Meconium Aspiration Syndrome (MAS)

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Objectives

- Review:
  - the significance of MSAF
  - the pathophysiology of MAS
  - the risk factors for MAS
  - the neonatal consequences of MAS
  - The management of MAS
  - the NRP guidelines in the management of MSAF in L and D

Abbreviations

- **MSAF**
  - Meconium-stained amniotic fluid
- **MAS**
  - Meconium aspiration syndrome

μηκονειον

- *mekoneion*

  = Greek word for poppy juice or opium

  – the sedative effects on the unborn infant observed by Aristotle and the physical resemblance with poppy juice explain why the sticky dark green material from the fetal intestinal tract is called **meconium**.

de Boufort *Early Human Devt* 2009

Meconium

First seen in the fetal intestine during the 3rd month of gestation

- Sterile, thick, blackish green (due to bile pigments), odorless
- Collects in the distal SI and colon
- Consists of intestinal secretions, bile, desquamated cells from the GIT and skin, lanugo hairs, fatty material from the vernix caseosa, and amniotic fluid
- comprises 72 to 80% water and contains cholesterol and its precursors, lipids, enzymes including pancreatic phospholipase A2, mucopolysaccharides, protein (decreases throughout gestation), bile acids and salts as well as drug metabolites
- 94 % of newborn pass meconium stool within 24 h after birth
- Delayed passage in preterms because rectal sphincteric reflexes may be absent or impaired

Scope of the problem

- 10-18 % of deliveries with **MSAF** (500,000/y US)
  - 7-22% of term deliveries overall
  - 23-52% after 42 wks (Hofmeyr, 2009)
  - is associated with:
    - reduced amniotic fluid index (<5 cm)
    - reduced middle cerebral artery pulsatility index
    - maternal fever
    - opiate and cocaine use
    - multiple nuchal cord loops in postdate pregnancies
- 3-6 % of infants born through **MSAF** develop **MAS**
- 30 % of require mechanical ventilation (Vidyasagar, 1975)
- 11% will develop pneumothoraces
- Overall mortality is 3-5 % (Desmond, 1975) ; 5-10 % (Wiswell, 2008)
    - 2**%** of all perinatal deaths

MSAF: Frequency

In a cohort of 45,673 term pregnancies:

Gestational age (wks)	(n)	MSAF (%)
37	(3964)	3
38	(8865)	5*
39	(13,839)	8*
40	(12,456)	13*
41	(5685)	17*
>42	(864)	18*

*P<0.001 compared with the prior week of gestation.

Poggi *Early Human Devt* 2009

MAS: Definition

- (Rossi)
  - respiratory distress, in the setting of MSAF, in the first 4h after birth with O_2 requirement and CXR showing characteristic features of MAS.

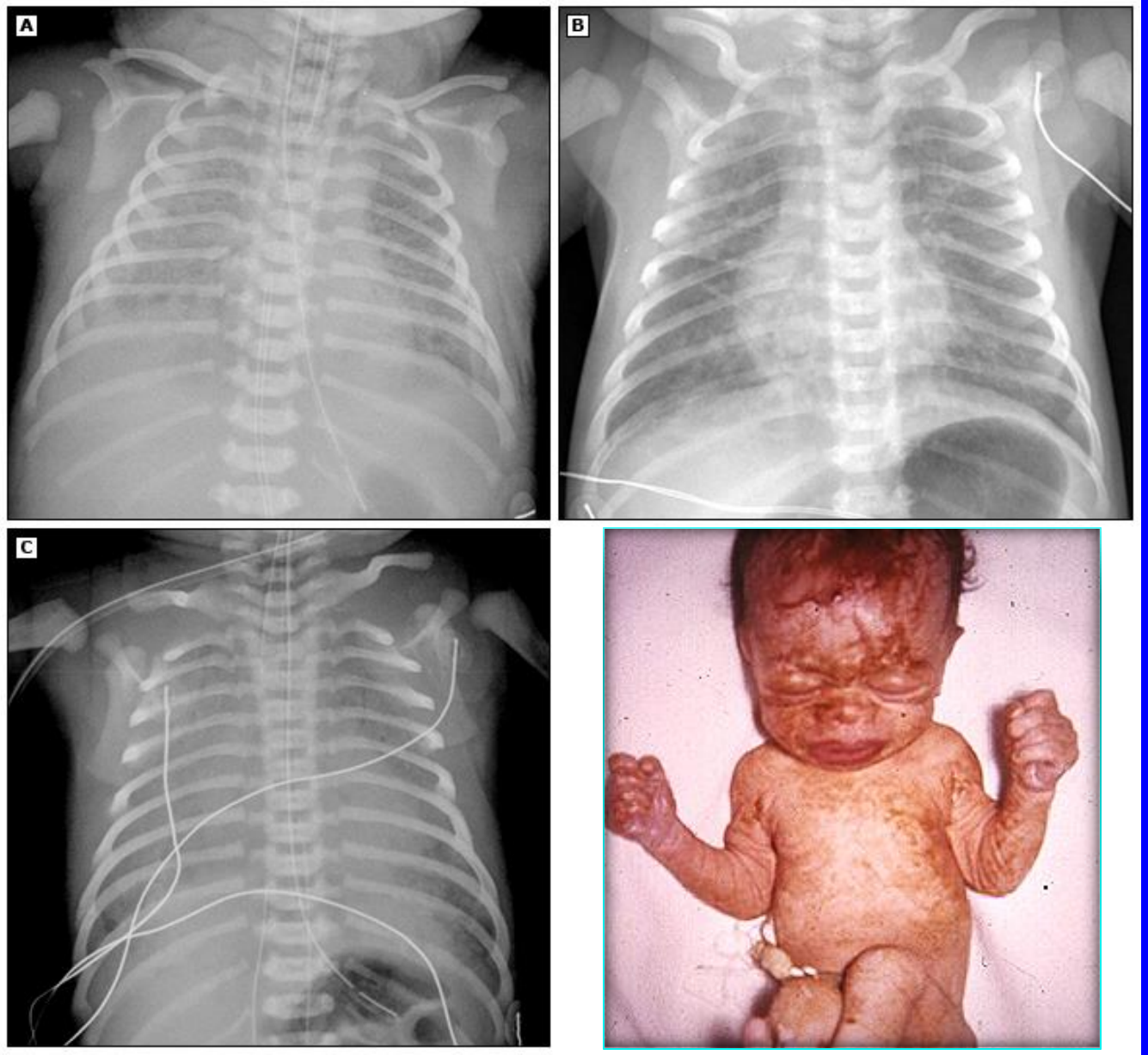
- (Cleary and Wiswell)
  - respiratory distress in an infant born through MSAF, which "cannot be otherwise explained."
    - Mild MAS = requiring <40% O_2 for <48 h
    - Moderate MAS = requiring >40% O_2 for at least 48 h
    - Severe MAS = requiring assisted mechanical ventilation; often associated with persistent pulmonary hypertension

  - The severity of MAS does not necessarily correspond to the degree of CXR abnormality.

Clinical Presentation

- Low Apgar Scores
- MAS pts are often postmature, with visible meconium staining of nails, skin, and cord
  - Tachypnea
  - Retractions
  - Cyanosis
  - Barrel-chest (lung over-inflation)
  - Coarse breath sounds (rhonchi; rales)
  - Poor peripheral perfusion
- Resp distress may persist with prolonged O_2 requirement for days
- Shorter course usually are retained lung fluid issues (TTN) rather than true MAS

Clinical presentation



MAS: CXR

- The severity of MAS does not necessarily correspond to the degree of CXR abnormality.

- MAS is associated with a range of X-ray features including:
  - coarse, patchy infiltrates
  - consolidation
  - atelectasis
  - pleural effusions
  - air leaks
  - hyperinflation
  - wet-lung picture
  - hypovascularity
  - (Pneumothorax and Pneumomediastinum are common)

- In some cases, the CXR may be interpreted as normal.

Differential Diagnoses of MAS (when MSAF is present at delivery)

Transient tachypnea of the newborn (TTN)

Aspiration of amniotic fluid or blood

Respiratory distress syndrome (RDS)

Sepsis with pulmonary edema

Pneumonia

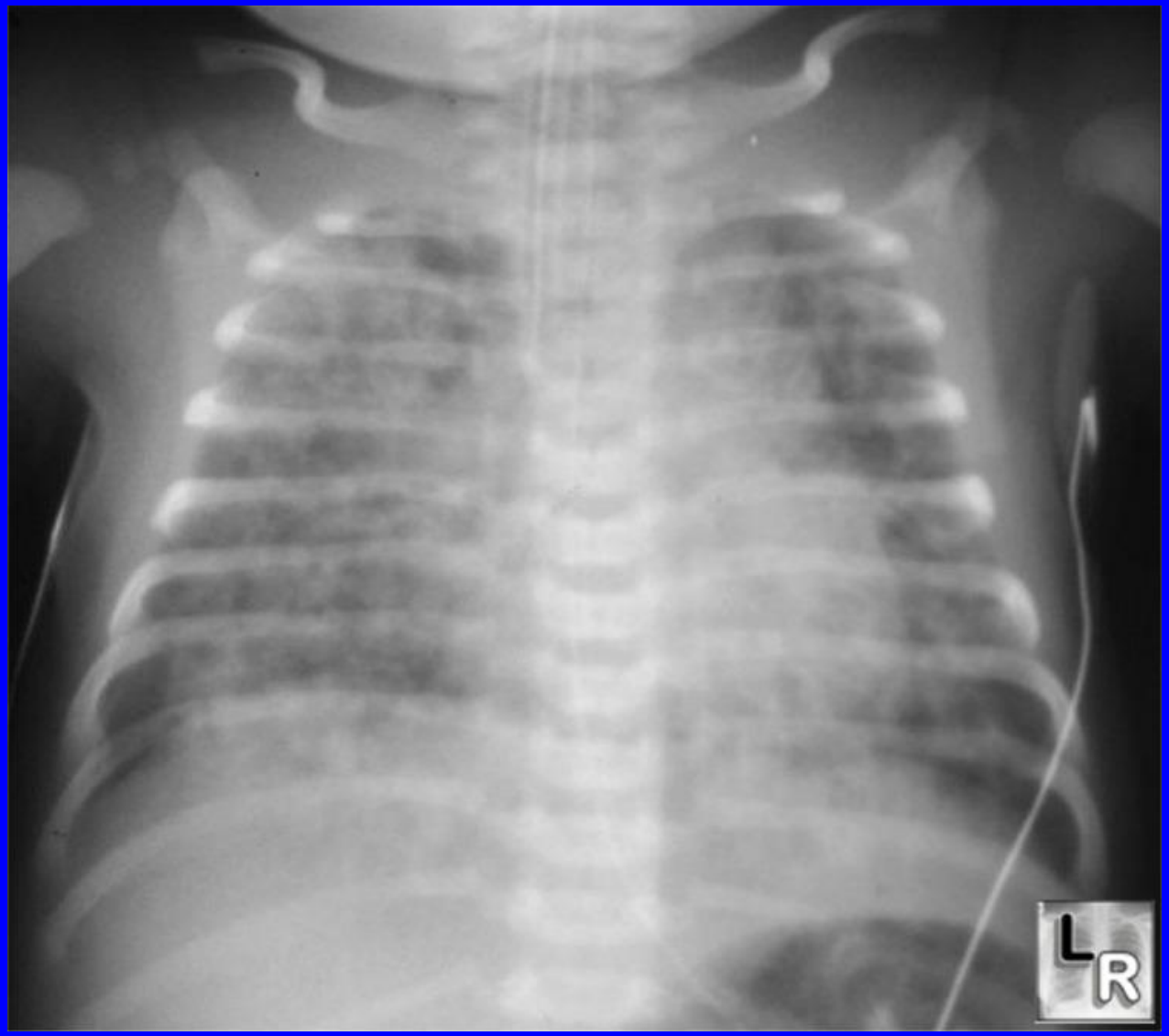
Congenital heart disease

Intrapartum asphyxia with cardiomyopathy

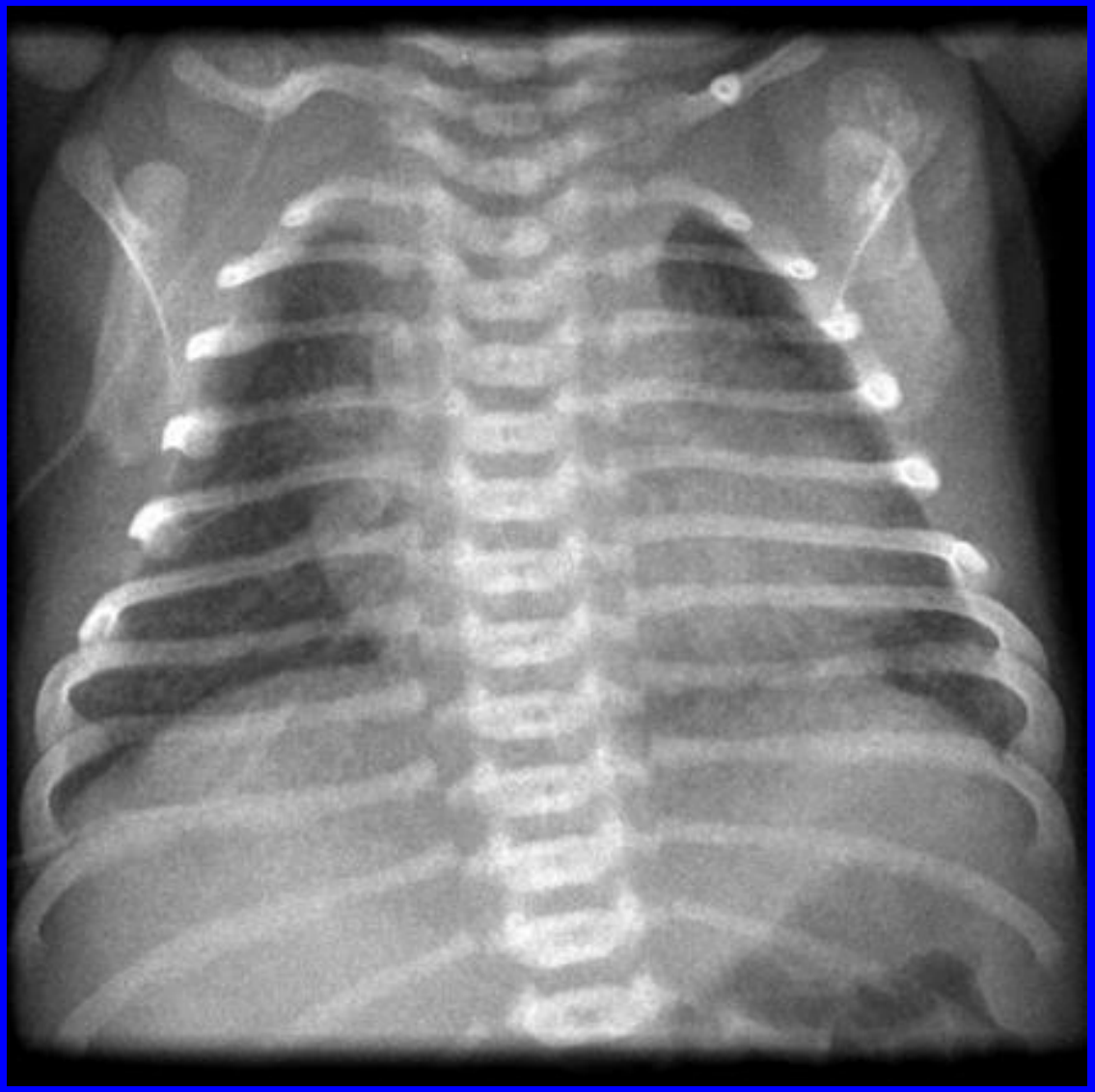
Persistent pulmonary hypertension of the newborn (PPHN)

Delayed transition

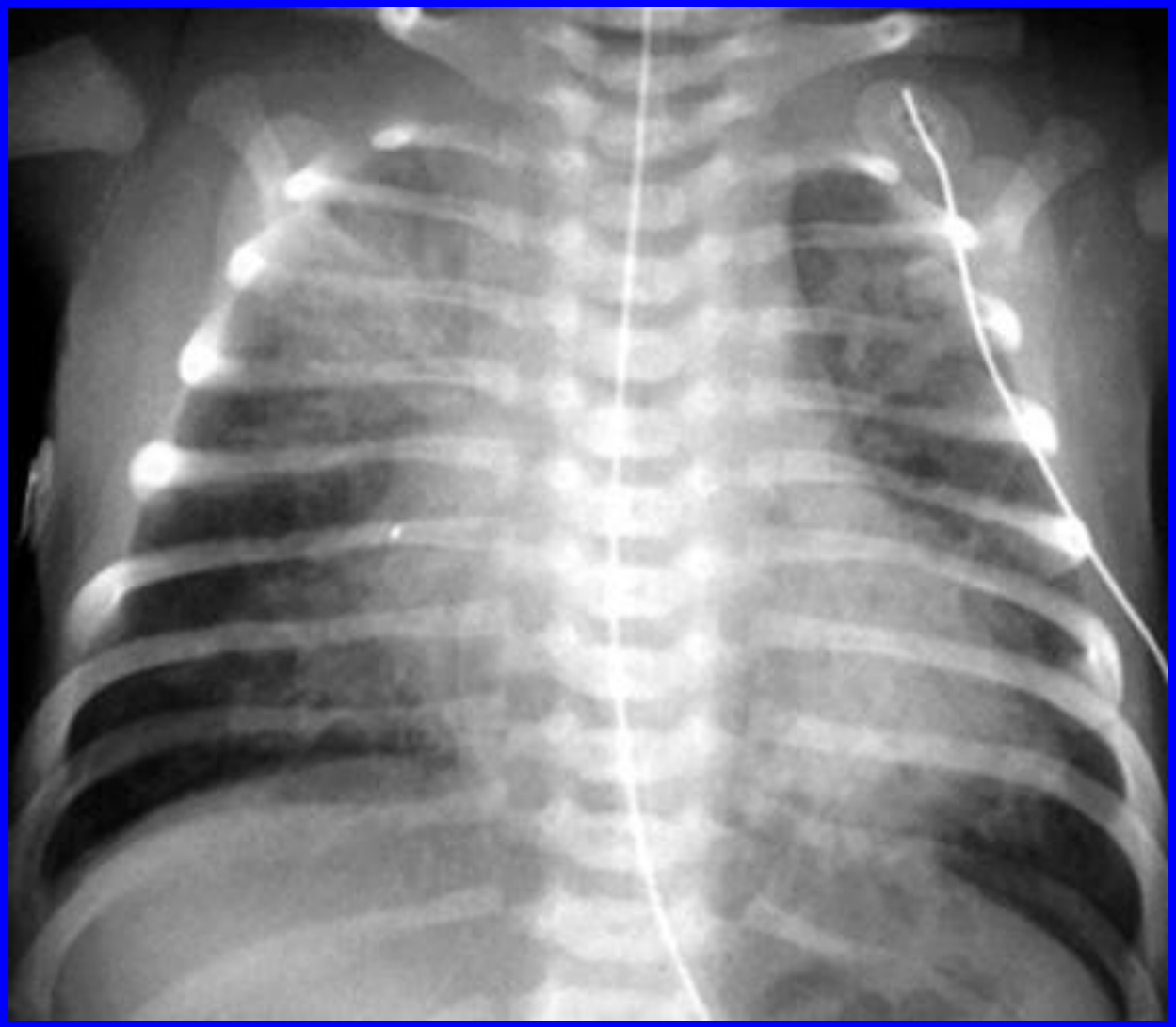
CXR: Post-mature with MAS

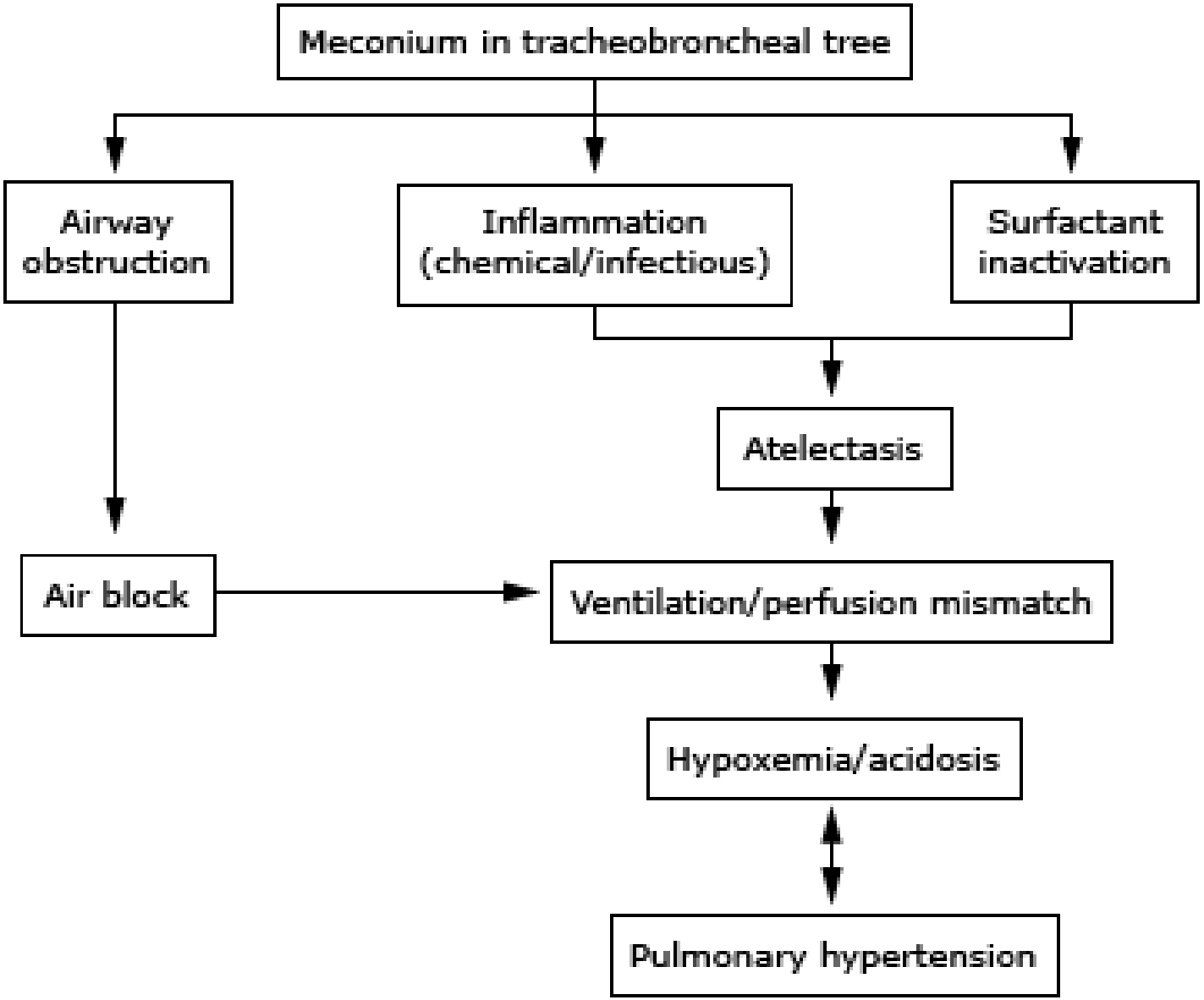


CXR: MAS mimics TTN

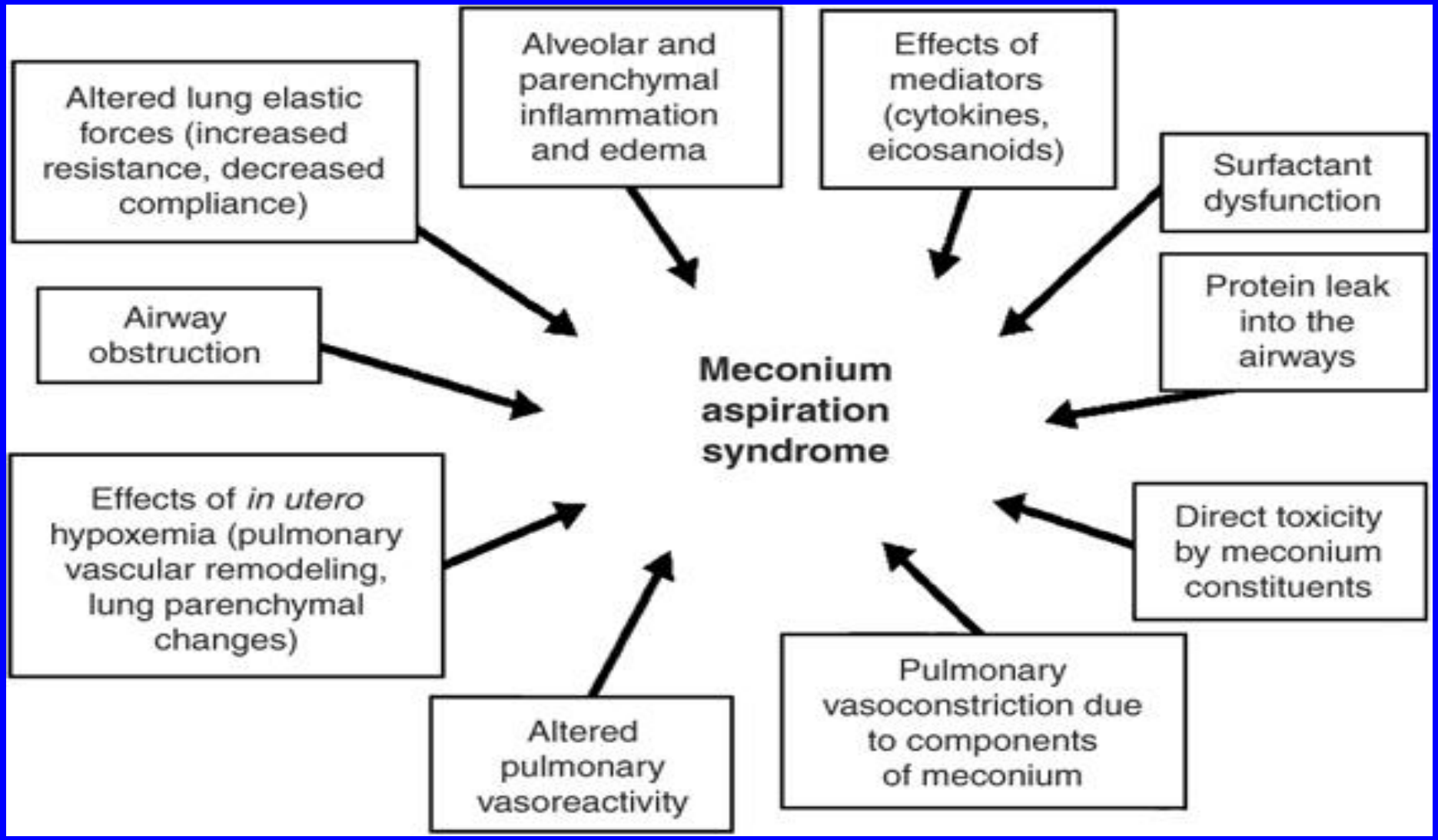


CXR: MAS (patchy, asymmetric densities with hyperinflation)




Meconium in tracheobroncheal tree
Airway obstruction
Inflammation (chemical/infectious)
Surfactant inactivation
Atelectasis
Air block
Ventilation/perfusion mismatch
Hypoxemia/acidosis
Pulmonary hypertension

Mechanisms playing role in development of MAS



Goldsmith *J Perinat* 2008

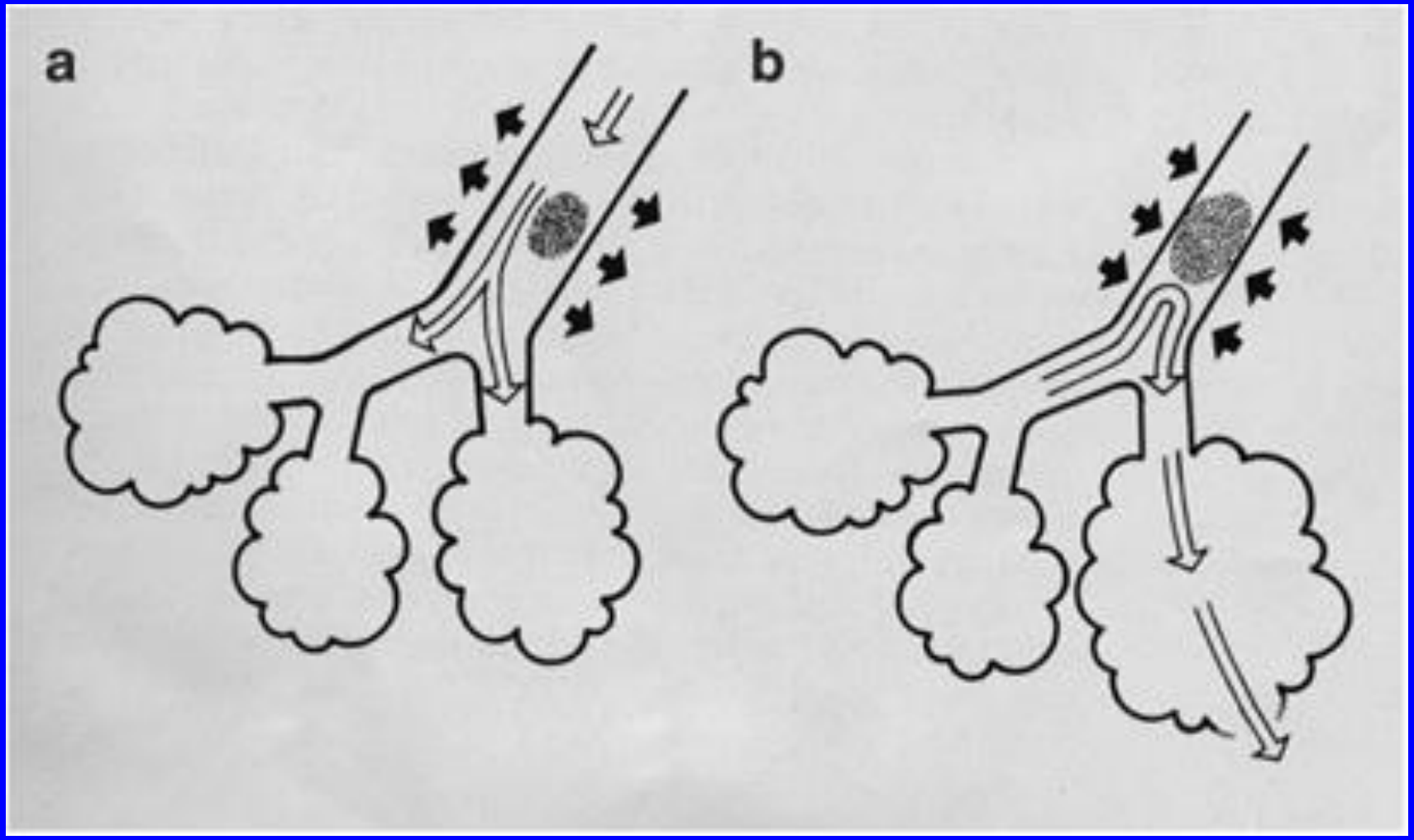
Meconium: Mechanical effects

- Aspirated meconium - partially or completely obstruct smaller airways

  - **Partial** obstruction (ball valve phenomenon) will lead to air trapping and hyperinflation of certain lung fields.
    - Pneumothorax may occur.
    - Cellular necrosis may develop within 48 h
    - Ventilation–perfusion mismatch → fall in PaO_2

  - **Complete** obstruction of the smaller airways
    - Leads to atelectasis
    - Inflammatory response

MAS: Ball–valve effect



Goldsmith *J Perinat* 2008

Meconium: Mechanical effects

- Direct damage on alveolar cells
- A rise in FRC leads to an increase in pulmonary vascular resistance.
- Right→left shunting across the PDA and/or PFO exacerbates hypoxemia.
- Chronic hypoxia will lead to an increase in PVR → persistent pulmonary hypertension (PPHN).

Meconium: Chemical effects

- Surfactant (SA) inactivation (functional deficiency)
  - Free fatty acids in meconium replace SA phospholipids, changing lung compliance.
  - Meconium interfere with surface tension lowering capacity of SA.
    - SA inhibition → decreased lung compliance, increased $paCO_2$, and atelectasis
    - SA administration → improved compliance and ventilation
  - SA Rx in MAS (with moderate or severe respiratory failure) → decrease ECMO referral
  - However, SA Rx did not significantly affect mortality in infants with MAS.

Meconium: Inflammatory responses

- Aspirated meconium -- associated with pneumonitis in neonates
- Inflammatory mediators and reactive O_2 species are involved in the pathophysiology of MAS, eventually leading to local injury and interference with surfactant function.
- The term “meconium-associated pulmonary inflammation” (MAPI) is (probably) more accurate to use than ‘chemical pneumonitis’.

Meconium: Cytokine and chemokine activation

- Intrapulmonary meconium trigger lung inflammatory cells to express inflammatory cytokines and O_2 radicals, resulting in lung airway epithelial cell injury and death through apoptosis.

- Meconium provokes a chemotactic reaction *(Zagaraya, et al)*.
  - In the rabbit lung cells, meconium stimulated the production of pro-inflammatory cytokines, such as IL-1β, IL-6, IL-8 and TNFα.

- Meconium is an extrinsic source of other proinflammatory cyto- and chemokines, such as IL-1β, IL-6, GM-CSF, INF-γ and TNF-α, which may contribute in vivo to local pulmonary inflammation with influx of leucocytes, T-lymphocytes, monocytes and macrophages, leading to parenchymal injury and remodeling of lung tissue.

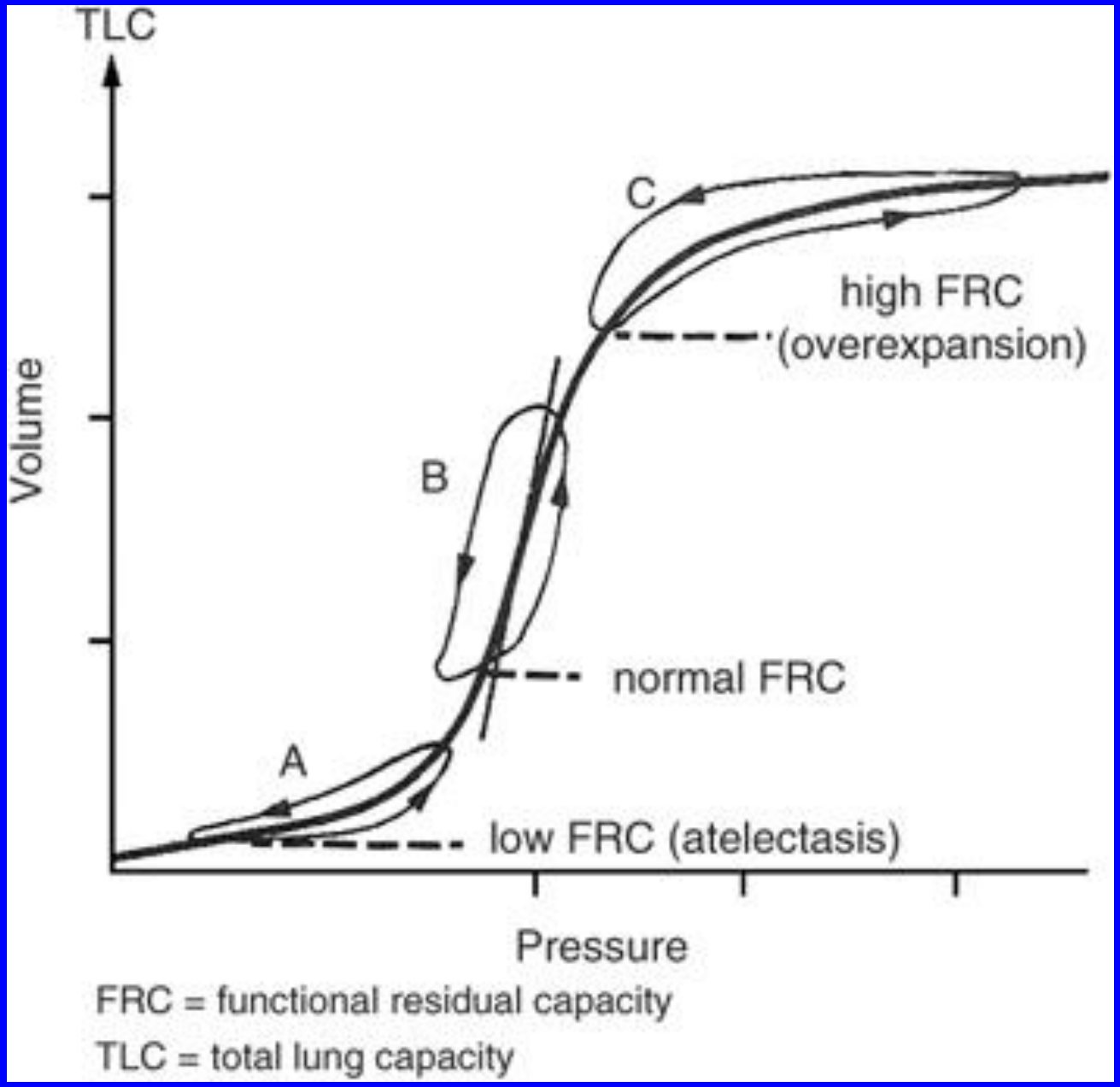
Risk factors for MAS

- Risk higher in black vs other ethnic groups
- Advanced gestational age (GA)
- High birth weight (BW)
  - BW > 4500 g associated with increased risks of perinatal & infant mortality and morbidity, incl. MAS
- Oligohydramnios
- Male gender
- Thick vs thin meconium (?) increase the incidence of MAS

Classification of Neonatal Pulmonary Disorders

	Atelectatic	Obstructive
Example	**RDS**	**MAS**
Physiol.	Dec Lung volume	Inc Lung volume
	Dec Compliance	Inc Compliance
	Dec FRC	Dec FRC
	Normal airway resistance	Inc Airway resistance
	Normal time constant	Inc Time constant

Adapted from Goldsmith JP, Karotkin EH

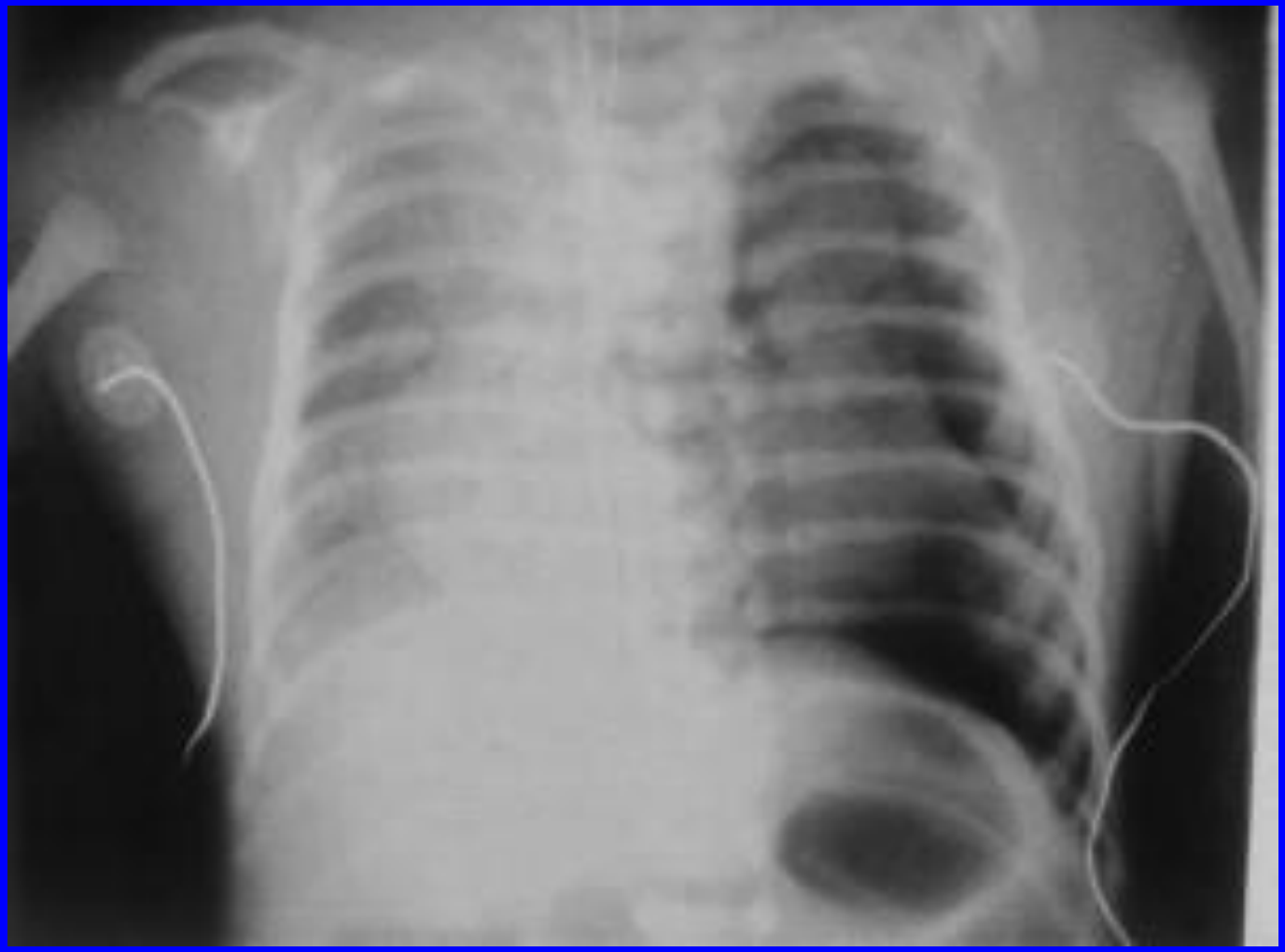


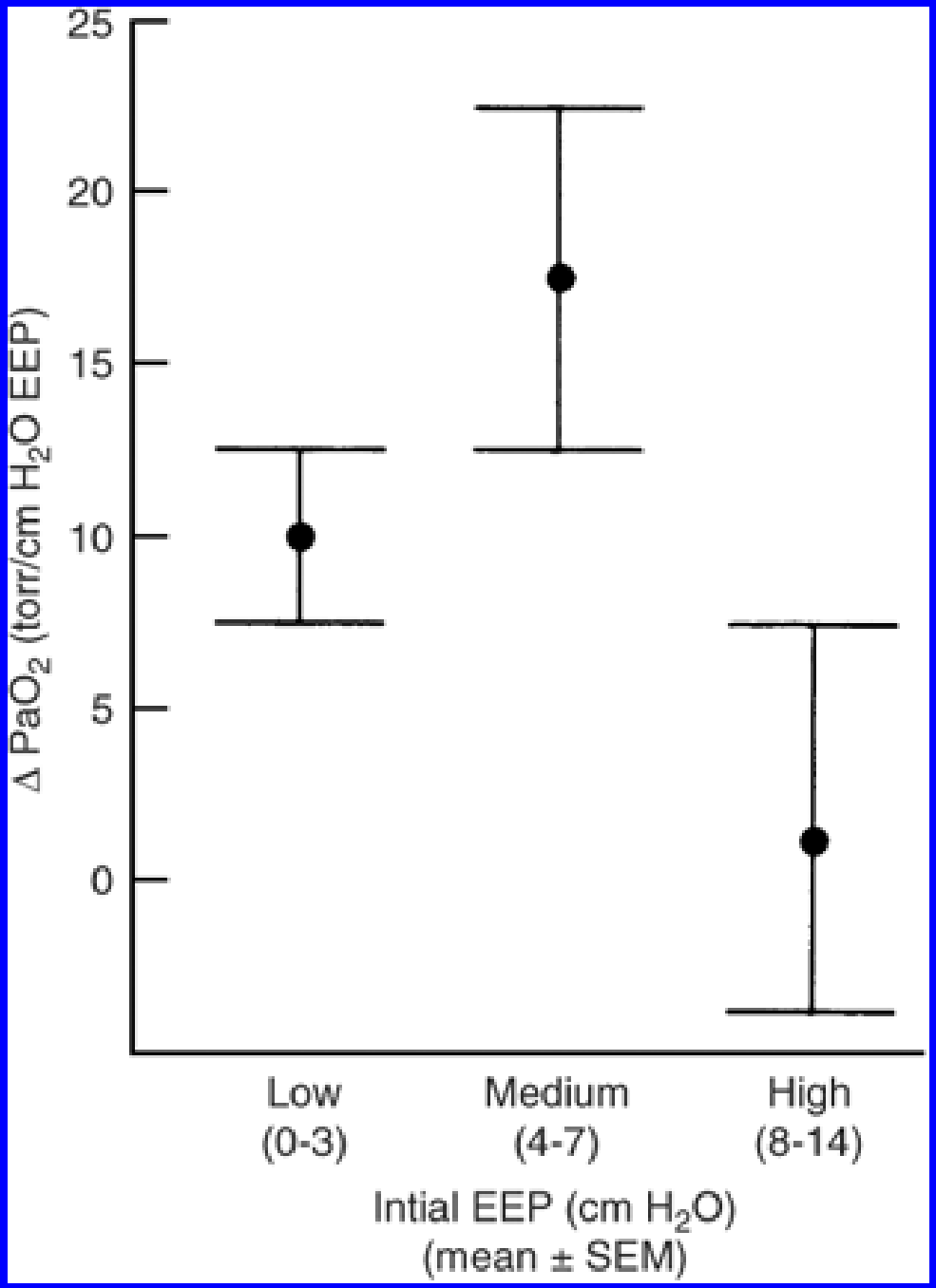
MAS

RDS

Goldsmith *J Perinat* 2008

PTX in MAS





Goldsmith *J Perinat* 2008

Meconium aspiration

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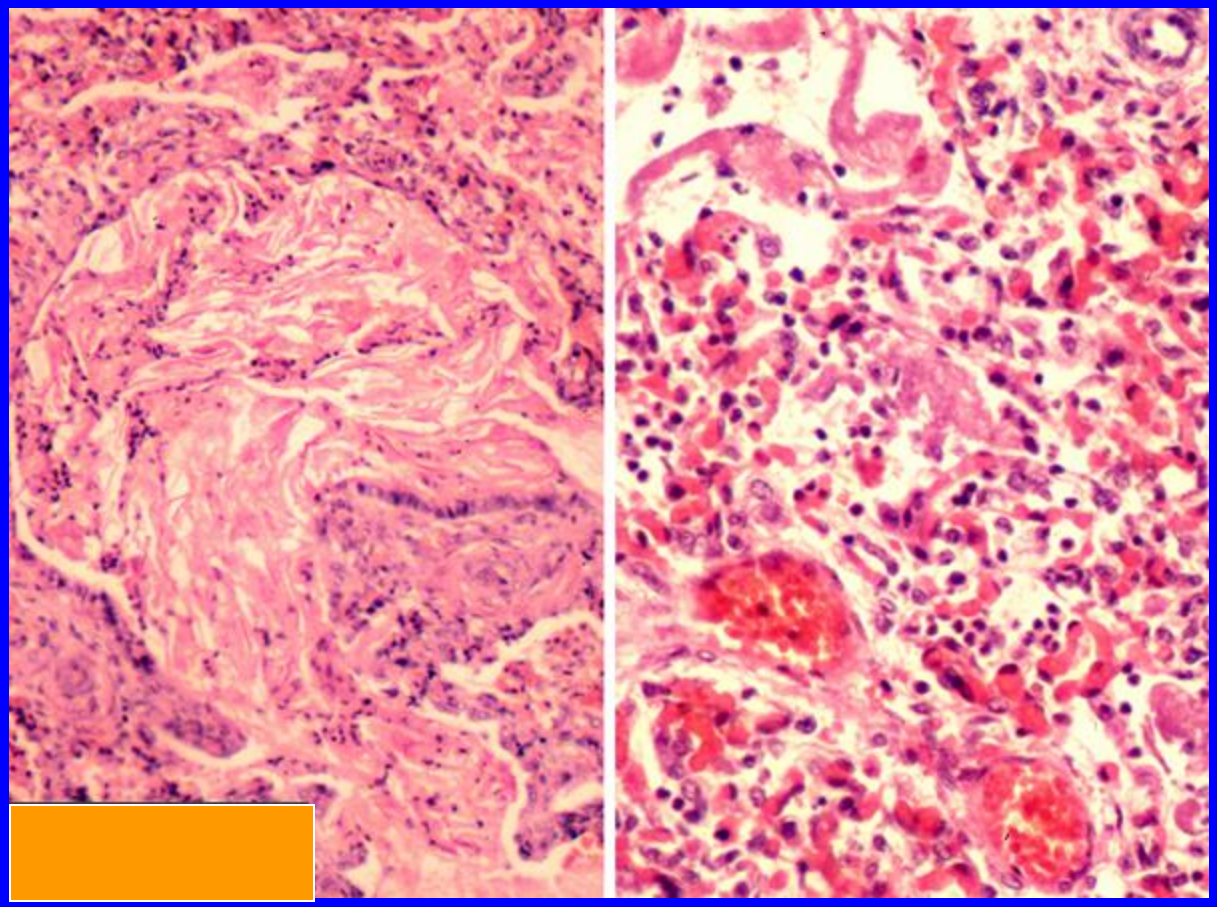

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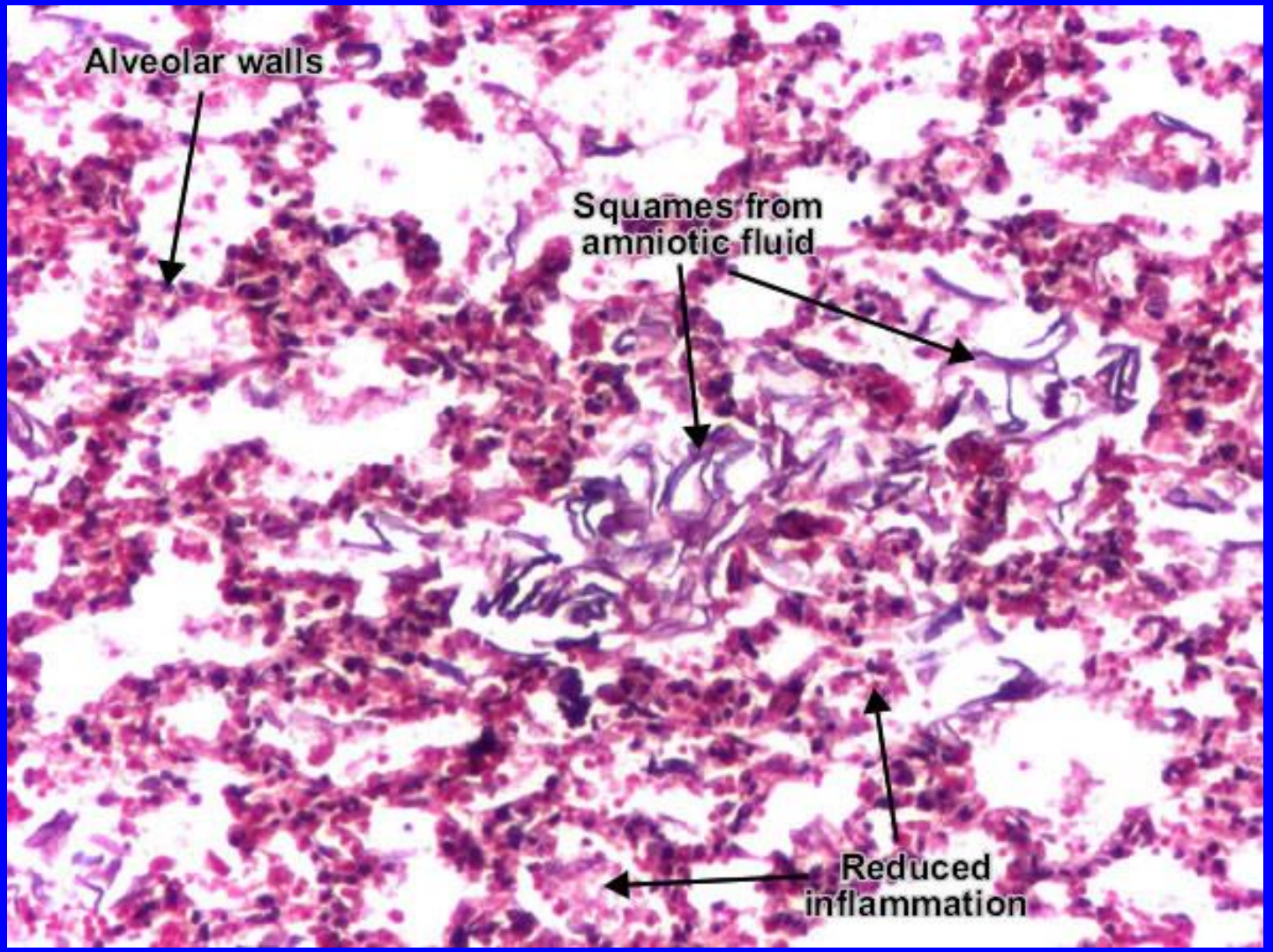
(L) a bronchiole is filled with aspirated meconium and squames.
(R) peripheral airspaces contain meconium; with acute inflammation.

MAS: Histology



NICU Management

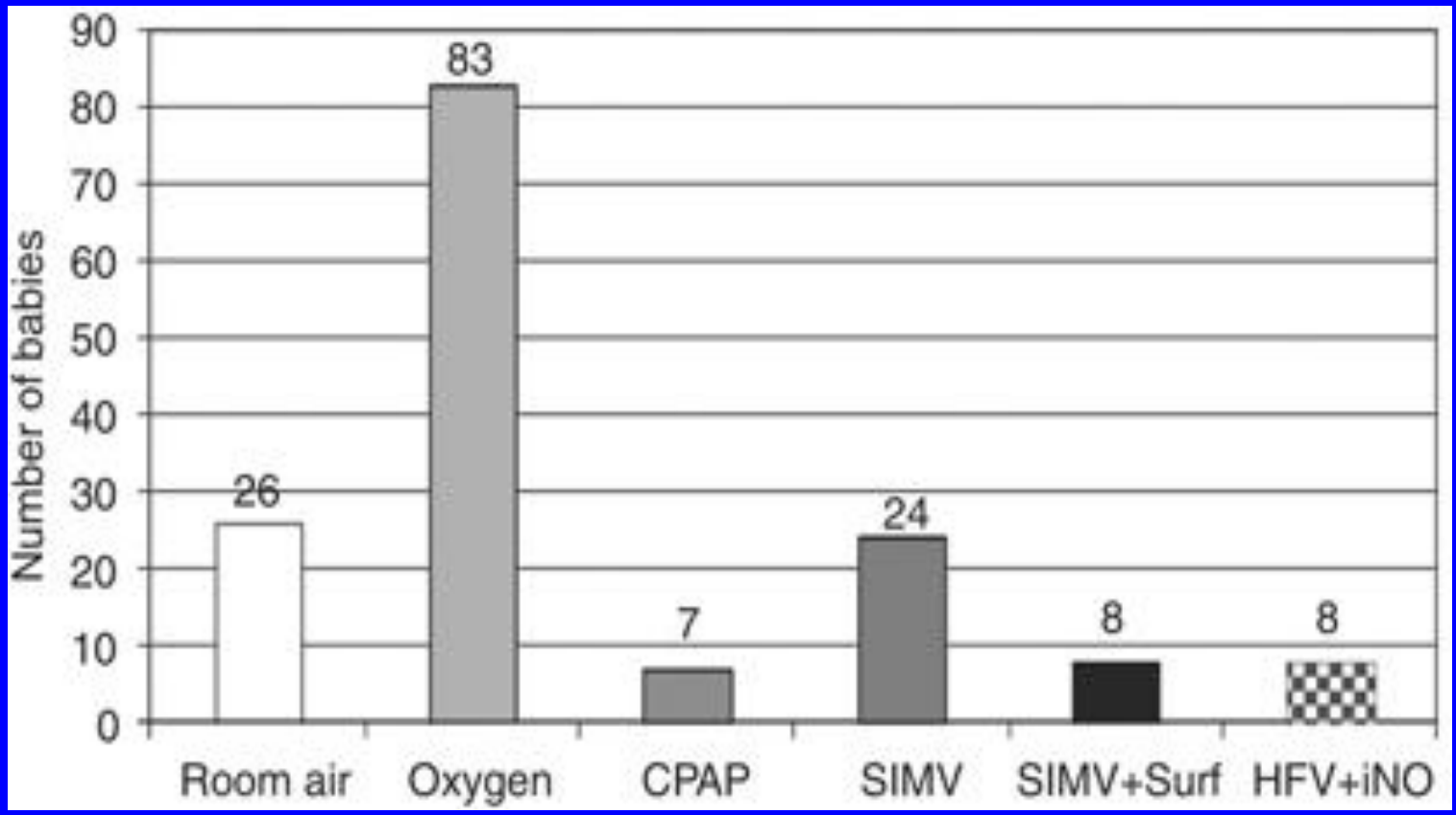
- Chest PT and O2 (warmed and humidified)

- Pulmonary toilet
  - Lung lavage may lead to pulmonary deterioration (lung function)

- Ventilatory Support:
  - Correct hypoxia and acidosis
  - $PaCO_2 > 60$ or $PaO_2 < 50$ → mech ventilation
  - Avoid high pressure PPV bec of inc air leaks
  - Avoid inadvertent PEEP bec of prolonged expiratory phase in MAS

Respiratory Support for MAS

Modes of respiratory support in newborns with MAS (*n*=47 needed ventilatory support/156 live births with MAS, 30%).



Bhutani *J Perinat* 2008

NICU Management

- **Respiratory support**
  - O2
    - Avoid high [O2] and limit duration to avoid free O2 radical damage.
    - Use TcO_2 saturation limits of 90 and 95%
    - Aim to maintain a paO_2 between 50–90 mm Hg
  - Assisted ventilation when [O2] needed to maintain these limits > 70%, or when respiratory acidosis or apneas develop
    - No strong evidence to recommend the use of CPAP, and CPAP may even increase the risk of pneumothorax.
  - Indications for mechanical ventilation are arbitrary.
    - Start conv (IMV) or synchronized mechanical ventilation (SIMV)
      - $FiO_2 \geq 0.7$ to maintain O_2 sats > 90%
      - Repeated sudden drops of the O_2 sats secondary to marked pulmonary hypertension
      - Apnea
      - Respiratory acidosis (paCO2>60 mm Hg), or pH<7.25) which may exacerbate pulmonary hypertension

NICU Management

- Supportive Care:
  - Thermoregulation
  - Fluid and electrolyte balance
  - Blood glucose monitoring

- Antibiotics - controversial (mec enhances bacterial growth by reducing host resistance).
  - No studies have shown that infection plays a role in MAS pathogenesis

- Steroid use not recommended *(Yeh, 1977; Frantz, 1975)*
- Sedation / neuromuscular blocking agents (pts are usually vigorous and tend to fight the vent)

NICU Management

- Additional therapies (in severe cases):
  - Sedation, analgesia, muscle paralysis (esp in PPHN)
    - because of difficulties in managing mechanical ventilation

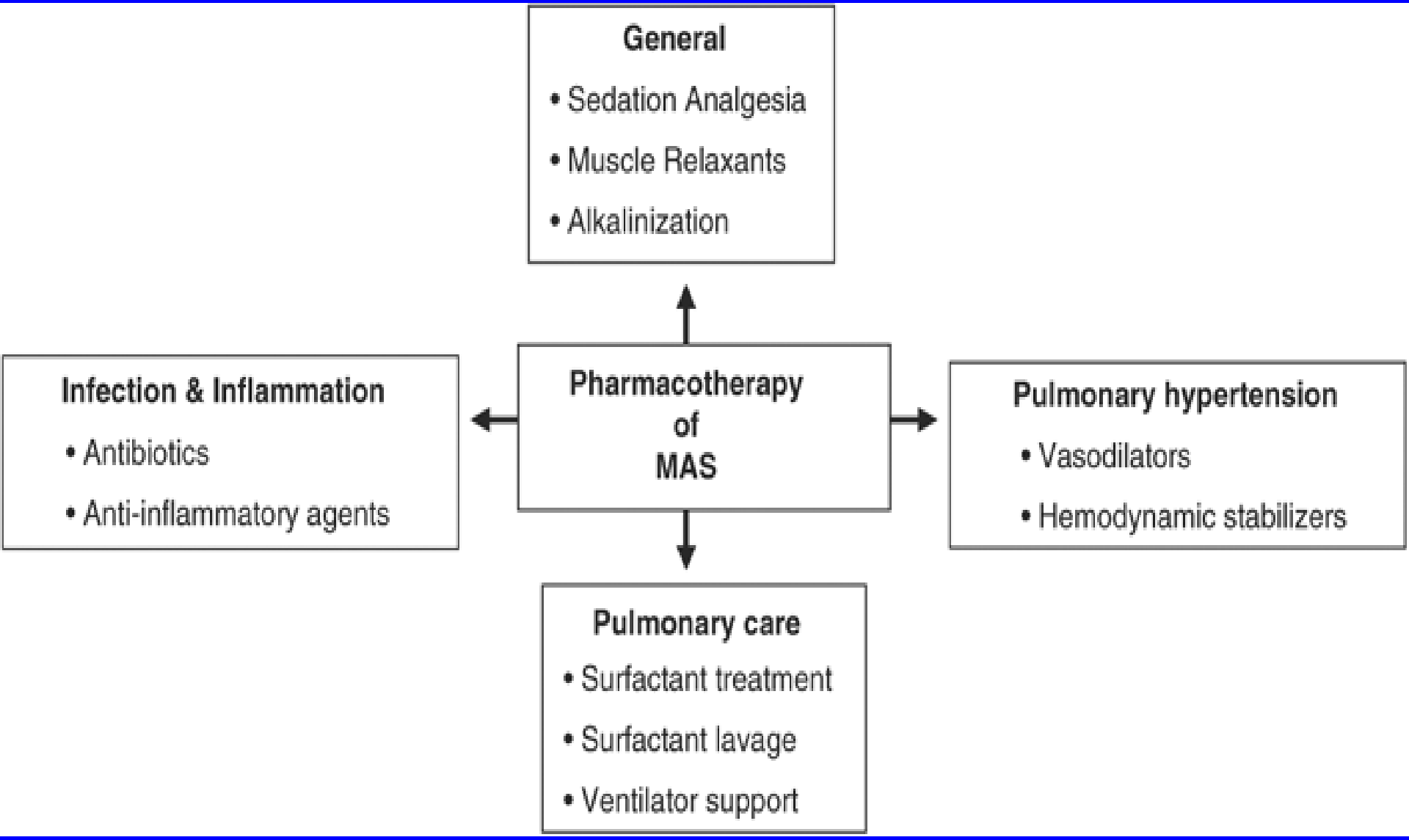
- Sodium bicarbonate has been used to raise the pH and decrease right to left shunting, again, more empirically than scientifically.

- Vasoactive drugs to increase systemic BP or improve heart contractility.

- **Nitric oxide (iNO)** for pulmonary hypertension.
  - variable response and dependent on the lung areas that can be reached by the gas (echo with no structural heart disease).

- **ECMO** should be used, when available, for infants with MAS who do not respond to the aforementioned therapies.
  - MAS comprise ~ 40-50% of the newborns treated with ECMO.

Pharmacotherapy for MAS (Asad, *J Perinat* 2008)



Extracorporeal membrane oxygenation (ECMO) and MAS

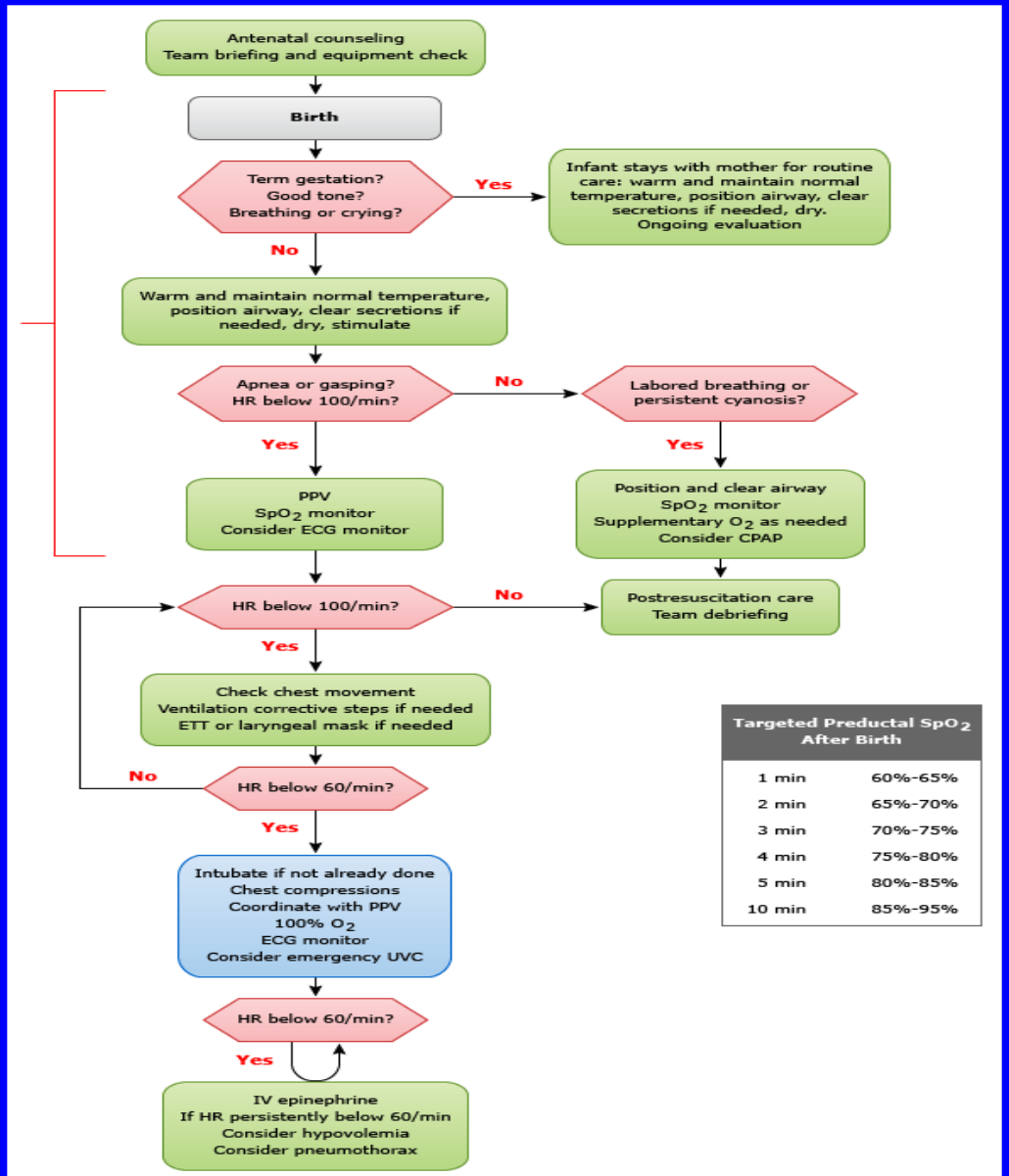
- ECMO registry: the highest survival rates (>90%) seen in patients with MAS who qualified for ECMO.

- With evidence-based approach to prevention of MAS and the initiation of better less-invasive therapies, including iNO, SA therapy, SA lavage and various modes of mechanical ventilation, including HF ventilation → decreasing trend of ECMO referral for MAS

NRP Guidelines: MSAF

Postpartum approach to the infant born through MSAF:

Tracheal suctioning no longer indicated



Escobedo *Peds* 2020

Delivery Room Interventions

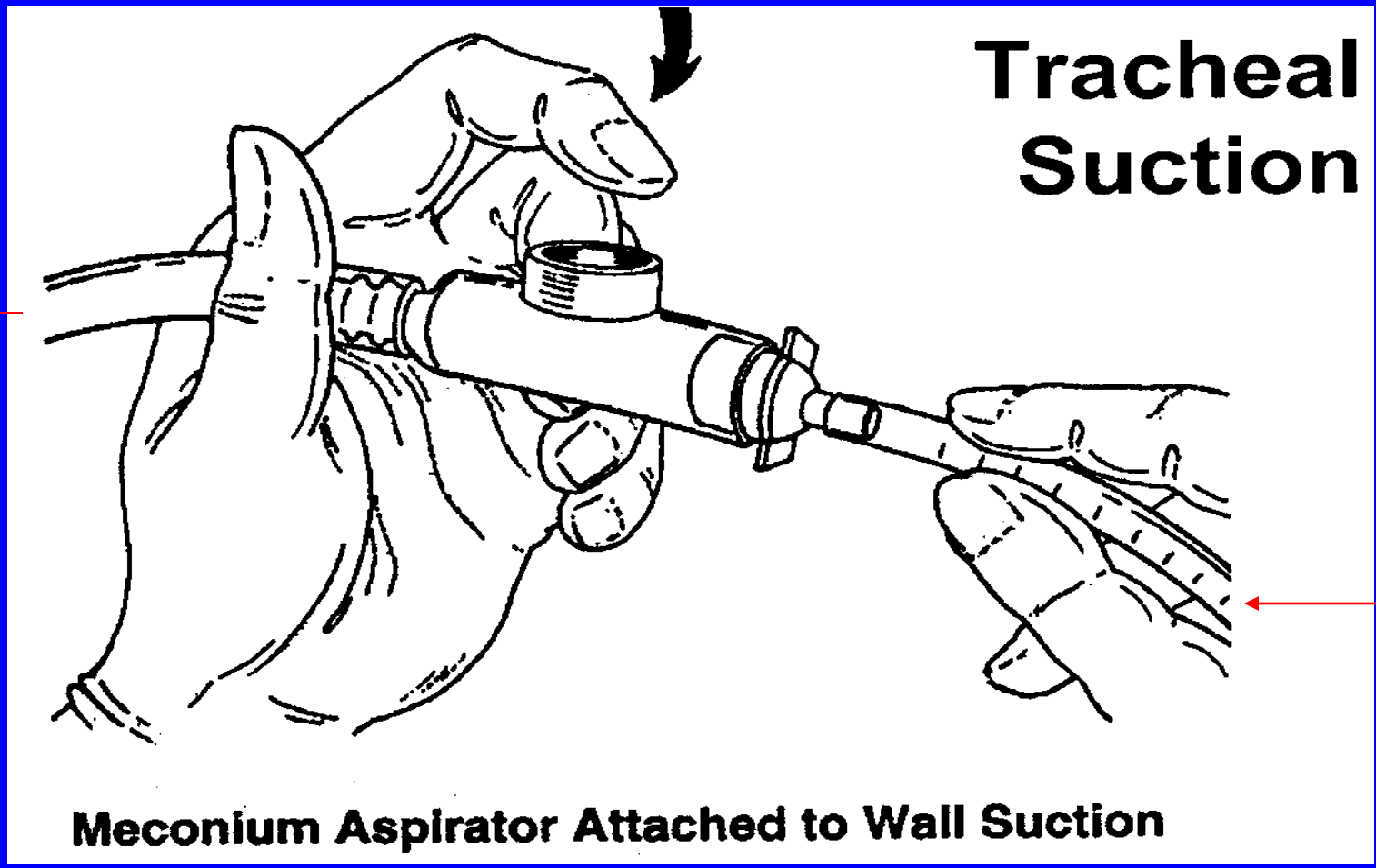
- **CPT (Chest physiotherapy)**
  - to prevent accumulation of debris and to improve mobilization of airway secretions
  - percussion, vibration, postural drainage, saline administration and suctioning
  - theoretically, help remove meconium from the airways, prevent its consequences and improve gas exchange
  - widely performed on infants born through MSAF, as well as those with MAS

- Caution!
  - there are no data to support CPT in mec-stained neonates, either in the DR or thereafter (no clinical trials).
  - potential complications of CPT (pneumothorax, hypoxemia, arrhythmia, airway perforation and tissue damage).

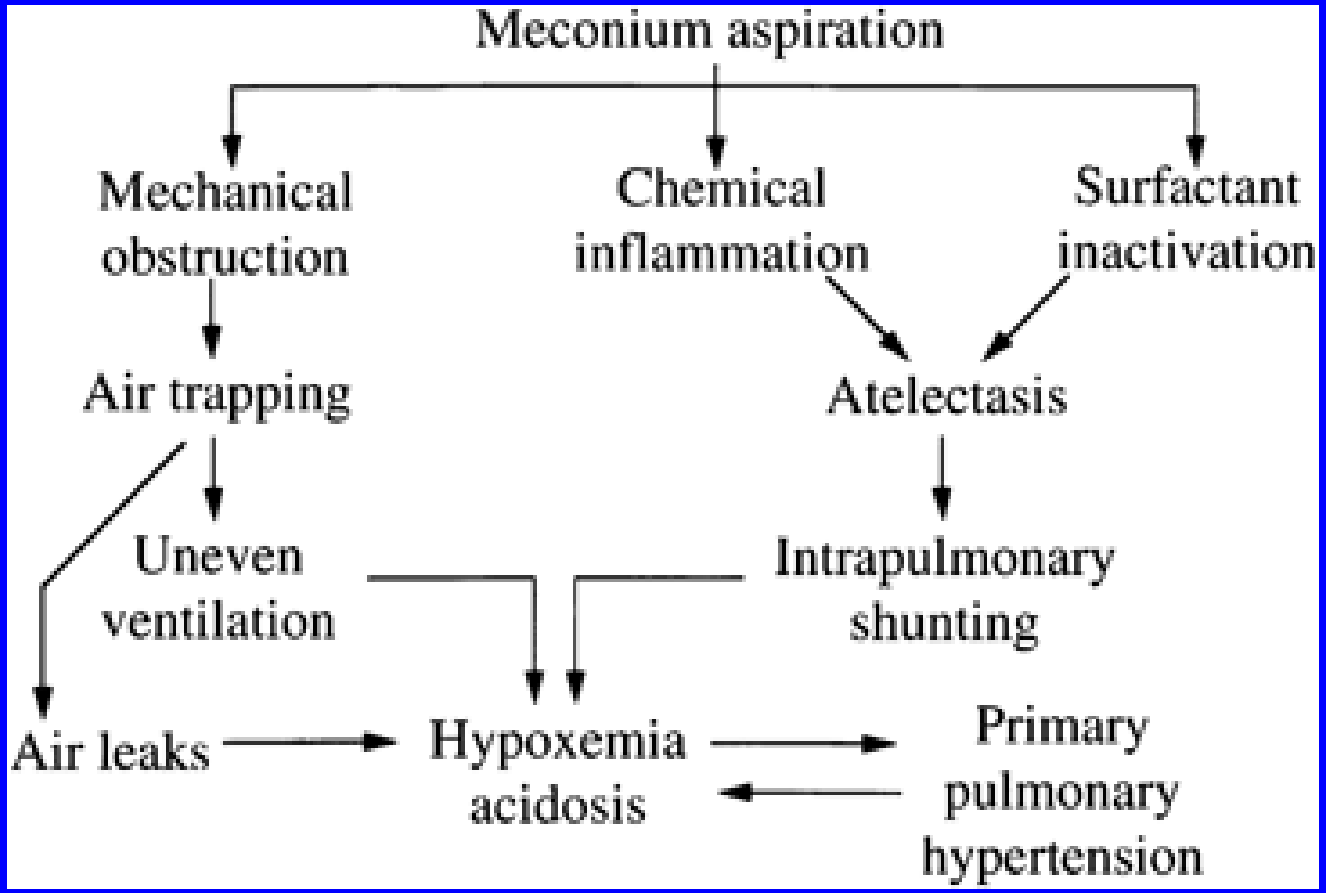
Delivery Room Interventions

- **Gastric suctioning**
  - suctioning of the stomachs of all meconium-stained neonates soon after delivery *(Karlowicz, et al)*
  - some cases of MAS could potentially be caused by the postnatal reflux of gastric contents into the oropharynx, then potentially be aspirated into the airways
  - has never been evaluated for efficacy in preventing MAS (no clinical trials)

Meconium Aspirator



MAS: Pathophysiology (Fanaroff *J Perinatol* 2008)



Fanaroff and Martin's *Neonatal Perinatal Medicine, Diseases of the Fetus and Infant* 8th ed, ed by R Martin, A Fanaroff and M Walsh, 2006.

Bad news!

Meconium aspiration continues to be a threat to many newborns.

MAS has an estimated neonatal mortality of ~ 5%, in addition to short- and long- term pulmonary and neuro-developmental sequelae.

Intrapartum electronic fetal monitoring (EFM)

- Goal of continuous EFM is to detect fetal hypoxemia (a risk factor for MAS)
- Questionable effectiveness have been reported
  - RCTs of EFM found no evidence in reducing the risk of fetal or neonatal mortality or morbidity.
- EFM tracings:
  - in the presence of MSAF, fetal tachycardia, variable and late decelerations and decreased long-term variability are risk factors for MAS.
- No increased correlation between abnormal FHR patterns during labor and MSAF & adverse outcomes (low arterial cord blood pH, and low Apgar scores) have been reported
- Umstad *et al.* reported the positive predictive value of abnormal FHR patterns in early labor and MSAF

Why does the fetus release meconium in the AF?

- Meconium in the AF
  - at delivery is associated with adverse outcome
  - Is usually considered abnormal
    - Associated with the ff abnormal conditions:
      - fetal hypoxia
      - intrauterine infections
      - gestational cholestasis
- Meconium passage is physiologic
    - the result of fetal gastrointestinal maturation

Intrapartum Oro-/Naso-pharyngeal Suctioning

- International prospective, randomized controlled trial of MSAF of any consistency, FT gestation and vertex presentation *(Vain, et al)*
  - (1) suctioning of the oropharynx and nasopharynx prior to delivery of the thorax OR
  - (2) no suctioning prior to delivery.
    - No differences were found in the incidence of MAS between suctioned (4.1%) and non-suctioned (3.8%) infants.
    - No differences in other key outcome variables including mortality, the need for mechanical ventilation, duration of mechanical ventilation and duration of supplemental oxygen use.
- Both the NRP and the American College of Obstetricians and Gynecologists (ACOG) **no longer recommend** intrapartum oropharyngeal and nasopharyngeal suctioning prior to delivery when MSAF is present.

Strategies to prevent MAS

- Key guidelines
  - Curtailment of prolonged pregnancy reduces the risk of MSAF and MAS.
  - Labor induction with prostaglandins, particularly misoprostol, appears to be associated with the occurrence of MSAF.
  - Amniotomy during labor may increase the risk for MAS.
  - No evidence as to whether expediting delivery because of MSAF alone improves outcome.
  - Amnioinfusion for suspected umbilical cord compression has no clear effect on the occurrence of MSAF.
  - Amnioinfusion for MSAF has no clear effect on the risk of MAS, except in centers with limited peripartum surveillance where the effects may be indirect.

MAS: Long-term consequences

- Related to mode of intervention
  - The initial follow-up report on follow-up of MAS by Marshall *et al.* in 1978 included a 1-year cohort of 17 patients, representing 3.7% of all admissions to their unit.
    - None of the survivors had persistent chronic lung disease but two of three patients with MAS and seizures had significant psychomotor retardation at follow-up examination.
    - There is an increased prevalence of asthmatic symptoms and abnormal bronchial reactivity among survivors of the MAS.
- Deafness reported in Hyperventilation intervention

Summary

- 3% to 4% of pregnancies complicated by MSAF develop MAS.
- Meconium aspiration may occur before birth, or during the birth process.
- MAS is an important cause of neonatal mortality in otherwise healthy term or post-term infants, with a case fatality rate of 5%-40%.
- Airways suctioning of the neonate may reduce but does not eliminate the occurrence of meconium aspiration.

Thank you!