The Respiratory System: Development and Physiology in the Neonate

11

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11.1 Introduction

The most common body system invaded and manipulated by the anesthesiologist is the respiratory system. All surgeries are performed under general anesthesia during the neonatal period, and most common technique involves inhalational induction, intubation, and assisted or controlled ventilation. Quite a few babies are already on preoperative respiratory support for alveolar ventilation and oxygenation, which may need to be continued postoperatively.

Ventilation is an important tool in the hands of the anesthesiologist, which when effectively used, can improve the postoperative outcomes. Use of high or low volumes, pressures, and inspired oxygen concentration, can have adverse short- and long-term consequences in these babies. Hence, it becomes imperative for the neonatal anesthesiologist to have a detailed thorough knowledge about the respiratory system, to be able to use it to ones' advantage in the perioperative period, the key to successful anesthetic management and optimum post anesthesia outcomes while avoiding untoward iatrogenic consequences.

This chapter will cover the developmental anatomy and physiology of the respiratory system, lung volumes and capacities, respiratory mechanics, pulmonary compliance and resistance, gas exchange and related problems, breathing patterns, apnea of prematurity and postoperative apnea, respiratory diseases, and clinical implications.

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11.2 Respiratory System

During the intrauterine life, lungs are filled with water and have no function. At birth, the newborn baby undergoes respiratory and cardiovascular adaptations for survival. The maturation of circulatory and respiratory system should be sufficient to withstand these changes which are drastic and occur rapidly within minutes of birth. This requires effective neuronal output and respiratory muscle function to displace the liquid filling the alveoli and airways and breathing in of sufficient air against the surface force so that sufficient alveolar surface for gas exchange is established [1]. Simultaneously, pulmonary blood vessels must dilate rapidly to allow pulmonary blood flow and establish adequate alveolar pulmonary perfusion. The neonatal adaptation of lung mechanics and respiratory control takes several weeks to complete. However, maturation of lungs continues at rapid pace even beyond the first year of life. Respiratory function in infants, especially during the first 6 months of life is both qualitatively and quantitatively different from older children and adults, as is the response to pharmacologic agents and anesthetic drugs.

11.2.1 Anatomical and Physiological Development

The organogenesis is nearly complete after 12 gestational weeks, i.e., end of 1st trimester.

11.2.1.1 Anatomical Development

1. The lungs begin as a bud on the embryonic gut round about 4th week of gestation. Failure of separation of lung bud from gut (later on) gives rise to tracheoesophageal fistula (TEF) [1].
2. The diaphragm forms during 4th–10th week of gestation dividing abdominal and thoracic cavities:
   (a) If the diaphragm is not completely formed when the midgut reenters the abdomen from the umbilical pouch, the abdominal viscera can enter the thorax leading to congenital diaphragmatic hernia (CDH).
   (b) The presence of abdominal contents within the thorax is associated with arrest of lung growth.
   (c) The lungs of a newborn with CDH are hypoplastic and have decreased number of arterioles. The pulmonary arterioles are abnormally thick, muscular, and highly reactive, resulting in increased pulmonary vascular resistance (PVR).

11.2.1.2 Physiological Development

1. Lung development is not sufficient in a fetus less than 23 week gestation. The alveolar or saccular stage takes place at around 24 weeks, accompanied by thinning of the pulmonary interstitium due to decrease in collagen fiber deposition, increased cellular differentiation, and capillary development, important for gas exchange.

2. Secretion of surfactant, which reduces alveolar wall surface tension and increases alveolar distension and aeration, is often inadequate until last month of gestation (34 weeks):
   (a) Birth before 32 weeks of gestation is associated with respiratory distress syndrome (RDS).
   (b) Glucose metabolism affects lung surfactant maturation, and babies of diabetic mothers are at increased risk of RDS, especially when born premature.
   (c) Antenatal steroid therapy is associated with decreased incidence of RDS and reduced mortality.
3. At birth, the onset of breathing is stimulated by hypoxia, hypercarbia, tactile stimulation, sudden exposure to cold, and decrease in plasma prostaglandin E. After aeration and distention of lungs, PVR decreases, and pulmonary blood flow increases nearly tenfold. Failure of reduction of PVR at birth is associated with extra pulmonary shunting and severe hypoxemia, leading to persistent pulmonary hypertension of newborn (PPHN).

11.2.2 Anatomical Fundamentals of the Neonatal Respiratory Tract and Airways

The neonatal respiratory tract is unique, and its understanding is essential for safe administration of anesthesia:

(a) A neonate's nostril, oropharynx, and trachea are relatively narrow. Breathing can be hindered by irritation of the mucous membrane due to edema building up in this area.
(b) The trachea is short and measures approximately 4 cm from the larynx to the carina. It is also narrow with a diameter of 6 mm.
(c) The tongue is relatively large and tends to fall backwards during sleep and under anesthesia, causing airway obstruction.
(d) Newborns, neonates, infants, and small children have a very soft and short thorax compared to adults. The ribs run horizontally unlike diagonally as is adults. The intercostal muscles are immature and do not have rigidity of adults.
(e) The salivary secretions are more pronounced.
(f) The larynx is more ventrally located, at the level of the 3rd and 4th cervical vertebrae, a whole vertebra higher than that in adults (cervical 4–6).
(g) Until the age of 8–10 years, the narrowest area of the lower airway is the very sensitive mucous membrane at the level of the cricoid cartilage and not glottis, as in adults.
(h) The epiglottis is relatively large, floppy, and U shaped, overhanging the glottis.
(i) Small babies breathe through their nose until they reach an age of 5 months (**obligatory nose breathers**). Inserting a stomach tube through the nose can be a massive respiratory hindrance. Hence, all nasal manipulations should be avoided.

11.2.3 Upper Airway Muscles and Anesthesia

The genioglossus, geniohyoid, and other pharyngeal and laryngeal abductor muscles have phasic inspiratory activity synchronous with diaphragmatic contraction. Their tonic activity maintains the patency of the upper airway [2]. The genioglossus and geniohyoid muscles increase the caliber of the pharynx by displacing the hyoid bone and tongue anteriorly. They are the most important muscles for the maintenance of oropharyngeal patency. The tone of all the laryngeal and pharyngeal muscles, including the abductors, is depressed during general anesthesia with resultant upper airway obstruction.

In neonates, under GA and inhalational anesthesia, the work of breathing (an index of the degree of upper airway obstruction) is significantly increased when breathing by mask, without an oral airway in place, even when partial upper airway obstruction is not clinically apparent. An addition of CPAP (5–6 cm of H_2O) opens-up the pharynx and improves airway patency as shown by a significant decrease in the work of breathing.

11.2.4 Controlling the Respiratory Process

Control of breathing in the neonates evolves gradually during the first month of extrauterine life and beyond and is different from that in older children, especially in response to hypoxia. Inspiration is an active process, initiated by contraction of the diaphragm, which creates negative intrathoracic pressure that allows air to be drawn into the lungs. Expiration, on the other hand, is passive, due to the elastic recoil of the lungs and thorax. It may be increased actively by contraction of abdominal and thoracic expiratory muscles during exercise.

The respiratory process in both premature and term newborns, and neonates is controlled by changes in $PaCO_2$, PaO_2, and pH. At birth the breathing regulation and response to hypoxia is not fully developed. The $PaCO_2$ and PaO_2 values of newborns and neonates are lower than those of adults until the end of the first year of life. (Table 11.1)

Table 11.1 Normal range of arterial blood gas values*

	ELBW (<1000 g)	VLBW (<1500 g)	Term infant36.–toddler	Child–adult
Parameters	**<28 weeks of GA**	**28–40 weeks of GA**	**Up to 2 years age**	**2 years**
pH	≥7.25 (≥7.20)	≥7.25 (≥ 7.20)	7.3–7.4	7.35–7.45
$PaCO_2$ (mm of Hg)	45–55 (60)	45–55 (60)	30–40	35–45
PaO_2 (mm of Hg)	45–65	50–70	80–100	80–100
HCO_3 m Eq/L	15–18	18–20	20–22	22–24

ELBW Extremely low birth weight, *GA* Gestational age, *VLBW* Very low birth weight. Values in parenthesis for lung protection strategies.

*Pagtakhan RD, Pasterkamp H, Intensive care for respiratory disorders. In Chernick V, editor: Kendig's disorders of respiratory tract in children, ed 5. Philadelphia: WB Saunders, 1990:205–224 and Durand DJ, Philips P, Boloker J: Blood gases; technical aspects and interpretation. In Goldsmith JP, Karotkin EH, editors: Assisted ventilation of the neonate, ed 4, Phiadelphia: WB Saunders/Elsevier Science, 2003

11.2.5 Response to Hypoxemia

During the first 2–3 weeks of age, both term and preterm neonates, in a warm environment, show a biphasic response to hypoxemia (FiO_2—15%). There is an initial transient (30 s) increase in ventilation followed by sustained ventilatory depression or apnea [3]. If hypothermia or hypoglycemia occurs simultaneously, the initial period of transient hyperpnea is abolished; hypoventilation is the immediate result, indicating the importance of maintaining a neutral thermal environment and prevention of hypoglycemia. By 3 weeks after birth, hypoxemia induces sustained hyperventilation, as it does in older children and adults.

11.2.6 Response to CO_2

Neonates responds to hypercapnia by increasing ventilation but less so than in infants. The slope of CO_2 response curve increases appreciably (response becomes more vigorous) with postnatal age, independent of postconceptual age (PCA) [4].

11.3 Patterns of Breathing in Neonates

The respiratory control mechanism and O_2 receptors are immature and still developing in neonates. Premature babies often experience respiratory arrest (apnea) either at regular **(periodical breathing)** or irregular intervals. Periodical breathing is considered as an episode of 3 or more respiratory pauses of at least 3 s (usually 5 to 10 sec) with normal breathing periods of less than 20 s. Apnea phases can be due to a central cause (no physical breathing exertion) or less often caused by an obstruction (no airflow despite physical breathing exertion). Most commonly, apnea of the prematurity is usually of the mixed type, i.e., central and obstructive. Periodical breathing is seen in all babies during the neonatal age and is not usually dangerous. The clinically relevant forms of apnea are discussed below.

11.3.1 Clinical Importance of Severe Forms of Apnea in Neonates

11.3.1.1 Apnea is defined as cessation of respiration for more than 15 s, or less than 15 s if associated with bradycardia (HR<100/min), cyanosis or pallor [5]

1. **Central apnea**

   The control of breathing and oxygenation even in healthy term newborns is not precise, because respiratory center is immature, more so in preterm neonates. 2–3% of term newborns commonly have prolonged apnea (explained below) lasting 30 s, associated with desaturation, with a central, obstructive, or mixed cause. The risk of having such episode is 20–30 times higher among preterm than term newborns, before 43 week PCA. Central apnea occurs more frequently in the in-hospital neonates due to depression of respiratory center by sedatives and narcot-

ics, and exacerbated by metabolic disturbances such hypoglycemia, hypocalcemia, hypothermia, and sepsis. Central apnea is treated with methyl xanthenes, such as caffeine citrate [especially in premature born (<34 week gestation age)].

Apparent life-threatening events (ALTE) are characterized by an episode of sudden onset apnea, color changes (pallor, cyanosis) tone changes (limpness or rarely stiffness) which require immediate resuscitation for revival and restoration of normal breathing pattern. Treatable pathologic conditions are found in about 30% of neonates, while in others, no cause may be found.

2. **Obstructive apnea**

   This occurs due to inconsistent maintenance of a patient airway. It can result from incomplete maturation and poor coordination of upper airway musculature. This form of apnea may respond to changes in head position, insertion of oral/nasal airway or placing the baby in prone position, occasionally administration of CPAP or high flow oxygen nasal cannula may be beneficial. This therapy is effective in neonates with large tongue, such as with trisomy 21.

3. **Mixed apnea**

   This represents a combination of both central and obstructive apnea.

11.3.1.2 Postoperative Apnea

Life threatening apnea is a serious postoperative event in prematurely born babies and may occur up to 60 week PCA. Though it is more frequent following general anesthesia, apnea may occur even after regional or local anesthesia, up to 12–24 h postoperatively. Postoperative hypoxemia, hypothermia, and anemia (Hct <30%) are significant risk factors regardless of gestational or PCA [6]. Both theophylline, and especially caffeine, are effective in reducing apneic spells in preterm neonates.

If it is not possible to delay surgery until the baby is more mature, it is mandatory to use postoperative apnea monitoring in neonates who undergo anesthesia at less than 60 week PCA, for at least 24 h.

11.4 Respiratory Mechanics

11.4.1 Characteristics of Neonatal Lungs and Thorax

The development and growth of lungs and surrounding thorax continue with fast pace during the first year of life. At birth the number of terminal sacs (most of which are saccular) are 20–50 million only, one tenth of fully grown lungs of a child during the first year, and is essentially completed by 18 months of age [7].

11.4.2 Compliance of Lungs

In neonates, static (elastic) recoil of lungs is very low (i.e., compliance normalized for lung volume is unusually high or highly compliant), because elastic fibers do not develop until postnatal period [8]. The elastic fibers in lungs give shape to alveoli and respiratory bronchioles and do not allow them to collapse as it gives outward

Table 11.2 Relationship between age and compliance

	Newborn	Infants	Small child	School aged
Age	1–28 days	Up to 1 year	2–5 years	6–14 years
Weight	2.5–5 kg	5–10 kg	10–20 kg	>20 kg
Compliance mL/mbar	5	10–20	20–40	100

traction to these structures. Since elastance is proportional to elastic fibers present and compliance is inverse of elastance ($C = 1$/elastance) the compliance of neonate lungs is high (also called that elastic recoil pressure of neonatal lungs is very low).

11.4.3 Compliance of Neonatal Thorax (Chest Wall)

The elastic recoil pressure of neonate's thorax (chest wall) is extremely low (highly compliant) because of its compliant cartilaginous ribcage and poorly developed thoracic muscle mass, which does not add rigidity. As neonate's thorax is more compliant than adults' it offers little resistance to over inflation. As the child grows older and the size also continuously grows; in absolute terms the total compliance (i.e., compliance of lung and chest wall) increases, as shown in Table 11.2.

11.4.4 Clinical Implications

The low lung compliance means more pressure or energy is required to provide the normal amount of air volume brought into the neonate lungs with each breath. The neonate chest wall is more compliant as explained above. With significant lung disease, the chest wall may actually be more compliant than the lungs, causing retractions, in which the ribs and sternum distort inward during inspiration instead of expanding the lungs.

Because of high lung and thoracic compliance, both lungs and thorax have a tendency to collapse; in other words, negative intrathoracic pressure is poorly maintained. Therefore, each tidal breath is accompanied by functional airway closure. In addition, adults have high proportion of slow-twitch, high oxidative, fatigue-resistant fibers in their diaphragm and intercostal muscles. Whereas adults have 65% of these fibers in the intercostal muscles and 60% in the diaphragmatic muscles, neonates have only 19–46% of these fibers in their intercostal muscles and 10–25% in the diaphragm. Consequently, neonates are more vulnerable to muscles fatigue and decreased stability of the chest wall. These unique characteristics make neonates more prone to lung collapse, especially under general anesthesia when inspiratory muscles are markedly relaxed.

In neonates, because of the horizontal placement of ribs and consequent inability to increase the transverse diameter of the thorax, the diaphragm does almost all the work expended for breathing. Abdomen hindrances, for example splinting of the diaphragm from raised intra-abdominal pressure, can lead to insufficient spontaneous breathing.

11.5 Surface Activity and Pulmonary Surfactant

The alveolar surfaces in human lungs are lined with surface active material that decreases the surface tension of gas fluid interface in the alveoli and is responsible for the stability of the air spaces in the lungs. This surfactant is secreted by Type II pneumocytes in the alveolar lining. The relationship among pressure (P), surface tension (T), and radius of a sphere, such as soap bubble, is expressed by the Laplace equation as follows:

$$P = 2T / r$$

It can be seen from this equation that if surface tension is constant in a number of connected spheres, the pressure is inversely proportional to the radius of the sphere, smallest sphere has the highest pressure. Thus, the smallest spheres would empty their gas contents into the larger ones, during the emptying phase. If this concept is applied to lung units, the lungs would be unstable, with most units collapsing into several large ones, as seen in the lung of a neonate with RDS, a condition deficient in the amount of surfactant. Surfactant consists of mainly lipids (90%), 10% protein and minimal carbohydrates (0.1%). The lipids lower the surface tension, but proteins allow absorption and dispersion of the lipids in the air liquid interface. They become more concentrated, i.e., greater reduction in alveolar surface tension, when the alveoli are smaller, as during expiration, and become less concentrated during inspiration, when alveoli expand and become larger. Therefore, in normal lungs, the surface tension decreases as the alveolar radius decreases (during exhalation) and vice versa and ratio T/r in above equation remains same, in other words the pressure of the alveoli remains same during exhalation and inhalation. Thus, physiologically the stability of air spaces is maintained regardless of the size of each alveolus or lung unit.

11.6 Pulmonary compliance

Pulmonary compliance can be reduced from various causes in neonates, chiefly, due to parenchymal damage, surfactant disorders or from reduced lung volume. The following are relevant to anesthetist:

1. **Parenchymal damage:** bronchopneumonia, pulmonary edema, RDS, and pulmonary fibrosis.
2. **Functional surfactant disorders**: alveolar pulmonary edema, atelectasis, aspiration, and RDS.
3. **Reduced volume**: pneumothorax, raised diaphragm.

11.7 Pulmonary Volumes

Relative to its size, the volume of a baby's lung is equivalent to that of an adult's. A term newborn has a total lung capacity (TLC) of approximately 160 mL, a functional residual capacity (FRC) of 80 mL and a tidal volume (Vt) of approximately

16 mL. One-third of the Vt is equal to dead space (Vd) volume. The proportion of Vd to Vt remains constant for spontaneously breathing children; it can, however, increase during controlled ventilation. In order to keep total Vd volume to minimum, accessories of anesthetic system should be operated using the smallest possible dead space available, especially when ventilating a neonate with a Vd of only 5 ml.

The following four static volumes and 4 static capacities (values in neonates) can be distinguished:

1. Tidal volume (Vt): is the volume normally expired and inspired. (4–6 mL/kg).
2. **Residual volume (RV)**: is the volume remaining in the lungs after a maximal expiration.
3. **Expiratory reserve volume (ERV)**: is the additional volume which can be exhaled after a normal expiration.
4. **Inspiratory reserve volume (IRV):** is the additional volume which can be inspired after a normal inspiration.
5. **Total lung capacity (TLC):** includes total air volume in the lungs after a maximal inspiration (FRC + IC) (63 mL/kg).
6. **Vital capacity (VC):** is the maximum volume which can be exhaled after a maximal inspiration (ERV + IC) (40 mL/kg).
7. **FRC:** is the volume remaining in the lungs after normal expiration (RV + ERV) (30 mL/kg).
8. **Inspiratory capacity (IC)**: is the maximum volume which can be inspired after maximal expiration (Vt + IRV).

In addition to the above volumes and capacities, closing volume is a very important parameter. Although all respiratory paths (airways) are open in a completely filled lung, decreasing expiatory volume may cause peripheral paths to become blocked, as peripheral paths easily collapse in neonate because of lack of elastic fibers that gives outward traction to peripheral airways and keep it open in older child and adults. The closing volume of neonates and small children is rather large compared to that of adults, and may exceed the FRC during normal ventilation, and impair or encroach normal Vt.

Intubation eliminates physiologically intrinsic PEEP in the larynx. The larynx undergoes some adduction which acts as an expiratory retard normally in neonates due to tonic activity of these mussels during expiration which counteracts peripheral respiratory path blockage. Autogenic PEEP can be compensated for in most anesthetic machines or ventilators using slightly extrinsic PEEP (3–5 mbar).

The alveolar ventilation (ventilation of the alveoli for the purpose of blood gas exchange) of a neonate, 100–150 mL/kg/min, is twice that of an adult. This is achieved mainly through an increase in respiratory rate and not through increase in TV. As pulmonary blood flow is continuous, the O_2 present in the lungs in form of FRC provides oxygenation of the blood during expiratory phase, expiratory pause or apnea. The ratio of alveolar ventilation to FRC is 5:1 for neonates and 1.5:1 for adults (i.e., the 'Buffer' or reserve of FRC of total alveolar ventilation in adults is much larger compared to neonates). As a result, the FRC of a neonate is only a slight or small "buffer" against fluctuations in the volumes and

Table 11.3 Average respiratory rates, tidal volumes and resistance values as per age

	Neonate	Infants	Small children	School age
Age	1–28 days	Up to 1 year	2–5 year	6–14 year
Weight	2.5–5 kg	5–10 kg	10–20 kg	>20 kg
RR/min	40–60	30–60	30–40	12–20
Vt (mL/kg)	7–10	7–10	7–10	7–10
Resistance (mbar/L/s)	40	20–30	20	1–2

concentrations of the inspiratory gases and anesthetic agents so that changes in anesthetic agent concentrations are reflected very quickly in the arterial blood gas values. Any reduction in FRC, e.g., by anesthetics or muscle relaxant, can lead to blockage in the smaller airways, uneven gas distribution, and consequent hypoxemia.

11.8 Airway Size and Resistance to Flow

The actual size of airway from nose to larynx to bronchioles in neonates is much smaller than in children and adults, and therefore, the flow resistance in absolute terms is extremely high. When normalized for body size, however, neonates' airway size is relatively much larger, airway resistance much lower than adults.(Table 11.3) Infants and toddlers, however, are prone to severe obstructions of the upper and lower airways, because their absolute (not relative) airway diameters are much smaller than those in adults; resistance to air flow increases by fourth power of radius with any decrease in airway diameter. Consequently, mild airway inflammation, edema or secretions can lead to far greater degree of airway obstruction in neonates than in adults (e.g., subglottic croup of laryngotracheobronchitis or accumulation of secretions).

Similarly, during surgery and anesthesia, significant fluctuations in respiratory resistance can occur. For example, bronchial dilatory effect of inhalational anesthesia reduces respiratory resistance while even a slight swelling or accumulation of secretion in the respiratory tract or tiniest obstruction in the tube area, can increase total flow resistance greatly.

11.9 Oxygen Requirements

At 7 mL/kg/min the O_2 needs of a neonate are twice as high as that of an adult. At the same time, the level of O_2 consumption depends on the baby's state of health, bodily maturity and stress due to cold, e.g., postoperative hypothermia doubles the O_2 requirement (15–16 mL/kg/min), whereas under general anesthesia it decreases as the body temperature falls. The O_2 consumption according to body weight is shown in Table 11.4.

Neonates are significantly more susceptible to hypoxia than adults because of higher O_2 consumption (twice that of adult), higher alveolar ventilation (twice that of adults), and in addition, less surface area for gas exchange (as alveoli are still developing and far less in number) and small FRC. The ventilatory requirement per

Table 11.4 Interdependency of O_2 consumption and FRC to body weight

Body weight kg	O_2 consumption	FRC
5	9 mL/kg × min	10 mL/kg
10	7 mL/kg × min	15 mL/kg
20	6 mL/kg × min	30 mL/kg
Adults	3.5 mL/kg × min	

unit of lung volume in neonate is markedly increased. The FRC is reduced even more after anesthetics have been administered (60% reduction of FRC in neonates vs. 30% reduction in adults after anesthesia from awake level). The small O_2 reserve available to a newborn or small child is quickly used up during hypoventilation or apnea of short duration, and therefore, they desaturate rapidly; hypoxia can occur within 10–20 s of apnea. For comparison, a healthy adult has apnea tolerance of 2–3 min.

Premature and low birth weight newborns (<1500 gm) do not react to hypoxia, such as an adult, with tachycardia, but rather with a reduced heart rate (bradycardia). This state is not remedied by administering medication such as atropine but responds only to increasing the O_2 supply.

The use of pulse oximetry routinely has improved ability to monitor and properly maintain oxygenation during the care of the neonate in the NICU or the OT. This is especially true in premature neonates who are susceptible to O_2 toxicity and retinopathy (ROP). The risk of retinopathy increases with the degree of immaturity, the duration of O_2 application, and the height of partial pressure. Babies in acute danger of developing ROP are premature babies born before the 44th week of pregnancy and exposed to:

(a) PaO_2 of more than 80 mmHg for more than 3 h or
(b) PaO_2 of more than 150 mm of Hg for more than 2 h

The risk of damaging the retina by excessive partial pressure of O_2 depends on the postnatal age and is practically nonexistent when premature neonate reaches the infant stage.

In neonate, whose P50 is 18–20 mmHg, the range of SaO_2 to maintain adequate PaO_2 (60–80 mmHg) is 97–98%. At PaO_2 value more than 80 mm of Hg the manifestation of ROP increases as saturation drops, PaO_2 also decreases significantly, at 1-day age, SaO_2 of 91% corresponds to PaO_2 of 41 mmHg, and at 2-week age it is 50 mmHg, which is dangerously low. Hence, FiO_2 should be such that it maintains SaO_2 at 97–98% (PaO_2 targeted at 70 mmHg) [1]. Table 11.5 shows the relationship between O_2 saturation values and corresponding PaO_2 values. (Note - as the baby desaturates, rate of decrease in PaO_2 is significant, reaching hypoxic levels).

Under anesthesia hyperventilation induced respiratory alkalosis, shifts the oxygen dissociation curve (ODC) curve to further left with further decrease in P50 value. This is hazardous in neonate whose P50 is unusually low even without respiratory alkalosis. Hence, maintenance of normal $PaCO_2$ by monitoring $EtCO_2$ under anesthesia is prudent.

Table 11.5 Relationship between P_{50}, SaO_2 and corresponding PaO_2

	1 day	2 weeks	6–9 weeks	Adult
P50 (mm of Hg)	19	22	24	27
SaO_2 (%)	**Estimated PaO_2 mm of Hg**			
99%	108	130	143	156
98%	77	92	101	111
97%	64	77	84	92
96%	56	68	74	82
95%	52	62	68	74
92%	43	52	57	62
91%	41	50	55	60

11.10 Functional Residual Capacity (FRC) and Anesthesia

The main mechanism that maintains FRC is the tonic contraction of both diaphragm and intercostal muscles throughout respiratory cycle (inspiration + expiration) in awake neonates. This mechanism effectively stiffens the chest wall. This intrinsic tone of inspiratory muscles maintains the outward recoil and rigidity of thorax and maintains a higher end expiratory lung volume. Anesthesia and paralysis would abolish this muscle tone reducing thoracic compliance (outward movement of thorax is reduced), while elastic recoil of lungs is not altered. This change alters the balance between elastic recoil of lungs and thorax in opposite direction and consequently diminished FRC. The compliance of the lungs decreases shortly thereafter with resultant airway closure (in matter of few minutes) from reduced FRC. The average decrease in FRC is 46–70% under anesthesia (while in adults this varies 9–25%).

The compliance of respiratory system as a whole (Crs, or total compliance) under general anesthesia decreases to about 35% (a value comparable with adult). The reduction in Crs occurs both during spontaneous and manual ventilation with low Tv and after muscle relaxant administration. When Vt is doubled, however, Crs returns to preanesthetic control levels. Hence, higher Tv is maintained under anesthesia depending on SaO_2, and $PacO_2$ values. It is explained more later.

11.11 Mechanical Modes of Ventilation

All known ventilation modes used in pediatric anesthesia come from adult anesthesia. These modes include the conventional modes of anesthesia, volume control mode (VCM), synchronized intermittent mandatory ventilation (SIMV), and pressure controlled ventilation (PCV).

11.11.1 Volume Control Mode (VCM)

VCM is a time cycled volume-controlled ventilation mode. The ventilator delivers a preset volume at a constant inspiratory flow rate. Time and frequency are set or given. The patient does not breathe on his/her own. The pressure which develops

inside the breathing system and the lungs is derived from both set parameters, and pulmonary resistance and compliance. Pressure monitoring is of great importance in order to avoid high peaks of pressure. The anesthetist must set a maximum pressure limit, Pmax, which cannot be exceeded. IPPV is primarily used on those babies with healthy lungs and ensures that the patient constantly receives a defined minute volume.

11.11.2 Synchronized Intermittent Mandatory Ventilation (SIMV)

SIMV is a mixture of both spontaneous and controlled ventilation, in which the inspiratory strokes of the respirator are synchronized with those of the patient. The patient is able to breathe spontaneously at regular, predetermined intervals. Mandatory ventilatory strokes ensure the minimum ventilation within these intervals. Mechanical respiratory strokes triggered by the patient means they take place within a time frame anticipated by the patient and his or her inspiratory efforts, not during the unsynchronized delivery of respiratory strokes. SIMV is a useful mode in pediatric anesthesia, for instance, during the recovery phase.

11.11.3 Pressure Controlled Ventilation (PCV)

PCV is ideal for general use in pediatrics anesthesia. The lungs of children are susceptible to over inflation during anesthesia. Reasons for this are insufficient flexibility of the alveoli, shallow breaths and highly compliant thorax.

Having set maximum pressure, which makes it possible to limit the pressure at which the gases are delivered into the respiratory tract, minimizes the risk of barotrauma and helps avoid high pressure peaks. Barotrauma can also occur during VCM secondary to very high inspiratory flows, secretions, mucus deposits, or bronchospasm. In these situations of blockade of airways, where resistance becomes too high, in VCM, the ventilator increases the peak flow to reach a set TV.

The major advantage of PCV over VCM is in being able to use uncuffed endotracheal tubes (ETT) in neonates, which allows large amounts of leakage (>20% of minute volume). By increasing the flow to maintain the set pressure, loss caused by leakage is automatically compensated to a certain degree. However, not only is ETT leakage counteracted, leakages caused by lungs (e.g., lung fistulas) are also counteracted. In IPPV mode the leakages will initiate low pressure alarm and prevent the Tv to be achieved.

In addition, gas distribution disorders within the lungs can be better compensated for in PCV than in VCM. For example, if the lungs are nonhomogeneous, conventional volume-controlled ventilation, overinflates the healthy lung areas and under inflates the obstructed lung areas. This results in temporary pressure differences and different volume throughout the lungs, which are exposed to great mechanical loads. PCV ensures that the lungs fill more evenly and that the healthy lung is not damaged by excess pressure.

Table 11.6 Initial respirator settings in Volume and Pressure Control Modes

Initial respirator settings in VCM			
		Neonates (5 kg)	Small children
Respiratory rate		20–30/min	15–20/min
I:E Ratio		1:2	1:2
Inspiratory pressure limit		<20 mbar	<20 mbar
PEEP		3 mbar	3–5 mbar
FiO_2		0.5	0.5
Tidal volume		10–15 mL/kg	10–15 mL/kg
Initial Respirator Setting in PCV			
	Premature (2 kg)	**Neonate (5 kg)**	**Small children**
Pressure Limit (mbar)	16–18	25	25
RR/min	30–60	20–30	15–25
I:E	1:2	1:2	1:2
PEEP (mbar)	2	2	2
Inspiratory flow (L/min)	4–6	4–8	4–12

11.11.4 Clinical Implications

The initial ventilation parameters are shown in Table 11.6 for both VCM and PCV modes.

(a) **Tidal Volume**

The anesthesiologist often controls a neonate or pediatric ventilation manually or mechanically during general anesthesia, because most anesthetics techniques cause spontaneous ventilation to decrease or cease. This is because most anesthetics are potent respiratory depressants, and because the ETT and anesthesia circuits add elastic and resistive loads to breathing. Because anesthesia causes a decrease in FRC, the uneven distribution of ventilation and an increase in physiological Vd, the Tv must be increased. The mechanical Vd and internal compliance of anesthetic equipment must also be taken into account for proper estimation of ventilatory requirement. Physiological Vd is further increased in patients with preexisting lung dysfunction. Therefore, it is practical to start with Tv of 10-/kg body or roughly 1.5–2 that is required in awake individual. In awake individuals Vt of 4–6 ml/kg for premature neonates and 6–8 mL/kg for term neonates, are taken as normal.

In VCM, tidal volume can be set directly, while in PCM, the desired tidal volume is influenced by patient's respiratory characteristics (compliance) and by pressure settings of the ventilator. Tidal volumes settings are monitored by the resulting $EtCO_2$ and capillary CO_2 values.

(b) Respiratory Rate

Neonates are ventilated with a frequency of 30–60/min.

(c) The I:E Ratio

It should be between 1:1 and 1:2 for uncomplicated cases during mechanical ventilation. If O_2 exchange disorders are present (e.g., RDS), neonates can be ventilated such as adults using an inverted I:E ratio and low inspiratory flow

(inverse ratio ventilation). In this case, a change in the I:E ratio affects the mean airway pressure and, in conjunction with FiO_2, oxygenation. A short inspiratory phase with high peak pressure of up to 35 mbar are less likely to cause barotrauma than long inspiratory phases (>0.6 s).

(d) PEEP

Physiologically, premature neonates and newborns build up a physiological PEEP in the larynx area during expiration which is eliminated by intubation. By setting the PEEP the risk of bronchial and alveolar collapse, which is easily triggered by high closing volume of neonate, is reduced. PEEP helps keeping the alveoli open throughout the respiratory phase and also increases the FRC. Ventilating the neonate with a PEEP of 5 mbar increases the FRC of intubated or anesthetized neonate by 28%.

Depending on the patient's oxygenation level, PEEP pressure is set to 4–8 mbar. Higher levels are not well-tolerated by neonates. Changing the setting should take place in increments of 1–2 mbar. One side effect of PEEP is the disruption of cardiac and circulatory systems, e.g., a decrease in cardiac output due to a lessening in venous return flows and cardiac compression.

(e) Peak Pressure

Peak pressure affects alveolar ventilation via $PaCO_2$ during artificial respiration and depends on resistance, compliance, inspiratory flow and tidal volume. Pressure limiting is of utmost importance in VCM to reduce the risk of alveolar overinflation. Peak pressure should not be set higher than 20–25 mbar. Peak pressure of >35 mbar should be avoided altogether, since the risk of brain hemorrhage increases. Peak pressure between 6 and 8 mbar are usually sufficient for ventilating premature and low birth weight neonates (<1000 g). Changes is the setting should be made in increments of 2 mbar.

(f) Inspiratory Flow

While the inspiratory flow is regulated directly in PCV modes, it can only be indirectly regulated in VCM through I:E ratio, Tip (inspiratory plateau time), inspiratory time and the respiratory rate. If, during PCV mode the inspiratory flow chosen is too low, the desired volume cannot be delivered in the preset time and ventilation will be insufficient. The steepness of the rise in pressure increases in VCM as the inspiratory flow increases, and peak pressure increases simultaneously. In order to protect the airway, alarm is triggered whenever the respiratory pressure reaches the set upper limit. Standard flow rates are 6–10 L/min for neonates. Much of this is not delivered to the to the baby, rather is used to drive the ventilator. Babies on PIP more than 20 cm H_2O and respiratory rates more than 60/min, may require higher flow rates (12–16 L/min) so as to achieve the peak pressure and deliver a larger tidal volume.

(g) Inspiratory O_2 (FiO_2) on ventilator

The following dictum supports the theory about maintaining he FiO_2 in neonates:

Keep it as low as possible, but as high as necessary.

The FiO_2 should be set so that PaO_2 value is less than <70 mmHg (higher PaO_2 promotes ROP).

(h) $EtCO_2$ or $PaCO_2$ monitoring

Once the mechanical ventilation is established, RR and Tv can be decreased and refined with the aid of capnography. The changes in $PaCO_2$ reflect alveolar ventilation, thus $EtCO_2$, PCO_2 or capillary $paCO_2$ is useful for adjusting and monitoring alveolar ventilation and it is targeted at 30–40 mmHg. In patients with lung disease, time constant duration (inspiratory time and inspiratory pause), should be increased to allow sufficient time for passive lung gas diffusion. The addition of low level of PEEP (5–7 cm H_2O) restores the volume (FRC) lost from relaxation of inspiratory muscles and helps prevent end expiratory airway closure.

The various parameters that need to be considered for improving oxygenation (PaO_2) and ventilation ($PaCO_2$) are shown in Box 11.1

Box 11.1 Parameters That May Need a Change to Improve Oxygenation (PaO_2) and Ventilation ($PaCO_2$)

1. Improving oxygenation (↑PaO_2) by
   (a) Increasing the Inspiratory O_2 concentration (FiO_2)
   (b) Increasing Mean Airway Pressure by
      – Increasing PEEP in PCV/VCV modes
      – Lengthening the Inspiratory phase in PCV/VCV modes
      – Increasing plateau pressure in PCV mode
      – Increasing Inspiratory flow in IPPV mode
2. Improving ventilation (↓$PaCO_2$) by
   (a) Increasing Minute Volume (MV) by
   (b) Increasing frequency
   (c) Increasing tidal volume
   (d) Optimizing form of ventilation
      • Adequate I:E ratio
      • Adequate Inspiratory flow

11.12 Considerations in Neonatal Respiratory Diseases

11.12.1 Clinical Presentation

Signs of respiratory distress are tachypnea, grunting, nasal flaring, intercostal and subcostal retractions, rales, rhonchi, asymmetry respiratory sounds on auscultation, and apnea. Pulse oximetry (SpO_2) is a useful noninvasive tool to screen systemic oxygenation in neonates. Blood gas tension (PaO_2 and $PaCO_2$), the invasive monitoring tool, is essential for suspected pulmonary and cardiopulmonary abnormalities.

Various disease states that present similarly as parenchymal diseases should be considered when evaluating neonates with respiratory distress:

1. **Airway obstruction**: choanal atresia, vocal cord palsy, laryngomalacia, laryngeal stenosis, compression of trachea by external masses, such as cystic hygroma, hemangioma, and vascular rings.
2. **Developmental Anomalies**: TEF, CDH, congenital lobar emphysema, pulmonary sequestration, bronchial cysts, congenital pulmonary airway malformations.
3. **Non pulmonary diseases:** cyanotic heart disease, persistent pulmonary hypertension of neonate, congestive heart failure, metabolic disturbances.

11.12.2 Laboratory Studies

For a neonate in respiratory distress, laboratory studies should include arterial blood gas, pre and post ductal O_2 saturation by SpO_2, hemoglobin, 12 lead ECG, and chest X ray.

If these results are abnormal, potential cardiac disease should be re-evaluated by ABG, while neonate breathes 100% O_2 **(Hyperoxia test)**. This is used in cyanotic babies to rule out cardiac cause.

11.12.3 Hyperoxia Test Methodology

1. Pre-oxygenation PaO_2. Baby allowed to breathe 100% O_2 for 10 min in a hood or via ETT. Repeat PaO_2 (right radial artery). There should be an increase in PaO_2 of 30 mmHg or more from the pretest value. If not, then most probable cause of cyanosis is cardiac (intracardiac shunt of >30%).
2. In terms of absolute PaO_2 values after breathing 100% O_2 for 10 min:
   (a) If PaO_2 is >150 mmHg, cyanosis is of pulmonary etiology, and if less than 150 mmHg, cyanosis is of cardiac origin.
   (b) PaO_2 of 50–150 mmHg is seen in cardiac disease without restriction of pulmonary blood flow (single ventricle with PDA, Truncus arteriosus), and
   (c) PaO_2 less than 50 mmHg—indicative of cardiac disease with restricted pulmonary blood flow (TOF Tetralogy of Fallot's, TA Tricuspid Atresia, TGA Transposition of great arteries).

However, echocardiography and cardiac consultation will be needed for further evaluation and management.

11.13 Respiratory Distress Syndrome (RDS)

11.13.1 Pathophysiology

RDS results from physiologic surfactant deficiency. Surfactant is essential for normal alveolar development in the intrauterine life, and expansion after birth. Surfactant deficiency causes decrease in lung compliance, alveolar instability, progressive atelectasis, intrapulmonary shunting and hypoxemia.

Premature babies have increased incidence of RDS and can be identified prenatally by amniocentesis and measuring lecithin to sphingomyelin ratio (>2), and saturated phosphatidyl choline levels (>500 μg).

Causes of RDS in a neonate, beside surfactant deficiency, include Bronchopulmonary dysplasia (BPD), and Hyaline membrane disease (HMD), and Meconium Aspiration Syndrome (MAS). *(These are discussed in the chapter on transitional changes in the newborn).* However, presentation, diagnosis and management is similar in all four conditions.

Antennal Glucocorticoid (betamethasone) treatment (once a day for 2 days to the mother), at least 48 h prior to premature delivery, decreases the incidence and severity of RDS in the newborn baby.

Clinically tachypnea, nasal flaring grunting and retraction is seen. Cyanosis appears soon after birth. Because of large intrapulmonary shunt due to atelectatic lung units, newborn remains hypoxic despite high FiO_2.

11.13.2 Initial Treatment

Symptomatic newborns should be kept in a warm humidified hood. O_2 can be provided in the hood or via nasal catheter:

- FiO_2 should be adjusted to maintain PaO_2 of 50–80 mmHg (SaO_2 = 88–92%).
- If FiO_2 >60% is required, nasal CPAP or even intubation may be indicated.
- Endotracheally given exogenous surfactant decreases morbidity and mortality.
- High frequency oscillation ventilation (HFOV) is helpful in decreasing air leaks and chronic lung disease.

11.14 Pneumothorax

Pneumothorax is a very serious condition which if undiagnosed can be fatal.

11.14.1 Causes of Pneumothorax

(i) **Iatrogenic Pneumothorax** can occur in neonates requiring positive pressure ventilation in ICU or intraoperatively during anesthesia.

(ii) **Spontaneous pneumothorax** can occur in 1–2% of otherwise healthy term neonates who often remain asymptomatic or mildly symptomatic and require no intervention.

11.14.2 Clinical Features

The diagnosis should be considered in any neonate with acute deterioration in clinical condition, such as sudden cyanosis and hypotension. Occasionally asymmetric chest movements and asymmetric breath sounds may be appreciated. However, endobronchial intubation should be ruled out.

11.14.3 Laboratory Studies

Transillumination of the thorax with strong light usually will show hyperlucent hemithorax. If the patient is stable, chest X ray can be done to confirm the diagnosis, but those in distress and are hemodynamically unstable, need immediate intervention.

11.14.4 Treatment

Immediate aspiration of the air with an IV catheter must be performed. Puncture is done in the 2nd intercostal space of the affected side, remembering that the neonates' chest wall is very thin, and the depth of insertion is not more than 0.5–1 cm (to avoid injury to the lung and heart). A three-way stopcock should be attached to the needle. At no time should the need be left open to the air. Once confirmed (by air gushing out, and improvement in the clinical condition), a chest tube drain will need to be inserted under LA at the same site, with a continuous draining tube and underwater seal attached, under all aseptic precautions, at the bed side, as re-accumulation is a potential occurrence, until the air leak gets sealed off.

11.15 Conclusion

This chapter covers the developmental anatomy and physiology of the lung, normal parameters, gas exchange, importance of FiO_2, ventilatory patterns and problems of ventilation in the newborn and the neonate, various ventilatory modes commonly used, and ventilatory parameters, and concerns regarding neonates with respiratory diseases and surfactant deficiency. Fortified with this knowledge, the anesthesiologist will be able to better understand and manage neonates during and after surgical procedure, according to the probable lung pathology or disease. Importance of keeping FiO_2, airway pressures and volumes, to the minimal, but enough to maintain parameters within normal range, should be the prime concern. Maintenance of PaO_2 and $PaCO_2$ are the two main goals of ventilation and these can be easily

monitored noninvasively using pulse oximetry and capnography, without the need of repeated arterial punctures, which are reserved for those with major cardiac defects and major shunt fractions. Apnea of prematurity is a real threat and must be anticipated and prevented in the immediate postoperative period, though the risk may persist up to 12–24 h. Pneumothorax is a potential cause of sudden deterioration in the clinical condition and must always be kept in mind as timely air aspiration may save the baby.

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