RESPIRATORY DISEASES

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Introduction

- Respiratory disorders are the **most frequent cause of admission** in term and preterm.
- It is occasionally **difficult to distinguish respiratory from non-respiratory** etiologies on the basis of clinical signs alone.
- **Timely and appropriate therapy** is essential to improve outcome.
- **Signs and symptoms of respiratory distress** include **cyanosis, grunting, nasal flaring, retractions and tachypnea**.

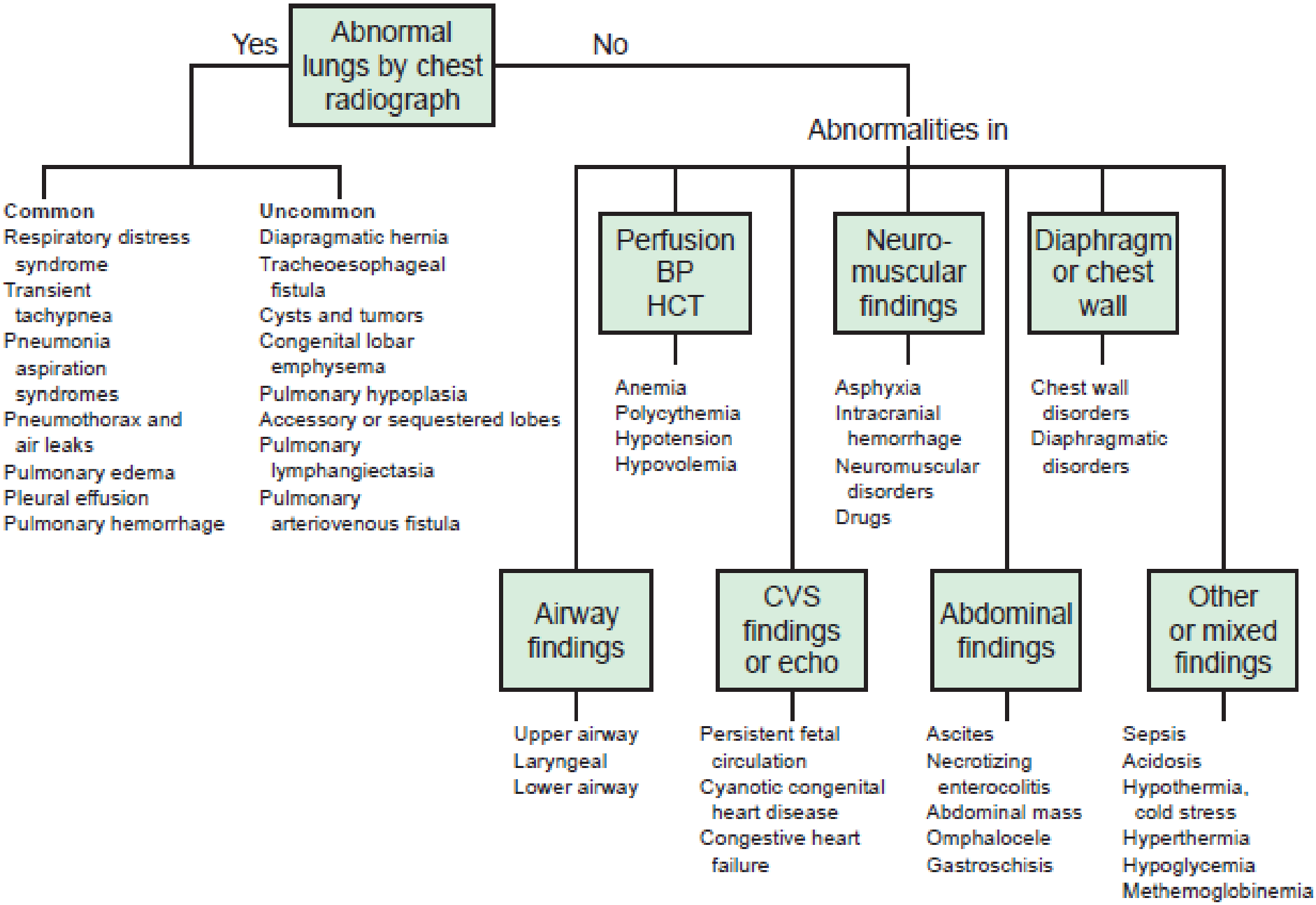
Introduction

- **Apnea:** No respiratory effort for **greater than 20 seconds** or if cessation of breathing lasts for **more than 10 seconds and is accompanied by bradycardia and or desaturation.**

- **Periodic breathing** pattern, which shifts from a regular rhythmicity to cyclic brief episodes of intermittent apnea, is **more common in preterm infants, who may have apneic pauses of 5-10 sec followed by a burst of rapid respirations at a rate of 50-60 breaths/min for 10-15 sec.**

- Periodic breathing, a **normal characteristic of neonatal respiration**, has no prognostic significance.

Neonate with acute respiratory distress



Respiratory Distress Syndrome (Hyaline Membrane Disease)

INCIDENCE

- Respiratory distress syndrome occurs primarily in premature infants; its **incidence is inversely related to gestational age and birth weight**.

- It occurs in
  - 60-80% of infants <28 wk of gestational age,
  - 15-30% of those between 32 and 36 wk of gestational age,
  - rarely in those >37 wk of gestational age.

INCIDENCE

The risk for development of RDS *increases* with

1. Maternal diabetes,
2. Multiple births,
3. Cesarean delivery,
4. Precipitous delivery,
5. Asphyxia or hypoxemia
6. Cold stress or hypothermia
7. Hypovolemia and hypotension
8. Maternal history of previously affected infants.

The risk of RDS is *reduced in*

1. Pregnancies with chronic or pregnancy-associated hypertension,
2. Maternal heroin use,
3. Prolonged rupture of membranes,
4. Antenatal corticosteroid prophylaxis

ETIOLOGY AND PATHOPHYSIOLOGY

- **Surfactant deficiency (decreased production and secretion; increased consumption) is the primary cause of RDS.**

- **Synthesis of surfactant depends on**
  1. normal pH,
  2. temperature,
  3. perfusion.

- **Although rare, genetic disorders of mutations** in protein part of the surfactant may contribute to respiratory distress.

- **The major constituents of surfactant are dipalmitoyl phosphatidylcholine (lecithin)**, phosphatidylglycerol, apoproteins (surfactant proteins SP-A, SP-B, SP-C, and SP-D), and cholesterol.

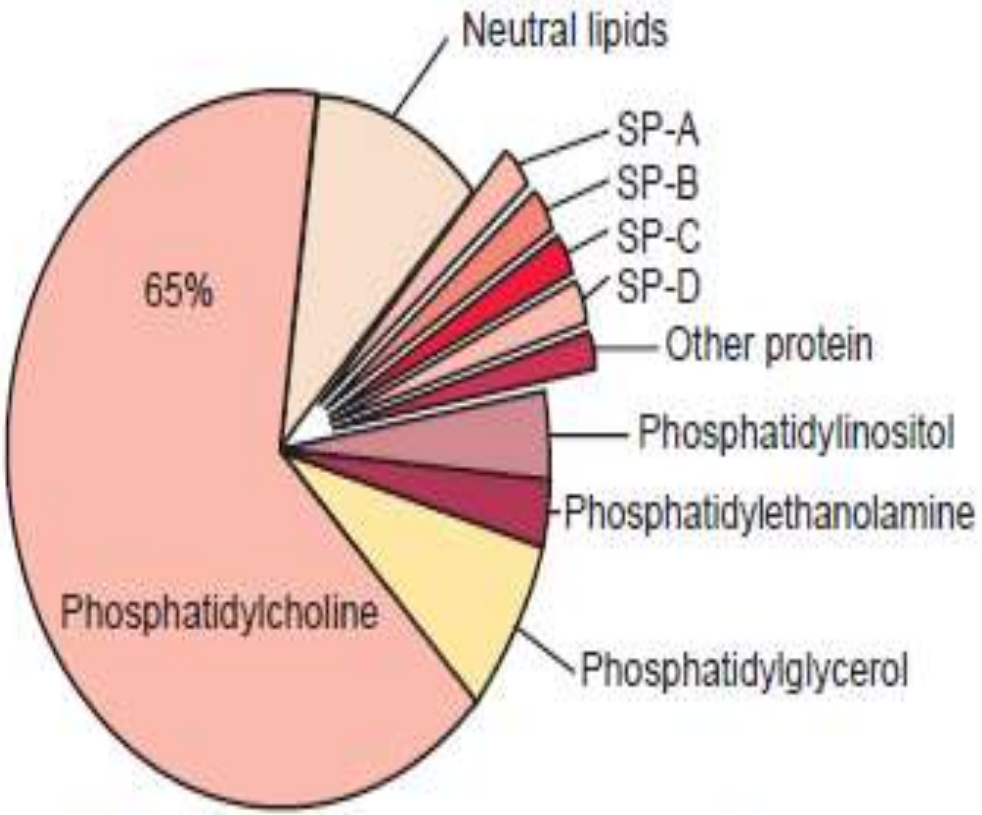
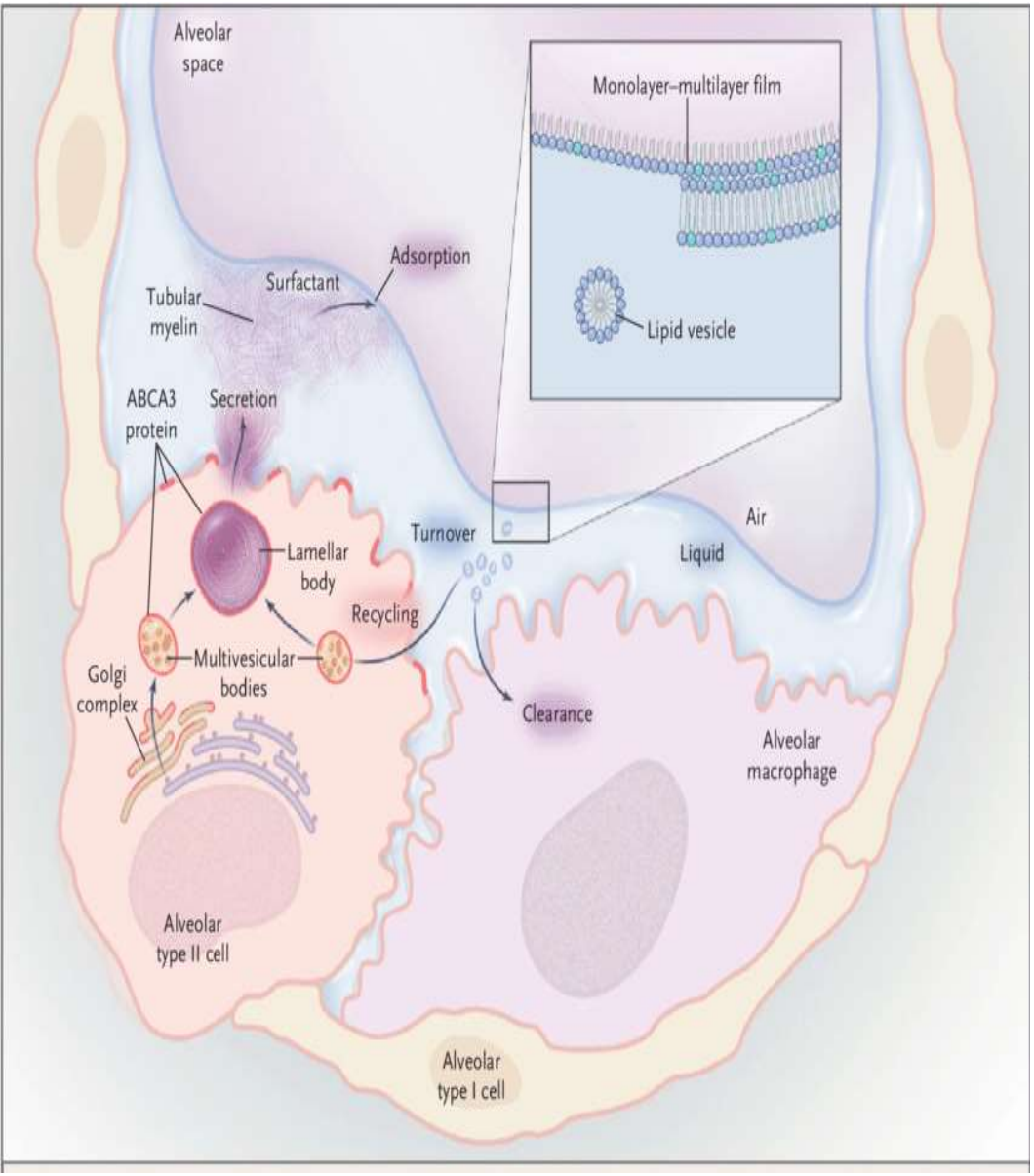


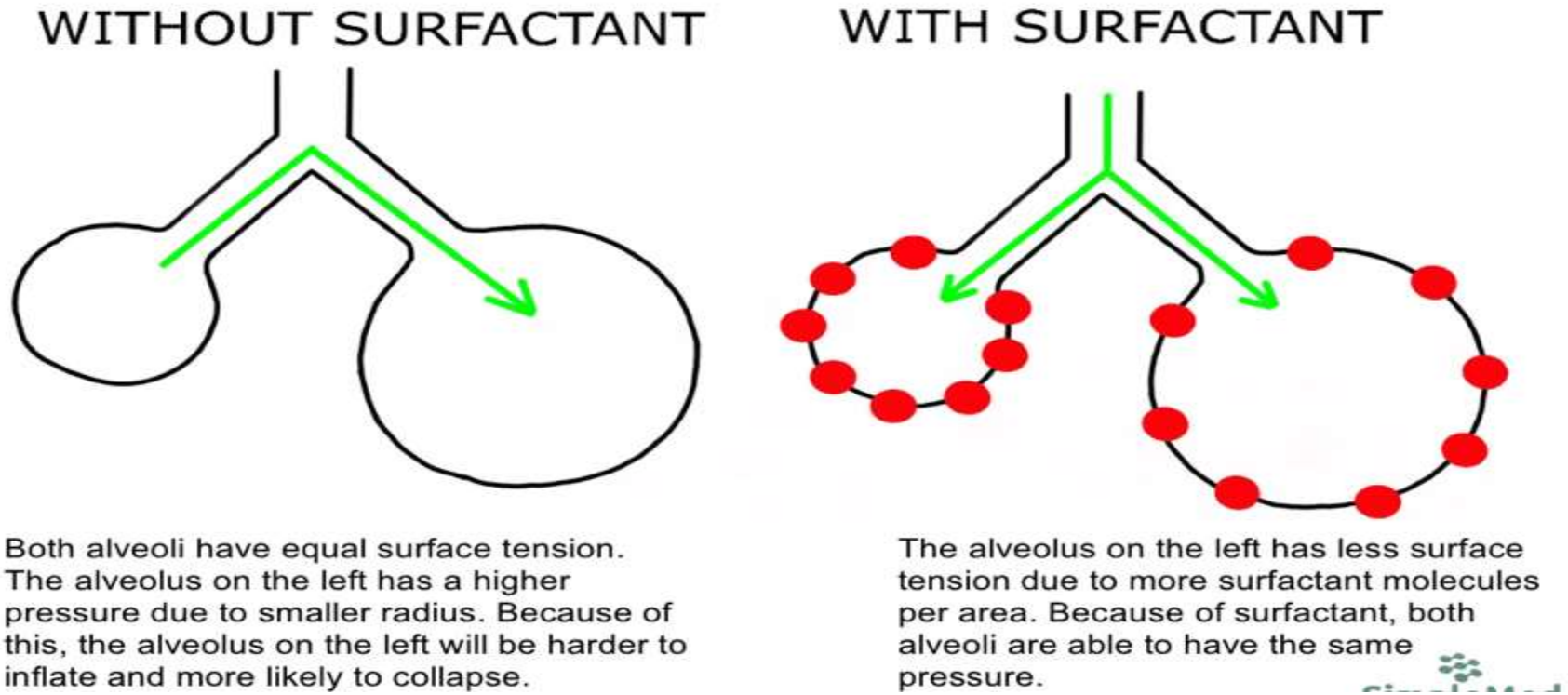
Figure 101-2 Composition of surfactant recovered by alveolar wash. The quantities of the different components are similar for surfactant from the mature lungs of mammals. SP, surfactant protein. *(From Jobe AH: Fetal lung development, tests for maturation, induction of maturation, and treatment. In Creasy RK, Resnick R, editors:* Maternal-fetal medicine: principles and practice, *ed 3, Philadelphia, 1994, WB Saunders.)*

- **Composition:**
  - **90% lipids**
  - **10% proteins**



- With advancing gestational age, increasing amounts of phospholipids are synthesized in **type II alveolar cells**.
- Surfactant is present in high concentrations in fetal lung homogenates by 20 wk of gestation, but it does not reach the surface of the lungs until later.
- **It appears in amniotic fluid between 28 and 32 wk of gestation**.
- **Mature levels of pulmonary surfactant are present usually after 35 wk of gestation.**
- **Normal**

Lecithin : Sphingomyeline ratio is >=2 which indicates mature lungs.



- **Function of lung surfactant**
  1. **Decreases surface tension during expiration**
  2. **Allows the alveolus to remain partly expanded**
  3. **Maintains functional residual capacity**

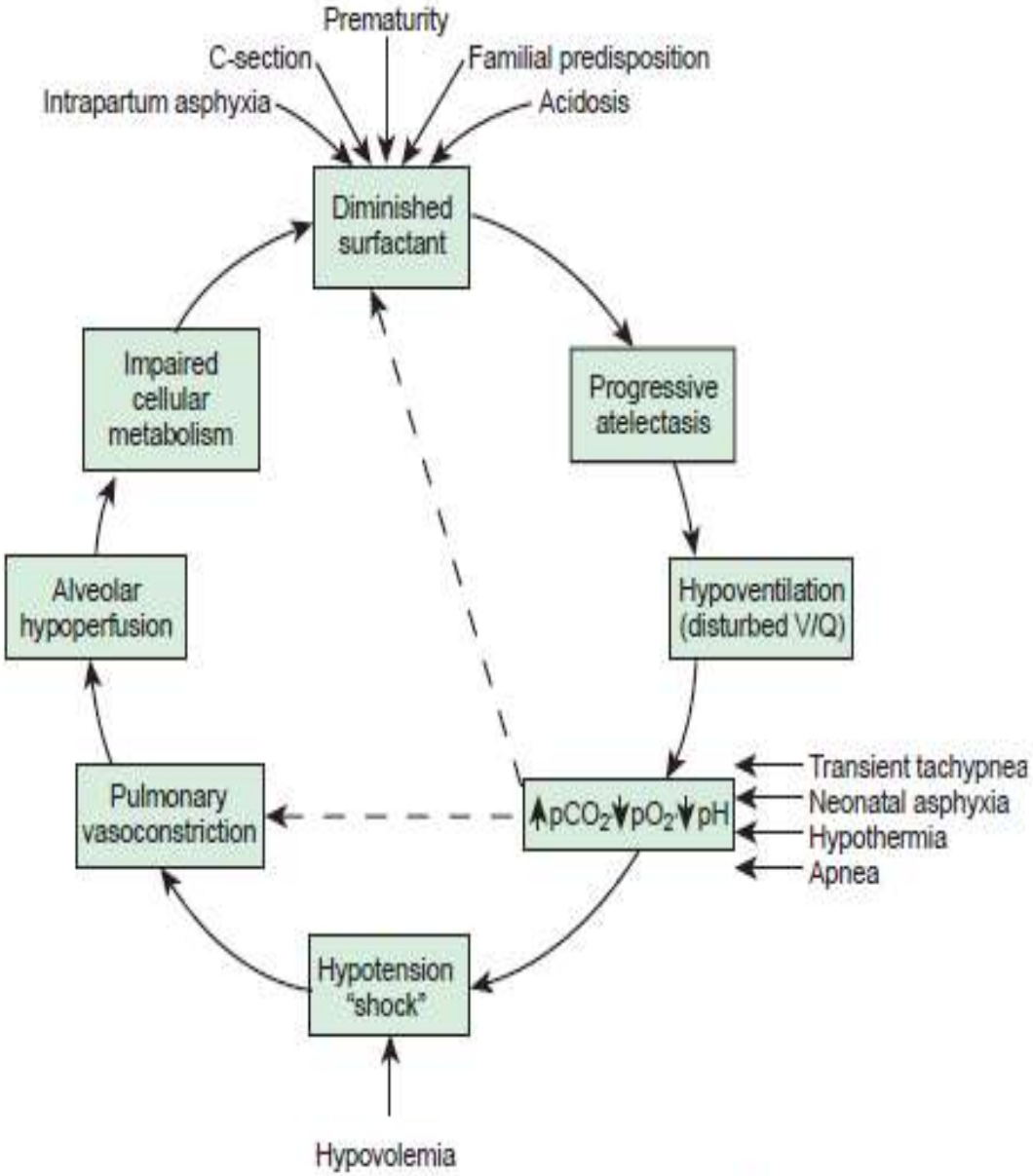


Figure 101-4 Contributing factors in the pathogenesis of hyaline membrane disease. The potential "vicious circle" perpetuates hypoxia and pulmonary insufficiency. *(From Farrell P, Zachman R: Pulmonary surfactant and the respiratory distress syndrome. In Quilligan EJ, Kretchmer N, editors:* Fetal and maternal medicine, *New York, 1980, Wiley. Reprinted by permission of John Wiley and Sons, Inc.)*

ETIOLOGY AND PATHOPHYSIOLOGY

- Alveolar atelectasis, hyaline membrane formation, and interstitial edema make the **lungs less compliant in RDS**, so **greater pressure is required to expand** the alveoli and small airways due to **increased surface tension**.
- Thus, at end-expiration, the volume of the thorax and lungs tends to approach residual volume, and **atelectasis may develop**. Results in perfused but not ventilated alveoli, causing **hypoxia.**
- Decreased lung compliance, small tidal volumes, increased physiologic dead space, and insufficient alveolar ventilation eventually result in **hypercapnia.**
- The combination of hypercapnia, hypoxia, and acidosis produces pulmonary arterial vasoconstriction with **increased right-to left shunting** through the foramen ovale and ductus arteriosus and within the lung itself.
- Progressive injury to epithelial and endothelial cells from atelectasis (atelectrauma), volutrauma, ischemic injury, and oxygen toxicity results in effusion of proteinaceous material into the alveolar spaces.>> **Bronchopulmonary dysplasia**

CLINICAL MANIFESTATIONS

- Signs of RDS usually appear within **minutes to hours of birth**.
- **History of resuscitation** at birth because of asphyxia or initial severe respiratory distress (especially with a ELBW).
- **Characteristically, tachypnea, grunting, intercostal and subcostal retractions, nasal flaring, and cyanosis are noted.**
- Breath sounds may be normal or diminished with a **harsh tubular quality**, and inspiratory fine crackles may be heard.
- In most cases, **the peak within 3 days**, after which improvement is gradual.
- **Improvement is often heralded by spontaneous diuresis and improved blood gas at lower inspired oxygen levels and/or lower ventilator support.**

CLINICAL MANIFESTATIONS

- The course of untreated RDS is characterized by

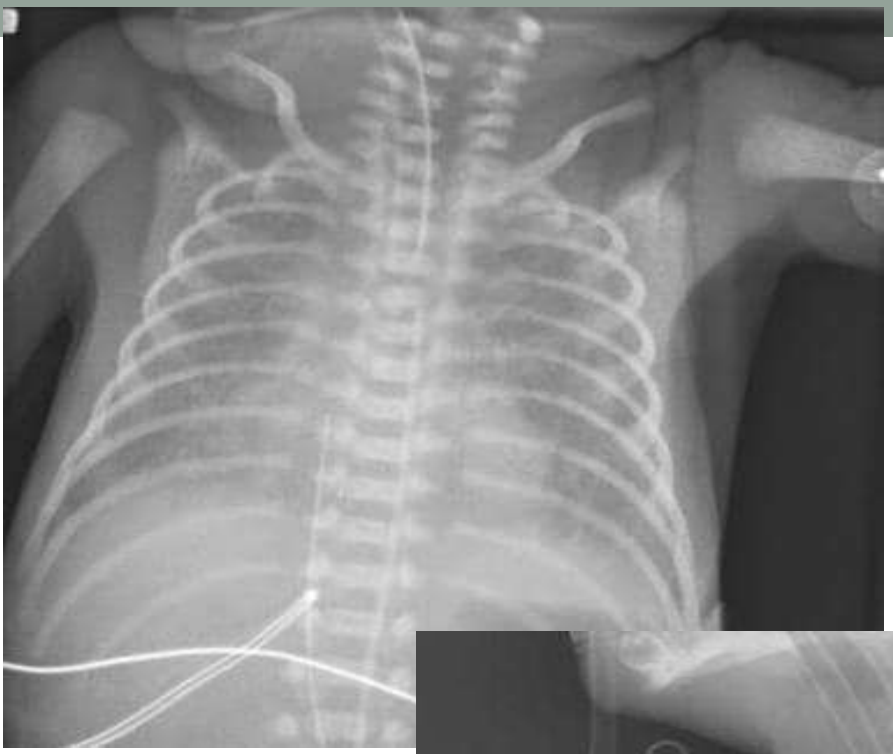
1. **Worsening of cyanosis, dyspnea and blood pressure**.
2. **Apnea and irregular respirations**.
3. **mixed respiratory-metabolic acidosis, edema, ileus, and oliguria**.
4. **Respiratory failure** may occur in infants.
5. finally death can result from severe impairment of gas exchange, alveolar air leaks (interstitial emphysema, pneumothorax), pulmonary hemorrhage, or IVH.

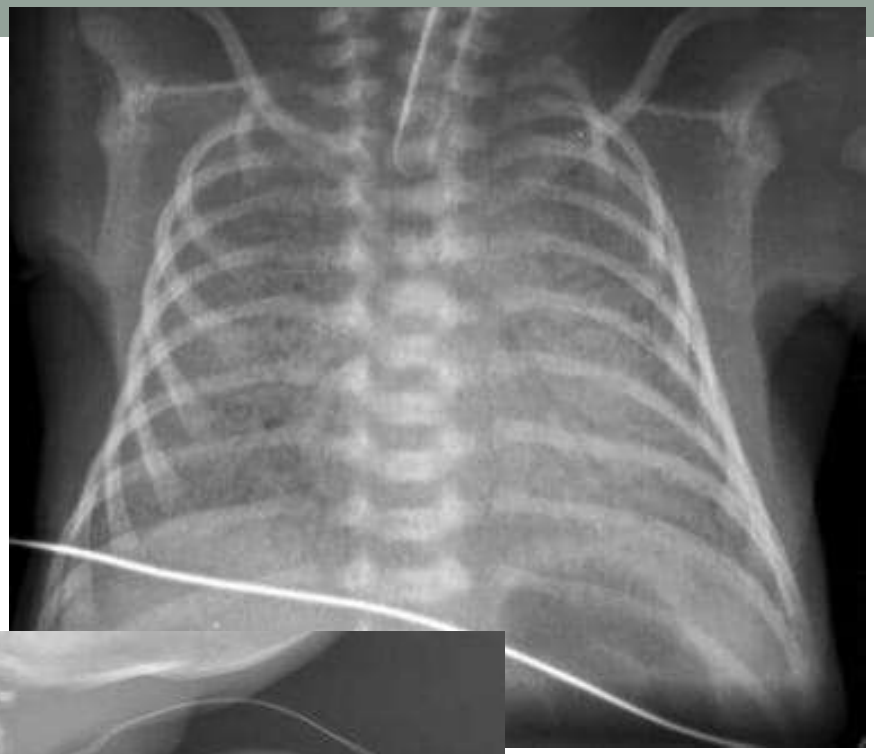
- **BPD is a form of chronic lung disease that often develops in infants with severe RDS.**

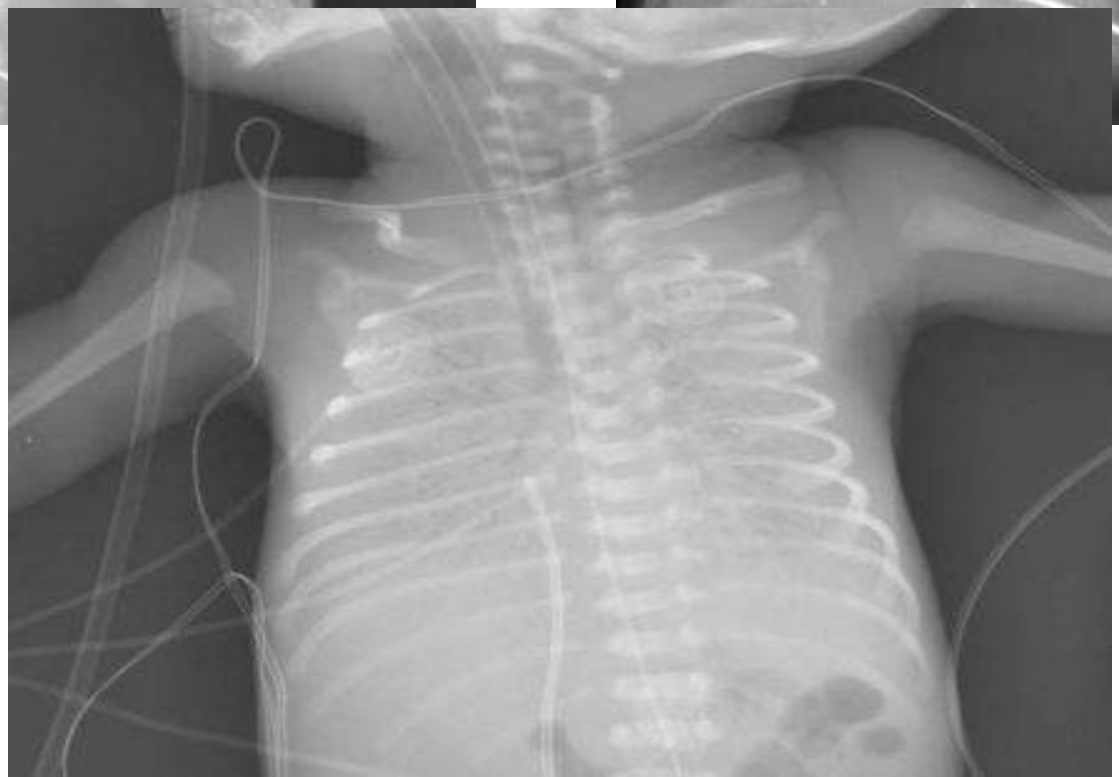
DIAGNOSIS

- The clinical course, chest x-ray findings, and blood gas and acid–base values help establish the clinical diagnosis.

- **On chest x-ray**, the lungs may have a characteristic but not pathognomonic appearance that includes a
  1. **fine reticular granularity** of the parenchyma (**Ground glass appearance**)
  2. **air bronchograms**: Prominent air bronchograms represent aerated bronchioles superimposed on a background of collapsed alveoli.
  3. **Small lung volume**







DIAGNOSIS

- Laboratory findings are characterized

1. initially by **hypoxemia that may progress,**
2. **hypercapnia with respiratory acidosis**
3. **then variable metabolic acidosis.**

- **Echocardiography** to rule out cyanotic congenital heart disease as well as ascertain patency of the ductus arteriosus and assess pulmonary vascular resistance (PVR).

DIAGNOSIS

- **Differential diagnoses are**

1. **GBS pneumonia**
2. **TTN,**
3. **Persistent pulmonary hypertension,**
4. **aspiration (meconium, amniotic fluid) syndromes,**
5. **spontaneous pneumothorax,**
6. **pleural effusions**,
7. **congenital anomalies**.

- **Transient tachypnea (TTN)** may be distinguished by its shorter and milder clinical course and is characterized by low or no need for oxygen supplementation.

- In the differential diagnosis**, early-onset sepsis** may be indistinguishable from RDS.
  - In neonates with GBS **pneumonia**, the chest radiograph may be identical to that for RDS. **So septic workup should be done**.

PREVENTION

- **Avoidance of unnecessary or early cesarean section (<39 wk) or induction of labor.**

- **Administration of antenatal corticosteroids to women before 34 wk of gestation significantly reduces the incidence and mortality of RDS** as well as

1. overall mortality,
2. the need for and duration of ventilatory support and admission to a neonatal ICU,
3. the incidence of severe IVH, necrotizing enterocolitis, and neurodevelopmental impairment.

  - Steroids are recommended for all women in preterm labor who are likely to deliver **within 1 wk** and are **safe** with no adverse effects.
  - **Betamethasone** better than dexamethasone.

- ***CPAP*** *started at birth is as effective as prophylactic or early surfactant and is the approach of choice for the delivery room management of a preterm neonate at risk for RDS.*

TREATMENT

- Therapy requires careful and frequent **monitoring of**
  1. **Heart and respiratory rates**
  2. **Oxygen saturation**
  3. **Pao2, Paco2, pH and serum bicarbonate**
  4. **Electrolytes**
  5. **Glucose**
  6. **Hematocrit**
  7. **Blood pressure and perfusion**
  8. **Kidney function tests**
  9. **Temperature**

TREATMENT

- **Avoid hypothermia** and minimize oxygen consumption, the infant should be placed in an **incubator or radiant warmer**, to keep core temperature between **36.5 and 37°C**.

- **Calories and fluids** should initially be provided intravenously with D10%W and amino acids.
  - Excessive fluids (>140 mL/kg/ day) contribute to the development of patent ductus arteriosus (PDA) and BPD.

- Because of the difficulty of distinguishing other bacterial infections from RDS, **empirical antibiotic therapy is indicated until the results of blood cultures are available**.
  - Ampicillin with an aminoglycoside is suggested.

TREATMENT

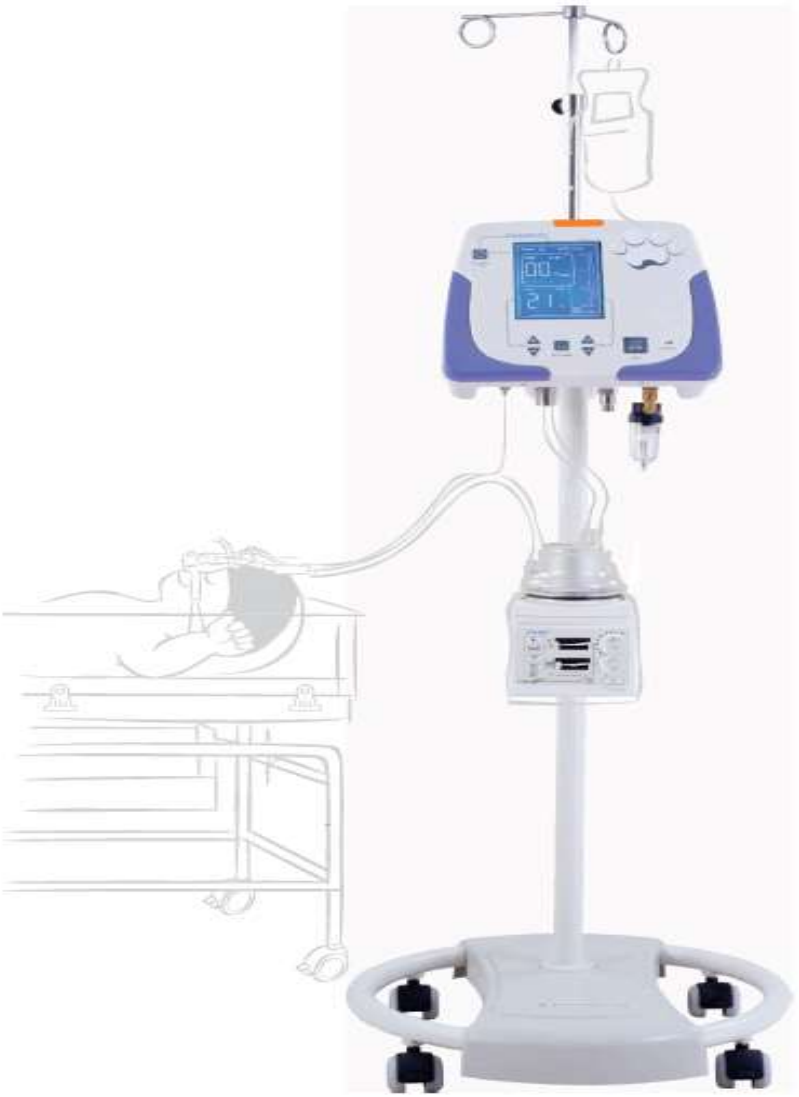
❖**Oxygen therapy:**

- Warm humidified oxygen should be provided at a concentration initially sufficient to keep **saturation 88-94%** **in order to maintain normal tissue oxygenation while minimizing the risk of oxygen toxicity**.

- If oxygen saturation cannot be kept >90% at inspired oxygen concentrations of 40-70% or greater, applying **CPAP**.

- Another approach is to **IN**tubate the preterm infant, administer intratracheal **SUR**factant and then **E**xtubate the infant and begin CPAP - **INSURE**.

- **Early nasal CPAP is beneficial as compared to intubation and prophylactic surfactant**, including lower mortality or BPD with CPAP treatment.



TREATMENT

❖Oxygen therapy:

- If an infant with RDS undergoing CPAP cannot keep oxygen saturation >90% while breathing 40-70% oxygen, Infants with respiratory failure or persistent apnea **assisted mechanical ventilation and surfactant are indicated**.

- **Reasonable measures of respiratory failure** are:

1. arterial blood pH <7.20,
2. arterial blood Pco2 of 60 mm Hg or higher,
3. oxygen saturation <90% at oxygen concentrations of 40-70% and CPAP of 5-10 cm H2O.

- **Permissive hypercapnia** in which priority is given to the prevention or limitation of lung injury from the ventilator by tolerating relatively high levels of Paco2 rather than maintenance of normal blood gas values.

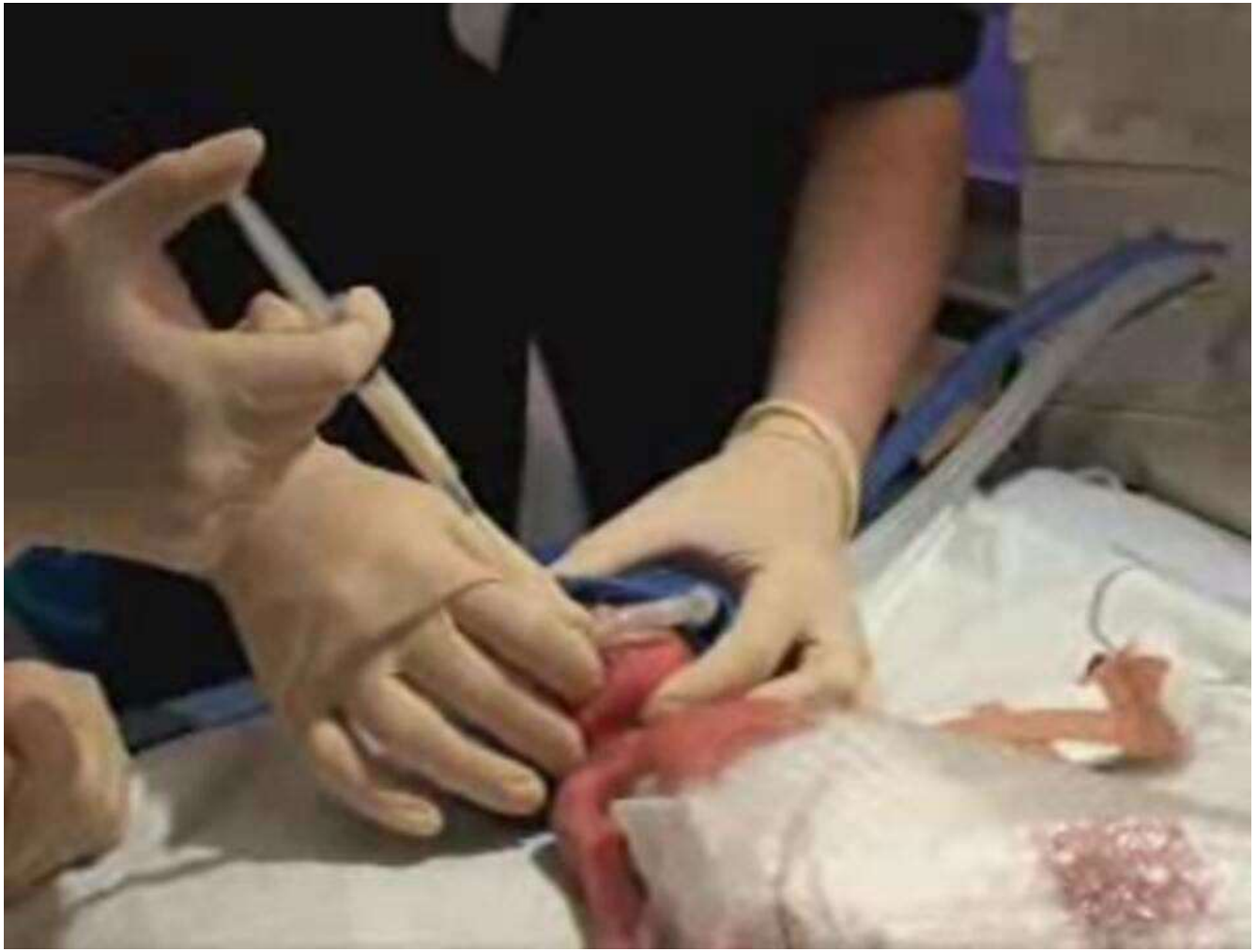
TREATMENT

❖ **Surfactant:**

- Immediate effects of **endotracheal surfactant replacement therapy** include
  1. improved oxygenation,
  2. reduced ventilatory support,
  3. increased pulmonary compliance,
  4. improved chest radiograph appearance.

- **Repeated dosing** is given every 6-12 hr for a total of 2 to 4 doses, depending on the preparation.

- **Complications of surfactant therapy** include
  1. transient hypoxia,
  2. hypercapnia,
  3. bradycardia and hypotension,
  4. blockage of the endotracheal tube,
  5. pulmonary hemorrhage.



COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

A. Complications of **tracheal intubation**.

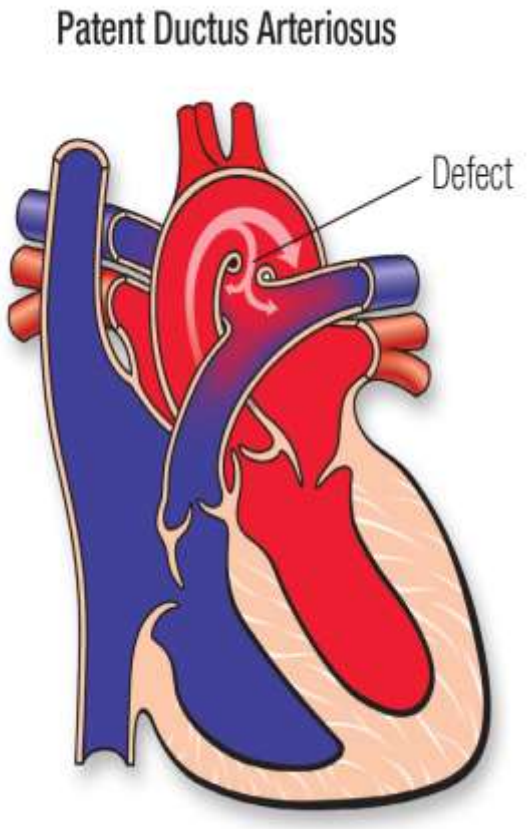
B. Risks associated with **umbilical *arterial* and venous catheterization.**

- **Renovascular hypertension** may occur days to weeks after umbilical arterial catheterization in a small proportion of neonates.

C. Air leaks are a common complication of the management of infants with RDS.

COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

D. Some neonates with RDS may have clinically significant shunting through a **PDA diagnosed** by echocardiography**.**



- Manifestations of PDA may include

1. a hyperdynamic precordium, bounding peripheral pulses, wide pulse pressure, and a continuous (machinery) or systolic murmur with or without extension into diastole;
2. radiographic evidence of cardiomegaly and increased pulmonary vascular markings;
3. hepatomegaly;
4. increasing oxygen dependence;
5. carbon dioxide retention.

COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

E. Bronchopulmonary dysplasia (BPD) :

- BPD was defined as **persistent oxygen dependency up to 28 days of life**.

- The severity of BPD-related pulmonary dysfunction and neurodevelopmental impairment in early childhood is more accurately predicted by an **oxygen dependence at 36 weeks' postmenstrual age (PMA) in infants <32 weeks' gestational age (GA) and at 56 days of age in infants with older GA**.

- The occurrence of BPD is **inversely related to gestational age**.

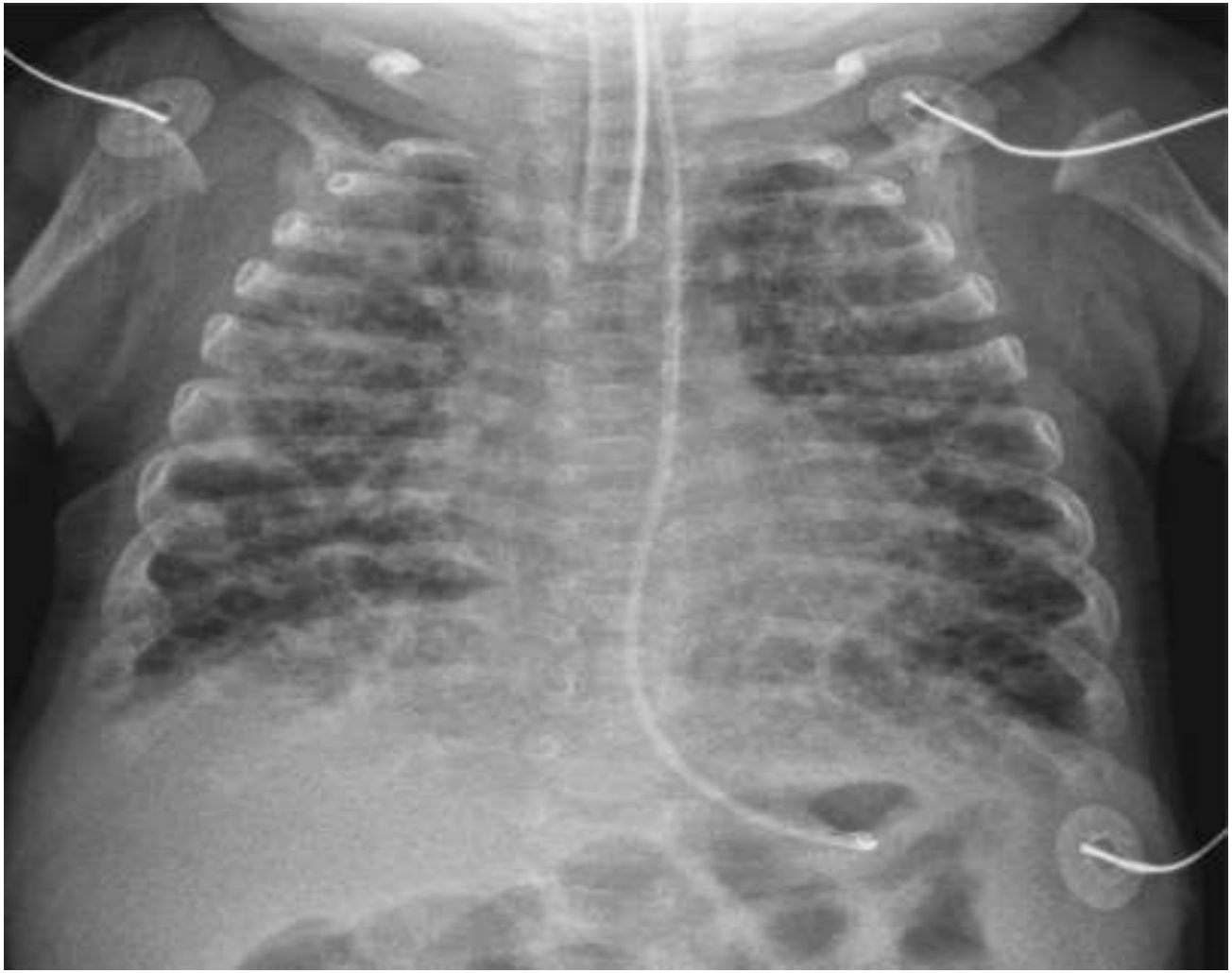
COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

❖ Bronchopulmonary dysplasia (BPD) :

- **Diagnosis:**

- Instead of showing improvement on the 3rd or 4th day, which would be consistent with the natural course of RDS, some infants demonstrate an **increased need for oxygen and ventilatory support**.

- **The chest radiograph may reveal** pulmonary interstitial emphysema, wandering atelectasis with concomitant hyperinflation, and cyst formation (chronic lung changes).



COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

❖ Bronchopulmonary dysplasia (BPD) :

- **Treatment** of BPD includes nutritional support, fluid restriction, drug therapy, maintenance of adequate O2, and prompt treatment of infection.
- **Vitamin A supplementation** in VLBW infants reduces the risk of BPD.
- **Early use of nasal CPAP and rapid extubation** with transition to nasal CPAP are associated with a decreased risk of BPD.
- **Nutritional supplementation**.
- Diuretic therapy(**Furosemide)**.

COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME AND INTENSIVE CARE

❖ Bronchopulmonary dysplasia (BPD) :

- **Inhaled bronchodilators (beta-2 agonist) and Ipratropium bromide** improve lung mechanics by decreasing airway resistance.

- **Methylxanthines** (theophylline and Caffeine) are used in infants with BPD to increase respiratory drive, decrease apnea, improve diaphragmatic contractility, decrease PVR and increase lung compliance.

- Preventive therapy of BPD with **postnatal dexamethasone** may reduce the time to extubation and may decrease the risk of BPD but is associated with substantial short- and long-term risks.

PROGNOSIS

- Antenatal steroids, postnatal surfactant use, and improved modes of ventilation have resulted in low mortality from RDS (≈10%).
- Mortality increases with decreasing gestational age.
- Although 85-90% of all infants surviving RDS after requiring ventilatory support are normal, the outlook is much better for those weighing >1,500 g.
- Survivors with BPD often go home on a regimen of oxygen, diuretics, and bronchodilator therapy.

PROGNOSIS

- **Cardiac complications of BPD** include pulmonary hypertension, cor pulmonale, systemic hypertension and left ventricular hypertrophy.

- Infants are at risk for **severe respiratory syncytial virus infections and must receive prophylactic therapy**.

- **Noncardiorespiratory complications of BPD** include **growth failure, psychomotor retardation**, and parental stress, as well as sequelae of therapy.


WHEN UR BORN IN 2020:
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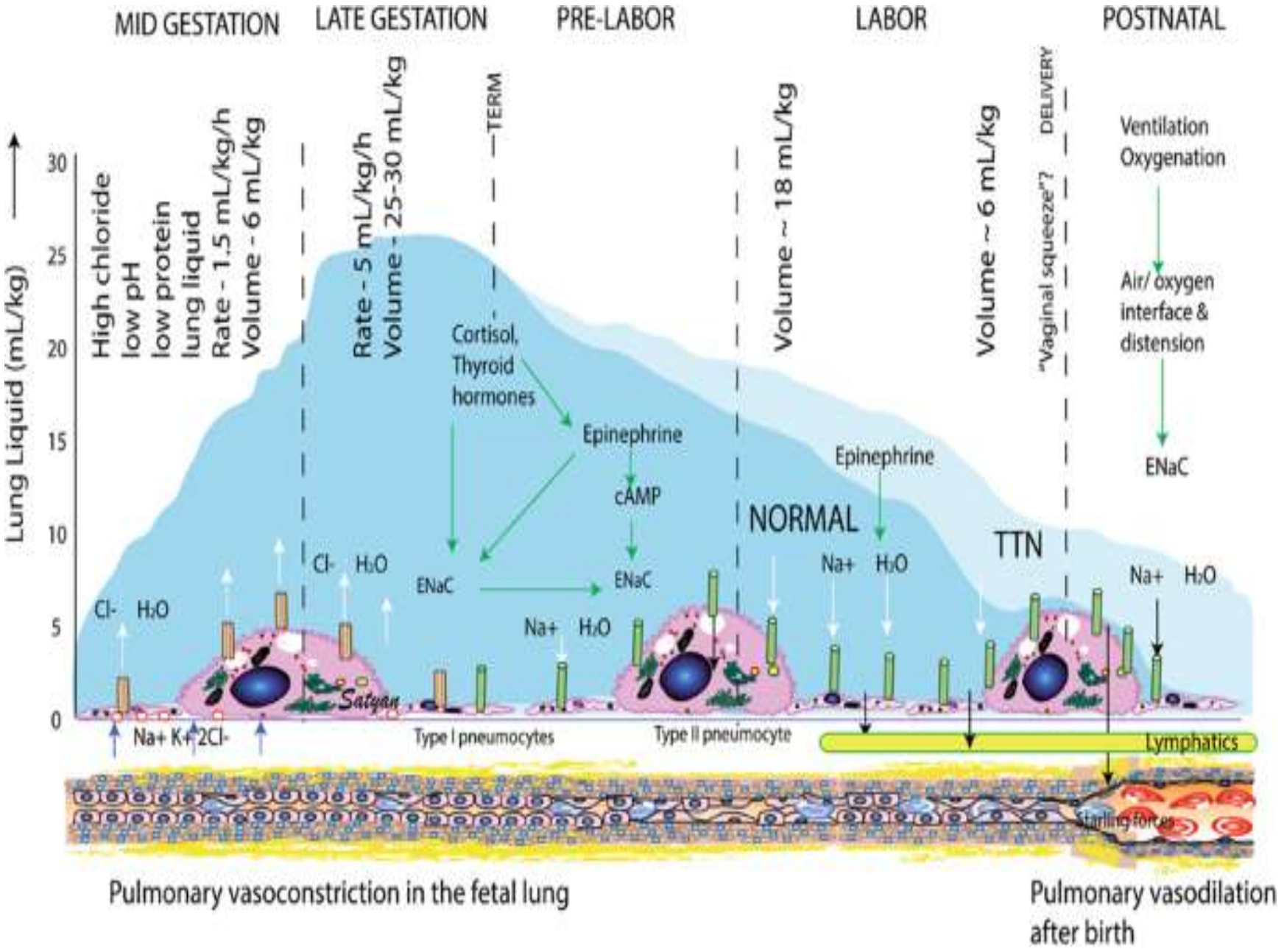
Transient Tachypnea of the Newborn

Transient Tachypnea of the Newborn

- Normally after delivery, **Air entry into the lungs displaces fluid**. **The remaining fluid is removed via the pulmonary lymphatics**, **upper airway, mediastinum, and pleural space**.

- The syndrome is believed to be secondary to **slow absorption of fetal lung fluid**, resulting in decreased pulmonary compliance and tidal volume and increased dead space.

- **In severe cases**, retained fetal lung fluid may interfere with the normal postnatal fall in PVR, **resulting in persistent pulmonary hypertension**; a mild surfactant deficiency may be present.


MID GESTATION
LATE GESTATION
PRE-LABOR
LABOR
POSTNATAL
Lung Liquid (mL/kg)
30
25
20
15
10
5
0
High chloride
low pH
low protein
lung liquid
Rate - 1.5 mL/kg/h
Volume - 6 mL/kg
Rate - 5 mL/kg/h
Volume - 25-30 mL/kg
TERM
Volume ~ 18 mL/kg
Volume ~ 6 mL/kg
DELIVERY
"Vaginal squeeze"?
Ventilation
Oxygenation
Air/ oxygen
interface &
distension
ENaC
Cortisol,
Thyroid
hormones
Epinephrine
cAMP
ENaC
Epinephrine
NORMAL
TTN
Cl-
H2O
Na+
H2O
Satyan
Na+ K+ 2Cl-
Type I pneumocytes
Type II pneumocyte
Lymphatics
Starling forces
Pulmonary vasoconstriction in the fetal lung
Pulmonary vasodilation
after birth

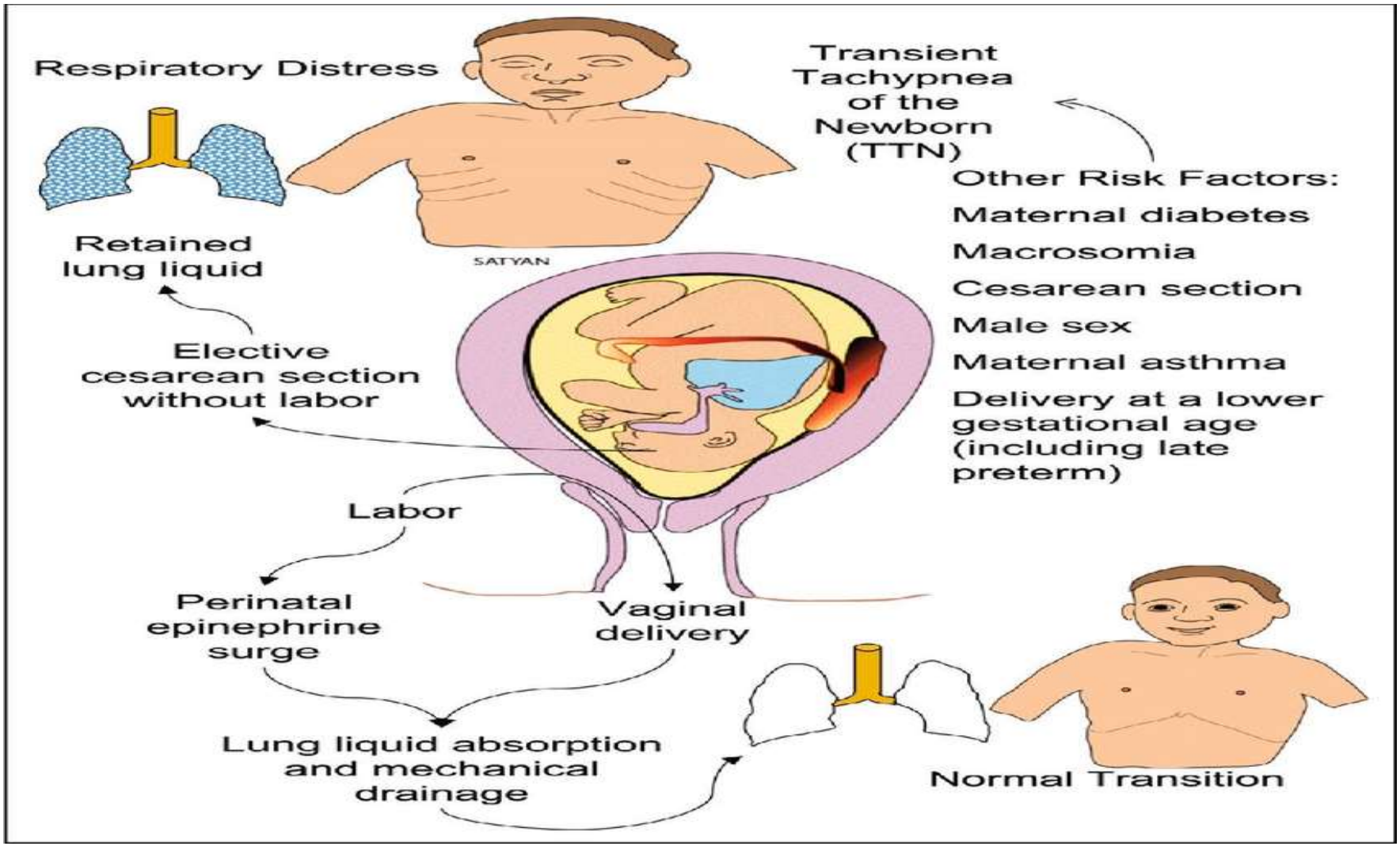
Transient Tachypnea of the Newborn

- Transient tachypnea is frequently **a diagnosis of exclusion**.

- The **distinctive features of transient tachypnea** are

1. rapid recovery of the infant
2. the absence of radiographic findings for RDS and other lung disorders.
3. Occur in term and late term infants.

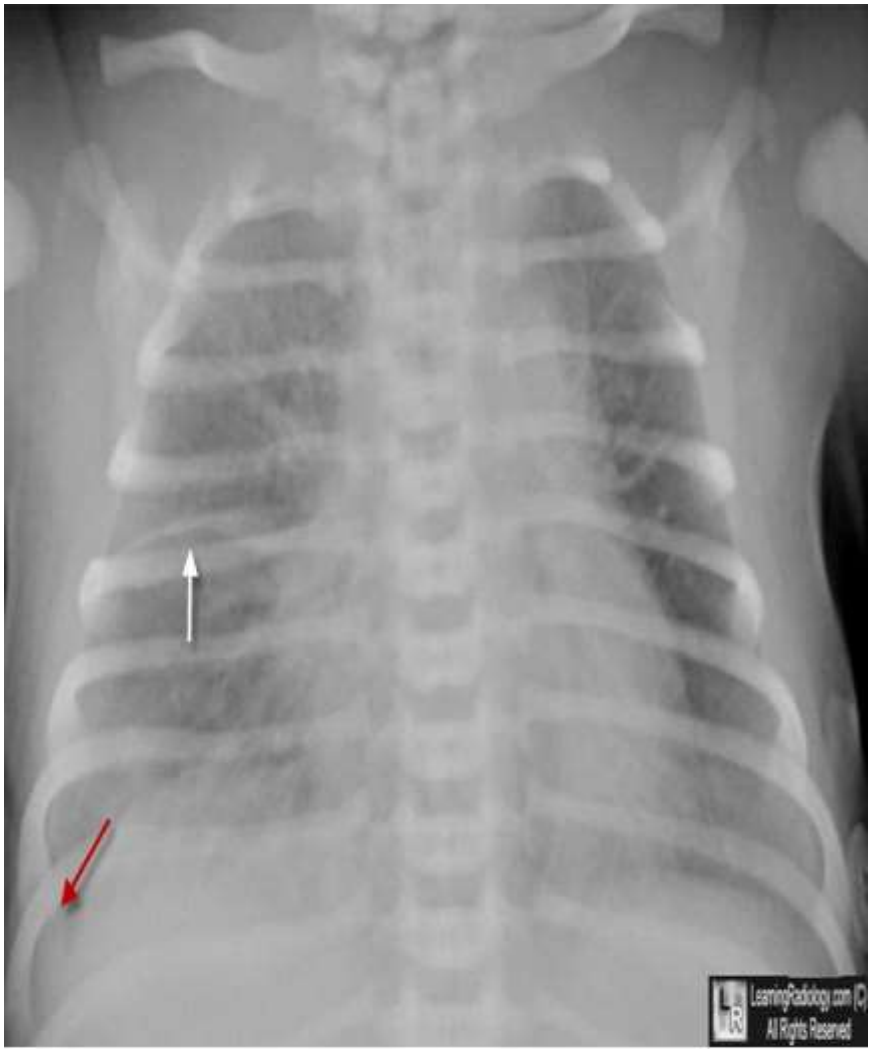
Risk factors



Transient Tachypnea of the Newborn

- Transient tachypnea is most common after **term cesarean delivery**.
- It is characterized by the **early onset of tachypnea**, sometimes with retractions, or expiratory grunting and, occasionally, cyanosis that is relieved by minimal oxygen supplementation (<40%).
- Most infants **recover rapidly**, usually within 3 days.
- Hypercapnia and acidosis are uncommon.

TTN



- The chest generally sounds clear without crackles or wheeze, and the chest radiograph shows

1. **prominent pulmonary vascular markings**,
2. **fluid in the intralobar fissures**,
3. **overaeration, flat diaphragms**,
4. rarely, **small pleural effusions**.

Transient Tachypnea of the Newborn

- **Treatment**
- **Supportive.**

- **Antibiotics started when baby need O2 support more than 6 hours due to difficulty to differentiate from sepsis.**

- The term "**malignant transient tachypnea of the newborn**" has been used to describe the refractory hypoxemia as a result of **pulmonary hypertension** and require ECMO support.
  - The initial approach to these infants is similar to that of RDS plus the concern for pulmonary hypertension.

Meconium Aspiration

Meconium Aspiration

- Meconium-stained amniotic fluid is found in 10-15% of births and usually occurs in **late-term, term or post-term infants**.
- Meconium aspiration syndrome (MAS) develops in 5% of such infants; 30% require mechanical ventilation and 3-5% die.
- Usually, but not invariably, **fetal distress and hypoxia** occur before the passage of meconium into amniotic fluid.
- The infants are **meconium stained** and **may be depressed and require resuscitation at birth (low APGAR score)**.
- Infants with MAS are at increased risk of persistent **pulmonary hypertension**.

Composition of meconium :

Meconium is the first intestinal discharge of the newborn infants. Which is greenish black in colour & contains:

* Water (75%)
* Mucopolysaccharides
* Proteins
* Cholesterol, lipids
* Bile acids & salts
* Enzymes
* Vernix & squamous cells

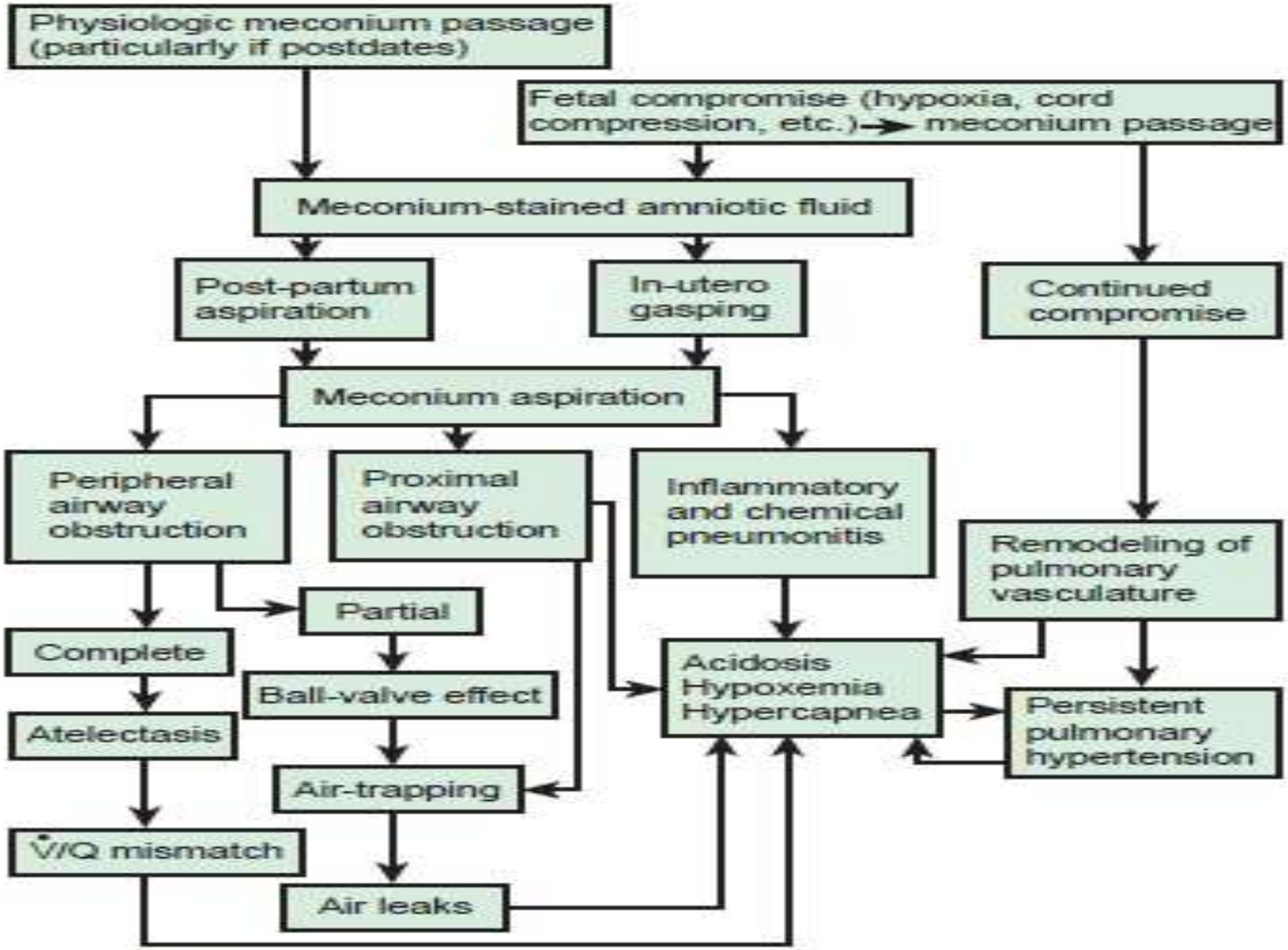


Figure 101-8 Pathophysiology of meconium passage and the meconium aspiration syndrome. V̇/Q, ventilation-perfusion ratio. *(From Wiswell TE, Bent RC: Meconium staining and the meconium aspiration syndrome: unresolved issues,* Pediatr Clin North Am *40:955–981, 1993.)*

CLINICAL MANIFESTATIONS

- Respiratory distress **within the first hours**, with tachypnea, retractions, grunting, and cyanosis observed in severely affected infants.

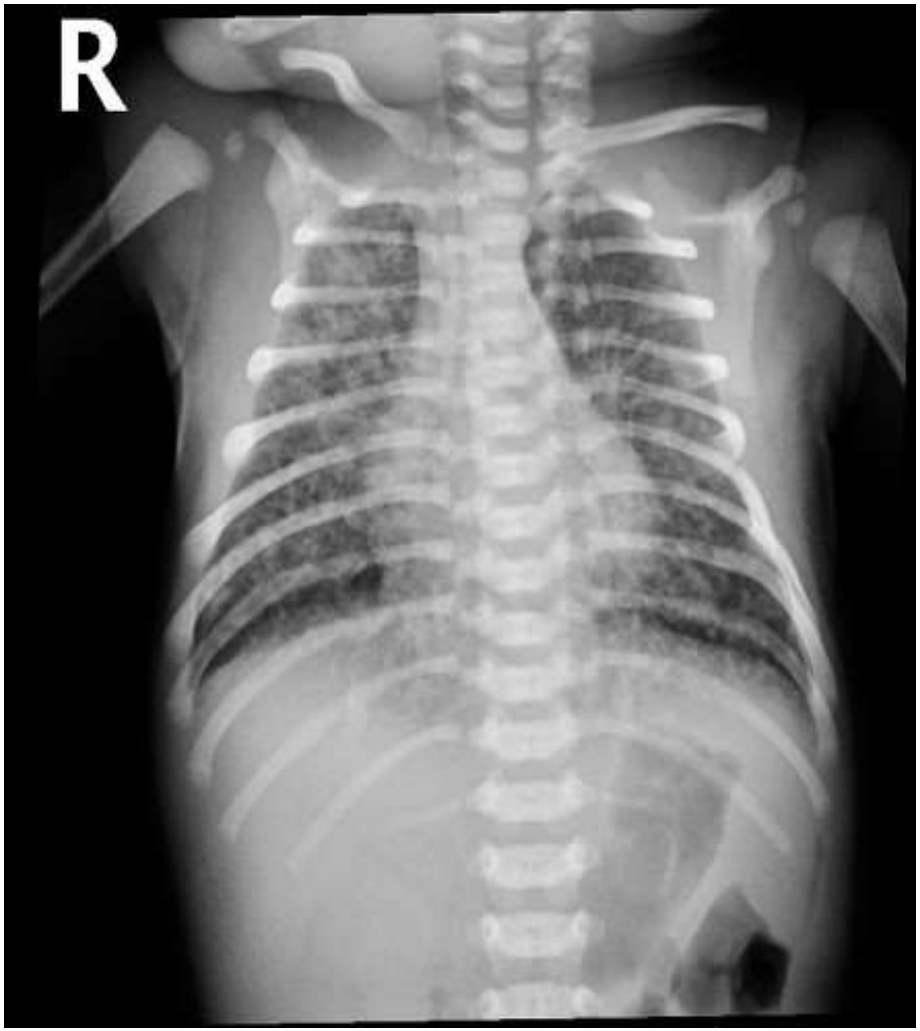
- Partial obstruction of some airways may lead to pneumomediastinum, pneumothorax, or both. **Overdistention of the chest** may be prominent.

- The condition usually improves within 72 hr, but **when its course requires assisted ventilation, it may be severe with a high risk for mortality**.

Diagnosis

- The typical chest radiograph is characterized by

1. **patchy infiltrates**,
2. **coarse streaking of both lung fields,**
3. **increased anteroposterior diameter**,
4. **flattening of the diaphragm**.



PREVENTION

- The risk of meconium aspiration may be decreased by **rapid identification of fetal distress** and initiation of prompt delivery in the presence of late fetal heart rate deceleration or poor beat-to-beat fetal heart rate variability.

- **Amnioinfusion**, it does not reduce the risk of MAS, cesarean delivery, or other major indicators of maternal or neonatal morbidity.

- **Intrapartum nasopharyngeal suctioning in infants with meconium-stained amniotic fluid does not reduce the risk for MAS**.

European Resuscitation Council Guidelines 2021

Meconium

- Non-vigorous newborn infants delivered through meconium-stained amniotic fluid are at significant risk for requiring advanced resuscitation and a neonatal team competent in advanced resuscitation may be required.
- Routine suctioning of the airway of non-vigorous infants is likely to delay initiating ventilation and is not recommended. In the absence of evidence of benefit for suctioning, the emphasis must be on initiating ventilation as soon as possible in apnoeic or ineffectively breathing infants born through meconium-stained amniotic fluid.
- Should initial attempts at aeration and ventilation be unsuccessful then physical obstruction may be the cause. In this case inspection and suction under direct vision be considered. Rarely, an infant may require tracheal intubation and tracheal suctioning to relieve airway obstruction.

TREATMENT

- **Routine intubation to aspirate the lungs of *vigorous and non-vigorous infants* born through meconium-stained fluid is not effective in reducing the MAS or other major adverse outcomes.**

- Treatment of the MAS includes **supportive management** for respiratory distress.

- Administration of **surfactant and/or iNO** to infants with MAS and hypoxemic respiratory failure, or pulmonary hypertension.

- ECMO.

PROGNOSIS

- The mortality rate of meconium-stained infants is considerably higher than that of non-stained infants.
- The decline in neonatal deaths caused by MAS during the last decades is related to improvements in obstetric and neonatal care.
- Residual lung problems are rare, but include symptomatic cough, wheezing, and persistent hyperinflation for up to 5-10 yr.
- The ultimate prognosis depends on the extent of CNS injury from asphyxia and the presence of associated problems such as pulmonary hypertension.

Extrapulmonary Air Leaks (Pneumothorax, Pneumomediastinum, Pulmonary Interstitial Emphysema, Pneumopericardium)

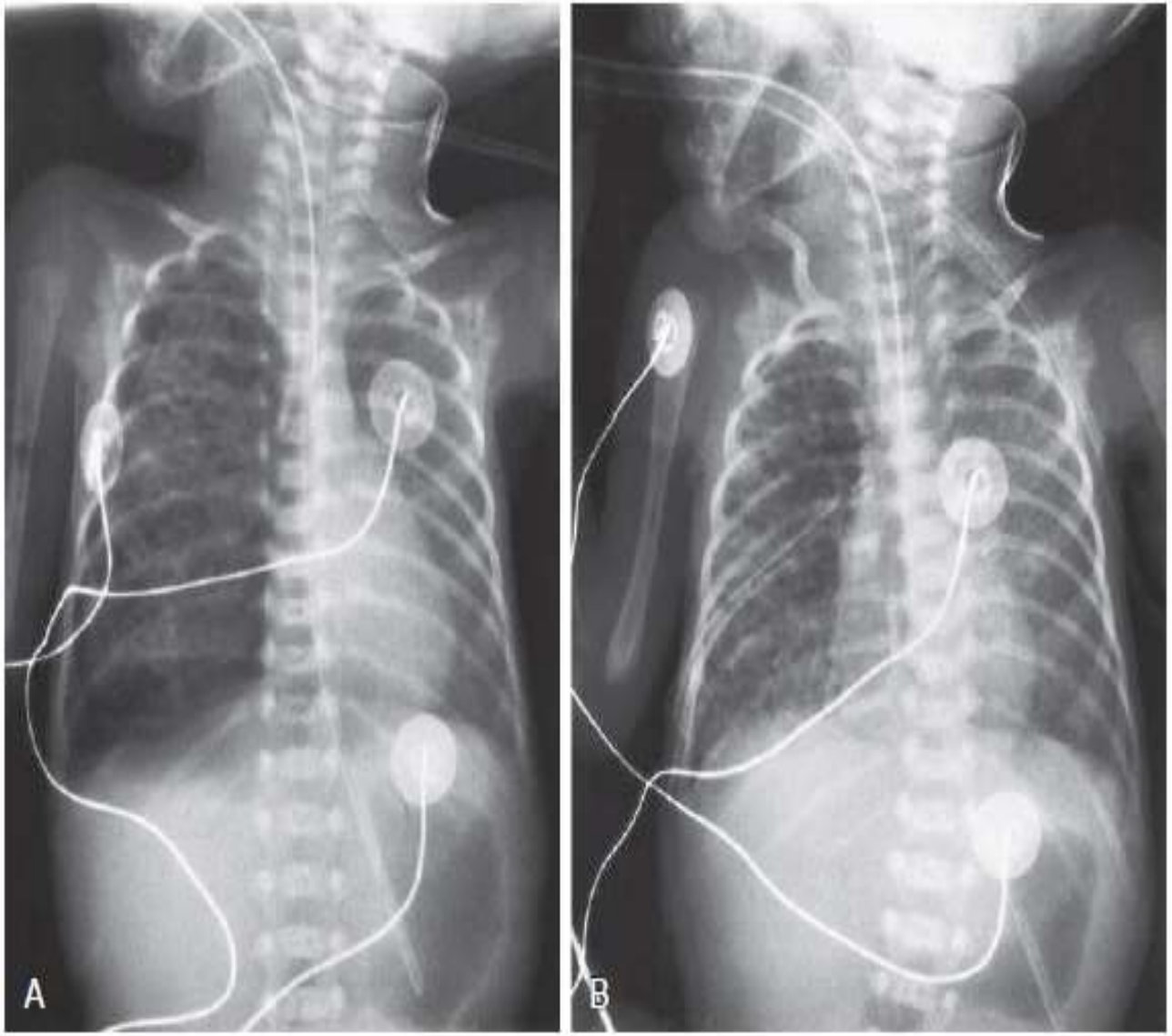


Figure 101-14 A, Right-sided tension pneumothorax and widespread right lung pulmonary interstitial emphysema in a preterm infant receiving intensive care. **B,** Resolution of pneumothorax with a chest tube in place. Pulmonary interstitial emphysema (PIE) persists. *(From Meerstadt PWD, Gyll C:* Manual of neonatal emergency x-ray interpretation, *Philadelphia, 1994, WB Saunders, p. 73.)*

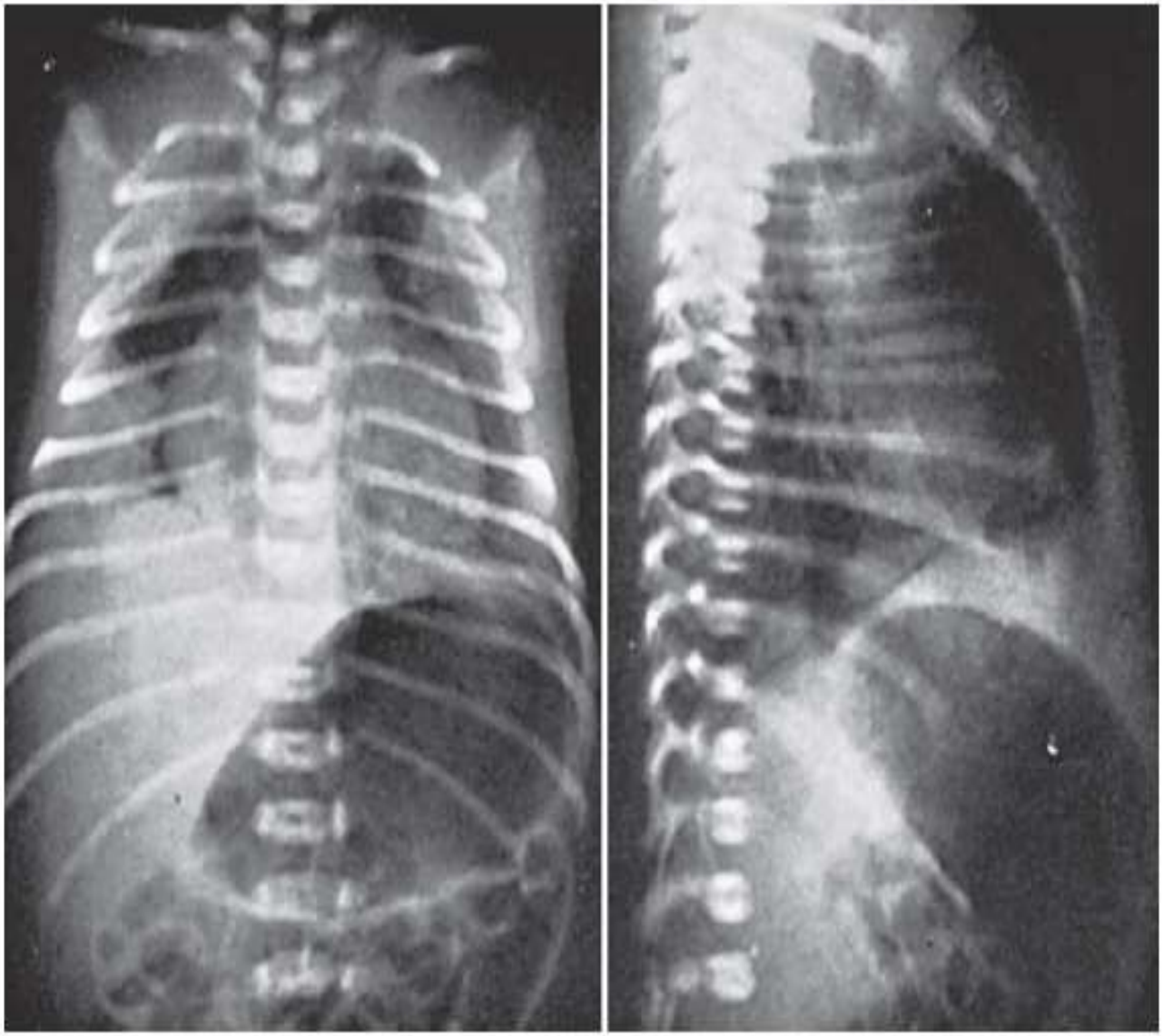


Figure 101-15 Pneumomediastinum in a newborn infant. The anteroposterior view (*left*) demonstrates compression of the lungs, and the lateral view (*right*) shows bulging of the sternum, each resulting from distention of the mediastinum by trapped air.