

*Pulmonary Diseases: Structure-Function
Correlation I*

Review of Histology/Histopathology
and Airway Diseases (Obstructive)

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*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.

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.

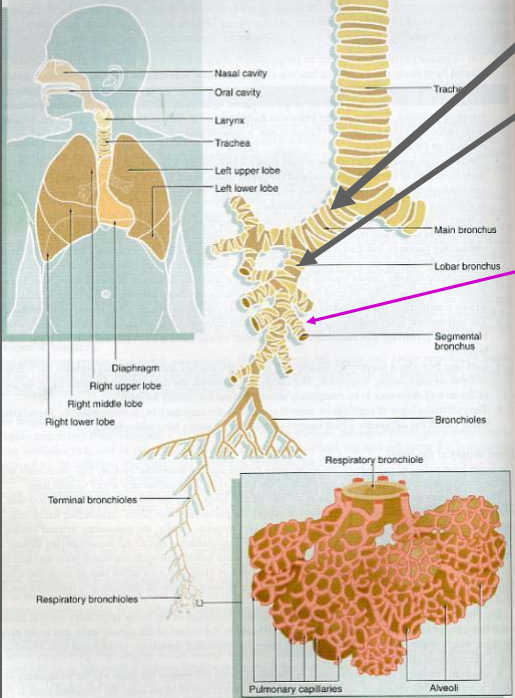


Pulmonary Diseases: Structure-Function Correlation I

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

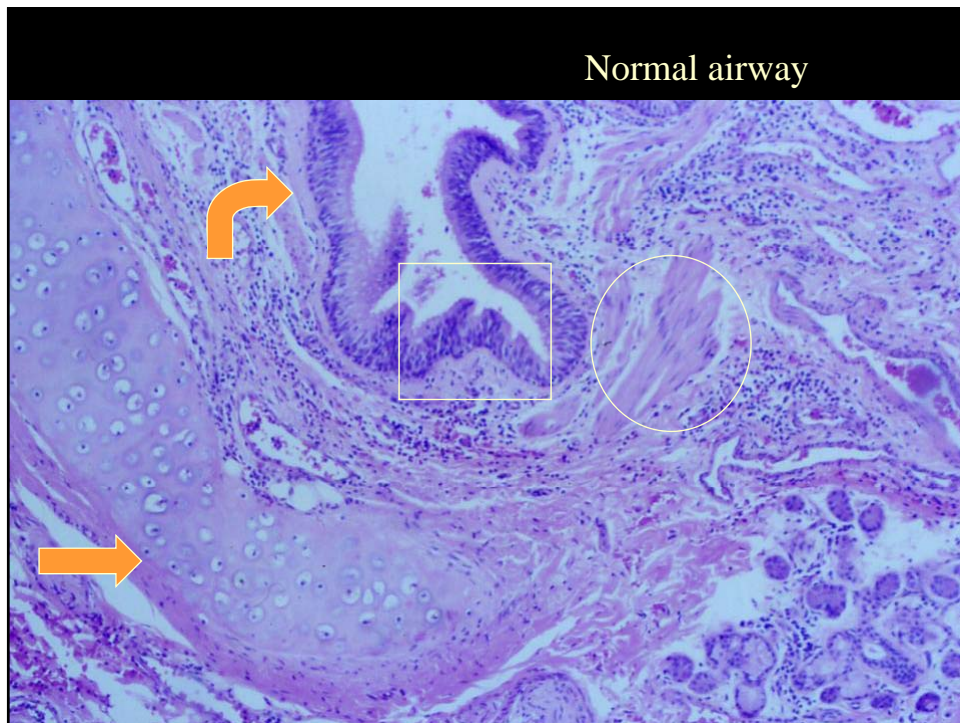
Pulmonary Diseases: Structure-Function Correlation I

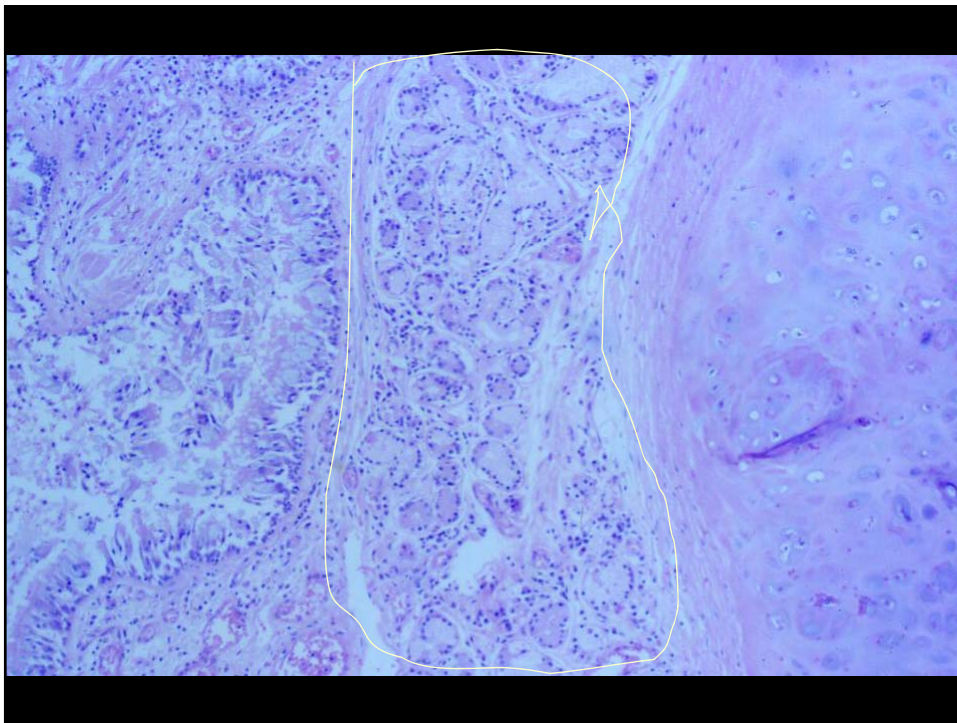
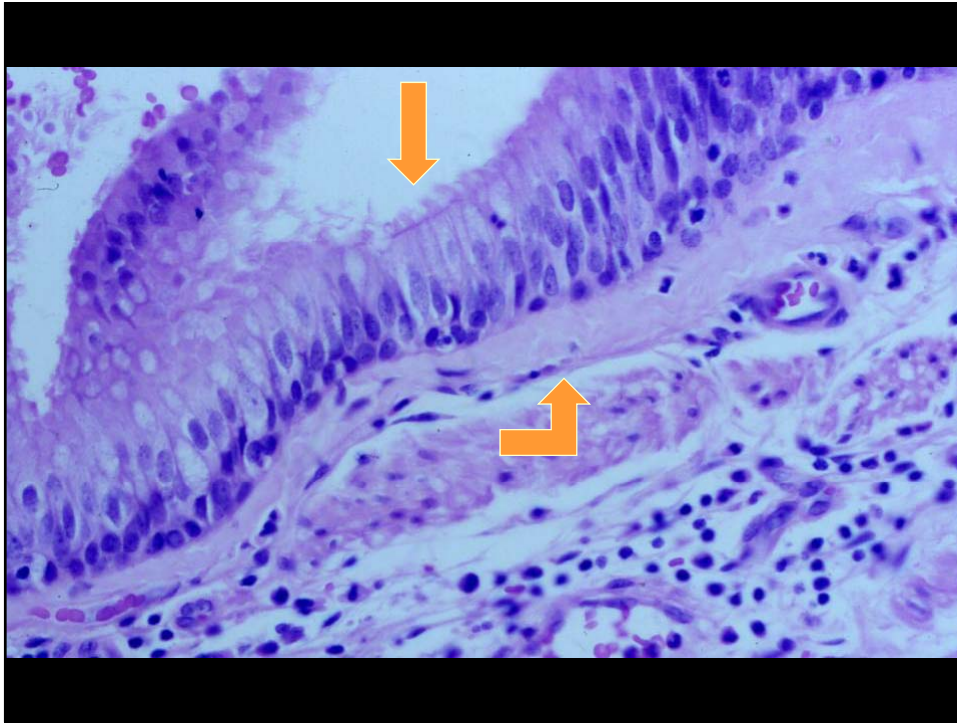
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| <ul style="list-style-type: none"> • Airways Conducting Zone <ul style="list-style-type: none"> • Trachea • <u>Bronchi</u> - ciliated and goblet cells, elastic tissue, smooth muscle, glands, cartilage • <u>Bronchioles</u> - (1 mm) - No cartilage or bronchial glands, ciliated lining, no goblet cells, smooth muscle | <ul style="list-style-type: none"> • Cell types <ul style="list-style-type: none"> – <u>CILIATED CELL</u> - beating of cilia contribute to mucociliary elevator – <u>GOBLET CELL</u> - Mucus secretion – <u>BASAL CELL</u> - reserve cell – <u>KULCHITSKY CELL</u> - neuroendocrine cells. |
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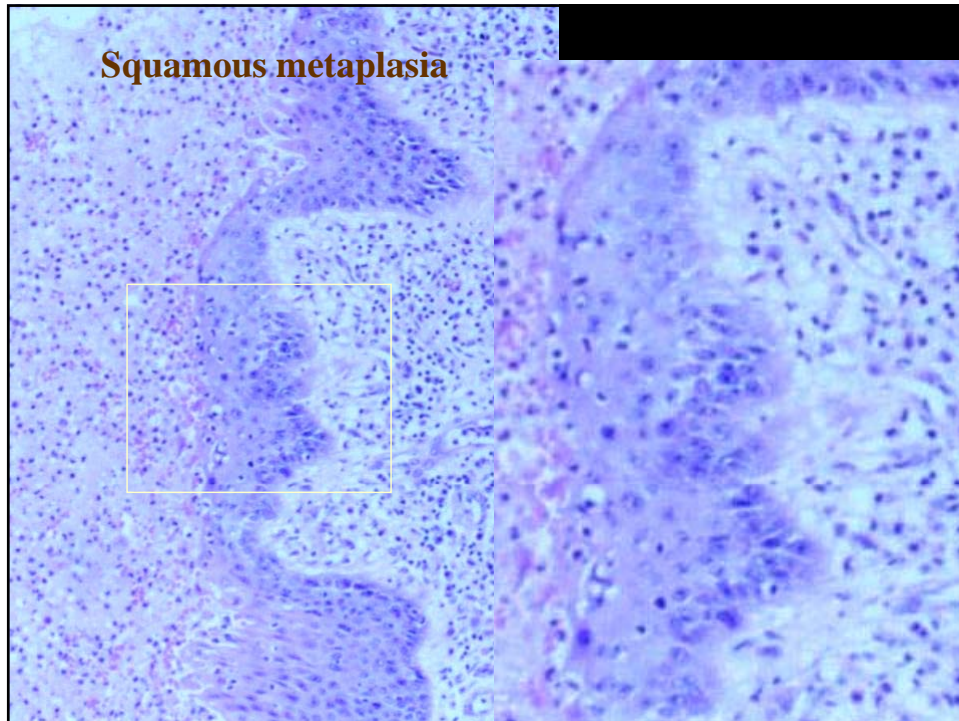


The diagram illustrates the human respiratory system. On the left, a sagittal view shows the nasal and oral cavities leading to the larynx and trachea. The lungs are shown with lobes: left upper and lower, and right upper, middle, and lower. The diaphragm is also indicated. On the right, a detailed tree diagram shows the branching from the trachea to the main bronchus, lobar bronchus, segmental bronchus, bronchioles, terminal bronchioles, and respiratory bronchioles. An inset shows the terminal end of a respiratory bronchiole branching into alveoli, with pulmonary capillaries nearby.

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

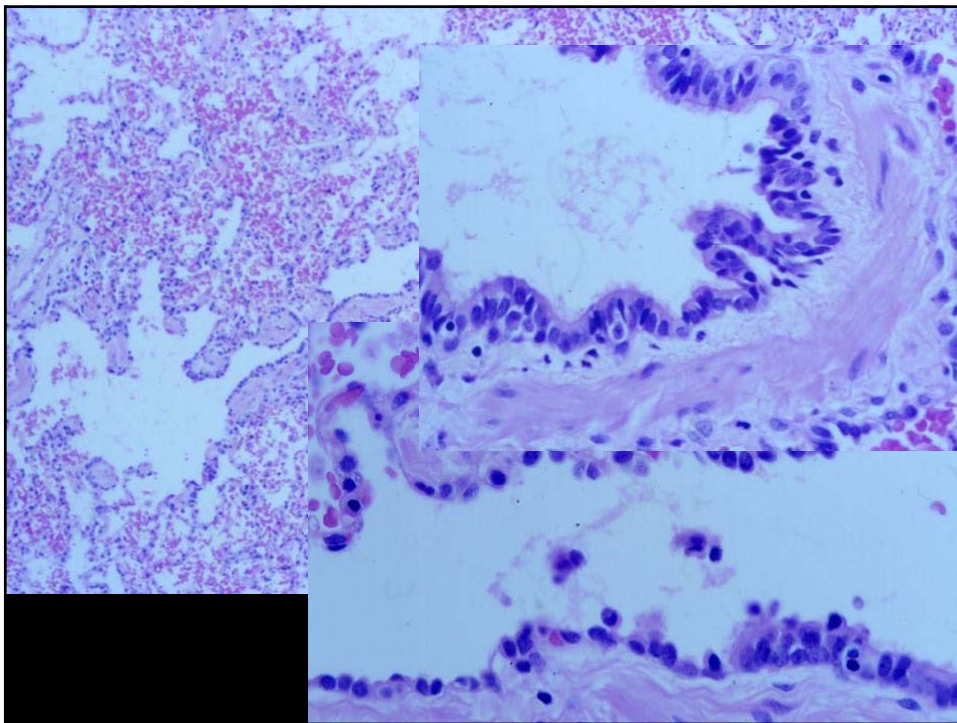
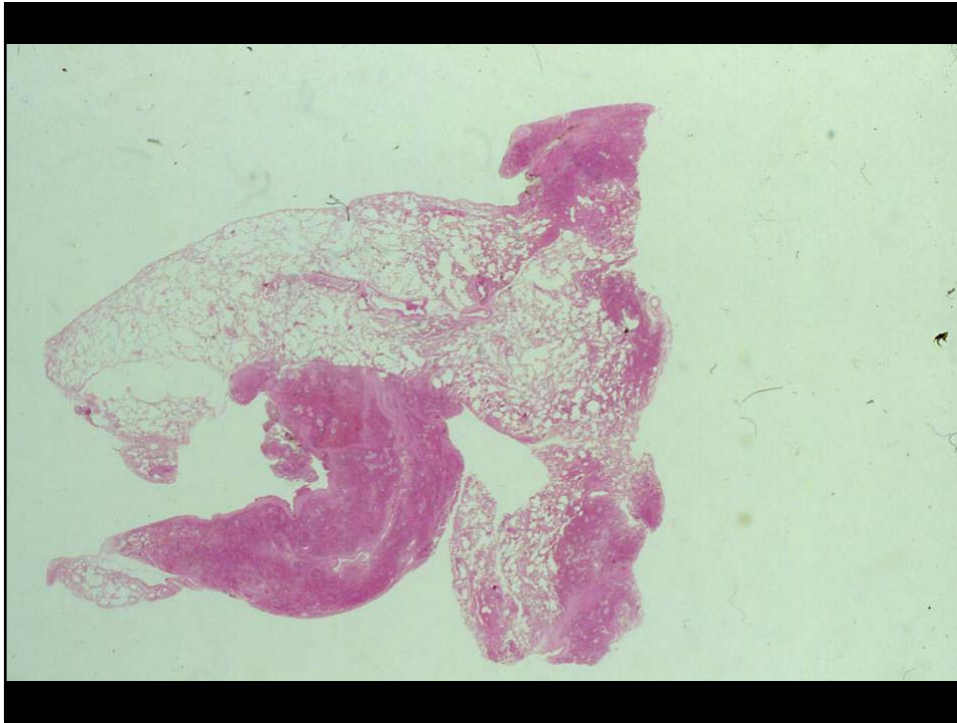


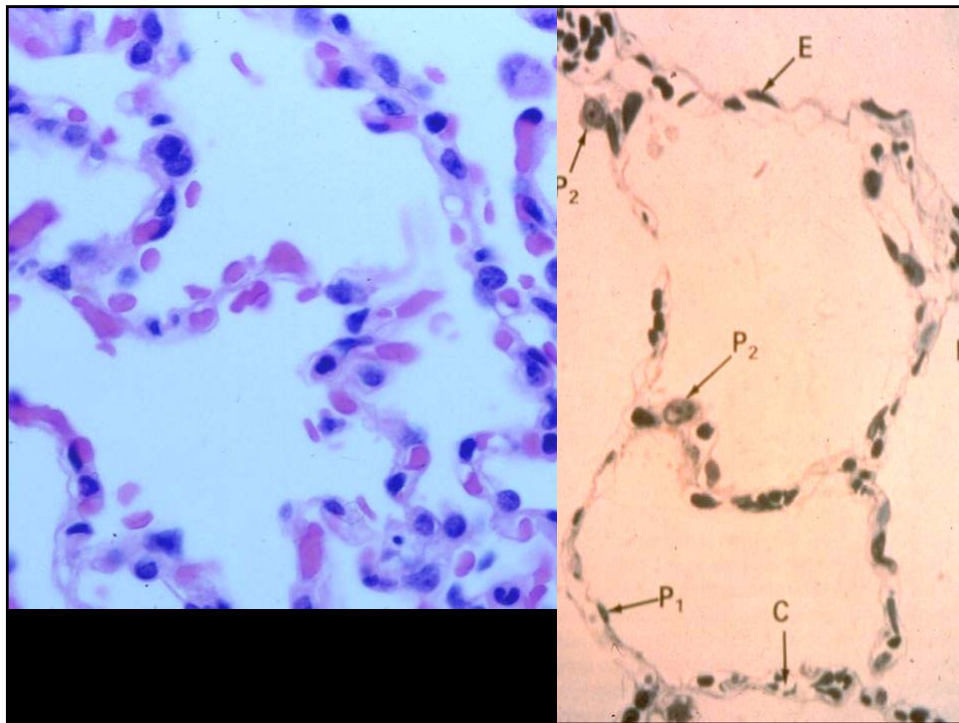
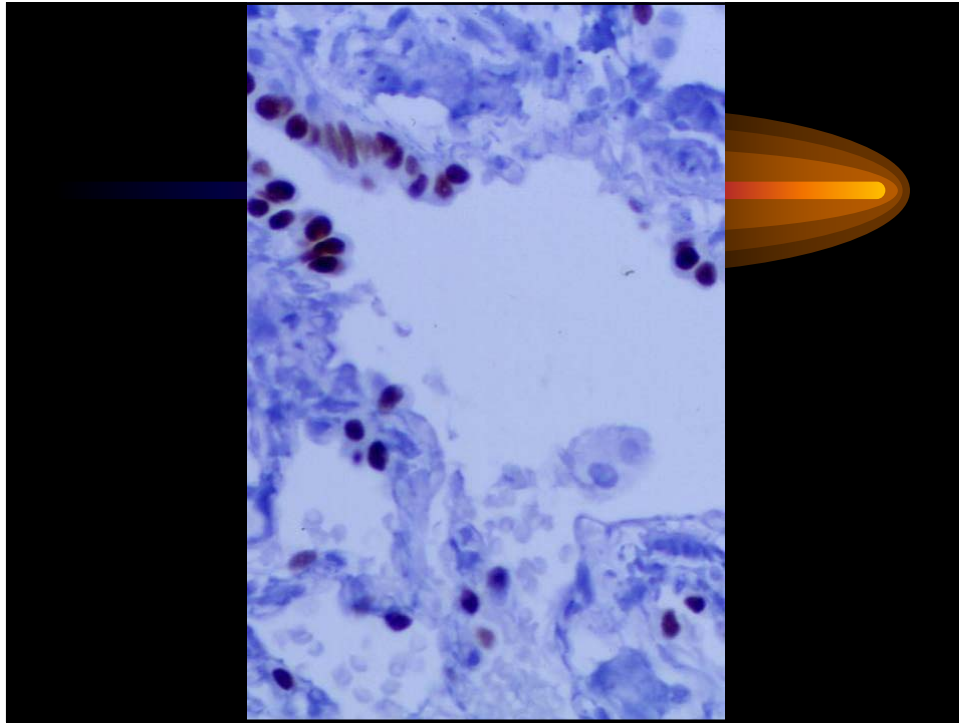


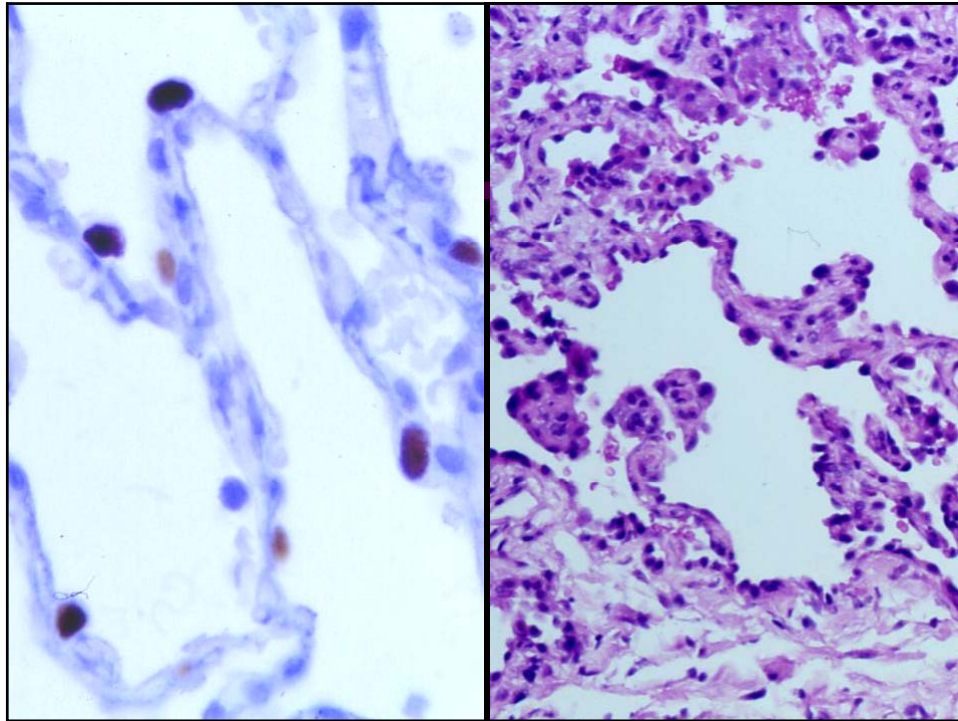


Pulmonary Diseases: Structure-Function Correlation I

- 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

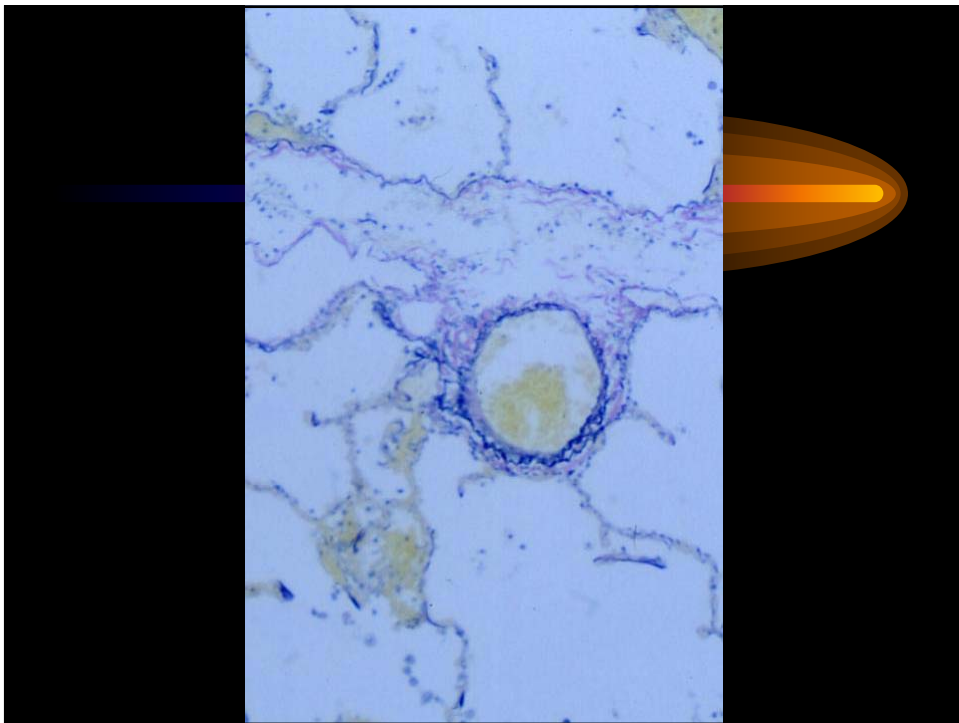
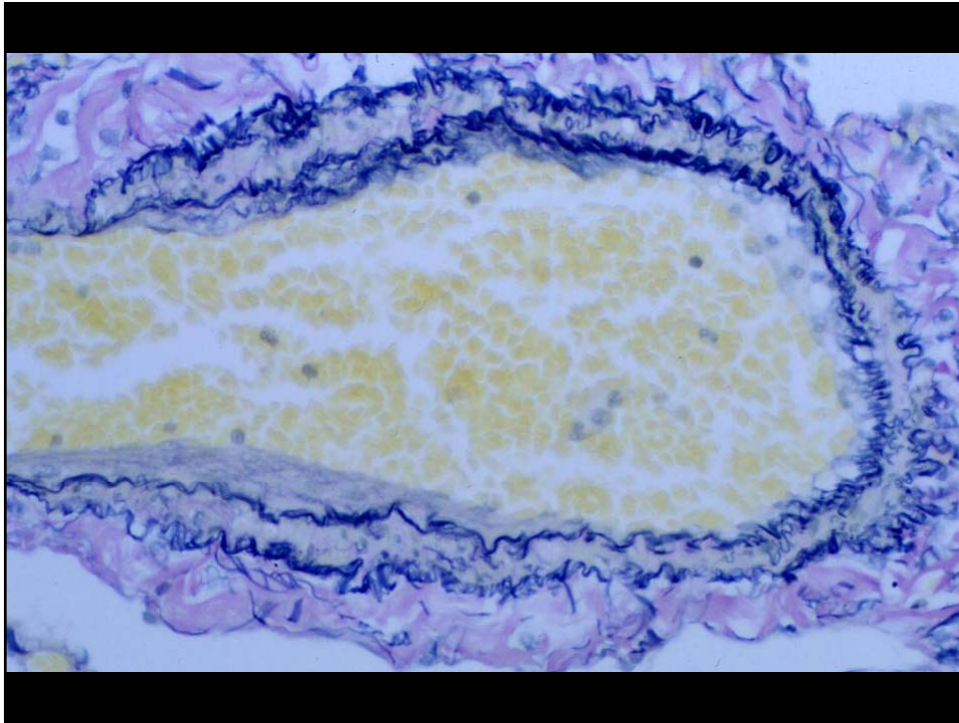






Pulmonary Diseases: Structure-Function Correlation I

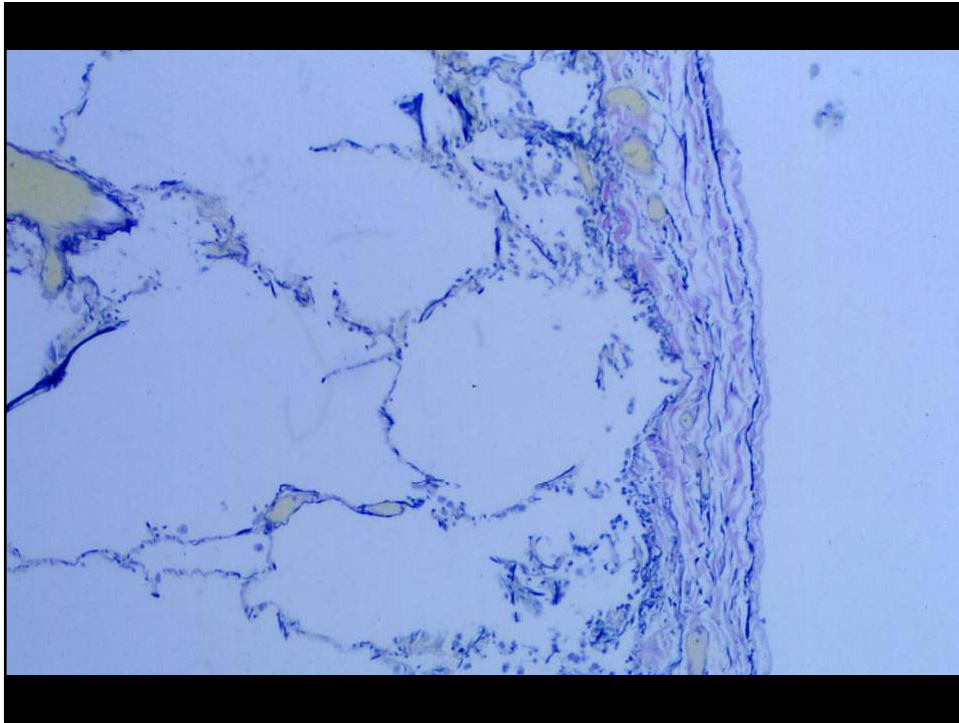
- **Vessels - Pulmonary**
 - Arteries/arterioles - travel and divide with bronchi and bronchioles
 - Produce capillary bed in alveoli for gas exchange
 - Venules collect capillary blood into lobular septa, forming veins and joining at the hilum.
- **Vessels - Bronchial**
 - Artery from aorta
 - Supplies bronchial tree up to respiratory bronchiole
 - Venous drainage to azygous/hemiazygous





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*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
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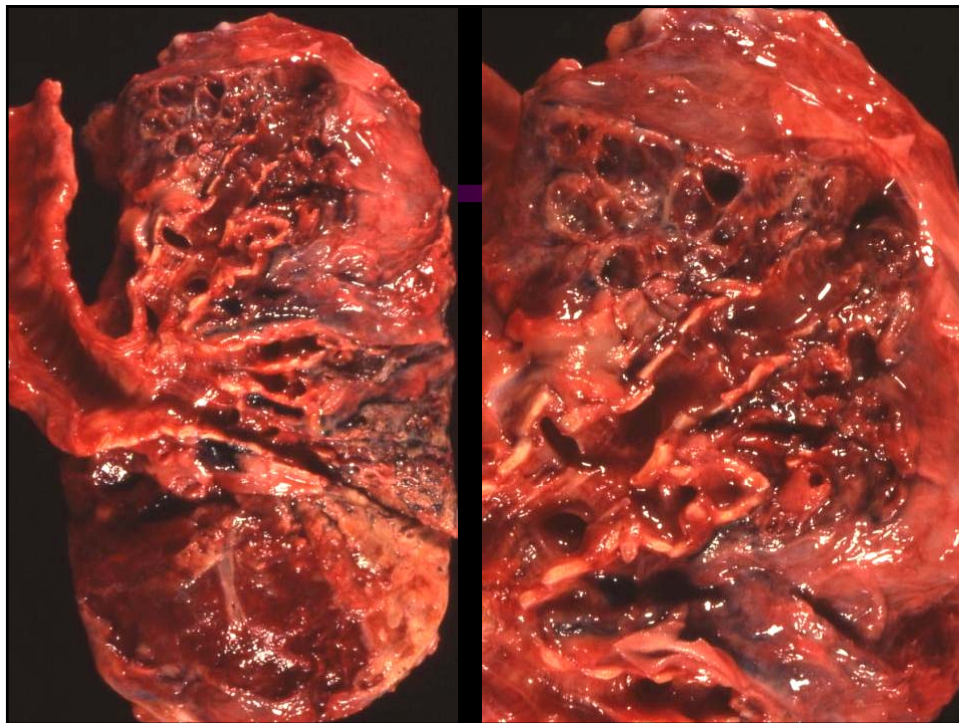
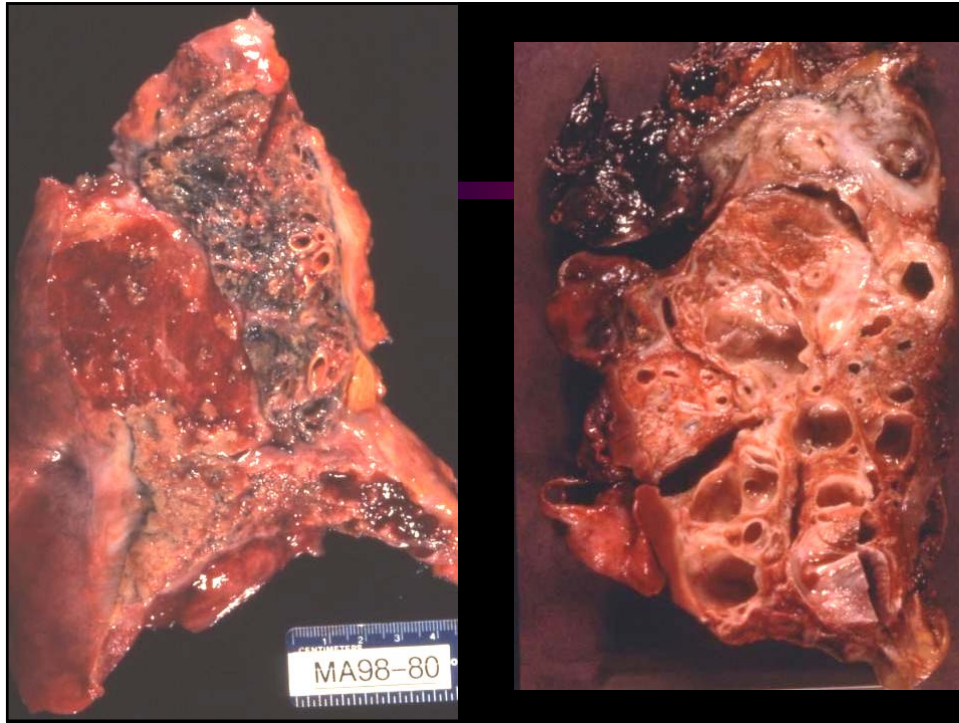
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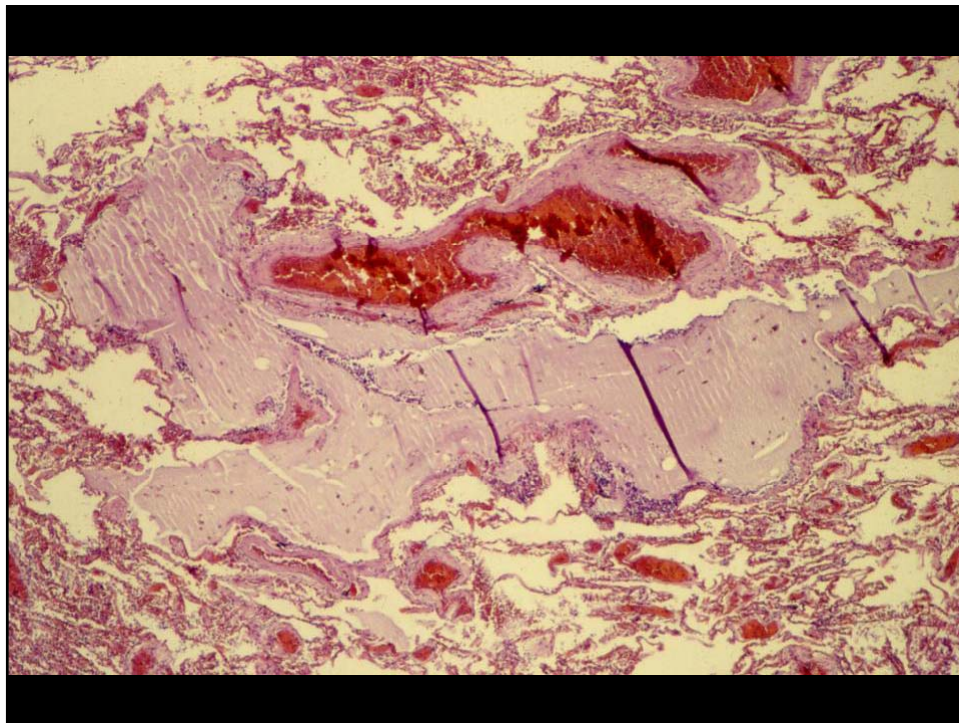
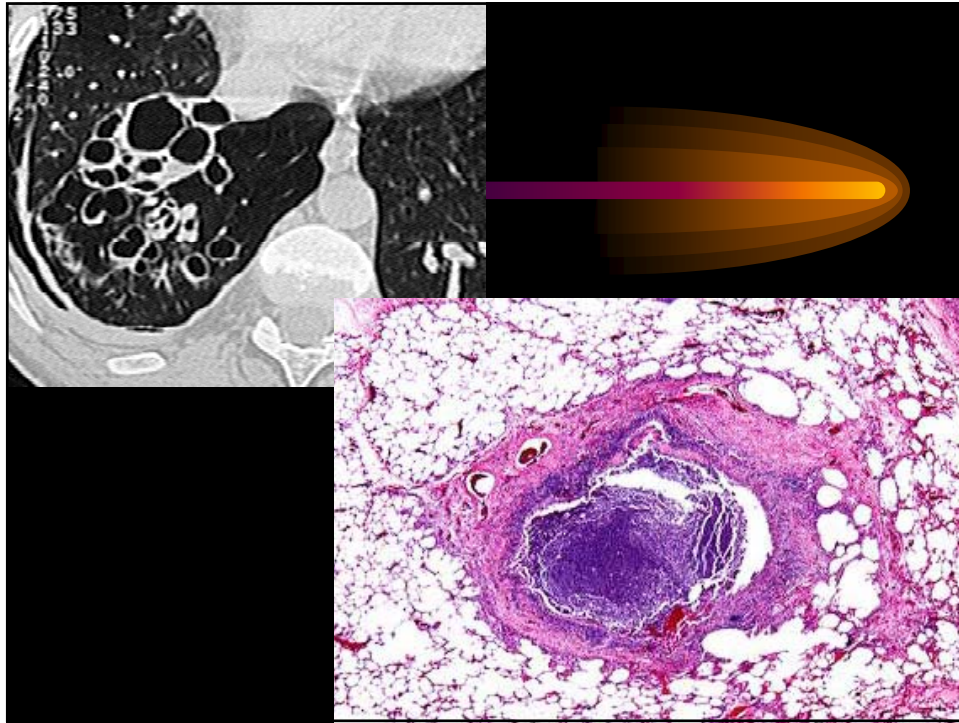
Pulmonary Diseases: Structure-Function Correlation I

- 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
 - Mucoïd 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





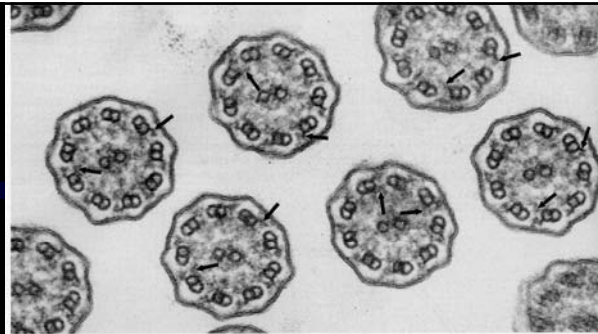
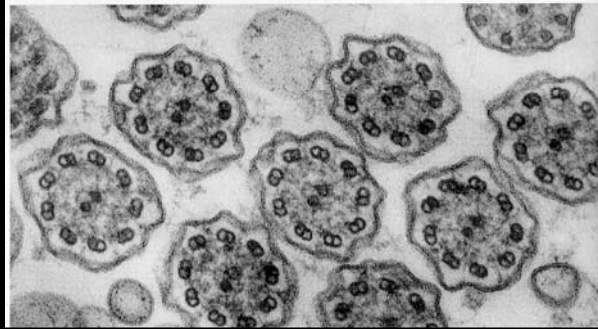


Figure 11.59. Normal cilia (nasal mucosa). Outer and inner dynein arms (arrows) are apparent in these cilia. Inner arms are usually blurred and less distinct than outer arms. ($\times 150,000$)

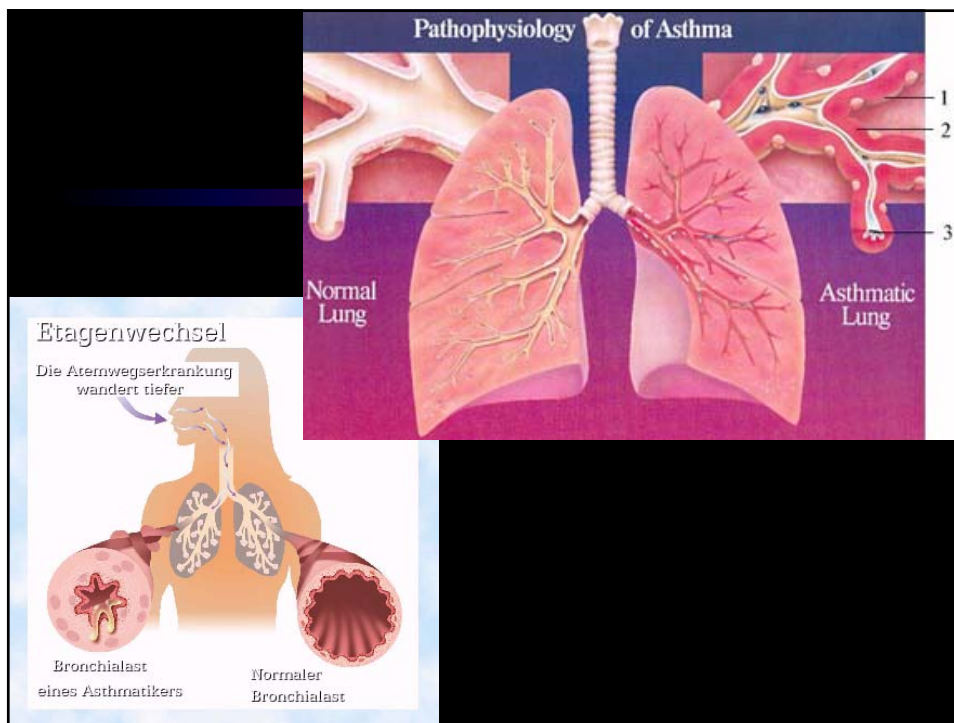


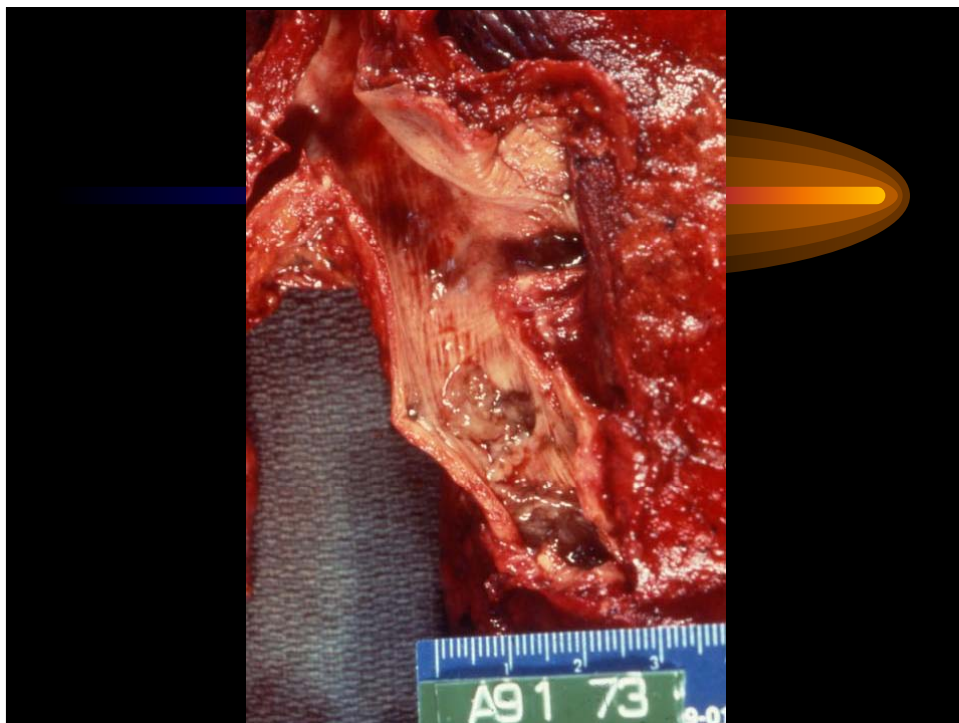
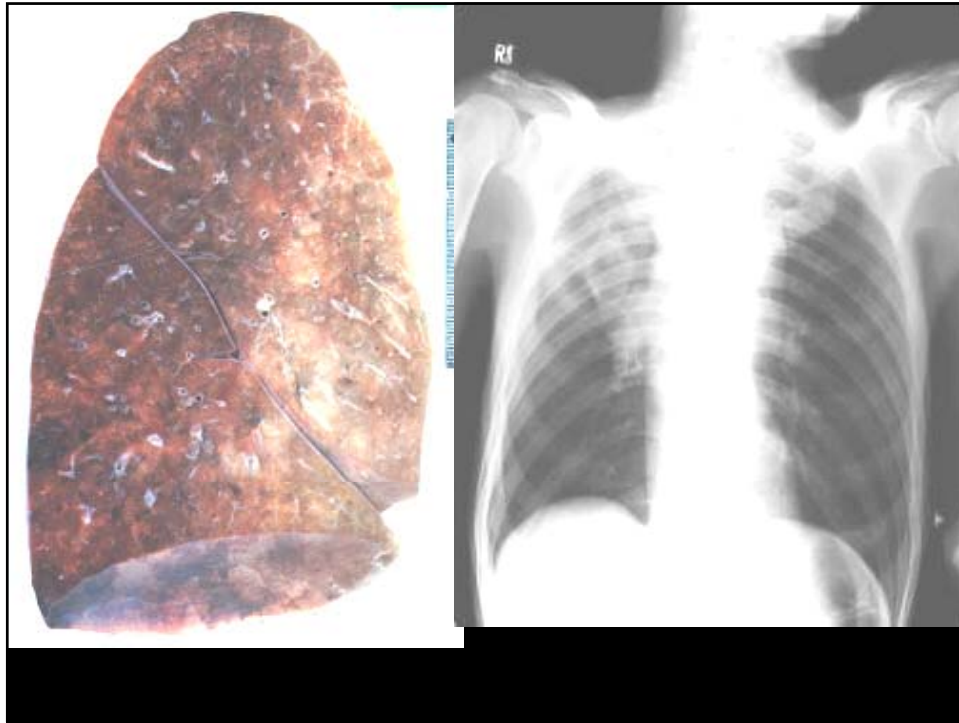
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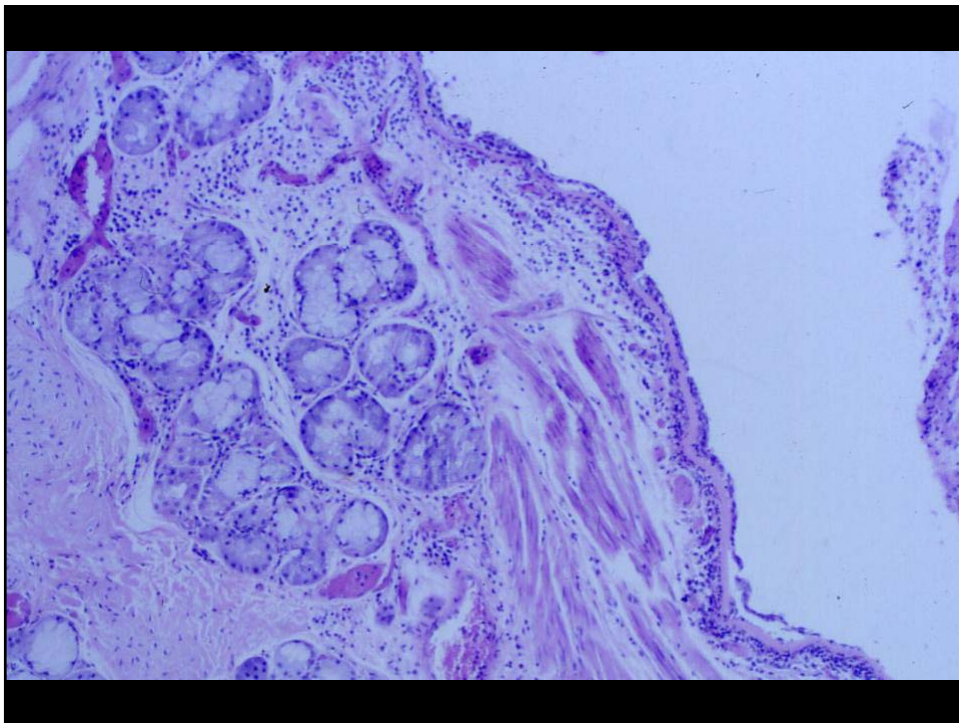
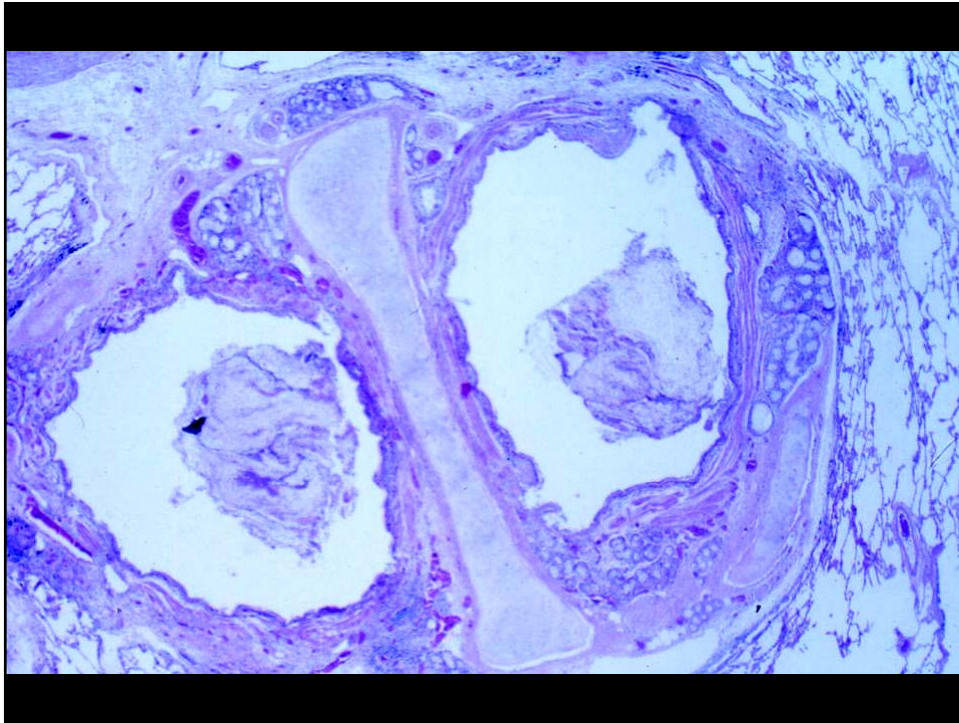
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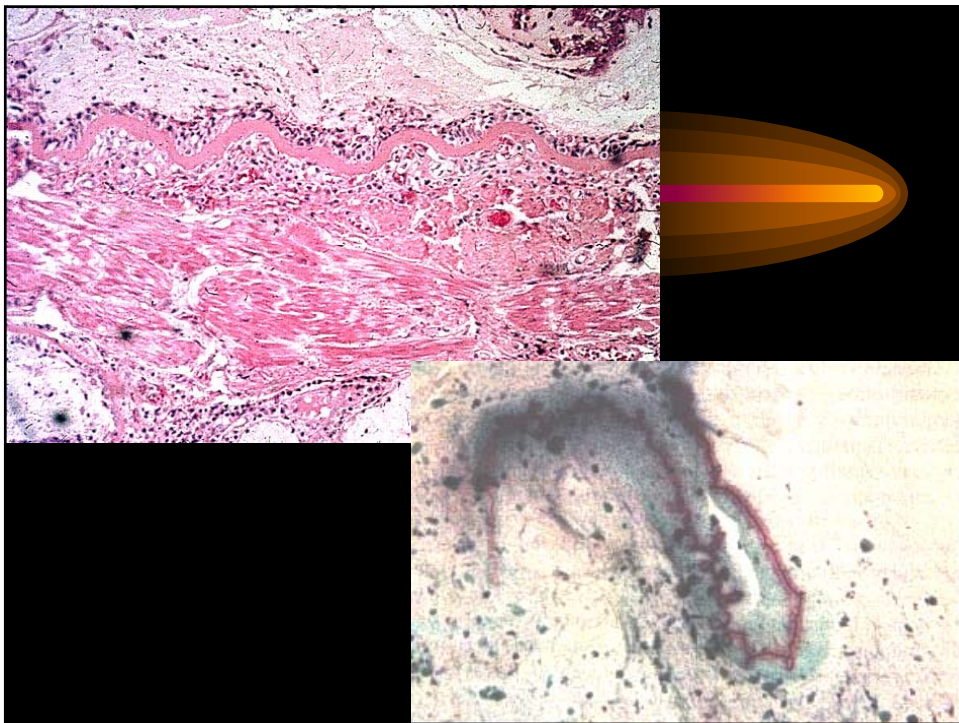
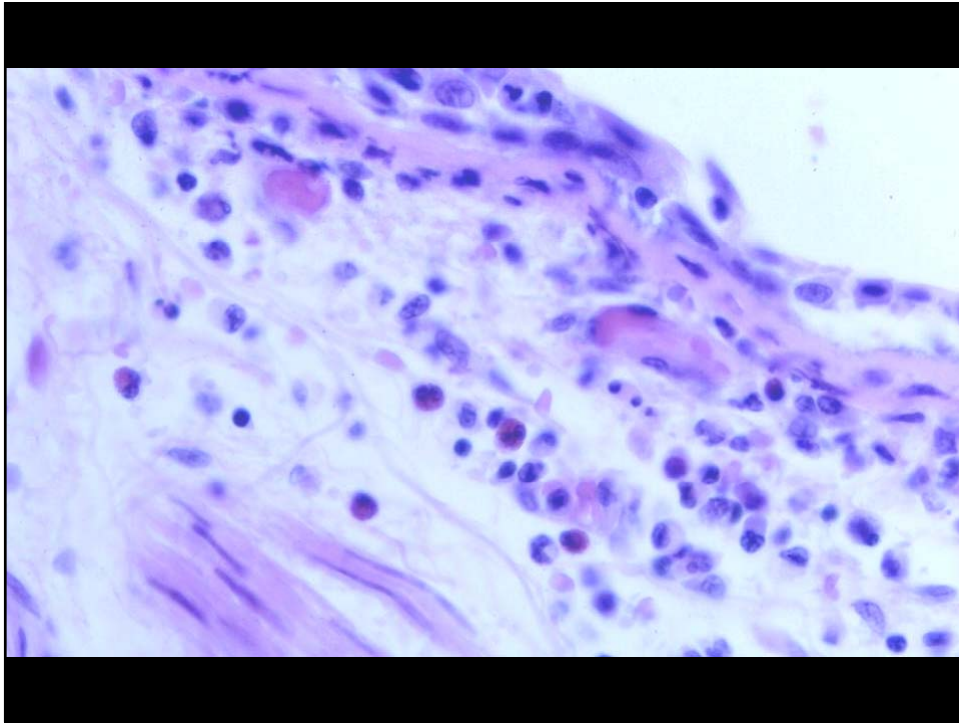
Disease of the conducting airways - ASTHMA

- **Bronchospasm, usually reversible**
 - Allergic trigger
 - non-allergic airway hyperresponsiveness
- **Anatomical target is 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**









Disease of the conducting airways - ASTHMA

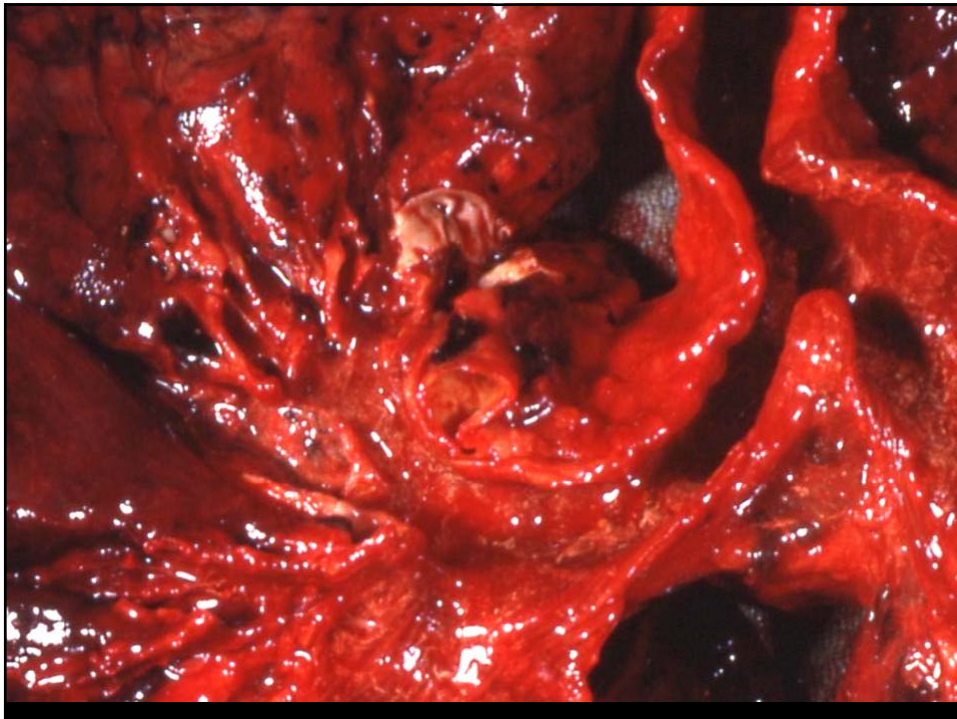
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|---|---|
| <ul style="list-style-type: none"> • Gross pathology <ul style="list-style-type: none"> –hyperinflation –Mucus plugging • Microscopic <ul style="list-style-type: none"> –Smooth muscle hypertrophy –Inflammation, eosinophils –Basement membrane thickening –edema | <p>Functional significance</p> <ul style="list-style-type: none"> • Total lung capacity - increased during attack • Work of breathing increased due to airway resistance • Airway resistance increased, on expiration more than inspiration |
|---|---|

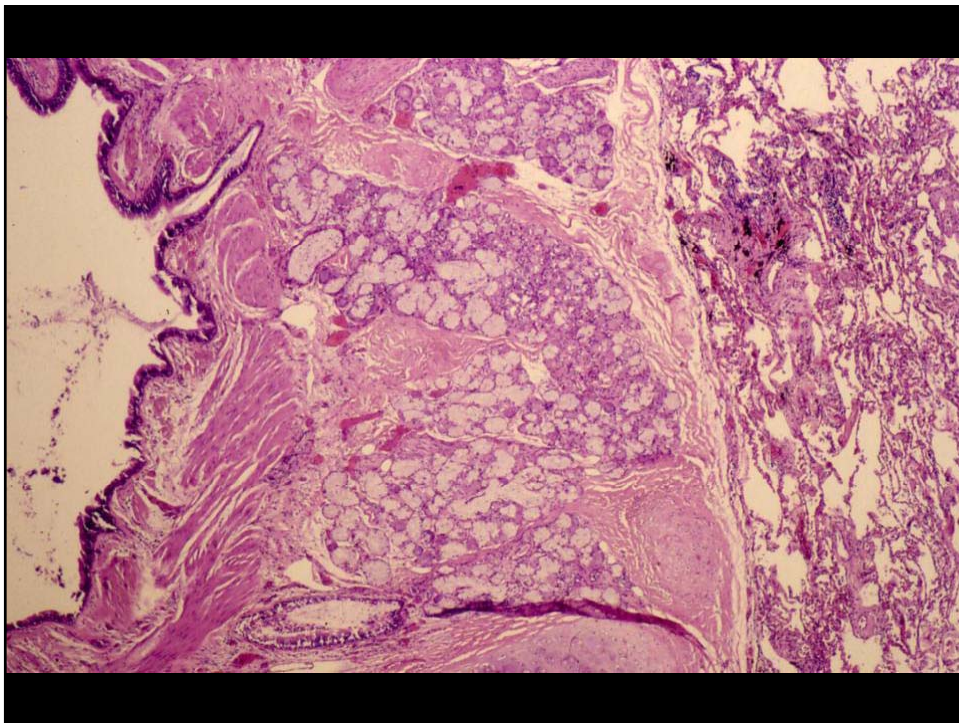
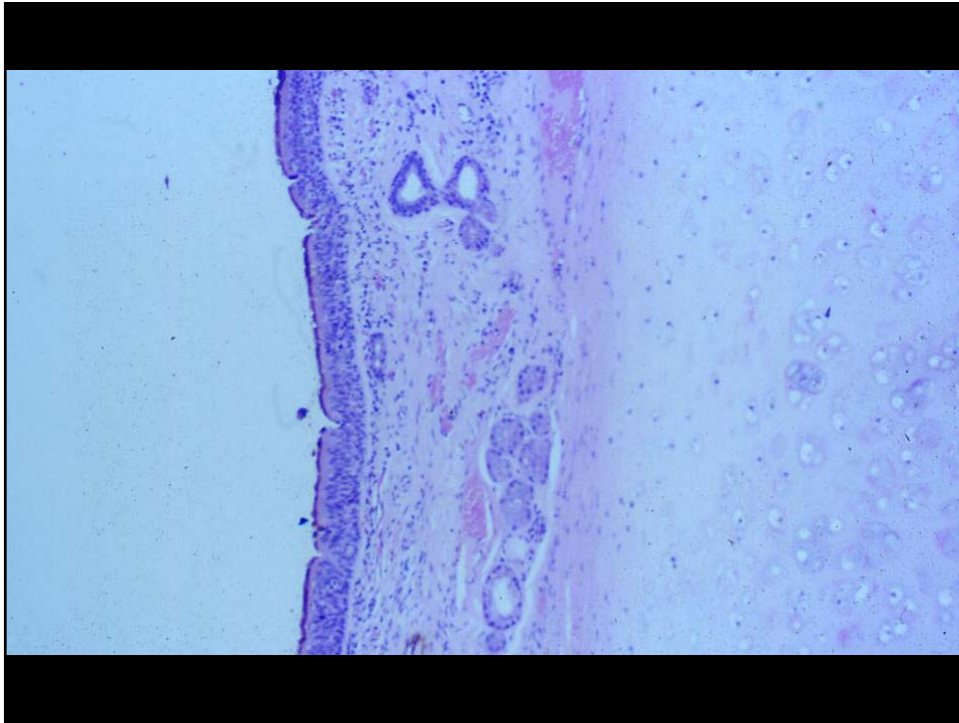
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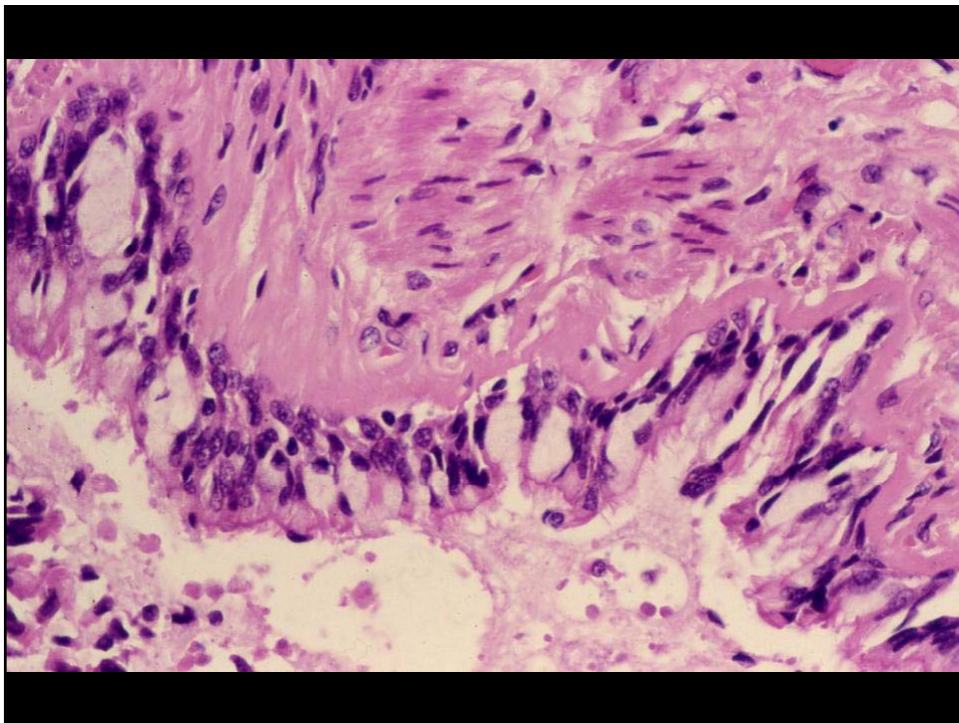
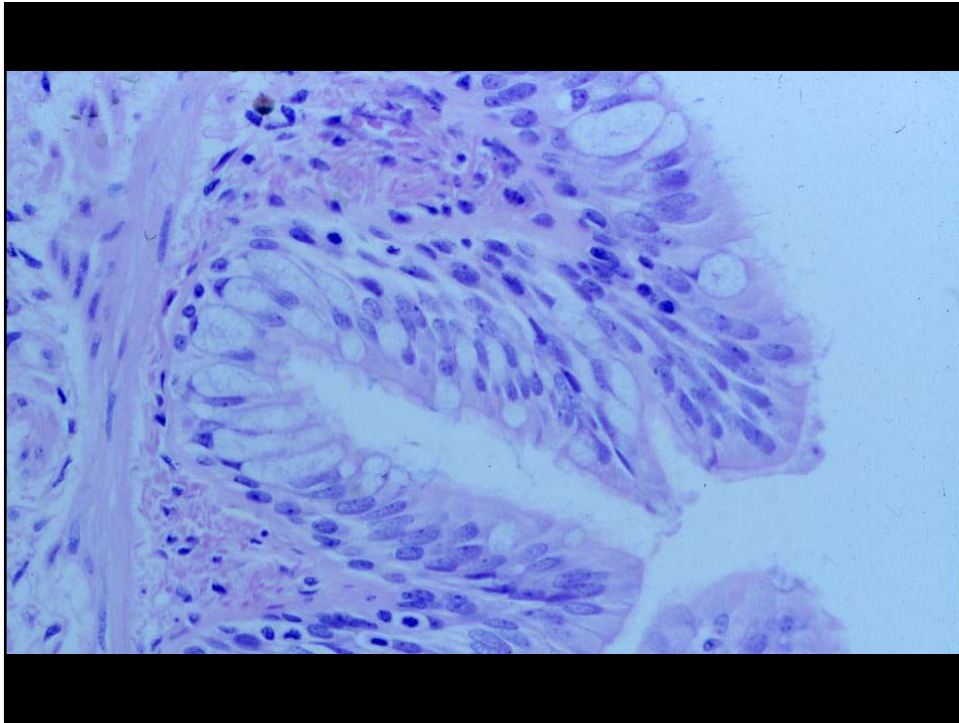
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Disease of the conducting airways - Chronic bronchitis

- 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







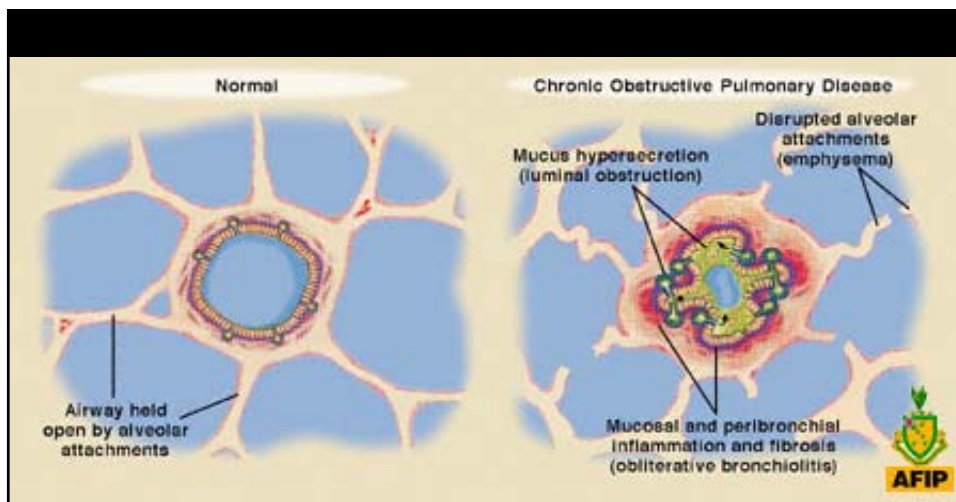


Disease of the conducting airways - Chronic bronchitis

- **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

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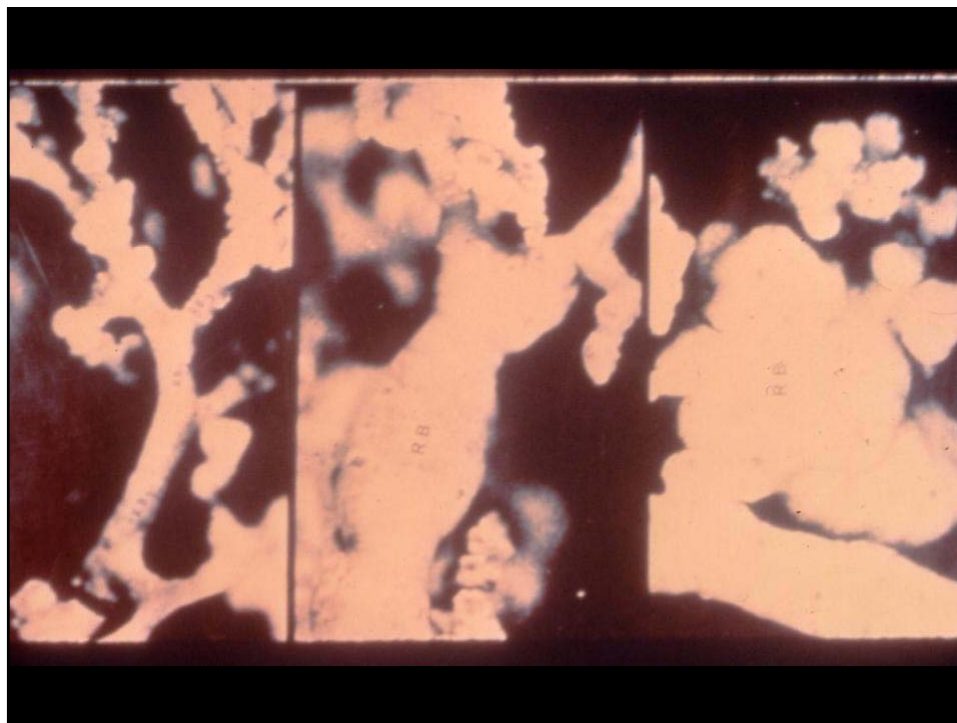
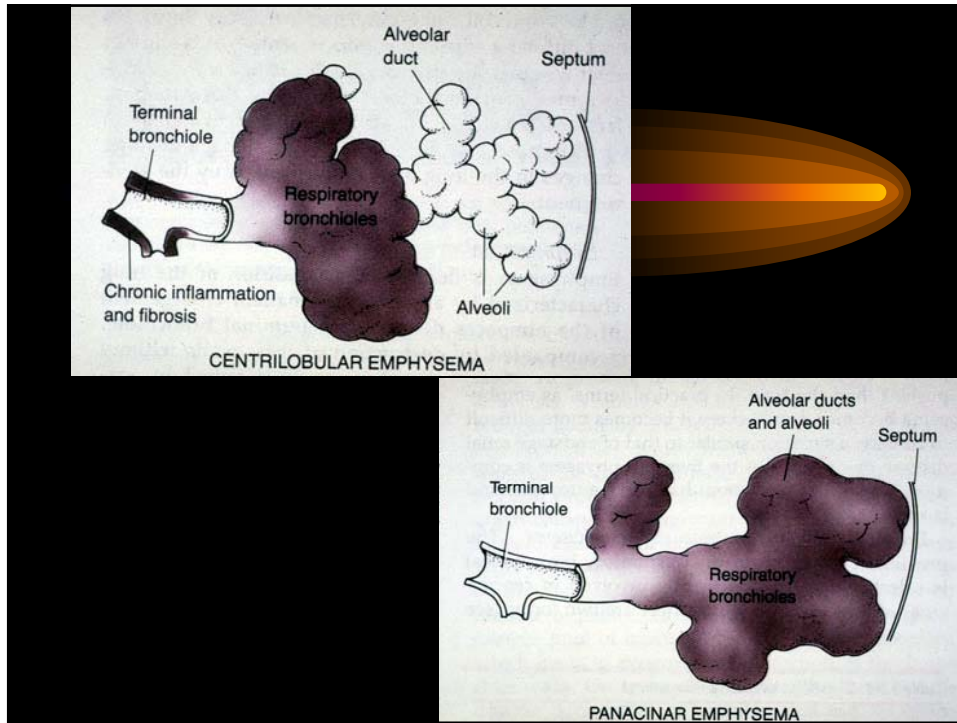
From NEJM
2000;343:270

*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

*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

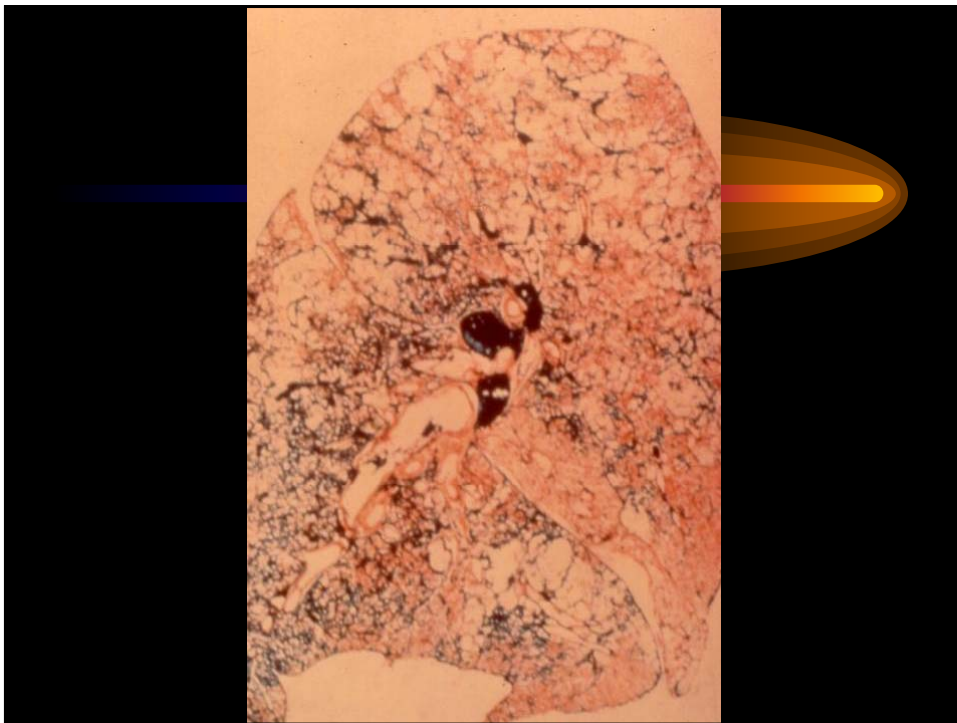
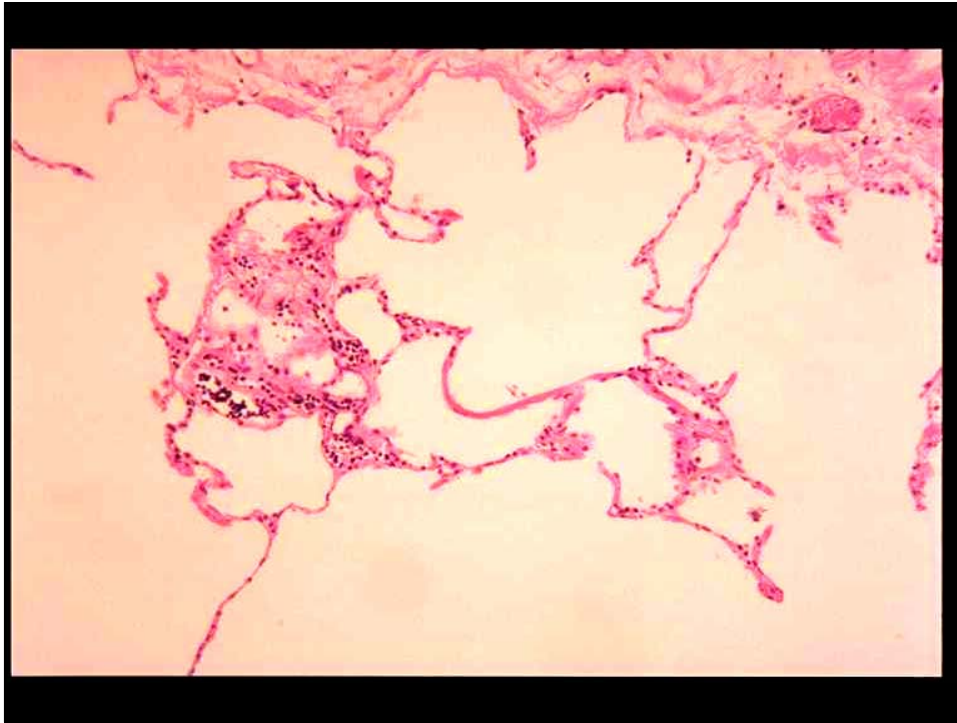
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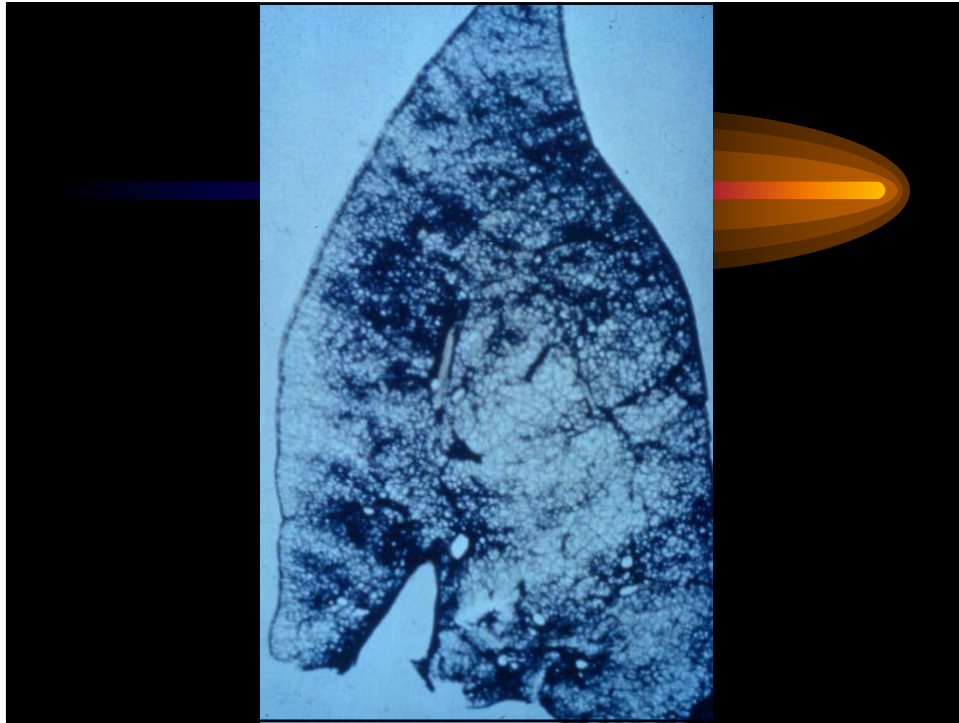
CENTRILOBULAR

VS. PANACINAR

- | | |
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| <ul style="list-style-type: none"> • Gross pathology <ul style="list-style-type: none"> – Upper lobe, irregularly dilated airspaces – Thin walled and grossly apparent • Microscopic <ul style="list-style-type: none"> – Dilated spaces, alongside normal alveoli – Anthracotic pigment | <ul style="list-style-type: none"> • Gross Pathology <ul style="list-style-type: none"> – Lower lobe, more uniformly dilated spaces – Voluminous lungs • Microscopic <ul style="list-style-type: none"> – Dilated spaces, uniformly dilated. |
|--|---|







*Destruction of acinar walls -
Emphysema*

CENTRIOLOBULAR

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*Destruction of acinar walls -
Emphysema*

STRUCTURAL

VS.

FUNCTIONAL

- | | |
|--|--|
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|--|--|