Changes in the Newborn at Birth: Fetal-to-Newborn Transition

3

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3.1 Introduction

In the intrauterine life, fetus is totally reliant on the mother for nutrition for growth and development, for gas exchange (oxygenation and carbon dioxide removal), and for clearing of metabolic waste products.

Placenta is the link between the mother and the fetus. Maintenance of normal maternal–placental–fetal physiology and metabolism, and regulation of placental circulation is extremely important.

At birth, this equation changes and the newborn baby must adapt to the extrauterine life when it needs to fend for itself. Transition is a complex process, and several factors interplay to make it a success. Of significance is the short time over which these changes must take place. All body systems undergo changes, cardiovascular and respiratory being prime, others being endocrine, metabolism, hepatic, hemopoietic, and thermoregulatory [1–3].

Abnormal adaptation increases the morbidity and mortality in the newborn baby and is more common in in-hospital and operative deliveries, and in premature and syndromic babies [4].

Neonatal anesthesiologists must understand and have complete knowledge of the intricacies of the transition process, **normal and abnormal adaptation,** factors in the perioperative period that can revert these changes (fetal asphyxia, respiratory distress in the newborn, neonatal hypoxia), and role of Surfactant.

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3.2 Placenta

Placenta is a temporary fetal organ, formed soon after implantation of the embryo. Its role is to provide nutrition and oxygen to the fetus and remove waste products. It is a barrier between fetal and maternal circulation, preventing direct mixing of maternal and fetal blood. Umbilical cord, the link between placenta and the fetus, contains two arteries and one vein. Umbilical arteries carry waste material and deoxygenated blood from the fetus to the placenta, while the umbilical vein carries nutrients and oxygen from the mother to the fetus. Placenta assumes its full function by the end of 1st trimester and continues to grow with the fetus.

Placenta also has an important role in the transitional process after birth and baby's adaptation to the external environment.

3.2.1 Feto-placental Maternal Circulation

This consists of two circulations: **1. utero-placental circulation and 2. feto-placental circulation.**

There is no mixing of maternal and fetal blood and exchange occurs by diffusion. Placenta is highly vascular. At term, it weighs about 500 g and has blood flow of 600–700 mL/min (80% of uterine perfusion).

Uterine arterial pressure is 80–100 mmHg and it drops to 10 mmHg in the inter-villous spaces on the maternal side. Pressure in the umbilical arteries is 50 mmHg which falls to 30 mmHg on the fetal side. Umbilical venous pressure is 20 mmHg. Higher uterine arterial pressure allows forward flow through the placenta. Maintenance of maternal systolic blood pressure (SBP) and uterine blood flow is essential for normal utero-placental fetal circulation. Maternal hypotension, hypovolemia, anemia, and poor oxygenation (lung disease and high altitude) may adversely affect placental circulation and fetal growth. Placental circulation has poor neurovascular regulation and is not affected by catecholamines. Feto-placental circulation is vulnerable to hypoxia. Reoxygenation is associated with release of excessive free radicals, contributing to pre-eclampsia and other pregnancy-related complications. Endothelins and prostanoids cause vasoconstriction, while nitric oxide (NO) has a vasodilatory effect. Melatonin has an anti-oxidant role.

3.2.2 Functions of Placenta

1. **Nutrition** and **gas exchange** between fetus and mother
2. **Removal of waste** products (urea, uric acid, creatinine, and CO_2)
3. Placental nutrient metabolism plays a key role in limiting transfer of some nutrients. Conditions such as diabetes and obesity affect nutrient transport, resulting in over or restricted growth (IUGR)
4. **Physical barrier** to microbe transmission from the mother
5. **Immune role:**
   (a) **IgG** antibodies can pass through placenta by 20th week, providing immunity to the fetus and newborn up to first few months of life.

(b) **IgM** antibodies cannot pass through the placental barrier. They are the first immunoglobulins expressed in the fetus, at 20 weeks, and are the first responders to an infection. Intravenous immune globulin (IVIG) can prevent neonatal infections, and sepsis in premature and low birth weight (LBW) neonates.
(c) **Immunological barrier**: small lymphocytic suppressor cells in the fetus inhibit maternal cytotoxic cells and prevent maternal rejection of the fetus as foreign body.

6. **Endocrine function**: placenta produces hormones that regulate maternal fetal physiology during pregnancy
   (a) Chorionic gonadotrophic hormone (CGH):
      - Is responsible for fetal survival
      - Stimulates release of progesterone and estrogen
      - Protects fetus from being rejected by the maternal body
      - Its deficiency is associated with risk of spontaneous abortions
      - Stimulates testis to produce testosterone and sex organ development in male fetus
   (b) Progesterone:
      - Helps in implantation of the embryo
      - Its uterine relaxant effect decreases the risk of spontaneous abortions
   (c) Estrogen:
      - Crucial for proliferation process (breasts, milk production, uterus, and fetus)
      - Increases blood supply (vasodilator effect) near end of pregnancy
      - Level is 30 times more than nonpregnant female
   (d) Human placental lactogen (hPL):
      - Necessary for fetal growth, development, and metabolism
      - Stimulates production of insulin-like growth factor that regulates intermediary metabolism
      - Necessary for production of IgF, insulin, surfactant, and adrenocortical hormone
      - Higher levels in multiple pregnancies, diabetes, molar pregnancy, and in RH incompatibility
      - Low levels in toxemia, choriocarcinoma, and placental insufficiency
   (e) It is a reservoir of blood for the fetus (500 mL), delivering to it in case of hypotension and viceversa.

3.3 Lung Development

Primordial lung appears as a lung bud off the esophagus, caudal-to-laryngotracheal sulcus by about 3–4 weeks of gestation. It elongates, divides, and stems into future lung.

i. 16–26 weeks: canalicular stage—peripheral lung development and differentiation of epithelium takes place.
ii. 20 weeks: surfactant production starts.
iii. 32 weeks: 17 generations of airways have developed.

iv. 36 weeks: 4 million distal saccules (respiratory bronchioles and alveolar ducts) are present.
v. Alveolarization (increase in number of alveoli) begins 36 week preterm (3–4 weeks of gestation) and continues until 36 months postnatal (3 years of age).
vi. Alveoli are lined by two types of epithelial cells (pneumocytes)—type 1 and type 2.
vii. Type 2 Pneumocytes produce and secrete surfactant.
viii. Alveoli have a property to collapse because of their spherical shape, but are prevented by surfactant (natural surfactant reduces ST to < 6 dynes/cm).

3.4 Surfactant [5]

Surfactant is a phospholipid, a surface-active lipoprotein, produced by the type 2 pneumocytes. The main active component is dia-palmitoyl-phosphatidyl-choline (DPPC). Surfactant forms a layer inside the alveolus to stabilize it and reduce the surface tension (ST). It has a hydrophobic area (facing air) and a hydrophilic area (facing water). ST acts as air–water interface of a bubble and makes it smaller by decreasing the surface area at the interface. Lowering of ST prevents the collapse of the alveolus. With decrease in ST, surface pressure increases, according to Laplace Law, i.e., gas pressure (P) needed to keep equilibrium between collapsing forces (ST = y) and expanding forces of gas in an alveolus of a radius (r) is represented by the formula:

$$P = 2y / r$$

3.4.1 Surfactant Production

Surfactant production begins by the 20th week and gradually increases. It appears in the amniotic fluid by 28 weeks, and by 35 weeks, fetus has adequate quantity of surfactant. A term newborn has alveolar surfactant pool of about 100 mg/kg, which is much lower in preterm newborns (4–5 mg/kg), as in an adult. Once secreted, it has a half-life of 5–10 h. Its unique property is that it is recycled. Up to 90% is reabsorbed by the pneumocytes themselves and remaining 10% is digested by the macrophages. Metabolism of surfactant is slower in newborns as compared to in adults.

3.4.2 Role of Surfactant

ST of water is 70 dynes/cm, and in lungs, it is 25 dynes/cm. At the end of expiration, as alveoli reduce in size, ST will reduce to zero (in the absence of surfactant). Surfactant reduces ST to 5–6 dynes/cm (preventing it to reach zero), and thereby prevents complete collapse at end of expiration, allowing alveoli to inflate more easily, with less work of breathing and less energy expenditure. Clinical surfactants reduce the ST to 5–10 dynes/cm. Role of surfactant:

- ↑**Pulmonary compliance**: by reducing ST, allowing alveoli to inflate more easily, with less work of breathing and less energy expenditure
- **Facilitate recruitment of collapsed alveoli**: by decreasing the required inflation pressure
- **Prevention of atelectasis**: smaller the alveolar size, greater the effect of surfactant
- **Reduces fluid accumulation** and keeps airways dry
- **Immune role**—by regulating inflammatory responses and interacting with adaptive responses. Two constituent proteins (SP-A and SP-D) bind to sugars on the surface of the pathogens and opsonize them, facilitating their phagocytosis
- **Surfactant deficiency** has two consequences: (**a**) Shrunken and fibrotic alveoli [as in respiratory distress syndrome (RDS)] and (**b**) enhanced pulmonary inflammation and infections.

3.4.3 Clinical Effects of Surfactant

1. Increase in pulmonary compliance
2. Prevention of atelectasis at the end of expiration
3. Facilitate recruitment of collapsed airways and alveoli

Adaptations at Birth - At birth, fetus must make several changes to adapt to the extrauterine life. Timing and appropriateness of these changes are essential for successful transition and survival of the newborn baby. Two systems undergo major changes—a respiratory and b cardiovascular system. In most newborns, complete changes occur at birth itself, but in some, it may take a few hours, latest 24 h of birth. Various factors can interfere with normal transition (Fig. 3.1).

Neonatal anesthesiologists need to be aware of these changes and factors affecting. Functional changes occur at birth, but permanent changes take place over a period of weeks to months. If care is not taken during the peri-operative period of the surgical neonate, these changes revert, with adverse postoperative outcome and high morbidity (delayed recovery, failure to extubate, need for prolonged, and more intense care), and mortality.

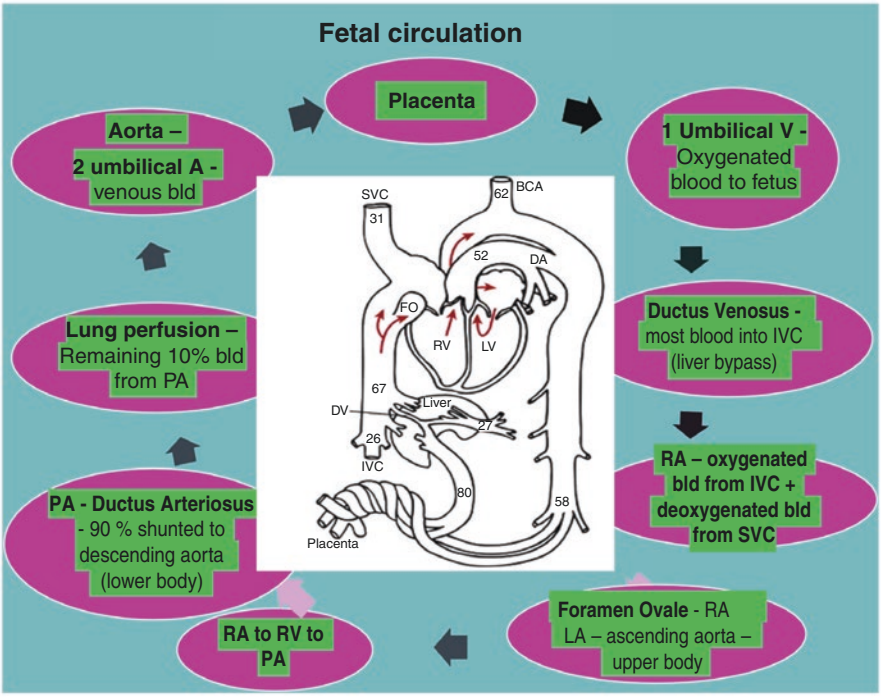

Fig. 3.1 Fetal circulation, *DA* Ductus Arteriosus, *DV* Ductus Venosus, *FO* Foramen Ovale

3.5 Fetal Circulation

In utero, blood, rich in nutrition and oxygen, is delivered to the fetus via the umbilical vein. Umbilical arteries carry venous blood back to the placenta. Heart acts as a conduit to blood flow and fetal lungs are non-functional. Pulmonary vascular resistance (PVR) is high due to hypoxic pulmonary environment (PaO_2 = 17–19 mmHg). Systemic vascular resistance (SVR) is low. Left atrial saturation is about 65%, which falls to 30% during labor, and within 5 min of birth, it increases to 90% (preductal SpO_2).

In a term fetus, cardiac output from both the ventricles is about 450 mL/kg/min, that of right ventricle (RV) being double of left ventricle (LV). At birth, circulation changes from "parallel" to "series", and total cardiac output increases to 800 mL/Kg/min. LV output increases and that of RV decreases, to become equal (LV output = RV output = 400 mL/kg/min), keeping pace with the increased O_2 consumption. Blood flow to lungs, heart, kidneys, liver, and the gastrointestinal tract increases. Cortisol, catecholamines, rennin–angiotensin system, vasopressin, and thyroid hormones, all play an important role.

Characteristic feature of Fetal circulation is the presence of three shunts: **ductus venosus (DV), ductus arteriosus** (DA)**, and foramen ovale** (FO)**.**

Umbilical vein carries blood from the placenta, toward the liver, where >80% blood bypasses the liver via the 1st shunt, DV (between portal vein and inferior vena cava (IVC)) toward the right atrium (RA). With increasing gestational age, blood flow to the liver increases. By 32 weeks, it is almost 80% of umbilical blood flow. Blood from the IVC (venous, from the lower body) mixes with the arterial blood from the DV. In the RA, blood from the IVC (O_2 rich) and superior vena cava (SVC) (venous, from head and upper extremities) mix. RA contains mixed venous blood (O_2 content < than in IVC but > than of SVC). 50–60% of blood in the RA is directed through the 2nd shunt, FO into the left atrium (LA), LV, and ascending aorta, to be supplied to the upper part of the body. This is facilitated because of low SVR and the flaplike aperture of FO, which acts as a one way valve, allowing blood flow from right to left only. Remaining 50–40% blood enters the RV and pulmonary artery (PA).

Fetal lungs are fluid filled, not fully developed, have high airway and PVRs. They have no role in fetal gas exchange. In the PA, 90% blood is shunted off into the descending aorta through the 3rd shunt, DA, to perfuse the lower part of the body, and eventually drains back to the placenta through the umbilical arteries. Remaining 10% blood in the PA (8% of cardiac output) perfuses the lungs to meet its metabolic demands. After 30 weeks of gestation, lung perfusion gradually increases.

3.6 Transition from Fetus to Newborn (Fig. 3.1)

This is a complex physiological process that takes place rapidly, over a short period, at the time of delivery [6]. **Two events initiate these changes:**

1. **Newborn baby's 1st cry or breath**
2. **Clamping of the umbilical cord**

1. **Newborn baby's cry or 1st breath** (Box 3.1): at birth, exposure of the head to cold, stimulates the baby to gasp (1st breath). Air rushes into the airways and alveoli, opening them up, and airway pressure falls. As air enters the lungs, pul-

Box 3.1 1st Breath: What Happens?

- **Delivery of Head**: Gasp—1st breath
- Generates -ve intrathoracic pressure: air flows into the lungs—lung expansion
- Opening of airways and alveoli: ↑FRC (functional residual capacity)
- Blood flows from PA to pulmonary capillaries: ↓ PVR (pulmonary vascular resistance)
- ↓ Blood flow through DA and FO—functional closure
- During vaginal delivery: chest gets compressed—**1/3rd lung fluid expelled** thru nose/mouth
- **After delivery:** chest wall relaxes—-ve intrathoracic pressure—air flows into the lungs
- **Crying**: generates +ve Intrathoracic P—keeps alveoli open and remaining fluid forced out

Box 3.2 Cord Clamping: Cutoff from Maternal Circulation

(a) Stimulation of aortic and carotid chemoreceptors, respiratory center from hypoxia, hypercarbia and acidosis
(b) ↑ SVR, SBP and LV pressure: ↓ flow through FO and DA
(c) Functional closure of foramen ovale: at birth (anatomic closure 3 months–1 year age)
(d) PA to DA flow ↓: functional closure—within 10–15 h of birth (anatomical closure—4–6 weeks)
(e) ↓ Prostaglandins from the placenta: DA closure
(f) Umbilical vessels and ductus venosus: become nonfunctional—anatomic closure by the end of 1st week

Box 3.3 Facilitation of Transitional Changes at Birth

1. Hormone surges at labor: cortisol, catecholamines, and thyroid hormones
2. Negative intrathoracic pressure by chest compression during vaginal delivery
3. Exposure to cold: gasping—1st breath—alveolar expansion, increase in FRC
4. ↑ PaO_2 and ↓ PGE2 stimulate DA spasm and closure
5. Clamping of umbilical cord: ↑ SVR–↑ Resistance to flow through Ductus Arteriosus
6. Alveolar expansion, loss of HPV: decrease in PVR, ↑ pulmonary blood flow
7. Activation of sodium pump and clearance of lung water
8. ↑ SVR–↑ LAP: closure of FO
9. Cord ligation: cessation of blood flow to umbilical vein–passive closure of DV
10. Lungs take over its function: gas exchange

monary vascular bed dilates [elimination of hypoxic pulmonary vasoconstriction (HPV)], PVR decreases, allowing forward blood flow from PA into pulmonary capillaries. RA, RV, and PA pressures decrease, with cessation of flow through the FO and DA. Further cries of the newborn generate +ve intrathoracic pressure that keeps airways and alveoli open and forces out remaining lung fluid.

2. **Clamping of the Umbilical cord** (Box 3.2)
   With the clamping of the umbilical cord two things take place:
   (a) Pulmonary arteries face resistance and can no longer drain into the placenta, with resultant increase in SVR, SBP, LV, and LA pressures.
   (b) Pulmonary vein is no longer fed by the placenta, with cessation of flow through DV. Systemic venous pressure falls, umbilical vessels constrict, with immediate closure of DV (Fig. 3.1).

Factors that facilitate transition at birth are summarized in Box 3.3

Prostaglandins are secreted by the Placenta and metabolized in the lungs. Fetal Prostaglandin levels are high because lung is unable to metabolize them. Prostaglandins maintain the patency of the DA, important for fetal circulation. With clamping of the cord and removal of placenta, airways open, alveoli expand, and pulmonary perfusion increases. Lungs start the process of gas exchange and can

metabolize prostaglandins. As levels of prostaglandins fall, DA goes into spasm and closes.

3.7 Other Adaptations

3.7.1 Respiratory Adaptaions

Fetal lungs are filled with fluid secreted by the lung epithelium, and alveoli are collapsed. Lungs are in a hypoxic environment, initiating pulmonary vasospasm (HPV). Lung fluid is rich in chloride and low in protein. Toward the end of gestation, production of lung fluid gradually diminishes. Endocrinal adaptations (cortisol, catecholamines, and thyroid) are critical to lung fluid clearance.

3.7.2 Pulmonary Changes at Birth:

- **Exposure** of the newborn to external cold environment stimulates a gasping breath.
- Lungs are **HEAVY–HIGH inspiratory pressures are** required to open the Alveoli.
- **One (1st) breath may not be enough, and MORE BREATHS** are required.
- **Initiation of 1st breath** is a complex process, involving several biochemical, neural, and mechanical factors. Hypoxia, hypercarbia, and acidosis stimulate aortic and carotid chemoreceptors, and trigger medullary respiratory center at birth.
- **Vaginal delivery**—1/3rd fluid expelled thru nose/mouth, and remaining gradually drains via the lymphatics.
- **How quickly fluid leaves the lungs depend on the effectiveness of the 1st few breaths in expanding the alveoli.**
- **Crying** creates a positive intrathoracic pressure, keeps alveoli open and forces fluid out.
- **Simultaneous** ↓ PVR **and** ↑ pulmonary blood flow occurs.
- As the baby's breathing becomes regular, lungs resume their function.

In 90% newborns, lungs assume their normal function, but 10% require assistance, while 1% newborns need extensive resuscitative measures.

Pulmonary Response:

- Pulmonary vasoconstriction occurs in response to hypoxia, acidosis, and hypercarbia
- Arteriolar constriction in the gastrointestinal tract, kidneys, muscles, skin occurs allowing redistribution of blood flow to vital organs (heart and brain)
- In prolonged asphyxia, myocardial function gets adversely affected, with decrease in Cardiac output and cerebral and myocardial ischemia.

Table 3.1 Cortisol levels

Gestational age	Fetal cortisol levels
30 weeks	5–10 μg/mL
36 weeks	20 μg/mL
Pre labor	45 μg/mL
Few hours post delivery	200 μg/mL

3.7.3 Endocrine Adaptations

Cortisol, vasoactive mediators, and thyroid hormones play an important role in transition at birth.

1. **Cortisol**: fetal cortisol synthesis and release is under fetal hypothalamic control. Fetal levels are low and increase with the period of gestation. (Table 3.1)
   Role of cortisol in adaptation process:
   (a) **Pulmonary effects**: in lung maturation, surfactant production, and clearance of lung fluid
   (b) **Increased β receptor density** in heart and lungs
   (c) **In catecholamine release**
   (d) **In conversion of T_4 to T_3**
   (e) **Maturation of thyroid axis**
   (f) **Metabolic and energy substrate** metabolism in the liver
   (g) **Gut maturation** and increase in digestive capacity
2. **Vasoactive substances:** catecholamines (norepinephrine, epinephrine, and dopamine), Angiotensin II and renin increase at birth, indicating presence of stress response in fetus and neonates. Levels are higher in preterms, probably because organs immature and less responsive, and lower in Cesarean delivery, when there is no stress of labor.
   Role of catecholamines in adaptation process:
   (a) Increase in blood pressure
   (b) Metabolic (glucose and fatty acids)
   (c) Brown fat thermogenesis
3. **Thyroid Hormones:** at birth, there is an increase in levels of T_3 and T_4 in response to cortisol surge, cord clamping and cold stimulus of birth.
   Role of thyroid hormones in adaptation process:
   (a) **In fetal lung fluid clearance** (activating the Na^+, K^+, ATPase)
   (b) **Congenital hypothyroidism:** no adaptation abnormality
   (c) **Very preterm babies**: blunted thyroid functional transition from fetal to newborn life (depressed adaptive behavior)

3.7.4 Metabolic Adaptations

Fetal energy needs are met with transplacental transfer of glucose. Fetal liver stores glycogen fat and other substrates. In early hours of birth plasma, glucose levels fall.

Catecholamine and cortisol surge and fall in insulin levels at birth help maintain plasma glucose and free fatty acid levels at birth.

Preterm babies have abnormal responses to cortisol and catecholamines, with increase in catecholamine release. They have minimal glycogen and fat stores and low substrate pool, which make birth adaptation difficult. They need glucose infusion to prevent hypoglycemia and as substrate for energy production.

Fetal heart is a mere conduit, and not much energy is consumed by the myocardial activity. At birth, it assumes its role in maintaining cardiac output, peripheral circulation, and vascular resistance. This is high energy consuming. Availability of substrates to the newborn depends on:

(a) Adequate gas exchange in the lungs
(b) Coronary blood flow
(c) Nutritional intake
(d) Efficiency in shifting from carbohydrate to fatty acid utilization

Neonatal myocardium is capable of anaerobic energy production and can maintaining cardiac function even at low PaO_2, providing some protection from ischemic injury to the myocardium in conditions of hypoxemia. However, persistent hypoxia or asphyxia adversely affects transitional changes much before the direct myocardial effects become apparent.

3.7.5 Thermal Adaptation and Thermogenesis

Core temperature of the fetus is 0.5 °C above the maternal temperature. Fetus does not expend energy to maintain body temperature and glucose is converted to glycogen in the liver and stored. After birth, the newborn utilizes these stores to maintain body temperature and other organ functions. Heat production is twice as much in a growing baby than adult.

Hormone surge (cortisol, catecholamines, and thyroid) at birth activates brown fat thermogenesis. Brown fat is 1% of body weight and is abundant around the kidneys and in the intrascapular areas. It generates heat by uncoupling of mitochondrial oxidative metabolism from ATP synthesis. **Neonates are extremely prone to hypothermia,** due to:

1. Large body surface area in relation to body weight, and greater heat loss
2. Limited fat reserves
3. Inability to shiver
4. Higher energy utilization for maintaining body functions.

Methods by Which Term Neonate Maintains Core Body Temperature:

1. **Brown fat metabolism** (non-shivering thermogenesis), that produce twice the amount of heat as compared to white fat metabolism
2. **Shivering thermogenesis** (from physical activity of kicking and crying)—minor role in heat production
3. **Peripheral vasoconstriction** secondary to exposure to cold, and decreased heat loss from skin surface

Key Points

1. Heat production is an active process needing O_2 and glucose—newborn should be allowed to breathe O_2 rich air for a few hours after birth.
2. Persistent hypothermia will result in metabolic acidosis, hypoglycemia, and decreased surfactant production, growth retardation and long-term effects—newborn should be kept in a warm environment.
3. Catecholamine surge at birth mobilizes glycogen, still glucose levels decline to a lowest point at 1 hour of age. Newborns should be given dextrose water orally or IV until initiation of regular feeds.

3.7.6 Hepatic Adaptation

Fetal liver is the main erythropoietic tissue at midterm. Besides storing glycogen, it is also the major store for Iron. Fetal liver is involved in all the three mechanisms of RBC formation:

1. **Initiation of erythropoiesis** in the embryonic liver
2. **Conservation of a high erythropoietic activity** for several weeks until bone marrow can take over
3. The **switch mechanism** from fetal to adult hemoglobin
   This process is regulated by two hormones:
   (a) **Testosterone** which stimulates heme and hemoglobin synthesis in liver at about 10–13 weeks of gestation
   (b) **Erythropoietin** in 2nd trimester (>12 week gestation)
   After birth, liver gradually takes on all the functions, chiefly:
      i. Production of clotting factors
      ii. Breakdown of glycogen to glucose
      iii. Anabolic and catabolic processes
      iv. Bilirubin metabolism: defects in bilirubin metabolism can lead to newborn jaundice

3.8 Normal Transitional Findings

Most of transitional changes occur within a few hours of birth, but permanent changes occur earliest by 6 weeks. This period is critical in the life of a newborn because of the risk of reversal to fetal status and reopening of the functionally closed shunts in event of hypoxia, acidosis, hypothermia, or respiratory infections. Some tachypnea, lung crackles from remaining fluid, tachycardia, flow or systolic murmur, and acrocyanosis for a few hours, but usually settles by 24 h of age [transient

Table 3.2 PVR and factors affecting PVR

↓ **PVR**: promote closure of DA and FO	↑ **PVR:** Encourages PFC/PPHT
i. High FiO_2	i. Airway resistance/pressure
ii. Alkalosis	ii. Poor RV function
iii. Nitric oxide	iii. Hypoxia
iv. Magnesium	iv. Asphyxia
v. Histamine	v. Acidosis
vi. Acetyl choline	vi. Hypercarbia
vii. ß-Sympathetic stimulation	vii. α-Sympathetic hyperactivity
viii. K+ channel activation	viii. Ca++ activation

tachypnea of the newborn (TTN)]. Several factors can interfere with the normal transition process at birth, by affecting **normal breathing or respiratory responses to hypoxia.** In an attempt to establish normal respirations, newborn can develop two problems:

1. Fluid may remain in the alveoli
2. Pulmonary blood flow may not increase as desired.

This can have several adverse consequences. Basic pathophysiology is continued high PVR, and all consequences are severe or minor forms of raised PVR. Decrease in **PVR** promotes functional closure of the DA and FO. High **PVR** encourages persistence of fetal circulation (PFC)/persistent pulmonary hypertension of the newborn(PPHN), patent DA (PDA)/patent FO (PFO), and shunt reversal. Factors that affect PVR are listed in Table 3.2.

3.9 Abnormalities of Transitional Changes at Birth

Incomplete removal of alveolar fluid has several adverse consequences, with immediate- and long-term impacts (Box 3.4). Several factors can interfere with complete removal of fluid from the lungs:

1. **APNEA at birth/birth asphyxia:** alveoli do not expand and remain small, collapsed, HEAVY, and fluid filled—more number of breaths with additional inflatory pressure are required to inflate them.
2. **Gasping irregular respiration following primary apnea**: poor alveolar expansion.
3. **Poor muscle tone and weak respiratory efforts.**
4. **Absent or weak crying.**
5. **High PVR.**
6. **Surfactant deficiency,** as in premature birth.

Box 3.4 Clinical Implications of Incomplete Lung Clearance

1. Inadequate lung expansion
2. Pulmonary crackles, noisy breathing, and wheeze
3. Transient tachypnea of the newborn (TTN)
4. Recurrent chest infections
5. Failure to thrive
6. Persistence of fetal circulation (PFC)
7. Risk of respiratory distress syndrome (RDS)

Table 3.3 High-risk pregnancies

Maternal Factors	Prepartum Factors	Intrapartum Factors	Intrinsic Factors
age >35, alcohol/substance abuse, Diabetes Mellitus, Hypertension, Cardiac disease Respiratory disease Severe anemia Infections	APH, PET, multiple births, no ANC IUGR, Placenta previa/ Abruptio Fetal–maternal hemorrhage PIH Illicit or drug exposure	Preterm/post term delivery Amnionitis Fetal distress/meconium-stained liquor/Prolapsed cord Premature rupture of membranes (PROM) Narcotic, $MgSO_4$ administration Malpresentations Prolonged labor Instrumental/Operative delivery	Prematurity, Congenital defects RDS Birth trauma

3.9.1 Apnea at Birth

Apnea at birth: babies of all high-risk pregnancies are at a risk of developing Apnea, primary and secondary (Table 3.3).

Primary apnea: in response to O_2 deprivation, there is initial rapid breathing, and if asphyxia/hypoxia continues, there is a decrease in respiratory movements (apnea) and bradycardia. Initial management consists of high FiO_2 and tactile stimulation. Usually, these suffice, but if apnea persists, management is as for secondary apnea.

Secondary apnea: if primary apnea remains unresolved, *secondary apnea occurs, during which HR, BP, and* PaO2 fall further. Management includes

(a) **High FiO_2** (50–60%)
(b) Check for any **obstruction** to respiration: use oropharyngeal (preferred)/nasopharyngeal airway
(c) **Respiratory support:** in a baby who has spontaneous efforts, continuous positive airway pressure (CPAP) should be tried through oropharyngeal or nasopharyngeal route

Table 3.4 Factors that affect respiration at birth

Stimulate respiration	Depress respiration
Mild acidosis	Severe acidosis
Hypercarbia	CNS damage
Hypoxia	Hypoxia
Sensations—pain, cold, touch, noise	**Drugs**—magnesium, alcohol, opioid, barbiturates

(d) **Mechanical ventilatory support (IPPV)**: babies with no respiratory effort or who do not respond to above measures, will need to be intubated and provided positive pressure ventilation
(e) **Early O_2 and IPPV** to prevent hypoxic ischemic injury to the brain
(f) Provide care in a **thermoneutral** environment
(g) Once stabilized, look for additional **avoidable causes of apnea** and accordingly manage

Important to Note:
- **Avoid nasal instrumentation** as far as possible because of narrow nares and they are obligate nasal breathers
- **Avoid 100% O_2**, and if required, use for the shortest duration (risk of developing ROP and BPD).
- Eliminate **other causes of apnea** that depress respiration (Table 3.4)

3.9.2 Vaginal vs Cesaritan Delivery

There is some difference in clearing of alveolar fluid in a baby born by normal labor and vaginal route compared to one born by cesarian section. The catecholamine surge during labor and the process of baby squeezing out through the cervix and vagina, helps in two ways:

1. **Compression of the chest** of the fetus during its passage down the birth canal and the elastic recoil of the thorax after birth creates a negative intrathoracic pressure, allowing air to gush in and expand the lungs.
2. **Expulsion of lung fluid**: 1/3rd fluid is expelled through nose/mouth during vaginal delivery, while remaining gradually passes into the interstitial spaces, to be carried away by the Lymphatics over a few hours after delivery.
3. **Crying** of the baby generates a positive intrathoracic pressure, further aiding in alveolar expansion, distribution of air throughout the lung, and exudation of lung fluid.

This benefit is lost during operative delivery, with cesarian babies more likely to have residual lung fluid, noisy breathing, wheeze, and pulmonary crackles. They are at a greater risk of developing TTN, recurrent chest infections, and failure to thrive.

3.9.3 Persistence of Fetal Circulation (PFC)/Persistent Pulmonary Hypertension of Newborn (PPHN)

PFC/PPHN [7, 8]: this is an extremely rare condition associated with poor survival, high morbidity and mortality in the newborn baby. Fetal circulation persists even after birth, i.e., right-to-left shunts at atrial and pulmonary arterial levels, high PVR, with PPHN, hypoxemia, and cyanosis. **Newborns at risk of PFC** include all high-risk pregnancies (Table 3.3) fetal or birth asphyxia, meconium aspiration syndrome (MAS), RDS, and sepsis. **Prevention is the only cure** (avoidance of factors that increase PVR, antenatal and neonatal care, and use of antenatal steroids in high-risk cases). **Management** includes early diagnosis and prompt intervention. **Baby presents with features of** severe hypoxemia, low Hb SpO_2, need for high FiO_2 and respiratory support, initial tachycardia followed by bradycardia, cyanosis and cardiac arrest. **Investigations include** hematocrit, platelet counts, serum glucose and calcium levels, X-ray chest (pulmonary haze or ground glass appearance), and ECG pattern of right axis deviation, RV strain and arrhythmias. **Hyperoxia (100% oxygen) challenge test**: if the shunt is >30% of the cardiac output, even 100% O_2 will not relieve cyanosis. Preductal PaO_2 >postductal PaO_2 is diagnostic. Echocardiography is indicated to rule out cyanotic congenital heart disease. Monitoring includes SpO_2, NIBP, ECG, and PaO_2. **Treatment** is by surfactant replacement, NO inhalation, beta-adrenergic drugs, and respiratory support.

3.9.4 Patent Foramen Ovale PFO/Patent Ductus Arteriosus PDA

PFO/PDA: in few newborns, there is minor maladaptation at birth that can lead to incomplete closure of FO or DA. Pressure changes occur as in normal transition with increase in SVR and decrease in PVR. The shunt is usually left to right, because of high left-sided pressures, or through the PFO/PDA. There is no cyanosis, and symptoms are due to pulmonary congestion. In PFO, left-to-right shunting leads to high pulmonary blood flow, and pulmonary congestion. In PDA, shunt is from the descending Aorta to the PA, and outflow of aortic blood leads to low diastolic blood pressure with wide pulse pressure. These babies are at **risk of complications,** such as necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), and sudden death. **Management** is **medical** (O_2 supplement, fluid restriction, diuretics, NSAIDS), and **surgical** (usually undertaken by 3–6 months of age).

3.9.5 Reversal of Shunt

Reversal of shunt: these are situations of PFO/PDA, with left-to-right shunts. As already stated, at birth closure of all shunts is functional. Permanent closure of DV takes place by 1 week, DA by 3–4 weeks and FO by 3–12 months of life. Any insult or exposure to factors that can increase PVR, in the neonatal period can lead to

reversal of shunt, which now becomes right to left through the PFO or PDA. Acyanotic congenital cardiac defect converts to cyanotic cardiac disease. **Resultant shunt is an interplay of SVR and PVR. Caution must be exercised by the anesthesiologist in such all neonates to avoid causative or precipitating factors** (Table 3.2)**. Broadly speaking, increases in right-sided pressures and decrease in left-sided pressure must be always avoided. The goal is to maintain high SVR and low PVR.**

Reversal of shunt results in increased venous admixture, decreased O2 carrying capacity, desaturation and low SpO_2, hypoxemia, cyanosis, pulmonary edema, and sudden death.

3.9.6 Pulmonary Consequences of Lung Fluid Retention

Pulmonary consequences of lung fluid retention include TTN and RDS.

TTN is the mildest and transient complication of incomplete clearance of fetal lung fluid. It is more frequent in preterm babies. They are tachypneic, have lung crackles, crepitations on auscultation, tachycardia, flow (systolic) murmur, and acrocyanosis for a few hours, but usually settle by 24–48 h of age. Factors contributing are decreased Na^+ transport, and low surfactant. If surfactant deficiency is severe, features of become evident.

Note L → R shunt is Preferable over R → L shunt

Key Points for an Anesthesiologist

1. DA is thick and muscular, and its constriction is a gradual process. With increase in PaO_2, ductus goes into spasm and its functional closure occurs at birth. Spontaneous closure occurs over a period of 96 h (4 days) of life in almost all babies. Most newborns have a PDA in the first 8 h of life, in 505 newborns at 24 h, and in 10% by 48 h of age. Permanent anatomic closure occurs by fibrosis by 4–6 weeks. It can reopen any time there are factors similar to intrauterine life, hypoxemia, acidosis, increase in PVR, and decrease in SVR, with reversal to fetal circulation (R–L shunt). It is crucial that neonatal anesthesiologist takes special care and precautions in the perioperative period, especially in the first 4 days of life, but through the entire neonatal period, to prevent this from happening.
2. Fetal pulmonary vessels have a thick layer of smooth muscle, thereby prone to vasoconstriction. It takes about 6–8 weeks for the muscle layer to thin out and less prone to vasospasm. Hypoxia is a very potent stimulus to pulmonary vasospasm and should be avoided.
3. Functional closure of FO occurs at birth or within 24 h. Permanent closure occurs by 3 months to 1 year of age. This also can reopen any time.
4. Cyanosis is a late sign of distress in neonates. It becomes visible in the presence of at least 5 g% of deoxygenated hemoglobin. A polycythemic baby, with high Hb concentration, may have cyanosis even at higher or normal O_2 saturation

levels, while an anemic baby with low total Hb concentration may be quite hypoxic before becoming visibly cyanotic.

In all newborns, neonates, especially premature, present for surgery, anesthesiologist must carry out a thorough detailed evaluation in the form of detailed antenatal and birth history, APGAR scores, examination and evaluation of investigations, to establish or rule out any other medical disease or metabolic derangement or congenital abnormality, besides the surgical condition, that may impact anesthetic management, and appropriate perioperative anesthetic care can be provided, to reduce morbidity and mortality, in the already high risk baby.

Make Special Note of

- **Medications received by the newborn:** in general, all newborns receive intramuscular Vit K to facilitate normal clotting and preventing Hemorrhagic disease of the Newborn, until intestinal bacteria can start synthesizing Vit K.
- **APGAR Score** as it provides an estimate of how well the newborn is adapting. It takes into consideration Color, HR, Resp, Reflex Response, Muscle tone and each is scored as 0, 1, 2. Max score is 10. A 10 min Apgar is significant and is graded as 7–10 normal, 4–6 is low, and 3 is critically low.

Special Care and Precautions:

(a) Supplemental O_2
(b) Maintenance of airway and ventilation
(c) Temperature controlled environment: incubator
(d) Strict maintenance of IV fluid transfusion, acid base, serum electrolytes and glycemic balance
(e) Maintenance of systolic perfusion pressures and need for vasoactive drug support
(f) Avoidance of triggering factors: hypoxia, hypercarbia, acidosis, hypotension and peripheral vasodilatation, increase in PVR

Anesthetist has a great responsibility during the perioperative management of neonates because of the potential to reopen these shunts and revert to fetal circulation with postoperative adverse outcome (delayed recovery, failure to extubate, need for prolonged and more intense care), high morbidity with long-term consequences, and mortality. Premature babies are at a greater risk.

3.10 Key Points

i. The transition from fetal to extrauterine life involves rapid adaptations of several organs in a very short time.
ii. Hormones play an important role in normal transition process, namely, cortisol, catecholamines and thyroid hormones.
iii. Pulmonary adaptation requires clearance of lung fluid, surfactant secretion, and onset of breathing.
iv. Cardiovascular adaptation requires changes in pulmonary and SVRs, pressures blood flow, and closure of shunts.
v. Abnormalities in adaptation are more frequent preterm birth or operative delivery.

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