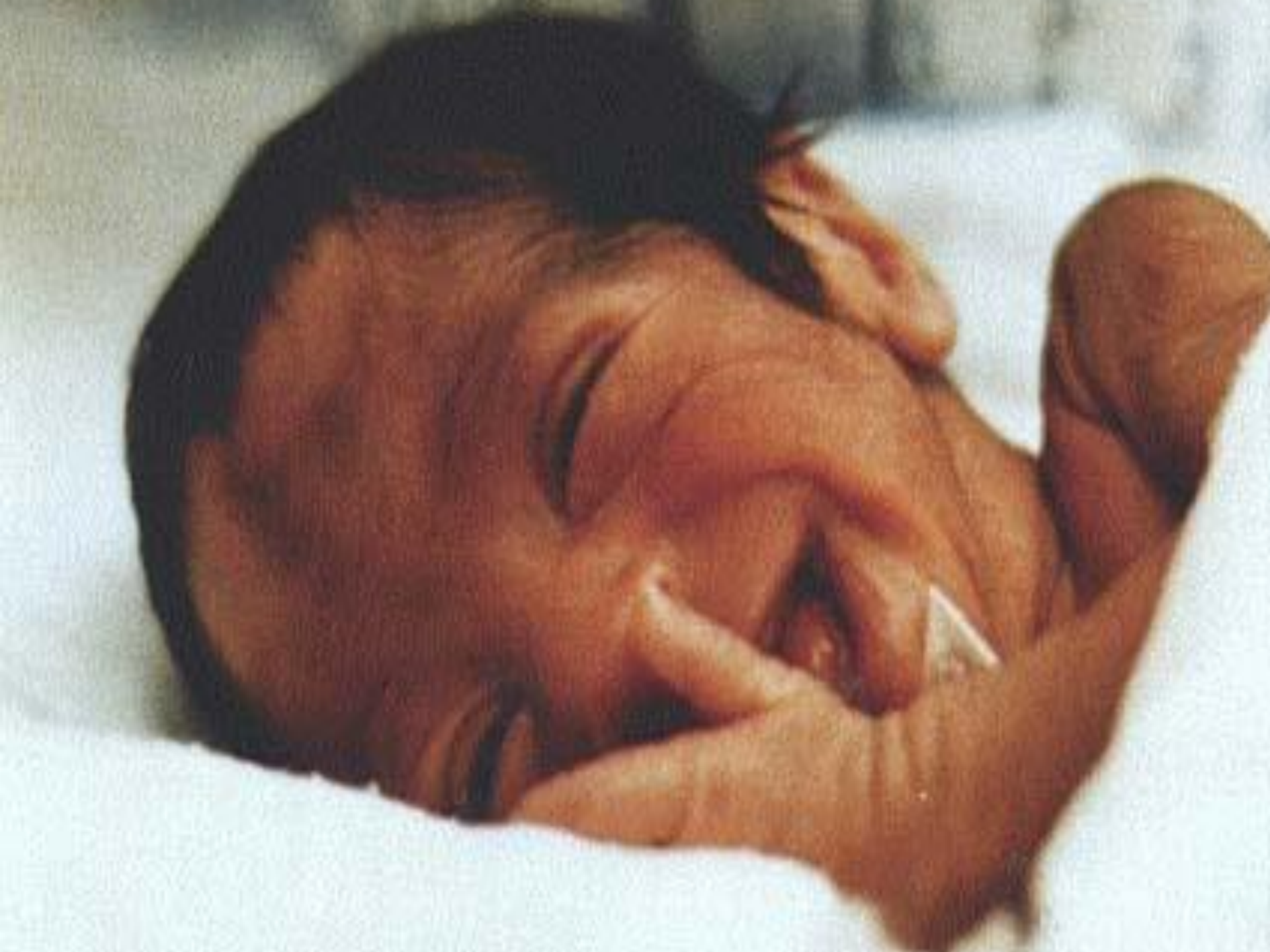


# Birth asphyxia

## hypoxic ischemic encephalopathy

DR: Mohamed Masood
assistant professor
head of neonate department and genetic clinic
Benghazi children hospital

# Case Scenario

- **The baby is delivered via C-section and is brought to the radiant warmer. Initial assessment reveals an unresponsive floppy infant with no respiratory effort and a heart rate of 80bpm. Resuscitation is undertaken. Subsequent Apgar scores are 1, 4, and 7 at 1, 5 and 10 minutes, respectively. The baby is transferred to the NICU for further care.**

# Case Scenario

- **What complications should you expect from this delivery and what is the underlying pathophysiology?**
- **What diagnostic and prognostic studies should be done in the NICU?**
- **What treatments are available for this baby and what are the criteria to treat?**

Hypoxic ischemic encephalopathy is an important cause of permanent damage to CNS cells which may result in neonatal death or manifest later as cerebral palsy or mental deficiency.

birth asphyxia is defined simply as the failure to initiate and sustain breathing at birth

Anoxia: is a term used to indicates the consequence of a complete lack of oxygen.

Hypoxia : refers to an arterial concentration of oxygen that is less than normal.

Ischemia: refers to blood flow to cells or organ that is insufficient to maintains there normal function

# Fetal circulation:

1: In the fetus the organ of gas exchange is the placenta.

2: The fetal pulmonary vascular resistance is high and the fetal systemic vascular resistance is low .

3: The umbilical vein carries the oxygenated blood from the placenta to the fetus.

# Transition at birth

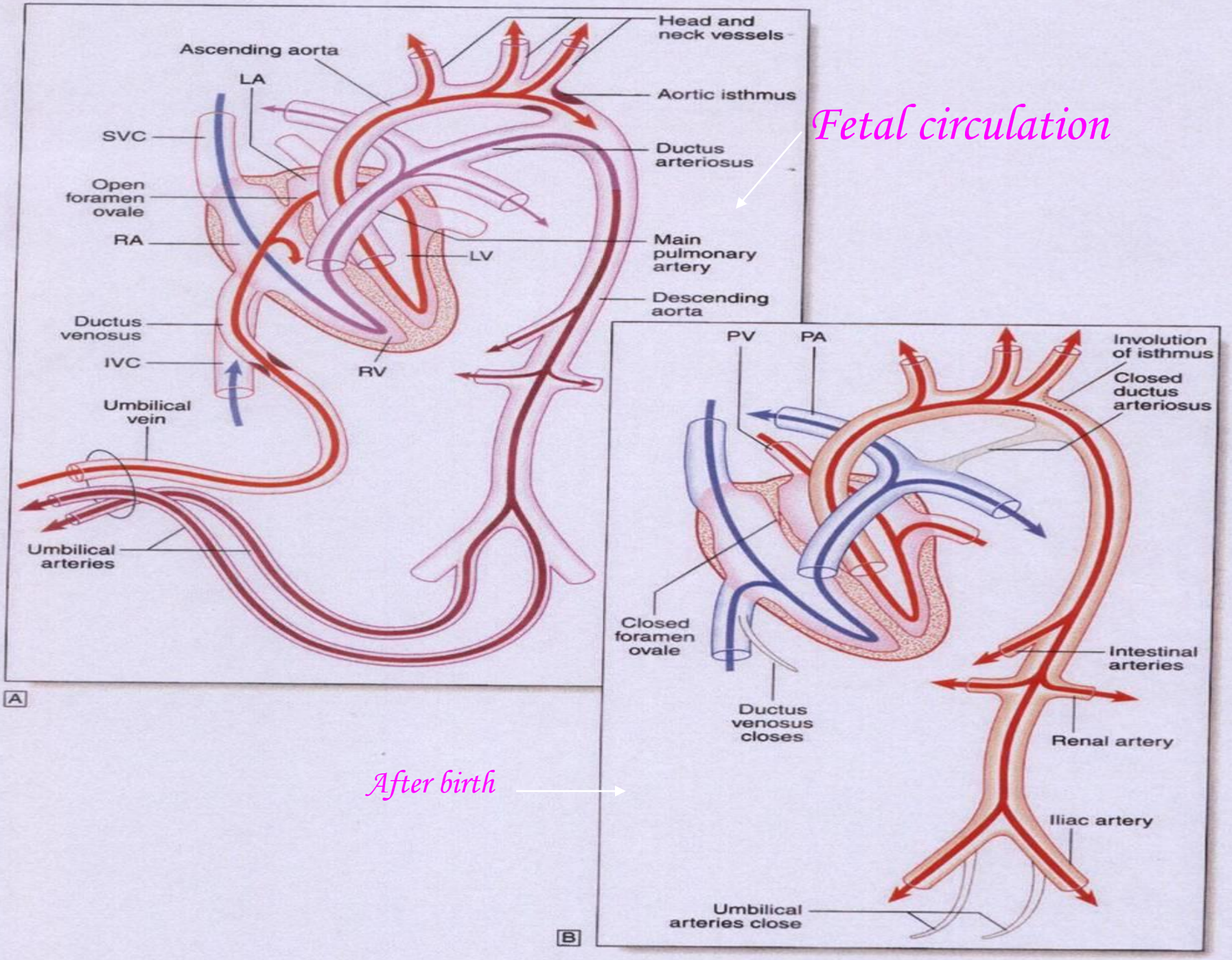
- ***The fetal circulatory system assumes the adult pattern coincident with clamping of cord.***

  ***Elevation of partial pressure of oxygen from fetal level (25 mmHg ) to (50-70 mmHg ) is associated with:-***

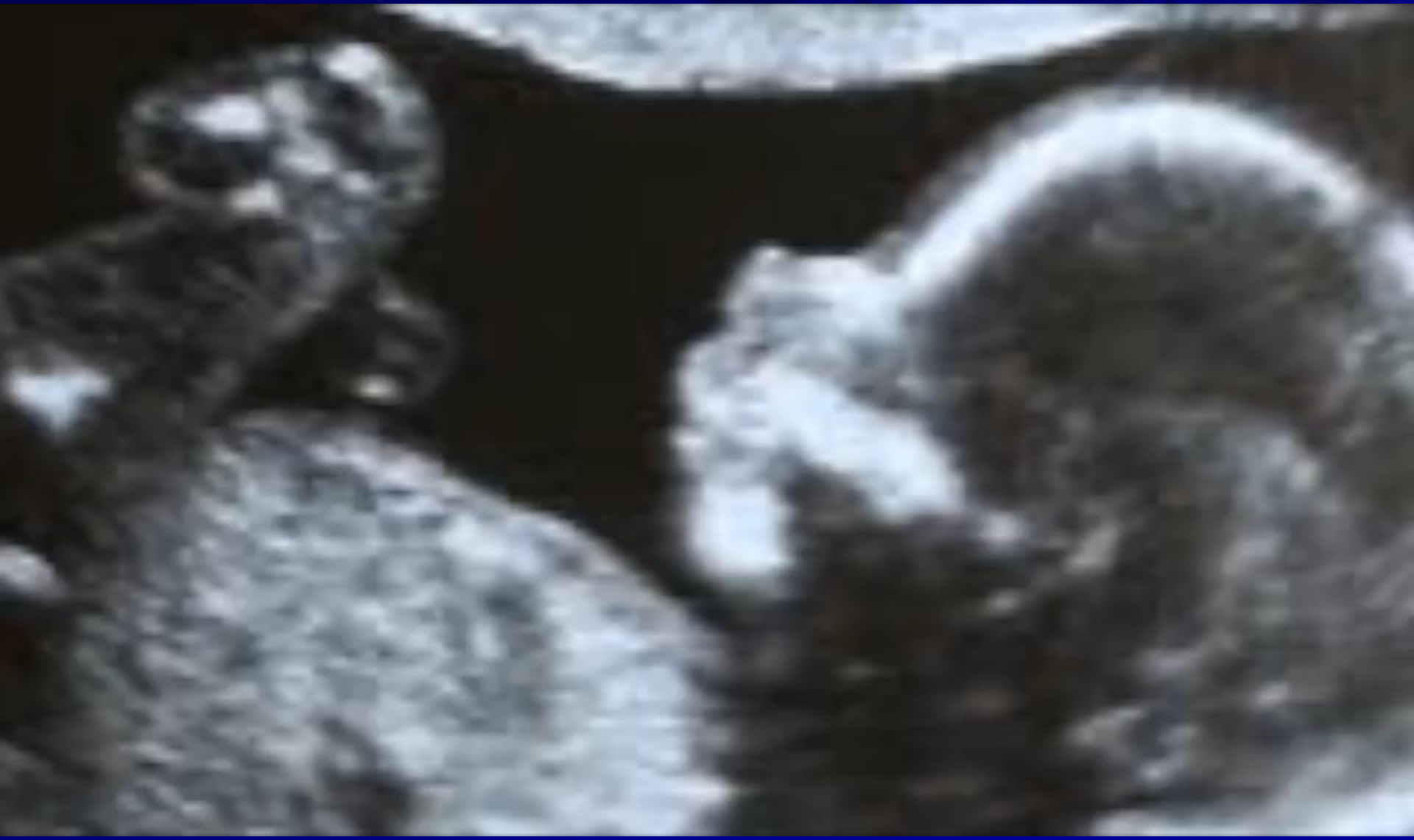
  ***1: Decrease in pulmonary vascular resistance.***

  ***2: Decrease in (Rt –Lt) shunt via ductus arteriosus.***

# *Fetal circulation*




*After birth*



## * what can go wrong during transition ?

1. The baby may not breath sufficiently to force fluid from the alveoli or foreign material (as meconium) block air ways as a result the lung will not fill with air.
2. Excessive blood loss may occur or decrease H.R from hypoxia ⟶ systemic hypotension.
3. Lack of O2 or failure of lung distension ⟶ sustained pulmonary arterioles constriction ⟶ persistent pulmonary HTN + hypoxia ⟶ V.C of arterioles in the bowel , kidneys , muscles , skin while blood flow to heart & brain is preserved . If hypoxia continue brain & other organs damage ⟶ DEATH

# HOW DOES ASPHYXIA OCCUR?

- Interruption of umbilical cord blood flow, eg: cord compression during labour
- Failure of exchange across the placenta, eg: abruption
- Inadequate perfusion of maternal side of placenta, eg: maternal hypotension
- Compromised fetus who cannot tolerate transient intermittent hypoxia of normal labour
- Failure to inflate lungs

# ABC's of Resuscitation

**A B C (A: Airway, B: Breathing, C: Circulation)**

A - establish open airway

Position, suction

B - initiate breathing

Tactile stimulation

Oxygen

C - maintain circulation

Chest compressions

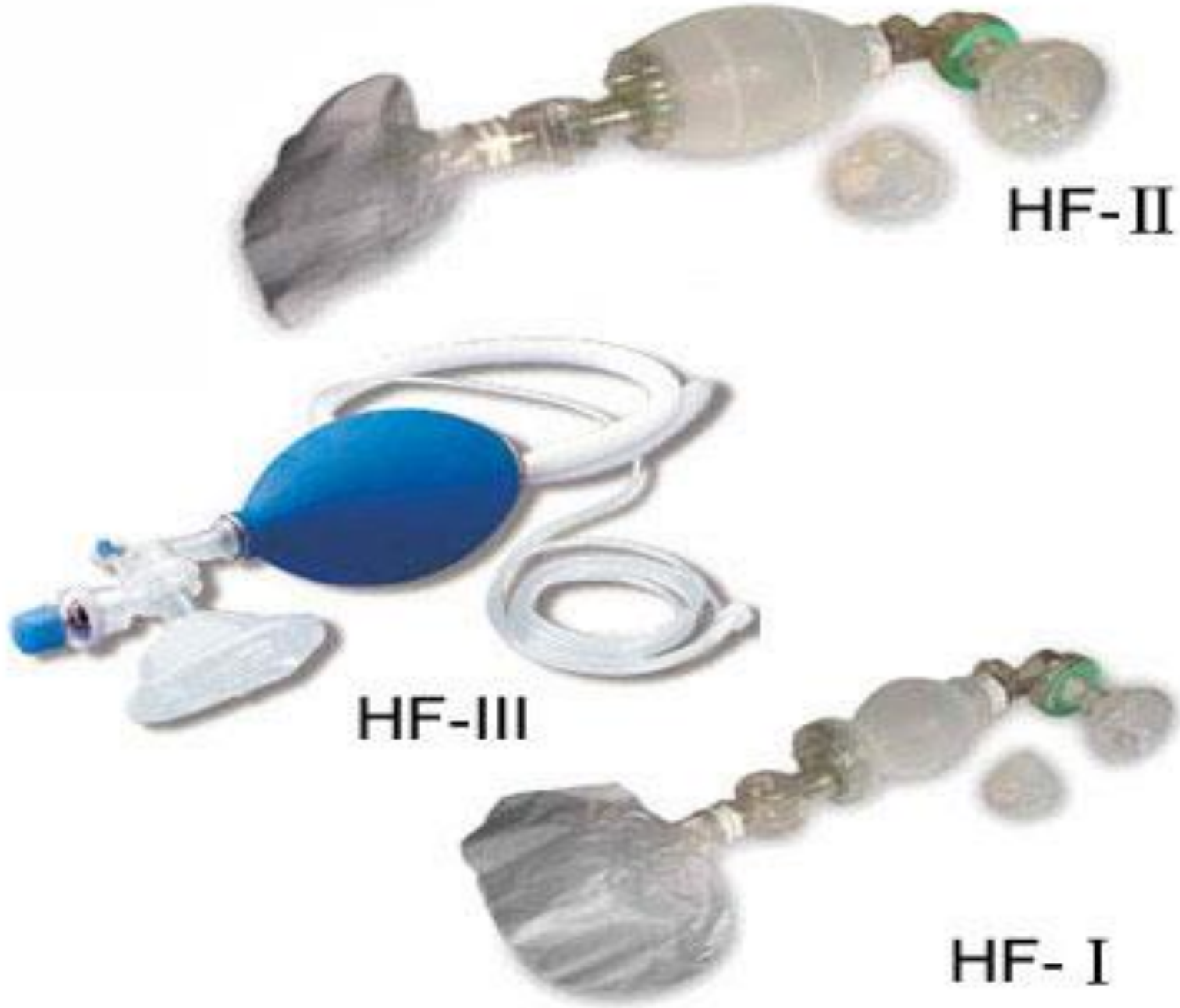
Medications

# Adequate preparation

## For resuscitation:

1. A self-inflating Ambo bag (newborn size)
2. Two infant masks (for normal and small newborn),
3. A suction device (mucus extractor),
4. A radiant heater (if available), warm towels, a blanket and
5. A clock

**are needed**


HF-II
HF-III
HF- I

Race : no predilection exists

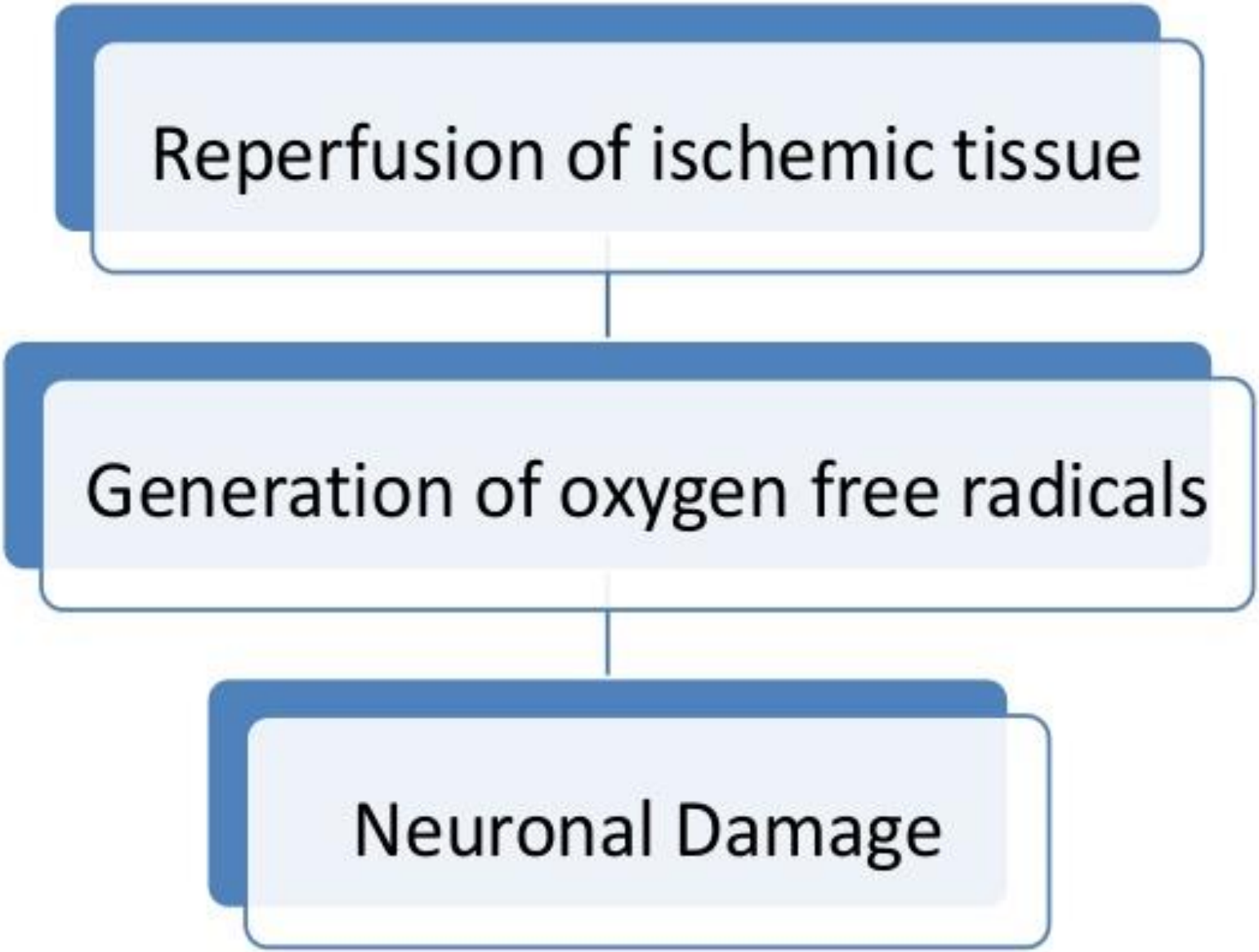
Sex : equal in males and females

Age : by definition , this disease is seen in the newborn period. In most cases the disease manifests at birth or within a few hours after birth.

Background: in spite of major advances in monitoring technology and knowledge of fetal and neonatal pathology , prenatal asphyxia remains a serious condition causing significant mortality and long term morbidity.

Pathophysiology: HIE is similar to stroke syndrome in adult except that in neonates the pathology is more generalized and the causes are different. Hypoxia and hypercapnia are important and powerful stimuli to increase CBF and thus oxygen delivery. During early phase of shock , the cardiac output is redistributed and the systemic BP is increased to maintains CBF.

By 6-24hours after the initial injury, a new phase of neuronal destruction sets in , characterize by apoptosis, this phase may continue for days to weeks. The severity of brain injury in this phase correlates well with the severity of long-term adverse neurodevelopment outcome in infants.


Reperfusion of ischemic tissue
Generation of oxygen free radicals
Neuronal Damage

# Incidence and risk factors

About 1 to 1.5 percent in most centers and usually related to gestational age and birth weight .

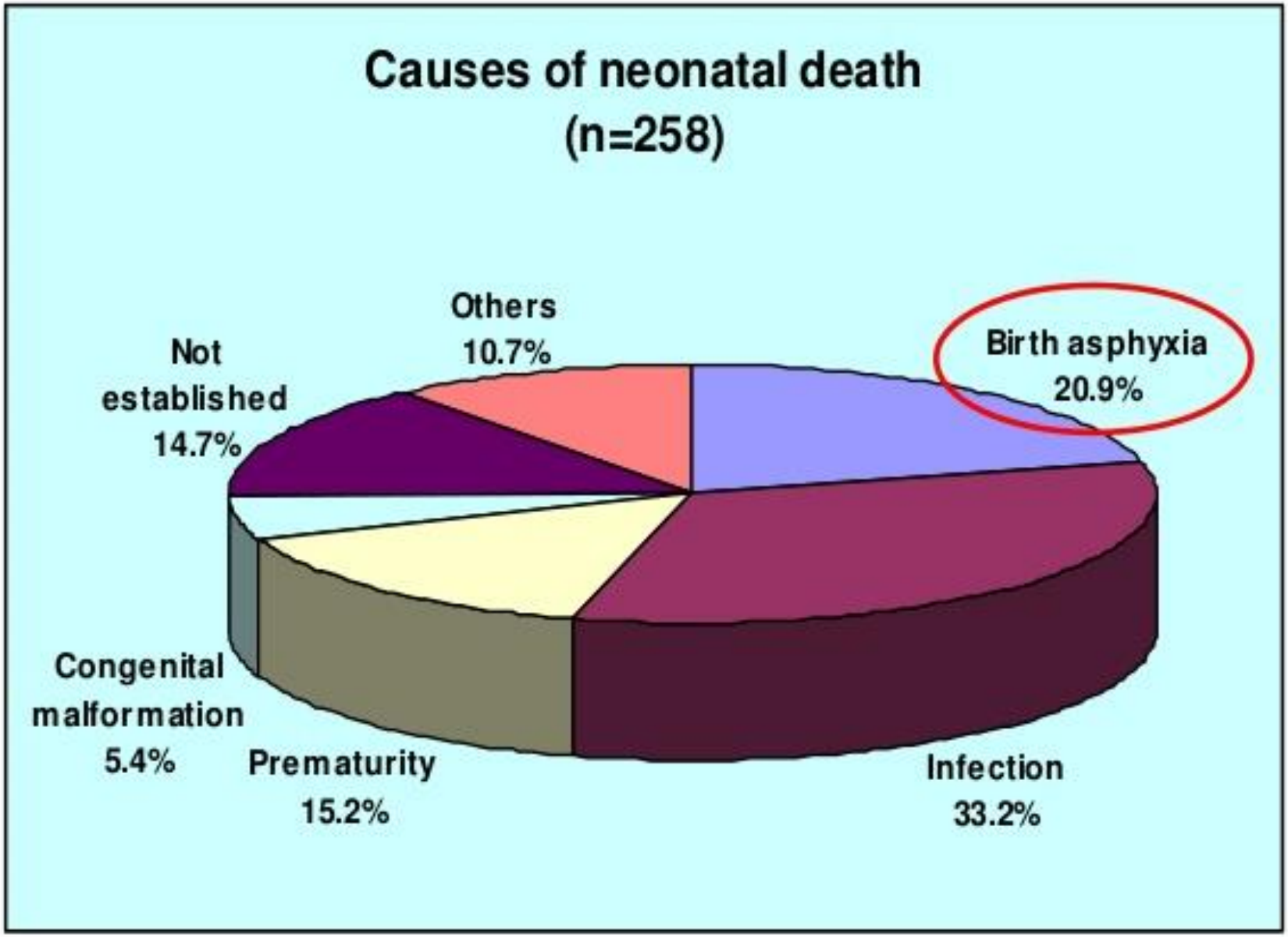
**Risk factors:**

1-pre-eclampsia
2-abrupto placenta
3-hydrops fetalis
4- post-maturity
5-unphysiological labor
6-IUGR
7-mal-presentation.
8-fetal abnormalities

# Why it is important?

# Primary cause of death: NNPD

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

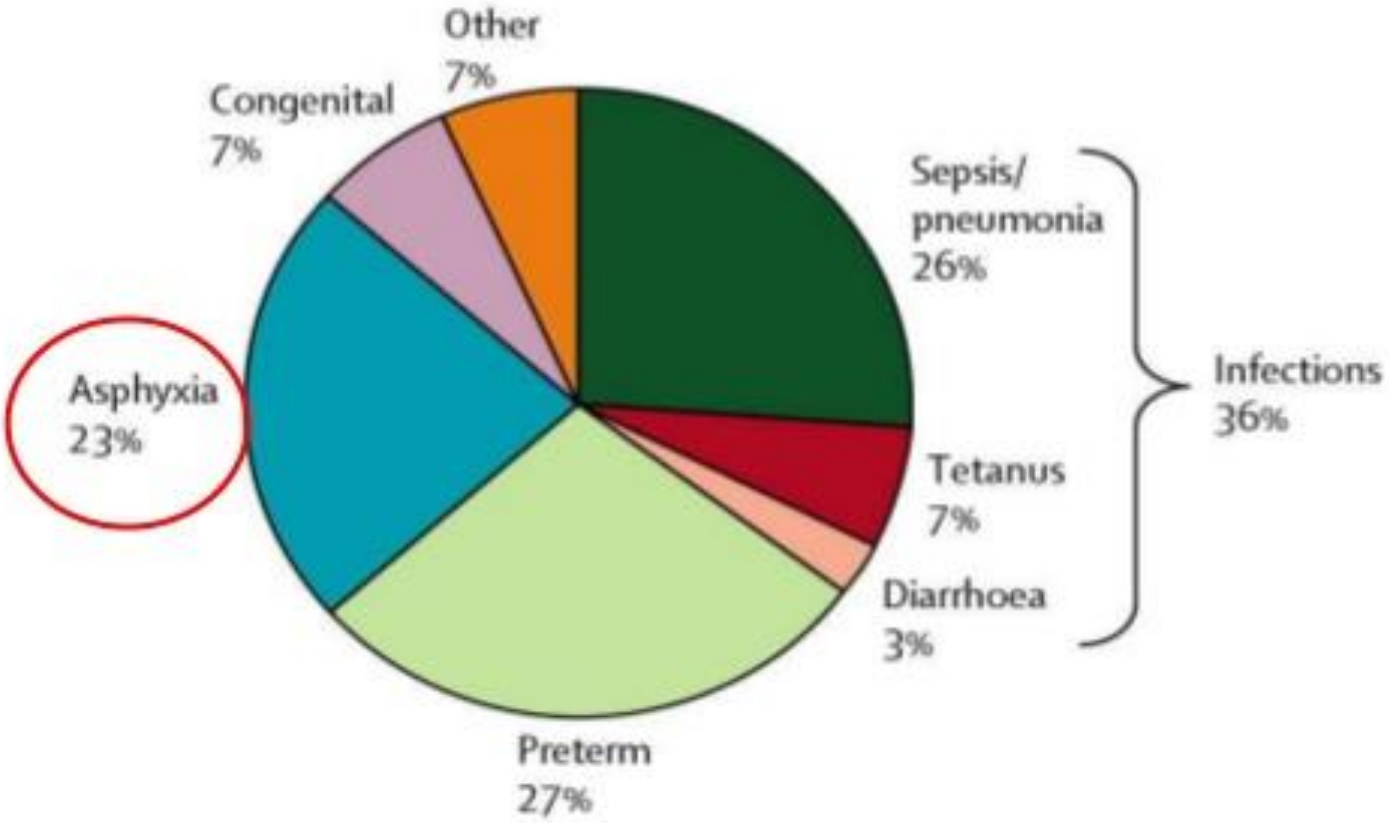



*Others: Hypothermia, RD, Jn, Pulm. Haemorrhage, Seizure etc.*

ICMR 2006

# 4 million newborn deaths – Why?

## almost all are due to preventable conditions



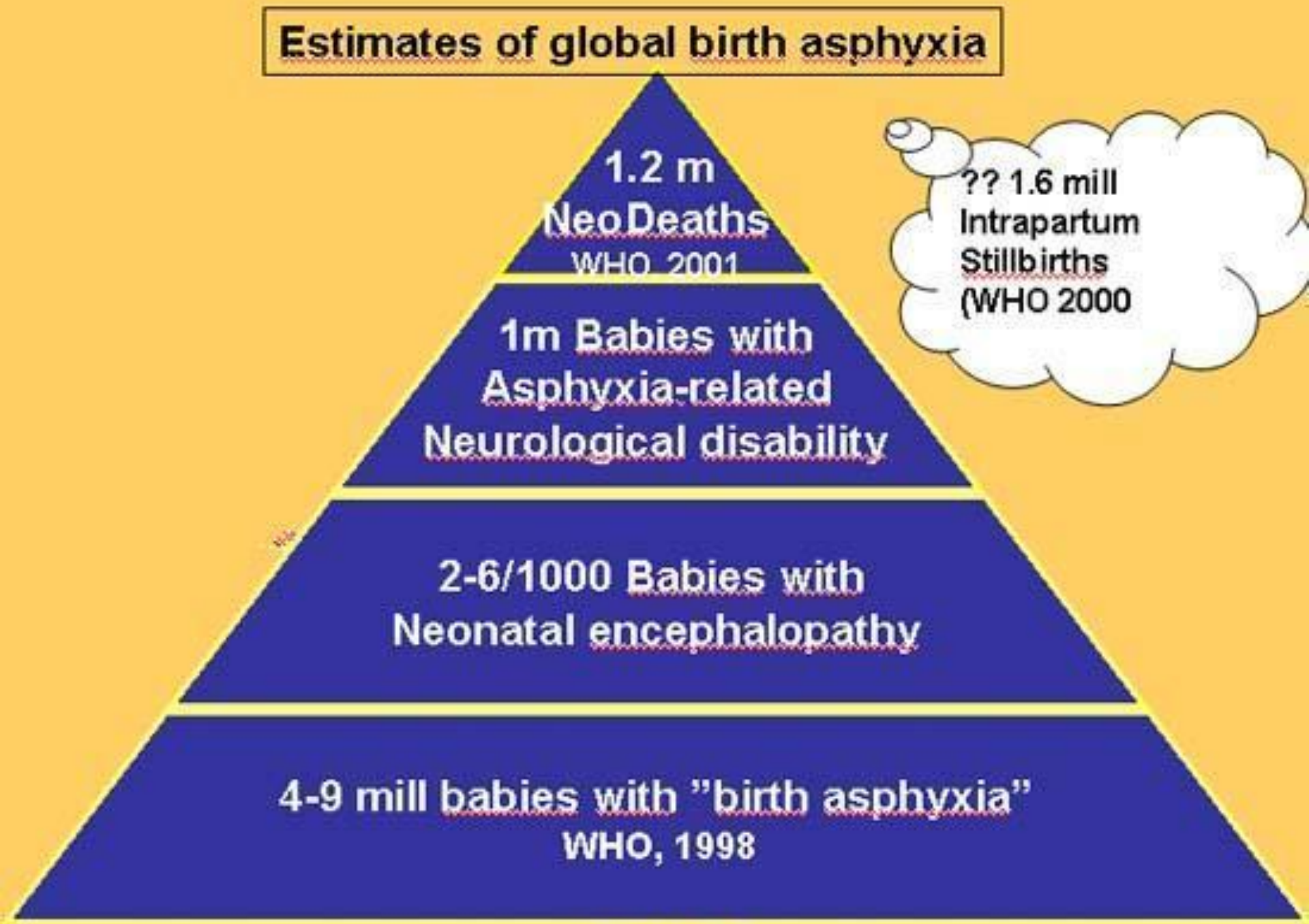
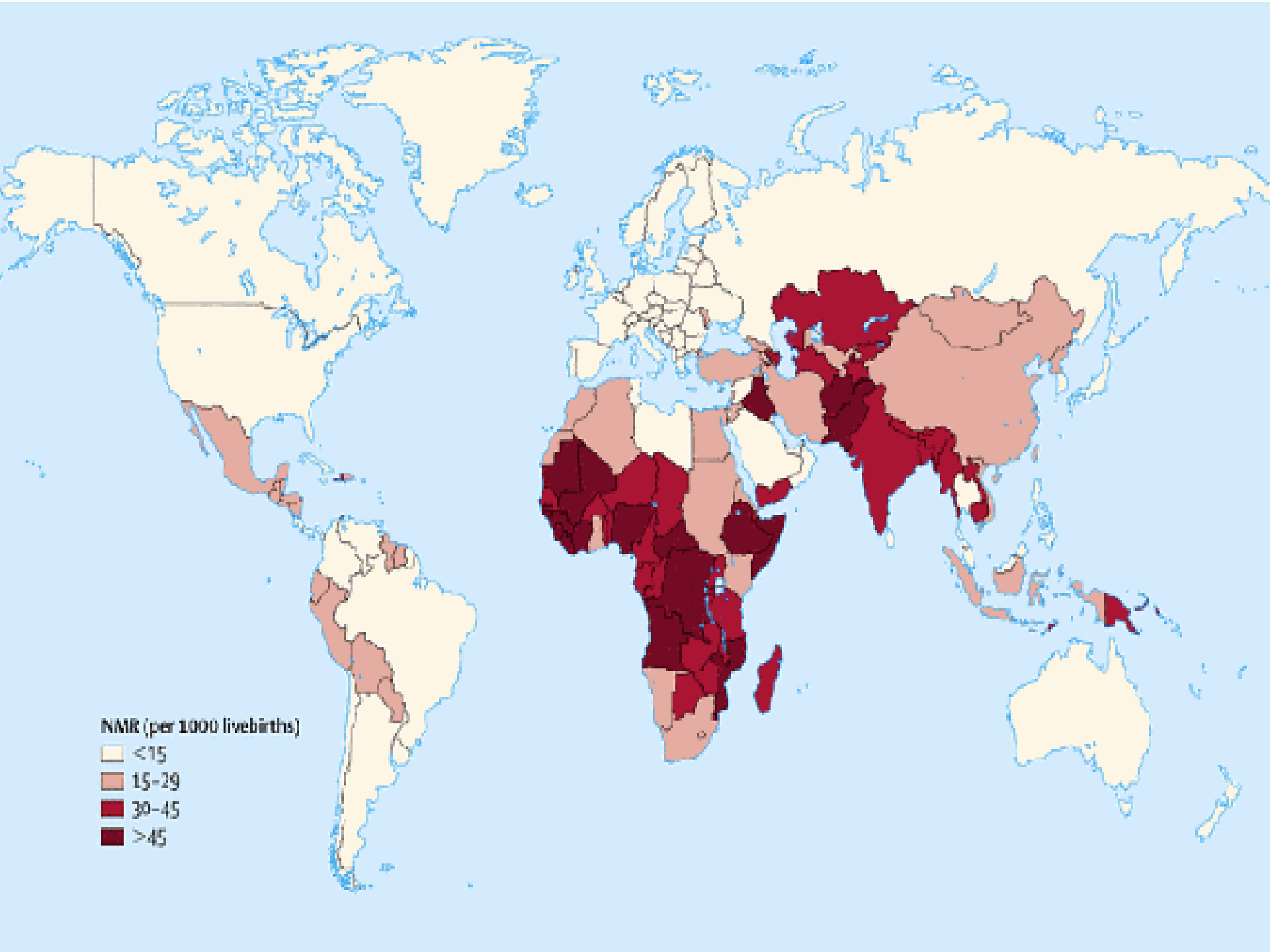
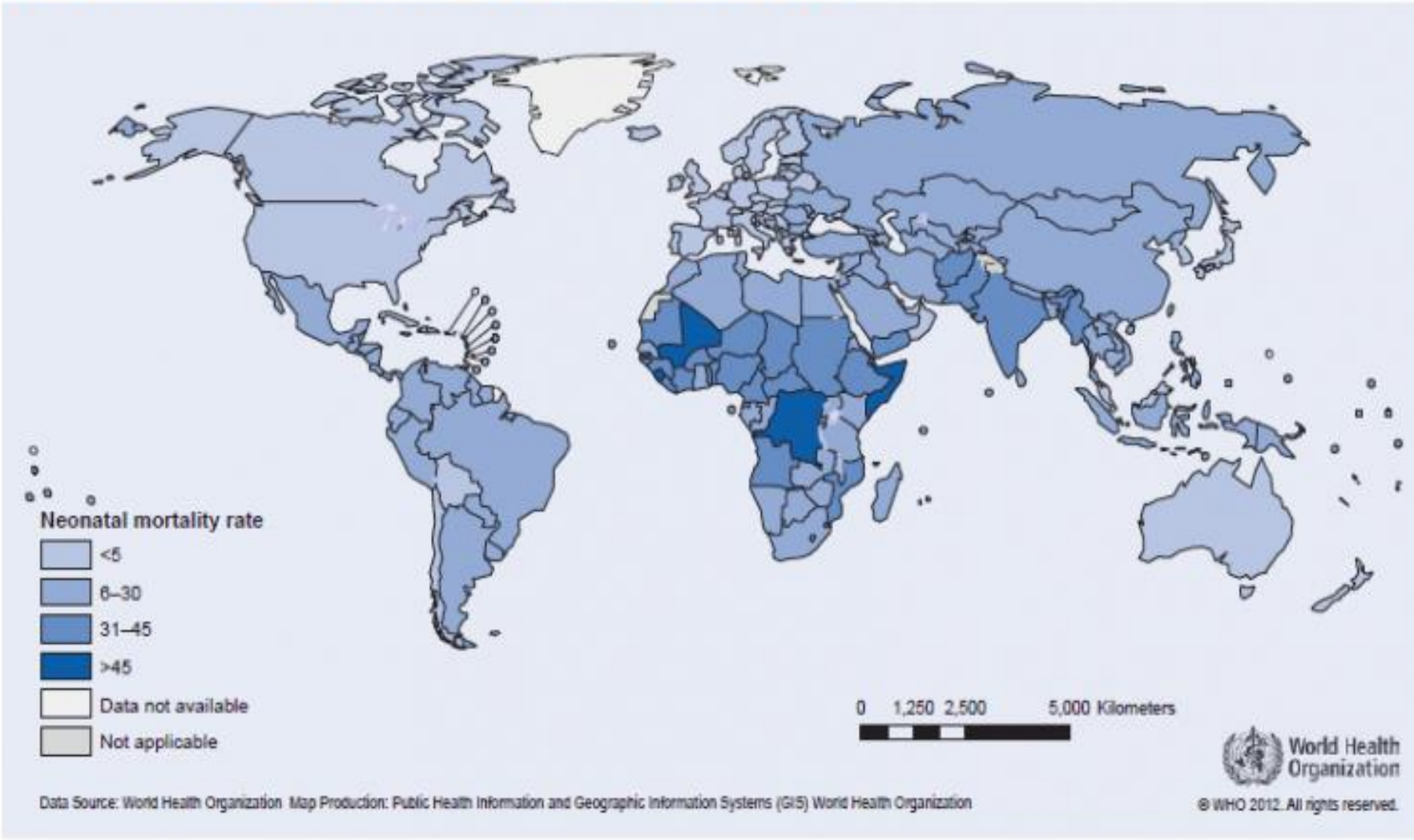

Estimates of global birth asphyxia
1.2 m
NeoDeaths
WHO 2001
?? 1.6 mill
Intrapartum
Stillbirths
(WHO 2000
1m Babies with
Asphyxia-related
Neurological disability
2-6/1000 Babies with
Neonatal encephalopathy
4-9 mill babies with "birth asphyxia"
WHO, 1998

Figure 3.2


NMR (per 1000 livebirths)
<15
15–29
30–45
>45

# NEONATAL MORTALITY RATES, 2010



# Detection of infants at risk of prenatal asphyxia:

Only half of the infants needing resuscitation are predicted by antenatal history or signs during labor.

The following predictors have been assessed for detection of perinatal asphyxia:

1-fetal movement counting

2-non stress testing

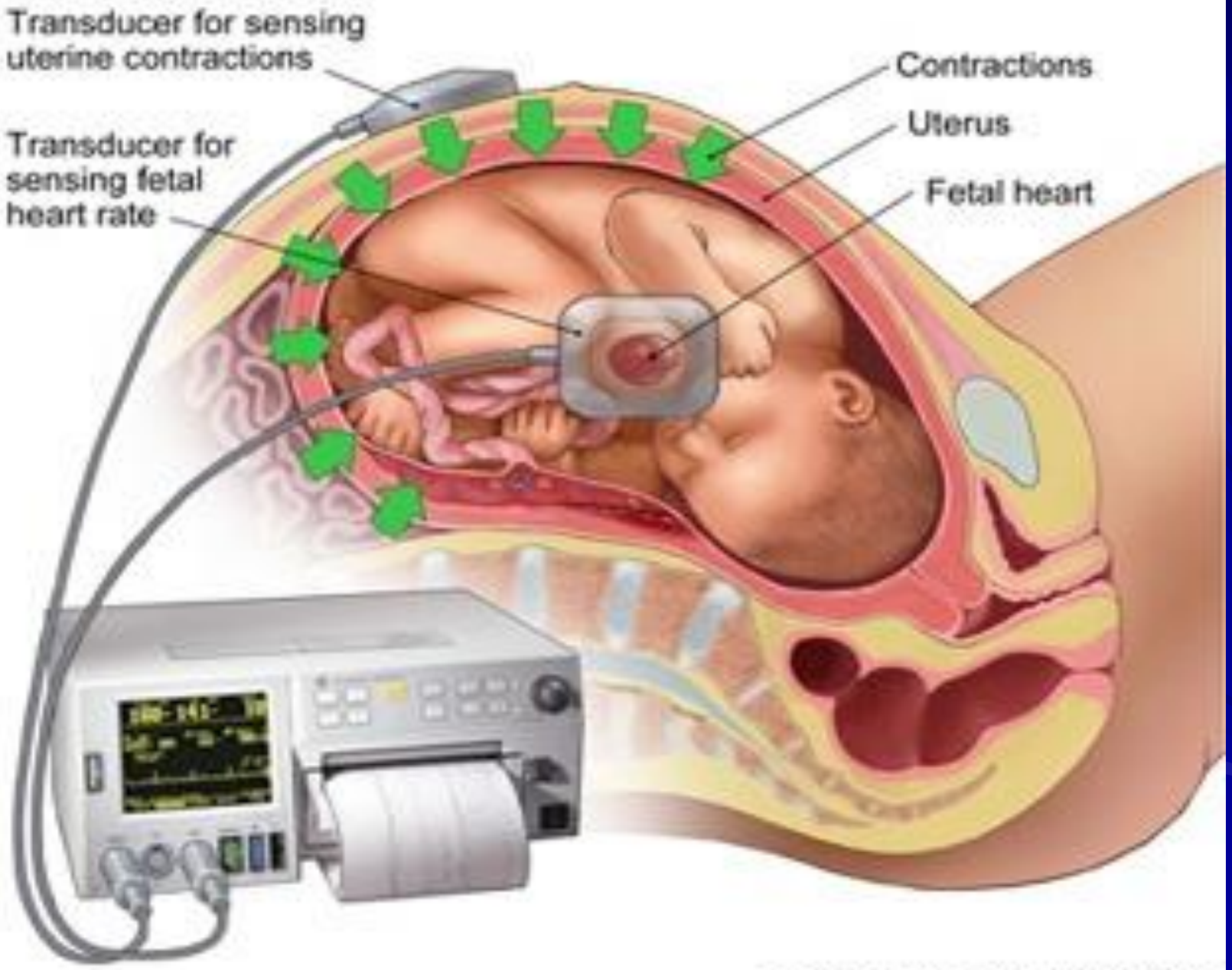
3-Fetal biophysical profile

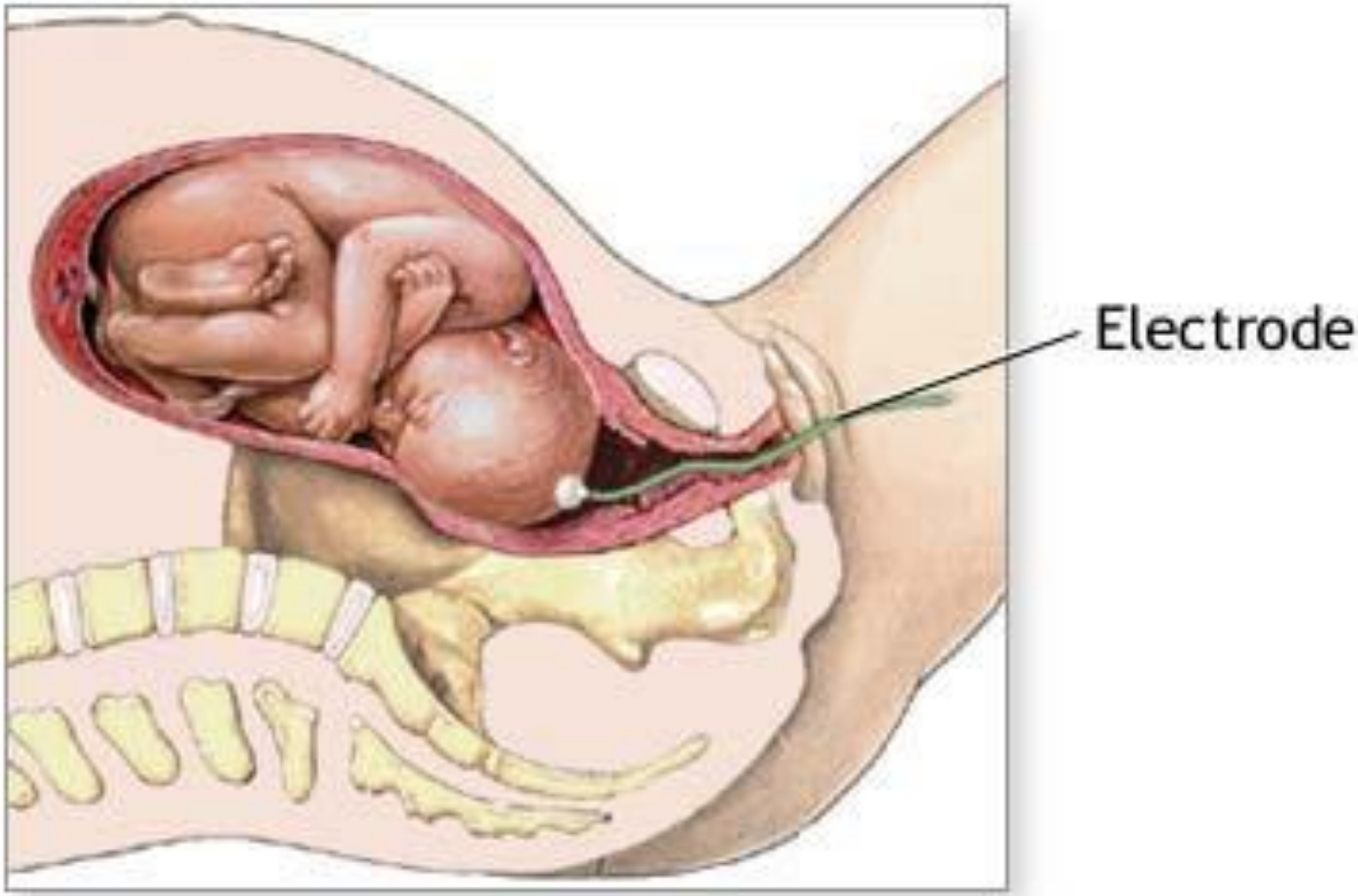
4-abonormal fetal heart rate recording (CTG)

5-fetal scalp pH

6-reduction of liquor volume.

# External Fetal Monitor






Internal fetal monitoring

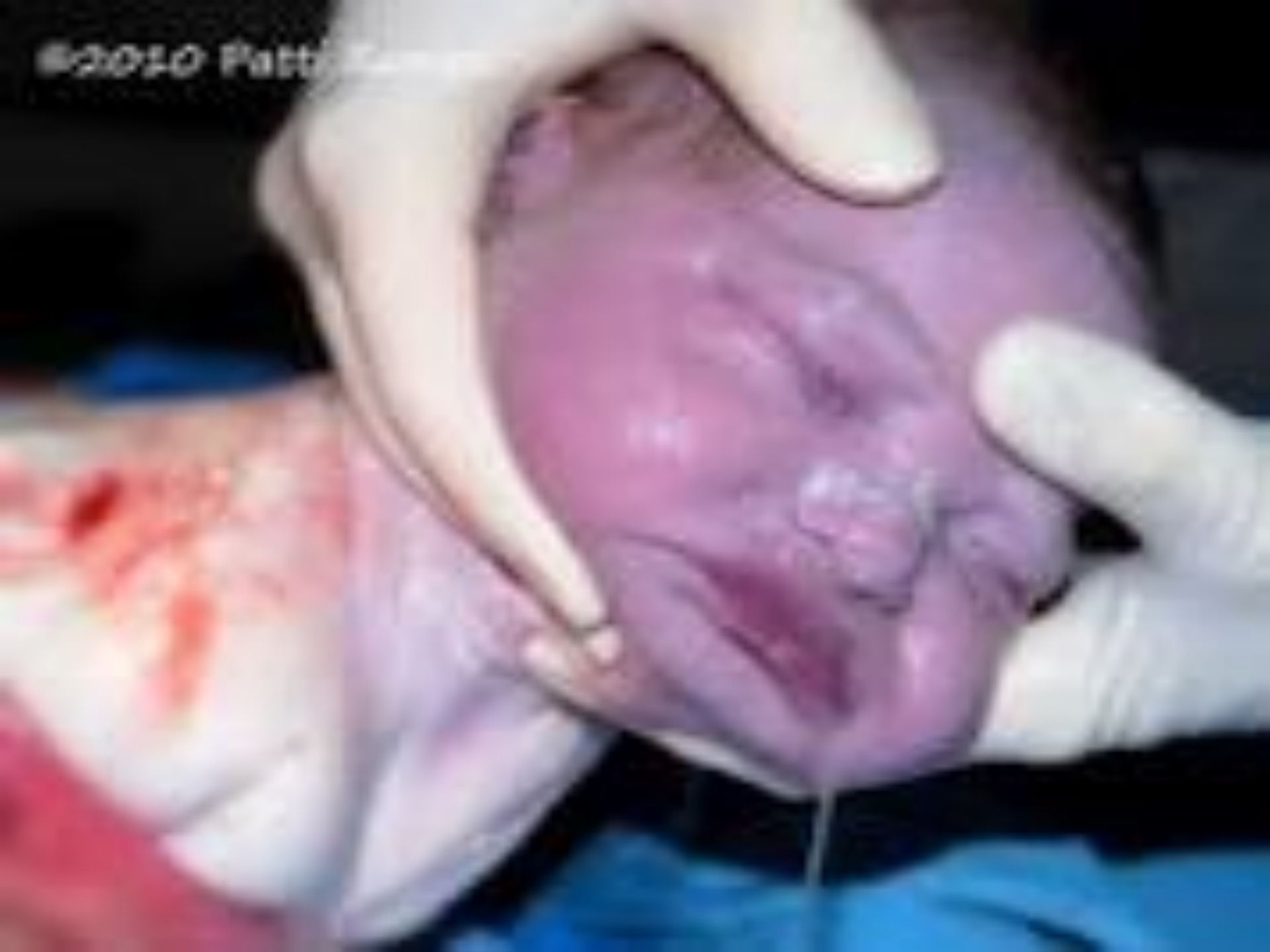
External monitor

Internal monitor

A.D.A.M.

# Apgar Score

| Sign | 0 | 1 | 2 |
|---|---|---|---|
| Heart rate | Absent | <100 beats/min | >100 beats/min |
| Respirations | Absent | Weak cry | Strong cry |
| Muscle tone | Limp | Some flexion | Active motion |
| Reflex | No response | Grimace | Active withdrawal |
| Color | Blue, pale | Body: pink Extremities: blue | Completely pink |



The Apgar score consists of the total assigned to five objective signs in the newborn.

The 5 objective signs are evaluated and given score of 0,1,or 2.

Score at 1 and 5 minutes after birth are usually noted in the chart.

If the 5-minutes score is < 6 the score should be continue to be noted at 5-minute interval until it is greater than 6

Score 0-2 severe asphyxia, 3-4 moderate asphyxia, 5-7 mild asphyxia, 8-10 normal.

# Apgar Score

| | Total Score = 10 |
|---|---|
| normal | score 7-10 |
| mild birth asphyxia | score 5-6 |
| moderate birth asphyxia | score 3-4 |
| severe birth asphyxia | score 0-2 |

# Physical examination

clinical manifestations and course vary depending on severity of HIE.

*Mild HIE:*

- muscle tone may be increased slightly and tendon reflexes may be brisk during the 1st few days of life.
- Transient behavioral abnormalities, such as poor feeding, irritability or excessive crying may occur.
- By 3-4 days of life the CNS examination finding became normal.

# Physical examination

*Moderate HIE:*

- Lethargy, hypotonic and diminished tendon reflexes are common.
- Primitive reflexes are sluggish or absent.
- May have occasional periods of apnea.
- Convulsions may occur within 1st 24hrs of life
- Full recovery within 1-2 weeks is possible and is associated with a long term outcome.

# Physical examination

*Severe HIE:*

- Stupor or coma is typical.
- Breathing may be irregular , often requires ventilatory support.
- Generalized hypotonia and depressed deep tendon reflexes.
- Primitive reflexes are absent.
- Disturbance of ocular motion , such as nystagmus, bobbing, deviation and loss of doll eye movement.
- Pupils may be dilated , fixed or poorly reactive.
- Seizures occur early and often initially difficult to control.
- Irregularities of heart beat and BP are common.

## ***Infants who survive severe HIE:***

The level of alertness improves by 4-5 days, hypotonia and feeding difficulties persist, requiring tube feeding for weeks to months.

Involvement of multiple organs besides the brain is the hallmark of HIE

- Renal failure seen in about 40%
- Respiratory distress and persistent P.H. in ~25%
- Hypoxic cardiomyopathy,hypotension,TR..etc~25%
- DIC
- Hepatic failure.
- Adrenal hemorrhage
- NEC
- Fluid, electrolyte and metabolic abnormalities, including ; IADH, hyperkalemia, hypoglycemia, hypocalcaemia and acidosis.
- ~ 33% or more of infants with HIE will have 2 or more organ system involvement

# 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 | Normal | Mild hypotonia | Flaccid |
| Posture | Mild distal flexion | Strong distal flexion | Intermittent decerebration |
| Strech reflexes | Overactive | Overactive | Decreased or absent |
| Primitive reflexes | | | |
| Suck | Weak | Weak or absent | Absent |
| Moro | Strong | Weak, incomplete | Absent |
| Tonic neck | Slight | Strong | Absent |
| Autonomic function | | | |
| Pupils | Normal | Miosis | Mydriase or variable, unequal |
| Heart rate | Tachycardia | Bradycardia | Variable |
| Seizures | None | Common | Uncommon |

Stage 0 = Normal

# Effects of Asphyxia

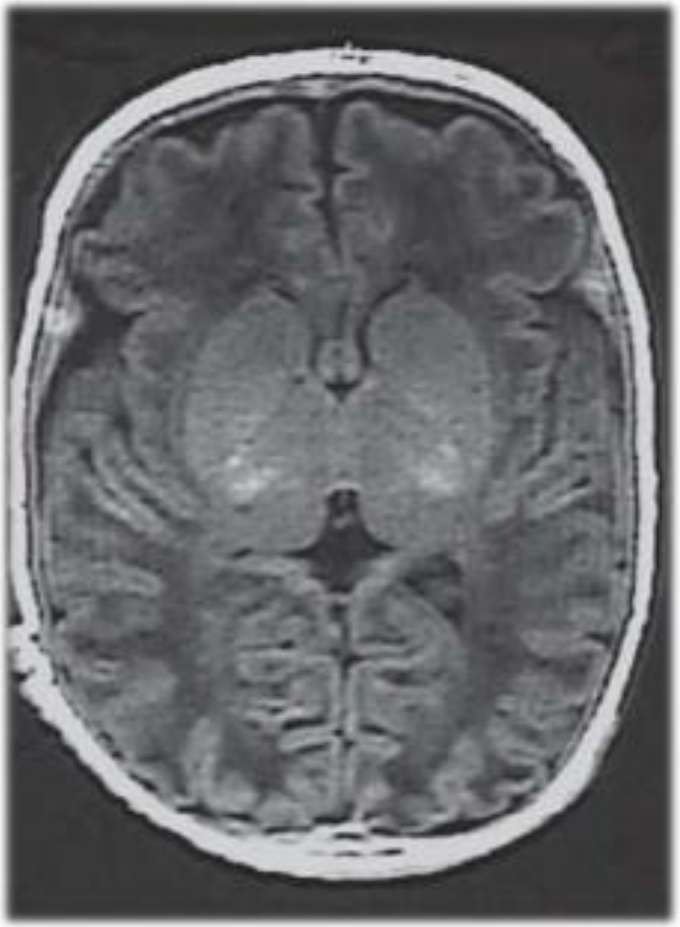
## Central nervous system

infarction, intracranial hemorrhage, cerebral edema, seizure, hypoxic-ischemic encephalopathy

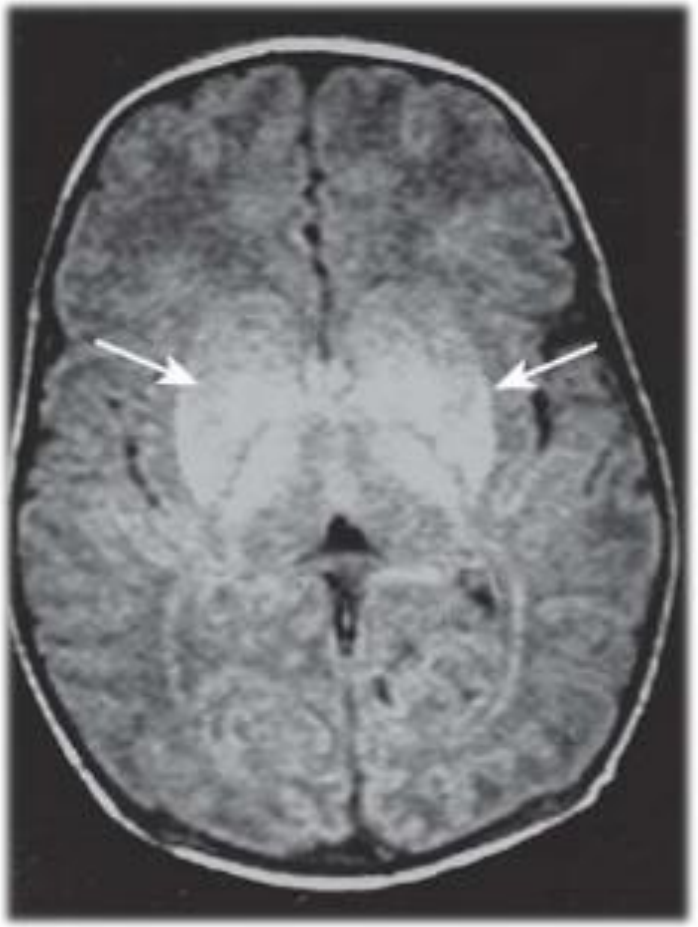
## Cardiovascular

bradycardia, ventricular hypertrophy, arrhythmia, hypotension, myocardial ischemia ,TR

# Neuro-imagery in HIE



Normal



HIE

# Effects of Asphyxia

Respiratory system

apnea, respiratory distress syndrome

cyanosis

KUB

acute tubular necrosis, bladder paralysis

Gastrointestinal tract

necrotizing enterocolitis , stress ulcer

# Effects of Asphyxia

## Hematology

disseminated intravascular coagulation

## Metabolic

hypoglycemia, hyperglycemia, hypocalcemia, hyponatremia

## Skin

subcutaneous fat necrosis

Differential diagnosis;

- developmental defects
- inherited metabolic disorders
- infections
- drug withdrawal

# Laboratory studies

No specific test excluding or confirms a diagnosis of HIE.

The diagnosis is based on the history and physical examination. All tests are performed to assess the severity of brain injury and status of systemic organs.

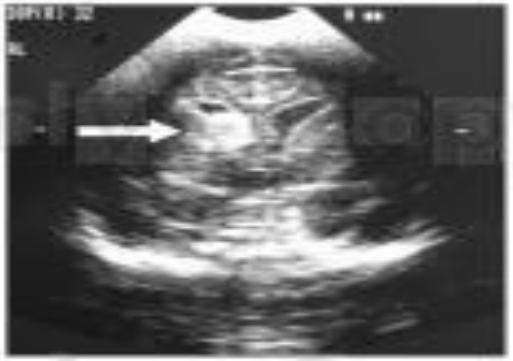
- Serum electrolytes and RFT.
- Liver function tests, PTT, PT, blood sugar
- complete blood picture, platelets ,blood gases.

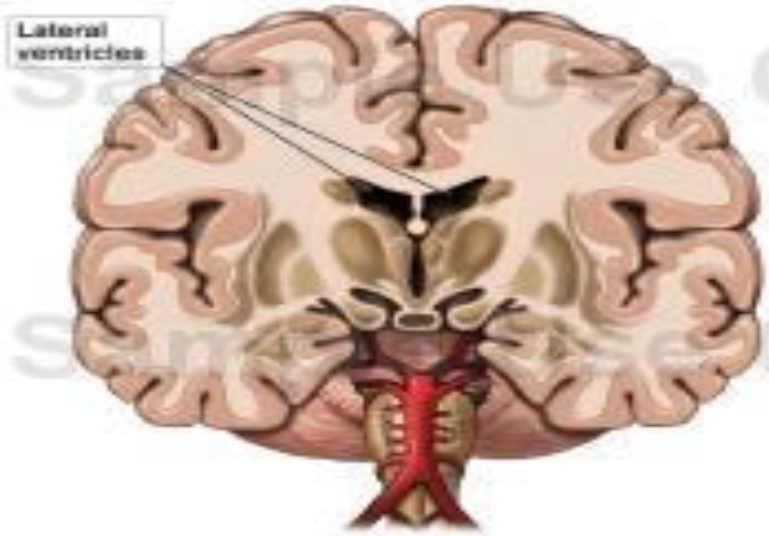
# Imaging studies

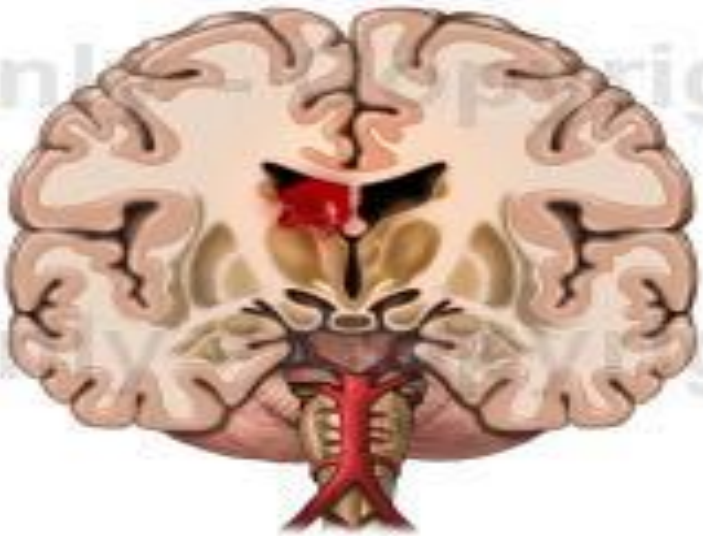
- Cranial ultrasound:
  is portable and provides a quick assessment of brain insult, may reveals hemorrhage and cerebral edema.
- CT scan, MRI of the head:
  may reveal cerebral edema , infarction and hemorrhages.
- Echocardiography:
  to assess cardiac contractility and valvular lesions and structural defects.
- EEG: changes depend on severity of HIE.

- Somatosensory evoked potentials : correlate closely with the outcome.

# Brain Hemorrhage in Infant

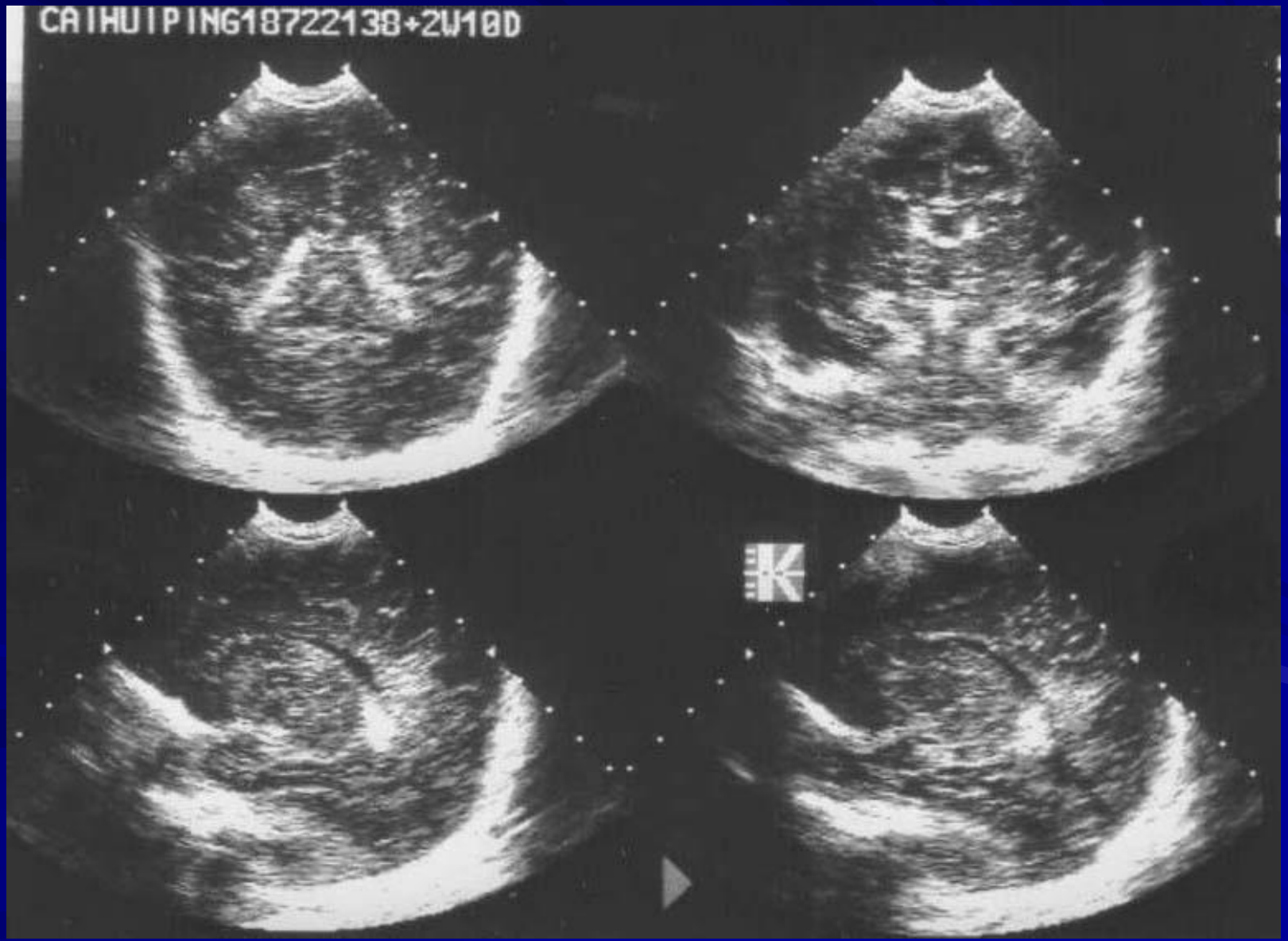




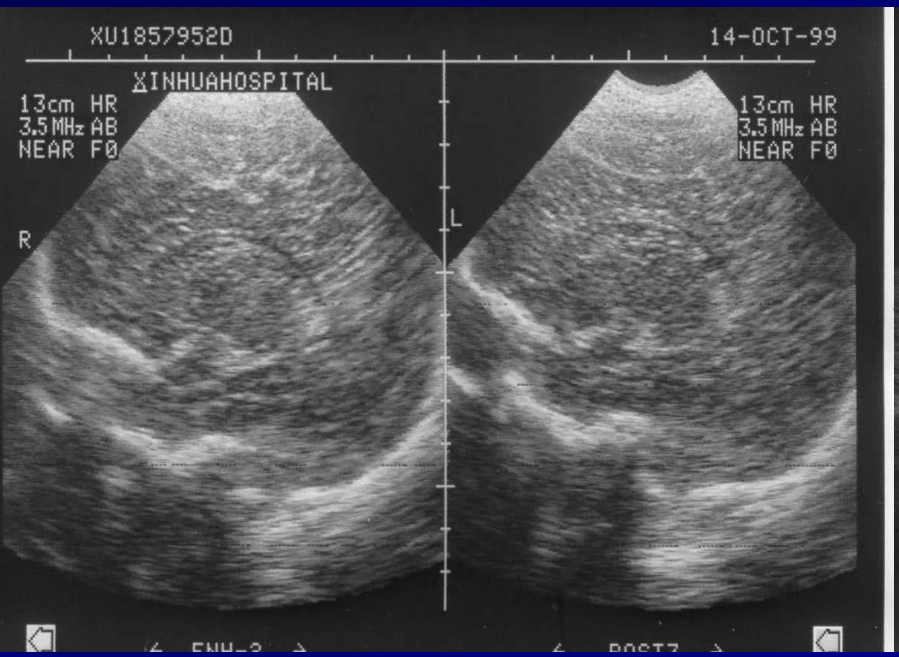



Sample Use Only - Copyrig

# Brain edema



# Brain odema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XINHUAHOSPITAL
13cm HR
3.5MHz AB
NEAR F0
R
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13cm HR
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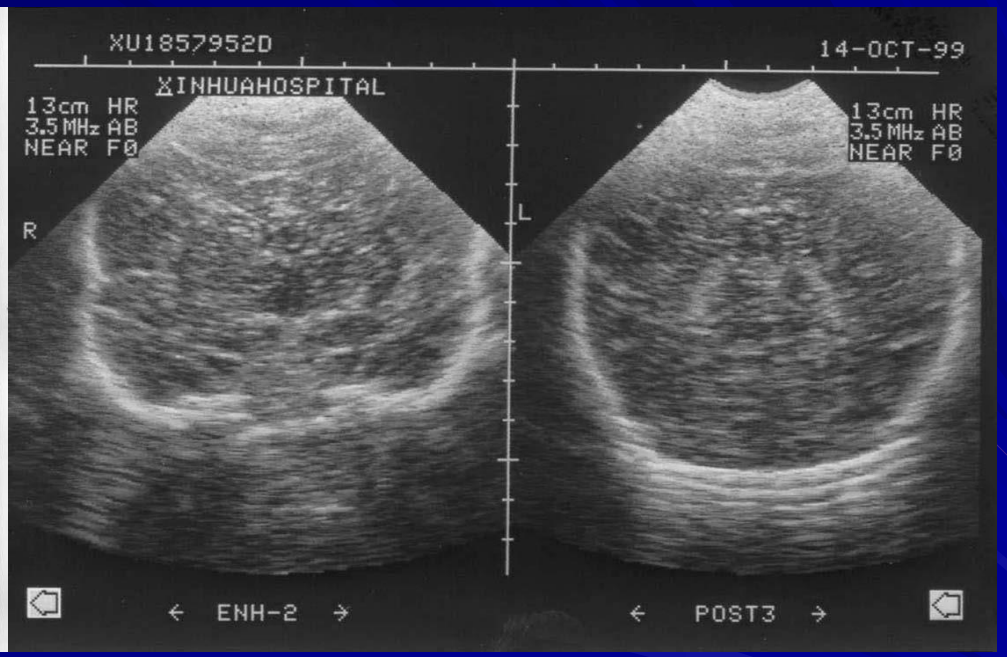
NEAR F0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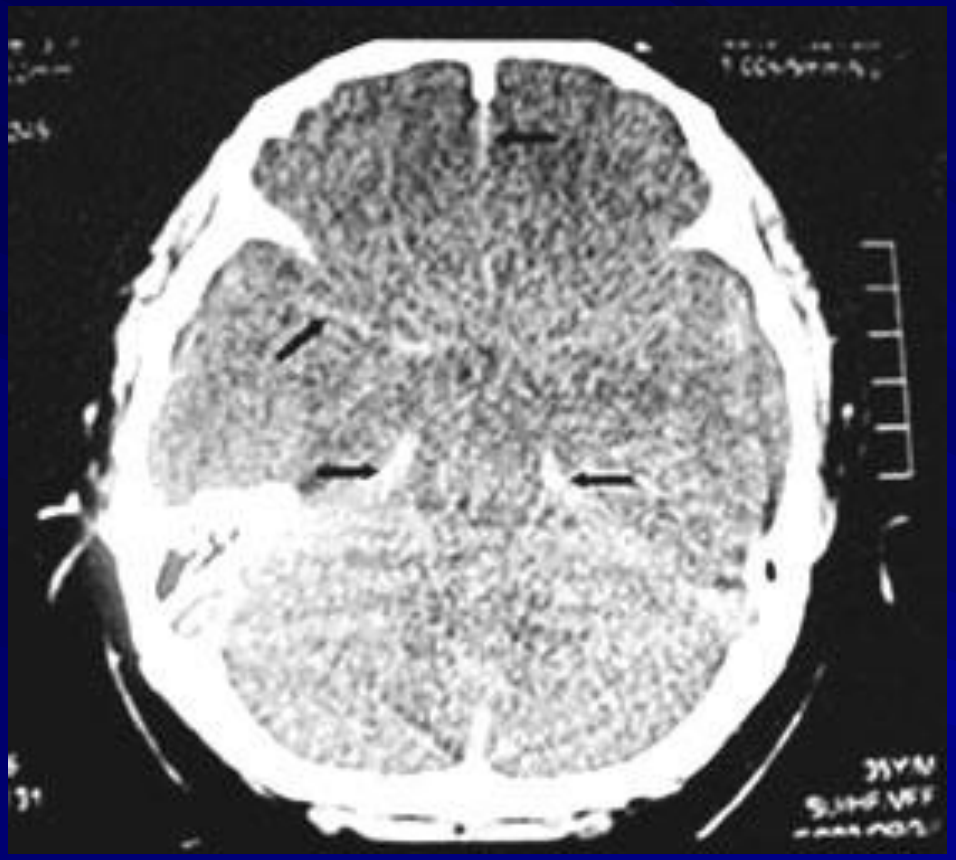

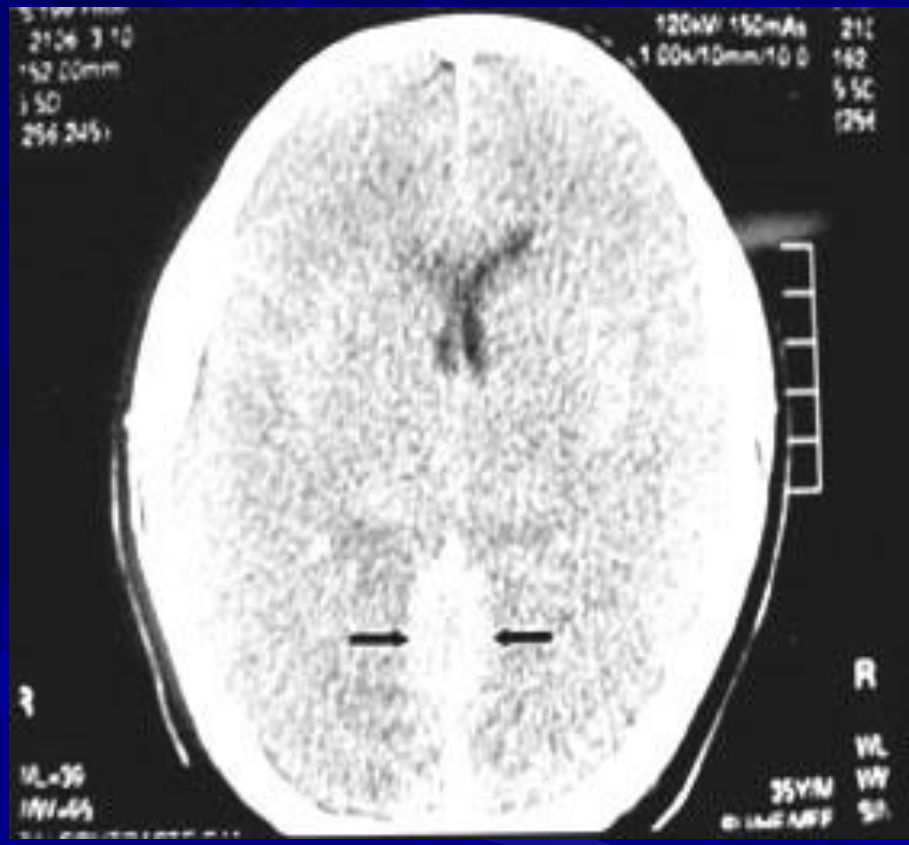

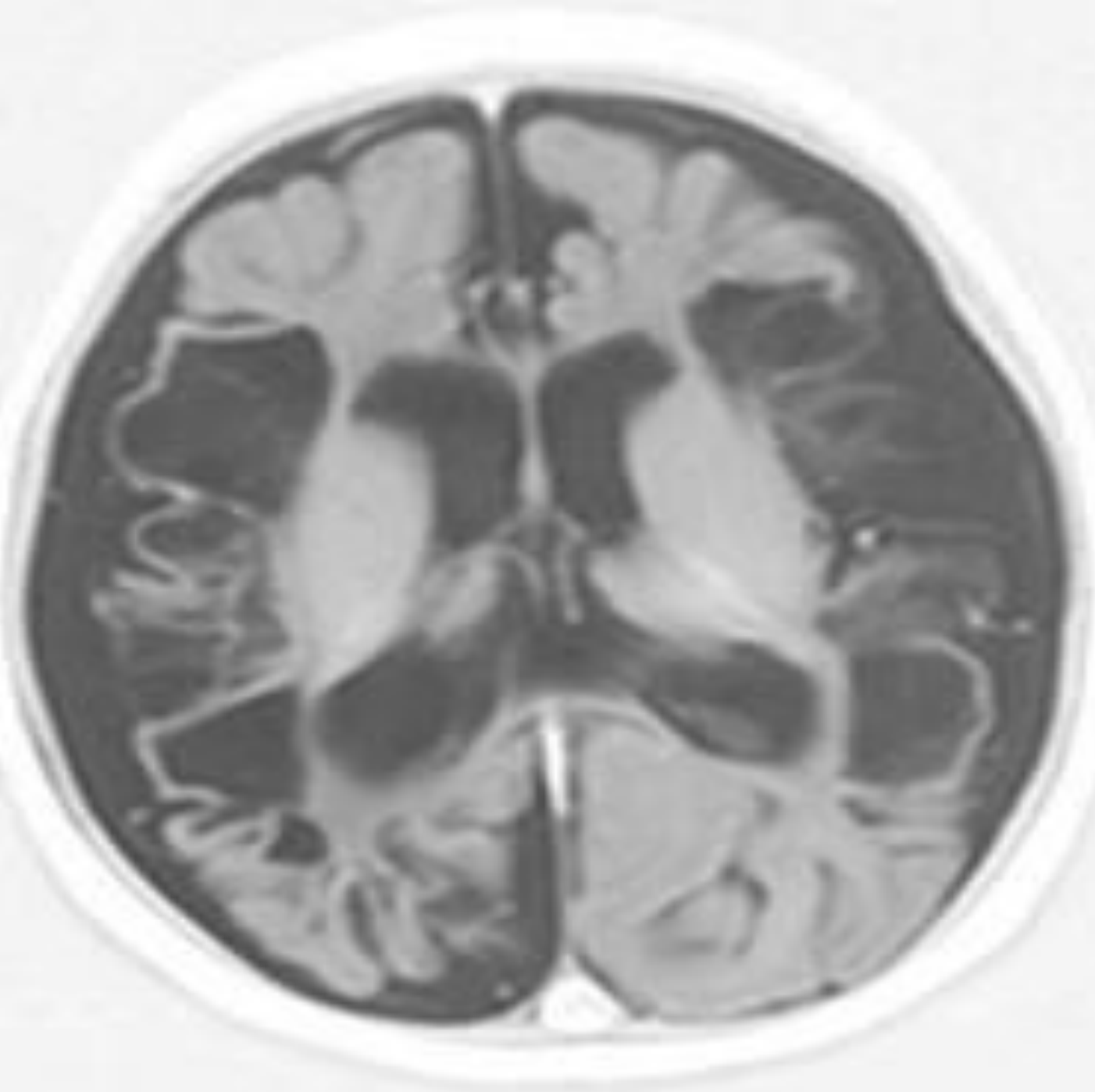


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2s2s.com

# treatment

Limiting the exposure of neonates to perinatal asphyxia requires the use of appropriate obstetric monitoring pregnancy and labor for risk factors.

Principles: clinical management is directed at appropriate and rapid resuscitation, and preventing hypoxia, hypercapnia and acidosis.

# Principles of Management

- Supportive Therapy,
- Anticonvulsants,
- Cerebroprotective interventions, and
- Monitoring.

# Supportive Therapy

- IV Fluid:
  - **10% Dextrose,**
  - **60 ml/kg/day.**
- Treat Hypotension:
  - **Dobutamine, and**
  - **Dopamine.**
- Temperature:
  - **Cool Therapy (33-34$^0$ C)**

# Supportive Therapy (continued)

- Glucose:
  - Treat hypoglycemia,
  - Maintain BS at 75 to 100 mg/dl.

- Calcium:
  - Calcium level should be kept in the normal range (9 – 11 mg/dl)

# Anticonvulsants

- 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.

# Cerebroprotective Interventions

- Therapeutic Hypothermia (cool therapy),
- Free Radical Scavengers,
- Antagonists of excitotoxic amino acids,
- Calcium Channel Blockers.

# Treatment

- Selective Cerebral or Whole Body Therapeutic Hypothermia (Cool Therapy),
- Control Seizures,
  - Phenobarbitone/Phenytoin/Midazolam.
- Mechanical Ventilation, (or ECMO),
- Volume Expansion,
- Pressure Amines.

# Monitoring

- Regular clinical assessment,
- Biochemical monitoring,
- $SpO_2$.

# treatment

- Correction of hypoglycemia
- Correction of respiratory status and acidosis…by ventilatory support and bicarbonate.
- Convulsions ; should be detected early and well controlled , by phenobarbiton , phenytoin and lorasepam…..
- Fluid therapy and renal impairment: infants with anuria /oliguria should receive 40-60mls/kg/day until adequate urine output occurs.

  regular assessment of fluid balance, electrolytes, RFT should be performed.

# treatment

- BP: these infants prone to hypotension , should be corrected by fluids and inotropes ( dopamine& doutamine)
- DIC: if there is evidence of bleeding or petecchiae perform platelets count and coagulation profile, if abnormal give vitamine K and FFP.
- Gastro-intestinal feeding: most cases they kept NPO in the 1$^{st}$ few days of life . Begin feeding by diluted formula or breast milk, observe for gastric retention or NEC.
- Temperature: maintain core temp. 36-37c , ovoid hyperthermia.

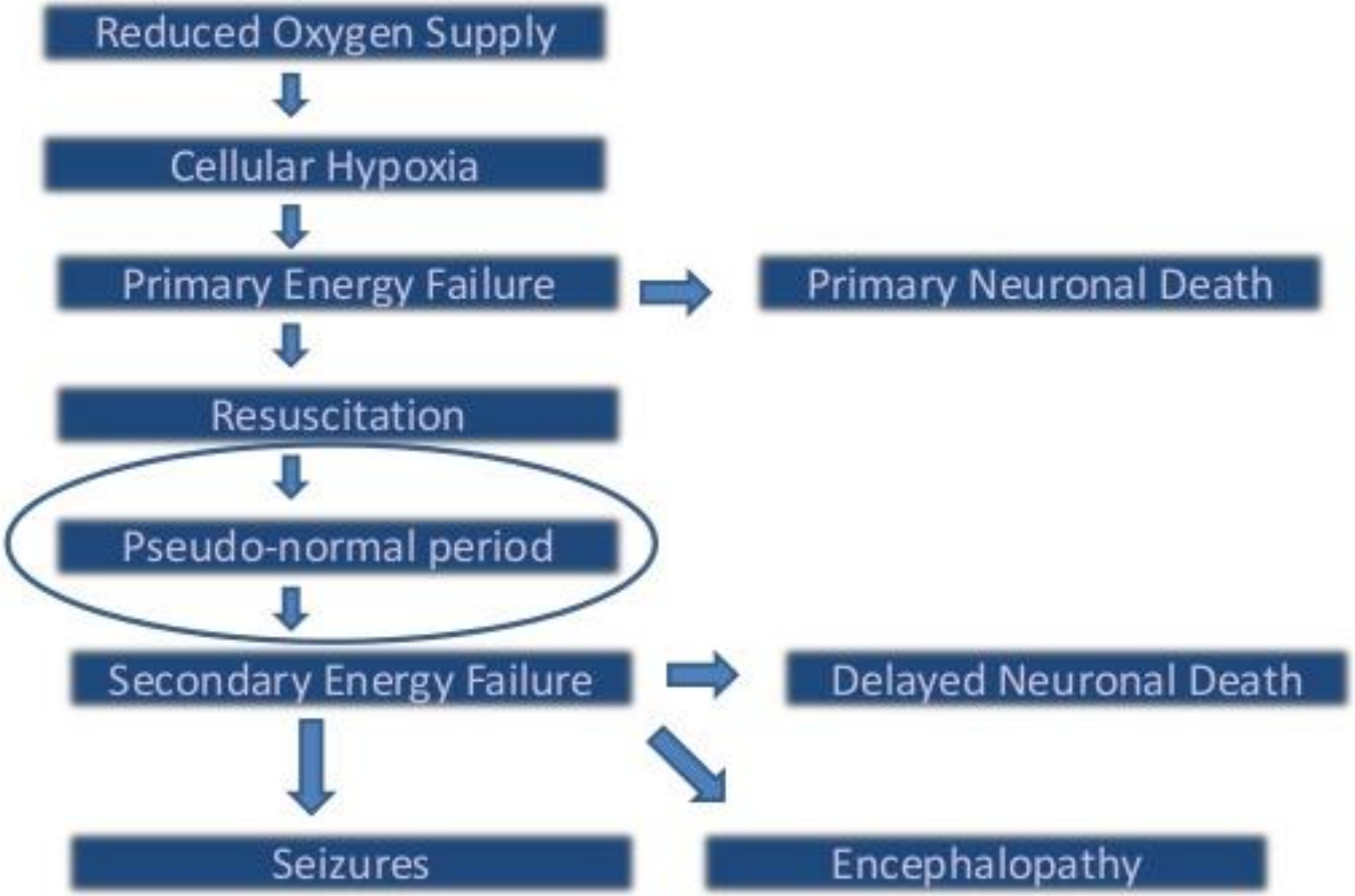
# treatment

**Needs further evaluation:**

- hypothermia: cooling the brain below normal temperature suggesting potential outcome.
- Allopurinol.
- Steroids : no clear good outcome.
- Mamitol
- Magnesium sulphate.
- MK-801 an EAA antagonist : has shown promising results in animals..
- Erythropiiotin under study

*Follow up:* physiotherapy and developmental assessment are needed, anti convulsion treatment should be continued depend on CNS symptoms.

# 1. Hypothermia



# 1. Hypothermia

**Mechanism**

- Modifies cells programmed for apoptosis
- Reduces cerebral metabolic rate, therefore production of toxic NO and Free Radicals.

**Who is treated?**

- Neonates with an abnormal aEEG- fairly predictive

**What happens?**

- Aims to lower basal ganglia temperature 32-34°c
- Whole body or Just head

**Disadvantages**

- Little benefit if severe brain damage
- Not yet trialled in pre-term infants

# Management - Hypothermia

- **Has become standard of care**
- **Whole-body and head-cooling** available
  - Unclear if one regimen is superior to the other - currently either one is utilized, based on availability
- **Aim to get core (rectal) temperature to 33-35° C for 72 hours**
  - ***based on Cool Cap and NICHD Neonatal Research Network trials***

# Hypothermia - Mechanism of Action

- **Reduces cerebral metabolism, prevents edema**
- **Decreases energy utilization**
- **Reduces/suppresses cytotoxic amino acid accumulation and nitric oxide**
- **Inhibits platelet-activating factor, inflammatory cascade**
- **Suppresses free radical activity**
- **Attenuates secondary neuronal damage**
- **Inhibits cell death**
- **Reduces extent of brain damage**
  - **DEATH OR SEVERE DISABILITY AT 18 MONTHS OF AGE SIGNIFICANTLY REDUCED!!**

# Criteria for Hypothermia

- **Hypothermia is not effective for every baby**
  - **Currently only used in infants ≥ 35 weeks**
- **Time interval between birth and initiation of treatment important**
  - **Treatment must be started within 6 hours of birth to be effective**

# How Does Hypothermia Therapy Work?

Babies with hypoxic-ischemic encephalopathy (HIE) undergo cooling . But what does the process look like, and how does it help stop the spread of brain damage?

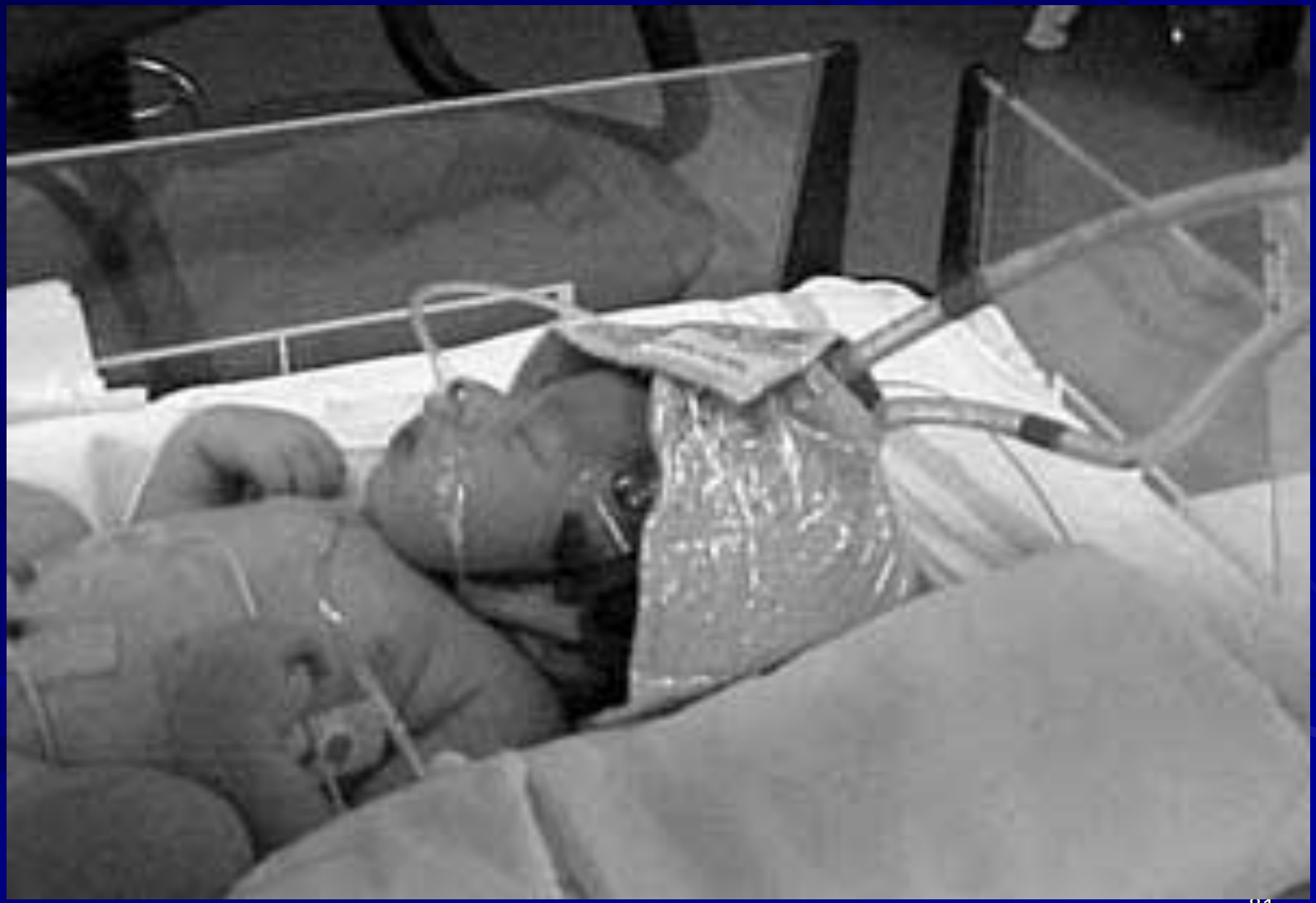
## THE PROCESS

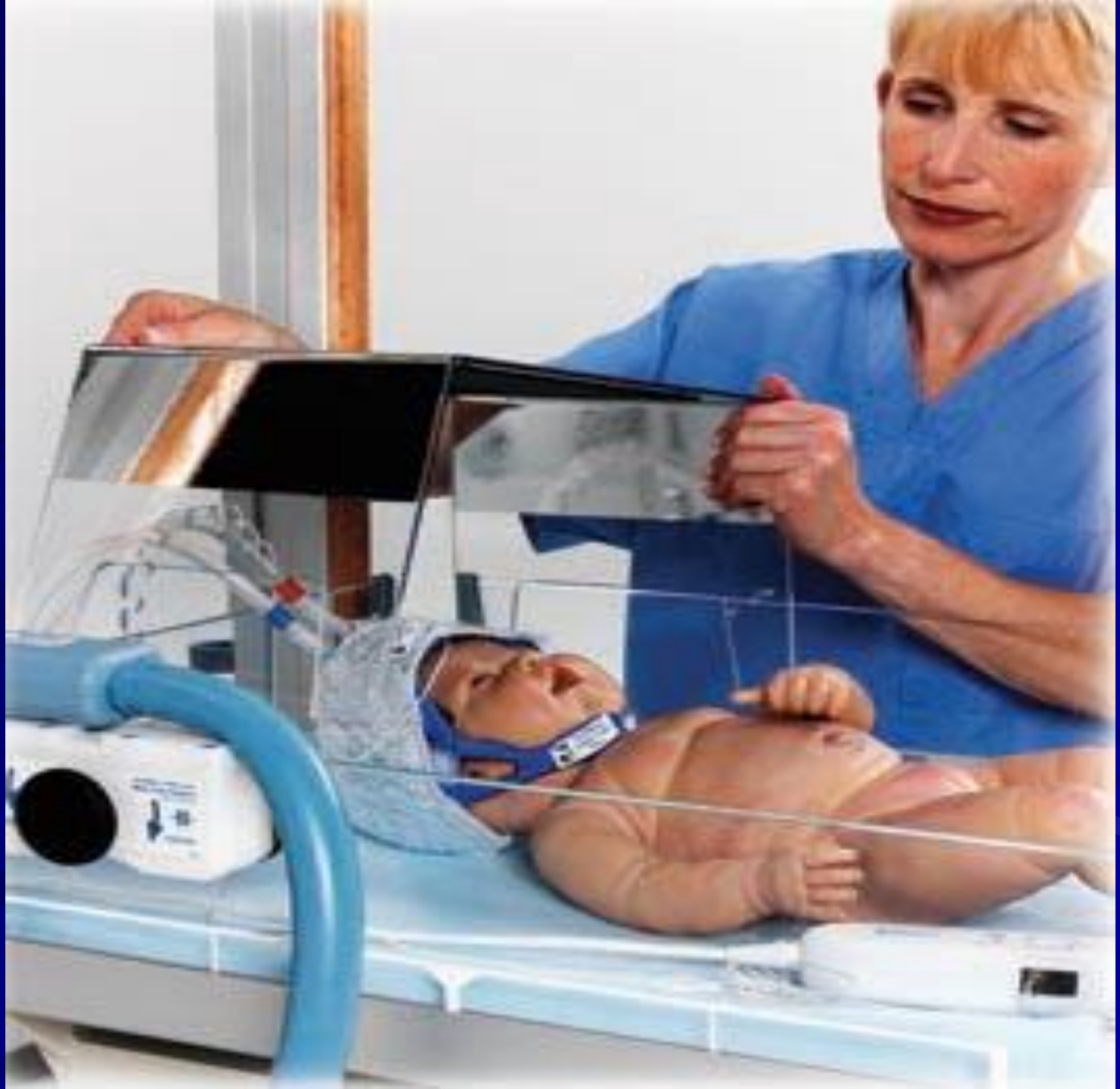
Using a cooling cap or blanket, a newborn's body temperature is lowered to 33.5 degrees Celsius.

The newborn's body temperature is lowered for 72 hours.

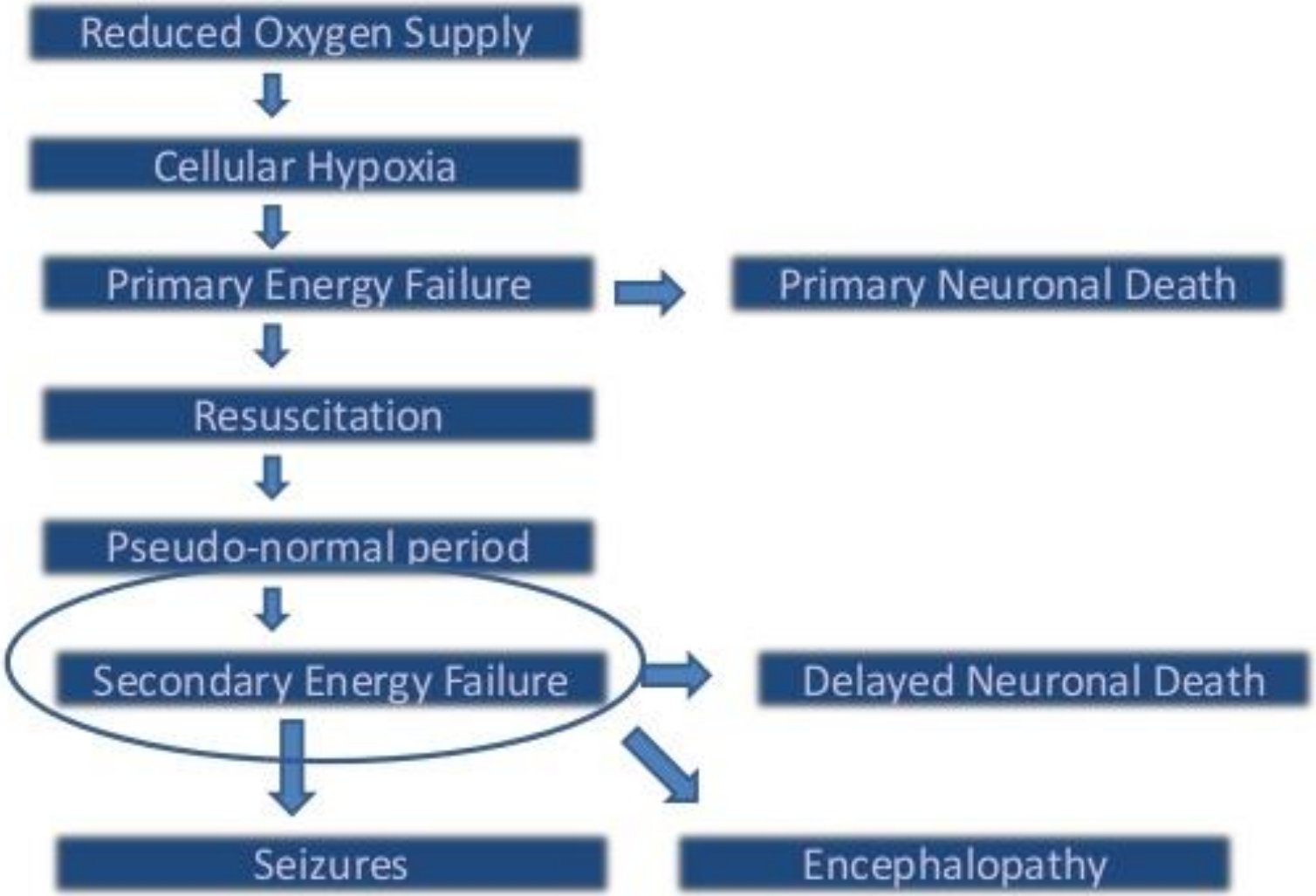
Decreased body temperature slows the baby's metabolic rate.

Cells are able to recover, preventing the spread, severity and permanence of brain damage.





# 2. Chemical Therapy



# 2. Chemical Therapy

Agents that inhibit glutamate release, uptake, or blockage of glutamate receptors

- Magnesium
- Xenon

Blockade of free radical generation or removal- free radical inhibitor

- Deferoxamine
- Allupurinol
- Indomethacin

Blockade of downstream effects and inhibitors of inflammatory effects

- Erythropoetin

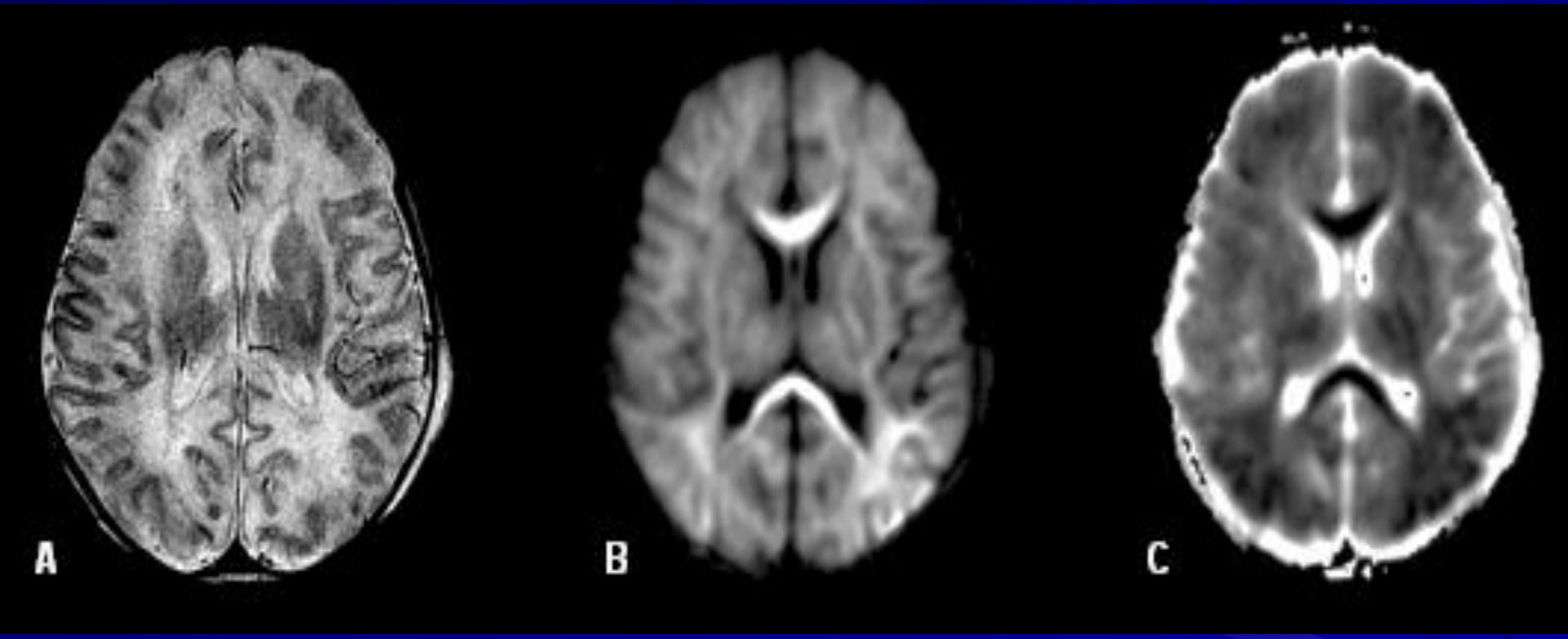
# 3. Cellular Therapy

Stem cells that may help repair ischaemic neuronal tissue

- Neural Stem cells
- Multi-potent adult progenitor stem cells
- Mesenchymal Stem cells (MSCs)
- Human Umbilical Cord Stem Cells

MSCs can differentiate into neurones and oligodendrocytes, therefore help repair ischaemic neural tissue.

May also help with restoration of functional networks via axonal sprouting and synaptogenesis.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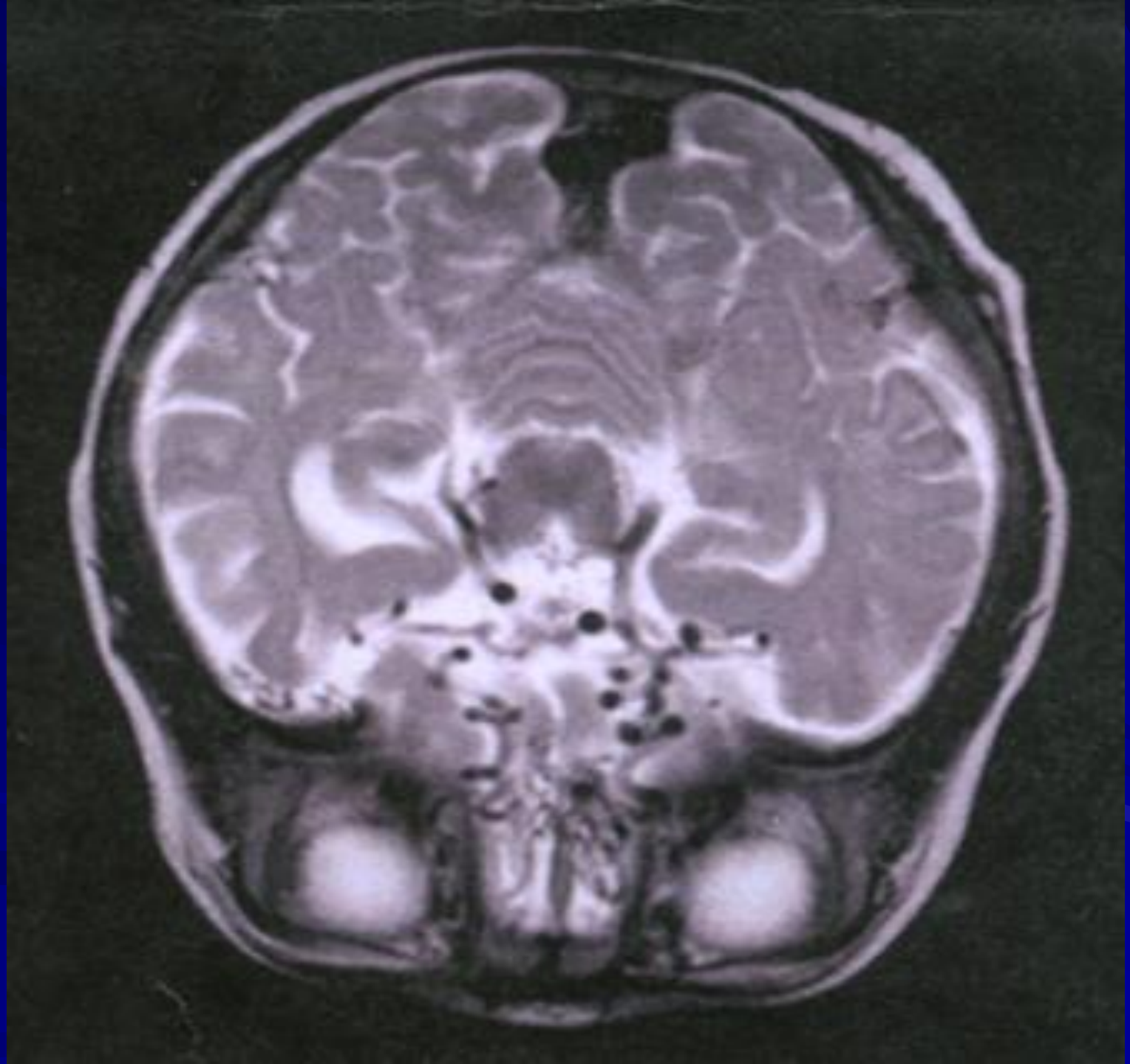

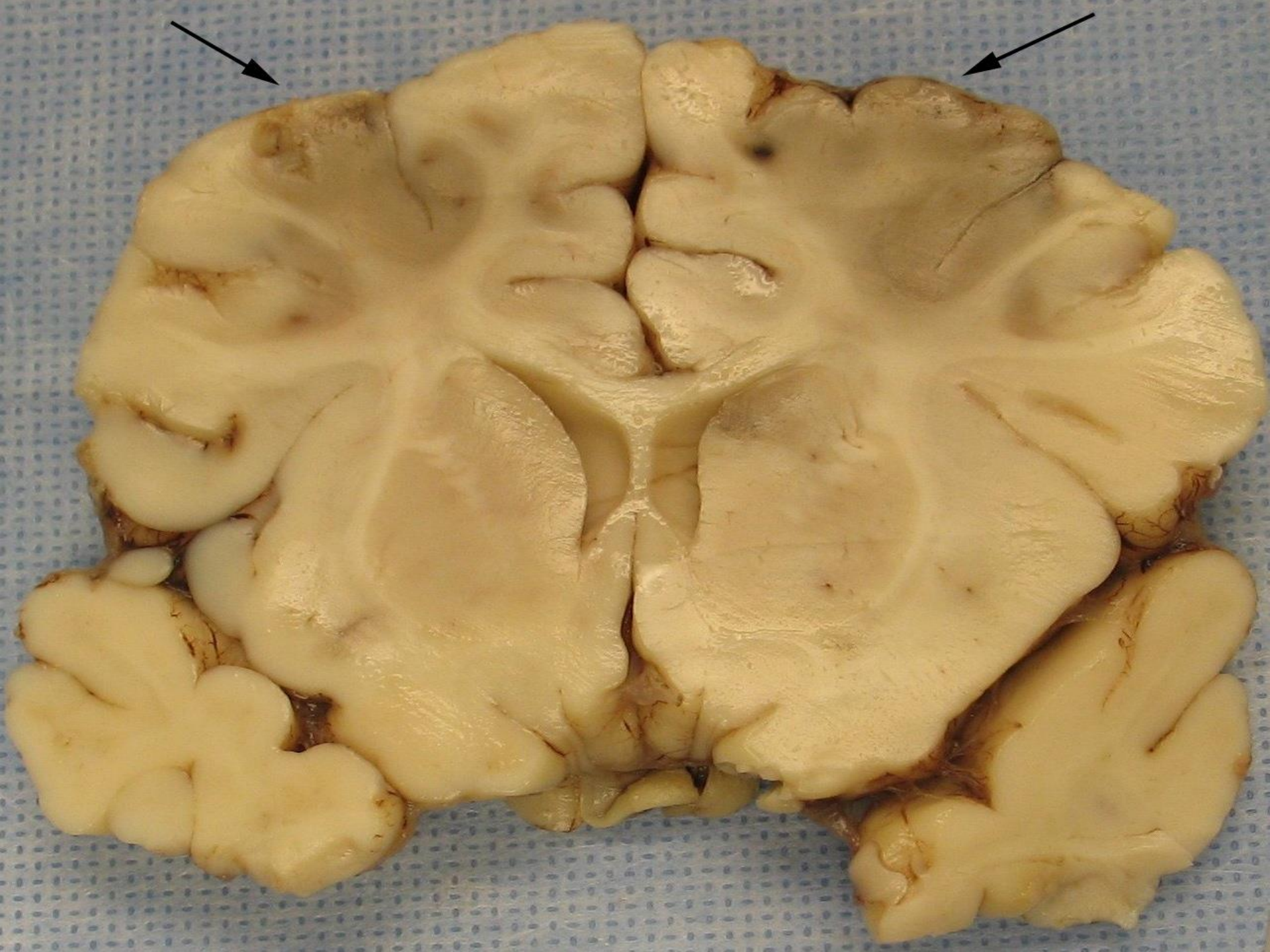

# prognosis

- Mild HIE: tends to be free from serious CNS complications.
- Moderate HIE: about 30-50% have serious long term complications, and 10-20% minor complications mainly learning difficulties.
- Severe HIE: mortality rate about 50% ,usually in 1st month.

among survivals , 80% have serious complications, the most frequent sequelae are mental retardation, epilepsy , and cerebral palsy.

# prognosis

Accurate prediction of the severity of long term complication is difficult, these pointers may be used:

- lack of spontaneous breathing within 20-30 minutes of birth is associated with high mortality.
- The presence of seizures is an ominous sing especially poorly controlled one.
- Abnormal clinical neurological finding beyond 1st 7-10 days of life indicate poor prognosis.
- Poor head growth during the postnatal period and 1st year indicate neurological deficit.


THANK
YOU!


Let's
STAY
Home