Care of Infants with Bronchopulmonary Dysplasia

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Learning Objectives

- Define bronchopulmonary dysplasia (BPD).
- List the risk factors for BPD.
- Identify current strategies to prevent BPD.
- Describe current management of BPD.
- Discuss implications for the practicing pediatrician.
Definition

- Originally defined by Northway
  - Clinical, radiological, and pathologic changes
  - Prolonged mechanical ventilation
  - High inspiratory oxygen levels
  - Subsequently, BPD defined by clinical characteristics present at 1 month in association with radiological changes

Births in the United States

- Number of births: 3,932,181
- Birth rate: 12.4 per 1000 population
- Percent born low birthweight: 8%
- Percent born preterm (<37 weeks gestation): 11.4%

# National Institutes of Health Consensus Definition of BPD

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>&lt;32 weeks</th>
<th>&gt;32 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time at assessment</td>
<td>36 weeks PMA or discharge to home, whichever comes first</td>
<td>&gt;28 days but &lt;56 days postnatal age or discharge to home, whichever comes first</td>
</tr>
</tbody>
</table>

**Treatment with oxygen >21% for at least 28 days PLUS**

<table>
<thead>
<tr>
<th>Mild BPD</th>
<th>Breathing room air at 36 weeks PMA or discharge, whichever comes first</th>
<th>Breathing room air by 56 days postnatal age or discharge, whichever comes first</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate BPD</td>
<td>Need* for &lt;30% oxygen and/or positive pressure (PPV or NCPAP) at 36 weeks PMA or discharge, whichever comes first</td>
<td>Need* for &lt;30% oxygen and/or positive pressure (PPV or NCPAP) at 56 days postnatal age or discharge, whichever comes first</td>
</tr>
<tr>
<td>Severe BPD</td>
<td>Need* for &gt;30% oxygen and/or positive pressure (PPV or NCPAP) at 36 weeks PMA or discharge, whichever comes first</td>
<td>Need* for &gt;30% oxygen and/or positive pressure (PPV or NCPAP) at 56 days postnatal age or discharge, whichever comes first</td>
</tr>
</tbody>
</table>

Abbreviations: BPD, bronchopulmonary dysplasia; NCPAP, nasal continuous positive airway pressure; PMA, postmenstrual age; PPV, positive pressure ventilation.

*Physiologic test of oxygen requirement required.

Physiologic Test for Diagnosis of BPD

- Infants receiving <30% O2 or >30% O2 with oxygen saturations >96%
  - O2 progressively weaned to 21% (room air)
  - No BPD if saturations remain >90% in room air for 30 minutes
  - Reduces the incidence of the diagnosis of BPD

## Incidence of BPD

<table>
<thead>
<tr>
<th>Birthweight (g)</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>501-750</td>
<td>46</td>
</tr>
<tr>
<td>751-1000</td>
<td>33</td>
</tr>
<tr>
<td>1001-1250</td>
<td>14</td>
</tr>
<tr>
<td>1251-1500</td>
<td>6</td>
</tr>
</tbody>
</table>
Lung development – Pathology

Risk Factors for BPD

- Genetic predisposition, male gender, Caucasian
- Peripartum infection
- Mechanical ventilation
- Fluid management
  - Excessive fluids in the first few days
- Patent ductus arteriosus (PDA)
  - Left to right symptomatic PDA
Role of Mechanical Ventilation

- Major role
  - Barotrauma, volutrauma
  - Use of excessive inflation pressures
  - Not allowing permissive hypercapnea (as long as pH is satisfactory)
  - Even a small number of inflations (for example, bagging) and use of high oxygen concentrations soon after birth can affect surfactant deficient lungs: implications for delivery room management
Risk Factors for BPD

Other Factors

- Oxygen toxicity (use current targeted oxygen saturations)
- Nutrient deficiencies
  - Vitamin A
- Immature antioxidant systems
  - Superoxide dismutase
  - Glutathione peroxidase
- Infections, inflammation
  - Sepsis: bacterial and fungal
Symptoms of BPD

- Rapid, shallow breathing
- Continued need for oxygen or ventilatory support
- Peripheral cyanosis
- Intercostal retractions
- Use of accessory muscles of respiration
Other Issues

- Trouble feeding
- Increased work of breathing
- Delayed growth
- Development of pulmonary hypertension
- Cor pulmonale
Representative X-Ray

Diagnosis

- Premature infants, especially those <30 weeks, and still requiring oxygen therapy at original due date
- Mild, moderate, or severe
- Chest x-ray findings: infiltrates/atelectasis
- Blood gas: low O2, high pCO2, low (initially) and later normal pH with compensation
Treatment Goals

- Prenatal steroids to reduce respiratory distress syndrome
- Reduce lung injury by minimizing ventilatory support
- Appropriate oxygen saturation targets
- Appropriate nutrition to promote growth and prevent extra uterine growth failure/restriction
- Aggressive treatment of infections
Treatment Goals: Drugs that Prevent BPD

- **Vitamin A:** Intramuscular vitamin A* (5000 IU, IM, 3 x week, over 4 weeks)  
  Relative risk of death or BPD at 36 weeks PMA: 0.91, 95% CI 0.83, 1.00  
  Relative risk of reducing death or O2 requirement at 1 month of age: 0.93, 95% CI 0.88, 0.99  
  Oxygen requirement at 36 weeks, 0.87, 95% CI 0.77-0.99  
- **Meta-analysis** confirmed the reduction of BPD with vitamin A

*Would be considered a therapeutic dose.

Treatment Goals

- **Caffeine citrate**
  - Caffeine for apnea trial: 2006 infants treated for apnea with primary outcome of death, cerebral palsy, cognitive delay, deafness, or blindness at 18-21 months corrected age
  - Secondary analysis: BPD, retinopathy of prematurity, and necrotizing enterocolitis
  - Infants treated with caffeine had lower risk of BPD than placebo: relative risk 0.63, 95% CI 0.52,0.73
  - Caffeine citrate use in premature infants resulted in a significant reduction in BPD with few side effects.

Treatment Goals: Other Drugs

- Late steroids: may have a role
- Inositol
- Azithromycin/Clarithromycin (eradication of Ureaplasma urealyticum) reduced BPD: does not have FDA-labeled instructions
- Inhaled nitric oxide
- Other

Nutrition and Other

- Total energy needs may be increased: need to provide energy and protein to satisfy growth requirements
- Fluid restriction often required, necessitating calorically dense feedings
- Diuretics: electrolyte imbalance; little evidence that they improve outcome

Prevention

- Vitamin A
  - Involved in regulation of lung development and repair
  - Prophylactic vitamin A decreases incidence of BPD
  - Need to treat ~14-15 infants to have 1 infant survive without BPD

- Caffeine
  - Reduces BPD; mechanism not known
Prevention

- **Corticosteroids**
  
  - High-dose prolonged therapy with dexamethasone used to be standard therapy for BPD.
  
  - Increase in adverse neurodevelopment
  
  - AAP policy statement recommends limited use under “exceptional clinical circumstances.”\(^a\)
  
  - When given after 14 days of life, corticosteroids may have short- and long-term benefits that need to be confirmed in larger trials.

BPD and the Pediatrician

- Abnormal lung function through school age and beyond
- More respiratory symptoms, asthma treatment
- Pulmonary and systemic hypertension, cor pulmonale
BPD and the Pediatrician

- Poor neurodevelopmental outcome
  - Language delays
  - Fine and gross motor impairment

- Other
  - Feeding difficulty
  - Gastroesophageal reflux
  - Increased energy expenditure
  - Growth failure
Outpatient Management

- Home oxygen to maintain saturations >90%*
- Home mechanical ventilation*
- Nutritional support
  - Appropriate fortification of breastmilk
  - Appropriate formulas
- Routine immunizations, including against influenza
- Respiratory syncytial virus prophylaxis by AAP criteria
- Developmental follow up and intervention*

*Use of a multidisciplinary group or consultation suggested.
Approach to Caring for an Infant with BPD

Conclusions

- BPD is a known complication in premature infants with initial lung disease.
- Incidence increases with decreasing gestational age.
- Prenatal steroids reduce the incidence of RDS; effects on incidence of BPD are not shown.
- Appropriate resuscitation, judicious use of positive pressure ventilation, and targeted oxygen saturations reduce the incidence of BPD.
Conclusions

- Vitamin A has a preventative role.
- Early and sustained appropriate nutrition to support growth may reduce BPD.
- Caffeine therapy in high-risk infants has been shown to reduce BPD.
- Post-natal growth failure is common in infants with BPD.
- Post-discharge attention to nutrition can ameliorate the growth failure.
Conclusions

- A multidisciplinary team approach, including a nutritionist, cardiology/pulmonary specialists, speech therapist, and developmentalists, is recommended.
- Adjunctive therapy should be tailored to individual cases: postnatal steroids, diuretics, and bronchodilators.
- Complications, including pulmonary artery and systemic hypertension, should be addressed.
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