Neonatal Encephalopathy

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HYPOXIC ISCHEMIC ENCEPHALOPATHY
First 12 Hours

- Depressed level of consciousness
- Periodic breathing
- Cranial nerve function may be spared
- Hypotonia with decreased movement or jitteriness
- Seizures
  - 50% of severely affected by 6-12 hours
  - often subtle
  - multifocal or focal clonic with infarcts
• *Apparent* increase in level of alertness
• More seizures
  • additional 15%-20%
• Apnea, jitteriness, shrill cry
• Weakness in the proximal limbs
• Exaggerated stretch reflexes
• Level of consciousness deteriorates
• Respiratory arrest
• Brain stem dysfunction
  • loss of oculo-vestibular response, fixed and dilated pupils
• Death (?)
Beyond 72 hours

- Improved level of consciousness
- Not improved suck and swallow
- Hypotonia
- Weakness of the proximal limbs, face and bulbar musculature
## Sarnat Staging

<table>
<thead>
<tr>
<th>Category</th>
<th>Mild Encephalopathy</th>
<th>Moderate Encephalopathy</th>
<th>Severe Encephalopathy</th>
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<tbody>
<tr>
<td>1. Level of consciousness</td>
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<td>Moro</td>
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<td>Dilated, responsive</td>
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### Thompson Score

Consider therapeutic hypothermia if total score ≥ 7 and aEEG discontinuous

<table>
<thead>
<tr>
<th>Sign</th>
<th>Score 0</th>
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<th>3</th>
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<tr>
<td>Tone</td>
<td>Normal</td>
<td>Hyper</td>
<td>Hypo</td>
<td>Flaccid</td>
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<td>Grasp</td>
<td>Normal</td>
<td>Poor</td>
<td>Absent</td>
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<td>Normal</td>
<td>Poor</td>
<td>Absent + bites</td>
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<td>Normal</td>
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<td>Normal</td>
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<td>Tense</td>
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Mild Encephalopathy 0-10  
Moderate Encephalopathy 11-14  
Severe Encephalopathy 15-22
Therapeutic Hypothermia guidelines

Infant should fulfill all 4 criteria:

1. Less than 6 hours post delivery OR sentinel event
2. GA greater than or equal to 35 weeks
3. Evidence of intrapartum hypoxia (see below)

- Any 2 of the following:
  - Cord or postnatal blood gas within one hour of birth with pH less than or equal to 7.00 OR base deficit of greater than or equal to -16
  - Evidence of acute perinatal event that may result in HIE (e.g. abruptio placentae, cord accident, uterine rupture, maternal trauma or cardiorespiratory arrest, late or variable decelerations etc.)
  - Apgar score 5 or less at 10 minutes, need for mechanical ventilation or resuscitation at 10 minutes

4. Signs of moderate or severe encephalopathy OR presence of seizures
Therapeutic Hypothermia

Exclusion Criteria
1. Neonate less than 1.8 kg
2. Clinically significant coagulopathy despite treatment
3. Moribund neonates, or neonates with major congenital or genetic abnormalities, in whom no further aggressive treatment is planned

- Target temperature: 33.5 rectal x 72 hours

- Routine:
  - Labs as per protocol
  - Fluid restriction to 60 ml/kg/day
  - CFM-if discontinuous → cEEG
  - MRI-post rewarming

Dexmeditomidine infusion → 0.05ug/kg/hr
## HIE Clinical Care Pathway

<table>
<thead>
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<th>0-24 hrs</th>
<th>24-72 hrs</th>
<th>3-4 days</th>
<th>4-8 days</th>
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| 1. Complete HIE admission order ("HIE" order set)  
2. Complete baseline vitals and blood work  
3. Ensure neonate is monitored closely for seizure activity  
4. If vented, assess for ongoing respiratory support  
5. Initiate/maintain cooling protocol (if indicated) | 1. Monitor ins and outs  
2. Ensure neonate is voiding  
3. Maintain therapeutic hypothermia  
4. Control seizures as required  
5. If intubated, complete spontaneous breathing trial  
6. Book MRI for day 4/5 post rewarming  
7. Book family meeting with both parents | 1. Rewarm to normothermic (if cooled)  
2. Prepare for MRI  
3. Confirm family meeting for day 4-5 (post MRI)  
4. Review enteral nutrition status  
5. Continue to assess for readiness for extubation | 1. MRI on day 4/5  
2. Discuss prognosis with parents/caregivers  
3. Initiate enteral/l oral feeds  
4. Discuss day 8 discharge and disposition |
| • Ensure continuous cardiorespiratory monitoring  
• Follow cooling protocol  
• Maintain BLANKETROL at 33.5°C (if cooled)  
• Establish central venous and arterial access  
• Assess need for urinary catheter  
• Cerebral Function Monitoring (CFM)  
• If seizure activity/depresseed background on CFM, initiate seizure management and continuous EEG monitoring  
• Assess need for low dose morphine infusion  
• Maintain NPO status  
• Restrict fluid intake to 40-60 mL/kg/day | • Complete and document full neurological examination  
• Complete labs as per HIE protocol  
• Ensure urine output is > 1ml/kg/hr  
• Stop antibiotics if blood cultures negative at 48 hours  
• Reassess TPN orders  
• Follow-up on blood cultures  
• Discuss lactation status with parents  
• Start mouth care with breast milk  
• Start TPN | • Complete and document full neurological examination  
• Monitor hemodynamics closely in rewarming phase  
• Discontinue CFM if no seizure activity 6 hours post rewarming  
• Determine discharge destination  
• Keep NPO if MRI within 12 hours; otherwise start enteral feeds  
• Prepare sedation orders for MRI  
• Ensure team is available for MRI  
• Remove Foley catheter  
• Remove arterial line  
• Attempt oral feeding  
• Initiate discharge summary | • Complete and document full neurological examination  
• Complete follow-up blood work for any previous abnormalities  
• Discontinue umbilical lines  
• Day 4, discontinue sedation medications (post MRI)  
• Day 5, complete follow-up EEG (if required)  
• Ensure nutritional goals are being met |
| • Head ultrasound  
• X-ray to confirm lines and tubes placement  
• Neurology consult within 24 hours of admission or within 1 hour if seizures present | • If ongoing hemodynamic instability; consider echocardiogram  
• Complete MRI checklist  
• Initiate lactation consult (if required) | • OT consult if feeding difficulties  
• Consider pediatrician for follow-up in community | |
| • Introduce team and review plan of care  
• Ensure that mum is encouraged to start pumping and storing breast milk | | | |
| • Update parents re: neonate clinical status and expectations for the next 48 hours  
• Book for follow-up meeting on day 4/5 (post MRI) to discuss prognosis  
• If neonate has seizure activity, bedside RN to initiate seizure teaching  
• Initiate EBM teaching | • Bedside RN to continue seizure teaching  
• Order teaching meds (if required)  
• Provide follow-up package  
• Facilitate infant holding by parent | • Complete hydration status teaching  
• Complete Well Baby Care teaching  
• Confirm follow-up plans: Neonatal Follow-up Clinic and Pediatrician | |
Modified Sarnat Stage

Number of Cases

Level of Encephalopathy

- Mild
- Moderate
- Severe
## Demographics

<table>
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<tr>
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<th>Mild (n-16)</th>
<th>Moderate (n-42)</th>
<th>Severe (n-16)</th>
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<tbody>
<tr>
<td>GA (mean)</td>
<td>38.5</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Sex</td>
<td>F 10</td>
<td>F 17</td>
<td>F 5</td>
</tr>
<tr>
<td>Apgar Scores (mean)</td>
<td>2 (1) 5 (5)</td>
<td>3 (1) 5 (5)</td>
<td>1.7 (1) 3.6 (5)</td>
</tr>
<tr>
<td>Cord Art. Gas (mean)</td>
<td>7.99</td>
<td>6.95</td>
<td>6.95</td>
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<tr>
<td>Therapeutic Hypothermia</td>
<td>13</td>
<td>34</td>
<td>10</td>
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<tr>
<td>Seizures</td>
<td></td>
<td>Clinical only 15</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical + Sub 6</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Subclinical 4</td>
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<tr>
<td>Brain injury</td>
<td>Normal 9</td>
<td>Normal 7</td>
<td>DR 8</td>
</tr>
<tr>
<td></td>
<td>T2 changes 2</td>
<td>T2 Changes 11</td>
<td>Hem 2</td>
</tr>
<tr>
<td></td>
<td>DR 3</td>
<td>DR 13</td>
<td>N/A 6</td>
</tr>
<tr>
<td></td>
<td>Hem 1</td>
<td>Hem 7</td>
<td></td>
</tr>
<tr>
<td>Disposition</td>
<td>Referral 14</td>
<td>Referral 33</td>
<td>Referral 4</td>
</tr>
<tr>
<td></td>
<td>Home 2</td>
<td>Home 9</td>
<td>Home 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Died 11</td>
</tr>
<tr>
<td>LOS</td>
<td>5.15 TH 8</td>
<td>8.5 TH 10.25 no TH</td>
<td>4.6 TH 6.3 no TH</td>
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</tbody>
</table>

Patterns of Injury
SEIZURES: CAUSES

- Metabolic
  - hypoxemia
  - hypoglycemia
  - hypo/hypernatremia
  - hypocalcemia, hypomagnesemia
- Genetic/inborn errors
- Structural
  - trauma
  - IVH, ICH
  - brain malformation
- Infectious – meningitis
- Withdrawal
- Familial
- Most common...HIE
Guidelines for the Management of Seizures in Late Pre-term and Term Neonates  
(Gestational age ≥ 34 weeks AND postmenstrual age < 44 weeks)

Seizure Onset

- Support ABCs
- Establish IV Access
- Rapid glucose check & lactate, gas, electrolytes (include Ca and Mg)
- Attach bedside CFM, if available
- Early referral to SickKids NICU for consideration of eEEG (outside patient)  
- Monitor closely for loss of airway reflexes and respiratory depression, hypotension, or cardiac arrhythmias.
- Consider need for intubation

Seizures ongoing for 3 minutes

Lorazepam
0.1 mg/kg IV/PR

Phenobarbital
20 mg/kg IV push over 10 minutes

Seizures ongoing for further 2 minutes

Lorazepam
0.1 mg/kg IV/PR

Phenobarbital
10 mg/kg IV push over 5 minutes

Seizures ongoing for further 2 minutes

Phenobarbital
10 mg/kg IV push over 5 minutes

If IV Levetiracetam unavailable consider:

Fosphenytoin
Load 20 mg PE/kg IV
May repeat load after 5 minutes: 10-20 mg PE/kg IV

Levetiracetam
Load 60 mg/kg IV

Seizures ongoing for further 2 minutes

Refractory Seizures / Status Epilepticus

Midazolam infusion
- 0.15 mg/kg IV bolus followed by 2 mcg/kg/min IV infusion
- Increase as needed by 2 mcg/kg/min every 10 min
- Bolus 0.15mg/kg with each increase in infusion rate
- Maximum infusion rate: 24 mcg/kg/min

Phenobarbital
10 mg/kg IV push over 5 minutes

Phenobarbital
10 mg/kg IV push over 5 minutes

• Consult Neurology service for consideration of video EEG (eEEG)
• Consider Pyridoxine 50 mg BID PO/NG/IV in all neonates with unexplained seizures.
• Consult Biochemical Diseases service (if metabolic condition suspected)

Phenobarbital
10 mg/kg IV push over 5 minutes

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Lorazepam
0.1 mg/kg IV/PR

Phenobarbital
10 mg/kg IV push over 5 minutes

Lorazepam
0.1 mg/kg IV/PR

Seizure Onset
Seizure Onset

- Support ABC
- Establish IV Access
- Glucose check, lactate, electrolytes
- Attach CFM if available
- Refer to tertiary center for EEG consideration
- Monitor airway, respiratory effort, BP
- Consider need for intubation
Treatment

- Lorazepam 0.1 mg/kg IV/PR
- Lorazepam 0.1 mg/kg IV/PR
- Phenobarbital 20 mg/kg IV
- Phenobarbital 10 mg/kg IV
- Phenobarbital 10 mg/kg IV
- Levetiracetam
  Load 60 mg/kg IV

- Consult Neurology service for consideration of video EEG (cEEG)
- Consider Pyridoxine 50 mg BID PO/NG/IV in all neonates with unexplained seizures,
- Consult Biochemical Diseases service (if metabolic condition suspected)
Refactory Seizures/Status Epilepticus

Midazolam infusion

• 0.15 mg/kg IV bolus followed by 2 mcg/kg/min IV infusion
• Increase as needed by 2 mcg/kg/min every 10 min
• Bolus 0.15mg/kg with each increase in infusion rate
• Maximum infusion rate: 24 mcg/kg/min
Paradigm Shift in Use of EEG...

- From a **Diagnostic Tool** ...
  - Intermittent recordings
  - Offline interpretation by neurologists

- ... To a **Monitoring Tool**
  - Continuous recordings +/- video
  - Possibility for real-time interpretation
aEEG for Seizure Detection

• aEEG is a monitoring / screening tool
  • Sensitivity 40-70%
  • Poor at detecting brief or very focal seizures
  • False positives common due to artifacts
  • Must examine the underlying raw EEG tracing to confirm aEEG findings

• Interpreted by neonatologist at bedside
  • Permits more rapid intervention

• Confirmation by conventional EEG is required
  • especially when aggressive anticonvulsant therapy is being considered
Normal trace (continuous with +/- cycling)

- Upper margin is > 10 µVolts
- Lower margin is > 5 µVolts
- Widening and narrowing of the trace [sleep wake cycling (SWC)]
24 hrs following admission
Moderately abnormal trace (discontinuous pattern)

- No evidence of Sleep/Wake cycling
- Upper margin > 10 μVolts
- Lower margin < 5 μVolts
- Increased variability (trace is broad)
Severely abnormal (inactive, flat trace)

- May be accompanied with brief bursts of higher voltage (burst suppression)
- No evidence of sleep/wake cycling
- Upper margin < 10 μVolts
Seizures

- Seizure onset shows continuous high activity
- Causes CFM to narrow and rise up
- Frequent and prolonged periods of elevation in both the lower and upper margins that coincide with an EEG repetitive rhythmic pattern.
Maternal History
  • 31 year old; G2P1, healthy

Delivery
  • Spontaneous labour at 38+2 weeks gestation
  • Emergency C/S due to cord prolapse
  • APGAR 2 & 4 at 1 & 5 minutes; no respiratory effort; HR <100
  • Intubation for thick meconium; inotropes
  • Arterial cord gas: pH 6.93/BD -14; Lactate 4.5
  • Moderate encephalopathy

NICU Course
  • Therapeutic hypothermia x 72 hrs
## Modified Sarnat Staging

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*The neurological examination must be performed by a physician skilled in neurological assessment to determine the degree of encephalopathy.*

☐ Presence of Clinical Seizures
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TOTAL

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Moderate Encephalopathy 11-14
Severe Encephalopathy 15-22
What is the most likely outcome?

A. Normal
B. Mild Disability
C. Moderate Disability
D. Severe Disability
18 mth Neurodevelopmental Outcome

- Normal
• **Maternal History**
  • 42 year old, primagravida
  • Pregnancy complicated by PIH and IDM on insulin

• **Delivery**
  • Induction at 41 weeks gestation
  • C/S for failure to progress after 20 hours of labour
  • APGAR 5 & 7 at 1 & 5 minutes respectively
  • Arterial cord gas pH 7.13/BD -9, lactate 4.6

• **NICU**
  • Severely encephalopathic
  • Seizures noted at 5 hours of life, status epilepticus
  • Therapeutic Hypothermia
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- ✔ Presence of Clinical Seizures
A. Normal
B. Mild Disability
C. Moderate Disability
D. Severe Disability
18 month Neurodevelopmental Outcome

• Infantile spasms

• Spastic cerebral palsy (quad)
  • Wheelchair, not sitting or rolling

• Growth parameters:
  ▪ Weight 85th to 97th percentile
  ▪ Head circumference < 0.1 percentile
HYPOTHERMIA: ADVERSE EFFECTS

• **Cardiac**
  • Contractility, BP
  • **Bradycardia**
  • Arrhythmias(< 28°C)
  • Pulmonary hypertension
  • Hyper viscosity
  • Diuresis

• **Gastrointestinal**
  • NEC

• **Coagulopathy**
  • Platelet dysfunction

• **Metabolic**
  • Acidosis*
  • $O_2$ dissociation curve to left
  • Hypokalaemia
  • Hypoglycemia

• **Dermatological**
  • Traumatic Fat necrosis

• **Immunological**
  • Sepsis
• Maternal History
  • 32 year old primigravida
  • Uncomplicated pregnancy

• Delivery
  • Spontaneous labour at 37 weeks
  • Shoulder dystocia, poor respiratory effort at birth, PPV
  • Apgars 4 & 7 at 1 & 5 minutes
  • Cord Arterial pH 6.98/BD-12
  • Encephalopathy, but improving

• NICU
  • 8 hrs of age focal seizures, right eye deviation with right arm extension; recurrent
  • Seizures treated with Lorazepam, Phenobarbital and Midazolam
A. Normal
B. Mild Disability
C. Moderate Disability
D. Severe Disability
18 mth Neurodevelopmental Outcome

No further seizures
Mild speech delay
Walking
Right hand fine motor delay
• Maternal History
  28 year old G2, P0, uneventful pregnancy

• Delivery
  Induced at 41 + 2 weeks gestation
  Vacuum assisted delivery,
  Cord Arterial pH 7.0/BD-21, Apgars 3, 6 & 7 at 1, 5 & 7 mins
  Resuscitation with PPV for HR 80 and no respiratory effort

• NICU
  Seizures at 24 hrs of age
  Severity of encephalopathy worsening over first 3 days
A. Normal
B. Mild Disability
C. Moderate Disability
D. Severe Disability
18 mth Neurodevelopmental Outcome

• Poor weight gain, failure to thrive-G-tube fed
• Ongoing encephalopathy with progressive seizure disorder
• Followed by palliative care team
• Maternal History
 Primagravida
 Uncomplicated pregnancy
 • Delivery and initial course
 Apgars 9/9
 Discharged at 24 hours of age
 Arrived in ER on DOL 3 with history of poor feeding and lethargy x 12 hrs
Next Steps

Assessment

Differential Diagnosis
  Sepsis
  Dehydration
  Hyperbilirubinemia

Interventions to stabilize
  Fluids
  Sepsis work up
  Lytes, glucometer, bilirubin
## Modified Sarnat Staging

<table>
<thead>
<tr>
<th>Category</th>
<th>Mild Encephalopathy</th>
<th>Moderate Encephalopathy</th>
<th>Severe Encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Level of consciousness</td>
<td>□ Hyperalert</td>
<td>☑ lethargic</td>
<td>□ Stupor/coma</td>
</tr>
<tr>
<td>2. Spontaneous activity</td>
<td>□ Normal</td>
<td>□ Decreased</td>
<td>□ No activity</td>
</tr>
<tr>
<td>3. Posture</td>
<td>□ Mild distal flexion</td>
<td>□ Strong distal flexion</td>
<td>□ Decerebrate (arms extended and internally rotated, legs extended with feet in forced plantar flexion)</td>
</tr>
<tr>
<td>4. Tone</td>
<td>□ Normal</td>
<td>□ Mild hypotonia</td>
<td>☑ Flaccid tone</td>
</tr>
<tr>
<td>5. Primitive reflexes</td>
<td>□ Weak</td>
<td>☑ Weak</td>
<td>□ Absent</td>
</tr>
<tr>
<td>Suck Moro</td>
<td>□ Strong</td>
<td>☑ Incomplete</td>
<td>□ Absent</td>
</tr>
<tr>
<td>6. Autonomic system</td>
<td>□ Dilated, responsive</td>
<td>☑ Constricted</td>
<td>□ Skew deviation, dilated/non-reactive to light</td>
</tr>
<tr>
<td>Pupils</td>
<td>□ Tachycardia</td>
<td>☑ Bradycardia</td>
<td>□ Variable HR</td>
</tr>
<tr>
<td>Heart rate</td>
<td>□ Normal</td>
<td>☑ Periodic breathing</td>
<td>□ Apnea</td>
</tr>
<tr>
<td>Respirations</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The neurological examination must be performed by a physician skilled in neurological assessment to determine the degree of encephalopathy.

- Presence of Clinical Seizures
Findings

• Na 150, K 4, Cl 104
• Glucometer < 1
• CBC Hbg 180, WBC 10.2, plts 195
Discussion

• Spastic quad, epilepsy (infantile spasms) --> 12 months
• Family support essential
INTERPRETATION

• All diagnostic tests must be taken in the context of the clinical evaluation.

• CLINICAL EXAMINATION IS THE MOST IMPORTANT PROGNOSTIC FACTOR IN NEURODEVELOPMENTAL OUTCOME.