

Hypoxic Ischemic Encephalopathy in Newborns

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Epidemiology

- In U.S., severe HIE is rare
- 2-4 cases / 1000 live births
- Mortality up to 50% in severe HIE
- 15-20% mortality overall
- Up to 80% of surviving infants with severe HIE develop serious complications; 10-20% develop moderately serious disabilities
- 25% of survivors have permanent neuropsychologic deficits

Asphyxia

- Criteria per AAP and ACOG
 - Profound metabolic or mixed acidemia (pH < 7.0) in cord blood
 - Persistence Apgar score of 0-3 for > 5 minutes
 - Neurologic sequelae (seizures, coma, hypotonia)

Grading of HIE Severity

Mild HIE	Moderately Severe HIE	Severe HIE
<ul style="list-style-type: none"> ■ Slightly increased tone and brisk DTRs in first few days ■ Transient behavioral abnormalities (crying, irritability, sleepiness) ■ Normal CNS exam by 3-4 days of life 	<ul style="list-style-type: none"> ■ Lethargic, hypotonic and diminished DTRs ■ Sluggish or absent brainstem reflexes ■ Apnea ■ Seizures usually within first 24 hrs ■ Fully recovery within 1-2 weeks associated with better long term outcome 	<ul style="list-style-type: none"> ■ Stupor or coma with diminished responsiveness to stimuli ■ May require ventilatory support ■ Hypotonic and depressed DTRs ■ Abnormal cranial nerve exam ■ Seizures which occur early and often initially resistant to treatment ■ Autonomic irregularities

Sarnat & Sarnat Clinical Staging of Perinatal Hypoxic Ischemic Brain Injury (1976)

	Stage 1	Stage 2	Stage 3
Mental State	Hyperalert	Lethargic or obtunded	Stuporous
Cranial nerves	Weak suck	Weak or absent	Absent
Motor	Normal	Mild hypotonia Cortical thumbing	Severe hypotonia
Reflexes	Mildly brisk	Brisk	Suppression
Primitive Reflexes	Normal	Suppressed	Suppression
Autonomic Reflexes	Sympathetic activation	Parasympathetic activation	Both systems suppressed
Seizures	None	Common	Uncommon
EEG	Normal	First day low voltage then bursting pattern and multifocal electrographic sz	Deep, periodic EEG with burst pattern
Duration	Less than 24hrs	2-14 days	Hours to weeks
Prognosis	Less than 24 hrs No sequelae	Good prognosis if recovery within 5 days	Microcephaly, MR, CP, seizures

Labs & Studies

- Serum electrolytes
- Imaging
 - Head ultrasounds
 - CT scans of head with/without contrast
 - MRI of brain with DWI
- Electrophysiology
 - EEG
 - SSEPs and/or VEPs
- Metabolic studies

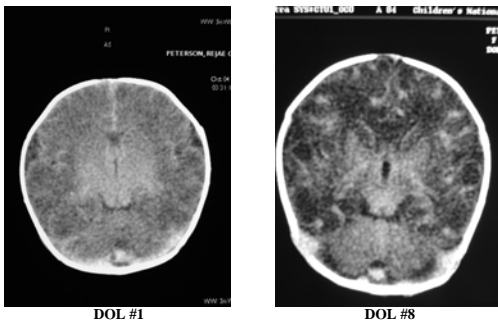
Histologic Findings

- Selective neuronal necrosis
 - Most common
 - Status marmoratus (delayed, lesions in basal ganglia)
- Parasagittal cerebral necrosis (bilateral)
- Focal and multi-focal ischemic brain necrosis (MCA territory most common)
- Periventricular leukomalacia
 - Preterm infants

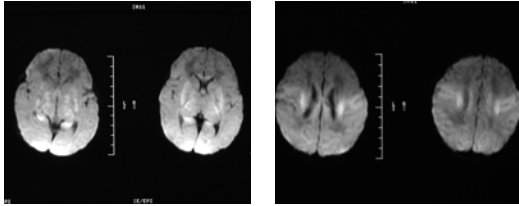
EEG



Neuroimaging

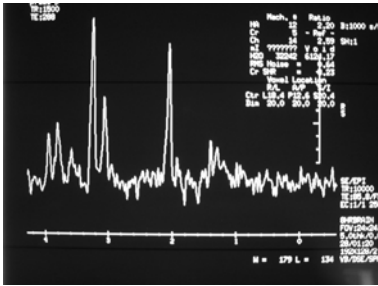


Neuroimaging



1 week old

Neuroimaging



Treatment

- Support care
 - Ventilation, perfusion, metabolic status
- Cerebral edema
- Treatment of seizures
 - Phenobarbital, fosphenytoin, lorazepam
- Neuroprotection
 - Allopurinol, high-dose PB, NMDA antagonists (MK801), hypothermia

Seizure Treatment

- Phenobarbital
 - Loading: 20 mg/kg IV (may need multiple)
 - Dosage: 4-6 mg/kg/d divided q12hrs
 - Levels
 - 10-30 µg/mL → 40% seizure free
 - 40 µg/mL → 70% seizure free
 - 100 µg/mL → 77% seizure free
 - Addition of 2nd AED → 88% seizure free
- Fosphenytoin
 - Loading: 20 mg/kg P.E. IV (usually multiple loads)
 - Dosage: 7-12 mg/kg/d divided q8hrs
- Lorazepam 0.05-0.1 mg/kg/dose

Neuroprotection Therapies Under Investigation

- Oxygen-free radical inhibitors
 - Superoxide dismutase, endoperoxidase, catalase, allopurinol, indomethacin
- Endogenous scavengers
 - Cholesterol, vitamin E, ascorbic acid, glutathione, 21-amino steroids
- Excitatory Amino Acid Antagonists (NMDA or AMPA/QA antagonists)
 - MK801, ketamine, dextromethorphan, phencyclidine, NBQX
- Calcium channel blockers
- Growth Factors
- Phenobarbital
- Hypothermia (systemic or focal cooling)

Biochemical Indicators of Moderate or Severe HIE

	PPV (%)	NPV (%)	Sens (%)	Spec (%)
S-100 & CK-BB	83	91	71	95
CK-BB and cord pH	71	91	71	91
CK-BB and cord BD	67	91	67	91
CK-BB and Apgar(1min)	83	96	83	95
S-100 and cord pH	100	88	57	100
S-100 and cord BD	100	92	67	100
S-100 and Apgar(1min)	80	88	57	96

THE END
