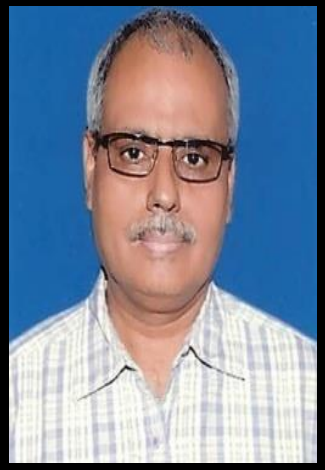
Perinatal asphyxia &

Hypoxic Ischemic Encephalopathy



Dr. Binod Kumar Singh

Professor & HOD, NMCH, Patna
President, IAP Bihar -2019
Vice President, IAP Bihar-2018
CIAP Executive board member-2015
NNF State president, Bihar- 2014
IAP State secretary,Bihar-2010-2011
NNF State secretary,Bihar-2008-2009
Fellow of Indian Academy of Pediatrics (FIAP)

- Chief Consultant

Shiv Shishu Hospital :K-208, P.C Colony.Hanuma Nagar, Patna – 800020
Web site : www.shivshishuhospital.com

OBJECTIVES

- Definition – perinatal asphyxia
- Etiology
- Epidemiology
- Manifestations of PA
- Evaluation and staging of HIE
- Pathophysiology of asphyxial injury
- Management

PERINATAL ASPHYXIA

Perinatal asphyxia is defined as a reduction of oxygen delivery and an accumulation of carbon dioxide owing to cessation of blood supply to the fetus ANTEPARTUM,INTRAPARTUM(90%) OR POSTPARTUM(10%)

Etiology

- Pathologically, any factor which interferes with the circulation between maternal and fetal blood exchange could result in perinatal asphyxia.
- These factors can be maternal factor, placental factor or fetal factor.

Etiology–High Risk Factors

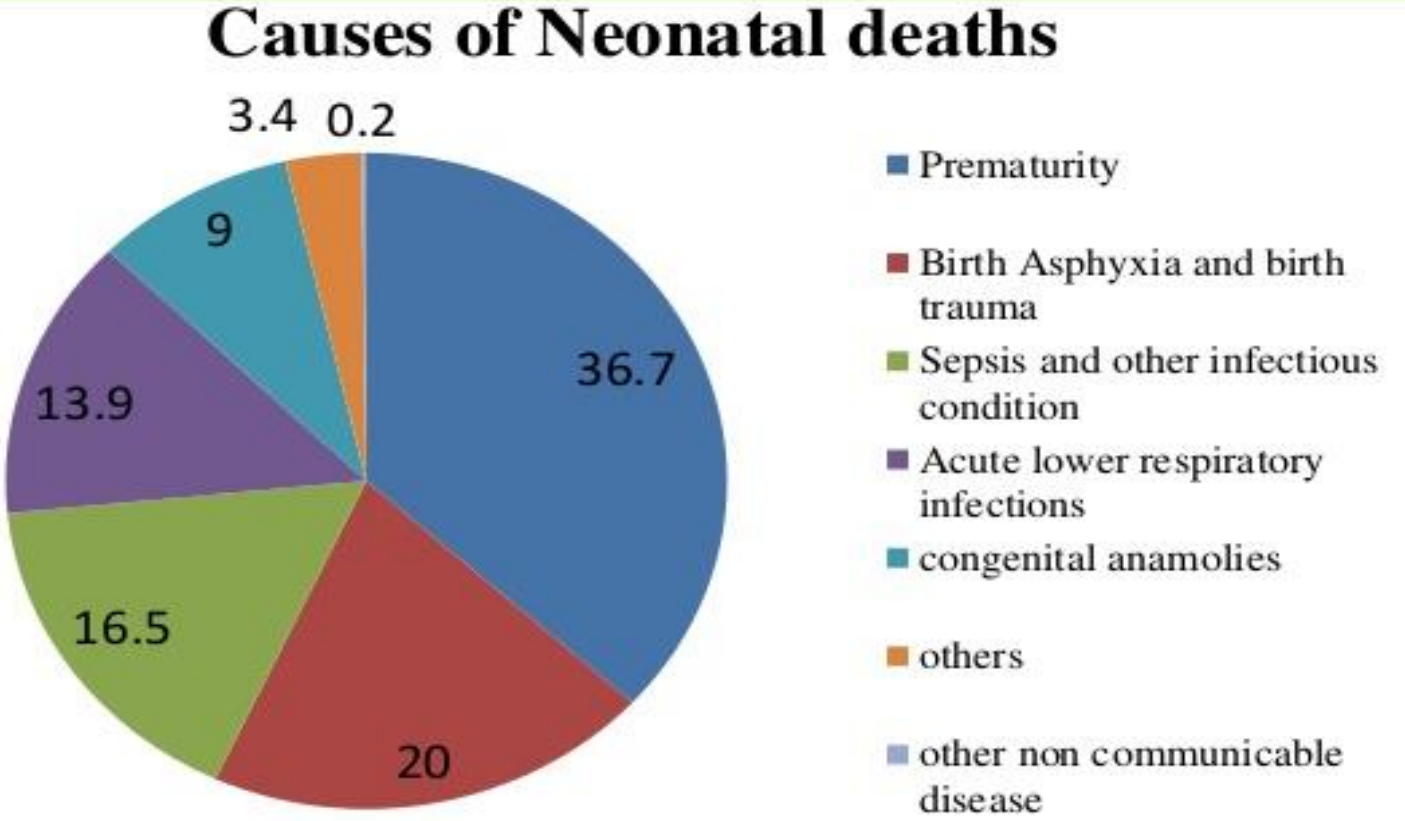
- Maternal factors:
  - Hypoxia due to respiratory or cardiac cause
  - Anemia
  - Diabetes
  - Hypertension
  - Smoking
  - too old or too young(<16 years or >35 years)
- DELIVERY CONDITIONS-
  - Abruption of placenta
  - placenta Previa
  - prolapsed cord
  - Cord tie
  - premature rupture of membrane
  - Prolonged labour
- Fetal factors:
  - Multiple birth
  - congenital or malformed fetus

ESSENTIAL CRITERIA FOR diagnosis of PERINATAL ASPHYXIA AAP

- Profound metabolic or mixed acidosis (pH< 7.00) and a base deficit of >16mmol /litre in umbilical artery cord blood
- Persistence of low Apgar scores less than 3 for more than 5 minutes
- Signs of neonatal neurologic dysfunction (e.g., seizures, encephalopathy, tone abnormalities)
- Evidence of multiple organ involvement (such as that of kidneys, lungs, liver, heart and intestine).

Epidemiology

DISEASE BURDEN(why is it so important?)



Source: *Mengying Li, Colin Mathers, Robert E Black, for the Child Health Epidemiology Reference Group of WHO and UNICEF, Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000, The Lancet, Volume 379, Issue 9832, 9–15 June 2012, Pages 2151-2161*

Primary cause of death: NNPD

Cause	Deaths (n = 1800)
Prematurity	27 %
Infection	17 %
Perinatal hypoxia	29 %
Malformation	09 %
Other causes	18 %

Report of the National Neonatal Perinatal database ,2002-2003

PATHOPHYSIOLOGY

1) .Birth asphyxia causes reduction of arterial oxygen concentration

2) Accumulation of CO_2 (hypercarbia)

3.) Fall in blood pH (acidosis)

- Initially-

Hypoxia

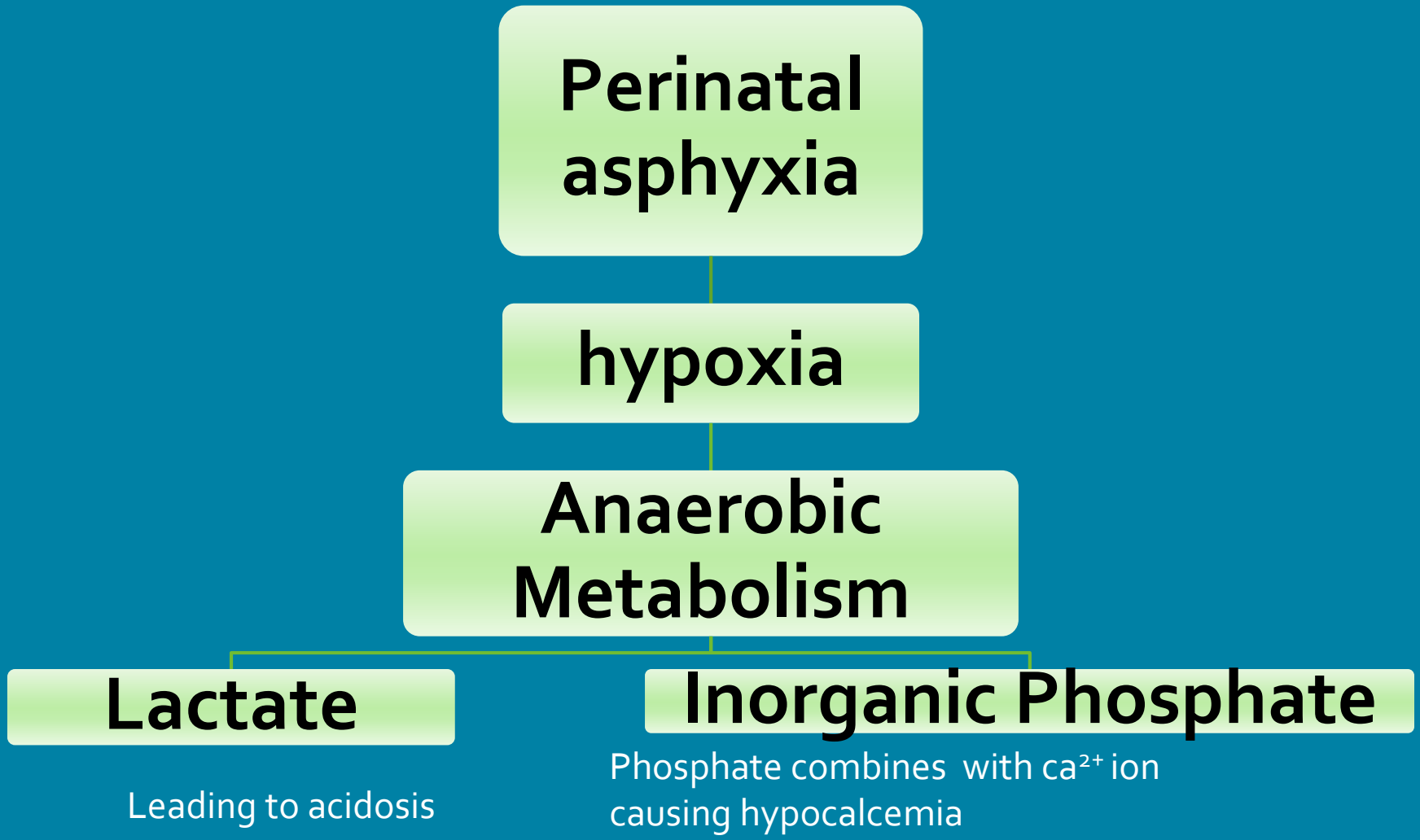
Diving sea reflex

Shunting of blood to

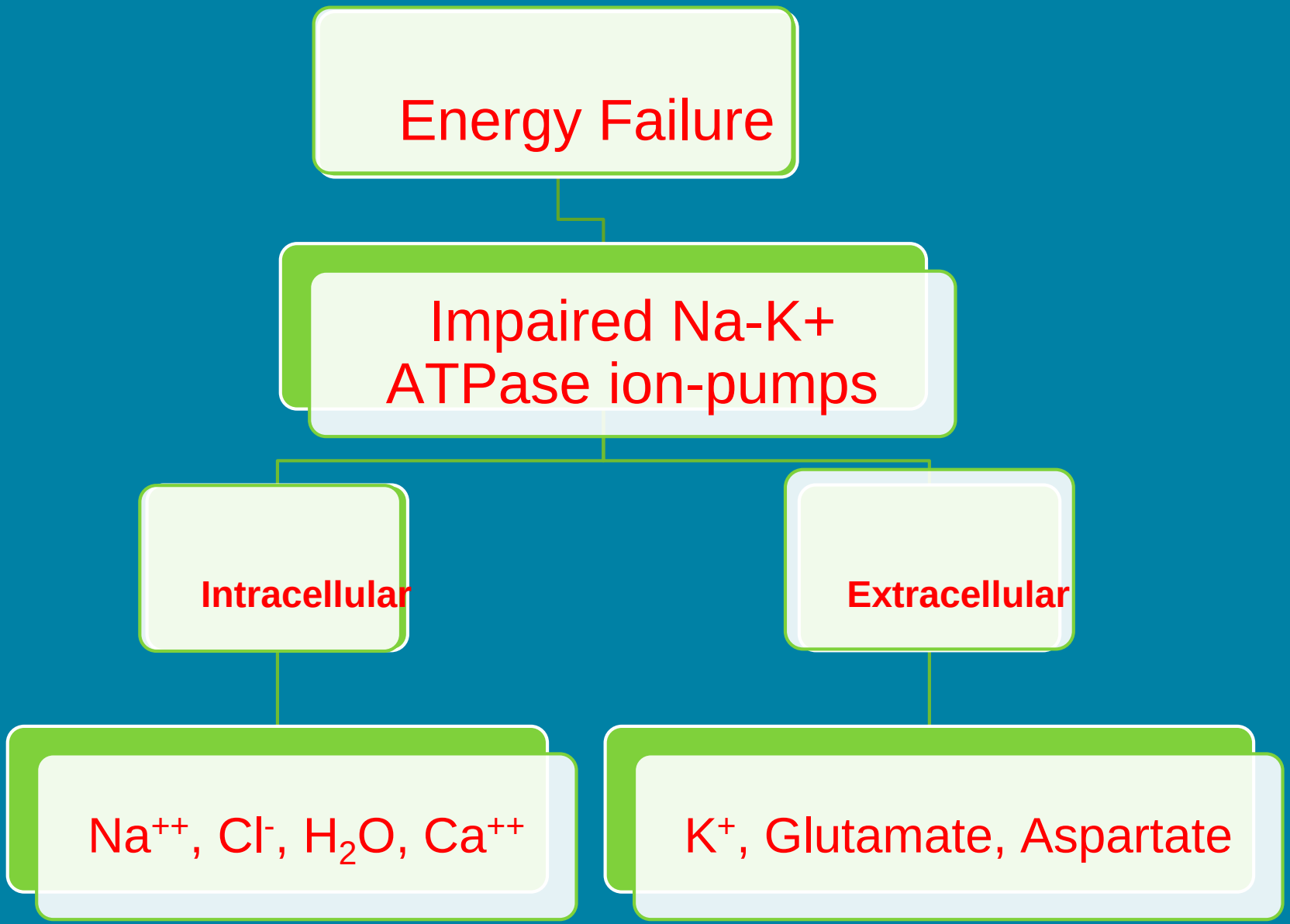
- ✔ Brain
- ✔ Heart
- ✔ Adrenal gland

Away from lungs, kidney, gut & skin

If it continues……



Anaerobic metabolism leads to failure of the pumps



Ca2+ causes activation of enzymes like lipase,protease, ROS)

Pathophysiology

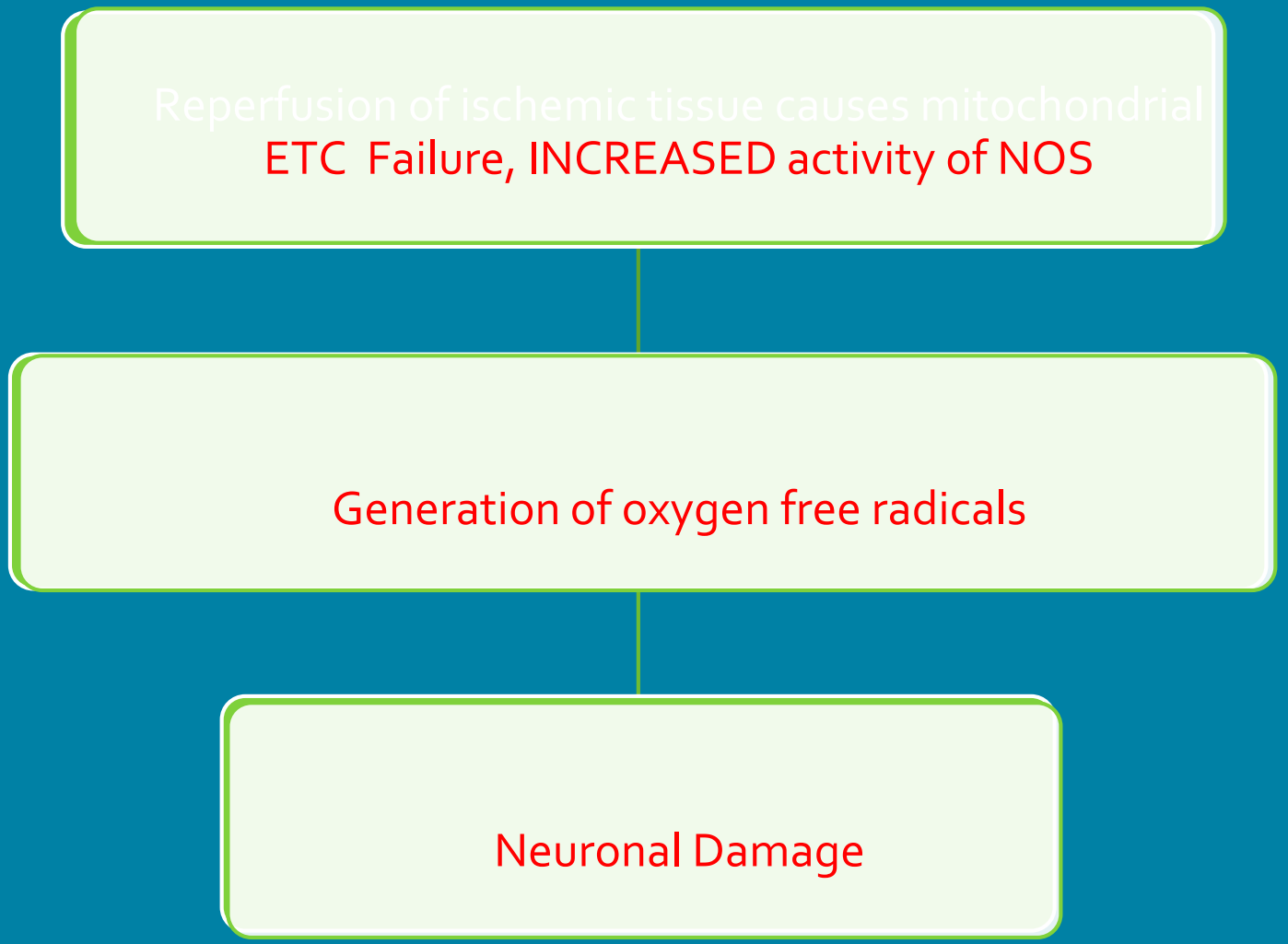
Accumulation of AA (glutamate) in damaged tissue.

Increased amount of intracellular Na & Ca

Tissue Swelling

Cerebral Oedema

Again if there is reperfusion , it leads to formation of ROS even aggravating the damage



CLINICAL MANIFESTATIONS-

- Clinical manifestations-

multi organ involvement almost every organ is affected

- Target organs of perinatal asphyxia
  - Kidney 50%
  - Brain 28%
  - Heart 25%
  - Lung 25%
  - Liver, Bowel, Bone marrow < 5%

t/t is oriented towards the severity of organ dysfunction by providing appropriate support for recovery

- Though kidney is the most common affected organ(50%),we are most concerned about asphyxic injury to the brain because it can kill the neurons or lead to long term neuromotor deficit

- In more pronounced cases an infant will survive but will have damage to the brain manifested as either mental or physical disability

SYSTEMIC MANIFESTATIONS

Brain(28%)- HIE, Intracranial hemorrhage, infarction, seizure

Heart(25%)- Myocardial dysfunction,

Valvular dysfunction, CCF

Lungs(23%)- Meconium aspiration, Pulmonary hemorrhage, edema, Pneumothorax, pneumonia,

PPHN, Surfactant depletion, resp.failure

Kidney(50%)- Hematuria, ARF, ATN, RVT

GIT- NEC, Paralytic ileus, Hepatic dysfunction

SYSTEMIC MANIFESTATIONS

- **Hematologic-** DIC, sepsis
- **Endocrine-** SIADH, Adrenal hemorrhage
- **Metabolic-** Hypoglycemia
  Hypocalcaemia
  Hyponatremia
  Acidosis

Staging of HIE (Sarnat & Sarnat staging)

	Stage-I	Stage-II	Stage-III
Level of consciousness	Hyper-alert	Lethargic	Stupor/coma
Muscle Tone	Normal	Hypotonic	Flaccid
Posture	Normal	Flexion	Decerebrate
DTR/Clonus	Hyperactive	Hyperactive	Absent
Myoclonus	Present	Present	Absent
Moro Reflex	Strong	Weak	Absent

HIE Staging

	Stage-I	Stage-II	Stage-III
Pupils	Dilated	Constricted	Unequal
Seizures	None	Common	Decerebrate
Duration	< 24 hrs	24 hrs-14 d	Days & Weeks
Outcome	Good	Variable	Death or Severe Deficit
EEG	Normal	Low Voltage	Bursts

CLASSIFICATION OF HIE (LEVENE)

Feature	Mild	Moderate	Severe
Consciousness	Irritable	Lethargy	Comatose
Tone	Hypotonia	Marked	Severe
Seizure	No	Yes	Prolonged
Sucking / Resp.	Poor Suck	Unable to suck	Unable to sustain spont. Resp.

Management

MANAGEMENT IS MAINLY SUPPORTIVE IT SHOULD BE DIRECTED TOWARDS

1. Early detection

2. Determining the severity of dysfunction of critical organs

3 . Providing appropriate support for self recovery to happen

1.DELIVERY ROOM CARE

Management should start in the delivery room it self. Health care professionals should we trained and the baby should be transferred to NICU IF

1.Apgar score is 0-3 at 1 minute

2.Prolonged bag and mask ventilation is required ≥ 60 s

3. Chest compression is required for resuscitation

Umbilical artery cord blood should be obtained for ABG analysis and appropriate diagnosis

2.SUPPORTIVE CARE IN NICU

TABCFMFMCF

- T - Temperature
- A - Airway
- B - Breathing
- C - Circulation
- F - Fluid
- M - Medications
- F - Feed
- M - Monitoring of vitals
- C - Communication
- F - Follow up

Relevant investigations-

- Blood Sugar
- ABG
- SpO_2 monitoring
- Serum electrolytes

Investigations (continued)

- Renal Function Tests:
  - **Blood Urea,**
  - **Serum Creatinine.**
- Liver Function Tests
- Coagulation Profile
  - **PT and**
  - **PTT.**

NICU CARE -

.

1. *Maintain normal temperature*
   - Avoid Hyperthermia (thermo neutral environment)

2. *Maintain normal oxygenation and ventilation*
   - Maintain saturations between 90% and 95% and avoid any hypoxia or hyperoxia
   - Avoid hypocarbia, as this would reduce the cerebral perfusion
   - Avoid hypercarbia, which can increase intracranial pressure and predispose the baby to intracranial bleed.

3. *Maintain normal tissue perfusion (It is the main corner stone of therapy)*

- Start intravenous fluid
- Administer IONOTROPICS to maintain adequate cardiac output, as required.
- Do not restrict fluid as this practice may predispose the babies to hypoperfusion.
- Restrict fluid only if there is hyponatremia (Sodium<120 mg%) secondary to syndrome of inappropriate secretion of ADH (SIADH) or if there is renal failure.

4. *Maintain normal hematocrit and metabolic milieu*

- maintain blood glucose levels between 75 mg/dL and 100 mg/dl.
- Correct Anaemia and maintain haematocrit between 45% and 55%.
- Check blood gases to detect metabolic acidosis as needed and maintain pH above 7.30.
- In case of severe asphyxia, provide calcium in a maintenance dose of 4 mL/kg/day (of 10% calcium gluconate)

5. *Treat seizures*
6. *Nutrition:*
   - *Start oral feeding once baby is hemodynamically stable*
7. *Miscellaneous*
   - Administer Vitamin K (1 mg IM) to all infants with perinatal asphyxia

8.communication and follow up

all newborns with stage 2 and 3 HIE should have proper neurological assessment and appropriate interventions if required

The parents should be informed properly about the prognosis

HIE STAGE 1 -98%-100% WILL HAVE NORMAL OUTCOME

MORTALITY ,1%

HIE STAGE 2-20% TO 37% have abnormal neurological outcome

HIE STAGE3 - 50% DIE & those alive will have 100% sequelae

Anticonvulsants

metabolic causes of seizures should be checked and treated appropriately

- Control Seizures:
  - Phenobarbitone:
    - Loading Dose: 20 mg/kg slowly
    - Maintenance Dose: 5 mg/kg/day
  - Phenytoin as a second line drug
  - Lorazepam
    - (0.05-0.1 mg/kg/dose I. V.) for seizures not responding to Phenobarbitone and/or Phenytoin.

Levetiracetam-Loading dose-20 mg/kg iv
Maintenance dose-10 mg/kg/day iv

Special investigations

Includes
1. *EEG*
2. *aEEG*
3. *Cranial USG*
4. *CT SCAN*
5. *MRI*

These are not indicated routinely . Mainly used for prognosticating long term outcomes

Electroencephalography (EEG):

- The prognosis is likely to be poor if the EEG shows:
  - Long periods of inactivity (more than 10 seconds)
  - Brief period of bursts (less than 6 seconds) with small amplitude bursts
  - Interhemispheric asymmetry and asynchrony
  - Isoelectric and low voltage (less than 5 microvolts)

Amplitude-integrated electroencephalography (aEEG)

- Simplified form and can be performed on continuous basis in NICU.
- Following abnormalities would indicate poor prognosis:
  - Wide fluctuations in the amplitude with the baseline voltages dropping to near zero
  - Peak amplitudes under 5 mV
  - Seizure spikes

Specific management

Therapeutic hypothermia

- Started within 4-6 hrs & continued for 72 hrs of life
- Moderate to severe HIE
- Both total body & head cooling is safe & effective
- Target temperature is 33 to 34

Inclusion criteria-

A- Post menstrual age > 36 wk , B.wt ->2 kg.

B- Evidence of fetal distress by any 1 of the following:

- H/o acute perinatal event
- pH < 7 or base deficit > 16 mmol/l in cord gas or post natal blood within 1 hr of life
- Apgar score < 5 at 10 mint
- Assisted ventilation initiated at birth & continued for at least 10 mint

C- Evidence of mod to severe neonatal encephalopathy by exam/ or aEEG as follows:

- 1- Primary method for determining is physical exam
- 2- If shows mod to severe encephalopathy aEEG should be perform
- 3-If physical exam is unreliable aEEG should be perform

4- patterns on aEEG that indicate mod to severe encephalopathy with minimum 20 minutes recording:-

- A- Severely abnormal- upper margin < 10 mcv
- B- Moderately abnormal- upper margin > 10 mcv & lower margin < 5 mcv
- C- seizure identified by aEEG

Exclusion criteria

- Chromosomal abnormality
- Severe cong. anomalies
- Symptomatic systemic cong. viral infection
- Symptomatic systemic cong. bacterial infection
- Bleeding diathesis
- ICH

Cooling devices

1 .Whole body cooling devices

- a) High technology devices like tecotherm, blanketrol, medithers
- b) Low technology devices
- Selective head cooling device :examples- olympic cool cap system

Mechanism of action of TH-

- 1-Decreased cerebral metabolism & blood flow- decreased energy requirement & cerebral edema
- 2-Decreased brain lactic acid, glutamate ,and nitric oxide concentrations- less excitotoxic & oxidative injury
- Inhibits protease activation, mitochondrial failure, free radical damage, lipid peroxidation- less apoptosis & necrosis

How to initiate whole body hypothermia

- Counsel the parents
- Prepare the cooling system for operation
- Set the cooling blanket temp 33 to 34 c
- Monitor & document the infants pre-cooling vital signs
- Place central & arterial lines before starting hypothermia
- Gently insert the rectal probe 2 cm into the infant's rectum & secure to the infant's leg with tap

- Place the infant on the warmer in supine position with the entire head & body resting on the cooling blanket
- The infant must lie directly on the cooling blanket wearing a diaper only.

Monitoring after initiating TH-

- For 72 hrs (3 days)
- Vitals 1 hrly
- Neurological monitoring 12 hrly
- Urine output ,glucose , skin integrity 6 hrly
- ECG, aEEG continuously
- Blood gas 1st 6 hrly then 12 hrly
- RFT, S.electrolytes once daily
- Complete hemogram if required
- Neurosonogram if abnormal

Rewarming

- Increase the infant's core temperature by 0.5c every 2 hrly until 36.5 c has been reached.
- If temp is 36.5c remove the patient from the cooling blanket
- Re-activate the radiant warmer, monitor & document the temp with the skin probe
- Problems during warming- seizures & hypotension

- Supportive therapy during TH-
- Sedative
- Enteral feeding, TPN
- Antibiotics
- Anticonvulsants
- PLT
- FFP

S/E of TH-

- Sinus bradycardia (H.R < 80/min)
- Thrombocytopenia
- Sepsis

Drugs under investigation-

- Block production of free radicals- allopurinol, oxypurinol, melatonin
- Scavengers of oxidants- superoxide dismutase,glutathione, N-acetyl cysteine
- CCBs- Flunarizine, nimodipine
- NMDA receptors blockers- Mg, xe, dextromethorpan
- Inflammatory mediators blockers-phospholipase A2, indomethacin, erythropoietin
- Stem cell therapy

Prognosis

Following features a/w poor prognosis-

- *Lack of spontaneous respiratory effort within 20-30 mints of birth*
- *HIE-3*
- *Abnormal neurogical findings persisting > 7-10 days of life*
- *Oliguria(<1 ml/kg/d) during the 1st 36 hrs*

Follow up-

- Infant's with stage 2,3
- Psychometric assessment at 18 m of age

Long term outcome-

- Mental retardation
- Epilepsy
- Cerebral palsy- hemiplegia, paraplegia, quadriplegia.


THANK YOU
WELLS FARGO
JDRF 2005
We're on Track For a Cure