Bronchopulmonary Dysplasia

Fellows Track Symposium

ATS 2020

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Bronchopulmonary Dysplasia

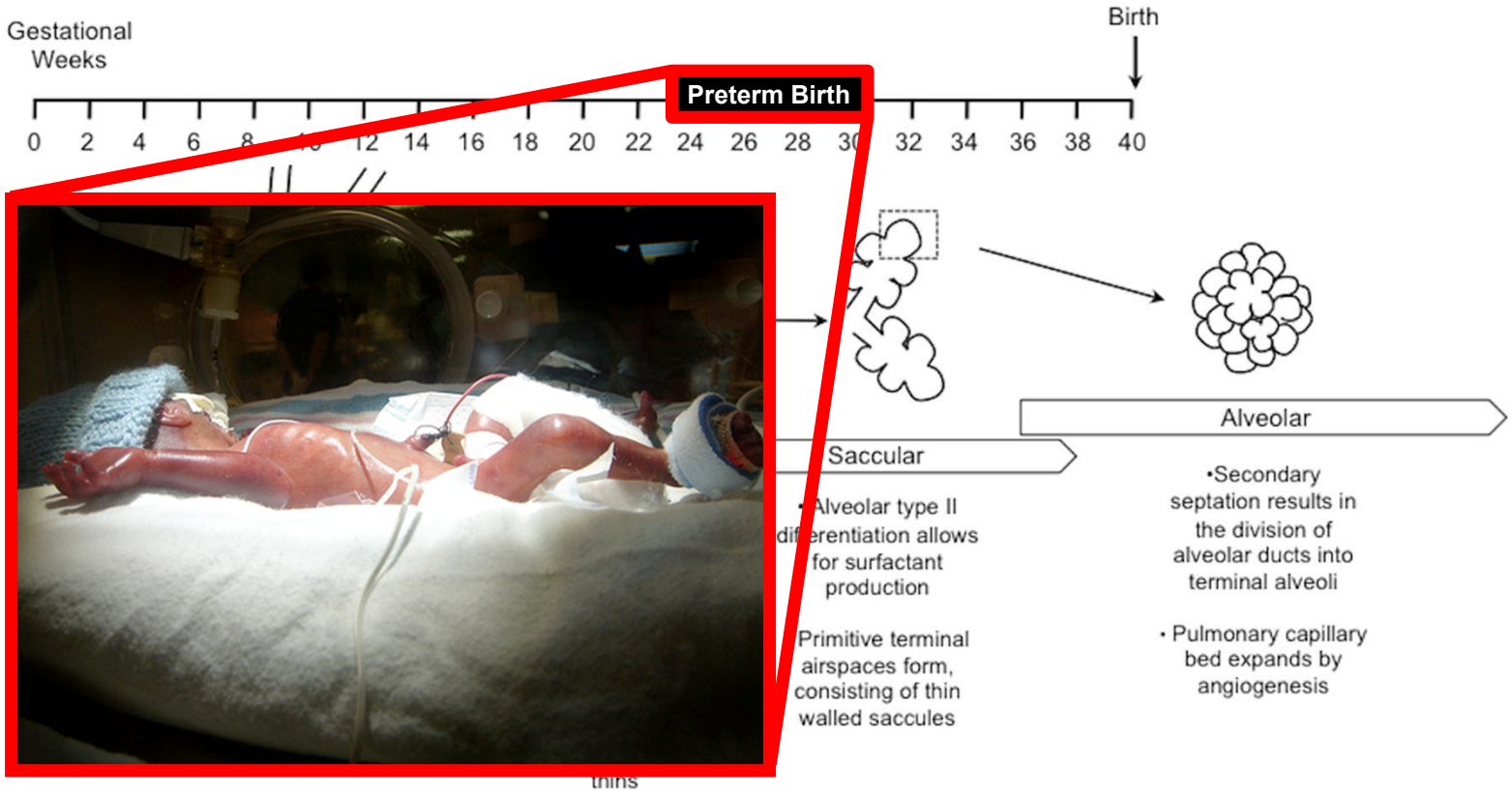
Relevant financial relationships with a commercial interest:

No relevant commercial interests.

BPD: Learning Objectives

- After this lecture, participants will be able to:
  - Review the **pathogenesis** of Bronchopulmonary Dysplasia (BPD)
  - Summarize the **vascular hypothesis** of lung development
  - Differentiate between **protective** and **supportive (chronic) ventilation** strategies in preterm infants
  - Recognize the indications for **chronic mechanical ventilation** in infants with severe BPD
  - Determine **which patients would benefit** from chronic ventilatory support (potentially via tracheostomy)

BPD: Lung Development

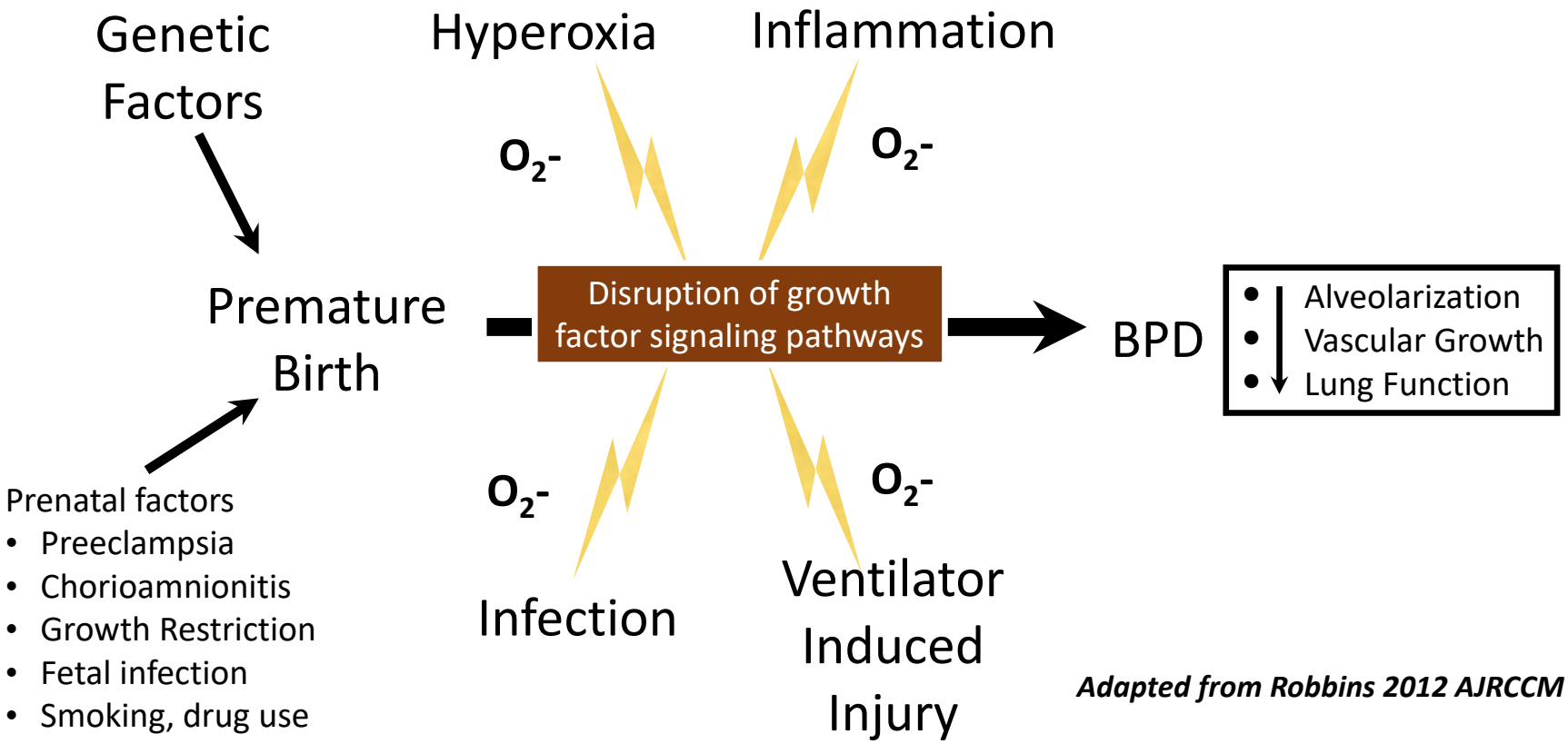


Baker / Alvira 2014 Curr Opin Pediatr 26:306;
Coalson 1999 CLD of Early Infancy 85-124

Bronchopulmonary Dysplasia

- Bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is associated with mechanical ventilation and oxidative stress. ***Northway 1967 NEJM 276:357***
- In infants born at 23-26 weeks gestation, BPD consists of an arrest in lung vascular and alveolar growth. ***Jobe 1998 Early Hum Dev 53:81***

Pathogenesis of BPD



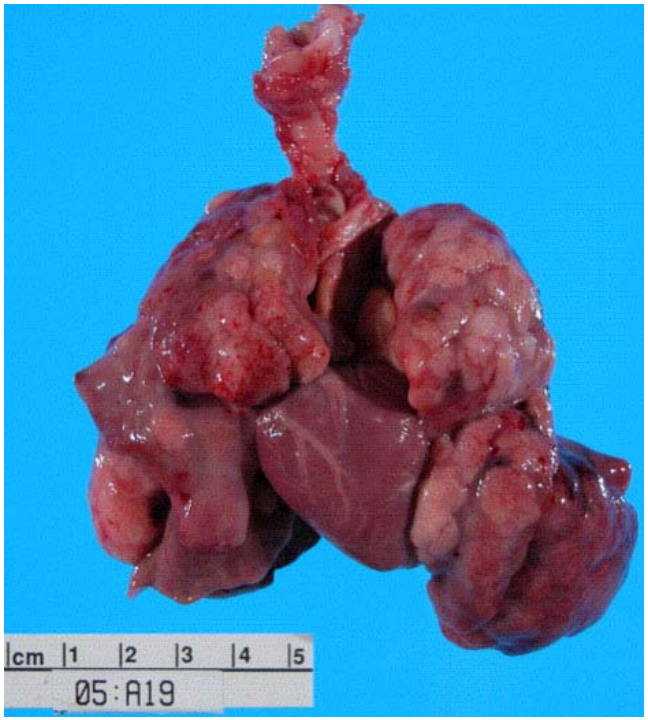
Adapted from Robbins 2012 AJRCCM 185:1015

Bronchopulmonary Dysplasia

"Old BPD" Pre-surfactant Era

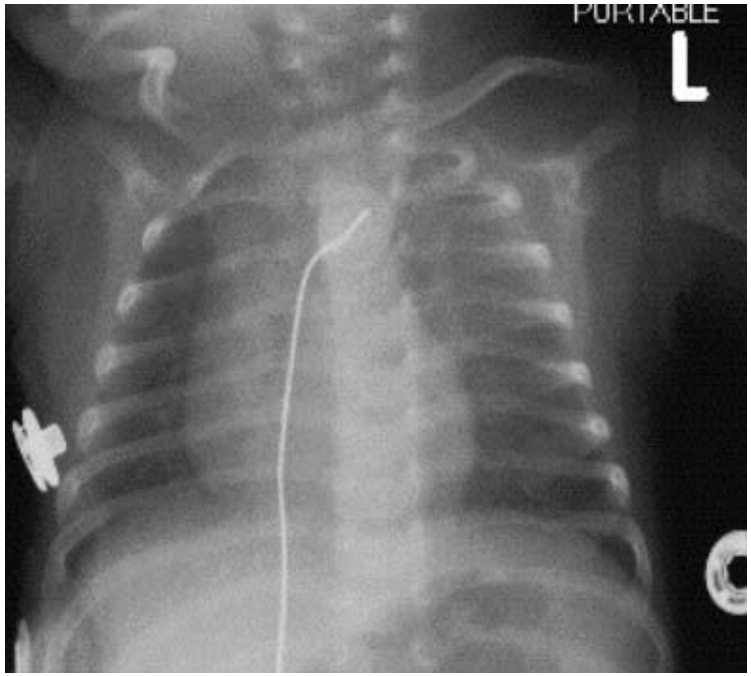
INJURY TO LUNG

- Atelectasis/Hyperinflation
- Airway epithelial lesions
- Smooth muscle hyperplasia
- Diffuse fibroproliferation
- Remodeling of pulm arteries
- Decreased alveolarization



Courtesy of SH Abman

Bronchopulmonary Dysplasia



<u>"New BPD" Post-surfactant</u>

ARREST OF DISTAL LUNG DEVELOPMENT

- **Rare fibrosis**
- **Less regional heterogeneity**
- **Rare epithelial lesions**
- **Decreased, dysmorphic lung capillaries**
- **Alveolar simplification**

Jobe 1999 Pediatr Res 46:641;

Coalson 2003 Semin Neonatal 8:73

BPD Severity: NIH Diagnostic Criteria

TABLE 1. DEFINITION OF BRONCHOPULMONARY DYSPLASIA: DIAGNOSTIC CRITERIA

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

Jobe 2001 AJRCCM 163:1723

BPD: The Spectrum of Severity

- By these criteria, the following have **severe BPD**:
  - **3 month old 26-wk F:** 1/8L NC; orally feeding; ready for discharge; O_2 reduction test: FiO_2 0.31
  - **3.5 month old 24-wk M:** CPAP 6 (FiO_2 0.21); NG fed; unstable during O_2 reduction test
  - **4 month old 24-wk twin M:** early HFOV; still intubated, conventional vent (FiO_2 0.80); frequent desaturation “spells”; pulmonary hypertension; tracheostomy planned

Severe “Type 2” or ”Grade 3” BPD

Table I. BPD definition with severity

BPD severity	Definition (Modified from Jobe and Bancalari[4])	Relative incidence (Data from Ehrenkranz et al[5])	Postdischarge mortality (Data from Ehrenkranzet al[5])
None	O_2 treatment <28 d and breathing room air at 36 wk PMA or discharge home, whichever comes first	23.1%	1.8%
Mild	O_2 treatment at least 28 d and breathing room air at 36 wk PMA or discharge home, whichever comes first	30.3%	1.5%
Moderate	O_2 treatment at least 28 d and receiving <30% O_2 at 36 wk PMA or discharge home, whichever comes first	30.2%	2.0%
Severe (type 1)	O_2 treatment at least 28 d and receiving ≥30% O_2 or nasal CPAP/HFNC at ≥36 wk PMA	16.4%	4.8%
Severe (type 2)	O_2 treatment at least 28 d and receiving mechanical ventilation at ≥36 wk PMA.		

HFNC, high flow nasal cannula; *O_2*, oxygen.

Abman 2017 J Pediatr 181:12
Higgins 2018 J Pediatr 197:300

A New Baby with "Old" BPD

Abman SH, In: The Newborn Lung, 2012, 21.21-21.29

Severe "Old" + "New" BPD

"Old BPD"

INJURY TO LUNG

- Altered inflation pattern of atelectasis and overinflation
- Severe airway epithelial lesions (hyperplasia, squamous metaplasia)
- Airway smooth muscle hyperplasia
- Extensive fibroproliferation
- Prominent vascular hypertensive lesions
- Decreased internal surface area and alveoli

+

"New BPD"

ARRESTED LUNG DEVELOPMENT

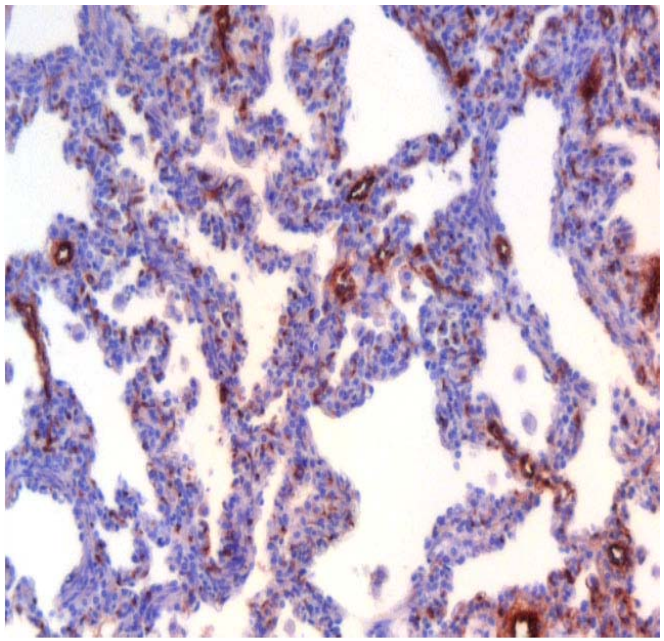
- Decreased, large and simplified alveoli (alveolar hypoplasia, decreased acinar complexity)
- Decreased, dysmorphic capillaries
- Variable interstitial fibroproliferation
- Less severe arterial/arteriolar vascular lesions
- Negligible airway epithelial lesions
- Variable airway smooth muscle hyperplasia

Coalson 2003 Semin Neonatol 8:73

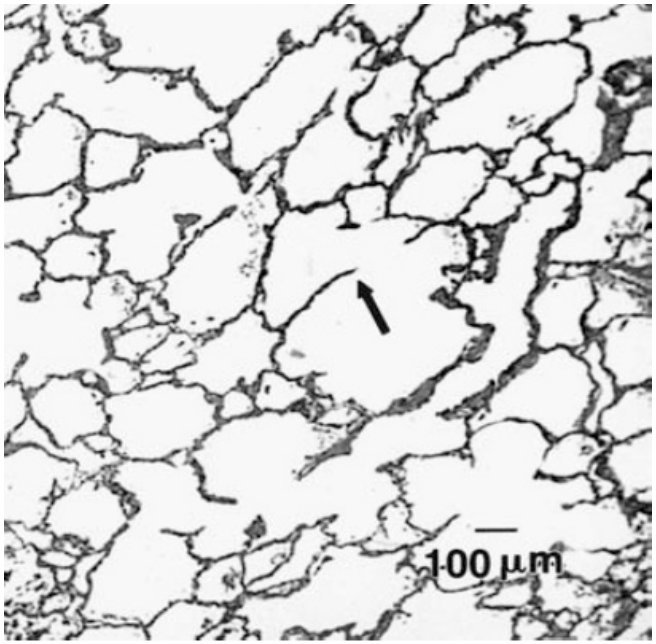
Severe BPD = "the worst of both worlds…"

Severe “Old” + “New” BPD

Increased Fibro-proliferation



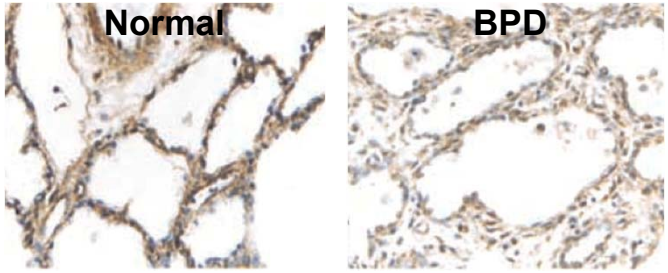
Alveolar Simplification

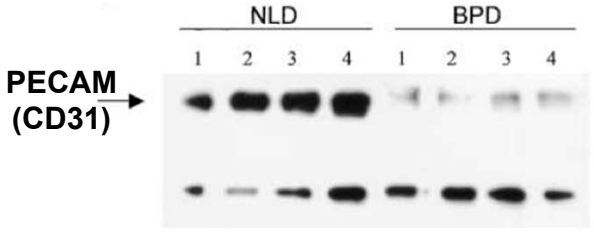


Coalson 2003 Semin Neonatal 8:73

BPD: A Vascular Hypothesis

- The lungs of preterm infants who die from BPD have markedly decreased vessels.





Bhatt 2001 AJRCCM 164:1971

- **Disrupted vascular growth impairs alveolarization.**

Abman 2001 AJRCCM 164(10):1755

- In neonatal rats, angiogenic inhibitors decrease pulmonary vascular growth and alveolarization. ***Jakkula 2000 AJP Lung 279:L600***
- Can we augment vascular growth to prevent/treat BPD?

BPD: Prevention and Treatment

BPD Prevention

- Delay preterm birth
  - Degree of prematurity and birth weight are the two biggest risk factors
- Antenatal steroids
  - Decreases respiratory distress syndrome, intraventricular hemorrhage, mortality
  - BPD incidence unchanged (due to increased survival)
- Exogenous surfactant
  - First dose during the first hour
  - Consider less invasive approaches
  - Can give up to two more additional doses if unstable during the first 72 hours of life

BPD Prevention

- Protective ventilation strategies
  - CPAP (even if must forego surfactant), high-frequency oscillatory/jet ventilation, noninvasive ventilation
- Judicious fluid management
  - Moderate fluid restriction (negative balance), higher fluid intake associated with BPD and death
- Caffeine
  - Not only for apnea of prematurity, but early caffeine therapy may reduce the risk of developing BPD
- Vitamin A
  - Some meta-analyses and multicenter studies show modest benefit, injections (3x/week)

BPD Treatment

- Ventilation strategies
  - Approach differs for chronic ventilation
  - Support breathing (rather than avoid injury)
  - For established disease: larger tidal volume, lower rate
  - Ideal time to stop weaning attempts?
- Oxygen Therapy
  - Avoid toxicity, optimal SpO2 target unclear (91-95%?)
- Diuretics
  - Improve lung compliance
  - Side effects: osteopenia, nephrocalcinosis, hearing loss
  - Long-term benefit unclear (avoid when possible)

Respiratory Outcomes in BPD

Respiratory Outcomes in Children

- **7-8y**: VLBW have ↓ FEV_1, ↑ RV/TLC

Finland: *Korhonen 2004 Acta Paediatr 93:316*

- **9.5y**: VLBW+BPD have ↓ FEV_1, FVC, FEF_{50}

Germany: *vom Hove 2014 J Pediatr 164:40*

- **11y**: <26wk+BPD have ↓ FEV_1, ↑ bronchoreactivity

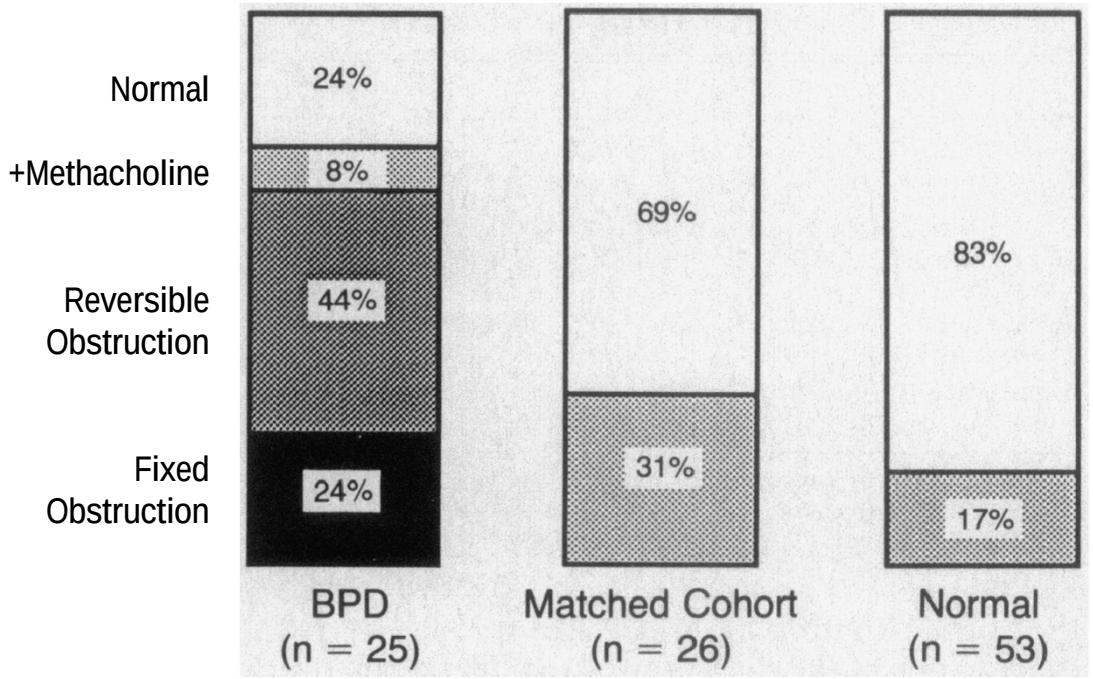
EPICure; UK: *Fawke 2010 AJRCCM 182:237*

- **1991-92** vs. **1997** vs. **2005** (at 8y)
  - 2005: ↓ MV / ↑ CPAP, lung function unchanged

Australia: *Doyle 2017 NEJM 377:329*

Young Adults with "Old" BPD Have Airways Disease

AIRWAYS DISEASE AT ~18 YRS



Northway 1990 NEJM 323:1793

Respiratory Outcomes in Young Adulthood

- **17y**: ↑ asthma, ↓ FEV_1
- **25y**: ↓ lung function, ↑ RV/TLC, +methacholine response

Norway: *Halvorsen 2004 Acta Paediatr 93:1294*

Norway: *Vollsæter 2015 ATS Annals 12:313*

- **19y**: ↓ FEV_1, FVC, FEV_1/FVC; normal lung volumes

Australia: *Doyle 2006 Pediatrics 118:108*

- **25y**: persistently ↓ airflows, no air trapping

Australia: *Gibson 2015 Pediatr Pulmonol 50:987*

Ventilation Strategies: Protective vs. Supportive

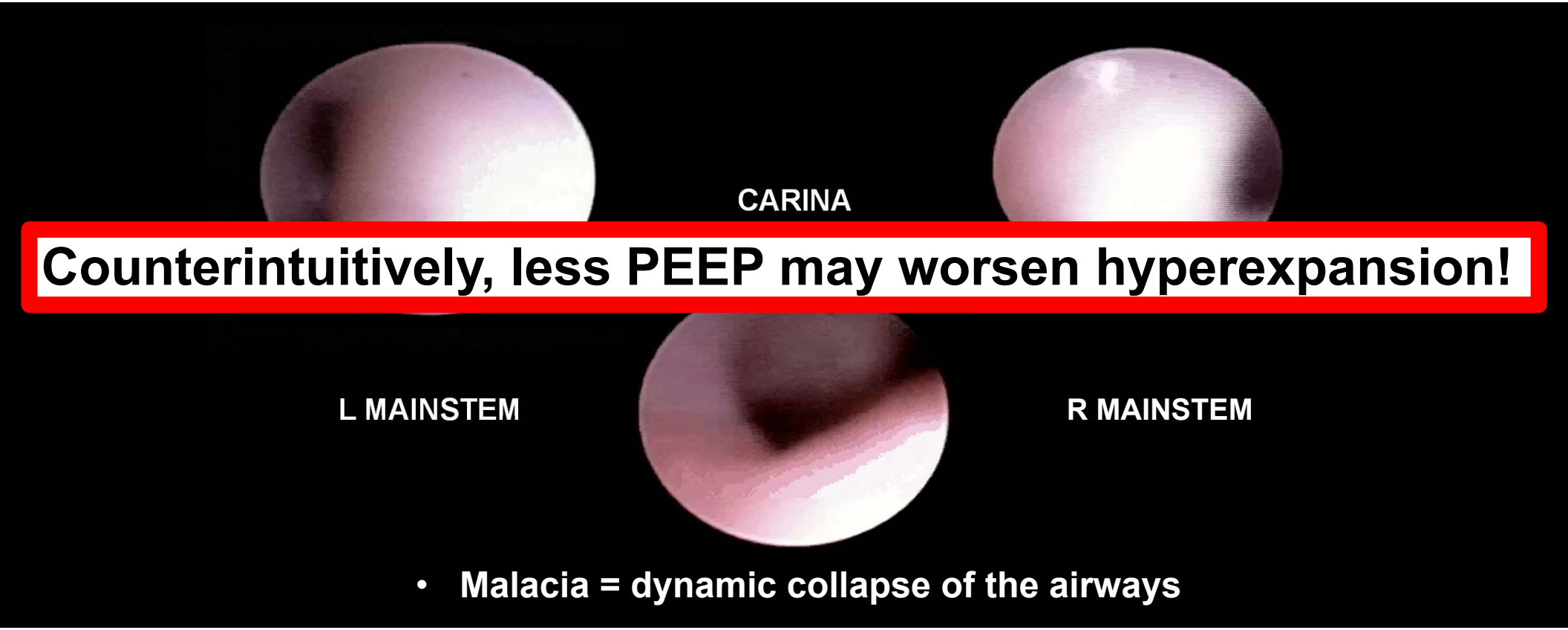
Protective Ventilation

- **GOAL:** avoid lung injury
  - “Gentle-ation”, early extubation
- Appropriate in the immediate postnatal period
- Consider less-invasive approaches:
  - Continuous positive airway pressure (CPAP)
  - High-frequency oscillatory ventilation
  - Small tidal volume / high rate vent strategy
- Delivery room CPAP (in lieu of postnatal surfactant)
- Minimally-invasive surfactant therapy (by catheter)
- Treatment of acute respiratory distress in children

Supportive Ventilation

- **GOAL:** support breathing, promote growth and development, stability, baby is happy
- Appropriate for established / chronic lung disease
- Heterogeneous lung: regions of fibrosis/atelectasis as well as regions of marked hyperinflation
- Supportive approaches to ventilation:
  - Larger tidal volume / lower rate vent strategy
  - PEEP to overcome dynamic airway collapse
- Support breathing for months/years; defer weaning
- Consideration of tracheostomy

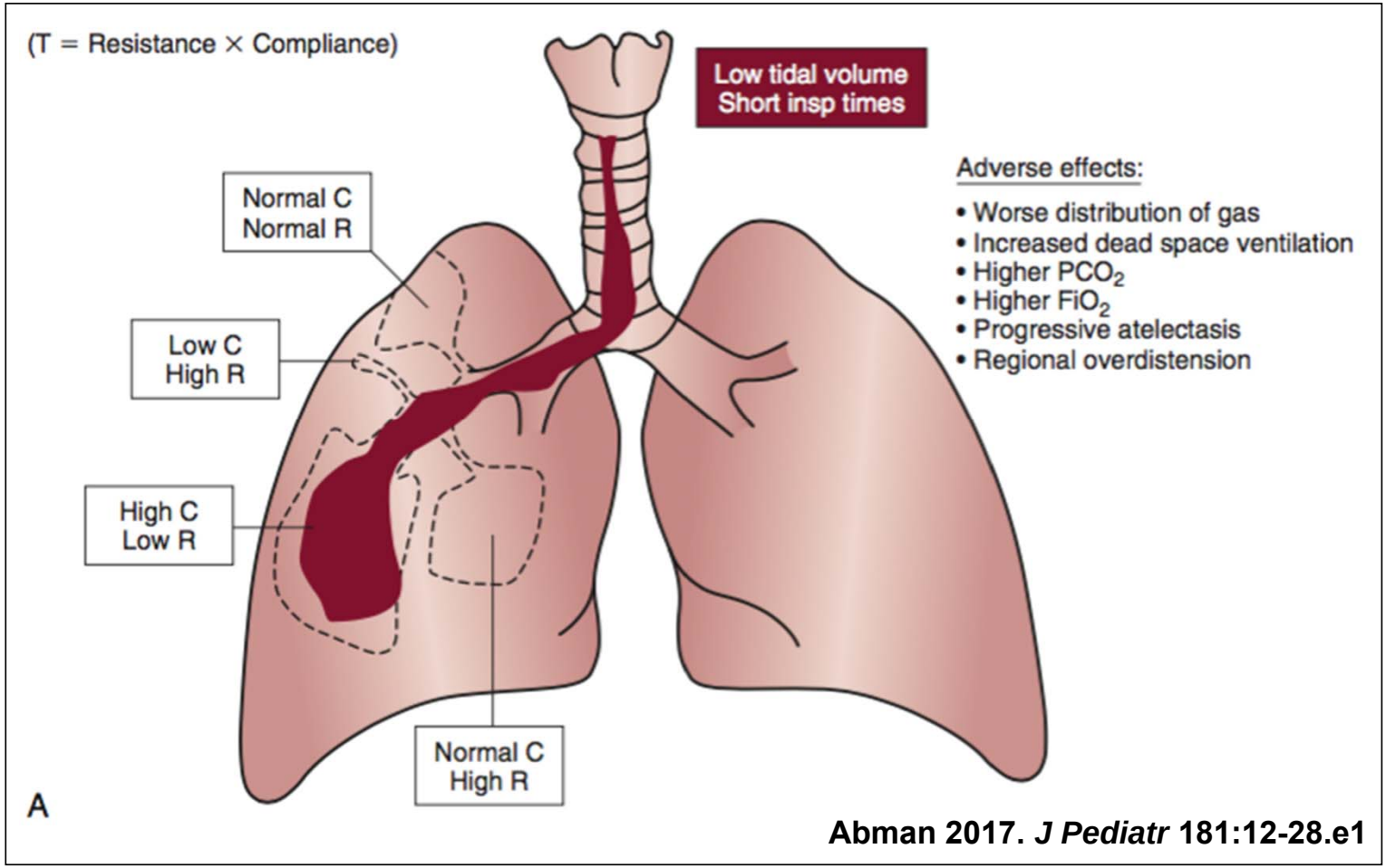
Tracheobronchomalacia



Counterintuitively, less PEEP may worsen hyperexpansion!

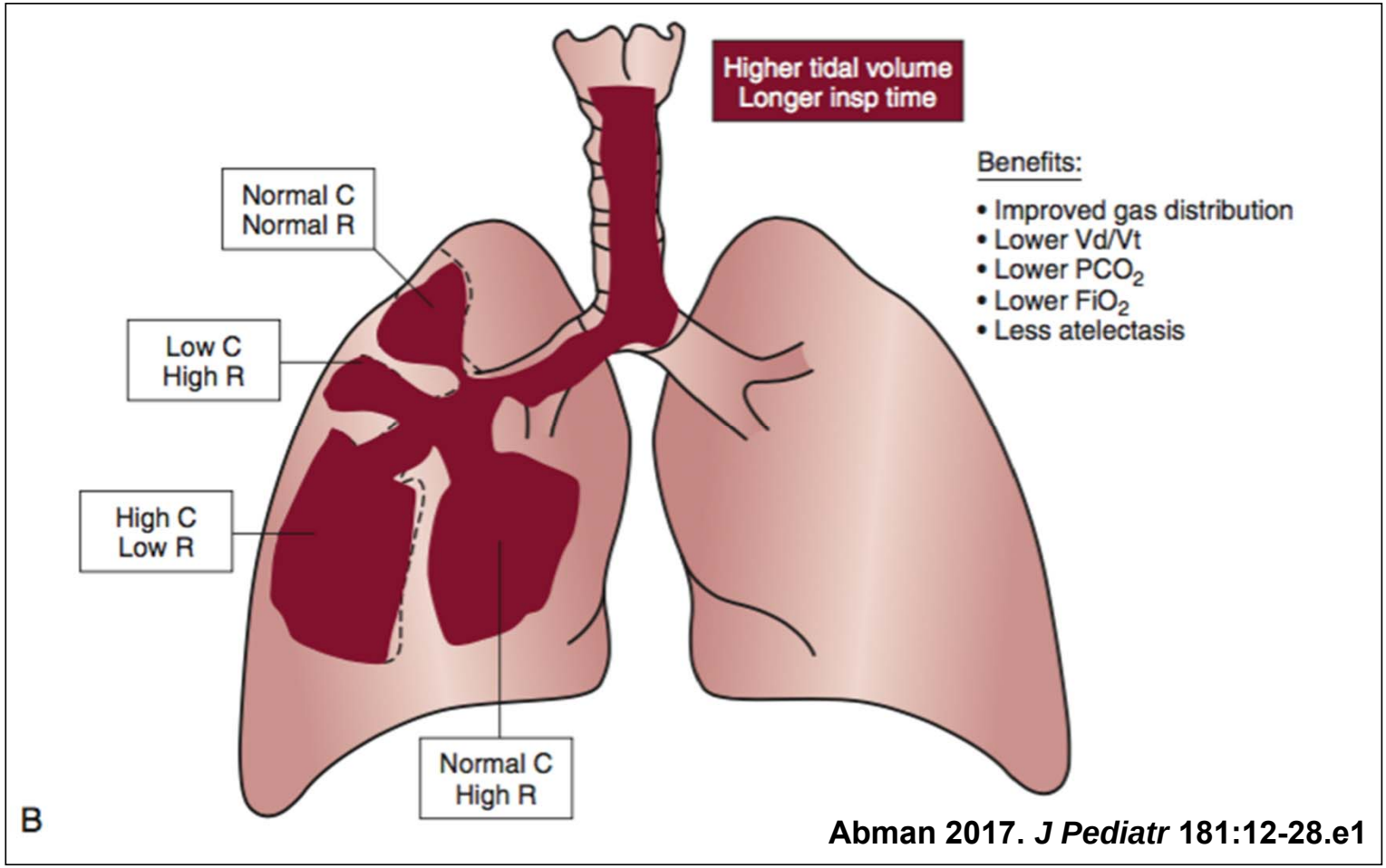
- Malacia = dynamic collapse of the airways

Ineffective Chronic Ventilation



Abman 2017. *J Pediatr* 181:12-28.e1

Effective Chronic Ventilation



Abman 2017. *J Pediatr* 181:12-28.e1

Chronic Ventilation: Other Factors

- Optimal nutrition for linear growth without obesity
- Aspiration – need for gastric fundoplication?
- Airway clearance / suctioning of secretions
- Medications (e.g., inhaled/enteral steroids, bronchodilators, diuretics)
- Pulmonary hypertension – screening, treatment
- Bedside emergency management – still A-B-C!
- Agitation, dyssynchrony – sedation, NAVA
- Developmental therapy – PT, OT, speech, feeding

Interim Summary

- The respiratory sequelae of BPD persist into young adulthood
- Strategies for protective and supportive ventilation differ dramatically
- More importantly, the goals of care are very different
- Chronic ventilation gives a baby with (Type 2) severe BPD the best chance at a positive outcome

Case: NICU Consult

Case: NICU Consult

3 month-old 24-week preterm twin girl, failed extubation multiple times despite aggressive steroid therapy (dexamethasone), has frequent desaturation spells.

Current ventilator settings: volume control, Vt 5ml/kg, i-time 0.4 sec, rate 35, PEEP 5 cm H_2O, PS 12 cm H_2O, FiO_2 0.50

Blood gas: pH 7.36, p_aCO_2 64, p_aO_2 118

Medications: Lasix 1 mg/kg BID, prednisolone 0.5 mg/kg every 48 hours, albuterol q4h PRN

Studies: CXR: hyperinflation, patchy atelectasis

Echocardiogram: no interventricular septal flattening

Flexible bronchoscopy: severe tracheobronchomalacia

What changes in ventilator strategy do you suggest?

A. Change to non-invasive ventilation
B. Increase Vt, i-time, and PEEP; decrease rate
C. Increase Vt and rate
D. Increase pressure support and decrease inspiratory time
E. Change to high frequency oscillatory ventilation (HFOV)

Correct answer:

B. Increase Vt, i-time, and PEEP; decrease rate

Answer Rationale

- Child will likely not tolerate extubation
- In severe BPD, larger Vt with longer i-time optimizes gas distribution
- A slower rate permits adequate exhalation
- PEEP supports dynamic airway collapse
- Increasing the rate may lower the pCO2, but increases V/Q mismatch
- HFOV is challenging in established BPD due to highly variable time constants and heterogeneous lung injury

Interdisciplinary Ventilator Care Program

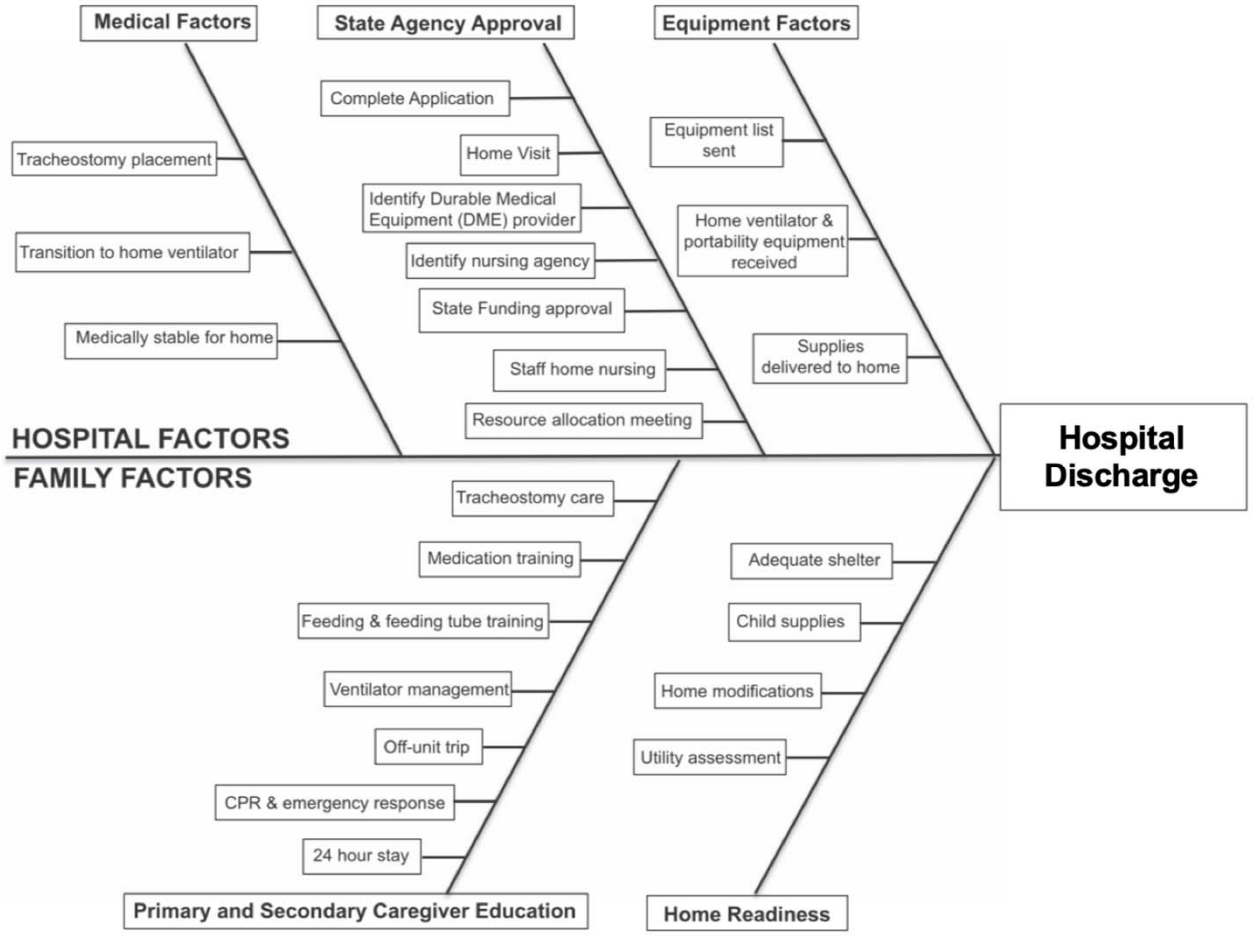
Ventilator Care Program (VCP)

- **VCP History in CO:** Pulm/Neo collaboration (Abman, Gien)
- **Mission**: Quality inpatient-to-outpatient care
- **Team approach** – many key contributors
- **Transition to PRCU (out of ICU)** before discharge
- **Clinical rounds:** two meetings/week since 2007
  - NICU rounds: at bedside, families participate
  - VCP rounds: conference room, discharge planning
- **Pulm-NICU Consult team:** since Jan 2019
- **Impact on families:** mortality, LOS/cost, traumatic stress

Ventilator Care Program (VCP)

- **Point-prevalence:** 20+ inpatients, 100+ outpatients (in seven state region)
- **Key discharge barrier:** inadequate in-home private duty nursing (worse in 2018-2019)
- 96% of U.S. survey respondents either “Disagreed” or “Strongly Disagreed” that there was “an adequate supply of home nursing services.” *Sobotka S 2018, Pediatric Pulmonol 54:40-46*

Many Factors Delay Discharge



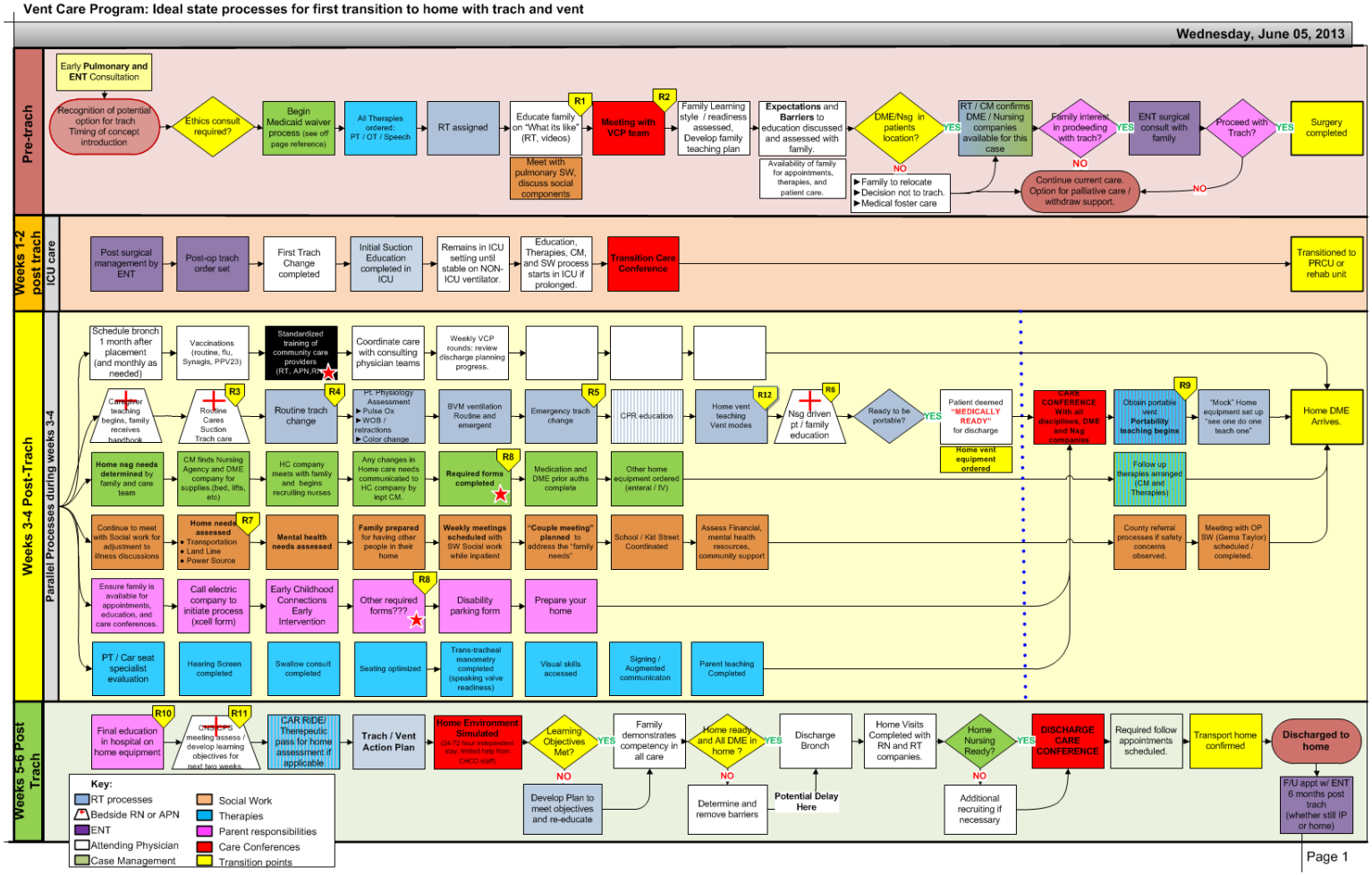
Sobotka 2016 Hosp Pediatr 6(9):552-7

VCP Standardized Process

- **Quality Improvement** (may not be generalizable)
- **Process map:** increases safety, improves efficiency, defines roles, ensures nothing overlooked
- Focus on **care coordination** (case management)
- Summarizes caregiver **responsibilities**
- **Standarized** process; highly **customized**
- Used to create the family-friendly "**Road Map**"
- **Reduced length of stay** (LOS) by 42% and post-ICU LOS by 55%

Baker 2016 Pediatrics 137:e20150637

Process Mapping



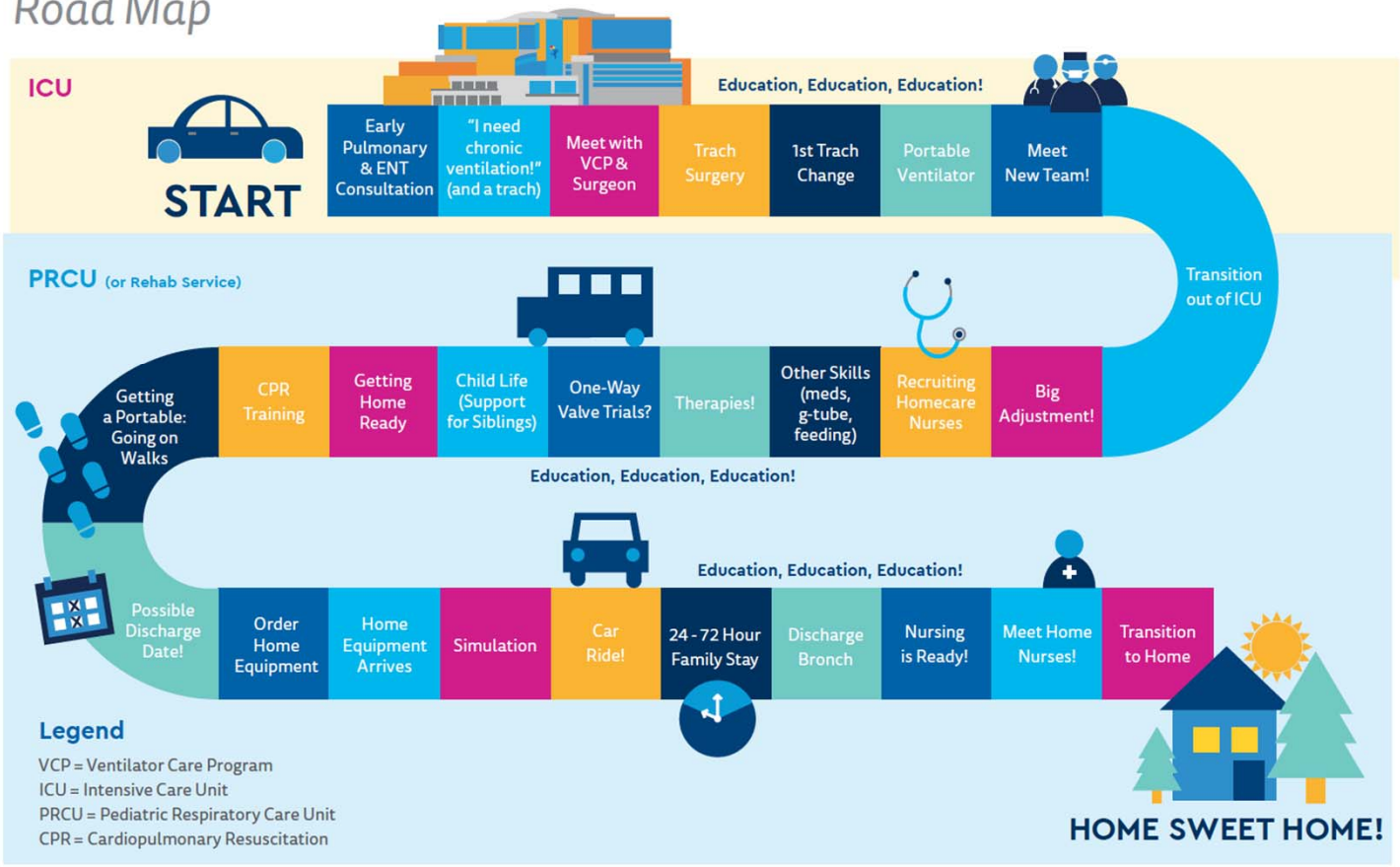
Baker 2016 Pediatrics 137:e20150637

BREATHING INSTITUTE

Chronic Ventilation

Road Map

Children's Hospital Colorado



Baker 2016 Pediatrics 137:e20150637 (revised; rebranded)

VCP Caregiver Education

- Interdisciplinary collaborative: led by RT and Nursing
- Teach-back Method
- Multiple modalities utilized (verbal, written, videos, CPR, high-fidelity SIM)
- Bilingual (English/Spanish)
- Address learning needs (language barriers, dyslexia)
- Timelines, checklists, color-coded medications

High-Fidelity Simulation (SIM)

- AIM: To recreate emergencies in a safe/artificial setting
- Two Complex Scenarios (90 min, including debriefing):
  - Plugged tracheostomy – requires suctioning the trach
  - Ventilator malfunction – requires full CPR and calling 911
- To date: **100+ children (200+ caregivers)**

High-Fidelity Simulation (SIM)

- SIM scheduled during week before discharge (to confirm/reinforce skills)
- Families identify gaps in understanding
- Not a pass/fail “test”
- Limitations: cost, time, difficult to repeat
- Subjectively, SIM improved caregiver confidence

Tofil 2013 Clinical Pediatrics 52(11):1038

- In our population, caregivers ranked post-SIM debriefing the most beneficial element of training *Thrasher/Baker 2018 J Pediatr Nurs 38:114*
- **2018: Expanded to all “tracheostomy” patients (n=20+)**

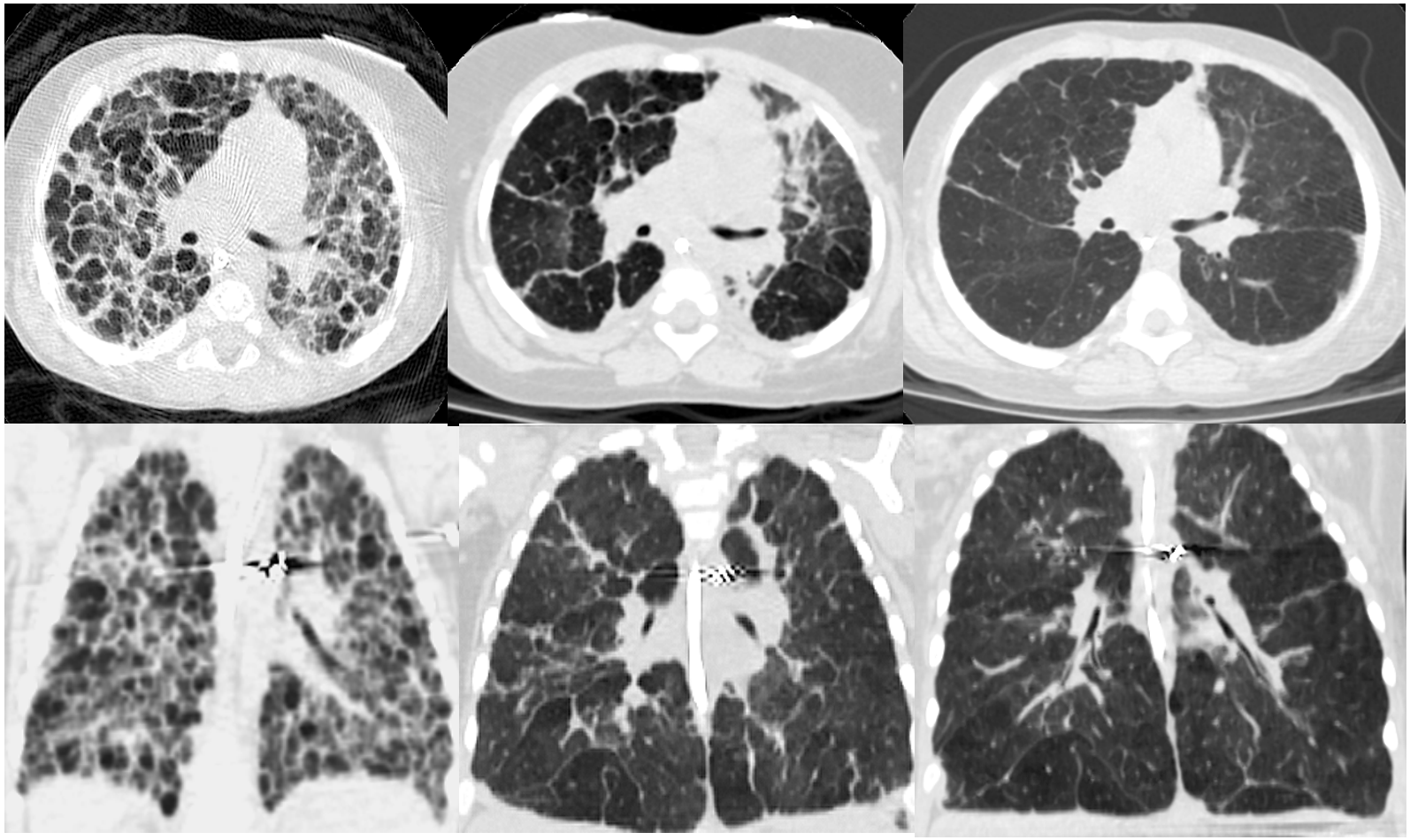
Summary

- BPD consists of an interruption in pulmonary vascular and alveolar growth after preterm birth
- Preterm infants with severe BPD can develop features of both “new BPD” and “old BPD”
- Optimal approaches to preventing and treating BPD remain unclear
- Children and young adults with BPD often have airflow obstruction
- Supportive Ventilation: chronic lung disease can improve over time (years)
- The care of chronically-ventilated children is improved with an **interdisciplinary program**

Should We Chronically Ventilate Infants with Severe Chronic Lung Disease?

Severe Bronchopulmonary Dysplasia

Age 6 months **Age 14 months** **Age 23 months**



Abman SH, The Newborn Lung, 2011 (Castile RG)

Thank you.

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