3.1 FETAL, NEONATAL AND TRANSITIONAL CARDIOVASCULAR PHYSIOLOGY:

Fetal circulation:

Before birth Placenta is the organ for exchange of gases for the fetus. Oxygen diffuses across the placental membrane from mother’s blood to the fetal blood. The oxygenated, nourished blood from the placenta is returned by umbilical vein which enters the liver where half of it enters the portal vein and the rest by passes liver via ductus venosus to enter Inferior venacava (IVC) just before it enters the right atrium. IVC also carries the deoxygenated blood that is returning to the heart from the lower limbs. In the right atrium blood stream of the oxygenated blood is directed towards the left atrium by the Eustachian valves via the Foramen Ovale.

In left atrium it mixes with the small amount of blood returning from lungs via pulmonary veins and is pumped into the left ventricle. This oxygenated blood mainly flows through the coronaries, head, and upper extremities.
The deoxygenated blood from superior vena cava and Inferior Vena cava directly traverses through tricuspid valve to enter right ventricle. 10-15% of right ventricular output passes through the fetal lung but it does not play a role in fetal oxygenation or acid-base balance. Pulmonary vascular resistance is high which decreases the flow of blood through the lungs. The high degree of pulmonary vascular resistance has been explained on basis of active and passive resistance.\textsuperscript{[20]} The passive resistance is due to compression of pulmonary capillaries by fetal lung fluid. The active vasomotor tone secondary to hypoxic level of pulmonary venous blood is mainly responsible for the pulmonary vasoconstriction in the fetus.

Increased levels of Prostaglandin E2 and adenosine have also been thought to be responsible for in-utero high pulmonary vascular resistance.\textsuperscript{[21]} Fetal lung vasculature also has a large muscle mass compared to that of the adult.

Because of the high pulmonary vascular resistance, majority of the blood pumped from the right ventricle enters the descending aorta through ductus arteriosus for distribution to the lower extremities and returns back to the placenta via umbilical arteries for oxygenation. Studies by Kiserud et al have shown oxygenation in ascending aorta is 65%, descending aorta (60%), where as in pulmonary trunk it is 55%. Oxygenation in pulmonary veins and pulmonary arteries is similar ie.45%.\textsuperscript{[22]}
Transitional Neonatal circulation:

Dramatic changes occur during fetal to neonatal transition at birth in order to immediately adapt to the extraterrestrial life. With increase in oxygenation level following first breath, there is marked decrease in pulmonary vascular resistance and increase blood flow from the right ventricle to the lungs. Fig 3.2 shows changes that occur in fetal circulation immediately after birth with closure of PDA and Foramen Ovale. The oxygenated blood returning from lungs is now being supplied to the whole body.

Figure 3.3 shows the sequence and factors responsible for the drop in pulmonary vascular resistance that occurs following birth. Many factors regulate pulmonary blood flow in this critical perinatal period. This includes mechanical factors and release of various vasoactive substances by pulmonary vascular endothelium such as Prostacyclin and Nitric Oxide.

The decrease in pulmonary vascular resistance increases the blood flow to the left atrium. The pressure in the left atrium increases which closes the Foramen Ovale.
by pressing the valve of the Foramen Ovale against the septum secundum. The Foramen Ovale closes functionally at birth.

As the pulmonary vascular resistance is now lower than the systemic resistance, blood flow in the ductus arteriosus reverses passing from the aorta to the pulmonary trunk. The ductus arteriosus constricts at the birth but there is often a small left to right shunt for 24 to 48 hours in a normal, healthy infant. Several events promote ductus constriction in the full term newborn. These include an increase in arterial partial pressure of oxygen, a decrease in blood pressure within ductus (due to postnatal decrease in pulmonary vascular resistance), a decrease in circulating PGE2 (due to loss in placental PG production and increase in PG removal by the lung), and a decrease in number of the PGE2 receptors in the ductus wall.

Fifty percent of ducts are functionally closed at the end of 24 hours, ninety percent by 48 hours and hundred percent by 72 hours (pulsed doppler echocardiography). Anatomical closure of the ductus and formation of the ligamentum arteriosum occurs by twelfth week.

Removal of the low resistance placental circulation and clamping of the cord also results in increase in systemic blood pressure. The major decline of pulmonary resistance from high fetal levels to low adult levels occurs within the first 2-3 days but may be prolonged to seven days or more. The sphincter in the ductus venosus constricts so that blood entering the liver passes through the hepatic sinusoids. Over the next few weeks pulmonary vascular resistance decreases even further secondary to remodeling of pulmonary vasculature including thinning of the vascular smooth muscle and recruitment of new vessels.
3.2. PREVIOUS STUDIES DONE ON FETAL AND NEONATAL CARDIOVASCULAR ADAPTATION:

Physiologic events that occur during transition from fetal to extrauterine life at birth have attracted the attention of investigators for several decades.\cite{22-25} Because of the very critical life threatening possibilities during transition Professor Clement Smith of Boston called this period from birth to first breath as “Period of Grace”\cite{23} (quoted in the eleventh Blackader lecture by Lind J).\cite{23} which highlights how important those few seconds are in view of those few children who never manage to adapt to extra-uterine life without additional help.

Several investigators in the past worked simultaneously to understand the fetal and newborn physiology. The concept of newborn care was developed based on research in the field that had been carried out mainly in non human mammalian fetuses and newborns such as rats, rabbits, pigs, lambs and monkeys. With advances in ultrasound in Obstetrics lot of human studies have investigated fetal and neonatal physiology with results that are similar but not identical to the animal studies.\cite{22}

In second century AD Galen described what is now known as Foramen Ovale and ductus arteriosus.\cite{26} In 1561 the word placenta was initiated by Fallopio and it was in 1626 Spigel showed that there is no direct communication between umbilical vessels of the fetus and uterine vessels of the mother.\cite{27} Pohlman in 1909 injected starch in fetal blood vessels to study the fetal blood circulation.\cite{28} However the important contributions came through work by Barcroft at Cambridge and Dawes in Oxford, UK on fetal and neonatal physiology through their experiments on fetal and newborn lambs.\cite{29-31} Barcroft and Barron for the first time in 1938 gave a direct record of circulation in the fetal lamb.\cite{32}
In 1939 Dawes and his associates presented data on normal distribution of the blood flow derived from oxygen saturation of blood withdrawn simultaneously from various vessels in mature fetal lamb delivered by C-section. This group, for the first time described the changes in the circulation at birth such as sudden drop in pulmonary resistance with increase in pulmonary blood flow and reversal of blood flow in ductus arteriosus.\

In 1959 Dawes published the paper on changes in oxygen consumption of lamb after birth. He and the team measured umbilical blood flow using velodyne flowmeter. They explained the increase in oxygen consumption after birth on the basis of increased metabolism to maintain body temperature in the newborn lamb. Their experiments on effect of vascular tone of fetal lung, effect of hypoxemia at the time of delivery on fetal lamb, changes in fetal and neonatal blood gas homeostasis gave a strong framework for care of newborn infants. Rudolph AM and colleagues conducted studies on previable human fetus and found that the flow through umbilical arteries increases from 17% at 10 weeks to 33% at 20 weeks of gestation.

In the series of quantitative studies of the human neonatal circulation published by Lind and associates different modes of respiratory and hemodynamic adjustment during the first hours of life were understood. The total blood volume of the late clamped infants was found to be 25-30% higher in the first half an hour of life. The blood volume in this group was measured as 100ml/kg at half an hour and decreased gradually to 90 ml/kg at four and 24 hours and 90-95 ml/kg at 72 hours. Nearly 40 ml of blood entered the infant in the first 15 seconds (quarter of total transfusion) and 80ml (one half of total) in 60 seconds after birth. Between 4 and 24 hours of age there was increase in plasma volume of majority of the infants significantly higher in those with delayed clamping of the cord. Higher pulmonary
arterial pressure in the late clamped group in the first nine hours of life was attributed to the comparatively greater pulmonary vasoconstriction secondary to greater filling or distension of the pulmonary vascular bed.

Recent Doppler studies in low risk pregnancies by Kiserud and colleagues found that the umbilical blood flow increases from 36 ml/min at 20 weeks to 265 ml/min at 40 weeks of gestation. One third of the fetal combined cardiac output is directed to the placenta by 20-32 weeks (similar to studies by Rudolph AM) but this decreases to one fifth beyond 32 weeks of gestation. The studies also show that the oxygen saturation in abdominal IVC (35%) is the lowest but the difference between left and right ventricles is found to be only 10% which increase to 12% during hypoxemia. This could be due to abundant volume of oxygenated blood presented to the Foramen Ovale with a spillover to the right side.

With advances in research modalities and techniques the knowledge of fetal and neonatal cardiovascular physiology will continue to expand in future.

3.3. FETAL, NEONATAL AND TRANSITIONAL PULMONARY PHYSIOLOGY:

Barcroft performed series of observations on fetal lambs delivered under maternal spinal anesthesia in a bath full of warm saline and concluded that fetal breathing movements were present or could be elicited by stimulation of the snout between 40 and 60 days gestation. It was latter proved that fetus has breathing movements that start midway through the gestation. These are intermittent breathing movements lasting for varying period but about 20 minutes every hour near term. Sensory stimulation and cooling of the skin, changes in the arterial oxygen and carbon dioxide levels, and the detachment
of the placenta are the factors found to be responsible for the onset of continuous breathing after birth.\textsuperscript{14,34} Prostaglandin E2 and adenosine are thought to be inhibitors of continuous breathing movements during experiments in fetal lamb.\textsuperscript{21}

Jost and Policard discovered that ligating the trachea of fetal rabbits causes distension of lungs and thus provided evidence for formation of lung fluid but the evidence that this fluid is different from the amniotic fluid was found by Adams in 1963.\textsuperscript{35,36} In 1966 Strang provided interesting information as to the means by which fluid is removed from the tracheobronchial tree after birth\textsuperscript{37} and Aherne\& Dawkins had found histological evidence of distended pulmonary lymphatics in newborn rabbits.\textsuperscript{38} Bland and colleagues measured the excess liquid in the lungs of unanaesthetized term fetal lambs before and during delivery.\textsuperscript{39}

Dawes paper on “The Central Control of Fetal Breathing and Skeletal Muscle Movements” gives idea on the systematic work done by him and several other investigators on fetal breathing.\textsuperscript{14}

These and many other investigators added to the fundamental knowledge about changes in respiratory physiology immediately after birth which laid down the basis for ventilation of newborn infants. Remarkable advances in the respiratory management of the premature infant occurred during the 1970s. The landmark study by Gregory illustrating the benefits of CPAP resulted in a dramatic improvement in the successful respiratory support of premature infants.\textsuperscript{40}

3.4. SCIENCE OF FIRST BREATH:

Replacement of fetal lung fluid with air is an important step towards establishment of smooth respiration. Fetal lung fluid is produced by the pulmonary epithelial cells and is high in chloride but low in bicarbonate and protein. In- utero
this fluid comes out of trachea and gets mixed with amniotic fluid. It has been found essential in the development of lungs in utero. The production of fetal lung fluid decreases before birth and there is increased absorption into the lung interstitial spaces followed by uptake in the lymphatic. The normal volume of fetal lung fluid present near term is approximately 20 ml/kg, and this volume decreases just before birth leaving approximately 6 ml/kg of lung fluid to be cleared after birth. An osmotic gradient is created by increase in interstitial sodium and protein which facilitates absorption of this fluid. As the infant begins breathing after birth the residual lung fluid is replaced with air. Surfactant present in the lung helps in retaining a small amount of air during exhalation and keeps the alveoli open. This air is known as the functional residual capacity (FRC) and is important to the development of effective respiration. A healthy newborn when taking the first breath after birth exerts a negative intrathoracic pressure of approximately 50 cm H2O (0-100 cm H2O) and with adequate surfactant supply will develop an FRC of approximately 5–6 ml/kg.\textsuperscript{[41,42]}

There is increased production of adrenaline by fetus and Thyrotropin releasing hormone and glucocorticoids by the mother with onset of labor that stimulates reabsorption of fluid by pulmonary epithelial cells. During vaginal delivery at term, up to 35 ml of fluid is expelled from the lungs by uterine contraction and passage through the birth canal.

Mechanics of first breath were studied as early as in 1958 on mature fetuses of guinea pigs, cats etc by Agostoni et al\textsuperscript{[43]} and they reported that many breaths were necessary before the lungs got completely aerated and all the liquid was removed immediately after birth. Marked resistance to lung expansion was found to be due to the high viscosity of the liquid present in the airways, the surface tension of the air-liquid interphase, the involvement of only the inspiratory muscles for the expansion of
the thorax which is not facilitated by the tendency of the thorax to expand due to elastic forces as seen in adults.

In 1959 Karlberg and in 1978 Milner successfully conducted studies on newborns to understand changes that occur with first breath.\[^{15,41,42}\] They took serial X-rays starting at the time of birth and also studied pressure and volume changes using intraesophageal catheter, face mask and low resistance pneumotach. They reported changes with the first and subsequent breaths as follows: With the first inspiration the pressure generated was 10-70 cm H\(_2\)O and the inspiratory volume was 20-75 ml. Expiration was passive and there was no pause at the end of inspiration.

Residual volume varied from 0 to 70 ml and subsequent earliest breaths required lower intra thoracic pressures.

Total respiratory work was equal to square of tidal volume. The total inspiratory work during first three breaths showed no difference. Milner reported that opening pressures are not required frequently (which was reported earlier) because air/liquid interface is not formed until first breath, and tension is reduced by surfactant.

A significant correlation has been shown between first inspiratory volume and functional residual capacity (FRC) at the end of the first breath.

![Diagram](image)

**Fig. 3.4.** Sequential changes with first and subsequent breaths (provided by Dr. Vidyasagar) Note that less pressure is required to open alveolus with subsequent breath, air displaces fluid from the alveolus with each breath, ductus arteriosus & foramen ovale closes.
breath (p <0.004). Fig.3.4 shows the sequential changes that occur in inspiratory pressure, fluid in alveoli, ductus arteriosus and Foramen Ovale with each breath.

Full inflation and prolonged expiration associated with the baby’s crying drives out nearly 100ml of fluid with first few breaths. Further breaths require less effort due to aerated alveoli and decreased surface tension in presence of surfactant.

In summary, with the first breath there is mechanical expansion of lungs, fluid from the alveoli is pushed out and absorbed in to the lymphatics. With subsequent breaths alveoli get filled with air which contains 21% oxygen. As a result of gaseous distension and increased oxygen in the alveoli the blood vessels in the lungs relax, the pulmonary blood flow increases and well oxygenated blood is pumped for the whole body.

3.5. EFFECTS OF NORMAL CARDIOPULMONARY TRANSITION ON OXYGENATION

Recent studies have shown that it takes 8-10 minutes to attain saturation level of 95 % in healthy term and preterm infants after the first breath. The classic studies of Karlberg et al and later of Vyas et al on first breath have shown that it takes several breaths for the newborn to attain “normal” lung volume before cardio pulmonary stabilization takes place. With steady lung expansion during this phase the existing fetal state of high pulmonary vascular resistance gradually decreases allowing increased blood flow to lungs. The blood flow through ductus arteriosus changes direction from the fetal state of R –to- L to no-flow state as the pulmonary vascular resistance drops. This natural course of cardiopulmonary hemodynamics spans through first few minutes of life during which time the initial fetal oxygen saturation
of 60-70% gradually improves with each breath and each cardiac cycle, reaching “normal” oxygen saturation. These changes are summarized in Table 3.1.

**Table 3.1. Summary of events during cardiopulmonary adaptation after birth**

<table>
<thead>
<tr>
<th>Events</th>
<th>Physiologic Consequence</th>
<th>Changes in CVS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar Ventilation</td>
<td>↓PVR</td>
<td>↑ LA Pressure</td>
</tr>
<tr>
<td></td>
<td>↑Pulmonary Blood Flow</td>
<td></td>
</tr>
<tr>
<td>Placental Separation</td>
<td>↓IVC return</td>
<td>↑ RA Pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ SVR</td>
</tr>
<tr>
<td>↑LA Pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↓RA Pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↓PVR</td>
<td>Reverse Ductal flow</td>
<td></td>
</tr>
<tr>
<td>↑SVR</td>
<td>O₂ in Ductus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Closure of Foramen Ovale</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**3.6. ROLE OF PULSE OXIMETRY IN UNDERSTANDING NEONATAL TRANSITION:**

Oxygen in blood is carried in 2 forms, 98-99% bound to hemoglobin (Oxyhemoglobin) and rest dissolved in the blood plasma (PO₂). Together oxygen content is represented in ml O₂/100ml of whole blood.

Tissues utilize dissolved form of oxygen. The oxygen hemoglobin dissociation sigmoid shape curve explains the relationship between these two forms of oxygen. Oxygen bound to the hemoglobin is released into the blood's plasma.

![Oxyhemoglobin equilibrium curves of blood from term infants at birth & from adults (ref Fetal & Neonatal Physiology 3rd Edition, Chapter 86)](image-url)
and absorbed into the tissues. Each hemoglobin molecule has the capacity to carry four oxygen molecules. How much of that capacity is filled by oxygen at any time is called the oxygen saturation. The oxygen saturation is the ratio of the amount of oxygen bound to the hemoglobin, to the oxygen-carrying capacity of the hemoglobin which is expressed in percentage.

Various physiological factors in the newborn period affect oxygen dissociation curve. Fetal hemoglobin has high affinity for oxygen and so there is high percentage of oxyhemoglobin. This shifts the curve to left thus decreasing the amount of oxygen available for utilization by tissues. It constitutes 75% of the total hemoglobin in term infants. Hypothermia, a common neonatal problem also shifts the curve to the left. Low pH secondary to metabolic acidosis in a hypoxic infant and decrease amount of 2, 3-DPG are other factors that can cause the shift of curve to left. The difference in Neonatal and adult oxygen dissociation curve is shown in Fig 3.5.

In normal infants $P_{50}$ (PaO$_2$ at 50% oxygen saturation) on day 1 of life is 20 mmhg in contrast to 27mmhg in adults. $P_{50}$ in term infants increases gradually and reaches adult values by 4-6 months of life. Further a less than 24 hours infant can have saturations in mid 90s and yet PaO$_2$ measurements of 50-60mmHg. This infant may appear pink despite low PO$_2$’s because of the high oxygen affinity associated with fetal hemoglobin. It should also be noted that lower PO$_2$’s in the newborn infant or changes in PO$_2$ do not accurately indicate the amount of Oxygen available to the tissues as it may be hardly affected.

Immediately after birth there is a small amount of adult hemoglobin which shifts the curve to the left compared to adults. In addition the steep portion of the curve which indicates tissue extraction of large amounts of oxygen with minimal drop
in PO$_2$ also shifts the curve to left. Therefore even a major drop on PO$_2$ from 80 to 40 mmHg will not affect oxygen saturation drastically.

Oxygen saturation is therefore a more precise indicator of oxygen content in blood and more important to monitor physiologically since it gives a complete picture of amount of oxygen available for use.

Measurements of oxygen saturation levels soon after birth also indicate the degree of interactions between ventilation and pulmonary blood flow.

### 3.7. USE OF OXYGEN IN CARE OF NEONATES

Oxygen was used in neonatal resuscitation in 1780, first described by Francoise Chaussier, Professor of Obstetrics in France and it was in 1900, Budin recommended the use of oxygen for premature infants during episodes of cyanosis.$^{45}$ In 1923, Bakwin noted that oxygen administration not only relieved cyanosis but also diminished the number of subsequent cyanotic episodes. He recommended extended periods of oxygen administration.$^{46}$ The association between oxygen therapy and Retrolental Fibroplasia (RLF) was eventually determined by Campbell K of Australia in 1951.$^{47}$ This led to decreased use of oxygen in Neonatal ICU increasing the risk of mortality. The earliest method of quantitation of O$_2$ administration was to count the number of bubbles when O$_2$ was delivered through water. Until the 1960's, O$_2$ was administered in terms of liters/minute rather than by concentration. In 1961, Silverman in his textbook, for the first time mentioned that "oxygen concentration must be determined by means of oxygen analyses, as often as necessary, to keep it properly stabilized, but at least every four hours".$^{48}$ In 1963 Cook and associates and in 1964 Cassin and co-workers showed the importance of low PO$_2$ in maintaining pulmonary vasoconstriction in the fetus and increase in pulmonary blood flow with
ventilation of lungs using oxygen.\textsuperscript{49,50} It was also recognized that high concentration of inspired oxygen leads to increased incidence of chronic lung disease. Use of pulse oximetry for neonatal care was started in 1980 and the earliest reported use in delivery room is in 1985 by Sendak and Harris to monitor the changes in SpO\textsubscript{2} immediately after birth.\textsuperscript{51,52} Since then investigators got interested in monitoring SpO\textsubscript{2} changes in the newborn immediately after birth and develop guidelines to use oxygen in the delivery room. Avery M and colleague showed association of surfactant deficiency and hyaline membrane disease as early as in 1956 however surfactant replacement therapy for Respiratory distress syndrome was introduced only in 1980s.\textsuperscript{53} Table 3.2 summarizes studies reported so far on changes in SpO\textsubscript{2} immediately after birth in newborns.

**Table 3.2. Studies on SpO\textsubscript{2} changes immediately after birth**

<table>
<thead>
<tr>
<th>Author</th>
<th>Gestation</th>
<th>Technology</th>
<th>Duration</th>
<th>No of infants</th>
<th>Site of monitoring</th>
<th>Values obtained SpO\textsubscript{2}%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamlin\textsuperscript{[54]}</td>
<td>&gt;31wks</td>
<td>Massimo</td>
<td>15 min/ SpO\textsubscript{2}&gt;90 %</td>
<td>205</td>
<td>Preductal</td>
<td>63,70,76,81,90 At 1,2,3,4,5 min</td>
</tr>
<tr>
<td>Altuncue\textsuperscript{[55]}</td>
<td>Term</td>
<td>Nellcor Oximax N-550B</td>
<td>Till SpO\textsubscript{2}&gt;95 %</td>
<td>150</td>
<td>Preductal</td>
<td>71,92,98 at 1,5,15 min</td>
</tr>
<tr>
<td>Rabi \textsuperscript{[56]}</td>
<td>&gt;35 wks</td>
<td>Masimo</td>
<td>10 min</td>
<td>45</td>
<td>Preductal</td>
<td>87,91 at 5, 8 min</td>
</tr>
<tr>
<td>Dimich\textsuperscript{[57]}</td>
<td></td>
<td>OhmedaBio x 3700</td>
<td>24 hours</td>
<td>100</td>
<td>Preductal</td>
<td>71,9,83,3,90,7, 95.7 at 1,5,10 min &amp; 24 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Postductal</td>
<td>64,4,76,6,87,1,9 5.2 at 1,5, 10 min &amp; 24 hours</td>
</tr>
</tbody>
</table>

20
<table>
<thead>
<tr>
<th>Author</th>
<th>Study Type</th>
<th>Instrument</th>
<th>Time Points</th>
<th>Saturation Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toth[58]</td>
<td>Term</td>
<td>Nellcor 300</td>
<td>20 min</td>
<td>Preductal: 73,84,92,92 at 1,5,10,15 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Postductal: 67,78,89,92,94 at 1,5,10,15 &amp; 20 min</td>
</tr>
<tr>
<td>Harris[51]</td>
<td>Term</td>
<td>Nellcor 100</td>
<td></td>
<td>Postductal: 61 at 1 min</td>
</tr>
<tr>
<td>House[59]</td>
<td>All infants</td>
<td>Nellcor N100/</td>
<td>First 15 min</td>
<td>Preductal: 64.4,70.4,78.6,8 0.7,83.2,86.4,86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ohmeda Bio 3700</td>
<td></td>
<td>.9,87.7,88.8,90,4,90.6 at each minute from 1-15 min</td>
</tr>
<tr>
<td>Dawson[44]</td>
<td>All healthy infants</td>
<td>Masimo</td>
<td>First 10 min</td>
<td>Preductal: 468 Gave reference range for SpO2 from 1 to 10 minutes of birth</td>
</tr>
<tr>
<td>Mariani[60]</td>
<td>Term</td>
<td>Novametrix 515A</td>
<td>Till 90% saturation 1,3,5,&amp;10 min</td>
<td>Preductal: 69.3,82.3,89.3,9 3.7 at 1,3,5,10min</td>
</tr>
<tr>
<td>Rao &amp; Ramji[61]</td>
<td>Term</td>
<td>Nellcor N 20</td>
<td>1,2,3,4,5,10,15,30 min 1,2,8,24 hours</td>
<td>Postductal: 60.60 ± 1.20, 91.10 ± 0.5% At 1,15 min, a plateau thereafter</td>
</tr>
</tbody>
</table>

However, the role of oxygen in neonatal resuscitation was unclear because the normal values of oxygen in a newborn immediately after birth were not known. Lind and colleagues during their study on neonatal circulation had studied various levels of SpO2 by direct angiocardiography of the neonate immediately after birth.[17] After the introduction of pulse oximetry in newborn Harris et al showed that the level of oxygen saturation is low even in the presence of normal Apgar score.[51] A great interest in assessing the accurate oxygenation status of the newly born baby in the
delivery room developed in 90s since the saturation values would guide the clinician on use of oxygen in resuscitation. Vento et al also showed that newborns resuscitated with 100% oxygen have an increased oxidative stress for at least a month.\(^{[63]}\) Oxidative stress is known to influence apoptosis and cell growth and an urgent need was perceived to know the optimal oxygen saturation levels at different ages of postnatal life. Various investigators since then studied changes in oxygen saturation immediately after birth (Table 3.2). Dawson et al published values of SpO\textsubscript{2} based on studies in 468 infants (62,150 data points).\(^{[44]}\) The authors referred them as the “reference values” for future studies.

3.8. CHANGES IN HEART RATE (HR) AFTER BIRTH:

Presence of heart rate is a sign of life and assessment of life in the newborn baby by palpating the umbilical pulse is known to be age old practice. An increasing heart rate in response to resuscitation is the most important clinical assessment of newborns well being in the delivery room (DR). Virginia Apgar found it to be the most important diagnostic and prognostic sign of the five signs of Apgar Score.\(^{[64]}\) Contis et al in 1963 showed significant decrease in heart rate during the first hours of life in healthy term normal infants measured by auscultation\(^{[65]}\) while Bustos et al reported no significant difference in heart rate of normal infants to those who were mildly depressed at birth.\(^{[66]}\)

With the introduction of pulse oximetry in the delivery room (DR) it became an important tool for assessment of heart rate immediately after birth. Kamlin and team compared heart rates determined clinically (auscultation/palpation of umbilical cord- counting for 6 sec and multiplying by 10) with ECG in healthy newborns in the DR.\(^{[67]}\) Clinical assessment was found to be inaccurate and underestimated ECG HR. Same group later studied the accuracy of pulse oximetry in measurement of heart rate
in newborns in DR and found the sensitivity and specificity of PO for detecting HRECG <100 bpm was 89% and 99%, respectively.\textsuperscript{68} Likewise, Toth et al found that the heart rates from pulse oximetry recordings were up to 30% lower than those from ECG recordings.\textsuperscript{57}

Heart rate more than 100bpm is taken as normal during newborn resuscitation. Recently Dawson et al published the reference charts derived from pulse oximetry measurements on 468 infants. They reported heart rate <100/minute in normal healthy newborns at one minute of life which increased to >100 bpm by 2-3 minutes.\textsuperscript{69}

Desmond et al found that the fetal heart rate decreased briefly just prior to delivery and was then irregular immediately after delivery. By 2–3 min of life the heart rate became regular at a slightly elevated level (approximately 180 /min) and then began decreasing to 140 beats/min or less by 30 min of life. Additionally they also reported that the heart rate was somewhat unresponsive to activity in the first 2–3 hours of life.\textsuperscript{70} Table 3.3 gives summary of studies done on HR in DR immediately after birth.

### Table 3.3. Studies on heart rate immediately after birth

<table>
<thead>
<tr>
<th>Author</th>
<th>No of infants</th>
<th>Duration and method of monitoring</th>
<th>Heart rate recorded</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bustos\textsuperscript{66}</td>
<td>23</td>
<td>90 min Auscultation</td>
<td></td>
<td>No difference in HR in vigorous and depressed infants, stabilizes by 50 minutes from birth.</td>
</tr>
<tr>
<td>Brady &amp; James\textsuperscript{71}</td>
<td>18</td>
<td>Welsh electrodes to shoulder</td>
<td>150(75-187)</td>
<td>Respiration prior to cord clamping Respiration after cord clamping</td>
</tr>
<tr>
<td>Meier-Strauss\textsuperscript{72}</td>
<td>53</td>
<td>3-20 min ECG &amp; PO</td>
<td>155-165 by ECG</td>
<td>HR by PO was less than recorded by ECG</td>
</tr>
<tr>
<td>Toth\textsuperscript{58}</td>
<td>50</td>
<td>2 min 10min 20min PO</td>
<td>157(89-199)</td>
<td>HR by PO less than recorded by ECG</td>
</tr>
<tr>
<td>Contis G\textsuperscript{65}</td>
<td>40</td>
<td>15,30 min, 1,2,3, hours</td>
<td>160bpm at 15 min</td>
<td>Significant drop in first hour to 130bpm</td>
</tr>
<tr>
<td>Rao &amp; Ramji\textsuperscript{61}</td>
<td>30</td>
<td>Till SpO\textsubscript{2} reached 90%</td>
<td>161.1±198 at 1 minute</td>
<td>This study was primarily to monitor SpO\textsubscript{2}</td>
</tr>
</tbody>
</table>
3.9. BLOOD PRESSURE MONITORING IN THE NEWBORN:

Systemic blood pressure is the product of systemic blood flow and systemic vascular resistance. Stephen Hales was the first to measure blood pressure using invasive techniques, in a horse.[73] Sphygmomanometer was developed by Von Bosch in 1876, for noninvasive blood pressure monitoring in humans based on palpation of arterial pulse while inflating.[74] This was however useful to obtain the systolic blood pressure only. In 1805, Korotkoff used the stethoscope to monitor the pulse and found the characteristic sounds heard during cuff inflation and deflation due to passage of blood through constricted artery.[74] Application of ultrasound techniques to measure infants’ blood pressure became available in the late 1960s.[75]

Blood pressure in the neonate has been measured by many different techniques. Vieroidt made the first blood pressure measurement in the newborn in 1894.[76] Earlier studies using Gartner's Tonometer and Riva Rocci's sphygmomanometer gave wide range of systolic blood pressures in newborn.[74,76] Celander and Thunell in 1961 measured blood pressure in newly born infants by modified mercury-in-rubber strain gauge earlier introduced by Whitney. Ballard studied blood pressure from birth, at one hour intervals for 12 hours, then each day for ten days using oscillatory method.[75,77]

Forfar reported a series of 513 blood pressure estimations carried out by modification of the flush method used by Goldring and Woltman on 143 full-term normal newborn infants during the first 11 days of life. A rapid rise in first 3 days followed by a slow rise was reported by them.[78] The mean blood pressure in arm in first 12 hours was 59.5±12.5mmHg. It was not until 1969 that the importance of intra-arterial measurement of blood pressure in the neonate became apparent. Routine intra-arterial as well as noninvasive blood pressure has become a standard procedure in the
NICU through extensive work done by Phibbs et al. In continuation of these studies Versmold et al also made a significant contribution to understanding of normal blood pressure in healthy preterm newborns by measurement of aortic blood pressure during the first 12 hours of life and published normograms for infants with birth weight 610 to 4,220.

In a similar study Nuntaramit et al recorded intra-arterial blood pressure from 103 infants with gestational age 23-43 weeks with no ionotropic support and no intraventricular hemorrhage during first 72 hours. From these observations they constructed normograms that show the mean predicted blood pressure of neonates of different ages. They found a closer correlation of mean blood pressure with birth weight than with gestational age in first 12 hours of life. Their measurements began at 30 minutes of age and all values were averaged for first hour. They did not see a marked drop in blood pressure in first hour. This could be explained based on the policy in their institution to clamp the cord only after infant began to breathe.

During this period the device for indirect non invasive mean arterial pressure by automated oscillometric method (DINAMAP) was introduced. Park and Lee published data on 219 healthy newborn on arm and calf blood pressure measurements using DINAMAP.

How does blood pressure change after birth?

Ashworth and Neligan found(using xylol pulse indicator) that within 15 minutes after birth there was a peak in the systolic blood pressure which was followed by a decline over the next 24 hours. The lowest reading was recorded within four to six hours of birth. Contis and Lind reported highest blood pressure 15 minutes (72-110mmhg) after birth, a rapid drop till 3 hours (68-110mmhg) and then
gradually increasing till seventh day. A positive correlation was found between birth weight and blood pressure. In an Indian study by Firdaus et al the BP in the newborns measured using Dianamap was found to have increased from day 1 to day 3 at a rate of 2 mmHg/ day.\(^{[85]}\) Additionally, they reported that BP did not vary with sex, race and socioeconomic status. The normograms constructed by Nunturamit and Versmold also show that Blood pressure increases with time from birth, birth weight and gestational age but the drop in blood pressure as found in other studies has not been reported.

The reasons for increase in systemic blood pressure after birth that have been found are 1) Removal of placenta, low pressure organ during in utero period 2) clamping of the cord and 3) increased return of blood to left atrium from pulmonary circulation.

3.10. THERMOREGULATION IN NEWBORN INFANT:

Thermal adaptation is one of the prime adjustments a newborn infant has to undergo in the extra-uterine life right from birth.

In-utero placenta functions as major heat excretory organ. The fetal temperature averages about 0.5°C higher than maternal temperature. The fetus does not have a system for temperature regulation and is poikilothermic which means that it adapts to the temperature of the mother. As a result the fetal central and extremities temperatures are the same and have a value determined by the central temperature of the mother. A newborn baby is physiologically homeothermic (can maintain stable body temperature that is warmer than the environmental temperature) and tachymetabolic that is the basal metabolic rate is several times higher than
poikilothermic animals. The normal range of core body temperature for a newborn infant is $36.5^0\text{C} - 37.4^0\text{C}$ regardless of weight and gestation.

**Mechanism of heat loss/Heat exchange:**

Heat exchange between the baby and the environment occurs through the skin and to some extent through the respiratory tract. Infant loses heat with every gram of water evaporated from the body surface or the respiratory tract.

Heat exchange through skin takes place through conduction, Evaporation, Radiation and Convection. Enormous amount of heat loss occurs soon after birth when infant’s body is covered with amniotic fluid, through evaporation. Heat loss on direct contact with cold surfaces such as cold clothing, tray etc can cause heat loss by conduction. Likewise heat gain occurs in Kangaroo mother care by direct skin to skin contact of the baby and mother. Convection currents can cause some cooling in the baby in DR and postnatal ward (PNW) if precautions are not taken to prevent draughts of cold air. Exposure to cold walls, large windows can lead to loss of heat by radiation. Similarly, babies can gain heat under radiant warmer or with any other external heat source.

Heat losses lead to increased metabolic rate and is reflected in an increase in oxygen consumption. Newborn babies have large body surface area per unit body mass. Compared to that of an adult for example the body mass of a newborn baby is only 5% where as the body surface area is 15% to that of an adult. Therefore in a newborn baby heat loss is at least four times per unit body mass as compared to that of an adult. It is therefore important to keep the oxygen consumption at minimal basal level.
Thermoneutral Zone:

The thermoneutral zone for newborn is been defined as the range of ambient temperature at which metabolic rate is at a minimum and within which temperature regulation is achieved without changes in metabolic heat production or evaporative heat loss.\[^{86}\] In the unclothed resting adult the lower range of thermoneutral range is 26-28\(^\circ\)C but it is 32-35\(^\circ\)C in the naked full term newborn.\[^{87}\] The lower end of thermoneutral range varies with increasing postnatal age and size of the baby. Several investigators have demonstrated that oxygen uptake which is directly related to thermogenesis is much higher at 23\(^\circ\)C than at 28\(^\circ\)C or at 32 – 35 \(^\circ\)C even during the first few hours of life. Maximum thermogenesis determines the lower limit of thermoregulatory range. When ambient temperature continues to remain below this point hypothermia sets in. In adult this value is 5\(^\circ\)C where as in full term newborns it is 23\(^\circ\)C. Oxygen uptake value measured at 23\(^\circ\)C in a one week old full term neonate is 15ml/kg/min compared to that of 16.8 ml/kg/min at 26\(^\circ\)C.Adamson et al found that the oxygen consumption began to rise when the gradient between skin and environmental temperature exceeded 1.5\(^\circ\)C.\[^{88}\]

The control of body temperature also depends on an integrated system which consists of sensors, central regulating system and effector components.\[^{89}\]

Sensors:

The external sensors or thermo-receptive structures are basically the cutaneous thermo-sensors and the internal structures are hypothalamus, lower brain stem and spinal cord. Thermal sensors have also been found in the dorsal wall of the abdominal cavity and in the musculature.
Cutaneous Thermal receptors:

They are fine unmyelinated nerve endings present into the basal layer of the epidermis. These endings contain numerous mitochondria, providing energy for a temperature sensitive Na$^+$, K$^+$ pump which transduces cold stimulus into an electrical signal. There is scarcely any area on the body surface which does not respond to cold but the number of cold spots/cm$^2$ is found to be more on the face than on the palms and soles.

Internal Thermoreceptors:

Anterior Hypothalamus and Preoptic area have been identified to be thermo-sensitive structures but the warm sensitive cells are more than cold sensitive cells. Midbrain and Medulla Oblongata are comparatively less thermo-sensitive than the Hypothalamus whereas Spinal Cord has been found to be extremely sensitive.

Afferent Pathways:

These are thin myelinated and unmyelinated axons which belong to Group 3 and group 4 nerves. They enter through the dorsal root ganglion, cross over to contralateral side and ascend within the spinothalamic tract in the anterolateral section. The fibres join the medial leminiscus and then project in to the Hypothalamus. Some cutaneous thermal sensors are connected via the spinoreticular pathway to the reticular formation from where it is projected to the Hypothalamus. The spinal cord thermal sensors are connected to the posterior hypothalamus via anterolateral pathway in the spinal cord.

Central regulating mechanism (Integration of the thermal inputs)

The Posterior Hypothalamus has mainly the thermoresponsive cells which respond to changes in temperature of distant structures but not to changes in their own
temperature. Anterior hypothalamus and Preoptic area also have some thermo responsive cells.

**Efferent Pathway:**

The thermoregulatory effector responses include: Thermogenesis, Skin blood flow changes, Sweat secretion and behavioral responses.

This is carried out mainly by nervous system via the somatomotor system and the sympathetic System. The whole effort is towards maintenance of the desired set point by regulating heat production and heat loss. This set point is the core body temperature routinely measured within the tympanic canal, the rectum or the esophagus.

**Response to cold environment** occurs through physiological and behavioral measures.

**Physiological:** There is extra heat production through shivering and non shivering thermogenesis.

**Nonshivering thermogenesis:**

Non shivering thermogenesis is the main mechanism of heat production in human neonates. It results from the metabolic activity in a specialized organ of heat production that is brown adipose tissue.[90]

In the newborn infants brown adipose tissue is found superficially in the interscapular region, at the nape of the neck, axillae, groin and deep around kidneys and adrenals. It is characterized by presence of a large number of mitochondria, many fat vacuoles and increased vascular supply as compared to the white fat.
Non shivering thermogenesis is controlled from the hypothalamic Ventromedial nucleus through sympathetic nervous system.\textsuperscript{[91]} It releases norepinephrine which acts on the adrenergic \( \beta \)-receptors located in the cell membrane and activates a cascade of reactions that splits triglycerides into glycerol and nonesterified fatty acids (NEFA). The NEFA is oxidized, re-esterified to triglycerides or released in to the circulation. This oxidation process has been found to be highly exothermic process with generation of heat which is distributed to the various parts of the body through blood stream.

Immediately after birth newborn is exposed to cold delivery room temperature. This mechanism of exposure to cold air and oxygen from room air stimulates the sympathetic nervous system to release norepinephrine. Norepinephrine in turn induces brown adipocytes to activate adenyl cyclase. This leads to increase in cytoplasmic cyclic adenosine phosphate (cAMP) that causes phosphorylation of hormone sensitive lipase. Lipase initiates lipolysis and energy production. An intracellular uncoupling protein UCP1 or thermogenin is needed to release energy as heat during lipolysis. Prostaglandin E2 and adenosine produced by placenta inhibit this process and cytoplasmic cAMP facilitates release of heat. Decrease in the level of PGE2 and adenosine following clamping of the cord takes away the inhibition on non shivering thermogenesis in the newborn infant. Thyroid hormone has also been shown to play a role in development of brown tissue and UCP production. Non shivering thermogenesis may persist for 3-6 months of life.

Shivering has been observed in human neonate with severe hypothermia at birth but it occurs at much lower temperature than that in adults. It is controlled by the somatomotor system. The descending axons from the Posterior hypothalamus project to the reticular formation of the midbrain and Pons. There they contact supraspinal...
pathways and descend to the motor nucleus of the anterior horns of the spinal cord. The motor nerves that leave the anterior root give signals for the rhythmic contraction of the muscles. The inhibitory influence of shivering is exerted mainly by the spinal cord warm receptive structure. The cervical spinal cord is the region that preferentially receives the heat generated in the interscapular brown adipose tissue and so the shivering remains suppressed.

**Vasomotor Response:**

Constriction of skin blood vessels occurs in response to cold both in full term and preterm infants. This is to increase the internal temperature gradient thereby increasing tissue insulation to maximum.

**Behavioral:**

These have not been clearly understood. The newborn infants may continue to sleep when cold. However, they may show signs of thermal discomfort, sleep less to increase heat production. They may adopt a flexed posture in an attempt to decrease heat loss.

**Significance of understanding Thermal adaptation:**

The baby is typically born into a wet and cold environment (comfortable for adults). Under normal delivery room conditions fall in deep body and skin temperatures are about 0.1°C and 0.3°C per minute respectively. This corresponds to heat loss of approximately 200cal/kg/min. In addition, the deep body temperature of the newborn is higher by 0.5°C at the time of birth compared to later in life. Furthermore, the infant loses heat if necessary steps are not taken to ensure that the infant is received on a warm cloth, placed on a warm surface, room temperature maintained at least 26°C and cold draughts of air are avoided.
Essential Newborn care by WHO also includes maintenance of warm chain through out the neonatal period.\cite{92} The 10 steps of warm chain are: Warm delivery room($26^0$C), warm resuscitation, immediate drying, skin to skin contact between the baby and mother, breastfeeding, postponement of bathing and weighing, appropriate clothing and bedding, mother and baby together, warm transport, and training of health care providers.

**Care of Premature Baby:**

A preterm baby is particularly vulnerable to hypothermia due to inadequate mechanism of thermoregulation and thermal adaptation. It is essential that appropriate precautions are taken to prevent heat by the four mechanisms discussed earlier and extra source of heat may need to be provided.

The response to cold stress in a preterm baby is primarily by vasoconstriction, which is seen with core and peripheral temperature difference.\cite{93} Simultaneous continuous monitoring of core and peripheral temperature gives us the information, whether babies are in their "thermo neutral" range. It should be the target of nursing care to keep the baby in its "thermo neutral" range to provide the best conditions for growth and maturity.\cite{94}

Thermal adaptation in the newborn depends on gestation. Most of the preterms may become unwell during early neonatal period due to other problems of prematurity. Once the baby has activated its own body temperature regulation systems it is more stable and able to cope better with changes in environmental conditions without any effect on central body temperature.
3.11 CONTRIBUTION OF VARIOUS INVESTIGATORS IN UNDERSTANDING THERMOREGULATION IN NEWBORNS:

The experiments on human infants started with the use of incubators to regulate environmental temperature. The first incubator was introduced in 1835 by Von Ruehl in St. Petersburg, Russia.\cite{95} This generated the interest to gather information on temperature regulation in newborn infants.

Response to cooling of the environment in poikilothermic animals such as the newborn rat and mouse was studied by Fairfield in 1948 and Fitzgerald in 1953.\cite{96,97} The metabolic rate, effect of environmental temperature on metabolism and temperature maintenance in newborn pig was studied by Mount in 1958.\cite{98} They studied the rate of rise in oxygen consumption with fall in environmental temperature in newborn piglet. A quantitative estimate of the changes in \( O_2 \) consumption and respiratory minute volume in the neutral environment was studied in newborn rabbit by Adamsons in 1959.\cite{88} Various investigators such as Day R\cite{99} Silverman\cite{100}, Baumgart\cite{93,94} studied temperature regulation in premature infants, mechanism of heat production, basal metabolic rate in preterm infants etc. However the major breakthrough came following work by Bruck K in Germany in 1960 on heat production and heat regulation in newborn infant and laid down the basis for temperature regulation in the neonates.\cite{101,102} In 1964 Dawkins and Hull\cite{90} through their work in unanaesthetized rabbits gave evidence that the energy for heat production is provided by the oxidation of fat stored in the brown adipose cell and that under the influence of catecholamines triglycerides are split into glycerol and NEFA. They showed that the thermocouples inserted over the intrascapular brown adipose tissue of the newborn rabbit recorded a temperature 2-3\(^{\circ}\)C higher than the deep colonic temperature during exposure of the animal to cold environment. Edmund
Hey and coworkers described thermoneutral environment for premature infants in 1969.[86] As more premature babies survived in 1980s the clinical implications of mechanism of thermoregulation were better understood.

Prevalence rates of hypothermia (more than 50% in some studies) in developing countries have been reported in studies from Nepal[103-5], Malawi[106], Ethiopia[107], Zimbabwe[108], Pakistan[109], India[4,110-111], Uganda[112], Zambia[113] and Bangladesh.[114]

Studies from India on hypothermia have reported varying but significant incidence of hypothermia. Table 3.4 gives the findings of these studies from India. Kumar and Agarwal measured axillary temperature in home delivered newborns within 24 hours of birth in India; 11% were hypothermic (temperature<35.5°C) but the incidence increased to 19% in winter season. They found a strong correlation between room temperature and newborn temperature. In nearly half (42%) of the cases of newborn hypothermia, the mother was even colder than her infant.

Table 3.4. Studies on neonatal hypothermia from India

<table>
<thead>
<tr>
<th>Author</th>
<th>Methods of assessment</th>
<th>Personnel &amp; site of study</th>
<th>No of babies</th>
<th>Time of assessment</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singh M et al[115]</td>
<td>Palpation of foot &amp; Abdomen by back of hand/palm Simultaneous local temperature recorded by electronic thermometer</td>
<td>Pediatrician/TCH</td>
<td>50</td>
<td>Postnatal period</td>
<td>20% had cold stress but 1 had core temperature &lt; 36°C Sensitivity of HTM Forehead 96%, Abdomen 83%, Foot 98%</td>
</tr>
<tr>
<td>Green, Kumar &amp; Khanna[116]</td>
<td>Thermospot On abdomen, simultaneous recording with DT</td>
<td>Local volunteers/Urban Slums</td>
<td>32</td>
<td>Every day from 1 to 7 days</td>
<td>Prevalence of Hypothermia 4% Axillary temperature&lt;35°C Sensitivity 88% Specificity 97%</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Methodology</td>
<td>Measurment</td>
<td>Participants</td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-------------------------------------------</td>
<td>--------------</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Agarwal et al[117]</td>
<td>Dorsum of right hand, simultaneous axillary DT</td>
<td>Trained field worker/Urban Slums</td>
<td>152</td>
<td>21.7%</td>
<td>74.5%</td>
</tr>
<tr>
<td>Kumar &amp; Aggarwal[118]</td>
<td>Touch of abdomen, simultaneous axillary temperature</td>
<td>Mother &amp; Field worker</td>
<td>189</td>
<td>32%</td>
<td>24.6%</td>
</tr>
<tr>
<td>Aggarwal et al[119]</td>
<td>Human Touch, simultaneous axillary DT</td>
<td>Trained non-medical field investigator</td>
<td>148</td>
<td>74%</td>
<td>96%</td>
</tr>
<tr>
<td>Kumar &amp; Aggarwal[120]</td>
<td>Axillary temperature</td>
<td>Field worker Home delivered Newborns</td>
<td>189</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td>Pejaver, Nisarga &amp; Gowda[121]</td>
<td>Thermospot, simultaneous rectal temperature</td>
<td>Maternity ward</td>
<td>20</td>
<td>310/313</td>
<td></td>
</tr>
<tr>
<td>Kumar V et al[121]</td>
<td>Continuous monitoring during specific activities such as bathing, breastfeeding, changing soiled diapers etc.</td>
<td>Field workers /Home delivered Newborns</td>
<td>139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bang et al 2005[10]</td>
<td>Axillary temperature by thermometer</td>
<td>Trained village health workers Home delivered newborns</td>
<td>763</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Kaushik et al[123]</td>
<td>Axillary temperature</td>
<td>Mother and Resident on duty, Medical College</td>
<td>206</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

An observational study was conducted nested in the parent trial in Shivgarh village of Uttar Pradesh, North India over a period of one year. Continuous ambulatory recording was done in home delivered newborn infants during routine activities such as bathing, breast feeding, changing soiled diapers etc. The study
highlights factors that lead to interruption of warm chain during routine newborn care. Delivered on to ground (85.3%), body not wiped(81.6%), lies uncovered for >60 min(67.5%), bathed and scrubbed within 24 hours(88.6%), bathed 3-4 times in a week, massaged uncovered (89.5)% , massaged >3 times a week (49.8%), and prelacteal feeds given (80%) were the important factors noted by these researchers. This study however did not look at the cold stress experienced by newborns by simultaneous recording of core and peripheral temperature.

This study group also noted seasonal variation in hypothermia 14.8% incidence in rainy season increasing to 21.5% in winter and decreasing to 13.8% in summer. The differences were statistically significant. In the study done by Kumar & Agarwal on body temperature of home delivered newborns during winter months 19.1% were hypothermic as compared to only 3.1% in summer whereas 8.5% were hyperthermic in winter compared to 36.8% in summer. Room temperature was below the recommended ambient temperature by WHO (Room air temperature of <24°C) in 41% readings. These studies done in community have shown high prevalence of hypothermia due to various social and cultural factors.

3.12 THERMAL STRESS:

Difference between core and mean skin temperature is considerably low due to small amount of tissue insulation in a neonate. Routinely, a single body temperature is measured (axillary or abdomen) to ascertain the whether the baby is euthermic (36.5-37.4°C). This measurement of a single temperature tells us how well the baby is maintaining body temperature but gives no idea about how much energy is being spent to maintain thermal balance. Through his study on preterm babies Lyon A has shown how it is essential to continuously monitor both core and peripheral temperature to detect cold stress.\cite{124}
In a baby with minimum basal metabolic rate difference in core and peripheral body temperature $< 1^\circ$C is considered normal. An increase in core peripheral temperature difference of more than $2^\circ$C indicates cold stress and it occurs before drop in central temperature.$^{[125]}$ In hypothermia, body tries to minimize heat loss by peripheral vasoconstriction. This also occurs in hypotension in an attempt to raise the blood pressure but there are other signs such as tachycardia and low volume pulses. These babies have cold extremities and drop in peripheral foot temperature. However, immediately after birth a newborn tends to have increased core–peripheral temperature difference due to various factors such as 1) poor control of environmental temperature, 2) inadequate clothing, 3) inadequate source of external heat supply such as close contact with the mother 4) cultural practices such as bathing and messaging with inadequate cover. Effect of this thermal stress on the normal healthy infant baby due increased core- peripheral temperature difference has been studied by few investigators. Increased oxygen consumption is known to be the gold standard for measurement of thermal stress.$^{[125,126]}$

Table 3.5 shows important studies that have significantly influenced the newborn care practices by highlighting the effect of core–peripheral temperature difference in the newborn.

Adamson et al observed minimal values (mean 4.6 ml.$\pm$0.68 S.E. $O_2$/Kg/min.) when the core–peripheral temperature gradient did not exceed $1.5^\circ$ C.$^{[88]}$
Table 3.5. Studies on Core-peripheral temperature difference in newborn

<table>
<thead>
<tr>
<th>Author</th>
<th>No &amp; Gestation of infants</th>
<th>Environment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karlsson[127]</td>
<td>25 healthy term newborns</td>
<td>Controlled environmental temperature 28-32(^{0})C</td>
<td>Regional dry heat losses closely followed the external temperature gradient (difference between skin and operative temperature).</td>
</tr>
<tr>
<td>Adamson[88]</td>
<td>50 healthy term newborns</td>
<td>Varying environmental temperature</td>
<td>Oxygen consumption is a function of the temperature gradient between skin and environment and not of the absolute values of either skin or deep body temperature.</td>
</tr>
<tr>
<td>Andrew Lyon[124]</td>
<td>83 VLBW infants in first five days</td>
<td>NICU</td>
<td>Significant increase in core – periphery temperature difference associated with routine nursing procedures</td>
</tr>
<tr>
<td>M Singh[115]</td>
<td>50 term infants</td>
<td>Maternity ward</td>
<td>20% had cold stress</td>
</tr>
<tr>
<td>Osborn[128]</td>
<td>128 infants &lt;30weeks</td>
<td>NICU</td>
<td>CPT difference did not detect infants with low SVC flow</td>
</tr>
<tr>
<td>Fransson&amp; Karlsson[129]</td>
<td>27 healthy newborns</td>
<td>Adequately dressed in maternity ward</td>
<td>Max difference between abdominal and foot skin temperature was when baby was in cot then when baby was with mother.</td>
</tr>
<tr>
<td>Ellis M[105]</td>
<td>35 healthy term newborns</td>
<td>Maternity ward</td>
<td>Core-skin (axillary-forehead) temperature difference exceeding 3(^{0})C for more than half of the first 24 hours.</td>
</tr>
<tr>
<td>Azaz et al[130]</td>
<td>22 normal healthy infants</td>
<td>Inside plethysmograph wearing light clothing</td>
<td>Within the first week, there was a 19% rise in oxygen consumption on cooling to 19-22(^{0})C during rapid eye movement sleep and a 6% rise during quiet sleep.</td>
</tr>
</tbody>
</table>

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39
3.13. USE OF CLINICAL PARAMETERS FOR MONITORING OF THE NEWBORN:

Clinical monitoring of the newborns is the mainstay of neonatal care universally. Monitoring of the neonate can be classified into three major categories: (a) clinical (b) biochemical and (c) electronic. Clinical monitoring is mainly based on clinical findings of inspection, palpation and auscultation.

Biochemical monitoring is mainly dependent on blood withdrawal and biochemical analysis but noninvasive biochemical monitoring is being used more frequently in neonates.

Electronic monitoring used primarily for monitoring physiological variables can either be invasive or noninvasive. Electronic monitoring is used only to help the health care workers to provide continuous monitoring and some times trends in clinical parameters.

We reviewed the literature on assessment of newborn based on 3 clinical parameters Color, Capillary refill time and Warmth.

Color

Color of the newborn has been used as an integral component of assessment of sick newborn. It is known that oxygen imparts a strong red color to the heme group and deoxygenated blood is a darker shade of red. In 1973 Goldman et al reported that they found no positive correlation between color of the trunk and ears especially when arterial oxygen saturation was <80%. They carried out simultaneous clinical assessment and arterial oxygen saturation in 93 infants less than 2 weeks of age. Color of the newborn was used to assess the need for resuscitation as per NRP protocol. But accuracy of the clinical assessment of color, in the minutes
after delivery, is not known, nor the pulse oximetry oxygen saturation (SpO₂) when they start to look pink.\textsuperscript{133} Not many clinical studies are available on clinical assessment of color at birth. Bang et al reported that pale or yellow color of the skin present on day of birth had significant association with neonatal death (p<.016).\textsuperscript{10} O’Donell et al conducted a study by showing video clippings of newborn babies to medical staff. There was no agreement on when the babies turned pink after birth and the color had no relation to Oxygen saturation.\textsuperscript{134} Daga SR used an algorithm to treat newborns with dusky soles presupposing it to be due to hypoxemia, hypothermia or hypotension.\textsuperscript{18}

Clinical assessment of color of newborn and its use in management of the newborn still continues to remain a dilemma. No studies till date have reported the change in color of the palms and soles in relation to time from birth.

**Capillary Refill Time**

There is no consensus on use of this clinical method to assess perfusion. Table 3.5 gives studies done so far in India and rest of the countries. Investigators have tried to find normal values of CRT in newborns and its use to detect hypoperfusion. In India Raichur et al\textsuperscript{19} found CRT <4 seconds to be normal in healthy term neonates. The factors they identified that led to inter observer difference were local skin temperature during the CRT estimation, finger skin temperature of the observers, behavioral state of the baby, subjective variations in deciding the end-point of measurement, variations in the size (in square units) of blanching produced, amount of pressure applied, the position and side of the limbs used for estimation and effect of observer bias regarding 'normal' CRT.
Table 3.6. Studies done on capillary refill time in assessment of newborn

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Findings</th>
<th>Time from Birth to assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miletin, Pichova &amp; Dempsey</td>
<td>38 VLBW infants</td>
<td>Poor correlation between CRT, mean BP and SVC flow</td>
<td>First day</td>
</tr>
<tr>
<td>Osborn, Evans &amp; Kluckow</td>
<td>128 infants &lt; 30 weeks</td>
<td>CRT&gt;3secs 55% sensitivity &amp; 81% specificity to detect low SVC flow</td>
<td>First day</td>
</tr>
<tr>
<td>Leflore &amp; Engle</td>
<td>42 Term AGA infants</td>
<td>Prolongation of CRT with BP</td>
<td>1–4 hours after birth</td>
</tr>
<tr>
<td>Strozik et al</td>
<td>469 Healthy newborns 28-42 weeks</td>
<td>Normal CRT &lt; 3 sec forehead &amp; chest</td>
<td>1-7 days of birth in controlled room temperature</td>
</tr>
<tr>
<td>Raju et al</td>
<td>137 well term healthy newborns 36-42 weeks</td>
<td>Mean CRT 4.23±1.47 s (SD) (range 1.63-8.78 s) in the hand4.64±1.41s (range 2.15-9.94 s) in the foot</td>
<td>1-120 hours</td>
</tr>
<tr>
<td>Raichur</td>
<td>155 healthy term newborns</td>
<td>CRT chest &amp; Forehead &lt; 3 sec, Palm &amp; Feet &lt; 4 sec</td>
<td>1-168 hours</td>
</tr>
</tbody>
</table>

Assessment of warmth by human touch:

This method of clinical assessment of temperature has been widely accepted worldwide as per WHO recommendation and has become an integral part of training of all health workers involved in care of newborn.\(^{[92]}\)

Table 3.4 shows studies done in India to determine the accuracy of this method to detect hypothermia in newborn. The studies have been done from 1-28\textsuperscript{th} day of life and compared the sensitivity and specificity of human touch to detect hypothermia. Interobserver difference has been reported in accuracy of assessment of hypothermia. Training of the mothers has been considered in detection of hypothermia but not yet studied extensively. It has also been found necessary that mothers should be kept warm if they are to detect and provide warmth to the baby.\(^{[117]}\)

Though the sensitivity and specificity of human touch method (HTM) to detect hypothermia has been studied, no studies till date have reported the time from birth when infants become warm on clinical assessment.