Smith Seminars
Continuing Education Credits
AARC-Approved for 2 CRCE
Respiratory Disorders in Neonates and Infants

Objectives
List the causes of respiratory distress in neonates and infants
Summarize the factors of apnea in the premature infant
Identify factors of bronchopulmonary dysplasia & meconium aspiration
Explain the etiology, diagnosis, pathophysiology, prognosis, and treatment of persistent pulmonary hypertension, respiratory distress syndrome, transient tachypnea, children with chronic health conditions, death and dying, and the sick neonate

Respiratory distress in neonates and infants has multiple causes. Symptoms and signs vary and include nasal flaring; intercostal, subcostal, and suprasternal retractions; weak and/or irregular breathing; tachypnea and apneic spells; cyanosis, pallor, mottling, and/or delayed capillary refill; and hypotension. In neonates, symptoms and signs may be apparent immediately upon delivery or develop minutes or hours afterward.

Causes of Respiratory Distress in Neonates and Infants

Cardiac - Right-to-left shunting with normal or increased pulmonary flow: Transposition of the great vessels, total anomalous venous return, truncus arteriosus, and hypoplastic left heart syndrome.
Right-to-left shunting with decreased pulmonary flow: Pulmonary atresia, tetralogy of Fallot, critical pulmonic stenosis, tricuspid atresia, single ventricle with pulmonic stenosis, Ebstein's anomaly, persistent fetal circulation or persistent pulmonary hypertension.
Respiratory - Upper tract: Choanal atresia or stenosis, tracheobroncholaryngeal stenosis, compressive obstruction (vascular ring), tracheoesophageal anomalies (such as cleft, fistula).
Lower tract: Respiratory distress syndrome, transient tachypnea of the newborn, meconium aspiration, pneumonia, sepsis, pneumothorax, congenital diaphragmatic hernia, pulmonary hypoplasia, cystic malformation of the lung, and congenital deficiency of surfactant proteins B or C.
Neurologic - Intracranial hemorrhage or hypertension, oversedation (infant or maternal), diaphragmatic paralysis, neuromuscular disease, and seizure disorder.
Hematologic - Methemoglobinemia, polycythemia, and severe anemia.
Miscellaneous - Hypoglycemia, blood loss, metabolic disorders (acid-base disorders or hyperammonemia), or hypovolemic shock.

Evaluation starts with a thorough history and physical examination. History in the neonate focuses on maternal and prenatal history, particularly gestational age, maternal infection or bleeding, meconium staining of amniotic fluid, and oligohydramnios or polyhydramnios. Physical examination focuses on the heart and lungs. Chest wall asymmetry or sunken abdomen suggests diaphragmatic hernia. Asymmetric breath sounds suggest pneumothorax, and a displaced left apical impulse and/or heart murmur

suggests a congenital heart defect. Assessment of BP, femoral pulse, and capillary refill helps identify any concomitant circulatory compromise. In both neonates and infants, it is important to assess oxygenation and response to O2 administration by pulse oximetry. Chest x-ray is also recommended.

There are several significant differences in the physiology of the respiratory system in infants compared with that of older children and adults. These differences include a more compliant collapsible chest wall, more reliance on diaphragmatic excursions over intercostal muscles, and collapsible extrathoracic airways; also, infants' smaller airway caliber gives increased airway resistance and increased tendency toward atelectasis. Yet, other principles of respiration are similar in adults and children.

Apnea in Premature Infants

Apnea of prematurity is defined as respiratory pauses > 20 seconds or airflow interruption and respiratory pauses < 20 seconds associated with bradycardia (< 80 beats/min), central cyanosis, or O2 saturation < 85% in infants born at < 37 weeks gestation and with no underlying disorders causing apnea. Cause may be CNS immaturity (central) or airway obstruction. Diagnosis is by multichannel respiratory monitoring. Treatment is with respiratory stimulants for central apnea and head positioning for obstructive apnea. Prognosis is excellent; apnea resolves in most neonates by 37 weeks.

About 25% of preterm infants have apnea of prematurity, which usually begins 2 to 3 days after birth and only rarely on the 1st day; apnea that develops > 14 days after birth in an otherwise healthy infant signifies a serious illness other than apnea of prematurity. Risk increases with earlier gestational age.

Etiology and Pathophysiology

Apnea of prematurity may be central, obstructive, or both; a mixed pattern is most common. Central apnea is caused by immaturity of medullary respiratory control centers; insufficient neural impulses from the respiratory centers in the medulla reach the respiratory muscles, and the infant stops breathing. Hypoxemia briefly stimulates respiratory efforts but, after a few seconds, suppresses respirations. Obstructive apnea is caused by obstructed airflow, either from neck flexion causing opposition of hypopharyngeal soft tissues or from nasal occlusion. Both types of apnea can cause hypoxemia, cyanosis, and bradycardia if the apnea is prolonged. Among infants dying of SIDS (Sudden Infant Death Syndrome), 18% have a history of prematurity, but apnea of prematurity does not appear to be a precursor to SIDS.

Diagnosis

Diagnosis of apnea itself is occasionally made by observation alone, but high-risk infants are typically diagnosed by an apnea monitor worn for 5 to 7 days. Typical monitors use a chest band to detect chest wall movements and pulse oximetry to detect heart rate and O2 saturation; nasal airflow must also be monitored if obstructive apnea is suspected. Apnea of prematurity is a diagnosis of exclusion. Other causes of apnea in neonates include hypoglycemia, hypocalcemia, sepsis, intracranial hemorrhage, and gastroesophageal reflux; these causes are sought with appropriate testing.

High-risk infants who are not apneic and who are otherwise ready for discharge may be monitored at home. Parents need to be taught how to place the monitoring belt and leads; how to interpret the significance of alarms by assessing the infant's color and respirations; and how to intervene. They should also be instructed to keep a log of alarms and infant appearance and to contact medical providers if questions arise or apneic episodes occur. Many monitors store information, allowing providers to assess the type and frequency of events, compare them with events reported and logged by the parents, and determine if other treatment is needed or if monitoring can be stopped.

Prognosis and Treatment

Most preterm infants stop having apneic spells by the time they reach about 37 weeks gestation; apnea may continue for weeks in infants born at extremely early gestational ages (such as 23 to 27 weeks). Mortality, treated or untreated, is probably negligible.
The infant's head should be kept in the midline and the neck in the neutral position or slightly extended to prevent upper airway obstruction. All premature infants, especially those with apnea of prematurity, are at risk of apnea, bradycardia, and O2 desaturation while in a car seat and should undergo a car seat challenge test before discharge.
When apnea is noted, either by observation or monitor alarm, infants are stimulated, which may be all that is required; if breathing does not resume, bag-valve-mask or mouth-to-mouth-and-nose ventilation is provided. For infants at home, the physician is contacted if apnea occurred but ceased after stimulation; if intervention beyond stimulation is required, the infant should be rehospitalized and evaluated.
Respiratory stimulants are indicated for treatment of frequent or severe episodes, characterized by hypoxemia, cyanosis, and/or bradycardia. Caffeine is the safest and most commonly used drug. It can be given as caffeine base (loading dose 10 mg/kg followed by a maintenance dose of 2.5 mg/kg PO q 24 hours) or caffeine citrate, a caffeine salt which is 50% caffeine (loading dose 20 mg/kg followed by a maintenance dose of 5 mg/kg q 24 hours). Other options include IV methylxanthines, aminophylline loading dose 6 to 7 mg/kg infused over 20 min followed by a maintenance dose of 1 to 3 mg/kg q 8 to 12 hours (lower in younger, more premature infants) or theophylline loading dose 4 to 5 mg/kg followed by a maintenance dose of 1 to 2 mg/kg q 8 to 12 hours, with doses adjusted to maintain a serum concentration of 6 to 12 µg/mL, and doxapram (0.5 to 2.0 mg/kg/h continuous IV infusion). Treatment continues until the neonate is 34 to 35 weeks gestation and free from apnea requiring physical intervention for at least 5 to 7 days. Monitoring continues until the neonate is free of apnea requiring intervention for 5 to 10 days.
If apnea continues despite respiratory stimulants, the neonate may be given continuous positive airway pressure starting at 5 to 8 cm H2O pressure. Intractable apneic spells require ventilator support. Discharge practices vary; some providers observe infants for 7 days after treatment has ended to ensure that apnea or bradycardia does not recur, whereas others discharge with theophylline if treatment appears effective.

Bronchopulmonary Dysplasia

Bronchopulmonary dysplasia (BPD) is chronic lung injury in premature infants caused by supplemental O2 and prolonged mechanical ventilation.

Bronchopulmonary dysplasia is considered present when there is need for supplemental O2 in premature infants at 36 weeks gestation who do not have other conditions that require O2 (such as pneumonia or congenital heart disease). It is caused by high concentrations of inspired O2 typically in patients on prolonged mechanical ventilation. Incidence increases with degree of prematurity; additional risk factors include pulmonary interstitial emphysema, high peak inspiratory pressures, increased airway resistance and pulmonary artery pressures, and male sex. BPD is typically suspected when a ventilated infant is unable to wean from O2 therapy, mechanical ventilation, or both. Patients develop worsening hypoxemia, hypercapnia, and increasing O2 requirements. Chest x-ray initially shows diffuse haziness due to accumulation of exudative fluid; appearance then becomes multicystic or spongelike, with alternating areas of emphysema, pulmonary scarring, and atelectasis. Alveolar epithelium may slough, and macrophages, neutrophils, and inflammatory mediators may be found in the tracheal aspirate.

Prognosis and Treatment

Prognosis varies with severity. Infants who still depend on mechanical ventilation at 36 weeks gestation have a 20 to 30% mortality rate in infancy. Infants with BPD have a 3- to 4-fold increased rate of growth failure and neurodevelopmental problems. For several years, infants are at increased risk of lower respiratory tract infections (particularly viral) and may quickly develop respiratory decompensation if pulmonary infection occurs. The threshold for hospitalization should be low if signs of a respiratory infection or respiratory distress develop.

Treatment is supportive and includes nutritional supplementation, fluid restriction, diuretics, and perhaps inhaled bronchodilators. Respiratory infections must be diagnosed early and treated aggressively. Weaning from mechanical ventilation and supplemental O2 should be accomplished as early as possible.

Feedings should achieve an intake of > 120 calories/kg/day; caloric requirements are increased because of the increased work of breathing and to aid lung healing and growth. Because pulmonary congestion and edema may develop, daily fluid intake is often restricted to about 120 mL/kg/day. Diuretic therapy is sometimes used: chlorothiazide 10 to 20 mg/kg PO bid plus spironolactone 1 to 3 mg/kg once/day or split into twice-daily doses. Furosemide (1 to 2 mg/kg IV or IM or 1 to 4 mg/kg PO q 12 to 24 hours for neonates and q 8 hours for older infants) may be used for short periods, but prolonged use causes hypercalciuria with resultant osteoporosis, fractures, and renal calculi (kidney stones). Hydration and serum electrolytes should be monitored closely during diuretic therapy.

Weeks or months of additional ventilator support and/or supplemental O2 may be required for advanced BPD. Ventilator pressures and fraction of inspired O2 (FiO2) should be reduced as rapidly as tolerated, but the infant should not be allowed to become hypoxemic. Arterial oxygenation should be continuously monitored with a pulse oximeter and maintained at = 88% saturation. Respiratory acidosis may occur during ventilator weaning and treatment and is acceptable as long as the pH remains > 7.25 and the infant does not develop severe respiratory distress.

Passive immunoprophylaxis with palivizumab, a monoclonal antibody to respiratory syncytial virus (RSV), decreases RSV-related hospitalizations and ICU stays but is costly and is indicated primarily in high-risk infants. During RSV season (November through

April), children are given 15 mg/kg IM q 30 days until 6 months after treatment of the acute illness. Infants > 6 months should also be vaccinated against influenza.

Prevention

BPD often can be prevented by weaning infants to the lowest tolerated ventilator settings and completely off mechanical ventilation as soon as possible; early use of aminophylline as a respiratory stimulant may help preterm infants wean from intermittent mandatory ventilation. Prenatal corticosteroid administration, prophylactic surfactant administration in extremely low-birth-weight infants, early treatment of patent ductus arteriosus, and avoidance of large volumes of fluid also decrease BPD incidence and severity. When an infant cannot be weaned within the expected time, possible underlying conditions, including patent ductus arteriosus and nursery-acquired pneumonia, should be considered and treated.

Meconium Aspiration

Intrapartum meconium aspiration can cause chemical pneumonitis and mechanical bronchial obstruction producing a syndrome of respiratory distress. Findings include tachypnea, rales and rhonchi, and cyanosis or desaturation. Diagnosis is suspected when there is respiratory distress after delivery through meconium-tinged amniotic fluid and is confirmed by chest x-ray. Treatment is vigorous suction immediately on delivery before the neonate takes his 1st breath, followed by respiratory support as needed. Prognosis depends on the underlying physiologic stressors.

Etiology and Pathophysiology

Physiologic stress at the time of labor and delivery (such as hypoxia caused by umbilical cord compression or placental insufficiency or from infection) may cause the fetus to pass meconium into the amniotic fluid before delivery; meconium passage is noted in about 10 to 15% of births. During delivery, perhaps 5% of infants with meconium passage aspirate the meconium, triggering lung injury and respiratory distress, termed meconium aspiration syndrome. Postterm infants delivered through reduced amniotic fluid volume are at risk of more severe disease because the less dilute meconium is more likely to cause airway obstruction.

The mechanisms by which aspiration induces the clinical syndrome probably include nonspecific cytokine release, airway obstruction, surfactant inactivation, and/or chemical pneumonitis; the underlying physiologic stressors also may contribute. If complete bronchial obstruction occurs, atelectasis results; partial blockage leads to air trapping on expiration, resulting in hyperexpansion of the lungs and possibly pulmonary air leak with pneumomediastinum or pneumothorax. Continuing hypoxia may lead to persistent pulmonary hypertension of the newborn.

Infants may also aspirate vernix caseosa, amniotic fluid, or blood of maternal or fetal origin during delivery and can develop respiratory distress and signs of aspiration pneumonia on chest x-ray. Treatment is supportive; if bacterial infection is suspected, cultures are taken and antibiotics begun.

Symptoms and Signs

Signs include tachypnea, nasal flaring, retractions, cyanosis or desaturation, rales, rhonchi, and greenish yellow staining of the umbilical cord, nail beds, or skin. Meconium staining may be visible in the oropharynx and (on intubation) in the larynx and trachea. Infants with air trapping may have a barrel-shaped chest and also symptoms and signs of pneumothorax, pulmonary interstitial emphysema, and pneumomediastinum.

Diagnosis

Diagnosis is suspected when a neonate demonstrates respiratory distress in the setting of meconium-tinged amniotic fluid and is confirmed by chest x-ray demonstrating hyperinflation with variable areas of atelectasis and flattening of the diaphragm. Fluid may be seen in the lung fissures or pleural spaces, and air may be seen in the soft tissues or mediastinum. Because meconium may enhance bacterial growth and meconium aspiration syndrome is difficult to distinguish from bacterial pneumonia, cultures of blood and tracheal aspirate should also be obtained.

Prognosis and Treatment

Prognosis is generally good, although it varies with the underlying physiologic stressors; overall mortality is slightly increased. Infants with meconium aspiration syndrome may be at greater risk of asthma in later life.

Immediate treatment, indicated for all neonates delivered through meconium, is vigorous suctioning of the mouth and nasopharynx using a De Lee suction apparatus as soon as the head is delivered and before the neonate breathes and cries. If suction returns no meconium and the infant appears vigorous, observation without further intervention is appropriate. If the infant has labored or depressed respirations, poor muscle tone, or is bradycardic (< 100 beats/min), the trachea should be intubated with a 3.5- or 4.0-mm endotracheal tube. A meconium aspirator connected to a suction apparatus is attached directly to the endotracheal tube, which then serves as the suction catheter. Suction is maintained while the endotracheal tube is removed. Reintubation and continuous positive airway pressure are indicated for continued respiratory distress, followed by mechanical ventilation and admission to the neonatal ICU as needed. Because positive pressure ventilation enhances risk of pulmonary air-leak syndrome, regular evaluation (including physical examination and chest x-ray) is important to detect these complications; these should immediately be sought in any intubated infant whose BP, perfusion, or O2 saturation suddenly worsens.

Additional treatments may include surfactant for mechanically ventilated infants with high O2 requirements, which can decrease the need for extracorporeal membrane oxygenation, and antibiotics (usually ampicillin and an aminoglycoside).

Persistent Pulmonary Hypertension

Persistent pulmonary hypertension of the newborn (PPHN) is the persistence of or reversion to pulmonary arteriolar constriction, causing a severe reduction in pulmonary blood flow and right-to-left shunting. Symptoms and signs include tachypnea, retractions, and severe cyanosis or desaturation unresponsive to O2. Diagnosis is by history, examination, chest x-ray, and response to O2. Treatment is with O2,

alkalinization, inhaled nitric oxide, or, if medical therapy fails, extracorporeal membrane oxygenation.

Etiology and Pathophysiology

Persistent pulmonary hypertension of the newborn is a disorder of pulmonary vasculature that affects term or postterm infants. The most common causes involve perinatal asphyxia or hypoxia (a history of meconium staining of amniotic fluid or meconium in the trachea is common); hypoxia triggers reversion to or persistence of intense pulmonary arteriolar constriction, a normal state in the fetus. Additional causes include premature ductus arteriosus or foramen ovale closure, which increases fetal pulmonary blood flow and may be triggered by maternal NSAID use; polycythemia, which obstructs blood flow; congenital diaphragmatic hernia, in which the left lung is severely hypoplastic, forcing most of the pulmonary blood flow through the right lung; and neonatal sepsis, presumably from production of vasoconstrictive prostaglandins by activation of the cyclo-oxygenase pathway by bacterial phospholipids. Whatever the cause, elevated pressure in the pulmonary arteries causes abnormal smooth muscle development and hypertrophy in the walls of the small pulmonary arteries and arterioles and right-to-left shunting via the ductus arteriosus or a foramen ovale, resulting in intractable systemic hypoxemia.

Symptoms and Signs

Symptoms and signs include tachypnea, retractions, and severe cyanosis or desaturation unresponsive to supplemental O2. In infants with a right-to-left shunt via a patent ductus arteriosus, oxygenation is higher in the right brachial artery than in the descending aorta; thus cyanosis may be differential, such as O2 saturation in the lower extremities is 5% lower than in the right upper extremity.

Diagnosis

Diagnosis should be suspected in any near-term infant with arterial hypoxemia and/or cyanosis, especially one with a suggestive history whose O2 saturation does not improve with 100% O2. Diagnosis is confirmed by echocardiogram, which can confirm the presence of elevated pressures in the pulmonary artery using Doppler interrogation and simultaneously excludes congenital heart disease. Lung fields on x-ray may be normal or may demonstrate changes due to the underlying cause (such as meconium aspiration syndrome, neonatal pneumonia, congenital diaphragmatic hernia).

Prognosis and Treatment

An oxygenation index (mean airway pressure [cm H2O] × fraction of inspired O2 [FiO2] × 100/PaO2) > 40 predicts mortality of > 50%. Overall mortality ranges from 10 to 80% and is directly related to the oxygenation index but also varies with underlying disorder. However, many survivors (perhaps 1/3) exhibit developmental delay, hearing deficits, and/or functional disabilities. This rate of disability may be no different from that of other infants with severe illness.

Treatment with O2, which is a potent pulmonary vasodilator, is begun immediately to prevent disease progression. O2 is delivered via bag and mask or mechanical ventilation; mechanical distention of alveoli aids vasodilation. FiO2 should initially be 100% but can be titrated downward to maintain PaO2 between 50 and 90 mm Hg to minimize lung injury. Once PaO2 is stabilized, weaning can be attempted by reducing FiO2 in

decrements of 2 to 3%, then reducing ventilator pressures; changes should be gradual, because a large drop in PaO2 can cause recurrent pulmonary artery vasoconstriction. High-frequency oscillatory ventilation expands and ventilates the lungs while minimizing barotrauma and should be considered for infants with underlying lung disease in whom atelectasis and ventilation/perfusion (V/Q) mismatch may exacerbate the hypoxemia of PPHN.

Inhaled nitric oxide relaxes endothelial smooth muscle, dilating pulmonary arterioles, which increases pulmonary blood flow and rapidly improves oxygenation in as many as 1/2 of patients. Initial dose is 20 ppm, titrated downward by effect.

Extracorporeal membrane oxygenation may be used in patients with severe hypoxic respiratory failure defined by an oxygenation index > 35 to 40 despite maximum respiratory support.

Normal fluid, electrolyte, glucose, and Ca levels must be maintained. Infants should be kept in a neutral thermal environment and treated with antibiotics for possible sepsis until culture results are known.

Respiratory Distress Syndrome

Respiratory distress syndrome (RDS) is caused by pulmonary surfactant deficiency in the lungs of neonates born at < 37 weeks gestation. Risk increases with degree of prematurity. Symptoms and signs include grunting respirations, use of accessory muscles, and nasal flaring appearing soon after birth. Diagnosis is clinical; prenatal risk can be assessed with tests of fetal lung maturity. Treatment is surfactant therapy and supportive care.

Etiology and Pathophysiology

Pulmonary surfactant is a mixture of phospholipids and lipoproteins secreted by type II pneumocytes; it diminishes the surface tension of the water film that lines alveoli, thereby decreasing the tendency of alveoli to collapse and the work required to inflate them. With surfactant deficiency, the lungs become diffusely atelectatic, triggering inflammation and pulmonary edema. Because blood passing through the atelectatic portions of lung is not oxygenated (forming a right to left intrapulmonary shunt), the infant becomes hypoxemic. Lung compliance is decreased, thereby increasing the work of breathing. In severe cases, the diaphragm and intercostal muscles fatigue, and CO2 retention and respiratory acidosis develop.

Surfactant is not produced in adequate amounts until relatively late in gestation; thus, risk of respiratory distress syndrome increases with greater prematurity. Other risk factors include multifetal pregnancies and maternal diabetes. Risk decreases with fetal growth restriction, preeclampsia or eclampsia, maternal hypertension, prolonged rupture of membranes, and maternal corticosteroid use. Rare cases are hereditary, caused by mutations in surfactant protein (SP-B and SP-C) and ATP-binding cassette transporter A3 (ABCA3) genes. Males and whites are at greater risk.

Symptoms and Signs

Symptoms and signs include rapid, labored, grunting respirations appearing immediately or within a few hours after delivery, with suprasternal and substernal retractions and nasal

flaring. As atelectasis and respiratory failure progress, symptoms worsen, with cyanosis, lethargy, irregular breathing, and apnea.
Neonates weighing < 1000 grams may have lungs so stiff that they are unable to initiate and/or sustain respirations in the delivery room.
Complications of RDS include intraventricular hemorrhage, periventricular white matter injury, tension pneumothorax, bronchopulmonary dysplasia, sepsis, and neonatal death. Intracranial complications have been linked to hypoxemia, hypercarbia, hypotension, swings in arterial BP, and low cerebral perfusion.

Diagnosis

Diagnosis is by clinical presentation, including recognition of risk factors; ABGs demonstrating hypoxemia and hypercapnia; and chest x-ray. Chest x-ray shows diffuse atelectasis classically described as having a ground-glass appearance with visible air bronchograms; appearance correlates loosely with clinical severity.
Differential diagnosis includes group B streptococcal pneumonia and sepsis, transient tachypnea of the newborn, persistent pulmonary hypertension, aspiration, pulmonary edema, and congenital cardiopulmonary anomalies. Patients typically require cultures of blood, CSF, and possibly tracheal aspirate. Clinical diagnosis of group B streptococcal pneumonia is extremely difficult; thus, antibiotics are usually started pending culture results.
RDS can be anticipated prenatally using tests of fetal lung maturity, which measure surfactant obtained by amniocentesis or collected from the vagina (if membranes have ruptured) and which can help determine the optimal timing of delivery. These are indicated for elective deliveries before 39 weeks when fetal heart tones, human chorionic gonadotropin levels, and ultrasound measurements cannot confirm gestational age and for nonelective deliveries between 34 and 36 weeks. Risk of RDS is low when lecithin/sphingomyelin ratio is > 2, phosphatidyl glycerol is present, foam stability index = 47, and/or surfactant/albumin ratio (measured by fluorescence polarization) is > 55 mg/g.

Treatment

Prognosis with treatment is excellent; mortality is < 10%. With adequate ventilatory support alone, surfactant production eventually begins, and once production begins, RDS resolves within 4 or 5 days, but severe hypoxemia in the meantime can result in multiple organ failure and death.
Specific treatment is intratracheal administration of surfactant; this requires endotracheal intubation, which may also be necessary to achieve adequate ventilation and oxygenation. Less premature infants (those > 1 kg) and those with lower O2 requirements (FiO2 < 40 to 50%) may respond well to supplemental O2 alone.
Surfactant hastens recovery and decreases risk of pneumothorax, interstitial emphysema, intraventricular hemorrhage, bronchopulmonary dysplasia, and neonatal mortality in the hospital and at 1 year. However, neonates who receive surfactant for established RDS have an increased risk of apnea of prematurity. Options for surfactant replacement include beractant (a lipid bovine lung extract supplemented with proteins B and C, colfosceril palmitate, palmitic acid, and tripalmitin) 100 mg/kg q 6 hours prn up to 4 doses; poractant alfa (a modified porcine-derived minced lung extract containing

phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C) 200 mg/kg followed by up to 2 doses of 100 mg/kg 12 hours apart prn; and calfactant (a calf lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C) 105 mg/kg q 12 hours up to 3 doses prn. Lung compliance can improve rapidly after administration; the ventilator peak inspiratory pressure may need to be rapidly lowered to reduce risk of a pulmonary air leak. Other ventilator parameters (such as FiO2, rate) may also need to be reduced.

Prevention

When a fetus must be delivered between 24 and 34 weeks, giving 2 doses of betamethasone 12 mg 24 hours apart or 4 doses of dexamethasone 6 mg IV or IM q 12 hours to the mother at least 48 hours before delivery induces fetal surfactant production and reduces the risk of RDS or decreases its severity.

Transient Tachypnea

Transient tachypnea of the newborn is respiratory distress caused by delayed resorption of fetal lung fluid.

Transient tachypnea of the newborn affects premature infants, term infants delivered by cesarean section, and infants born with respiratory depression, all of whom have delayed clearance of fetal lung fluid. Maternal diabetes and asthma are also risk factors, for unknown reasons, and the disorder can occur in preterm infants with respiratory distress syndrome (RDS) and in term infants born through meconium-stained amniotic fluid. Rapid respirations, grunting, and retractions begin soon after delivery, and cyanosis may develop. Chest x-ray shows hyperinflated lungs with streaky perihilar markings, giving the appearance of a shaggy heart border while the periphery of the lungs is clear. Fluid is often seen in the lung fissures.

Recovery usually occurs within 2 to 3 days. Treatment is supportive and involves giving O2 by hood and monitoring ABGs or pulse oximetry. Rarely, extremely premature infants and/or those with neurologic depression at birth require continuous positive airway pressure and occasionally even mechanical ventilation.

Initial stabilization maneuvers include head positioning, suctioning of the mouth and nose, and tactile stimulation, followed as needed by supplemental O2, continuous positive airway pressure (CPAP), bag and mask ventilation, or mechanical ventilation. Infants who cannot be oxygenated by any of these means may require a full cardiac evaluation to exclude congenital heart disease and treatment with high frequency oscillatory ventilation, nitric oxide, and/or extracorporeal membrane oxygenation.

Oxygen: O2 may be given using a nasal cannula, face mask, or O2 hood, with O2 concentration set to achieve a PaO2 of 50 to 70 mm Hg in preterm infants and 50 to 80 mm Hg in term infants or an O2 saturation of 88 to 94% in preterm infants and 92 to 96% in term infants. Lower PaO2 in preterm infants provides almost full saturation of Hb, because fetal Hb has a higher affinity for O2; maintaining higher PaO2 may increase the risk of retinopathy of prematurity. No matter how O2 is delivered, it should be warmed (36 to 37° C) and humidified to prevent secretions from cooling and drying and to prevent bronchospasm. An umbilical artery catheter (UAC) is usually placed for sampling ABGs in neonates who require fraction of inspired O2 (FiO2) = 40%. If a UAC

cannot be placed, a percutaneous radial artery catheter can be used for continuous BP monitoring and blood sampling.

Neonates who are unresponsive to these maneuvers may require fluid administration to improve cardiac output and are candidates for CPAP ventilation or bag and mask ventilation (40 to 60 breaths/min). If the infant does not oxygenate with or requires prolonged bag and mask ventilation, endotracheal intubation with mechanical ventilation is indicated, although very immature infants (such as < 28 weeks gestation or < 1000 g) are typically begun on ventilatory support immediately after delivery so that they can receive preventive surfactant therapy. Because bacterial sepsis is a common cause of respiratory distress in neonates, it is common practice to draw blood cultures and administer antibiotics to neonates with high O2 requirements pending culture results.

Continuous positive airway pressure: CPAP delivers O2 at a positive pressure, usually 5 to 7 cm H2O, which keeps alveoli open and improves oxygenation by reducing the amount of blood shunted through atelectatic areas while the infant breathes spontaneously. CPAP can be provided using nasal prongs and various types of apparatus to provide the positive pressure; it can also be given using an endotracheal tube connected to a conventional ventilator with the rate set to zero. CPAP is indicated when FiO2 = 40% is required to maintain acceptable PaO2 (50 to 70 mm Hg) in infants with respiratory diseases that are of limited duration (such as diffuse atelectasis, mild respiratory distress syndrome, or lung edema). In these children, CPAP may preempt the need for positive pressure ventilation.

Mechanical ventilation: Endotracheal tubes 2.5 mm in diameter (the smallest) are typically used for infants < 1250 g; 3 mm for infants 1250 to 2500 g; and 3.5 mm for those > 2500 g. Intubation is safer if O2 is insufflated into the infant's airway during the procedure. Orotracheal intubation is preferred; the tube should be inserted such that the 7-cm mark is at the lip for infants who weigh 1 kg; 8 cm for 2 kg; and 9 cm for 3 kg. The endotracheal tube is properly placed when its tip can be palpated through the anterior tracheal wall at the suprasternal notch. It should be positioned about halfway between the clavicles and the carina on chest x-ray, coinciding roughly with vertebral level T2. If position or patency is in doubt, the tube should be removed and the infant supported by bag and mask ventilation until a new tube is inserted. Acute deterioration of the infant's condition (sudden changes in oxygenation, ABGs, BP, or perfusion) should trigger suspicion of changes in the position and/or patency of the tube.

Ventilators can be set to deliver fixed pressures or volumes; can provide assist control (A/C, in which the ventilator is triggered to deliver a full breath with each patient inspiration) or intermittent mandatory ventilation (IMV, in which the ventilator delivers a set number of breaths within a time period, and patients can take spontaneous breaths in between without triggering the ventilator); and can be normal or high frequency (delivering 400 to 900 breaths/min). No mode or type of ventilation is proven better than the other. Nevertheless, volume ventilators are considered useful for larger infants with varying pulmonary compliance or resistance (such as bronchopulmonary dysplasia), because delivering a set volume of gas with each breath ensures adequate ventilation; assist-control mode is often used for treatment of less severe pulmonary disease and in decreasing ventilator dependence while providing a small increase in airway pressure or a small volume of gas with each spontaneous breath; and high-frequency jet, oscillatory,

and flow-interrupter ventilators are used in extremely premature infants (< 28 weeks) and in some infants with air leaks, widespread atelectasis, or pulmonary edema.

Initial ventilator settings are estimated by judging the severity of respiratory impairment. Typical settings for an infant in moderate respiratory distress are FiO2 = 40%; inspiratory time (IT) = 0.4 sec; expiratory time = 1.1 sec; IMV or A/C rate = 40 breaths/min; peak inspiratory pressure (PIP) = 15 cm H2O for very low-birth-weight and up to 25 cm H2O for near-term infants; and positive end-expiratory pressure (PEEP) = 5 cm H2O. These settings are adjusted based on the infant's oxygenation, chest wall movement, breath sounds, and respiratory efforts along with the arterial or capillary blood gases.

PaCO2 is lowered by increasing the minute ventilation through an increase in tidal volume (increasing PIP or decreasing PEEP) or an increase in rate. The PaO2 is increased by increasing the FiO2 or increasing the mean airway pressure (increasing PIP, PEEP, or rate or prolonging IT). Patient-triggered ventilation is often used to synchronize the positive pressure ventilator breaths with the onset of the patient's own spontaneous respirations. This appears to shorten the time on a ventilator and may reduce barotrauma. A pressure-sensitive air-filled balloon attached to a pressure transducer (Graseby capsule) taped to the infant's abdomen just below the xiphoid process can detect the onset of diaphragmatic contraction, or a flow or temperature sensor placed at the endotracheal tube adapter can detect the onset of a spontaneous inhalation.

Ventilator pressures or volumes should be as low as possible to prevent barotrauma and bronchopulmonary dysplasia; an elevated PaCO2 is acceptable as long as pH remains = 7.25 (permissive hypercapnia). Likewise, a PaO2 as low as 40 mm Hg is acceptable if BP is normal and metabolic acidosis is not present.

Paralytics, sedation, and nitric oxide are adjunctive treatments used with mechanical ventilation in some patients. Paralytics such as vecuronium or pancuronium bromide 0.03 to 0.1 mg/kg IV q 1 to 2 hours as needed with pancuronium, (a test dose of 0.02 mg/kg is recommended in neonates) and sedatives such as fentanyl 1 to 4 µg/kg IV push q 2 to 4 hours or midazolam 0.05 to 0.15 mg/kg IV over 5 min q 2 to 4 hours may facilitate endotracheal intubation and can help stabilize infants whose movements and spontaneous breathing prevent optimal ventilation. These agents should be used selectively, however, because paralyzed infants may need greater ventilator support, which can increase barotrauma. Inhaled nitric oxide 5 to 20 ppm may be used for refractory hypoxemia when pulmonary vasoconstriction is a contributor to hypoxia, such as idiopathic pulmonary hypertension, pneumonia, or congenital diaphragmatic hernia, and may prevent the need for extracorporeal membrane oxygenation.

As respiratory status improves, the infant can be weaned from the ventilator by lowering the FiO2, inspiratory pressure, and rate. Continuous-flow positive pressure ventilators permit the infant to breathe spontaneously against PEEP while the ventilator rate is progressively slowed. After the rate has been reduced to 10 breaths/min, the infant usually tolerates extubation. The final steps in ventilator weaning involve extubation, possibly support with nasal (or nasopharyngeal) CPAP, and, finally, use of a hood or nasal cannula to provide humidified O2.

Very low-birth-weight infants may benefit from the addition of a methylxanthine during the weaning process. Initial dosing for aminophylline is 5 mg/kg IV loading followed by a maintenance dose of 1.5 to 3 mg/kg IV q 8 hours; for theophylline a 4 mg/kg loading dose is given orally or by gastric tube, followed by a maintenance dose of 2 mg/kg bid.

Doses of both agents are adjusted as needed to maintain a blood theophylline level of 7 to 12 µg/mL (39 to 67 µmol/L). Methylxanthines are CNS-mediated respiratory stimulants that increase ventilatory effort and may reduce apneic and bradycardic episodes that may interfere with successful weaning. Corticosteroids, once used routinely for weaning and treatment of chronic lung disease, are no longer recommended in premature infants because risks (such as impaired growth and neurodevelopmental delay) outweigh benefits. A possible exception is as a last resort in near-terminal illness, in which case parents should be fully informed of risks.

Complications of mechanical ventilation more common in neonates include asphyxia from endotracheal tube obstruction; ulceration, erosion, or narrowing of airway structures due to adjacent pressure; and bronchopulmonary dysplasia.

Extracorporeal membrane oxygenation (ECMO) is a form of cardiopulmonary bypass used for infants who cannot be adequately oxygenated or ventilated with conventional ventilators. Eligibility criteria vary by center, but in general, infants should have reversible disease (such as persistent pulmonary hypertension of the newborn, congenital diaphragmatic hernia, or overwhelming pneumonia) and have been on mechanical ventilation < 7 days. After systemic heparinization, blood is circulated through large-diameter catheters from the internal jugular vein into a membrane oxygenator, which serves as an artificial lung to remove CO2 and add O2; oxygenated blood is then circulated back to the internal jugular vein (venovenous ECMO) or to the carotid artery (venoarterial ECMO). Venoarterial ECMO is used when circulatory in addition to ventilatory support is needed (as in overwhelming sepsis). Flow rates can be adjusted to obtain desired O2 saturation and BP. ECMO is contraindicated in infants < 34 weeks and/or < 2 kg because of the risk of intraventricular hemorrhage with systemic heparinization. Complications include thromboembolism, air embolization, neurologic (stroke, seizures) and hematologic (hemolysis, neutropenia, thrombocytopenia) problems, and cholestatic jaundice.

Children with Chronic Health Conditions

Chronic health conditions (both chronic illnesses and chronic physical disabilities) are generally defined as those conditions that last > 12 months and are severe enough to create some limitations in usual activity. It has been estimated that chronic health conditions affect 10 to 30% of children, depending on the criteria. Examples of chronic illnesses include asthma, cystic fibrosis, congenital heart disease, diabetes mellitus, attention deficit hyperactivity disorder, and depression. Examples of chronic physical disabilities include meningomyelocele, hearing or visual impairments, cerebral palsy, and loss of limb function.

Children with chronic health conditions may experience limitations in some activities; frequent pain or discomfort; abnormal growth and development; and more hospitalizations, outpatient visits, and medical treatments. Those with severe disabilities may be unable at times to participate in school and activities.

A child's response to a chronic health condition largely depends on his developmental stage when the condition occurs. Children with chronic conditions that appear in infancy will respond differently than children who develop conditions during adolescence. School-aged children may be most affected by the inability to attend school and form relationships with peers. Adolescents may struggle with their inability to achieve

independence if they require assistance from parents and others for many of their daily needs; parents should encourage self-reliance within the adolescent's capability and avoid overprotection. Adolescents also find it particularly difficult to be viewed as different from their peers.

Health care practitioners can be advocates for appropriate hospital services for children with chronic health conditions. Age-appropriate playrooms can be set up and a school program initiated with the oversight of a trained child life specialist. Children can be encouraged to interact with peers whenever possible. All procedures and plans should be explained to the family and child whenever possible so the family knows what to expect during the hospitalization, thus relieving the anxiety that can be created by uncertainty.

For the families, having a child who has a chronic health condition can lead to loss of their hope for an "ideal child," neglected siblings, major expense and time commitment, confusion caused by conflicting systems of health care management, lost opportunities (such as family members providing primary care to the child and are therefore unable to return to work), and social isolation. Siblings may resent the extra attention the ill child receives. Such stress may cause family breakup, especially when there are preexisting difficulties with family function.

Conditions that affect the physical appearance of an infant (such as cleft lip and palate or hydrocephalus) can affect the bond between these children and family or caretakers. Once the diagnosis of abnormality is made, parents may react with shock, denial, anger, sadness or depression, guilt, and anxiety. These reactions may occur at any time in the child's development, and each parent may be at a different stage of acceptance, making communication between them difficult. Parents may express their anger at the health care practitioner, or their denial may cause them to seek many opinions about their child's condition.

Without coordination of services, care will be crisis-oriented. Some services will be duplicated, while others will be neglected. Care coordination requires knowledge of the child's condition, his family, and the community in which he functions.

All professionals who care for children with chronic health conditions must ensure that someone is coordinating care. Sometimes the coordinator can be the child's parent. However, the systems that must be negotiated are often so complex that even the most capable parents need assistance. Other possible coordinators include the primary care physician, the subspecialty program staff, the community health nurse, and staff of the third-party payer. Regardless of who coordinates services, the family and child must be partners in the process. In general, children from low-income families who have chronic conditions fare worse than others in part because of lack of access to health care and care coordination services. Some children with terminal illness benefit from hospice care.

Death and Dying

Families often have difficulty dealing with an ill and dying child; children who are trying to make sense of the death of a friend or family member may have particular difficulty. Most often the death of a child happens in the hospital or emergency department. Death can occur after a prolonged illness, such as cancer, or suddenly and unexpectedly, such as following injury or sudden infant death. The death of a child can be difficult for families to comprehend and accept. For parents, the death of a child means that they must give up their dreams and hopes for their child. The grieving process may also mean that they are

unable to attend to the needs of other family members, including other children. Health care practitioners can help in the process by being available to the family for consultation and to provide comfort whenever possible. In some circumstances, referral to specialists skilled in working with families who have experienced the death of a child is appropriate.
Many children experience the death of a loved one. The way the child perceives the event is affected by the child's developmental level. Preschool children may have limited understanding of death. Relating the event to previous experience with a beloved pet may be helpful. Older children may be able to understand the event more easily. Death should never be equated with going to sleep and never waking up because the child may become fearful of sleeping.

The Sick Neonate

Difficulties arise when a sick or premature infant must be taken away from the family after birth because of illness. The parents may not be able to see a critically ill infant during stabilization and may be separated from the infant because of transport to a different hospital. Some infants require prolonged separation from their families because of lengthy hospitalizations and treatments.
Many hospitals have recognized the importance of encouraging contact between infants and their families. In most places, parents are encouraged to visit, taking precautions to minimize the risk of spreading infections. Many hospitals have unlimited visiting hours for parents. Some hospitals have areas in which parents can stay for prolonged periods to be near their infants.
In most hospitals, parents are encouraged to interact with their sick infants as much as possible. No neonate, even one on a respirator, is too ill for the parents to see and touch. Parents are also encouraged to provide direct care for the infant as a way to get to know the infant and to prepare for taking the infant home. Some hospitals increase contact between parents and premature or sick infants by encouraging skin-to-skin contact; this may help parents feel more confident about taking care of their infants at home. Infants who experience skin-to-skin contact gain weight faster when compared with those who do not receive such care. Mothers can also provide breast milk directly or pumped to be given through a feeding tube.
When an infant has a birth defect, the parents should see the infant as soon after birth as possible, regardless of the medical condition. Otherwise, they may imagine the appearance and condition to be much worse than the reality. Intensive parental support is essential, with as many counseling sessions as are needed for parents to understand their infant's condition and recommended treatment and to accept the infant psychologically. To balance discussion of abnormalities, the physician should emphasize what is normal about the child and his potential.
When an infant dies without the parents having seen or touched him, the parents may later feel as though they never really had a child. Such parents have reported exaggerated feelings of emptiness and may develop prolonged depression because they could not mourn the loss of a “real infant.” Parents who have not been able to see or hold their infants during life will usually be helped in the long term if allowed to do so after the infant has died. In all cases, follow-up visits with the physician and a social worker are helpful to review the circumstances of the infant's illness and death, answer questions that often arise later, and assess and alleviate feelings of guilt. The physician can also

evaluate the parents' grieving process and provide appropriate guidance or a referral for more extensive support if necessary.

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