Pulmonary Pathology I

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Pulmonary Lecture Series Outline
• Normal Lung, Congenital Anomalies and Acute lung injury – I
• Obstructive Lung Diseases – II
• Restrictive Lung Diseases – III
• Neoplasms – IV

ANATOMY AND HISTOLOGY
TRACHEA

C: Cartilage
E: Epithelium
SG: Submucous Glands

PRIMARY BRONCHIAL EPITHELIUM

Cilia
Goblet cells
Basal cells

Histologically, similar to trachea, but discontinuous cartilaginous plates

TERTIARY BRONCHUS (Fig A.)
AND BRONCHIOLE (Fig B.)

Bronchioles lack cartilage (c) and submucous (sm) glands. These are seen in the tertiary bronchus.
Mucociliary escalator

- Goblet cells secrete mucus.
- Cilia beat rhythmically upwards, pushing mucus up and out of the airways.
- Particles that are deposited on the mucus are removed from the lungs.
- Escalator function negatively affected by:
  - Smoking
  - Dusts
  - Low humidity
  - Mucostasis
  - Ciliary dyskinesia
Respiratory Unit

- Respiratory units are responsible for the transport of oxygen from the airspace into the blood, and transport of carbon dioxide from the blood to the airspace.
- Any process that reduces alveolar surface area, capillary surface area, increases the distance from the airspace to the capillary, reduces ventilation or perfusion, or causes ventilation-perfusion mismatch will reduce gas exchange.

Cell types in alveoli

- Type I cells or squamous pneumocytes - gas exchange
- Type II cells or granular pneumocytes - secrete surfactant
Cell types in alveoli (cont’d)

• Alveolar macrophages - ingest foreign matter. Arise from blood monocytes.
• Endothelial cells - line blood vessels, gas exchange
• Connective tissue cells (fibroblasts) - provide structural support.
• Rare Lymphocytes, Mast cells in the inter alveolar septa. Play immunological role.

DEVELOPMENT
CONGENITAL ANOMALIES

Develops as an outgrowth from the foregut and undergoes progressive dichotomous branching
Congenital Anomalies

- Agenesis
  - Unilateral, bilateral or lobar
  - Maybe associated with cardiovascular anomalies
- Hypoplasia
  - Associated with prolonged oligohydramnios, decreased intrathoracic space (renal cystic disease, diaphragmatic hernia), and decreased breathing movements (anencephaly, musculoskeletal disorders).

Trachea or bronchial anomalies

Atresia
Stenosis
Fistulas
• Congenital Cystic Adenomatoid Malformation (CCAM)
  – Also known as Congenital Pulmonary Airway Malformation (CPAM)
  – "Hamartomatous lesions"
  – Usually lower lobes.
  – Classification based on size of cysts and level of origin based on histologic appearance.
  – Type 1-5 (Most common type 1, large cysts, Type 2 Medium cysts)
  – Can be surgically resected in most types

Multiloculated Cysts

Cysts of Varying Sizes
ACUTE LUNG INJURY

Acute Lung Injury/Non-Cardiogenic pulmonary edema

Spectrum of bilateral pulmonary damage (epithelial and endothelial) which manifests as
a) Acute onset dyspnea
b) Hypoxemia
c) Development of bilateral pulmonary infiltrates in the absence of cardiac failure

Clinical causes of ALI

Direct Lung Injury
• Pneumonia
• Aspiration
• Trauma
• Fat embolism
• Near drowning
• Inhalation injury
• Reperfusion injury after lung transplantation
• Drug overdose

Indirect Lung Injury
• Sepsis
• Severe trauma with shock
• Acute pancreatitis
• Drug overdose
• Uremia
• DIC

IF SEVERE ALI CAN PROGRESS TO ARDS
### Etiology – ARDS - Nutshell

- **A** – Aspiration, acute pancreatitis, air/amniotic fluid embolism
- **R** – Radiation
- **D** – Drug overdose, DIC, drowning
- **S** – Shock, sepsis, smoke inhalation

### Acute Respiratory Distress Syndrome (ARDS) - synonyms

- Adult respiratory distress syndrome
- Traumatic wet lung
- Noncardiogenic pulmonary edema
- Adult hyaline membrane disease

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![Diagram: Pathogenesis of ARDS](image.png)

**NORMAL ALVEOLUS**
- Bronchial epithelium
- Type I cell
- Alveolar macrophage
- Alveolus
- Type II cell

**ACUTE LUNG INJURY**
- Sputcher bronchial epithelium
- Necrotic type I cell
- Edema fluid
- Neutrophil sequestration and migration into alveolus
- Hyaline membrane

**Pathogenesis**

*Fig: Robbins and Cotran*
ARDS

- Incidence
  - 1.5 to 8.3 per 100,000 people/year
  - 7% of all ICU admissions
  - ~ 40% mortality rate
- ACUTE Onset: 24-72 hrs of precipitating event
- Tachypnea, Dyspnea, cyanosis (due to hypoxemia)
- Bilateral lung infiltrates in the absence of cardiac dysfunction
- Approach to Dx: clinical history, imaging studies (X-ray, CT), bronchoscopy (r/o aspiration, hemorrhage, infection, malignancy)
- Treatment: Treat underlying condition + supportive care

ARDS - Pathology

- Early Exudative Phase (Acute)
- Subacute Proliferative Phase (Organizing)
- Fibrotic Phase (Late)

[Image of EARLY EXUDATIVE PHASE: Hyaline membranes composed of dead pneumocytes, endothelial cells, and plasma proteins. Widened Septa. Sparse inflammation. Hyaline Membrane.]
Histologic Manifestation of ARDS is Diffuse Alveolar Damage (DAD)

ARDS – CLINICAL TERM
DAD – PATHOLOGICAL TERM

ARDS: late proliferative and fibrosis stages.
Respiratory Distress Syndrome (RDS) – In Neonates ???

There are many causes of respiratory distress in the newborns!

**Etiology:**
- Fetal injury during delivery
- Aspiration of blood and amniotic fluid,
- Cord compression
- Excessive sedation of the mother
- Hyaline membrane disease/RDS (most common)

Neonatal Respiratory Distress Syndrome - Synonyms

- Infant respiratory distress syndrome (IRDS)
- Respiratory distress syndrome of newborn
- Hyaline membrane disease: Because of the formation of “membranes”
Fundamental Abnormality in RDS

Insufficient pulmonary surfactant production by immature lungs resulting in failure of lungs to inflate after birth

Surfactant

- Synthesized in type II pneumocyte
- Composition:
  - Dipalmitoyl phosphatidylcholine/lecithin (DPPC)
  - Unsaturated phosphatidyl cholines (PC)
  - Phosphatidylglycerol (PG)
  - Surfactant specific proteins SP-A, SP-B, SP-C and SP-D.
- Can be secreted as early as 20 weeks
- Not produced in adequate amounts till 34 weeks
Surfactant Deficiency: Pathophysiology

- **Function:**
  - Stabilizing the lung by reducing surface tension
  - Host defense mechanism as a barrier for inhaled particles
- **Deficiency:** Increased alveolar surface tension → resistance to inflation → surface collapse → stress on alveolar wall leads to alveolar injury → DAD
**Neonatal Respiratory Distress Syndrome**

**Incidence:** 24,000 cases/year

Incidence inversely proportional to the gestation age
- 60% < 28 weeks
- 15-20% < 32-36 weeks
- < 5% > 37 weeks

**Predisposing factors:**
- Prematurity
- Maternal diabetes
- C-section

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**Surfactant synthesis modulated by:**
- Glucocorticoids – increases production
- Insulin – decreases production
- Labor induces production
- Prolactin
- Thyroxine
- TGF-β

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**Control and treatment of RDS**

- Prevention and treatment
  - Delaying labor if possible to permit fetal lung maturity
  - Prophylactic administration of exogenous surfactant to infants less than 28 weeks
- Assess maturation of fetal lungs:
  - Amniotic fluid assays: Lecithin: Sphingomyelin ratio > 2:1
  - Amniotic fluid: Lamellar body counts
Neonatal Respiratory Distress Syndrome - Complications

Long term complications of oxygen therapy used in NRDS:
- Retrolental fibroplasia (retinopathy of prematurity)
- Bronchopulmonary dysplasia- (chronic lung disease characterized by large alveolar sacs)

Other complications due to prematurity:
- Patent Ductus Arteriosus (PDA)
- Intraventricular hemorrhage (IVH)
- Necrotizing enterocolitis (NEC)

<table>
<thead>
<tr>
<th>ARDS</th>
<th>NRDS</th>
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<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>Numerous, direct and indirect injury to the lung</td>
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<tr>
<td><strong>Pathophysiology</strong></td>
<td>Imbalance of pro-inflammatory and anti-inflammatory mediators</td>
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<tr>
<td><strong>Age</strong></td>
<td>Adults</td>
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<tr>
<td><strong>Sx</strong></td>
<td>Tachypnea, dyspnea</td>
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<tr>
<td><strong>Histology</strong></td>
<td>DAD, hyaline membrane formation</td>
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<td><strong>Treatment</strong></td>
<td>Treat underlying cause + supportive measures</td>
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Miscellaneous

• Collapse
• Pneumothorax
• Pulmonary edema
Atelectasis/ Collapse

Greek words *ateles* and *ektasis*, which mean incomplete expansion

- **Neonatal**
  - Incomplete expansion

- **Acquired**
  - **Resorption or obstruction**
    - Asthma, COPD, bronchiectasis, aspiration, postop patients
  - **Compression**
    - Effusions, air, tumors, CHF
  - **Contraction**
    - Fibrosis of lung/pleura

Types of Atelectasis

Robbins and Kumar

Pneumothorax

- **Pneumo**: air, gas; **thorax**: chest wall
- **Types**: Spontaneous, Traumatic
- **Pathophysiology**: Causes compression and atelectasis, leading to respiratory distress
- **Most commonly associated with**: Emphysema, asthma, TB
- **Spontaneous idiopathic form**: in younger people, rupture of peripheral small pleural blebs
Where do you think the needle got stuck?
Bronchoscopic Findings

Question

A 30-year-old woman develops multiple organ failure, bleeding diathesis post-partum. Sputum and blood cultures are negative. Nevertheless, she requires intubation with mechanical ventilation, but it becomes progressively more difficult to maintain her oxygen saturations. A portable chest radiograph shows increasing opacification of all lung fields. Capillary wedge pressure is normal.
Which of the following pathologic processes is most likely now to be present in her lungs?
A Emphysema
B Diffuse alveolar damage
C Extensive intra-alveolar fluid (i.e. pulmonary edema)
D Intraalveolar neutrophils (i.e. Pneumonia)
E Normal lung

Summary

• Normal Histology
• Development anomalies
• Difference between ARDS and pulmonary edema
• ARDS – clinical term; DAD- pathology term
• NRDS – clinical term, HMD- pathology term

Thank You!
Questions?