



Neonatal Seizures

Neonatal seizures are defined as involuntary alterations in neurologic function, including motor behaviors, and can include autonomic functions such as heart rate, respiratory rate, and blood pressure. Neonatal seizures are age specific and occur in term infants less than 28 days of life and preterm infants less than 44 weeks adjusted age. Due to both relative excitability in the neonatal brain and the risk for brain injury in the perinatal period, the threat for seizures is highest in the first year of life, with the first 1 to 2 days being the most vulnerable time.

The incidence of neonatal seizures is difficult to determine and is related to gestational age and birth weight, but is estimated to occur in one to two of every 1,000 term infants, 57.5 of 1,000 infants less than 1,500 g, and 2.8 of 1,000 infants weighing 2,500 to 3,999 g (Crowell, 2017; Parsons, Seay, & Jacobson, 2016). Seizures are one of the most frequent—and sometimes the only—signs of neurological dysfunction and can signify an underlying brain injury or anomaly. Neonatal seizures require urgent diagnosis and management and are considered a neurological emergency.

Etiology

Determination of the etiology is crucial. Not only does it guide treatment strategies, but it is a determining factor of prognosis. Determining etiology can be a challenge for care providers. A detailed prenatal, perinatal, and family history can be helpful in narrowing down the differential diagnosis. Hypoxic ischemic encephalopathy (HIE) remains the most common etiology of neonatal seizures in the first 48 hours of life and accounts for approximately 80% of all neonatal seizures. Seizures caused by HIE are usually transient, and although they may be initially difficult to control, pharmacological therapy is usually short term.

Bacterial or viral exposure should be considered in all neonates with seizures. Meningitis is a common cause of neonatal seizures within the first few days of

life, with infections most commonly caused by *Group B Streptococcus* (GBS) and *Escherichia coli*. Other congenital infections include herpes simplex virus (HSV) type 2, rubella, toxoplasmosis and congenital cytomegalovirus (CMV). Congenital viral exposures caused by Zika, enteroviruses, and parvoviruses also should be considered.

Central nervous system malformations, trauma and cerebrovascular lesions (intraventricular, intracranial, or periventricular hemorrhages) are commonly associated with seizures and should be diagnosed by imaging studies.

Acute metabolic disorders such as hypoglycemia, hypocalcemia, hyponatremia, and hypernatremia constitute a large portion of neonatal seizures, and these indices should be part of the initial workup after seizures present. Although rare, persistent metabolic disorders or inborn errors of metabolism such as urea cycle defects, organic acidurias, and aminoacidopathies can cause seizures in the neonatal period.

An uncommon cause of neonatal seizures is drug withdrawal in infants born to mothers with barbiturates, alcohol, heroin, cocaine, or opiate/methadone abuse. Infants of mothers who were on selective serotonin reuptake inhibitors during pregnancy may exhibit tremors and jitteriness that can be mistaken for seizures. The infant can present with withdrawal symptoms in addition to seizures possibly occurring as long as 4–6 weeks after birth. Seizures caused by maternal drug use can occur due to substance withdrawal or may be associated with utero-placental insufficiency due to chronic substance abuse and poor health maintenance.

Genetic causes of seizures are rare and include epileptic encephalopathy and benign familial neonatal convulsions. These should be considered when other diagnoses have been ruled out or a concerning family history is present.



Clinical Presentation and Classification

Due to central nervous system immaturity and incomplete myelination patterns in the brain, neonatal seizures have characteristics that are unlike seizures in other age groups. Neonates may have minimal seizure expression, and only 10% of suspected seizures have ictal electroencephalography (EEG) activity. Subclinical seizures, or seizures identified by EEG without any motor or behavioral activity, are common in the neonatal period. Seizure-like clinical activity not associated with changes in EEG may be caused by excessive neuronal activity or generated from subcortical brain structures and are considered a type of primitive reflex. EEG is not only useful in identification of seizures, but it also can evaluate background brain activity, which is an important prognostic factor.

Management and Treatment

The dissociation between clinical and electrographic seizures makes monitoring and treating neonatal seizures a challenge. Neonatal seizures require immediate evaluation and treatment to prevent or reduce brain injury. In 2011, the World Health Organization (WHO) set treatment guidelines and recommendations for neonates with seizures. Management and treatment begins with recognizing seizures, ensuring ventilation and perfusion stability, monitoring neurological status, ruling out electrolyte abnormalities, and providing education and support to the family. Any electrolyte abnormalities should be corrected prior to starting antiepileptic medications.

Phenobarbital (see *Phenobarbital* in Diagnoses) is the first-line antiepileptic drug of choice. A common side effect of phenobarbital is sleepiness. If seizures are not controlled after the maximum dose, a benzodiazepine (Valium, Ativan), phenytoin (Dilantin), or Keppra (see *Keppra* in Step 9) can be used as a second-line treatment. Pharmacological treatment and duration of treatment remain a topic of discussion and debate due to the lack of data for long-term use in the neonatal and early infancy population.

Outcomes

Early recognition and prompt intervention may protect the brain and improve outcomes. Infants with a history

of neonatal seizures are at increased risk for adverse neurological outcomes such as cerebral palsy, epilepsy, behavior problems, and abnormal cognitive development. The etiology for neonatal seizures has the best predictive value for estimating outcomes. Neonatal seizures caused by HIE, meningitis, structural anomalies, and intracranial hemorrhages have more severe outcomes. Outcomes are also related to prematurity and birth weight. Fifty percent of neonates with seizures will have long-term neurological complications. Neonatal neurological exams are a good predictor of outcomes as is the severity of EEG abnormalities, such as burst suppression and severe low voltage and multifocal abnormal discharges. Infant with neonatal seizures should be followed at a high-risk clinic to monitor development and achievement of milestones.

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Neonatal Seizures: Information for Parents

The brain is made up of millions of nerve cells, all connected together, that create and receive signals. These signals control many functions of our body. A seizure can occur when there is a disruption in the communication between brain nerve cells, which alters the signals or causes them to not fire as they should.

Neonatal seizures are seizures in a baby who is less than 28 days old or in a preterm baby who is less than 44 weeks adjusted age. Neonatal seizures are different from seizures in older children and adults. Babies are at higher risk for having seizures because their brain is immature and still developing. Neonatal seizures can be caused by many different things, and just because your baby has seizures now does not mean that your baby will have seizures later in life.

Some causes of seizures in your baby include

- a decrease or lack in oxygen or blood flow to your baby's brain before or during birth
- an infection caused by certain bacteria or viruses, before or after birth, that can cause meningitis or encephalitis
- bleeding in or around the brain
- brain structure abnormalities
- abnormal metabolic or electrolyte levels, including low blood sugar, low calcium, and low or high sodium
- problems in the body's chemistry or metabolism
- family history of seizures or "fits"
- drug withdrawal, which may be seen in infants born to mothers using barbiturates, alcohol, heroin, cocaine, methadone, painkillers, or other substances.

Neonatal seizures do not usually last long and it may be hard to tell if your baby is actually having a seizure. Seizures in a newborn can include any of the following behaviors:

- change in facial movements (repeated movements of the eyes, lips or tongue)
- movements of the arms or legs that look like riding or pedaling a bike

- staring
- stopping breathing
- rhythmic jerking
- stiffening or tightening of arms or legs
- quick jerks involving legs, arms, or the whole body.

Newborn babies can have a variety of different movements that might look like seizures but are not. Some examples are simple things, like sucking and stretching, or jitteriness when they are crying or disturbed. The jitteriness should diminish over the first few weeks after birth and should be less frequent when the baby is quiet and awake. Other babies have single jerks of their arms or legs during sleep. This is called *benign neonatal sleep myoclonus* and should stop when the baby wakes up. Both of these examples are not concerning and do not need any treatment.

So how do you recognize seizures in your baby? Look for movements that the baby repeats over and over and are not provoked, or if your baby seems to be staring or not present during these movements. Many times these movements will occur in clusters for a short period of time. If you are unsure, try to video the movements to show your healthcare provider.

If seizures are suspected, it is important to monitor your baby's brain waves and function of the nerve cells using an electroencephalogram (EEG). An EEG can show how the brain cells are talking to each other and if there is a problem. Wires and gentle "paste" are used to hold electrodes to the baby's skin. It is not a painful procedure.

These electrodes then send wavy lines to a machine to graph the impulses, and the graphs tell the providers if something is abnormal and if there are seizures occurring. During an EEG recording, you may notice many different waves and changes on the screen—these do not always represent abnormal brain activity. Some changes may result from movement of the head or stimulation. Heart



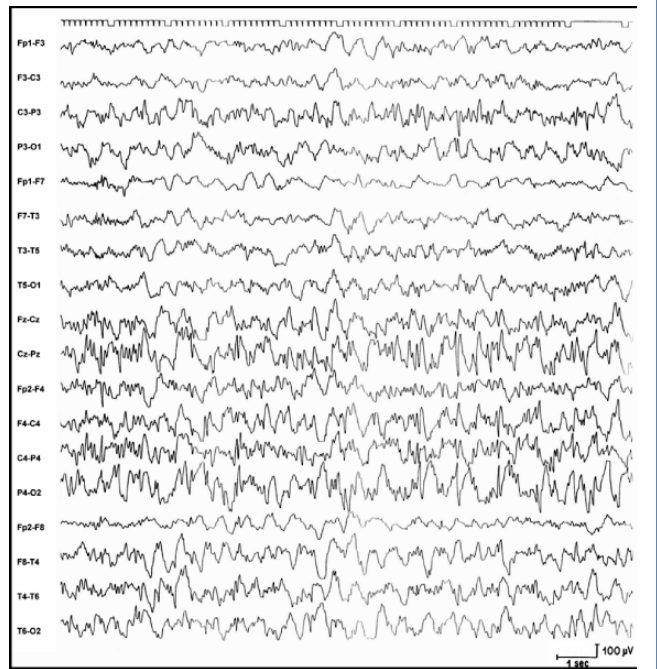
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rate and oxygen level changes will be monitored, as these may be associated with seizures.

If your baby is having seizures, it may be necessary to do other tests such as blood work, magnetic resonance imaging (MRI), or computed tomography (CT) scan to determine the cause of the seizures.

There is evidence that seizures may affect the brain function and development, so it is important to identify and control the seizures. Your baby's healthcare team will look for the cause of the seizures and treat them as needed. The healthcare team will first try to correct any abnormalities of blood sugar or electrolytes (other normal substances in our body). If the seizures continue, your baby may need an antiepileptic drug (a drug to treat and stop the seizures).

Phenobarbital is the first drug of choice to treat neonatal seizures. Sleepiness is one of the major side effects and may be observed, especially in the first days of treatment. If the seizures are not controlled with this medication, there are others that can be added. Often, newborns that have seizures only need medication for a



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short time. Many times, the medication is stopped before going home. If your baby still needs medication at home, your baby will need to be monitored by a neurologist (pediatrician who specializes in the brain and spinal cord) as an outpatient.

If your baby is diagnosed with neonatal seizures, the outcome may be different depending on the cause of the seizures. Talk to your baby's healthcare providers to find out what the future effects will be for your baby. If your baby's seizures are caused by an underlying brain injury or abnormality, his or her long-term outcome may be more serious. It is important to provide the healthcare team with as much information as possible regarding family history (especially of seizures or "fits"), birth history, and prenatal history. This may help the healthcare team identify a cause for the seizures and give more information to guide treatment and improve outcome expectations.