Chronic Respiratory Failure in Neonates

48

Educational Aims

- Describe and contrast the original and new forms of bronchopulmonary dysplasia
- Describe and discuss different definitions of bronchopulmonary dysplasia
- Present the issues and discuss some of the principles for the management of infants with bronchopulmonary dysplasia

48.1 Bronchopulmonary Dysplasia

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48.1.1 Clinical Presentation

The original publication on bronchopulmonary dysplasia (BPD) by Northway and collaborators described a group of preterm infants who after prolonged mechanical ventilation developed chronic respiratory failure and characteristic radiographic findings (Northway et al. 1967). The lung damage was attributed primarily to the use of aggressive positive-pressure ventilation and high inspired oxygen concentrations. Today, with the widespread use of antenatal corticosteroids and the use of postnatal surfactant and less aggressive mechanical ventilation, this severe form of BPD has been replaced by a milder form that presents in the more immature infants who frequently have only mild initial respiratory disease (Charafeddine et al. 1999; Parker et al. 1992; Rojas et al. 1995). Therefore, these infants are not exposed to the very high airway pressures or oxygen concentrations, the two main factors in the pathogenesis of the original form of BPD. This milder form of the disease has been described as "New BPD." This new presentation has created some inconsistencies and confusion in the definition and the diagnostic criteria of BPD (Bancalari et al. 2003).

The severe form of BPD was usually seen in infants who had severe respiratory failure from the time of birth and received aggressive ventilation and prolonged exposure to high inspired oxygen concentrations. These infants had characteristic changes in their chest radiographs and remained on ventilation and supplemental oxygen for long periods of time. This BPD was characterized by severe pulmonary damage that included emphysema, atelectasis, and fibrosis and marked epithelial squamous metaplasia and smooth muscle hypertrophy in the airways and in the pulmonary vasculature. These changes were associated with severe respiratory failure with airway obstruction, pulmonary hypertension, and cor pulmonale. This presentation is uncommon today, but there are still some infants who have

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this course and end up with severe respiratory failure, pulmonary hypertension, and marked alterations in their chest radiographs. The radiographs of infants with the milder forms of BPD show a more diffuse pattern reflecting loss of volume or increased lung fluid. Occasionally they also have dense areas of segmental or lobar atelectasis or pneumonic infiltrates but they do not show the areas of severe overinflation characteristic of the original BPD. These different clinical and radiographic manifestations reflect the different pathogenic process that underlines the new presentation of BPD.

This milder form of BPD seen more frequently today is characterized mainly by increased lung fluid, a diffuse inflammatory response, and by a striking decrease in alveolar septation and impaired vascular development (Abman 2000; Coalson et al. 1995; Husain et al. 1998; Jobe 1999; Margraf et al. 1991; Thibeault et al. 2003). These changes are more compatible with an arrest in lung development than with mechanical injury. It is not clear to what extent this arrest in lung development is secondary to the exposure of the premature lung to gas breathing versus the effects of overdistension and oxygen toxicity. Additional factors including incomplete lung development, inflammatory processes due to ante or postnatal infections, (Groneck et al. 1994; Groneck and Speer 1995; Hannaford et al. 1999; Pierce and Bancalari 1995; Watterberg et al. 1996; Yoon et al. 1997) and the exposure of the immature pulmonary vasculature to increased blood flow because of a persistent ductus arteriosus (Gonzalez et al. 1996; Marshall et al. 1999) are also implicated in the pathogenesis of the new BPD.

48.1.2 Definition

There has been a striking lack of uniformity in the diagnostic criteria for BPD among clinicians and in the literature. This explains some of the variation in the reported incidence of BPD among different centers. A major problem with most of the definitions of BPD is that they are based primarily on the need for supplemental oxygen that is used as a surrogate of the severity of the pulmonary damage. Supplemental oxygen is an important part in the management of these infants but in addition, it is implicated in the pathogenesis of BPD. Because there is no clear evidence on what the optimal arterial oxygen levels for these infants are, the indications for supplemental oxygen vary significantly from center to center. In addition, the need for supplemental oxygen can be influenced by altitude, drugs such as steroids or respiratory stimulants, and by the use of other forms of respiratory support such as nasal CPAP or mechanical ventilation. The proposed criteria to define BPD suggested in a National Institutes of Health (NIH) sponsored workshop in 1979 included a continued oxygen dependency *during the first 28 days* plus compatible clinical and radiographic changes (Bancalari et al. 1979). While these criteria were appropriate for the classic presentation of BPD, most infants today have intervals during the first days after birth when they do not require supplemental oxygen. Therefore, this criterion is not appropriate for the "New BPD." To address this issue, some authors and clinicians have simplified this criterion and diagnose BPD in infants who are oxygen dependent "at" day 28. Although this simplified approach may work in most cases, it is possible that some infants who do not have significant lung disease may require supplemental oxygen only around day 28 because of acute conditions. This results in the erroneous labeling of those infants as BPD when in reality they do not have chronic lung damage. It is also possible that a premature infant may be on room air on day 28 and subsequently develop chronic lung damage and prolonged oxygen dependency. In order to avoid these problems, it is essential to include other indicators such as persistent radiographic changes and a minimal duration of oxygen therapy to reflect the chronicity of pulmonary damage.

The variation in the incidence of BPD when the different diagnostic criteria are applied to the same population of premature infants is illustrated in Fig. 48.1. Approximately one half of the infants who require oxygen *at* day 28 or for more than 28 days have a need for oxygen that persists to 36

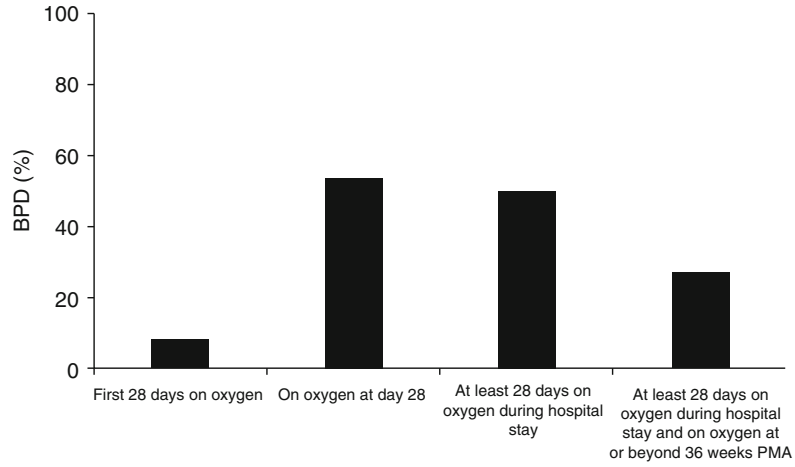

Fig. 48.1 Incidence of BPD using different definitions. Very few infants require oxygen continuously during the first 28 days after birth. In contrast, large proportions need oxygen at day 28 and for at least 28 days during their hospitalization. Only half of the latter group have a persistent need for oxygen at or beyond 36 weeks PMA (Data from 673 infants born at JMH, years 2004–2008; gestational age, 23–30 weeks; and alive at 36 weeks PMA)

weeks postmenstrual age (36 weeks PMA). Only a small fraction of infants from this cohort have an uninterrupted need for oxygen during the first 4 weeks. This accounts for the very low BPD incidence when using this definition. Although small in number, most infants who continuously require oxygen during the first 28 days go on to become oxygen dependent at 36 weeks PMA, very much like in the classic form of BPD. These infants, however, account only for a minority of infants who develop BPD today. Presently, most infants born ≤30 weeks of gestation do not have continuous oxygen need during the first month of life but still many of them go on to develop BPD. This presentation accounts for most of the BPD cases today.

In order to circumvent some of these problems, and to focus on the more severely afflicted infants, it has been proposed to use the need for supplemental oxygen *at* 36 weeks PMA as a better criterion for BPD (Shennan et al. 1988). Because this is a stricter criterion than the 28 days oxygen supplementation, it identifies a group of infants with more severe lung damage and therefore better predicts poor long-term outcome. The criterion of oxygen dependency at 36 weeks PMA requires for an infant born at 24 weeks of gestation to be on oxygen for 12 weeks, while an infant born at 32 weeks of gestation would be labeled as BPD if he or she requires oxygen for only 4 weeks after birth.

Figure 48.2 shows the incidence of BPD among infants born at Jackson Memorial Hospital (JMH) within different birth weight and gestational age strata according to the criteria of oxygen dependency for ≥28 days in combination with oxygen need at 36 weeks PMA.

In order to address the inconsistencies in the diagnostic criteria of BPD and to come up with a better definition a workshop was organized by the NIH in 2000 (Jobe and Bancalari 2001). As a result of this effort, the recommendation was to use oxygen need for ≥28 days and at 36 weeks PMA to identify different severity of BPD and also to use the oxygen concentration at 36 weeks PMA to further define the severity of lung injury. It was also agreed that a minimum of 28 days of supplemental oxygen was necessary to make the diagnosis of BPD (Table 48.1). These recommendations solve many of the problems with previous criteria but it still has the limitations of using 36 weeks PMA that were discussed earlier.

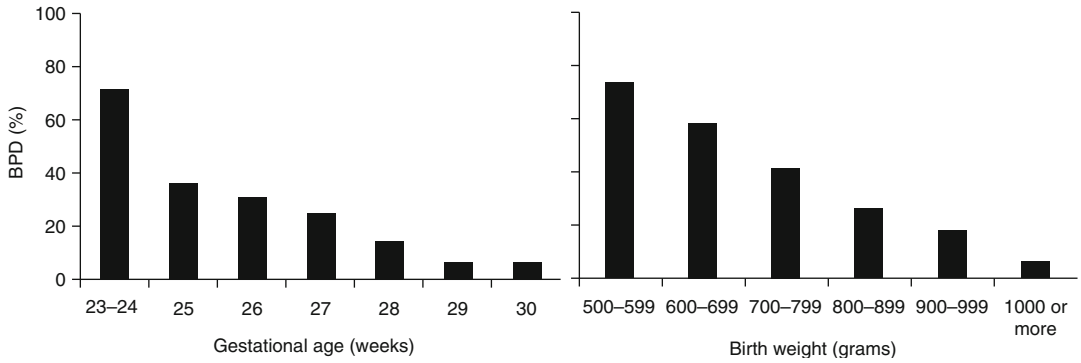

Fig. 48.2 Incidence of BPD by gestational age and birth weight. BPD defined as oxygen need for ≥28 days and at or beyond 36 weeks PMA (Data from 673 infants born at JMH during years 2004–2008; gestational age, 23–30 weeks; and alive at 36 weeks PMA)

Table 48.1 NIH consensus definition of BPD

Gestational age	<32 weeks	≥32 weeks
Time point of assessment	36 weeks PMA or discharge to home, whichever comes first	>28 days but <56 days postnatal age or discharge to home, whichever comes first
Treatment with oxygen >21 % for at least 28 days plus		
Mild BPD	Breathing room air at 36 weeks PMA or discharge, whichever comes first	Breathing room air by 56 days postnatal age or discharge, whichever comes first
Moderate BPD	Need[a] for <30 % at 36 weeks PMA or discharge, whichever comes first	Need[a] for <30 % at 56 days postnatal age or discharge, whichever comes first
Severe BPD	Need[a] for ≥30 % oxygen and/or positive pressure (PPV or NCPAP) at 36 weeks PMA or discharge, whichever comes first	Need[a] for ≥30 % oxygen and/or positive pressure (PPV or NCPAP) at 56 days postnatal age or discharge, whichever comes first

Adapted from Jobe and Bancalari (2001)

BPD usually develops in neonates being treated with oxygen and positive-pressure ventilation for respiratory failure, most commonly respiratory distress syndrome

Persistence of clinical features of respiratory disease (tachypnea, retractions, rales) is considered common to the broad description of BPD and has not been included in the diagnostic criteria describing the severity of BPD. Infants treated with oxygen >21 % and/or positive pressure for non-respiratory disease (e.g., central apnea or diaphragmatic paralysis) do not have BPD unless they also develop parenchymal lung disease and exhibit clinical features of respiratory distress. A day of treatment with oxygen >21 % means that the infant received oxygen >21 % for more than 12 h on that day. Treatment with oxygen >21 % and/or positive pressure at 36 weeks PMA, or at 56 days postnatal age or discharge, should not reflect an "acute" event but should rather reflect the infant's usual daily therapy for several days preceding and following 36 weeks PMA, 56 days postnatal age, or discharge

Definition of abbreviations: *BPD* bronchopulmonary dysplasia, *NCPAP* nasal continuous positive airway pressure, *PMA* postmenstrual age, *PPV* positive-pressure ventilation

[a]A physiologic test confirming that the oxygen requirement at the assessment time point remains to be defined. This assessment may include a pulse oximetry saturation range

An important factor that is often ignored in the literature is the detailed and clear description of the base population in which the incidence of BPD is being reported. For example, reports that include only ventilated infants would have a higher rate of BPD than studies that include all live-born infants. Therefore, calculations of risk reduction and number needed to treat cannot be extended to the general population of infants even within the same range of birth weight or gestation. Benchmarking comparisons should also account for differences in the base population in regard to mortality. The reported incidence per total admissions may be much lower than the incidence among premature infant surviving the neonatal period, at 36 weeks PMA or

at discharge. Inaccurate estimation of GA can also affect the calculated BPD incidence in a population where a consistent over- or underestimation of GA occurs.

Data combining results from competing outcomes are frequently found in the literature. For example, BPD or death, or survival without BPD is frequently reported as a combined outcome. This is done because BPD cannot be diagnosed in infants who die before the time point when diagnosis is made but it is essential that the outcomes are also reported separately. Regardless of the beneficial effect of a given intervention to prevent BPD, an increase in mortality or other serious complication beyond what is expected would nullify its use.

48.1.2.1 Prediction of Outcome

One of the main objectives of a diagnostic criterion for BPD is to predict the long-term pulmonary and neurodevelopmental outcome of preterm infants. The predictive value of the oxygen for ≥28 days, oxygen at 36 weeks PMA, and the NIH consensus definition was evaluated in a large cohort of infants from the National Institute of Child Health and Human Development (NICHD) neonatal network at 18–22 months corrected age (Ehrenkranz et al. 2005). The more liberal 28 days of oxygen criterion is more sensitive in detecting post-discharge respiratory complications but has poor specificity. Stricter definitions that use oxygen dependency at 36 weeks PMA and the more severe cases of need for ≥30 % oxygen are clearly more specific but at a cost of not classifying as BPD some infants that may later need additional respiratory care. These findings are similar to those reported from data obtained in the Trial of Indomethacin Prophylaxis in Preterms (TIPP) where oxygen need after day 28 was shown to be a more sensitive test (although less specific) than oxygen beyond 36 weeks PMA in predicting poor long-term pulmonary outcome (Davis et al. 2002). These results emphasize the importance of considering the respiratory evolution during the neonatal period in addition to the need for supplemental oxygen at a given point.

The BPD definition of oxygen at 36 weeks PMA is slightly more sensitive in predicting mental and psychomotor developmental impairment but the definition of severe BPD (oxygen ≥30 % at 36 weeks PMA) increases the predictive sensitivity. A recent multivariate analysis indicated an increased risk of poor neurologic outcome among infants deemed to have BPD based on their oxygen need at 36 weeks PMA (Schmidt et al. 2003). Interpretation of these findings however is difficult because of the confounding effects of some risk factors for BPD as they may also be independently associated with poor neurologic outcome.

48.1.2.2 Physiologic Definition

In order to reduce the influence of different strategies for oxygen supplementation on the reported incidence of BPD (Ellsbury et al. 2002), Walsh and collaborators have devised a physiologic test to standardize the need for oxygen at the time when BPD is being diagnosed (Walsh et al. 2004). To accomplish this, infants with moderate dependency on oxygen at 36 weeks PMA (<30 % oxygen) are challenged with room air breathing following a set weaning protocol to determine whether the supplemental oxygen is in fact needed. Although this test was applied in only 14 % of their entire cohort, it reduced the incidence of BPD from 35 to 25 % compared to the clinically prescribed oxygen supplementation. The use of this test clearly demonstrated that part of the reported variation in incidence of BPD among centers participating in the NICHD neonatal network was due to differences in clinical practice with respect to oxygen therapy. While the overall reduction in BPD incidence was 10 %, it ranged from 0 to 44 % in different centers demonstrating the wide variation in the use of supplemental oxygen. Over 40 % of the infants tested passed the challenge test and did not need the clinically prescribed oxygen.

Application of any diagnostic criteria also needs to consider other forms of respiratory support such as CPAP or IPPV. These interventions are included in the NIH consensus definition and can significantly influence the results of a diagnostic assessment and its relevance on outcome. However, they are rarely considered in the literature. Most definitions of BPD use supplemental

oxygen as the main parameter to define chronic lung damage. This is associated with a number of limitations. Whether a small preterm infant remains on supplemental oxygen for 28 days or until 36 weeks PMA may not be very important because most of these infants remain hospitalized past the 36 weeks PMA for reasons other than their oxygen requirement. Therefore, the duration of oxygen therapy is not very important unless it predicts poor long-term outcome. Unfortunately, the reported predictive value of oxygen need in terms of long-term outcome has not been very strong.

48.1.3 General Management of the Infant with BPD

The management of the infant with BPD is aimed at preserving adequate gas exchange and at the same time preventing the progression of the disease by reducing factors that predispose to lung damage. The difficulty in the management of these infants is that many of the therapies used to maintain gas exchange such as supplemental oxygen and mechanical ventilation are major contributors in the pathogenesis of this disease.

48.1.3.1 Fluid Management and Diuretics

Infants with BPD frequently accumulate excessive fluid in their lungs and tolerate even normal amounts of fluid intake poorly. The pulmonary edema contributes to the respiratory failure and ventilator dependency. For this reason, water and salt intake should be limited to the minimum required to provide the necessary calories for their metabolic needs. When evidence of pulmonary edema persists despite fluid restriction, diuretic therapy can be used. The use of diuretics in infants with BPD can be associated with an improvement in lung compliance and decrease in resistance, but the effect on gas exchange is less consistent. Chronic diuretic therapy can be associated with serious side effects that include hypokalemia, hyponatremia, metabolic alkalosis, hypercalciuria with nephrocalcinosis, hypochloremia, and hearing loss. Some of these side effects may be reduced by using an alternate-day therapy with furosemide.

Because of the side effects and the lack of evidence that prolonged use of diuretics changes the long-term outcome in infants with BPD (Kao et al. 1994), this therapy should be left only for acute episodes of deterioration associated with evidence of pulmonary edema. Distal tubular diuretics such as thiazides and spironolactones are also used in infants with BPD but the improvement in lung function with these diuretics is less consistent than with proximal loop diuretics. However, the side effects such as nephrocalcinosis and hearing loss may be less prevalent than with furosemide and for this reason, these diuretics are used in infants with established BPD who receive diuretic therapy for prolonged periods of time.

48.1.3.2 Bronchodilators

Infants with severe BPD may have airway smooth muscle hypertrophy and airway hyperreactivity. Hypoxia can increase airway resistance in these patients, and therefore, maintenance of adequate oxygenation is important to avoid bronchoconstriction. Inhaled bronchodilators including β agonists, such as isoproterenol, salbutamol, metaproterenol, and isoetharine, and anticholinergic agents, such as atropine and ipratropium bromide, have been used to reduce airway resistance in infants with BPD. Their effect is usually short-lived and many of these drugs have cardiovascular side effects such as tachycardia, hypertension, and possible arrhythmias so they should be used with caution and only when indicated.

Methylxanthines (aminophylline and caffeine) also have been shown to reduce airway resistance in these infants. These drugs have other potential beneficial effects, such as respiratory stimulation and mild diuretic effect, and aminophylline may also improve respiratory muscle contractility. These drugs must also be used with caution because of their multiple side effects.

There is no evidence that prolonged use of bronchodilators changes the course of infants with BPD and for this reason it is advisable to limit their use to episodes of acute exacerbation of airway obstruction.

48.1.3.3 Anti-inflammatory Drugs/ Corticosteroids

Inflammation is an important factor in the pathogenesis of BPD, and therefore, anti-inflammatory agents have been used during the early stages of the disease to ameliorate its progression. Several studies have shown rapid improvement in lung function after the administration of steroids, facilitating weaning from the ventilator and a reduction in BPD incidence when compared with controls who received placebo. The possible mechanisms for the beneficial effect of steroids include enhanced production of surfactant and antioxidant enzymes, decreased bronchospasm, decreased pulmonary and bronchial edema and fibrosis, improved vitamin A status, and decreased responses of inflammatory cells and mediators in the injured lung. Potential complications of prolonged steroid therapy include masking the signs of infection, arterial hypertension, hyperglycemia, increased proteolysis, adrenocortical suppression, somatic and lung growth suppression, and hypertrophic myocardiopathy. In addition, long-term follow-up studies suggest that infants who received early or prolonged steroid therapy have worse neurologic outcome, including an increased incidence of cerebral palsy (Committee on Fetus and Newborn 2002; O'Shea et al. 1999; Yeh et al. 1998). Because of the seriousness of these complications, specifically when systemic steroids are used early after birth, and until more information on safety is available, it is recommended to use systemic steroids after the first 2 weeks of life and only in infants who show evidence of severe and progressive pulmonary damage and remain oxygen and ventilator dependent. The dose and duration of therapy should be limited to the minimum necessary to achieve the desired effects, usually 4–7 days and the potential side effects should be discussed with the family.

Steroids have also been administered by nebulization to minimize the systemic side effects, but data on effectiveness and side effects are not conclusive enough to recommend their routine use (Cole et al. 1999; Groneck et al. 1999).

48.1.3.4 Pulmonary Vasodilators

Pulmonary hypertension is a common and serious complication in infants with severe BPD. Because pulmonary vascular resistance is extremely sensitive to changes in alveolar PO_2, it is important to maintain normal oxygenation at all times.

In infants with severe pulmonary hypertension and cor pulmonale, the calcium channel blocker nifedipine has been shown to decrease pulmonary vascular resistance but this drug is also a systemic vasodilator and can produce a depression of myocardial contractility. Its safety and long-term efficacy in these infants has not been established.

Inhaled nitric oxide is also administered to infants with BPD in an attempt to improve ventilation-perfusion matching, reduce pulmonary vascular resistance, and reduce inflammation. Although NO has been shown to improve oxygenation (Banks et al. 1999), there is no clear evidence that this therapy improves long-term outcome, hence should still be considered experimental. Phosphodiesterase inhibitors (sildenafil), prostacyclin (epoprostenol), and ET-1 antagonists are potent pulmonary vasodilators that have been used to treat pulmonary hypertension but there is not enough information on their safety and efficacy to recommend their routine use in infants with BPD.

48.1.3.5 Nutrition

Adequate nutrition is an important aspect of care for the infant with BPD. Malnutrition can delay the development of new alveoli and can decrease muscle strength, making successful weaning from mechanical ventilation more difficult. Malnutrition can also make infants more prone to infection and oxygen toxicity. High-calorie formulas and supplements of protein, calcium, phosphorus, and zinc are used to maximize the intake of calories while restricting fluid intake to prevent congestive heart failure and pulmonary edema (Brunton et al. 1998). When enteral nutrition is not possible, parenteral alimentation must be used until the gastrointestinal tract again becomes functional. Bone demineralization is frequently observed in infants with BPD as a

manifestation of rickets secondary to deficiency of calcium or vitamin D and excessive calciuria resulting from chronic diuretic therapy. Administration of extra calcium and vitamin D is necessary to prevent rickets in these infants. Infants who receive exclusively parenteral nutrition for prolonged periods are more susceptible to developing deficiency of specific nutrients, such as vitamins A and E, and trace elements, such as iron, copper, zinc, and selenium, all of which play a role in antioxidant function, protection against infection, and lung repair. Decreased caloric intake potentiates oxygen-induced lung damage and interferes with cell multiplication and lung growth. Deficiency of sulfur-containing amino acids may also affect lung levels of glutathione, a potent antioxidant. Infants with severe BPD have been shown to have lower plasma levels of vitamin A and a deficiency of this vitamin in experimental animals results in loss of ciliated epithelium and squamous metaplasia in the airways, changes similar to those observed in severe BPD. Clinical studies in preterm infants with prolonged respiratory failure suggest that maintenance of normal plasma levels of vitamin A reduces the incidence and severity of BPD (Shenai 1999; Shenai et al. 1987; Tyson et al. 1999). The use of supplemental vitamin A by intramuscular injection to maintain normal serum levels is effective, but its use is not widespread because of the relatively small effect on BPD and the reluctance to give repeated intramuscular injections to very small infants.

Gastroesophageal reflux is common in infants with BPD and it may contribute to malnutrition and lung damage. When severe reflux is documented, aggressive anti-reflux management, including surgery, may be indicated to alleviate the respiratory symptoms.

48.1.4 Respiratory Care in the Infant with BPD

48.1.4.1 Oxygen Therapy

While it is important to reduce the use of oxygen as much as possible to avoid toxicity, it is also important to ensure adequate tissue oxygenation and to avoid the pulmonary hypertension and cor pulmonale that can result from chronic hypoxemia. There is no conclusive information to recommend a specific range of oxygen saturation in these infants, but there is clear evidence that oxygen saturations above 95 % and PaO_2 above 70 mmHg are associated with higher incidence of ROP and worse respiratory outcome (Askie et al. 2003; Bancalari et al. 1987; Tin 2004). Because of this, it is recommended to maintain the saturations between 90 and 95 % and the PaO_2 between 50 and 70 mmHg to minimize the detrimental effects of hypo- and hyperoxemia. In many cases, oxygen therapy is required for several months or even years and many of these patients are discharged with oxygen therapy at home.

Adequacy of gas exchange is monitored by determining arterial blood gas levels at intervals dictated by the child's clinical condition. Blood gas determinations obtained by arterial puncture may not be reliable because the infant usually responds to pain with crying or apnea. Transcutaneous PO_2 electrodes are also inaccurate in these infants because they frequently underestimate the true PaO_2. Pulse oximeters offer the most reliable estimate of arterial oxygenation and have the advantage of simplicity of usage and the possibility of assessing continuous oxygenation.

Because of the increased metabolic demands in infants with BPD, associated in severe cases with low arterial oxygen tension, it is important to maintain a relatively normal blood hemoglobin concentration.

48.1.4.2 Mechanical Ventilation

Mechanical ventilation is one of the main factors associated with the pathogenesis of BPD, and therefore, it is essential to use the lower settings necessary to maintain gas exchange and reduce the duration of mechanical support to a minimum. In order to minimize overdistension and injury the peak airway pressure should be the minimal necessary to obtain adequate tidal volumes. Inspiratory times between 0.3 to 0.5 s with flow rates between 5 and 10 l/min are used because shorter inspiratory times and higher flow rates may exaggerate the maldistribution of the

inspired gas. Longer inspiratory times may increase the risk of overdistension and alveolar rupture and negative cardiovascular side effects. End-expiratory pressure is adjusted between 4 and 8 cm H_2O to maintain lung volume so that the minimum oxygen concentration necessary to keep oxygen saturation above 90 % (PaO_2 above 50 mmHg) is used. In infants with severe airway obstruction, especially those with bronchomalacia, the use of higher PEEP levels of up to 10 cm H_2O may be necessary to avoid expiratory airway collapse and preserve alveolar ventilation. The duration of mechanical ventilation must be limited as much as possible to reduce the risk of further ventilator-induced lung injury and infection. Weaning these patients from mechanical ventilation is very difficult and must be accomplished gradually. When the patient is able to maintain an acceptable PaO_2 and $PaCO_2$ with low peak inspiratory pressures (lower than 15–20 cm H_2O) and a FiO_2 lower than 0.3–0.4, the ventilator rate is gradually reduced to allow the infant to perform an increasing proportion of the respiratory work. The use of patient-triggered ventilation and pressure support of the spontaneous breaths can accelerate the process of weaning and reduce the total duration of mechanical ventilation (Greenough 2001; Reyes et al. 2006).

During the weaning process, the need to increase the FiO_2 to maintain oxygen saturation within an acceptable range is common. The $PaCO_2$ may also rise to values in the 50–60 mmHg or higher. As long as the pH is within acceptable limits, certain degree of hypercapnia must be tolerated in order to wean these patients from the ventilator. In small infants with poor central respiratory activity, respiratory stimulants such as aminophylline or caffeine are used during the weaning phase. When the patient is able to maintain acceptable blood gas levels for several hours on low ventilator rate (10–15 breaths/min), extubation can be attempted. During the days that follow extubation, it is important to provide chest physiotherapy to prevent airway obstruction and lung collapse caused by retained secretions. In smaller infants with poor respiratory drive and frequent apneic episodes, the use of nasal CPAP or nasal IMV can stabilize respiratory function and reduce the need for reinstitution of mechanical ventilation. Despite all these steps to facilitate weaning, it is not uncommon that small infants fail extubation and need to be placed back on mechanical ventilation. In infants with severe BPD it sometimes becomes necessary to perform a tracheostomy to facilitate their respiratory care and be able to wean them from mechanical ventilation.

Essentials to Remember

- The severe forms of BPD seen before are relatively uncommon today. Instead many premature infants present with milder forms of BPD that result from a different multifactorial pathogenic process.
- Definitions of BPD are primarily aimed at standardizing terminology and providing a prognostic insight into the respiratory condition in childhood. Use of standardized definitions is key for intra- and inter-center benchmarking purposes.
- Strategies used in the care of infants with BPD should focus in breaking the cycle of dependency for respiratory support and injury that results from this support.

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