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National Neonatology Forum, DELHI

Delhi Neocon 2020

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Foreword

SECTION 1

Perinatal Management

Protocol 1: Methods of fetal monitoring and surveillance

Goal of fetal monitoring

(i)Prevention of intrauterine death

(ii) avoiding unnecessary interventions

At risk patients to be considered for surveillance:

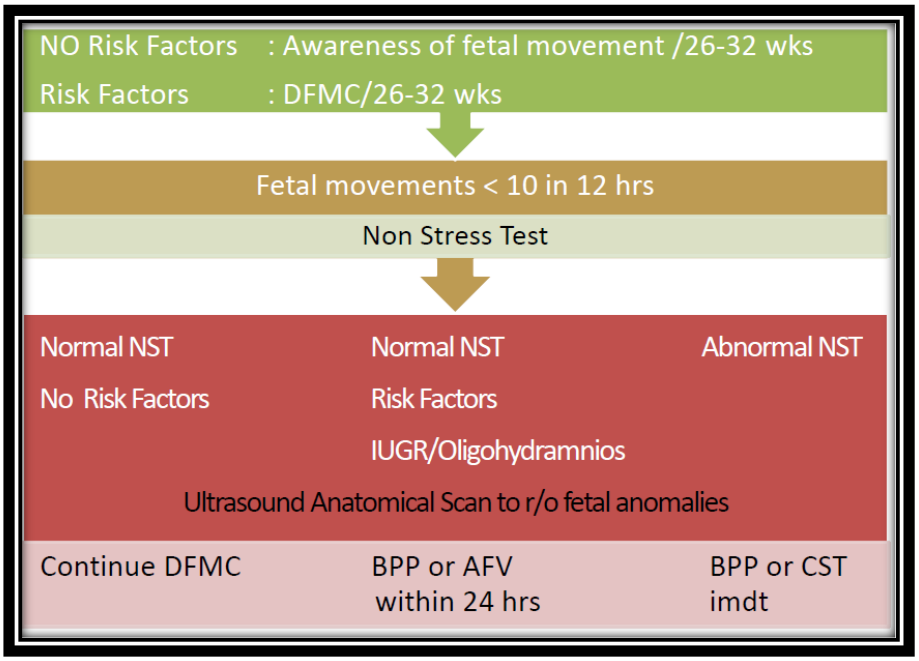
- Previous obstetrical history
  - PIH/Abruptio Placenta/IUGR/Stillbirth
- Current Pregnancy: Maternal
  - PIH/GDM/pPROM/Vaginal Bleeding/Post Term/ Rh Isoimmunization
- Current Pregnancy: Fetal
  - IUGR/Suspected Oligohydramnios/Decreased fetal movement/Multiple Pregnancy/Preterm Labor/ Malpresentation

Methods of fetal monitoring and surveillance

1. Daily Fetal Movement counts (DFMC)
2. Non stress test (NST)
3. Contraction stress test (CST)
4. Biophysical profile (BPP)
5. Umbilical artery doppler changes

Recommendations

1. Daily fetal movement count (DFMC)



2. Non stress test (NST)

Parameter	Normal/Reactive NST	Abnormal/Non Reactive NST
• Baseline	• 110-160 bpm	• Bradycardia Tachycardia
• Variability	• 6-25 bpm	• ≤ 5 for > 80 min ≥ 25 for > 10 min
• Decelerations	• None or occ variable < 30 s	• Late Decelerations/ Variable for > 60 s
• Accelerations • Term	• ≥2 with acme of ≥ 15 bpm, ≥ 15 s in < 40 min.	• ≤ 2 with acme of ≥ 15 bpm, lasting 15 sec. in > 80 min.
• Preterm < 32 wks	• ≥2 with acme of ≥ 10 bpm, ≥ 10 s in < 40 min.	• ≤ 2 with acme of ≥ 10 bpm, lasting 10 sec. in > 80 min.

3. Contraction stress test (CST)

Interpretation	Findings	Follow Up
• Negative	• No late or significant variable decelerations	• No further intervention , continue NST
• Positive	• Late or significant variable decelerations ≥ 50 % contractions	• High false positive rate
• Equivocal	• Intermittent late or variable decelerations < 50 % of contractions	• High false positive rate
• Unsatisfactory	• Fewer than 3 contractions in 10 min	• Further testing

4. Biophysical Profile (BPP)

Components

Manning et al, 1980

Non Stress Test	
Fetal Breathing movements	• At least one episode continuing for more than 30 seconds
Gross Body Movements	• At least 3 limb or body movements
Fetal Muscle Tone	• An episode of active extension with return to flexion of a limb or trunk OR opening or closing of the hand
Amniotic fluid volume	• At least one cord and limb-free fluid pocket which is 2 cm by 2 cm in two measurements at right angles.

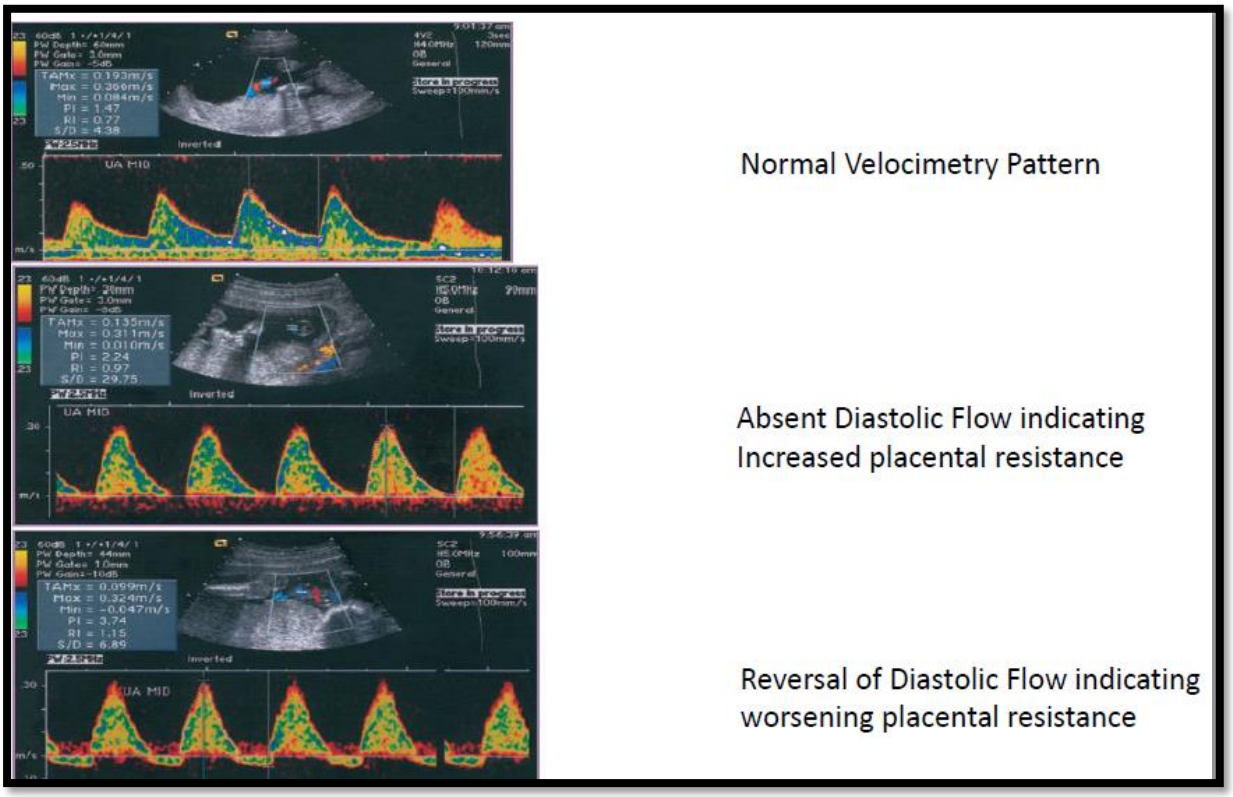
Interpretation of BPP

Score	Risk of perinatal mortality in 1 week without intervention	Intervention
10/10	1/1000 fetal asphyxia extremely rare	No intervention
8/10 (abnormal fluid)	89/1000 chronic fetal compromise	If intact renal function and membranes, delivery for term fetus intense surveillance < 34 weeks
6/10 **Abnormal fluid** **Normal fluid**	Variable possible fetal asphyxia 89/1000	Repeat test within 24 hours Term – deliver < 34 weeks intense surveillance
4/10	91/1000 high probability of fetal asphyxia	Delivery for fetal indications
2/10	Fetal asphyxia almost certain	Immediate delivery
0/10	600/1000 fetal asphyxia certain	Immediate delivery

Diagnostic accuracy of various methods

Test	False Negative	False Positive %
Non-Stress Test	1.9–5	50%
Contraction Stress Test	0.4	40%
Biophysical Profile	0.6	40%
Modified BPP	0-0.8	60%

5. Umbilical fetal artery Doppler



Intevention based on umbilical artery doppler changes

Abnormality	BPp Frequency	Decision to Deliver (Fetal)
Elevated Indices only	Weekly	Abnormal BPP or Term or > 36 wks with no fetal growth
AEDV (Absent End diastolic velocity)	Twice weekly	Abnormal BPP or > 34 wks proven maturity
REDV (Reversal of end diastolic velocity)	Daily	Any BPP < 10/10 or > 32 wks (ANS given)
REDV-UVP	Three times daily	Any BPP < 10/10 or > 28 wks (ANS given)

Protocol 2: Approach to antenatal hydronephrosis

Antenatal Hydronephrosis

Classify

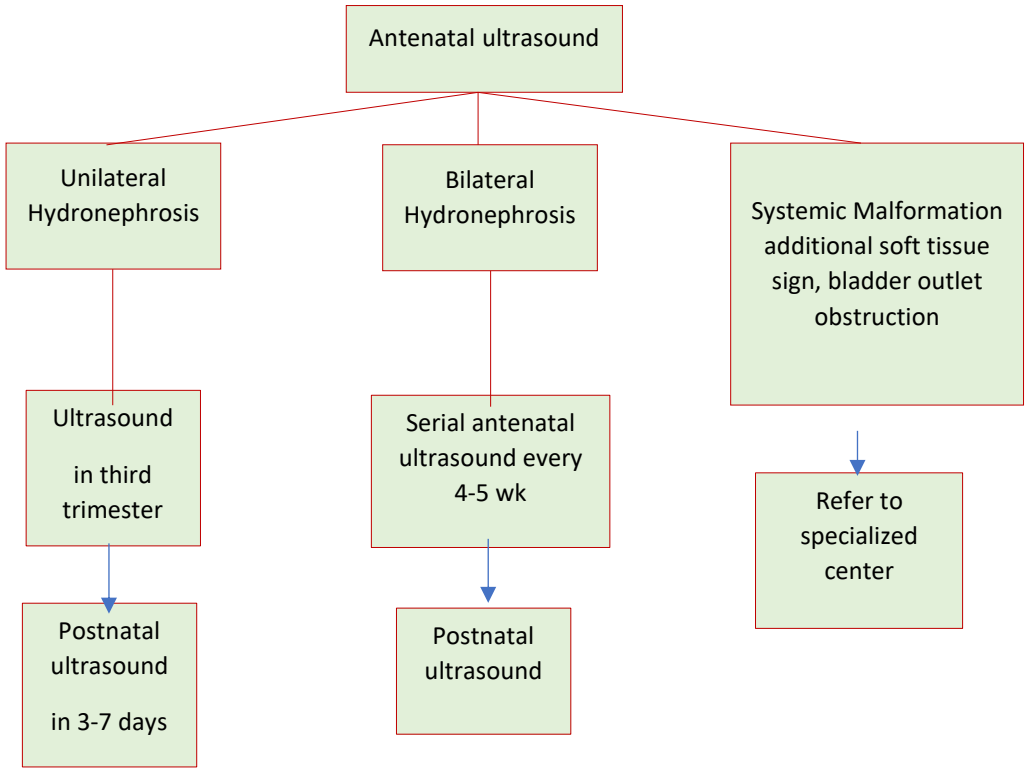
Severity of ANH by Antero-posterior Diameter

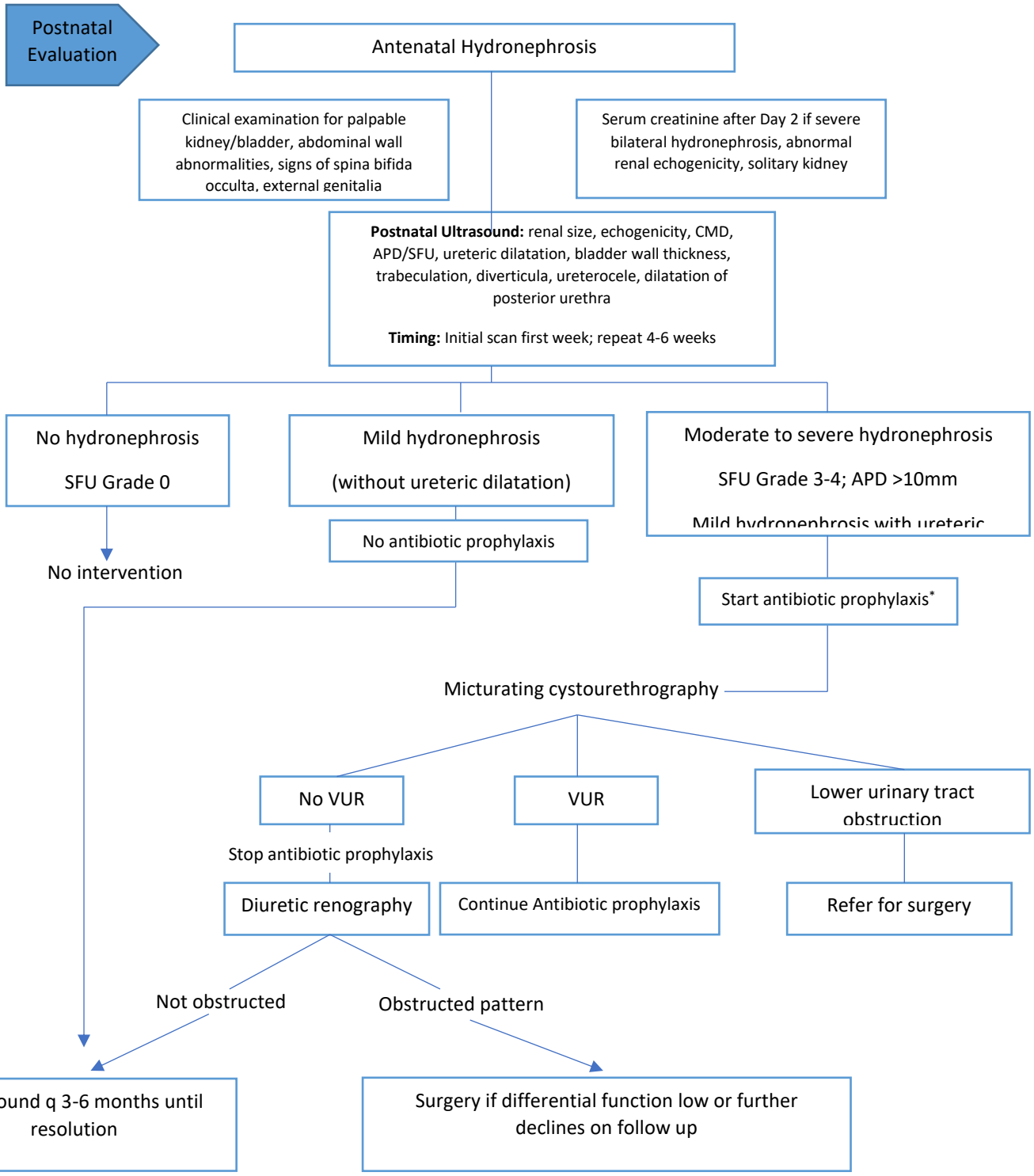
Degree of ANH	Second Trimester	Third Trimester
Mild	4 to 6 mm	7 to 9 mm
Moderate	7 to 10 mm	10 to 15 mm
Severe	> 10 mm	>15 mm

SFU Grading of ANH

SFU Grade	Ultrasound Findings
0	No splitting
1	Pyelectasis
2	Pyelectasis with dilatation of 1 or more major calyces
3	Pyelectasis with dilatation of all 3 major calyces
4	Pyelectasis with parenchymal thinning as compared to contralateral kidney

Monitor





*Commonly used antibiotics

Antibiotic	Dose mg/kg/day
Cephalexin	10
Cefadroxil	5
Cotrimoxazole#	1-2
Nitrofurantoin#	1-2

Avoid in <3 months, G6PD deficiency

Abbreviations

ANH	Antenatal hydronephrosis
APD	Antero-posterior diameter

Protocol 3: Approach to fetal ventriculomegaly

Definition: Dilatation of ventricles
- Ventricle width >10 mm on antenatal USG

Classification
- Mild (ventricle dia 10-12 mm)
- Moderate (ventricle dia 12.1-15 mm)
- Severe (ventricle dia >15 mm)

Aetiology

Obstructive
- Arnold chiari II malformation
- Dandy walker malformation
- Aqueductal stenosis
- Obstructing masses

Dysgenesis
- Agenesis of corpus callosum
- Septo optic dysplasia
- Holoprosencephaly
- Schizencephaly

Destructive
- Intracranial hemorrhage
- Hydrancephaly
- Periventricular leukomalacia
- Infections:
  - CMV
  - Toxoplasma
  - Zika virus (endemic area)

Investigations: Level II USG, fetal MRI brain
- Fetal echocardiogram
- Amniocentesis – fetal karyotype
- Maternal TORCH testing
- Genetic studies

Management

Mild
- Serial USG scan to follow progression / regression
- Counselling of parents

Vaginal delivery
- Outcome favourable
- Infant likely to be normal

Moderate
- Serial USG scan to follow progression / regression Counselling of parents

LSCS
- Increased chances of neurodevelopment abnormalities

Severe
- If diagnosis made prior to fetal viability → termination of pregnancy

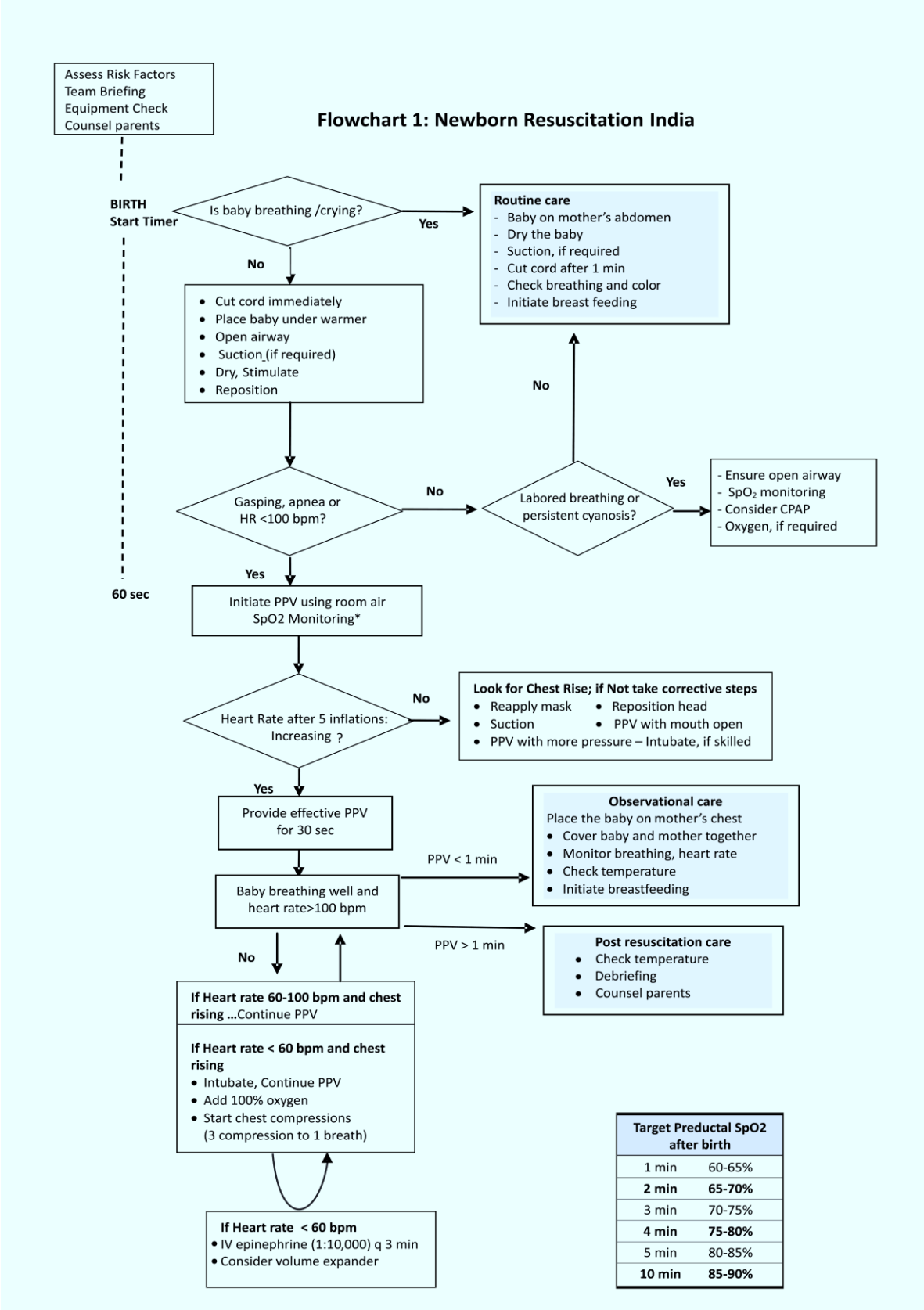
If diagnosis made after a period of fetal viability
- Cephalocentesis prior to delivery
- Ventriculoamniotic shunt
- Shunting after birth
- Frequently associated with other congenital anomalies

References

SECTION 2

Delivery room management and Essential newborn care

Protocol 1: Neonatal Resuscitation



Recent Modifications in AAP NRP 2020

1.Delayed cord clamping mentioned as " longer than 30 seconds" ; 2015 version stated " at least 30 to 60 seconds"

2. PPV may be initiated with air (21% oxygen) in term and late preterm babies, and up to 30% oxygen in preterm babies. (In NRP India, it is < 32 weeks – 30 % , 32 weeks or more – room air)

3. If all steps of resuscitation are effectively completed and there is no heart rate response by 20 minutes, redirection of care should be discussed with the team and family

Protocol 2: Decision making in Periviable gestation

There is no clear-cut timeline for peri viability and differs amongst different countries.

- **ACOG Guidelines** defines it as 'Delivery occurring from 20 0/7 to 25 6/7 weeks of gestation'.
- **NRP** defined a cut off age of 24 weeks and a weight of 400 gms which can be used to initiate resuscitation.

There are no specific guidelines in India to tackle the issue of Periviability.

- **IAP consensus statement 2017** said decisions during periviability should be based on local survival data and possibility of intact survival in a given set-up. In tertiary care centres, 24 weeks can be used as criteria for full scale neonatal interventions and in other centres, 28 weeks can be used as a cut off. Discussion with parents antenatally regarding the prognosis (both survival and neurodevelopmental outcome) should be basis of interventions before cut off gestations, whether to provide palliative care or perform full scale neonatal interventions. The discussion should be documented and signed by unit-in-charge or clinician, the parent and any other witness, if present.
- The guiding principles for the neonatologist are beneficence (doing good), non-maleficence (doing no harm), autonomy (respecting individual preferences) and justice.

However, the decision arrived during discussion with parents can change, if after delivery, the clinician feels that resuscitation and other interventions would be in the best interest of the baby.

President's commission in 1983,

Physician assessment of treatment	**Parents prefer to accept treatment**	**Parents prefer to forego treatment**
Clearly beneficial to infant	Provide treatment	Provide treatment (seek legal review)
Ambiguous or uncertain benefit to infant	Provide treatment	Withhold/ Withdraw treatment
Futile	Provider treatment unless provider declines to do so	Withhold/ Withdraw treatment

Calculation of exact gestational age is the most important 1st step while tackling issues of periviability. Calculations should be based on 1st ultrasound (Dating scan), Last menstrual period, Embryo transfer date.

Where none of information is available or there is no time available, actual weight at birth can be used as an indicator to initiate and perform full scale neonatal interventions. As per NRP, 400 gms is considered as a cut off for resuscitation.

2 Important aspects are involved during threshold of Periviability, Parental counselling and interventions. Parental counselling should include chances of survival and chances of long-term neurodevelopmental outcome in details along with expected complications of extreme prematurity.
In-utero transfer to a centre with tertiary care NICU facility should always be offered.

Obstetric interventions			
	< 22 weeks	**22-24 weeks**	**> 24 weeks**
Antenatal steroids	Not recommended	Consider	Recommended
Tocolysis to prolong labour for steroids	Not recommended	Consider	Recommended
Magnesium sulphate for neuroprotection	Not recommended	Consider	Recommended
Antibiotics to prolong latency during PPROM	Consider	Consider	Recommended
Caesarean delivery for fetal indication	Not recommended	Not recommended	Recommended
Neonatal Interventions			
Palliative care	Offer	Offer	Not offered
Level III care	Not offered	Consider after parental discussion	Recommended

- Palliative care might be offered to babies born below cut off gestations after discussion with parents and should include providing warmth, gentle handling, skin to skin contact, syringe drop feed, pain relieving interventions, emotional support to parents by social workers or psychologists.
- After 24 weeks gestation, sometimes the parents might not want neonatal interventions; they should be presented with facts of survival and neurodevelopmental outcome. If they do not want resuscitation, according to Law commission of India 2012, it is mandatory to seek High court's opinion for making a decision to withdraw life support.
- The guidelines are based on the data from the western literature and multi-centric data would be required from Indian institutions for framing the specific guidelines.

Protocol 3: Management of hypothermia

Axillary temperature < 36.5 degree Celsius

Look for possible causes of hypothermia

Check room temperature

Hypothermia

Mild hypothermia 36 to 36.4

- Ensure room is warm (maintain at 25◦C to 28◦C)
- Position baby skin to skin with mother continue breastfeeding
- Recheck temperature in 1 hour
- If temperature is normal, cover the baby adequately including head, hands and feet
- If no improvement, treat as Moderate Hypothermia

Moderate hypothermia 32◦C – 35.9◦C

- Provide warmth using a warmer
- If no warmer is available, start skin to skin with mother (KMC).
- Cover mother and baby together optimally using pre-warmed clothes
- Ensure room is warm (maintain at 25◦C – 28◦ C)
- Continue breast feeding
- Measure blood glucose, if hypoglycaemic, treat for hypoglycaemia

Severe hypothermia (< 32◦ C)

- Provide warmth using a warmer
- Rapid re-warming till baby is 34oC and then slow re-warming*
- Start oxygen and maintenance IV fluids
- Give Inj Vitamin K, if not given or status unknown
- Ensure room is warm (maintain at 25◦C – 28◦C)
- Measure blood glucose, if < 45v mg per dL, treat for hypoglycaemia
- Reassess every 15 minutes, if temperature does not improve, increase settings of warmer
- If no improvement, work up for sepsis and manage accordingly

*Initially use high setting of the warmer and if the baby's temperature has been increasing at least 0.5ºCelcius per hour in l at three hours, rewarming is successful, shift to lower setting of warmer and continue measuring the baby's temperature every two hour s

SECTION 3

Management of cardiorespiratory disorders of neonate

Protocol 1: Management of apnoea

Apnea is absence of breathing for 20 seconds or longer or a shorter pause associated with bradycardia (<100 beats per minute), cyanosis, or pallor. Can be of central (25-40%), obstructive (10-25%) or mixed type (50%). Periodic breathing is a normal breathing pattern in preterm neonates characterized by pauses of breathing < 5-10 seconds followed by a series of rapid breathing episodes and return to normal breathing without stimulation.

Incidence: Inversely proportional to gestation age (Varies from <10% at 34 weeks to >60% at 28 weeks)

Etiology	
Preterm Neonates	
Idiopathic	Apnea of Prematurity
CNS	IVH, Meningitis, Perinatal Asphyxia, Seizures, Depressant Drugs
Respiratory	RDS, Pneumonia, Pulmonary Hemorrhage, Obstructive Airways Lesion, Hypoxemia, Hypercarbia, Pneumothorax, Airway Obstruction Caused by neck flexion
Cardiovascular	PDA, CHF, Hypo/Hypertension, Congenital heart diseases
Gastrointestinal	GERD, abdominal distension, NEC
Infection	Sepsis, Meningitis Pneumonia
Metabolic	Hypoglycemia, Hypocalcaemia, Hypo/Hypernatremia, Acidosis
Haematological	Anemia, Polycythemia
Temperature instability	Hypothermia/ Hyperthermia
Term Neonates	
Intrapartum Asphyxia	Hypoxia, acidosis, Brainstem depression,
Placental transfer of drugs	Narcotics, magnesium sulfate, General anesthetics
Neuromuscular disorders	Congenital Neuropathies and Myopathies
Trauma	Intracranial Haemorrhage ,Spinal cord transaction
Infection	Pneumonia, Sepsis, Meningitis
Central nervous system	Seizures, Congenital central hypoventilation syndrome, Malformations

Apnea of Prematurity

- Diagnosis of exclusion; related to immaturity of central and peripheral chemoreceptors along with immature airway reflexes.
- Usually presents after 1-2 days of life and within the first 7 days. Frequency and duration of apnea decreases with advancing postnatal age. Apneic spells stops by 37 weeks' PMA in 92% of infants and by 40 weeks' PMA in > 98% infants.
- More severe events requiring intervention resolves first and, spontaneously resolving apnea/ bradycardia events of uncertain clinical significance are last to resolve.

Investigations

Apnea in infants < 28 weeks, with no other signs, requiring only tactile stimulation & responding to single loading of caffeine can be monitored clinically without any investigation till they require second loading of caffeine.

- Each apnea episode DOES NOT warrant repeated work up unless a new etiology is suspected.
- Any apnea requiring BMV should undergo investigation.

Suspected Etiology	Investigations
Sepsis, pneumonia, meningitis	Sepsis screen, Blood culture ,LP, X-Ray chest
Metabolic	RBS ,Serum Ca, Serum Na
Anemia / Polycythemia	Hematocrit
PDA	X-Ray chest ,2D-Echo
IVH	USG Cranium

Treatment

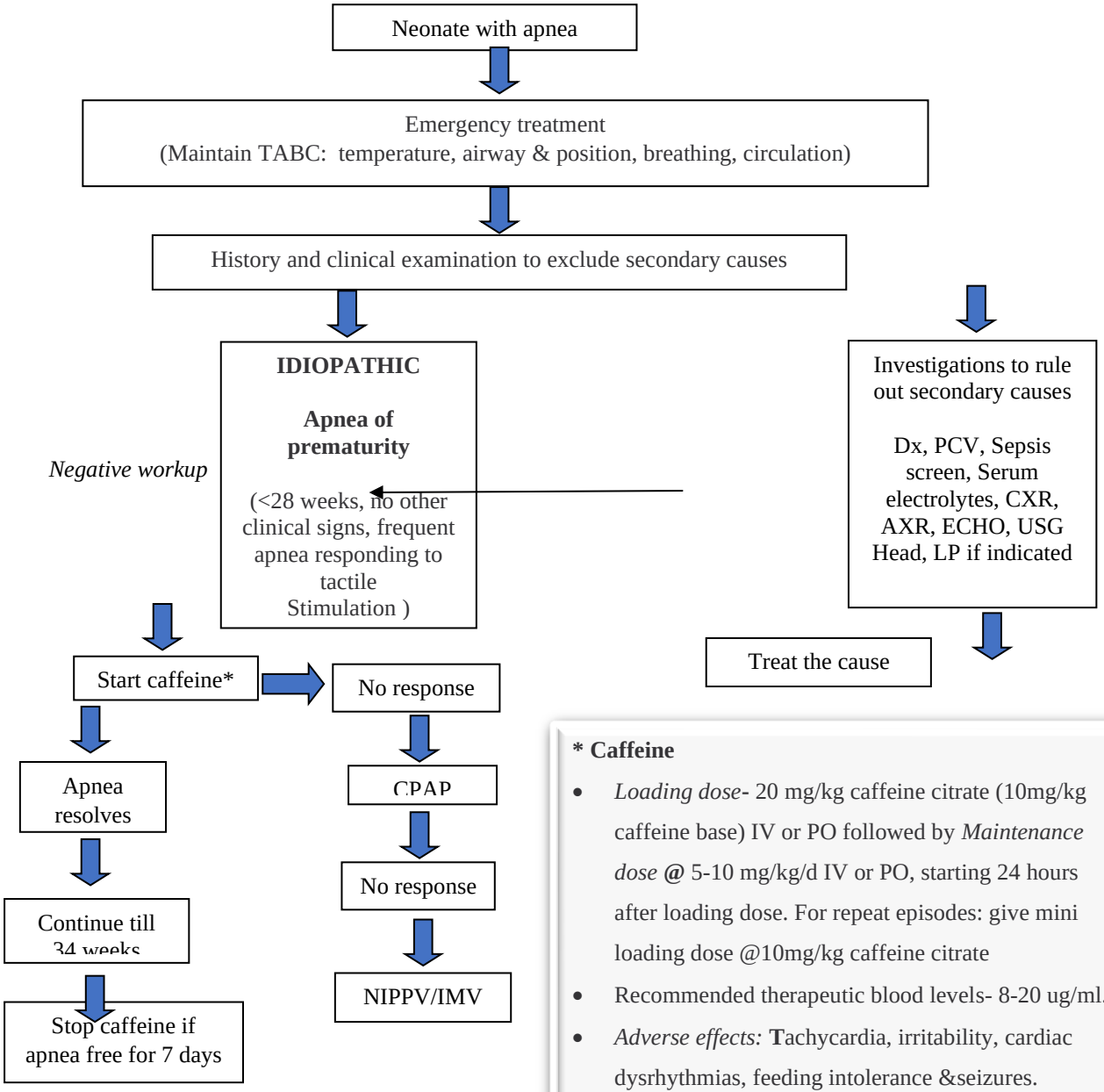
1. Supportive measures: Maintain TABC
    - Maintain temperature between 36.5-37.5 degree Celsius
    - Place in sniffing position to maintain airway. Prone positioning in preterms, stabilizes the chest wall and may reduce apnoea.
    - Supplemental oxygen if required, to maintain the SpO2 between 91-94 %
    - Treatment of the underlying cause (hypoglycemia /hypocalcemia/ anemia, sepsis etc)

2. Specific treatment

- Caffeine- Non selective adenosine receptor antagonism (A1 and A2a) resulting in increase in minute ventilation & diaphragmatic contraction, improved CO2 sensitivity and decreased hypoxic depression of breathing.
- Indication:
- Apneas are frequent ≥3 episodes/hour or ≥3 episodes over 24 hrs
- Need of positive pressure ventilation for apnea unresponsive to tactile stimulation
- Effective in reducing the number of apnea attacks and use of mechanical ventilation in 2-7 days after starting treatment.
- Continue till 34 completed weeks corrected gestational age if apnea free in last 7 days and monitor the baby for apnea recurrence for next 5-7 days after caffeine discontinuation.

- CPAP @ 4–5 cmH2O splints upper airway stabilizes chest wall with increases FRC. Indications are:
- >2 episodes per hour over 4 hours requiring tactile stimulation,
- 1 episode requiring PPV despite of optimal caffeine therapy
- NIPPV/ Mechanical ventilation: if apneas continue to occur despite optimal caffeine and CPAP.

Algorithm for management of neonatal apnea



*** Caffeine**

- *Loading dose*- 20 mg/kg caffeine citrate (10mg/kg caffeine base) IV or PO followed by *Maintenance dose* **@** 5-10 mg/kg/d IV or PO, starting 24 hours after loading dose. For repeat episodes: give mini loading dose @10mg/kg caffeine citrate
- Recommended therapeutic blood levels- 8-20 ug/ml.
- *Adverse effects:* **T**achycardia, irritability, cardiac dysrhythmias, feeding intolerance &seizures.

Protocol 2: Approach to respiratory distress in a preterm neonate

The respiratory distress syndrome (RDS) common in preterms. (1) grunt, (2) tachypnea (> 60/ min) and (3) retractions.

Presence of any of the 2 of the above with prematurity would indicate a high possibility of RDS.

Differentials of RDS in a Preterm:

The RDS s not only the cause of respiratory distress in preterm, important not uncommon differentials are ;

1. Delayed Adaptation (Transient Tachypnea)
2. Congenital Pneumonia/ Early onset sepsis (EONS)
3. Congenital Malformation (Congenital Diaphragmatic Hernia; CDH)
4. Cardiac disease / failure or Shock, Persistent Pulmonary Hypertension of newborn (PPHN)
5. Early Pneumothorax
6. Hemodynamic Significant PDA (Generally late onset)

Examination of a Preterm with Respiratory distress:

The respiratory distress should be graded using a scoring like the “Silverman Andersons Score”.
These retraction scores give an objective way to assess the condition of the baby.
In addition, the SPO2 , vitals, chest expansion, air entry and the ongoing ABG analysis should be done as and
when required.
The transillumination should be performed on suspicion of pneumothorax. The extra-pulmonary causes of respiratory
distress
viz, PPHN, CDH, intracranial bleed also should be considered and the baby examined for the same.
The chest x ray of the baby should be examined for reticulogranular opacities / poor expansion (HMD), Cardiomegaly with hyper-inflation (TTNB),air leaks with mediastinal shift (Pneumothorax) , congenital abnormalities (CDH) and oligemic lung fields (PPHN)

Management of a Preterm baby with RDS:

In a preterm baby with respiratory distress, the CPAP should be initiated at the earliest, as the commonest cause

in these babies is RDS. However, the EONS should be considered in all the spontaneous preterms and a sepsis workup performed.

The decision to give surfactant (SF) should be taken early (within 2 hrs) if the baby is not able to maintain saturations and/or has retractions even on moderate CPAP pressures and fio2 of 30%.

If the spontaneous efforts are good and the baby is hemodynamically stable the SF may be delivered by INSURE (**I**ntubation- **S**urfactant_**R**apid _ **E**xtubation) or by Minimal Invasive technique if the team is experienced.

Presence / worsening of respiratory distress and / or hypoxemia (PaO2 <50 mmHg) on a CPAP of 7cmH_2O and 70% FiO_2 should be considered as failure of CPAP and mechanical ventilation (MV) initiated without delay.

If the HMD is complicated with asphyxia, PIE (pulmonary interstitial emphysema), PDA or sepsis, multiple doses of SF. (All surfactants available have comparable efficacy, even though some studies have **reported** porcine SF to be better n smaller babies)

Invasive Ventilation:

The MV should be initiated immediately when required. There are different types of MV with different modes available.

Any mode of the ventilation if used strategically and rationally are good.

Lately, it has been recognized that the volutrauma contributes significantly in the ventilator induced lung injury (VILI).

Hence, the volume and the hybrid modes are now used as primary modes in many units.

The usual settings to be offered on invasive MV are the PIP (Peak Inspiratory Pressures), PEEP (Peak Expiratory End Pressures), Ti (Inspiratory Time), TV (Tidal Volume) and RR (Respiratory Rate), the Fio2 is adjusted in addition depending on the condition of the baby in concurrence with the pressures.

In HMD /RDS ; the initial settings would be PIP of 10-20 based on chest rise , PEEP of 4-5 adequate for expansion avoiding hyperinflation , short Ti of 0.3 to 0.4 and a rapid rate of 50-60. When a volume mode is used a target TV of 4-6ml/kg is used .

The ongoing changes in the settings are to be done based on clinical examination and the diagnostics like chest X ray, ABG reports and the natural course of the disease as required.

Ventilator adjustment:

The ongoing changes in the settings of the ventilator parameters should be based on the detail clinical examination of the baby and the ABG analysis. A general guideline, is detailed in the Table No.1

Table No.1: Adjustments to be made in the ventilator settings in different situations

Clinical / Biochemical Situation	Important Adjustment
Poor Chest expansion or decrease breath sounds Paco2 > 50 with inspired O2 > 60%	Increase PIP
Chest expansion Visible and the breath sounds heard PaCO2 : 40-50 with inspired O2 <60%	Maintain PIP
Chest appears to be expanding excessively Co2 <40 with inspired O 2 < 50%	Decrease PIP
Chest expanding but baby fighting against ventilator Paco2 > 50, with Inspired O2 <60% and acidosis	Increase frequency
Paco2 40-50 with inspired O2 > 60%	Increase PEEP
Paco2 < 40 with inspired O2 > 60%	Decrease PEEP

Weaning from Ventilation:

- The goal of MV should be to get the baby out of the ventilation. The Weaning should be a gradual, measured reduction of ventilator settings to a minimum point at which risk of VILI is the least and from where the infant can be safely taken off ventilator support.
- The method depends on the severity underlying RDS and the mode of ventilation from which he / she has to be weaned off. Some of the prerequisites for weaning a baby are clinically & hemodynamically stable; good and regular spontaneous respiratory efforts; basic lung disease improved and acceptable blood gases. A prior initiation of caffeine when extubation is planned decreases the chances of extubation failure in preterms Lately, caffeine started early and continued to PMA of 34 to 36 weeks in sicker and small babies also prevents BPD and is neuroprotective.
- The baby who has been ventilated also needs the post extubation care and chest physiotherapy to prevent and manage the complications of the ventilation. The long term follow up of these babies for the respiratory morbidity and the neuro-developmental impairment should also be undertaken in all these cases.

Protocol 3: Surfactant therapy

Early Initiation of CPAP/PEEP within delivery room

Initiate early PEEP/CPAP of at least 6 cm H2O in infants of < 30^{+0} weeks of gestation at highest risk of developing RDS/ Infants showing signs of RDS

'Surfactant prophylaxis' or 'Early Rescue Surfactant' protocol

Surfactant Prophylaxis

Prematurity-requiring intubation for initial stabilisation or transport

Ventillation strategies which minimise the risk of volutrauma

Extubate to non- Invasive ventillation as soon as is safe and possible

Routine prophylactic surfactant- no benefits with higher incidence of BPD of death in prophylactic surfactant group.

Early Rescue Surfactant
(within 2 hours)

Optimise non invasive respiratory support (CPAP)

Early Rescue surfactant should be given in case of **CPAP failure** indicated by FiO2 requirement **>30 %** on CPAP pressures of atleast 6 cm of H2O in first hour.

Early Rescue Surfactant - decreased mortality, BPD and air leak syndromes.

European consensus Guidelines on management of respiratory distress syndrome - 2019 update.

Rescue surfactant may also be considered in:

Severe meconium aspiration

Pneumonia

Pulmonary haemmorhage

Surfactant Preparations	***Surfactant Administration***
➢ *Babies with RDS should be given animal derived surfactant preparation – improved survival and decreased BPD* ➢ *Poractant alpha at initial dose of 200 mg/kg (2.5 ml/kg) is superior to 100 mg/kg of poractant alpha or 100 mg/kg (4 ml/kg) of beractant (Surventa)* ➢ *Synthetic preparations containing SP-B and SP- C under trials. Lucinactant (Surfaxin) containing SP-B licensed for use in USA*	➢ *Rapid bolus technique- recommended method of surfacatant administration.* ➢ ***In**tubate – **Sur**factant – **E**xtubate (InSurE) vs Non InSurE- lower incidence of mechanical ventillation, air leaks and BPD.* ➢ *Repeat second or occasional third surfactant dose should be considered if oxygen requirement i persistently high with evidence of RDS- lower incidence of pneumothorax and decreased trend towards mortality.*

Less Invasive/Non Invasive techniques:	LISA/MIST
➢ Using feeding tube / stiff catheter using Mcgill forceps- Less invasive Surfactant administration (LISA) / minimally Invasive surfactant therapy (MIST) ➢ Through laryngeal mask airway ➢ Nebulised surfactant therapy LISA – preferred mode of surfactant administration in spontaneously breathing newborns on CPAP, if clinician is experienced in technique	➢ Metaanalysis of LISA vs InSurE – decreased need for mechanical ventillation, reduced composite outcome of death/BPD or BPD at 36 weeks. ➢ Concerns – less CPAP delivery, loss of surfactant needing 10-15 % higher dose, less homogenous distribution, associated pain etc.

Protocol 4: Protective strategies for BPD prevention

Antenatal:

1. Prevent prematurity
2. Antenatal steroids in impending delivery in prematurity (24-34 weeks): Although steroids don't have a direct role in reduction of BPD but reduce chances of RDS and neonatal death.

Labour room care:

- In case the baby has respiratory distress, Start CPAP early: CPAP is superior to Intubation and PPV. No role of prophylactic surfactant
- Use blender, avoid hyperoxia.

NICU care:

- If the baby has respiratory distress, continue CPAP. No benefit of NIPPV over CPAP in terms of reduction of BPD or mortality.
- CPAP + Early surfactant better than waiting for CPAP failure and then intubating and giving surfactant. LISA (Less invasive surfactant administration) is better than INSURE to administer surfactant.
- Avoid intubation and mechanical ventilation as much as possible. If unavoidable, then only intubate. High frequency ventilation marginally reduces death and BPD as compared to conventional ventilation. In conventional ventilation, volume target ventilation is better than pressure target ventilation.
- Ventilation strategies (Based on physiological principles. None based on evidence from large RCTs/meta-analyses):
- Be liberal with PEEP, while avoiding overdistention.
- Minimise PIP (Δ P)
- Permissive Hypercapnea, especially after 1st few days of ventilation
- Extubate at the earliest opportunity even if it means high CPAP or high NIPPV settings
- Drugs: Postnatal dexamethasone definitely decreases Death/BPD, but at the cost of increased cerebral palsy. Therefore, not routinely recommended. The risk: benefit ratio of giving steroids is in favour of steroids if patient's chances of developing BPD are high, but not otherwise.
- Caffeine (preferably started within first 3 days of life) reduces the risk of BPD.
- Marginal reduction in Death/BPD with prophylactic vitamin A, but only when given intramuscularly, which is practically difficult.
- Consider Azithromycin if Ureaplasma colonisation is proven.

Protocol 5: Management of Persistent Pulmonary Hypertension (PPHN)

- Disproportionality Sever hypoxemia (PaO2 < 35-45 mmHg) for clinical, radiological correlation & ABG parameter
- Differential cyanosis (Pre &Post ductal SpO2 > 5-10%)

↓

Hyperoxia Test

- PaO2 > 100 mmHg - Parenchymal lung disease
- PaO2= 50-100 mmHg - Parenchymal lung disease or cardiovascular disease
- PaO2 < 50 mmHg- CCHD (R-L shunt) or PPHN

↓

Routine Hematological
ABG,
R/O Hypoglycemia,
Hypocalcemia,
Polycythemia

← **Diagnostic Evaluation** →

CXR
Characteristics
Appearance s/o
CCHD

↓

ECHO

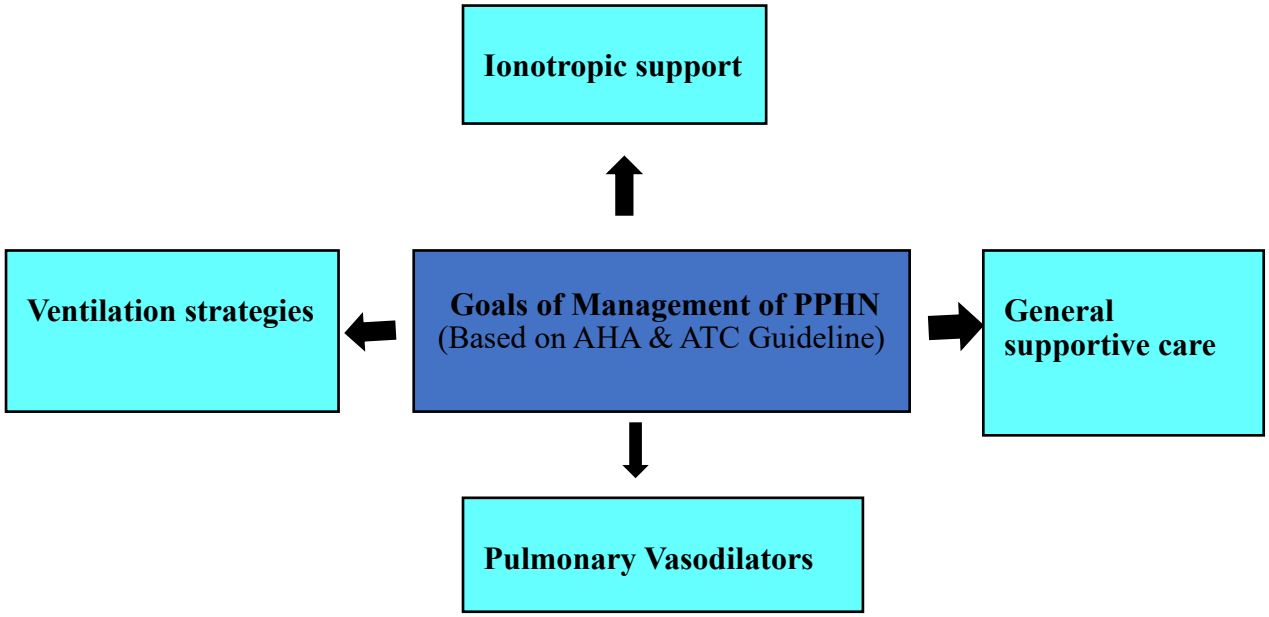
(Gold standard for diagnosis & Monitoring to the response to the therapy)

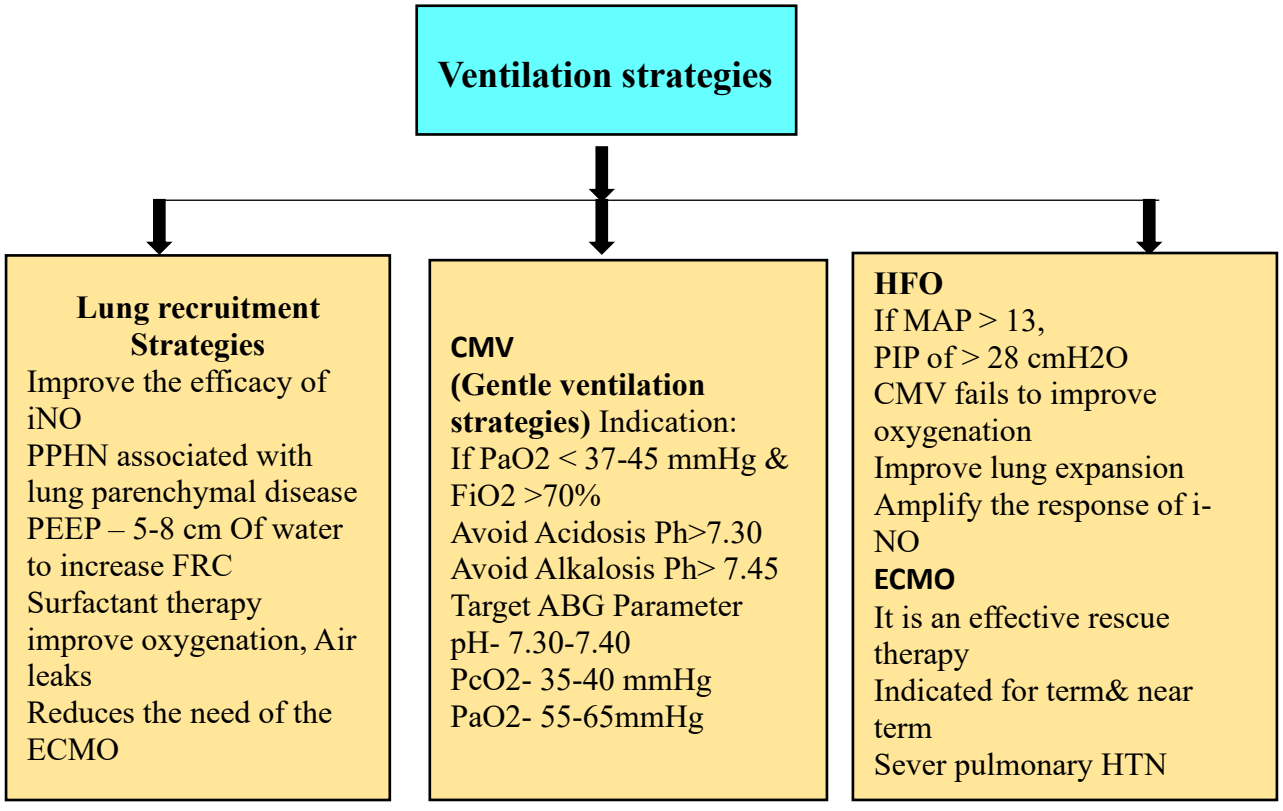
Diagnostic feature…

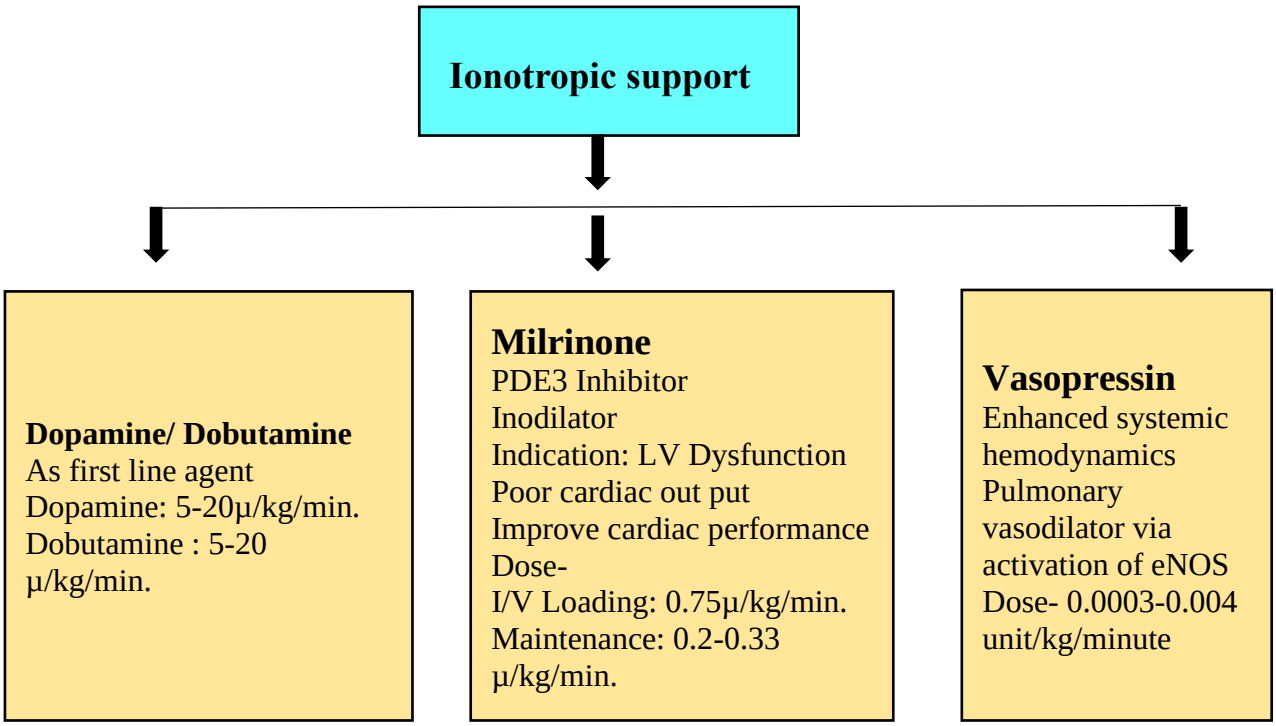
- Right-to-left or bidirectional shunt at the ductus or foramen ovale and/or,
- Flattening or leftward deviation of the interventricular septum and/or,
- Tricuspid regurgitation, and finally
- Absence of structural heart disease (COA, TAPVR)

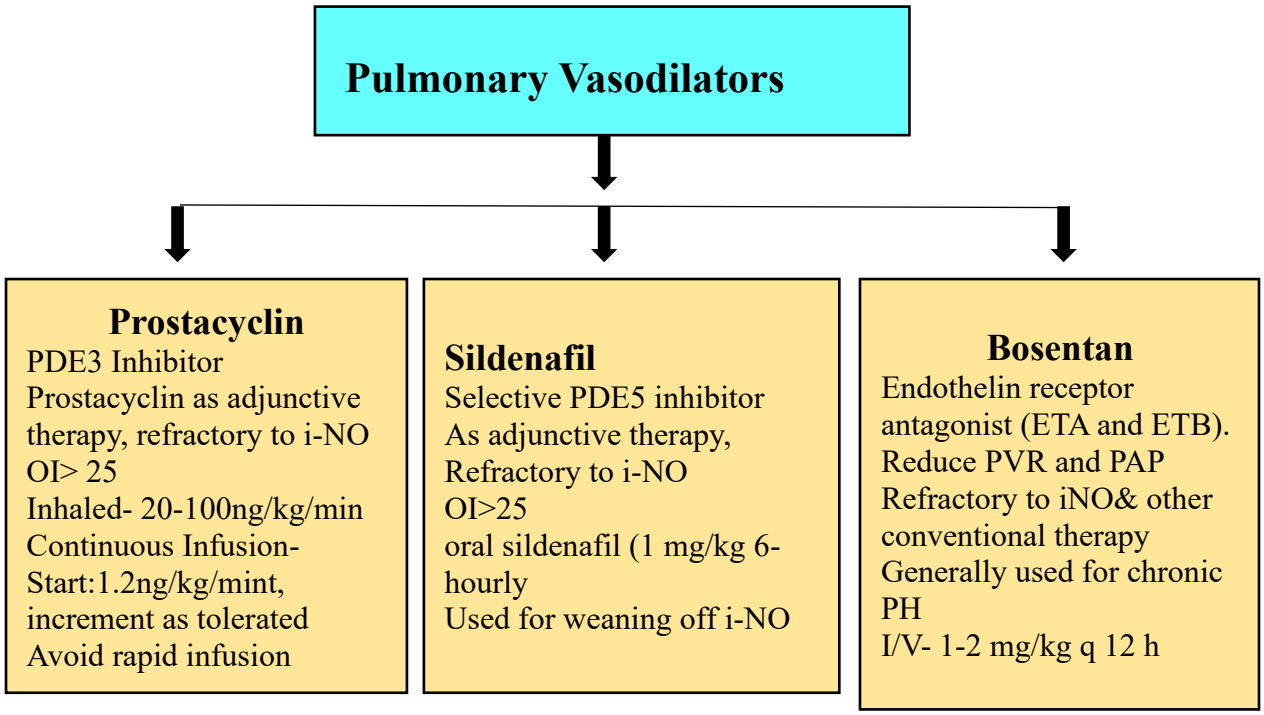
Other feature

- Direction of flow across the duct& PFO (Bi-Directional Rt to Lt)
- Increase Rt Ventricular Dilation
- RVF/LVF (TAPSE & Speckle Tracking)


Ionotropic support
Ventilation strategies
Goals of Management of PPHN
(Based on AHA & ATC Guideline)
General supportive care
Pulmonary Vasodilators


Ventilation strategies
Lung recruitment Strategies
Improve the efficacy of iNO
PPHN associated with lung parenchymal disease
PEEP – 5-8 cm Of water to increase FRC
Surfactant therapy improve oxygenation, Air leaks
Reduces the need of the ECMO
CMV
(Gentle ventilation strategies) Indication:
If PaO2 < 37-45 mmHg & FiO2 >70%
Avoid Acidosis Ph>7.30
Avoid Alkalosis Ph> 7.45
Target ABG Parameter
pH- 7.30-7.40
PcO2- 35-40 mmHg
PaO2- 55-65mmHg
HFO
If MAP > 13,
PIP of > 28 cmH2O
CMV fails to improve oxygenation
Improve lung expansion
Amplify the response of i-NO
ECMO
It is an effective rescue therapy
Indicated for term& near term
Sever pulmonary HTN


Ionotropic support
Dopamine/ Dobutamine
As first line agent
Dopamine: 5-20µ/kg/min.
Dobutamine : 5-20 µ/kg/min.
Milrinone
PDE3 Inhibitor
Inodilator
Indication: LV Dysfunction
Poor cardiac out put
Improve cardiac performance
Dose-
I/V Loading: 0.75µ/kg/min.
Maintenance: 0.2-0.33 µ/kg/min.
Vasopressin
Enhanced systemic hemodynamics
Pulmonary vasodilator via activation of eNOS
Dose- 0.0003-0.004 unit/kg/minute



i-NO: High yielding facts

- NO has a very short duration of action; Avoid overexposure.
- Only after their lung volume has been optimised and their cardiovascular status stabilized (LV Dysfunction).
- Insufficient evidence to recommend in premature babies or in term babies with CDH.
- Administer only if continuous NO and nitrogen dioxide (NO2) monitoring are available and there is immediate access to methaemoglobin analysis
- Associated with an increased bleeding time &Thrombocytopenia
- Continuously recording of pre & post ductal *P*aO2 OR Spo2

General supportive care

Temp & Oxygenation
Maintain Normothermia to decrease O2 consumption
Target Spo2 90%- 94%
Pre & Post ductal PaO2 between 60-80 mmHg

Correct Hematological & Metabolic derangements
Avoid Polycythemia
Maintain PCV- 40%
Thrombocytopenia
Hypoglycemia
Hypocalcemia

Antibiotics
Judicious use of antibiotics OR
As per C/S pattern

Weaning the baby with PPHN

- Once the baby has acceptable blood gases weaning can begin.
- The ventilator pressure should be reduced to <30 cmH2O first, and then reduced the rate of infusion of the vasodilator drugs.
- In PPHN, the ventilator pressures should never be reduced by more than 1–2 cmH2O increments and the oxygen concentration by no more than 3–5% increments.

Protocol 6: Management of Patent Ductus Arteriosus (PDA)

DEFINITION: Clinical-hsDA (i) respiratory signs, increased respiratory support, unable to wean respiratory support or oxygen need; (ii) physical signs, murmur, hyperdynamic precordium or bounding pulses; (iii) blood pressure problems, decreased mean or diastolic pressure or increased pulse pressure, and/or (iv) signs of congestive heart failure, including cardiomegaly, hepatomegaly or pulmonary congestion. ECHO based (Table 1): (i) left heart dimensions, including the left-atrium-to-aorta ratio (LA/Ao ratio) and left ventricular dimensions, (ii) left-to-right shunting, including the presence of a colour jet in the mean pulmonary artery (iii) Doppler parameters, ductal jet size and/or (iv)ductal diameter

Table 1 Comparison of echocardiographic markers of HSDA

Feature quantified	Modality/position of sample gate	No PDA	Small	Moderate	Large
Characteristics of the ductus arteriosus					
Transductal diameter (mm)	Two-dimensional, short axis view	0	<1.5	1.5–3	>3
Ductal velocity V_{max} (cm/s)	PWD at pulmonary end of duct	0	>2	1.5–2	<1.5
Antegrade PA diastolic flow (cm/s)	PWD within left pulmonary artery	0	>30	30–50	>50
Pulmonary overcirculation					
Left atrial/aortic ratio	m-mode, long axis view	1.13±0.23	<1.4:1	1.4±1.6:1	>1.6:1

Management

1. **Fluid restriction**: Cochrane review 2014 suggests that a restricted fluid intake with avoidance of dehydration, in the first few weeks of life for <30 weeks infants has a trend towards lower incidence of PDA 7 associated morbidities. During management of PDA, iv fluids are kept to 120 ml/k/d & full enteral feeds till 150 ml/k/d.
2. **Diuretics (Furosemide)**- Multiple RCt's using furosemide in indomethacin treated PDA infants, has not shown any benefit or improved long term outcomes. It is therefore not routinely advised
3. **Pharmacological Management**

   INDOMETHACIN: *Prophylactic treatment with indomethacin is no longer recommended.* Review of current data suggest it decreases the incidence of symptomatic PDA following treatment of an asymptomatic duct. Platelet counts and renal parameters to be checked prior to starting therapy with indomethacin and repeated after 24 hours.

   IBUPROFEN: *Current evidence does not support the use of ibuprofen for prevention of PDA.* Ibuprofen is as effective as indomethacin in closing a PDA. Ibuprofen reduces the risk of NEC and transient renal insufficiency. It therefore appears to be the drug of choice. Oro-gastric

administration of ibuprofen appears as effective as IV administration. Higher dose regime (20-10-10) has shown better closure rates after conventional failure, but side effects unclear. PARACETAMOL: *Moderate-quality evidence suggests paracetamol is as effective as ibuprofen*; low-quality evidence suggests paracetamol to be more effective than placebo or no intervention; and low-quality evidence suggests paracetamol as effective as indomethacin in closing a PDA.

Dosage
Indomethacin-(iv infusion over 30 min) Loading: 0.2 mg/k/dose
Subsequent (as per PNA)- <2 days- 0.1 mg/k/dose 12 hrly two doses
2-7 days- 0.2 mg/k/dose 12 hrly two doses
>7 days- 0.25 mg/k/dose 12 hrly two doses
Ibuprofen (iv or oral)- Loading 10 mg/k/dose
Subsequent- 5 mg/k/dose 24 hrly two doses.
Paracetamol-(iv or oral) 15 mg/k/dose 6 hrly for 3-7 days

4. **Timing:**

- ✓ Prophylactic- no long-term improvement in outcomes seen. Currently not routinely recommended
- ✓ Early asymptomatic (>12 hrs age) based on ECHO findings of an unrestrictive PDA. Some advantages seen but data to suggest routine use still not there.
- ✓ Early (2-7 days) &/or Late symptomatic (10-14): studies indicate lesser incidence of CLD and mechanical ventilation duration with “early” management. Late therapy has lower need for medical treatment but higher pharmacological failure chances

5. **Surgical Ligation**: after failure of drug therapy or in case of contraindications to available drugs. Known for adverse effects, such as vocal cord dysfunction, impaired neurological outcome, risk of BDP, retinopathy of premature (ROP), chylothorax and diaphragmatic paralysis, bleeding, pneumothorax, and cardiorespiratory failure.

Protocol 7: Management of shock

Diagnosis of Neonatal Shock

Shock is defined as a state of energy failure at cellular level resulting from an inadequate tissue oxygen delivery that fails to meet the tissue oxygen demand.

Phases of Shock

Compensated phase	• "Diving reflex" present - Blood flow to vital organs maintained • Clinical findings - Tachycardia, delayed CFT, cold peripheries, ↓urine output but normal blood pressure
Uncompensated phase	1. If not treated in compensated phase, uncompensated phase begins 2. Blood flow to vital organs also decreases 3. Clinical features - All features of compensated phase + presence of hypotension
Irreversible phase	If treatment not initiated promptly in uncompensated phase, multi organ failure and permanent damage to vital organs ensue; further treatment will not be effective

Aetiology

Hypovolemia	**1. Absolute hypovolemia (Hemorrhagic shock – APH, TTTS, IVH, pulmonary bleed; Increased IWL in extreme prematurity, Diarrhea, vomiting, Third space losses associated with severe sepsis, NEC etc).** **2. Relative hypovolemia: Sepsis, DIC, NEC**
Cardiac	**Post asphyxia myocardial dysfunction, Sepsis, Congenital heart diseases (Critical aortic stenosis, Critical coarctation, HLHS), Hemodynamically significant PDA**
Obstructive	**1. Tension pneumothorax, pneumopericardium, Cardiac tamponade (post surgical, Complication of central line insertion)** **2. Mechanical ventilation - Excessive PIP/ PEEP**
Distributive	**Impaired peripheral vasomotor tone: ELBW, sepsis**
Septic Shock	**Combination of hypovolemic, distributive and cardiogenic shock**

Differential diagnosis for common clinical scenarios based on history and physical examination

Gestation Age

- **Preterm baby**
  - **Baby well (BP low but other parameters within normal limits): Transient circulatory compromise in first 24 hours is common in ELBW and VLBW infants**
  - **Sick Preterm: Sepsis, IVH, Large PDA, adrenal insufficiency**
  - **ELBW infant with excessive weight loss: hypovolemic shock**
- **Term < 24 hours with asphyxia, H/O meconium aspiration: HIE, MAS, PPHN**
- **Term > 24 hours, initially normal:**
  - **Gradual onset : Sepsis**
  - **Sudden onset: Suspected Duct Dependent cardiac disease**

Antenatal History

- **Maternal antepartum hemorrhage, cord accidents, Monochorionic twins: Hypovolemic shock**
- **Risk factors for EONS Chorioamnionitis in mother: Septic shock**
- **Maternal TORCH profile - Viral myocarditis**
- **Maternal diabetes - Cardiac anomalies, Maternal SLE - Congenital heart block**

Perinatal events

- **H/O Birth asphyxia: Hypoxic-ischemic injury of myocardium, PPHN**
- **Meconium stained liquor: MAS, PPHN**

Interventions in the immediate past

1. **Surfactant administration / Mechanical ventilation - excessive PIP/PEEP and obstructive shock, pheumothorax**
2. **Post central line insertion - Pneumothorax in subclavian line insertion, cardiac tamponade in PICC line/ Umbilical line insertion**
3. **Post DVET - Air embolism**

Assessment of Shock

Clinical Parameters

- **HR > 160 bpm**

1. **Earliest sign but non- specific**
2. **Bradycardia can be seen in hypoxic ischemic injury**

- **Prolonged capillary refill time > 3 seconds**

1. **Flash CFT in early warm shock (sepsis)**

- **Pulse volume: Weak/ absent peripheral and central pulses**

1. **Bounding in PDA / Warm shock**

- **Blood pressure**

1. **NIBP is not accurate in reading low BP records; most accurate is Systolic BP > mean BP > diastolic BP**
2. **Gestational age and postnatal age influence BP**
3. **Hypotension : crudely defined as MAP less than the baby's gestational age in weeks in the first 48 hours of life or Mean BP < 30 mm of Hg**

- **Urine output < 1 ml/kg/hr after 48 hours**
- **Lethargy and decreased sensorium**

Laboratory Parameters

2. **Base deficit > 5**
3. **Arterial lactate > 2 mmmol/L**

Echocardiography

- **Assessment of preload:**

1. **IVC collapsibility > 30% in spontaneously breathing and IVC variability index >18% in ventilated infants**
2. **LV, RA size and volume**

- **Assessment of myocardial contractility**

1. **Ejection fraction (EF) < 50%**
2. **Fractional shortening < 23 in Preterm and < 25 in term neonates**
3. **Decreased Cardiac output < 150 ml/kg/min**

- **Assessment of after load**

1. **Superior Vena Caval (SVC)flow < 50ml/kg/min**

Management of Neonatal Shock

Recognition of early signs
Maintain TABC
Initial stabilization, airway, and ventilation, IV access, ECG, blood culture. antibiotics

Quick examination &history
Assess possibility of CCHD, IEM
Start PGE1 if duct dependent lesion suspected

Fluid bolus @ 10-20ml/kg (0.9% NS) slowly over 30 mins (more slowly in case of cardiogenic shock)

Can give upto 40-60 ml/kg in septic shock

Complete blood counts
Lactate, Blood gas
Electrolytes
Renal & liver function tests
Chest X ray
Blood culture
Monitor fluid by IVC status

Fluid Refractory shock
Start Dopamine @ 10 ug/kg/min ± Dobutamine (cardiogenic shock)

Dopamine Refractory Shock
Start Adrenaline (0.05-0.3 ug/kg/min) & add hydrocortisone

Correct Anaemia
Hypoglycaemia,
Hypocalcemia
Pheumothorax
Tamponade

Catecholamine refractory shock
Consider goal directed therapy
Evaluate for Pneumothorax, Pericardial effusion, HsPDA

PPHN with normal BP, poor cardiac function:
inhaled NO,
milrinone

Warm shock or Cold shock with low BP

1. Start adrenaline at 0.3 ug/kg/ minute and titrate till 1.5 ug/ kg/minute
2. Start hydrocortisone in cases requiring a third inotrope

Cold shock with normal BP

1. Start Dobutamine at 10 ug/kg/ min and titrate till 20 ug/kg/min
2. Start hydrocortisone in cases requiring a third inotrope

Consider Non-Adrenaline/ low dose vasopressin if no response

Consider Milrinone if no response

Supportive Therapy:

Maintain TABCD

Maintain euthermia (36.5-37.5 degree celcius)

Respiratory support – Support airway and breathing in form of non-invasive or invasive ventilation; Maintain SpO2 from 91-95 %.

Correction of Metabolic and haematological derangements: euglycemia, normocalcemia and hematocrit

Administration of first line antibiotics in suspected septic shock

Inotropic support - To be started in neonates with fluid refractory shock.

(i) Dopamine is the 1st choice in almost all cases of neonatal shock. The starting dose is 10 ug/ kg/min; titrate by 5 ug/kg/minutes every 15-20 minutes till a maximum of 20 ug/kg/min

(ii) Dobutamine is useful in the following cases –

- 1st line - Cardiogenic shock (Eg. Post asphyxial, PPHN related, later stages of septic shock)
- 1st line - Delayed transition in very preterm infants
- 2nd line - Cold shock with normal BP in cases not responding to maximal doses of dopamine

Dopamine	**1. Dosage - 10- 20 ug/kg/minute** **2. Mechanism - Dopaminergic receptor (<2ug/kg/minute; endocrine and renal effects - Decreased throtropin, thyroxin, renal vasodilatation); b1 receptor (2-6 ug/kg/min; increased myocardial contractility) ; a1 receptor (>6 ug/kg/min; vasoconstriction) [Indirect action on a1, b1 receptors via release of catecholamine)** **3. Side effects - Pulmonary vasoconstriction at all doses (can be detrimental PPHN); arrhythmia, endocrine effects**
Dobutamine	**1. Dosage - 10-20 ug/kg/min** **2. Mechanism - Direct action on dopaminergic, b1 (myocardial contractility), b2 receptor (peripheral vasodilatation) at dose of up to 10 ug/kg/minute; at doses of 10-20 ug/kg/ min - vasoconstriction** **3. Better agent to improve blood flow** **4. Side effects - arrhythmias, hypotension** **5. Not to be started in babies with severe hypotension (<3rd centile)**
Adrenaline	**1. Dosage - For improving myocardial contractility and decreasing after load - 0.1-0.3 ug/kg/min; for increasing BP - 0.3- 1.5 ug/kg/min** **2. Mechanism - a1,a2,b1,b2 receptor actions** **3. Side effects - Lactic acidemia, hyperglycemia, tachycardia, pulmonary**

	vasoconstriction (at high doses only)
Nordrenaline	**1. Dosage - Similar to adrenaline; Mechanism - a1,a2,b1 (no b2 action)** **2. Used in catecholamine refractory septic shock (warm shock) in pediatric population - improves outcome, limited studies in neonates**
Milrinone	**1. Dosage - Loading - 50-75 ug/kg over—— followed by 0.5 -1.5 ug/kg/min** **2. PDE-III inhibitor, inotropic, lusitropic and inodilatory effects** **3. Use - Post cardiac surgery myocardial dysfunction, PPHN related myocardial dysfunction** **4. Side effects - Hypotension, tachycardia, tachyarrhythmia, thrombocytopenia**
Vasopressin	**1. Dosage - Low dose preferred (0.0007 IU/Kg/min); High dose - 0.001-0.02 IU/kg/min); High dose is associated with significant side effects** **2. V1, V2 Receptor - Increases vasomotor tone and increases cortisol release** **3. Side effects - Cutaneous schema, necrosis and hyponatremia at high doses** **4. Used in catecholamine refractory shock , warm shock and PPHN (Selective pulmonary vasodilator and systemic vasoconstrictor)**

Therapeutic End Points

- Normal pulse volume & Capillary refilling time < 3 seconds
- Normal heart rate 110-160 bpm
- Blood pressure - Between 10th – 90th centile for gestational and postnatal age
- Urine output - > 1 ml/kg/hour (valid only beyond 48 hours of life)
- Improvement in mental status
- Difference in pre-post ductal spo2 < 5 %
- Echocardiographically - SVC flow > 50 ml/kg/min, EF > 50%, LVO - > 150 ml/kg/min (if PDA has closed) or RVO (P V max>2 m/second; if PDA is patent),

Monitoring

Parameter	Frequency
Temperature	**Maintain temperature between 36.5-37.5 degree Celsius**
Vitals - HR/ RR/ CFT/peripheral pulses/ SPO2/ BP	**2 hourly**
Urine output	**6-8 hourly**
Blood dextrose	**6 hourly ; Confirm any abnormal reading with RBS sample since peripheral blood flow compromised**
Hematocrit/ Serum Calcium and electrolytes/ Renal function tests	**At least once daily or more frequently as per the treating physicians discretion**
Arterial pH / Lactate/ Other parameters of blood gas	**Depending on clinical status**
Echocardiography	**Depending on clinical status**

Tapering inotropes

1. Start tapering if the baby remains stable for a period of atleast 4-6 hours after inotrope initiation
2. Taper inotropes if BP readings > 90th centile at any point of time.
3. Decrease @ 5 ug/kg/min hourly for dopamine and dobutamine infusions. For other inotrope infusions it should be @ 0.3 ug/kg/min hourly
4. Omit when infusion rate is 5 ug/kg/min for dopamine and dobutamine; and o.3 ug/kg/minute for others.
5. Inotrope added last should be tapered first and omitted, followed by the previous one

Protocol 9: CPAP-Indications, starting and weaning

Indications:
Spontaneously breathing preterm Neonate with respiratory distress Silverman Anderson score (SAS) 3/10 (esp < 32 weeks, < 1500 grams, Inadequate steroid cover)
Start delivery room CPAP @ PEEP 5, Fio2 0.21 with suitable interface short binasal prongs
Others are: Postextubation, pneumonia, apnoea

Contraindications → CDH, TEF, Choanal atresia, Cleft palate, GI malformations, Shock

Monitor respiratory distress with SAS, If persists 3/10 or more, Optimize CPAP by increasing PEEP by 1 cm water every 20 minutes till SAS less than 3/10
Titrate Fio2 by 0.05 to keep Preductal target SpO2 between 90-95%

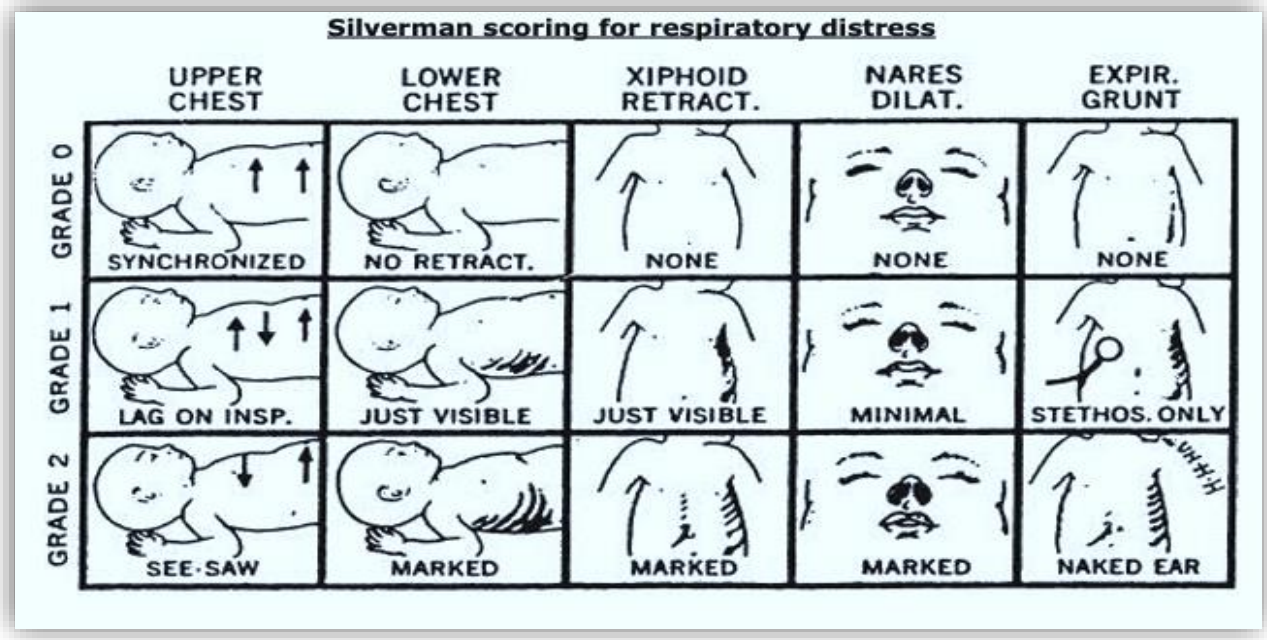
Nursing care
-Ensure correct size and fixation of prongs, make sure mouth is closed
-Bubbling is continuous with depth of immersion of expiratory limb
-Humidifier is on at 37^0Cwith adequate water level
-Keep Oro-gastric tube in place and open after 30 minutes of feed

Adequate CPAP: baby comfortable, no retractions, CRT < 3 seconds, SPo2 90-95%, ABG: ph 7.35-45, PO2 50-80 mm Hg, PCO2 40-60 mm Hg

Indication of Surfactant: Setting PEEP 7-8, FiO2> 30% to keep SpO2 > 90% → Surfactant by INSURE/LISA/MIST and put back on CPAP

CPAP Faliure: Setting PEEP 7-8, FiO2> 60%, SpO2 < 90%
SAS >2, continuous moderate to severe retractions
Recurrent apnoea, Shock, poor respiratory effort
PH < 7.2, PaO2 < 50, Paco2 > 60 → Ventilation

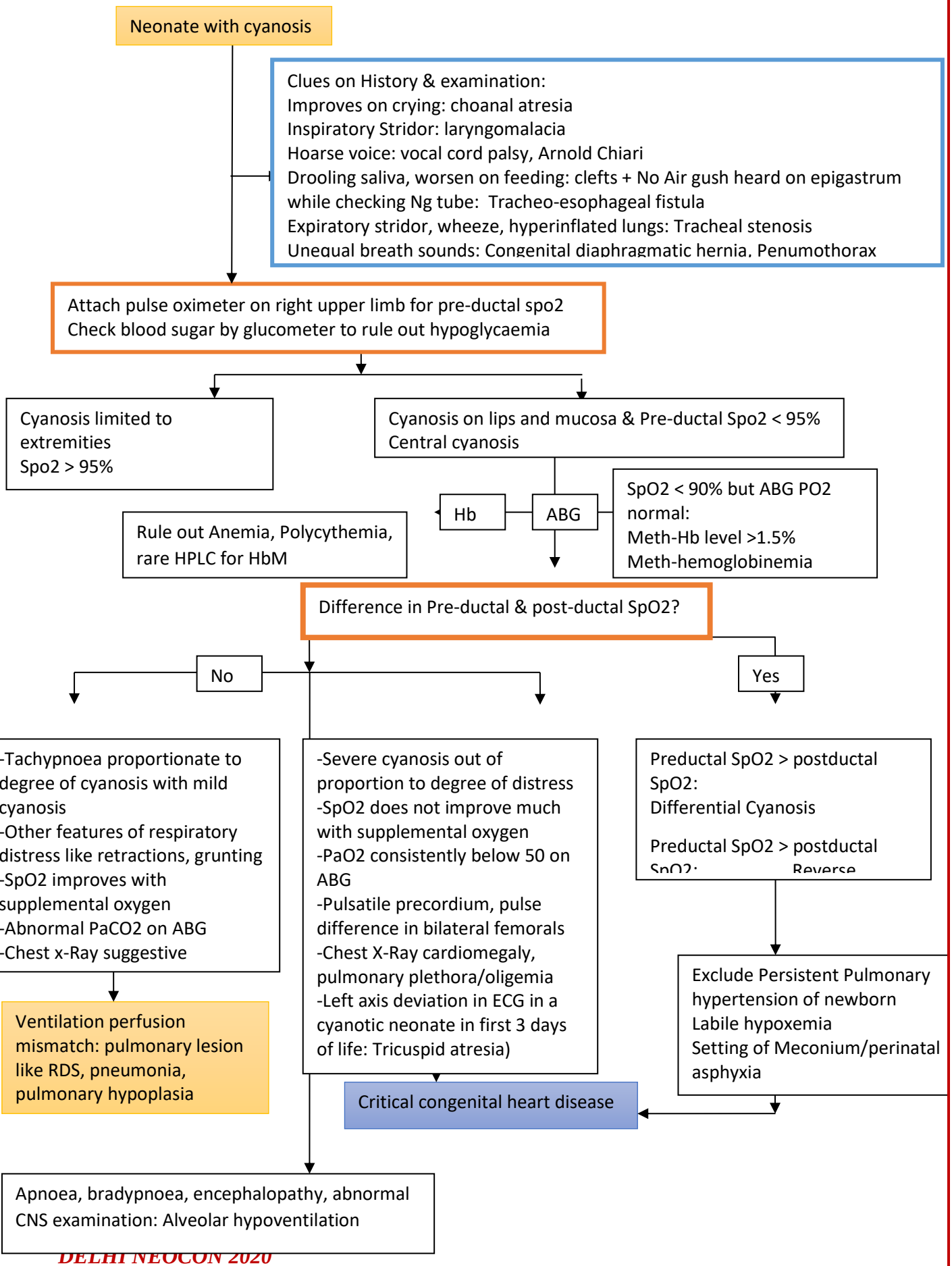
Weaning of CPAP: Reduce Fio2 in steps of 5% if SpO2 > 95%
Reduce CPAP pressure by 1 cm till CPAP is 5 cm and Fio2 50%
Reduce Fio2 in steps of 5% till 30% reached and then decrease PEEP to 4 cm
Once stable on this for 12-24 hours, CPAP can be taken off



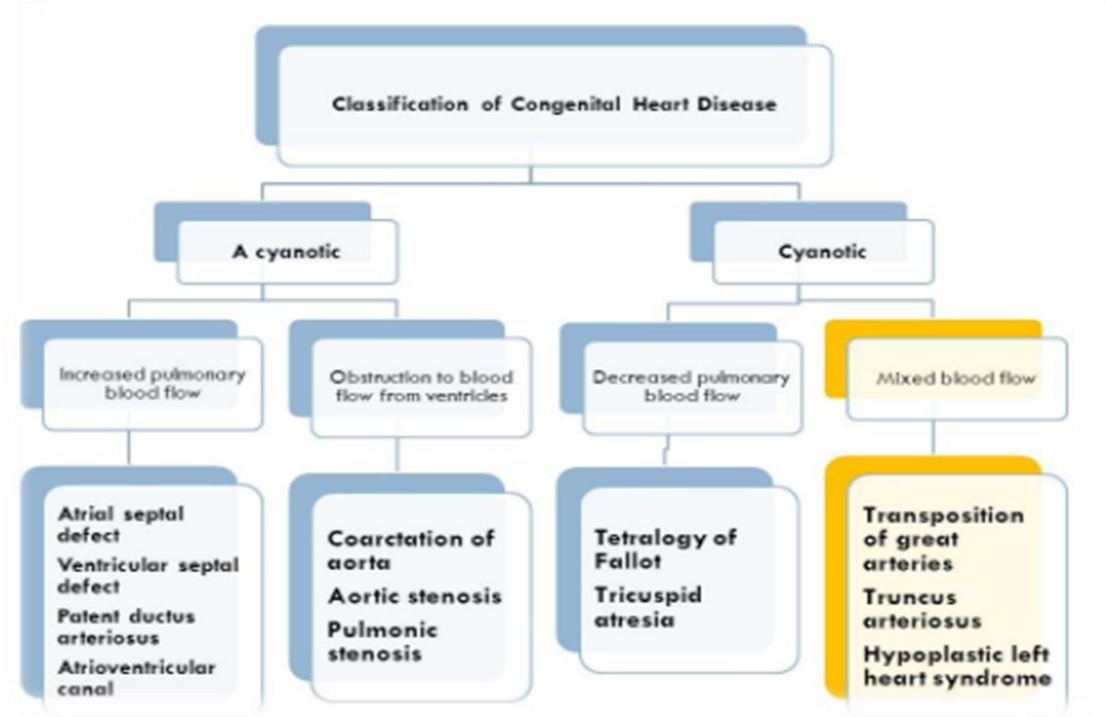
Interpretation: Score 0-3: mild respiratory distress, 4-6: moderate respiratory distress, >6 impending respiratory failure

Troubleshooting				
SpO2	Retractions	Air Entry	Bubbling	Diagnosis
Low	++/+++	poor	yes	Lung disease
Low	+/ nil	good	yes	PPHN/CHD
Normal	++/++++	good	yes	Metabolic acidosis
Low	++/+++	poor	yes	obstructions
Low	++/+++	poor	no	leaks

Protocol 10: Approach to a cyanotic neonate



Protocol 9: Approach to suspected congenital heart disease in a neonate



Distribution of fetal heart diseases according to their classification and management

Group	Cardiac anomalies
IA	Left to right shunt heart diseases: ASD, VSD, AVSD, and Ao-P window Diseases with mild outflow tract obstructions: PS, AS, and CoA Complex congenital heart diseases without significant obstructions of systemic or pulmonary outflow tracts: TOF, complex TGA, DORV, univentricular hearts, and CTGA
IB	Isolated extrasystoles; mild, isolated TR
IIA	Heart diseases with critical obstruction of systemic or pulmonary outflow tracts: PAIVS, Critical PS, Critical AS, and HLHS Heart diseases that need interatrial shunt: HLHS and variations, TGA, and TA Heart diseases with severe valve insufficiencies: Ebsteins anomaly and tricuspid valve dysplasia, pulmonary valve agenesis, severe primary or secondary MR, secondary TR, and truncal valve insufficiency
IIB	Cardiomyopathies and myocarditis, arrhythmias, obstructive tumors, extrinsic compressions, (CDH and CCAM), ductal constriction, restrictive foramen ovale, ductus venosous agenesis, AVMs, TTTS, and twin gestation with 1 acardiac fetus
III	Severe chromosomal disorders; multiple malformations, cardiac defects that are not correctable, very severe forms of Ebsteins anomaly or tricuspid valve dysplasia with lungs hypoplasia, LV aneurysms, or diverticula associated with fetal hydrops

Group IA. Structural fetal heart diseases without in utero hemodynamic compromise, which do not require immediate neonatal care. Class of recommendation/level of evidence: IB

Heart disease	In utero outcome	In utero follow up	Delivery	Postnatal assessment
VSD AVSD ASD Ao-P window	Stable	Repeat the study a few weeks before birth is recommended	Delivery type according to obstetric indication Level 1 center	Maternity ward or outpatient clinic

Ao-P: aortopulmonary; ASD: atrial septal defect; AVSD: atrioventricular septal defect; VSD: ventricular septal defect.

Group IA. Structural fetal heart diseases without in utero hemodynamic compromise that may progress during fetal life and may or may not require immediate neonatal care. Class of recommendation/level of evidence: IB

Heart disease	In utero outcome	In utero follow up	Delivery	Postnatal assessment
TOF DORV Complex TGA CTGA TA	May progress to significant obstruction to systemic or pulmonary outflow tracts	After diagnosis, repeat the study every 46 weeks A new study a few weeks before birth is highly recommended	Delivery type according to obstetric indication Level 1; Level 2 or 3 centers in case the in utero hemodynamic condition worsens or precipitates immediate neonatal decompensation (significant obstruction of the systemic or pulmonary outflow tracts)	In all cases, before hospital discharge, cardiac assessment with echocardiogram is required

CTGA: corrected transposition of great arteries; DORV: double outlet right ventricle; TA: tricuspid atresia; TOF: tetralogy of Fallot; TGA: transposition of great arteries.

Group IB. Functional fetal heart diseases without in utero hemodynamic compromise, that do not require immediate neonatal care. Class of recommendation/level of evidence: IB

Heart disease	In utero outcome	In utero follow-up	Delivery	Postnatal assessment
trial or ventricular extrasystoles Mild TR	Stable	Repeat the study a few weeks before birth is recommended	Delivery type according to obstetric indication Level 1 center	Maternity ward or outpatient clinic

TR: tricuspid regurgitation.

Group IIA. Structural fetal heart diseases with possible in utero hemodynamic compromise and chance of fetal treatment, which require immediate neonatal care. Class of recommendation/level of evidence: IB

Heart disease	In utero outcome	In utero follow-up	Delivery	Postnatal assessment
PS PAIVS AS Ebsteins anomaly	Risk of ventricular hypoplasia Risk of ventricular dysfunction or fetal hydrops Risk of circular shunt Risk of fetal arrhythmia	Repeat the study every 2 to 4 weeks is recommended If signs of in utero progression, consider fetal intervention between 22 and 32 weeks If circular shunt, consider induced ductal constriction	Without hydrops, induced vaginal delivery or programmed C-section With hydrops, programmed C-section Level 2 or 3 center	Immediate neonatal cardiac assessment PAIVS requires neonatal treatment Severe or critical PS and AS, may require neonatal treatment Ebsteins anomaly needs treatment if pulmonary atresia and lung hypoplasia

AS: aortic stenosis; PAIVS: pulmonary atresia with intact interventricular septum; PS: pulmonary stenosis.

Group IIA. Structural fetal heart diseases that inevitably require neonatal care. Class of recommendation/level of evidence: IB

Heart disease	In utero outcome	In utero follow-up	Delivery	Postnatal assessment
Simple TGA HLHS IAA Severe CoA TAPVR Truncus Complex heart diseases with severely restricted systemic or pulmonary outflow tracts	FO may be restrictive during gestation Although they are complex heart diseases, they tend to remain stable, without hemodynamic compromise during gestation	Repeat study every 4 to 6 weeks is recommended In HLHS or anatomical variations with restrictive ASD, consider fetal intervention Perform a new evaluation a few weeks before delivery	Induced vaginal delivery or programmed C-section Level 2 or 3 center	Immediate neonatal cardiac evaluation The majority are duct dependent CHD and require prostaglandin infusion + interventional or surgical treatment during the first week of life TAPVR and Truncus are diseases with early presentation of HF and PH, and thus require treatment during the first weeks of life, even when they are not duct dependent

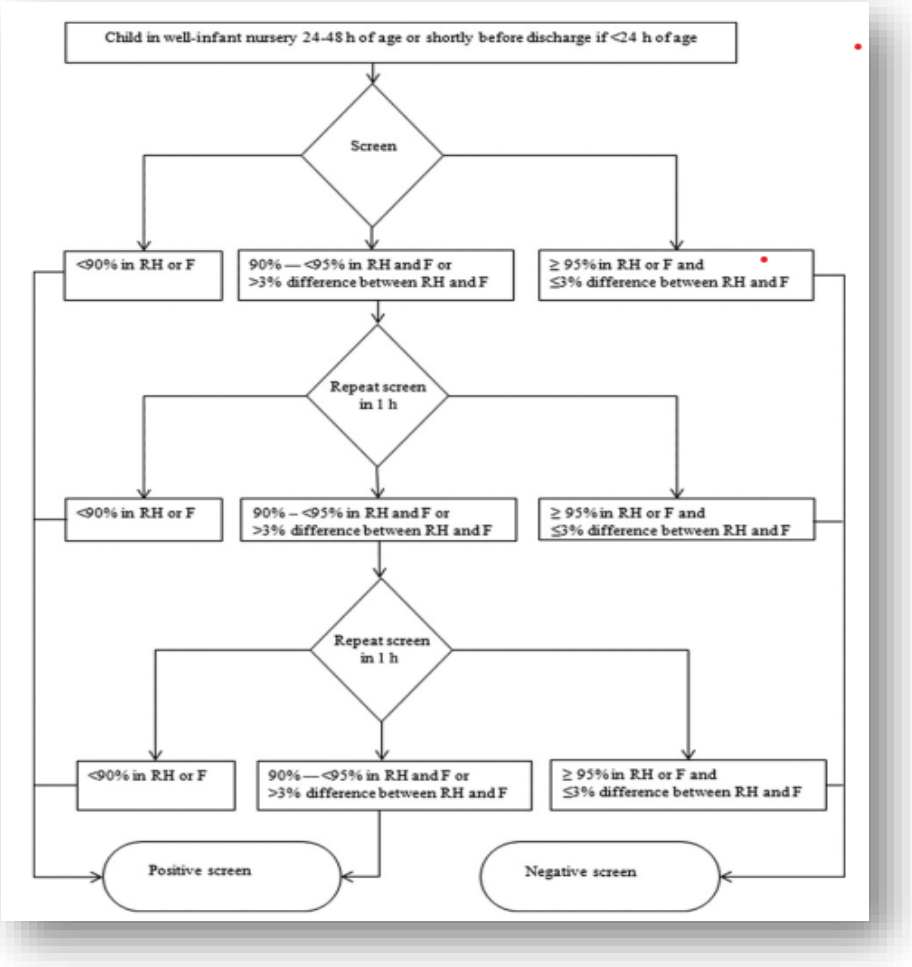
CoA: coarctation of the aorta; FO: foramen ovale; HF: heart failure; HLHS: hypoplastic left heart syndrome; IAA: interrupted aortic arch; PH: pulmonary hypertension; TAPVR: total anomalous pulmonary venous return; TGA: transposition of great arteries.

Group IIB. Functional fetal heart diseases with hemodynamic compromise. Class of recommendation/level of evidence: IIb

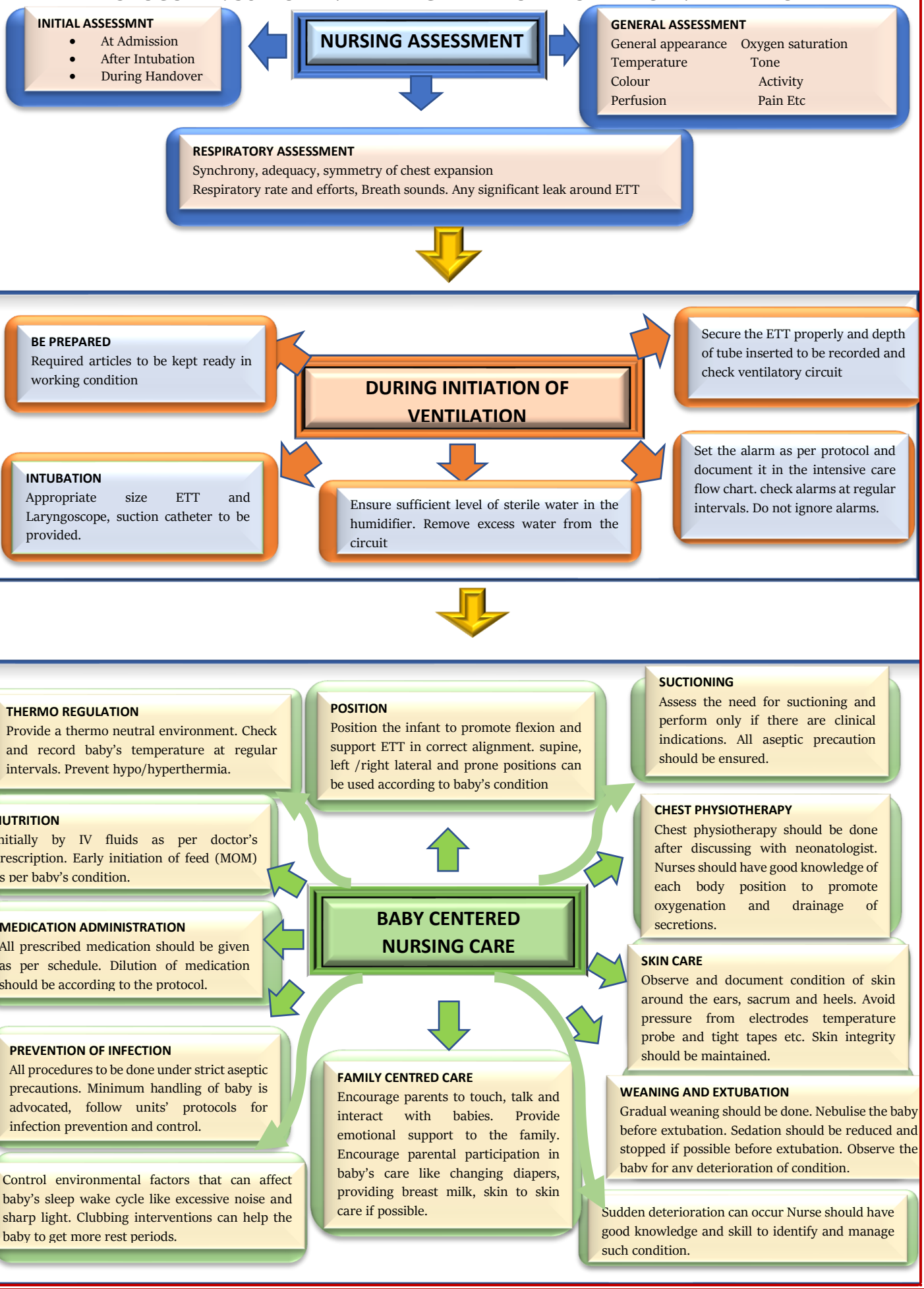
Heart disease	In utero outcome	In utero follow up	Delivery	Postnatal assessment
Restricted FO **Ductal constriction** **Pericardial effusion** **Extrinsic compressions** **Anemia** **High-output AV fistulas** **TTTS**	May evolve with ventricular dysfunction or fetal hydrops	Serial echocardiogram every 4 to 6 weeks is recommended May need fetal treatment	With hydrops, programmed C-section; Without hydrops, induced vaginal delivery or programmed C-section Level 2 or 3 centers Evaluate the need for preterm delivery	Immediate neonatal cardiac evaluation May require clinical, interventional or surgical treatment immediately after birth

AV: arteriovenous; FO: foramen ovale; TTTS: twin-twin transfusion syndrome.

Pulse oximetry screening for critical congenital heart disease



PROTOCOL 11: SUPPORTIVE MANAGEMENT OF NEONATE ON VENTILATOR



Protocol 12: Sedation and analgesia in a sick neonate

In NICU, normally a newborn receives nearly 10-14 painful stimuli everyday esp. during first 2 weeks of life. By 24 weeks of gestation, lateral spinothalamic tract which carries pain fibers develops so a viable preterm can feels pain. Painful stimulus has impact on both short- and long-term neurological outcomes. Hence every neonatal unit must have pain management policy for better neonatal outcomes.

Step 1. Develop NICU policy for management of pain (select pain champions and methods of pain assessment tools like PIPP, NIPS, N-PASS, COMFORT, CRIES, CHIPS, MAPS, FLACC, Bernese scale etc)

Step2.

Minimise pain full procedure by

- Eliminating unnecessary laboratory or radiographic procedures
- Using transcutaneous measurements for bilirubin assessment, noninvasive assessment of co2 by capnography and O2 by SpO2
- Decreasing the number of repeat procedures performed after failed attempts
- using umbilical venous /arterial line during first 10 days for routine sampling
- Using point of care devices which analyse blood gas and multiple bichemical values from single small blood sample

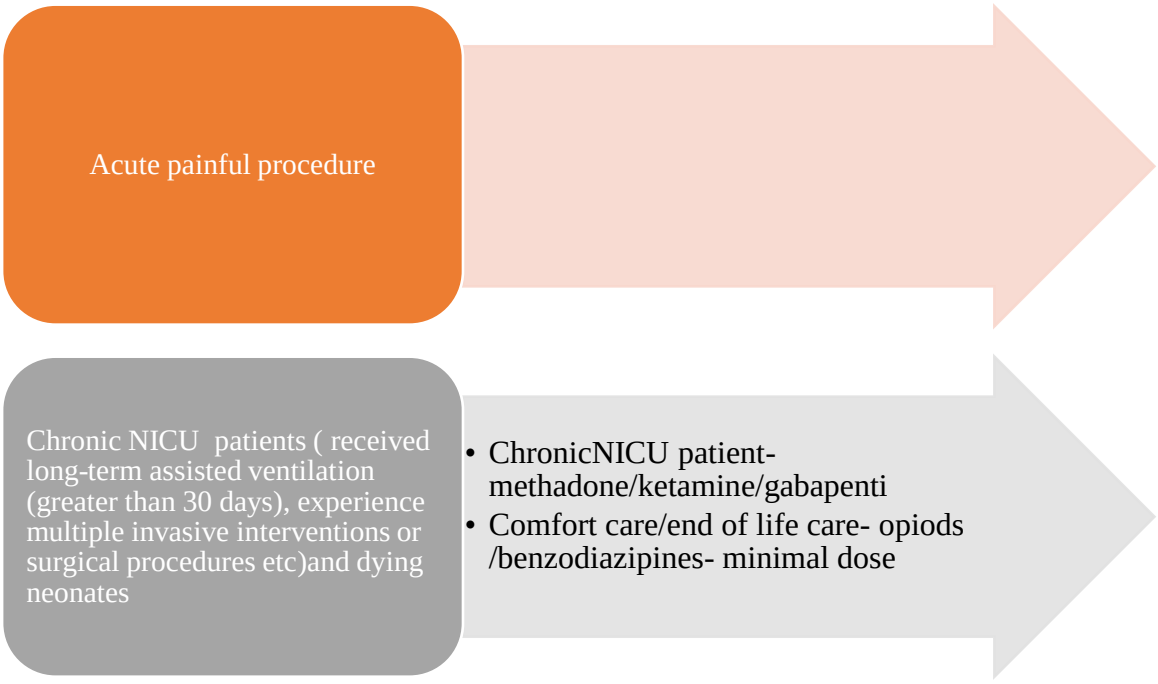
DO IN ALL BABIES to minimise stress/pain

- Clustered care
- Nesting,Facilated tucking,Swaddling
- NNS,Music therapy,KMC,Massage therapy

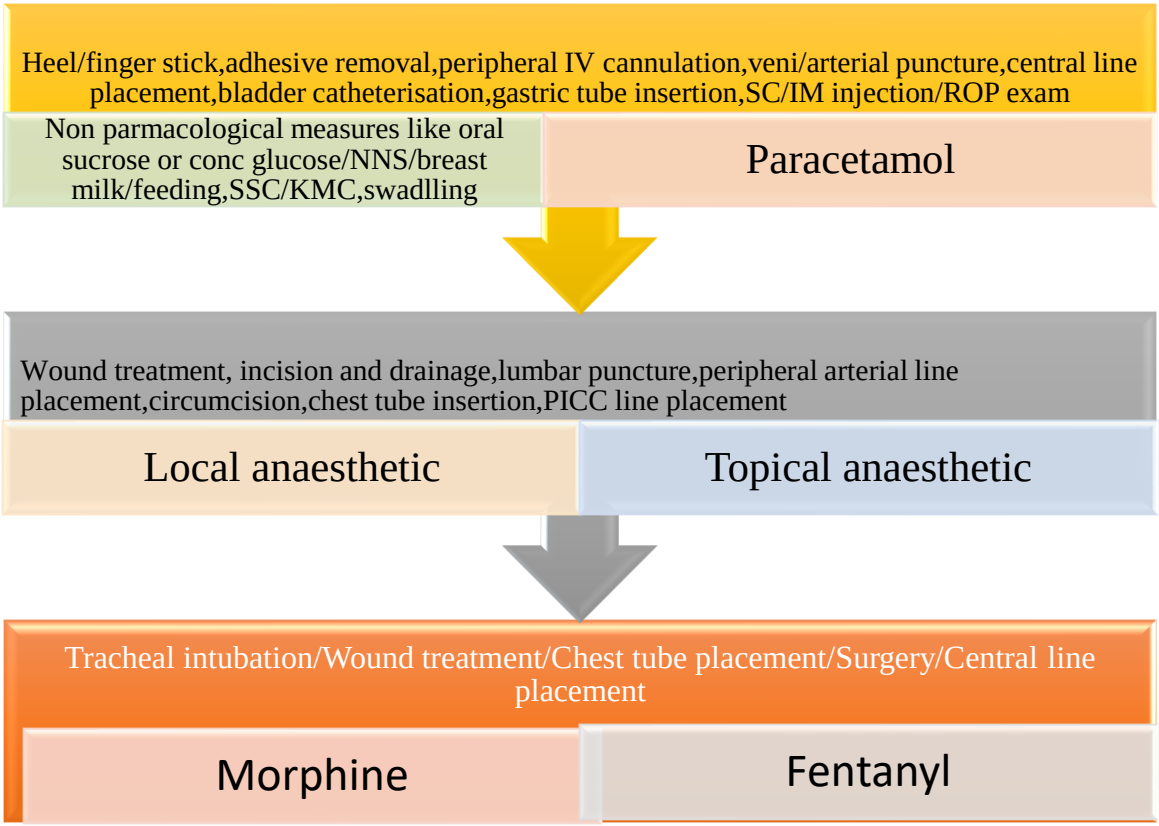
In elective intubation GIVE

- Fentanyl
- Rocuronium/Vecuronium and Atropine

3. Most common neonatal painful procedures and their management



3(a) Acute painful procedures like-



4.In mechanically ventilated neonates, fentanyl doses of 1–3 μg/kg can be given to provide analgesia/sedation

Drugs dose used in neonates for analgesia/sedation

Sucrose (24%)/glucose(20-30%)	**Less conc.solution is preferred in preterm.** **0.05-2 ml per dose, oral.** **Peaks effects occurs at 2 minutes, duration of analgesia is 4 minutes**
Fentanyl	0.5-1 μg/kg/dose, IV/IM
Dexmedetomidine	1-3 μg /kg/dose, IV
Paracetamol	10-15 mg/kg/dose, oral, maximum 4 times a day
Vecuronium	0.1 mg/kg, IV
Atropine	0.02 mg/kg, IV
Propofol	2.5 mg/kg, IV
Ketamine	0.5-2 mg/kg/dose, IV/IM
Morphine	0.05-0.1 mg/kg/dose, IV
EMLA cream	0.5-1 gm, covered under occlusive dressing before 45-60 minutes of procedure
Lidocaine inj	3-5 mg/kg/dose, SC
Gabapentin	5 mg/kg every 8-12 hrly

SECTION 4

Management of neonatal neurological disorders

Protocol 1: Management of neonatal seizures

Neonatal seizure(lasting for≥ 3mins)

Baby with suspected seizure activity

Observe and monitor: · Seizure activity· Temperature, heart rate, respiratory rate & effort, BP, O2 saturation

Treat cardiorespiratory compromise

Assessment: · Review history (maternal, perinatal, family)· Physical examination· Neurological examination·

Investigate for underlying cause as required

Check RBS

Put i.v line/O_2

If RBS below 45 mg/dl

Give iv dextrose (10%) @ 2ml/kg bolus followed by maintenance

If RBS is normal and if bedside facility of serum/ionic calcium is not available- i.v loading calcium gluconate(10%) @ 2ml/kg over 10 minutes under strict cardiac monitoring. If calcium is low continue calcium @ 8ml//kg for 3 days If seizures continue despite

If seizures still continue give i.v loading Phenobarbitone @20 mg/kg The maintenance dose is 3-5 mg/kg/day in 1-2 divided doses, started 12 hours after the loading dose

Whether seizure ceased

yes

Maintenance therapy:
· For difficult to control or prolonged seizures or abnormal EEG
Consider ceasing AEDs if: · Seizures controlled and neurological examination normal OR Neurological examination abnormal but EEG normal

No

Additional doses of phenobarbital: 5–10 mg/kg IV (to total dose of 40 mg/kg)

Seizure persisting consider

Second line drug:o Phenytoin 15-20 mg/kg IV

Midazolam 0.15 mg/kg IV

Levetiracetam 10 mg/kg IV twice per day

Protocol 2: Therapeutic hypothermia

Subject headings:

A) Selection of neonates
B) Starting therapeutic hypothermia
C) Equipment and supplies
D) Monitoring plan
E) Adjunctive therapies

A) Selection of neonates:

Flow chart to assess and decide for eligibility for TH

- In a 36 weeks or greater pregnancy and the newborn being asphyxiated requiring resuscitation (Accuracy of gestation to be ascertained by - LMP / USG / NBS)

↓

- Check umbilical cord pH and BE immediately after stabilization

↓

- Calculate Apgar score at 10 minutes
- Enquire specifically for acute perinatal event (e.g. cord prolapse, cord around neck, antepartum haemorrhage, severe fetal heart rate abnormality on intra-partum monitoring such as late or variable decelerations)

↓

- Weigh the baby once stabilized
- Check eligibility to undergo therapeutic hypothermia (see below for criteria)
- Counsel the parents for need for NICU care, risk of neurodevelopmental impairment and other relevant financial implications

Who is eligible for hypothermia?

To undergo therapeutic hypothermia, a neonate should be ≥36 weeks and ≥1800 grams and should satisfy point **a & b** (stated below)

(a). At least one of the following

1. Apgar score of ≤ 5 at 10 min after birth
2. Continued need for Resuscitation (IPPV) at 10 min after birth
3. Acidosis within 60 min of birth (Defined as any occurrence of umbilical cord or Arterial or Capillary pH < 7.00)
4. Base deficit ≥ 16 mmol/L in umbilical cord or any blood sample within1 hour of birth (arterial, venous or capillary)

Infants that meet criteria (a) should be assessed for whether they meet the neurological abnormality criteria (b)

(b). Seizures (or) Moderate to severe encephalopathy

Moderate to severe encephalopathy consists of (all are required to be present):

1. Altered state of consciousness (reduced or absent response to stimulation)
2. Abnormal tone (focal or general hypotonia, or flaccid)
3. Abnormal primitive reflexes (weak or absent suck or Moro response)

Note:

- ***Seizures detected by EEG or aEEG without a clinical component (subclinical seizures) would also be considered as seizures***
- ***In babies who satisfy criteria (a) & (b), start therapeutic hypothermia at the earliest, but not later than 6 hours***
- ***Examine and record a baseline (pre-TH) encephalopathy severity score (Thompson's score)***
- ***Use the same score for ongoing monitoring as it would objectively help to assess the effect of TH***

Who should not undergo Therapeutic Hypothermia?

a. Gestational age <36 weeks (confirmed by reliable LMP or early antenatal ultrasound or New Ballard scoring system – in this order of importance)
b. Birth weight <1800 grams
c. Postnatal age greater than 6 hours
d. Presence of known chromosomal anomalies
e. Presence of major congenital malformations
f. Active bleeding (Bleeding from > 2 sites)
g. Grade 3 and above Intracranial hemorrhage (Therapeutic hypothermia not to be delayed if USG has not been done, but USG head to be done within 24 hours of birth and a decision regarding discontinuation of hypothermia has to be taken in Gr III IVH / Intra-Parenchymal Bleed)
h. Moribund neonate

B) Starting therapeutic hypothermia (Informing consultant area / on-call once a potential neonate for TH is identified is essential)

In the Delivery room:

Once eligible to receive hypothermia therapy follow the steps described below:

1. Inform the NICU team
2. Maintain temperature of the baby (skin or axillary) in the range of 36.1 to 36.5 deg.C while being in the delivery room as well as during transport. Do not attempt to do passive cooling by switching off the warmer (evidence to support the efficacy of rectal temperature not in the range of 33.0 to 34 deg.C is absent and it may be counter-productive)

In the NICU:

a) Spread the cooling device on the warmer
b) Place a thin plastic sheet (Interlayer sheet with wax coated side on the mattress side and soft tissue side on baby's side) on the mattress so that it is between the patient and cooling mattress. This plastic sheet should be slightly larger than the mattress and fully cover the mattress with a border for wrapping the mattress
c) Place patient supine over the plastic sheet with patient's head over narrower portion of the cooling mattress and trunk over the broader portion.
d) Insert patient end of the rectal probe 3 cm into the rectum. Secure it with a tape over thigh
e) Attach skin probe to the right flank of the abdomen
f) Attach pulse oximeter sensor to the right wrist/hand and choose 'Max' mode in the Masimo SET technology pulse oximeters or similar monitor with Masimo SET technology
g) Attach ECG leads for continuous ECG monitoring
h) Place Umbilical venous access in addition to peripheral venous access as obtaining venous access in a cooled baby may be very difficult to obtain.
i) Place arterial line (radial or umbilical) for invasive arterial pressure monitoring (remember – non-invasive blood pressure monitoring may be difficult and erroneous in cooled babies and clinical monitoring may be extremely difficult and unreliable in such babies)

Starting to perform cooling

a) Switch on the cooling machine in case one is using a 'servo controlled' device. For phase changing material, the cooling starts as soon as the baby is placed.
b) Switch radiant warmer to manual mode with zero heater output. Alternatively, radiant warmer can be switched off
c) Anticipate significant bradycardia once cooling has been initiated.

Stopping therapeutic hypothermia:

a) Identification of a contraindication that was previously undetected
b) Persistent signs of brain death as detected and confirmed by the treating team
c) Parents wish to withdraw the treatment and intensive care

Note: Apart from the above three conditions, the hypothermia treatment should be continued uninterrupted for 72 hours and rewarming over 6-7 hours after that.

C) Equipment and supplies:

In addition to the standard equipment, disposables, intravenous fluids and drugs, availability of the following equipment and supplies must be ensured

a) Cooling device
b) Rectal temperature probe
c) Skin temperature probe (separate from the one used with radiant warmer)
d) Plastic sheet for keeping in between cooling mattress and baby
e) ECG electrodes
f) Multi-parameter monitor
g) aEEG machine (if available)
h) Invasive BP monitoring module (preferred) or NIBP cuff
i) Injection morphine/fentanyl
j) Radiant warmer
k) Pulse oximeter (preferably Masimo)

Protocol 3: Strategies to reduce preterm brain injury

The two most important acquired brain injuries in preterm infants are intraventricular haemorrhage (IVH) and periventricular leukomalacia (PVL) respectively. These injuries are commonly seen in very and extreme preterm infants and contributes significantly to the in-hospital mortality and morbidity, as well as it also increases the risk of developing long-term neurodevelopmental impairment. The various strategies to reduce brain injury in preterm infants in NICU along with their current evidence.

Time frame	Intervention	Evidence
Antenatal Period	Inuetro transfer for anticipated preterm delivery	Mortality is reduced [OR 0.73 (0.59- 0.9)] and morbidity free survival is increased (OR 1.92 (1.02 to 3.6)
	Antenatal steroids	• IVH (all grades) is reduced [RR 0.54 (0.43–0.69)] • Developmental delay at 3 years is reduced [RR 0.49 (0.24–1.00)] • CP (all severities) at 2–6 years is reduced [RR 0.60 (0.34–1.03)]
	Magnesium sulphate for pregnant women at risk of imminent preterm birth < 32 weeks of gestation	• CP (all severities) at 12–24 months is reduced [RR 0.68 (0.54–0.87)] • CP (moderate to severe) at 12–24 months is reduced [RR 0.64 (0.44–0.92)] • Gross motor dysfunction at 18–24 months is reduced RR 0.61 (0.44–0.85)
	Antibiotics following preterm premature rupture of membranes	• Prolongation of pregnancy, reduction in neonatal infection [RR 0.67(0.52- 0.85)] and abnormal cranial ultrasound scans [RR 0.81(0.68 to 0.98)]. • At school age, no difference in functional, behavioural or attainment outcomes.
Peripartum period	Delayed cord clamping	• Reduction in IVH (all grades) [RR 0.59 (0.41–0.85)] • Reduction in Gross motor dysfunction at 18–22 months [RR 0.32 (0.10–0.90)]
Postnatal period	Prevention of hypothermia	• Moderate and severe hypothermia is associated with increased risk of IVH [RR 1.3 (1.1-1.6) for moderate] and death [RR 1.5 (1.3-1.9) for moderate and RR 5.6 (1.1-28.1) for severe hypothermia]. • Plastic wraps reduces hypothermia on admission to the nursery or up to two hours after birth [RR 0.67 (0.62-0.72)[7] • Skin to skin contact reduces hypothermia at birth for infants with birth weight ≥ 1200 and ≤ 2199 grams [RR 0.09 (0.01 to 0.64)]
	Judicious management of hypotension	• No evidence for very preterm infants without cardiovascular compromise and insufficient evidence for very preterm infants with cardiovascular compromise regarding routine use of volume expansion for severe disability [RR 0.80 (0.52, 1.23)], cerebral palsy (CP) [RR 0.76 (0.48, 1.20)]

		• One should be cautious using volume expansion and inotrope in premature infants
	Prophylactic indomethacin	• Reduction in IVH (Grades 3 and 4) [RR 0.66 (0.53–0.82)] • Reduction in ventriculomegaly, PVL or other white matter echo abnormalities [RR 0.80 (0.65–0.97)]
	Caffeine	• Reduction in cerebral palsy (CP) (all severities 12–22 months) AOR 0.58 (0.39-0.87) • Reduction in cognitive delay (18–22 months) AOR 0.81 (0.66–0.99)
	BPD prevention	
	Volume ventilation	Reduction in PVL and IVH (Grades 3 and 4) [RR 0.48 (0.28–0.84)]
		Observational studies have shown that hypercapnia (PCO2>60 mmHg) and hypocapnia (PCO2 <35 mmHg) can cause brain injury and should be avoided particularly during initial 72 hours after birth (target PCO2 between 45-55 mmHg, to a maximum of 60 mmHg).
	Head positioning	Limited evidence
	Nurturing environment and optimising postnatal growth	
	Prevention of sepsis & NEC	Postnatal infection and neurodevelopmental outcome: [14] CP (all types) Late (1.14–2.56) Early onset sepsis (EOS)—OR 1.7 (0.84-3.45) onset sepsis (LOS)—OR 1.71 EOS+LOS—OR 2.33 (1.02–5.33)
	Restrictive blood transfusion policy	

SECTION 5

Management of neonatal sepsis

Protocol 1: Approach to suspected neonatal sepsis

Perinatal risk factors

1. Rupture of membranes > 24 hours
2. Spontaneous preterm labour
3. Chorioamnionitis (Intraamniotic Infection)
4. Prolonged labour
5. Unclean Per vaginal examinations

Extreme risk factors *

1. Rupture of membranes > 72 hours
2. Chorioamnionitis (Intraamniotic Infection)
3. Foul smelling liquor

Definition of Intraamniotic Infection or Inflammation or both (Triple I)

Maternal fever: Maternal oral temperature >/=39 0c on any one occasion. If oral temperature is 38 (100.4) to 38,9 (102 F) repeat after 30 minutes, if repeat value remains at least 38 C (100.4) it is defined as fever

Suspected triple I: Fever without a clear source plus any of : (i) baseline fetal tachycardia (> 160.m for > 10 min)

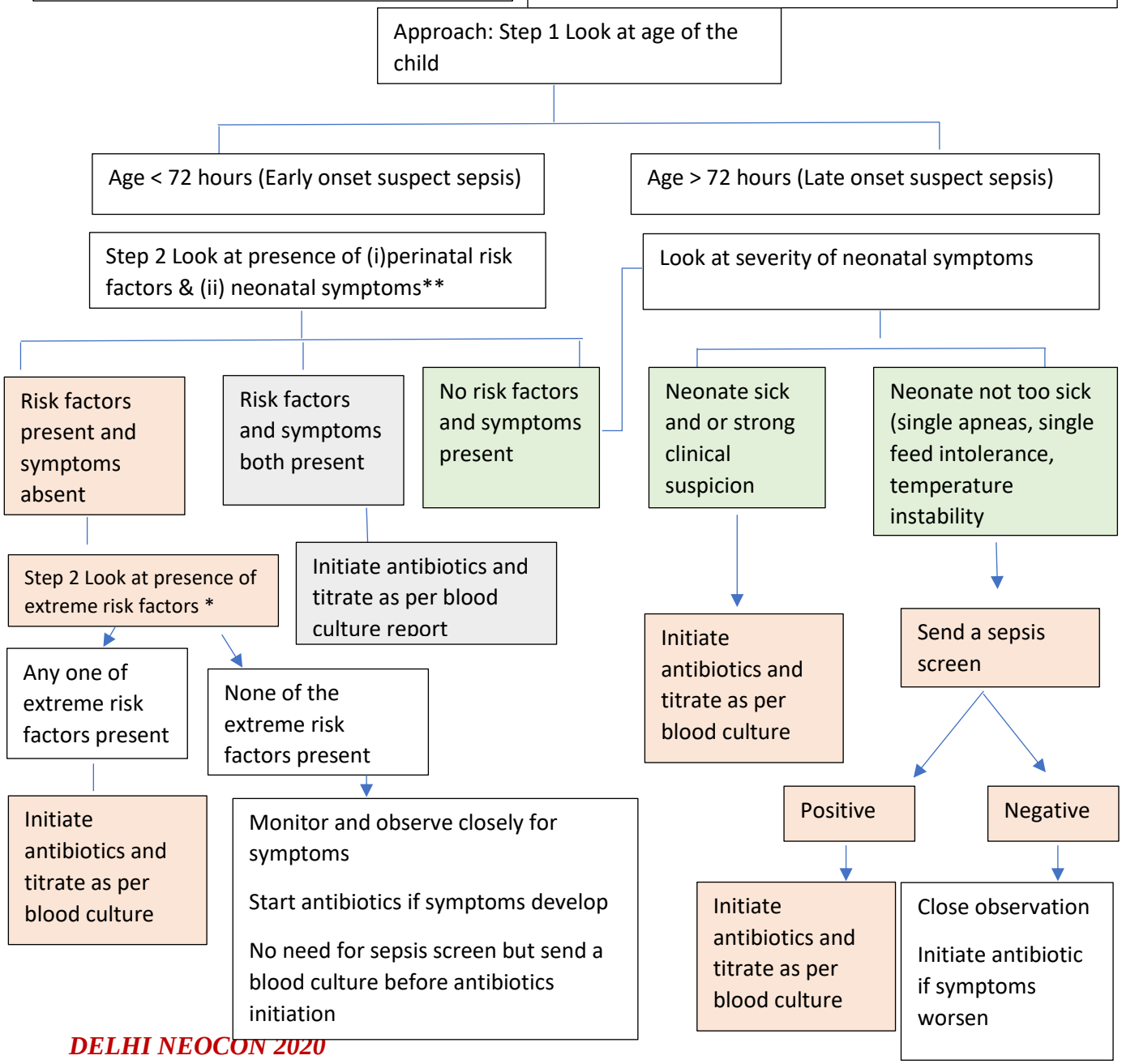
Maternal TLC > 15000/cmm in absence of corticosteroids

Definite purulent fluid from cervical os

Confirmed Triple I: All the above plus lab findings such as:

Positive amniotic fluid gram stain/culture

Histopathological evidence of infection or inflammation or both in placenta



Symptoms of sepsis**

Lethargy

Poor feeding

Mother/nurse reports that baby is not well

Fever

Hypothermia

Vomiting, Diarrhea, abdominal distension

Seizures, encephalopathy

Poor perfusion, shock

Rarely: bleeding, sclerema, renal failure

Components of sepsis screen

Total leucocyte count (TLC)

Absolute neutrophil count (ANC)

Micro ESR

C Reactive Protein (CRP)

Immature to Total count (IT Ratio)

TLC < 5000/cmm, ANC below cut off for age (<1800/cmm), Micro ESR > 15 mm Hg, CRP > 10 mg per dL and I/T ratio > 0.2- any two of the above constitute a positive sepsis screen

Always send a blood culture before starting antibiotics.

Lumbar Puncture should be performed in all symptomatic neonates (irrespective of early onset or late onset of symptoms).

Protocol 2: Management of fungal sepsis

Invasive fungal infections encompass infections largely caused by *Candida* species (C.*albicans*> C. *parapsilosis*>C. *glabrata)* and with a small portion caused by *Aspergillus*, *Zygomycetes*, *Malassezia*, *and Trichosporin*.

Invasive *Candida* infections (ICI) in neonates include: Congenital Cutaneous Candidiasis (CCC) and Late-onset Cutaneous Candidiasis, Bloodstream infections (BSIs), Urinary tract infections (UTIs), Meningitis, Peritonitis, and infection of other sterile sites (bone and joint infections).

Incidence: inversely proportional to birth weight & gestational age- 1-4% in VLBW & 2-8% in ELBW and 20% in < 26 weeks/ < 750 gram neonates.

Risk factors for Invasive Candida Infection

Immunity	Medications facilitating fungal growth*	Medications that suppress immune defense	Diseases	NICU practices
• **Extreme Prematurity: Under developed immune system** • **Immune suppression** • **Neutropenia**	• Cephalosporins* • Carbapenams* • Postnatal steroids*	• Histamine receptor antagonists* • PPIs* • Postnatal steroids*	• NEC • Prior BSI • SIP/ Focal bowel perforation • GI malformations • Hyperglycemia	• Prolonged use of antibiotics > 5 days* • Multiple antibiotic usage* • Lack of enteral feeds* • Use of intralipid > 7 days* • Indweller central venous catheter* • Mechanical ventilation*

***** Modifiable risk factors

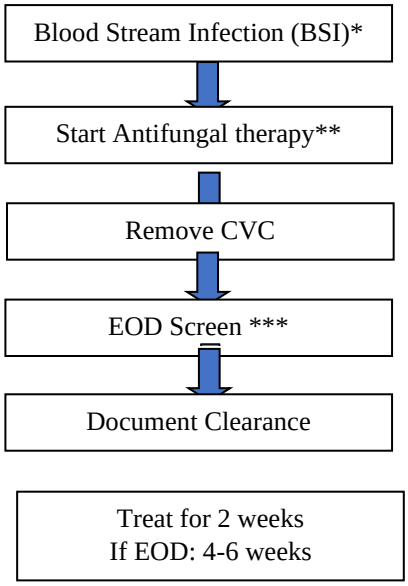
Clinical presentation

Non-specific and variable course ranging from localized skin infection to disseminated end organ involvement.

Signs & Symptoms	Common Lab Parameters
• **Mucocutaneous: oral thrush, diaper dermatitis**	• Thrombocytopenia • Immature to Total neutrophil ratio >0.2 • Increased CRP Elevated WBC > 20000/ cumm^3 • Hyperglycemia • Metabolic Acidosis • Neutropenia < 1500/cumm^3
• **Respiratory: Frequent apnea ,Respiratory distress, Pneumonia, increased oxygen requirement & need for assisted ventilation**	
• **CNS: Lethargy, Hypotonia, Meningitis, Ventriculitis, Cerebral abscess**	
• **GI symptoms: Feed intolerance, abdominal distension, blood in stools, Peritonitis, SIP**	
• **Renal: UTI, renal abscess**	
• **Cardiac: Hypotension , Endocarditis , thrombi**	
• **Eye: Endophthalmitis, Chorioretinitis**	
• **Bones & Joints- Septic arthritis & osteomyelitis**	

Management of Fungal Infections

- **Blood stream Infections**



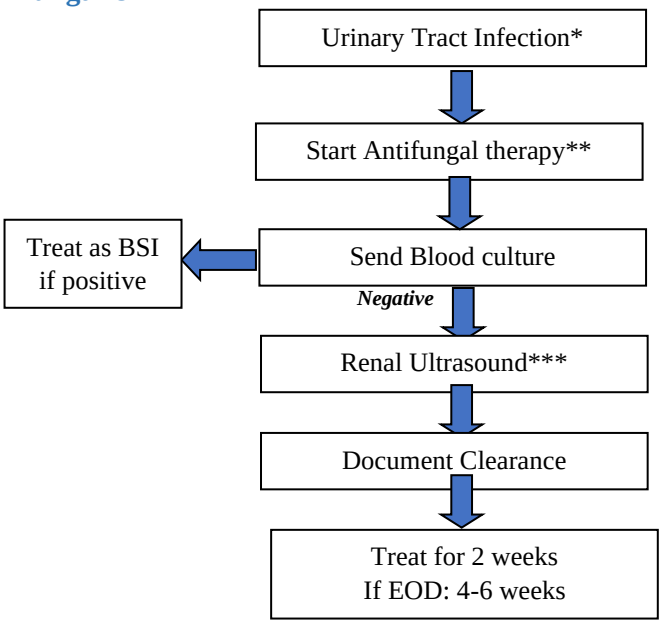
* Isolation of Candida species in blood culture

** Amphoteracin B @ 1mg.kg.day IV is initial DOC > Fluconazole 12 mg/kg IV or PO
Monitor for hypokalemia, renal tubular dysfunction, bone marrow toxicity

** *Perform EOD screen (End organ dysfunction screen) at presentation and after 5-7 days of start of therapy.
Involves:

- Eye examination : retinitis/ endophthalmitis
- Renal USG for Fungal ball
- ECHO
- Cranial USG/CT/MRI

- **Fungal UTI**

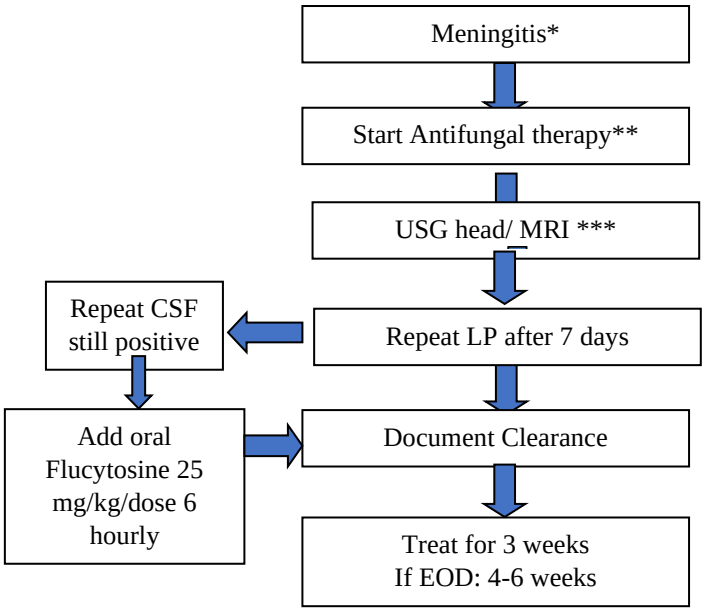


* Isolation of fungal species in urine collected by supra-pubic aspiration/ sterile catheterization.
Defined as $\geq 10^4$ CFU of Candida species/ml

** Amphoteracin B @ 1mg.kg.day IV is initial DOC > Fluconazole 12 mg/kg IV or PO
Monitor for hypokalemia, renal tubular dysfunction, bone marrow toxicity

** *Perform Renal USG for fungal ball at presentation and after 5-7 days of start of therapy.

- **Fungal Meningitis**

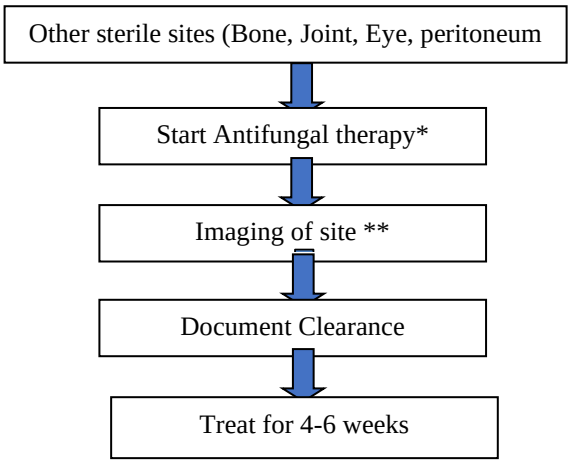


* Isolation of Candida in CSF or CSF cytology or biochemistry suggestive of meningitis with Candida BSI

** Begin monotherapy with Amphoteracin B @ 1mg.kg.day IV
- Remove shunt if present
- Monitor for hypokalemia, renal tubular dysfunction, bone marrow toxicity

** *Perform EOD screen (End organ dysfunction screen) at presentation and after 5-7 days of start of therapy. Involves:
- Eye examination : retinitis/ endophthalmitis
- Renal USG for Fungal ball
- ECHO
- Cranial USG/CT/MRI

- **Other Sterile Site Infections (**bone, joint, eye)

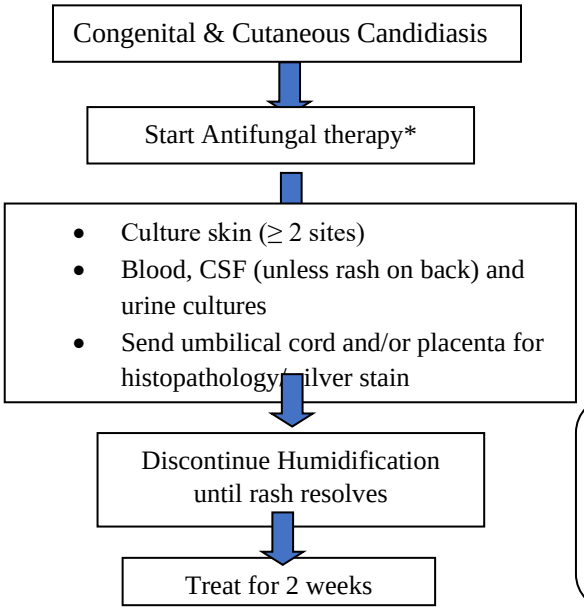


* Amphoteracin B @ 1mg.kg.day IV is initial DOC > Fluconazole 12 mg/kg IV or PO
Monitor for hypokalemia, renal tubular dysfunction, bone marrow toxicity

** Perform EOD screen (End organ dysfunction screen) at presentation and after 5-7 days of start of therapy.
Involves:

- Eye examination : retinitis/ endophthalmitis
- Renal USG for Fungal ball
- ECHO
- Cranial USG/CT/MRI

- **Congenital & Cutaneous Candidiasis**

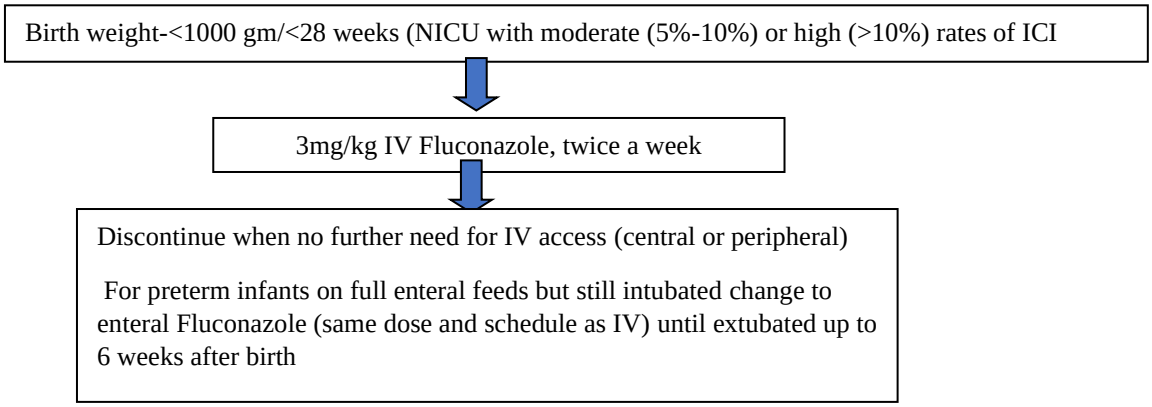


*Amphoteracin B @ 1mg.kg.day IV is initial DOC > Fluconazole 12 mg/kg IV or PO
Monitor for hypokalemia, renal tubular dysfunction, bone marrow

- **Treatment of Diaper Dermatitis:** Healthy term infants without symptoms, feeding well, and at low risk of invasive Candidiasis: Nystatin/ Miconazole / Clotrimazole local application. If no response; give Fluconazole @3 mg/kg OD for 7 days

Antifungal Prophylaxis

- Routine antifungal prophylaxis for preterm infants is **NOT recommended**
- Antifungal prophylaxis is reserved for ELBW in **NICUs with a high baseline rate (> 5-10%) of systemic fungal infection**
- Consistent with American Academy of Pediatrics and the Infectious Diseases Society of America recommendation, indicated in **congenital & cutaneous Candidiasis**



Good NICU Practices to Prevent Invasive fungal Infection

- Early initiation and rapid advancement of enteral feeds
- Minimize use and duration of IV alimentation
- Rational use (dose, duration, type and mode) of antibiotics
- Removal of indwelling catheters when no longer required (within 7-10 days)
- Avoid usage of PPIs, H2 antagonists, 3 rd generation Cephalosporins

Protocol 3: Approach to intrauterine infections

Management algorithm of newborn born to mother with tuberculosis

Aim: Active search for tubercular lesion to diagnose congenital tuberculosis, and prevention of transmission of infection to the neonate from the mother or treatment of active tubercular infection in neonate. However, till date the topic is quite controversial and as such there is no uniformity in the recommendations from various paediatric societies across the globe.

Table 1. Diagnosis, treatment, vaccination and follow up

Paediatric society	Diagnosis of congenital tuberculosis	Treatment of congenital tuberculosis	BCG vaccination	Follow up
WHO[1]	Cantwell criteria	Areas with low HIV prevalence and/or low prevalence of isoniazid resistance: HRZ for 2 months followed by HR for 4 months Areas with high HIV prevalence and/or high prevalence of isoniazid resistance**:** HRZE for 2 months followed by HR for 4 months	Delay until INH therapy is completed. BCG after 2 weeks of completing therapy only if TST remains negative and the baby is HIV-negative	Every 2 months till the treatment is complete
AAP[2]	TST and IGRA test, CXR, lumbar puncture, placental examination and appropriate cultures	HRZ, and either E or an aminoglycoside. Corticosteroid for meningitis	Only if mother is having MDR TB, or poorly adherent to treatment	Monthly while on INH prophylaxis. Mtx repeated at 6, 9, 12 months to detect congenital TB
DOTS/RNTCP[3]	-	-	BCG vaccination at birth even if	-

			INH prophylaxis therapy is planned.	
IAP[4]	-	-	BCG vaccination at birth even if INH prophylaxis is planned.	-
New Zealand guidelines[5]	Cantwell criteria*	-	Delay until 3 to 4 months old, perform a TST and CXR. If normal and the infant is asymptomatic, stop isoniazid and consider BCG	-
Merk's Manual[6]	Culture of tracheal aspirate, gastric washings, urine, and CSF CXR, Mtx.	HRZ, aminoglycoside ± pyridoxine (breastfed infant) for 2 months. After 2 months HR continued for 6 to 12mo. depending on disease category	If adherence in a non tuberculous environment cannot be ensured	-
Kenya Guidelines[7]	Clinical signs and symptoms Placental examination	-	Mother MDR TB negative: Delay until 2 weeks after completion of INH therapy Mother MDR TB positive: at birth	monthly
NICE guidelines[8]	CXR, CT thorax, histology, 3 gastric lavages	-	Both MTx and interferon-gamma release assay is negative	Regular

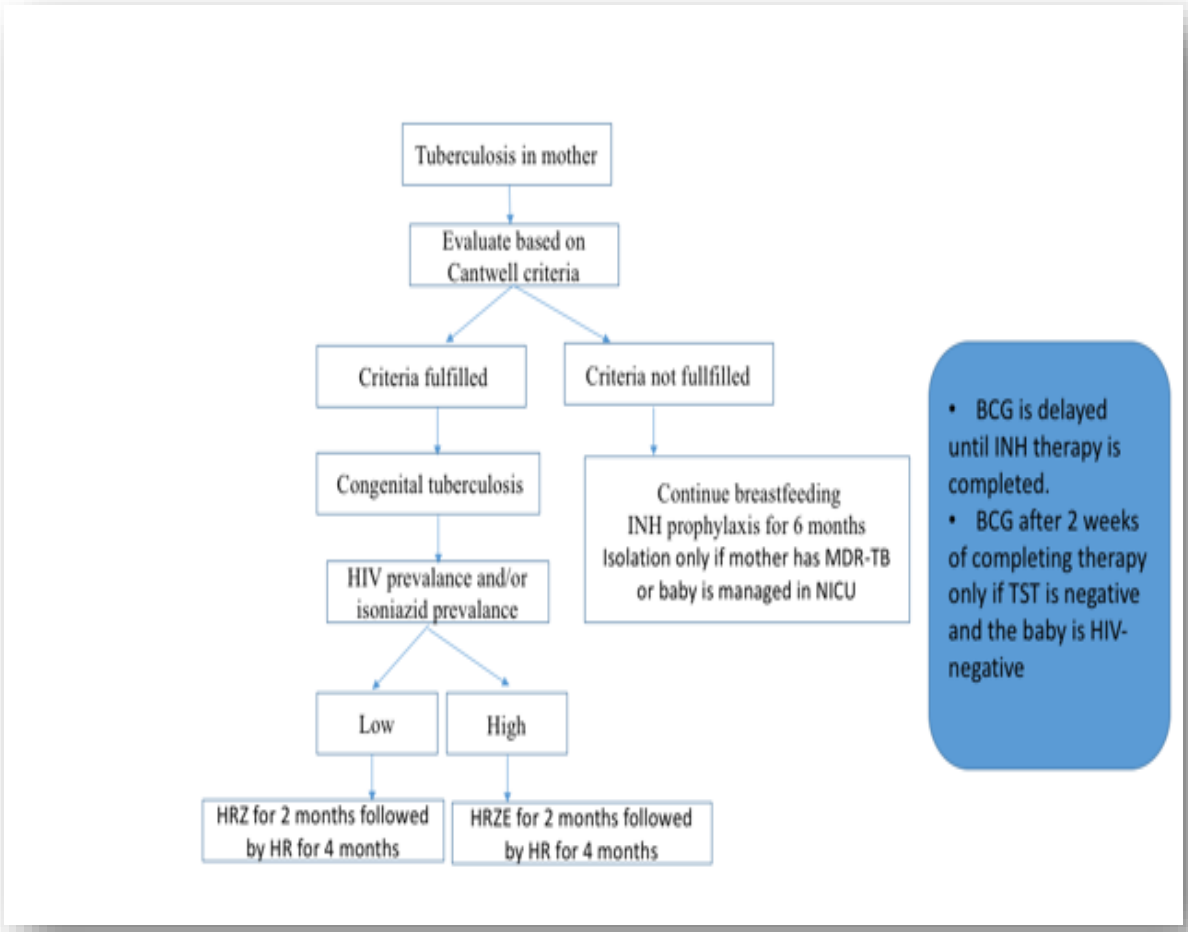
Table 2: Prevention of transmission of tubercular infection to the neonate from the mother			
Pediatric society	Breastfeeding	Isolation	Prophylaxis
WHO[1]	Continue	Only if mother has MDR-TB or baby is managed in NICU (give expressed breast milk)	INH prophylaxis continued for 6 months
AAP[2]	Only if the mother is on ATT	Only if mother is MDR-TB, non-compliant to therapy and before starting ATT.	INH for 3-4 months followed by Mtx test. i. MTx negative: stop INH. ii. Mtx positive: search for congenital TB. If positive treat as congenital TB, if negative give INH for 9 months
DOTS/RNTCP[3]	Breastfeeding	MDR TB or mother having active disease and noncompliant to treatment.	INH prophylaxis should be started after ruling out congenital TB and continued for 6 months. Chemoprophylaxis in MDR contacts is not recommended
IAP[4]	Continue	mother is sick, non-adherent to therapy or has MDR-TB.	INH prophylaxis should be started after ruling out congenital TB and continued for 6 months
New Zealand guidelines[5]	Continue	Mother having MDR TB, active disease or noncompliant to treatment.	INH prophylaxis after ruling out congenital TB and continued for 3-4 months After 3-4 months TST and CXR performed. If TST is positive and CXR and systemic examination is normal treat with isoniazid for six months.
Merk Manual[6]	Continue	mother having MDR TB, active disease and noncompliant to treatment	INH + pyridoxine for breastfed babies for 3 months Mantoux test at 3 months

			a. Negative: stop if the contact has adhered to treatment and has a positive response b. Positive: CXR and AFB cultures, if active disease is excluded, treatment with INH is continued for a total of 9 mo.
Kenya Guidelines[7]	continue	Not mentioned	Isoniazid for 6 months Chemoprophylaxis in MDR contacts is not recommended
NICE[8]	Continue	Mother and baby should not be separated	INH + pyridoxine for exclusively breastfed babies for 6 weeks MTx at 6 weeks a. Positive: reassess for active TB; if negative, continue isoniazid for 6 months. b. Negative: reassess for active TB and consider an interferon-gamma release assay: i. negative: stop INH ii. positive: reassess for active TB; if negative, continue isoniazid for 6 months.

*** Cantwell criteria**

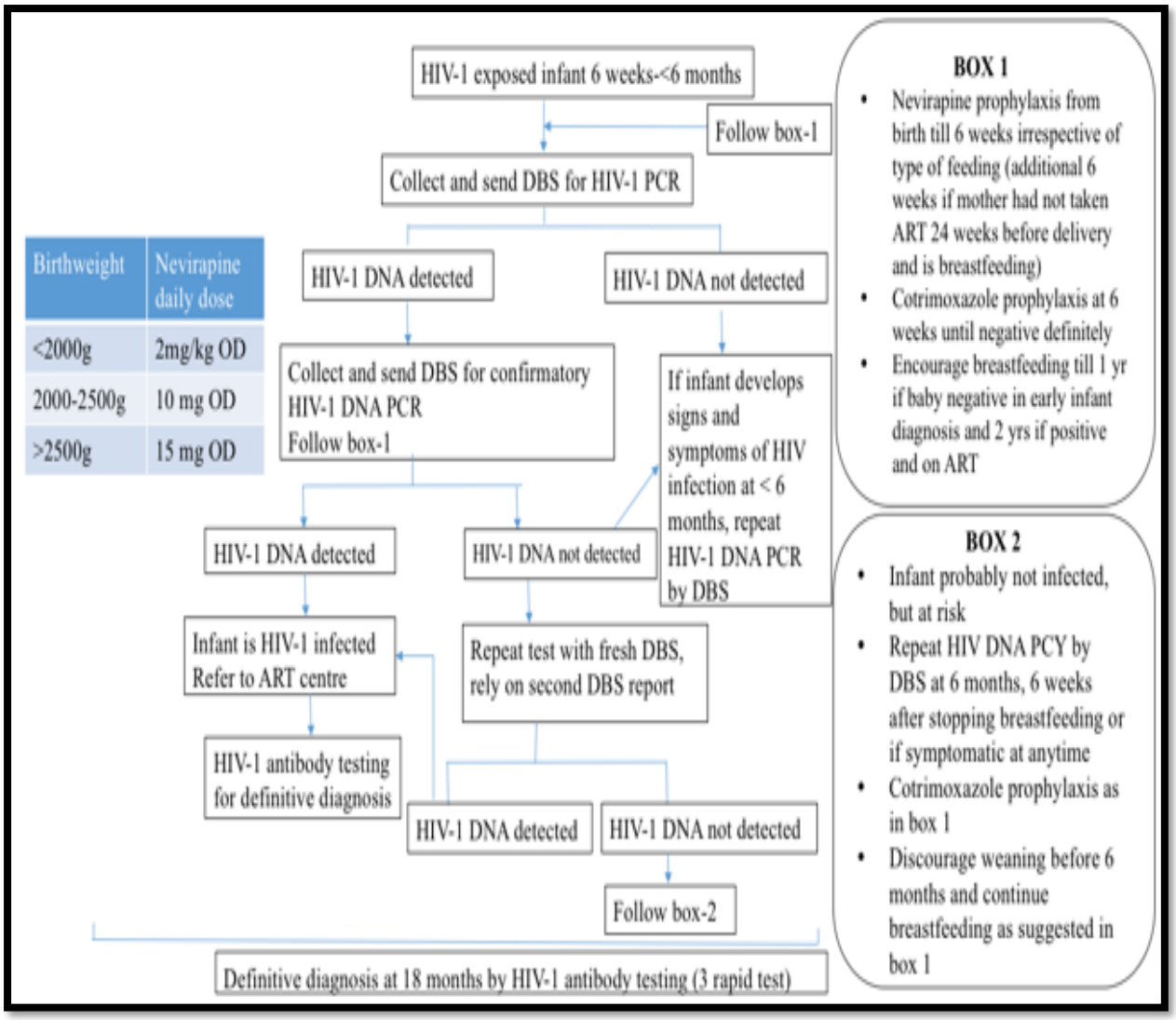
Diagnosis of congenital tuberculosis is made in the presence of proven tuberculous lesion and at least one of the following; *(i)* lesions in 1st week of life; *(ii)* primary hepatic complex or caseating hepatic granulomata; *(iii)* tuberculous infection of the placenta or the maternal genital tract; and *(iv)* exclusion of postnatal transmission by thorough contacts .

Middle path approach



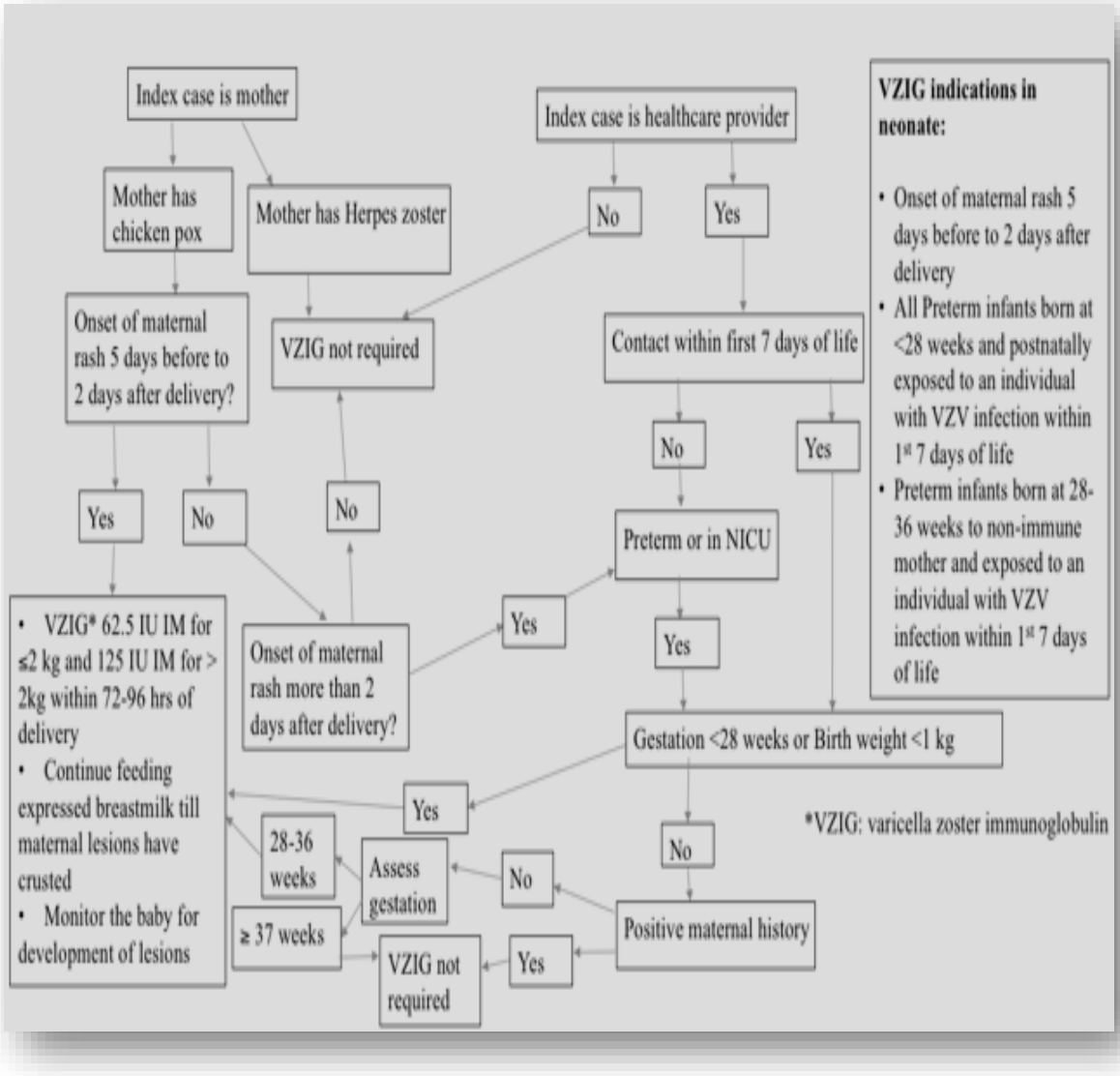
Management algorithm of babies born to HIV positive mother[9]

Aim: Actively search for perinatal HIV infection, continued surveillance for HIV infection during breastfeeding, prevention of transmission of infection to the neonate from the mother during breastfeeding and prevention against the development of opportunistic infection



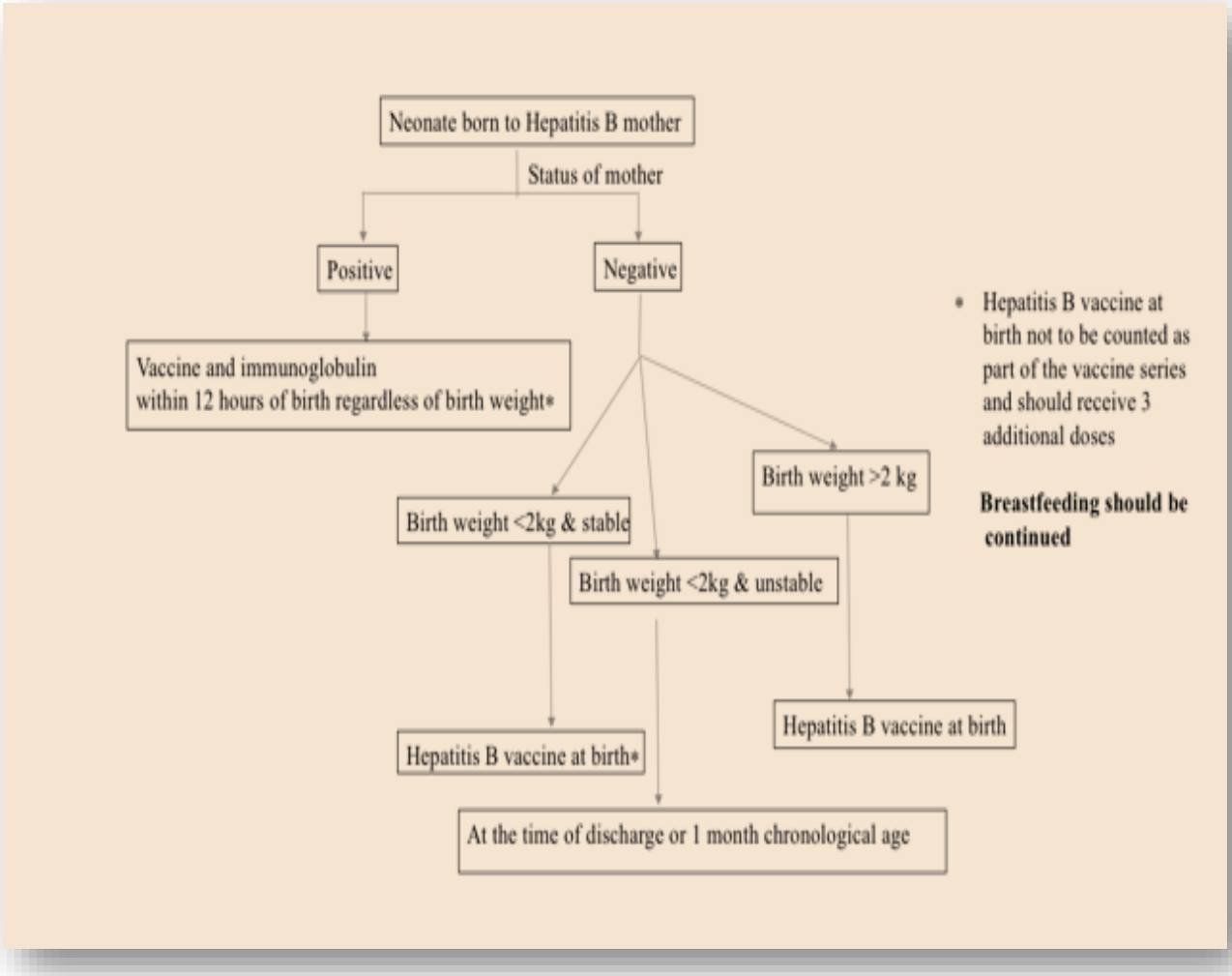
Management algorithm of babies born to varicella positive mother[10]

Aim: Prevent developing varicella infection in neonates born to mothers having active chicken pox around delivery as well as in neonates admitted in NICU and exposed to healthcare provider with active chicken pox



Management algorithm of babies born to Hepatitis B positive mother

Aim: To prevent the development of perinatal Hepatitis B Virus infection and hence early childhood infection and later chronic carrier state.



Protocol 4: Approach to antibiotic therapy in NICU

Indications of initiating antibiotics

1. First 72 hours of life: Presence of extreme risk factors in the mother but asymptomatic neonate
2. First 72 hours of life: Presence of risk factors and symptomatic neonate
3. More than 72 hours of life: Strong clinical suspicion of sepsis based on signs and symptoms, sick neonate
4. More than 72 hours of life: Doubtful clinical symptoms and signs (single episode of fever/single apnoea /single feed intolerance episode) and well-baby: start if investigations are suggestive of sepsis.

Which should be the first line antibiotic?

- It is not possible to recommend a single antibiotic policy for use in all newborn units.
- It should be based on local culture and sensitivity data and profile of organisms for last 6-12 months. If not available, use data from nearby units or NNPD.
- Individual antibiotics and rational combinations of antibiotics must be evaluated for the percentage of organisms that they cover. The simplest and cheapest rational combination of antibiotics must be selected for each line
    - First line: must cover approximately 75-80% of isolates
    - Second line: must cover approximately 90-95% of isolates
    - Third line: must cover approximately 95-100% of isolates
- Initial combination should cover both Gram negative and Gram-positive organisms. One should use the lowest generation antibiotic combination which would cover about 70% of organisms. This is to ensure you have something to fall back on.
- Avoid cephalosporins as first line antibiotics---proven harm (high risk of ELBS organisms, increased Candida infections, NEC, and mortality)—units who do not use have shown multiple benefits.
- Have a written unit/departmental/institutional antibiotic policy and practice antibiotic stewardship---i.e. have a written policy, write the reasons for starting the antibiotics, review the plan for antibiotics at 48 hrs and again at 5 days based on culture reports and clinical course, have a EXIT plan, do not use reserve drugs without consultation.

Antibiotic Stewardship is the way forward to reducing the use of multiple antibiotics and resistance.

Titration of antibiotics

- Antibiotics need 48-72 hours to show effects—till that time aggressive supportive treatment should be the focus
- When going from second line to third line antibiotics, give 72-96 hours at least for the effects to be seen.
- Empirical upgradation must be done if the expected clinical improvement with the ongoing line of antibiotics does not occur.
- Before changing, consider alternative diagnoses and metabolic complications. Check whether dose is correct, dilution is correct, drug is not beyond shelf-life and some drugs work better as infusions over few hours.
- Always take a repeat culture before changing.
- If the culture shows that the organism is sensitive to a lower generation antibiotic, in general one should downgrade

No role of prophylactic antibiotics

No benefits—rather harmful. Increased mortality, increased NEC, increased fungal infections.

Hence ***no antibiotics should be started*** in situations like

I. For all ELBW/VLBW,
II. For all babies born by caesarean,
III. For all twin of symptomatic baby,
IV. Just if baby is getting IV fluids
V. For colonization of —ET tube or elsewhere.
VI. MSL is not an indication to give antibiotics if baby is well. There are RCTs to prove this.
VII. Before or after exchange / partial transfusion

SECTION 6

Feeding protocols in NICU

Protocol 1: Feeding of low birth weight neonate

Goal for nutrition of the preterm and LBW infants is to '*Achieve postnatal growth rate approximating that of the normal foetus of the same gestation age.* Establishing adequate nutrition in preterm & low birth weight babies can be challenging especially in the initial few days owing to structural and functional immaturity of the GI tract, poor body stores increased susceptibility to infections, resulting in increased risk of extra uterine growth retardation and poor neuro-developmental outcomes later in life.

1. When to start feeds?

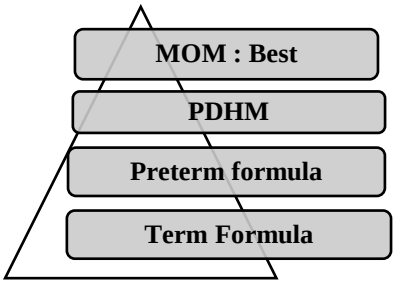
Enteral feeding should be initiated **as early as possible** in all babies.

- Early versus delayed introduction of feeds: No difference in Feed intolerance and/or NEC
- Delayed initiation : Intestinal villous atrophy, longer time to achieve full feeds, poor growth , delay in regaining birth weight, prolonged duration of hospital stay, complications of IV alimentation (sepsis, cholestasis)
- Presence of RD, need for ventilation, moderate asphyxia, PDA and extreme prematurity are NOT Contraindication to feeding.
- Contraindication to feed initiation: Presence of hemodynamic instability requiring vasopressor support,

2. Which Milk to give?

Mothers own milk (MOM) is the best option**.** Results in dose specific reduction in risk and severity of

- NEC
- Late onset sepsis
- Retinopathy of prematurity
- Rehospitalisation after NICU discharge
- Neurodevelopment problems at 18-22 months



3. What should be the volume and frequency of feeding?

- Start fluids at 80 ml/kg/day (< 1500 g) & 60 ml/kg/day (1500-2500g)
- Daily increment: 20-30 ml/kg/day to a maximum of 180-200 ml/kg/day
- Frequency of feeding: every 2 hourly
- Slow (15-20 ml/kg/day) versus fast advancement (30-40 ml/kg/day) : No difference in FI and/or NEC, mortality
- Slow advancement of feeds: delayed establishment of full enteral nutrition, increased risk of infection

4. What is Minimal enteral nutrition (MEN) or Trophic feeds?

MEN is small volumes of expressed breast milk @ 12-24 ml/kg/day every 1-3 hourly
Started in sick and extremely preterm babies; NOT contraindicated in asphyxia, RD, Hypotension
Benefits:

- Enhance the gut growth , motility &hormonal
- Less feed intolerance
- Reduction in days required for attaining full feeds ; Fewer days on parenteral nutrition
- Improved weight gain & decreased hospital stay

5. What is role of Early Total enteral feeding (ETEF) in VLBW babies?

ETEF is an effective intervention to improve outcomes in VLBW neonates in resource limited settings
Benefits:

- Avoid prolong intravenous access and its related complications
- Improved postnatal growth
- Gut maturation and reduced intestinal permeability
- Stimulates gut motility, enzyme production, GI hormone release
- Preserves gut microbiota

6. What should be the ideal mode of feeding?

Gestation	Maturation of feeding skills	Initial feeding method
28 weeks and below	• No proper sucking efforts • Increasing propulsive motility of gut	• Initiate **Tropic feeds / MEN** • **Initiate ETEF if clinically stable** • Hike the feeds after monitoring for feed intolerance
29-31 weeks	• Sucking bursts develop • No suck/swallow and breathing coordination	**Oro-gastric tube feeding**
32-34 weeks	• Slightly mature sucking pattern • Breathing & swallowing coordination develops	**Spoon/ Paladai feeds**
>34 weeks	• Mature sucking pattern • Sucking/ swallow & breathing coordination develops	**Breast feeding**

7. What nutritional supplements should be given in LBW and VLBW infants?

LBW, especially preterm need supplements to meet their high demands.

Nutritional Supplementation in LBW infants

- Require iron and Vitamin D supplementation till 1year of age

Nutritional Supplementation in VLBW infants

- Feeds should be supplemented for Protein, Energy, Calcium, Phosphorous, Trace elements (Iron, zinc) & Vitamins (A, D, E, K) till term gestation (40 weeks) or 2000g, whichever is earlier).
- After 40 weeks requirement is similar to those with birth weight 1500-2499 grams.

Methods of supplementation:

- Giving individual nutrients
- Fortification with preterm formula/ Human milk fortifier (HMF)

Supplementation with individual nutrients in LBW infants

Nutrients	Dose	When to start	Till
Vitamin D	400 IU/day	Feeds at 100 ml/kg/day	1 year of age
Iron	3 mg/kg/day	2-4 weeks	1 year of age

Supplementation with individual nutrients in VLBW infants

Nutrients	Dose	When to start	Till
Vitamin D	400 IU/day * ELBW: 800-100 IU	Feeds at 100 ml/kg	1 year of age
Calcium & phosphorus	140-160 ml/kg/day (Syp. Osteocalcium 8-10 ml/kg/day)	Feeds at 100 ml/kg	40 weeks PMA or 2 kg whichever is later
Zinc, Vit A, B6	Multivitamin drops (visyneral z 1 ml OD)	Feeds at 100 ml/kg	40 weeks PMA or 2 kg whichever is later
Iron	2-3mg/kg/day	2 weeks	1 year of age

Fortification of breast milk

- Supplementation with multi-component HMF improves short term increase in weight, length and HC
- It reduces hospital stay, TPN days with no effect on biological activity of Human milk
- Started when neonate is on 100 ml/kg/day enteral feeds with EBM @ 0.4 gram per 10 ml and continued till weight of 2 Kg or PMA 40 weeks, whichever is later.
- Provide optimal calories, protein, micronutrients except zinc which needs to be added separately.

8. What are the good NICU practices to promote optimal feeding?

- Family participatory care : involvement of mothers in the care of their babies
- Promoting and supporting KMC
- Oropharyngeal therapy with MOM in all preterm < 32 weeks soon after birth (sick as well as healthy) @ 0.2 ml q 2 hourly- has Immunomodulatory effects & decreases NEC/Late onset sepsis
- Non- Nutritive sucking on empty breast as soon as baby is clinically stable.

9. How to monitor growth in LBW infants?

- All LBW infants should be weighed daily till the time of discharge from the hospital. Both term and preterm LBW infants tend to lose weight (about 10% and 15% respectively) in the first 7- 14 days of life
- Birth weight is regained by 10-14 days. Thereafter, the weight gain should be at least 15-20 g/kg/day till a weight of 2-2.5 kg is reached. After this, a gain of 20 to 30 g/day is considered appropriate.

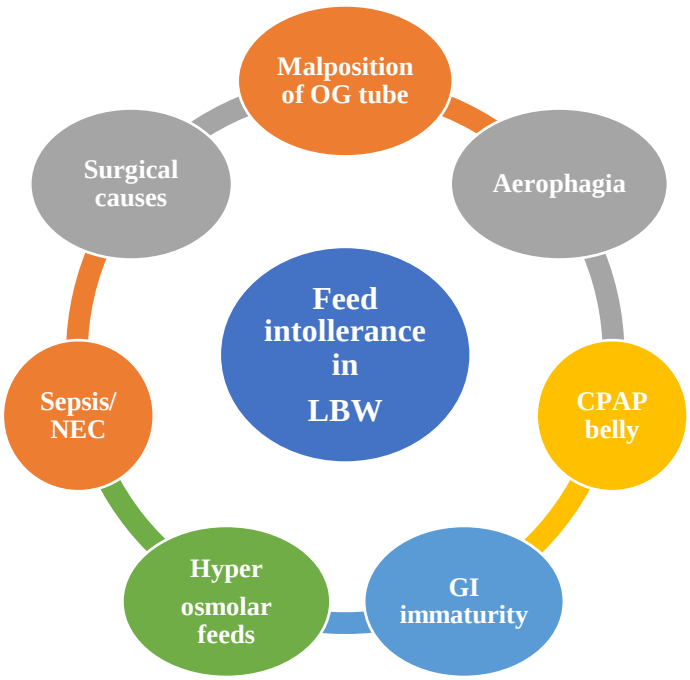
Protocol 2: Approach to feed intolerance in neonates

Feed intolerance is common in very preterm infants especially in the first few days of life and represents structural and functional immaturity of the gastrointestinal tract.

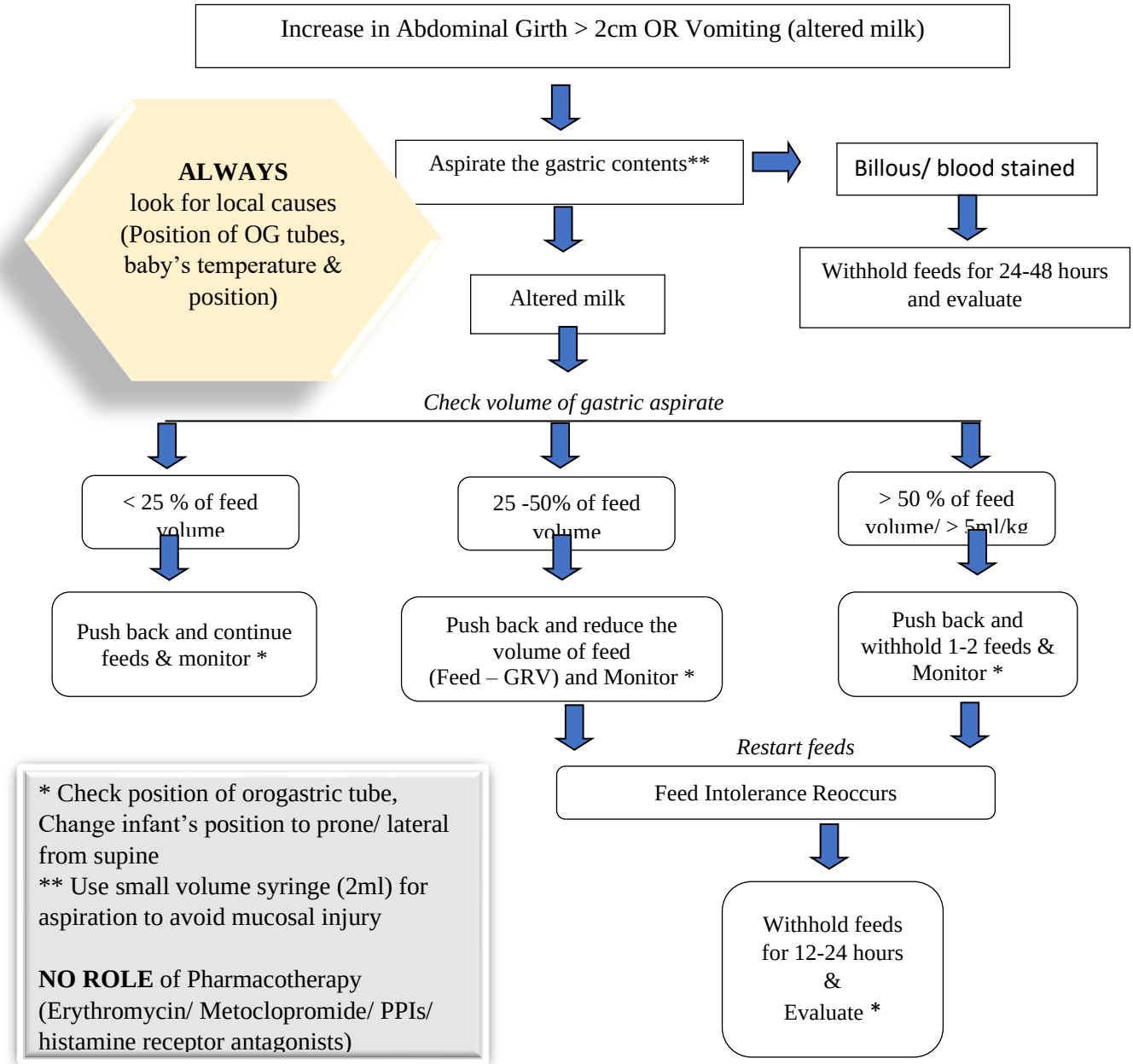
NO UNIVERSALLY AGREED UPON CRITERIA. Can be diagnosed by the presence of one or more of the following:

- Vomiting
  - Any episode of bile- or blood-stained vomiting
  - Recurrent vomiting more than three times during any 24 h period
- Abdominal distention (with or without visible bowel loops) :
  - Abdominal girth (AG) increase >2 cm (measured at umbilicus—pre-feed)
  - Abdominal wall erythema or tenderness
  - Absent/ reduced bowel sounds
- Increased gastric residuals
  - Non-specific indicator: > 5 ml/kg or > 50 % of the gastric residual volume (GRV) is abnormal
  - Routine pre feed aspiration of gastric contents is NOT recommended
- Gross or occult blood in stools
- Presence of systemic features (lethargy, apnea, cyanosis, bradycardia etc)

Cause of Feed intolerance



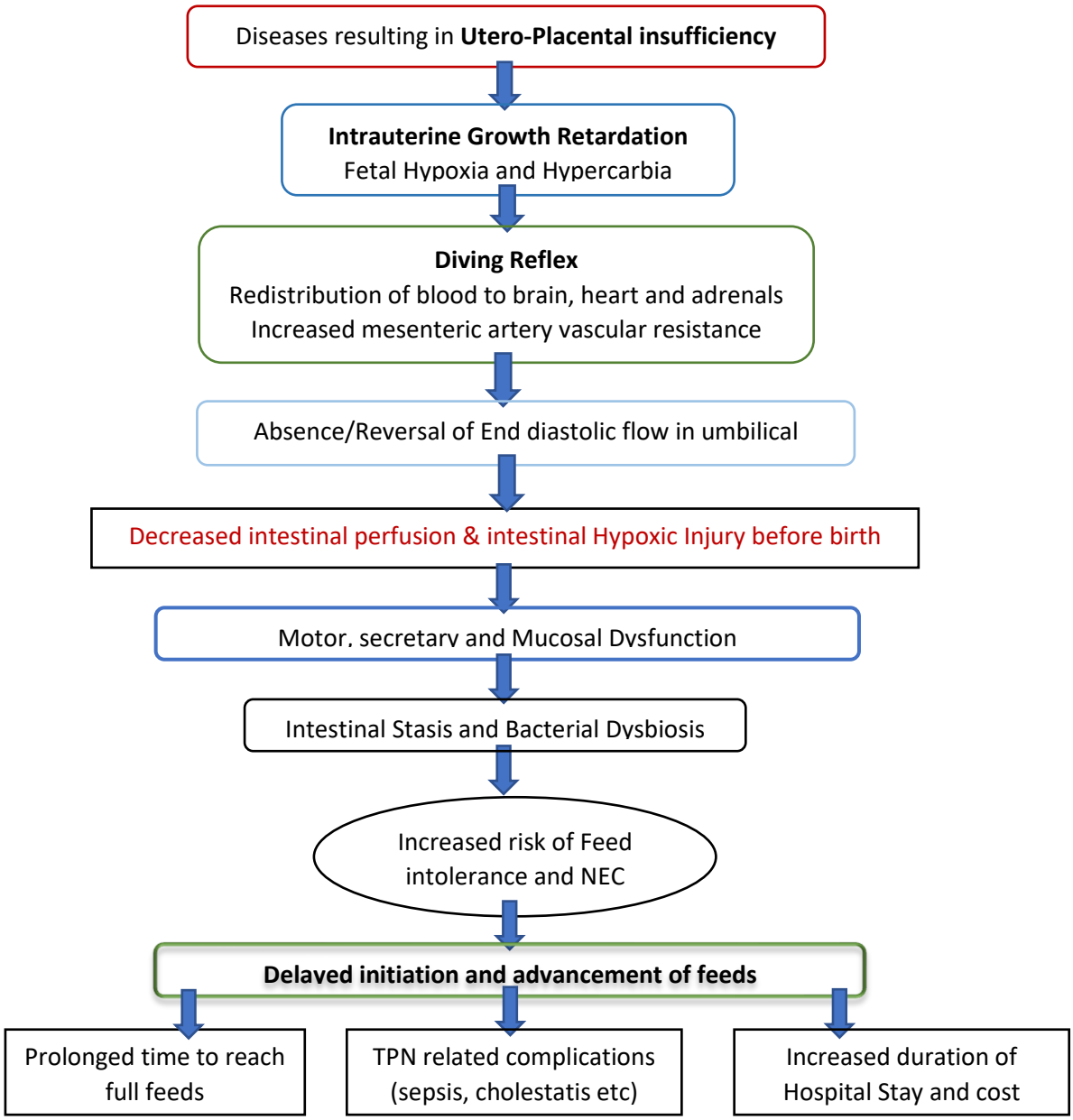
Approach to Feed Intolerance



Protocol 3: Management of feeding in neonates with absent/reversal of end diastolic flow

- Incidence: 6% in high risk pregnancies.
- Preterm neonates born to mothers with AREDF in umbilical artery dopplers are at an increased risk of **feed intolerance (FI) and necrotizing enterocolitis (NEC)** leading to undue delay in initiation and advancement of enteral feeding resulting in prolonging the time to reach full enteral feeds as well the duration of hospital stay.

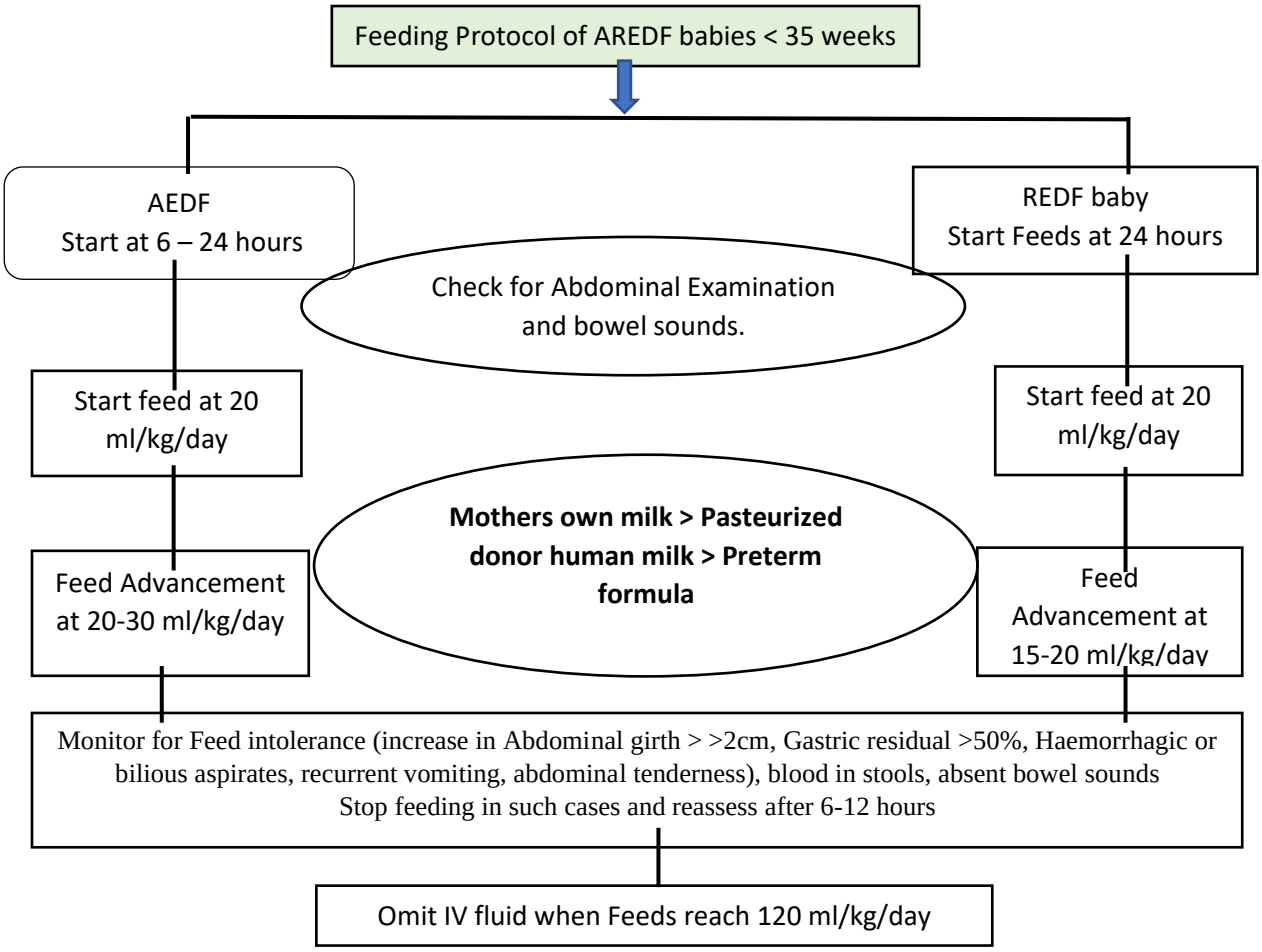
• Pathophysiology:



Feeding in AREDF: What does the current evidence suggest?

- **Early (6-48 hours) versus delayed initiation of enteral feeds:** No difference in incidence of FI and/or NEC. Delayed feed initiation group: increased time to reach full feeds
- **Slow (10-20 ml/kg/day) versus Rapid (20-40 ml/kg/day):** No difference in FI and/ or NEC

- **Feeding Protocol in AREDF**
  - 35 weeks and above: Start full enteral feeds as per daily total requirement
  - < 35 weeks:



SECTION 7

Management of neonatal haematological disorders, neonatal jaundice, AKI, and metabolic disorders

Protocol 1: Approach to inborn errors of metabolism

Approach to Inborn error of metabolism

For a baby with suspected inborn error of metabolism (IEM) basic workup should be initiated as soon as the possible as outcome of many of them particularly those associated with hyperammonemia, metabolic acidosis and hypoglycaemia is directly related to the rapidity with which problems are detected and appropriate management is instituted. Disease category in IEM can be based on blood ammonia levels, blood gas analysis and urinary ketone testing. This can be done as a part of 1st line investigation. The second line investigations can be performed in a targeted manner, based on presumptive diagnosis reached after first line investigations as shown in box 1

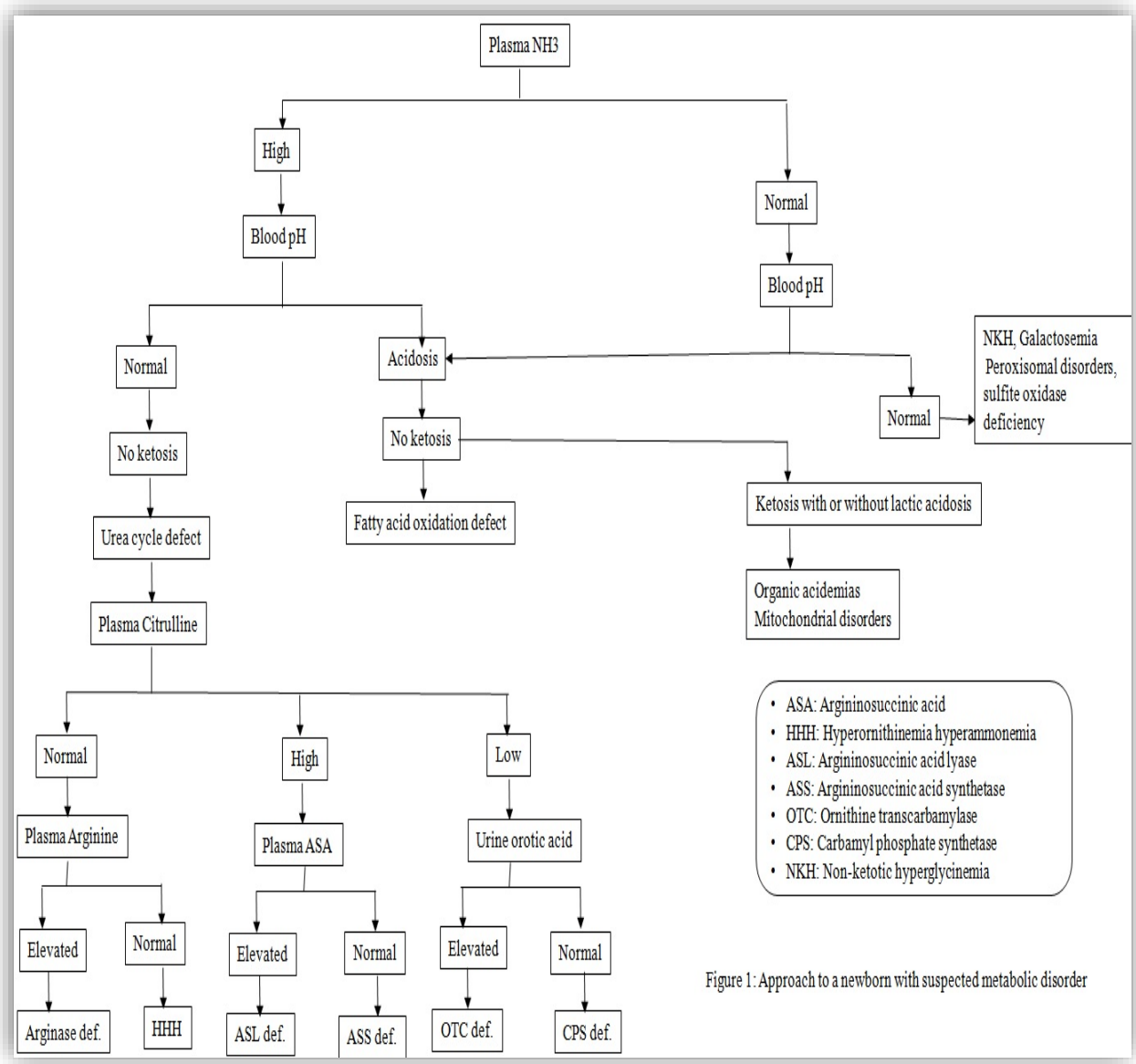


Figure 1: Approach to a newborn with suspected metabolic disorder

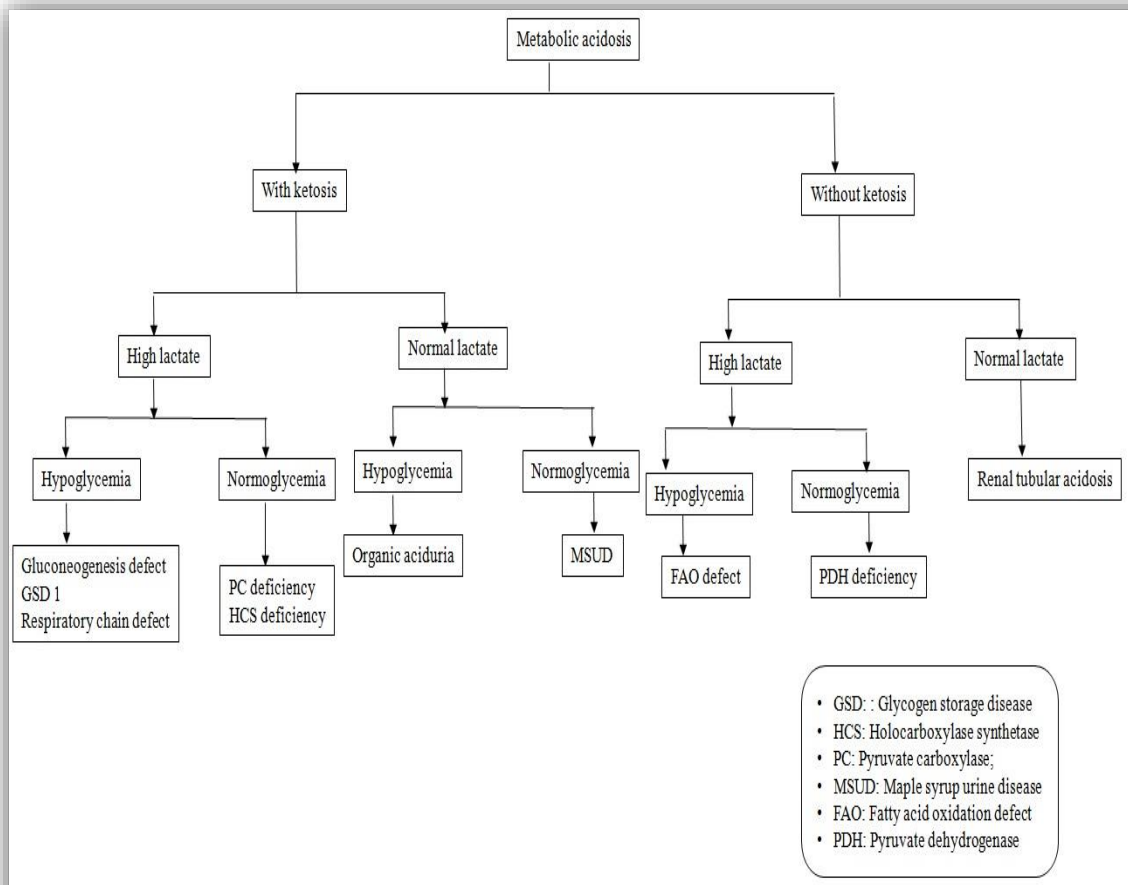


Figure 1: Approach to a newborn with metabolic acidosis

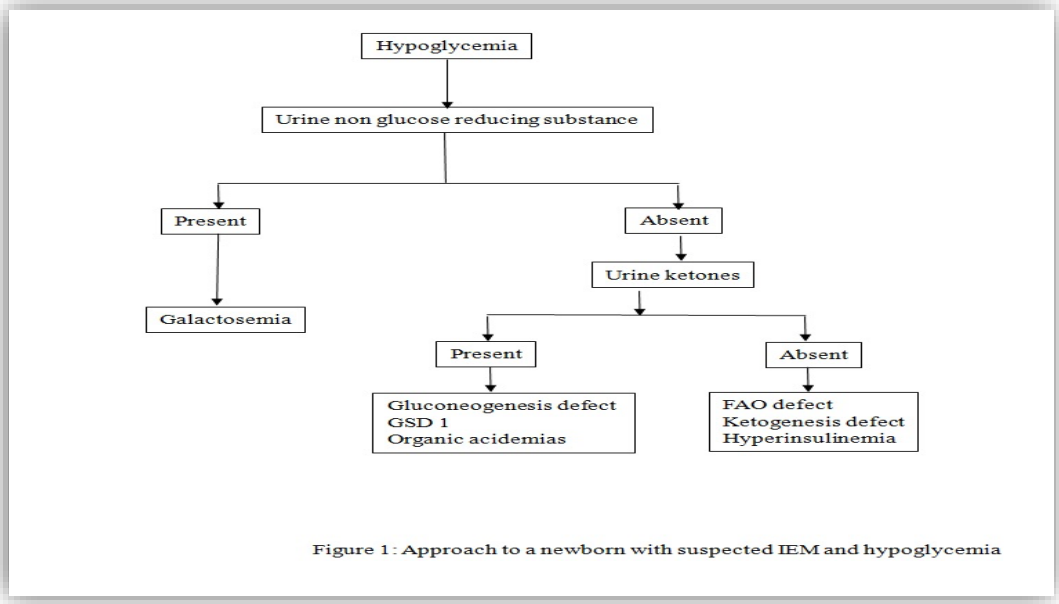


Figure 1 : Approach to a newborn with suspected IEM and hypoglycemia

Box 1: Screening, axillary and confirmatory investigations for a baby with suspected IEM

Screening investigations

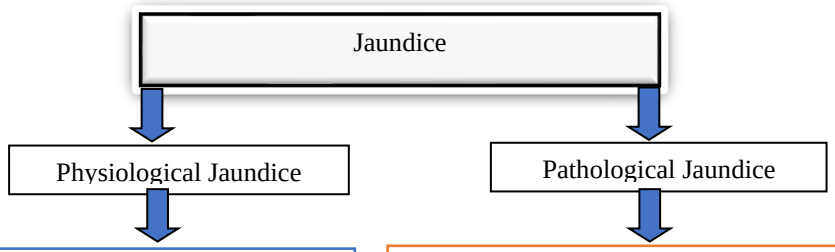
- **Complete blood count: (neutropenia and thrombocytopenia seen in organic acidaemia)**
- **Arterial blood gases and electrolytes (pH, PCO2, base excess)**
- **Blood glucose**
- **Plasma ammonia (Normal values in newborn: 90-150 mg/dl or 64-107 mmol/L)**
- **Arterial blood lactate (Normal values: 0.5-1.6 mmol/L)**
- **Liver function tests**
- **Urine ketones**
- **Urine non glucose reducing substances**
- **Serum uric acid (low in molybdenum cofactor deficiency).**

Auxiliary and confirmatory investigations

- **Gas chromatography mass spectrometry (GCMS) of urine- for organic acidemias.**
- **Tandem mass spectrometry (TMS)- for organic acidemias, urea cycle defects, aminoacidopathies and fatty acid oxidation defects.**
- **Lactate/pyruvate ratio**
- **Urinary urea cycle defect metabolites-**
- **Enzyme assay: biotinidase assay, GALT (galactose 1-phosphate uridyl transferase)**
- **Neuroimaging:**
- **a. MRI: useful pointers towards etiology while results of metabolic workup are pending.**
  b. Magnetic resonance spectroscopy (MRS): To detect metabolite peak
- **Electroencephalography (EEG): To detect characteristics EEG abnormalities e.g. comb-like rhythm in MSUD, burst suppression in NKH and holocarboxylase synthetase deficiency.**
- **Plasma very long chain fatty acid (VLCFA) levels: elevated in peroxisomal disorders.**
- **Mutation analysis when available.**
- **CSF aminoacid analysis: CSF Glycine levels elevated in NKH.**

Protocol 2: Approach to neonatal jaundice

Neonatal Hyperbilirubinemia (NNH) is the most common neonatal morbidity in first week of life occurring in 60% in Term & 80% in Preterm infants. In majority, it is benign and only 5-10% develop clinically significant jaundice requiring treatment.



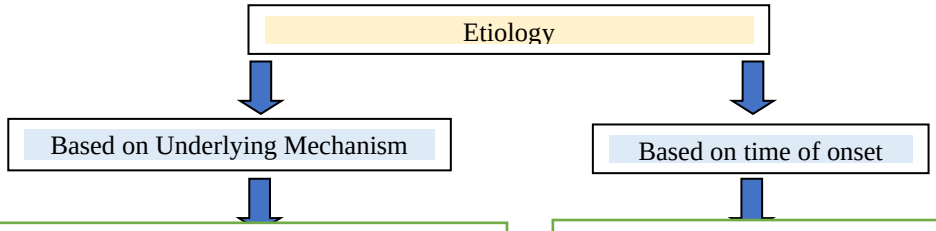
- Represents **physiological immaturity** to handle increased bilirubin production.
- Apparent by 24 -72 hrs of age;
- **Term**: TSB rises to a peak of 12-15 mg/dl by 3rd day & falls thereafter
- **Preterm**: Can rise to 12- 15 mg% around 3-7 day of life
- Clinically not detectable after 14 days
- **No treatment required**

- Elevation of TSB levels to level **requiring treatment**
- Visible jaundice in **first 24 hrs** of life
- Presence of jaundice on arms & legs on day 2
- Yellow staining of **palms & soles**
- TSB increasing > **0.2mg/dL/hour** or > **5 mg/dL in 24 hrs**
- TSB concentration **> 95centile** as per age specific bilirubin normogram
- Signs of **acute bilirubin encephalo**pathy
- Clinical jaundice persisting > 2 wks in term & 3 wks in preterm neonates

Breastfeeding jaundice versus Breastmilk jaundice

	Breastfeeding Jaundice	Breast milk jaundice
Incidence	• Occurs in 1/3rd babies by end of 1st week	• Incidence 2-4% of Exclusive breast fed babies
Presentation	• Can persist till 2-3rd month • Baby is dehydrated	• Begins after 3-5 day, peaks within 2 weeks, and normalize over 3-12 weeks if BF is continued
Cause	• Due to inadequate BF and resultant increased entero-hepatic circulation	• Exact cause not known: due to factors (b-glucuronidase) in human milk
Treatment	• Ensure optimum BF	• Continue BF

Etiology



Hemolytic

- Rh ,ABO or minor blood group incompatibility
- Red cell enzyme deficiency (G6PD deficiency),Hereditary Spherocytosis
- TORCH, Sepsis
- Drug administration to mother (Sulfisoxazole, Salicylates, Vit K)

Decreased conjugation (liver enzyme immaturity)

- Criggler Najar
- Gilbert Syndrome

Increased entero-hepatic circulation

- Insufficient breast feeding
- Preterm
- GI obstruction

- **Extravasated blood**
- Cephalhematoma, Extensive bruising,
- Polycythemia

Within 24 hours of age

- Hemolytic disease of newborn: Rh, ABO & minor Blood group incompatibility
- Infections: TORCH, malaria, bacterial
- G6PD deficiency

Between 24-72 hours of age

- Physiological
- Sepsis
- Polycythemia, Concealed Hemorrhage, SAH, IVH , cephalohematoma,
- Increased Entero-hepatic circulation

Between 72hours – 1 week of age

- Sepsis, Neonatal Hepatitis
- Breast milk Jaundice
- Surgical & Metabolic disorders

After First Week

- Septicemia, Neonatal hepatitis
- Surgical & Metabolic causes
- Drug-induced hemolytic anemia
- Hypothyroidism

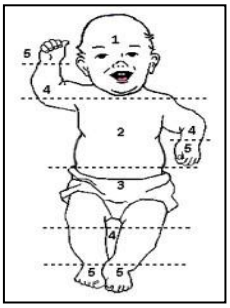
Approach to Jaundice

Visual assessment (Krammer' rule *) of jaundice every 8 to 12 h during initial 3 to 5 days of life.
Use transcutaneous bilirubinometry (TcB), if available

Does the baby have Pathological Jaundice?

- Yes → Start phototherapy → Measure TSB and determine need for phototherapy or exchange transfusion
- No → Presence of significant jaundice to require TSB measurement**
  - Yes → Measure TSB and determine need for phototherapy or exchange transfusion
  - No → Continued observation every 12- 24 hr for initial 3 to 5 days

Determine cause of jaundice & provide supportive along with follow up care



***Visual Assessment by Krammer Rule**

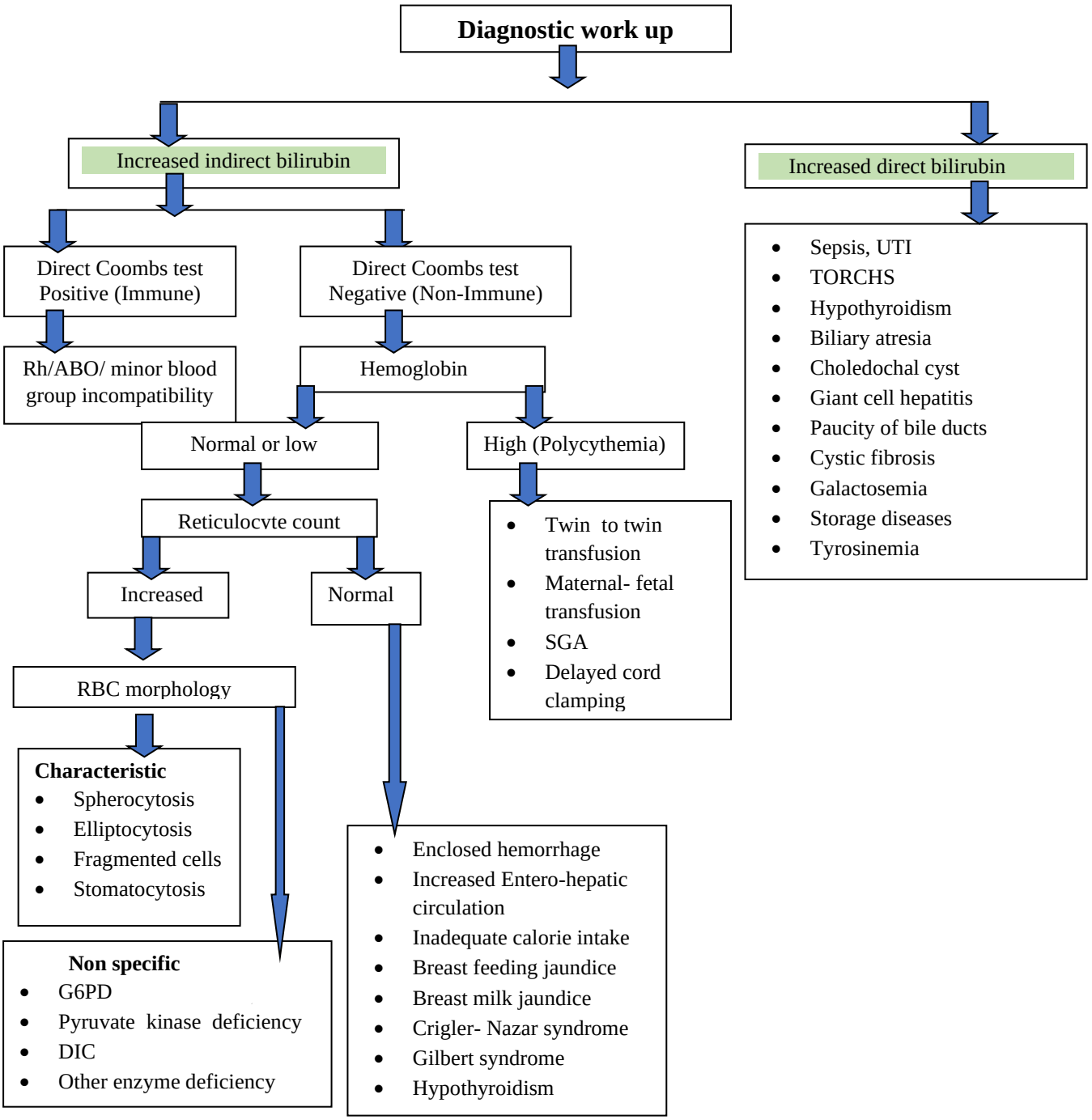
1.	Face	4-8mg/dl
2.	Upper trunk	5-12 mg/dl
3.	Lower trunk & thighs	8-16 mg/dl
4.	Arms ad lower legs	11-18 mg/dl
5.	Palms and soles	>15 mg/dl

ilirubin if

- Occurrence in first 24 hour
- **L**ikely to be more than 12 to 14 mg/dl or requiring PT on visual assessment and/or TCB

Risk factors for JAUNDICE

J -Jaundice within first 24 hrs of life
A -Sibling who was jaundiced as neonate
U -Unrecognized hemolysis
N -Non-optimal sucking/nursing
D -Deficiency of G6PD
I -Infection
C -Cephalhematoma /bruising
E -East Asian/North Indian


Diagnostic work up
Increased indirect bilirubin
Increased direct bilirubin
Direct Coombs test Positive (Immune)
Direct Coombs test Negative (Non-Immune)
Sepsis, UTI
TORCHS
Hypothyroidism
Biliary atresia
Choledochal cyst
Giant cell hepatitis
Paucity of bile ducts
Cystic fibrosis
Galactosemia
Storage diseases
Tyrosinemia
Rh/ABO/ minor blood group incompatibility
Hemoglobin
Normal or low
High (Polycythemia)
Twin to twin transfusion
Maternal- fetal transfusion
SGA
Delayed cord clamping
Reticulocyte count
Increased
Normal
RBC morphology
Characteristic
Spherocytosis
Elliptocytosis
Fragmented cells
Stomatocytosis
Non specific
G6PD
Pyruvate kinase deficiency
DIC
Other enzyme deficiency
Enclosed hemorrhage
Increased Entero-hepatic circulation
Inadequate calorie intake
Breast feeding jaundice
Breast milk jaundice
Crigler- Nazar syndrome
Gilbert syndrome
Hypothyroidism

Protocol 3: Approach to prolonged neonatal jaundice

Prolonged Jaundice: Visibly detectable jaundice beyond 2 weeks of age in a term and beyond 3 weeks of age in a preterm infant.

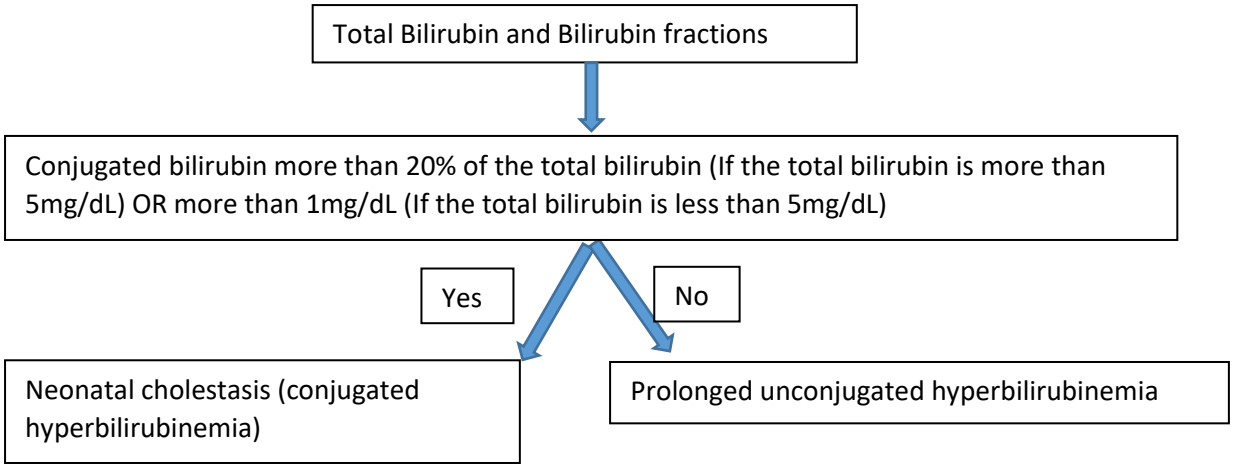
History:

- Mode of feeding, Adequacy of feeding- Pattern of weight (including birth weight & current weight), number of wet nappies.
- Color of stool and history of delayed passage of meconium
- Urine color
- Activity and behaviour during sleep/waking up
- Any abnormal body movements
- Any bleeding/bruising
- Family history of blood or liver disorders
- Mother's blood group, Baby's blood group

Examination:

- Plot available weights on a growth chart (the majority of healthy infants should have regained their birth weight by 10-14 days of age). There are special charts for plotting post-natal weights to see whether the weight loss is acceptable or excessive. (Refer to *www.newbornweight.org*).
- Anthropometry: To rule out microcephaly
- Head to toe exam: Look for Cataracts, Jaundice, Pallor, Petechiae/purpura, Hydration status
- Abdominal exam: Look for hepatosplenomegaly
- CNS exam: Any feature of bilirubin induced encephalopathy

Get Total Serum Bilirubin, Direct and Indirect Bilirubin levels



Prolonged unconjugated jaundice

Common causes:

1. Hemolysis
   - Immune mediated (Coombs positive): Rhesus incompatibility, ABO incompatibility, Minor group incompatibility
   - RBC membrane defects
   - RBC enzyme abnormalities
   - G6PD deficiency
   - Pyruvate kinase deficiency
   - Hemoglobinopathies: Alpha-thalassemia, Gamma-thalassemia
   - Infection induced hemolysis
2. Decreased conjugation
   - Hypothyroidism
   - Prematurity
   - Polymorphism/mutation in the *UGT1A1* gene (*Crigler-Najjar Syndrome (CNS)*
3. Increased enterohepatic circulation
   - Pyloric stenosis
   - Ileal atresia
   - Hirschprung's disease
4. Breast milk jaundice (diagnosis of exclusion)

Investigations

- Bilirubin (Total and direct)
- Complete Blood Count, Reticulocyte Count, Peripheral blood smear
- Blood grouping and typing
- Direct Coombs test
- G6PD activity
- Liver Function Tests
- Thyroid profile
- Urine routine & culture
- Genetic evaluation if polymorphism/mutation in the *UGT1A1* gene is suspected.

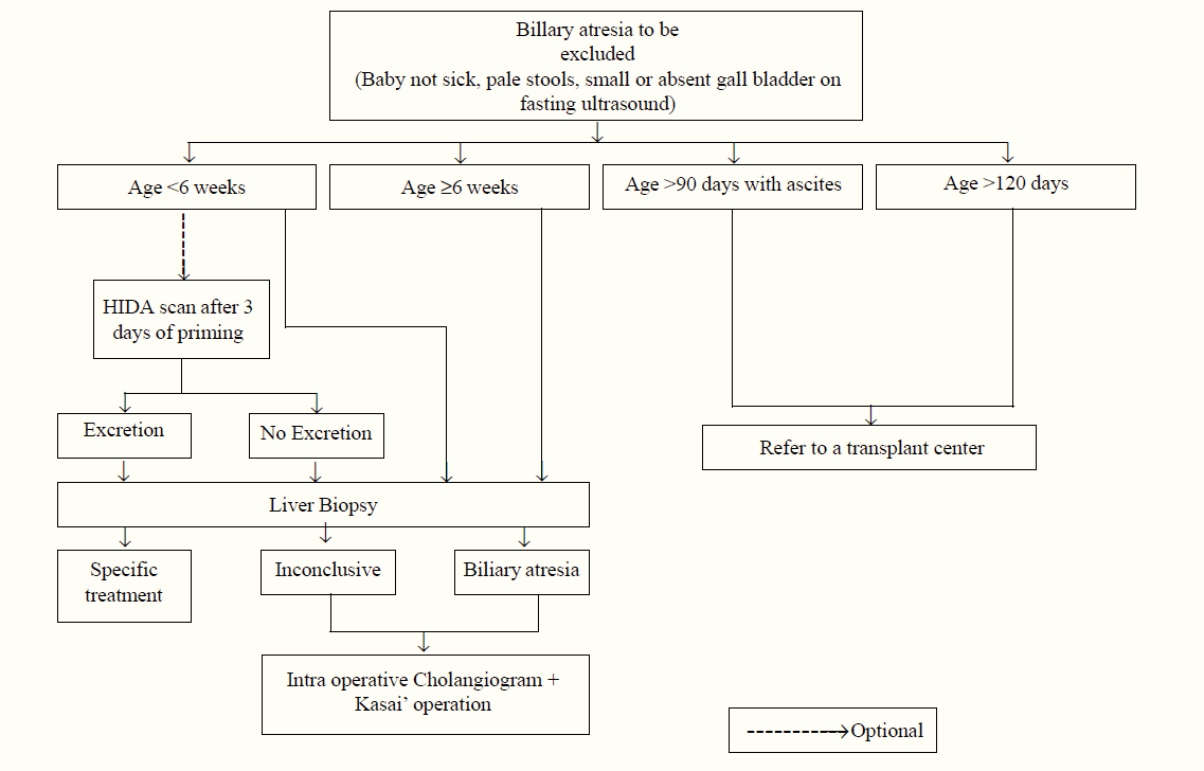
Treatment of unconjugated jaundice

- Try to identify an underlying cause and treat accordingly.
- Phototherapy/Exchange transfusion: There are no separate guidelines for prolonged unconjugated jaundice. The thresholds in AAP charts (2004) at day 6-7 of age can be used for babies more than a week old as the curves flatten after day 6.
- Breast milk jaundice is a diagnosis of exclusion and should be made only after other causes have been ruled out. Interruption of breastfeeding for treatment of jaundice is not recommended.
- Trial of phenobarbitone can be given whenever the bilirubin levels are high enough to cause encephalopathy ($\geq$18mg/dL). Should be used only when other causes of prolonged jaundice have been ruled out and diagnosis is either genetic or breast milk jaundice. Phenobarbitone may be considered for lower levels of bilirubin (15-18mg/dL), if the parents are anxious and contemplating stoppage of breastfeeding.
- Refer to a Pediatric gastroenterologist if there is conjugated hyperbilirubinemia or a suspicion of underlying liver disease (unconjugated jaundice with deranged LFTs).

Neonatal Cholestasis (conjugated hyperbilirubinemia)

Causes:

1. Obstructive causes: Biliary atresia, Choledochal cysts
2. Hepatocellular causes: Idiopathic giant cell hepatitis, Infections (Sepsis, TORCH, Malaria, UTI), Metabolic causes (Galactosemia, AIAT deficiency, Tyrosinemia, Storage disorders, Hemochromatosis), Miscellaneous
3. Ductal paucity (Syndromic or Non-syndromic)
4. Undifferentiated



Treatment:

- Nutritional support: Calories 125% of RDA. Supplement fat soluble vitamins.
- Treatment of underlying cause.
- In infants with pruritus due to severe cholestasis, the group recommended, in the following order: Ursodeoxycholic acid (UDCA) (20 mg/kg/d), rifampicin (5-10 mg/kg/d), and phenobarbitone (5–10 mg/kg/d).
- Liver Transplantation, the standard therapy for decompensated cirrhosis due to any cause.

Protocol 4: Approach to hypoglycaemia

A. Definition

Hypoglycemia is one of the most common metabolic problems in neonates. If left untreated may cause permanent brain damage. There is no concrete evidence to show the causation of adverse outcome by a particular level or duration of hypoglycemia. Hence an "Operational threshold" for hypoglycemia has been defined as plasma glucose level less than 45 mg/dL.

B. Screening for hypoglycemia

1 Low birth weight infants (<2000 grams)

2 Preterm infants (≤35 weeks)

3 Small for gestational age infants (SGA)

4 Infant of diabetic mothers (IDM)

5 Large for gestational age (LGA) infants

6 Infants with Rh-hemolytic disease

7 Infants born to mothers receiving therapy with terbutaline/propranolol/labetalol/oral hypoglycemic
agents.

9 Any sick neonate such as those with perinatal asphyxia, polycythemia, sepsis, shock, hypothermia.

10 Infants on total parenteral nutrition

C. Time schedule for screening

The infants at risk for hypoglycaemia should be screened within 1-2 hrs of birth and frequently thereafter 6-8 hrs for next 72 hrs. IDMs frequently experience hypoglycaemia in first 12 hrs of life. However, preterms and SGA are at highest risk till 36 hrs of life

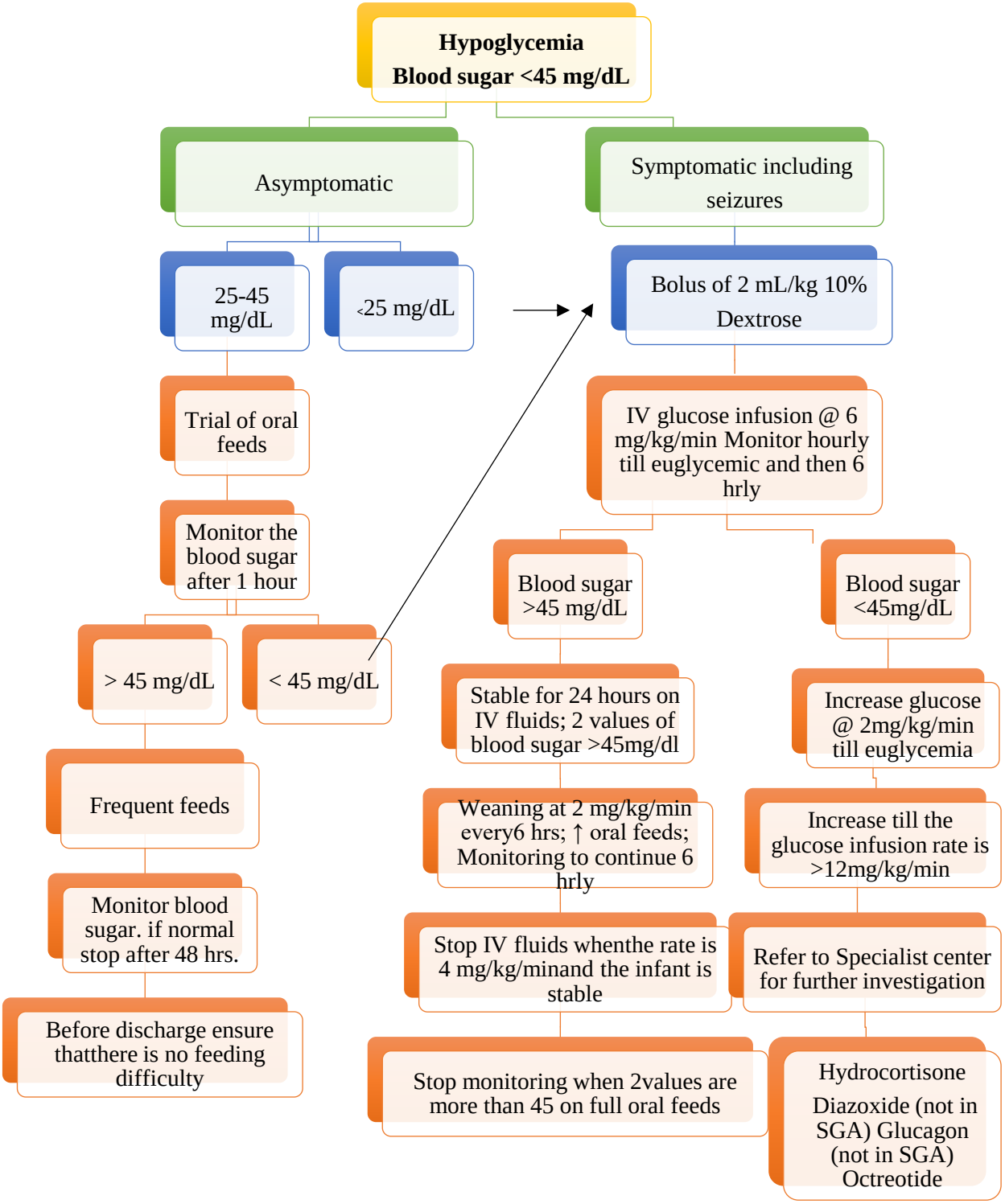
D. Method of blood glucose level estimation

1. **Reagent strips** - Rapid screening method but low values should be confirmed by laboratory analysis.
2. **Laboratory diagnosis**: This is the most accurate method. Glucose oxidase(calorimetric) and glucose electrode are two commonly used methods. Whole blood sugar is 10-15% lower than plasma sugar.

E.Clinical Presentation

• **Asymptomatic hypoglycemia** is said to be present when blood glucose level is less than 45 mg/dL (to be confirmed by laboratory estimation) and the infant does not manifest with any clinical features.

. **Symptomatic hypoglycemia** should be diagnosed if hypoglycemia coexists with clinical symptoms. Clinical signs include stupor, jitteriness, tremors, apathy, episodes of cyanosis, convulsions, intermittent apneic spells or tachypnea, weak and high pitched cry, limpness and lethargy, difficulty in feeding, and eye rolling. Episodes of sweating, sudden pallor, hypothermia and cardiac arr*est* have also been reported.


Hypoglycemia
Blood sugar <45 mg/dL
Asymptomatic
Symptomatic including seizures
25-45 mg/dL
<25 mg/dL
Bolus of 2 mL/kg 10% Dextrose
Trial of oral feeds
IV glucose infusion @ 6 mg/kg/min Monitor hourly till euglycemic and then 6 hrly
Monitor the blood sugar after 1 hour
Blood sugar >45 mg/dL
Blood sugar <45mg/dL
> 45 mg/dL
< 45 mg/dL
Stable for 24 hours on IV fluids; 2 values of blood sugar >45mg/dl
Increase glucose @ 2mg/kg/min till euglycemia
Frequent feeds
Weaning at 2 mg/kg/min every6 hrs; ↑ oral feeds; Monitoring to continue 6 hrly
Increase till the glucose infusion rate is >12mg/kg/min
Monitor blood sugar. if normal stop after 48 hrs.
Stop IV fluids whenthe rate is 4 mg/kg/minand the infant is stable
Refer to Specialist center for further investigation
Before discharge ensure thatthere is no feeding difficulty
Stop monitoring when 2values are more than 45 on full oral feeds
Hydrocortisone
Diazoxide (not in SGA) Glucagon (not in SGA)
Octreotide

Recurrent / Persistent hypoglycemia

This condition should be considered when infant fails to maintain normal blood glucose level despite a GIR of 12 mg/kg/min or when stabilization is not achieved by 7 days of therapy. Investigations for hyperinsulinism, endocrine disorders and inborn errors of metabolism should be undertaken. **'critical sample'** should be sent for insulin ,GH, cortisol, ketones and FFA.**Insulin > 2 µU/ml** and **Insulin/Glucose ratio>0.4** is abnormal.

Drugs that are used for resistant hypoglycemia include the following:

1. Hydrocortisone 5 mg/kg/day IV or PO in two divided doses for 24 to 48 hrs
2. Diazoxide can be given orally 10-25 mg/kg/day in three divided doses .
3. Glucagon 100 µg/kg subcutaneous or intramuscular (max 300 µg) – maximum of three doses.
4. Octreotide (synthetic somatostatin in dose of 2-10 µg/kg/day subcutaneously two to three times a day.
5. Surgery may be required for insulin secreting tumors.

Follow up and Outcome

Repeated and prolonged episodes of hypoglycaemia may cause mental retardation, developmental delay, epilepsy, visual disturbances. MRI at 4-6 weeks or before discharge, neurodevelopmental, visual and hearing assessment in regular follow up till 20-24 months.

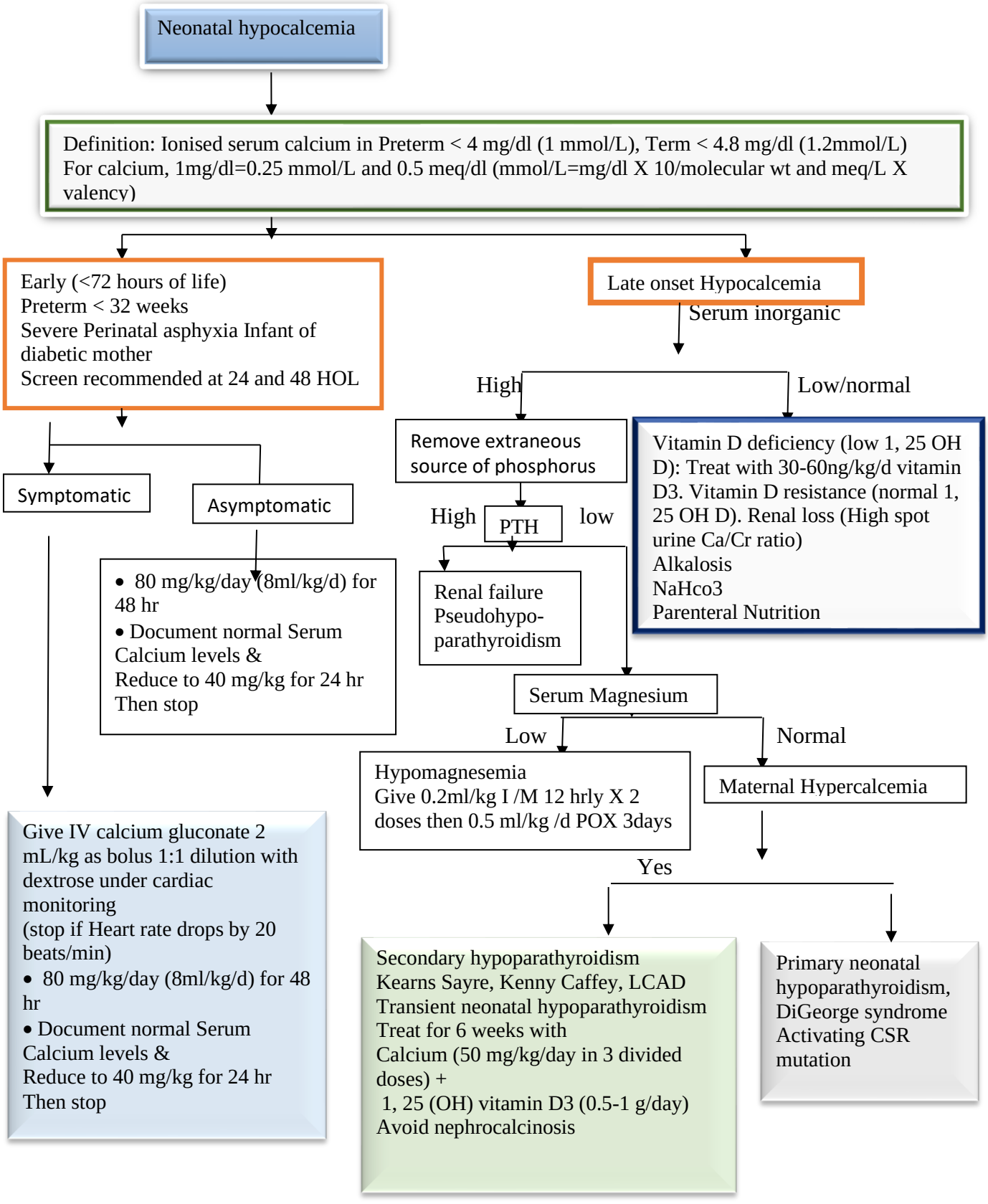
I. Useful formulae

(a) GIR (mg/kg/min) $= \frac{\%\text{ of dextrose being infused x rate (mL/hr)}}{\text{body weight (in kg) x 6}}$

(b) Infusion rate (mg/kg/min) $= \frac{\text{IV rate (mL/kg/day) x \% of dextrose}}{144}$

(c) Infusion rate (mg/kg/min) = Fluid rate (mL/kg/day) x 0.007 x % of dextrose infused

Protocol 5: Approach to hypocalcaemia



Protocol 6: Screening for congenital hypothyroidism

- Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation and has an incidence of 1 in approximately 1000 Indian newborns.
- This may be transient or permanent.
- The most common cause of permanent CH are thyroid dysgenesis or agenesis followed by thyroid dyshormonogenesis. However recent evidence indicates an increased incidence of dyshormonogeneis as a cause from India and worldwide.

Clinical features

The neonate may present with:

Delay in skeletal maturation (absence of femoral and tibial epiphyses)

Hypothermia, Jaundice, Lethargy/decreased activity, Poor feeding

Macroglossia, Macrosomia

Umbilical hernia, Wide anterior fontanelle, open posterior fontanelle

During infancy they may present with:

Constipation, hoarse cry, Decreased muscle tone

Coarse skin, brittle hair

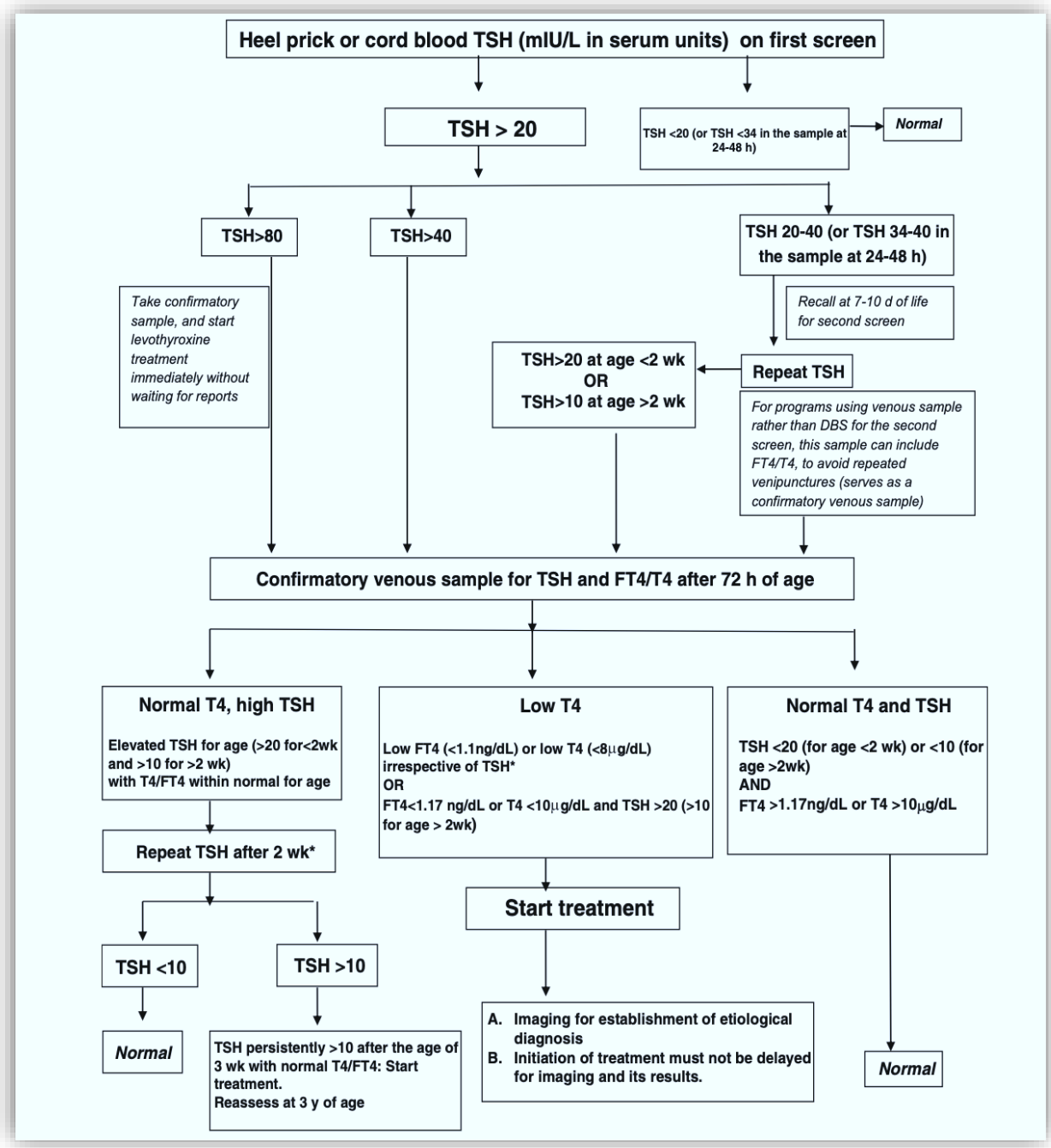
Delayed milestones

Failure to thrive, Poor linear growth

Diagnosis

CH is diagnosed by TSH and low Free/Total T4 values. The initial CH screen is done by either cord blood or postnatal blood sample of TSH.

ISPAE recommends the following flowchart for screening and follow up of children diagnosed with raised TSH.


Heel prick or cord blood TSH (mIU/L in serum units) on first screen
TSH > 20
TSH <20 (or TSH <34 in the sample at 24-48 h)
Normal
TSH>80
TSH>40
TSH 20-40 (or TSH 34-40 in the sample at 24-48 h)
Take confirmatory sample, and start levothyroxine treatment immediately without waiting for reports
Recall at 7-10 d of life for second screen
TSH>20 at age <2 wk OR TSH>10 at age >2 wk
Repeat TSH
For programs using venous sample rather than DBS for the second screen, this sample can include FT4/T4, to avoid repeated venipunctures (serves as a confirmatory venous sample)
Confirmatory venous sample for TSH and FT4/T4 after 72 h of age
Normal T4, high TSH
Elevated TSH for age (>20 for<2wk and >10 for >2 wk) with T4/FT4 within normal for age
Low T4
Low FT4 (<1.1ng/dL) or low T4 (<8μg/dL) irrespective of TSH*
OR
FT4<1.17 ng/dL or T4 <10μg/dL and TSH >20 (>10 for age > 2wk)
Normal T4 and TSH
TSH <20 (for age <2 wk) or <10 (for age >2wk)
AND
FT4 >1.17ng/dL or T4 >10μg/dL
Repeat TSH after 2 wk*
Start treatment
TSH <10
TSH >10
Normal
TSH persistently >10 after the age of 3 wk with normal T4/FT4: Start treatment.
Reassess at 3 y of age
A. Imaging for establishment of etiological diagnosis
B. Initiation of treatment must not be delayed for imaging and its results.
Normal

Management

- Criteria for initiation of levothyroxine therapy (based on venous sample values)
- Low T4 (100nmol/L) or Low FT4 (<1.1ng/dl) - irrespective of TSH.
- Mild low T4 (128nmol/L) or FT4 (<1.17ng/dl) in presence of TSH >20mIU/L [age <2 wks] or TSH >10mIU/L if age>2 wks
- Normal T4/FT4 with persistently elevated TSH >10mIU/L at >3 wks

Dosage

- Initial recommended dose in neonatal period is 10-15microgm/kg/day given as single dose.
- Target is to maintain T4/FT4 in upper normal range and TSH in normal range(<5mIU/L).If T4/FT4 are in upper normal range one should not pursue for a normal TSH.

Follow up

- Serum T4/FT4 is measured at 2 wk and TSH with T4/FT4 at 1 mth
- Then T4/FT4 and TSH are measured every 2 mo till 6mth of age
- Every 3mths during 6mth- 3y
- Every 3–6 mo thereafter, till completion of growth and puberty.

Protocol 7: Approach to osteopenia of prematurity

Definition

- MBD is defined as decreased bone mineral content relative to the expected level of mineralization for a fetus or infant of comparable size or gestational age seen in conjunction with biochemical and/or radiographic changes.
- MBD has been estimated to occur in **16- 40%** of VLBW and ELBW infants. It presents between 6- 16 weeks.
- Bone mineralization occurs predominantly in the third trimester. Nearly, 80% of calcium (120mg/kg/day) and phosphorus (60mg/kg/day) transfer occurs between the 24th week of gestation and term.
- MBD occurs as a result of inadequate calcium and phosphorus stores exacerbated by inadequate intake and the high degree of skeletal growth occurring in the weeks following birth.

Postnatal changes

There is nadir at 24- 36 hours after birth in preterm leading to increase in PTH and Vitamin D. PTH increases calcium absorption in kidney and intestine and increase active Vitamin D level. PTH increases phosphate absorption in intestine and excretion in kidney. Vit D increases calcium and phosphate absorption in kidney and intestine. *Since PTH response predominate in kidney so hypercalcemia and hypophosphatemia are seen*. With insufficient calcium intake over time these changes become persistent and cause MBD.
Hypophosphatemia manifests as the earliest marker of disrupted mineral metabolism, as early as 7-14 days after birth. Thus, phosphate deficiency disrupts calcium balance, potentially leading to hypercalcemia, hypercalciuria, and nephrocalcinosis.

Which serum markers to be used

- ALP >900 IU/l with serum phosphorus levels <5.6 mg/dl (<1.8 mmol/l) yields 100% sensitivity with 70% specificity
- A PTH level of > 180 mg/dL or a Phosphate level of < 4.6 mg/dL was associated with a sensitivity of 100% and specificity of 94%
- Vitamin D- Not routinely checked. In the majority of cases of MBD, 25(OH) D levels are normal as vitamin D is readily transferred across the placenta. While 1, 25(OH) 2D is the metabolically active form of vitamin D, 25(OH) D should be the biomarker measured exclusively for vitamin D status. Indications for screening for vitamin D deficiency in preterm infants
  - Maternal vitamin D deficiency (if known)
  - Short gut syndrome and other malabsorptive conditions, and
  - Anticonvulsant therapies that may increase vitamin D catabolism (e.g. phenobarbital)

Prevention of Osteopenia of Prematurity

Recommended intake of supplements in preterm (VLBW)

	Calcium(mg/kg/day)	**Phosphate(mg/kg/day)**	**VitaminD(IU/day)**
AAP 2013	150-220	75-140	200-400
Canadian Paediatric society 1995	160-240	78- 118	400-800
ESPGHAN	70-140	50-90	800-1600
Global consensus recommendation (2016)	200 mg/day	Half of calcium	400

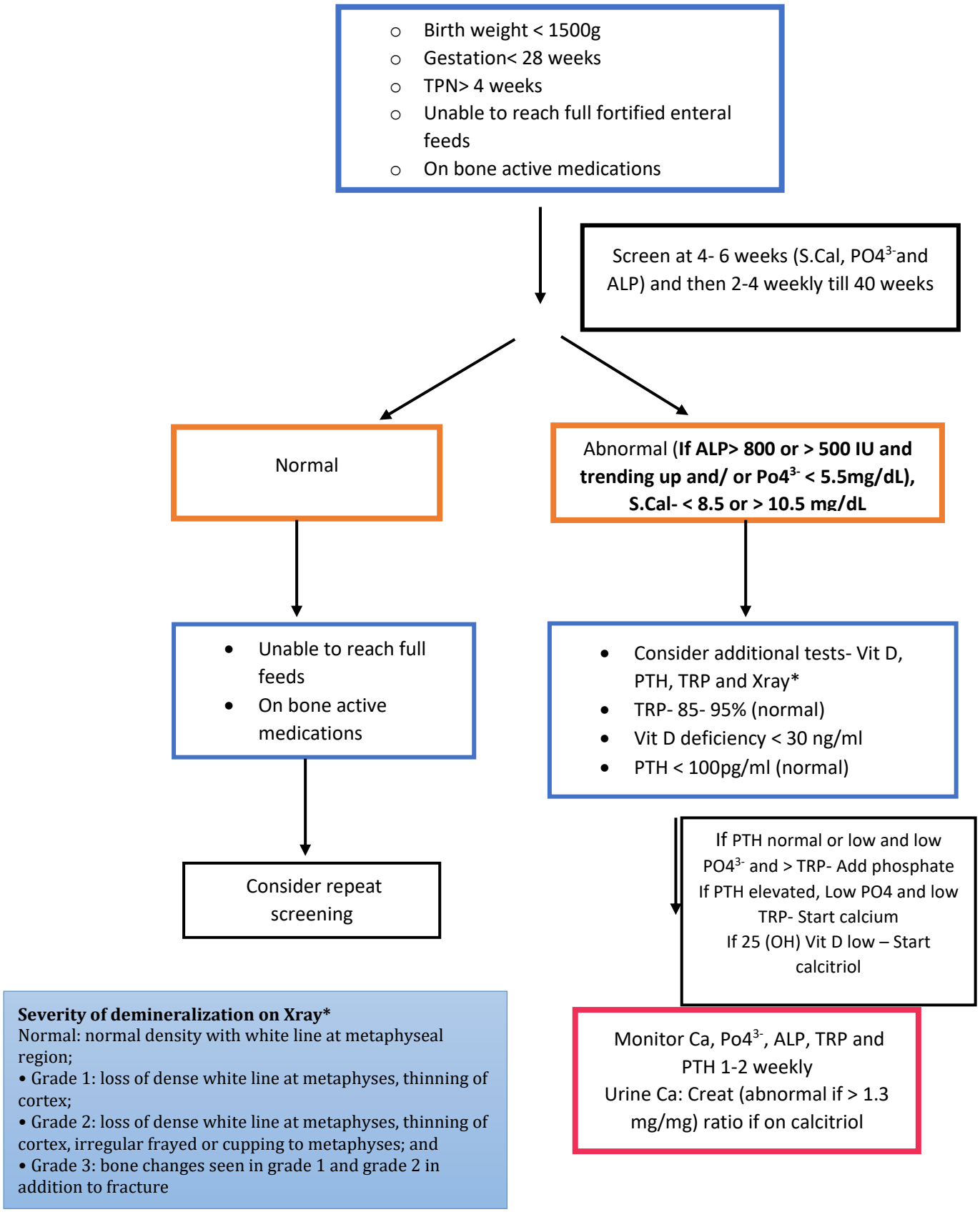
Treatment

- Optimizing nutrition, calcium, phosphate and Vitamin D
- Vitamin D – 2000 IU/day for 3 months with maintenance dose of 400IU/day until it resolves and calcium of 500mg/day (Global consensus recommendation 2016)
- Limiting use of bone active medications
- Physical activity for 15 min /day

Targets to achieve

- $PO4^{3-}$ - > 5.5 mg/dL (in babies with hypophosphatemia)
- Normalize PTH and ALP
- The AAP Clinical Report recommends rechecking radiographs every 5-6 weeks until improved mineralization is

Algorithm for Metabolic bone disease management



Severity of demineralization on Xray*
Normal: normal density with white line at metaphyseal region;
• Grade 1: loss of dense white line at metaphyses, thinning of cortex;
• Grade 2: loss of dense white line at metaphyses, thinning of cortex, irregular frayed or cupping to metaphyses; and
• Grade 3: bone changes seen in grade 1 and grade 2 in addition to fracture

Protocol 8: PRBC and platelet transfusions in neonates

80% of babies < 1500g are transfused at least once.

Indications in preterm

- Phlebotomy losses
- Anemia of prematurity

Liberal vs restrictive

For the restrictive group, Iowa study reported an increase in episodes of apnea, and at 18-21-month follow-up the PINT study found a statistically significant cognitive delay in a post-hoc analysis.
For the liberally transfused group, the Iowa study patients had significantly poorer learning outcomes and reduced brain volume on magnetic resonance imaging. **As per Cochrane** 2011, modest reduction in exposure to transfusion occurs in the restrictive transfusion groups and no significant difference in mortality, major morbidities or survival without major morbidity.

ETTNO Trial (Effects of Liberal vs Restrictive Transfusion Thresholds on Survival and Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants) -Strategy of liberal blood transfusions compared with restrictive transfusions did not reduce the likelihood of death or disability at 24 months of corrected age.

Volume and rate of transfusion

The typical transfusion volume is 10–20 mL/kg (higher end of dose for severe anemia or bleeding) administered at 5 mL/kg/h. Top-up transfusions in excess of 20 mL/kg are not recommended because of the risk of transfusion-associated circulatory overload (TACO).

Characteristics of blood

- Hematocrit-0.5-0.7
- Upto 35 days old
- Should have anticoagulant as CPD- A
- Group O (or ABO-compatible with baby and mother) and RhD negative (or RhD compatible with the neonate). Preferably use **O Rh D –ve**
- CMV seronegative for neonates

Cut offs for transfusion in preterm depending on postnatal age and respiratory support (BCSH) (< 32 weeks)

Postnatal age	Hb threshold for transfusion(g/L)		
	Ventilated	**O_2/CPAP**	**Off O_2**
First 24 hours	<12	<12	<10
1-7 days	<12	<10	<10
8-14 Days	<10	<9.5	8.5-7.5
>15 days	<10	<8.5	<7.5

Note: Use of **paedipacks** reduces donor exposure for multiply transfused preterms.

Transfusion of a total of 10 mL/kg PRBC causes a 9-10% increase in the Hct value.

- ***ARIPI (Age of Red Blood Cells in Premature Infants)*** trial reported no effects on clinical outcomes for preterm neonates using red cells of different storage ages.
- The routine use of ***EPO or darbepoetin alfa*** is not recommended in preterm infants to reduce transfusion.
- Where the term neonate or preterm neonate does not require resuscitation, undertake ***delayed cord clamping***.
- Every 10 mL/kg of blood lost increased the number of transfusions by 0.66; every 10 days on mechanical ventilation increased the number of transfusion by 0.59; and the adoption of liberal criteria increased this number by 0.55

Platelet transfusion in preterm

Thrombocytopenia is defined as platelet count < 1.5 lakh. It affects 18–35% of all patients admitted to NICUs and approximately 70% of ELBW

There is no clear correlation between the severity of thrombocytopenia and major bleeding and other clinical factors (gestation < 28 weeks, postnatal age < 10 days and NEC) are important. Audits show that, contrary to many published guidelines, the majority of platelet transfusions are given as 'prophylaxis' in the absence of bleeding. Single donor apheresis platelets manufactured to neonatal specifications are used. A new major bleeding episode or death occurred 1.57 times more in the high-threshold group (< 50,000) as compared to the low-threshold group (< 25000) [Planet-2 trial].

Characteristics of platelet transfused

They should be CMV-negative and ABO RhD identical or compatible with the recipient. A typical dose is 10– 20 mL/kg at 10-20 ml/.kg/hour.

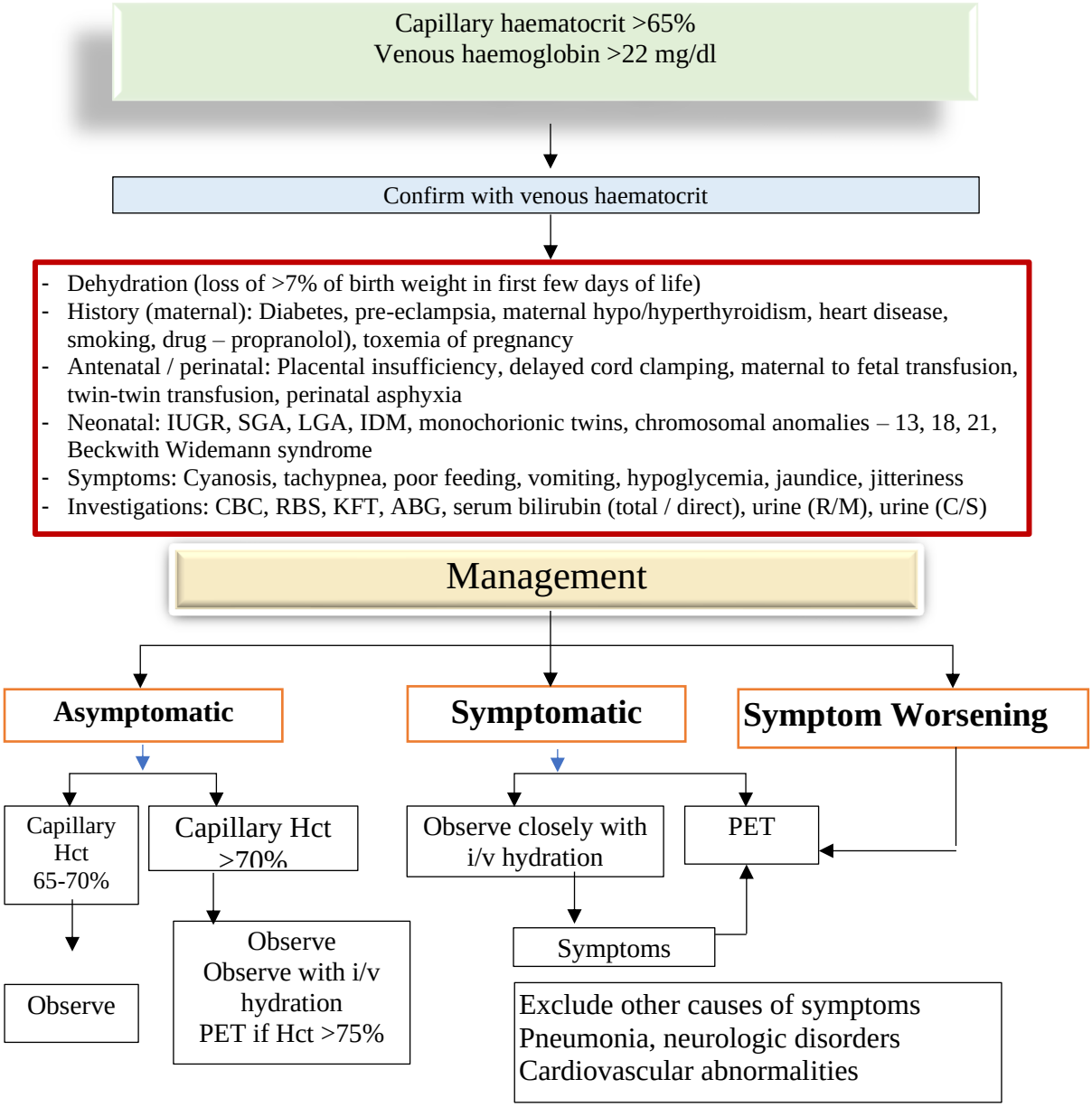
Note: HPA-compatible with maternal platelet antibody for neonates with NAIT

Transfusion threshold (BSCH)

Platelet count (**X 10^9/ L)**	**Indication for platelet transfusion**
< 25,000	Neonates with no bleeding (including neonates with NAIT if no bleeding and no family history of ICH).
<50,000	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with ICH
< 100,000	Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)

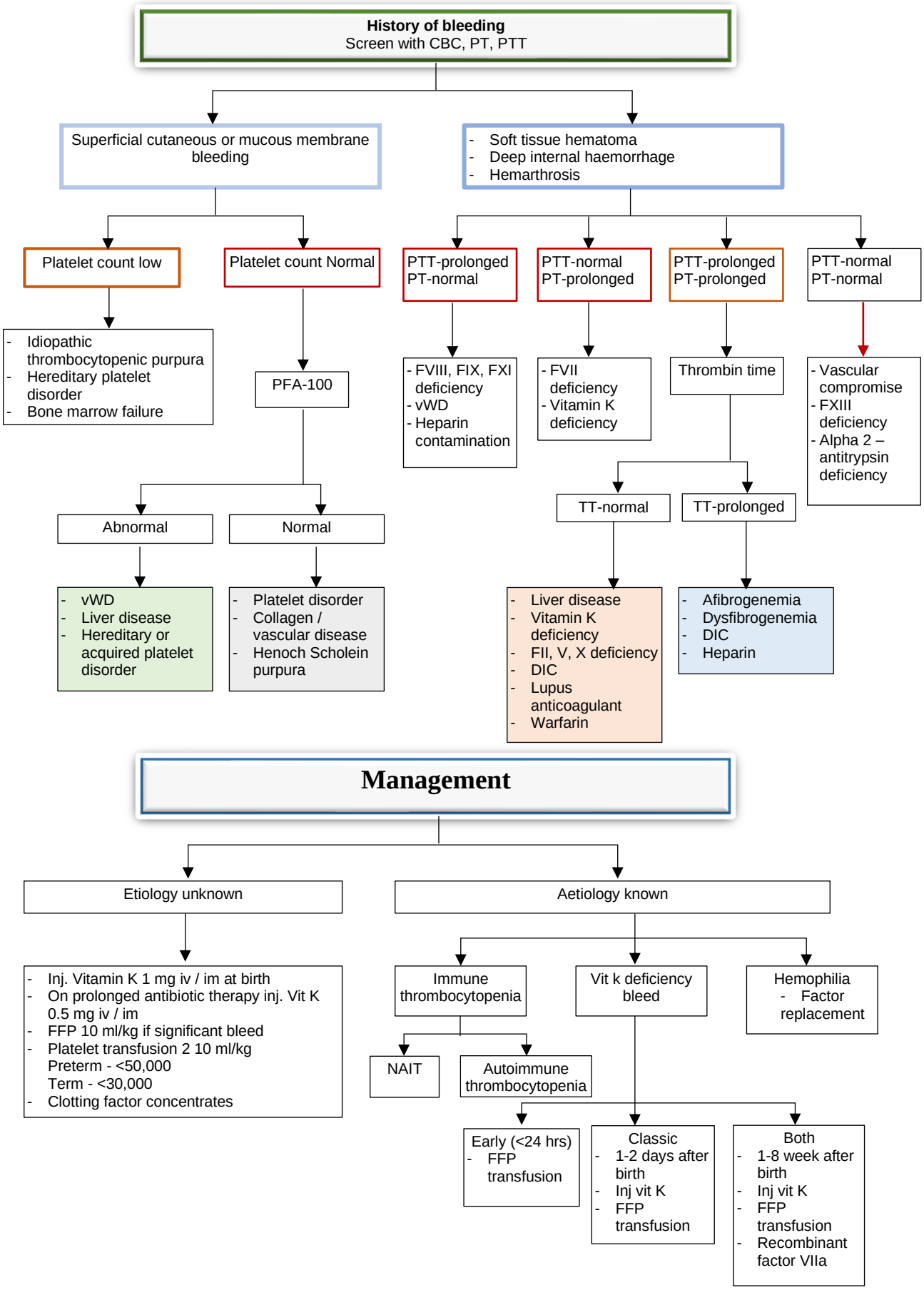
Note: A blood count should be performed 1 hour and 24 hours after completion of the transfusion in order to evaluate the efficacy of the transfusion

Protocol 9: Management and approach to polycythaemia



Complications: NEC, kidney failure, seizure, stroke, decreased fine motor control.

Protocol 10: Approach to bleeding neonate



Protocol 11: Approach to acute kidney injury in neonates

Neonatal Acute Kidney Injury

Definition

Acute kidney injury is characterised by a sudden impairment in kidney function that results in the retention of nitrogenous waste products and alters the regulation of extracellular fluid volume, electrolytes and acid-base homeostasis[1].

Table 1: Causes of Neonatal AKI

Prerenal Azotemia	**Intrinsic AKI**	**Obstructive renal failure**
Loss of effective blood volume Haemorrhage Dehydration Hypoalbuminemia Congestive heart failure Renal hypoperfusion Relative loss e.g. sepsis, NEC, ECMO	Acute tubular necrosis Severe renal ischaemia Nephrotoxins Infections Renal artery/vein thrombosis DIC Intrarenal obstructions Congenital malformations Renal dysplasia Polycystic kidneys	Congenital malformations Urethral stricture Posterior urethral valves Ureterocele Megaureter Extrinsic compression Intrinsic obstruction Renal calculi Fungal ball Neurogenic bladder

Table 2: Neonatal modified AKI KDIGO staging[2,3]

Stage	Serum creatinine (mg/dl)	Urine output
0	No change in SCr or rise ≤ 0.3 mg/dl	≥ 0.5 mL/kg/h
1	SCr rise ≥0.3 mg/dL within 48 h or SCr rise ≥1.5–1.9 times reference SCr[a] within 7 days	<0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0–2.9 times reference SCr	<0.5 mL/kg/h for ≥ 12 h
3	SCr rise ≥3 times reference SCr or SCr ≥2.5 mg/dL[b] or need for dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h
KIDIGO- Kidney Disease: Improving Global Outcomes a -reference serum creatinine is defined as the lowest previous serum creatinine value and b-Serum creatinine value of 2.5 mg/dl represents a glomerular filtration rate of <10ml/min/1.73m^2		

Table 3: Pointers in the history and examination[4]

History **Antepartum:** • **Family history** • **antenatal ultrasound scans** • **maternal illness and drug usage (especially NSAIDs)** **Intrapartum:** • **Congenital or peripartum infections** • **hypoxic/ischaemic insults** **Nephrotoxic drugs**	**Postpartum:** • **respiratory/cardiovascular support** • **evidence of sepsis or necrotising enterocolitis, etc.** **Examination** • **Dysmorphic features** • **gestational age - more common if preterm** • **blood pressure and assess peripheral pulses, perfusion** • **presence (or history) of venous or arterial catheter or thrombotic tendency**
Investigations **Urinalysis and microscopy:** • **haematuria** • **haemoglobinuria** • **myoglobinuria** • **proteinuria** **Serum biochemistry:** • **urea** • **creatinine** • **electrolytes, calcium** **Urine biochemistry:** • **creatinine, sodium ,osmolality**	Blood: • haemoglobin (evidence of polycythaemia) • pH • base deficit or bicarbonate Ultrasound: • abnormalities of renal structural or parenchyma • renal tracts including bladder size • Doppler assessment of renal vasculature

Table 4: Management of Neonatal AKI

Pre- renal	**Intrinsic renal**	**Post renal obstructive**
Cautious fluid resuscitation	Correct electrolyte disturbances	Correct obstruction
Vasopressor support	Stop all nephrotoxic agents	Correct electrolyte disturbances
Consider diuretics	Strict input- output charting	Support diuresis
	Dialysis if indicated	

Fluid management

Restricted to insensible water loss (IWL) along with urinary loss[5,6]. Replace urine volume for volume. The insensible water loss in a term neonate is 25 mL/kg/day. IWL can be assumed to be 40mL/kg/day in preterm infants. In preterm neonates this can vary widely depending on gestation, postnatal age, use of radiant warmers, phototherapy etc. The fluid should be electrolyte free 10% dextrose water.

Hyponatremia

Hyponatremia due to dilution secondary to water retention has to be corrected with fluid restriction. In most of the cases, there is no sodium deficit and fluid restriction will suffice. If symptomatic or hyponatremia is less than 120 mEq/L it requires prompt correction with 3% hypertonic saline in a dose of 5 mL/kg over 4-5 hrs.

Hyperkalemia

The first step in the management of hyperkalemia is to stop all potassium in the fluids. If ECG changes are evident, give calcium gluconate 10%. This should immediately be followed by methods to decrease the potassium levels.

Table 5: Management of hyperkalemia[1]

Medication	Dose	Onset of action
Calcium gluconate	0.5 to 1 mL/kg over 10 min	1-5 min
Sodium bicarbonate	1 mEq/kg over 10 min	5-10 min
Glucose and insulin	1 IU insulin /5 gm glucose	15-30 min.
Cation exchange resin	1g/kg intrarectally q 6 h	1-2 hours
Peritoneal dialysis	Dialysate with low K+ concentration	Immediate

Hypocalcemia

Symptomatic hypocalcemia should be corrected by infusing calcium gluconate at a dose of 100 to 200mg/kg over 10 to 20 minutes and repeated every 4 to 8 hours as necessary.

Nutrition

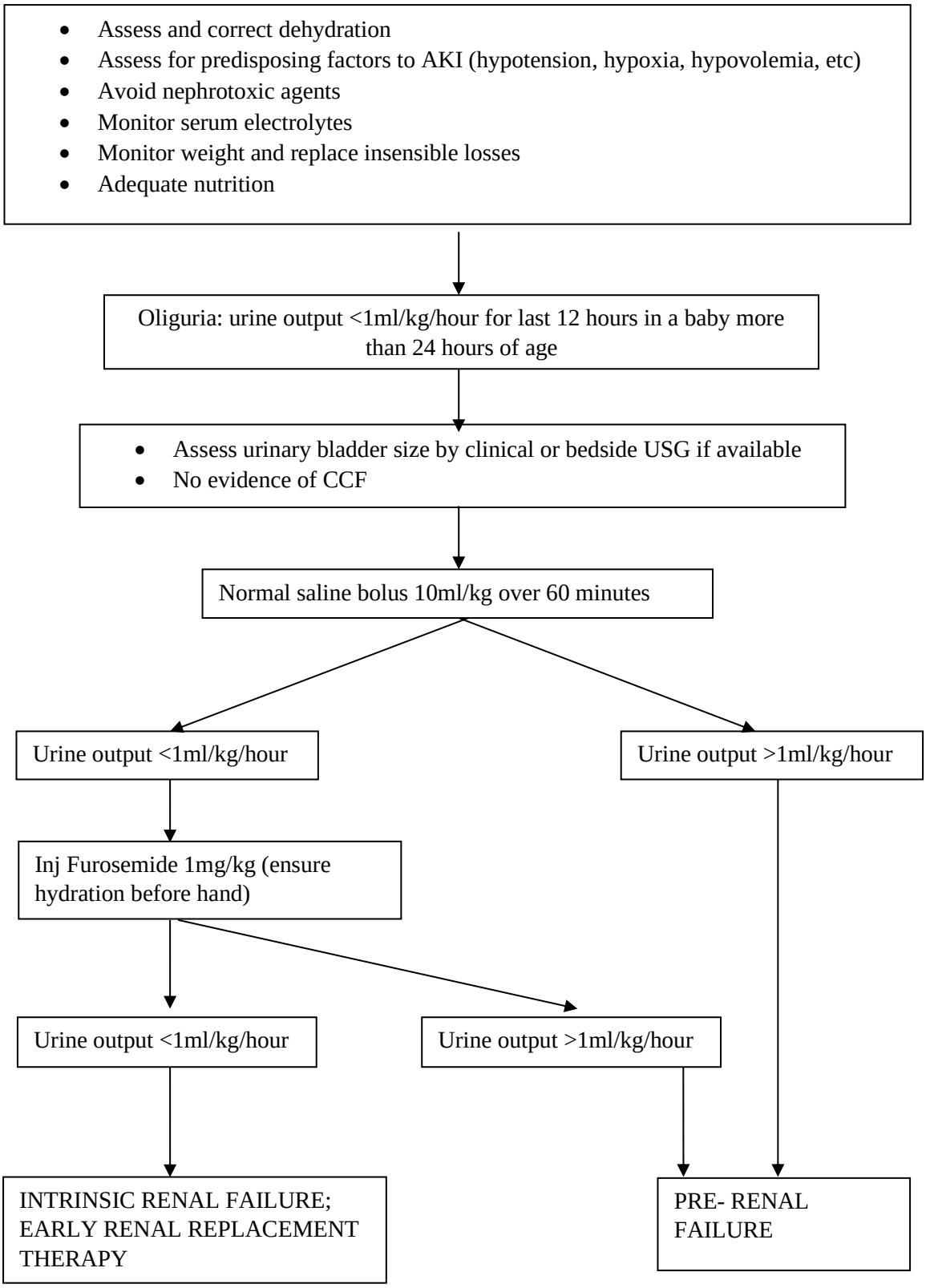
The goal is to provide 100 kcal/kg/day. Proteins or amino acids can be provided in a dose of 1-2 g/kg/day1. If on enteral feeds, breast milk can be used.

Acidosis

Mild metabolic acidosis is common. Replacement with bicarbonate or acetate is indicated to treat metabolic acidosis.

Renal replacement therapy

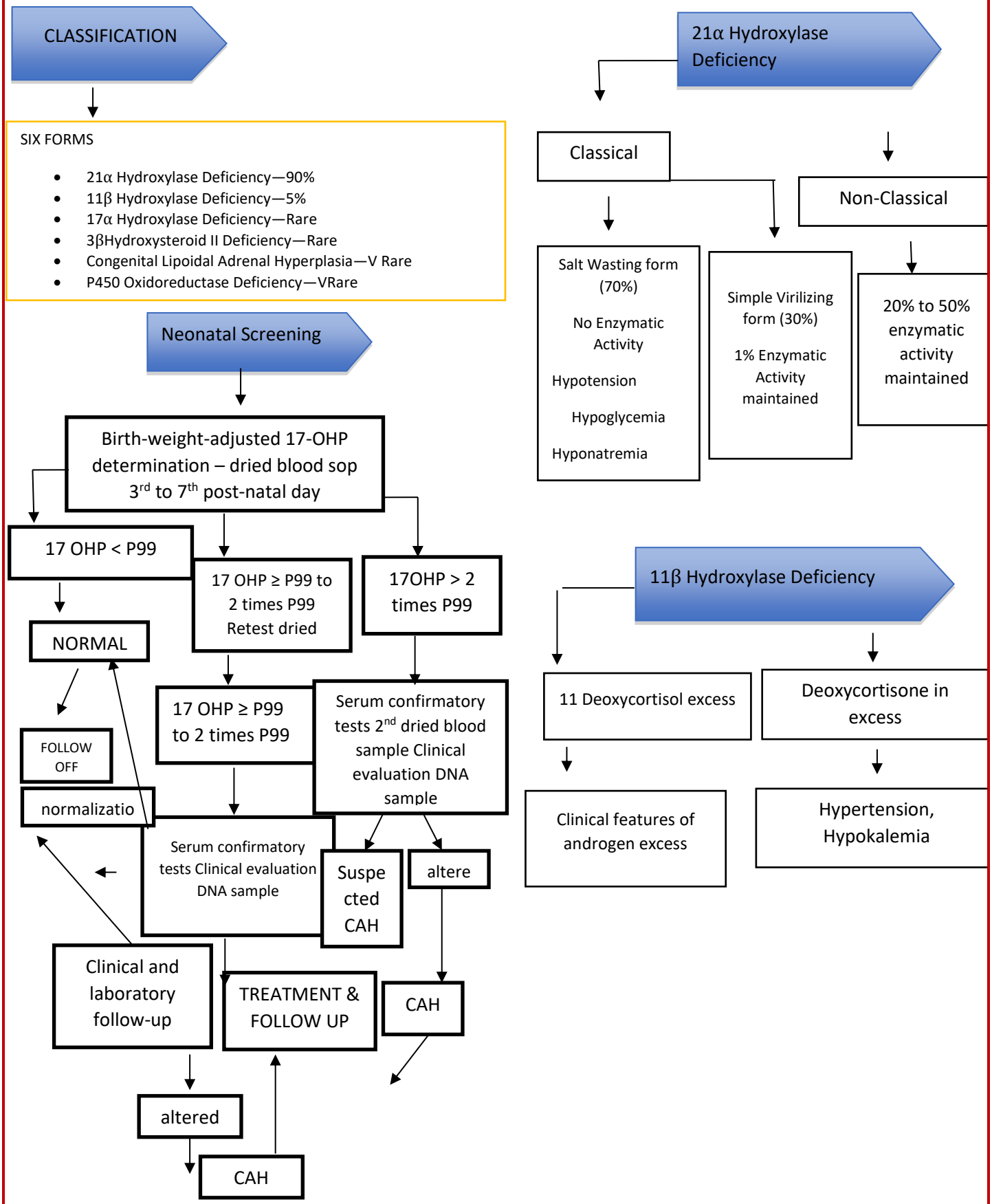
The common indications for renal replacement therapy are fluid overload, hyperkalemia, hyponatremia and severe metabolic acidosis which are unresponsive to medical management.

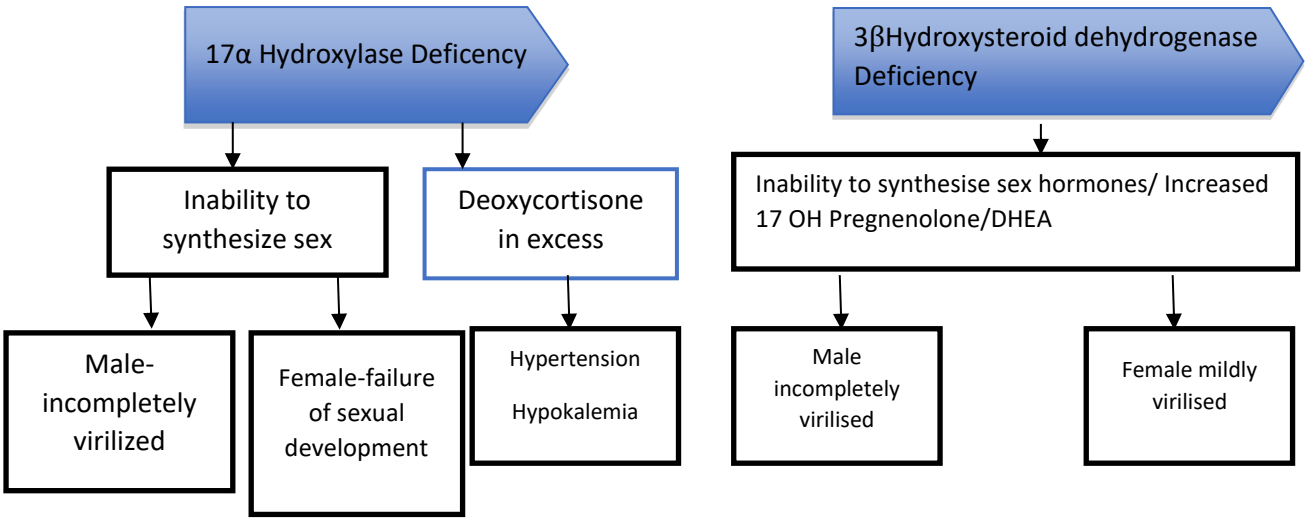


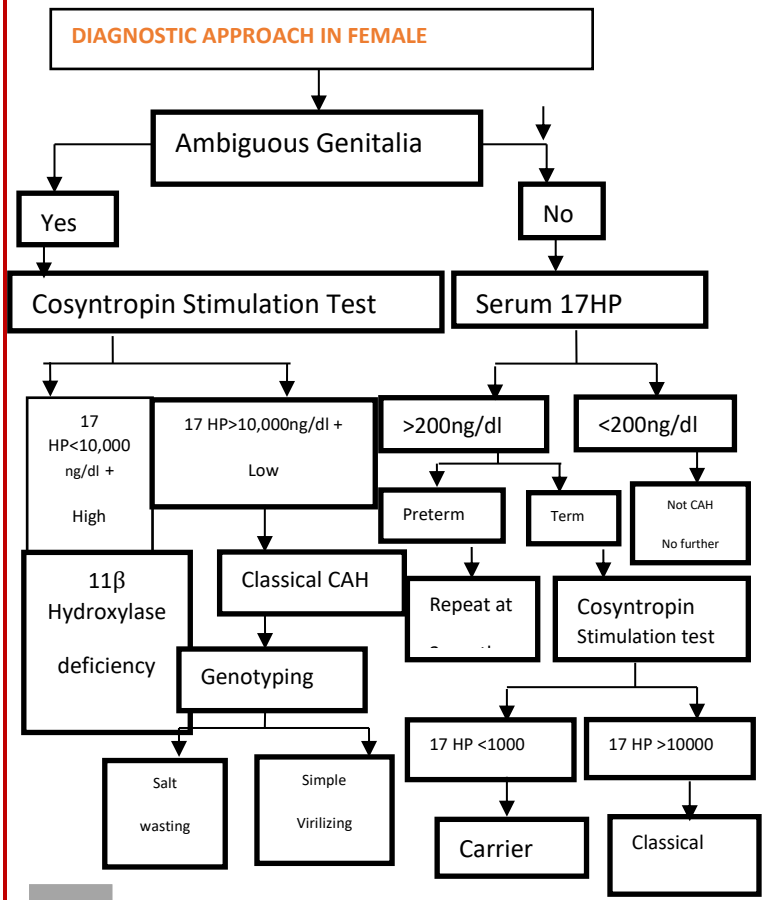
CCF- Congestive cardiac failure

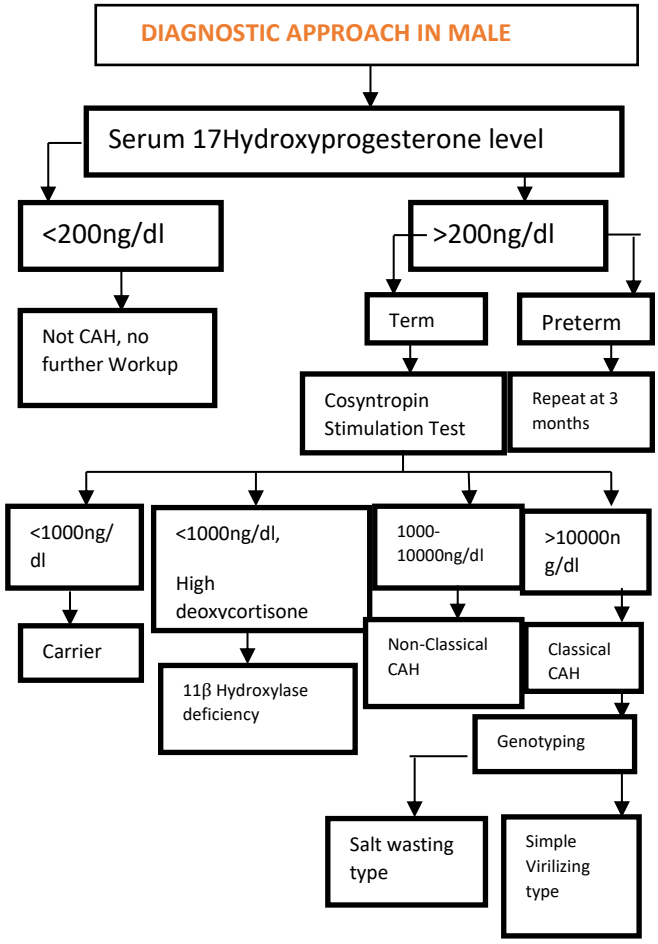
Fig 1. Approach to a neonate with AKI

Protocol 12: Approach to Congenital Adrenal Hyperplasia (CAH)









TREATMENT

MINERALOCORTICOID DEFICIANCY-FLUDROCORTISONE 0.1-0.3 mg/kg/day in divided doses

GLUCOCORTICOID DEFICIANCY- HYDROCORTISONE 15-20 mg/m^2/day in divided dose

SURGICAL CORRECTION AND COUNSELLING

Reference Values in ng/ml-

P99 (99^{th} percentile) - 17 OHP Cut off points to diagnose

CAH: Birth weight ≤ 1500 gm-110.4 ng/ml

Birth weight 1501 gm to 2000 gm – 43.0 ng/ml

SECTION 8

Charts, centiles, and common drugs

Protocol 1: Inotropes and calculation of dose

Drug	Dose	How to make it
Dopamine (1 ml = 40 mg)	5 to 20 mcg/kg/min	Take 1.5 ml/kg of dopamine and add 5% dextrose to it. Final volume – 50 ml. 1ml/hr of this solution is equivalent to 20 mcg/kg/hr
Dobutamine (1 ml = 50 mg)	5 to 20 mcg/kg/min	Take 1.2 ml/kg of dobutamine and add 5% dextrose to it. Final volume – 50 ml. 1ml/hr of this solution is equivalent to 20 mcg/kg/hr
Adrenaline (1 ml = 1 mg)	0.05 to 0.5 mcg/kg/min	Take 1.5 ml/kg of epinephrine and add 5% dextrose to it to make final volume of 50 ml. 1 ml/hr of this solution is equivalent to 0.5 mcg/kg/min
Noradrenaline (1 ml = 1 mg)	0.05 to 0.5 mcg/kg/min	Take 1.5 ml/kg of epinephrine and add 5% dextrose to it to make final volume of 50 ml. 1 ml/hr of this solution is equivalent to 0.5 mcg/kg/min
Milrinone (10 ml = 10 mg)	**Loading** – 50 mcg/kg IV over 30 min **Maintenance** – 0.3 to 0.75 mcg/kg/min	**Dilution (Prepared solution)** Dilute 10 ml of milrinone with 90 ml of NS/ D5 (Resultant 1 ml = 100 mcg) **Loading dose** Take 0.5 ml/kg (50 mcg/kg) of prepared solution and add D5 to it to make total volume 5 ml. Give it over 30 min at rate of 10 ml/hr. **Maintenance** Running rest of prepared solution at 0.3 ml/kg/hr is equivalent to 0.5 mcg/kg/min
Sildenafil (10 mg = 12.5 ml)	**Loading** 0.4 mg/kg over 3 hrs **Maintenance** 1.6 mg/kg/day (0.067 mg/kg/hour)	**Strength** – 0.8 mg/ml **Prepared solution** - To 10 ml of sildenafil, add 90 ml of Normal saline. Resultant conc. = 0.08mg/ml **Loading** Take 5 ml/kg of prepared solution and give it over 3 hours. **Maintenance** Run rest of prepared solution at 0.8 ml/kg/hr (1.6 mg/kg/d)
PGE1 (Prostin) 1 ml = 500 mcg	0.05 to 0.1 mcg/kg/min	Dilute 1 ml of drug with 49 ml NS to give final conc of 10 mcg/ml and then 0.3 X wt = …. ml/hr (0.05 mcg/kg/min) 0.6 X wt = …. ml/hr (0.1 mcg/kg/min)

Which inotrope in which condition

Scenario	Presenting features	Pathophysiology	Suggested Management
Sepsis Warm shock	Low diastolic pressure Tachycardia	Vasodilation, Capillary leak, Absolute or relative hypovolemia, High cardiac output	1. Volume (Crystalloid) 2. Vasopressor - Dopamine 3. Vasopressor - Epinephrine, norepinephrine, vasopressin
Sepsis: Cold Shock	Low systolic pressure or severe combined hypotension	Vasoconstriction, Low cardiac output	1. Volume expansion (crystalloid) 2. Positive inotropic agent - epinephrine 3. Second line – Hydrocortisone 4. Milrinone once blood pressure is better
Hypoxic Ischemic Injury	Low systolic pressure or severe combined hypotension	Right ventricular dysfunction or Left ventricular dysfunction or Combined	1. Positive inotropic agent - Dobutamine 2. Second line positive inotropic agent - Epinephrine 3. Hydrocortisone if refractory shock
Persistent Pulmonary Hypertension	Low systolic pressure or severe combined hypotension	Low Left ventricle preload, Right-to-left ductal shunt, Decreased LV and RV systolic function	1. Optimize lung recruitement 2. Inhaled Nitric Oxide, Sildenafil 3. Dobutamine (if low MAP/DAP) 4. Milrinone(if normal or high MAP/DAP) 5. Vasopressin(if low MAP /DAP)
ELBW/ VLBW (first 24 hours)	Low systolic pressure or severe combined hypotension	Cardiogenic shock secondary to high systemic vascular resistance, Sometimes hsPDA	1. Slow volume expansion (10 ml/kg over half hour) 2. Dobutamine 3. Dopamine/ Epinephrine 4. Close duct if hemodynamically significant 5. Hydrocortisone

Adapted from *Giesinger RE, McNamara PJ. Seminars in perinatology 2016 Apr;40(3):174-88*

Protocol 2: Central lines and its length calculation

Central Lines

- Centrally inserted Umbilical venous and umbilical arterial lines
- Peripherally inserted PICC lines

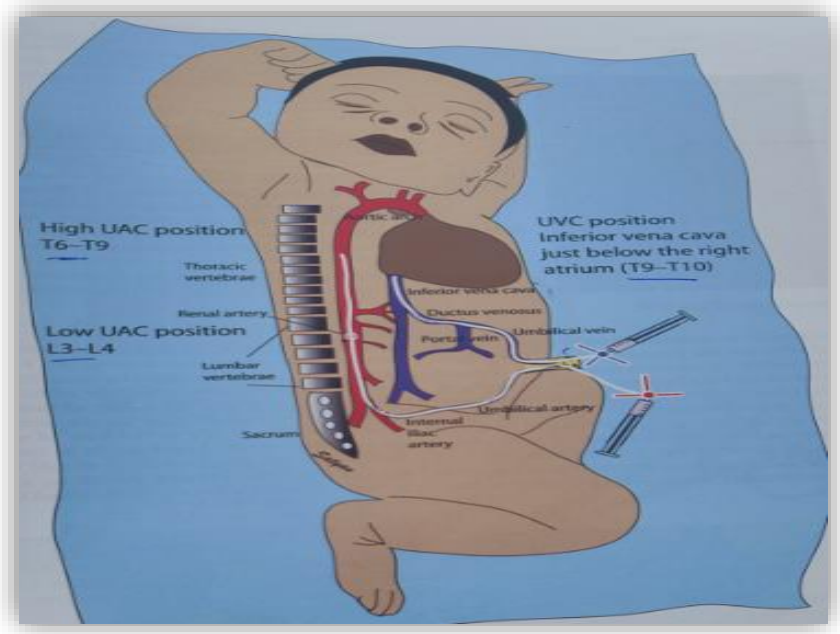


Fig: Position of the catheters

Correct positions of central catheters (Fig)

UAC: High position T6 to T10/Low position: L3 to L5

UVC: Tip 0.5 cm above the diaphragmatic level (on X Ray)

PICC line:

For upper limb: Tip position – lies between T3 and T6 vertebrae and must be well outside cardiac chambers(1 cm in preterm and 2 cm in term)

For lower limb: In the IVC just below the diaphragm(T9-T10) and above L4-L5 vertebrae level.

Methods of insertion

For Umbilical catheters

Method 1: By measuring shoulder umbilical length (distance from the tip of shoulder/lateral end of the clavicle to a point vertically below at level of the umbilicus and adding umbilical stump length to it.

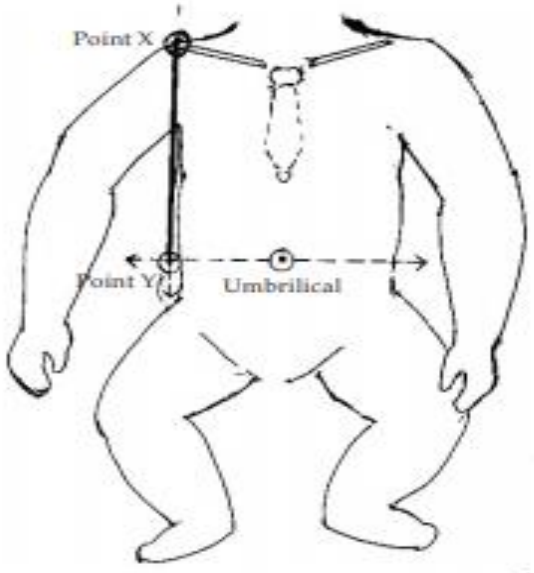


Figure 40.1A: Shoulder umbilical length : the distance from the tip of the shoulder/lateral end of the clavicle (point x) to a point vertically below at the level of the umbilicus (point y).

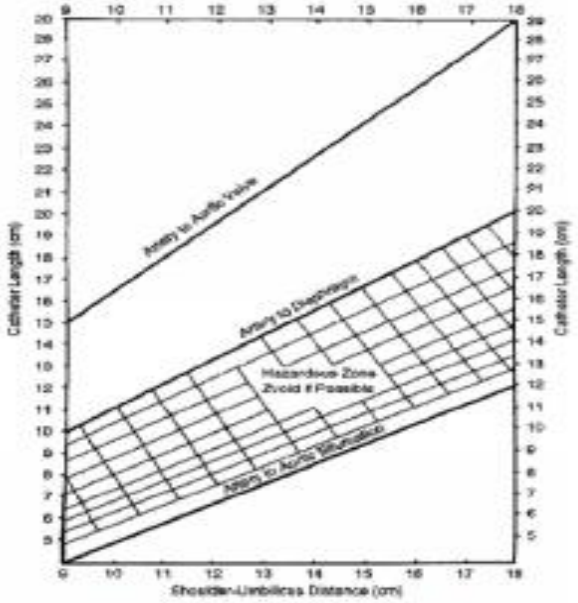


Figure 40.1B: Shoulder-umbilical length normogram (reproduced with permission From *dunn pm. Localization of the Umbilical catheter by post-mortem Measurement.* Arch dis child. *1966;41:69.*)

Method 2:

- infants > 1.5 kg= (birth wt in kg x 3) +9 +umbilical stump length
- infants < 1.5 kg= (birth wt in kg x 4) +9 +umbilical stump length

Method of PICC line insertion

vein selection

: in upper limb (basilic and cephalic vein)

: in lower limb (long saphenous vein and popliteal vein)

Estimating distance of insertion:

Upper limb: Measure distance from the point of insertion along venous pathway to suprasternal notch to right 3 rd intercostal space.

Lower limb: Measure distance from the point of insertion to umbilicus and then to xiphisternum.

Recommended catheter size:

<1.5 kg -3.5Fr

>1.5 kg-5Fr

Recommended duration:

- UAC line- short duration 5-7 days
- UVC line- preferred short duration (<7 days) and maximum 14 days
- PICC - intermediate duration: weeks

Protocol 3: Growth charts

3 types of charts available for growth monitoring during fetal, neonatal and infancy.

Fetal

Based on the ultrasound parameters of fetus

Used to monitor the growth of fetus antenatally

Neonatal size at birth/neonatal anthropometric charts

1. Intergrowth 21st neonatal charts
2. Fentons
3. Lubchenco
4. Regional charts (AIIMS, SJH)
5. WHO charts (start at 40 weeks gestation)

Any of the above

For classification of neonate at birth as Appropriate for gestation age (AGA), Small for gestational age (SGA) and Large for gestational age (LGA)

Postnatal charts

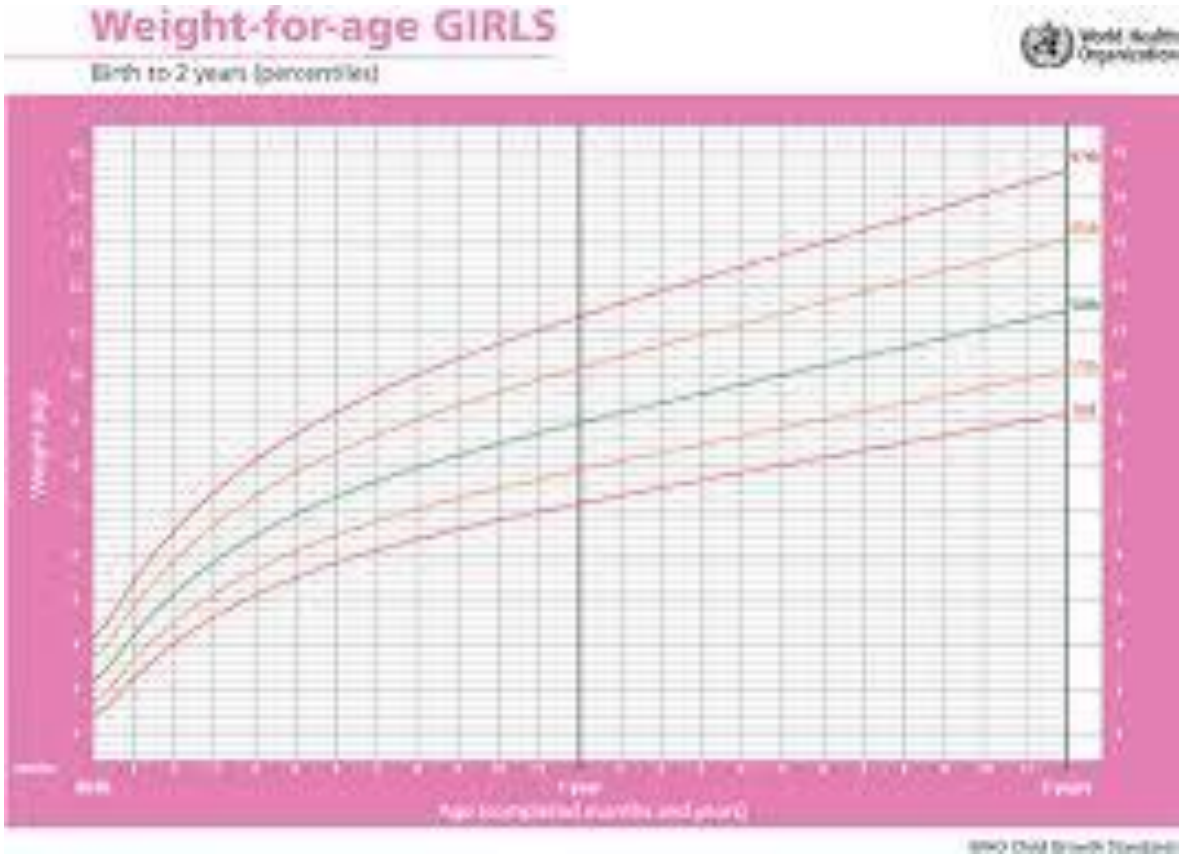
Exhibit the postnatal dip in weight due to extracellular fluid losses

1. Ehrenkranz
2. Modified Dancis charts
3. Intergrowth 21st postnatal charts

Should be used for postnatal monitoring of VLBW, inside NICU.

Fentons used in most units for postnatal monitoring though it is a size at birth chart

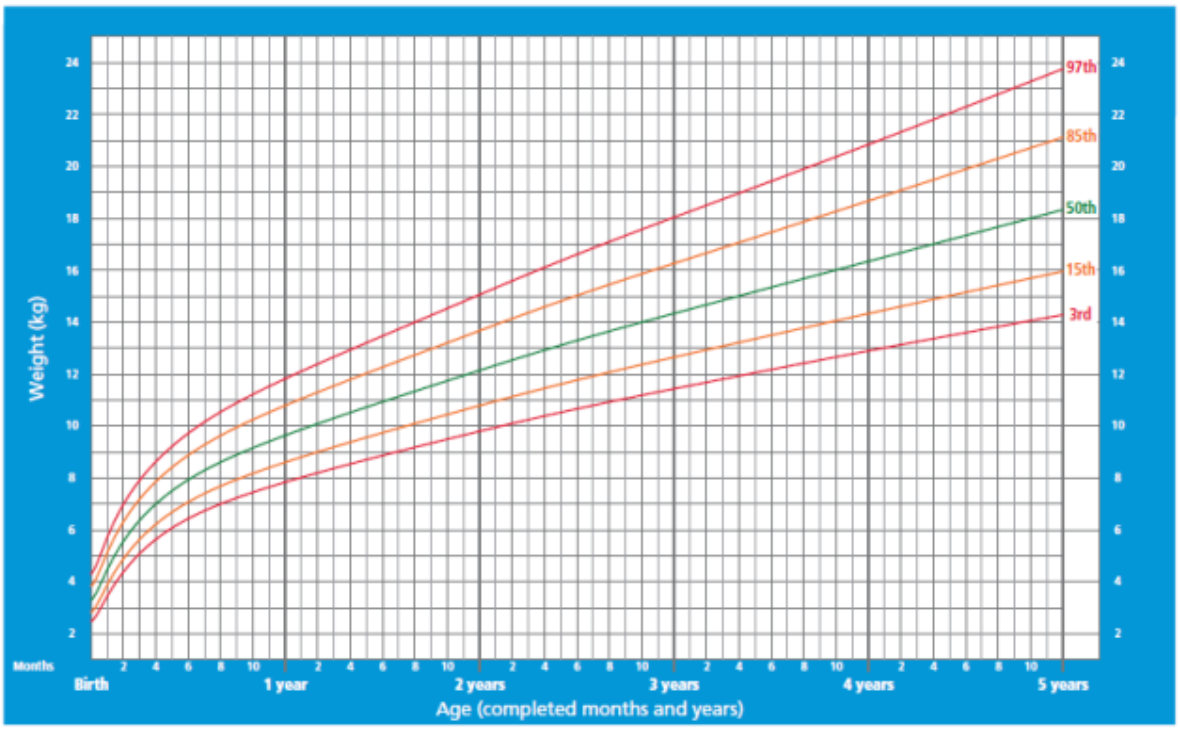
- Beyond 40 weeks PMA (Postmenstrual age) till childhood, WHO growth charts should be used for growth monitoring
- Fentons overlaps with WHO charts at 50 weeks PMA
- Intergrowth 21st postnatal chart overlaps with WHO charts at 64 weeks PMA.



Weight-for-age BOYS

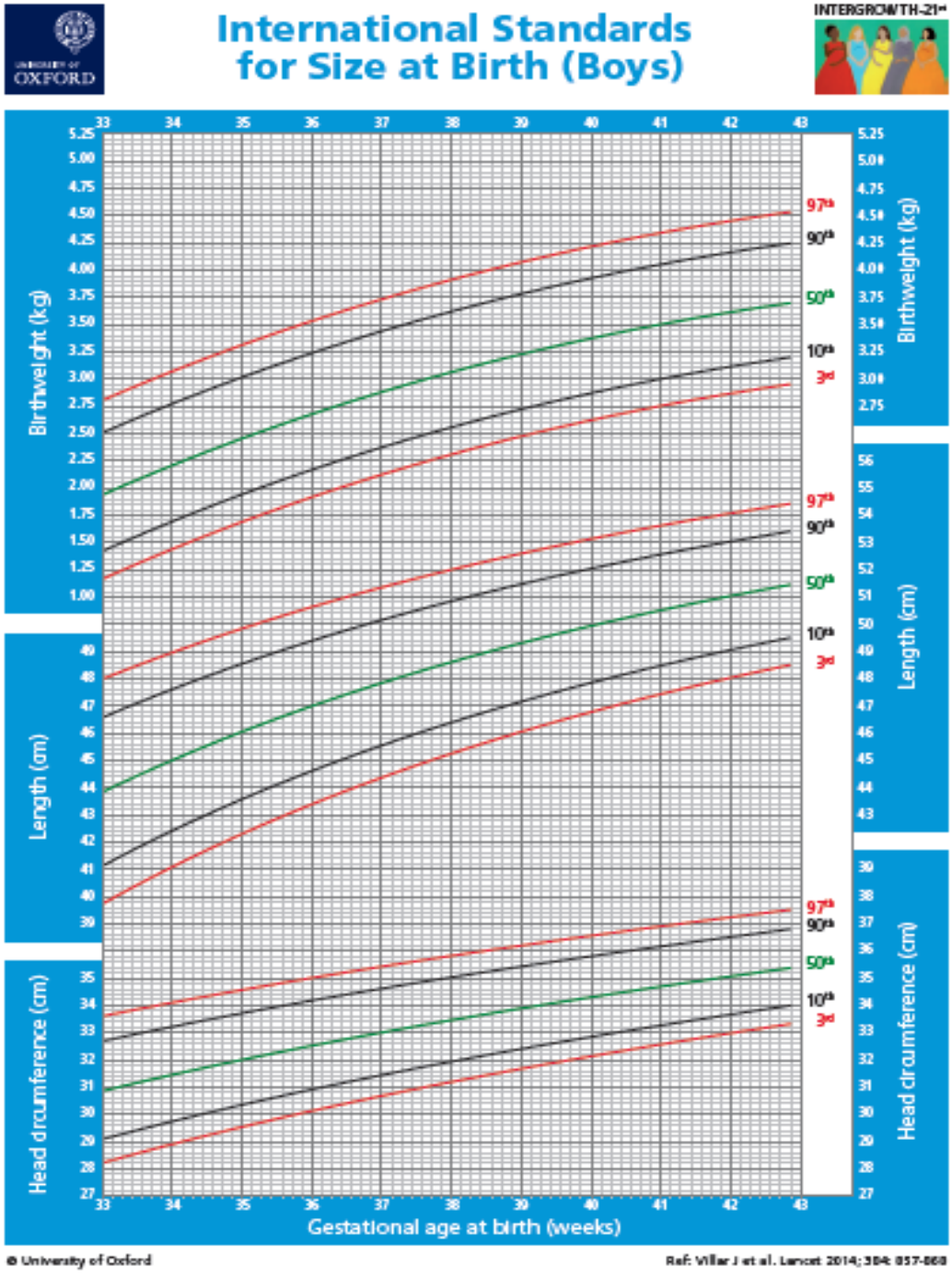
Birth to 5 years (percentiles)

World Health Organization

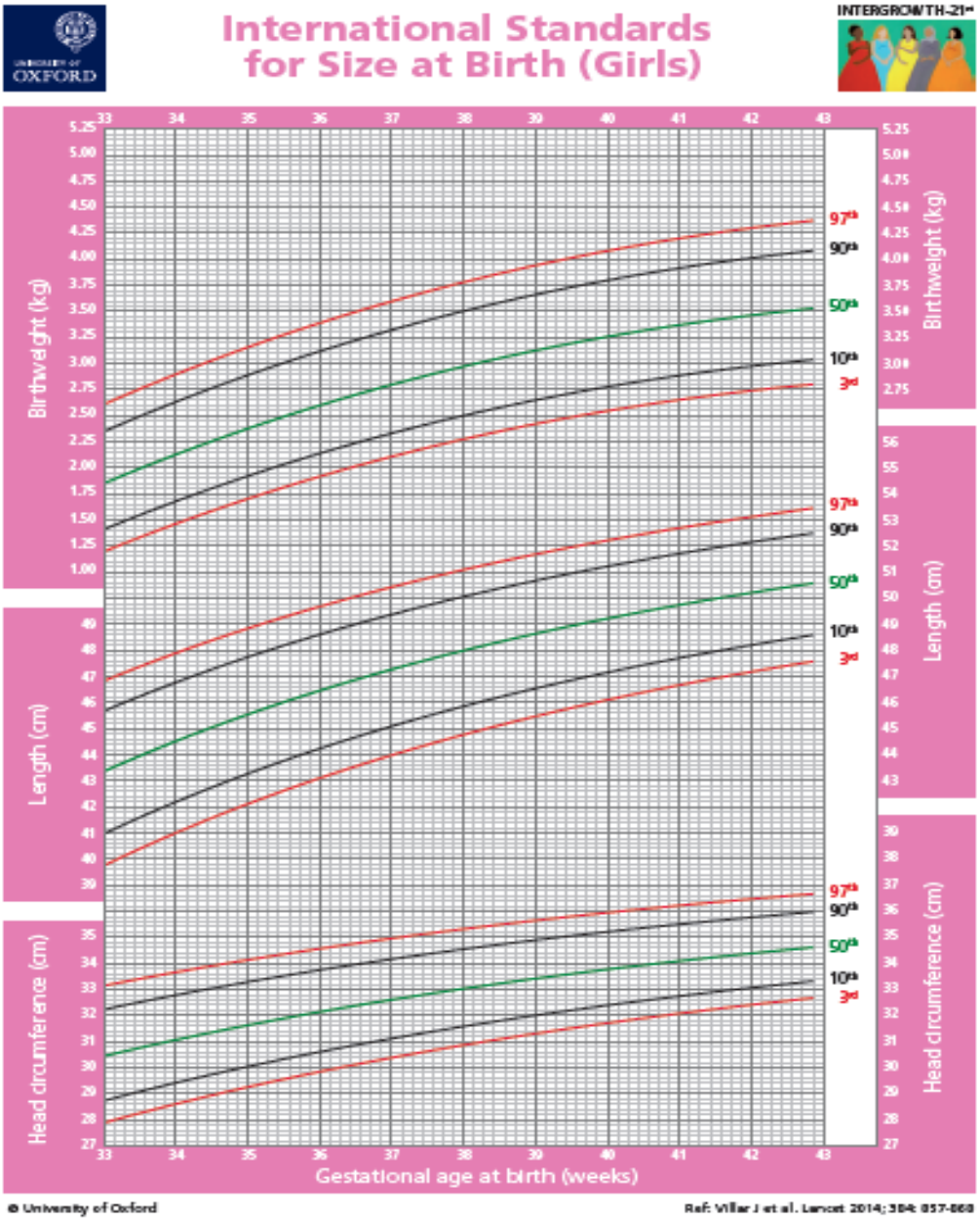


WHO Child Growth Standards

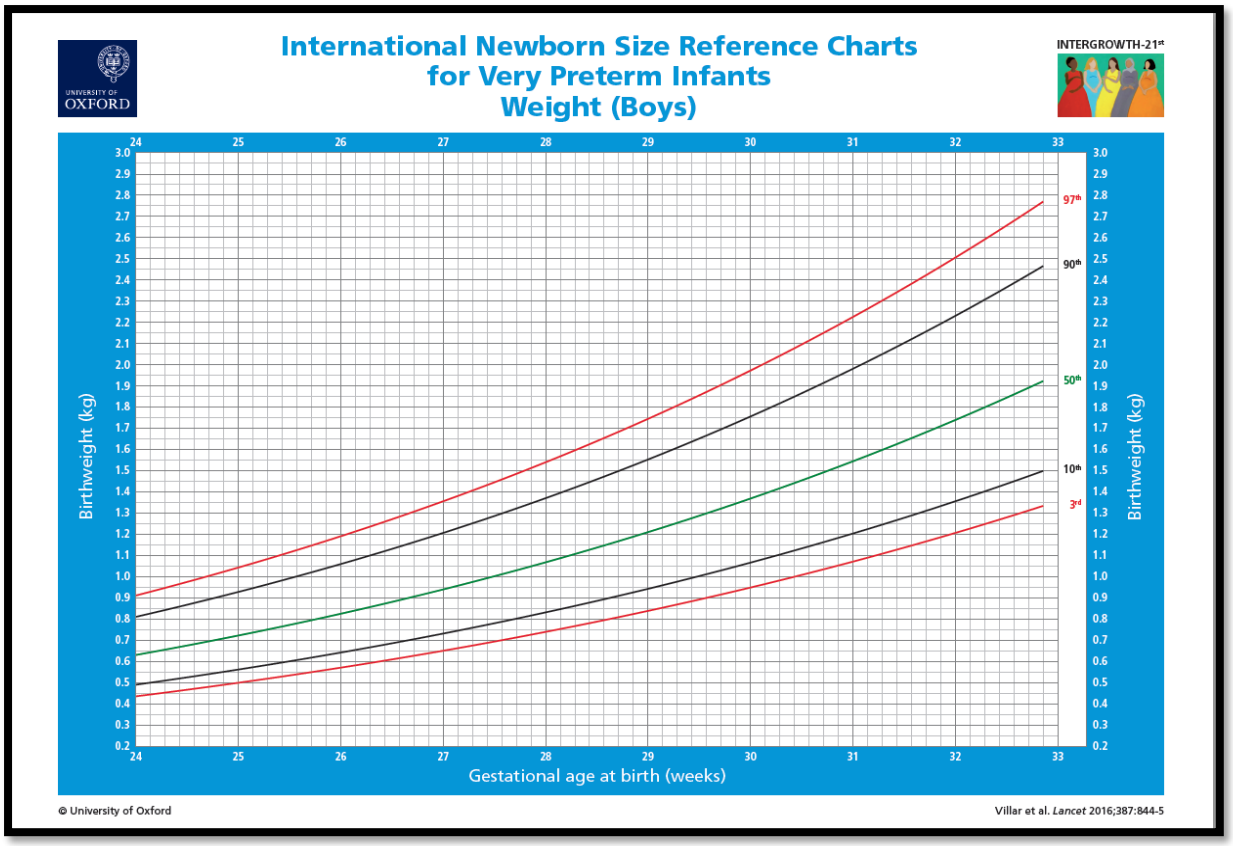
WHO weight for age charts

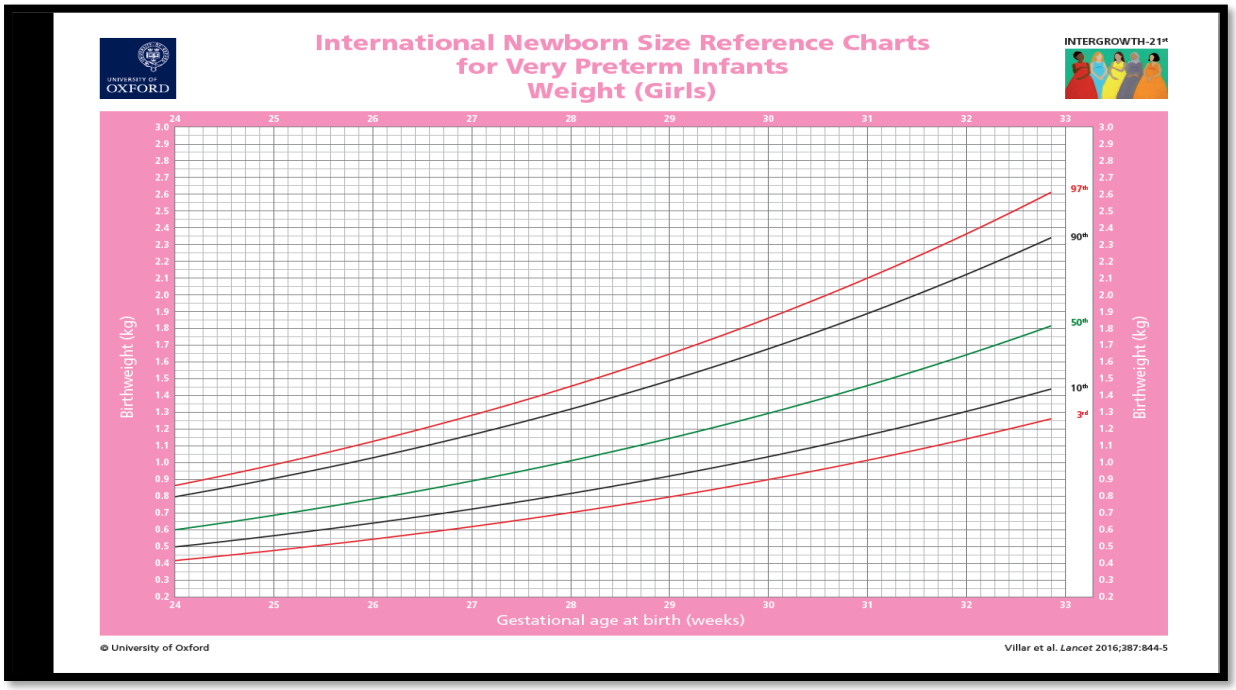


Intergrowth 21st size at birth chart (boys)

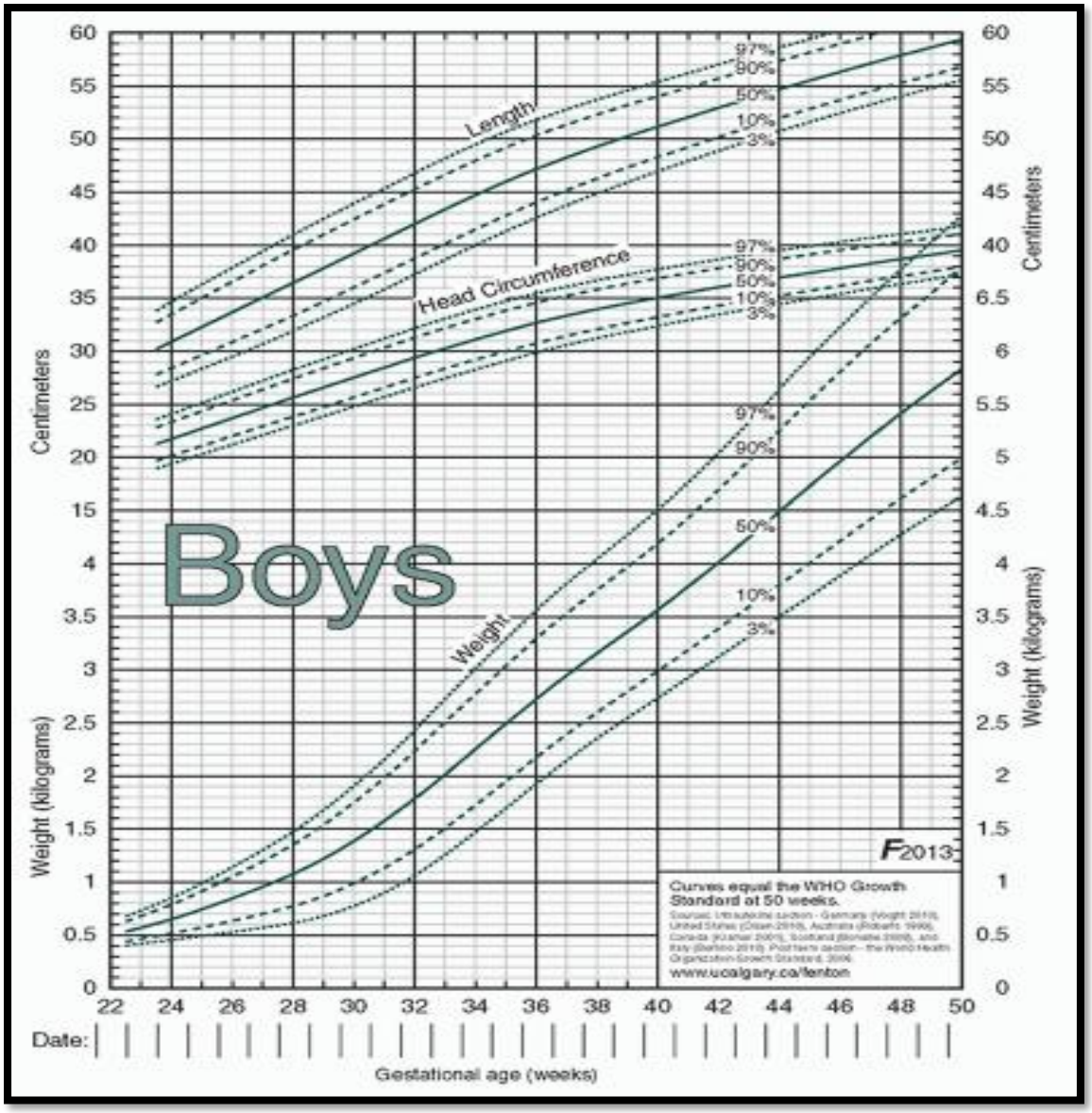


Intergrowth 21st size at birth charts (girls)

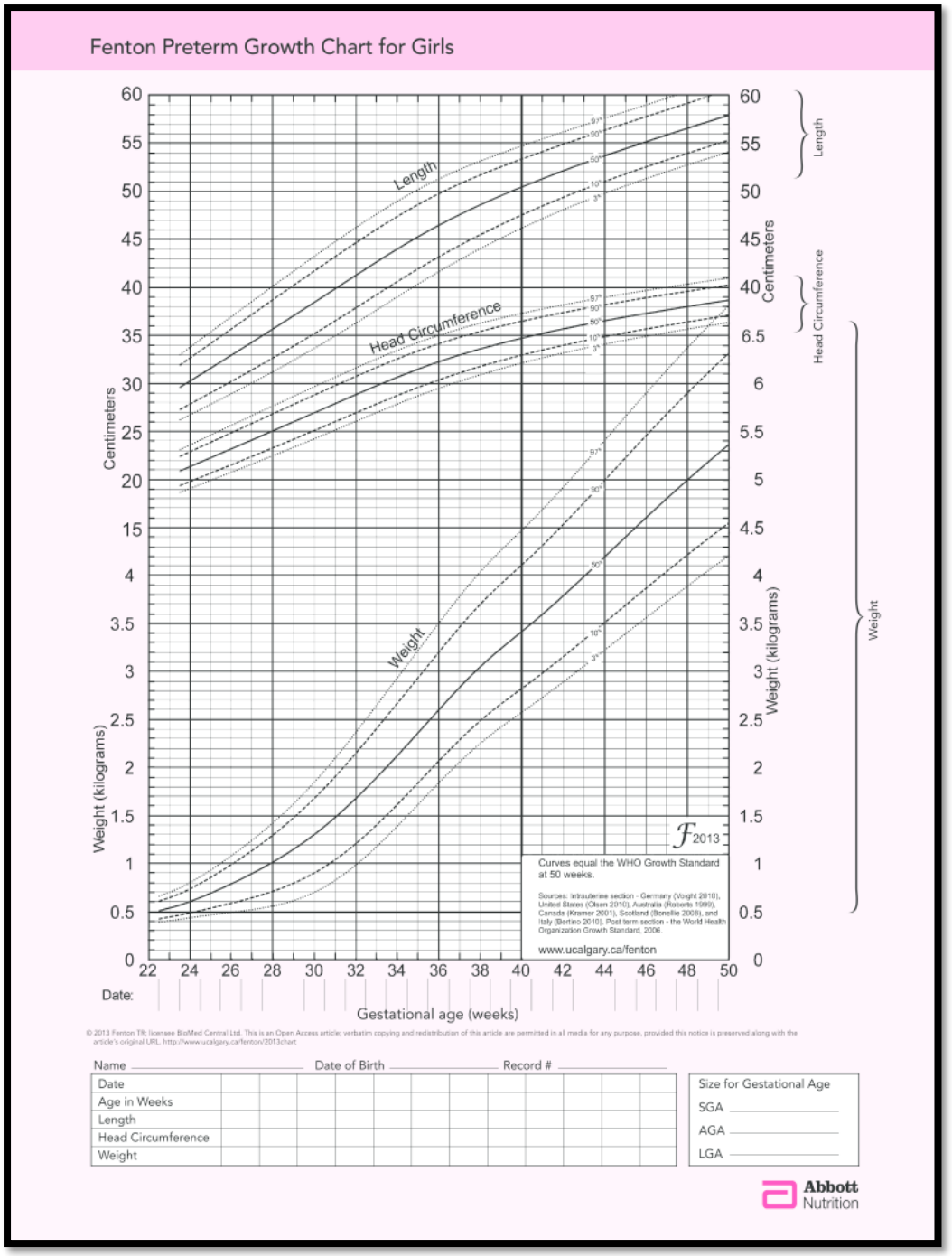

International Newborn Size Reference Charts
for Very Preterm Infants
Weight (Boys)
INTERGROWTH-21st
Birthweight (kg)
Gestational age at birth (weeks)
97th
90th
50th
10th
3rd
© University of Oxford
Villar et al. Lancet 2016;387:844-5


International Newborn Size Reference Charts
for Very Preterm Infants
Weight (Girls)
INTERGROWTH-21st
Birthweight (kg)
Gestational age at birth (weeks)
97th
90th
50th
10th
3rd
© University of Oxford
Villar et al. Lancet 2016;387:844-5

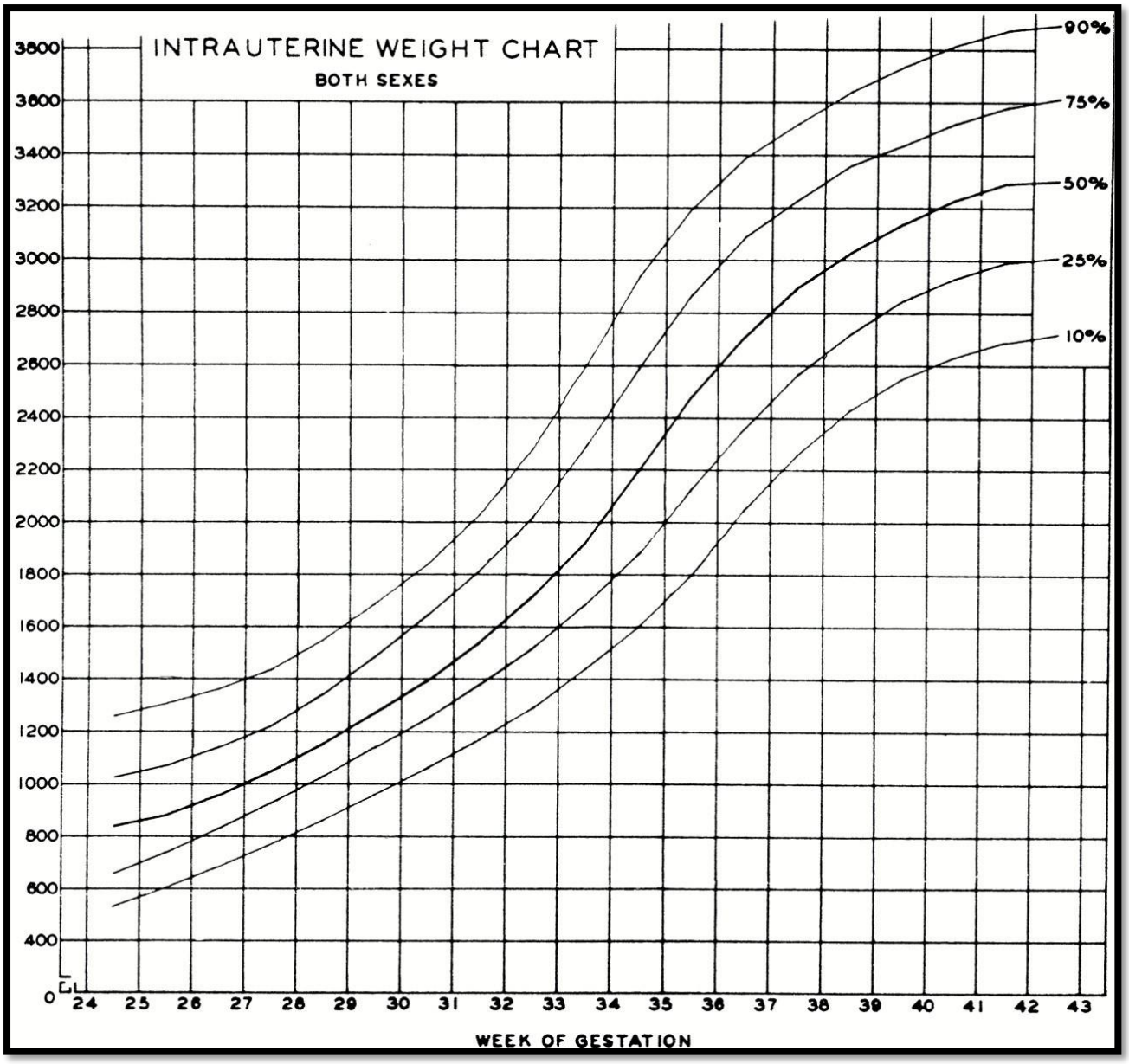
Intergrowth 21st size at birth charts for very preterm (buys and girls)



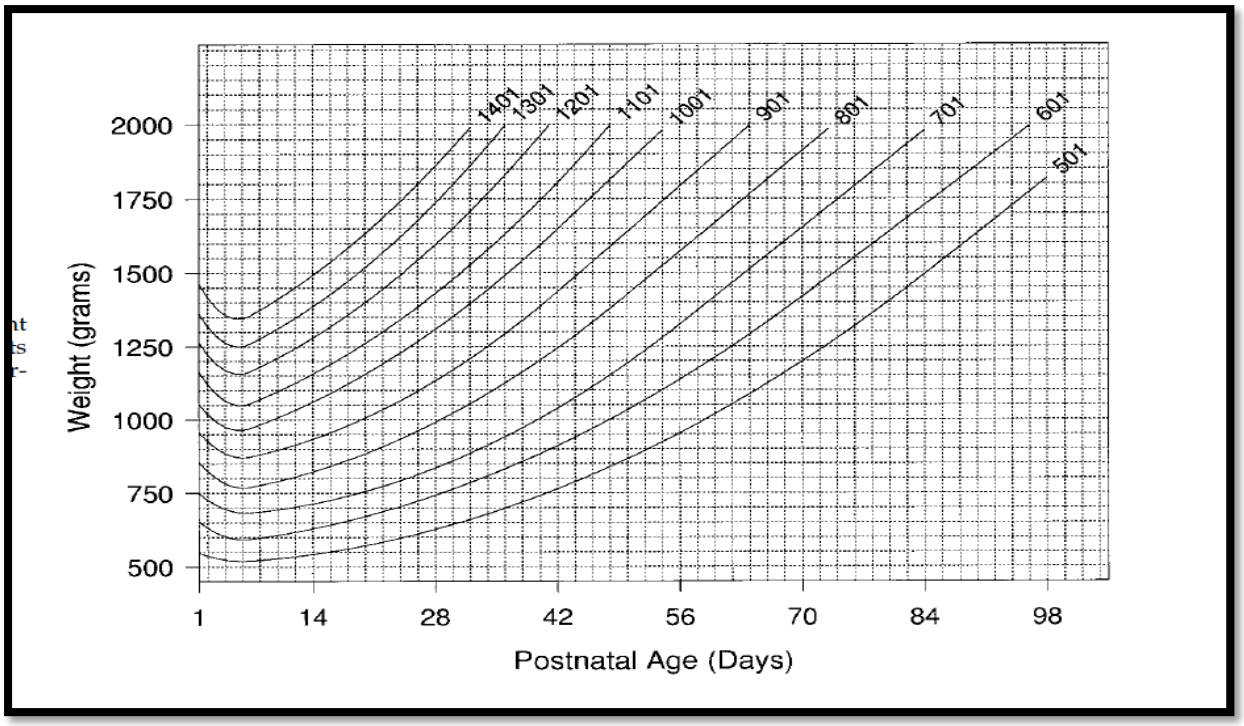
Fentons size at birth chart (Boys)



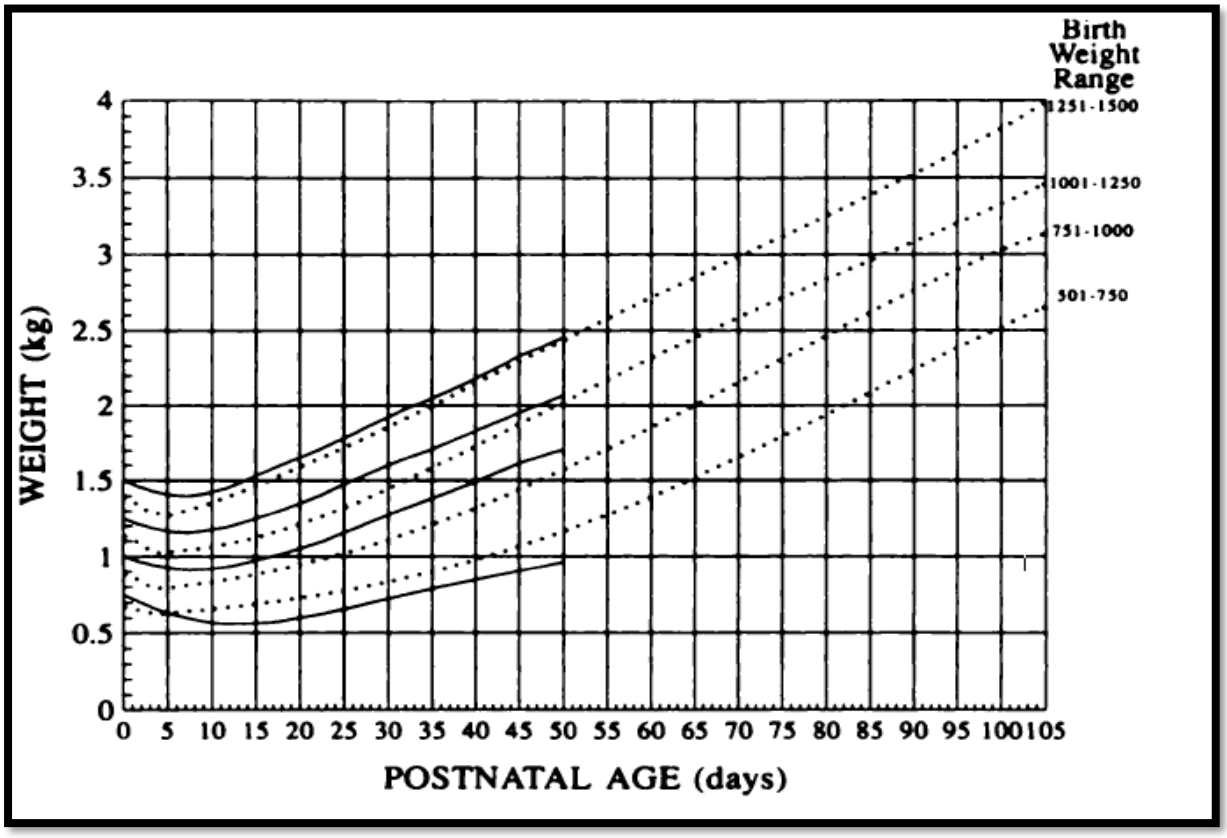
Fentons size at birth chart (girls)



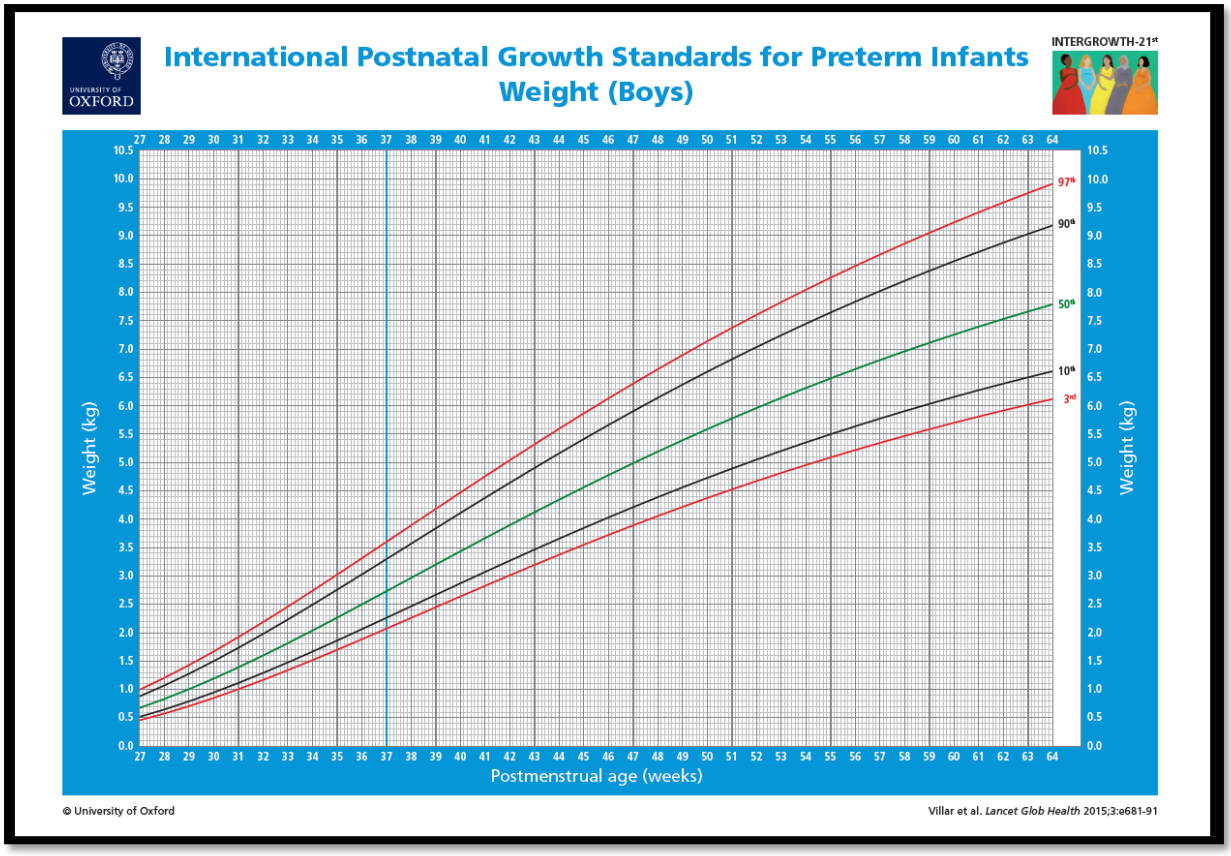
Lubchenco size at birth chart



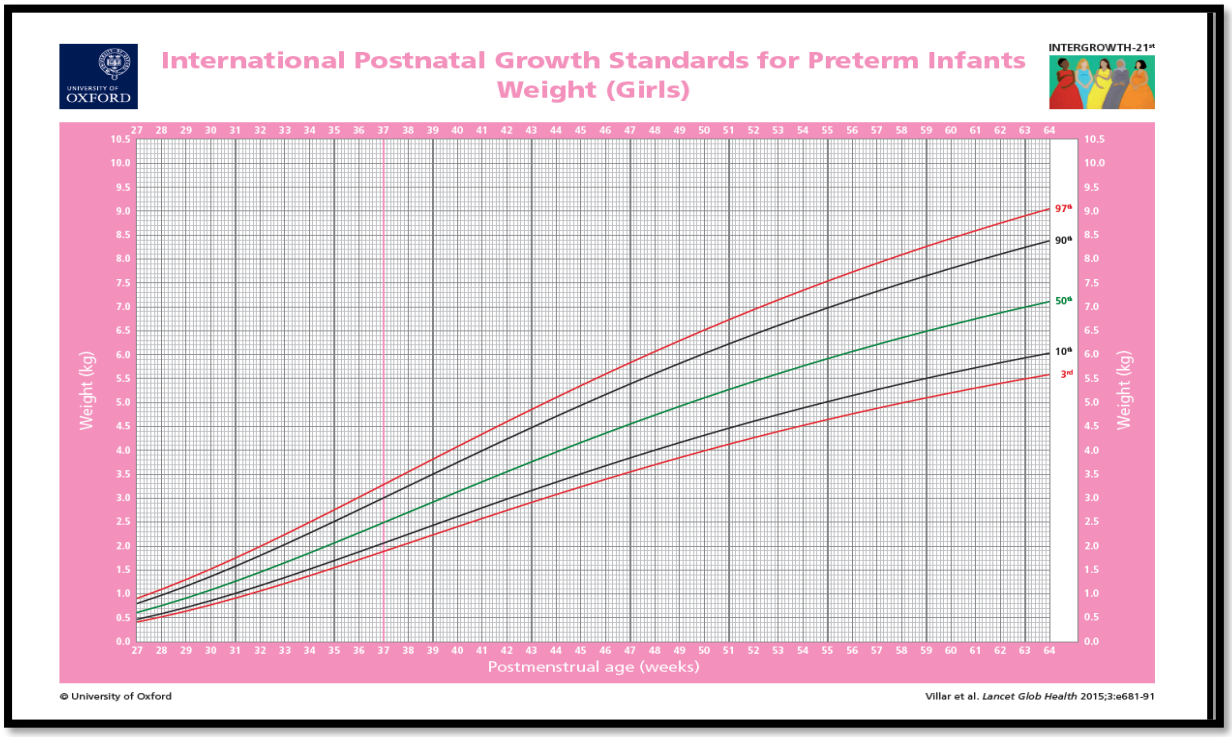
Ehrenkranz postnatal growth chart



Modified Dancis postnatal charts (Wrights modified)



Intergrowth postnatal charts (boys)



Intergrowth postnatal charts (girls)

Protocol 4: BP Centiles, AAP guidelines for neonatal jaundice

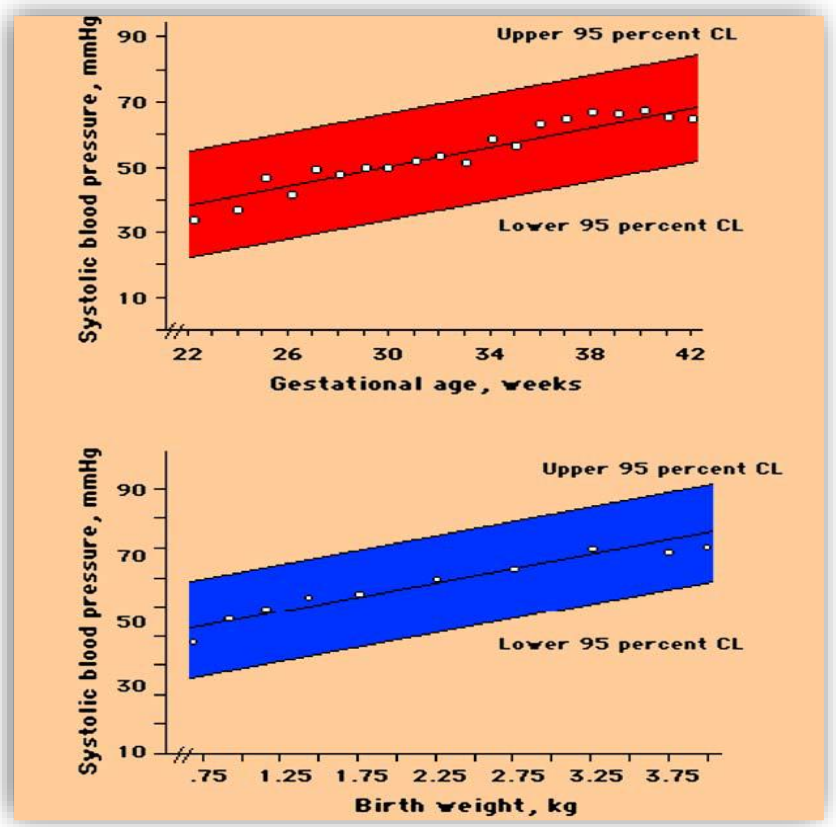


Fig 1: Linear regression of mean systolic blood pressure on gestational age and birth weight in infants admitted to NICU on day 1 of life.(Zubrow et al, J Perinatol 1995;15:470e9.)

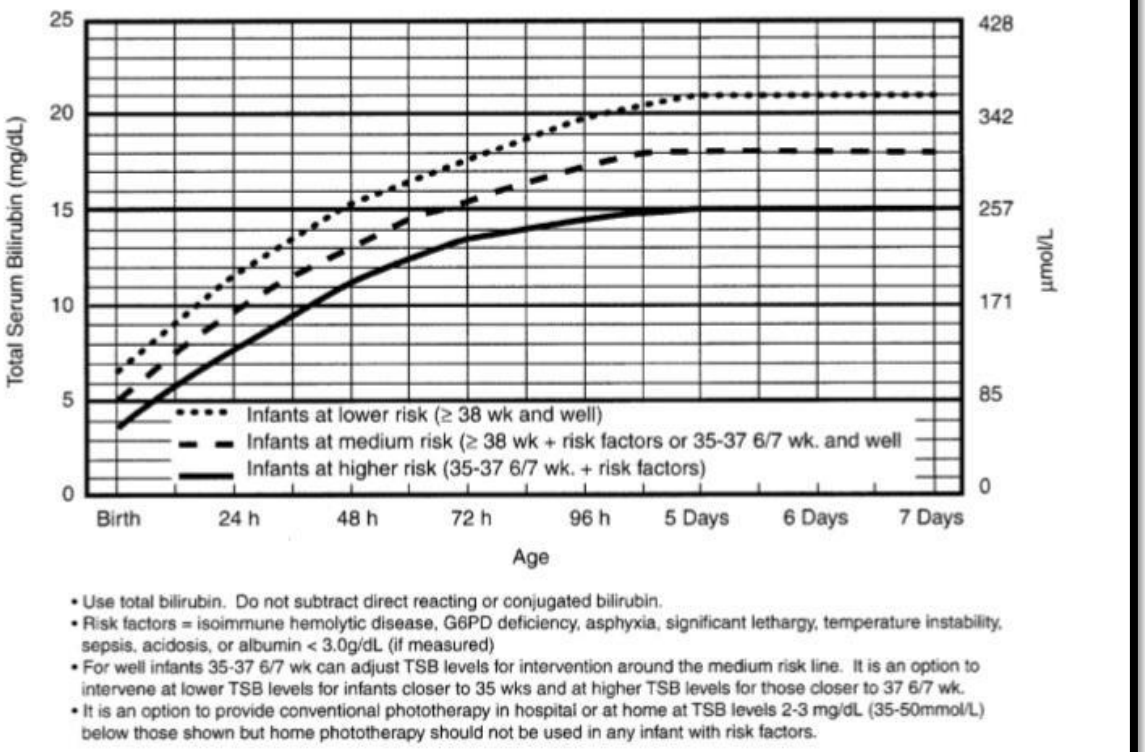


Fig 3. Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation.

Note: These guidelines are based on limited evidence and the levels shown are approximations. The guidelines refer to the use of intensive phototherapy which should be used when the TSB exceeds the line indicated for each category. Infants are designated as "higher risk" because of the potential negative effects of the conditions listed on albumin binding of bilirubin,[45–47] the blood-brain barrier,[48] and the susceptibility of the brain cells to damage by bilirubin.[48]

"Intensive phototherapy" implies irradiance in the blue-green spectrum (wavelengths of approximately 430–490 nm) of at least 30 $\mu W/cm^2$ per nm (measured at the infant's skin directly below the center of the phototherapy unit) and delivered to as much of the infant's surface area as possible. Note that irradiance measured below the center of the light source is much greater than that measured at the periphery. Measurements should be made with a radiometer specified by the manufacturer of the phototherapy system.

See Appendix 2 for additional information on measuring the dose of phototherapy, a description of intensive phototherapy, and of light sources used. If total serum bilirubin levels approach or exceed the exchange transfusion line (Fig 4), the sides of the bassinet, incubator, or warmer should be lined with aluminum foil or white material.[50] This will increase the surface area of the infant exposed and increase the efficacy of phototherapy.[51]

If the total serum bilirubin does not decrease or continues to rise in an infant who is receiving intensive phototherapy, this strongly suggests the presence of hemolysis.

Infants who receive phototherapy and have an elevated direct-reacting or conjugated bilirubin level (cholestatic jaundice) may develop the bronze-baby syndrome. See Appendix 2 for the use of phototherapy in these infants.

AAP Guidelines for Phototherapy

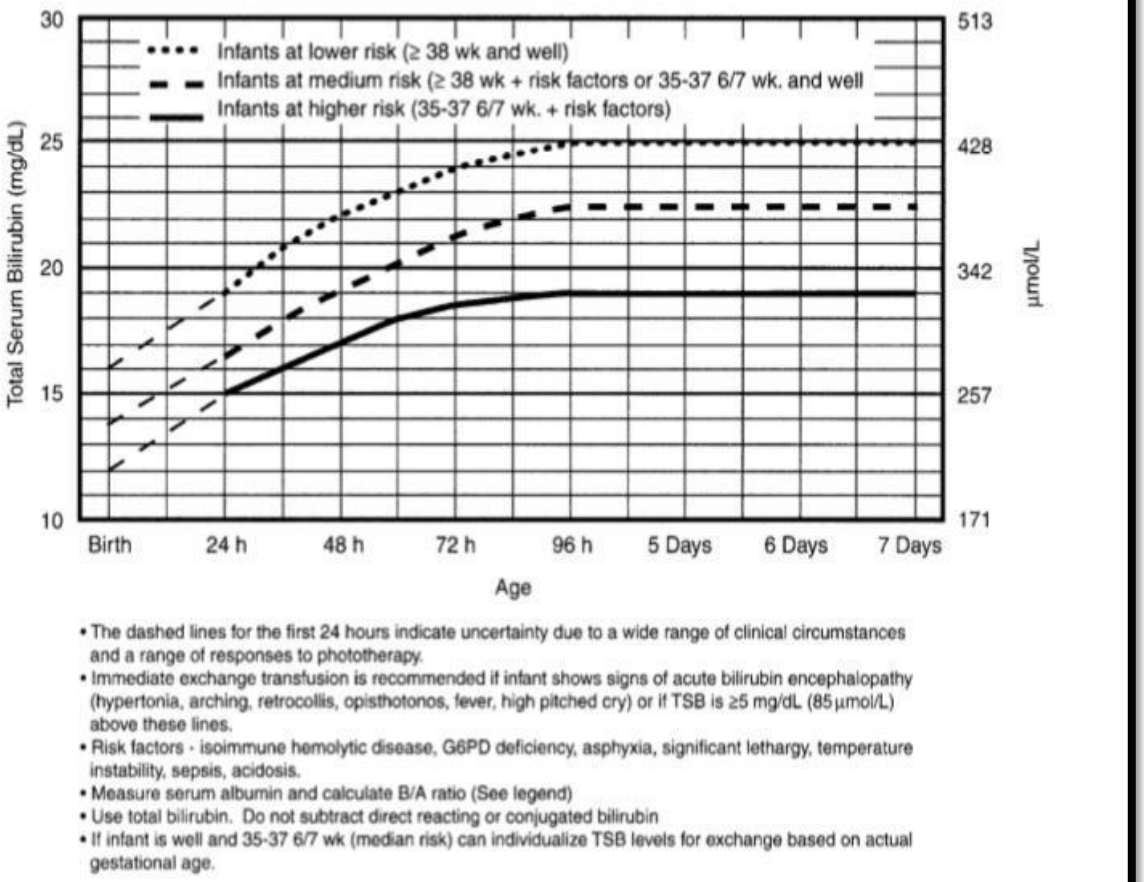


Fig 4. Guidelines for exchange transfusion in infants 35 or more weeks' gestation.
Note that these suggested levels represent a consensus of most of the committee but are based on limited evidence, and the levels shown are approximations. See ref. 3 for risks and complications of exchange transfusion. During birth hospitalization, exchange transfusion is recommended if the TSB rises to these levels despite intensive phototherapy. For readmitted infants, if the TSB level is above the exchange level, repeat TSB measurement every 2 to 3 hours and consider exchange if the TSB remains above the levels indicated after intensive phototherapy for 6 hours.
The following B/A ratios can be used together with but in not in lieu of the TSB level as an additional factor in determining the need for exchange transfusion[52]:

AAP Guidelines for Exchange Transfusion

SECTION 9

Discharge preparedness and Follow up of high-risk neonate

Protocol 1: Discharge preparedness and follow up of high-risk neonate

Improvement in maternal and neonatal care has led to increased survival of babies at risk of long-term morbidities which include growth failure, ongoing medical illness and long term neuro-developmental sequelae (motor, cognitive and sensorineural impairment). Comprehensive discharge and follow up program is required for early detection and management of these morbidities

Discharge planning

Should begin days before the discharge. Caregivers are trained to get oriented in the care of the baby.

Discharge Criteria

Infant Factors

- Baby is hemodynamically stable and able to maintain euthermia
- Weight greater than 1500g (Regained birth weight with consistent weight gain for 3 consecutive days)
- On full enteral feeds by spoon or breastfeeding
- Not on medications other than supplements (should be off caffeine for at least 5-7 days prior to discharge)
- Received vaccination as per schedule
- Completed newborn screening

Paternal Factors

- Parents confident in taking care of the baby including KMC
- Danger signs have been explained to the parents along with the follow-up plan.

Checklist at the time of discharge

1. **Morbidity**: Details of important morbidities in chronological order eg. HMD, Sepsis, Asphyxia, MAS, etc
2. **Therapy during NICU stay**: Oxygen, Antibiotics, Anticonvulsants, Ionotropes, Prolonged tube feeding etc.
3. **Anthropometry**: Weight, Length, OFC at birth and discharge
4. **Special consultation if any**. e.g: Endocrine, Genetics, Pulmonologist, etc
5. **Neurological Examination**: Mention abnormality in tone, posture, reflexes, movements, orientation and behaviour.
6. **ROP Screening as per RBSK**: Mention previous reports and date of next screen
7. **Hearing Screen** results at time of discharge and date of next screen.
8. **Neuro Imaging if required**: USG, CT &/or MRI: mention earlier reports along with date of next screen
9. **Nutrition counselling**: along with quality, quantity and the supplements
10. **Counselling regarding temperature maintenance** (including KMC) along with hand hygiene
11. **Immunization** : Mention date of next immunization visit
12. Explain **Danger signs** (as per IMNCI)
13. Date, time and place of next **follow up**

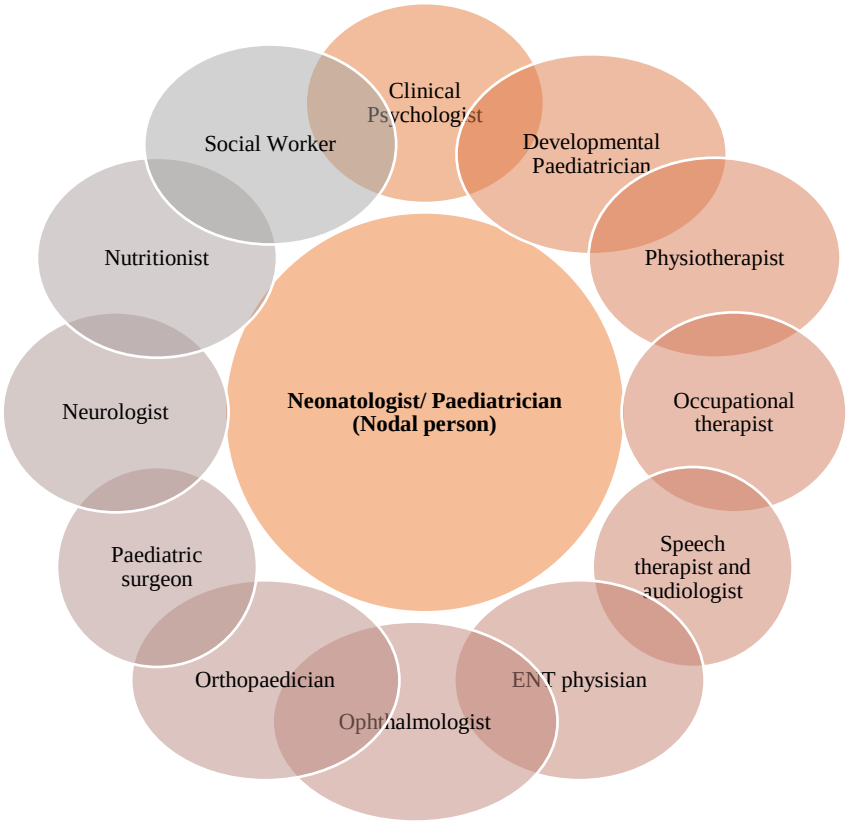
Follow up of High risk infant

High-risk neonates requiring follow-up

- Preterm <34 weeks, birth weight < 1800g
- Severe IUGR (< 3rd centile)
- Major Malformations
- Abnormal neurological examination at discharge
- Turbulent NICU course: Perinatal asphyxia (AS < 3 at 5 min, HIE stage 2 or more), Shock, Sepsis, Meningitis, Mechanical ventilation for 24 hours or more, hypoglycemia, seizures, NEC, cholestasis etc
- Major morbidities associated with prematurity: BPD, IVH, ROP, PVL
- Intrauterine infections
- Jaundice near exchange transfusion range
- Babies with suspected inborn errors of metabolism
- Infant of diabetic mother, multiple pregnancies, retrovirus positive mother
- Suboptimal home environment

Follow-up plan

- Done in a dedicated high risk clinic where all majority of the follow-up services are available under single roof under the primary care of Neonatologist/ Paediatrician
- Should be done until a minimum of 2 years corrected age and ideally till 8 years of age
- Use corrected age for assessing growth and development, and postnatal age for vaccination and establishing complementary feeding
- High Risk Follow up team:



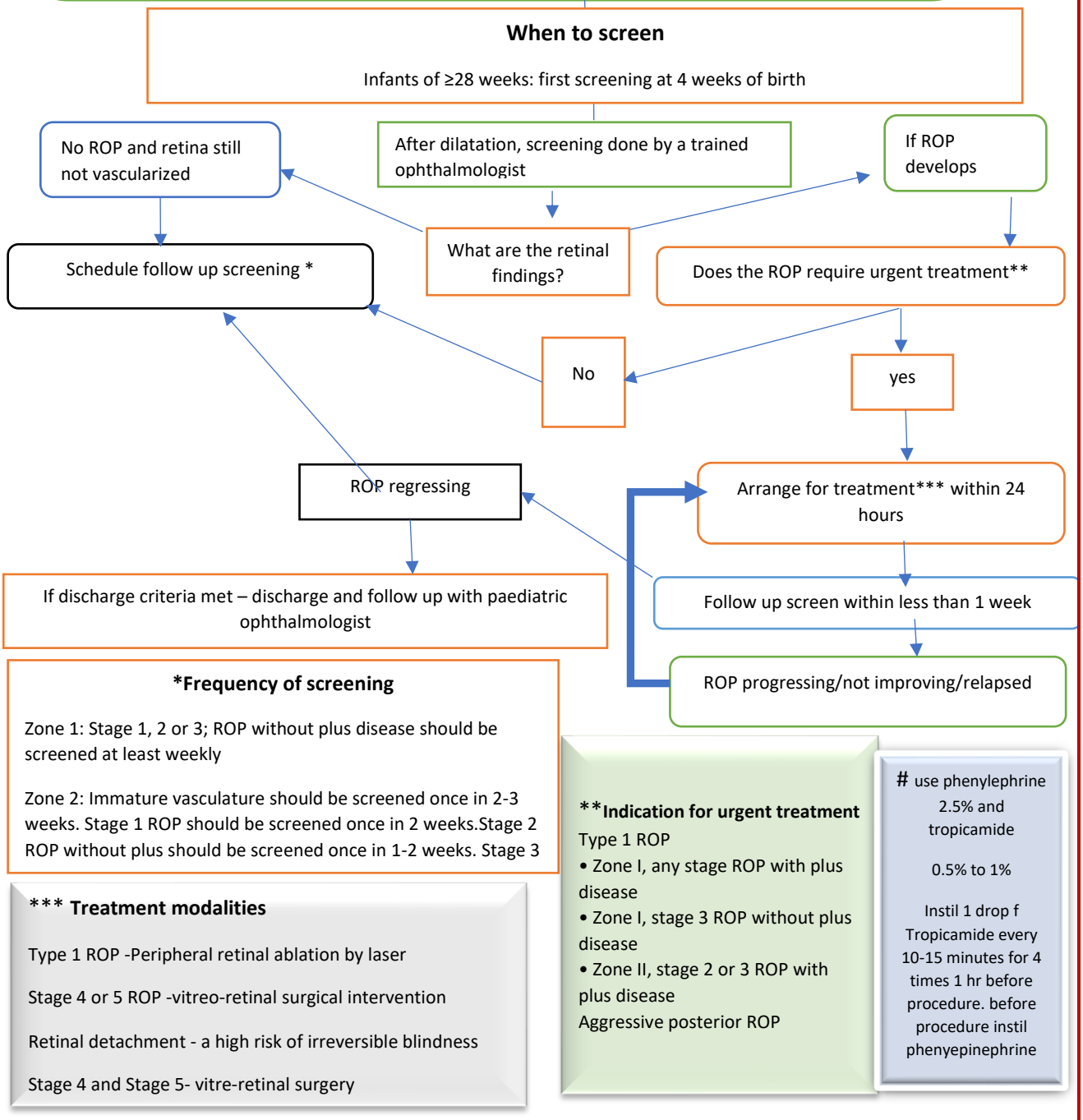
Follow-up schedule: 48h after discharge, 2 weeks after discharge, at 6, 10, 14 weeks, 3, 6, 9, 12, 15, 18 and 24 months

S.No	Intervention	Frequency	Details
A	Anthropometry	Every visit	Intergrowth postnatal follow-up charts till 64 weeks PMA followed by WHO charts after 64 weeks
B	Breastfeeding	Every visit	Address breastfeeding problems
C	Counselling	Every visit	Hygiene Feeding KMC Ongoing issues
D	Developmental screening and neurological examination	Every visit	Trivandrum developmental screening chart; DDST- II BSID
E	Eye	• ROP screen as per RBSK 4 weeks postnatal age (at 3 weeks if < 28weeks and/or < 1200g) and repeat as required based on stage of ROP until 44 weeks PMA • Evaluation for fixation at 3 months & refractive errors and visual acquity at 9 months	Formal visual assessment at 9-12 months
F	Follow up USG	At discharge/ 36 weeks PMA	To look for PVL and other abnormalities
G	Growth monitoring	Every visit	
H	Hearing	BERA at 34 weeks PMA	If normal, screen at 9 and 18-24 months, or if there is parental concern of hearing problems
I	Immunisation	6,10,14 weeks, 9months, 15-18 months, 24 months	As per UIP
L	Language / speech Behavior at / after IQ testing	1,2,3 years 1,3 years	Any delay detected should prompt early intervention

Protocol 2: ROP Screening

Eligible babies

1. Birth weight less than 2000 gm
2. Gestational age less than 34 weeks
3. Gestational age between 34 to 36 weeks but with risk factors such as: a) Cardio-respiratory support, b) Prolonged oxygen therapy, c) Respiratory distress syndrome, d) Chronic lung disease, e) Fetal hemorrhage, f) Blood transfusion, g) Neonatal sepsis, h) Exchange transfusion, i) Intraventricular haemorrhage, j) Apneas, k) Poor postnatal weight gain.
4. Infants with an unstable clinical course who are at high risk (as determined by the neonatologist or paediatrician).



***Frequency of screening**

Zone 1: Stage 1, 2 or 3; ROP without plus disease should be screened at least weekly

Zone 2: Immature vasculature should be screened once in 2-3 weeks. Stage 1 ROP should be screened once in 2 weeks.Stage 2 ROP without plus should be screened once in 1-2 weeks. Stage 3

***** Treatment modalities**

Type 1 ROP -Peripheral retinal ablation by laser

Stage 4 or 5 ROP -vitreo-retinal surgical intervention

Retinal detachment - a high risk of irreversible blindness

Stage 4 and Stage 5- vitre-retinal surgery

****Indication for urgent treatment**

Type 1 ROP

- Zone I, any stage ROP with plus disease
- Zone I, stage 3 ROP without plus disease
- Zone II, stage 2 or 3 ROP with plus disease

Aggressive posterior ROP

use phenylephrine 2.5% and tropicamide

0.5% to 1%

Instil 1 drop f Tropicamide every 10-15 minutes for 4 times 1 hr before procedure. before procedure instil phenyepinephrine

Protocol 3: Screening protocol for hearing assessment

Eligible babies:

1. Birth weight <1500 grams
2. Gestation <32weeks
3. Infants with BW of 1500 gm or more OR gestation 32 week or more ***AND***

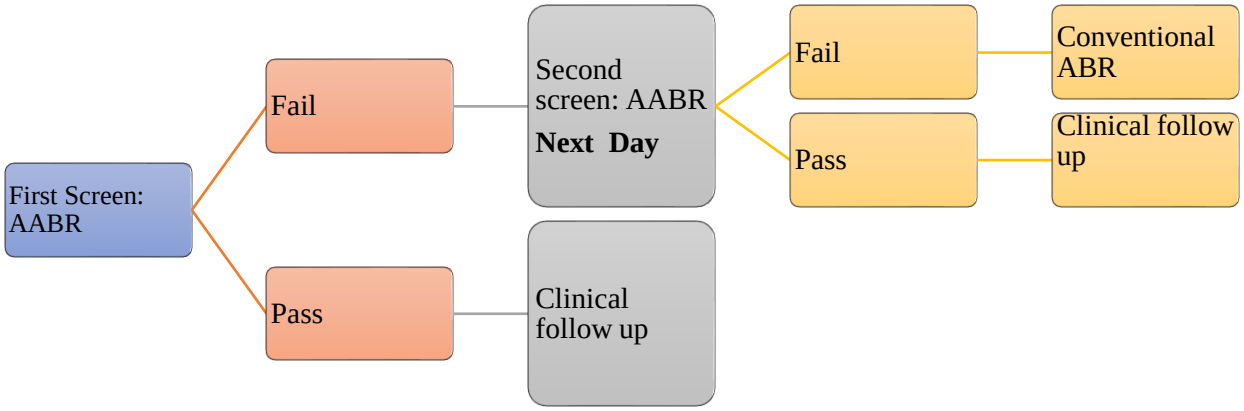
a) Intrauterine growth centile <3rd centile	**b) Symptomatic hypoglycemia**
c) Meningitis	d) Retrovirus positive mother
e) Received mechanical ventilation for 48 hours or more	f) Hyperbilirubinemia requiring exchange transfusion OR Rh isoimmunization/cholestasis
g) Hypoxic ischemic encephalopathy stage 2 or higher	h) Abnormal neurological examination at discharge/seizures
i) Major malformation	j) Major morbidities such as chronic lung disease, IVH hemorrhage Grade III or more (Papile's classification), and periventricular leucomalacia
k) Inborn error of metabolism/chromosomal or genetic disorders/intrauterine infections	

Time of screening:
Within 3-5 days prior to discharge.

Pre-requisites:
Baby should be quiet/ sleeping. (Usually half an hour after feeding)
Ensure outer part of ear canal is patent

Procedure of AABR

1. Switch on the laptop
2. Connect the BERA phone through USB cable
3. Open MBI software in laptop(Saved on desktop)
4. Enter baby details
5. Choose ear
6. Apply jelly on the surface electrodes and place on three points (Mastoid/Ground {in front of ear}/Vertex) on one side
7. Wait for light to blink as green
8. Click “measure”
9. Wait for the result
10. Result displayed as “Pass” or “Refer”
11. Repeat for other ear



Further reading

1. Avery's Diseases of the Newborn10th Edition
2. Rennie & Roberton's Textbook of Neonatology 5th Edition
3. Diseases of the Fetus and Infant. Fanaroff and Martin's Neonatal-Perinatal Medicine, 11th Edition
4. WHO website for reading resources: https://www.who.int/maternal_child_adolescent/newborns/guidelines/en/
5. NNF http://www.nnfi.org/
6. WHO newborn collaborating centre: https://www.newbornwhocc.org/
7. Cloherty Manual of Neonatal Care 8th Edition
8. Nelson Textbook of Pediatrics 21st Edition
9. Facility based newborn care: Training module for doctors and nurses – 2014
10. Echocardiography in the assessment and management of persistent pulmonary hypertension of the newborn. *Pediatr Res* **84,** 68–77 (2018).
11. Sahni M, Jain S Hypotension in Neonates.NeoReviews October 2016, 17 (10) e579-e589
12. Davis AL, Carcillo JA, Aneja RK, Deymann AJ, Lin JC, Nguyen TC et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. Crit Care Med. 2017 Jun;45(6):1061-1093
13. Singh Y, Katheria AC, Vora F. Advances in Diagnosis and Management of Hemodynamic Instability in Neonatal Shock. Front Pediatr. 2018 Jan 19;6:2.
14. Fanaro S. Feeding intolerance in the preterm infant. Early Hum Dev. 2013 Oct;89 Suppl 2:S13-20.
15. Dutta, S., Singh, B., Chessell, L., Wilson, J., Janes, M., McDonald, et al. Guidelines for feeding very low birth weight infants. Nutrients. 2015;7(1):423-442.
16. Kumar RK, Singhal A, Vaidya U, Banerjee S, Anwar F, Rao S. Optimizing Nutrition in Preterm Low Birth Weight Infants-Consensus Summary. *Front Nutr*. 2017;4:20.
17. AAP. Follow-up care of high risk infants. Pediatrics 2004;114:1377– 97

18. Leaf A, Dorling J, Kempley S, McCormick K, Mannix P, Linsell L et al. Early or delayed enteral feeding for pretermgrowth-restricted infants: a randomized trial. Pediatrics. 2012;129:e1260–e1268.
19. Jain S, Mukhopadhyay K, Jain V, Kumar P. Slow versus rapid enteral feed in preterm neonates with antenatalabsent end diastolic flow. J MaternFetal Neonatal Med. 2016;1-24.
20. Subramanian S, Murki S. The feeding conundrum. *Transl Pediatr*. 2017;6(2):86-87.
21. Tewari VV, Dubey SK, Kumar R, Vardhan S, Sreedhar CM, Gupta G. Early versus late enteral feeding in preterm intrauterine growthrestricted neonates with antenatal doppler abnormalities: an open-label randomized trial. J Trop Pediatr. 2018;64:4–14.
22. Aradhya AS, Mukhopadhyay K, Saini SS, Sundaram V, Dutta S, Kumar P. Feed intolerance in preterm neonates with antenatal reverse end diastolic flow (REDF) in umbilical artery: a retrospective cohort study. J Matern Fetal Neonatal Med. 2020 Jun;33(11):1846-1852.