Hipoxic ischemic encephalopathy

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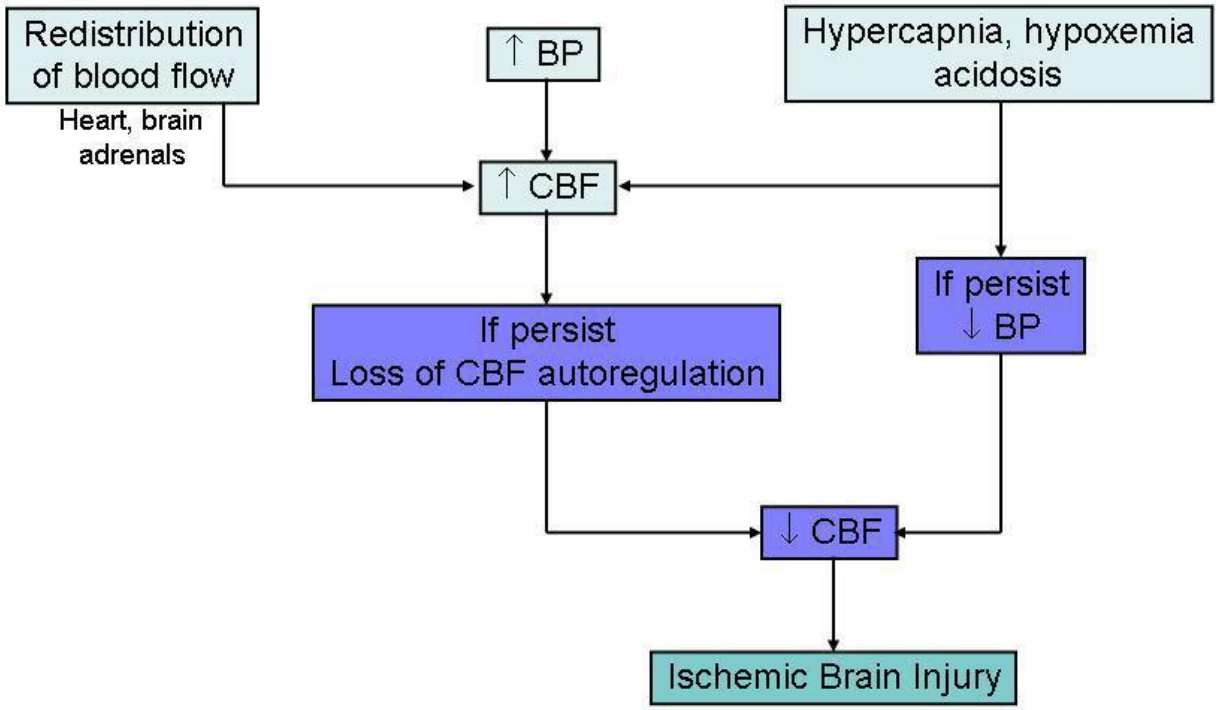
Perinatal asphyxia

- 1. Definition
- **Perinatal asphyxia-** more appropriately known as **hypoxic – ischemic encephalopathy –** is characterized by clinical and laboratory evidence of **acute brain injury due to asphyxia**
- **The primary causes** of this condition are systemic hypoxemia and/or reduced cerebral blood flow (CBF)

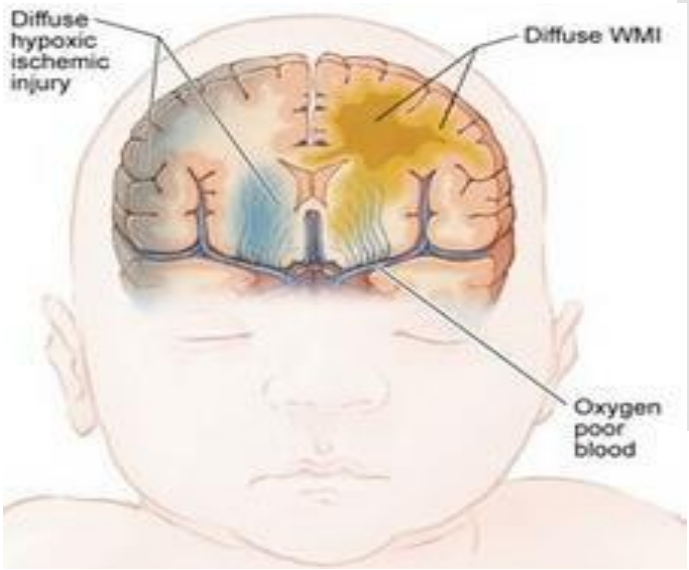
Perinatal asphyxia

Fetal response to asphyxia illustrating the initial redistribution of blood flow to vital organs. With prolonged asphyxial insult and failure of compensatory mechanisms, cerebral blood flow falls, leading to ischemic brain injury.



Neonatal encephalopathy- clinical signs

- **Disturbance in neurologic function, demonstrated by** :
- Difficulty in maintaining respirations
- Hypotonia
- Altered level of consciousness
- Depressed or absent primitive reflexes, seizures, poor feeding

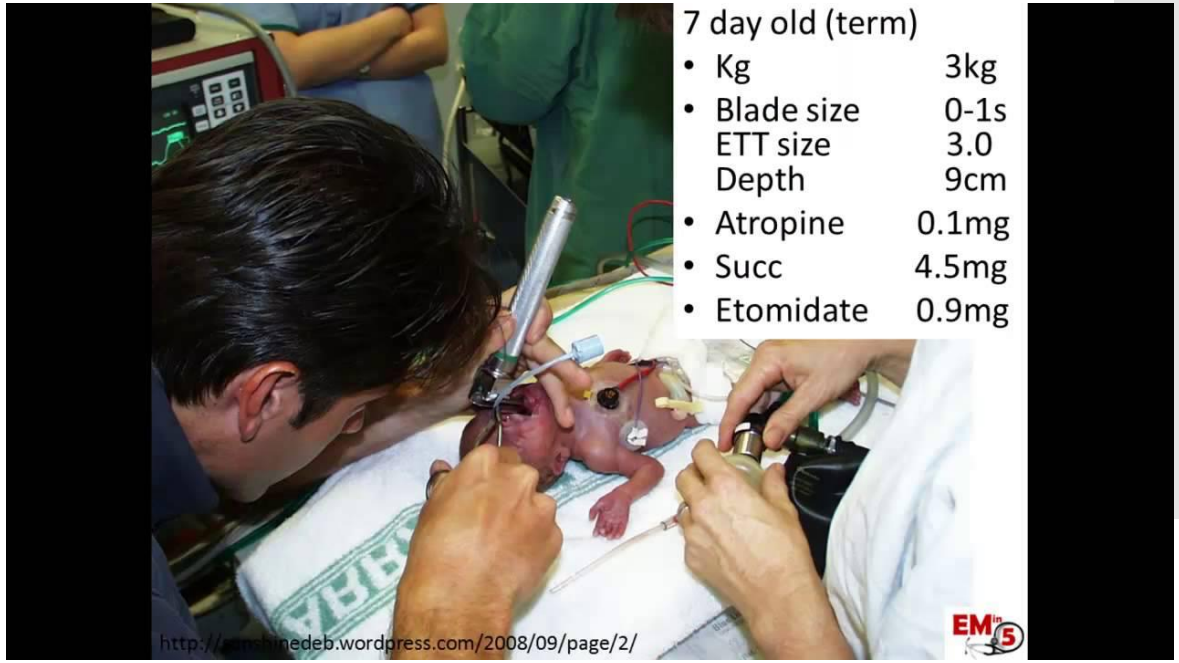


Diagnosis (AAP, ACOG)

all of the following must be present for the designation of perinatal asphyxia severe enough to result in neurologic injury

- Profound metabolic or mixed acidemia (pH < 7 in an umbilical artery blood sample, if obtained)
- Persistance of an Apgar score of 0-3 for longer than 5 minutes
- Neonatal neurologic sequele (seizures, coma, hypotonia)
- Multiple organ involvements (kidneys, lungs, liver, heart, intestines)

- Lab studies
- Imaging studies
- Additional studies

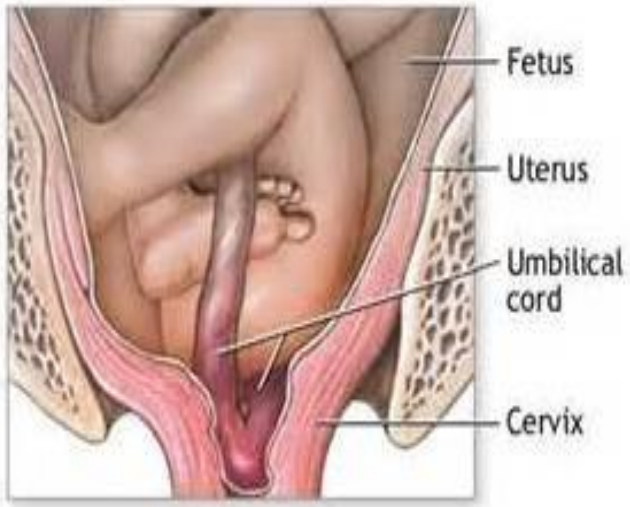


Etiology

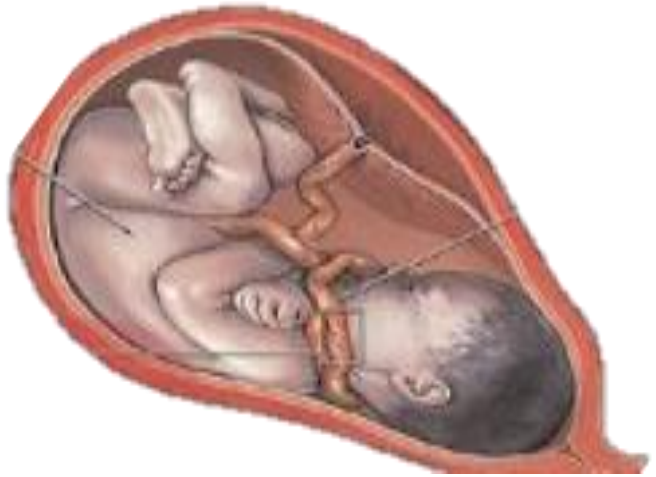
(Also the important role of the placental analysis (chronić villitis, chorioamnionitis)

- Etiology multifactorial – but typically results from a serious hypoxic- ischemic event occuring before or during labor or at delivery,
- Maternal problems- hypotension, preeclampsia, chronic vascular disease
- Primary placental perfusion problems (true knot, abruptio placenta, uterine rupture)
- Fetal oxygenation/perfusion problems (fetomaternal hemorrhage, fetal thrombosis)

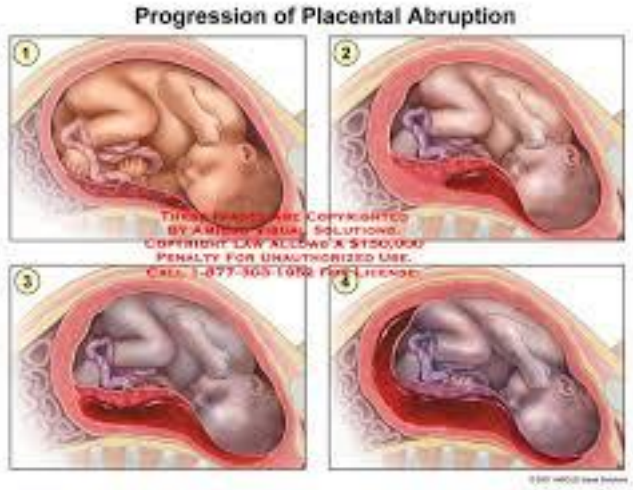
Knotted cord



Prolapsed cord

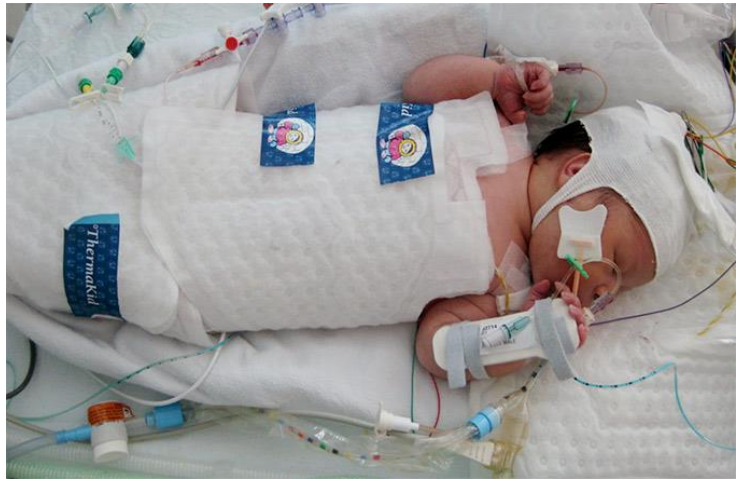


Nuchal cord



Placental abruption

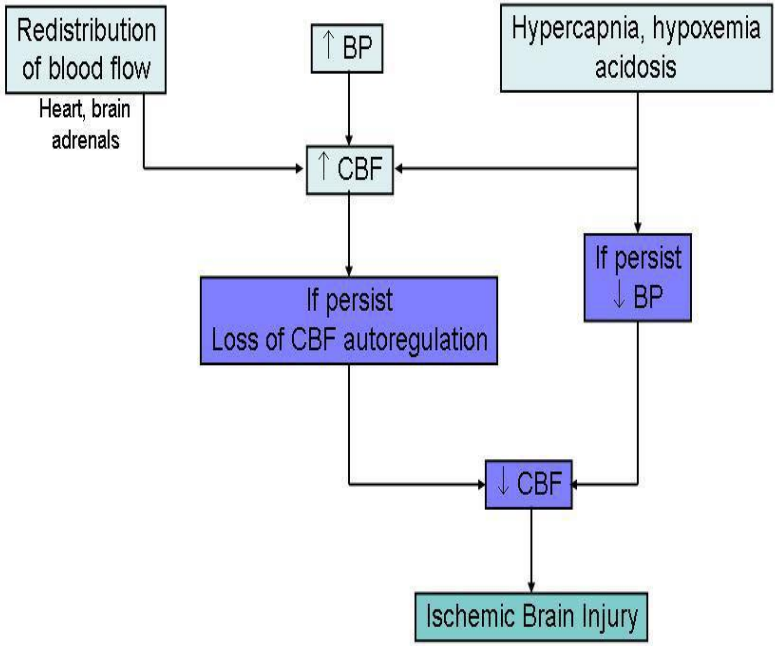
Treatment



- Hypothermia should be induced as early as possible to achieve maximum neuroprotection and edema blocking effect.
- The terapheutic hypothermia must be started within 6 hours from birth

Background – pathophysiology

- Global ischemic events may cause **decreased perfusion** and i**njury** to vulnerable watershed regions of the developing brain
- Poor perfusion leads to lack of **oxygen** and **glucose**, resulting in Energy failure and loss of mitochondrial function, which is the central cellular problem underlying HIE

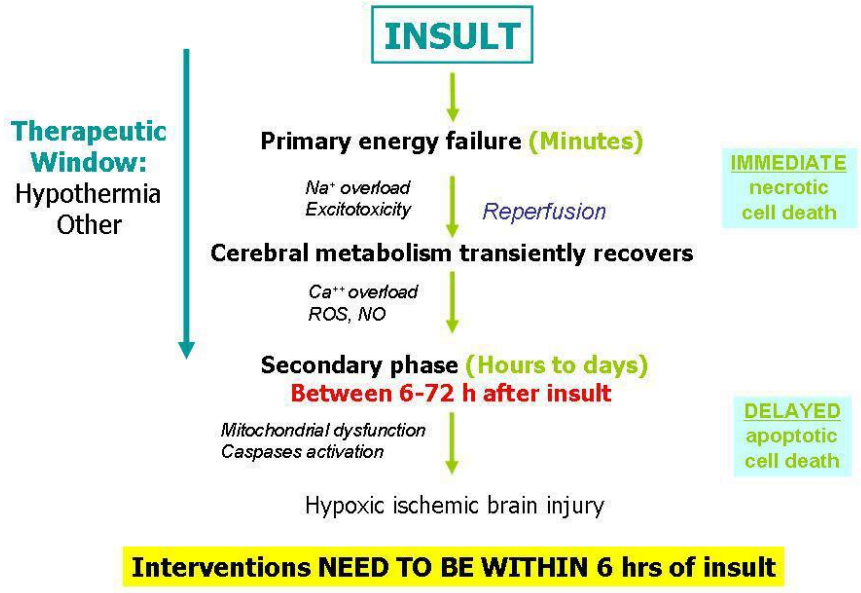


Backround- pathophysiology

- In fetuses and newborns suffering from acute asphyxia after the adjustments fail, the **CBF can become pressure passive** , at which time the brain perfusion depends on systemic BP

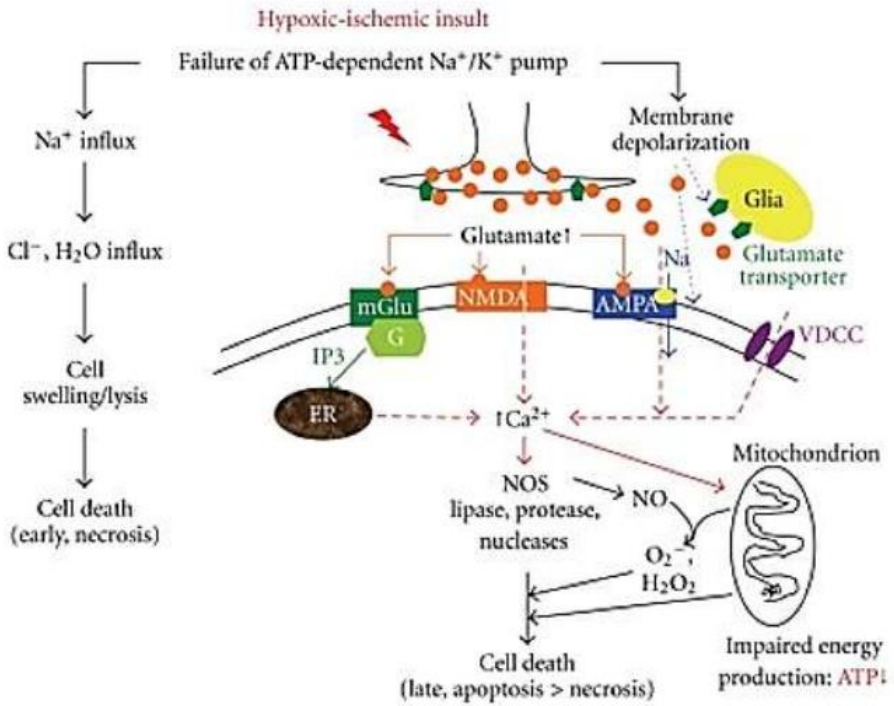
- CBF falls below critical levels which leads to brain injury secondary to diminished blood suply and a lack of sufficient oxygen

- This leads to intracellular Energy failure



Background - pathophysiology

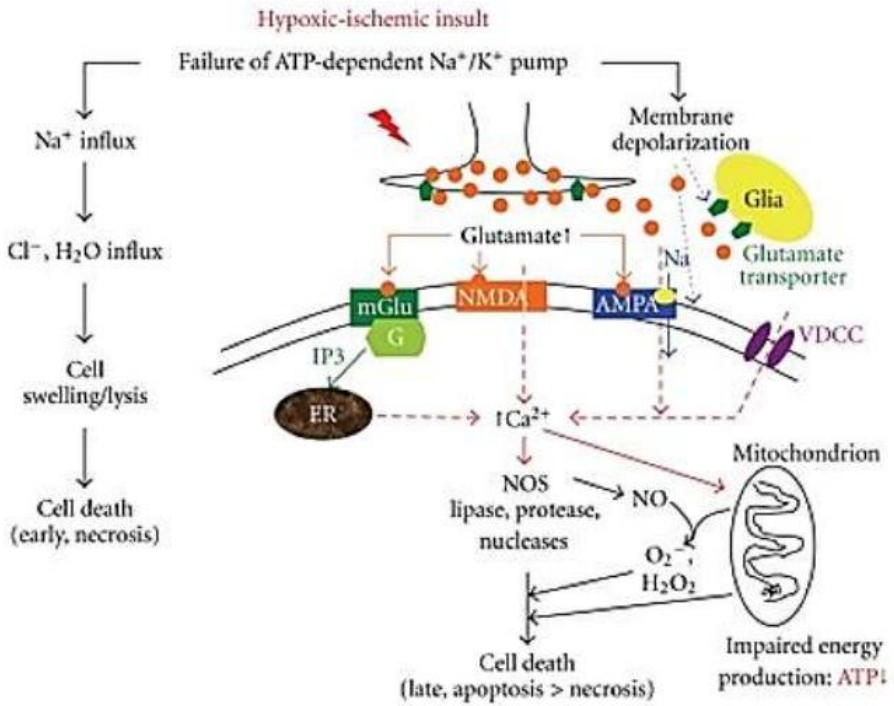
Without sufficient oxygen and glucose, adenosine triphosphate (ATP) production diminishes and Energy depdendent membrane pumps fail, resulting in neurotransmiter release(glutamate), induction of destructive enzymes and free radical damage



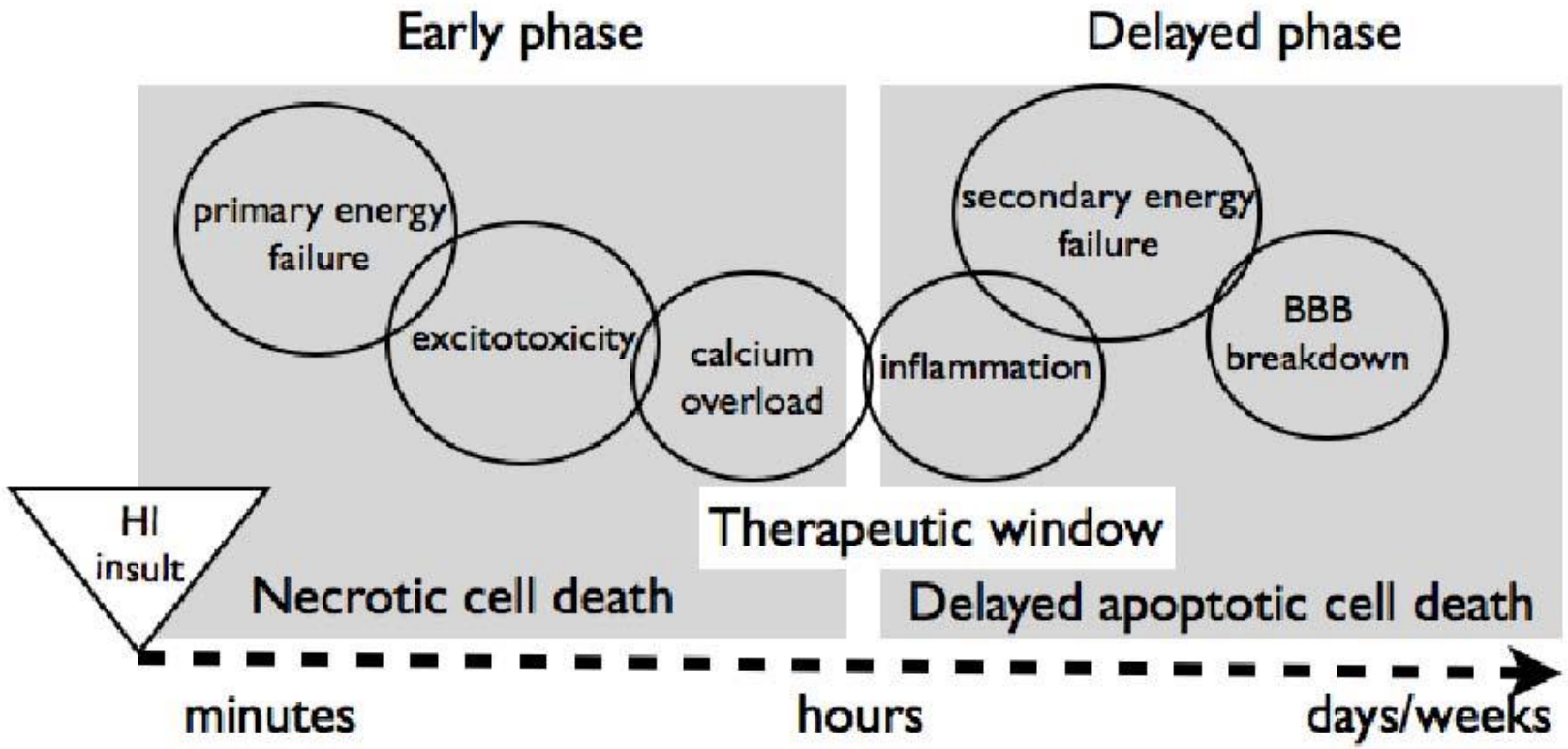
Background - patophysiology

Excitotoxic **glutamate receptor-mediated injury** can occur through overactivation of NMDA receptors, intracellular calcium accumulation- which triggers apoptosis.

Activation of AMPA receptors may result in necrotic death of mature oligodendrocytes



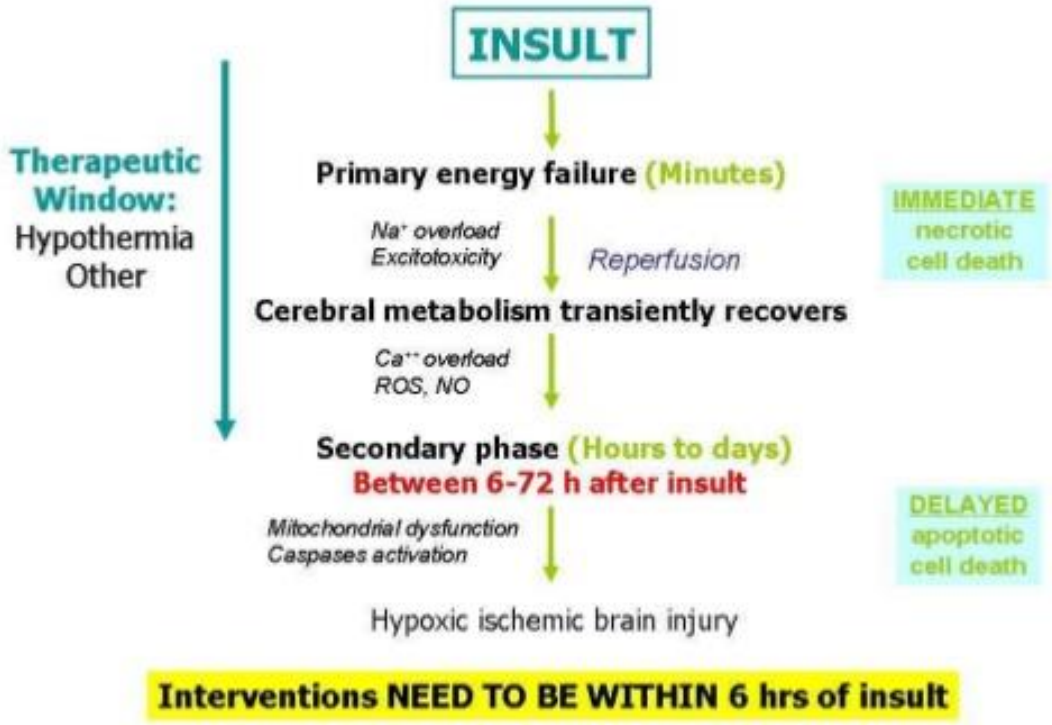
If the newborn is resuscited afer a hypoxic –ischemic event, brain tissue reperfusion occurs, which may propagate series of cellular events that evolve rapidly through reactive oxygen species, cytokines and caspases- that induce cell dysfunction and death



HIE – pathophysiology – delayed phase of neuronal injury

Following the initial phase of Energy failure from the injury, cerebral metabolism may recover following reperfusion, only to deteriotare in a secondary Energy failure phase.

It starts 6-24 hrs after and is characterized by miotochndrial dysfunction and inititation of the apoptotic cascade.

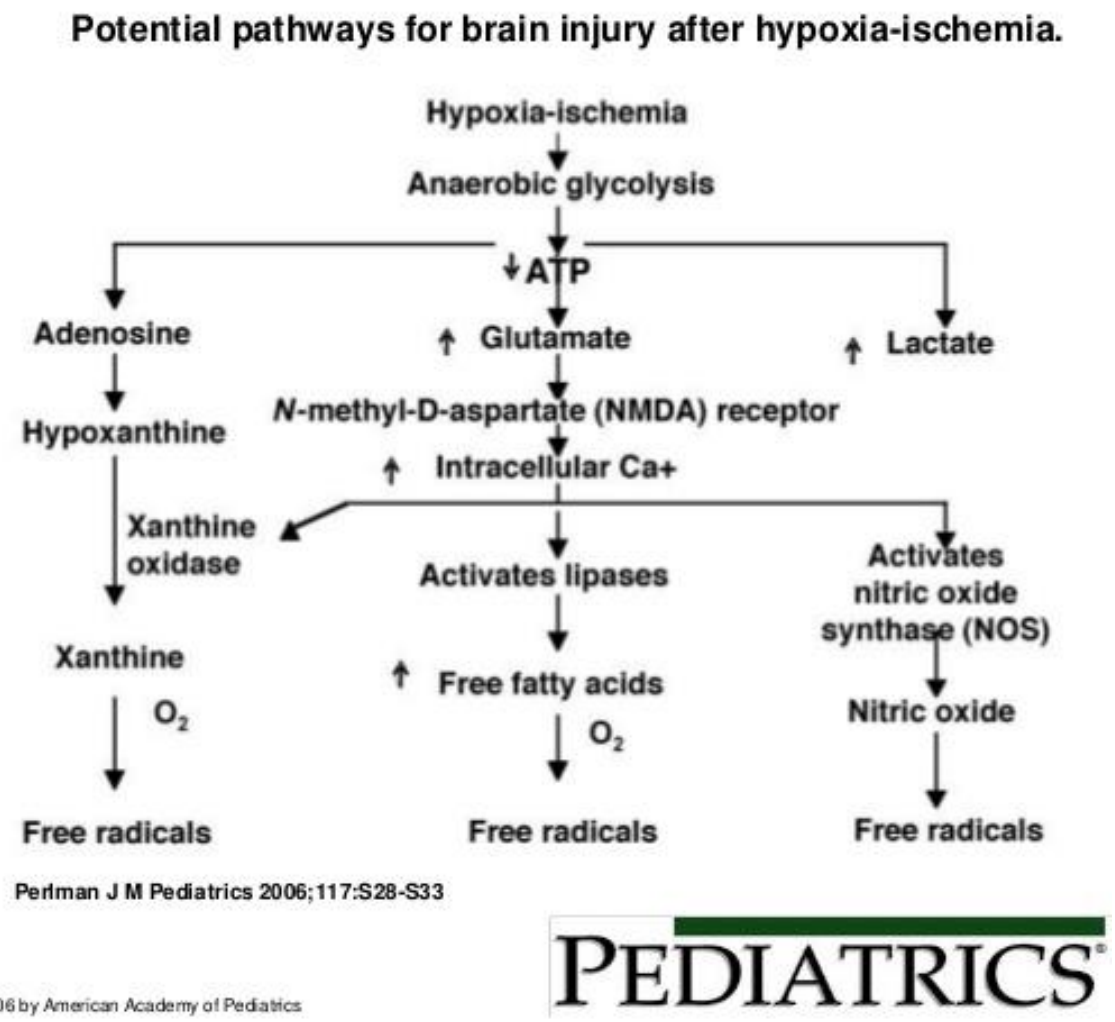


Background- patohysiology

At the cellular level, neuronal injury is an evolving proces.

The magnitude of the final neuronal damage depends on the duration and severity of the initial insult, combined with the effects of reperfusion injury, and apoptosis.

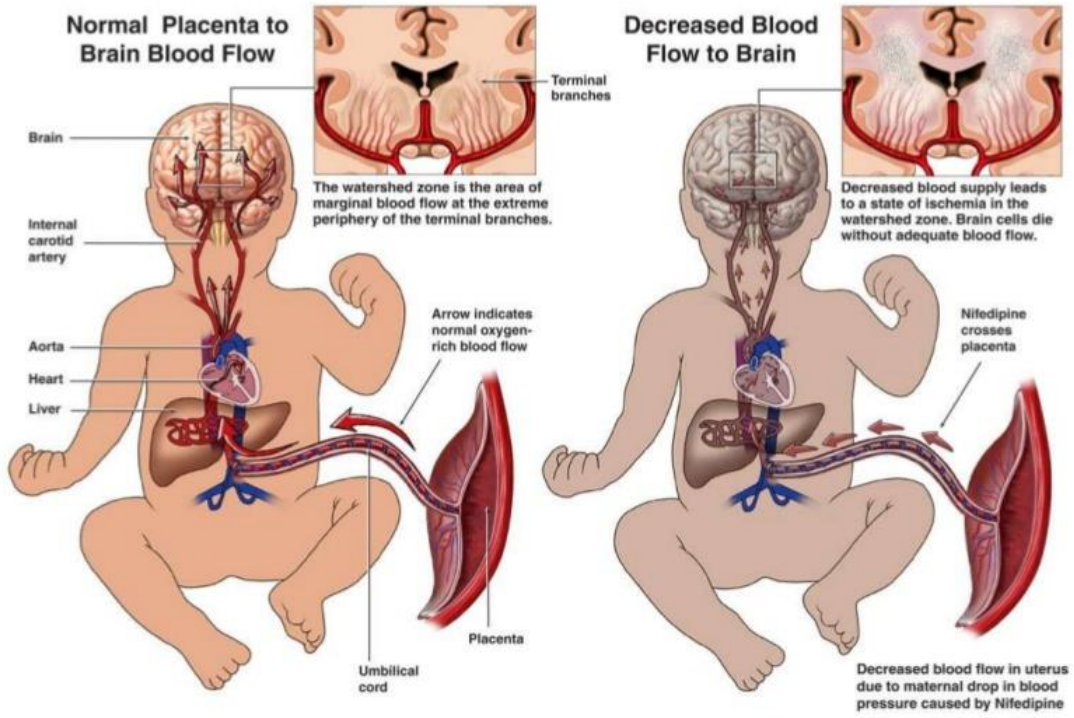
At the biochemical level, a large cascade of events follow HIE



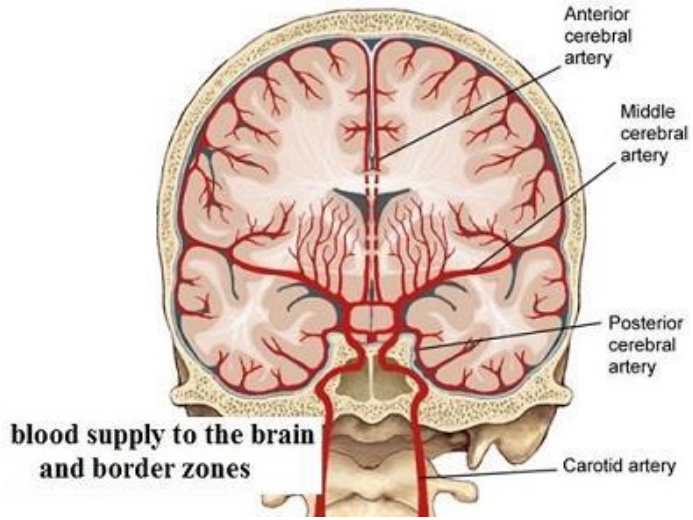
HIE – pathophysiology

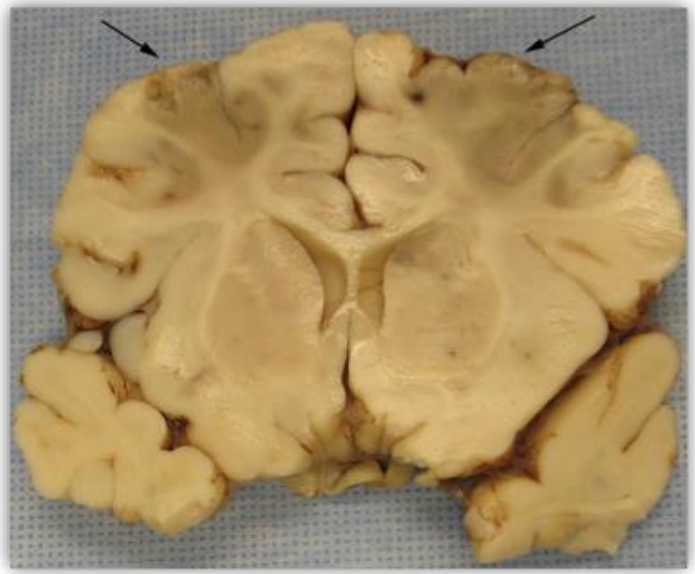
The pattern of injury seen after hypoxia – ischemia can be largely explained by the excitatory circuit at this age (putamen, thalamus)

Finally, developing oligodendroglia is uniquely susceptible to hypoxia-ischemia. This white matter injury may be the basis for the disruption of long-term learning and memory faculties in infants with hypoxic- ischemic encephalopathy



HIE – pathophysiology





diagnosis

Is made by careful birth history, neurologic examination, lab studies

- Birth histories consistent with HIE include description of intrauterine stress (fetal heart rate tracing abnormalities, meconium passage, history of difficult labour and delivery)

- Newborn with HIE typically have respiratory failure requiring positive pressure ventilation, may develop cardiac arrest,
- Low Apgar scores (< 5) at 5 min and 10 min of life
- pH of fetal umbilical artery less than 7,0; or base defcit greater than or equal to 12-15. mmol/l; or both

Clinical signs and symptoms

The clinical presentation of affected neonates may evolve over a period of 72 hrs, and is often categorized using sarnat staging :

- Mild encephalopathy
- Moderate encephalopathy
- Severe encephalopathy

Sarnat & Sarnat staging (1976)

	Stage 1	Stage 2	Stage 3
Consciousness	hyperalert	Lethargic of obtunded	Stupor or coma
Activity	Normal	Decreased	Absent
Neuromuscular control Muscle tone Posture Strech reflexes	 Normal Mild distal flexion Overactive	 Mild hypotonia Strong distal flexion Overactive	 Flaccid Intermittent decerebration Decreased or absent
Primitive reflexes Suck Moro Tonic neck	 Weak Strong Slight	 Weak or absent Weak, incomplete Strong	 Absent Absent Absent
Autonomic function Pupils Heart rate	 Normal Tachycardia	 Miosis Bradycardia	 Mydriase or variable, unequal Variable
Seizures	None	Common	Uncommon

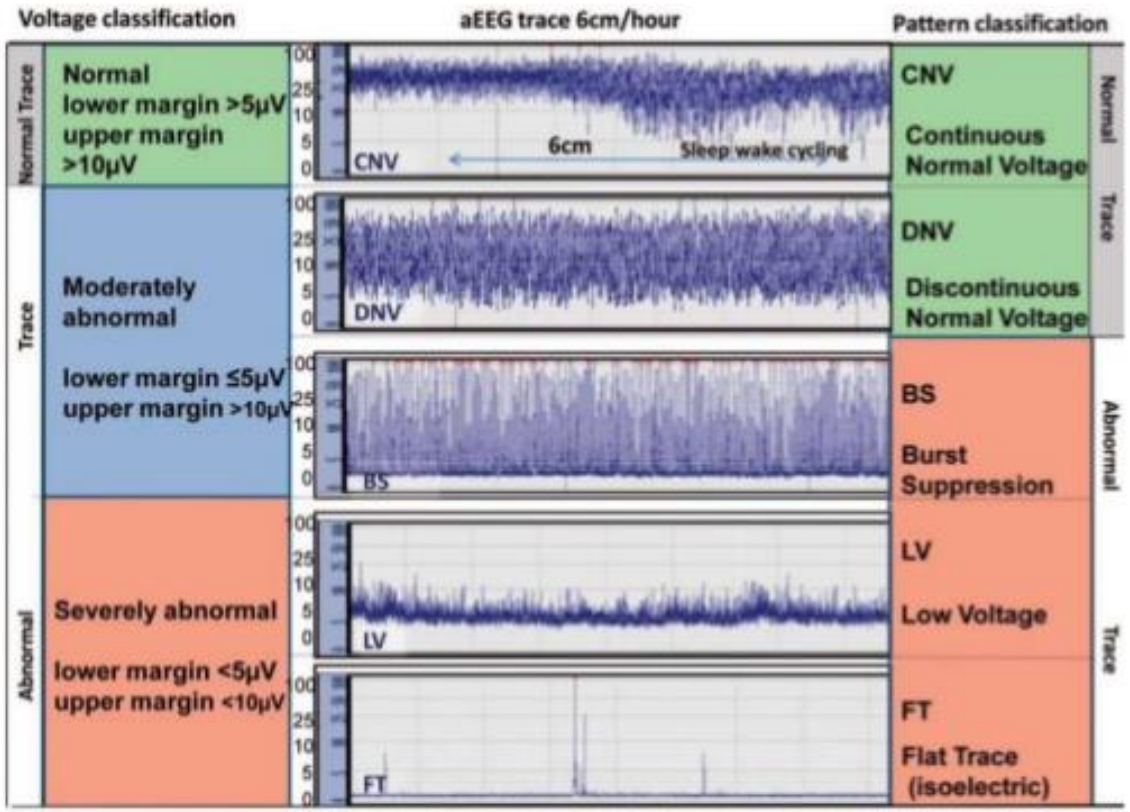
Stage 0 = Normal

Diagnosis

HIE is the most common cause of seizures in the neonatal period

Seizures may be noted in the first 24 hours after birt h

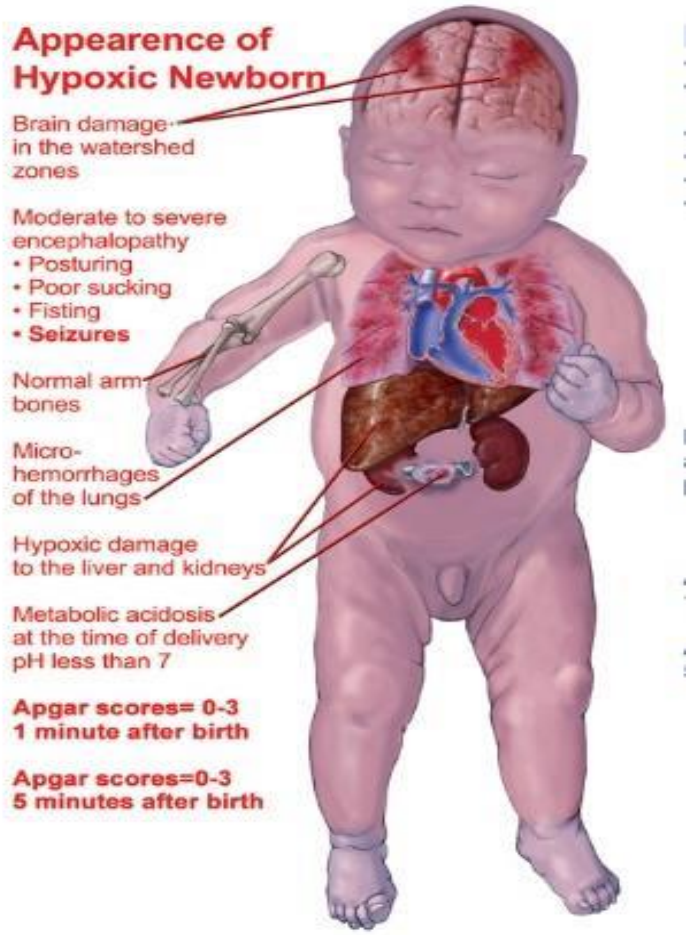
Apneic events and vital sign instability may also be presentation of seizure activity



From Thoresen M, et al. Effect of hypothermia on amplitude-integrated electroencephalogram in infants with asphyxia. Pediatrics. 2010 Jul;126(1):e131-9. PMID:9563847 Reprinted with permission of The American Academy of Pediatrics

Diagnosis

Serial examinations and monitoring are important to assess neonates with HIE since the clinical signs and symptoms often evolve over time



Neonates with mild HIE may develop a normal examination by 12 hours of age , whereas neonates with more severe HIE remain **stuporous**, often with **respiratory failure** and **dialted pupils that are fixed** and poorly reactive to light

In general, neonates who have a quick clinical recovery and a normal examination a 1 week of age typically have normal long-term outcomes

Laboratory and ancillary studies

- Multisystem organ failure is comon, evidenced by metabolic and hematologic abnormalities, hepatic, renal gastrointestinal and cardiac dysfunction

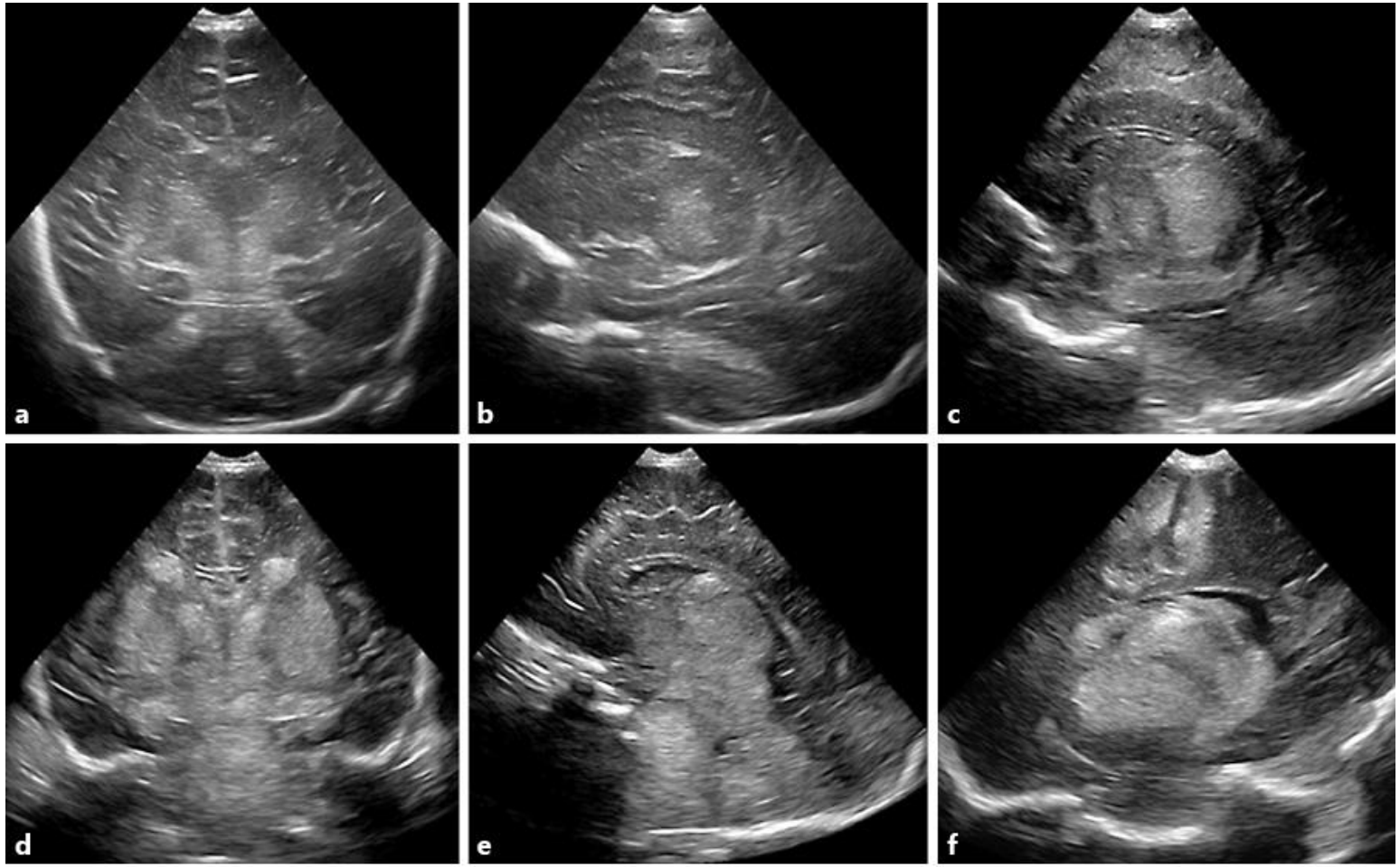
- Basic metabolic panel and an arterial blood should be obtained shortly after delivery
- Comlete blood count
- Coagulation studies
- Liver function labs
- creatinine

Neuroimaging

Cranical ultrasonography (US) can be used as a first line imaging tool in newborns with HIE

Subtle signs of HIE may be difficult to detect with US

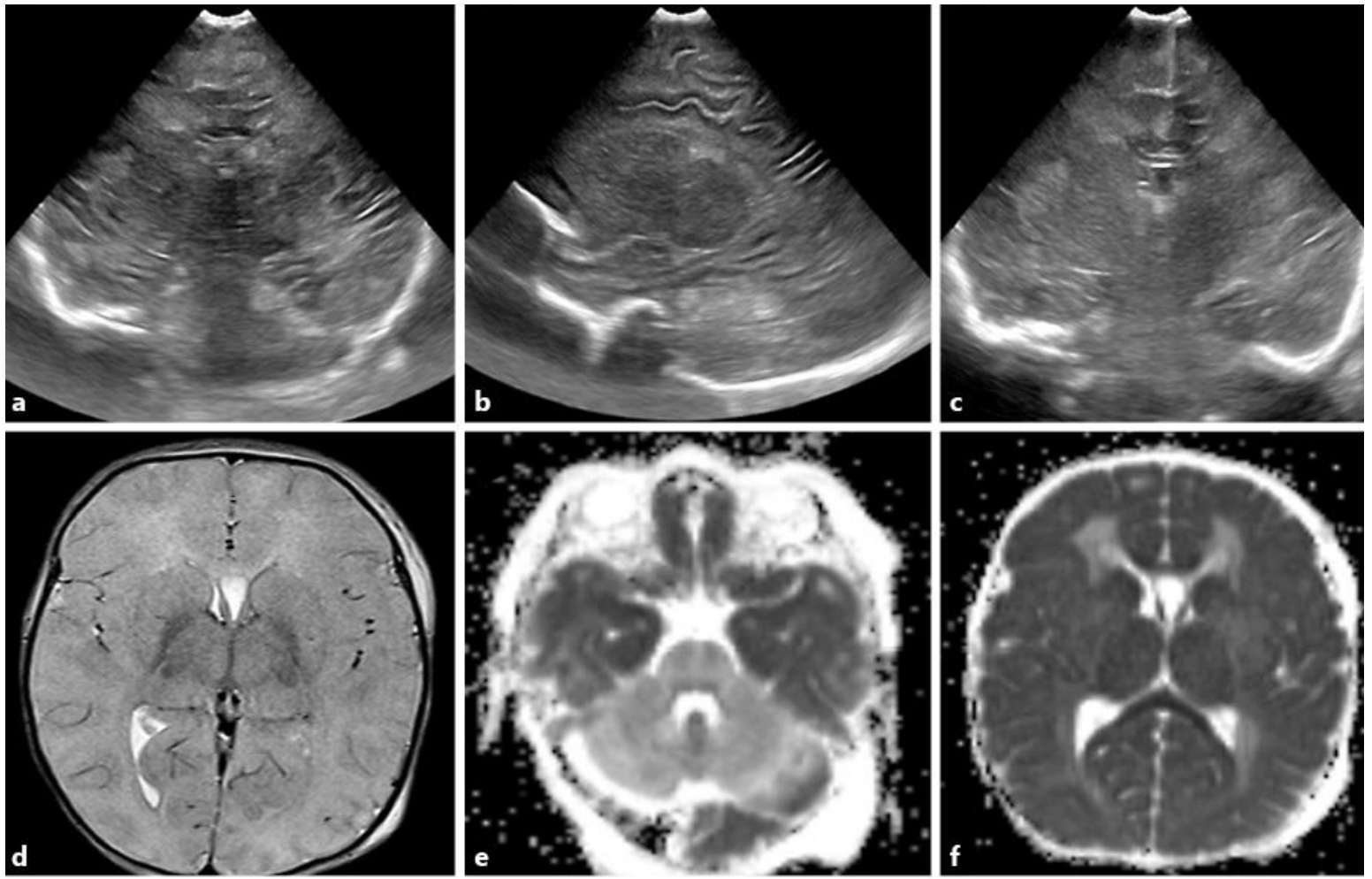
In Severe HIE – US may demonstrate increased focal or diffuse brain parenchyma echogenicity, slit like ventricules, obliteration of extracerebral CSF

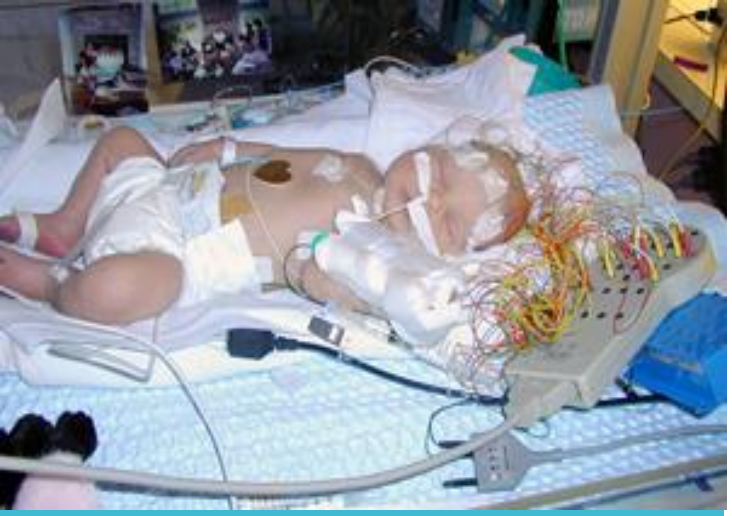


Neuroimaging

MRI is the study of choice for neonates with HIE,

MRI performed in the newborn period has a high predictive value in neonates





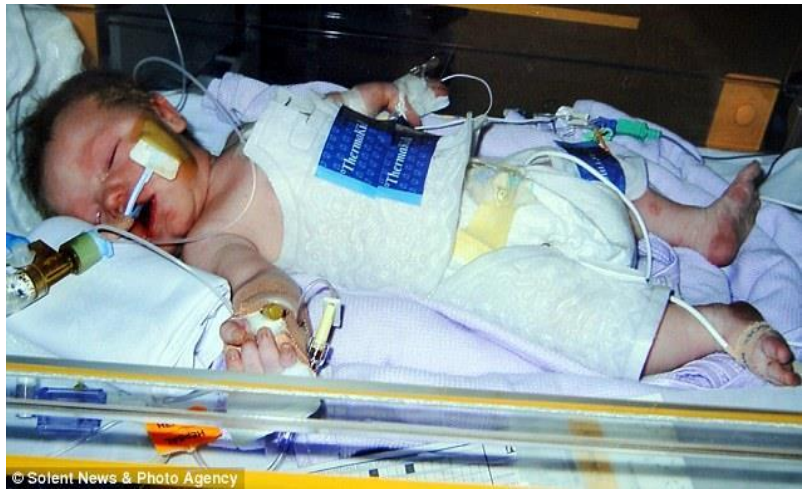
Management

- Initial steps should focus on promoting adequate oxygenation, ventilation, circulation.
- Serial monitoring of laboratory tests (blood gas basic metabolic panel, ionized calcium, lactate, CBC, liver enzymes, coagulation studies)
- Correction of metabolic derangements (hypoglycemia, hyperglycemia, hypocalcemia)
- Assesment of clinical and electrographic seizure activity
- Inotropic agents may be useful for hypotension
- Close monitoring of renal function/ electrolytes

Management

TH (therapeutic hypothermia) 72 hours of cooling to 33.5 +/-0.5° followed by slow rewarming, 0.5° per hour to normothermia is now the **standard of care** to treat neonates with moderate to severe HIE

The benefit of TH for improving outcomes of newborns wit HIE was investigated in numerous studies

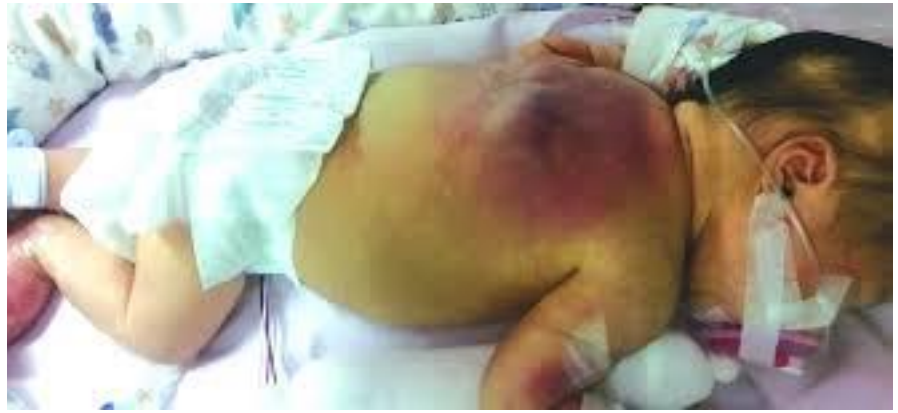


Whole body hypothermia

Selective head cooling

TH – complications

- Arrythmias – bradycardia, ventricular tachycardia
- Persistent acidosis
- Bleeding
- Subcutaneous fat necrosis
- Death



TH

- less death and better neurodevelopmental outcomes for survivors
- TH has not been associated with a significant increase in the rates of major cardiac arrythmia and hypotension or in the need for inotropic agents
- It appears that TH increaes survival without incerasing the rates of major disability, an IQ score below 70, or cerebral palsy in surviving children

Thank you for the attention