

## Follow up of High Risk Newborns

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### Summary of Recommendations

- All health facilities caring for sick neonates must have a follow up program. It requires establishment of a multidisciplinary team.
- The level of follow up can be based on anticipated severity of risk to neurodevelopment. The frequency of follow up and the type of tests depend on “intensity or level of follow up” assigned. The schedule for follow up must be planned before discharge from birth admission.
- Prior to discharge, a detailed medical and neurological assessment, neurosonogram, ROP screen and hearing screen should be initiated. A psychosocial assessment of the family should also be done.
- The follow up protocol should include assessment of growth, nutrition, development, vision, hearing and neurological status.
- Formal developmental assessment must be performed at least once in the first year and repeated yearly thereafter till six years of life. In Indian context, DASII is the best formal test for developmental assessment (till 2 year 6 months).
- Ideally, the follow up should continue till late adolescence, at least till school as many cognitive problems, learning problems and behavioral problems that are more common in at-risk neonates are apparent only on longer follow up.
- Early intervention programme (early stimulation) must be started in the NICU once the neonate is medically stable.
- Timely specific intervention must be ensured after detection of deviation of neurodevelopment from normal.

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## Introduction

Last two decades have witnessed a steady improvement in the quality of perinatal care in India. In the last 2 decades, the neonatal care has improved and more VLBW and ELBW babies are surviving in our country. (89 % survival of the 14.5 % preterm babies and 70 % survival of 3.4 % VLBW babies, NNPD 2002-3) Close Neonatal - Obstetric collaboration, successful implementation of NALS programs, better understanding of pathophysiology and management of neonatal problems, technological advances in neonatal care and above all the concern of pediatricians to enhance the intact survival of newborn babies have contributed to this increased survival of high risk newborns. These improvements have been most dramatic in infants born ELBW (<1000g) and at extremes of viability (22-25 weeks).<sup>1-3, 5-8</sup> Even though there has been a substantial improvement in neonatal survival, the incidence of chronic morbidities and adverse outcome in survivors continues to be high.<sup>2, 4-7, 9-15</sup> The incidence of severe disabilities like Cerebral palsy has remained quite unrelenting at 4.5-10% over the past two decades.<sup>16</sup> This is also associated with reports of increasingly high incidence of neuro-sensory impairment (blindness and deafness), cognitive, learning disabilities and behavioral problems like ADHD and depression.<sup>16-18</sup> Perinatal risk factors and course of neonatal illness define a group of neonates at increased risk of neurodevelopmental disability. Timely and appropriate intervention can prevent or modify many of these disabilities (example – laser photocoagulation for ROP, timely hearing aid for hearing impaired). There is a lack of knowledge among neonatal specialists, primary health care providers, lack of coordination among health care providers and lack of parent understanding of need for follow up. Structured follow up programme can result in improvement of implementation and compliance of the multidisciplinary follow up.

### Importance of follow up care

*Surveillance:* The mission of a neonatal follow up program is to provide a continuum of specialized care to sick babies discharged from NICUs. The objective is to identify early deviation of growth, development or behavior from normal and provide support and interventions as indicated. The neonate “at-risk” of neurodevelopmental disability must be identified before discharge from birth admission. A discharge summary must be provided to primary care provider and parents, the discharge summary should describe the prenatal and perinatal risk factors, neonate’s hospital course and therapies that can increase the risk of neurodevelopmental disability. (Level 2 evidence).

*Bench marking: Auditing of perinatal care practices:* It is now known that short term outcomes of survival or absence of major anomalies in early infancy are not sufficient to assess efficacy and safety of therapies. Long term follow up will enhance understanding of association between risk factors, therapies and intact survival. There is increasing awareness of the importance of reporting long-term outcomes in RCTs studying interventions and not just survival or short term medical outcomes. There is also an increased recognition of the potential disconnect between perinatal outcomes and long-term outcomes. There is lack of evidence based data on the sequelae of these at - risk newborns and most therapies used in neonatal period.

*Data base helps in anticipatory counseling of parents/ health planning:* In India, we have no systematic database of outcomes of at-risk neonates. The NNPD provides only a database of sick neonates, illnesses and survival. A uniform structure of follow up will go beyond improving care of these at-risk babies, will allow a database that will guide regional and national health care planners. These databases will also allow objective anticipatory guidance of parents based on actual local scenario, rather than information obtained from more equipped and developed world.

**Efforts to improve compliance to follow up programs:** Parents must be informed of the risk factors for neurodevelopmental disability and the need for follow up. Structured follow up programme will result in improvement of implementation and compliance with the multidisciplinary follow up.

- Integrate multi-disciplinary follow up: Assessments at various points are done by a team of Neonatologist/Pediatrician (coordinator), developmental pediatrician / therapist, ophthalmologist, ENT specialist, audiologist, physiotherapist / occupational therapist, pediatric neurologist, clinical psychologist, orthopedician etc. Effort must be made to integrate the developmental follow up with health visit for immunization or routine care. A social worker / a public health nurse must integrate the multidisciplinary team, facilitate parent communication and improve patient confidence. The date of subsequent visits / purpose / place of next visit for developmental assessment must be explained and documented.
- Communication: Address, phone numbers and emails of parents must be recorded and updated. The parents and primary care physicians must be provided contact phone numbers for clarification and emergency.
- Continuity of care must be ensured. The primary care physician must be identified before discharge. He must be communicated regarding the risk factors and follow up plan.

**Recommendations:**

- All health facilities caring for sick neonates (“at-risk” of neurodevelopmental disability) must have a follow up program.
- Make efforts to improve compliance to follow up programs.

**Who needs follow up and assigning the level of follow up?**

The “at –risk” neonates may seem healthy and can be missed on a routine follow up. An active surveillance is necessary, both at **birth admission and in follow up** for pointers to abnormal neurodevelopmental outcome. Timely and appropriate screening or assessment must be offered even before symptoms or signs of disability appear.

1. Identify at-risk infants: The neonate “at-risk” of neurodevelopmental disability must be identified before discharge from birth admission. Prenatal, Perinatal risk factors, course of neonatal illness and therapies identify a group of “at – risk” neonates - at increased risk of neurodevelopmental disability. It is important to prospectively record the risk factors and communicate them to parents and document them in the discharge summary. **Documentation:** discharge summary must have gestation, birth weight, discharge weight and discharge head circumference, feeding method and dietary details, diagnosis (medical problems list), medications and references to other departments, days on oxygen and gestation when baby went off oxygen, date and findings of last hematological assessment, metabolic screen, ROP screen, hearing screen, thyroid screen, ultrasound cranium, immunization status, and assessment of family.
  - A. Biological risk factors Prematurity, Low birth weight, Asphyxia, Shock, Need for ventilation, CLD, Sepsis, Jaundice, PDA, NEC , Malformations
  - B. Interventions – e.g. post natal steroids/ hypocarbia
  - C. Socio – economic

Various risk factors have been identified for adverse developmental outcome in NICU graduates. Biggest factor among them is probably gestational age and birth weight. There has been remarkable improvement in survival of VLBW and ELBW babies,<sup>1,3,7,11,23,24</sup> but this improvement has not been associated with a similar improvement in neurodevelopmental outcome. Hence most centers treat neurodevelopmental outcome as a measure of success and undertake follow up of preterms.<sup>2,4-7,9-15</sup>

Neonatal sepsis is another recognized risk factor for neurodevelopmental impairment (NDI). Stoll et al have described in a large cohort from NICHD Neonatal Research Network that infants with neonatal infections were more likely to have lower mean developmental index (MDI) scores, lower psychomotor development index, visual problems and cerebral palsy.<sup>25</sup> Moreover incidence of CNS damage is present in 20 to 60% cases of neonatal meningitis and incidence of hearing loss is 15% in case of gram negative meningitis while 30% suffer disorder ad developmental delay.<sup>26</sup>

In a meta-analysis of infants with NEC overall, 45% of children who had neonatal NEC were neurodevelopmentally impaired. Infants with NEC were significantly more likely neurodevelopmentally impaired than infants of similar age and gestation who did not develop NEC, including a higher risk of cerebral palsy (1.5 (1.2 to 2.0),  $p = 0.001$ ), visual (2.3 (1.0 to 5.1),  $p = 0.04$ ), cognitive (1.7 (1.4 to 2.2),  $p < 0.0001$ ) and psychomotor impairment (1.7 (1.3 to 2.2),  $p < 0.0001$ ). The odds ratio of neurodevelopmental impairment was also 2.3 times higher in neonates with Bell's stage III disease or requiring surgery ((1.5 to 3.6),  $p = 0.0001$ ).<sup>27</sup> Schulke and colleagues have described that the risk of long-term neurodevelopmental impairment was significantly higher in the presence of at least stage II NEC vs no NEC (odds ratio, 1.82; 95% confidence interval, 1.46-2.27). Significant heterogeneity ( $I^2 = 47.9\%$ ;  $P = .06$ ) between the studies indicated variations in patient, illness, and intervention characteristics and in follow-up methods. Patients with NEC requiring surgery were at higher risk for neurodevelopmental impairment vs those managed medically (odds ratio, 1.99; 95% confidence interval, 1.26-3.14).<sup>28</sup>

Invasive ventilation alone has been described as a risk factor for NDI. Marlow and colleagues who studied neurological and respiratory outcomes at 2 year of age of babies ventilated with either high frequency ventilation (HFOV) or conventional ventilation (CV) found at 24 months of age, severe neurodevelopmental disability was present in 9% and other disabilities in 38% of children, but the prevalence of disability was similar in children who received HFOV or CV (relative risk 0.93; 95% confidence interval 0.74 to 1.16).<sup>29</sup> Infants with BPD-2 were found to have a lower mean developmental quotient (comparison group: 97.4 (15.0) vs BPD-1: 97.9 (11.6) vs BPD-2: 90.7 (19.3)).<sup>30</sup> Teberg et al<sup>31</sup> and Gray and coworkers<sup>32</sup> concluded that VLBW and preterm infants with BPD present a higher risk of neurodevelopmental delay but that risk is associated with neonatal brain lesions and not respiratory problems. Neonatal jaundice associated with prematurity, birth weight < 1000g and bilirubin encephalopathy were likely to have an adverse outcome.<sup>33-35</sup> Also therapeutic interventions like prolonged postnatal steroid therapy to prevent or ameliorate BPD seems to be associated with negative CNS outcomes.<sup>36,37-39</sup>

### ***Recommendations for at risk newborn follow up :***

Social class also has a role to play. In a review of social class and developmental outcomes in 37 studies conducted in 2000,<sup>40</sup> low social class as determined by several different means, was associated with poorer growth, greater academic difficulties including reading and spelling problems, lower IQ, poorer language skills, poorer fine motor skills, more aggression and externalizing behavior, more depression and other psychiatric disorders, poorer sibling relationships, and poorer social development<sup>40</sup>. Accordingly

these risk factors can be broadly classified into biological risk, interventions and social/environmental risk<sup>41</sup>.

The frequency of follow up and the type of tests used would depend on “intensity or level of follow up” assigned. Determinants of level of follow up include – severity of perinatal risk factors, interventions required at birth admission to NICU, demographic factors of the family, and resources of the follow up service.

**High Risk:**

1. Babies with <1000g birth weight and/or gestation <28 weeks
2. Major morbidities such as chronic lung disease, intraventricular hemorrhage, and periventricular leucomalacia
3. Perinatal asphyxia - Apgar score 3 or less at 5 min and/or hypoxic ischemic encephalopathy
4. Surgical conditions like Diaphragmatic hernia, Tracheo-oesophageal fistula
5. Small for date (<3<sup>rd</sup> centile) and large for date (>97<sup>th</sup> centile)
6. Mechanical ventilation for more than 24 hours
7. Persistent prolonged hypoglycemia and hypocalcemia
8. Seizures
9. meningitis
10. Shock requiring inotropic/vasopressor support
11. Infants born to HIV-positive mothers
12. Twin to twin transfusion
13. Neonatal bilirubin encephalopathy
14. Major malformations
15. Inborn errors of metabolism / other genetic disorders
16. Abnormal neurological examination at discharge

**Moderate Risk:**

1. Babies with weight – 1000 g- 1500g or gestation < 33 weeks
2. Twins/triplets
3. Moderate Neonatal HIE
4. Hypoglycemia, Blood sugar<25 m/dl
5. Neonatal sepsis
6. Hyperbilirubinemia > 20mg/dL or requirement of exchange transfusion
7. IVH grade 2
8. Suboptimal home environment

**Mild Risk:**

1. preterm, Weight 1500 g - 2500g
2. HIE grade I
3. Transient hypoglycemia
4. Suspect sepsis
5. Neonatal jaundice needing PT
6. IVH grade 1

**Risk factors for NDD - Assign the baby to the highest level indicated by risk**

<b>Mild risk for NDD</b>	<b>Moderate risk for NDD</b>	<b>High-risk for NDD</b>
Prenatal risk factors	Abnormal Fetal growth	Fetal distress
≥37 weeks	33 – 36	< 33 weeks
>2500 gms	1500 - 2500	<1500 grams
Booked pregnancy / intramural baby	Sub optimal perinatal care	Sub optimal transport (extramural)
Completed course of ANS	Incomplete course of ANS	No ANS
No need for resuscitation	Need for resuscitation at birth	APGAR < 3 at 5 min Encephalopathy, Multi-organ injury
Levene grade 1	Levene grade 2	Levene grade 3
Not required ventilation	Uncomplicated course of ventilation	Ventilation more than 7 days, Hypocarbica, Pneumothorax Apnoea requiring resuscitation
No shock	Shock	Refractory shock Hemodynamically significant PDA
Transient hypoglycemia	Hypoglycemia, blood sugar < 25 mg / dL, > 3 days	Symptomatic hypoglycemia, seizure
Suspect sepsis (screen negative)	Sepsis (culture +ve / clinical and screen +ve)	Meningitis
Neonatal jaundice needing phototherapy	Neonatal jaundice leading to Exchange transfusion	Kernicterus
NICU admission	(Complex course – NEC & PDA (needing surgery)	CLD
Preterm IVH grade 1 or 2 , no abnormality at 40 wks	Intra-Ventricular Hemorrhage (IVH) > grade 2 on Neurosonogram	Ventriculomegaly and / or cystic periventricular leukomalacia (at 40 weeks), hydrocephalus
Normal neurologic exam at discharge	Severe / prolonged encephalopathy Any cause	Abnormal neurologic examination at discharge / Suspect development
Good home environment + optimal follow up	Sub-optimal Home Environment (Parent coping poor/ low socio-economic)	Parent concern for NDD

## Where should the baby be followed up and who should do the follow-up?

Place of follow up should be easily accessible to the parents and the directions to the place should be mentioned in the discharge card. Low risk infants can be followed up at a well baby clinic. Moderate and High risk infants should be followed up in or near to a facility providing Level II and Level III NICU care respectively due to multidisciplinary approach required and increased frequency of ongoing illness in these cohorts.

A comprehensive follow up program requires a multi disciplinary approach involving a team of experts who include a pediatrician, a child psychologist, pediatric neurologist, ophthalmologist, audiologist, occupational therapist, social worker and a dietician all under one roof.

1. Low risk: follow up with pediatrician / primary care provider with objective to screen for deviation in growth and development.
2. Moderate risk: follow up with neonatologist and developmental pediatrician: screen for developmental delay, manage intercurrent illnesses
  - Developmental pediatrician
  - Developmental therapist
  - Radiologist
  - Ophthalmologist
  - Audiologist
  - Physiotherapist
  - Social worker
  - Dietician
3. For babies with high risk of Neurodevelopmental delay: Neonatologist: supervise and screen for developmental delay

Team as for Moderate risk and

- Pediatric neurologist
- Geneticist
- Occupational therapist
- Speech therapist
- Endocrinologist
- Pediatric surgeon
- Orthopedician

### **Recommendations:**

- A discharge summary must be provided to primary care provider and parents, the discharge summary should describe the prenatal and perinatal risk factors, neonate's hospital course and (and therapies) that can increase the risk of neurodevelopmental disability. (level 2 evidence)

- The frequency of follow up and the type of tests used would depend on “intensity or level of follow up” assigned. Determinants of level of follow up – severity of perinatal risk factors, interventions required at birth admission to NICU, demographic factors of the family, and resources of the follow up service.

**Active surveillance is required before discharge from NICU and in follow up.**

**Pre-discharge**

- A) Medical examination
- B) Neurobehavior and Neurological examination
- C) Neuroimaging
- D) ROP screening
- E) Hearing screening
- F) Screening for congenital hypothyroidism
- G) Screening for metabolic disorders
- H) Assessment of parent coping and developmental environment

**Follow up**

- I) Medical examination - nutrition and growth, Immunization
- J) Neurological examination
- K) Development assessment
- L) Ophthalmologic assessment – squint and refraction
- M) Hearing and Language and speech
- N) Function
- O) Behavioral, cognitive and intelligence status

**Recommendations:**

- An active surveillance is necessary, both **Pre-discharge and in follow up** for pointers to abnormal neurodevelopmental outcome.
- The schedule for follow up must be planned before discharge from birth admission. The “at-risk” neonates must be followed till at least one year age (follow up into school years is desirable)

**Medical examination** – physical examination, nutrition and growth, Immunization, unresolved medical issues, laboratory tests (Hemoglobin, Calcium, Phosphate, Alkaline phosphate)

**Head circumference (OFC)**

- Head circumference (OFC) is the most important and simple tool that can predict abnormal brain growth. (level 2)
  - OFC centile < (microcephaly) / > length centile (hydrocephalus)
  - Static / dropping centile of OFC in relation to length centile on serial follow up



- Growth – weight and length plotted on growth chart and compare centiles
  - Birth weight and discharge weight must be compared. Weight centile must be interpreted against length centile.
  - Poor growth may be a pointer to medical problems (can affect Neuro – development)
  - Poor growth is also often seen in babies with NDD (as the feeding is not optimal)
- A complete physical examination must look for common anticipated medical problems some of which may have impact on developmental outcomes – e.g hip examination, dysmorphism, signs of IU infections, neuro-cutaneous markers etc.
  - Hip examination – risk group – breech, oligohydramnios, and girl, family h/o DDH – look for asymmetry
- In preterm babies use special growth chart for preterm babies/ corrected age after the baby is “term”
- Unresolved medical problems must be addressed and medications reviewed
  - Chronic lung disease
  - Gastro-esophageal reflux disease
  - Reactive airway disease

### **Neurobehavioral and Neurological examination**

Neurobehavioral assessment and neonatal neurological examination must form a part of routine clinical examination of a newborn infant. When carefully performed, it is of great value in predicting subsequent abnormality. Several tools have been found effective—Hammersmith neonatal neurological screener, neurodevelopmental risk examination, Amiel-Tison—all examine different domains eg. tone, reflexes, sensory and behavioral responses. They are useful predictors of neurodevelopmental disability on follow up.

### **Neurobehavioral assessment**

Although predictive power of isolated neurological signs is not great, certain abnormal findings are associated with greater frequency with abnormal outcomes. In a large population study, as a part of the Collaborative perinatal project of NIH, when infants who developed cerebral palsy (mostly term) were compared with those who did not, certain neurological abnormalities were valuable predictors.

<b>Neurological signs in neonate (mostly term)</b>	<b>Increased risk of CP</b>
Abnormal Tone – limb, neck, trunk	12-15 fold
Diminished cry for > one day	21 fold
Weak or absent suck	14 fold
Need for gavage or tube feeding	16-22 fold
Diminished activity > one day	19 fold

Similarly, severity of neonatal neurological insult in neonatal period is a predictor of abnormal outcome. Perinatal asphyxia - Levene’s modification of Sarnat & Sarnat score.

<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>
No seizure	Seizure	Prolonged seizure
Irritable	Lethargy	Comatose
Hypotonia mild	Marked tone abn	Severe hypotonia
Poor sucking	Requires Tube feed	Needs ventilation*

\* Fails to maintain spontaneous respiration

In preterm babies - NAPI (neurobehavioral assessment of preterm infants)- It can be used for babies between 32 weeks gestation and term.

Requires training, it includes assessment of

- Motor development & vigor
- Scarf sign
- Popliteal angle
- Alertness & orientation
- Irritability
- Vigor and crying
- Percentage sleep ratings

Also score rating scales for quality of spontaneous movements, crying and visual behavior.

VLBW and ELBW babies, who had CP, had low scores of NAPI.

### **Neurological examination**

**Hammersmith neonatal neurological examination** (screening) is a simple test. It is best used for evaluation of term born “normal” neonates in maternity ward/ first follow-up in a busy follow up clinic. If two items are in “blocked/ shaded area, the neonate should have a detailed assessment.

The full Hammersmith test evaluates a baby in following areas-

- Posture and tone
- Tone patterns
- Reflexes
- Movements
- Abnormal signs or patterns
- Orientation / behavior

An optimality score is generated in the full test. It is mostly used as a research tool.

### **Neuroimaging – USG/CT/MRI**

Neuroimaging is a very important complement to clinical assessment in the management of preterm and term neonates with encephalopathy. It serves 2 purposes (1) diagnosis of brain pathology for appropriate immediate management and (2) detection of those lesions which are associated with long term neurodevelopmental disability. Problems associated with imaging are the choice of right technique, timing, risk of radiation, need for sophisticated machines and trained manpower etc. Many of these babies are quite often sick and testing outside the NICU may not be possible. The growing brain differs in maturity and interpretation of MRI / ultrasound images requires a sound knowledge of “normal” at various gestations and postnatal ages.

Currently the most widely used and available modalities are

1. Ultrasound
2. CT Scan
3. MRI

### ***Recommendations:***

- All preterm babies born before 32 weeks and < 1500 grams birth weight must undergo screening neurosonograms at 1-2 weeks and 36 – 40 weeks corrected age.
  - Ultrasounds may be performed more often if the preterm baby has a catastrophic event like seizure, frequent apnea that may reflect IVH.

- With limited facility available, it is advisable to have at least one ultrasound at ~ 40 wks of gestation in preterm babies.
- Babies with ventriculomegaly and cystic PVL have a very high incidence of cerebral palsy as compared to those with a normal neurosonogram. The sonographic assessment of brain injury is a better predictor of neuromotor outcome than gestation and perinatal risk factors.
- MRI is more sensitive in detection of preterm brain injury, but, ultrasound has similar specificity in detection of severe lesions (ventriculomegaly, cystic PVL and grade 3, 4 IVH).
- Encephalopathy in term born babies
  - Suspected hemorrhagic encephalopathy – pallor, raised anterior fontanel, history of birth trauma – CT scan is the preferred imaging modality. CT is better in detection of intracranial calcifications.
  - MRI is the diagnostic imaging modality in all babies with encephalopathy if ICH is not suspected.

Limitations – USG is operator dependant, CT has risk of radiation exposure and MRI requires sedation and monitoring is not possible during the procedure unless monitors that are MRI compatible are available.

## Follow up protocol

Schedule for follow up of infants is driven by several factors such as developmental milestones at a given age, availability and applicability of appropriate test instruments at specific ages, and cost and feasibility of follow up of a cohort of patients.

Initial weekly examination is done to ascertain whether the infant has settled in the home environment and if he is gaining weight or not. The neuromotor examination at discharge and at 1 and 3 months of age has been used to predict CP at 1 year of age.<sup>44</sup> At 12 months of Corrected age, environmental factors are less influential and a broad range of cognitive and behavioral processes can be assessed. Neuro assessment at 12 months can be used to predict cognitive performance at 36 months.<sup>45</sup> Indices of neurodevelopment in infants and toddlers are less stable over time and, at least before 24 months, lack substantial predictive validity for later morbidity. This is partly because of the means by which infants are able to express their cognitive abilities (i.e., primarily through sensorimotor acts) and the lack of continuity in response modalities from infancy to older childhood and adolescence.<sup>46</sup> By 24 months of age, environmental factors begin to exert influence on the test results and there is improved prediction to early school performance. At 3-4 years intelligence can be assessed and later IQ scores predicted. School achievement can be assessed at 6 years and IQ, neurophysiological functions and school performance at 8 years.<sup>47</sup>

## Medical follow up

### A. Growth and Nutrition

*Growth:* It is a well established fact that preterm very low birth weight babies grow poorly in postnatal period. During postnatal life though the target growth is to achieve intrauterine growth rate as well as to maintain fetal body composition, however in reality they grow very poorly due to several factors like sickness and inadequate nutrition which contribute to their poor growth. According to NICHD reports,<sup>8</sup> 97% of all VLBW babies and 99% of ELBW babies had weights <10<sup>th</sup> centile at 36 weeks PMA. These babies subsequently also continue to grow poorly throughout childhood. This growth restriction is believed to persist in adult life as shown by some researchers and they<sup>55</sup> found VLBW infants are twice as

likely to have a height less than 3<sup>rd</sup> centile at 20 years of age than that of normal birth weight controls. Hence there is a need for early and aggressive nutrition policy to prevent significant catabolic losses and early catch up growth.

Data regarding post discharge growth of VLBW infants scanty in our country. In our follow up study (abstract presented in Pedicon 2008)<sup>56</sup> we found the similar trend of growth failure till corrected age (CA) of 1 yr. At 40 wks CA, 85% VLBW babies were less than <10<sup>th</sup> centile. They showed some catch up growth by 6 months but again by CA 1 year 78% were <10<sup>th</sup> centile probably due to delayed weaning.

The growth failure is more marked in SGA babies as described in various studies. A report from Hongkong<sup>57</sup> observed in a cohort of their LBW (<2500 g) babies that one third of their babies were SGA who were term or near term. At 6-12 months, 33-35% babies were still short as compared to 7-12% of AGA babies. Probably this reflects poor fetal growth has a long term impact on long term growth potential.

The standard anthropometric measurements which are followed in routine practice are as follows

- Weight
- Length
- Head circumference

Other anthropometric measurements which are mostly used for research purposes are

- Mid arm circumference
- Triceps skin fold thickness
- Weight for length ratio
- Growth velocity
- Energy intake and energy expenditure
- Bone density

*Which chart to follow?*

There is controversy about which chart to use in the neonatal period as both have merits and demerits.

- Intrauterine growth chart or
- Postnatal growth chart

The IU growth charts are based on reference fetal growth.<sup>58</sup> However this can not be used as these data based on a small sample and based on chemical composition and the optimal weight gain was calculated based on body weight obtained at different gestations. Though the actual measurement of body composition would give an accurate assessment of optimal growth but a large number of fetuses to be studied for this and practically it will be difficult.

There are several other intrauterine growth charts.<sup>59,60,61</sup> Though currently they are taken as gold standards for ideal postnatal growth but it does not take into account of postnatal weight loss, sickness and

metabolic losses. In addition many of these growth charts are from US and Canada and there is a need for developing our own chart which should be multicentric by keeping in mind the wide variation in ethnicity and in babies who are born to mothers with no antenatal problem and from upper socio economic status.

Though intrauterine growth standards are still the gold standard but one needs to keep in mind that weight gain is not the only criteria but the body composition is important consideration to prevent metabolic syndromes in later life. It has been found that aggressive nutrition does improve the nutrition status but it is not clear whether it will have any adverse metabolic effect in later life or not.

Due to above problems with IU growth chart, some like to use postnatal growth charts which represent the longitudinal growth of VLBW neonates. The advantages of these charts are that they take into account the postnatal weight loss. However, the disadvantages are that postnatal illness are not uniform and policies of nutrition are very variable and also one needs to take into account the intrauterine growth status and multiple gestations while developing such charts. There are several postnatal growth charts which have been developed in last 2-3 decades.

#### *Which postnatal chart to follow?*

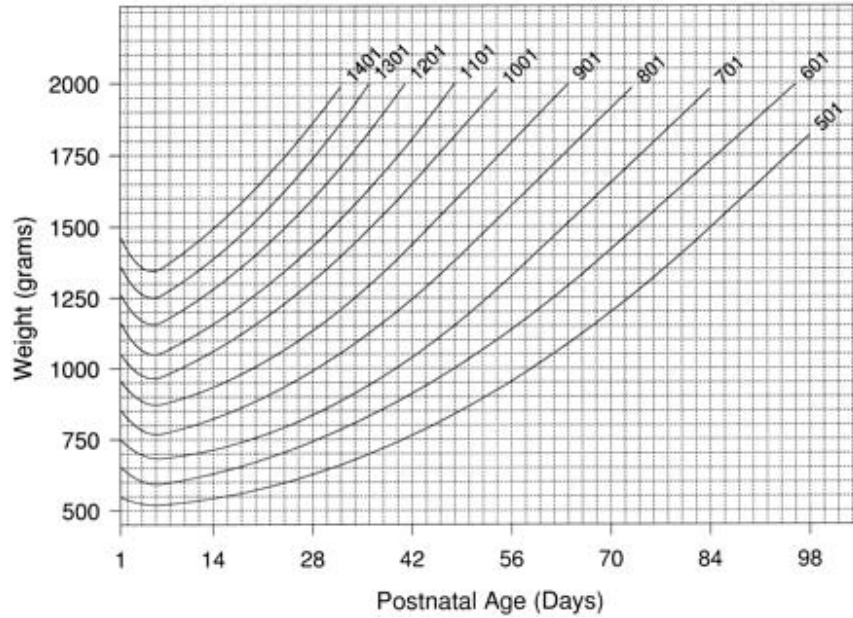
There are several postnatal growth charts with relative merits and demerits.<sup>62,63</sup> We propose to use either Kelly-Wright chart<sup>62</sup> or NICHD growth chart.<sup>63</sup> Kelly Wright's chart involves all 3-parameters (weight, length and HC) and up to 105 postnatal days but it gives data only for singleton AGA babies, where as NICHD growth chart includes SGA babies and well and sick babies as well. After 40 weeks, one can use CDC growth charts. However in CDC charts, VLBW babies were not included and as is known that VLBW babies grow differently than normal birth weight babies, to develop a new reference to compare the growth of VLBW babies is the need of the hour, specially in our country due to our genetic and environmental differences from that of western countries. CDC charts can be used throughout childhood and the growth status percentiles and/or Z scores are easily available on the CDC website. ([www.cdc.gov/growthcharts](http://www.cdc.gov/growthcharts))

There is a new growth chart (Fenton TR. A new growth chart for preterm babies: Babson and Brenda's chart updated with recent data and a new format. BMC Central 2003; 3: 13) which is an updated version of original Babson and Brenda's chart, beginning at 22 weeks upto 50 weeks which is based on a meta analysis of published reference studies though like other graphs the validity is limited by the heterogeneity of the data sources. For post 40 weeks section, CDC growth chart was used.

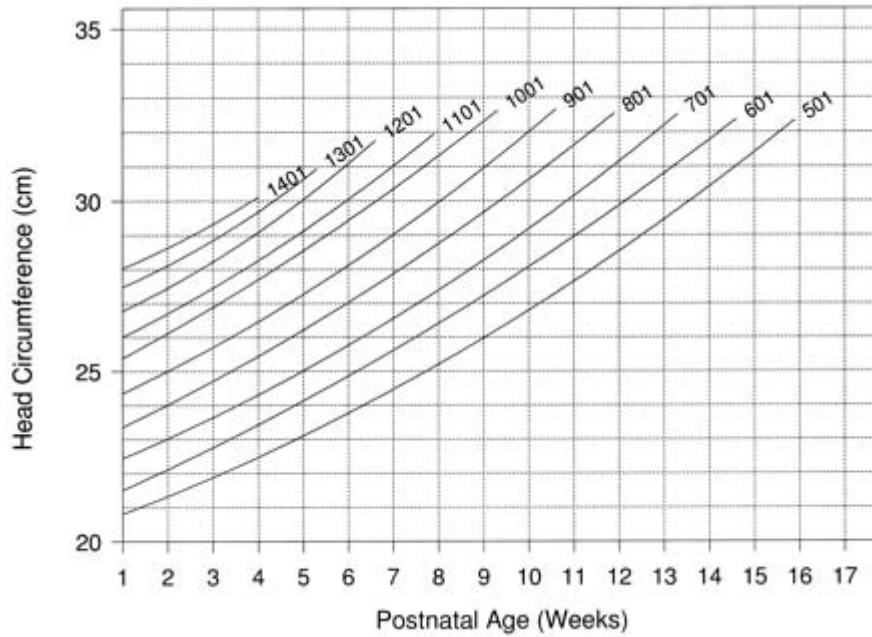
#### ***Recommendations***

- Use a standard Intrauterine growth chart to plot centiles for weight, length and HC
- Follow with an appropriate postnatal growth chart

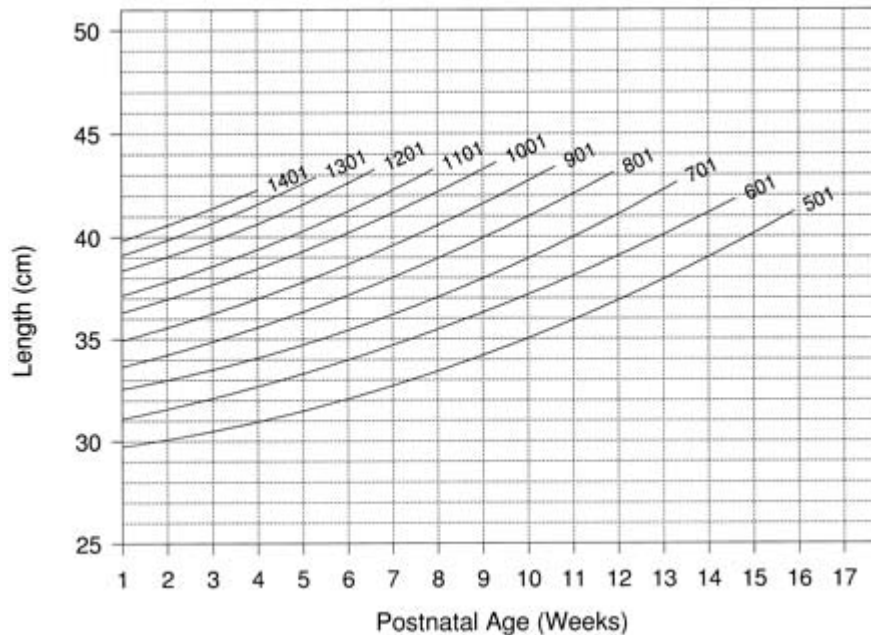
**Growth charts for VLBW (Ehrenkranz)**



**Average daily body weight versus postnatal age in days for infants**



**Average weekly head circumference versus postnatal age in weeks**



**Average weekly length versus postnatal age in weeks for infants**

**Recommendations:**

- OFC must be recorded and plotted serially every health visit till two years age. (Level 2 evidence)  
It must be assessed in context of length of the baby.
- Weight and length must be plotted at every health visit till 6 years of age. (Level 3 evidence)

**Nutrition**

**Post discharge nutrition**

Though the in hospital growth affects significantly the nutritional status at discharge, post discharge feeding and nutrition issues have not been researched as much as pre-discharge nutrition issues. The conventional diet after discharge has been unfortified human milk or term formula once the baby reached 2 -2.5 kg however from mid 90's the issues regarding post discharge nutrition has gained lot of attention due to significant growth failure during follow up.

**Human milk fortifier:** As evident from the previous data that preterms and VLBW babies continue to grow poorly, post discharge nutrition remains a major issue during follow up. Fortification of human milk remains debatable after discharge. Because of their poor postnatal growth there is a need for continuation of higher energy intakes. Though post discharge enriched formulas are available for formula fed babies, there are no reference data available for breast fed babies after discharge. On one hand premature babies



may be unable to take breast feed ad libitum to maintain growth and on the other side for a fully breast fed baby; it is a difficult proposition to express the milk and add fortifiers. Some studies have reported un-supplemented human milk feeding after discharge resulted in slower accretion of both radius and whole body bone mass compared with infants fed standard formula.<sup>64,65</sup> The risk of continued fortification is that concentration of nutrients may be excess when the baby reaches corrected age term and beyond. The post discharge follow up of premature babies found no differences in growth either during their first year or at 8 years (both remaining below 50th centile) whether fed human milk or term formula. Thus close observation is mandatory for the babies who show poor growth on full breast feeds or have biochemical abnormalities in the form of low levels of blood urea nitrogen, albumin, phosphorus and high alkaline phosphatase. This group forms a special at risk group and may need some fortification or extra mineral supplements. Deficiencies have been described with nutrients like Vitamin A, E, D, Iron, Zinc, Copper etc and most of these needs to be supplemented in preterm diet either by fortification or using preterm formula as they are deficient in preterm mature milk.

The most extensively studied metabolic deficiency state is osteopenia of prematurity which manifests after 6 -8 wks of life due to poor bone mineralization arising due to deficiency of calcium and phosphate and sometimes due to vitamin D deficiency in the diet of a VLBW and ELBW infants.<sup>66</sup> Mineral fortified diet and adequate vitamin D intake can help to minimize this complication. The preterm babies are also at risk of developing late hyponatremia due to massive sodium (Na) loss in the urine due to tubular immaturity. Preterms babies may need extra Na supplements during the growing phase. By 34 weeks nephrogenesis is complete and tubules become more mature and hence the Na loss continues to decrease and by the time the baby is discharged, hyponatremia gets corrected. Iron supplementation should be started by 4-6 weeks of postnatal life and continued till 1-2 years. Recommended dose is 3 mg/kg per day of elemental iron.

**Supplementary feeding of preterm neonates:** There are no standard guidelines regarding age of starting supplementary feeding in preterm babies. In general it is decided by readiness of eating semisolids by these babies. Some prefer to start it by corrected age of 4 months however one should not be in a hurry of starting semisolids too early as it can compromise weight gain.

***Recommendation:***

- Ensure adequate postnatal nutrition.
- Ensure adequate vitamin, minerals and Iron supplementation
- Start supplementary feeding as per baby's readiness

## **B. Immunization**

The preterm/VLBW babies should be immunized according to chronological age and as per guidelines for full term newborns. For Hepatitis B, one should wait till the baby is 2000 g.<sup>107</sup>

**Combined follow up and immunization schedule**

Age / Date	Immunization	Given	Dev test	Interpretation
Hep B at birth (if mothers status is HBSAg positive or unknown)				
HBIG at birth if mother HBSAg +ve				
1 – 2 week after discharge	BCG after 34 weeks corrected age OPV		Medical exam including growth Neuro behavior Neonatal neuroexam OAE (if not done before) /BERA ROP follow up if not completed	
2 months	DTaP / DTP HIB hep B OPV / IPV PCV		OAE (if not done before)  Medical exam including growth  Neurological exam  <ul style="list-style-type: none"> <li>• Hammersmith</li> <li>• Amiel tison</li> </ul> Development test  <ul style="list-style-type: none"> <li>• TDSC / CDC grading</li> <li>• DDST</li> <li>• DASII</li> </ul>	
4 months	DTaP / DTP HIB hep B OPV / IPV PCV			
6 months	DTaP / DTP HIB hep B OPV / IPV PCV			
9 months	Measles			
12 months				
15 months	MMR			
18 months	DTaP / DTP HIB OPV / IPV PCV			
Yearly till 5 years				
Adolescence				
Adult				

**Medical examination**

Date / age				
Urine stream - boys				
Murmur				
Hepatosplenomegaly				
GERD				
HRAD				
Hernia: Umbilical/ Inguinal				
Hemangioma				
Undescended testis				
Hb				
Iron				
Ca / P / ALP				
Calcium supplement				
Multivitamin supplement / HMF				
Change from LBW to term formula (if not exclusively breast fed)				
Unsorted medical problems				
Medications				
Squint / refraction				

An assessment of refraction and examination for squint, other visual problems must be performed at least at 1 year and yearly thereafter till school age (5 years). Squint and refraction: test at 9 mo – 1year age for babies born at 32 weeks or less.

**Neurological examination**

The neurological examination of infant, toddler and child is an integral part of follow up care. Infants with mild or moderate abnormalities may improve with time. This is known as transient neuromotor dysfunction and in growing brain with plasticity, many infants become normal. The infants with severe early neurologic dysfunction is unlikely to make complete recovery and likely to have worst neurodevelopmental outcome.<sup>72</sup>

**Amiel Tison Scale**<sup>73</sup>

Evaluation of the tone is a fundamental part of this assessment. There is a definite pattern of development of tone in neonates which is gestation dependent which needs to be considered while assessing tone. From 28 to 40 weeks the acquisition of muscle tone and motor function proceeds in a caudo-cephalic direction. After 40 weeks, the process is reversed, so that relaxation and motor control proceed downward for the next 12-18 months. (cephalocaudal)

The assessment is done under the following headings:

1. Neuromotor
  - Tone in upper limb , lower limb and axial
2. Neurosensory
  - Hearing and vision
3. Neurobehavioural
  - Arousal pattern, quality of cry, suckling , swallowing
4. Head growth
  - Head circumference and also skull for sutures, size of anterior fontanel

Following parameters are recorded for evaluation of tone

1. Spontaneous posture
2. Passive tone
3. Active tone

*Spontaneous posture* is evaluated by inspecting the child while he or she lies quiet

*Passive tone* is evaluated by measuring the angles at extremities. The resistance of the extremity to these maneuvers is measured as angle as given below

Adductor and Popliteal angles are best studied. Adductor and popliteal angle measured with a goniometer.

<b>Months</b>	<b>3</b>	<b>6</b>	<b>9</b>	<b>12</b>
<b>Adductor angle</b>	40-80	70-110	100-140	130-150
<b>Popliteal angle</b>	80-100	90-120	110-160	150-170

Test schedule - 3, 6, 9, 12 months

Tone abnormalities

- Normal tone
- Hypotonia (mild / severe)
- Hypertonia (mild / severe)

a. Pattern of tone abnormalities

- Diplegia
- Hemiplegia
- Differential extensor tone against flexor tone

**Look for asymmetry**

- Assessment of Passive tone (Amiel Tison) in the first year of life is a useful tool in early detection of motor developmental disability. (comparable to BSID at 3, 6, 9 months).

**Word of caution** – it has been seen that, tight angles at 4 months (<2000 gm birth weight) do not always predict abnormal outcome, many of which become normal, where as persisting hypertonia at 8-12 months is associated with poor outcomes.

*Active tone* is assessed with the infant moving spontaneously in response to a given stimulus.

- *For extremities it is assessed by looking at posture resting and posture recoil and for the axial tone (neck and trunk tone), it is assessed by response to pull to sit or pull to stand.*
- In addition deep tendon reflexes, abnormal persistence of primitive reflexes, like ATNR, fisting and cortical thumb are also recorded.
- Amiel –Tison scale is a good screening test for neuromotor assessment, the predictive value at 3 months examination for normal outcome at 12 months is 93%. The main draw back of using this solely is that this scale does not take into account the mental development. Hence one still needs to do a formal development tests as developmental delay can be present in a baby with normal neurological examination.

a. Primitive reflexes at 3 months

- Palmar grasp
- Automatic walking
- Moro reflex
- Asymmetric tonic neck reflex

All disappear by 3 months in Indian infants

Primitive reflexes are difficult to interpret even by experts. In infants with diffuse bilateral cerebral injuries, stronger, sustained reflexes with no signs of habituation (stereotyped, not decreasing with repeated elicitation) are obtained.

b. Postural reflexes at 9 months

- Parachute
- Lateral propping

Postural reactions are relatively easier to interpret, and a slow appearance indicates delay in acquiring postures and hence, CNS injury. Vojta's system of kinesiological diagnosis (based on the evaluation of 7 postural reactions) enables one to identify infants at risk for neurodevelopment delay as early as 3 months of age with 100 % accuracy when 3 reactions were abnormal.

***Recommendations:***

A structured, age-appropriate Neuro-motor assessment should be performed by corrected age at least once during the first 6 months, once during the second six months, and once yearly.

- Assessment of neurobehavior in neonatal period may have great predictive value and can guide further imaging, intervention planning.
- Neurological Assessment by Amiel –Tison scale, Hammersmith neonatal / infant neurological examination at discharge and periodically as indicated
- Assessment of severity of disability (function) by GMFCS at 2 years

**Developmental assessment**

Each baby follows his or her own schedule of development (acquiring skills) within fairly broad limits of age. Development assessment in infancy is not a predictor of intelligence and has limited ability in predicting eventual normal neurodevelopment. Deviations from normal identify an at-risk group of babies/ children who may require further evaluation and intervention. Developmental tests must be performed in conjunction with medical examination to identify the cause of deviation and plan the interventions. The interpretation of the developmental test must be discussed with parents.

**General principles**

Parental concerns regarding development must be recorded and respected. Development may be assessed by

- Developmental history (assessment by report)
- Direct observations and interaction with examiner - Administration of specific tests

Factors that may affect development

Prematurity - **How long to use corrected age (CA)?**

Though there is controversy about how long to use CA most of the researchers correct completely for prematurity up to 2-3 years for neuro developmental assessment.

- Assess child's environment and developmentally relevant stimulation
- Medical illness that may interfere with normal development

**Developmental Tests:** Various development scales which are used commonly are

1. DOC with CDC grading
2. Trivandrum Developmental Screening Chart (TDSC)
3. Denver Development Screening Test (DDST) / Denver II
4. Development Assessment scale for Indian Infants (DASII)

Babies at mild / no risk may be followed by primary care physician in the clinic along with well baby care / immunization visits

- Development observation card
- Trivandrum development screening chart

Development observation card (DOC) (with CDC grading)

**DOC is a self-explanatory card that can be used by parents. Four screening milestones**

- Social Smile by 2 months
- Head holding by 4 months
- Sit alone by 8 months
- Stand-alone by 12 months
- Make sure the baby can see, hear and listen

Further grading of each milestone helps in defining stage of development accurately.

*Trivandrum development screening chart (TDSC)*

TDSC is a simple screening test. There are 17 items taken from Bayley Scale of Infant development. The test can be used for children 0-2 years age. No kit is required. Anybody, including an Anganwadi worker can administer the test. Place a scale against age line; the child should pass the item on the left of the age-line. Currently TDSC is being validated for children till 6 years of age.

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**For at- risk babies (moderate / severe)**

A multidimensional development-screening test (Denver development screening test (DDST / Denver II) should be documented using standardized instruments (LOE 3)

- At least once during first 6 months
- At least once during next 6 months
- Once every year till 5 years.

A formal developmental evaluation Development assessment scale for Indian infants –DASII and diagnostic work up and intervention should be performed within 2 months of parental concern / abnormal screening test for development / once every year in babies at moderate – high risk of disability

*Denver development screening test (DDST)*

The Denver Developmental Screening Test is a simple, clinically useful tool for early detection of **children with serious developmental delays**. The test is best used for apparently normal children (asymptomatic, but, having perinatal risk factors), confirming suspicions with objective tool and in monitoring children with developmental problems, serially. The test compares the index child against children of similar age. The test is **not designed to derive a developmental or mental age**, nor a development or intelligence quotient; it is to be **used only to alert professional child workers to the possibility of developmental delays** so that appropriate diagnostic studies may be pursued. The parents should be informed that **DDST is not an IQ test but a developmental screening device to obtain an estimate of the child's level of development**.

DDST has 4 sectors – gross motor, fine motor, language and social. All 4 are to be treated as independent tests and interpreted separately. This allows diagnosis of the probable differential diagnosis of developmental disability.

The test has been developed for use by people who are not trained in psychological testing.

***Recommendations:***

- In settings where formal developmental tests cannot be performed or in mild/ moderate risk neonates, a multi-dimensional screening test for development must be performed at 0- 6 months age, preferably 4 months corrected age between 6-12 months preferably 8 months corrected age and yearly thereafter till at least 6 years age. DDST is a simple screening test. CDC grading is a test validated on Indian population.
- In case a development screening test is abnormal or in case of parental concern, a formal test for development assessment must be performed within 2 months.
- Formal development assessment must be performed at least once in the first year and repeated yearly thereafter till six years of life. In Indian context, DASII is the best formal test for development assessment (below 30 months).



### **Squint and refraction assessment**

By 9-12 months age, irrespective of ROP.

### **Language and speech assessment**

Babies with risk factors for hearing loss, who have passed the newborn hearing test, must have a repeat diagnostic hearing test at 12 months age- retesting of hearing by behavioral audiometry at 1 year. Comprehensive assessment of speech and language must be done between one and two years age using Language Evaluation Scale Trivandrum (0-3). Reference TEENS. Adequate receptive and expressive language is fundamental for communication, adaptive behavior, academic success and literacy. Assessment is not easy as different skills emerge at different ages. For complete assessment of language, both receptive and expressive language as well as organization and grammars are required. Various test batteries are available to test the above parameters.

#### ***Recommendation:***

Language assessment at 9 months and 18 months using LEST (0-3)

### **Gross motor functioning**

Gross motor function is an important adjunct to the neurologic assessment. A gross motor functional classification scale<sup>74</sup> (GMFCS) is used in many western centers. This scale can be used from 18 months and up to 12 years and this scale contains a scoring system for gross motor skill levels by direct observation. It has 5 levels, starting from normal category to severe disability and this way it not only reports rate of CP but also severity of CP.

### **How long to follow up?**

Most follow up studies follow the infant for a short term (18-24 months). The problems with longer follow up are challenges of cost, tracking, and feasibility. But there is now increasing evidence of adverse outcomes into school age and adolescence.<sup>48-49</sup> Currently, in India there is no standardized guideline for follow up services for high risk infants.

A recent meta analysis<sup>98</sup> reported that very preterm and/or VLBW children have moderate to severe deficits in academic achievement, attention problems, and internalizing behavioral problems and poor executive function and all these adverse effects were strongly correlated with their maturity at birth. During transition to young adulthood these children continue to lag behind term born peers.

Ensure follow up till late adolescence, at least till school. Many cognitive problems, learning problems, behavioral problems that are commoner in at-risk neonates are apparent only on longer follow up.

In our country large number of dropout happens due to movement and most of the high risk babies born in the tertiary care are usually referred from far off places leading to drop out in follow up. In cases of expected drop out, the follow up can be continued up to at least 3 years when an IQ check and behavioral assessment can be performed.

Motor outcomes of high risk infants can range from transient dystonia to cerebral palsy. At school age, low birth weight infants are more likely to have subtle neurologic impairment than their normal birth weight peers.<sup>61,70</sup>

On examination, 10% to 11% of low birth weight infants have neurologic soft signs, a twofold increased risk compared with their normal birth weight peers.<sup>23,71</sup> Soft signs are defined as deviations in speech, balance, coordination, gait, tone, or fine motor or visual motor tasks that do not signify localized brain dysfunction. These soft signs are associated with an increased the risk of subnormal IQ, learning disabilities, attention deficit disorder, and internalizing and externalizing behaviors at 6 and 11 years.<sup>71</sup>

### **Learning (psycho-educational) problems**

Other than neuromotor disabilities and developmental delay, the preterm VLBW babies are also at a high risk of learning difficulties.<sup>96</sup> Though these babies may be neurologically normal, have age appropriate adaptive skills and activities of daily living, they often have poor school achievement and behavioral difficulties as compared to their same age controls and these are even worse in ELBW babies especially in mathematics.<sup>97</sup>

In Pune low birth weight study<sup>99</sup> 180 high risk babies weighing less than 2000 g were followed up till 12 years and assessed for cognitive and educational abilities along with 90 controls of normal birth weight. The mean IQ ( $89.5 \pm 16.9$ ) was in normal range in study group though it was significantly lower ( $p < 0.05$ ) than normal controls ( $97.2 \pm 14.1$ ). Preterm SGA had the lowest IQ ( $85.4 \pm 17.7$ ). Visuo-motor perception and motor competence were poor in study group and they had writing and mathematics learning disability, poor academic achievement especially preterm SGA and VLBW group.

Hence all VBW and ELBW babies should be followed up till adolescence for early identification of school difficulties and development of intervention strategies to improve the outcome.

### **Cognition**

Cognitive impairment is the most common impairment among high risk infants defined as scores that are 2 standard deviations below the mean on standardized cognitive testing. Average score for ELBW infants at 18 to 22 months corrected age in the NICHD is 76<sup>20</sup> (mean score 100). Like rates of neurodevelopmental impairment, rates of cognitive impairment vary worldwide, and are inversely proportional to gestational age and birth weight. Worldwide rates of cognitive impairment throughout childhood range from 14% to 39% at 24 weeks, 10% to 30% at 25 weeks,<sup>2</sup> 4% to 24% at less than 26 weeks, and 11% to 18% at less than 29 weeks.<sup>5,14</sup> Mean IQ for ELBW and VLBW at school age ranges from 82-105 which though is within normal range it is significantly lower than their normal birth weight peers.<sup>22-24,41-43</sup> Children born VLBW or ELBW have relative impairments of executive functioning,<sup>29,41,60,61</sup> visual-motor skills,<sup>61</sup> and memory,<sup>29,41</sup> especially verbal memory.<sup>32</sup> They score lower on tests of academic achievement,<sup>29,30,42</sup> perceptual-organizational skills,<sup>31,41</sup> visual processing tasks,<sup>31,41</sup> and adaptive functioning<sup>29,41</sup> compared with their normal birth weight peers. A group of NICU cohorts comprising LBW followed in Pune had significant cognitive impairment at school age with learning difficulties and went to have poor IQ scores at 12 year of age with the study group having poor skills in mathematics.<sup>48</sup> Saroj Saigal et al<sup>49</sup> found significantly higher scores for depression and ADHD on questioning parents of teens born ELBW on parents questionnaire however there was no difference in self esteem in between the two groups.

Malin's Intelligence Scale for Indian Children (MISIC), Seguin Form Board (SFB) and Vineland Social Maturity Scale (VSMS) are freely available tools)

1. The scales which can be used to assess cognitive and functional status are Weschler's intelligence scale –revised (WISC-R)<sup>100</sup>- This is the most commonly used intelligence scale all over the world for school age children. An Indian adaptation by MC Bhatt is also available. It has 11 subtests and gives a separate verbal and performance score. It must be administered in a quiet room by a trained psychologist and takes about one and half hours. An intelligence quotient of below 70 is considered mental retardation, between 70-84 as borderline intelligence, between 85-109 as average and 110 or more above average intelligence.
2. Bender- Gestalt Test (BG)<sup>101</sup>This assesses the visuo- motor perception which is important for reading and writing. It consists of 9 figures characterized by their patterning and the child is instructed to copy the figures. This is scored as age appropriate, below normal (9-11 years), and poor (below 9 years).
3. Wide range achievement test (WRAT)<sup>10</sup> This test assesses the basic codes of reading, writing and mathematics. When used in conjunction with an IQ test like WISC, it can detect specific learning disabilities.
4. Human figure drawing: Emotional state of the child can be assessed by asking the child to draw a human figure on a prescribed piece of paper .Koppitz<sup>103</sup> has described 30 emotional indicators which can be interpreted from the drawings. The presence of 3 or more indicators is considered abnormal.
5. School performance: In addition to above tests, parents can be asked to bring the child's report which shows the child's school performance.

### **Behavioral assessment**

High risk infants have been associated with a wide array of behavioral and psychological disabilities. Recent concern has arisen that rates of Autism Spectrum Disorder (ASD) may be higher in ELBW infants than previously thought. Although low birth weight (<2500 g) may result in a two- to threefold increase in the risk of ASD,<sup>76,77</sup> At 14 and 17 years of age, VLBW children score significantly lower on measures of self-esteem.<sup>43,44</sup> They report less confidence in their athletic, school, romantic, and job-related abilities.<sup>44</sup> At the age of 20 years, VLBW adults report lower rates of alcohol and drug use, sexual activity, and pregnancy than adults born normal birth weight.<sup>46,49</sup>

For behavioral assessment, CBCL scale can be used. CBCL<sup>104</sup> (Achenbach Child behavior checklist) which is based on parental perception of children's behavior designed to assess the social competence and behavioral problems and can be used from 1.5-5 years aged children.

### **Fetal Onset Adult Diseases:**

Comparative cross sectional analysis of two groups of cohorts followed-up at 1 year and 16 years of age at Child Development Centre (CDC), Kerala showed that high triglyceride values and overweight/obesity were significantly more in LBW adolescents when compared to NBW adolescents. This has policy implications in planning adolescent nutrition and care programs in India. Nair MKC . Life Cycle Approach to Child Development. Indian Pediatr Suppl 2009;46: S7-S11)

**Recommendations:**

- Ensure follow up till late adolescence, at least till school entry. Many cognitive problems, learning problems, behavioral problems that are commoner in at-risk neonates are apparent only on longer follow up.
  - Behavioral assessment can be done after one year age
  - Formal cognitive development, IQ is tested by 3 years
  - BP, BMI and Lipid Profile at school exit

Children born below 28 weeks or 1000 grams birth weight must be referred for a Psycho-educational testing (pre-school assessment) to detect learning

**Early intervention – do we need/ when/ how ?**

The problems associated with at - risk infants are often identified very late when little can be done. No Drug has been conclusively proven to be effective in improving outcome in post-asphyxial encephalopathy. Pyritinol was not found useful in improving the neurodevelopmental status of babies with post-asphyxial encephalopathy at one year of age.

Hence, developmental follow up and early intervention is the answer to this problem.<sup>19</sup> The early intervention institute at Utah University reviewed 316 articles reporting results of 162 early intervention efficacy studies showing that there is compelling evidence in 150 of them that early intervention has immediate positive effect on one third to one half.<sup>20</sup> A recent Meta analysis showed that early intervention improved cognitive outcome at infant age (0-2 years).<sup>21</sup> Although, there is no uniform agreement as to the ideal group of babies who would benefit maximally from early intervention, the neonatal nursery graduates would probably form the best captive population for providing early stimulation. CDC model of ‘early stimulation therapy’ was effective at one year. The beneficial effect also persisted at two years, without any additional interventions in the second year. A reduction of 40% in poor performance could be achieved by early intervention in LBW babies in Trivandrum.<sup>22</sup>

A sick neonate in NICU experiences significant adverse environment and separation from mother which is very stressful and can lead to abnormal sensory input resulting in abnormal brain structure and function and as a result can develop developmental disabilities. Developmental supportive care is an intervention for preterm infants that focuses on environment and is designed to minimize the stress of the neonate in NICU environment. Interventions aiming at enhancing parent – infant relationship focuses on sensitizing the parents to infant cues and teach appropriate and timely response to the infant’s needs. There is evidence that early parent- infant interaction positively influences cognitive and social development in children.<sup>108</sup> NIDCAP (The Newborn Individualized Developmental Care and Assessment Program) is one developmental care framework. There are several NIDCAP based RCT which showed positive effects in the short term as well as long term outcome in the form of less disability specially mental delay in BSID scale.<sup>109</sup>

The Cochrane review published in 2007<sup>110</sup> which looked at the pooled result of 16 randomized controlled studies involving 2379 patients. Intervention was started within the first 12 months, in babies less than 37 weeks of gestation, either in hospital or after discharge. Meta analysis concluded that intervention improved cognitive outcomes at infant age, preschool age, however this effect was not sustained at school age though there was significant heterogeneity between studies for cognitive outcome at infant and school

ages. There was little evidence of an effect of early intervention on motor outcomes in the short, medium and long term but there were only 2 studies reporting outcome beyond 2 years.

Hence based on above evidence, it is recommended to start early intervention while the baby is still in NICU

### **Early intervention after discharge from NICU**

*Who should be initiated on an early stimulation programme?*

Babies at risk of Neurodevelopmental disabilities based on risk factors & Initial assessment

*When can early stimulation be started?*

As soon as baby is medically stable in the NICU

In the NICU

- Optimize lighting
- Reduce noise, gentle music
- Club painful procedures, allow suck sucrose / breast milk , hold hand
- Tactile stimulation – touch, gentle massage
- Kangaroo Mother Care
- Non-nutritive sucking
- Passive exercises

Motivate the parent to stimulate the baby with appropriate stimuli; the parents of an at-risk baby are likely to be demoralized & at-risk of not being involved in stimulation of the child.

*What is done in early stimulation?*

- Assess parenting –skills and educate
- Stimulate the child in all sectors of development – motor, cognitive, Neuro-sensory, language
- Developmentally appropriate - through the normal developmental channel (stimulate to achieve the next “mile-stone” rather than age-based)
- Physical stimulation – passive exercises to prevent development of hypertonia
- Caution – avoid over-stimulation (has shown negative effects on development when many inputs of different nature are simultaneously started)

At Home

- Bold patterns with strong contrasts / parent faces / moving objects
- Talk to the baby / music
- Touch - Rocking, walking and swinging

- Massage

***Recommendations:***

- Early intervention programme (early stimulation) must be started in the NICU itself once the neonate is medically stable and continued till at least till 1 year of age

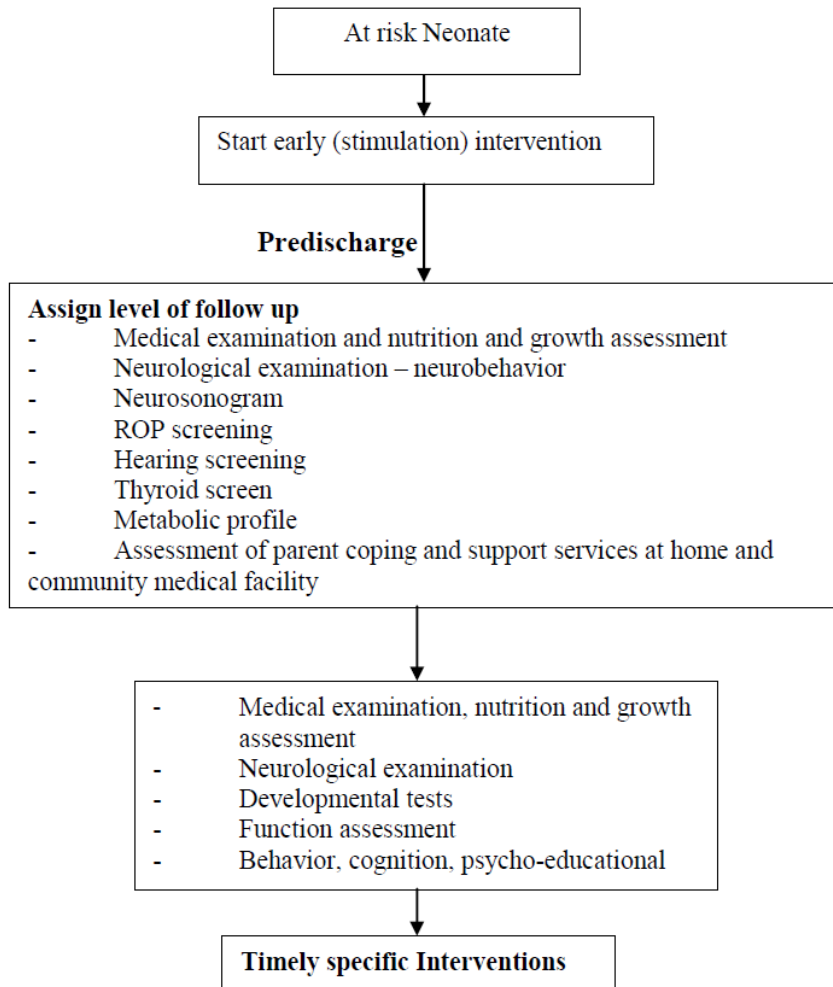
**Specific interventions**

- Motor impairment / Hypertonia – medications and physiotherapy
- Physiotherapy and occupational therapy
- Speech therapy
- Seizures
- DDH and other Orthopedic
- Squint correction
- Behavior therapy and pharmacotherapy for behavioral disorders
- Therapy for learning disabilities

***Recommendations :***

Timely specific interventions and compliance must be ensured after detection of deviation from normal.

**Algorithm for follow up of at-risk neonates**



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