Slide 1

Bronchopulmonary Dysplasia
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Slide 2

BPD - Objectives
1. Review the definition of bronchopulmonary dysplasia (BPD).
2. Evaluate different treatment modalities for infants with BPD.
3. Recognize some long term issues for patients with BPD.

Slide 3

BPD - Diagnosis
- Oxygen requirement at 28 postnatal days
- Oxygen requirement at 36 weeks postmenstrual age
- Based on gestational age and severity of disease
  – 2001 National Institute of Child Health and Human Development

References 2 and 11
Slide 5

BPD - Incidence

- Over time the changes in incidence are unclear
  - Decreased mortality and increased BPD
  - 25% for VLBW (<1500 grams)
- Birth weight in grams and incidence
  - 1251-1500 6%
  - 1001-1240 14%
  - 751-1000 33%
  - 501-750 46%

Reference 2

Slide 6

BPD - Pathogenesis

- Three key factors
  - Lung immaturity
  - Acute lung injury
  - Inadequate repair of the initial lung injury

Reference 8
Slide 7

**BPD - Pathogenesis**

- Prematurity
- Mechanical ventilation
- Oxygen toxicity
- Infection
- Fluid overload/PDA

Reference 2

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Slide 8

**BPD - Pathogenesis**

- Genetic factors
- Late surfactant deficiency
- Bombesin-like peptides

Reference 2

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Slide 9

**BPD - Pathogenesis**

- Prematurity
  - Poor airway support structures
  - Surfactant deficiency
  - Decreased compliance
  - Underdeveloped antioxidant mechanisms
  - Inadequate fluid clearance
- Inflammation
  - Mechanical injury
  - Oxygen toxicity
  - Infection

Reference 2
Slide 10

BPD - Oxygen Toxicity

- Exact level or duration for damage unknown
- Enzyme inactivation and lipid peroxidation
- Oxygen metabolites and inadequate antioxidant defenses
  - Superoxide free radical
  - Hydrogen peroxide
  - Hydroxyl free radical
  - Singlet oxygen

Reference 2

Slide 11

BPD-Pathology

- Pre-surfactant treated
  - Airway injury
  - Inflammation
  - Parenchymal fibrosis

Reference 2

Slide 12

BPD-Pathology

- Surfactant treated
  - Disruption of lung development
  - Alveolar simplification
    - Decreased septation and alveolar hypoplasia
    - Fewer and larger alveoli
  - Reduction of surface area for gas exchange
  - Minimal small airway injury
  - Reduced microvascular development

References 2, 4, and 5
Slide 13

**BPD-Pathology**

- Surfactant treated
  - Dysregulation of pulmonary vascular development
  - Abnormal distribution of alveolar capillaries
  - Thickened pulmonary arteriole musculature
    - Increased pulmonary resistance
  - Less airway injury and inflammation
    - Unless severe BPD

Reference 2

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Slide 14

**BPD-Natural History**

- Not well reported
- Better over 2 to 4 months
  - Healing and lung growth

References 2 and 5

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Slide 15

**BPD - Signs & Symptoms**

- Pathologic small airways
- Tachypnea
- Wheezing
- Chest wall retractions
- Paradoxical respirations
- Increased dead space ventilation

References 2 and 8
Slide 16

**BPD - Signs & Symptoms**

- Increased functional dead space
- Small/fast tidal volume
- Increased muscle activity/compliant chest wall retraction—wasted energy
- RAD - exercise (crying, feeding), cold air, infection
- Prolonged expiratory phase

References 2 and 5

Slide 17

**BPD - Signs & Symptoms**

- Tracheomalacia/bronchomalacia
  - 45% TM, 34% BM but likely higher
  - Large airway collapse
  - From barotrauma, infection, intubation
  - Positional (worse on back)

References 2 and 5

Slide 18

**BPD - Signs & Symptoms**

- BPD spells
  - Occur during agitation/crying
  - Natural history of TM/BM not reported

References 2 and 5
Slide 19

**BPD - Signs & Symptoms**

- Glottic and subglottic damage
- Stridor
- Stenosis/granuloma
  - Emphysema and atelectasis

Reference 2

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Slide 20

**BPD - Signs & Symptoms**

- Cyanosis/hypoxemia
- Pulmonary HTN
- Sleep related especially during REM
- Poor growth
- 10% supplemental oxygen after 1 year old

Reference 2

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Slide 21

**BPD - CXR**

- Diffusely hazy
- Patchy infiltrates/hyperinflation
- Edema especially during exacerbations
- Cystic changes/fibrotic changes
- Atelectasis
- Low lung volumes

Reference 2
Slide 22

**BPD – Overview of Therapy**

• Supportive
  – Survival of younger GA
• Minimize injury
  – Less aggressive ventilation/oxygen
• Antenatal steroids
• Surfactant
  
  Reference 2

Slide 23

**BPD - Overview**

• Studies of long term outcomes are difficult to compare and extrapolate
  – Non-standardized care in units
  – Different definitions
  – Changes in clinical care
  – Small numbers of patients studied
  
  Reference 5

Slide 24

**BPD - Therapy**

- Assisted ventilation
- Oxygen
- Monitoring
- Diuretics and fluid balance
- PDA closure
- Bronchodilators
- Corticosteroids
- Antibiotics/RSV prophylaxis
- Nutrition
  
  Reference 2
Slide 25

**BPD - Therapy**

- Mechanical ventilation (optimal strategy unknown)
  - Wean gradually from SIMV
  - Small tidal volumes (avoid injury) (4-6 ml/kg)
  - PEEP 5-7 cm water (avoid atelectasis)
  - Prolonged inspiratory time (0.4-0.5 sec)
  - Promote uniform lung inflation
  - Permissive hypercapnia with pH 7.3-7.4 (55-65+)

Reference 2

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Slide 26

**BPD - Therapy**

- HFOV
  - No clear improvement
- NIPPV and early CPAP
  - Not conclusive
- Caffeine
  - Less BPD in <1250 gram babies
- iNO
  - No significant benefit

Reference 2

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Slide 27

**BPD - Therapy**

- Tracheostomy
  - Optimal timing unclear
  - 48-52 weeks PMA and expected ongoing MV
- “Calibrated suctioning”
  - To distal tip of tube

Reference 2
Slide 28

**BPD - Therapy**

- Oxygen
  - Best therapeutic range (safe?)
  - No side effects of low flow
  - Optimal sats unknown
  - Better outcomes 88-95% sat in <30 weeks PMA
  - 90-95% sat if given supplemental oxygen
  - 95% - 96% pulmonary HTN ?

Reference 2

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Slide 29

**BPD - Therapy**

- D/C oxygen after diuretics
- Fluid restriction released corticosteroids
- Poor growth may be desaturation

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Slide 30

**BPD - Therapy**

- Diuretics
  - 3 to 4 weeks old
  - MV dependent/fluid restricted
  - Furosemide for more severe, pulmonary edema, after PRBC transfusions

Reference 2
BPD - Therapy

- Distal renal tubule
  - Thiazide and/or spironolactone
  - Improved lung mechanics
  - Did not decrease vent support, length of stay, long term outcome
  - Combination no difference in lung mechanics, electrolyte balance, need for supplements

Reference 2

BPD - Therapy

- Loop diuretics
  - Furosemide
    - Single IV dose with transient improvement (1 mg/kg)
    - Chronic dosing
      - Improved oxygenation and lung mechanics
      - No change in vent support, LOS, survival, long term outcome
      - Ototoxic especially rapid IV
      - Nephrocalcinosis/Nephrolithiasis

Reference 2

BPD - Therapy

Monitor electrolytes initiation, increase in dose, at least weekly
supplement NaCl/KCl/Ca
Monitor Ca/PO₄/alk phos

Reference 2
Slide 34

BPD - Therapy

• MDI vs. Nebulizer
  – Small proportion is delivered to lungs
  • 0.17-0.23 MDI
  • 0.21-0.23 Neb
  • Most in central lung regions
  • MDI may be preferable
    – More cost effective

Reference 2

Slide 35

BPD - Therapy

• Albuterol/levalbuterol
  – May help (observation)
    • Clinical trial
      – Gas exchange
        – Decreased respiratory effort
        – Increased oxygen saturation
      • dx if no benefit
      • Also for acute exacerbations of RAD
        – Less common

Reference 2

Slide 36

BPD - Therapy

• Bronchodilators
  – Tachycardia
  – HTN
  – Possibly arrhythmia
  – Worse symptoms if bronchomalacia

Reference 2
Slide 37

**BPD - Therapy**

**Bronchodilators**
- no effect on survival, diagnosis or severity, duration of vent support or oxygen therapy

Reference 2

Slide 38

**BPD - Therapy**

- Ipratropium bromide
  - 25 mcg/kg
  - Improved resistance and compliance
  - Synergistic with albuterol
    - Decreased hospitalization rates in asthma

Reference 2

Slide 39

**BPD - Therapy**

**Systemic Steroids**
- 1983 was first randomized trial
  - peak use 1997-9, lowest 2003-4
- In general:
  - Improves lung function but significant side effects
  - Complications may outweigh benefits

Reference 2
Slide 40

BPD - Therapy
Systemic Steroids—adverse effects
- Sepsis/infection
- Adrenal suppression
- Poor growth
- Hypertension
- Cardiac hypertrophy

References 2 and 8

Slide 41

BPD - Therapy
Systemic Steroids—adverse effects
- Hyperglycemia
- Bowel perforation and GI bleeding
- Overlap with indomethacin?
- Decreased bone mineralization
- Neurodevelopment abnormalities/CP

Reference 2

Slide 42

BPD - Therapy
- Issues with systemic steroid studies
  - Variations in methodologies
  - Preparation of glucocorticoid used
  - Dosing and timing of administration
  - Length of therapy
  - See the AAP/CPS recommendations

Reference 2
BPD - Therapy

- Early systemic steroids
  - Reduced incidence of BPD at 28 DOL and 36 weeks PMA
  - Lower rate of intubation at each interval
  - Earlier extubation
  - No difference in mortality

Reference 2

BPD - Therapy

- Late systemic steroids
  - Improved lung function
  - Reduced need for assisted ventilation/oxygen therapy
  - Reduced extubation failures
  - No difference in asthma rates
  - For acute exacerbations
    - 5-7 day course hydrocortisone (5 mg/kg)

Reference 2

BPD - Therapy

- Inhaled steroids
  - Early use does not prevent BPD
  - Treatment for BPD unclear
    - Dual dose for 1 week with exacerbation
  - No adverse effects
  - Appropriate dose unknown
  - Trial if severe BPD and >40 weeks PMA and RAD/OLD

Reference 2
Slide 46

**BPD - Therapy**

- Antibiotics if infection
  - CXR and culture of tracheal aspirate

Reference 2

Slide 47

**BPD - Therapy**

- RSV prophylaxis
  - Palivizumab per guidelines

Reference 2

Slide 48

**BPD - Nutrition**

- NG/OG/PG feeds
- High caloric density
- Fluid restricted
  - 140-150 ml/kg/day after DOL 7
  - Less earlier in life or more severe disease

Reference 2
Slide 49

BPD - PFT

- Less than three years of age—airflow obstruction and air trapping
  - Decreased forced expiratory flow rates
  - Increased functional residual capacity, residual volume, RV/TLC
  - 1/3 bronchodilator responsive
  - Increased respiratory effort and minute ventilation

Reference 2

Slide 50

BPD - PFT

Long term ("classic BPD")
- Airway obstruction
- Hyperinflation (elevated RV)
- Rarely clinically significant
- RAD 52% on MCh or BD change
- Reduced exercise tolerance/desaturation (some studies)

References 2 and 5

Slide 51

BPD - PFT

- Long term for "new BPD" (post surfactant/antenatal steroids) mostly unstudied and unknown
- Perhaps less airflow limitation
- Perhaps lower lung volumes

References 2 and 5
**Slide 52**

**BPD - Long Term**

- 30-40% mortality (severe BPD)
- Predictors
  - MAP and oxygen concentration
  - Longer duration of mechanical ventilation
  - Sepsis
  - Pulmonary HTN
  
  > Cor pulmonale
  
  Reference 2

**Slide 53**

**BPD – Long Term**

- Recurrent hospitalization (pneumonia, RAD, RSV)
  - First year 58% vs. 35%
    > Especially RSV and home oxygen dependent
  - Second year 37%
  - Viral
  
  > Life threatening
  
  References 2 and 5

**Slide 54**

**BPD - Long Term**

- Pulmonary HTN
  - EKG may underestimate abnormalities
  - May require cardiac cath
    
    > Gold standard, reactivity, collaterals
  - Echocardiogram
    
    > Every month if <32 wks GA, starting at 36-37 wks
    
    > PMA and if MV or CPAP, oxygen >30%, CO2 >60
    
    > Every 2-3 months for PHTN surveillance
    
    References 2 and 8
Slide 55

BPD - Long Term

• Airway hyperresponsiveness
  – 40-50% with abnormal exercise, histamine or methacholine response
  – No increase in atopy
  – May respond to ICS

Reference 5

Slide 56

BPD - Long Term

• Neurodevelopment
  – Motor and Cognitive performance
  • 50% have abnormal gross and/or fine motor skills
  • Solute signs
  • Cerebral palsy
  • Microcephaly
  • Behavioral problems
  • Dysphagia/aspiration

Reference 2

Slide 57

BPD - Long Term

• Radiography
  – CT scans with linear and triangular opacities, mosaic profusion, air trapping
  – CXR
  • At 6-9 years 40% minor fibrotic changes
  • At 8-10 years all had generalized hyperinflation
  – 40% with localized hyperinflation
  – 50% with parietal fibrosis

References 2 and 5
BPD - Long Term

- Avoid smoking
- Avoid respiratory irritants
- Good hand washing

Reference 2

References and Suggested Reading

2. UpToDate, 2012.

References and Suggested Reading

5. ScienceDirect.
References and Suggested Reading


References and Suggested Reading