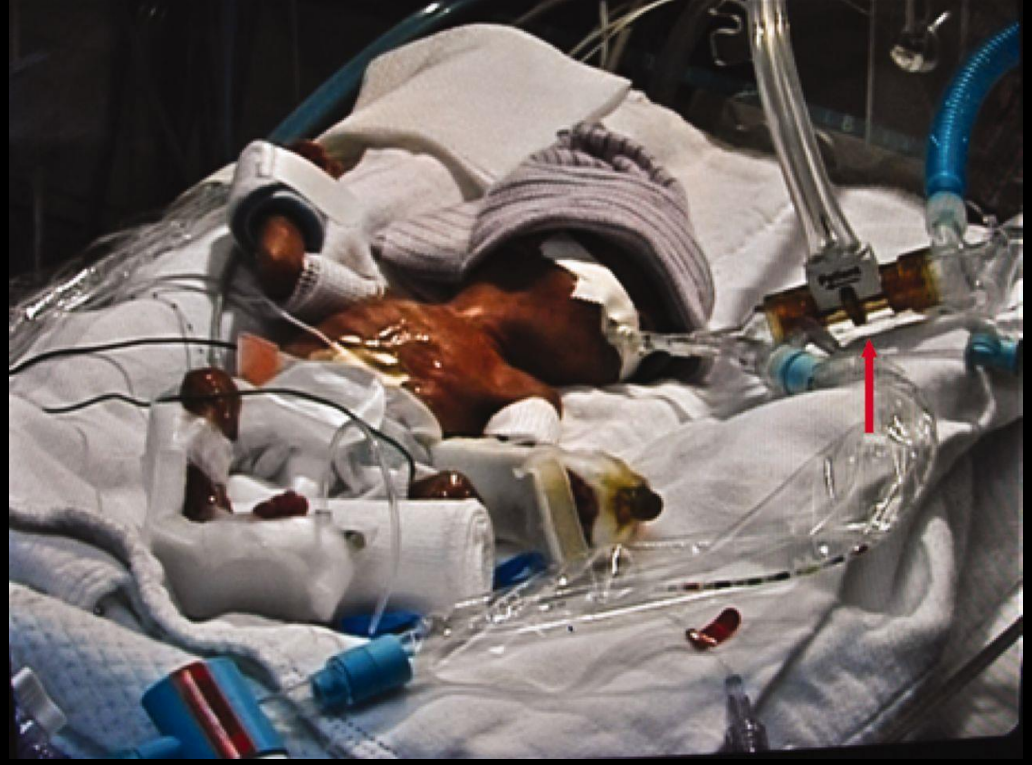


פגיעה ריאתית כתוצאה מהנשמה

ד״ר ווסים סעיד

מנהל יחידת טיפול נמרץ ביילוד

בית חולים משפחה קדושה, איטלקי

נצרת

Unique Challenges in NB Ventilation

Children ≠ Small Adults

Newborns ≠ Small Children

- Transitional circulation
- Compliant chest wall, stiff lungs
- Limited muscle strength and endurance
- Immature respiratory control
- Rapid RR, short time constants
- Small trachea, high ETT resistance
- Uncuffed ETT
- Awake, breathing patient

Need to understand the pathophysiology

INTRODUCTION

- Mechanical ventilation (MV) is a life saving intervention, but it also risks injury to the lungs, brain, and other organ systems.

- Supporting gas exchange while minimizing harm is the key therapeutic goal and challenge of MV in neonates.

Classification of prematurity categorized by birth weight or gestational age

	Birth weight
Low birth weight (LBW)	<2500 g
Very low birth weight (VLBW)	<1500 g
Extremely low birth weight (ELBW)	<1000 g
	Gestational age
Term	≥37 weeks
Late preterm	34 weeks to <37 weeks
Moderate preterm	32 weeks to <34 weeks
Very preterm	<32 weeks
Extremely preterm	<28 weeks

1- Ventilator-induced lung injury (VILI)

- **VILI** is lung injury caused by MV
- It can result from exposure to:

1. excessive pressure (***barotrauma***)
2. excessive stretching of the lung tissue (***volutrauma***)
3. cyclic collapsing of the alveolar spaces (***atelectrauma***)
4. exposure to ***high fraction of inspired oxygen***

Phase variables

A. Start

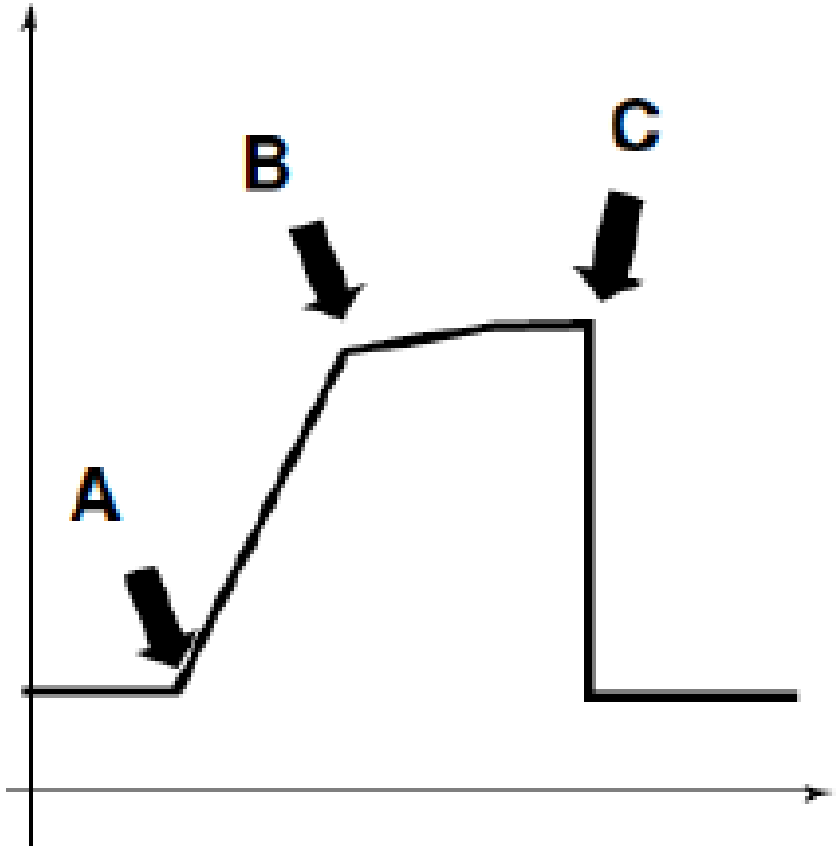
Trigger mechanism: What starts the breath?

B. Limits

What is controlled and what is variable?

C. End

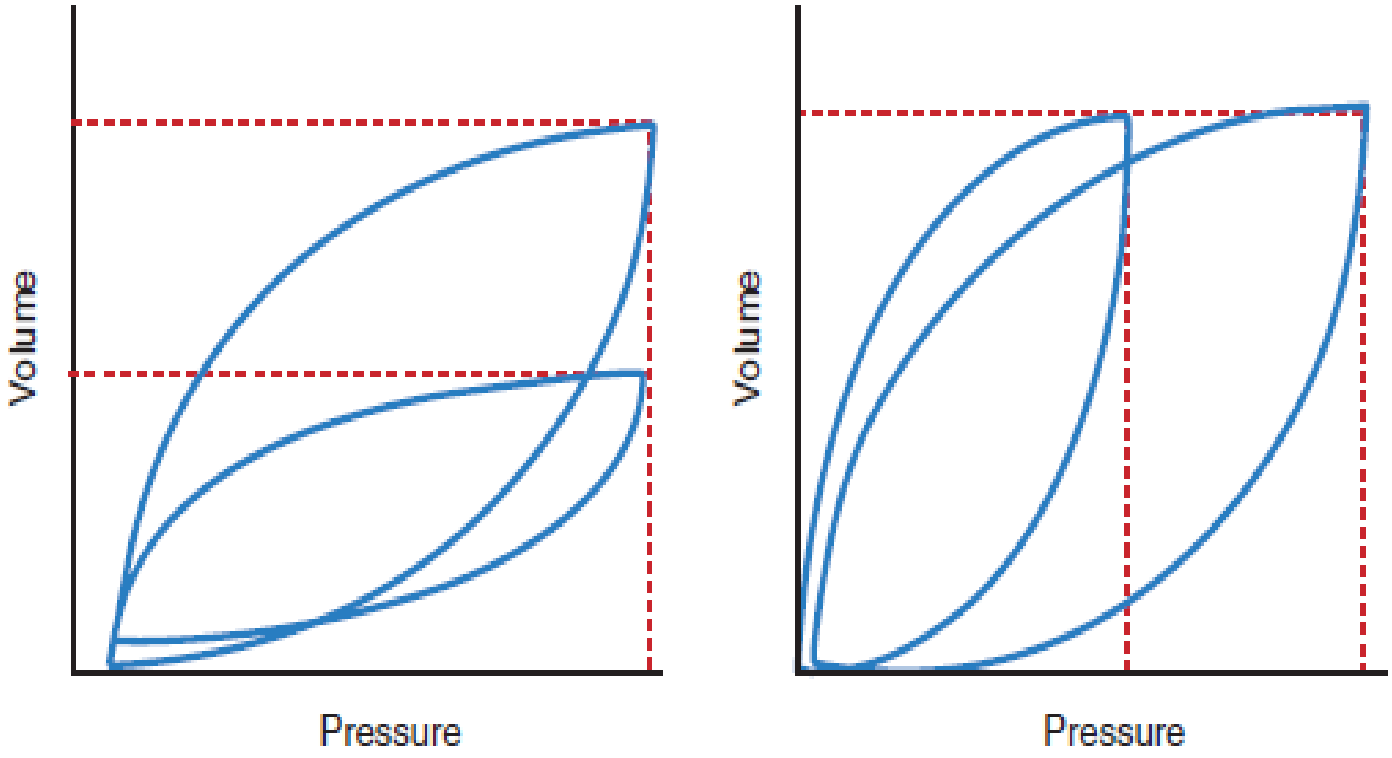
Cycle mechanism: what causes the breath to end?



Neonatal mechanical ventilation terminology

Broad categories of MV	
Conventional mechanical ventilation (CMV)	CMV generally refers to MV that provides breaths with Tvs and frequencies that approximate physiologic breathing. CMV is a broad category comprised of many different modes, with different types of breath triggering (eg, ACV, SIMV, PSV), and different types of breath limitation (eg, VTV and PLV).
High-frequency ventilation (HFV)	HFV refers to ventilation that delivers very small Tvs at very high frequencies on a sustained MAP. There are two types of HFV commonly used in neonates: ▪ High-frequency oscillatory ventilation (HFOV) ▪ High-frequency jet ventilation (HFJV)
Types of breath triggering in CMV	
Assist-control ventilation (ACV)	ACV provides mandatory breaths at a set rate (control breaths) and also supports spontaneous breaths above the set rate (assist breaths). The support is the same regardless of whether it is an assist or control breath. ACV can be used to deliver volume-targeted or pressure-limited breaths.
Pressure-support ventilation (PSV)	In PSV, all breaths are triggered by the patient's spontaneous effort (ie, there is no set rate). All breaths are pressure-limited.
Synchronized intermittent mandatory ventilation (SIMV)	In SIMV, all breaths are "mandatory" (ie, determined by a set rate), but the ventilator attempts to synchronize each breath with the patient's spontaneous effort, if present. SIMV can be used with either volume-targeted or pressure-limited breaths.
Synchronized intermittent mandatory ventilation + pressure support (SIMV + PS)	SIMV + PS is a combination of SIMV and PSV. Like ACV, it provides both mandatory and spontaneous breaths. Unlike ACV, the mandatory and spontaneous breaths are not the same. For example, if the SIMV component uses VTV, the mandatory breaths will be volume-targeted, while the spontaneous (PS) breaths will be pressure-limited.
Types of breath control or limitation in CMV	
Volume-targeted ventilation (VTV)	In VTV, the desired Tv is set, and the inspiratory pressure delivered to achieve it varies. There are different subtypes and terms for VTV, including VC, VG, and PRVC. The specific properties of each may differ among ventilator manufacturers.
Pressure-limited ventilation (PLV)	In PLV, the inspiratory pressure is set, and the size of the Tv depends on the compliance of the lungs and respiratory circuit. PC is the main mode in this category. In PC, the ventilator controls both the PIP and the Ti. PSV is another pressure-limited mode in which the ventilator controls the inspiratory pressure, but there is no Ti setting and breaths terminate based on declining flow.

PRESSURE VS. VOLUME
(CONTROL VARIABLES)



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Ventilator settings	
Inspiratory time (Ti)	Ti is the duration of the inspiratory phase for each breath. The Ti and the respiratory rate together determine the inspiratory to expiratory (i:e) ratio.
Mean airway pressure (MAP)	MAP is the average pressure applied over the entire respiratory cycle (including inspiration and expiration). In CMV, MAP is measured by the ventilator and is largely determined by the PEEP setting. In HFOV, MAP is a ventilator setting.
Minute ventilation (Ve)	The volume of gas exchanged per minute. It is determined by Tv and RR.
Peak inspiratory pressure (PIP)	PIP is the peak pressure during inspiration. In PLV, PIP is controlled by the ventilator (ie, it is a setting). In VTV, PIP will vary depending on the patient's lung compliance. However, some ventilators allow the clinician to set upper and lower PIP limits in VTV modes to provide some control over PIP.
Positive end-expiratory pressure (PEEP)	PEEP is the amount of pressure applied during expiration. PEEP acts to prevent atelectasis (derecruitment) and is a key setting for ensuring adequate oxygenation.
Respiratory rate (RR)	As a ventilator setting, RR refers to the number of mandatory breaths per minute.
Tidal volume (Tv)	Tv is the volume of each breath in mL. In VTV, Tv is controlled by the ventilator (ie, it is a setting). In PLV, Tv is not controlled by the ventilator and will vary depending on other settings (ie, inspiratory pressure and Ti) and the patient's lung compliance.

MV: mechanical ventilation; Tv: tidal volume; ACV: assist control ventilation; SIMV: synchronized intermittent mandatory ventilation; PSV: pressure support ventilation; VTV: volume-targeted ventilation; PLV: pressure-limited ventilation; MAP: mean airway pressure; VC: volume control; VG: volume guarantee; PRVC: pressure-regulated volume control; PC: pressure control; PIP: peak inspiratory pressure; Ti: inspiratory time; PEEP: positive end-expiratory pressure; RR: respiratory rate.

Minimizing ventilator-induced lung injury

- While lifesaving, MV also can cause lung injury and impact hemodynamics, with secondary consequences on the brain and other organs

- the impact of VILI and the imperative for utilizing lung-protective strategies are particularly important for preterm neonates

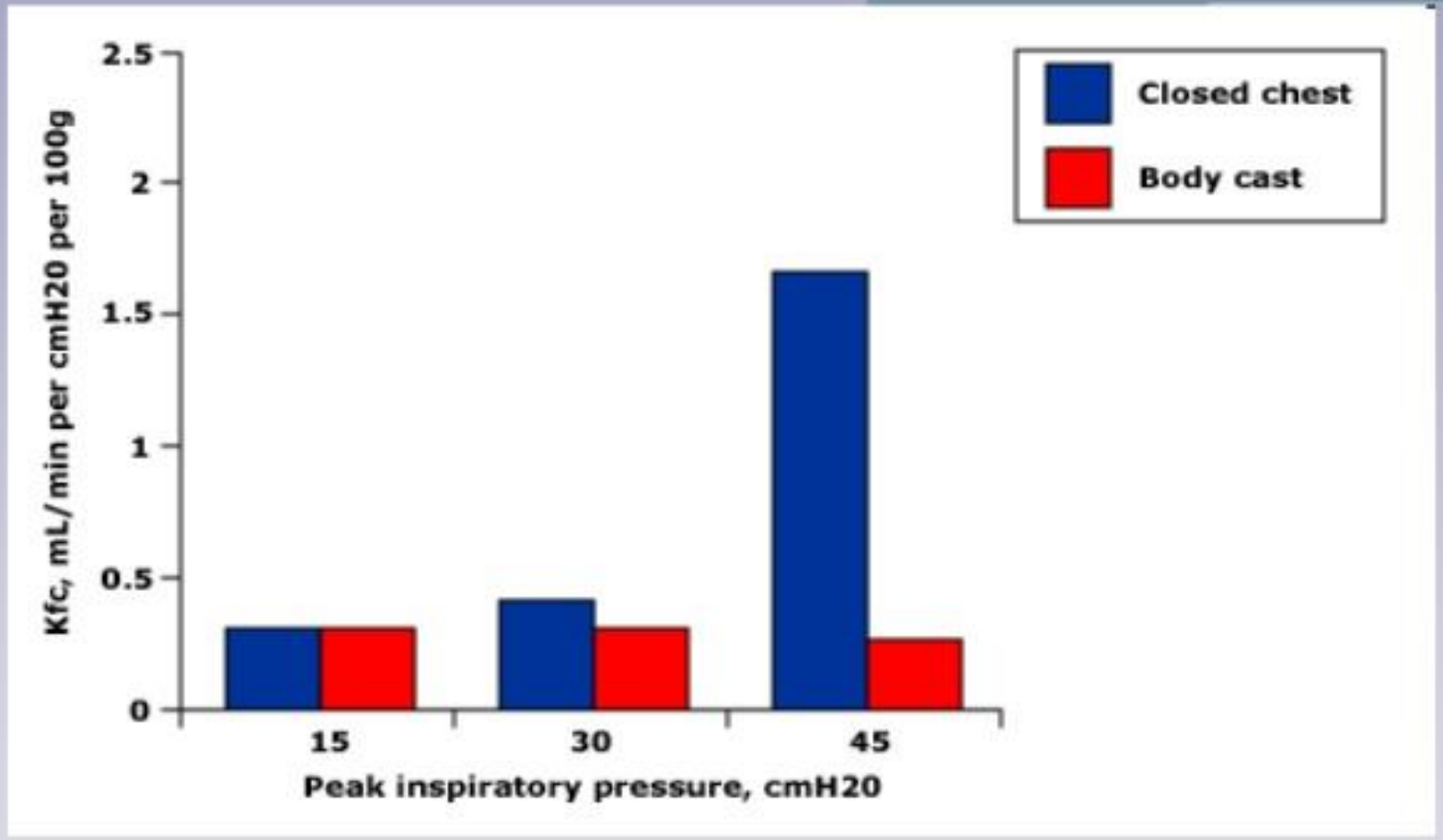
General Principles

1. Avoidance of MV through preferential use of non invasive respiratory support
2. Volume-targeting that supports gas exchange while minimizing volutrauma
3. Use of positive end-expiratory pressure (PEEP) to maintain lung recruitment and avoid atelectasis
4. Avoidance of high inspired oxygen levels
5. Setting targets for gas exchange that do not aim for normal levels (ie, modest permissive hypercapnia)
6. Use of HFV as a rescue therapy or as an initial ventilation strategy in neonates at high risk of developing VILI

Volutrauma

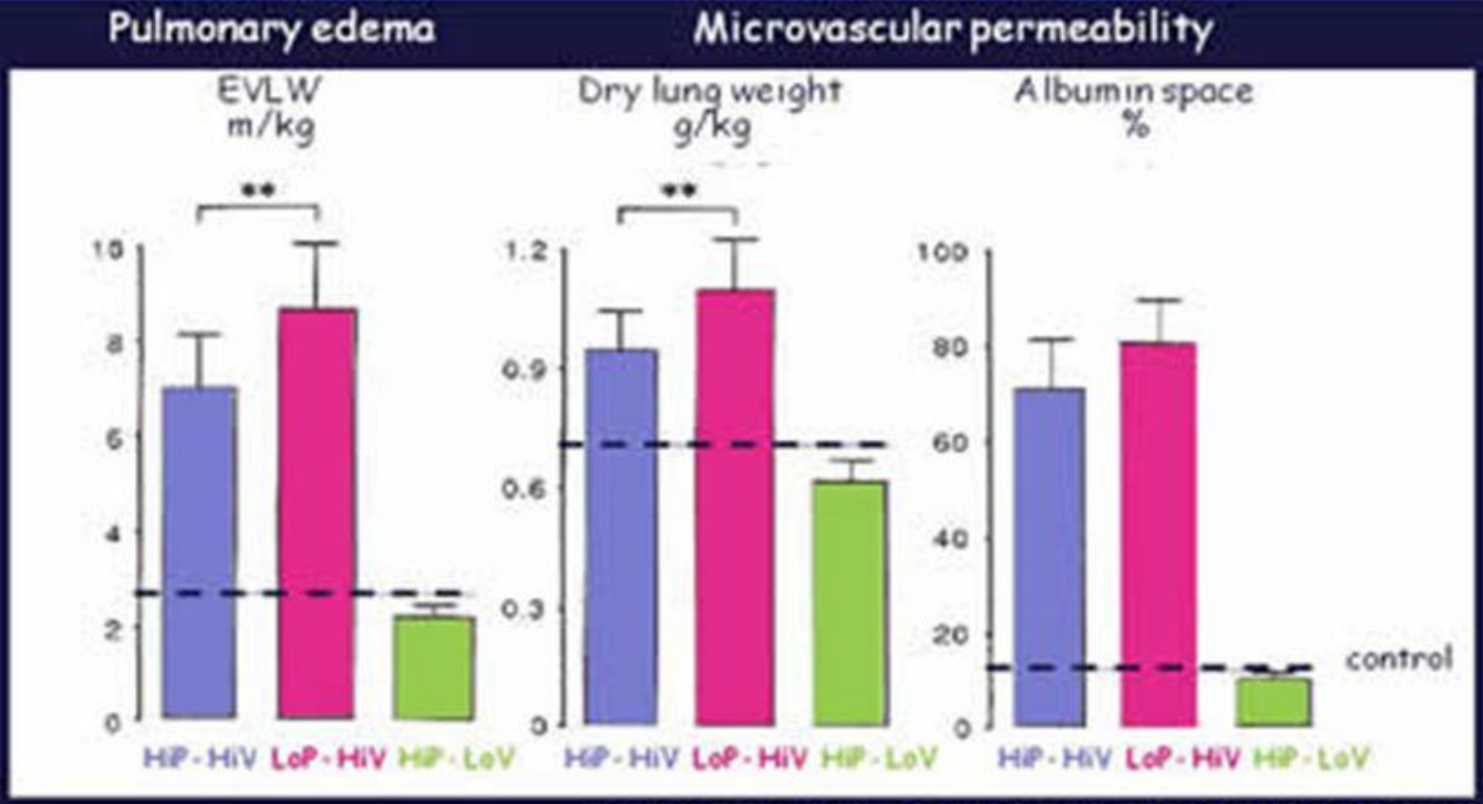
- Experimental data demonstrate that mechanical ventilation using both high tidal volumes and high peak pressures can cause lung injury

- however, data from various investigators consistently demonstrate that, regardless of the peak pressure, markers of lung injury in animals are increased with high tidal volume ventilation but not with low tidal volume ventilation



The effect of limited intrathoracic expansion by means of a body cast on ventilator-induced lung injury in rabbits. Rabbits were ventilated with 15, 30, and 45 cmH20 peak inspiratory pressure for one hour. *Redrawn from Hernandez, LA, Peevy, Kj, Moise, AA, Parker, JC, J Appl Physiol 1989.*

Volutrauma



Dreyfuss et al. Am Rev Resp Dis 1988; 132: 1159-64

Volutrauma

- At the microscopic and molecular level, volutrauma caused by mechanical overdistention leads to a diverse array of abnormalities:

1. Alveolar epithelial cell damage
2. alveolar protein leakage
3. altered lymphatic flow
4. hyaline membrane formation
5. and inflammatory cell influx

Hillman NH, Moss TJM, Kallapur SG, et al. Brief, large tidal volume ventilation initiates lung injury and a systemic response in fetal sheep. Am J Respir Crit Care Med 2007;176: 575–81.

Wada K, Jobe AH, Ikegami M. Tidal volume effects on surfactant treatment responses with the initiation of ventilation in preterm lambs. J Appl Physiol 1997;83(4):1054–61.

Volutrauma

- Volutrauma can also decrease lung compliance and alter surfactant structure and function
- The expression of genes involved in inflammatory signaling is up-regulated after mechanical ventilation with high tidal volumes

Veldhuizen RAW, Welk B, Harbottle R, et al. Mechanical ventilation of isolated rat lungs changes the structure and biophysical properties of surfactant. J Appl Physiol 2002;92: 1169–75.

Copland IB, Kavanagh BP, Engelberts D, et al. Early changes in lung gene expression due to high tidal volume. Am J Respir Crit Care Med 2003;168:1051–9

Volutrauma

- Because lung injury contributes to BPD, efforts to decrease volutrauma in preterm infants should decrease the risk of this disorder

- The shift towards increasing use of VTV in neonates was spurred by preclinical observations that tissue stretch from lung overdistension (volutrauma) caused more lung inflammation and injury than exposure to high pressure without excessive stretch (barotrauma)

Cochrane Database Syst Rev. 2017

Volume-targeted versus pressure-limited ventilation in neonates

- A 2017 systematic review and meta-analysis identified 20 randomized controlled trials comparing VTV and PLV in 977 neonates (predominantly preterm neonates)

Cochrane Database Syst Rev. 2017

1. Shorter **duration of MV** (mean difference 1.35 days shorter; 95% CI 0.86-1.83 days)
2. Lower incidence of **pneumothorax** (5 versus 9%; rate ratio [RR] 0.52, 95% CI 0.31-0.87)
3. Lower incidence of **BPD** at 36 weeks (23 versus 35%; RR 0.68, 95% CI 0.53-0.87)
4. Lower incidence of **PVL** or **grade 3 and 4 IVH** (8 versus 16%; RR 0.47, 95% CI 0.27-0.80)
5. *Nonsignificant* trend towards **lower mortality** (12 versus 16 percent; RR 0.75, 95% CI 0.53-1.07)

Cochrane Database Syst Rev. 2017

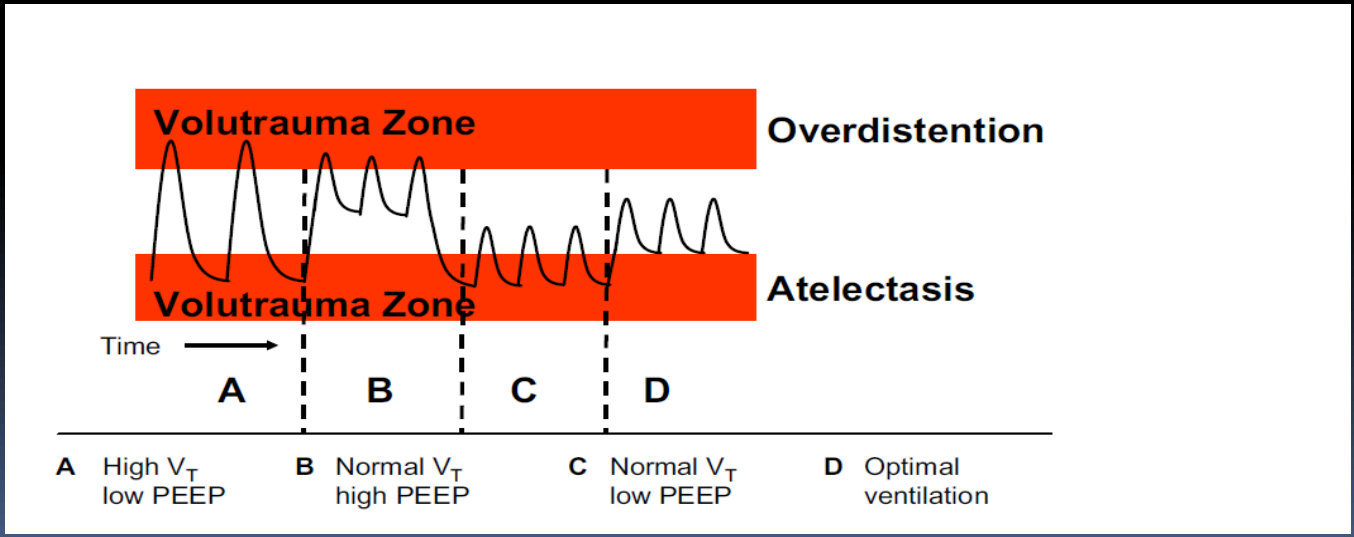
- All of the trials included in the meta-analysis compared volume-targeted with pressure-limited strategies, but there was:

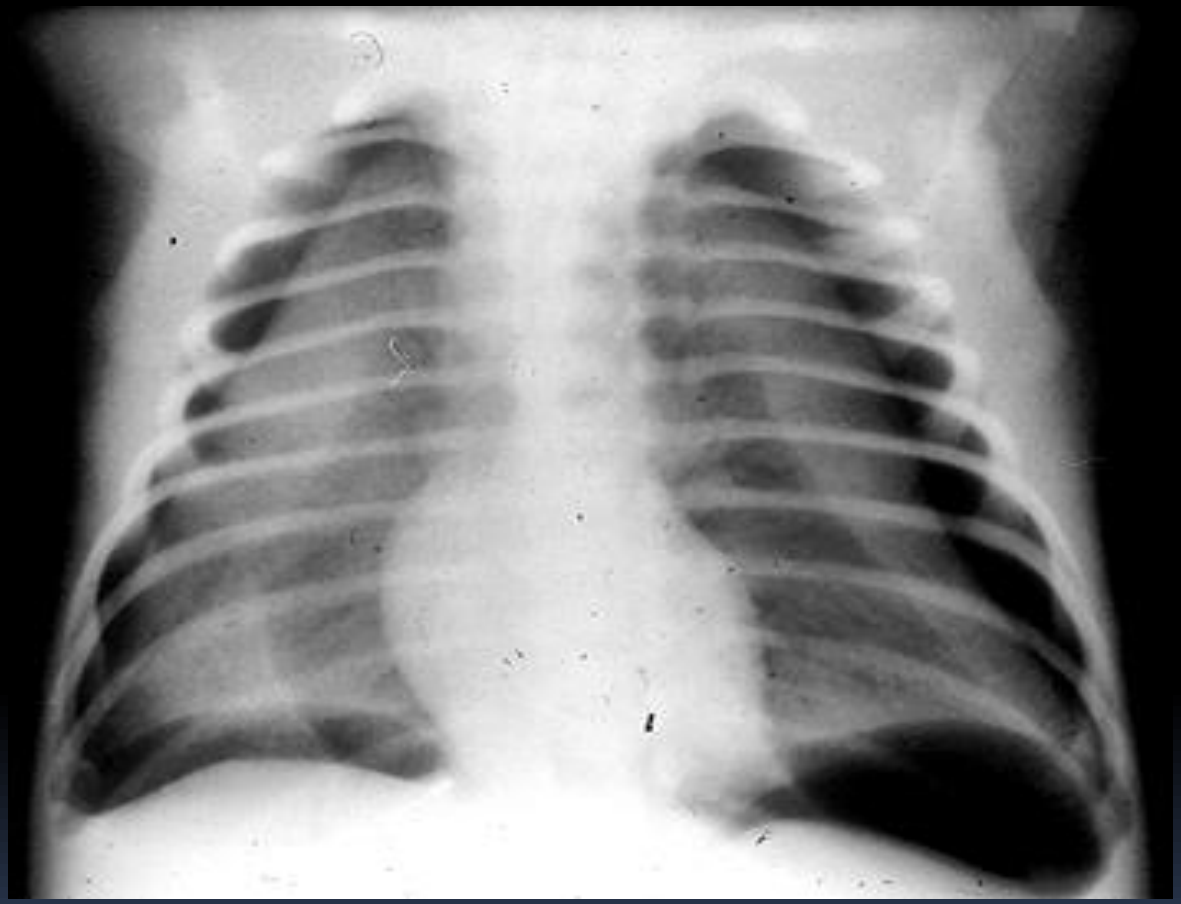
1. considerable heterogeneity with respect to the specific mode used in each arm.
2. In addition, the trials were conducted at centers with relative expertise in the use of VTV.

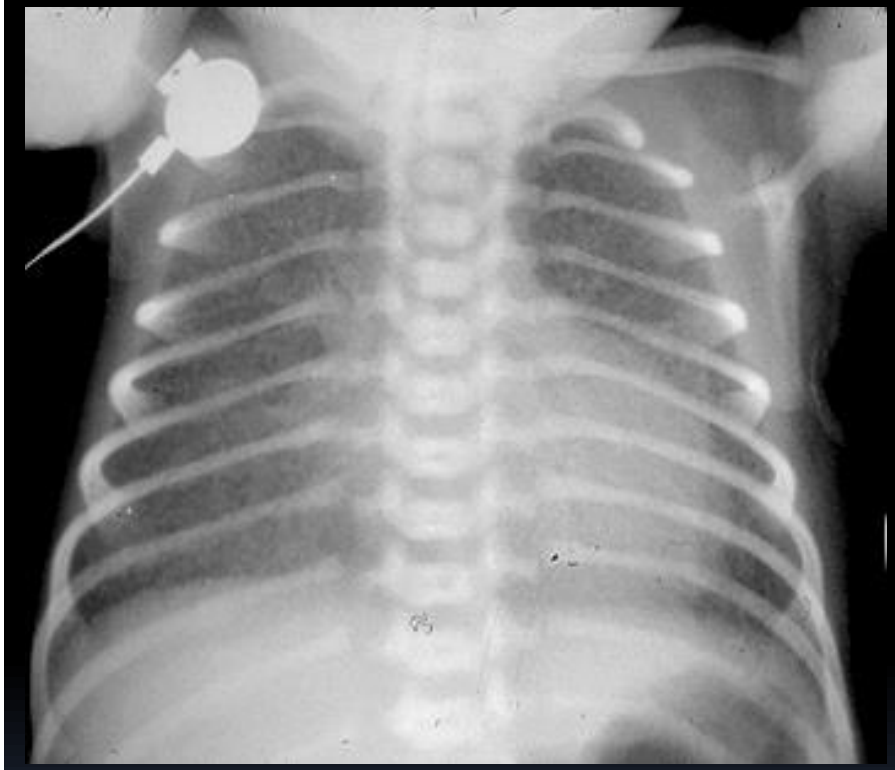
- The generalizability of these results to centers implementing the novel use of VTV remains uncertain

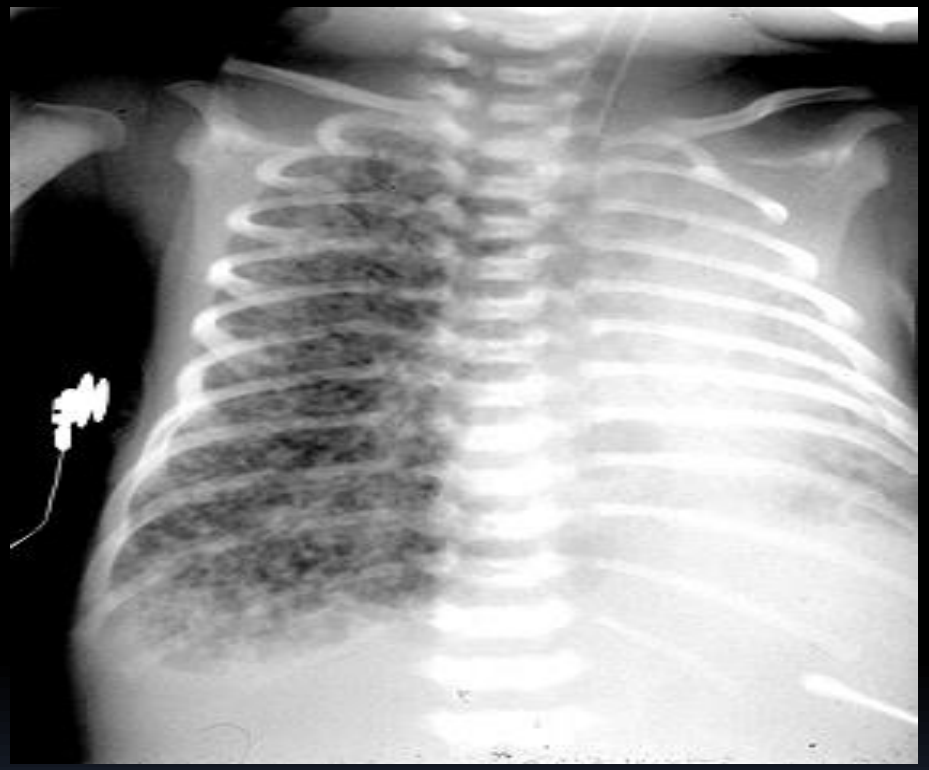
Ventilator-induced lung injury (VILI)

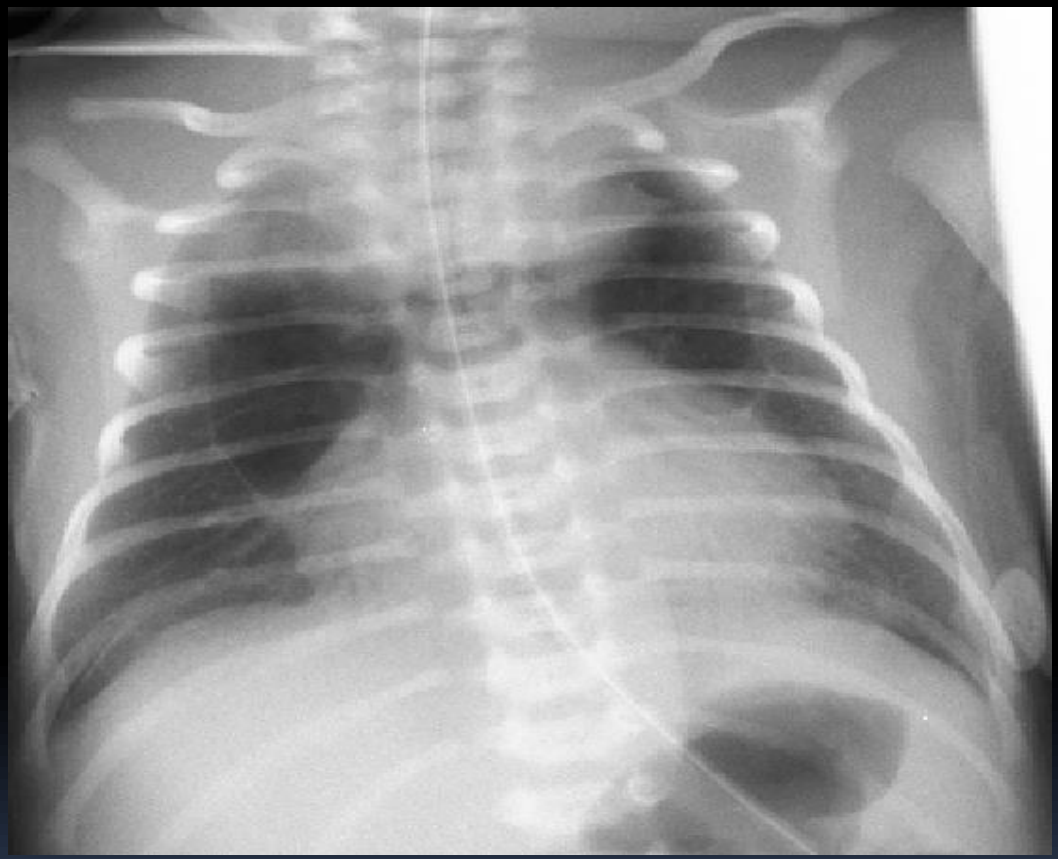
- The best ventilator strategy may consist of using adequate PEEP to maintain FRC to avoid atelectrauma and using an optimal tidal volume to avoid volutrauma

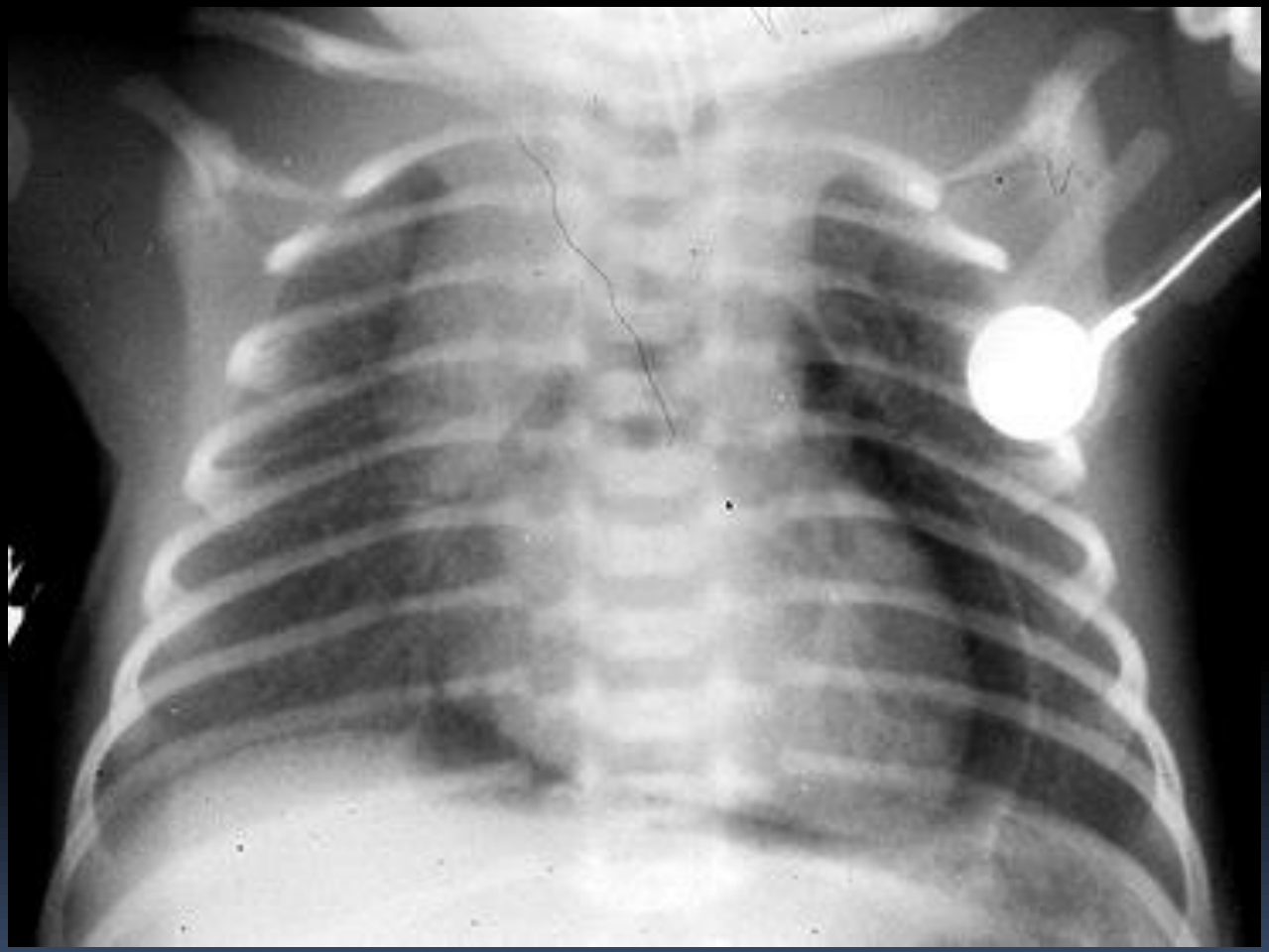












2- Pulmonary air Leak in the newborn

- Pulmonary air leak occurs more frequently in the newborn period than at any other time of life
- It occurs when air escapes from the lung into extra-alveolar spaces where it is not normally present
- The resulting disorders depend upon the location of the air:
- Pneumothorax , pneumomediastinum , pulmonary interstitial emphysema , and pneumopericardium . Rarer forms are pneumoperitoneum and subcutaneous emphysema.

INCIDENCE

- The incidence is higher in preterm infants, who often have pulmonary disease

- In a report from the Vermont Oxford database, pneumothorax was reported in 6.3% of 26,007 infants with BW 500 to 1500 grams in 1999
- Since that published report, the incidence of pneumothorax has decreased for infants with BW 500 to 1500 grams registered in the Vermont Oxford Network database (2014)

BMC Pediatr. 2014 bupE .14:208;2014Aug 23

PNEUMOTHORAX

- Clinical features
- Diagnosis
- Management:

1. Oxygen supplementation?

Shaireen H, Rabi Y, Metcalfe A, et al. Impact of oxygen concentration on time to resolution of spontaneous pneumothorax in term infants: a population based cohort study. BMC Pediatr 2014; 14:208.

2. In mechanically ventilated infants, ventilator settings should be adjusted,

- In some cases of infants who do not require high ventilatory settings, spontaneous resolution may occur without **Thoracentesis** or **chest tube placement**.

Litmanovitz I, Carlo WA. Expectant management of pneumothorax in ventilated neonates. Pediatrics 2008; 122:e975.

PULMONARY INTERSTITIAL EMPHYSEMA

- air trapped in the perivascular tissues of the lung
- This results in decreased compliance and overdistention of the lung
- It usually presents within 96 hours of birth with gradually worsening hypoxemia and hypercarbia.
- Ventilator settings are often increased in response to the poor gas exchange, which may exacerbate air trapping and lead to further worsening of oxygenation and ventilation
- decreased venous return and impaired cardiac output

PIE: Management

- There is no definitive treatment for PIE
- adequate gas exchange and minimizing the risk of further air leak:

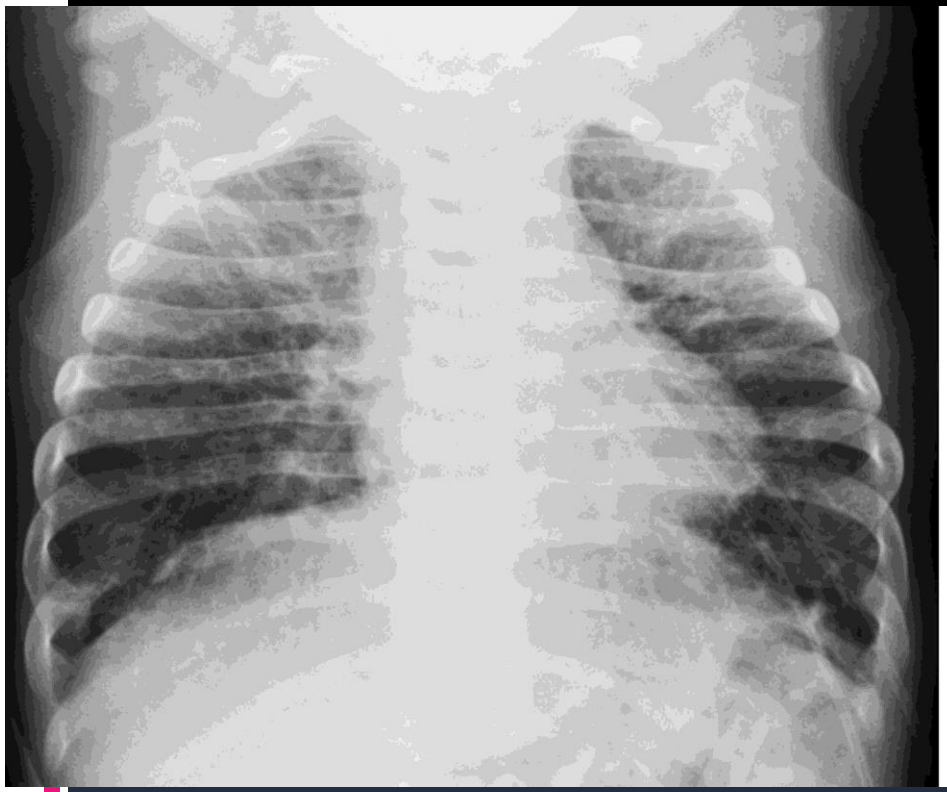
1. decreasing the MAP as much as possible (PIP, PEEP, Ti)
2. The FiO2 concentration should be increased to compensate for the decreased MAP
3. HFV to avoid large cyclic swings in tidal volume? (trials of this intervention are not available)

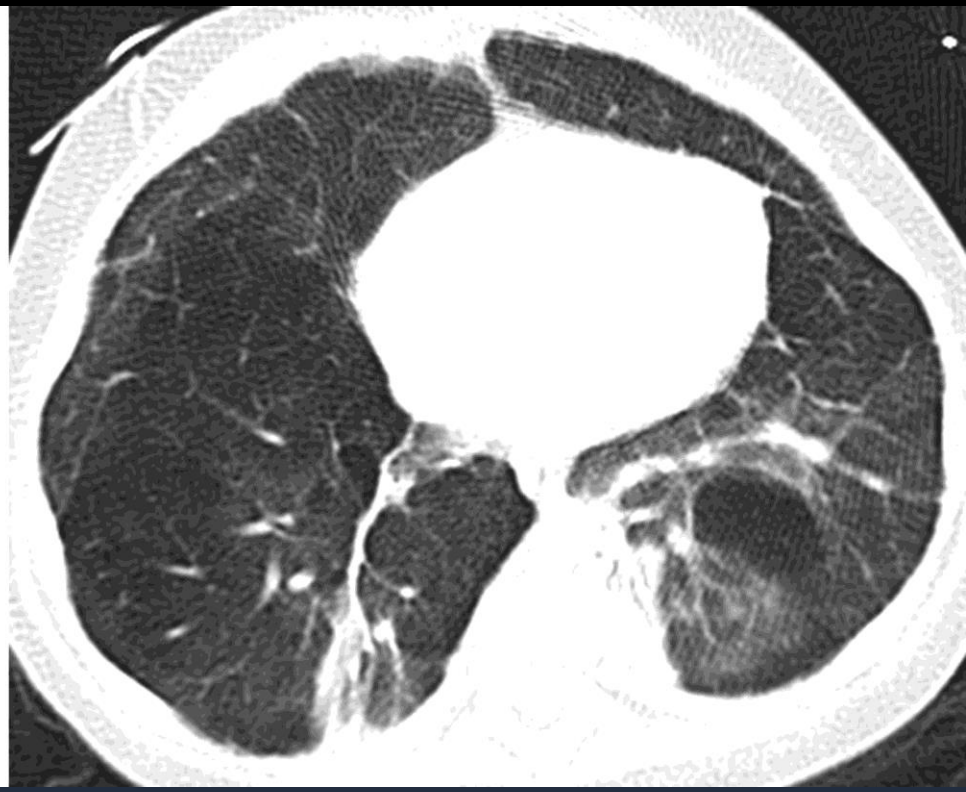
Unilateral PIE

- Placing the infant in the lateral decubitus position with the affected side down promotes aeration of the unaffected lung and reduces aeration of the lung with PIE

- In severe cases, selective bronchial intubation of the contralateral lung or occlusion of the bronchus of the affected lung by use of a Swan-Ganz catheter may promote decompression and healing of the affected lung

Rastogi S, Gupta A, Wung JT, Berdon WE. Treatment of giant pulmonary interstitial emphysema by ipsilateral bronchial occlusion with a Swan-Ganz catheter. Pediatr Radiol 2007; 37:1130





3-BPD

Abiramalatha T, Ramaswamy VV, Bandyopadhyay T, et al.

Interventions to Prevent Bronchopulmonary Dysplasia in Preterm Neonates: An **Umbrella Review of Systematic Reviews and Meta-analyses**.

***JAMA Pediatr.* 2022**;176(5):502–516

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
1-Delivery Room CPAP

- **High COE** indicated that initiation of CPAP in the delivery room compared with routine intubation with or without surfactant administration was associated with a lower risk of BPD or mortality

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
2- Surfactant Therapy

- **High COE** showed that prophylactic surfactant was associated with an increased risk of BPD or mortality when compared with stabilization receiving CPAP with selective surfactant administration

- **High COE** indicated that early (within 3 hours) selective surfactant administration compared with delayed surfactant therapy was associated with a lower risk of BPD or mortality

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
2- Surfactant Therapy

- **Moderate COE** suggested that surfactant therapy using LISA was associated with lower risk of BPD or mortality at 36weeks when compared with the INSURE technique

- **Moderate COE** suggested that porcine surfactant used at a dose of more than 100mg/kg, compared with bovine lung surfactant ,was associated with decreased risk of BPD or mortality

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
3- Inhaled Corticosteroids

- **High COE** suggested that inhaled corticosteroids administered in the first 2 weeks of life were associated with decreased risk of BPD or mortality at 36 weeks' PMA

-increased risk of mortality-

Ramaswamy VV, Bandyopadhyay T, Nanda D, et al.

Assessment of postnatal corticosteroids for the prevention of BPD in preterm neonates: a systematic review and network meta-analysis. *JAMA Pediatr. 2021*

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
3- Systemic Corticosteroids

Early Systemic Steroids (Started≤7Days)

- **High COE** showed that early systemic dexamethasone was associated with decreased risk of BPD or mortality at 36weeks' PMA

there is international consensus against its use in neonates during the first week of life

- **High COE** suggested that hydrocortisone initiated within the first week (for varying reasons, was associated with decreased risk of BPD or mortality in infants born at less than 32 weeks

Primary Outcome: BPD or Mortality at 36 Weeks' PMA: 4- Ventilation Strategies

Volume-Targeted Ventilation vs Pressure-Limited Ventilation

- volume-targeted ventilation was associated with decreased risk of BPD or mortality at 36 weeks' PMA with a **high COE**

Primary Outcome: BPD or Mortality at 36 Weeks' PMA: 4- Ventilation Strategies

Elective HFOV vs CMV

- **Low COE** suggested that elective HFOV was associated with decreased risk of BPD or mortality at 36 weeks' PMA when compared with CMV

Primary Outcome: BPD or Mortality at 36 Weeks' PMA:
5- High-Dose Caffeine

- 40-80mg/kg loading dose + 20mg/kg maintenance compared with standard dose 20 mg/kg in neonates less than 32 weeks' gestation and older than 14 days of life was associated with decreased risk of BPD or mortality at 36weeks'PMA

- The **COE was low**

Primary Outcome:BPD at 36 Weeks' PMA

- The interventions that were associated with significant decrease in BPD at 36weeks' PMA with **moderate to high COE** **but not the combined outcome of BPD or mortality** included:

1. Vitamin A supplementation
2. targeting lower oxygen saturation targets (85%-89%)
3. iNO use (routine use or within 3 days for hypoxic respiratory failure or after 3 days for decreasing the risk of BPD).

This suggests that they might be associated with an increased risk of mortality

4-Ventilator-Associated Pneumonia (VAP)

- pneumonia characterized by the presence of new and persistent focal radiographic infiltrates in a ventilated infant appearing more than 48 hours after admission to the neonatal intensive care unit

- It results from:

1. either dissemination of microorganisms from colonized mucosal sites
2. aspiration of gastric contents
3. Occasionally microorganisms may be transmitted from contaminated equipment

VAP

- 0.3-1.6 cases per 1000 ventilator days
- risk factors and associations

1. Prematurity
2. use of corticosteroids
3. H2 blockers
4. Antacids
5. proton pump inhibitors
6. Overcrowding
7. Understaffing
8. and inadequate disinfection of equipment

VAP

- One should suspect VAP in a ventilated infant if there is deterioration in the respiratory status unexplained by other events or conditions
- Radiographic findings are nonspecific and may be difficult to distinguish from chronic lung disease in the older baby
- Bacterial and fungal pathogens are the most common agents

VAP

- Tracheal aspirates?? (merely reflect colonization)
- Laboratory investigations (not specific)
- Management of VAP includes

1. broad-spectrum antibacterial and/or antifungal agents
2. hemodynamic support
3. and provision of adequate nutrition
4. inhaled NO and/or ECMO
5. Surfactant??

VAP

- more frequent positioning of babies on their sides, as opposed to supine, may decrease the incidence of VAP

Aly H, Badawy M, El-Kohly A, et al. Randomized, controlled trial on tracheal colonization of ventilated infants: can gravity prevent ventilator-associated pneumonia? *Pediatrics. 2008*

5-Airway Complication: Upper Airway

- result from mechanical damage to structures in the naso-or oropharynx, trachea, and larynx.
- These injuries include:

1. superficial mucosal erosion
2. damage to the alveolar ridge (with subsequent dental problems)
3. perforation of the esophagus or trachea
4. injury to the vocal cords
5. injury related to fixation devices such as tape

Upper Airway

- Long-term nasotracheal intubation may cause:

1. erosion of the nasal septum and nasal deformities
2. Acquired palatal grooves
3. and even cleft palate have been described after long-term orotracheal intubation

Trachea

- Less serious problems, which tend to resolve spontaneously over time:

1. tracheal and laryngeal mucosal metaplasia
2. subglottic cysts
3. tracheal enlargement
4. and tracheo-bronchomalacia

Trachea

Subglottic stenosis

- Is a life-threatening condition
- generally requiring tracheostomy
- Its etiology is still not completely understood, but associations have been demonstrated for:

1. duration of intubation
2. number of intubations
3. and the degree of prematurity

Trachea

Necrotizing tracheobronchitis

- highly lethal acquired entity
- This disorder was seen most commonly:

1. in the early days of HFJV
2. and was felt to be related to the effects of insufficient humidification of inspired gas

It has all but disappeared since refinements in <u>humidification systems</u>

6- Miscellaneous Complications

- ***Imposed Work of Breathing:*** increase in airway resistance, increase in dead space created------ Assist/Control Ventilation
- ***PDA***
- ***IVH and PVL***: hypercapnia and hypocapnia respictively, fluctuation in cerebral blood flow observed in babies who fight the ventilator (asynchronous breathing), overdistension, Increased intrathoracic pressure , endotracheal tube suctioning or re-intubation
- ***ROP***: degree of prematurity and a high arterial oxygen content

thank you