NEONATAL SEIZURES

Seizures are the most frequent manifestation of neonatal neurological diseases. It is important to recognize seizures, determine their aetiology and treat them because:

1. the seizures may be related to significant diseases that require specific treatment
2. the seizures may interfere with supportive measures e.g. feeding and assisted respiration for associated disorders
3. the seizures per se may lead to brain injury.

Table 1. Classification of neonatal seizures

Clinical seizure	EEG seizures	Manifestation
Subtle	common	*ocular phenomena* - tonic horizontal deviation of eyes common in term infants - sustained eye opening with fixation common in preterm infants - blinking
		oral-buccal-lingual movements - chewing common in preterm infants - lip smacking, cry-grimace
		limb movements - pedaling, stepping, rotary arm movements
		apnoeic spells common in term infants
Clonic		
Focal	common	well localized clonic jerking, infant usually not unconscious
Multifocal	common	multifocal clonic movements; simultaneous or in sequence or non-ordered (non-Jacksonian) migration
Tonic		
Focal	common	sustained posturing of a limb, asymmetrical posturing of trunk or neck
Generalized	uncommon	tonic extension of upper and lower limbs (mimic decerebrate posturing) tonic flexion of upper limbs and extension of lower limbs(mimic decorticate posturing) those with EEG correlates; autonomic phenomena e.g. increased blood pressure are prominent features.
Myoclonic Focal, Multifocal	common	well localized, single or multiple, migrating jerks usually of limbs
Generalized		single or several bilateral synchronous jerks or flexion movement occurring more in upper than lower limbs.

Aetiology

- *Hypoxic ischaemic encephalopathy*
  - usually secondary to perinatal asphyxia.
  - most common cause of neonatal seizures (preterm and term)
  - seizures occur in the first day of life (DOL)
  - presents with subtle seizures; multifocal clonic or focal clonic seizures
  - if focal clonic seizures may indicate associated focal cerebral infarction

Table 2. Major aetiology in relation to time of seizure onset and relative frequency

Etiology	Time of onset [1]		Relative frequency [2]	
	0-3 days	> 3days	Premature	Full term
Hypoxic –ischemic encephalopathy	+		+++	+++
Intracranial hemorrhage	+	+	++	+
Intracranial infections	+	+	++	++
Developmental defects	+	+	++	++
Hypoglycaemia	+		+	+
Hypocalcaemia	+	+	+	+
Other metabolic disturbances & IEM	+			+
Epileptic Syndromes	+	+		+

footnote: 1. postnatal age
2. relative frequency of seizures among all etiologies:
+++ most common, ++ less common, +least common
Abbreviations. IEM, inborn errors of metabolism

- *Intracranial hemorrhage (ICH)*
  - principally germinal matrix-intraventricular (GM-IVH), often with periventricular haemorrhagic (PVH) infarction in the premature infant
  - in term infants ICH are principally (may occur with HIE) and subdural(associated with a trauma , presenting with focal seizures in the first 2 DOL)
- *Intracranial Infection*
  - common organisms are group *B streptococci, E. coli., toxoplasmosis, herpes simplex, coxsackie B, rubella* and *cytomegalovirus*
- *Malformations of cortical development*
  - neuronal migration disorder resulting in cerebral cortical dysgenesis e.g. lissencephaly, pachygyria and polymicrogyria
- *Metabolic disorder*
  - *hypoglycemia* common in SGA infants and infants of diabetic mothers (IDM) (see protocol on *Neonatal Hypoglycemia*
  - *hypocalcaemia* has 2 major peaks of incidences:
    - first 2 to 3 DOL, in low birth weight infants, IDM and history of perinatal asphyxia.
    - later-onset of hypocalcaemia associated with endocrinopathy (maternal hypoparathyroidism, neonatal hypoparathyroidism) and heart disease (with or without Di George Syndrome), rarely with nutritional type (cow's milk, high phosphorus synthetic milk). Hypomagnesemia is a frequent accompaniment.
  - inborn errors of metabolism: represent <1% of all neonates who have seizures but among neonates with intractable neonatal seizure, ~30% are due to IEM

Table 3. Inborn errors of metabolism presenting with neonatal seizures

Treatable	Non-treatable
Pyridoxine-dependent epilepsy	Nonketotic hyperglycinemia (poor outcome though seizure may be better controlled with dextromethorphan)
Pyridoxal phosphate responsive epilepsy	Sulphite oxidase deficiency/ Molybdenum cofactor deficiency
Folinic acid-responsive seizures	Mitochondrial disorders
Biotinidase deficiency	Peroxisomal disorder
Glucose transporter 1 deficiency	Neuronal ceroid lipofuscinoses
Serine deficiency syndromes	Adenylosuccinate lyase deficiency (purine disorder)
Creatine deficiency syndromes	
Phenylketonuria	

Seizures versus Jitteriness and Other Non-epileptic Movements

Some movements e.g. jitteriness and other normal movement during sleep (Myoclonic jerks or generalized myoclonic jerks as infant wakes from sleep) or when awake/ drowsy (roving sometimes dysconjugate eye movements, sucking not accompanied by ocular fixation or deviation) in newborn may be mistaken for seizures.

Table 3. Differentiating seizures form non-epilpetic events, e.g. jitteriness

Clinical Features	Jitteriness	Seizure
Abnormality of gaze or eye movement	0	+
Movements exquisitely stimulus sensitive	+	0
Predominant movement	tremors[1]	clonic, jerking[2]
Movements cease with passive flexion of affected limb	+	0
Autonomic changes (tachycardia, ↑ BP, apnoea, salivation, cutaneous vasomotor phenomena)	0	+

footnote: 1. alternating movements are rhythmical and of equal rate and amplitude
2. clonic, jerking – movements with a fast and slow component

Management

- consensus is lacking on necessity for treatment of minimal or absent clinical manifestations.
- treatment with anticonvulsant is to prevent potential adverse effects on ventilatory function, circulation and cerebral metabolism (threat of brain injury)
- controversy regarding identification of adequacy of treatment, elimination of clinical seizures or electrophysiology seizures. Generally majority attempt to eliminate all or nearly all clinical seizures.

Duration of Anticonvulsant Therapy - Guidelines

Duration of therapy depends on the probability of recurrence of seizures if the drugs are discontinued and the risk of subsequent epilepsy. This can be determined by considering the neonatal neurological examination, cause of the seizure and the EEG.

Neonatal Period

- if neonatal neurological examination becomes normal, discontinue therapy
- if neonatal neurological examination is persistently abnormal,
  - consider etiology and obtain electroencephalogram(EEG)
  - in most cases – continue phenobarbitone, discontinue phenytoin
  - and reevaluate in a month

One Month after Discharge

- if neurological examination has become normal, discontinue phenobarbitone over 2 weeks
- if neurological examination is persistently abnormal, obtain EEG
- if no seizure activity or not overtly paroxysmal on EEG, discontinue phenobarbitone over 2 weeks
- if seizure activity is overtly paroxysmal continue phenobarbitone until 3 months of age and reassess in the same manner

Figure 1. Approach to neonatal seizures

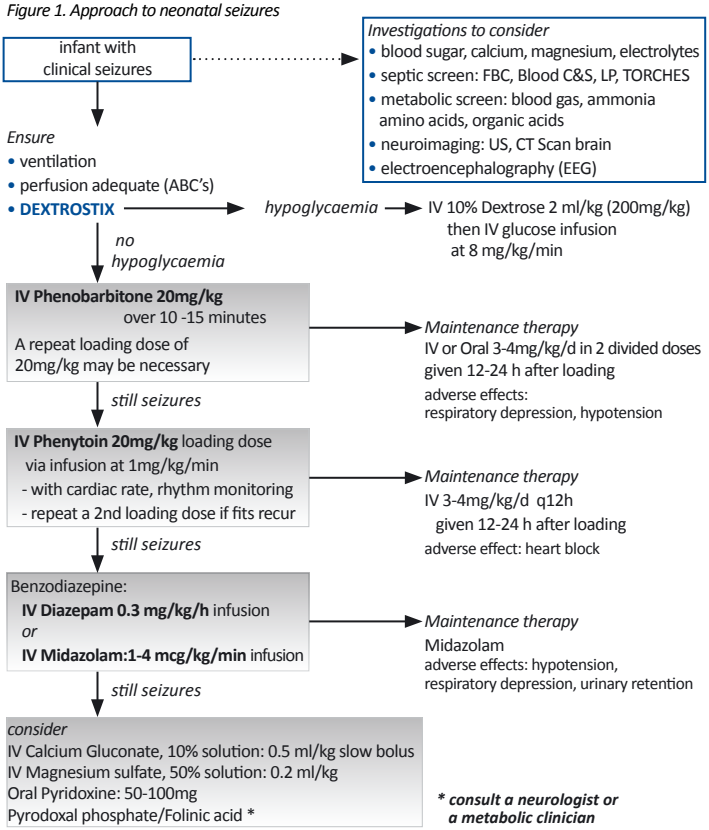

Table 4. Prognosis according to aetiology of neonatal seizures

Neurological Disorder	Normal Development (%)[1]
Hypoxic Ischemic Encephalopathy	50
Severe Intraventricular Haemorrhage with PVH infarction	10
Hypocalcaemia	
Early onset (depends on the prognosis of complicating illness, if no neurological illness present prognosis approaches later onset)	50
Later onset (nutritional type)	100
Hypoglycemia	50
Bacterial Meningitis	50
Developmental defect	0

footnote. 1. Prognosis is based on those cases with the stated neurological disease when seizures are a manifestation. This will differ from overall prognosis of the disease.