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# NEOCHAP BULLETIN

AN OFFICIAL PUBLICATION OF IAP NEONATOLOGY CHAPTER



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## EDITORIAL

It's indeed my pleasure to present this edition of NeoChap bulletin to you. Respiratory care is like bread and butter for the practising Neonatologist and Paediatrician. While we'll be quite familiar with the routine standard practices, few recent developments need to be noted. These developments like high flow oxygen therapy, current recommendations and future of surfactant, practical use of pulmonary graphics in day to day practice could have some impact in the way we'll manage a newborn with respiratory problem. At end follows an article on practical tips to follow up a newborn, who's been discharged after the hard work by you and your team. On the other hand it's noteworthy development in academic endeavour of NeoChap team to conduct Zonal CMEs. Already the west and east zone CMEs have been done at Mumbai and Bhubaneswar respectively, with excellent speakers and great attendance. Details can be seen in our ever active website .  
Jai Hind

**Dr Arjit Mohapatra**  
Guest Editor

## Chairperson's Message

Dear Fellow Academicians,  
Seasons Greetings !

I feel privileged to take over as Chairperson of the Neonatology Chapter of IAP. This organization has grown leaps and bounds in the last 5 years. Thanks to the hard work of all the members and the leadership during these formative years. Now is the time to consolidate and grow.

I have a good team of people to work with and would like to say that we will continue the good work the Chapter has been doing in improving the newborn healthcare, training and building a better Neonatal workforce in the country.

Strengthening the Fellowship program, publication of Atlas of Neonatology & Protocols in Neonatology, improving the newly created Chapter website, book on newborn parenting, and propagating neonatal care through Zonal workshops across the country, publishing member's directory would be some of the aspects our team we will be looking at achieving during the next two years.

I sincerely request you all to contribute and participate in this endeavor. Your feedback and support is vital.

With warm regards,  
**Dr Rhishikesh Thakre**

## Upcoming Academic Events of IAP Neonatology Chapter

"Cardiology for Neonatologists: in a nutshell"  
IAP Neonatology Chapter, West Zone CME  
Co-hosted by NNF Mumbai, IAP Mumbai & Kokilaben Dhirubhai Ambani Hospital.  
Date: 12th April 2015  
Venue : Convention Centre, 6th floor, Kokilaben Dhirubhai Ambani Hospital, Mumbai.

IAP Neonatology Chapter, South Zone CME on  
**Recent advances in "Care of Preterm Neonates"**  
**Hosted by : IAP Thrissur**  
In association with : NNF Kerela and  
Jubilee Mission Medical College & Research Institute, Thrissur, Kerela-680005  
**Venue:** Moher Teresa hall, Gate No:1, Jubilee Mission Medical College, Thrissur  
**Date:** 9 & 10 May 2015 (Noon to noon: Saturday & Sunday)

## **SURFACTANT : YESTERDAY, TODAY AND TOMORROW**

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RDS was first characterized as surfactant deficiency disease of the newborn by Avery and Mead in 1959 . The first clinical use of exogenous surfactant to treat RDS was by Fujiwara and colleagues in 1980 . These sentinel reports lead to our current strategies for the surfactant treatment of RDS in premature infants that began in 1989, with the Food and Drug Administration (FDA) approval of the synthetic surfactant colfosceril palmitate suspension (Exosurf®), closely followed by approval of beractant (Survanta®), the first animal derived surfactant. These were the first commercially available surfactant preparations in the United States and were associated with a greater decline in mortality in premature infants with RDS than in any other years in recent decades.

Endogenous surfactant is a biochemical compound composed of phospholipids, neutral lipids, and proteins that forms a layer between the terminal airways/alveolar surfaces and the alveolar gas. In 1961, Klaus and colleagues were the first to isolate alveolar surfactant from bovine lungs, and extracted a phospholipid fraction that displayed a surface active behavior. Ten years later, Gluck et al discovered a technique that allows fetal lung maturity to be measured using the lecithin/sphingomyelin ratio in amniotic fluid. Surfactant is secreted by the type-II pneumocyte and functions to reduce lung collapse during end- exhalation by decreasing surface tension within the terminal airways and alveoli. Infants who are born prematurely are more likely to have lungs that are surfactant-deficient at birth. Surfactant deficiency is associated with onset of respiratory distress syndrome (RDS), a major cause of morbidity and mortality in premature infants. Surfactant is also effective in treating infants with meconium aspiration syndrome (MAS), pulmonary hemorrhage, and pneumonia, although the evidence base for their use in these disease processes is much weaker than the primary indication of RDS.

Surfactant reduces surface tension, improves lung compliance, and stabilizes lung volumes at a lower transpulmonary pressure. Without surfactant, alveoli may never inflate or may collapse on expiration and require an inordinate amount of force to re-expand on inspiration, leading to the development of severe RDS and air leak syndromes. Surfactant's secondary function is to enhance macrophage activity and mucociliary clearance, and to reduce inflammation. The incidence of RDS is related more to lung immaturity than to gestational age. However, in general, the more premature the infant, the less the surfactant production and the higher the probability for RDS. Mechanical ventilation is often necessary for the treatment of RDS; however, ventilator-induced lung injury can deactivate the production of endogenous surfactant production and compromise the therapeutic effect of surfactant replacement therapy. Direct tracheal instillation of surfactant has been shown to reduce mortality and morbidity in infants with RDS.

Exogenous lung surfactant can be either natural or synthetic. Natural surfactant is extracted from animal sources such as bovine or porcine. Synthetic surfactant is manufactured from compounds that mimic natural surfactant properties. Both forms of surfactant replacement are effective at reducing the severity of RDS; however, comparative trials demonstrate greater early improvement in the requirement for ventilatory support and fewer pneumothoraces associated with natural surfactant extract treatment. On clinical grounds, natural surfactant extracts would seem to be the more desirable choice.

Two basic strategies for surfactant replacement have emerged: prophylactic or preventive treatment, in which surfactant is administered at the time of birth or shortly thereafter to infants who are at high risk for developing RDS from surfactant deficiency; and rescue or therapeutic treatment, in which surfactant is administered after the initiation of mechanical ventilation in infants with clinically confirmed RDS.

Prophylactic surfactant administration to infants at risk of developing RDS is associated with lower risk of air leak and mortality, compared to selective use of surfactant in infants with established RDS. Surfactant administration with brief lung-protective ventilation (followed by extubation to nasal CPAP) for premature infants at risk for developing RDS is associated with a lower incidence of mechanical ventilation, air leak syndromes, and chronic lung disease, compared to selective surfactant and continued mechanical ventilation.

Surfactant is traditionally administered by instilling through the ETT, but can also be delivered effectively by injection

through the nasopharynx during delivery or by using a thin catheter. Experimental evidence also supports the delivery of some surfactants using a nebulizer.

#### Currently Available Surfactants

Trade Name	Source		Dose
Poractant alfa	Curosurf	Porcine	100–200 mg/kg/dose (1.25–2.5 mL/kg)
Calfactant	Infasurf	Bovine	105 mg/kg/dose (3 mL/kg)
Beractant	Survanta	Bovine	100 mg/kg/dose (4 mL/kg)
Lucinactant	Surfaxin	Synthetic	5.8 mL/kg

#### Comparison of Different Natural Surfactant

Overall, calfactant and poractant were superior to beractant in terms of secondary outcomes (pneumothorax, ventilator weaning duration, need for supplemental oxygen), but rates of mortality and CLD remained similar amongst all three types.

A more recent meta-analysis has since been carried out comparing porcine and bovine surfactants with a total of five randomised controlled trials identified, all of which compare poractant versus beractant. Again, no difference is noted when the initial dose is at 100mg/kg for both cohorts, but significant reduction in mortality and need for re-dosing has been reported in the high-dose (200mg/kg) poractant cohort. Mortality is significantly lower and need for re-dosing was less in poractant alfa (200 mg/kg) treated infants vs. in infant treated with low dose poractant alfa (100 mg/kg) or beractant treated infants.

#### Natural vs Synthetic

All trials showed consistently that, natural surfactants were better than protein free synthetic surfactants. But, when natural surfactant is administered, there are a number of drawbacks, including the lack of cost-effectiveness, inconsistent efficacy, possible anaphylactic shock reaction, and risk of pathogen contamination. It is important to note that the pathogenic risks have not been identified on a clinical level.

However interesting developments have occurred in the field of synthetic protein containing surfactants. Lucinactant, also known as Surfaxin®, is considered a new-generation synthetic surfactant composed of DPPC, POPG (palmitoyloleoyl phosphatidylglycerol), palmitic acid, and sinapultide, a hydrophobic 21-amino acid KL<sub>4</sub> peptide with the hydrophobic-hydrophilic amino acid pattern of leucine and lysine repeating units. Despite its considerably smaller size relative to SP-B, sinapultide replicates SP-B action by mimicking a C-terminal amphipathic helical domain of SP-B.

In SELECT and STAR trial, in which Lucinactant was compared versus Beractant and Poractant respectively, Lucinactant reported better survival rates at 1 year in comparison to animal-derived surfactant (beractant and poractant), but again lacked significance. The authors concluded that lucinactant can provide an equal or possibly greater survival rate than animal-derived surfactants in the management of RDS.

#### Comparison Between Prophylactic and Rescue Therapy

Over the years, the administration technique of surfactant has undergone a series of advances. One primary change involves the indication for surfactant. Conventional method deemed surfactant administration as a means of rescue therapy. Surfactant was instilled in tandem with continued mechanical ventilation in the presence of confirmed RDS. A Cochrane meta-analysis assessed four different randomised controlled trials, with the criteria for early selective surfactant measured as administration within the first 2 hours of life. Patients in the early surfactant cohort reported significantly decreased risk of pneumothorax and pulmonary emphysema. There was also a reduced incidence of neonatal mortality and CLD. In summary, early selective surfactant treatment in preterm infants with RDS is more effective than delayed selective surfactant use in reducing neonatal mortality, pneumothorax, and BPD at 36 weeks. Prophylactic treatment also decreases the incidence of pneumothorax, pulmonary interstitial emphysema, BPD and neonatal mortality when compared with delayed selective treatment. However, prophylactic surfactant treatment is not superior to initial respiratory support with CPAP followed by selective surfactant treatment later on in

reducing the need for mechanical ventilation, pneumothorax and BPD or mortality in the era of antenatal corticosteroids and CPAP.

### **European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants – 2013 Update**

#### *Recommendations*

- (1) Babies with RDS should be given a natural surfactant preparation.
- (2) A policy of early rescue surfactant should be standard but there are occasions when surfactant should be administered in the delivery suite, such as extremely preterm infants in whom the mother has not had antenatal steroids or those who require intubation for stabilization.
- (3) Babies with RDS should be given rescue surfactant early in the course of the disease. A suggested protocol would be to treat babies <26 weeks' gestation when  $FiO_2$  requirements >0.30 and babies >26 weeks when  $FiO_2$  requirements >0.40.
- (4) Poractant alfa in an initial dose of 200 mg/kg is better than 100 mg/kg of poractant alfa or beractant for treatment of RDS.
- (5) Consider the INSURE technique. More mature babies can often be extubated to CPAP or nasal intermittent positive pressure ventilation (NIPPV) immediately following surfactant, and a clinical judgement needs to be made as to whether an individual baby will tolerate this.
- (6) A second, and sometimes a third, dose of surfactant should be administered if there is evidence of ongoing RDS such as a persistent oxygen requirement and need for MV.

#### **CONCLUSION**

While the efficacy of surfactant in the prevention and treatment of RDS has been well-documented, issues remain. These include surfactant type, as well as the mode and timing of administration. For the time being, natural surfactant is the surfactant of choice, but a superior subtype is still debatable. However, the development of synthetic surfactant containing peptides that mimic the action of surfactant proteins have demonstrated a similar, if not superior, efficacy to natural surfactant. It is hoped that further development will allow synthetic surfactant to supersede natural surfactant, resulting in a reliable, well-controlled product that will be more cost-effective and prevent the risk of immunogenicity. Lucinactant, a synthetic surfactant with a KL4 peptide that mimics SP-B. With regards to the mode and timing of surfactant administration, early surfactant instillation demonstrated greater impact in reducing the risk of RDS and its related complications. The INSURE technique is quickly becoming standard procedure in the management of RDS. Since nCPAP has become the first-line management of RDS, this approach along with early selective surfactant appears to provide a better option as illustrated in recent studies. Instillation is currently *via* endotracheal tube, but non-invasive methods are being trialled including aerosolised form and through catheter (MIST). Clearly further research and development into surfactant therapy is needed as more innovations are introduced, but its therapeutic potential in RDS is promising. With surfactant in its third decade the two most exciting things happening are Lucinactant and MIST, which time will clear the horizon.

#### **References**

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<sup>2</sup> **Rangasamy Ramanathan<sup>1</sup>, Karen Kamholz<sup>2</sup> and Alan M Fujii<sup>3\*</sup>** Is there a Difference in Surfactant Treatment of Respiratory Distress Syndrome in Premature Neonates? A Review *J Pulmon Resp Med* 2013, S13

3. R Ramanathan<sup>1</sup>, JJ Bhatia<sup>2</sup>, K Sekar<sup>3</sup> and FR Ernst<sup>4</sup> Mortality in preterm infants with respiratory distress syndrome treated with poractant alfa, calfactant or beractant: a retrospective study *Journal of Perinatology* (2013) 33, 119–125

4. Christopher Cheng-Hwa Ma<sup>\*</sup> and Sze Ma **The Role of Surfactant in Respiratory Distress Syndrome** *The Open Respiratory Medicine Journal*, 2012, 6, 44-53

5. Brian K Walsh RRT-NPS RPFT FAARC, Brandon Daigle RRT-NPS, Robert M DiBlasi RRT-NPS FAARC, and Ruben D Restrepo MD RRT FAARC AARC Clinical Practice Guideline. Surfactant Replacement Therapy: 2013 RESPIRATORY CARE FEBRUARY 2013 VOL 58 NO 2

## PULMONARY GRAPHICS

### DR K. SANKARA NARRAYANAN

DM (Neonatology)

MRCPH.

Senior Consultant Neonologist

#### Introduction:

In the care of a sick neonate, there is a need to optimize ventilation using techniques which are real-time, available at the cot side, accurate, objective and preferably non-invasive. The use of pulmonary graphics helps in optimizing ventilator care of the neonate in conjunction with clinical, radiological and laboratory data. Introduction of microprocessor based technology in the 1990s has revolutionized the monitoring of pulmonary functions on a real time basis in neonatal units.

#### Principles:

There are two types of sensors which measure variables like pressure, flow and volume and convert the signal to an electrical signal which can then be read on a screen. The more commonly used sensor is the heated wire anemometer.

The heated wire is maintained at a constant temperature. As gas flows across the heated wire, it is cooled and this results in an additional electrical supply to bring the wire back to its fixed temperature. The magnitude of this additional electrical current is converted into signals which calculate flow and volume.

The other type of sensor is the pneumotachometer. As gas flows across this sensor there is a differential pressure between the proximal and the distal ports of this sensor. The magnitude of this pressure difference is proportional to the flow.

Both these sensors have a small dead space and do not add significant additional weight to the ventilator tubing. Ventilators manufactured by several companies have the ability to calculate pulmonary mechanics and display the trends on a real time basis.

#### Indications

1. Optimise ventilator parameters
2. Assess the type of respiratory pathology e.g., obstructive, restrictive
3. Assess course of respiratory status, i.e., improving/ worsening
4. Assess response to interventions e.g. surfactant administration
5. Assess various mechanics e.g. compliance, resistance, time constants
6. Assess spontaneous respiration and readiness for extubation

#### The Graphics screen

The following two pictures are examples of neonatal ventilators displaying pulmonary graphics. The first picture demonstrates a ventilator screen displaying various mechanics on the screen. The subsequent picture demonstrates waveforms and loops on a real time basis.





### Limitations

The use of pulmonary graphics is limited by the availability of flow sensors and ventilators which can display graphics. It is also important to note that pulmonary graphics provide information about the pulmonary mechanics and not about gas exchange. It is important to note the trend displayed on the graphics monitor rather than look at spot measurements in isolation. In order to improve the accuracy and speed of measurement, many ventilators now have intelligent flow measurement software.

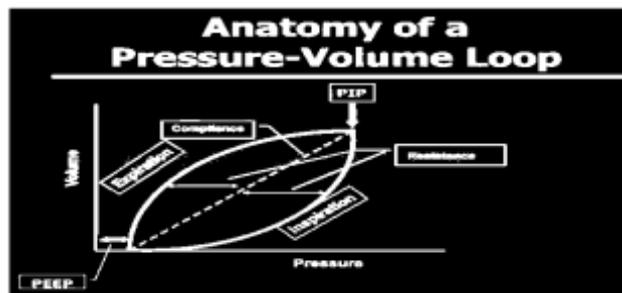
### Pulmonary waveforms and loops

Pulmonary waveforms are time-based and relate changes in pressure, flow, and volume to time, these parameters may also be presented relative to each other, referred to as loops. The two most frequently used in clinical practice are the pressure-volume (P-V) loop and the flow-volume (F-V) loop. The interpretation of these loops can provide valuable information about the mechanical properties of the lung and how it responds to changes in pathophysiology, mechanical ventilation and therapeutic interventions.

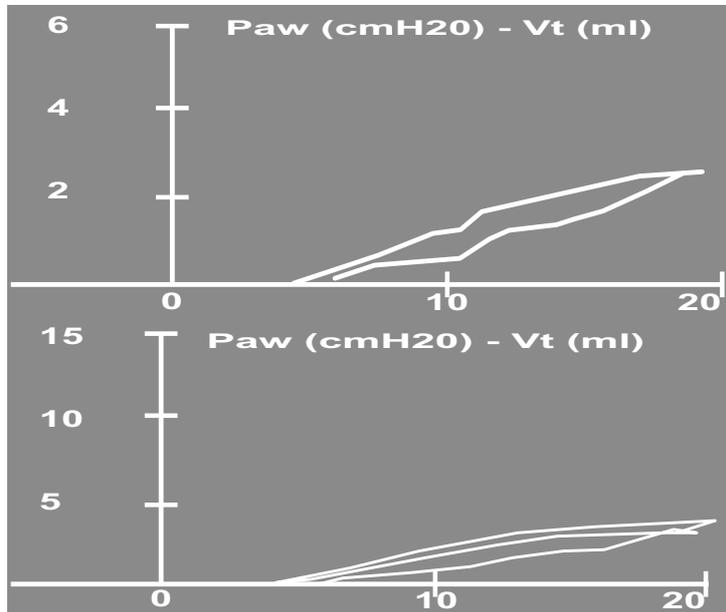
#### .The P-V Loop

The P-V loop displays the relationship of pressure and volume during a single breath. Pressure is displayed on the x-axis and volume on the y-axis. As inspiration begins, there is a rise in pressure and subsequently volume. This describes the inflation limb of the loop and terminates at the peak inspiratory pressure (PIP). As the lung deflates, pressure and volume decrease, and the deflation limb terminates at zero volume and the PEEP level. The P-V loop provides valuable information about lung mechanics. The dotted line is the *compliance axis*, a measure of the stiffness or elasticity of the lung. Compliance is defined as the change in volume divided by the change in pressure.

**RESISTANCE:-** A line drawn from the midpoint of the inflation limb to the compliance axis is a measure of inspiratory resistance; a line drawn from the midpoint of the deflation limb to the compliance axis is a measure of expiratory resistance.

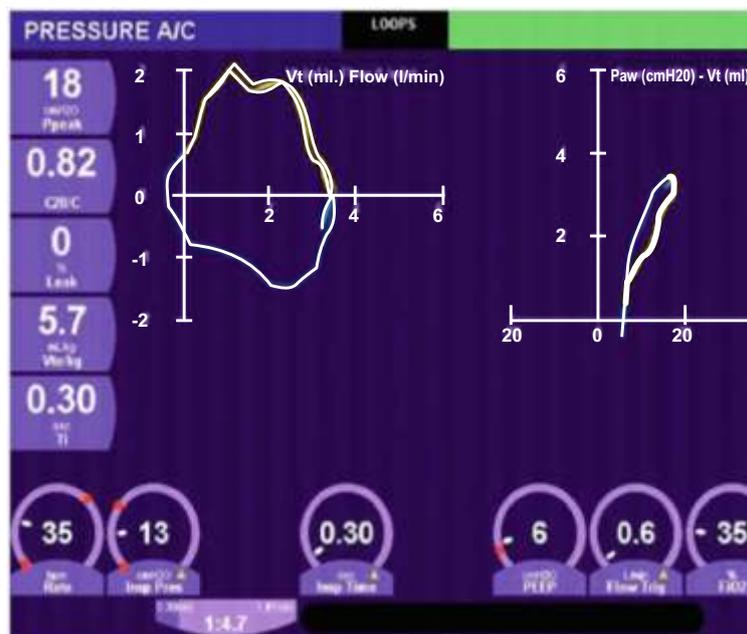


### Decreased Compliance

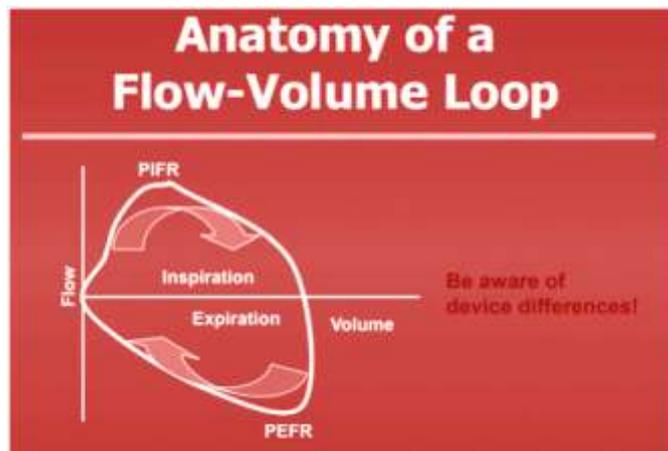
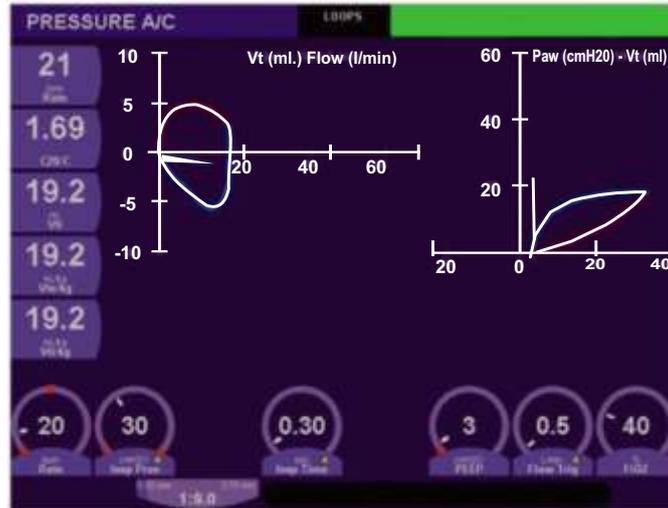


It may be seen in respiratory distress syndrome (RDS), pneumonia, or other conditions marked by surfactant inactivation or depletion. When compliance is low, the lung is stiff, requiring more pressure to deliver the same tidal volume ( $V_t$ ) compared to normal compliance.

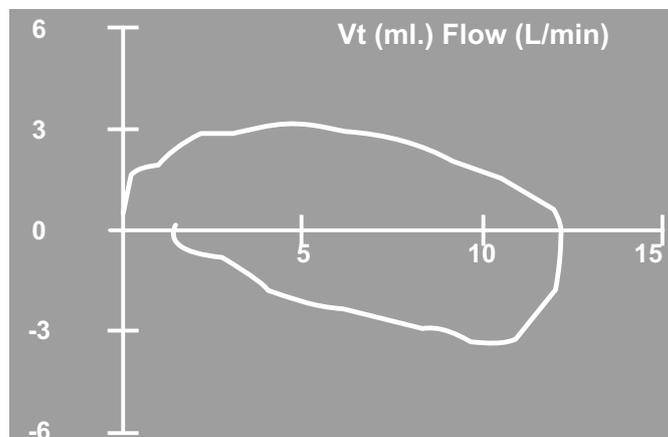
### HYPERINFLATION:-



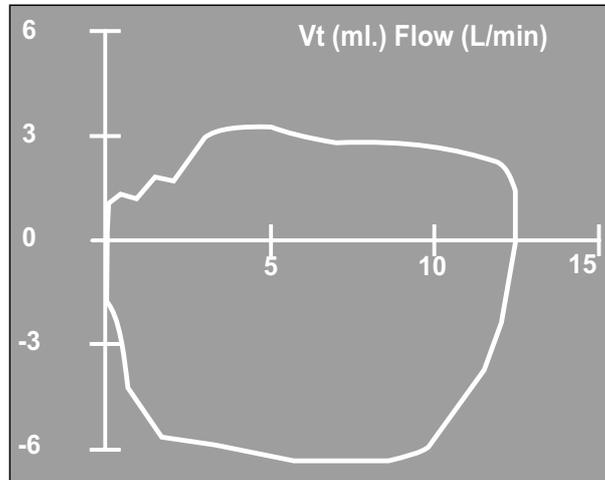
**Surfactant Administration and resulting improvement in compliance**



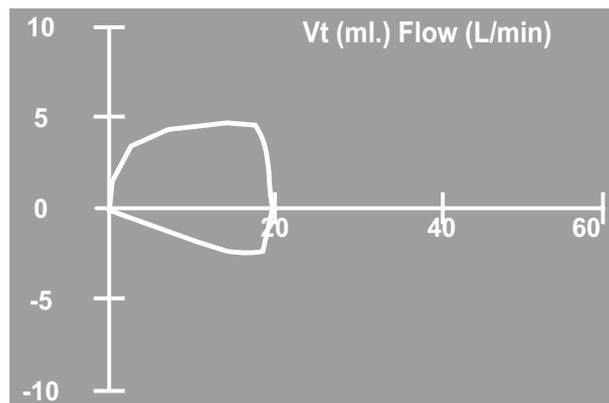
**Peritubal leak**



**Elevated Expiratory Resistance e.g. bronchoconstriction**

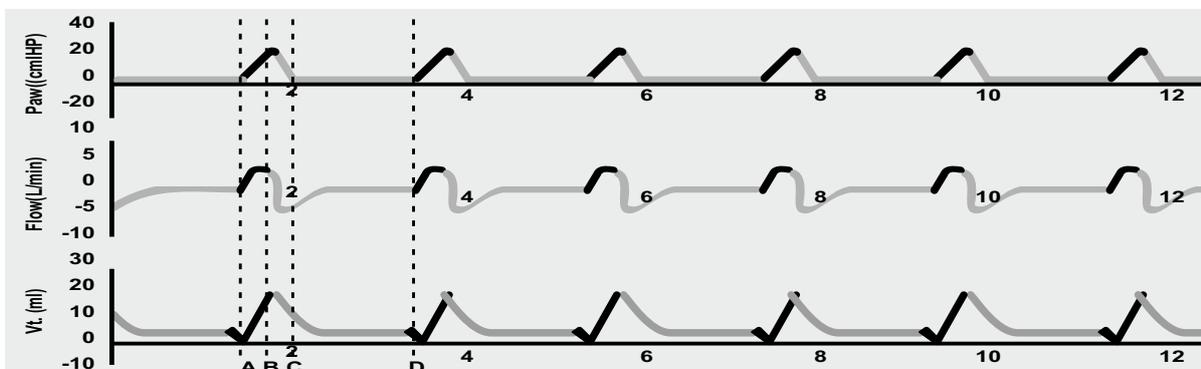


**Elevated Inspiratory Resistance (extra-thoracic obstruction)**



**Waveform**

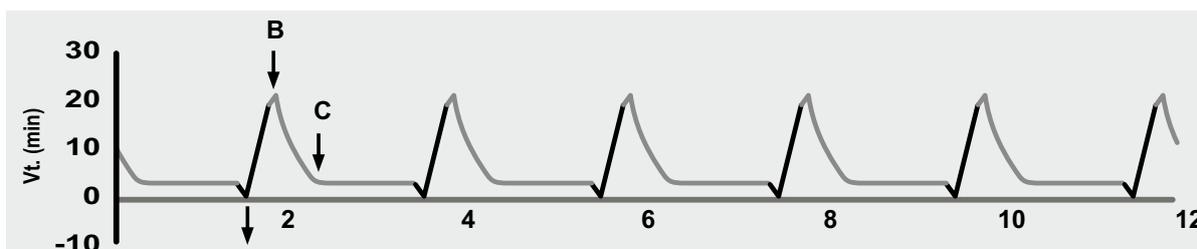
The waveforms depict the relationship between respiratory parameters and time on breath to breath basis. The three waveforms used are  
 1) pressure 2) volume and 3) flow waveform



The above picture depicts pressure waveform, flow waveform and volume waveform. A denotes start of inspiration, B–peak inspiration, C- end of inspiration, D-end of expiration

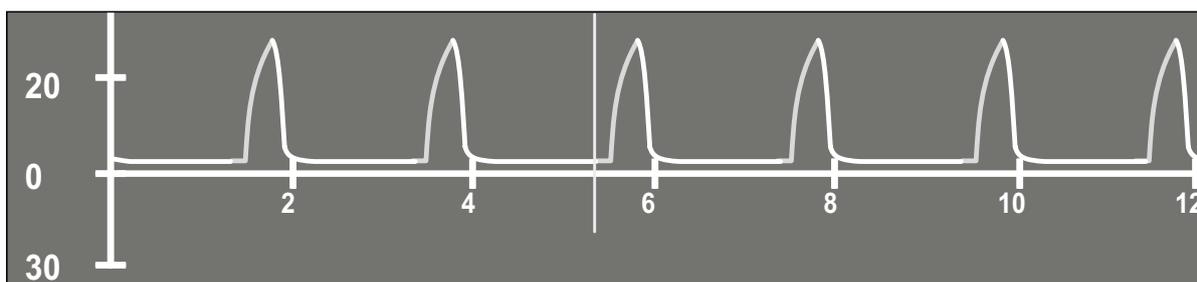
### Volume waveform

The volume waveform displays the changes in delivered volume over time. It is determined by integrating the inspiratory and expiratory flow signals.



### Pressure waveform

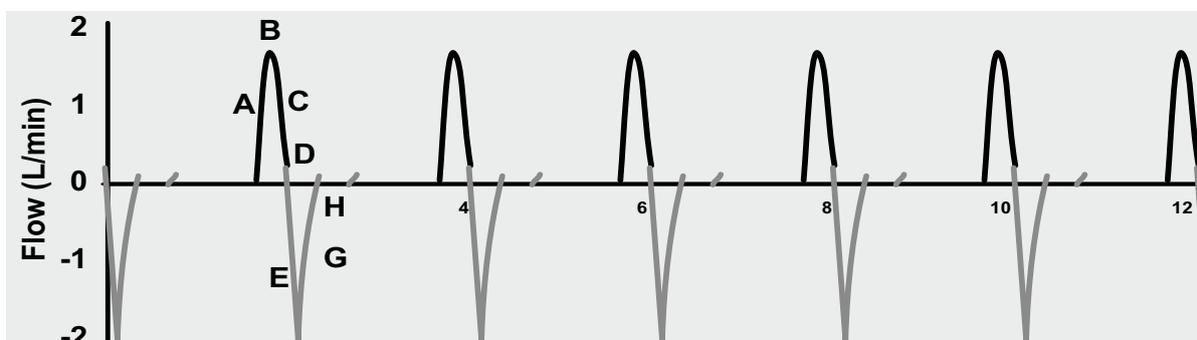
The pressure waveform represents the airway pressure throughout the respiratory cycle. The start of inspiration is above the baseline (PEEP). The peak pressure is PIP (Peak inspiratory pressure). The area under the curve is mean airway pressure. The pressure difference between PIP and PEEP is  $\Delta P$ .



### Flow waveform

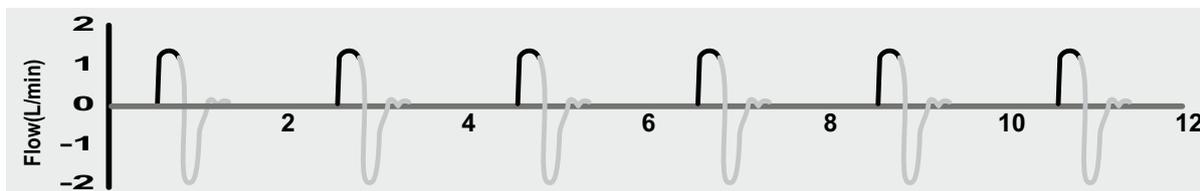
The flow waveform has inspiratory and expiratory phases each have two components. In this waveform, the baseline represents a zero flow state. There are two major ways in which inspiratory flow can be delivered to the patient, variable or constant (continuous) flow. Variable

*flow is utilized in pressure control and pressure support ventilation.*



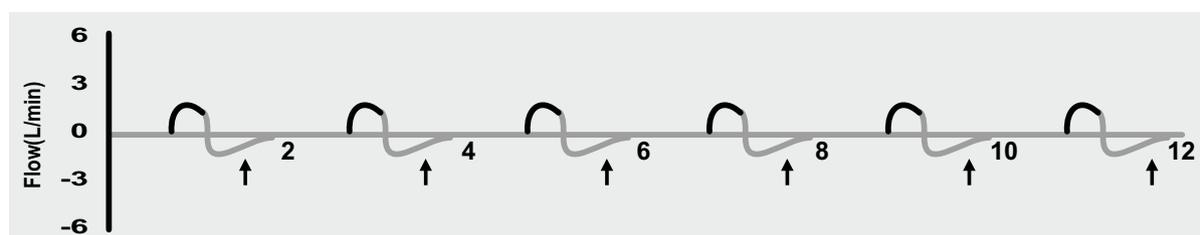
Volume control ventilation has the accelerating inspiratory flow peaks and then is held constant (continuous) until inspiration ends, creating a square waveform.

One major advantage of flow cycling is the improved synchrony between the baby and the ventilator because the baby both initiates and terminates the breath. The other advantage is that this prevents gas trapping during patient-triggered ventilation.

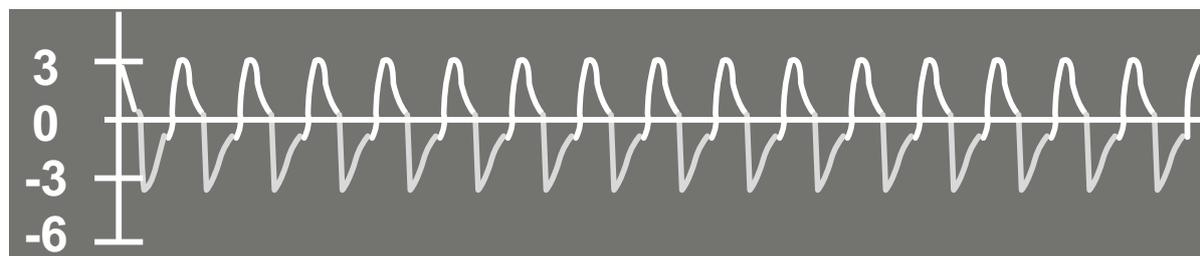


**The uses of waveform**

Identify increased expiratory resistance

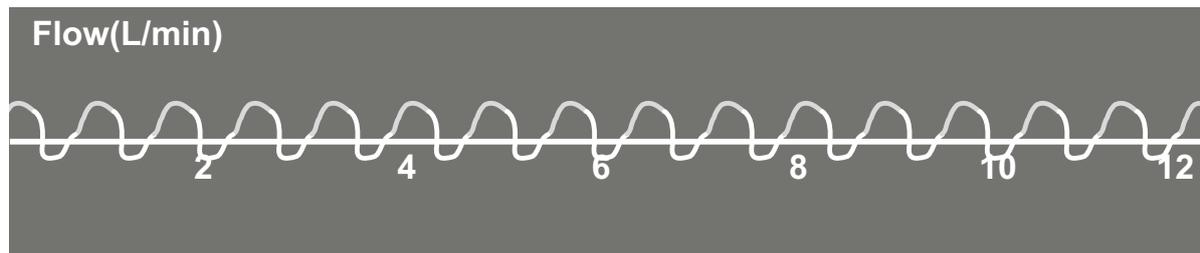


The above picture denotes the decreased slope and increase time for the decelerating slope to return to baseline. Gas trapping



The expiratory flow fails to reach the baseline before initiating the next breath.

Endotracheal tube leak



The above flow waveform denotes no expired volume.

**Summary and conclusions**

The use of pulmonary graphics is a useful adjuvant to optimizing the ventilator care of the ventilated newborn infant. Graphics are especially useful if the trend is closely followed. Pulmonary graphics can help in minimizing invasive blood tests and also in minimizing the use of radiological investigations. Studies to assess the impact of pulmonary graphics on neonatal respiratory morbidity will promote greater use of this very useful modality.

## Humidified high flow nasal cannula therapy in neonates

### Dr Rajesh Kumar

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Use of humidified high flow nasal cannula (HHFNC) in neonatal intensive care units has become popular in many parts of the world despite not having sufficient evidences from RCTs. HHFNC uses gas flow rates that is higher than the patient's normal inspiratory flow rate. Entrainment of room air is reduced as the flow rate increases, and hence HHFNC can deliver oxygen at higher concentrations than is possible by low flow therapy devices or head box. For neonates, flow rate of 2-8 litre/min by nasal cannula is generally accepted as high flow rate. HHFNC is used as a primary support for respiratory distress syndrome (RDS), for treating apnoea of prematurity (AOP), to support preterm infants after extubation and to wean from nasal continuous positive airway pressure (NCPAP). HHFNC is becoming popular because of ease of application and maintenance. This also allows greater access to the baby's face, which may improve feeding and bonding.

### Mechanism of action

Postulated mechanisms of action of HHFNC are:

**Washout of nasopharyngeal cavity:** This is thought to be the primary mechanism, reduction in the overall dead space which contributes to more effective CO<sub>2</sub> elimination. Reduction of the dead space also has an effect on oxygenation, due to reduced entrainment of room air. It is possible to deliver 100% oxygen to the airways with the use of HHFNC,

**Reduction of inspiratory resistance:** CPAP reduces inspiratory resistance (up to 60%) by splinting open the airway, while HHFNC does the same by matching/exceeding patient's inspiratory flow and thus way eliminating increasing nasopharyngeal resistance (caused by its inspiratory distensibility). Work of breathing on HHFNC at flow rates of 3-5 L/min has been shown to be equivalent to that of CPAP at 6 cmH<sub>2</sub>O in a 1 kg patient despite significantly lower oesophageal pressure with HHFNC. This suggests that mechanisms other than simply the airway distending pressure affects work of breathing in HHFNC.

**Warm, humidified gas improves respiratory mechanics:** Breathing cold, non-humidified gas for only five minutes decreases lung compliance and conductance. Cold, dry gas elicits bronchoconstriction (nasal mucosa receptors, muscarinic effect). Thus use of warm and humidified air is beneficial for respiratory mechanics of the baby. There is evidence to show that, there is improved function of muco-ciliary apparatus with the use of HHFNC.

**Reduced metabolic cost of gas conditioning:** The nasopharyngeal cavity provides effective warming and humidification to inspiratory gas but this requires a significant amount of energy. Babies on HHFNC have been shown to gain weight quicker than on CPAP.

**Provision of end distending pressure:** High gas flow generates positive airway pressure (although very unreliably and depending on factors like body weight, mouth leaks, etc). This also may be beneficial for the baby.

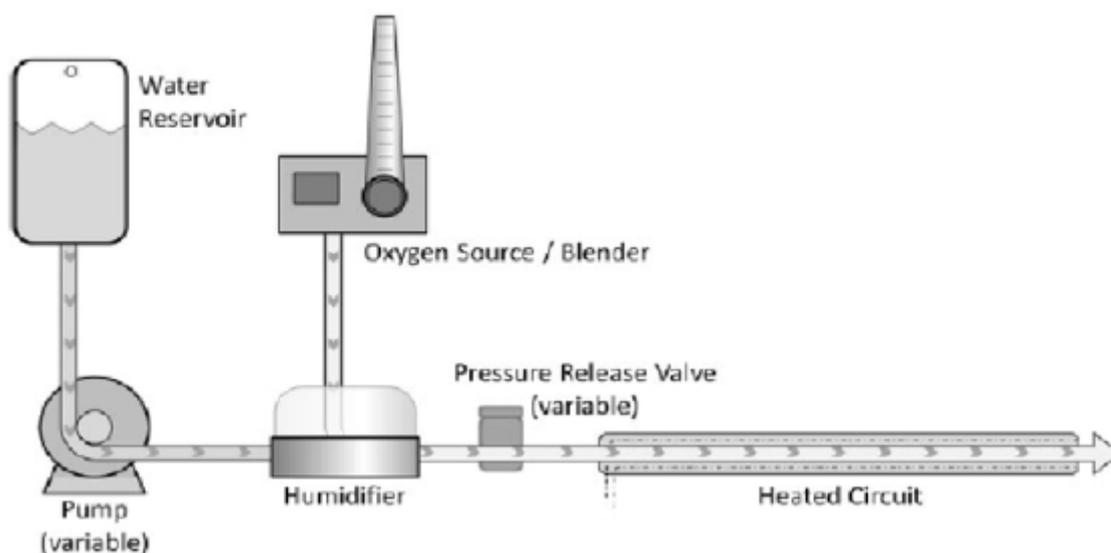
**Potential benefits:** The potential benefits of the use of HHFNC are;

- Avoidance of nasal septum trauma by using small nasal cannula interface.
- Avoidance of nasal mucosa irritation and thickened nasal secretion.
- Ease of administration and well tolerated by the babies.
- Lower cost than nasal CPAP.

**Potential risks:** The potential risk of the use of HHFNC is the inability to consistently predict the actual level of positive distending pressure being delivered to the baby. This has been the main criticism for the use of the HHFNC. But studies have shown that if HHFNC is used in the recommended way, the airway end distending pressure rarely goes beyond 6 cm of water.

**HHFNC set-up:** HHFNC is an open respiratory support system. Nasal cannula should not cover more than 50% of the nasal orifice. This is the most important concept in HHFNC. There is no need to keep the mouth closed as we do in NCPAP. HHFNC system is commercially available or it can be locally assembled. The requirement for the HHFNC system is:

- Compressed oxygen and air source
- Blender (to mix oxygen and air)
- Humidifier
- Heated wire circuit with pressure release valve
- Short nasal cannula



• **Indications for use: The indications of the use of HHFNC in neonates are**

- Infants with Chronic Lung Disease (ability to wean flow over FiO<sub>2</sub>)
- As a mode of weaning from ventilatory support
- As a mode of weaning NCPAP support
- Alternative to NCPAP in mild/moderate respiratory distress
- Post-op respiratory support
- Babies with nasal trauma from NCPAP
- Treatment or prevention of apnoea of prematurity

**Contraindications: The contraindications of the use of HHFNC in neonates are**

- Upper airway abnormalities
- Ventilatory failure
- Severe cardiovascular instability
- Frequent apnoea (despite caffeine in preterms)

**Recommended Settings**

- **Nasal prongs: It must** be smaller than 50% of patient's nares (tight fit of nasal cannulae may generate pressure of 6-10cm H<sub>2</sub>O at flow as low as 1.5-2 L/min)
- **Flow:** Flow 4-8 L/min (lower flow 4-6 L/min may be sufficient for smaller babies, flow rates > 6 L/min in infants < 1 Kg should avoided)
- **Fio<sub>2</sub>:** Starting Fio<sub>2</sub> should be 40-60%.
- **Operating temperature:** If using servo humidifier set the temperature at 36 - 38° C. If using humidifier with manual settings, use the heater output so that mild condensation is seen in the circuit.
- If the baby is requiring FiO<sub>2</sub> > 0.6 or has CO<sub>2</sub> retention, acidosis or apnoea, she/he is likely to need alternative support. Continuous monitoring of heart rate, respiratory rate and SpO<sub>2</sub> is indicated. The following is a guide for the size of the nasal cannula to be used, but the diameters of nares vary and appropriate size should be individualized for every baby.

**Table 1: Suggested cannula size to be used in neonates for HHFNC**

<b>Weight</b>	<b>Cannula Type</b>	<b>Maximum recommended flow rate</b>
<1.4 kg	Premature	6L/min
1.4kg-2.5 kg	Neonatal	7L/min
>2.5 kg	Infant	8L/min

- **Weaning from HHFNC:** We should start weaning from HHFNC when FiO<sub>2</sub> is <30%. After weaning from HHFNC
- Baby can be put on oxygen nasal cannula with flow < 1 L/min
- Attempt to reduce by 1 L/min 24 hourly if FiO<sub>2</sub> < 0.25-0.3 in babies > 1.5Kg
- Attempt to reduce by 0.5L/min 12 hourly if FiO<sub>2</sub> < 0.25-0.3 in babies < 1.5 Kg
- Attempt to reduce by 0.5L/min 24 hourly if FiO<sub>2</sub> = 0.25 – 0.3
- Attempt to stop if requiring 2.0 L/min or less

## TIPS TO FOLLOW-UP OF NICU GRADUATES IN CLINICAL PRACTICE.

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### Introduction:

Advances in perinatal intensive care have been associated with improved survival of high risk neonates but have not resulted in decreased morbidity.(1)

### Importance of early intervention:

Almost 80-90% of brain development occurs in the first 3 years of life. Research on early brain development has revealed the limited window of malleability of the developing brain, highlighting the need to identify and address emerging problems early. (2) Hence there is need to follow up and identify newborns with developmental and behavioural difficulties earlier. A method of early detection and thereby early and appropriate intervention can prevent or minimize future disabilities.

### Whom to follow up?

Ideally, all infants and children should be screened for developmental delay. In developing countries including India, this screening is neither feasible nor cost effective. (3) However perinatal risk factors and course of neonatal illness define a group of neonates at increased risk of neurodevelopmental disability, classified as high, moderate and mild risk.(4)

### Classification of newborns as per risk:

Mild Risk	Moderate Risk	High Risk
Preterm	Preterm<33 weeks	<28 weeks
Weight 1500-2500g	Weight 1000-1500g	Weight <1000g , SGA, LGA
HIE grade I	HIE moderate	Apgar's<3 at 5 min and or HIE
Transient hypoglycemia	Hypoglycemia(BSL<25 mg/dl)	Persistent prolonged hypoglycemia
Suspect sepsis	Sepsis	Meningitis, shock needing Inotropes/vasopressor support
Neonatal jaundice needing phototherapy	Neonatal jaundice s. bil>20 or needing exchange	Neonatal Bilirubin encephalopathy
Grade I IVH	IVH grade 2	Major morbidities IVH, PVL

		Abnormal neurology on discharge, Seizures
	Twins or triplets	Twin to twin transfusion
		Ventilation more than 24 hours, CLD
	Suboptimal home environment	Surgical conditions, major malformations
		Hypocalcemia
		Inborn errors of metabolism and or genetic disorders
		Infant of HIV+ve mother

The type of follow up provided is then based on severity. (4)

Risk	Mild	Moderate and high
Who will follow up	Primary care physician	High Risk team
Where	Clinic	High risk clinic
When	Well baby care or Immunization visit	*4 months, 8 months, 1 year and yearly till 6 years

**\*Age:** Age used for follow up is calculated as corrected age. Corrected age is the sum of chronologic age in weeks minus the difference between gestational age at birth and 40 weeks of gestation.

The correction is to be considered till 2 years of age.

#### **Possible Adverse Neurodevelopmental Outcomes in Newborns**

Rates of disabilities increase with decreasing birth weight and gestation. The table below gives the probable morbidities and the clinical manifestations.

Morbidity	Clinical manifestations
Developmental Delay	Delayed milestones, Speech delay
Motor deficits	Delayed motor milestones, Tone abnormalities, Cerebral Palsy, Visuomotor integration issues, Sensory processing difficulties, Speech clarity issues
Sensory impairment	Vision impairment Sensorineural hearing loss
Learning difficulties	Dyslexia, dysgraphia, dyscalculia
Behavioral issues	ADHD, Autism, others
Epilepsy	

**The components of the follow up include follow up of Cognitive development, Neuromotor development, Growth, Neurosensory and Behaviour.**

#### **I. Cognitive Development Follow up.**

##### **Developmental screening**

It is a quick and general measure of skills. Its purpose is to identify children who are in need of further evaluation. Simply using a screening test cannot make a diagnosis. If the results of a screening test suggest developmental delay, the child should be referred for a developmental evaluation. (3) A screening tool can be a form given to the parent or a test given to the child. Some examples are

- **Parent report Questionnaires:** This is a form given to parents. Some examples are the Ages and Stages Questionnaires (ASQ), Child Development Inventories, Parents' Evaluation of Developmental Status.(5)
- **Direct observation card (DOC):** This is a self-explanatory card that can be used by parents.
- **Trivandrum development screening chart (TDSC) :**The test has 17 test items include motor, mental, hearing and vision. A vertical line is drawn at the level of the child's chronological age being tested. If the child fails to achieve any items short of the 3rd centile, the child is referred for assessment.(6)
- **Denver Developmental screening test( DDST II):** It is a quick screen with 125 items gross motor, fine motor, social language items. It is used between 0-6 years. It has a parental question plus task. In review of its psychometric properties, it is a more appropriate surveillance tool that can provide a growth chart of milestones acquisitions. (7).

### Developmental Assessment

A developmental assessment is done if a child fails a screening test, at one year and yearly till 6 years of age. A developmental evaluation is a long, in-depth assessment used to create a profile of the child's strengths and weaknesses in all developmental areas. The results are used to determine if the child is in need of early intervention services and/or a treatment plan.

#### **DASII (Developmental assessment scales for Indian Infants).**

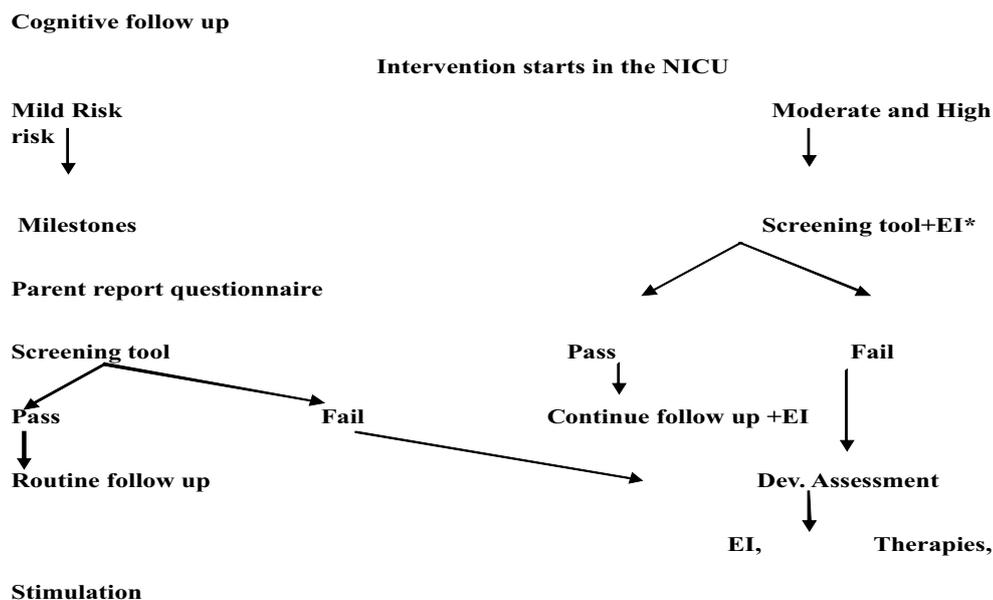
The DASII is based on revision of Baroda norms on BSID. It has 67 motor and 163 items in the mental scale. It covers age range 0-30 months. It helps to identify child's performance in 15 areas of development. The cluster scores help plan intervention. It also provides DQ (development quotient). In the Indian context, the DASII is the best formal test in children less than 2 and half years. (4)

#### **BSID III (Bayley Scale of infant development -III)**

This is an individually administered instrument that assesses developmental functioning between 1 month and 42 months of age. It assesses five scales: cognitive, language, motor, socio-emotional and adaptive scales. A score less than 70 is considered as delay.

**Intelligence tests:** These are used in children above developmental age of 2 and ½ years. These include the Wechsler Intelligence scale for children and the Stanford Binet test of intelligence.

#### **Cognitive Follow up algorithm**



\*EI- Early Intervention

#### **II Growth and Nutrition Follow up:**

Growth is a sensitive index of the infants well being. While monitoring growth, we should use corrected age for the same.

#### **Which charts?**

In preterm < 40 weeks gestation - use intrauterine growth charts Fenton, Infant Health and Development Program (IHDP), Casey P, Wrights, Gairdner and Pearson (Castlemead), Modified Babson Brenda charts. IHDP is preferred as recent compared to the Lubchenco. Later postnatal growth charts by CDC (Centre for Disease Control and Prevention) can be used. (4)

**Head size:** It is a simple tool to predict brain growth. It is usually the first parameter to demonstrate catch-up. Small head size indicates poor brain growth and identifies an infant at risk for developmental disability.

### III Neuromotor Follow up:

- **Amiel Tison** The Amiel Tison is a neurodevelopmental assessment in the first year assessing Tone, Primitive reflexes, Postural reactions and deep jerks. It helps in early identification of tone abnormality for early intervention. It is administered at 3, 6, 9 months and 1 year corrected age. Its predictive value at 3 months examination for normal outcome at 12 months is 93%. It has greater sensitivity for picking up abnormal motor development at 3,6,9 months than the Bayley Scales but loses advantage at 12 months. (8). Early intervention starts in the NICU itself.
- **Tone evolution:**  
Babies with tone abnormalities identified are started on intervention, investigated accordingly and followed diligently. Serial comprehensive assessments of both neurologic signs and motor skills by trained observers are indicated to give an idea of whether tone abnormalities are transient or persistent. A diagnosis of cerebral palsy is generally evident if the neurological signs persist by 18-24 months. Loss of abnormal neurological findings by 12 months is associated with better outcomes. (9)
- **Assessment of severity of motor disability (function)**  
The GMFCS (gross motor function classification system) after 2 years defines five levels of gross motor function helps in prognosis. It has been developed to systematically evaluate functional skills in prone roll over, sitting, crawl, walk and run. (10)

### IV Vision Screening for Retinopathy of Prematurity:

In preterm babies, there is a risk of developmental vascular proliferative retinal disorder.

#### Whom to screen:

Baby with any one of the following: BW < 1500 grams or Born at  $\leq$  32 weeks GA

When to screen: 4 weeks after birth or 32 weeks post menstrual age whichever is later. (11)

**Follow-up** - Follow-up examinations should be recommended by the examining ophthalmologist.

**Annual examinations: They are needed** for the presence of strabismus, nystagmus, light reflex, tracking ability, and roving or disconjugate eye movements. (9).

### V Hearing follow up:

**Risk factors for hearing loss:** NICU stay of > 5 days, Mechanical ventilation, Ototoxic drugs, Hyperbilirubinemia requiring exchange transfusion, Meningitis, TORCH infections.

#### How to follow:

**Screen**- OAE - Otoacoustic emission in NICU. This detects vibrations of hair cells in response to noise.

**Assessment** - BERA –Brain stem evoked auditory response. It measures the summation of action potentials from Cochlear nerve VIII to the inferior colliculus of the midbrain in response to a click stimulus.

#### When to test?

OAE at birth

BERA done at 3 months or if OAE is refer.

Babies with risk factors who pass the screen have a behavioural audiometry at 1 year. (4)

A DASII done at 1 year would evaluate language comprehension and thereby helping plan intervention.

Infants with permanent hearing loss who receive intervention services prior to 6 months of age have significantly better language outcomes. (9)

## VI Behavioural issues follow up

High risk newborns are more prone to behavior issues like attention issues. The Pediatrician monitoring follow up must probe for attention issues in social settings and its effect on learning. With the rise in incidence of autism, administering a simple screen like the M-CHAT-R Follow -Up at 18 months may help identify children with autistic features earlier. (12)

### Till when to follow up:

Ideally, follow up should continue till late adolescence as many cognitive, learning and behavioural problems more common in at risk newborn may only become apparent on longer follow up.

### Summary

1. A neonatal follow up programme based on early detection and early intervention should exist as an extension of all neonatal intensive care units.
2. Perinatal risk factors help classify neonates on the basis of risk and follow up is organized accordingly.
2. A screening test is not enough for diagnosis. It needs to be followed by a detailed evaluation.
4. Based on the assessment, an early intervention programme is initiated with parents in the loop. Serial follow up evaluations are necessary to ensure that appropriate interventions are in place.
5. Considering the high incidence of behavioural and academic difficulties in high risk newborns in school age, a surveillance for the same is warranted since the early follow up visits.
5. Early intervention reduces the impact of the disability and improves functional outcomes.

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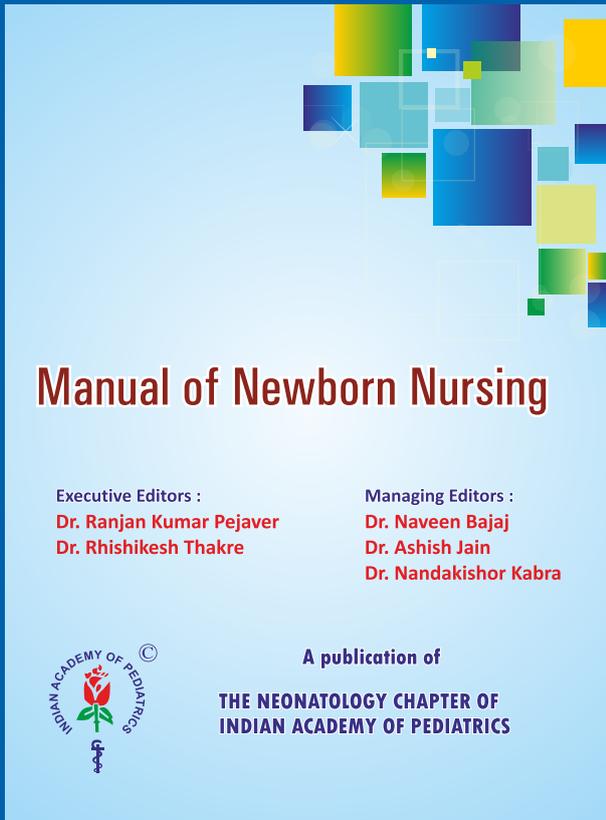


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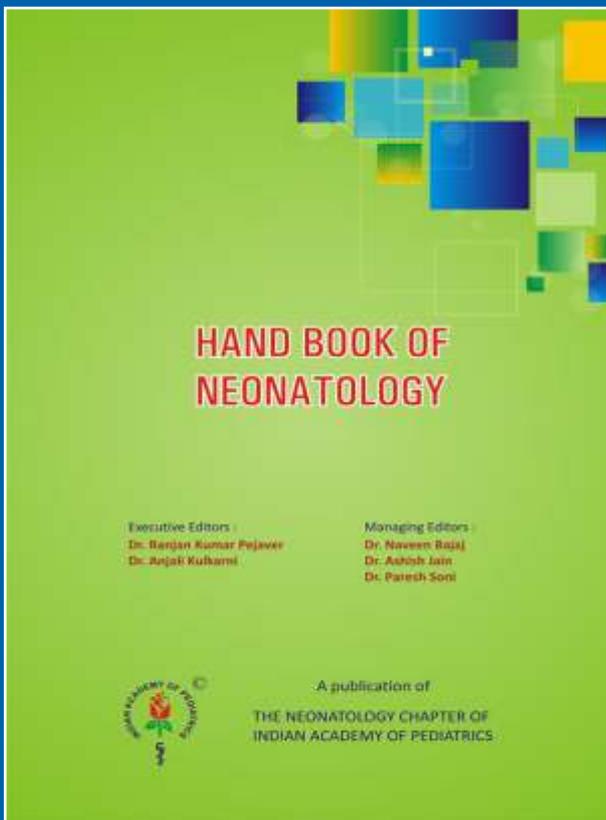
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