# Neonatal Respiratory System

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## CONTENTS



## EMBRYOLOGY AND SYSTEM DEVELOPMENT

There are five stages in the embryonic development of normal lung growth: embryonic, pseudoglandular, canalicular, terminal sac, and alveolar. As shown in Figure 1, the embryonic stage occurs from conception to week 5, with the major event being the formation of the proximal airways. The lung bud appears and begins to divide, the pulmonary vein develops and extends to join the lung bud, and the trachea develops. In stage 2, the pseudoglandular stage, formation of the conducting airways occurs (weeks 6-16). Cartilage appears and the main bronchi form. Formation of new bronchi is complete and the capillary bed is formed. During the canalicular stage (weeks 17-24), the major feature is formation of acini (gas-exchanging sites). There is an appearance of cuboidal cells, the capillaries invade the terminal air sac walls, type II alveolar cells appear, and the airway changes from glandular to tubular and increases in length and diameter. The alveolar sacs are formed and there is development of gas-exchange sites in

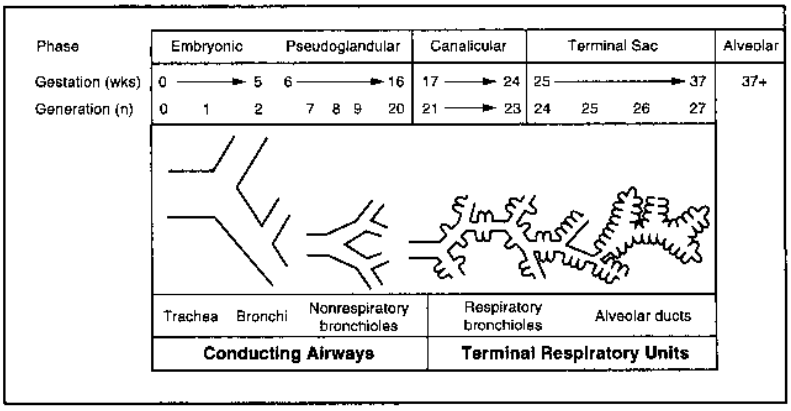


**Figure 1. The five phases of the process of tracheobronchial airway development.** n = number of branches. Reproduced, with permission, from Elliott and Leuthner: Anatomy and development of the lung, in Hansen TN, Cooper TR, Weisman LE (eds): *Contemporary Diagnosis and Management of Neonatal Respiratory Diseases,* ed 2. © 1998, Handbooks in Health Care Co, p 2.

the terminal sac stage (weeks 25-37). In the alveolar, or final, stage (week 37-postnatal), expansion of the surface area occurs. This stage continues up to 8 years after birth.

The surface of the lung is lined by a layer of fluid that creates an air-liquid interface. Surface-tension forces act on air-liquid interfaces, causing a water droplet to bead up. A surface-active compound called surfactant reduces the surface tension and allows the droplet to spread out into a thin layer. In the lungs, the surface-tension forces tend to cause the alveoli to collapse. Surfactant is needed to lower the surface tension within these alveoli to prevent their collapse at the end of expiration. Surfactant is a surface-active agent composed of phospholipids (including lecithin and sphingomyelin), cholesterol, lipids, and proteins and is synthesized in type II alveolar epithelial cells. These cells begin to appear in the lung between 20 and 24 weeks of gestation.

## TRANSITION FROM INTRAUTERINE TO EXTRAUTERINE LIFE

The transition from intrauterine to extrauterine environment and from fetal to postnatal life begins with the clamping of the umbilical cord and the infant's first breath.

In utero, fetal circulation (Figure 2) depends on the placenta and three fetal ducts: the ductus venosus, the foramen ovale, and the ductus arteriosus. The placenta allows for the exchange of gases, nutrients, and metabolic waste products. It is a low-resistance circuit that maintains a low fetal systemic vascular resistance, while the pulmonary fetal circuit maintains a high pulmonary vascular resistance. Subsequently, the increased pulmonary vascular resistance and low systemic vascular resistance promote right-to-left shunting through the fetal ducts. The ductus venosus allows part of the oxygenated blood carried by the umbilical vein to bypass the liver. Oxygenated blood entering the heart flows through the foramen ovale into the left atrium, then perfuses the brain and the heart via the carotid, subclavian, and coronary arteries. The ductus arteriosus directs blood from the main pulmonary artery to the descending aorta. Fetal admixture at the foramen ovale and ductus arteriosus lowers fetal arterial oxygen tension to ~ 25-35 mm Hg. The low fetal oxygen tension helps to maintain pulmonary artery vasoconstriction, allowing blood to bypass the lung and flow instead through the foramen ovale and ductus arteriosus.

In summary, fetal blood flows from the placenta via the umbilical vein, bypasses the liver via the ductus venosus, and enters the inferior vena cava. From the inferior vena cava, blood enters the right atrium, where the majority of it is shunted through the foramen ovale into the left atrium. Blood continues into the left ventricle, where it mixes with blood returning from the pulmonary veins, and is then injected into the ascending aorta. From the ascending aorta, it supplies the carotid, subclavian, and coronary arteries before mixing with blood shunted across

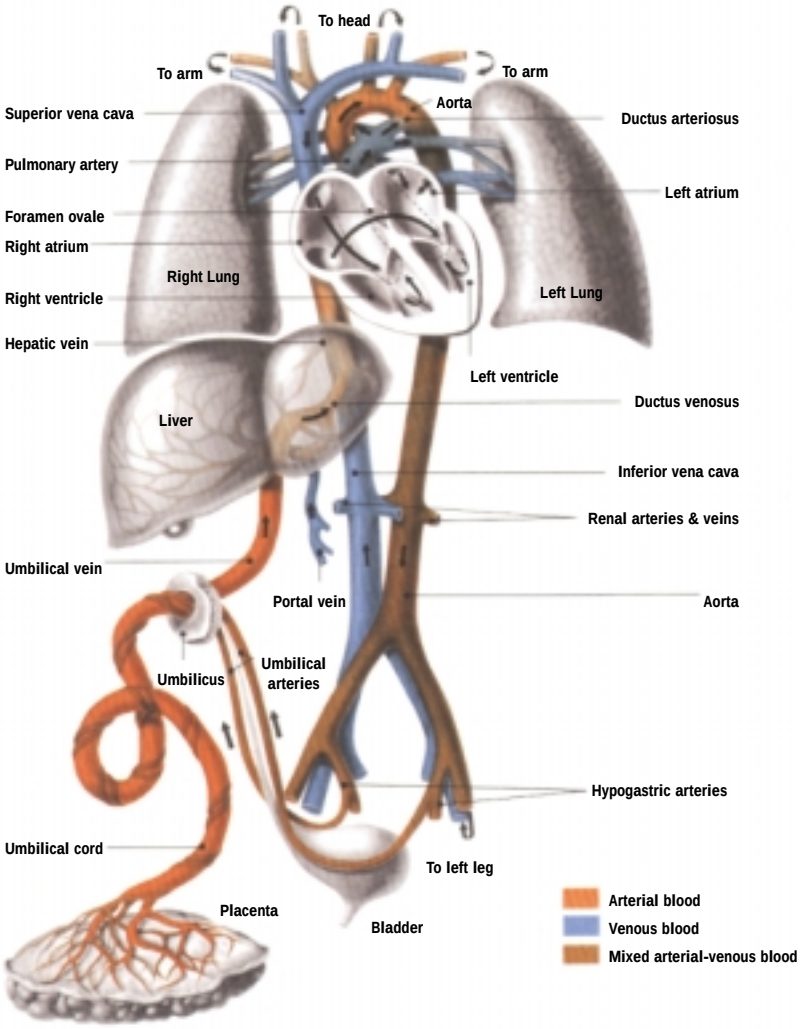


**Figure 2. The fetal circulation.**

the ductus arteriosus. The remainder of the blood entering the right atrium mixes with blood from the superior vena cava and continues into the right ventricle and pulmonary arteries. Most of this blood shunts across the ductus arteriosus into the descending aorta.

Once the infant is delivered and the transition to extrauterine life begins, respiratory and cardiovascular changes occur independently but simultaneously. Fetal lung fluid is replaced by air, so the liquid-liquid interface of alveoli becomes an air-liquid interface and surface tension forces begin. Surfactant decreases the surface tension with the first breath and arterial oxygen tension rises, resulting in reversal of hypoxemia-induced pulmonary vasoconstriction. The pulmonary vascular resistance begins to decline as a result of increasing oxygen saturations and decreasing carbon dioxide levels, resulting in an increase in pulmonary blood flow. Decreasing prostaglandin levels also will facilitate the reversal of the pulmonary vasoconstriction. Removal of the placental circuit by the clamping of the umbilical cord results in increasing systemic vascular resistance. Simultaneous cardiovascular changes include the closing of fetal shunts. The ductus venosus functionally closes as the umbilical cord is clamped. Functional closure of the foramen ovale occurs at birth from the changing atrial pressures and increasing systemic vascular resistance. The left atrial pressure is now greater than the right atrial pressure. With increasing arterial oxygen tension and decreasing levels of prostaglandin E, the ductus arteriosus closes functionally at 15-24 hours of age but does not close anatomically for 3-4 weeks (see Tables 1 and 2).

**Table 1. Summary of Main Transitional Events From Fetal to Neonatal Circulation**

| |
|---|
| Loss of fetal lung fluid |
| Secretion of surfactant |
| Establishment of functional residual capacity |
| Fall in pulmonary vascular resistance |
| Rise in systemic vascular resistance |
| Closing of fetal shunts |
| Increasing pulmonary blood flow |

## RESUSCITATION OF THE INFANT WITH RESPIRATORY DISTRESS

Anticipation is a key component of the successful resuscitation of a distressed newborn. Maternal or fetal conditions that place a newborn at risk for respiratory depression/distress at birth must be recognized. According to the American Academy of Pediatrics (AAP) and the American Heart Association (AHA), “Every newborn has a right to a resuscitation performed at a high level of competence. The proper

**Table 2. Transition From Fetal to Neonatal Circulation***

| | First Period of Reactivity (early reactivity) | Period of Relative Inactivity (deep sleep) | Second Period of Reactivity (secondary reactivity) |
|---|---|---|---|
| **Time Course** | Birth to 30-45 minutes | 45 minutes to 2-4 hours | 3-4 hours thereafter |
| **CNS** | Alert, eyes open; vigorous, active crying; increased tone and highly responsive to stimuli | Somnolent, eyes closed; difficult to arouse or interest; decreased tone and general responsiveness; can be awakened only briefly | Hungry; progresses normally through wake, feed, quiet alert, drowsy, and deep sleep in cyclic fashion |
| **Color** | Ruddy with acrocyanosis | Pale, no cyanosis | Pink, no cyanosis |
| **Heart Rate** | High (140-160 BPM) and very reactive | Low (90-120 BPM) and briefly reactive | Varies with wake/sleep cycle |
| **Respiratory Rate** | High (40-60 BPM), mild retractions, moist rales | Low (20-40 BPM), no retractions, no rales; occasional periodic breathing | Varies with wake/sleep cycle |
| **Blood Pressure** | Should rise slowly but steadily through all stages | | |
| **Bowel Sounds** | Active bowel sounds; belly distended; may pass meconium and urine | Inactive bowel sounds; less distention; belly easily palpated | Active bowel sounds; air swallowing and distention with crying |

*Adapted from Molteni RA: *Neonatal Respiratory Distress* Clinical Education Aid. © 1992 Ross Laboratories, p 3.

equipment must be immediately available at delivery, and healthcare professionals must be skilled in resuscitating a newborn and capable of working smoothly as a team" (Bloom et al, 1994, p O-1).

### Resuscitation Equipment

Resuscitation equipment should be available, ready to use, and functional at all times, and should include:

- Radiant warmer bed (prewarmed)
- Stethoscope
- Bulb syringe
- DeLee suction catheter
- Meconium aspirator
- Wall suction
- Suction catheters (6F, 8F, 10F)
- Resuscitation bag with a manometer
- Laryngoscope with Miller 0 and Miller 1 blades
- Straight blades; extra bulbs and batteries
- Endotracheal tubes (2.5, 3.0, 3.5, 4.0, 4.5 internal diameter mm)
- Stylet
- Tape (to secure endotracheal tube)
- #8 feeding tube; 20-mL syringe
- Face masks (newborn, premature sizes)
- Oxygen source with flowmeter and tubing

Medications recommended in the AAP/AHA Neonatal Resuscitation Program (NRP) and in *NeoFax*® (Young and Mangum, 1997) should also be readily available, including intravenous or umbilical vessel cannulation materials (see Table 3).

### Resuscitation Procedure

Mastery of neonatal resuscitation skills is necessary for performing successful resuscitation. The AAP/AHA NRP is a national program that provides health care professionals with the knowledge and skills to resuscitate newborn infants by using a standardized approach.

The American Academy of Pediatrics and the American Heart Association have developed a new algorithm for resuscitation of the newly born infant. The revised NRP algorithm follows the basics of the previous algorithm, but now includes three levels of post-resuscitation care: routine care, supportive care, and ongoing care. Evaluation continues to be based primarily on respirations, heart rate, and color, and the valuation-decision-action cycle. (See the *Textbook of Neonatal Resuscitation* for algorithm.)

## DIFFERENTIAL DIAGNOSIS

The differential diagnosis for neonatal respiratory distress is very broad (see Tables 4 and 5). The practitioner must carefully review the maternal history, observe the infant's disease course, and assess the results of the physical examination. Laboratory tests and radiologic findings are adjuncts to the differential diagnosis.

**Table 3. Medications for Neonatal Resuscitation***

| Medication | Indication | | Dose | Route | Administration |
|---|---|---|---|---|---|
| **Epinephrine** | HR<60 despite 30 seconds of assisted ventilation & another 30 seconds of coordinated chest compressions and ventilations | 1:10,000 concentration | 0.1-0.3 mL/kg | ETT or IV | Administer as quickly as possible |
| **Volume Expander** | No response to resuscitation Evidence of blood loss | Use normal saline (recommended), ringer's lactate, O-negative blood | 10 mL/kg | IV, umbilical vein | Administer over 5-10 minutes |
| **Sodium Bicarbonate** | Suspected or proven severe metabolic acidosis | 4.2% solution<br><br>(Do not administer if lungs are not adequately ventilated)<br><br>(Do not give per endotracheal tube) | 2 mEq/kg<br><br>(4 mL of 4.2% solution) | IV, umbilical vein | Administer slowly (no greater than 1 mEq/kg/min) |

*Naloxone is not necessary during ACUTE stage of resuscitation, so is no longer discussed under resuscitation medications.
Adapted from Kattwinkel J (ed): *Textbook of Neonatal Resuscitation*, ed 4. © 2000 American Academy of Pediatrics and American Heart Association.

## COMMON NEONATAL RESPIRATORY DISORDERS

### RESPIRATORY DISTRESS SYNDROME (RDS)

Respiratory distress syndrome (RDS) is caused by a primary absence or deficiency of surfactant. Endogenous surfactant prevents increased surface tension, which can lead to alveolar collapse.

#### Incidence (Moïse and Hansen, 1998; Cifuents et al, 1998)

40,000 infants per year
14% of low-birth-weight infants
60% of infants of < 29 weeks' gestational age
Inversely proportional to gestational age

#### Infants at Risk/Predisposing Factors

Premature infants
Male infants
Infants of diabetic mothers—surfactant production can be inhibited due to the infant's hyperinsulinemic state
Perinatal asphyxia—surfactant production can be decreased due to transient fetal distress

#### Pathophysiology

The absence or deficiency of surfactant results in increased alveolar surface tension, leading to alveolar collapse and decreased lung compliance (stiff lungs). With decreased lung compliance, greater and greater negative pressure must be generated to inflate the lung with each succeeding breath. Widespread alveolar collapse, or atelectasis, results in mismatches of ventilation and perfusion (V/Q ratio) and hypoventilation. Collapsed areas of the lung may continue to receive capillary blood flow, but gas exchange does not occur. Intrapulmonary shunting causes further hypoxemia. Hypercarbia also develops, which leads to respiratory acidosis. Hypoxia at the cellular level results in anaerobic metabolism and, subsequently, metabolic acidosis.

**Table 4. Pulmonary Disorders**

| Common | Less Common |
|---|---|
| Respiratory distress syndrome | Pulmonary hypoplasia |
| Transient tachypnea | Upper airway obstruction |
| Meconium aspiration syndrome | Rib-cage abnormalities |
| Pneumonia | Space-occupying lesions |
| Air-leak syndrome | Pulmonary hemorrhage |

With the hypoxemia and resulting acidosis there is increased pulmonary vascular resistance and vasoconstriction, leading to pulmonary hypoperfusion and additional hypoxemia.

#### Clinical Presentation

The usual clinical presentation is seen within 6 hours after birth and includes the following:

| | |
|---|---|
| Nasal flaring | An attempt to decrease airway resistance and take in more oxygen |
| Grunting | An attempt to maintain functional residual capacity |
| Retractions | A reflection of noncompliant or stiff lungs and compliant chest wall |
| Tachypnea | An attempt to maintain minute ventilation and prevent lung collapse |
| Hypoventilation | A result of muscle fatigue |
| Diminished breath sounds | A reflection of decreased air entry |
| Edematous extremities | A result of altered vascular permeability |
| Cyanosis | A result of increasing hypoxemia |

Arterial blood gases demonstrate hypoxemia in room air, hypercarbia, and mixed acidemia. With mild RDS, the chest radiograph shows a ground-glass, reticulogranular appearance (diffuse alveolar atelectasis surrounding open bronchi), air bronchograms (aerated bronchioles), and decreased lung volumes (diffuse atelectasis). With severe RDS, a "whiteout" pattern is seen on the chest film, with little aeration and with the heart border obscured or fuzzy.

**Table 5. Extrapulmonary Disorders**

| Vascular | Metabolic | Neuromuscular |
|---|---|---|
| Persistent pulmonary hypertension | Acidosis | Cerebral edema or hemorrhage |
| Congenital heart disease | Hypoglycemia | Drugs |
| Hypovolemia, anemia | Hypothermia | Muscle disorders |
| Polycythemia | | Spinal cord problems |
| | | Phrenic nerve damage |

## HISTORY AND RESPIRATORY SYSTEM ASSESSMENT

| Table 6. History | |
|---|---|
| **Mother** | Prenatal history and care<br>Family illnesses<br>Age<br>Pregnancy-related complications<br>Medications<br>Substance abuse<br>Gravida, para, abortions, living children<br>Blood type, antibody screening |
| **Intrapartum** | Intrapartal complications<br>Time of rupture of membranes (spontaneous or artificial)<br>Description of amniotic fluid (clear, foul-smelling, meconium-stained)<br>Onset and duration of labor (spontaneous or induced)<br>Medications<br>Evidence of fetal distress<br>Method of delivery:<br>Vaginal (especially forceps, vacuum extraction)<br>Cesarean |
| **Infant** | Apgar scores<br>Resuscitative interventions<br>Gestational-age examination<br>General physical examination |

| Table 7. Respiratory System Assessment | |
|---|---|
| **Color** | |
| Pink | Reddish-pink hue of skin, nailbeds, and mucous membranes |
| Cyanosis | Blue discoloration of skin, nailbeds, and mucous membranes |
| Acrocyanosis | Peripheral cyanosis of hands and feet |
| Plethora | Ruddy color |
| Pallor | Pale, white skin |
| **Type of Breathing** | |
| Apnea | Cessation of breathing for > 20 seconds, usually with color changes and bradycardia |
| Periodic respirations | Intermittent cessation of respiration; usually pauses between breaths < 15 seconds |
| Dyspnea | Labored or difficult breathing |
| Bradypnea | Abnormally slow respiratory pattern; 20-30 BPM of slower, deeper respirations |
| Tachypnea | Respiratory rate > 60 BPM |
| **Respiratory Effort** | |
| Chest movement | Depth of respiration, symmetry, synchrony |
| Paradoxical respiratory effort | Inward pull of lower thorax and bulging of abdomen with each breath |
| Retractions | Inward pull of chest wall on inspiration |

(continued)

| Table 7. Respiratory System Assessment (continued) | |
|---|---|
| **Other Respiratory Findings** | |
| Expiratory grunt | Audible, forced expiration through a partially closed glottis<br>Delays expiration and increases gas exchange by increasing end-expiratory pressure |
| Nasal flaring | Increased size of nares with respiration to decrease airway resistance |
| Stridor | High-pitched crowing sound caused by narrowing of glottis or trachea |
| Wheeze | High-pitched, continuous lung sounds similar to dry whistling sound produced by air passing through a narrowed lumen |
| **Chest Shape/Symmetry** | |
| Barrel-shaped chest | Suggests increased chest volume<br>eg, transient tachypnea of the newborn, meconium aspiration syndrome, persistent pulmonary hypertension |
| Bell-shaped chest | Suggests decreased chest volume<br>eg, respiratory distress syndrome, pulmonary hypoplasia |
| Chest wall asymmetry | Results from volume differences between two sides of thoracic cavity<br>eg, atelectasis, pneumothorax, unilateral pulmonary emphysema, cystic lung disease |
| **Auscultation of Breath Sounds** | |
| Assess air movement and quality of breath sounds: | |
| Normal breath sounds | Bronchovesicular (expiration equals inspiration) |
| Adventitious breath sounds | Rales<br>Rhonchi<br>Wheeze<br>Pleural friction rub |

The clinical course of RDS is variable but self-limiting. There is progressive worsening over the first 2 to 3 days, as evidenced by increasing oxygen requirements and poor lung performance. Postnatal surfactant production begins at ~ 48-72 hours of age and results in improved lung compliance and decreasing respiratory distress. This recovery phase is usually preceded by a period of spontaneous diuresis.

### Management

Management begins with preventive measures. Administration of antenatal steroids results in accelerated maturity of the fetal lungs. The incidence and severity of RDS are decreased in infants whose mothers received corticosteroids 24-48 hours before delivery. Corticosteroids are most effective when infants are less than 34 weeks' gestational age and the drug is administered for at least 24 hours but no longer than 7 days before delivery. There appears to be an additive effect in the improvement of lung function with the combined use of antenatal steroids and postnatal surfactant.

The goals of treating RDS are to prevent alveolar collapse, optimize tissue oxygenation and carbon dioxide elimination, minimize oxygen consumption, and provide supportive care. Administration of oxygen, continuous positive airway pressure, and positive-pressure ventilation may be needed to provide adequate tissue oxygenation, relieve hypoxic vasoconstriction, and reduce right-to-left shunting. Arterial blood gases, pulse oximetry, and transcutaneous oxygen monitors provide information needed to maintain the arterial oxygen tension within an acceptable range. Positive end-expiratory pressure, provided by either nasal prongs or tracheal intubation, can be used to prevent atelectasis by maintaining alveolar distention throughout the respiratory cycle. Sedatives and analgesics may be given if the infant's respiratory efforts interfere with effective positive-pressure ventilation (see Table 8). Supportive care includes maintaining a neutral thermal environment, hydration, and circulatory support; antibiotics; and standard neonatal care.

Other treatments for RDS include surfactant replacement therapy, high-frequency ventilation, and patient-triggered ventilation.

Surfactant replacement therapy has become a standard treatment. It improves oxygenation and stabilizes alveoli with a resultant reduction in the severity of RDS. Commercial preparations used in surfactant replacement therapy are usually given as a liquid bolus into the endotracheal tube, with the dose divided into aliquots and administered with the infant in different positions.

High-frequency ventilation, including high-frequency oscillation and high-frequency jet ventilation, appears to produce adequate gas exchange at lower peak airway pressures while potentially reducing barotrauma and the development of chronic lung disease. It uses small tidal volumes at near or less than anatomic dead space at rapid rates.

Synchronized intermittent mandatory ventilation and assist/control mode ventilation are referred to as patient-triggered ventilation. Synchronized intermittent mandatory ventilation uses airway flow, airway pressure, changes in chest wall impedance, or abdominal movements to detect the onset of inspiratory efforts. Spontaneous breaths trigger the ventilator to maintain the rate. During episodes of apnea, controlled breaths occur at the preset rate. In the assist/control mode, a spontaneous breath triggers a mechanical breath. This mode also delivers controlled breaths at the preset rate during apnea. Patient-triggered ventilation has been shown to improve gas exchange and reduce asynchrony between infant-generated and ventilator-generated breaths.

### Prognosis (Moïse and Hansen, 1998; Bhutani, 1996)

Most infants with RDS recover without further problems, usually within 3 to 5 days. With severe RDS, the requirement for assisted ventilation, the development of complications such as air leaks, patent ductus arteriosus, or the beginnings of bronchopulmonary dysplasia may delay recovery for days, weeks, or even months. Mortality is inversely proportional to gestational age. The incidence of chronic lung disease is < 10% in infants with a birth weight > 1000 g to ~ 50% in infants with a birth weight < 1000 g.

## TRANSIENT TACHYPNEA OF THE NEWBORN (TTNB)

The most commonly cited cause of transient tachypnea of the newborn (TTNB) is delayed absorption of fetal lung fluid.

### Infants at Risk/Predisposing Factors

Term or near-term infants
Precipitous delivery
Cesarean delivery, especially in the absence of labor

### Pathophysiology

In utero, the fetal lungs are filled with fluid. During normal vaginal delivery, the fluid is usually forced out by the thoracic squeeze. The remainder of the fluid in the lungs is cleared by the pulmonary veins and lymphatic system. With a precipitous or cesarean delivery, absence of the gradual chest compression that occurs during normal vaginal birth causes fluid to be retained. Accumulation of this interstitial fluid interferes with forces that tend to keep the bronchioles open and eventually causes the bronchioles to collapse (air trapping). Air trapping and hyperinflation can increase pulmonary vascular resistance and lead to potential persistent pulmonary hypertension.

### Clinical Presentation
The clinical presentation can be difficult to distinguish from that of other neonatal disorders such as bacterial pneumonia, sepsis, and RDS. The onset of symptoms is usually 0.5-6 hours after birth; respiratory rates up to 120-140 BPM are the most common symptom. Grunting, nasal flaring, and retractions may occur with varying severity. Arterial blood gases reveal hypoxemia in room air, mild hypercarbia, and mild to moderate acidosis. Chest radiographs show hyperinflation (from air trapping) and streaky infiltrates (interstitial fluid along the bronchovascular space) from the hilum.

### Management
Treatment of TTNB consists of supplemental oxygen (usually < 40% fractional inspiratory oxygen [$FiO_2$]), pulse oximetry and/or transcutaneous monitoring, antibiotics (if infection is suspected), a neutral thermal environment, and general supportive neonatal care. Oral feedings should be delayed to prevent aspiration from high respiratory rates.

### Prognosis
Although TTNB is self-limiting and usually clears within 1 to 3 days, it is a diagnosis of exclusion made after the infant has recovered. Infants generally recover completely without any residual respiratory problems.

## MECONIUM ASPIRATION SYNDROME (MAS)

Meconium aspiration syndrome (MAS) is the most common aspiration syndrome causing respiratory distress in newborns. Meconium-stained fluid is present in 9% to 20% of all deliveries, but not all meconium-stained infants develop MAS.

### Incidence (Orlando, 1997)
~ 520,000 infants per year are meconium-stained
~ 26,000 infants per year develop MAS
~ 1,000 infants per year die from MAS

### Infants at Risk/Predisposing Factors
Term, postterm infants
Term or postterm small-for-gestational age infants
Any event causing fetal distress, such as:
- Reduced placental or uterine blood flow
- Maternal hypoxia and/or anemia
- Placental or umbilical cord accidents

### Pathophysiology
Meconium is normally retained in the fetal gut until postnatal life, but passage of meconium occurs in response to fetal distress (hypoxic bowel stimulation). The rectal sphincter tone or muscle may relax after vagal reflex stimulation and release meconium into the amniotic fluid. The fetus begins gasping in response to asphyxia and may inhale meconium into the airway. With the infant's first breath, meconium can be aspirated into the lungs. This aspirated thick meconium can result in:
- Partial airway obstruction (a ball-valve obstruction), leading to air trapping and overdistention of the airways, with alveolar rupture and air leaks
- Complete airway obstruction, leading to small airway atelectasis
- Inflammatory response of the tracheobronchial epithelium to meconium, leading to chemical pneumonitis
- Possible surfactant displacement or inactivation of endogenous surfactant

Uneven pulmonary ventilation with hyperinflation of some areas and atelectasis of others leads to ventilation-perfusion mismatches and, subsequently, hypercarbia and hypoxemia. Hypoxemia may worsen pulmonary vasoconstriction, resulting in further hypoxemia and acidemia, and set up a vicious cycle.

### Clinical Presentation
Usually infants with MAS have a history of fetal distress and meconium-stained fluid. Respiratory distress can range from mild to severe, with varying degrees of cyanosis, tachypnea, retractions, grunting, nasal flaring, and coarse rales and rhonchi. The chest appears barrel-shaped (increased anteroposterior diameter) from gas trapping. Arterial blood gases may reflect varying degrees of hypoxemia, hypercarbia, and acidosis. The chest radiograph shows coarse, patchy areas of decreased aeration (atelectasis) and areas of hyperaeration (air trapping). Later, chemical pneumonitis can become apparent on the chest film.

### Management
Treatment of infants at risk for MAS begins with preventive management. Infusion of saline into the amniotic sac (amnioinfusion) has been used to dilute the meconium and correct the oligohydramnios often associated with meconium-stained amniotic fluid. Amnioinfusion may also decrease the risk of cord compression and acidemia, which could stimulate passage of meconium. Another preventive intervention, nasopharyngeal and oral suctioning, should be instituted as soon as the head is delivered and before the thorax is delivered. After delivery, a person skilled in neonatal resuscitation and intubation should provide direct tracheal suctioning before the infant begins breathing. This is usually necessary if the meconium is thick or particulate, and the infant is depressed.

Additional treatment is required for infants who develop MAS. Because meconium in the alveoli can injure type II alveolar epithelial cells and interfere

with endogenous surfactant production, surfactant replacement therapy may improve oxygenation. Respiratory status should be constantly monitored with pulse oximetry or transcutaneous monitoring, frequent blood gases, and clinical assessment to determine the need for oxygen and positive-pressure ventilation. Supportive care includes but is not limited to broad-spectrum antibiotics for suspected infection, correction of metabolic abnormalities, maintenance of fluid balance, a neutral thermal environment, and minimal stimulation. Sedatives and analgesics may be given if the infant's respiratory efforts interfere with effective positive-pressure ventilation (see Table 8). Potential complications

**Table 8. Sedatives, Analgesics, and Muscle Relaxants for Neonates**

| | **Dose** (Young and Mangum, 1997) | **Side Effects** (Alexander and Todres, 1998; Young and Mangum, 1997) |
|---|---|---|
| **Sedatives** | | |
| Lorazepan | 0.05-0.1 mg/kg/dose<br>IV slow push | Respiratory depression<br>Hypotension |
| Midazolam | 0.05-0.15 mg/kg/dose over at least 5 minutes<br>IV, IM<br>Continuous IV infusion: 0.01-0.06 mg/kg/hour | Respiratory depression<br>Hypotension<br>Seizure, seizurelike activity following rapid bolus administration |
| Chloral hydrate | 25-75 mg/kg/dose<br>PO or PR<br>Dilute oral preparation or give after a feeding | CNS, respiratory, myocardial depression<br>Ileus and bladder atony<br>Direct hyperbilirubinemia<br>Cardiac arrhythmias<br>Do not use in patients with significant liver or kidney disease |
| **Analgesics** | | |
| Morphine | 0.05-0.2 mg/kg/dose<br>IV, IM, SQ<br><br>Continuous IV infusion:<br>Loading dose first—<br>100 mcg/kg over 1 hour followed by<br>10-15 mcg/kg/hour | Respiratory depression<br>Hypotension<br>Urine retention<br>Decreased gut motility<br>Tolerance and withdrawal<br>(prolonged administration)<br>(weaning regimen needed)<br>Reversed with naloxone |
| Fentanyl | 1-4 mcg/kg/dose IV<br><br>Continuous IV infusion:<br>1-5 mcg/kg/hour | Fewer respiratory and cardiovascular effects than with morphine<br><br>With large, rapid boluses:<br>Muscle rigidity<br>Seizure activity<br>Hypotension<br>Bradycardia<br>Tolerance and significant withdrawal with continuous infusion ≥ 5 days (weaning regimen needed)<br>Reversed with naloxone |
| **Muscle Relaxants** | | |
| Pancuronium bromide | 0.1 mg/kg/dose IV<br>(0.04-0.15 mg/kg/dose), as needed for paralysis<br>Usual dosing interval: 1-2 hours<br>Continuous IV infusion: 0.05-0.2 mg/kg/hour | Tachycardia<br>Hypotension<br>Peripheral edema<br>Increased salivation<br>Reversed with atropine or glycopyrrolate followed by neostigmine |
| Vecuronium bromide | 0.1 mg/kg/dose IV<br>(0.03-0.15 mg/kg/hour), as needed for paralysis<br>Usual dosing interval: 1-2 hours | Few cardiovascular effects |

IV = intravenously, IM = intramuscularly, PO = orally, PR = rectally, SQ = subcutaneously

associated with MAS include air-leak syndrome, chemical pneumonitis, persistent pulmonary hypertension, and end-organ damage.

Other treatment interventions for MAS depend on the disease progression and may include high-frequency ventilation (discussed in RDS section), nitric oxide, and extracorporeal membrane oxygenation (ECMO).

Nitric oxide, a potent pulmonary vasculature dilator, appears to be an effective adjunct therapy for persistent pulmonary hypertension and may reduce the need for ECMO. Inhaled nitric oxide can selectively lower pulmonary artery pressure and improve oxygenation without causing adverse effects on cardiac performance or systemic blood pressure. It enhances gas exchange by improving ventilation-perfusion mismatching and decreasing intrapulmonary shunting. But nitric oxide is not without problems. Progressive atelectasis and decreased cardiac performance can limit its effectiveness. Potential toxicities include both methemoglobinemia and direct lung injury from nitric dioxide. Therefore, nitric oxide administration is still considered experimental and is reserved for extremely sick newborns.

ECMO is a process of prolonged cardiopulmonary bypass that provides cardiorespiratory support until the lungs recover. It is used with infants who have reversible lung disease and who have not responded to maximal medical therapy. ECMO is often used to treat infants with predictably fatal pulmonary failure from diseases such as MAS and infants with a birth weight > 2 kg with RDS, pneumonia and sepsis, and persistent pulmonary hypertension. ECMO can be performed by either venoarterial or venovenous techniques. It has significant complications, so selection criteria must be established to determine candidates who would die if conventional therapies were used.

### Prognosis (Orlando, 1997)

Meconium aspiration syndrome is usually resolved by 1 week of life for infants who do not require assisted ventilation, but may persist in infants requiring prolonged assisted ventilation. The outcome depends on the severity of the asphyxial insult and the extent of lung damage caused by the disease and its potential complications.

## PNEUMONIA

Neonatal pneumonia can be caused by bacterial, viral, protozoan, fungal, or other pathogens such as *Treponema pallidum* or *Chlamydia trachomatis*. It can occur as a primary infection or as part of a generalized infection.

### Incidence (Carey and Trotter, 1997)

1% of term neonates
10% of preterm neonates

### Infants at Risk/Predisposing Factors

Premature infants
Prolonged rupture of membranes > 24 hours
Excessive intrapartum manipulation
Maternal fever
Maternal viral, bacterial, or other infection
Prolonged labor
Maternal urinary tract infection
Amnionitis
Immature immune system

### Pathophysiology

Transmission occurs transplacentally, intrapartally, or postnatally. Pathologic organisms include but are not limited to those listed in Table 9. Transplacental pneumonia can develop from aspiration or ingestion of infected amniotic fluid or from transmission of organisms from an infected mother across the placenta to the fetus. Intrapartum pneumonia results from colonization of the infant by ascension of the organism after rupture of the membranes or by the infant's passage through the birth canal. Postnatal pneumonia usually develops from hospital-acquired or nosocomial sources such as unwashed hands and open skin lesions, as well as contaminated equipment, nutritional products, or blood products.

### Clinical Presentation

A high index of suspicion of pneumonia is the key to early diagnosis. The clinical presentation is often nonspecific and includes temperature instability, apnea, tachycardia, tachypnea, grunting, nasal flaring, retractions, lethargy, poor peripheral perfusion, and poor feeding. Skin lesions may be found in infants with congenital pneumonia caused by herpes simplex virus, *Candida* sp, or *T pallidum*.

**Table 9. Pneumonia: Pathologic Organisms**

| Transplacental | Intrapartum | Postnatal Nosocomial |
|---|---|---|
| Cytomegalovirus | Herpes simplex virus | *Staphylococcus aureus* |
| Rubella | *C trachomatis* | *Staph epidermidis* |
| *T pallidum* | Group B streptococci | Herpes simplex virus |
| *Toxoplasma gondii* | *Escherichia coli* | *Candida* sp |
| Varicella | *Klebsiella* sp | Cytomegalovirus |
| Enterovirus | | Group B streptococci |
| *Listeria monocytogenes* | | Enteroviruses |
| | | Respiratory syncytial virus |

A shocklike syndrome is often seen in the first 7 days of life with early-onset group B β-hemolytic streptococcus (GBS) sepsis. Bacterial and viral cultures, rapid viral screening tests, and antigen tests (latex agglutination, counterimmunoelectrophoresis) should be performed on infants with suspected pneumonia. A Gram's stain of tracheal aspirate may be useful if done during the first 8 hours of life, but it may not differentiate overt pulmonary infection from early colonization. A complete blood count with differential and platelets is a useful adjunct diagnostic test. The chest radiograph may show patchy opacifications, unilateral or bilateral alveolar infiltrates, pleural effusions, and/or changes in lung volume. GBS pneumonia is difficult to differentiate from RDS on a chest radiograph.

### Management

For an infant with suspected bacterial pneumonia, broad-spectrum antibiotics, such as ampicillin and an aminoglycoside, should be started immediately and adjusted, if necessary, once the organism has been identified. Some viral pneumonias can be treated with pharmacologic agents such as acyclovir or vidarabine for herpes simplex virus and ribavirin for respiratory syncytial virus (RSV). Supportive treatment is needed for respiratory problems, hematologic instability, and acid-base imbalance. Oxygen and positive-pressure ventilation may be required in addition to volume expanders, blood products, and vasopressors if the infant is in shock. With continued deterioration, the infant may require newer treatment options, including granulocyte transfusion, intravenous immunoglobulins, colony-stimulating factors, high-frequency ventilation, inhaled nitric oxide, and extracorporeal membrane oxygenation.

### Prognosis (Speer and Weisman, 1998)

Overall mortality from sepsis, both related and unrelated to pneumonia, ranges from 5% to 10% in term infants and is as high as 67% in infants with a birth weight < 1500 g.

## PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN)

Persistent pulmonary hypertension of the newborn (PPHN) has been described as the persistence of the cardiopulmonary pathway seen in the fetus, but without the passage of blood through the placenta. It is characterized by high resistance in the pulmonary arteries, which produces an obstruction of blood flow through the lungs and right-to-left shunting through the ductus arteriosus and/or foramen ovale. PPHN may be idiopathic or secondary to another disorder such as MAS or sepsis.

### Incidence (Walsh and Stork, 2001)

0.43 to 6.82 per 1,000 live births

### Infants at Risk/Predisposing Factors

Near-term, term, or postterm infants

Maladaptation of the pulmonary vascular bed—functional pulmonary vasoconstriction with normal structural development and anatomy (eg, MAS, cold stress, asphyxia, sepsis)

Maldevelopment of the pulmonary vascular bed—abnormal pulmonary vascular structure resulting in excessive muscularization (eg, fetal ductal closure, congenital heart disease)

Underdevelopment of the pulmonary vascular bed—decreased cross-sectional area of pulmonary vascular bed secondary to hypoplasia (eg, Potter's syndrome, diaphragmatic hernia)

### Pathophysiology

The neonatal pulmonary vasculature is sensitive to changes in arterial oxygen tension ($PaO_2$) and pH. With hypoxemia and acidemia, the pulmonary vasculature constricts, resulting in increased pulmonary vascular resistance. High pulmonary vascular resistance promotes blood flow away from the lungs through the ductus arteriosus into the systemic system and results in right-to-left shunting. It also maintains higher right-sided pressures in the heart. When right atrial pressure is greater than left atrial pressure and pulmonary artery pressure is greater than systemic pressure, blood flow follows the path of least resistance through the foramen ovale and ductus arteriosus, again bypassing the lungs. This promotion of right-to-left shunting results in hypoxemia due to venous admixture. The cycle repeats as hypoxemia increases pulmonary vascular resistance, resulting in further intrapulmonary shunting, hypoxemia, and pulmonary vasoconstriction.

### Clinical Presentation

Clinical presentation is variable due to the different etiologies of PPHN. Respiratory distress and cyanosis worsen despite high concentrations of inspired oxygen. Arterial blood gases demonstrate severe hypoxemia, normal or mildly elevated arterial carbon dioxide tension ($PaCO_2$), and metabolic acidosis. There is no classic chest radiograph finding for PPHN; rather, the x-ray reflects the underlying lung disease. It may show a prominent main pulmonary artery segment, mild to moderate cardiomegaly, and variable prominence of the pulmonary vasculature (normal or decreased vascular markings).

The diagnostic work-up for PPHN may include a hyperoxia/hyperventilation test and/or preductal and postductal $PaO_2$ tests. With the hyperoxia/hyperventilation test, the infant is placed in 100% $FiO_2$ and hyperventilated at rates > 100 BPM. An increase in $PaO_2$ from < 50 mm Hg before the test to > 100 mm Hg after the test is indicative of PPHN. Preductal and postductal blood is sampled to demonstrate a right-to-left shunt through the ductal arteriosus. Blood is drawn simultaneously from a preductal site (right radial or either temporal artery) and a postductal site (umbilical, femoral, or posterior tibial artery). In the hypoxemic infant, ductal shunting is demonstrated with a $PaO_2$ difference > 15 to 20 mm Hg between the preductal and postductal sites. Pulse oximetry also demonstrates an arterial oxygen percent saturation ($SaO_2$) difference between the right arm and the rest of the body and supports the diagnosis of PPHN. Diagnosis of PPHN can be made by demonstration of a shunt by two-dimensional echocardiogram.

### Management

The goal of treatment is to correct hypoxemia and acidosis and promote pulmonary vascular dilation. Treatment consists of positive-pressure ventilation, pharmacologic support, supportive care, and perhaps the use of high-frequency ventilation, nitric oxide, and ECMO. Alkalosis, with either mechanical ventilation or a bicarbonate infusion, produces pulmonary vasodilation. This subsequently decreases pulmonary vascular resistance and improves pulmonary perfusion and oxygenation. This approach is not without risks, as mechanical hyperventilation can impede venous blood return and reduce cardiac output, which further reduces oxygenation. Induced hypocarbia can also diminish cerebral blood flow. Also, alkali infusion increases carbon dioxide production, which may lead to use of increased ventilator settings.

A more conservative approach attempts to minimize barotrauma while maintaining $PaO_2$ between 50 and 70 mm Hg and $PaCO_2$ between 40 and 60 mm Hg. The appropriate peak inspiratory pressure for either ventilatory approach is then determined by the infant's chest excursion.

Nitric oxide or ECMO may be needed if an infant does not respond to maximal medical treatment (see section describing ECMO and nitric oxide).

Pharmacologic management includes a variety of agents. Vasopressors, which increase systemic vascular resistance, and volume expanders can be used to keep the systemic pressure normal or above normal in an attempt to reduce the pulmonary and systemic pressure gradient, thereby decreasing right-to-left shunting. Tolazoline, a vasodilator, dilates the pulmonary arteries, which results in decreased pulmonary vascular resistance. Because of its serious side effects, such as significant hypotension, gastrointestinal bleeding, thrombocytopenia, and renal dysfunction, tolazoline should be used with caution. Sedatives, analgesics, and muscle relaxants are used when the infant's respiratory efforts interfere with positive-pressure ventilation (see Table 8). Supportive care includes continuous monitoring of arterial blood pressure, pulse oximetry, maintenance of fluid and electrolyte balance, and provision of a neutral thermal environment, hematologic support, and minimal stimulation.

### Prognosis (Wearden and Hansen, 1998)

The prognosis varies according to disease etiology and severity. Improvement should be seen after 3 to 5 days.

## AIR-LEAK SYNDROME

Air leaks develop from alveolar rupture and the escape of air into tissue in which air is not normally present (pleura, mediastinum, pericardium, or extrathoracic areas).

### Incidence (Miller et al, 1997)

The incidence of air-leak syndrome varies with the underlying lung disease as well as with resuscitation and ventilation methods:
5% to 20% incidence in infants with RDS, with and without the use of assisted ventilation
20% to 50% incidence in term infants with MAS

### Infants at Risk/Predisposing Factors

Infants with hypoplastic lungs, RDS, MAS, or congenital malformations
Infants who require ventilatory assistance or vigorous resuscitative efforts
Infants who have undergone thoracic surgery

### Pathophysiology

Air leaks develop from abnormal distribution of gas and subsequent alveolar overdistention and rupture. Air ruptures out of the alveoli and moves along the pulmonary blood vessels or peribronchial tissues. The escaping air flows toward the point of least resistance. The location of the air leak determines which air-leak syndrome develops:

| | |
|---|---|
| Pulmonary interstitial emphysema (PIE) | Air that is trapped in interstitial space |
| Pneumomediastinum | Air that has traveled along the pulmonary blood vessels and entered the mediastinum |
| Pneumothorax | Air that has escaped directly into the pleural space |
| Tension pneumothorax | Free pleural air that compresses the lung |
| Pneumopericardium | Air that has entered the space between the heart and the pericardial sac |
| Pneumoperitoneum | Air that has traveled downward into the abdominal cavity and entered the peritoneal space via the postmediastinal openings in the diaphragm |
| Air embolism | Thought to arise when air ruptures out of alveoli into small pulmonary veins |

### Clinical Presentation and Management

The clinical presentation of air-leak syndrome is outlined in Table 10.

Transillumination provides a preliminary diagnosis for pneumothorax. It works by placing a high-intensity, fiber optic light source over the chest wall and comparing the ring of the light bilaterally. Normal lung and pleura are dense, so light is absorbed. The presence of air pockets produces light around the fiber optic light. However, negative transillumination does not rule out pneumothorax. The *definitive* diagnosis for air leaks is a chest radiograph, either an anteroposterior (A-P) view or an A-P and a lateral view. The chest radiograph will identify the location and extent of air outside the tracheobronchial tree.

A nitrogen washout can be used to treat pneumomediastinum or nontension pneumothorax. The infant is placed in 100% oxygen for 6 to 12 hours to establish a diffusion gradient between the pleural air and the pleural capillaries so that air is more rapidly absorbed by the capillaries. Nitrogen washout is not recommended for preterm infants because of the relationship between high oxygen concentrations in the blood and retinopathy of prematurity. Tension pneumothoraces require emergency treatment. Needle aspiration can be used to remove air quickly and the catheter can be left in place until a chest tube is inserted. A chest (thoracostomy) tube and chest drainage system will restore negative pressure and expand the lung. Local anesthesia with 1% xylocaine and an analgesic should be given for pain relief.

## CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

A congenital diaphragmatic hernia (CDH) is the herniation of the abdominal contents into the chest through a defect in the diaphragm. Ninety percent of these hernias occur on the left side and in the posterolateral portion of the diaphragm.

### Incidence

(Guillory and Cooper, 1998; Cifuents et al, 1998)

1:2000 to 1:5000 live births
Occurs more often in males than in females

### Infants at Risk/Predisposing Factors

None

### Pathophysiology

Closure of the diaphragm occurs at 8 to 10 weeks' gestational age. If closure is delayed, the bowel can move into the thoracic cavity and result in a diaphragmatic hernia. The stomach as well as the small and large bowel, spleen, and liver can also herniate into the chest. The presence of the abdominal contents in the thorax does more than just cause lung hypoplasia by compression. Decreased numbers of bronchial generations and alveoli are seen, and the pulmonary artery is small. Increased muscularization of the pulmonary arteries is also present. Both the bronchial and vascular changes restrict pulmonary blood flow, which can result in persistent pulmonary hypertension.

### Clinical Presentation

A history of polyhydramnios is frequently associated with CDH, because the thoracic location of the intestine interferes with the intrauterine flow of amniotic fluid. Severity of signs and symptoms and age at onset depend on the extent of lung hypoplasia and the degree of interference with ventilation. Clinical presentation includes a scaphoid abdomen, barrel-shaped chest, cyanosis, dyspnea, retractions, shifted heart sounds, and decreased or absent breath sounds on the affected side. Chest and abdominal radiographs show loops of bowel in the chest (although these may not be evident until the infant has swallowed adequate air), sparse or absent abdominal bowel gas, a mediastinal shift, and a markedly elevated or indistinct diaphragm.

**Table 10. Air-Leak Syndrome: Types, Symptoms, Diagnoses, Management**

| Air Leak | Clinical Presentation | Chest Radiograph Findings | General Management |
|---|---|---|---|
| Pulmonary interstitial emphysema | Increased oxygen requirements<br>$CO_2$ retention<br>Increased noncompliant lung | Small dark bubbles of air outside the tracheobronchial tree but trapped within the lung tissue | Positive-pressure ventilation<br>High-frequency ventilation<br>Optional: selective main stem bronchus intubation |
| Pneumomediastinum | Generally asymptomatic<br>Tachypnea<br>Bulging sternum | "Spinnaker sail sign": thymus gland lifted by the mediastinal air<br>"Angel wing sign": both lobes of thymus lifted | Usually none required |
| Pneumothorax | If symptomatic, see:<br>• Tachypnea<br>• Grunting<br>• Retractions<br>• Cyanosis | May not show any changes, or may show air in pleural space outlining the visceral pleura | Usually no specific management<br>Optional: nitrogen washout |
| Tension pneumothorax | Tachypnea<br>Grunting/retractions<br>Cyanosis<br>Hypotension<br>Decreased breath sounds<br>Chest asymmetry<br>Shift in point of maximal impulse<br>Distended abdomen | Pocket of air impinging on the lung<br>Mediastinal shift may/may not be evident | Needle aspiration<br>Chest tube placement |
| Pneumopericardium | Distant/absent heart sounds<br>Bradycardia<br>Diminished/absent pulses<br>Marked hypotension<br>Cyanosis and/or pallor<br>Reduced EKG voltage | Dark circle surrounding the heart<br>Decreased heart size | Needle aspiration<br>Optional: pericardial tube placement |
| Pneumoperitoneum | Distended abdomen<br>Pulmonary function may be compromised | Dark layer over the abdomen<br>Blurring or obscuring of normal bowel pattern | Usually none required<br>Optional: insertion of soft catheter into the peritoneum |
| Air embolism | Catastrophic<br>Sudden cyanosis<br>Circulatory collapse<br>Air-blood mixture crackles and pops with each heartbeat<br>Air-blood mixture aspirated from the umbilical artery catheter | Bizarre picture of intracardiac and intravascular air | No effective treatment |

## Management

Immediate recognition of the defect in the delivery room is a key component in management of an infant with a congenital diaphragmatic hernia. Bag-and-mask ventilation should be avoided to prevent the accumulation of air in the stomach and bowel, which will compromise respiratory expansion and worsen respiratory function. Instead, immediate intubation and ventilation, using the lowest possible pressure, should be instituted. A large double-lumen orogastric tube placed to low, intermittent suction prevents stomach and bowel distention. Other interventions include establishing intravenous access and providing a neutral thermal environment. Elevating the head of the bed and positioning the infant so that the affected side is down allows for maximal expansion of the unaffected lung. Sedatives, analgesics, and muscle relaxants are used for pain relief and asynchrony of infant- and ventilator-generated breaths (see Table 8). The definitive treatment is surgical correction of the hernia. The development of pulmonary hypertension is frequently seen postoperatively (see section on management of pulmonary hypertension).

### Prognosis (Miller et al, 1997)

Infants with CDH continue to have a high mortality rate (from 20% to 60%). Pulmonary hypoperfusion on the affected side may persist for years as the number of bronchi and alveoli remains reduced and increased muscularization of the pulmonary blood vessels continues. For survivors, gastro-esophageal reflux can be a long-term problem after surgical repair.

## APNEA OF PREMATURITY

Apnea is a cessation of respiration lasting 15 to 20 seconds and associated with bradycardia and/or color changes. It can be obstructive, central, or mixed. With obstructive apnea, respiratory efforts are observed, but there is blocked air flow from collapse of the upper airway. Central apnea involves the cessation of both respiratory efforts and air flow, with no airway obstruction. The most common classification in preterm infants is mixed apnea, which involves a pause in respiratory effort preceded or followed by airway obstruction at the upper airway level.

### Incidence (Adams, 1998)

~ 25% incidence in preterm infants
75% incidence in infants with a birth weight < 1000 g

### Infants at Risk/Predisposing Factors

Premature infants
Contributing factors shown in Table 11

| Table 11. Factors Contributing to Apnea |
|---|
| Sepsis |
| Intracranial hemorrhage |
| Prostaglandin E infusion |
| Gastroesophageal reflux |
| Poor thermoregulation |
| Antepartum narcotics or general anesthesia |
| Metabolic disorders |
| Anatomic abnormalities |
| Anemia of prematurity |
| Seizure activity |
| Electrolyte abnormalities |

### Pathophysiology

Apnea of prematurity is a diagnosis of exclusion when other underlying causes of apnea have been ruled out for infants of < 37 weeks' gestational age. It has been related to neuronal immaturity of brain stem function, which controls respirations. In addition, the central responsiveness to carbon dioxide is blunted in preterm infants. A diminished response to peripheral chemoreceptors located in both the aortic arch and the carotid arteries has also been noted. These receptors sense changes in $PaO_2$, pH, and $PaCO_2$ that affect the regulation of respirations and relay them to the respiratory center in the brain. Upper airway obstruction contributes to apnea because the negative pressure generated during inspiration may result in pharyngeal and laryngeal collapse.

### Clinical Presentation

Cessation of respiratory effort with cyanosis, pallor, hypotonia, or bradycardia is noted. Frequent swallowing-like movements in the pharynx during apnea can be a problem, because swallowing directly inhibits the respiratory drive.

### Management

Treatment of the infant with apnea of prematurity begins with assessment and monitoring (see Table 12). Tactile stimulation, oxygen administration, and/or bag-and-mask ventilation can be used to stimulate an infant who is experiencing an apneic episode.

The standard long-term treatment for apnea of prematurity is the use of methylxanthines, specifically theophylline, aminophylline, and caffeine, which act on the brain stem respiratory neurons to exert a central stimulatory effect. Other effects include improved sensitivity to carbon dioxide response, increased diaphragmatic contractions, increased catecholamine activity, enhanced resting pharyngeal muscle tone, and decreased diaphragm fatigue. Doxapram, a peripheral chemoreceptor stimulator, has also been used for infants with apnea; it increases both minute ventilation and tidal volume. However, doxapram contains benzyl alcohol and requires continuous infusion, so it is not recommended for newborns.

Infants who fail to respond to methylxanthines or who continue to have apnea while on these medications may respond to continuous positive airway pressure (CPAP), which increases functional residual capacity and stabilizes the chest wall. CPAP is beneficial to infants with mixed and obstructive apnea, but not central apnea. Infants who fail to respond to medications and CPAP require positive-pressure ventilation. Supportive care includes provision of a neutral thermal environment, use of pulse oximetry and/or transcutaneous monitoring, and positioning to prevent flexing of the neck.

### Prognosis (Menendez et al, 1996)

Apnea of prematurity usually resolves by a post-conceptional age of 34 to 52 weeks. Some infants may require home monitoring after discharge from the hospital.

## BRONCHOPULMONARY DYSPLASIA (BPD)

There is no consensus about the definition of bronchopulmonary dysplasia (BPD), but current definitions agree that it is a chronic neonatal respiratory problem with a multifactorial cause.

### Incidence (Oellrich, 1997; Verklan, 1997)

~ 20% in preterm infants with RDS
5% in infants with a birth weight > 1500 g
1 to 3 cases per 1,000 live births
~ 7,000 new cases reported annually

### Infants at Risk/Predisposing Factors

Preterm infants
Term infants (infrequent)
Early gestational age and low birth weight (risk inversely proportional)
Oxygen toxicity
Barotrauma
Nutritional deficiencies
Infection
Patent ductus arteriosus

### Pathophysiology

Lung injury from oxygen toxicity, barotrauma, and other contributory factors produces an inflammatory reaction, capillary leak, abnormal lung repair, and airway obstruction. A pattern of constant and recurring lung injury, repair, and scarring occurs. This produces cellular, airway, and interstitial changes, including inflammation, atelectasis, emphysema, inactivation of surfactant, pulmonary edema, decreased lung compliance, increased airway resistance, ventilation/perfusion mismatch, over-

**Table 12. Apnea Monitoring**

| Type of Monitor | Characteristics/Capabilities | Problems |
|---|---|---|
| Impedance monitoring with EKG electrodes | Detects changes in electrical impedance as size of thorax increases and decreases during respiration | Unable to detect obstructive apnea<br>Obstruction may not trigger a respiratory alarm<br>Heart rate may not decrease with episode of apnea<br>Sensitivity level usually set so monitor will sound in presence of shallow respirations (false alarm) |
| Pulse oximetry | Continuous measurement of hemoglobin saturation | Decreased accuracy during hypoperfusion, hypothermia, and active movement |
| Three-channel pneumocardiogram | Assesses respiratory effort, heart rate, pulse oximetry<br>Overnight or 24-hour recording | Motion and cardiogenic artifacts can interfere with respiratory signals |
| Two-channel pneumocardiogram | Assesses respiratory effort, heart rate<br>Continuous recording on memory chip x 2-3 weeks<br>Allows analysis of apnea, bradycardia, or both | Motion and cardiogenic artifacts can interfere with respiratory signals |
| Polysomnography | Expanded sleep study<br>EEG, ECG, EMG, chest wall, and abdominal movement analysis, end-tidal $CO_2$, oxygen saturation, continuous esophageal pH determination, nasal air flow | Involves use of transducers and electrodes |
| Inductance plethysmography | Uses chest and abdominal belts to monitor respirations<br>Detects obstructive apnea and decreases false alarms | Belt slippage<br>Changes in body position |

distention, air trapping, and increased production of mucus. These pulmonary function disturbances lead to hypoxemia, hypercarbia, and some degree of bronchial hyperactivity. Bronchial hyperactivity and airway smooth-muscle hypertrophy (which decreases lumen size) cause bronchospasms or constrictions. The hypoxemia or ongoing marginal oxygenation induces pulmonary artery vasoconstriction, vascular muscular hypertrophy, and hypertension, resulting in pulmonary hypertension and subsequently increasing stress of the right-sided cardiac function.

## Clinical Presentation

The most common alteration of pulmonary function in infants with BPD is increased airway resistance. In addition to low pulmonary compliance, this resistance results in increased work of breathing, hypoventilation, and retention of carbon dioxide. In infants with mild chronic lung disease, there is an initial need for positive-pressure ventilation, which must be maintained longer than was anticipated, followed by days or weeks of oxygen supplementation. Retractions, crepitant rales, and diminished breath sounds occur. In the early phase of moderate to severe BPD, oxygen and ventilatory pressure requirements increase relentlessly. Chest radiographs show progressive overdistention of the lungs. Clinically, a barrel-shaped chest is noted, and the infant demonstrates lability with handling and acute episodes of bronchospasms. Generally, if respiratory support can be decreased during the 1st month of life, the subsequent course of BPD is relatively benign. But if increased support is needed at this time, a severe, protracted course is usual. BPD often becomes a progressive disease if it persists beyond 1 month of age. Growth failure is prominent and osteopenia is common. Right-sided cardiac failure, bronchospasms, inspiratory stridor, overproduction of airway secretions, and systemic hypertension are common in infants with progressive BPD (see Table 13).

**Table 13. Overall Signs and Symptoms of Bronchopulmonary Dysplasia**

| | |
|---|---|
| Rapid and shallow respirations | Crackles |
| Increased work of breathing | Decreased air entry |
| Hyperinflated chest | Atelectasis |
| Hypoxemia | Hypercarbia |
| Pulmonary hypertension with right-sided cardiac failure | Intercostal/substernal retractions |

With mild BPD, chest radiograph findings are identical to those for RDS. As BPD progresses, coarse, irregular-shaped densities and air cysts start to develop. With advanced BPD, the lungs appear bubbly (air cysts continue to enlarge) and are extensively hyperinflated, emphysema has progressed considerably, and cardiomegaly (indicating right-sided heart failure) is present.

## Management

The treatment goals for BPD are to promote growth and to heal the infant's lungs. Oxygen administration and positive-pressure ventilation are both the cause of and the treatment for BPD. Adequate oxygenation is required to prevent recurrent hypoxemia and reduce pulmonary hypertension. This applies whether the infant is awake or asleep, crying or feeding. The lowest possible ventilator settings should be used and weaning should be accomplished slowly, based on the infant's tolerance. Ventilator settings can be reduced on the basis of acceptable blood gases of $PaO_2$ 55 to 70 mm Hg, $PaCO_2$ 50 to 60 mm Hg, and pH > 7.25. Oxygen saturation should be maintained between 90% and 95% to assure adequate tissue oxygenation and to avoid the effects of chronic hypoxemia (such as pulmonary hypertension and cor pulmonale). Hyperoxia is to be avoided, as it may worsen the BPD. Hemoglobin should be maintained at 12 to 15 g/dL to maximize oxygen delivery to the tissues.

Pharmacologic management is critical for infants with BPD. Excessive interstitial fluid accumulates in the lung and can result in deterioration of pulmonary function, adding to the existing hypoxemia and hypercarbia. Pharmacologic management includes diuretics, bronchodilators, and steroids (see Table 14). Diuretic therapy decreases excessive lung fluid. Bronchodilator and systemic methylxanthines have been used for both reactive airway disease and airway hyperreactivity. Corticosteroids promote weaning from the ventilator and decrease the inflammatory response, thereby improving pulmonary function.

Optimal nutrition is required for growth, for lung healing, and as compensation for increased oxygen and calorie consumption. Since optimal nutrition is often limited by increased caloric demands, fluid restriction, feeding intolerance, and gastroesophageal reflux, a high-calorie, nutrient-dense feeding is advisable. Adequate vitamin A is critical for normal growth and differentiation of epithelial cells, and appropriate intake of minerals and vitamin D is necessary to prevent the development of rickets.

**Table 14. Pharmacologic Management of Infants With Bronchopulmonary Dysplasia**

| Medication | Effects | Side Effects |
|---|---|---|
| **Diuretics** | **(Decrease interstitial fluid and pulmonary edema)** | |
| **Furosemide** | Decrease interstitial pulmonary edema<br>Lowers pulmonary vascular resistance and improves ventilation-perfusion ratios | Electrolyte imbalance<br>Dehydration<br>Ototoxicity<br>Renal stone formation |
| **Thiazide Diuretics**<br>• Chlorothiazide<br>• Hydrochlorothiazide<br>• Used in combination with spironolactone, a potassium-sparing drug | Decrease interstitial pulmonary edema<br>Improve pulmonary function<br>Decrease airway resistance<br>Increase pulmonary compliance | Electrolyte imbalance<br>Dehydration<br>Hyperglycemia<br>Glycosuria |
| **Bronchodilators** | **(Improve pulmonary mechanics)** | |
| ***Inhaled:***<br>• Albuterol<br>• Terbutaline sulfate<br>• Cromolyn sodium<br>• Isoetharine<br>• Isoproterenol<br>• Ipratropium bromide | Increase surfactant production<br>Decrease pulmonary edema<br>Enhance mucociliary transport<br>Overall: increase lung compliance and decrease airway resistance | Tachycardia<br>Tremors<br>Hypertension<br>Irritability<br>Gastrointestinal disturbances |
| ***Systemic:***<br>• Methylxanthines<br>Caffeine citrate | Decreases pulmonary resistance<br>Stimulates central nervous system<br>Increases inspiratory drive<br>Improves skeletal muscle and diaphragm contractility and increases lung compliance | Rare |
| Aminophylline<br>Theophylline | Actions as noted for caffeine citrate<br>Increase surfactant production | Vomiting, tachycardia, gastroesophageal reflux, electrolyte abnormalities, tremors, agitation |
| • Albuterol<br>• Terbutaline sulfate | Decreases pulmonary resistance/adjunct to methylxanthine | Tachycardia, tremors, hypertension, irritability, gastrointestinal disturbances, hypokalemia (albuterol) |
| **Corticosteroids** | **(Promote weaning from ventilator and decrease inflammatory response)** | |
| **Dexamethasone** | Improves pulmonary status, probably by decreasing tracheobronchial and alveolar inflammation and decreasing pulmonary edema<br>Facilitates gas exchange<br>Increases lung compliance<br>Diminishes airway resistance | Hypertension<br>Hyperglycemia<br>Gastrointestinal complications (perforated gastric and duodenal ulcers, upper GI hemorrhage)<br>Restlessness and/or irritability |

**Table 15. Premature Infants: Special Respiratory Considerations**

| Concern/Condition | Impact/Result |
|---|---|
| Brain respiratory control center | May lack sufficient maturity to consistently regulate respirations; therefore, may experience periodic breathing and apnea |
| Compliant (immature) chest wall | Insufficient breathing and retractions |
| Noncompliant lungs | Increased work for respiratory muscles, leading to increased work of breathing and retractions |
| Surfactant deficiency | Collapsed alveoli plus intrapulmonary shunting, resulting in hypoxemia |
| Pulmonary vascular smooth muscle | Not as well developed as in term infants, so fall in pulmonary vascular resistance occurs more rapidly |
| Immaturity of terminal air sacs and associated vasculature | Poor gas exchange |
| Immaturity of diaphragm and other muscles of respiration | Inspiratory difficulty |
| Peripheral chemoreceptors (in aortic arch and carotid arteries) | Blunted response; therefore, can experience apnea |
| Muscle fiber type distribution | Muscles may be more susceptible to fatigue |
| Ductus arteriosus | Ductal smooth muscle does not have a fully developed constrictor response to oxygen<br>Ductal tissue exhibits increased dilatory response to prostaglandins<br>Persistently high circulating levels of prostaglandins<br>May remain patent, shunting blood away from systemic organs |
| Lower hemoglobin | Limited oxygen-carrying capacity |

The environment surrounding the infant is important for recovery from BPD. Minimizing agitation to prevent the hypoxemia and bronchospasms that often accompany agitation is essential. Sedation may be needed in addition to evaluation of noise, light, and touch to avoid overstimulation, which has a negative effect on weight gain, respiratory function, and development.

**Prognosis** (Adams and Wearden, 1998; Barrington and Finer, 1998)
Survival to discharge is inversely related to duration of ventilation. Improvement in pulmonary function occurs slowly over 1 to 3 years. Morbidities include but are not limited to chronic respiratory difficulties, prolonged or recurrent hospitalizations, increased incidence of neurodevelopmental disabilities, and growth restriction. Overall mortality ranges from 25% to 40%, with most deaths related to infection or cardiopulmonary failure associated with pulmonary hypertension or cor pulmonale.

## SPECIAL CONCERNS WITH THE PREMATURE INFANT

The clinician or bedside caregiver should be alert to special concerns with the premature infant, as outlined in Table 15 (Donovan et al, 1998; Whitaker, 1997).

## RELATED NURSING CARE

### NURSING DIAGNOSIS:
**Impaired Gas Exchange**

### PATIENT OUTCOME
Infant will maintain adequate gas exchange and effective breathing pattern, as evidenced by:
- RR 40-60 BPM
- HR 110-160 BPM
- Clear and equal breath sounds
- Mild to no retractions
- Lack of nasal flaring and grunting
- Pink color
- Blood gases within normal limits

### INTERVENTIONS
- Assess for signs of impaired gas exchange/ respiratory distress every hour and as necessary (PRN)
  - Nasal flaring
  - Expiratory grunt
  - Tachypnea
  - Cyanosis
  - Retractions—note type and degree
    - Type: suprasternal, substernal, intercostal, subcostal
    - Degree: mild, moderate, severe
- Auscultate breath sounds and note adventitious sounds every 1 to 2 hours and PRN
  - Air movement
  - Equality—compare and contrast each side of chest
  - Clarity—clear, rales, rhonchi
- Maintain a patent airway:
  - Small roll under shoulders
  - With endotracheal tube (ETT):
    - Suction PRN
    - Assess and document ETT size and position—note insertion depth (mark located at infant's lips)
    - Use ETT adaptor or closed suction system to allow suctioning without removing infant from ventilator
  - With nasal continuous positive airway pressure (NCPAP):
    - Keep infant calm; swaddle if necessary (crying releases pressure through mouth)
    - Maintain patency of nares and nasal prongs
    - Guard against pressure necrosis
- Administer oxygen in correct amount and by correct route of delivery
  - Analyze and document inspired oxygen percentage every hour and with changes
  - Document oxygen administration temperature
- Document ventilator settings and alarm limits every shift and with changes
- Assess and document blood gas results as ordered
  - Notify physician/practitioner of results
- Maintain pulse oximetry (oxygen saturation) or transcutaneous monitor (transcutaneous and partial pressure of oxygen [$TcPO_2$] and carbon dioxide pressure [$TcPCO_2$])
  - Pulse oximetry:
    - Note probe site and change PRN
    - Place probe so light source and photodetector are opposite one another
    - Shield probe from ambient light, especially if phototherapy is in use
    - Set monitor alarms according to unit policy
    - Document readings every hour and PRN
  - Transcutaneous monitor:
    - Position probe on a flat, well-perfused area
    - Change probe position every 4 hours and PRN
    - Preferred temperature range: 43ºC for preterm infants, 44ºC for term infants
    - Set monitor alarms according to unit policy
    - Document readings every hour and PRN
- Maintain end-tidal $CO_2$ monitoring if ordered
- Provide chest physiotherapy as ordered
  - Monitor $O_2$ saturation, heart rate, respiratory rate, signs and symptoms of distress on an ongoing basis to assess tolerance of procedure
  - Percussion: 1 to 2 minutes over area to be drained
    - Emphasize atelectatic area
    - Do not percuss over liver or spleen
  - Vibration: Use padded electric toothbrush or vibrator
    - Base duration on infant's tolerance
- If chest tube required:
  - Assist with transillumination process
  - Assist with needle aspiration of chest
  - Assist with chest tube placement:
    - Administer analgesic
    - Monitor vital signs during procedure
    - Place chest tube to chest drainage system at 15 to 20 cm $H_2O$ pressure
    - Note bubbling activity
  - Document tolerance to procedure
- If chest tube in place:
  - Maintain tube stability:
    - Tape all connections securely
    - Secure tubing from infant to bed to relieve tension at insertion site
    - Assess for kinks in tubing
    - Do not strip/milk chest tube; this generates extremely high pressures

Bubbling activity slows several hours after chest tube placement and usually stops after 72 hours
If no bubbling noted for 24 hours, place chest tube to underwater seal (provides an outlet for any reaccumulated air after suction is discontinued); do not clamp tube
After discontinuing chest tube, use an occlusive dressing (such as petrolatum gauze) for 48 hours
Keep occlusive dressing at bedside for application at insertion site if chest tube becomes dislodged
Assess and document amount of chest tube drainage every hour or every shift
Assess and document bubbling activity every hour and PRN
Reposition infant every 2 to 4 hours to facilitate removal of air
Elevate head of bed

- Reposition infant every 2 to 4 hours
- Provide cluster care with minimal handling
- Assess infant's response to and tolerance of handling and procedures to determine appropriate nursing care
- Administer sedatives, analgesics, and muscle relaxants as ordered
  Assess response to medications
- Maintain neutral thermal environment
- Provide support to family

## NURSING DIAGNOSIS:
**Ineffective Airway Clearance**

## PATIENT OUTCOME
Infant will have an adequately clear airway, as evidenced by:
Clear and equal breath sounds
Respiratory rate 40-60 BPM
Pink color
Unlabored respirations

## INTERVENTIONS
- Assess respiratory status every 2 hours and PRN
- Provide chest physiotherapy and administer aerosol medications as ordered
- Assess need for suctioning on the basis of:
  Quality of breath sounds
  Current condition
  Blood gas results
  General clinical appearance: chest movement, color
  Oxygen saturation readings
- Suction PRN (most units have a minimal suctioning protocol)
  Use appropriate-sized suction catheters
  Wear protective goggles and mask (if not using a closed suctioning system)
  Use sterile technique and follow unit suctioning protocol
  Document amount, characteristics, and color of secretions
  Document auscultatory findings of breath sounds before and after suctioning
- Assess patient tolerance of suctioning procedure
- Initiate appropriate interventions to minimize hypoxia (bag ventilation presuctioning or postsuctioning)
  Determine degree of hypoxia by pulse oximeter or transcutaneous monitor readings and time to return to baseline
  Note degree of bradycardia, if any, and time to return to baseline
  Note any other physiologic changes
- Allow infant to rest after suctioning procedure and before other major stress activities
- Reposition infant every 2 to 4 hours and PRN
- Maintain adequate hydration

## ADDITIONAL NURSING DIAGNOSES
These include but are not limited to:

**High risk for injury:** intraventricular hemorrhage, air leaks, other, related to treatment for respiratory disorders

**Alteration in comfort:** pain, related to chest tube placement and other procedures

**High risk for fluid volume deficit:** related to disease process, fluid loss, and IV administration

**High risk for fluid volume excess:** related to renal inability to excrete any volume overload and to iatrogenic fluid volume excess

**Altered nutrition:** less than body requirements, related to increased caloric expenditures and decreased nutritional intake

**Knowledge deficit:** related to lack of parental understanding of the disease process

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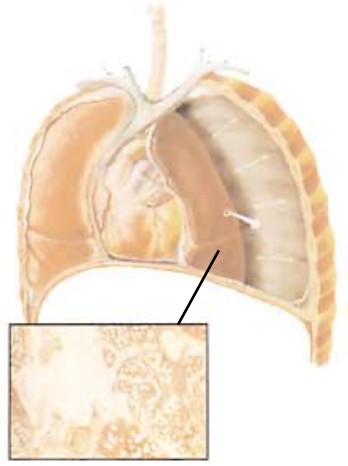
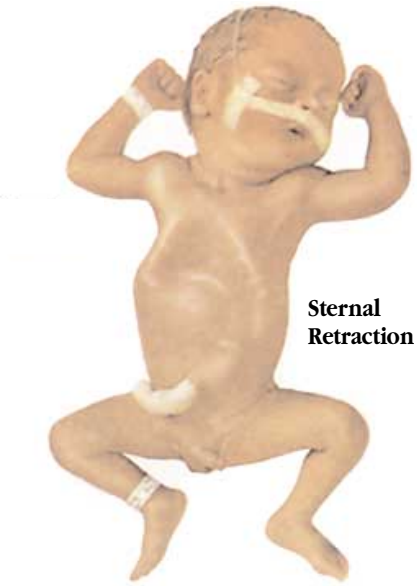
# Neonatal Respiratory System

**Tension Pneumothorax**

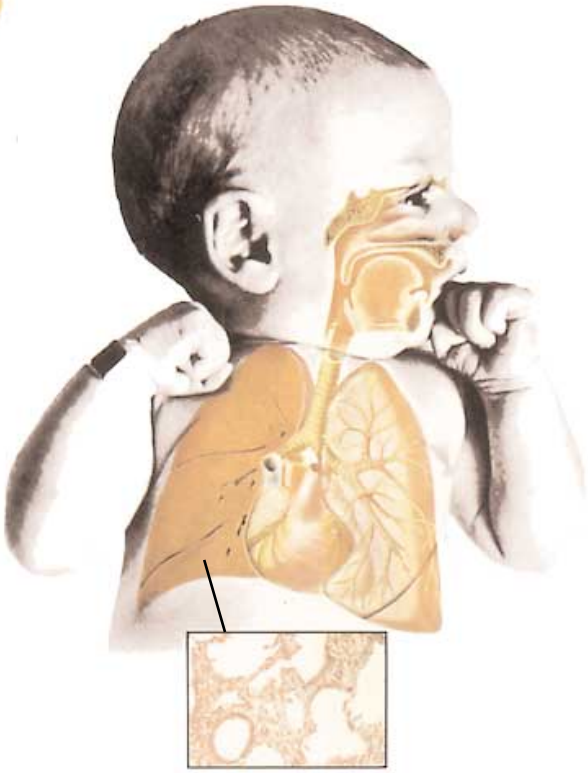


**Interstitial Emphysema**

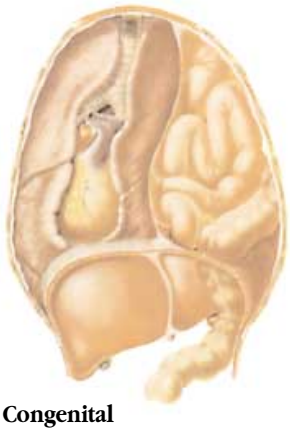


**Sternal Retraction**

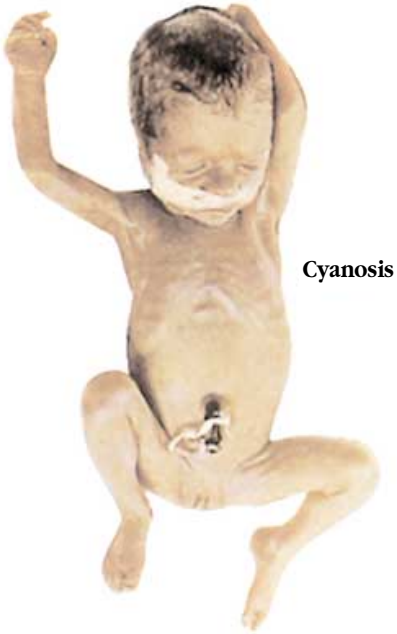
**Normal Respiratory Tract**



**Normal Lung Tissue**



**Congenital Diaphragmatic Hernia**



**Cyanosis**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