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HYPOXIC - ISCHEMIC ENSEPHALOPAHTY OF NEWBORN CLINICAL AND LABORATUARY FOLLOW UP

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- Annually asphyxia is responsible of 23 % of the 4,000,0000 neonatal deaths
- The rate of HIE is 1-2/1000 term newborns in developed countries
- Mortality 10-20 %

Why

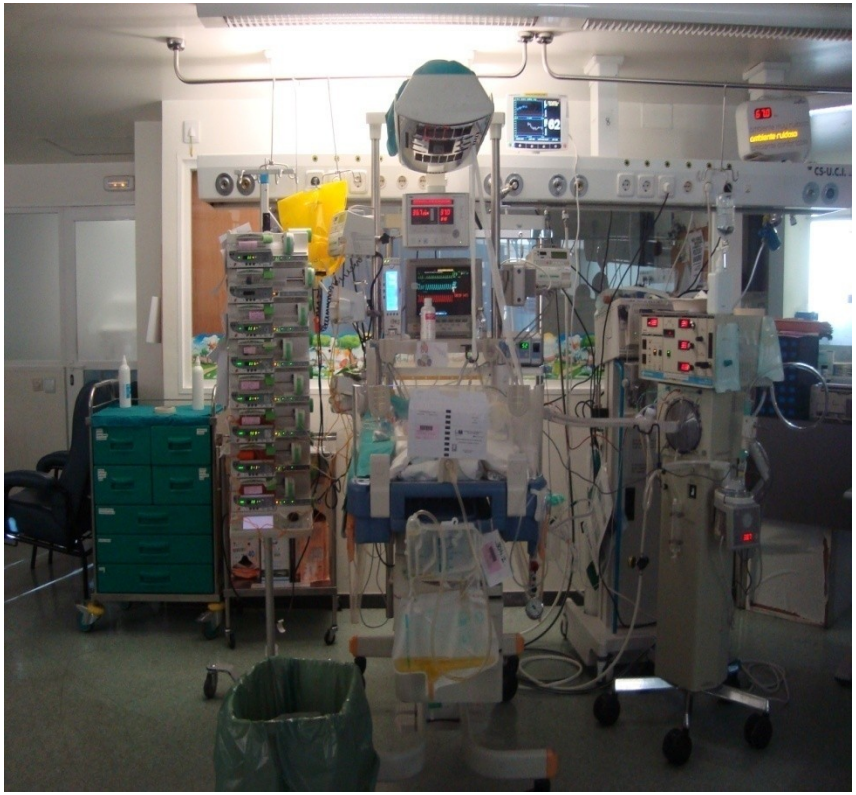
- Still looking for other methods to predict favorable or adverse outcome in asphyxiated newborns
- Still looking for methods to predict the therapeutic window and apply treatment
- Still looking for tests to assess treatment efficiency

Clinical Evaluation

Supportive Care

Delivery room

- Resuscitation beginning with room air



Temperature

- Avoid hyperthermia

Ventilation

Delivery room

- Cord blood gas
- APGAR
- A note should be made of

1. the time for respiration to be established

2. the return of tone as this may help indicate

"It's a new medical technology. Instead of crying, we can program your choice of 200 fun ring tones!"

Ventilation

Adequate respiratory functions

Avoid hypo/hyperoxemia

Avoid hypo/hypercarbia

- hypercarbia *loss of autoregulation*

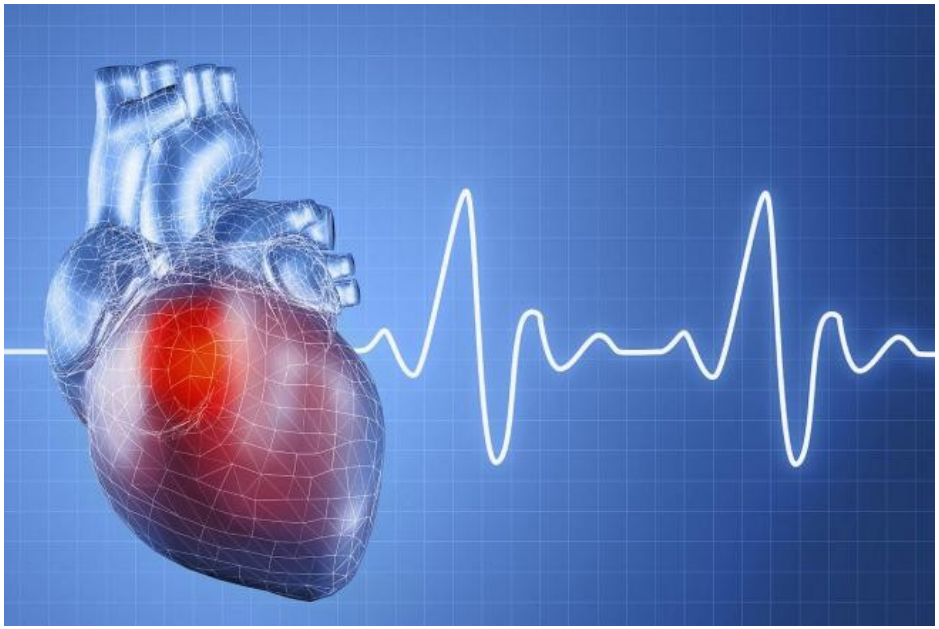
- hypocapnia *death, severe neurodevelopmental delay*

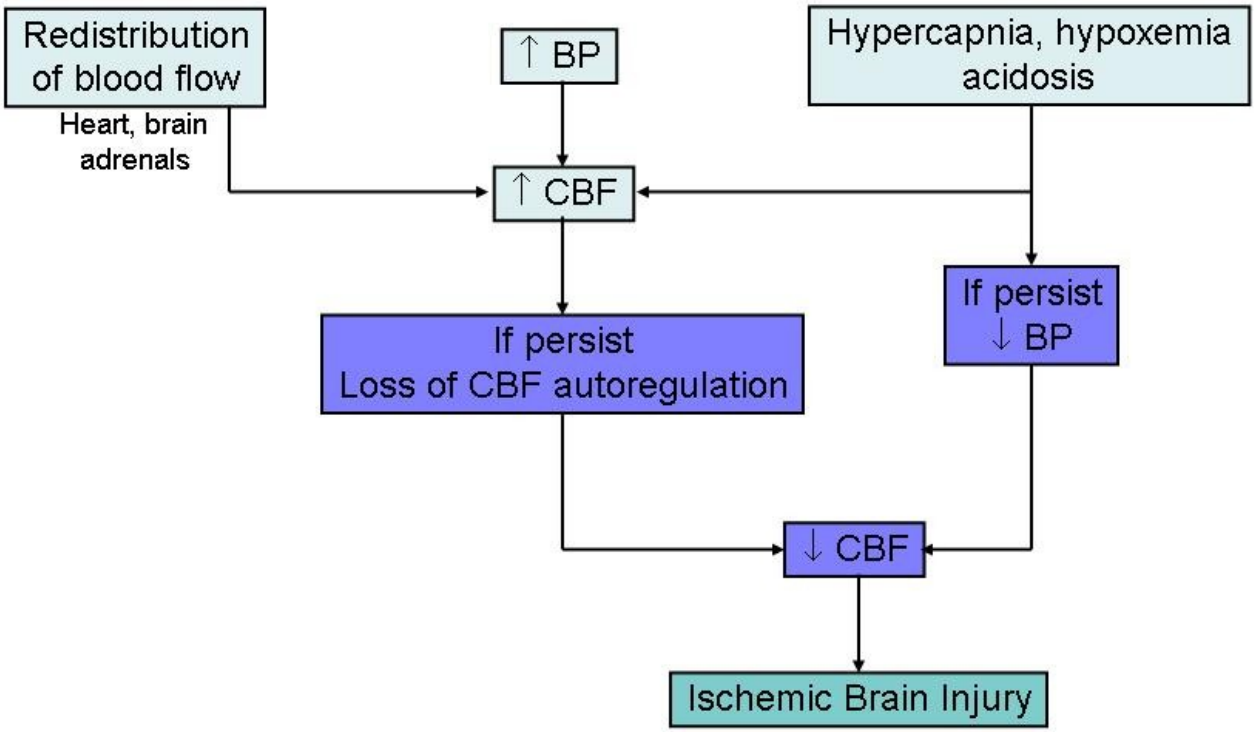
Kapadia VS, Chalak LF, Dupont TL, Rollins NK, Brion LP, Wyckoff MH. Perinatal Asphyxia with Hyperoxemia within the First Hour of Life Is Associated with Moderate to Severe Hypoxic-Ischemic Encephalopathy. J Pediatr. 2013 Oct;163(4):949-54.

Perfusion

Hypotension

- Myocardial dysfunction
- Endothelial cell damage
- Volume loss (rarely)




Redistribution of blood flow
Heart, brain adrenals
↑ BP
Hypercapnia, hypoxemia acidosis
↑ CBF
If persist Loss of CBF autoregulation
If persist ↓ BP
↓ CBF
Ischemic Brain Injury

Fluid status

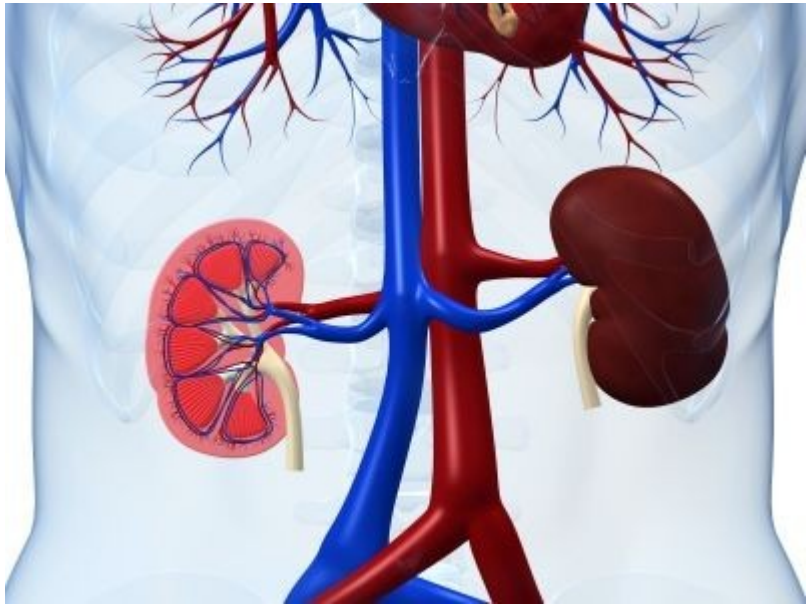
Often progress to fluid overload state

- Renal failure
- SIADH

↑ Weight

↓ Urine output

↓ Hyponatremia

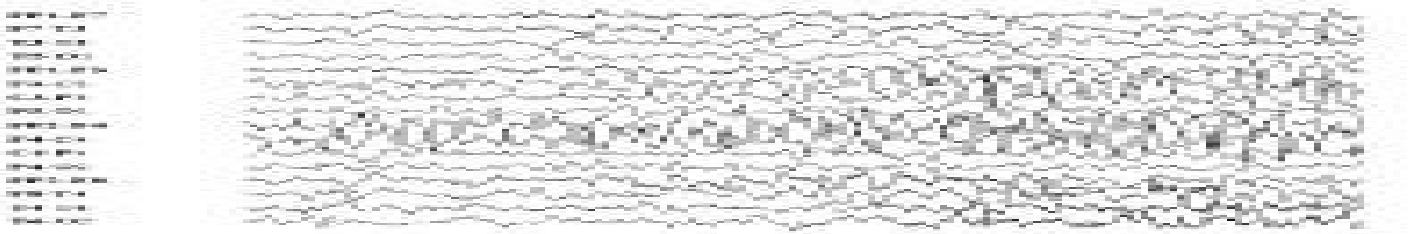


Seizures

- Most common cause in neonatal period
- Subsequent epilepsy risk
- Treat?

    Clinical seizures

    Electrographic seizures

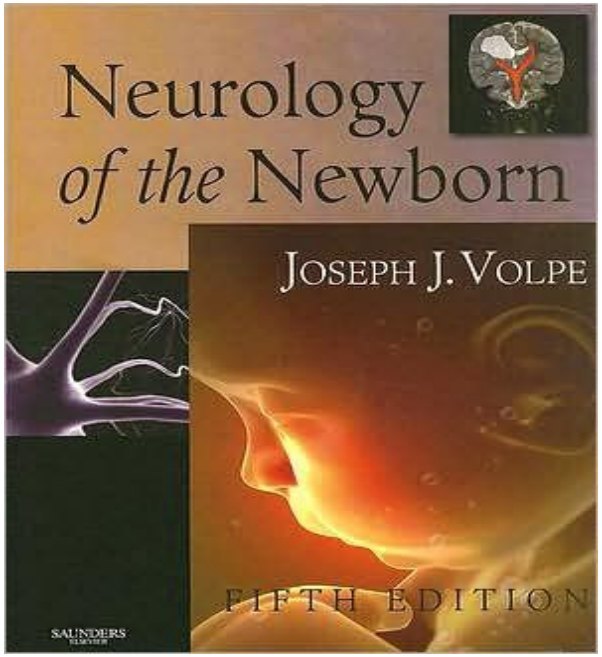


Others

- Pulmonary
  - PPHN
  - MAS
- Hematopoietic
  - Thrombocytopenia
  - Clotting abnormalities
- Hepatic
- Gastrointestinal

HIE=MODS?

Organ	%
None	22
CNS only	16
CNS with one or more organ systems	46
Other organ systems without CNS	16



Supportive treatment

- Correct metabolic abnormalities
- Correct hypotension/hypo-perfusion
- Fluid management
- Treatment of seizures
- Bleeding and/or thrombocytopenia
- Treatment of cerebral edema

Laboratory studies

- Serum electrolyte levels
- Renal function studies
- Cardiac and liver enzymes
- Coagulation system - Includes prothrombin time, partial thromboplastin time, and fibrinogen levels
- Arterial blood gas

  - ✓**On admission (within the first minutes of hypoxic insult)**
  - ✓**Daily**

Sarnat Grading Scale of HIE

Modified Sarnat Stage *			
STAGE **	**Stage 1**	**Stage 2**	**Stage 3**
Level of Consciousness	Hyperalert	Lethargic or obtunded	Stupor or coma
Activity	Normal	Decreased	Absent
Neuromuscular Control			
Muscle Tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration (extension)
Stretch Reflexes	Overactive	Overactive	Decreased or absent
Complex / Primitive Reflexes			
Suck	Weak	Weak or absent	Absent
Moro (startle)	Strong; low threshold	Weak; incomplete; high threshold	Absent
Tonic Neck	Slight	Strong	Absent
Autonomic Function			
Pupils	Mydriasis	Miosis	Variable; often unequal; poor light reflex; fixed; dilated
Heart Rate	Tachycardia	Bradycardia	Variable
Seizures	None	Common; focal or multifocal	Uncommon (excluding decerebration)

* Sarnat H.B., Sarnat M.S.: Neonatal encephalopathy following fetal distress. Arch Neurol. 33:698-705. 1976.
** STAGE 0 = Normal

Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol. 1976 Oct;33(10):696-705.

Staging of HIE

Stage	Mental	Resp Support	Feeding problem	Tone	Seizure
Mild (Sarnat I)	Hyperalert	No	Mild	Jittery	No
Moderate (Sarnate II)	Lethargy	No	Moderate	Decreased	Yes
Moderate-Severe	Lethargy	Yes	Moderate	Increased	Yes
Severe (Sarnat III)	Coma	Yes	Severe	Flask	Yes (early)

Allan WC,Sobel DB. Seminars in Pediatric Neurology 2004:11;119-128

Problem?

- Sarnat classification is for 12 h after birth and also can change during follow-up
- Neurological exam immediately after birth is not accurate enough for decisions like hypothermia treatment

Radiological Methods

- MR spectroscopy (generally when stable)
- Diffusion weighted MRI (when stable)
- Doppler Ultrasound (user dependent,shows flow velocity rather than flow)
- Echocardiography

Imaging

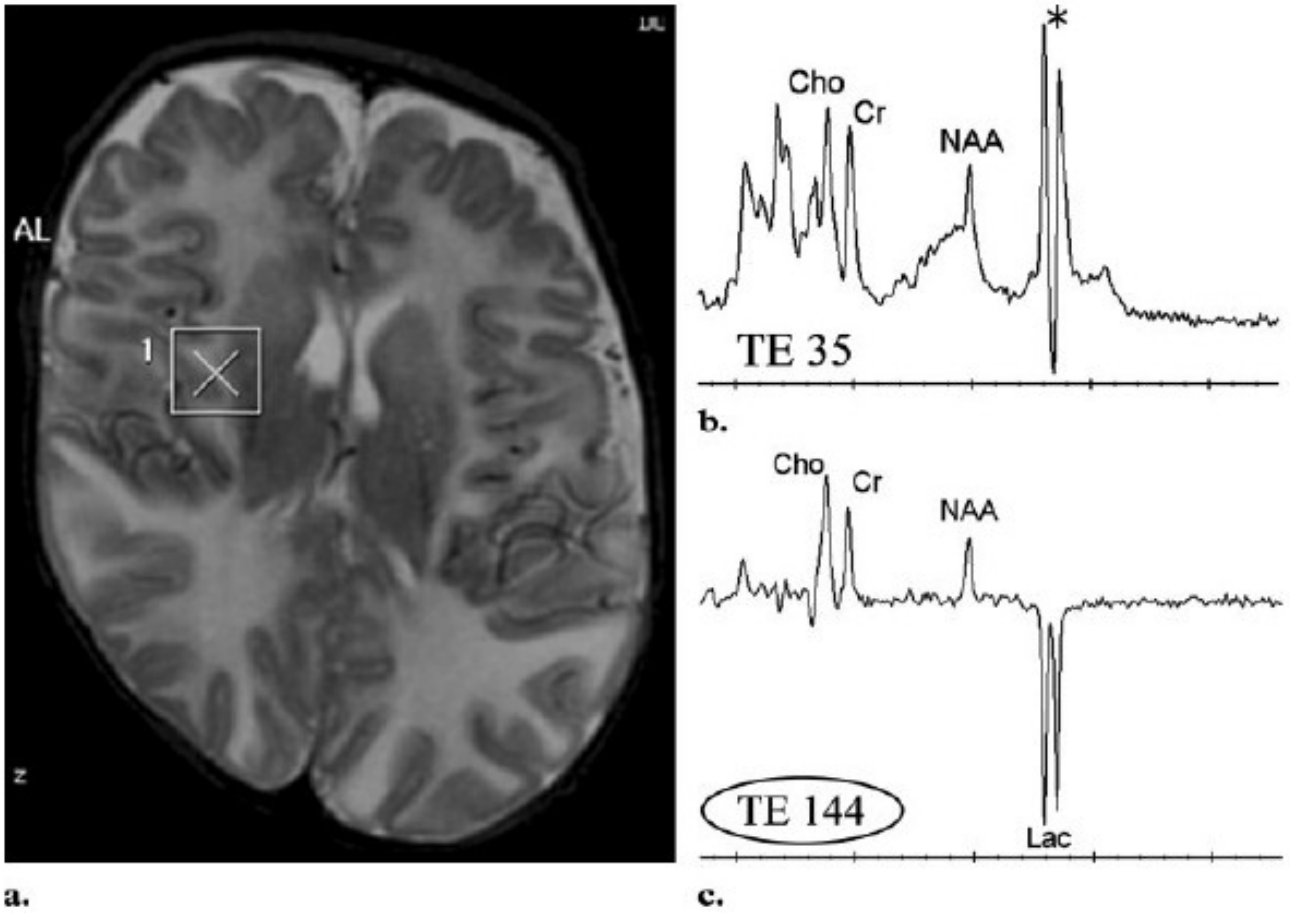
MR-S

For increased lactate or decreased high energy phosphates

Not practical

Not easy to obtain early on

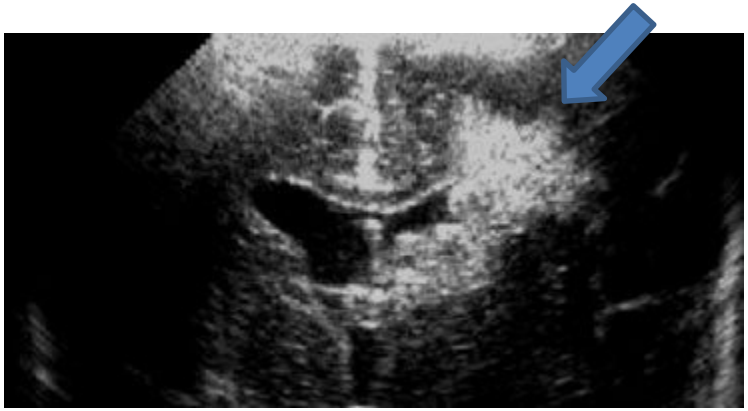
MR Spectroscopy in HIE
“Lactate peak”



Good but indirect

Cranial sonography

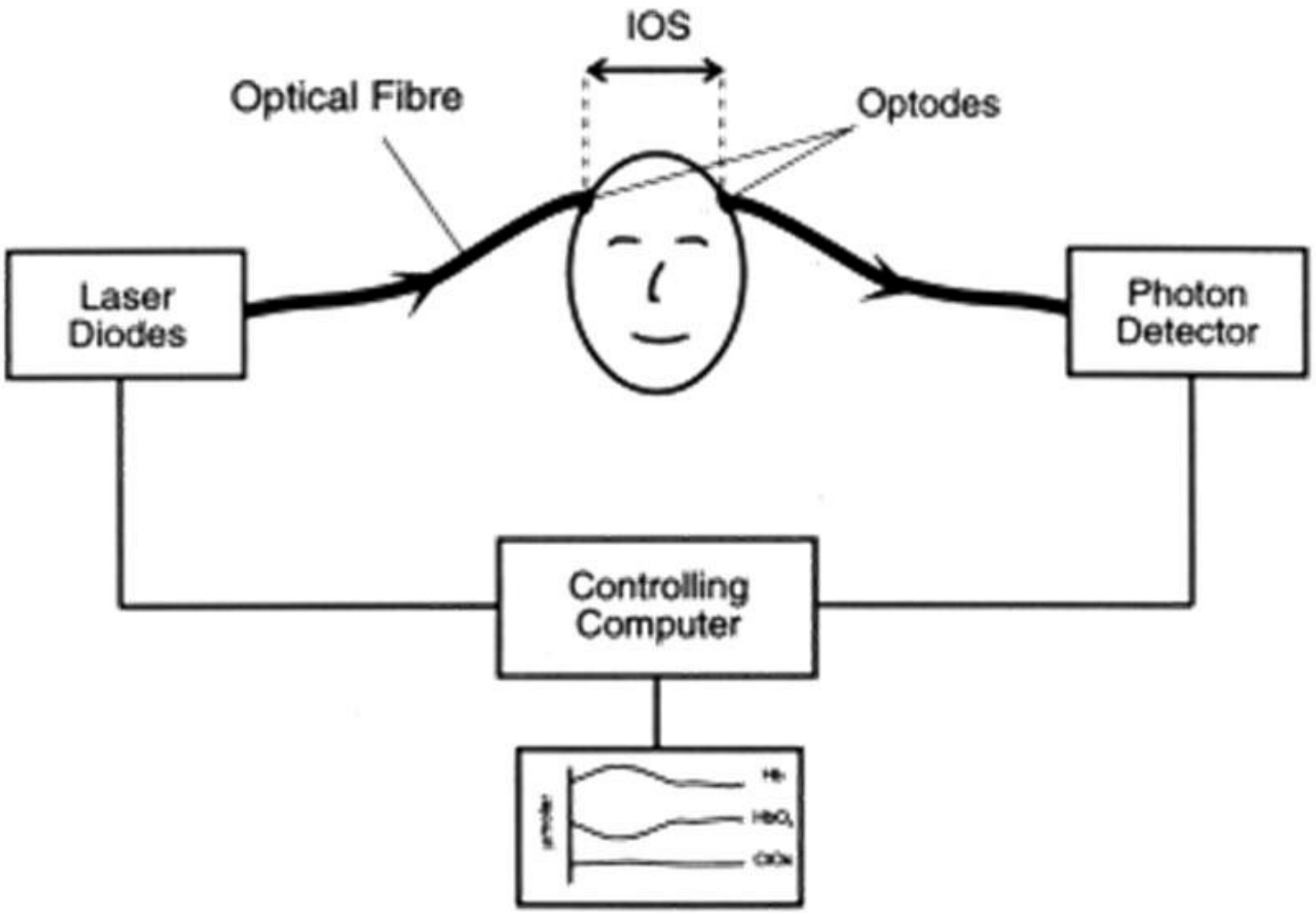
- Non-invasive
- Bed-side



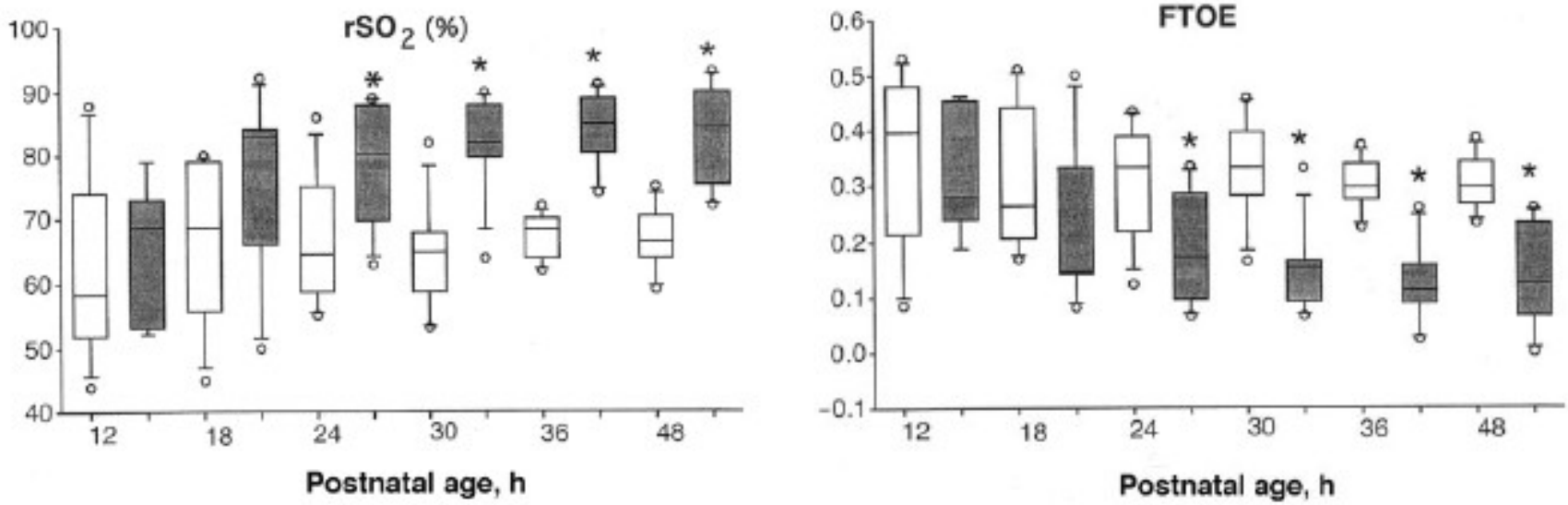
- Locating hemorrhages
- Defining ventricular size
- White matter damage?
- Edema

Shankaran S, Kottamasu SR, Kuhns L. Brain sonography, computed tomography, and single-photon emission computed tomography in term neonates with perinatal asphyxia. Clin Perinatol. 1993 Jun;20(2):379-94.

Near Infrared Spectroscopy



NIRS–HIE

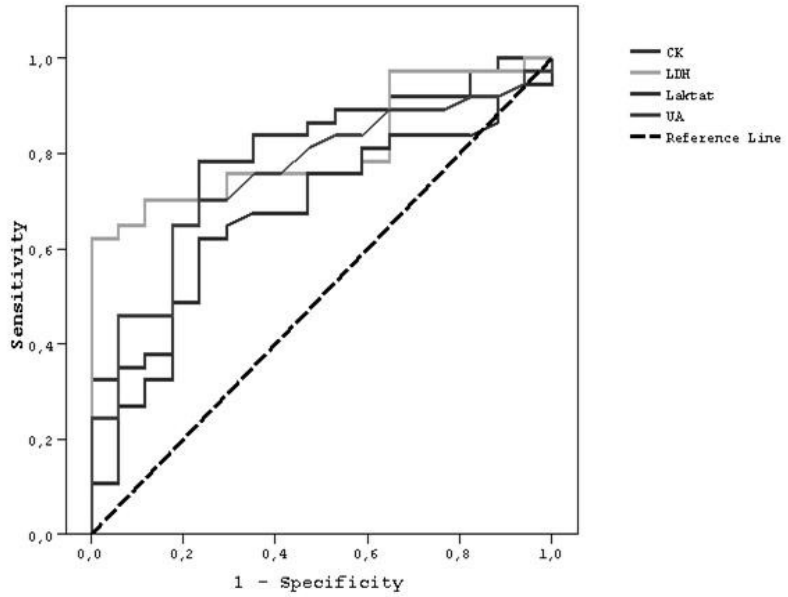


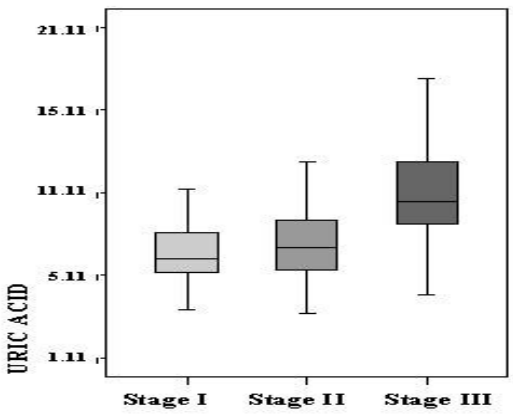
High rSO2 after 24 h of life is associated with adverse outcome in HIE. Low a-EEG score is associated with adverse outcome in HIE

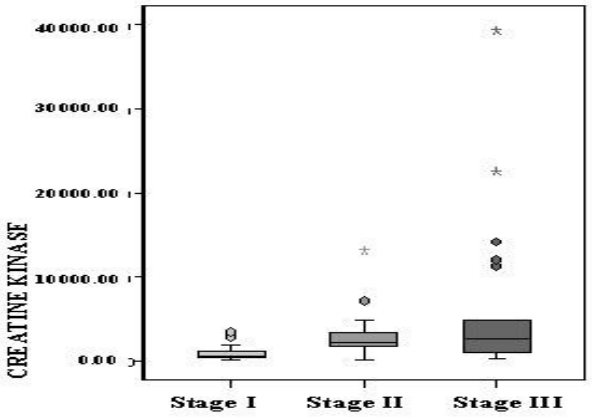
Toet MC Pediatrics 2006

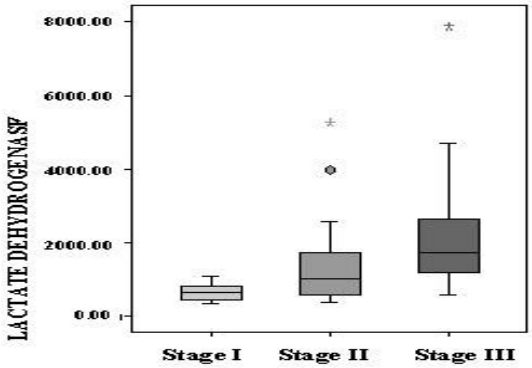
Laboratory

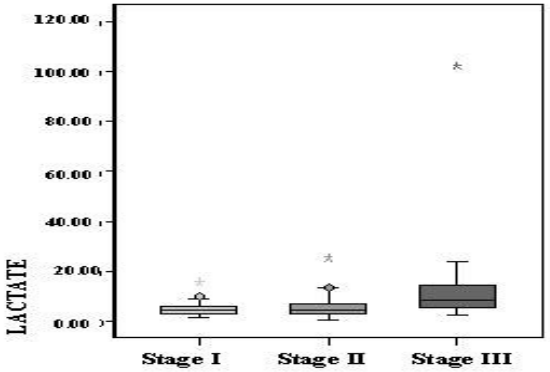
	Specificity	Sensitivity	PPD	NPD	Accuracy rate
CK	57%	90%	75%	80%	%76
LDH	56%	79%	76%	62%	%71
UA	48%	78%	73%	55%	%68
Lactate	39%	74%	66%	48%	%61
CK+LDH+UA+Lactate	87%	94%	94%	87%	%68




URIC ACID
21.11
15.11
11.11
5.11
1.11
Stage I
Stage II
Stage III


CREATINE KINASE
40000.00
30000.00
20000.00
10000.00
0.00
Stage I
Stage II
Stage III


LACTATE DEHYDROGENASE
8000.00
6000.00
4000.00
2000.00
0.00
Stage I
Stage II
Stage III

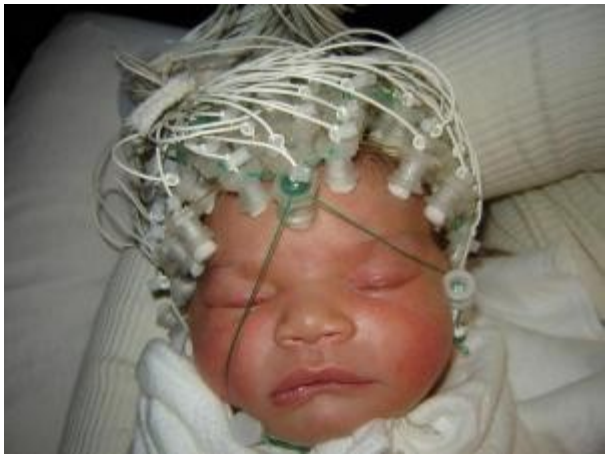

LACTATE
120.00
100.00
80.00
60.00
40.00
20.00
0.00
Stage I
Stage II
Stage III

Electroencephalography

Not helpful for determining the cause of neonatal encephalopathy

Presence and severity of encephalopathy

Prognostic information



aEEG and Perinatal Asphyxia

- The neontal EEG is depressed during and immediately after an acute hypoxic ischemic event
- The degree and duration of the EEG depresion correlates with the severity of the brain injury
- During the recovery the EEG contains valuable information on the severity of the former insult
- In neonates electrocortical activity when recorded after HIE is ahighly sensitive predictor of neurologic outcome

aEEG and Perinatal Asphyxia

- Several studies have shown that outcome can be accurately predicted from aEEG during the first hours after birth
- The predictive value of the presence of a poor background pattern (BS, CLV, FT) for neuro-developmental outcome at 18–24 months was assessed
- The predictive values obtained by different groups were very similar
- Both+&- predictive values were slightly lower when the aEEG was assessed at 3 instead of 6 h

a-EEG

Abnormal a-EEG

- More specific % 89 vs % 79
- Better PPV % 73 vs % 58
- Similar sensitivity
- Similar NPV

When compared with early abnormal neurological exam after hypoxia-ischemia

Shalak LF, Laptook AR, Velaphi SC, Perlman JM. Amplitude-integrated electroencephalography coupled with an early neurologic examination enhances prediction of term infants at risk for persistent encephalopathy. Pediatrics. 2003;111(2):351-7.

Abnormal a-EEG + Abnormal neuro exam;

- % 94 specificity
- % 85 PPV

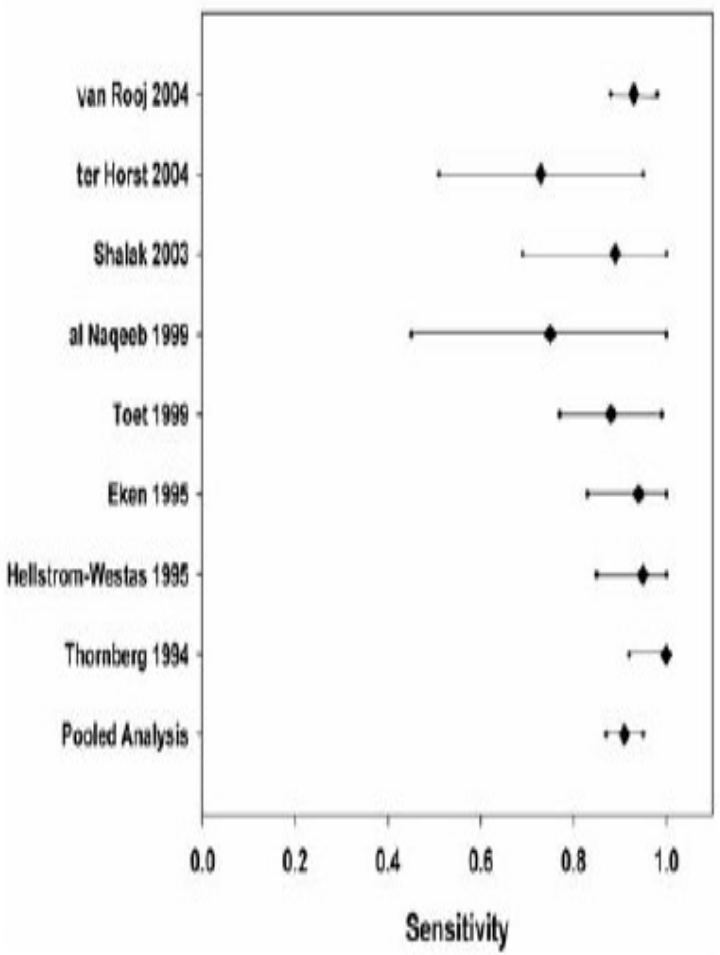
For early adverse outcome

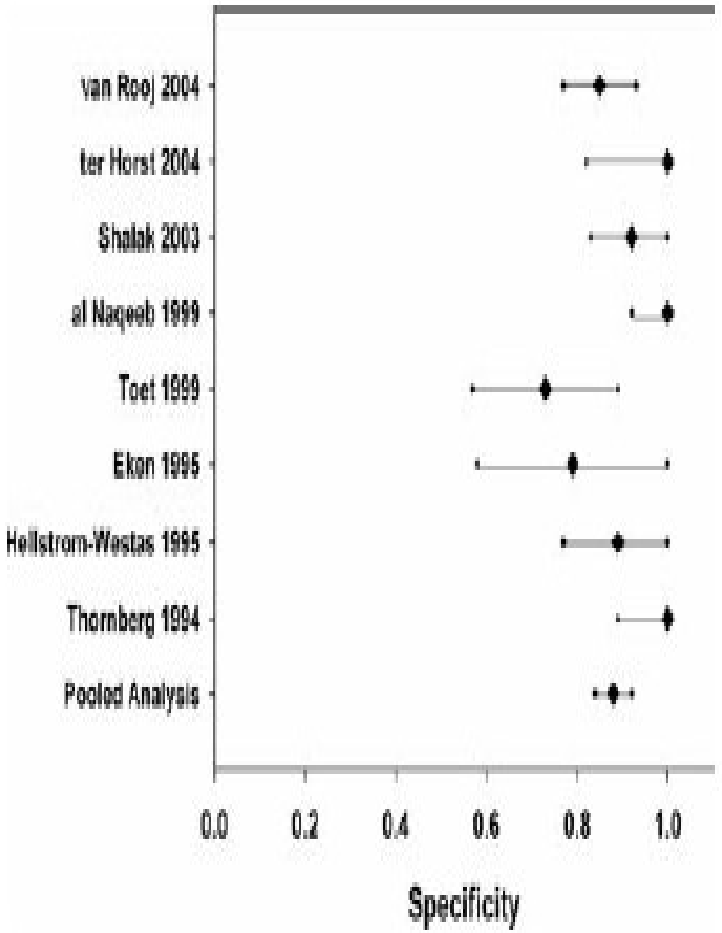
Shalak LF, Laptook AR, Velaphi SC, Perlman JM. Amplitude-integrated electroencephalography coupled with an early neurologic examination enhances prediction of term infants at risk for persistent encephalopathy. Pediatrics. 2003;111(2):351-7.

Recovery of abnormal background activity of a-EEG within 24 hours is considered to represent

<u>good prognosis</u>

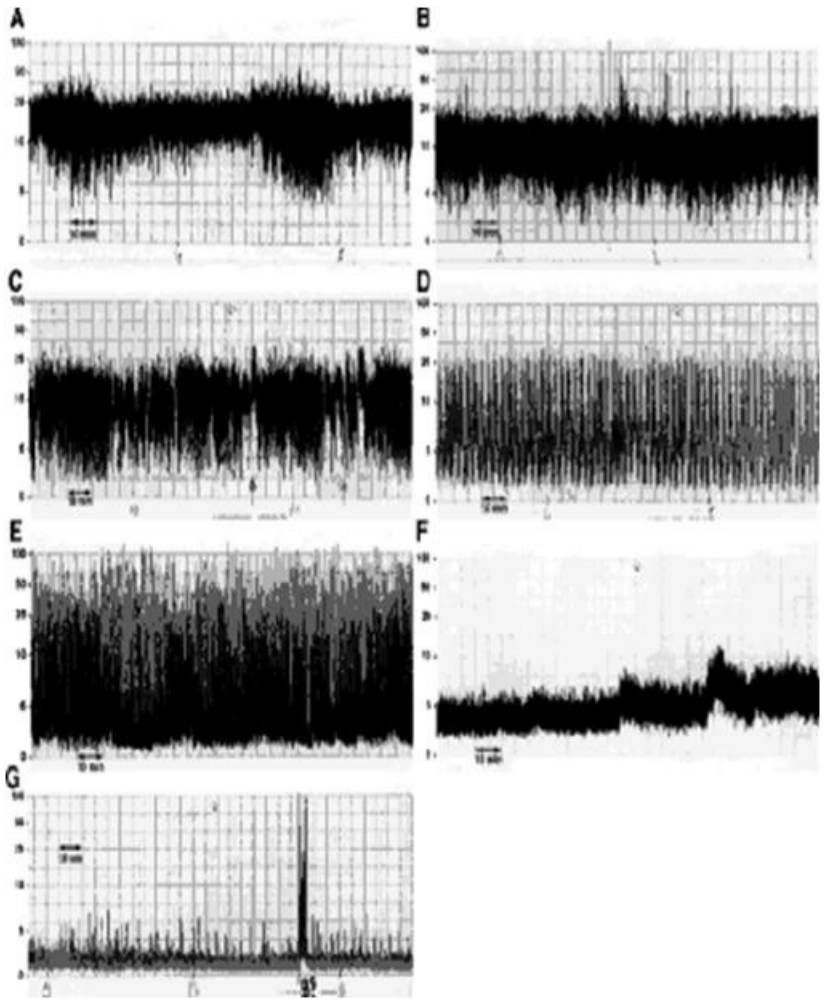
a-EEG For Predicting Adverse Outcome





Spitzmiller RE, Phillips T, Meinzen-Derr J, Hoath SB. Amplitude-integrated EEG is useful in predicting neurodevelopmental outcome in full-term infants with hypoxic-ischemic encephalopathy: a meta-analysis. J Child Neurol. 2007 Sep;22(9):1069-78.

aEEG – Typical Tracings



CFM studies have prognostic significance postasphyxial injury

Faster recovery of CFM yields better prognosis at two years

Normal early CFM, good prognosis

ter Horst HJ, Sommer C, Bergman KA, Fock JM, van Weerden TW, Bos AF. rognostic significance of amplitude-integrated EEG during the first 72 hours after birth in severely asphyxiated neonates. Pediatr Res. 2004 Jun;55(6):1026-33.

Sleep-Wake Cycling on aEEG in Term Newborns With HIE

- 96.1% of newborns who showed normal SWC< 36 hrs had good neurodevelopmental outcome
- Only 20% of thoe who developed abnormal SWC> 36 hrs had a good outcome
- The presence and time onset and the quality of SWC were related to the grade of HIE
- Good neurodevelopmental outcome was associated with early onset normal SWC
- aEEG monitoring should be continued until the onset and quality of SWC are established

Osredkar DJ Toet MC, van Rooij LG, van Huffelen AC, Groenendaal F, de Vries LS. Sleep-wake cycling on amplitude-integrated electroencephalography in term newborns with hypoxic-ischemic encephalopathy. Pediatrics. 2005 Feb;115(2):327-32.

Before Hospital Discharge

- Reference to developmental pediatrics
- Ophalmologic examination
- ABR
- Retinal and ophthalmic examination
- Head circumference and growth

Robertson CM, Perlman M. Follow-up of the term infant after hypoxic-ischemic encephalopathy. Paediatr Child Health. 2006 May;11(5):278-82.

After Hospital Discharge

- Developmental pediatrics
- Pediatric neurologist
- EEG if seizure is seen or if taking AED
- Neuroimaging (MRI)

Robertson CM, Perlman M. Follow-up of the term infant after hypoxic-ischemic encephalopathy. Paediatr Child Health. 2006 May;11(5):278-82.

The question is….

- To treat or not to treat
- Who to treat

THANK YOU….