Objective

At the end of this presentation, the participant will be able to:

- Recognize respiratory distress as a symptom associated with both respiratory and non-respiratory etiologies
- Review the common respiratory diseases that cause respiratory distress in newborns
- Itemize associated prenatal and perinatal risk factors
- Describe their pathophysiology, clinical and radiographic features and treatments

Respiratory Diseases of the Newborn

- Respiratory diseases
  - Often present with respiratory distress

- Respiratory distress
  - One of most common reasons for NICU admission
    - Most common causes for admission
      - Transient tachypnea of the newborn (TTN)
      - Infection (sepsis, pneumonia)
Respiratory Distress

- Extensive differential diagnoses
- Multiple disease etiologies
  - Non-respiratory disorders
  - Respiratory diseases

Non-respiratory Disorders Causing Respiratory Distress

- Cardiovascular
  - Essential to rule out cardiac disease
- Hematological
- Infectious
- Metabolic
- Musculoskeletal
- Neurological
  - CNS
  - PNS
  - Neuromuscular

Respiratory Diseases Causing Respiratory Distress

- Parenchymal conditions
- Developmental abnormalities
- Mechanical abnormalities
- Airway abnormalities
Respiratory Diseases Causing Respiratory Distress

- Parenchymal conditions
  - Transient tachypnea of the newborn (TTN)
  - Respiratory distress syndrome (RDS)
  - Pneumonia
  - Meconium aspiration syndrome (MAS)
  - Pulmonary hypertension (PPHN)

Respiratory Diseases Causing Respiratory Distress

- Developmental abnormalities
  - Congenital diaphragmatic hernia (CDH)
  - Congenital cystic adenomatoid malformation (CCAM)
  - Pulmonary sequestration
  - Tracheoesophageal fistula (TEF)
  - Pulmonary hypoplasia
  - Infantile lobar emphysema

Respiratory Diseases Causing Respiratory Distress

- Mechanical abnormalities
  - Pulmonary air-leak syndromes

- Airway abnormalities
  - Airway obstruction
    - Intrinsic
    - Extrinsic
Q1. Embryologically, the lung is derived from:

A. Lateral folds of embryonic mesoderm
B. Medial pharyngeal groove of the foregut endoderm
C. Epithelial cells of the neural crest
D. Subdivision of primordial mesenchyme
E. None of the above

Development of Lung

- Lung differentiation begins during 3rd week of gestation
- Embryonic period of fetal development
- Development of lung bud
  - Ventral outpouching of the floor of primitive foregut
Lung morphogenesis: 5 distinct periods

<table>
<thead>
<tr>
<th>Phase</th>
<th>Time (wk)</th>
<th>Key Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic</td>
<td>3–6</td>
<td>Lung bud: axillary, posterior, lateral, and segmental buds</td>
</tr>
<tr>
<td>Pseudoglanular</td>
<td>6–10</td>
<td>Subsegmental bronchi, terminal bronchi, acini, tubules, mucous glands</td>
</tr>
<tr>
<td>Canalicular</td>
<td>11–16</td>
<td>Regioinal bronchi, microconduits and conelations, capillary arteries</td>
</tr>
<tr>
<td>Saccular</td>
<td>17–20</td>
<td>Dilatation of terminal bronchi, acini, interstitial, capillaries</td>
</tr>
<tr>
<td>Alveolar</td>
<td>21–34</td>
<td>Alveoli development, until 2–6 years of age</td>
</tr>
<tr>
<td>Maturation</td>
<td>34–36</td>
<td>Alveoli development, until 2–6 years of age</td>
</tr>
</tbody>
</table>

- Embryonic/Pseudoglanular: conducting airways
- Canalicular/Saccular/Alveolar: terminal resp. units
- Alveoli development: until 2–6 years of age
- Relate common malformations to morphogenesis
  - Embryonic
    - TEF, tracheal stenosis
  - Pseudoglanular
  - CDH, CCAM

Q2. A term male newborn is delivered by repeat C/S. Rupture of membranes occurs at delivery. Apgars are 9 at 1 min and 9 at 5 minutes. At 15 minutes of life the infant is noted to have tachypnea and mild intercostal retractions. He is acyanotic with peripheral oxygen saturation at 88 to 90% on room air. There is no cardiac murmur. Chest radiograph shows expansion of the lungs to 8 to 10 anterior ribs, perihilar streaking, and a fluid density in the right horizontal fissure.

Of the following, the BEST therapy for this infant is:

- A. Intravenous furosemide
- B. Intravenous ampicillin and gentamicin
- C. Tracheal intubation and surfactant
- D. Intravenous prostaglandin E1
- E. Supplemental oxygen by hood
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Please key in your response

**Perihilar streaking, increased interstitial markings**

**Transient Tachypnea of the Newborn (TTN)**

- Most common cause of respiratory distress in newborns
- Term and preterm
- Results from delayed clearance of fetal lung fluid
- Mechanical forces
- Inhibited activation of apical Na+ channels
- G/F/R, tachypnea, +/-cyanosis
- Resolves by 48-72 hours
- Usually benign, self limiting
- Risk Factors
  - C/S delivery w/o labor, late preterm delivery, maternal diabetes, precipitous delivery, perinatal depression
**Transient Tachypnea of the Newborn (TTN)**

- **CXR**
  - Generally good lung volumes
  - Increased interstitial markings
  - Perihilar streaking without air bronchograms
  - Fluid in fissure(s), (pleural effusion- occasionally)

- **ABG**
  - Mild hypoxemia, +/- hypercarbia

- **DDx**
  - RDS, pneumonia, air-leak syndromes, congenital lung malformations

- **Rx:** Supportive
  - Oxygen supplementation, CPAP, IVF, monitoring

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Q3. A 1,600 g infant is born at 32 weeks gestation. Pregnancy was complicated by preterm labor and precipitous delivery. The mother received no antenatal steroids and her membranes ruptured just prior to delivery. At 1 to 2 hours of age the infant develops tachypnea, grunting, nasal flaring and subcostal retractions.

Of the following, the MOST likely radiographic finding in this infant would be:

A. Fine reticulogranular pattern
B. Diffuse coarse infiltrates
C. Pleural effusion
D. Raised thymic silhouette [sail sign]
E. Fluid in the fissures

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D. Raised thymic silhouette [sail sign]
E. Fluid in the fissures
**Respiratory Distress Syndrome (RDS)**

- Most common cause of SEVERE respiratory distress in newborn
- Disease of biological/biochemical immaturity
- Surfactant deficiency
  - Alveolar collapse at low lung volumes
    - \( \rightarrow \) lung compliance, atelectasis, pulmonary edema
    - \( \rightarrow \) V/Q mismatch, altered gas exchange
  - Hypoxemia, hypercarbia
- Incidence inversely proportional to gestational age
  - 23-25wks 100%
  - 29wks 60%
  - >37wks <1%

**Respiratory Distress Syndrome**

- Onset within minutes to hours after birth
- Respiratory distress
  - G/F/R, tachypnea, +/- cyanosis
- CXR
  - Fine reticulogranular pattern
  - “Ground-glass” appearance
  - Air-bronchograms
  - Diffuse atelectasis
- Peak severity at 24-72 hours
- Recovery usually coincides with diuresis
Respiratory Distress Syndrome

- Preventive strategies
  - Tocolytic agents to arrest premature labor
  - Acceleration of fetal lung maturity
    - Antenatal corticosteroid therapy
      - 24-48hrs prior to delivery
- Complications
  - Air leaks (20-50%)
  - CLD/BPD

Q4. A pregnant woman is counseled to have a repeat C/S as her pregnancy approaches term. To avoid delivering a newborn who has immature lungs and consequent respiratory distress syndrome, she undergoes antenatal assessment of her amniotic fluid.

Of the following, the amniotic fluid test MOST likely to predict fetal lung maturity is:

A. Phosphatidylglycerol
B. Alpha-fetoprotein
C. Surfactant protein A
D. Thyroxine
E. Sphingomyelin

Please key in your response.
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C. Surfactant protein A  
D. Thyroxine  
E. Sphingomyelin

Q5. The treatment of RDS with exogenous administration of surfactant is MOST likely to increase the incidence of:

A. Intraventricular hemorrhage  
B. Bronchopulmonary dysplasia  
C. Pulmonary hemorrhage  
D. Retinopathy of prematurity  
E. Pneumothorax
Q6. Before delivery of an infant at 41 weeks gestation, the obstetrician remarks that the amniotic fluid contains thick particulate meconium. As the infant is placed upon the warmer after the delivery, he appears limp and pale with depressed respirations.

Of the following, the MOST important initial step in resuscitation of the infant is to:

A. Determine the infant’s Apgar score  
B. Initiate tracheal intubation with suctioning  
C. Provide positive pressure ventilation  
D. Suction the hypopharynx  
E. Aspirate the gastric contents
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Q7. A newborn whose estimated gestational age is 42+ weeks is stained with meconium. Tracheal intubation reveals meconium below the vocal cords. The infant has respiratory distress. A chest radiograph is obtained.

Of the following, the MOST likely radiographic finding is:

A. Decreased lung volumes  
B. Coarse, patchy infiltrates  
C. Pleural effusion  
D. Reticulogranular pattern  
E. Mediastinal shift
Coarse, patchy infiltrates

Meconium Aspiration Syndrome (MAS)
- Meconium stained amniotic fluid
- 10-15% of all deliveries
- MAS
  - Incidence: 1-2%
  - Mortality: 5-20%
- Meconium
  - Lanugo hair, vernix, cellular debris, bile acid and pigments, mucus and blood
  - Appears in the fetal ileum 10-16 weeks gestation
- In utero passage 2° fetal hypoxia, acidosis
  - ↑ peristalsis, rectal sphincter relaxation, stooling
  - Gasping respiratory efforts, laryngeal incompetence
  - → MSAF aspiration into airways

Meconium Aspiration Syndrome
- Pathophysiology
  - Airway obstruction
    - Viscous particulate matter →
      - Partial obstruction (ball-valve) → hyperinflation
      - Complete obstruction → atelectasis
  - Chemical pneumonitis
    - Leukocyte infiltration, alveolar necrosis, edema
  - Surfactant inactivation
    - → abnormal compliance
    - O2 requirement
    - Air leaks (10-30%)
    - Hypoxic pulmonary vasoconstriction (PPHN)
Meconium Aspiration Syndrome

- Risk factors associated with MAS
  - Post-dates
  - Fetal distress
  - In-utero hypoxia
- Management: supportive
  - Ventilation (HFOV), O₂, iNO, surfactant, antibiotics
- Prevention
  - Amnio-infusion
  - MSAF & NRP guidelines
    - Indication for tracheal intubation and suctioning
      - “Non-vigorous” neonate
- DDx
  - TTN, RDS, pneumonia

Q8. A 3-hour-old infant delivered at term has respiratory distress. The clinical history is significant for meconium-stained amniotic fluid. CXR shows bilateral diffuse coarse infiltrates. The infant is receiving mechanical ventilation with FIO₂ 1.0 and a high mean airway pressure. ABG reveals PaO₂ of 35 mmHg.

Of the following, the manifestation MOST helpful for the diagnosis of persistent pulmonary hypertension is:

A. Elevated PaCO₂
B. Differential oxygen saturations between right arm and leg
C. Precordial Hyperactivity
D. Response to inhaled nitric oxide
E. Tricuspid regurgitation

Please key in your response.
Q9. Newborns who do not demonstrate a difference in the preductal to postductal values for SpO2 and PaO2 do not have PPHN.

A. True
B. False

**Persistent Pulmonary Hypertension of the Newborn (PPHN)**

- Clinical syndrome
- Abn elevated pulmonary vascular resistance (PVR)
  - Maladaption vs. maldevelopment of pulmonary vascular bed
  - Incidence 1:1000 live births
- Pathophysiology
  - Failure of normal decline in PVR after birth
  - Persistence ↑ pulmonary vascular resistance
    - → R to L shunting at atrial and/or DA
    - → ↓ pulmonary blood flow
    - → hypoxemia & acidosis
Persistent Pulmonary Hypertension of the Newborn

- **Associated disorders**
  - **Maladaptation**
    - Normal pulmonary structure, ↑ PVR
    - Bacterial sepsis, perinatal hypoxia/ asphyxia, pneumonia, MAS, hypothermia, post-dates
  - **Maldevelopment**
    - Excessive muscularization of pulmonary arterioles
    - Pulmonary hypoplasia (i.e. CDH), intrauterine hypoxia, alveolar capillary dysplasia, fetal ductus arteriosus closure

- **Presentation**
  - Typically in term or post-dates infant
  - 1st 24 hours of life
  - Respiratory distress, severe cyanosis

- **Diagnosis**
  - Severe hypoxemia (low PaO₂s)
  - CXR
    - Parenchymal lung disease
    - +/- oligemic appearing lungs (↓ PBF)
    - +/- Pre-Post-ductal splitting: ↓ SaO₂ > 10%
  - Echocardiography
    - R-sided pressures are systemic
    - TR, R→L shunting at PDA

- **Management**
  - Treatment of underlying cause
  - Antibiotics (i.e. sepsis, MAS)
  - Sedation
    - Maximize oxygen saturation
  - Support cardiac output/ SBP
    - Volume expansion, inotropes
    - Encourage ↑ PBF
  - Pulmonary vasodilation
    - FiO₂ (1.00), iNO, [Øalkalosis]
  - ECMO
Q10. A neonate born at 38 weeks has tachypnea, expiratory grunting, nasal flaring, subcostal retractions, and cyanosis shortly after birth. The mother had rupture of membranes 36 hours prior to vaginal delivery and has developed uterine tenderness and fever.

Of the following, the MOST likely chest radiographic finding in this infant is:

A. Mediastinal displacement
B. Diffuse reticulogranular pattern
C. Lung overinflation with coarse densities
D. Prominent perihilar streaking
E. Fine curvilinear lucencies

Q11. The most appropriate initial combination of antibiotics to treat neonatal pneumonia is:

A. Vancomycin and gentamicin
B. Cefotaxime and metronidazole
C. Ampicillin and gentamicin
D. Erythromycin and dicloxacillin
E. Cefaclor monotherapy
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D. Erythromycin and dicloxacillin  
E. Cefaclor monotherapy
Neonatal Pneumonia

- Causative agent is related to time of acquisition
  - Intrauterine (maternal infection/colonization)
    - Rubella, CMV, HVZ, HIV
    - Treponema p., Toxoplasma g., Mycobacterium tuberculosis, Listeria m.
  - At birth-perinatal
    - E. coli, GBS, GC, Chlamydia t., HSV
  - After birth
    - Respiratory viruses (adenovirus, RSV)
    - Gram positive (Staph. aureus)
    - Gram negative enteric (Pseudomonas, Serratia)

Neonatal Pneumonia

- Clinical presentation
  - Respiratory distress, +/- cyanosis
  - Apnea and desaturation
  - Temperature instability
  - Lethargy, poor feeding
  - Early-onset (<7days of age)
    - Intrauterine, perinatally-acquired
      - GBS, E. Coli, Klebsiella sp, Listeria
  - Late-onset (>7days of age)
    - Gram-negative enteric, fungal, Chamydia trach., HSV
    - Late onset often presents as systemic disease

Neonatal Pneumonia

- Diagnosis [CXR]
  - Radiographic features evolve with worsening during first 72hrs of disease/symptoms
  - Lung volumes increased (vs RDS)
  - Bacterial infections tend to be alveolar
    - Coarse patchy parenchymal infiltrates, consolidation, air bronchograms, pleural effusions, pneumatoceles
  - Viral infections interstitial
    - Perihilar streakiness, diffuse hazy or reticulonodular lungs, hyperexpansion
Neonatal Pneumonia

- **CXR features AND associated pathogens**
  - Listeria
  - Patchy parynchymal infiltrates WITH granular lungs OR streaky interstitial infiltrates
  - GBS
  - Diffuse b/L reticulogranularity, exaggerated air bronchograms [RDS]
  - Staph aureus
  - Consolidation [lobar], pleural effusions [+/- abscess, empyema, pneumatoceles]
  - G[-] Bacilli [e.g. E coli, Klebsiella]
  - Parenchymal consolidation [widespread]

Neonatal Pneumonia

- **CXR features AND associated pathogens (cont)**
  - Chlamydia
  - Hyperexpansion, b/L symmet interstitial infiltrates

- **Management**
  - Respiratory support and monitoring
  - Blood, tracheal secretions: culture & gram stain
  - Broad-spectrum antibiotic coverage
    - Ampicillin &
    - Aminoglycoside OR 3rd gen. cephalosporin

Q12. After successful intubation and manual ventilation of a 26 week gestation infant at delivery, the infant is pink and vital signs are stable. His color abruptly turns blue. Breath sounds are diminished on the right, normal on the left, and heart rate rapidly falls. The colorimetric carbon dioxide detector continues to display cyclical color changes.

Of the following, which intervention is MOST likely to resolve these findings?

A. IV bolus of normal saline
B. Endotrachial administration of epinephrine
C. Needle thoracotomy
D. Re-intubation
E. Surfactant therapy
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Right hemithorax:
- Extrapulmonary air
- Mediastinal shift

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Pulmonary Air Leak Syndromes

- In newborn most common forms:
  - Pneumothorax
  - Pneumomediastinum
- Other
  - Pulmonary interstitial emphysema (PIE)
  - Subcutaneous emphysema
  - Pneumoperitoneum
  - Pneumopericardium
Pulmonary Air Leak Syndromes

Pathophysiology
- Uneven alveolar ventilation, air trapping, high transpulmonary pressure swings →
  - Alveolar overdistention and rupture
  - Air tracks along root of lung
    - Perivascular connective tissue sheath
    - Rupture into:
      - Pleural space (pneumothorax)
      - Mediastinal space (pneumomediastinum)...
  - Direct mechanical trauma (i.e. suction catheter)

Pneumothorax
- Air dissection and leakage into thorax
  - Between visceral and parietal pleural reflections
- Occurs spontaneously in 1-2% of healthy term infants
  - High transpulmonary pressure swings with first breaths
  - Often asymptomatic
  - Pulmonary interstitial emphysema (PIE)
  - Air dissection and trapping in perivascular space
- More common amongst preterm infants
- May precede pneumothorax
- Associated with increased mortality rate

Risk factors
- Conditions with diminished/poor lung compliance
  - TTN, RDS, MAS, pneumonia
  - Pulmonary hypoplasia, CDH
- Asynchronous ventilation
- High ventilatory pressures
- Rapidly improving lung compliance
  - S/p surfactant administration
Pulmonary Air Leak Syndromes

- **Pneumothorax**
  - Clinical presentation
    - Dependent upon effects of trapped air on degree of lung collapse and cardiovascular compromise
    - Respiratory distress, tachypnea, ↑ WOB, +/- cyanosis
    - Affected side with ↓ BS
    - ↑ A-P diameter
    - Tension
      - Mediastinal shift
      - Acute ↓ HR/SV → ↓ cardiac output, ↓ BP, hypoxia
  - Dx: PE, transillumination, CXR
  - Rx: observation, nitrogen washout, needle aspiration, chest tube insertion, +/- respiratory support

Q13. Shortly after birth, a term infant presents with tachypnea, worsening retractions and persistent cyanosis. The abdomen appears scaphoid. Bag and mask ventilation is initiated. Auscultation reveals decreased breath sounds on the left and heart tones that are louder on the right.

The MOST likely explanation for these findings is:

A. Dextrocardia with situs solitus
B. Congenital cystic adenomatoid malformation
C. Esophageal atresia with tracheoesophageal fistula
D. Pneumothorax
E. Diaphragmatic hernia
Q14. The MOST appropriate initial treatment for this infant is:
A. Increased bag-mask ventilation
B. ECMO
C. Intubation and gastric decompression
D. Sodium bicarbonate infusion
E. Immediate surgical repair

Please key in your response

- Multiple bowel loops and stomach in left hemithorax
- Mass effect
- Deviation of trachea and cardiac silhouette across midline
- Minimal bowel gas in abdomen
Congenital Diaphragmatic Hernia (CDH)

- Developmental diaphragmatic defect
  - Prior to 8th week of embryonic life
  - Allow abdominal viscera to enter thoracic cavity
  - Incidence 1: 2-5,000 births
  - 2/3 male
  - 95% through posterolateral foramen of Bochdalek
  - 80% left-sided
  - Recurrence risk future pregnancies 2%
  - Mortality rates 25-75%
  - ↑ major malformations, liver herniation, degree of pulmonary hypoplasia, PPHN
  - 1/3 associated cardiac, renal, GI or chromosomal abnormalities

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Congenital Diaphragmatic Hernia

- Pathophysiology (classic)
  - Abdominal viscera herniate into thoracic cavity
  - → lung compression
  - → pulmonary hypoplasia, abnormal lung vasculature
  - → hypoxemia, respiratory failure, surfactant deficiency
- Clinical presentation
  - Respiratory distress shortly after birth
  - PE
    - Abdomen appears scaphoid
    - Air entry reduced on affected side
    - Displaced heart sounds to contralateral side

---

Congenital Diaphragmatic Hernia

- Treatment
  - Immediate
    - Intubation
    - Gastric decompression
      - Avoid intestinal distension
      - Prevent worsening CV compromise
  - Management approaches (varied)
    - HFOV, permissive hypercapnea
    - Surfactant administration, iNO
    - ECMO
    - Immediate vs. delayed surgical repair
Q15. All below listed conditions are associated with intrinsic airway abnormalities that may lead to airway obstruction, EXCEPT:

A. Vascular ring  
B. Choanal atresia  
C. Beckwith-Wiedemann Syndrome  
D. Laryngomalacia  
E. Pierre-Robin sequence  

Airway Abnormalities → Airway Obstruction

- Intrinsic
  - Nose & nasopharynx
    - Choanal atresia, edema 2o to suctioning
  - Mouth & Jaw
    - Pierre-Robin sequence, mandibular hypoplasia
  - Tongue
    - Macroglossia
      - Trisomy 21, Beckwith-Wiedemann Syndrome
    - Mass-effect
      - Thyroglossal duct cyst
**Airway Abnormalities → Airway Obstruction**

- **Intrinsic (cont.)**
  - **Larynx**
    - Laryngomalacia
    - Most common cause of neonatal airway obstruction
    - Inspiratory stridor
    - Epiglottis abnormalities
    - Laryngeal web
    - Vocal cord paralysis/ paresis (i.e. post op)
    - Laryngospasm (i.e. hypocalcemia)

- **Trachea/ Bronchi**
  - Tracheal bronchomalacia
  - Tracheal broncho/ subglottic stenosis
  - Congenital lobar emphysema

- **Extrinsic compression**
  - Thyroid enlargement
  - Vascular ring, aberrant blood vessel
  - Hemangioma **
  - Cystic hygroma
  - Mediastinal masses
    - Teratoma