Pulmonary Diseases: Structure-Function Correlation I

Review of Histology/Histopathology and Airway Diseases (Obstructive)

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• 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.
**Pulmonary Diseases: Structure-Function Correlation I**

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.
Pulmonary Diseases: Structure-Function Correlation I

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

Pulmonary Diseases: Structure-Function Correlation I

- 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

Normal airway
Squamous metaplasia

Pulmonary Diseases: Structure-Function Correlation 1

- 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
Pulmonary Diseases: Structure-Function Correlation 1

- **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
Pulmonary Diseases: Structure-Function Correlation I

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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
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
Pulmonary Diseases: Structure-Function Correlation I

• 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
  bronchial epithelium and smooth muscle.

• Inflammation
• Obstructive disease

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

• Microscopic
  smooth muscle hypertrophy
  – Inflammation, eosinophils
  – Basement membrane thickening
  – edema

Pathophysiology of Asthma

Etagenwechsel
Die Atemwegserkrankung wandert tiefer

Bronchialast
Normaler Bronchialast
Bronchialast
eines Asthmakerns

Normal Lung
Asthmatic Lung
**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

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**Pulmonary Diseases: Structure-Function Correlation I**

- Disease of the conducting airways
  - Asthma
  - Chronic bronchitis
  - Bronchiectasis
Disease of the conducting airways - Chronic bronchitis

- Persistent cough with sputum production for 3 months in two 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
Disease of the conducting airways - Chronic bronchitis

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

• **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
Pulmonary Diseases: Structure-Function Correlation I

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- Disease of the conducting airways
- Disease of the pulmonary vasculature

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

Destruction of acinar walls - Emphysema

- 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
**Destruction of acinar walls - Emphysema**

**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.

**Destruction of acinar walls - Emphysema**

**Pathogenesis**
- Protease/Antiprotease hypothesis
  - 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

**CENTRIOLOBULAR 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

CENTRILOBULAR VS. PANACINAR

• Gross pathology
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• Gross Pathology
  – Lower lobe, more uniformly diluted spaces
  – Voluminous lungs
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Destruction of acinar walls - Emphysema

**STRUCTURAL VS. FUNCTIONAL**

**STRUCTURAL**
- 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
