Neonatal Seizures

Neonates are at particular risk for the development of seizures because metabolic, toxic, structural, and infectious diseases are more likely to be manifested during this time than at any other period of life. Neonatal seizures are dissimilar from those in a child or adult because generalized tonic-clonic convulsions tend not to occur in the 1st mo of life. The arborization of axons and dendritic processes as well as myelination is incomplete in the neonatal brain. A seizure discharge, therefore, cannot readily be propagated throughout the neonatal brain to produce a generalized seizure.

CLINICAL MANIFESTATIONS AND CLASSIFICATION.

Focal seizures consist of rhythmic twitching of muscle groups, particularly those of the extremities and face. These seizures are often associated with localized structural lesions as well as with infections and subarachnoid hemorrhage. Multifocal clonic convulsions are similar to focal clonic seizures but differ in that many muscle groups are involved, frequently several simultaneously. Tonic seizures are characterized by rigid posturing of the extremities and trunk and are sometimes associated with fixed deviation of the eyes. Myoclonic seizures are brief focal or generalized jerks of the extremities or body that tend to involve distal muscle groups. Subtle seizures consist of chewing motions, excessive salivation, and alterations in the respiratory rate including apnea, blinking, nystagmus, bicycling or pedaling movements, and changes in color.

Neonatal seizures may be difficult to recognize clinically, and some neonatal behaviors that were previously considered to be convulsions are not substantiated by the EEG recording. Nonetheless, several clinical features distinguish seizures from nonepileptic activity in neonates. Autonomic changes such as tachycardia and elevation of the blood pressure are common with seizures but do not occur with nonepileptic events. Nonepileptic movements are suppressed by gentle restraint, but true seizures are not. Nonepileptic phenomena are enhanced by sensory stimuli that have no influence on seizures. Correct classification of neonatal seizures is important for appropriate selection of anticonvulsant therapy. Studies using polygraphic EEG recording with video monitoring have greatly enhanced the characterization of neonatal seizures and their medical management.

TABLE 593-6 -- Paroxysmal Disorders of the Neonatal Period

PAROXYSMAL NONEPILEPTIFORM DISORDERS
Jitteriness
Benign neonatal sleep myoclonus
ACUTE SYMPTOMATIC SEIZURES AND OCCASIONAL SEIZURES[*]
Hypoxic-ischemic encephalopathy
Intraventricular hemorrhage
Acute metabolic disorders[†]

Sepsis-meningitis
EPILEPTIC SYNDROMES
Benign idiopathic neonatal convulsions
Familial
Nonfamilial
Symptomatic focal epilepsy
Brain tumor
Malformations of cortical development
Inherited metabolic disease; mitochondrial disorders
Early-onset generalized epileptic syndromes with encephalopathy
Early myoclonic encephalopathy
Early infantile encephalopathic epilepsy

EEG CLASSIFICATION OF NEONATAL SEIZURES

CLINICAL SEIZURE WITH A CONSISTENT EEG EVENT.

In this category, a clinical seizure occurs in relationship to seizure activity recorded on the EEG and includes focal clonic, focal tonic, and some myoclonic seizures. These seizures are clearly epileptic and are likely to respond to an anticonvulsant.

CLINICAL SEIZURES WITH INCONSISTENT EEG EVENTS.

Neonates may have a clinical seizure without a corresponding seizure discharge. This is observed with all generalized tonic seizures and subtle seizures and with some myoclonic seizures. These infants tend to be neurologically depressed or comatose as a result of hypoxic-ischemic encephalopathy. Seizures in this category are likely to be of nonepileptic origin and may not require or respond to antiepileptics.

ELECTRICAL SEIZURES WITH ABSENT CLINICAL SEIZURES.

Electrical seizures associated with a markedly abnormal background EEG may develop in comatose infants who are not on anticonvulsants. Conversely, electrical seizures may persist in patients with focal tonic or clonic seizures without clinical signs after the introduction of an anticonvulsant.

ETIOLOGIC DIAGNOSIS.

Many additional disorders are likely to cause seizures, including metabolic, infectious, traumatic, structural, hemorrhagic, embolic, and maternal disturbances. Because seizures in neonates may indicate a serious, life-threatening, and potentially reversible disease, it is imperative that a timely and organized approach to the investigation of neonatal seizures be carried out.

TABLE 593-7 -- Causes of Neonatal Seizures

AGES 1–4 DAYS
Hypoxic-ischemic encephalopathy
Drug withdrawal, maternal drug use of narcotic or barbiturates
Drug toxicity: lidocaine, penicillin
Intraventricular hemorrhage
Acute metabolic disorders
Hypocalcemia
Perinatal asphyxia, small for gestational age
Sepsis
Maternal diabetes, hyperthyroidism, or hypoparathyroidism
Hypoglycemia
Perinatal insults, prematurity, small for gestational age
Maternal diabetes
Hyperinsulinemic hypoglycemia
Sepsis
Hypomagnesemia
Hyponatremia or hypernatremia
Iatrogenic or inappropriate antidiuretic hormone secretion
Inborn errors of metabolism
Galactosemia
Hyperglycinemia
Urea cycle disorders
Pyridoxine deficiency (must be considered at any age)
AGES 4–14 DAYS
Infection
Meningitis (bacterial), encephalitis (enteroviral, herpes simplex)
Metabolic disorders
Hypocalcemia
Diet, milk formula
Hypoglycemia, persistent
Inherited disorders of metabolism: galactosemia, fructosemia, leucine sensitivity
Hyperinsulinemic hypoglycemia

Anterior pituitary hypoplasia, pancreatic islet cell tumor
Beckwith syndrome
Drug withdrawal, maternal drug use of narcotic or barbiturates
Benign neonatal convulsions, familial and nonfamilial
Kernicterus, hyperbilirubinemia
AGES 2–8 WEEKS
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

Careful neurologic examination of the infant may uncover the cause of the seizure disorder. Examination of the retina may show the presence of chorioretinitis, suggesting a congenital infection in which case to xoplasmosis, rubella, cytomegalovirus, and herpes simplex (TORCH) titers of mother and infant are indicated. Blood should be obtained for determinations of glucose, calcium, magnesium, electrolytes, and blood urea nitrogen. If hypoglycemia is a possibility, a serum Dextrostix testing is indicated so that treatment can be initiated immediately. for a discussion of the diagnosis and treatment of hypoglycemia. Hypocalcemia may occur in isolation or in association with hypomagnesemia. A lowered serum calcium level is often associated with birth trauma or a CNS insult in the perinatal period. Serum electrolyte measurement may indicate significant hyponatremia (serum sodium <135 mEq/L) or hyponatremia (serum sodium >150 mEq/L) as a cause of the seizure disorder.

A lumbar puncture is indicated in virtually all neonates with seizures, unless the cause is obviously related to a metabolic disorder such as hypoglycemia or hypocalcemia secondary to feeding of high concentrations of phosphate. These latter infants are normally alert interictally and usually respond promptly to appropriate therapy.

Many inborn errors of metabolism cause generalized convulsions in the newborn period. The treatment consists of supportive measures and promotion of urine output

by administering intravenous fluids with appropriate monitoring to prevent fluid overload.

Benign familial neonatal seizures, an autosomal dominant condition, begins on the 2nd–3rd day of life, with a seizure frequency of 10-20/day. Patients are normal between seizures, which stop in 1–6 mo. Fifth-day fits occur on day 5 of life (4–6 days) in normal-appearing neonates. The seizures are multifocal and are present for less than 24 hr. The diagnosis requires exclusion of other causes of seizures. The prognosis is good. Pyridoxine dependency, a rare disorder, must be considered when generalized clonic seizures begin shortly after birth with signs of fetal distress in utero. These seizures are particularly resistant to conventional anticonvulsants, such as phenobarbital or phenytoin. The history may suggest that similar seizures occurred in utero. Some cases of pyridoxine dependency are reported to begin later in infancy or in early childhood. This condition is inherited as an autosomal recessive. The seizures abruptly cease, and the EEG normalizes in the next few hours. Not all cases of pyridoxine dependency respond dramatically to the initial bolus of IV pyridoxine. Therefore, a 6 wk trial of oral pyridoxine (10–20 mg/day) or pyridoxal phosphate is recommended for infants in whom a high index of suspicion continues after a negative response to IV pyridoxine. In the future, measurement of CSF and plasma pyridoxal-5- phosphate may prove to be the more precise method of confirming the diagnosis of pyridoxine dependency. These children require lifelong supplementation of oral pyridoxine, 10 mg/day

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. Indeed, many recommend imaging of all neonates with seizures unexplained by serum glucose, calcium, or electrolyte disorders. Infants with chromosome abnormalities and adrenoleukodystrophy are also at risk for seizures and should be evaluated with investigation of a karyotype and serum long-chain fatty acids, respectively.

TREATMENT.

Anticonvulsants should be used in the treatment of infants with seizures secondary to hypoxic-ischemic encephalopathy or an acute intracranial. Phenytoin and phenobarbital are equally but incompletely effective as anticonvulsants in neonates, controlling seizures in less than half of cases. The greater use of EEG recording in infants with subtle seizures has identified a number of patients with abnormal movements unrelated to seizure discharges.

PROGNOSIS.

This depends mainly on the primary cause of the disorder or the severity of the insult. In the case of hypoglycemic infants of a diabetic mother or hypocalcemia associated with excessive phosphate feedings, the prognosis is excellent. Conversely, a child with intractable seizures due to severe hypoxic-ischemic encephalopathy or a cytoarchitectural abnormality of the brain usually does not respond to anticonvulsants and is susceptible to status epilepticus and early death. The challenge for the physician is to identify patients who will recover with prompt treatment and to avoid delays in diagnosis that could lead to severe, irreversible neurologic damage