Pulmonary Diseases: Structure-Function Correlation I

Review of Histology/Histopathology and Airway Diseases (Obstructive)

Alain C. Borczuk, M.D.
Department of Pathology

Pulmonary Diseases: Structure-Function Correlation I

• Overview
  – Two lectures will follow the structure/function section of the syllabus:
    • Lecture 1 - Histology/histopathology review and Airways disease.
    • Lecture 2 - Interstitial and parenchymal disease, and vascular disease.

Goals:
• To review microanatomy/histology of normal lung and compare to pathologic alterations within those elements
• To observe the relationship between structural/morphologic manifestation of diseases to measurable functional parameters using prototypical diseases of the airways
• To describe the pathology, Gross and microscopic, of these pulmonary diseases.

• Cast of Characters
  – Airways
    • Conducting
    • Respiratory
  – Vessels
    • Arteries, arterioles - pulmonary and bronchial
    • Capillaries
    • Veins/Venules and Lymphatics
  – Pleura- visceral and parietal

• Airways Conducting Zone
  • Trachea
  • Bronchi - ciliated and goblet cells, elastic tissue, smooth muscle, glands, cartilage
  • Bronchioles - (1 mm) - No cartilage or bronchial glands, ciliated lining, no goblet cells, smooth muscle

• Cell types
  – CILIATED CELL - beating of cilia contribute to mucociliary elevator
  – GOBLET CELL - Mucus secretion
  – BASAL CELL - reserve cell
  – KULCHITSKY CELL - neuroendocrine cells.
Main stem bronchus
Lobar bronchus (5 lung lobes)
Segmental bronchus (10 bronchopulmonary segments on right, 9 on left)
Branching continues as airways become bronchioles, then at terminal bronchioles airways transition into respiratory bronchioles
About 20 branch generations from beginning to end

Squamous metaplasia

Normal airway

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- Airways Respiratory Zone
  - Respiratory bronchiole - lined by ciliated cells and **CLARA CELLS**
  - Alveolar ducts/sacs
    - **Type I cells**
      - 90% of alveolar surface
    - **Type II cells**

- Cell types
  - **CLARA CELLS** - produce a component of surfactant and are the bronchiolar reserve cell
  - **TYPE I CELLS** - thin lining cell for gas exchange
  - **TYPE II CELLS** - surfactant and alveolar reserve cell
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- Vessels - Pulmonary
  - Arteries/arterioles - travel and divide with bronchi and bronchioles
  - Produce capillary bed in alveoli for gas exchange
  - Venules collect capillary blood into lobular septa, forming veins and joining at the hilum.

- Vessels - Bronchial
  - Artery from aorta
  - Supplies bronchial tree up to respiratory bronchiole
  - Venous drainage to azygous/hemiazygous
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Correlation 1

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Pulmonary Diseases: Structure-Function Correlation I

- Disease of the acini and interstitium
  1) Replacement of air with fluid, inflammatory cells or cellular debris
  2) Thickening of alveolar walls and interstitium
  3) Destruction of acinar walls
- Disease of the conducting airways
- Disease of the pulmonary vasculature

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Pulmonary Diseases: Structure-Function Correlation I

- Disease of the conducting airways
  - Asthma
  - Chronic bronchitis
  - Bronchiectasis
    - Permanent dilation of bronchi and bronchioles, due to destruction of elastic tissue and muscle.

Disease of the conducting airways - Bronchiectasis

- Dilatation of bronchi and bronchioles, usually due to necrosis of wall and obstruction
  - Foreign body
  - Mucoid impaction
  - Aspergillus
  - Cystic fibrosis
  - Immotile cilia
  - Chronic bronchitis and infection
- Gross Pathol. - Dilated bronchi, filled with mucus or pus, lower lobes.
- Microscopic -
  - Can have acute and chronic inflammation
  - Varying degrees of fibrosis
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Correlation 1

• Disease of the conducting airways
  – Asthma
  – Chronic bronchitis
  – Bronchiectasis

Disease of the conducting airways - ASTHMA

• Bronchospasm, usually reversible
  – Allergic trigger
  – non-allergic airway hyperresponsiveness

• Anatomic targets, triggered by medications,
  smooth muscle hypertrophy
  bronchial epithelium and smooth muscle.

• Inflammation

• Obstructive disease

• Gross pathology
  – hyperinflation, severe if status asthmaticus
  – Macus plugging

• Microscopic
  – Inflammation, eosinophils
  – Basement membrane thickening
  – edema
Disease of the conducting airways - ASTHMA

• Gross pathology
  – hyperinflation
  – Mucus plugging
• Microscopic
  – Smooth muscle hypertrophy
  – Inflammation, eosinophils
  – Basement membrane thickening
  – edema

Functional significance
• Total lung capacity - increased during attack
• Work of breathing increased due to airway resistance
• Airway resistance increased, on expiration more than inspiration

Disease of the conducting airways - Chronic bronchitis

• Persistent cough with sputum production for 3 months in two 2 consecutive years.
• Smoking
• Repeated infections

• Gross Pathology: Brown discolored, mucus filled bronchi.
• Microscopic:
  – Bronchial gland hyperplasia
  – Goblet cell metaplasia
  – Chronic inflammation
  – Fibrosis of bronchioles
  – Loss of cilia

Pulmonary Diseases: Structure-Function Correlation 1

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Chronic bronchitis

- **Gross Pathology:** Brown discolored, mucus filled bronchi.

- **Microscopic:**
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- **Functional Significance**
  - Airway resistance, due to mucus, edema and narrowing. Obstructive disease
  - Degree of obstruction determines extent of V/Q mismatch
  - Lung capacity normal
  - Right heart failure and pulmonary hypertension can occur – hypoxic vasoconstriction and endothelial dysfunction

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From NEJM
2000;343:270
**Destruction of acinar walls - Emphysema**

- Obstructive disease
- Involves the airway distal to the terminal conducting bronchiole
- Airway wall is damaged, and fibrosis can be present.
- Is classified by pattern/location of damage within the respiratory acinus

**Centriacinar (Centrilobular)**
- Smoking
- Damage is to the respiratory bronchiole. When severe disease develops, whole acinus involved.
- Upper lobes, especially apical portions most affected

**Panacinar (Panlobular)**
- Damage is to the entire acinar unit from respiratory bronchiole to alveolar sac
- More severe at bases, but is more diffuse than CLE
- Alpha-1 antitrypsin deficiency

**Pathogenesis**

- Protease/Antiprotease hypothesis
  - Imbalance between neutrophil derived elastase and deficiency in anti-elastase activity from alpha-1-antitrypsin
  - Neutrophil elastase is unchecked, causing tissue destruction
  - Smoking causes more rapid evolution of panacinar emphysema.

- In panacinar emphysema, deficiency in alpha 1 anti-trypsin is a genetic defect
- In centrilobular emphysema, the interplay of cigarette smoke, acquired deactivation of A1AT activity and activation of a perhaps broader spectrum of neutrophils and macrophage derived proteases may be significant. These may include proteinase 3, cathepsins and matrix metalloproteinases (1,2,9,12)
- Other inhibitors of protease activity may also play a role – e.g. TIMPs
Destruction of acinar walls - Emphysema

CENTRILOBULAR VS. PANACINAR

• Gross pathology
  – Upper lobe, irregularly dilated airspaces
  – Thin walled and grossly apparent

• Microscopic
  – Dilated spaces, alongside normal alveoli
  – Anthracotic pigment

• Gross Pathology
  – Lower lobe, more uniformly dilated spaces
  – Voluminous lungs

• Microscopic
  – Dilated spaces, uniformly dilated.

Destruction of acinar walls - Emphysema

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Destruction of acinar walls - Emphysema

**Structural vs. Functional**

- **Gross pathology**
  - Upper lobe, irregularly dilated airspaces
  - Thin walled and grossly apparent

- **Microscopic**
  - Dilated spaces, alongside normal alveoli
  - Anthracotic pigment

- **Functional**
  - Total lung capacity increase
  - Lung compliance increased (elastin destruction)
  - V/Q mismatch mild - airway and capillary destruction
  - Recoil decreased; lose radial traction on airways
  - Obstructive; worsens on forced expiration