it.

An **unprovoked seizure** is one that is not an acute symptomatic seizure.

Epilepsy ….

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition.

Q / WHEN DO SEIZURES COSIDERED AS EPILEPSY?

The clinical diagnosis of epilepsy usually requires the occurrence of at least one unprovoked epileptic seizure with either:

1. A second seizure occurs in a time frame of longer than 24 hours in between them.
2. EEG and clinical information to convincingly establish an enduring predisposition to develop recurrences.

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 or of febrile seizures does not necessarily imply the diagnosis of epilepsy.

TERMS YOU SHOULD KNOW:

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.

EPILESY CATEGORAZATIONS

According to etiology, epilepsies are categorized into genetic, structural, metabolic, immune, infectious, or unknown categories.

It is important to note that these categories are not mutually exclusive, and a patient's epilepsy may have multiple concurrent etiologies (e.g., genetic and structural)

1. **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.

2. **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).

3. **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 encephalitides** such as anti–*N*-methyl- d-aspartate (NMDA) receptor encephalitis are examples of immune-mediated epilepsies.

4. **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.

5. **Unknown epilepsy**. 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

EVALUATION OF THE FIRST SEIZURE

1. ***A, B, C***: 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.
2. ***Vital Signs:*** measurement of temperature, blood pressure, and glucose conc.

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.

3. History:

- FIRST STEP …. The following questions should be answered:
  - ✓ Was it really seizure or not?
  - ✓ Factors that might have promoted the convulsion.
  - ✓ 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, the duration should be documented.

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. 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.

 # Tonic seizures =increased tone or rigidity (usually lasting 2 seconds up to several minutes)

 # Atonic seizures are characterized by flaccidity and lack of movement.

 # Clonic seizures consist of rhythmic, fast muscle contractions and slightly longer relaxations

 # Myoclonus is a shock like contraction of a muscle of <50 milliseconds that is often repeated.

 # Spasms consist of flexion or extension of the truncal and extremity musculature that is sustained for 1-2 seconds, shorter than the duration seen in tonic seizures.

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, or experiential (déjà vu 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. (Aura goes with focal seizure)

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

- Third step 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 autoimmune etiology.

4. ***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, uveitis, chorioretinitis…

- 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–type lesions usually better seen using an ultraviolet light (Wood lamp); of adenoma sebaceum, shagreen patches, or retinal phakomas (tuberous sclerosis); of multiple cafe-au- lait spots (neurofibromatosis); or of V1-or V2-distribution nevus flammeus (Sturge-Weber syndrome).

5. ***Lab Investigations***: In an acute setting such as the emergency department, the decision to pursue further laboratory testing, including serum electrolytes, a 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.

6. ***ECG***: to rule out long QT or other cardiac dysrhythmias and other tests directed at disorders that could mimic seizures may be needed.

7. ***A lumbar puncture*** is usually of limited value in an acute workup of a *non-febrile* 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.

8. ***A routine EEG*** *should be performed in all cases of a first unprovoked nonfebrile seizure to help predict the risk of seizure recurrence.*

9. ***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.

Brain MRI is preferred over a CT scan and performing it on a non-emergent basis should be considered in most patients. CT is useful if a rapid study is needed to look for trauma (Hmg), a mass, or signs of increased intracranial pressure.

EXAMPLE S OF EPILEPSY SYNDROMES

- ***BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS)***

The most common such syndrome is **benign childhood epilepsy with Centro temporal 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 Centro temporal spikes that are markedly increased in frequency during drowsiness and sleep.

MRI is normal.

TRATMENT Patients respond very well to AEDs such as oxcarbazepine and carbamazepine. In some patients who only have rare and mild seizures, treatment might not be needed.

- ***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.

EEG: 3-Hz spike–and–slow-wave discharges.

TREATMENT: initially treated with Ethosuximide then, valproate; lamotrigine. Other medications that could be used for absence seizures include acetazolamide, zonisamide, or clonazepam.

- ***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.**

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, In males, West syndrome can also be caused by *ARX* gene variants.

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.

EEG Hypsarrhythmia is a high-voltage, slow, chaotic background with multifocal spikes.

TREATMENT West syndrome is best treated with hormonal therapy in the form of either ACTH injections or, possibly, oral steroids (prednisolone).

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. The ketogenic diet is probably the third-line therapy.

Subsequent alternative treatment options for spasms include valproate, benzodiazepines, pyridoxine, and IVIG.

Febrile Seizures

DEFINITION:

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 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:

1. 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.
2. 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.

EPIDIOMOLOGY:

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

PROGNOSIS:

- 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.

Table 633.9	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%.

Table 633.10	Risk Factors for Occurrence of Subsequent Epilepsy After a Febrile Seizure*

RISK FACTOR	RISK FOR SUBSEQUENT EPILEPSY
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 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. Genes associated with febrile seizures include SCN1A, SCN1B, SCN9A.

EVALUATION

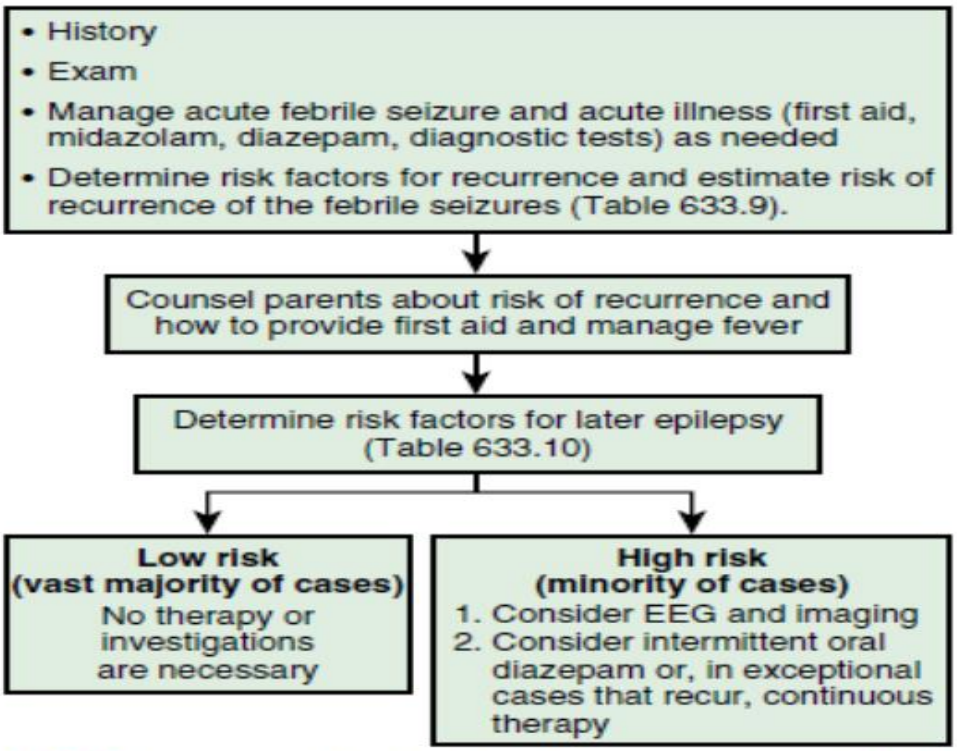


Fig. 633.5 Treatment algorithm for the management of febrile seizures. *(Modified from Mikati MA, Rahi A. Febrile seizures: from molecular biology to clinical practice. Neurosciences [Riyadh]. 2004;10:14–22.)*

- 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, so:

a. 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.
b. 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.
c. 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.EEGs performed within 2 weeks of a febrile seizure often have nonspecific. 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

- ***Blood 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).

- ***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***

a. In general, antiepileptic therapy, continuous or intermittent, is not recommended for children with one or more simple febrile seizures.
b. 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.
c. 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.
d. 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.
e. 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 thesedrugs.
f. Antipyretics can decrease the discomfort of the child but do not reduce the risk of having a recurrent febrile seizure.
g. 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.
h. Iron deficiency is associated with an increased risk of febrile seizures, and thus screening for that problem and treating it appear appropriate.

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:

TYPES OF NEONATAL SEIZURES

- Automatisms: 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.
- Clonic Seizures: Clonic seizures can be focal or multifocal. Multifocal clonic seizures incorporate several body parts and are migratory in nature.
  Notes: Generalized clonic seizures that are bilateral, symmetric, and synchronous are uncommon in the neonatal period, presumably because of decreased connectivity associated with incomplete myelination at this age.
- Epileptic Spasms: 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.
- 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.
- Tonic Seizures: Tonic seizures can be focal or generalized (generalized are more common). Focal tonic seizures include persistent posturing of a limb or posturing of the trunk or neck in an asymmetric way, often with persistent horizontal eye deviation.
- Behavioral Arrest: Behavioral arrest seizures include cessation of activity or immobilization. This seizure type is rarely seen in isolation then automatisms, and autonomic manifestations with varying lateralization.

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 and is usually induced by a stimulus.
While Seizures generally do not end with tactile or motor suppression and often involve eye deviation and autonomic changes.

ETIOLOGY

1. **Hypoxic-Ischemic Encephalopathy**: This is the most common cause of neonatal seizures, accounting for 50–60% of patients. Occur within 24 hours of birth.
2. **Vascular Events**: include intracranial bleeds and ischemic strokes and account for 10–20% of patients. Patients with arterial strokes or venous sinus thrombosis can present with seizure, and these can be diagnosed by neuroimaging.
3. **Intracranial Infections**: Bacterial and nonbacterial infections account for 5–10% of the cases of neonatal seizures and include bacterial meningitis, TORCH (*t*oxoplasmosis, other infections, *r*ubella, *c*ytomegalovirus, *h*erpes simplex virus) infections, and, particularly, herpes simplex encephalitis.
4. **Brain Malformations**: account for 5–10% of neonatal seizure cases
5. **Metabolic Disturbances**: include disturbances in glucose, calcium, magnesium, amino acids, or organic acids and pyridoxine dependency.
6. **Local anesthetic intoxication seizures** can result from neonatal intoxication with local anesthetics that are inadvertently administered into the infant's scalp.
7. **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, appear during the first 3 days of life.
8. **Genetic Syndromes** Seizure syndromes include **benign neonatal convulsions (fifth-day fits)**, start around the fifth day of life. Autosomal dominant **benign familial neonatal seizures** have an onset at 2-4 days of age.

TREATMENT

Treatment of the underlying etiology (e.g., HIE, hypoglycemia, hypocalcemia, meningitis, drug withdrawal, trauma) whenever one can be identified.

1. **Lorazepam** is often used in the acute treatment of neonatal seizure (0.1 mg/kg)

2. **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.

3. **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.

4. **Levetiracetam** (which can be given intravenously is commonly used as a second-or third-line agent. The maintenance dosages used are 40-60 mg/kg/day of levetiracetam, dosed 3 times daily. Topiramate, a possible third line agent, can be given at a dose of 5-10 mg/kg/day.

PROGNOSIS

The prognosis of neonatal seizures depends on the etiology and other organ system injury. Prematurity and high seizure burden have been shown to be associated with early death.

Patients with seizures secondary to severe hypoxic-ischemic encephalopathy have a 50% chance of typical development, whereas those with seizures caused by primary subarachnoid hemorrhage or hypocalcemia have a much better prognosis.

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 = 10-15 minutes, 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.

The incidence of SE ranges between 10 and 60 per 100,000 population in various studies. SE is most common in children younger than 5 years of age, with an incidence in this age-group of ∼100 per 100,000 children.

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

ETIOLOGY

- New-onset epilepsy of any type
- Drug intoxication (e.g., tricyclic antidepressants) in children
- Drug withdrawal or overdose in patients taking AEDs.
- Hypoglycemia; hypocalcemia; hyponatremia; hypomagnesemia.
- Acute head trauma.
- Encephalitis; meningitis; autoimmune encephalitis.
- Ischemic (arterial or venous) stroke.
- Intracranial hemorrhage.
- Vitamins dependency (b6, Folinic acid present in infants).
- Inborn errors of metabolism.

Management:

SE is a medical emergency that requires initial and continuous attention to securing the airway, breathing, and circulation (with continuous monitoring of vital signs including ECG) and determination and management of the underlying etiology (e.g., hypoglycemia).

Laboratory studies, including glucose, sodium, calcium, magnesium, complete blood count, basic metabolic panel, CT scan, and continuous EEG, are needed for all patients.

Blood and spinal fluid cultures, toxic drug screens, and tests for inborn errors of metabolism are often needed. AED levels need to be determined in all patients known already to be taking these drugs.

Neuroimaging must be considered after the child has been stabilized, especially if it is indicated by the clinical manifestations, by an asymmetric or focal nature of the EEG abnormalities, or by lack of knowledge of the underlying etiology.

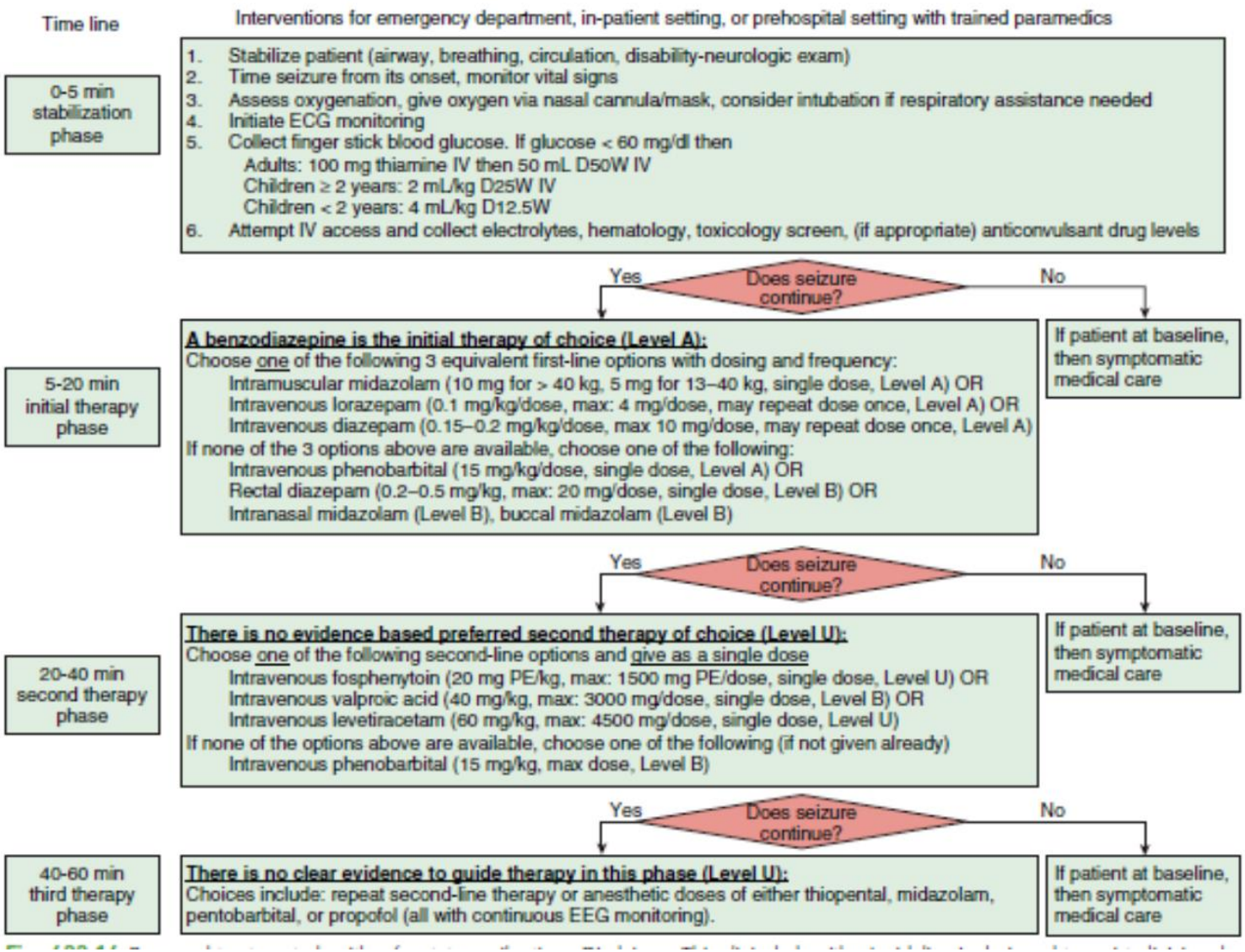
MEDICATIONS FOR SE

1. The initial emergent therapy should be started for convulsive seizures lasting longer than 5 minutes involves the use of a benzodiazepine medication {intravenous lorazepam as a first-line agent and, if the patient does not have intravenous access, using intramuscular midazolam, buccal or intranasal midazolam, intranasal lorazepam, or rectal diazepam}.
2. If seizures persist 5 minutes after the initial benzodiazepine dose, a second dose of the drug should be given. Additionally, in some infants, a trial of pyridoxine may be warranted.
3. If the emergency therapy with a benzodiazepine is unsuccessful (persistent seizures 5 minutes after the second benzodiazepine dose), fosphenytoin, valproate, or levetiracetam is the recommended option for urgent therapy.

- Fosphenytoin is given at a loading dose of 20 mg/kg, and a maintenance dose can be started 6 hours after the initial bolus.
- Valproate is given at a loading dose of 40 mg/kg, but its use should be avoided in patients younger than 2 years of age and in those with hepatic dysfunction or mitochondrial disease.
- Levetiracetam is given at loading doses of 60 mg/kg.
- If valproate, fosphenytoin, or levetiracetam is not available, Intravenous phenobarbital is an alternative option but is not recommended as a first-line urgent therapy because of its side effects. ((The phenobarbital dose used in neonates is usually 20 mg/kg as a loading dose))

4. If seizures persist, a decision must be made regarding re-dosing with another second-line agent or proceeding to a continuous infusion and intubation in a patient who has already had convulsive seizures for more than 30-60 minutes.

After the second or third medication is given, and sometimes before that, the patient might need to be intubated. All patients with SE, even the ones who respond, need to be admitted to the intensive care unit for completion of therapy and monitoring.


Time line
Interventions for emergency department, in-patient setting, or prehospital setting with trained paramedics
0-5 min stabilization phase
1. Stabilize patient (airway, breathing, circulation, disability-neurologic exam)
2. Time seizure from its onset, monitor vital signs
3. Assess oxygenation, give oxygen via nasal cannula/mask, consider intubation if respiratory assistance needed
4. Initiate ECG monitoring
5. Collect finger stick blood glucose. If glucose < 60 mg/dl then
Adults: 100 mg thiamine IV then 50 mL D50W IV
Children ≥ 2 years: 2 mL/kg D25W IV
Children < 2 years: 4 mL/kg D12.5W
6. Attempt IV access and collect electrolytes, hematology, toxicology screen, (if appropriate) anticonvulsant drug levels
Yes
Does seizure continue?
No
If patient at baseline, then symptomatic medical care
5-20 min initial therapy phase
A benzodiazepine is the initial therapy of choice (Level A):
Choose one of the following 3 equivalent first-line options with dosing and frequency:
Intramuscular midazolam (10 mg for > 40 kg, 5 mg for 13–40 kg, single dose, Level A) OR
Intravenous lorazepam (0.1 mg/kg/dose, max: 4 mg/dose, may repeat dose once, Level A) OR
Intravenous diazepam (0.15–0.2 mg/kg/dose, max 10 mg/dose, may repeat dose once, Level A)
If none of the 3 options above are available, choose one of the following:
Intravenous phenobarbital (15 mg/kg/dose, single dose, Level A) OR
Rectal diazepam (0.2–0.5 mg/kg, max: 20 mg/dose, single dose, Level B) OR
Intranasal midazolam (Level B), buccal midazolam (Level B)
Yes
Does seizure continue?
No
If patient at baseline, then symptomatic medical care
20-40 min second therapy phase
There is no evidence based preferred second therapy of choice (Level U):
Choose one of the following second-line options and give as a single dose
Intravenous fosphenytoin (20 mg PE/kg, max: 1500 mg PE/dose, single dose, Level U) OR
Intravenous valproic acid (40 mg/kg, max: 3000 mg/dose, single dose, Level B) OR
Intravenous levetiracetam (60 mg/kg, max: 4500 mg/dose, single dose, Level U)
If none of the options above are available, choose one of the following (if not given already)
Intravenous phenobarbital (15 mg/kg, max dose, Level B)
Yes
Does seizure continue?
No
If patient at baseline, then symptomatic medical care
40-60 min third therapy phase
There is no clear evidence to guide therapy in this phase (Level U):
Choices include: repeat second-line therapy or anesthetic doses of either thiopental, midazolam, pentobarbital, or propofol (all with continuous EEG monitoring).