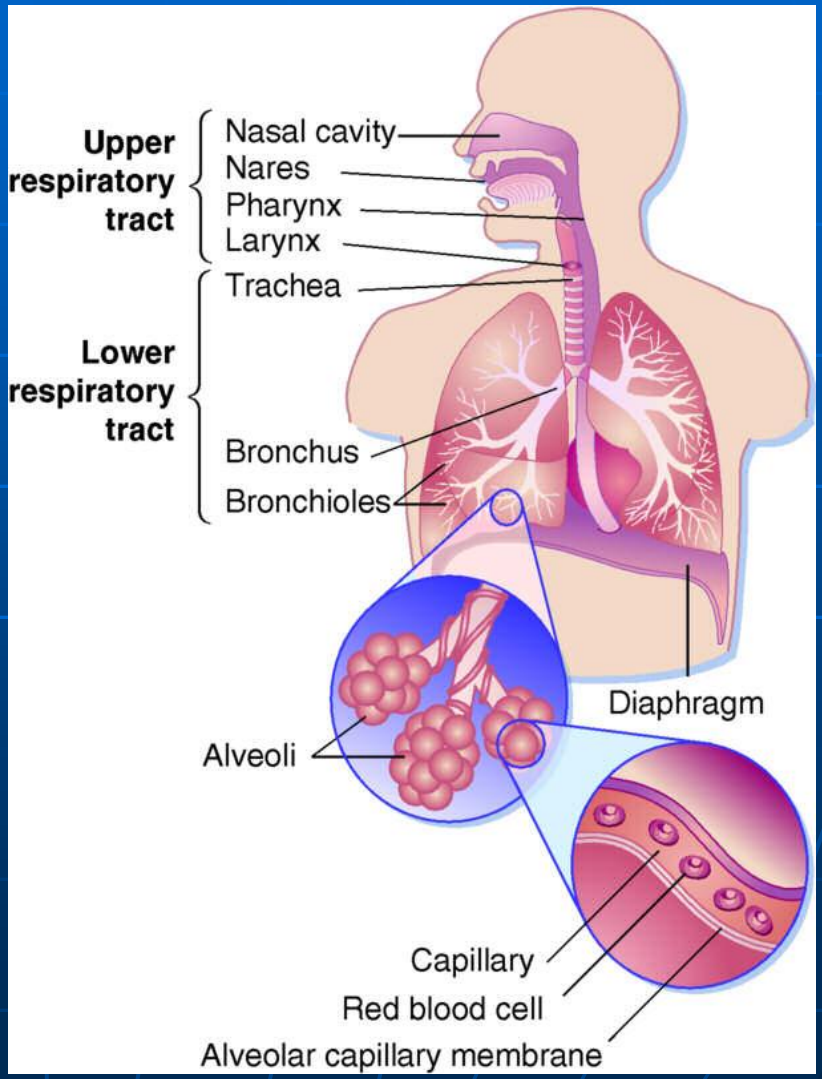
PULMONARY DISEASES

Respiratory Tract

- Upper respiratory tract includes: nares, nasal cavity, pharynx, and larynx.
- Lower respiratory tract includes: trachea, bronchi, bronchioles, alveoli, and alveolar-capillary membrane
- Air enters the upper resp. tract & travels to the lower tract where gas exchange takes place



Respiratory Tract

- Respiration = the process whereby gas exchange occurs at the alveolar-capillary membrane. 3 phases:

  1. Ventilation - movement of air from the atmosphere through the upper & lower airways to the alveoli

  2. Perfusion - blood from the pulmonary circulation is adequate at the alveolar-capillary bed

  3. Diffusion - molecules move from area of higher concentration to lower concentration of gases - O2 passes into the capillary bed to be circulated & CO2 leaves the capillary bed & diffuses into the alveoli for vent. excretion

Respiratory Tract

- Perfusion - influenced by alveolar pressure. For gas exchange, the perfusion of each alveoli must be matched by adequate ventilation. Mucosal edema, secretions, & bronchospasms increase the resistance to airflow & dec. ventilation & diffusion of gases
- Bronchial Smooth Muscle - In the tracheobronchial tube is smooth muscle whose fibers spiral around the tube → contraction → constriction of airway

- Parasympathetic Nervous system → releases acetylcholine → bronchoconstriction
- Sympathetic Nervous system → releases epinephrine → stimulates beta-2 receptors in bronchial smooth muscle → bronchodilation

- Upper Respiratory Infections (URI's) = common cold, acute rhinitis, sinusitis, acute tonsillitis, acute laryngitis

  - The common cold = most expensive > $500 million spent on OTC preparations

- Common Cold & Acute Rhinitis -

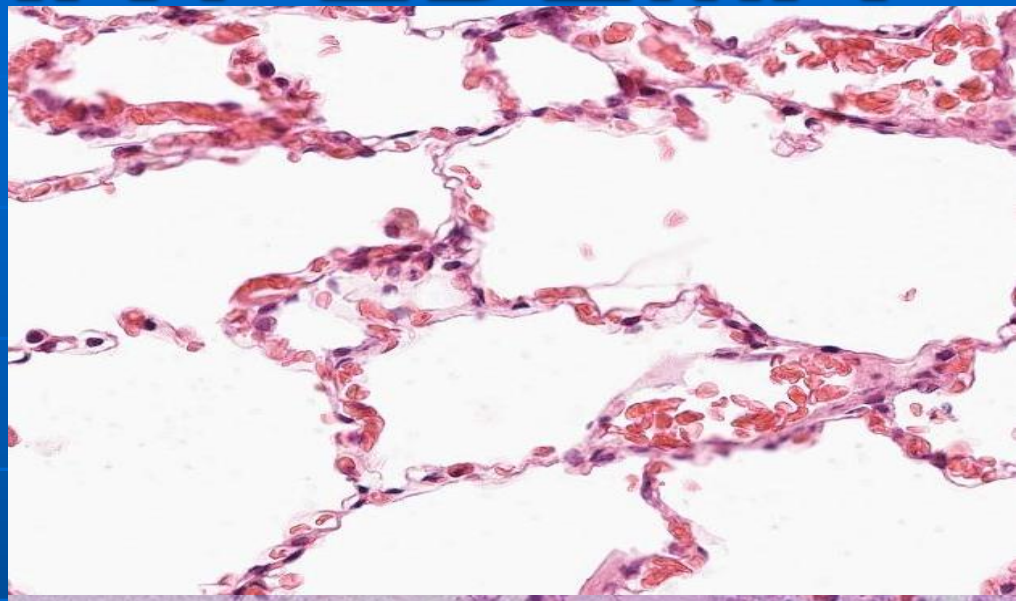
  - Common cold caused by the rhinovirus & affects primarily the nasopharyngeal tract.

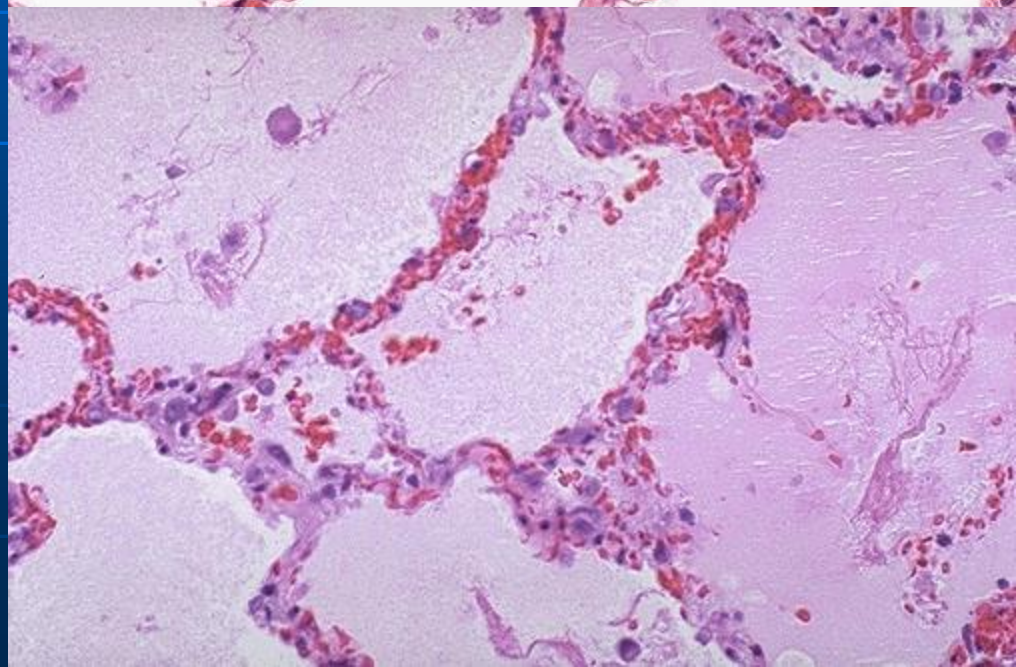
  - Acute rhinitis (inflammation of mucus membranes of nose) usually accompanies the common cold

  - Allergic rhinitis - caused by pollen or a foreign substance

PULMONARY EDEMA

- IN-creased venous pressure
- DE-creased oncotic pressure
- Lymphatic obstruction
- Alveolar injury



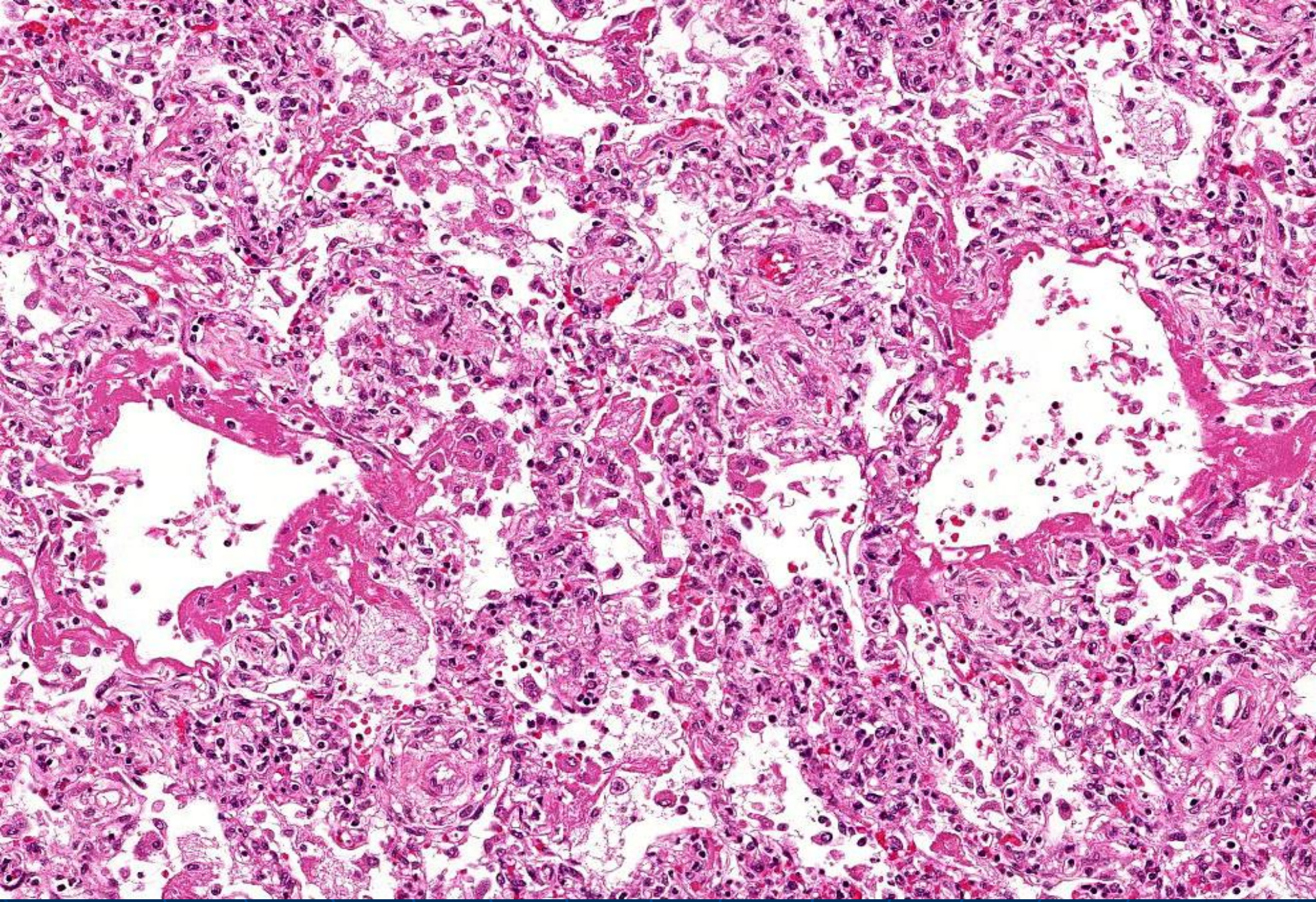


ARDS

- Definition — noncardiogenic pulmonary edema resulting from acute alveolar-capillary damage
- Epidemiology Due to direct injury to the lungs or systemic diseases
- Causes
- (1) Gram-negative sepsis (>40% of cases)
- (2) Gastric aspiration (>30% of cases)
- (3) Severe trauma with shock (>20% of cases)
- (4) Diffuse pulmonary infections Severe acute respiratory syndrome (SARS), hantavirus
- (5) Other causes: heroin, smoke inhalation, acute pancreatitis, cardiopulmonary bypass, disseminated intravascular coagulation, amniotic fluid embolism, and fat embolism

Pathogenesis

- a. Acute damage occurs in alveolar capillary walls and epithelial cells.
- b. Alveolar macrophages and other cells release cytokines.
- (1) Cytokines are chemotactic to neutrophils.
- (2) Neutrophils transmigrate into the alveoli through pulmonary capillaries.
- (3) Capillary damage causes leakage of a protein-rich exudate producing hyaline membranes.
- (4) Neutrophils damage type I and II pneumocytes.
- • Decrease in surfactant causes atelectasis with intrapulmonary shunting.
- c. Late findings
- (1) Repair by type II pneumocytes
- (2) Progressive interstitial fibrosis (restrictive lung disease)



ARDS

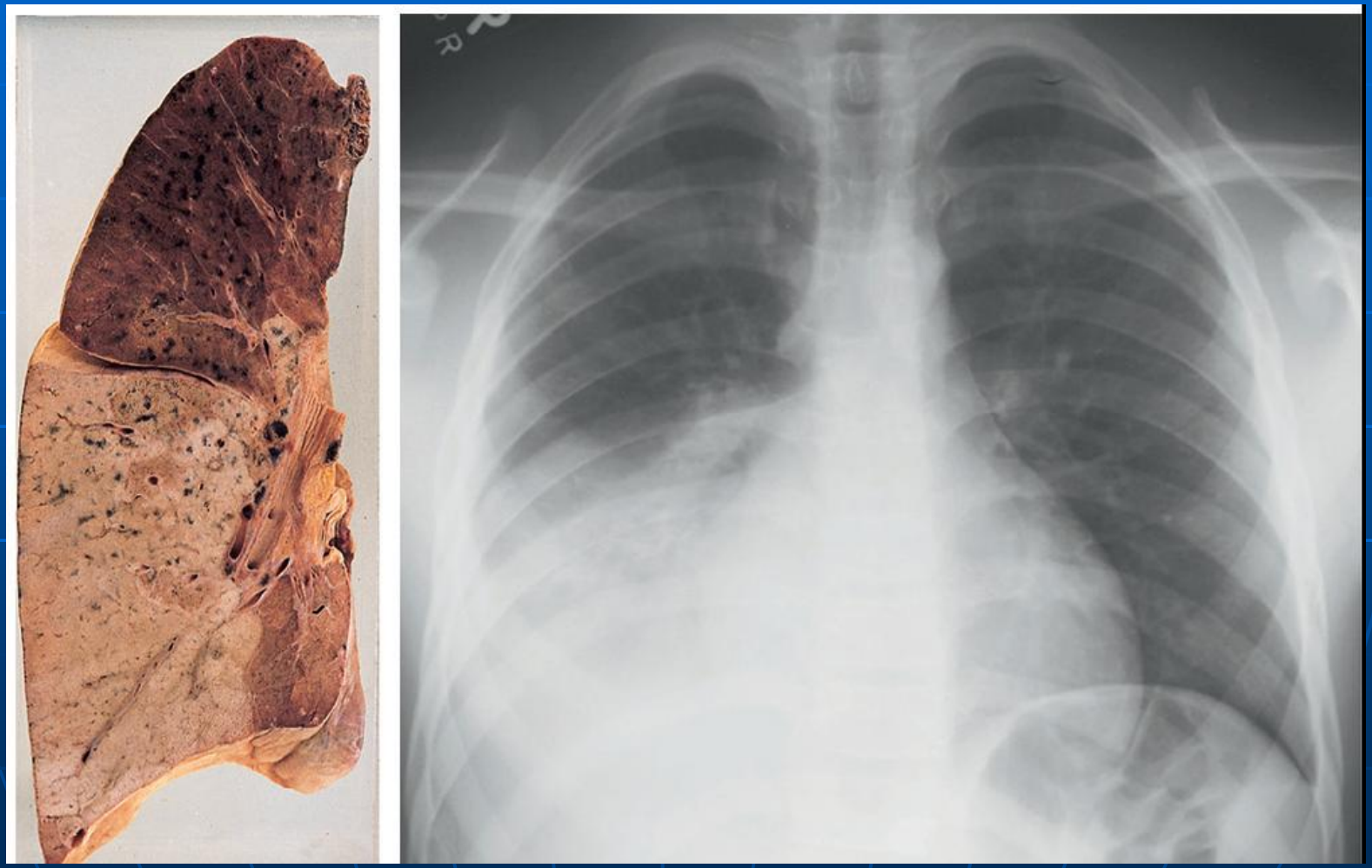
- According to the WHO vital statistics, **pneumonia** and **influenza** together account for 3 % of all death and are the fifth leading cause of death, exceeded only by heart disease, cancer, cerebrovascular disease, and accidents.
- With the use of potent therapies that deliberately or incidentally produce immunosupression, there is every prospect that respiratory infections will remain a serious clinical problem.
- For example, pneumonia develops in one third of patients receiving chemotherapy for leukemia.

BACTERIAL PNEUMONIA

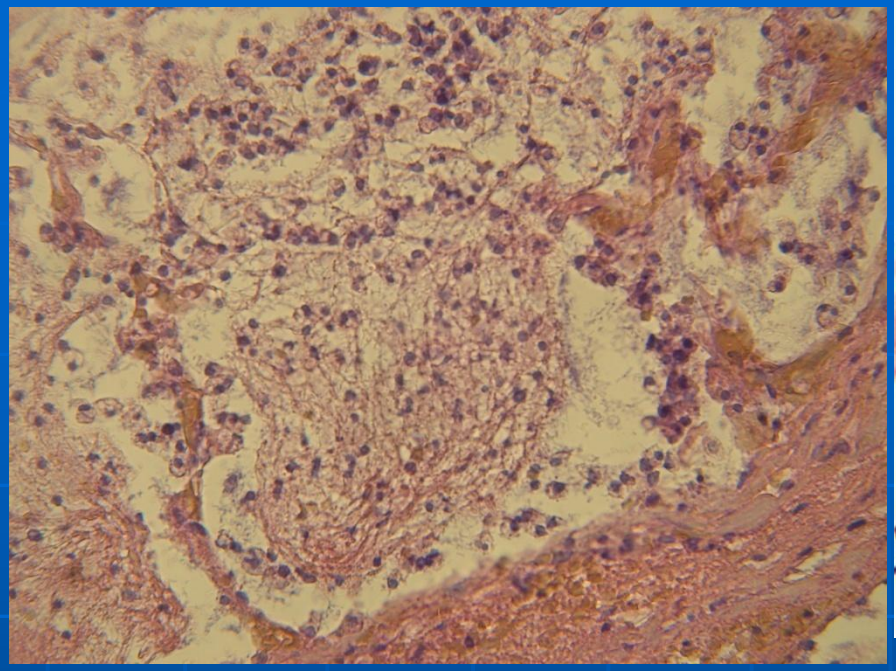
- **Pneumococcal pneumonia.**
- The pneumococcus continues to be responsible for 30 % to 80 % or more of community-acquired pneumonias. Groups at particular risk include the very young and very old, alcoholics, diabetics, spleenectomized subjects, and patients with multiple myeloma or circle cell disease.
- Pneumococcal pneumonia typically presents the picture of lobar pneumonia. One or occasionally several lobes of the lung are involved. Traditionally the progress of the disease is divided into four stages: **edema**, **red hepatization, gray hepatization** and **resolution or organization**.

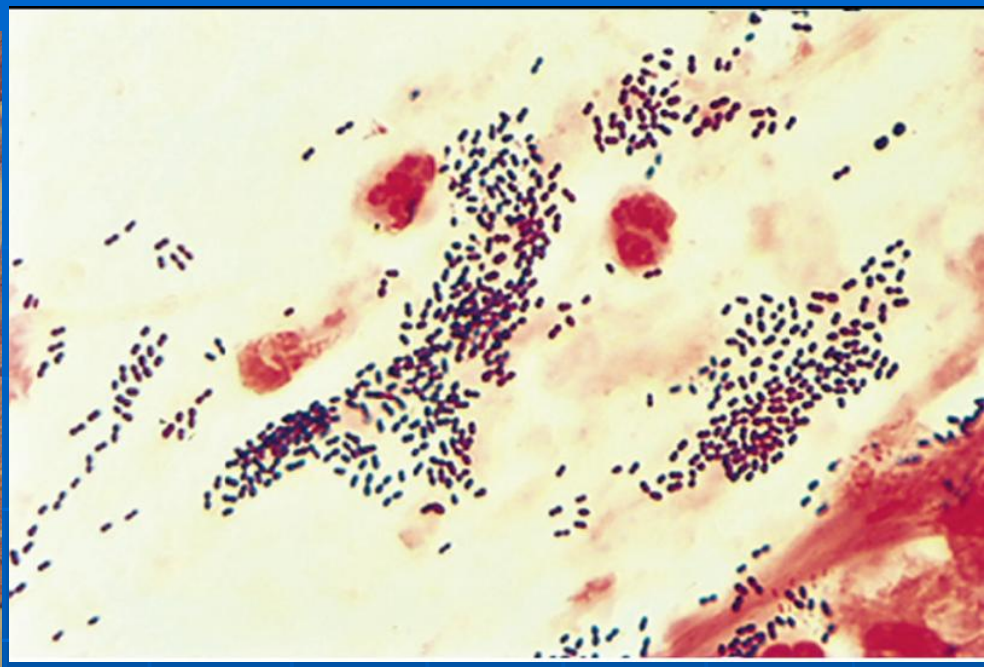
- The initial response of the organism is an outpouring of edema fluid, which provides a rich broth in which the organisms proliferate and which spreads them throughout the lobe through pores of Kohn and bronchioles.
- With the passage of time progressively more fibrin and neutrophils enter the alveoli.
- At first the alveolar capillaries are distended with erythrocytes and there is diapedesis of erythrocytes into the alveoli, giving the lobe a red color, while the filling of the air spaces with fibrin and leukocytes gives it a firm, liver like consistency. Classically the lobe at this phase is described as **red hepatization**.

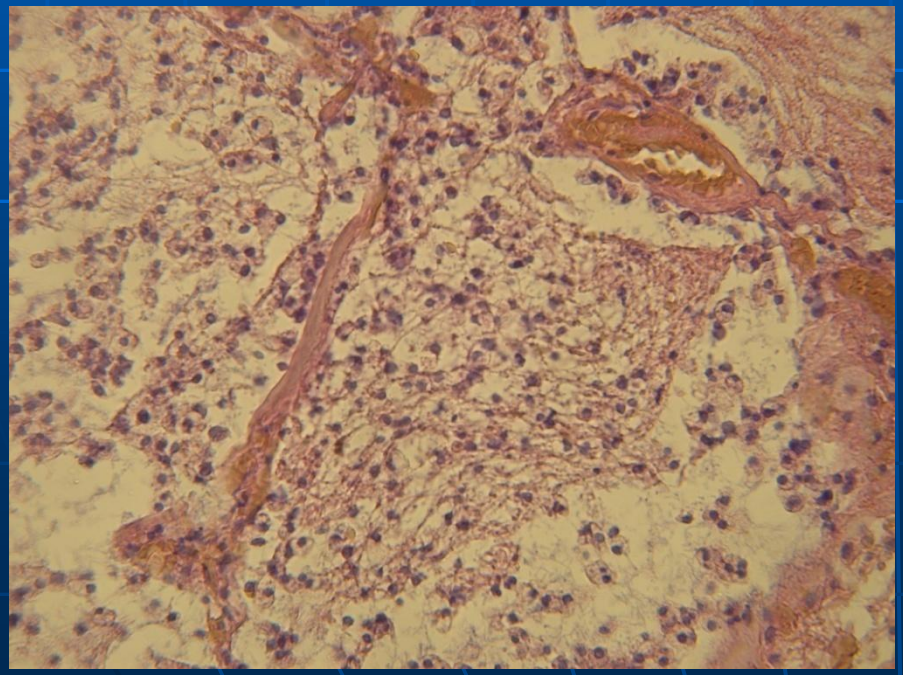
Lobar pneumonia



- With the further evolution of the process, increasing amounts of fibrin and leukocytes enter the air spaces, the alveolar capillaries appear compressed, and the lobe becomes progressively grayer in appearance, evolving into the stage of gray hepatization. In untreated persons, organisms decrease in number progressively after approximately 5 days.







Gram stain of *Streptococcus pneumoniae. The sputum stain shows* numerous lancet-shaped diplococci with the tapered ends pointing to each other. A few neutrophils contain phagocytosed bacteria.

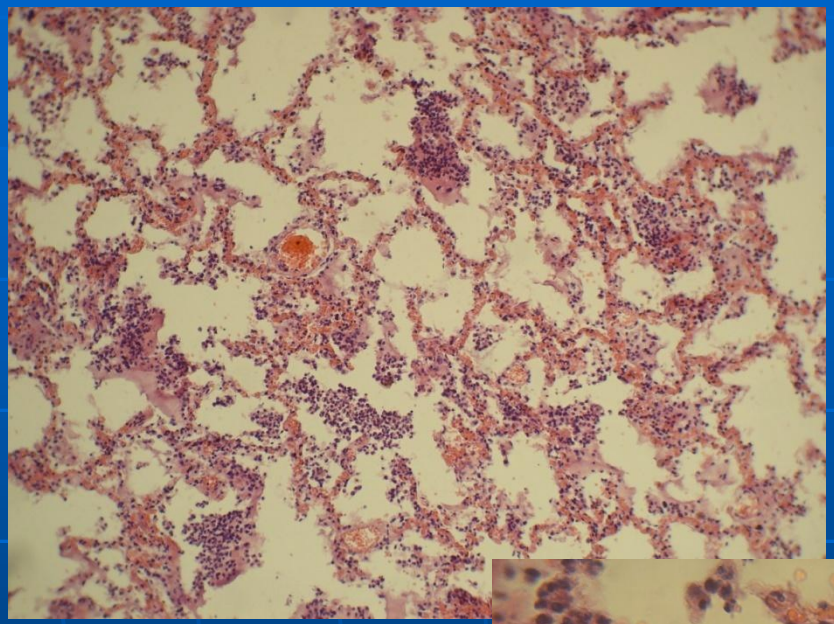
Complications.

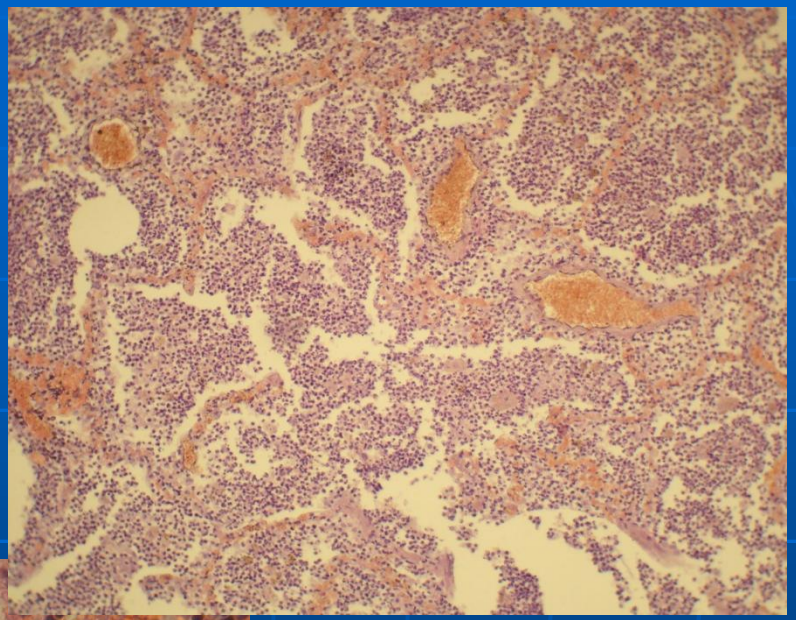
- Pleural involvement occurs commonly in lobar pneumonia. In two thirds of patients there is fibrinous pleuritis without infection of the pleural space. In 15 % to 25 % of patients, infection of the pleural space (empyema) develops and the pleural surface becomes covered with shaggy white layers of fibrin and neutrophils. Bacteremia occurs in 20 % to 35 % of patients with lobar pneumonia and a much smaller proportion of those with bronchopneumonia. Bacteremic spread leads to meningitis, bacterial endocarditis, arthritis, or pericarditis in small proportion of patients. Lung abscess results from the breakdown of alveolar walls.

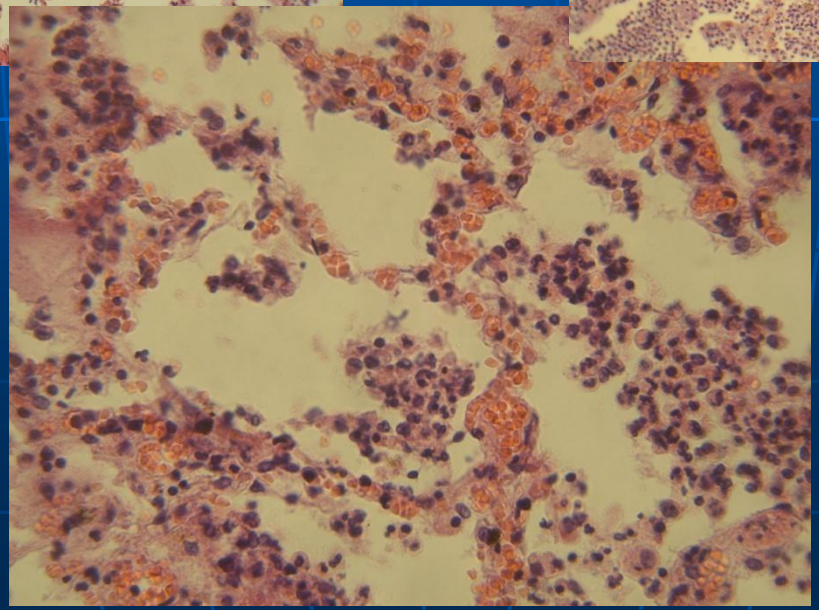
Bronchopneumonia

- Staphylococcal bronchopneumonia is not rare in children less than 6 months of age. A notable feature of Staphylococcal pneumonia in small children is the development of pneumatoceles, air-containing lesions that are seen roentgenographically within the areas of confluent pneumonia and that enlarge very rapidly, often over hours. It is unlikely that they are simple abscesses because they are thin-walled and can disappear over several weeks without residue. Although their morphology has rarely been described since patients commonly recover, most radiologists assume that they arise from the trapping of distal to partial obstruction to a bronchus, which acts as a check valve.

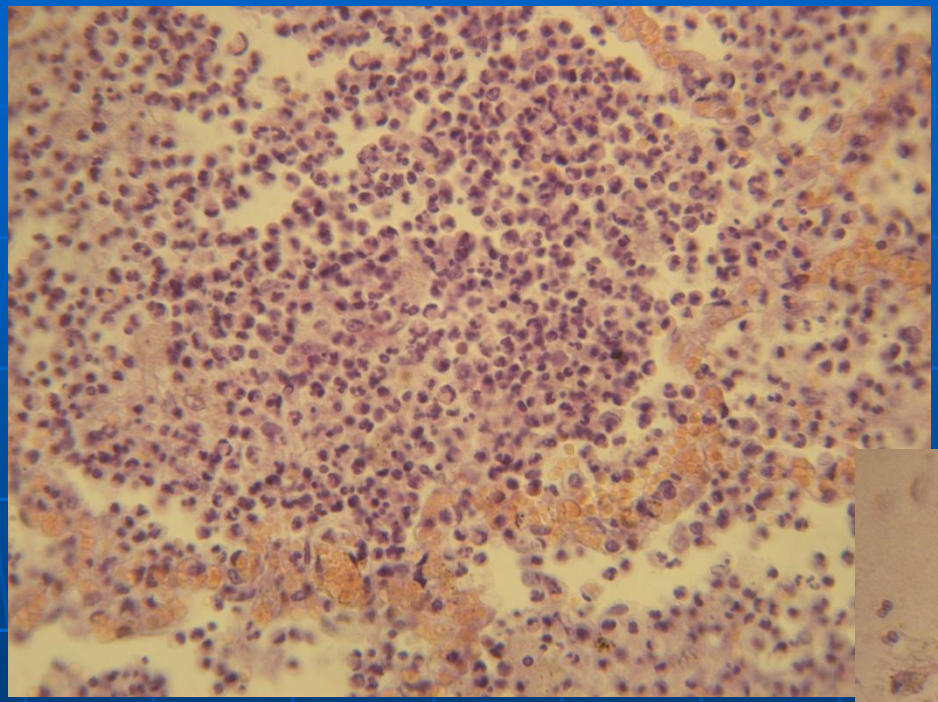
Bronchopneumonia showing patchy areas of consolidation *representing* collections of neutrophils in the alveoli and bronchi.

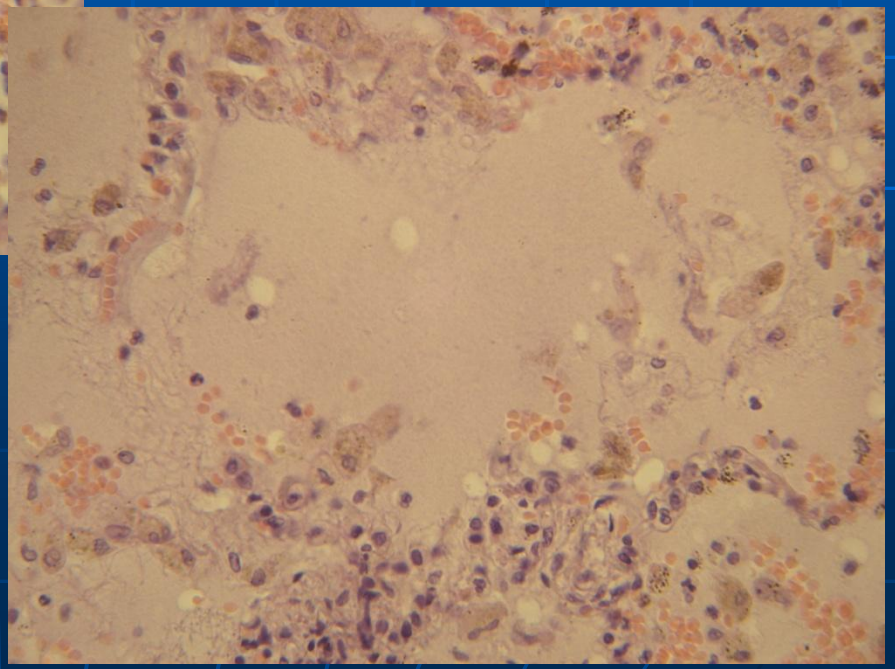






Bronchopneumonia





Bronchopneumonia

(1) It begins as an acute bronchitis and spreads locally into the lungs.

(2) The lower lobes or right middle lobe are usually involved.

(3) The lung has patchy areas of consolidation.

- Microabscesses are present in the areas of consolidation.

Lobar pneumonia

- Complete or almost complete consolidation of a lobe of lung

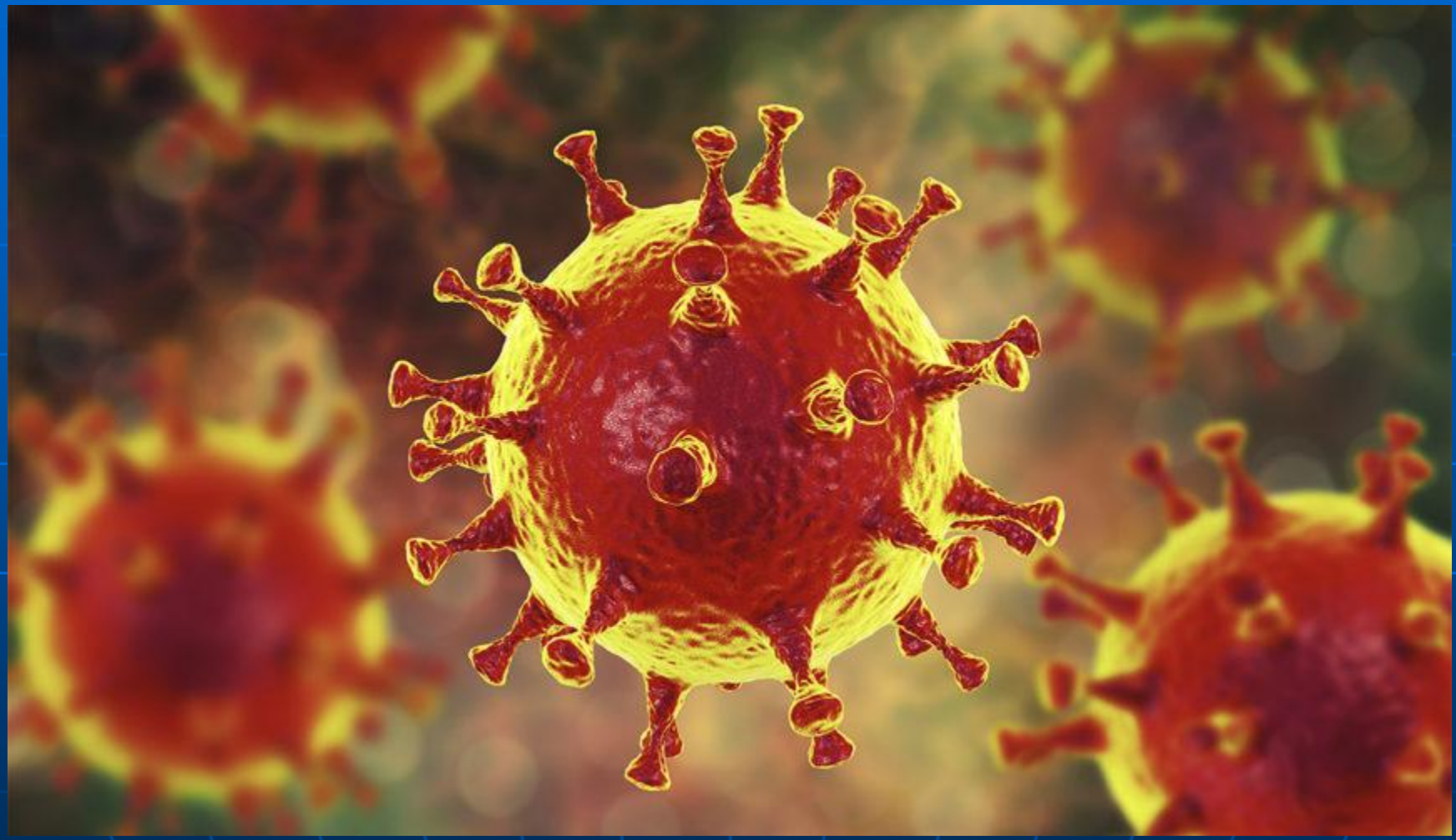
Complications

(1) Lung abscesses, empyema (pus in the pleural cavity)

(2) Sepsis

COVID-19

- The severe acute respiratory syndrome (SARS) coronavirus-2 is a novel coronavirus belonging to the family Coronaviridae and is now known to be responsible for the outbreak of a series of recent acute atypical respiratory infections originating in Wuhan, China. The disease caused by this virus, termed coronavirus disease 19 or simply COVID-19, has rapidly spread throughout the world at an alarming pace and has been declared a pandemic by the WHO on March 11, 2020.



COVID-19

- The virus is transmitted via respiratory droplets and aerosols from person to person. Once inside the body, the virus binds to host receptors and enters host cells through endocytosis or membrane fusion.
- ACE-2 has been identified as a functional receptor for SARS-CoV and is highly expressed on the pulmonary epithelial cells. It is through this host receptor that the S protein binds initially to start the host cell invasion by the virus.

COVID-19

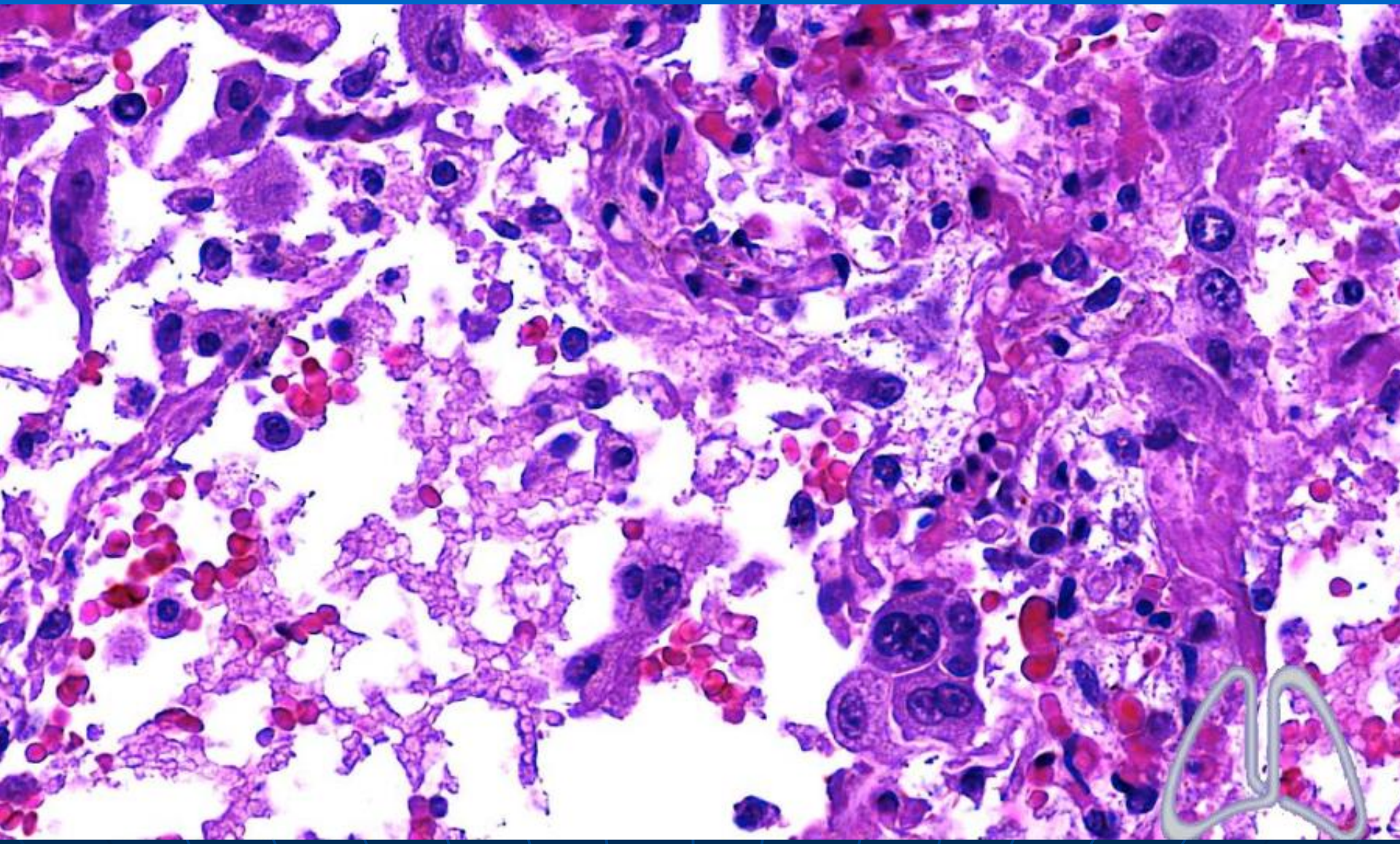
- About one-fifth of all infected patients progress to this stage of disease and develop severe symptoms. The virus invades and enters the type 2 alveolar epithelial cells via the host receptor ACE-2 and starts to undergo replication to produce more viral Nucleocapsids. The virus-laden pneumocytes now release many different cytokines and inflammatory markers such as interleukins (IL-1, IL-6, IL-8, IL-120 and IL-12), tumour necrosis factor-α (TNF-α), IFN-λ and IFN-β, CXCL-10, monocyte chemoattractant protein-1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α).

COVID-19

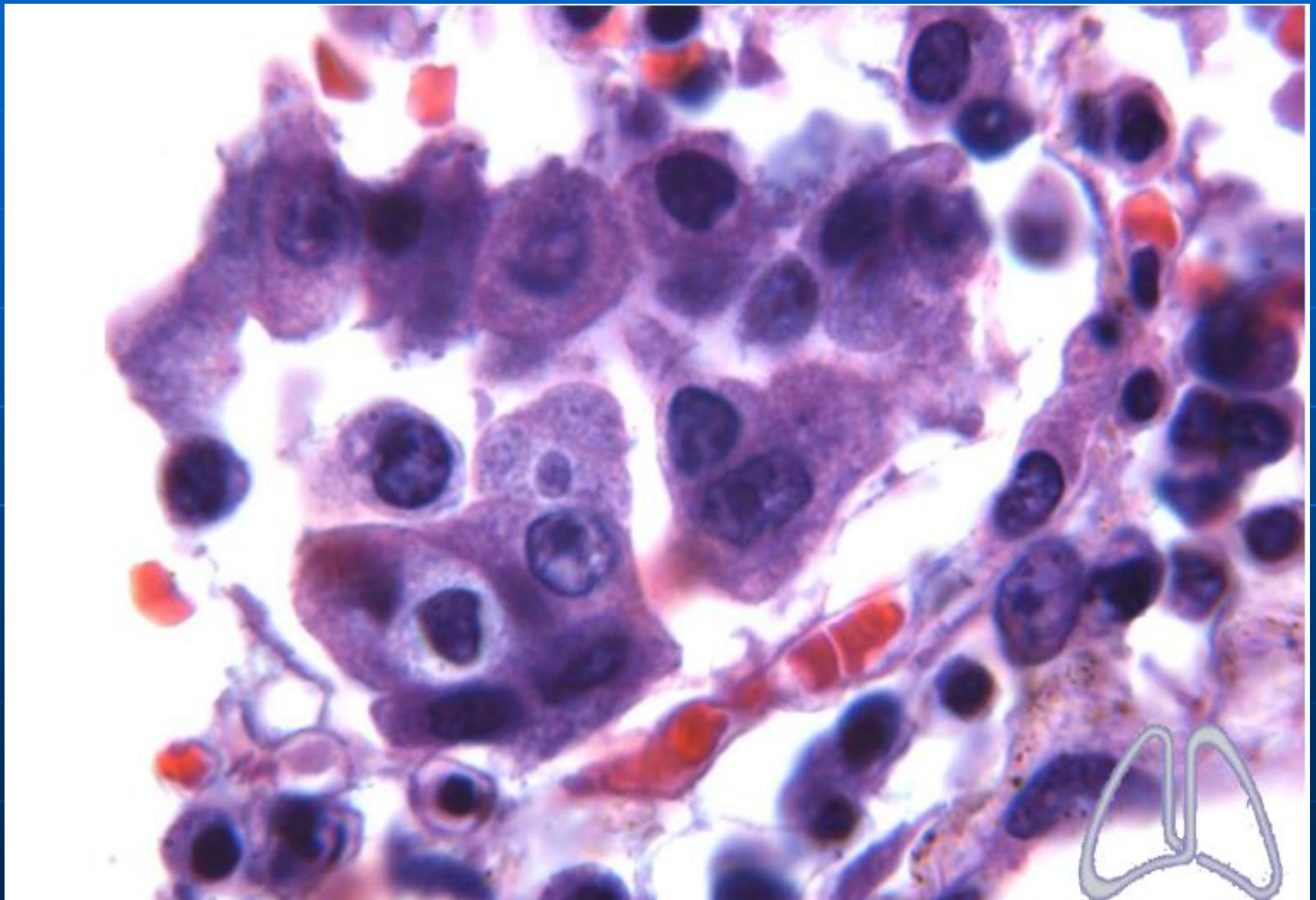
- 'Cytokine storm' acts as a chemoattractant for neutrophils, CD4 helper T cells and CD8 cytotoxic T cells, which then begin to get sequestered in the lung tissue. These cells are responsible for fighting off the virus, but in doing so are responsible for the subsequent inflammation and lung injury. The host cell undergoes apoptosis with the release of new viral particles, which then infect the adjacent type 2 alveolar epithelial cells in the same manner. Due to the persistent injury caused by the sequestered inflammatory cells and viral replication leading to loss of both type 1 and type 2 pneumocytes, there is diffuse alveolar damage eventually culminating in an acute respiratory distress syndrome.

http://patolog.ru/sites/default/files/mv_samsonova_covid-19_.pdf

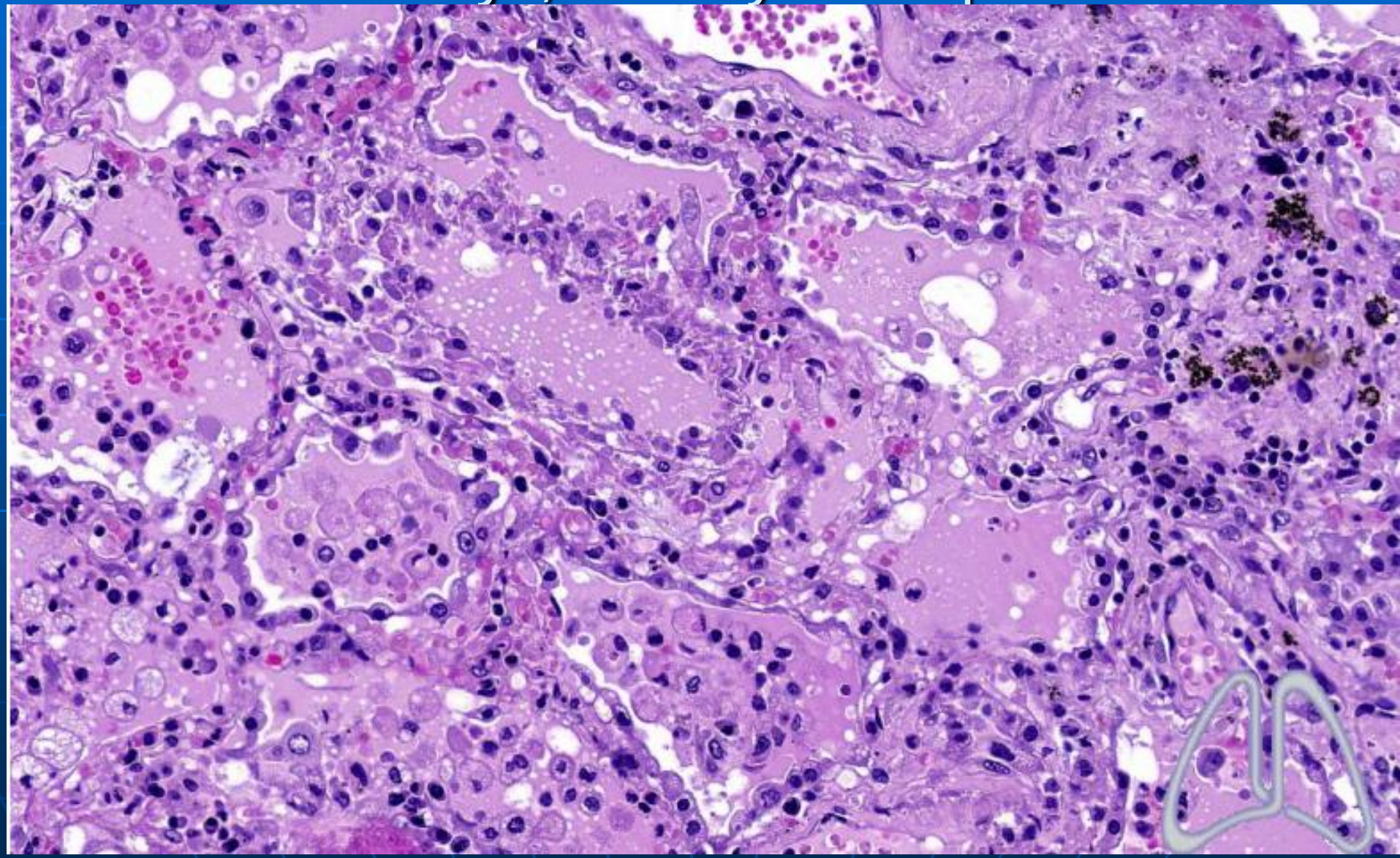
9 days, 8th day in hospital



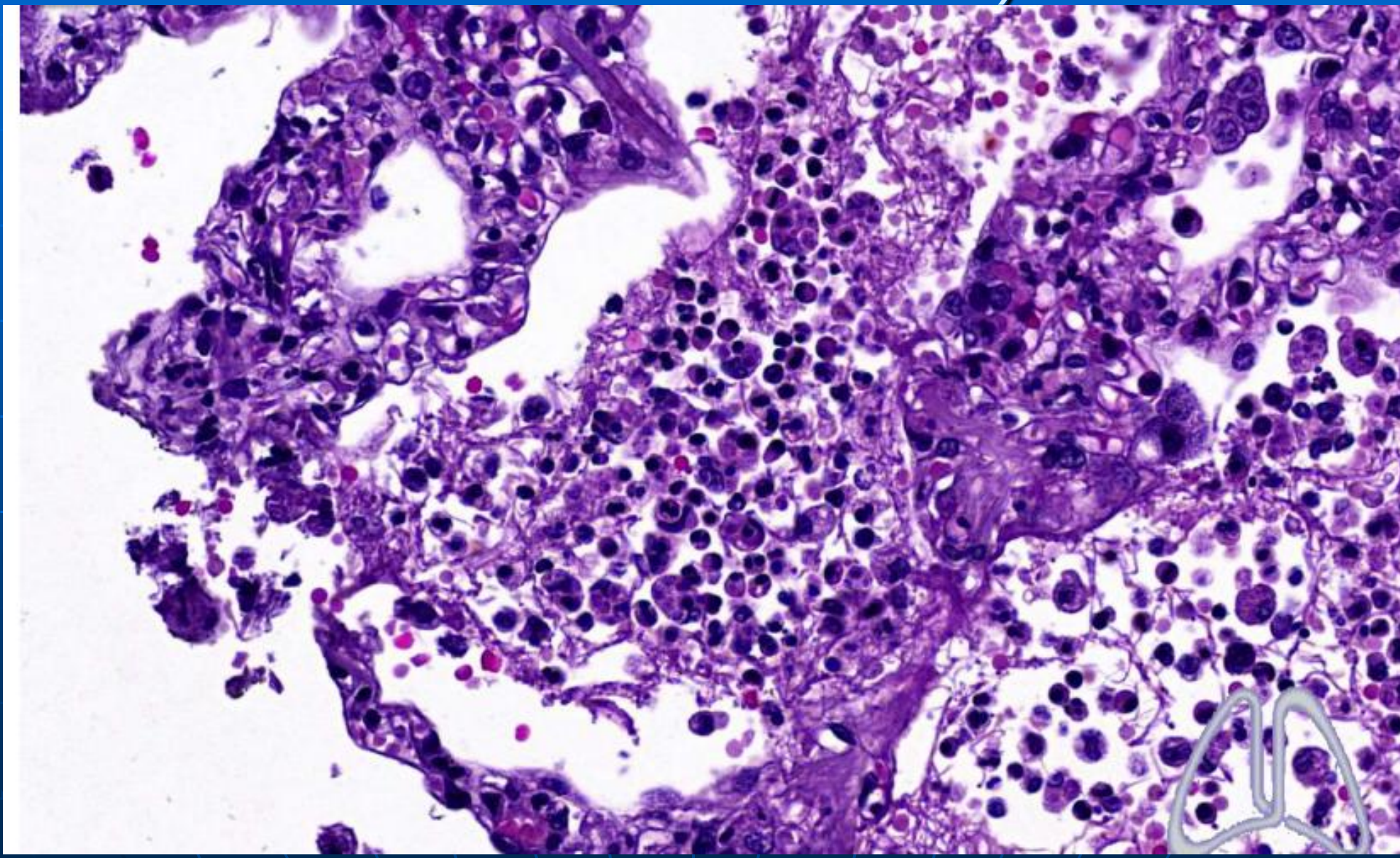
5 days, 3rd day in hospital (Mechanical ventilation 1 day)



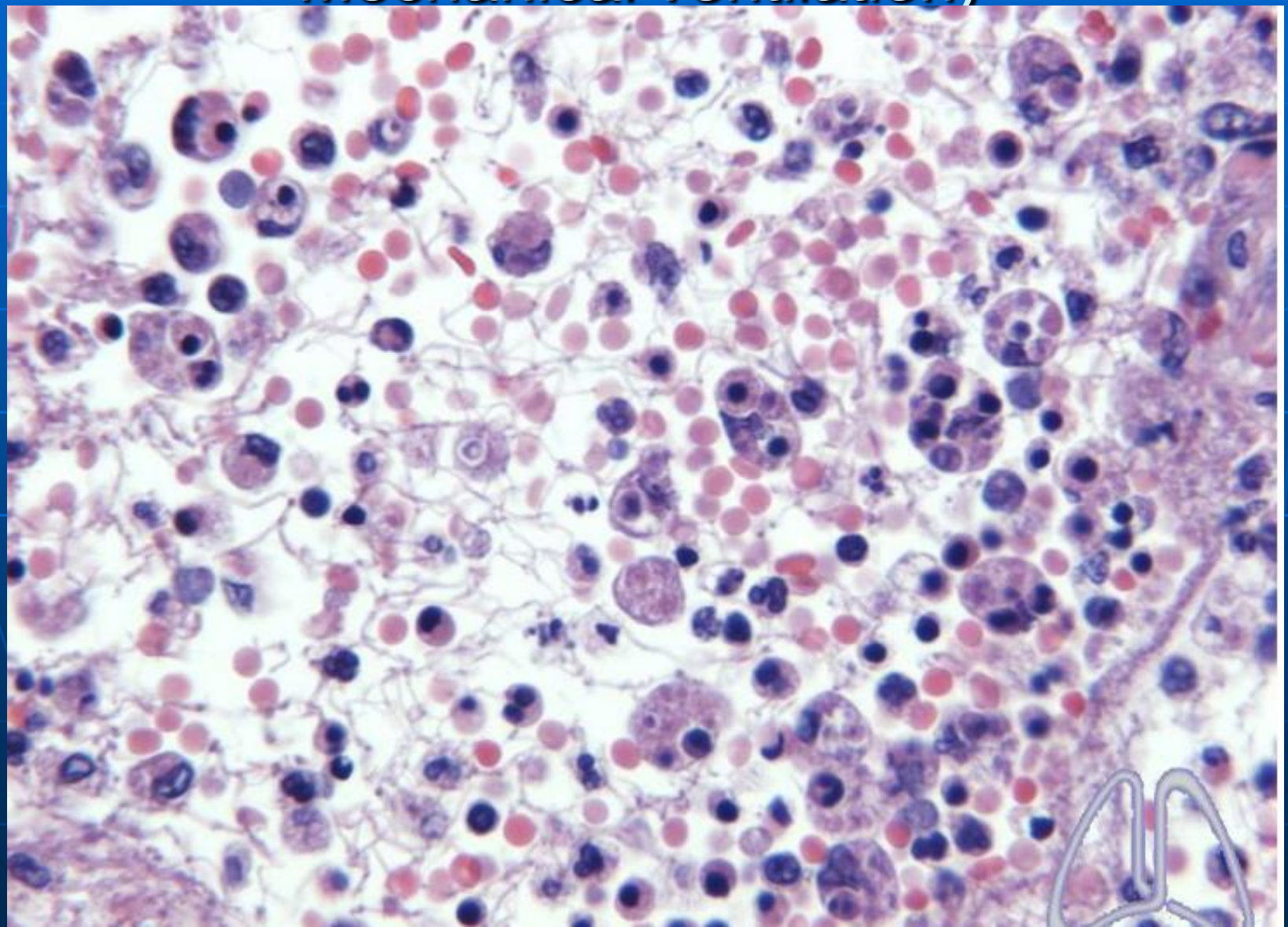
15 days, 9th day in hospital



10 days, 4th day in hospital (4 days of Mechanical ventilation)



10 days, 4th day in hospital (4 days of Mechanical ventilation)



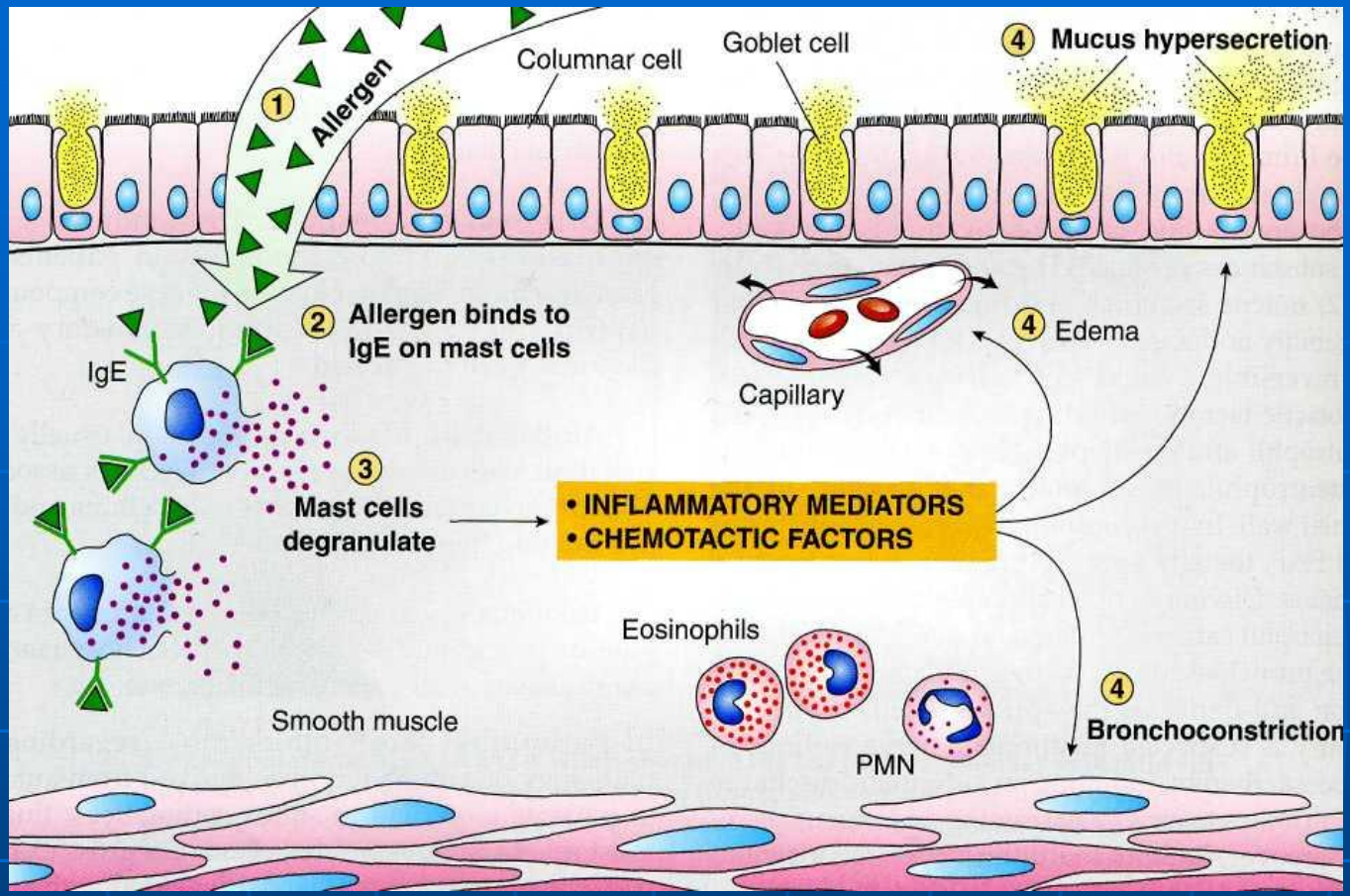
Asthma

Asthma is characterized by variable obstruction to the flow of air and increased responsiveness of the airways to a variety of stimuli. It is characterized clinically by paroxysms of wheezing, dyspnea, and cough. When severe acute asthma is unresponsive to therapy, it is referred to as **status asthmaticus.**

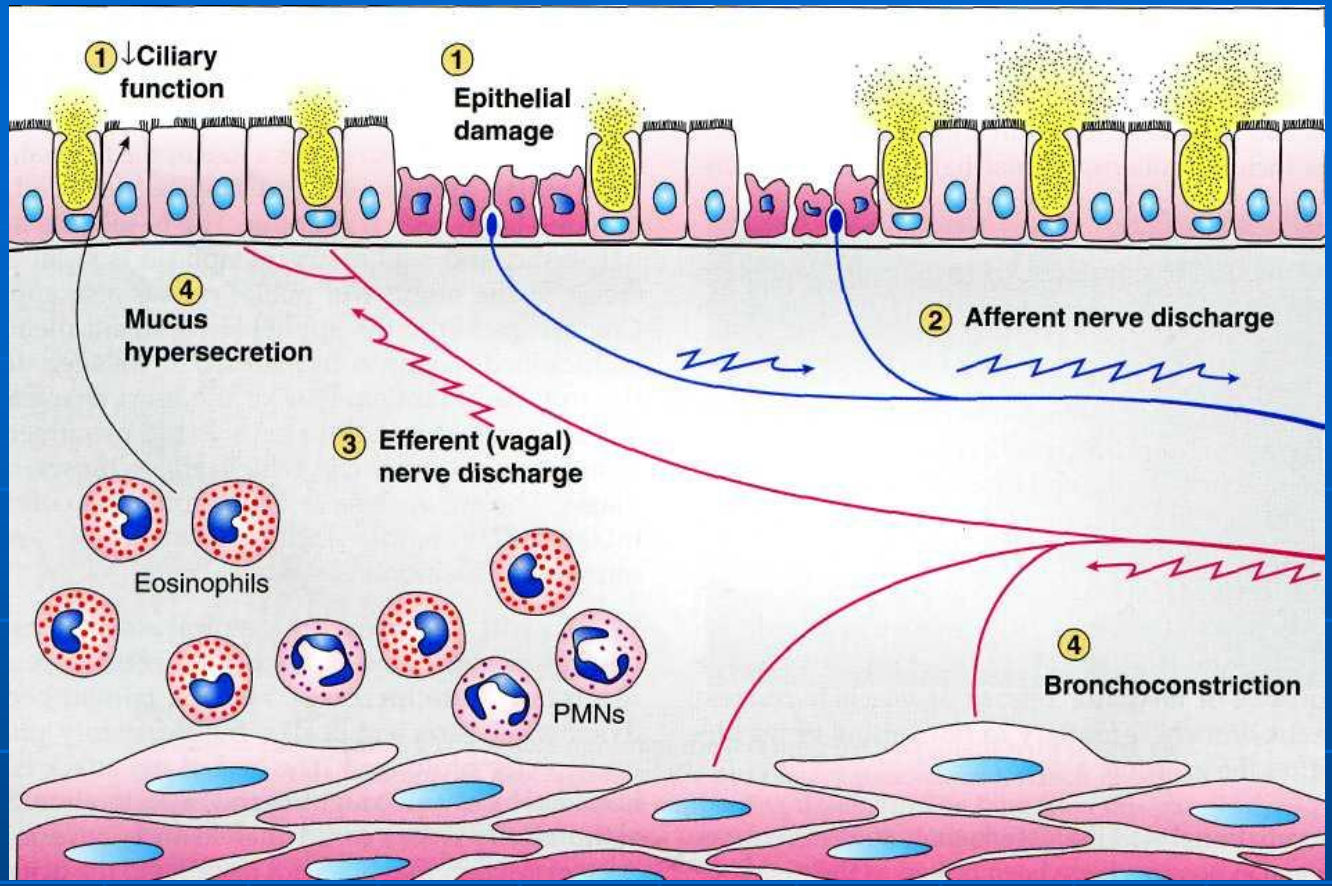
Pathogenesis: Asthma has been attributed to an increased airway responsiveness to an inflammatory reaction provoked by diverse stimuli. The best-studied situation associated with induction of asthma is the inhalation of allergens.

There are two major clinical forms of asthma that can overlap.

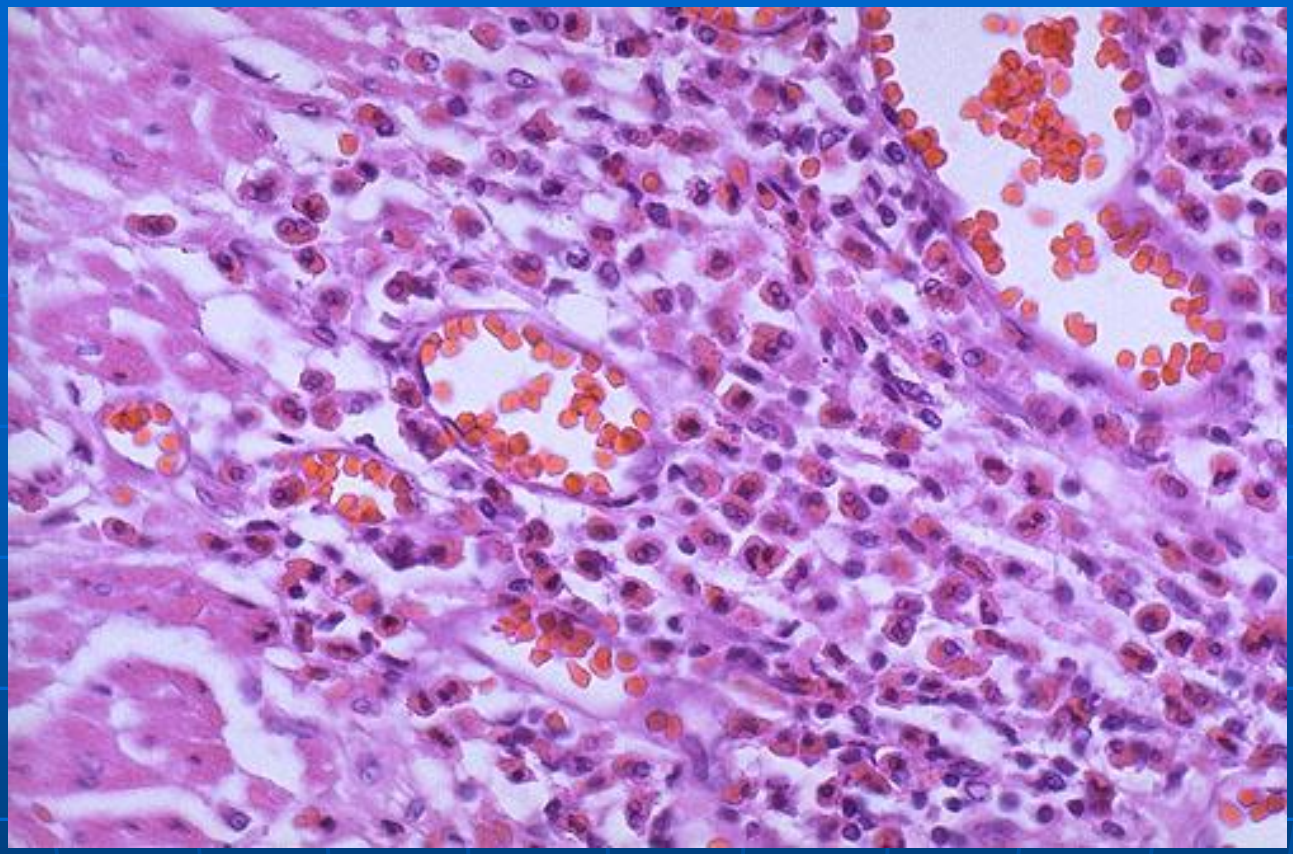
- Extrinsic asthma: there is typically an association with atopy (allergies) mediated by type 1 hypersensitivity, and asthmatic attacks are precipitated by contact with inhaled allergens. This form occurs most often in childhood.
- Intrinsic asthma: asthmatic attacks are precipitated by respiratory infections, exposure to cold, exercise, stress, inhaled irritants, and drugs such as aspirin. Adults are most often affected.



Pathogenesis of asthma. Immunologically mediated asthma. Allergens interact with immunoglobulin E on mast cells, either on the surface of the epithelium or, when there is abnormal permeability of the epithelium, in the submucosa. Mediators are released and may react locally or by reflexes mediated through the vagus.



Pathogenesis of asthma. Discharge of eosinophilic granules further impairs mucociliary function and damages the epithelial cells. In turn, epithelial cell injury stimulates nerve endings in the mucosa, thereby initiating an autonomic discharge that contributes to airway narrowing and mucus secretion.



- At high magnification, the numerous eosinophils are prominent from their bright red cytoplasmic granules in this case of bronchial asthma.

An inhaled allergen in a sensitized person interacts with IgE antibody that is bound to the surface of mast cells interspersed among the epithelial cells of the bronchial mucosa.

As a result, mast cells degranulate and release mediators of type I (immediate) hypersensitivity, including histamine, bradykinin,leukotrienes, prostaglandins,thromboxane A2, and platelet-activating factor (PAF). These substances produce:

(1) smooth muscle contraction,

(2) mucus secretion, and

(3) increased vascular permeability and edema, each of which is a potent, albeit reversible, cause of airway obstruction.

Allergic Asthma.

This is the most common form of asthma and is usually found in children. Common allergens include pollens, animal hair or fur, and contamination of house dust with mites.

- Histamines - A compound derived from an amino acid histadine. Released in response to an allergic rxn (antigen-antibody rxn) - such as inhaled pollen

  - When released it reacts w/ H-1 receptors = arterioles & capillaries dilate = inc. in bld flow to the area = capillaries become more permeable = outward passage of fluids into extracellular spaces= edema (congestion) = release of secretions (runny nose & watery eyes)

  - Large amts. of released histamine in an allergic rxn = extensive arteriolar dilation = dec. BP, skin flushed & edematous = itching, constriction & spasm of bronchioles = SOB & lg. amts. of pulmonary & gastric secretions

Infections.

A common precipitating factor in childhood asthma is a viral respiratory tract infection rather than allergic stimuli.

Exercise-Induced Asthma.

Exercise can precipitate some degree of bronchospasm in the majority (65%) of all patients with asthma, and in some patients, exercise may be the only inciting factor. The more rapid the ventilation (severity of exercise) and the colder and drier the air that is breathed, the more likely it is that an attack of asthma will occur.

Occupational Asthma.

More than 80 different occupational exposures have been linked to the development of asthma. In some instances, these substances provoke allergic asthma by IgE-related hypersensitivity mechanisms. Those affected include animal handlers, bakers, and workers exposed to wood and vegetable dusts, metal salts, pharmaceutical agents, and industrial chemicals.

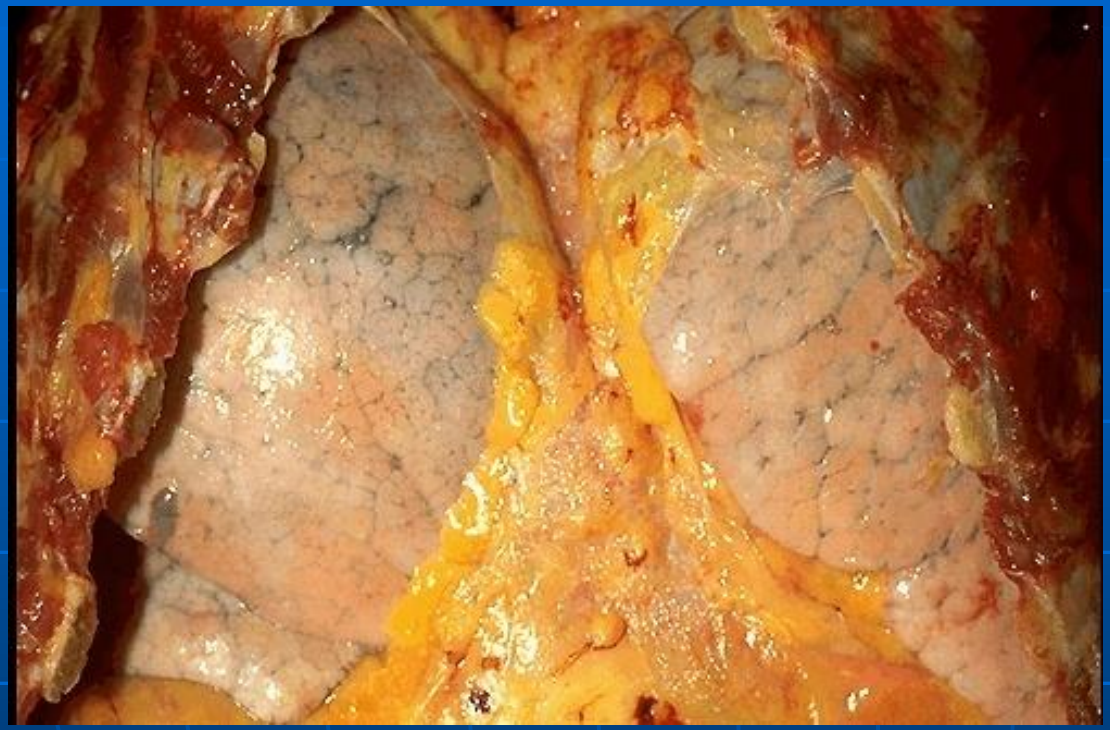
Drug-Induced Asthma.

Drug-induced bronchospasm occurs most commonly in patients with known asthma. The best known of these compounds is aspirin, but nonsteroidal anti-inflammatory agents have also been implicated.

Air Pollution.

Massive air pollution, usually in association with temperature inversions, is associated with bronchospasm in patients with asthma and other preexisting lung conditions.

Emotional Factors. Psychological stress can aggravate or precipitate an attack of bronchospasm in as many as half of all patients with asthma.

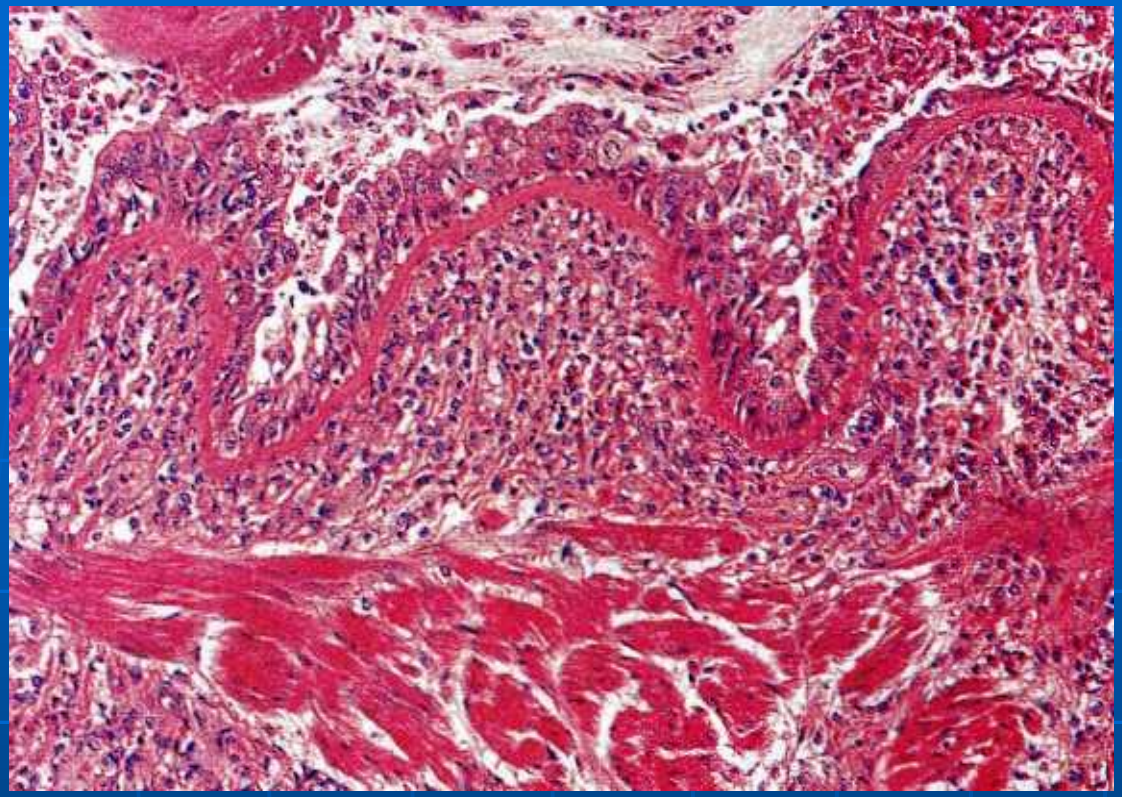


- These lungs appear essentially normal, but are normal-appearing because they are the hyperinflated lungs of a patient who died with status asthmaticus.

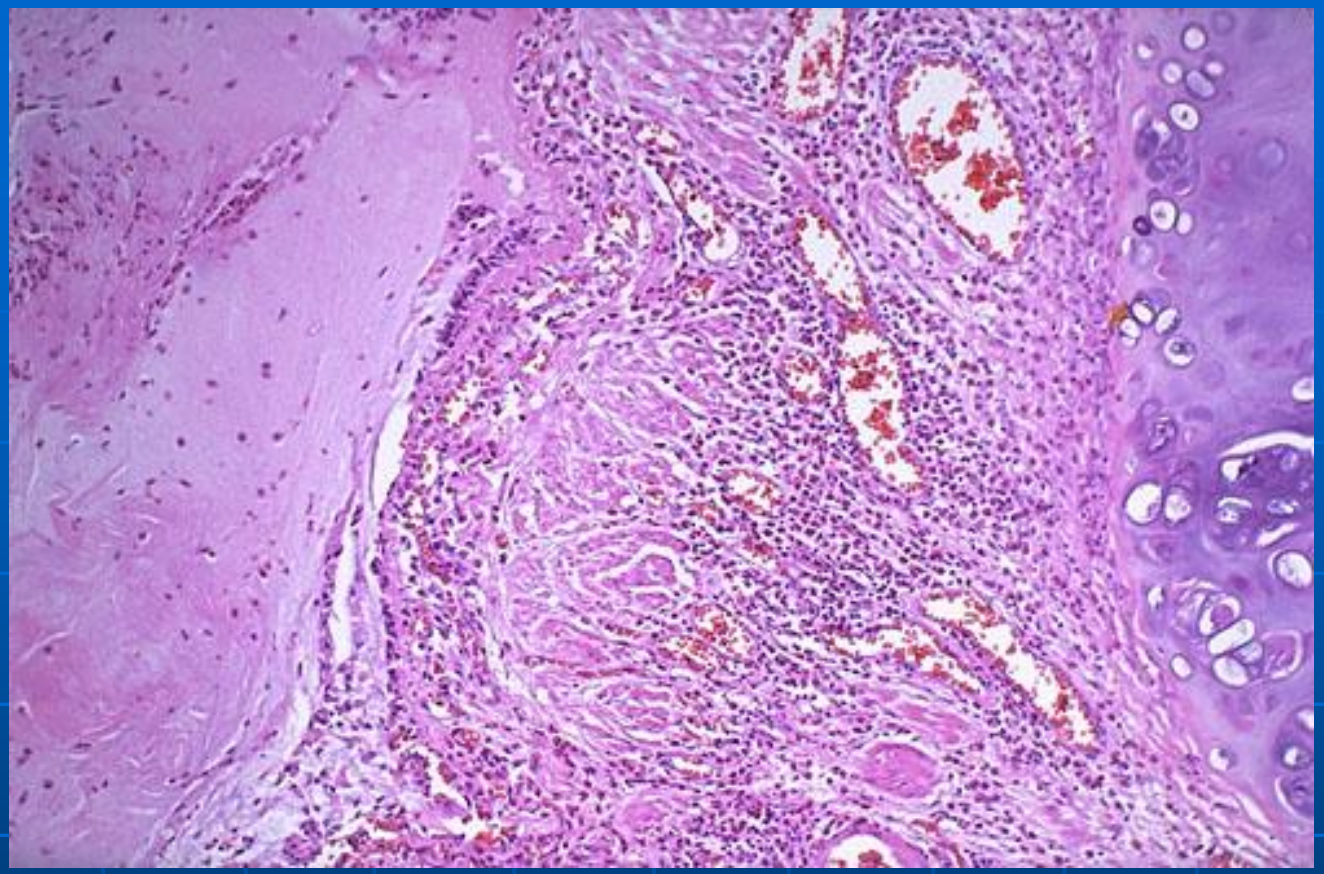
Pathology: Most information regarding the pathology of asthma has been derived from autopsies of patients who died in status asthmaticus; thus, the most severe lesions are described. On gross examination, the lungs are remarkably distended with air, and he airways are filled with thick, tenacious, and adherent mucous plugs.

Pathology: Microscopically, the plugs contain strips of epithelium and many eosinophils, the extruded granules of which coalesce to form needle-like crystals (Charcot-Leyden crystals). In some cases, the mucoid exudate forms a cast of the airways (Curschmann spirals), which may be expelled with coughing.

Asthma. A section of lung from a patient who died in status asthmaticus reveals a bronchus containing a luminal mucous plug, submucosal gland hyperplasia, and smooth muscle hyperplasia.



Asthma. Higher magnification shows hyaline thickening of the subepithelial basement membrane and marked inflammation of the bronchiolar wall, with numerous eosinophils. The mucosa exhibits an inflamed and metaplastic epithelium.



- Between the bronchial cartilage at the right and the bronchial lumen filled with mucus at the left is a submucosa widened by smooth muscle hypertrophy, edema, and inflammation (mainly eosinophils). These are changes of bronchial asthma. The peripheral eosinophil count or the sputum eosinophils can be increased during an asthmatic attack.

- This cast of the bronchial tree is formed of inspissated mucus and was coughed up by a patient during an asthmatic attack. The outpouring of mucus from hypertrophied bronchial submucosal glands, the bronchoconstriction, and dehydration all contribute to the formation of mucus plugs that can block airways in asthmatic patients.

CHRONIC OBSTRUCTIVE PULMONARY DISEASES

Chronic obstructive pulmonary disease (COPD) is a nonspecific term that describes patients with chronic increased resistance to conducting air & includes chronic obstructive bronchitis, chronic obstructive emphysema, bronchiectasis, chronic bronchiolitis.

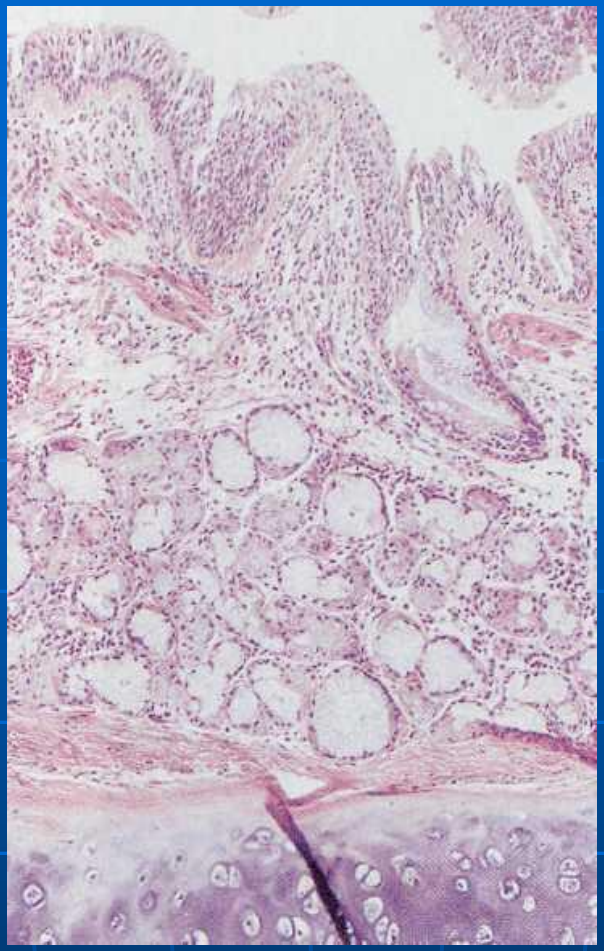
CHRONIC PULMONARY DISEASES

Restrictive pulmonary diseases show evidence for a decrease in forced expiratory volume as measured by spirometric pulmonary function tests.

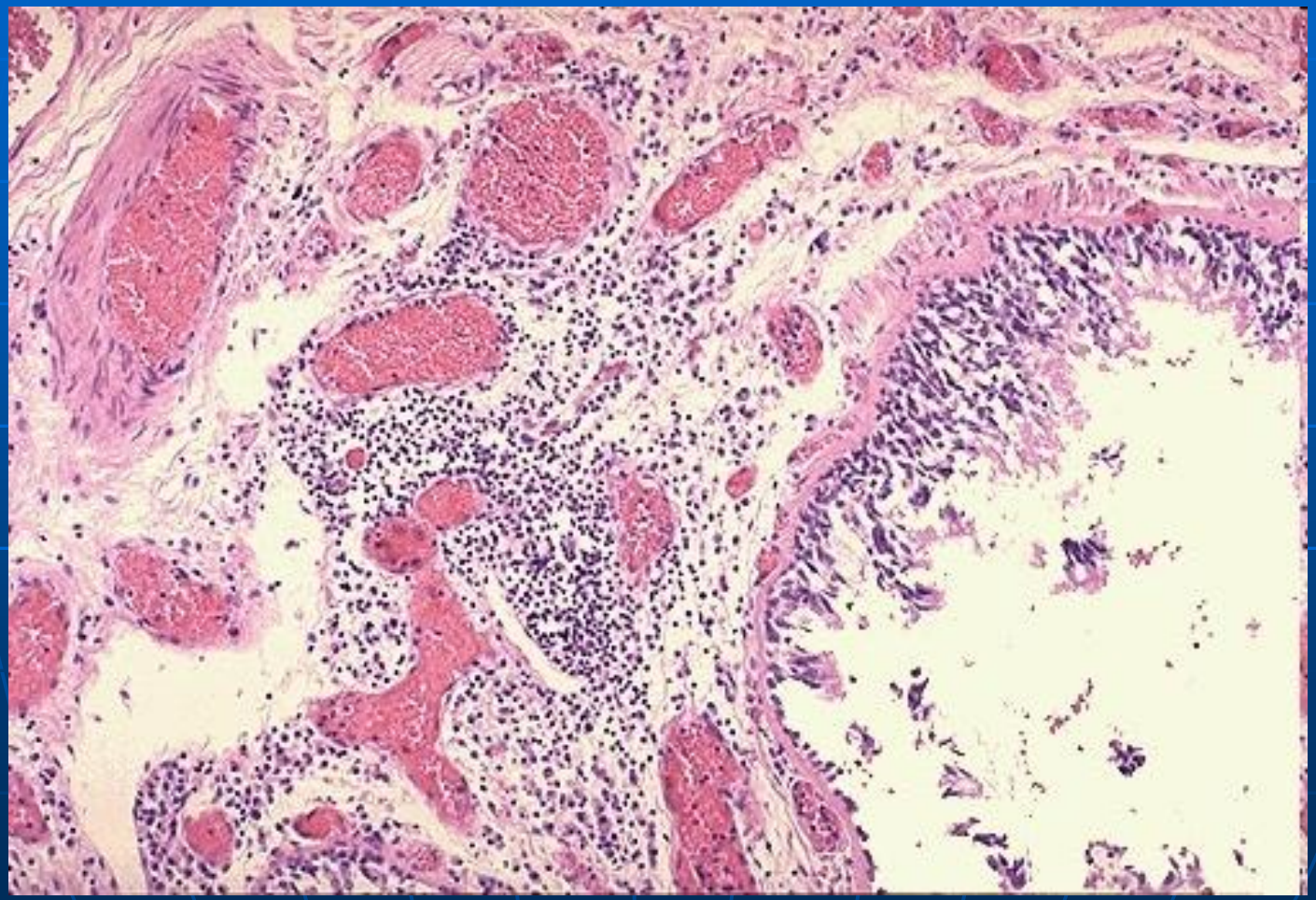
Chronic Bronchitis

Chronic bronchitis is defined clinically as the presence of a chronic, productive cough without a discernible cause for more than half of a 2-year period. **Chronic bronchitis** is primarily a disease of cigarette smokers. In fact, some 90% of all cases occur in smokers.

Pathology: Chronic bronchitis is characterized by hyperplasia and hypertrophy of the mucus-secreting cells and an increased proportion of mucous to serous cells.



Chronic bronchitis. The bronchial wall is thickened by hypertrophy and hyperplasia of the mucus-secreting glands. The Reid index is greater than 0.5. The submucosa shows increased smooth muscle and mild chronic inflammation.



Pathology: Other morphologic changes are variable and include:

(1) excess mucus in the central and peripheral airways;

(2) thickening of the bronchial wall by mucous gland enlargement and edema, which, in turn, leads to encroachment on the bronchial lumen;

(3) an increase in goblet cells;

(4) increased amounts of smooth muscle, which may indicate bronchial hyperreactivity.

Emphysema

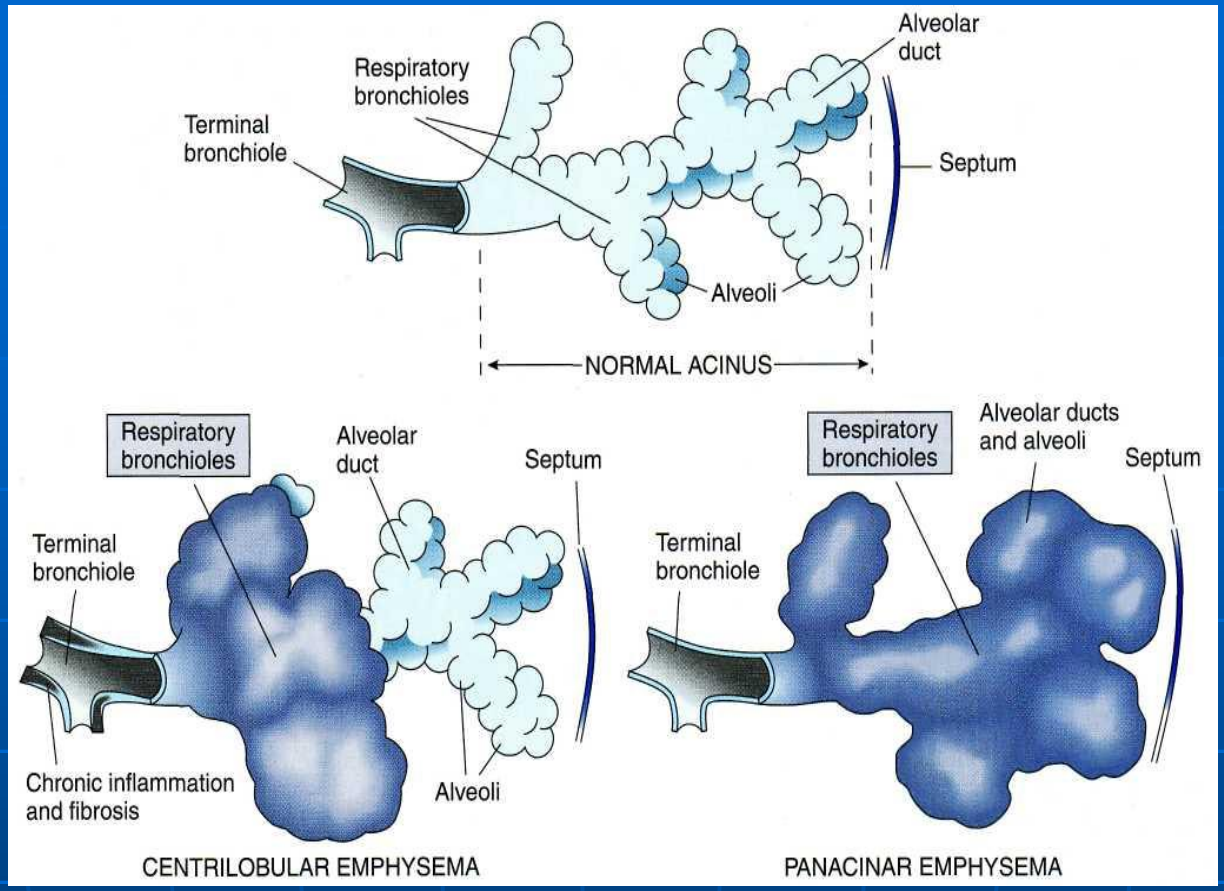
Emphysema is enlargement of the airspaces distal to the terminal bronchioles, with destruction of their walls but without fibrosis. Emphysema is classified in anatomic terms, but the classification should not obscure the fact that the severity of emphysema is more important than the type.

Pathogenesis:

The major cause of emphysema is cigarette smoking, and moderate to severe emphysema is rare in nonsmokers. Increased numbers of neutrophils, which contain serine elastase and other proteases, are found in the bronchoalveolar lavage fluid of smokers.

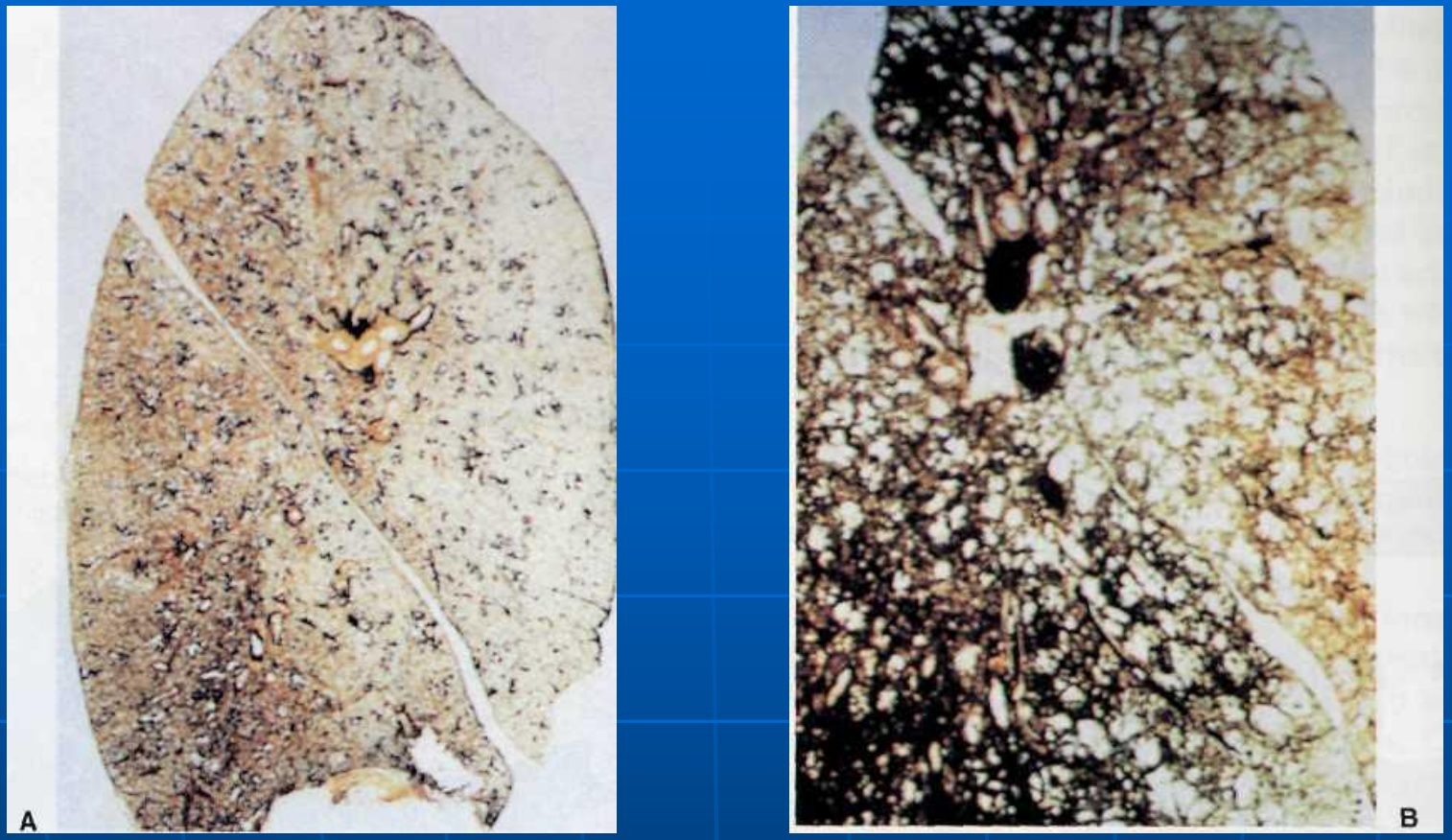
Smoking also reduces the a_1- antitrypsin activity in the lung owing to oxidation of methionine residues in the enzyme. In this way, unopposed and increased elastolytic activity leads to destruction of elastic tissue in the walls of the distal airspaces, thereby impairing elastic recoil.

Pathology: Emphysema is morphologically classified according to the location of the lesions within the pulmonary acinus



Types of emphysema. The acinus is the unit gas-exchanging structure of the lung distal to the terminal bronchiole. It consists of, in order, respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. In centrilobular (proximal acinar) emphysema, the respiratory bronchioles are predominantly involved. In paraseptal (distal acinar) emphysema, the alveolar ducts are particularly affected. In panacinar (panlobular) emphysema, the acinus is uniformly damaged.

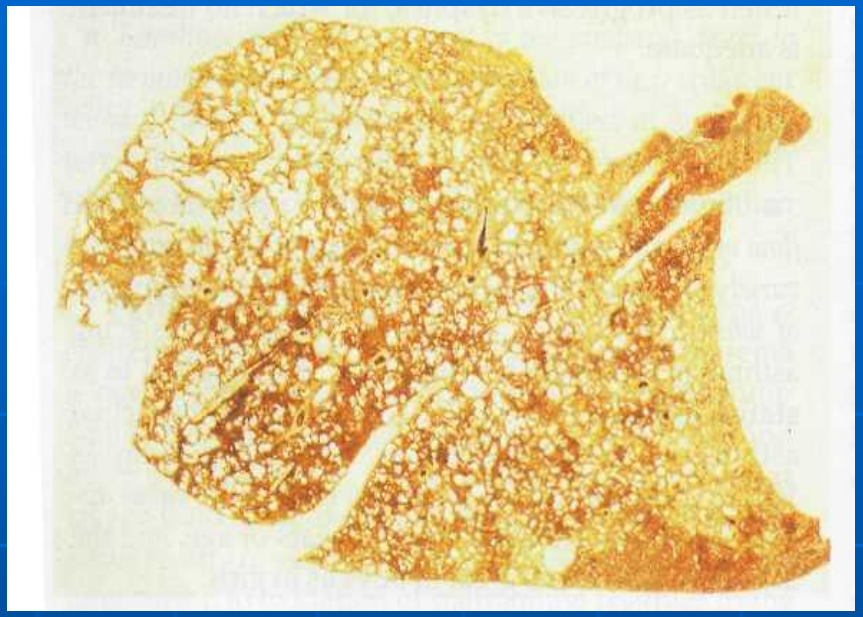
Centrilobular Emphysema. This form of emphysema is the most frequently encountered variant and the one that is usually associated both with cigarette smoking and with clinical symptoms. Centrilobular emphysema is characterized by destruction of the cluster of terminal bronchioles near the end of the bronchiolar tree in the central pulmonary lobule

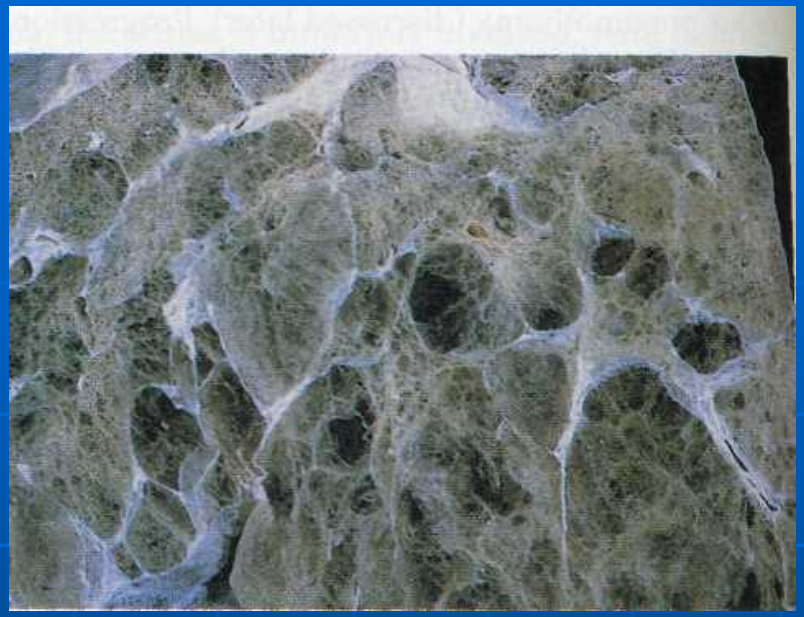


Centrilobular emphysema. (A) A whole mount of the left lung of a smoker with mild emphysema shows enlarged air spaces scattered throughout both lobes, which represent destruction of the terminal bronchioles in the central part of the pulmonary lobule. These abnormal spaces are surrounded by intact pulmonary parenchyma. (B) In a more advanced case of centrilobular emphysema, destruction of the lung has progressed to produce large, irregular air spaces.

Centrilobular Emphysema. The enlarged respiratory bronchioles form enlarged airspaces, which are separated from each other and from the lobular septa by normal alveolar ducts and alveoli. As centrilobular emphysema progresses, these distal structures may also be involved. The bronchioles proximal to the emphysematous spaces are inflamed and narrowed. Centrilobular emphysema is most severe in the upper zones of the lung, the upper lobe, and the superior segment of the lower lobe.

Panacinar Emphysema. In this type of emphysema, the acinus is uniformly involved, with destruction of the alveolar septa from the center to the periphery of the acinus



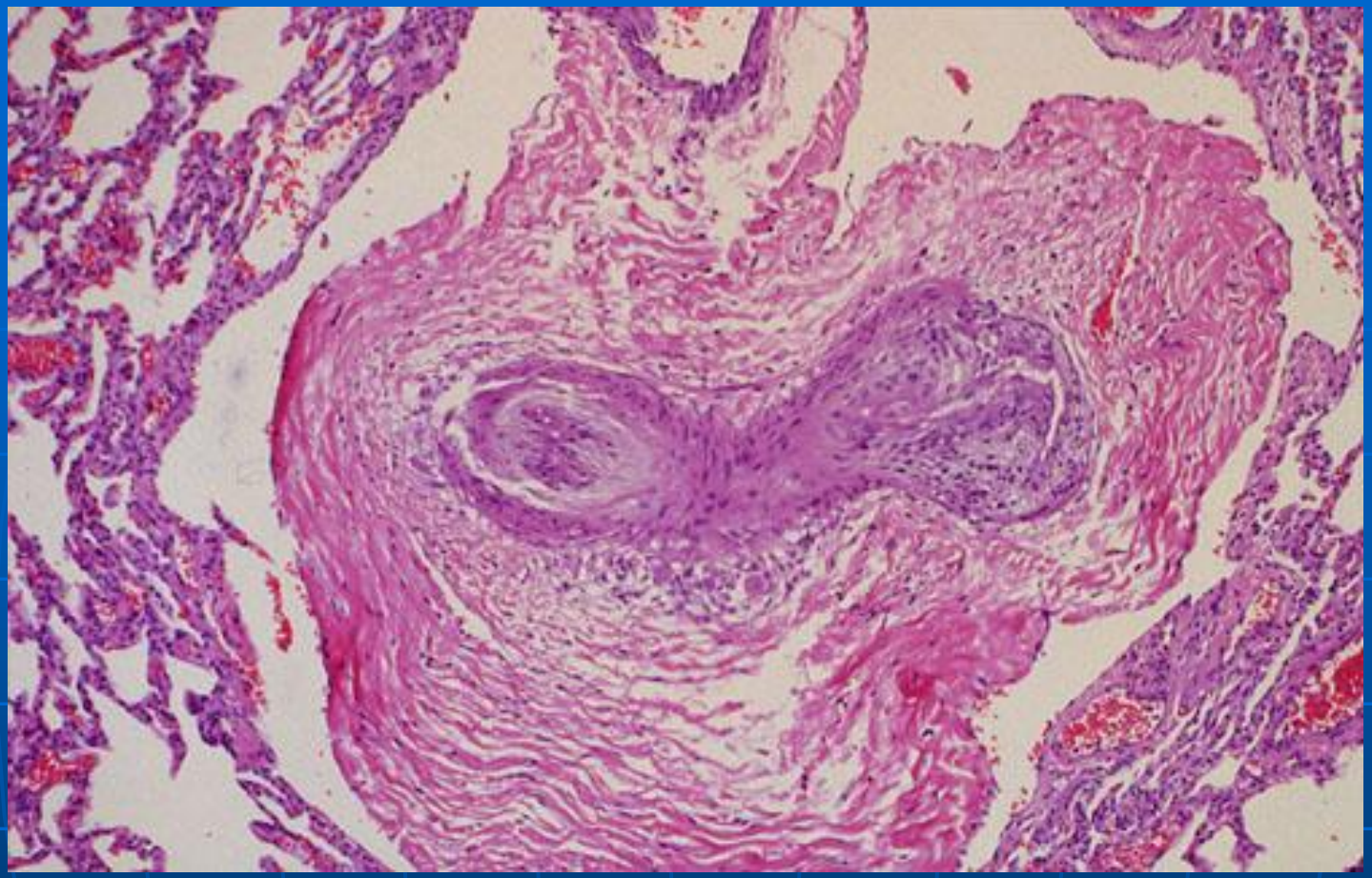


Panacinar emphysema. *(A) A* whole mount of the left lung from a patient with severe emphysema reveals widespread destruction of the pulmonary parenchyma, which in some areas leaves behind only a lacy network of supporting tissue. *(B)* The lung from this pa-tient with a_1-antitrypsin deficiency shows a panacinar pattern of emphysema. The loss of alveolar walls has resulted in markedly enlarged air spaces.

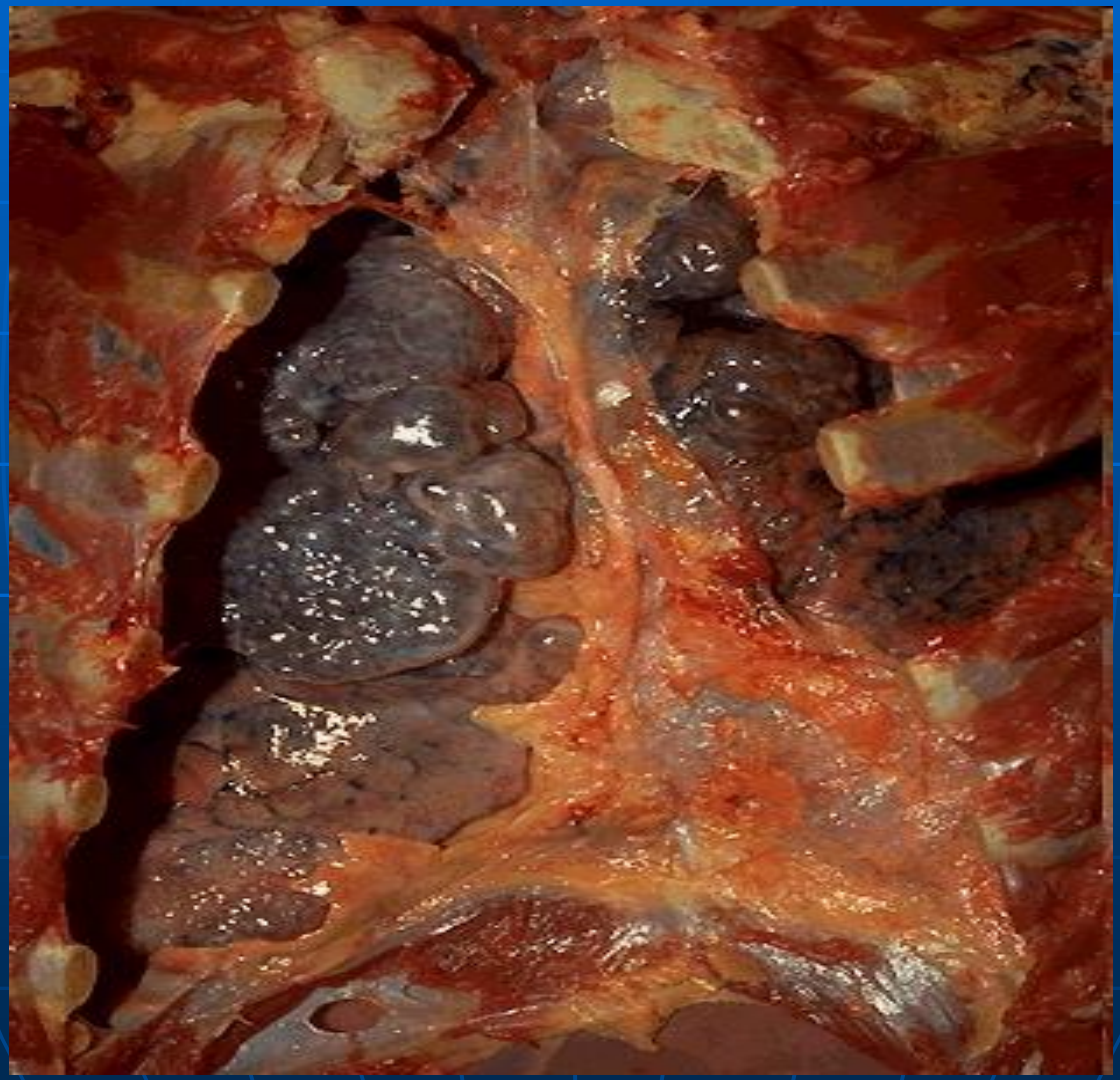
In the final stage, panacinar emphysema leaves behind a lacy network of supporting tissue ("cotton-candy lung"). This variant occurs in several different situations, but is often found in cigarette smokers in association with centrilobular emphysema. In such cases, the panacinar pattern tends to occur in the lower zones of the lung, whereas centrilobular emphysema is seen in the upper zones.

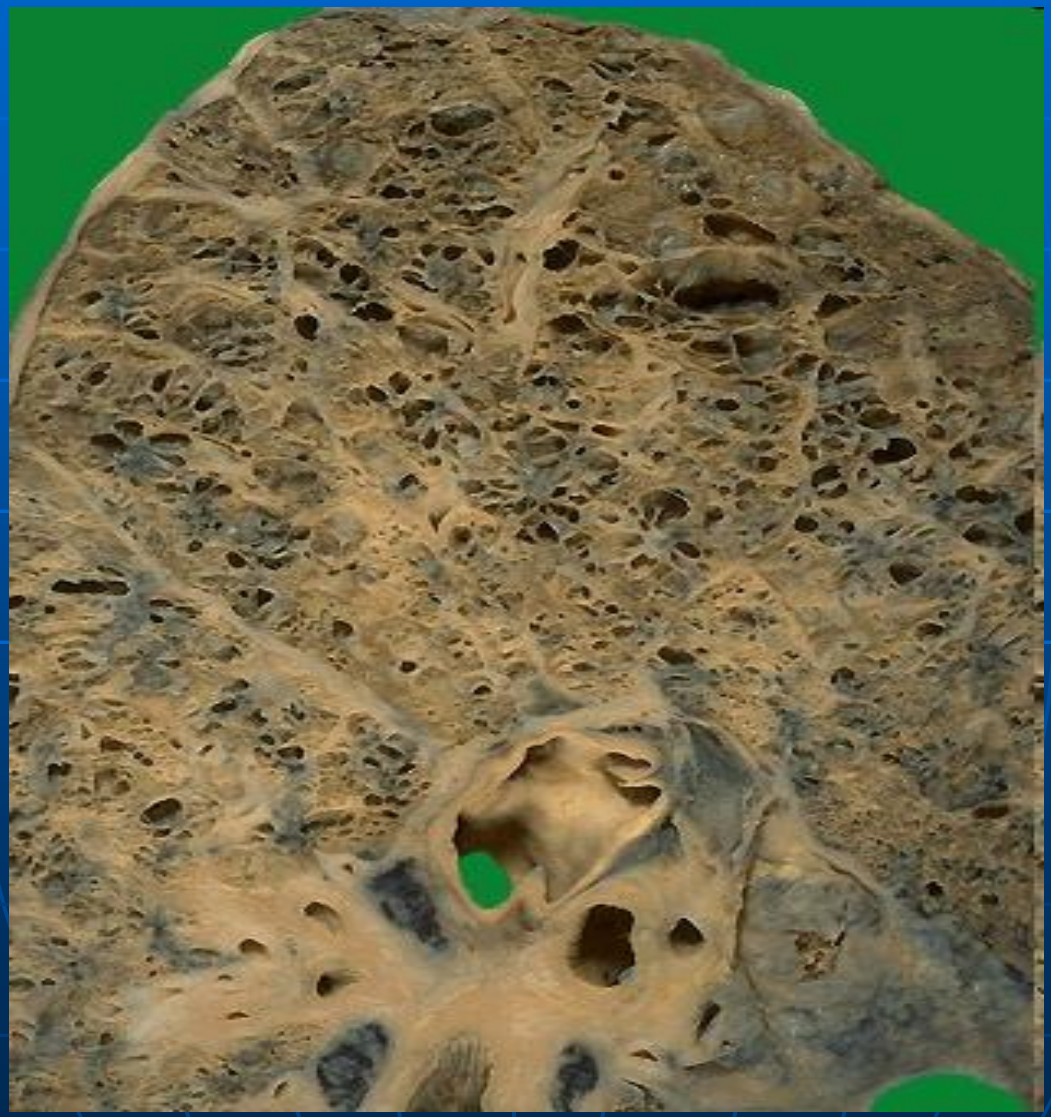
Localized Emphysema. This condition, which was previously known as paraseptal emphysema, is characterized by the destruction of alveoli and resulting emphysema in only one or, at most, a few locations, with the remainder of the lungs being normal.

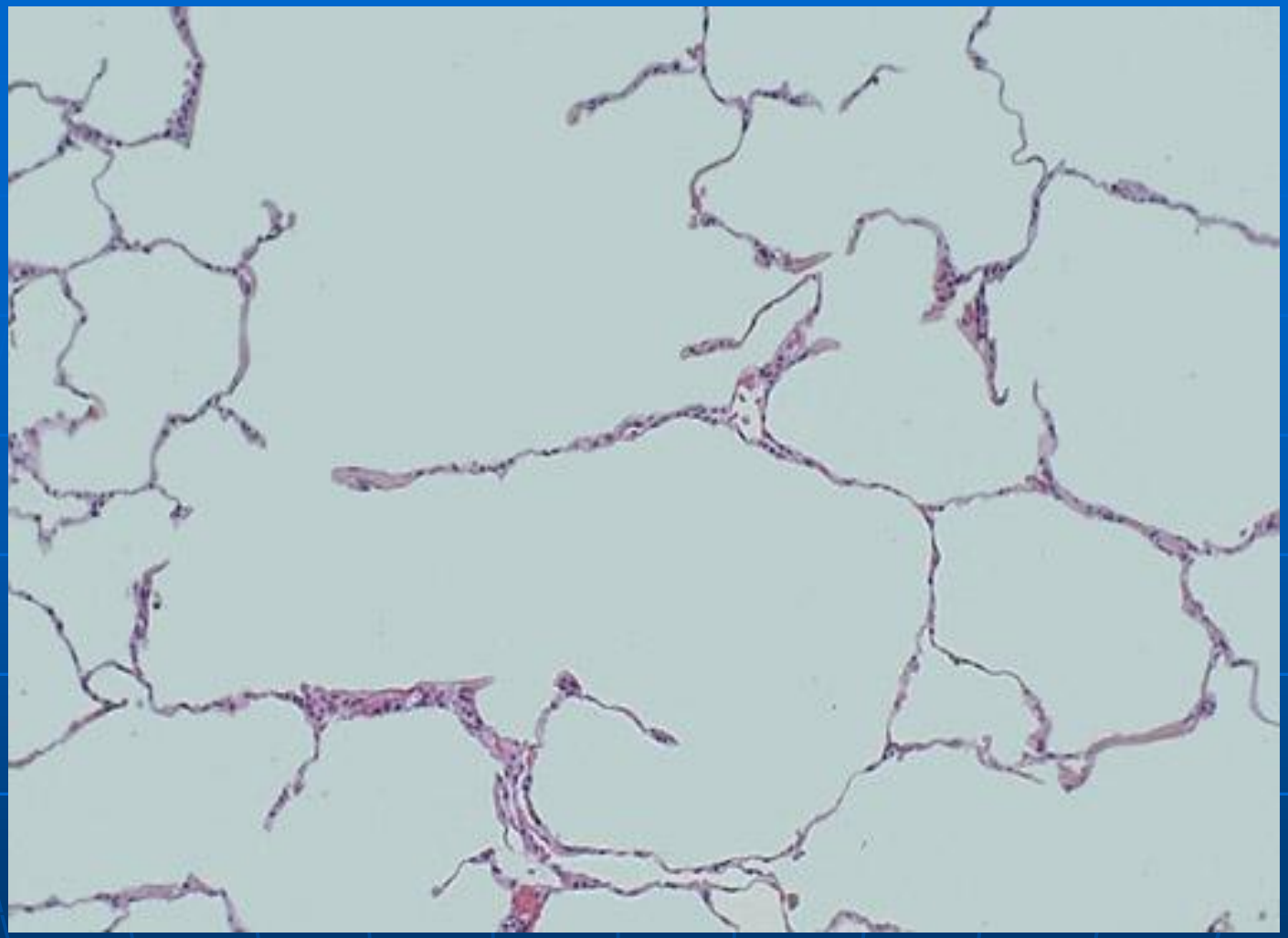
Although it has no clinical significance itself, rupture of an area of localized emphysema produces spontaneous pneumothorax. Progression of localized emphysema can result in a large area of destruction, termed a **bulla.** Bullae range in size from as small as 2 cm to large lesions that occupy an entire hemithorax.



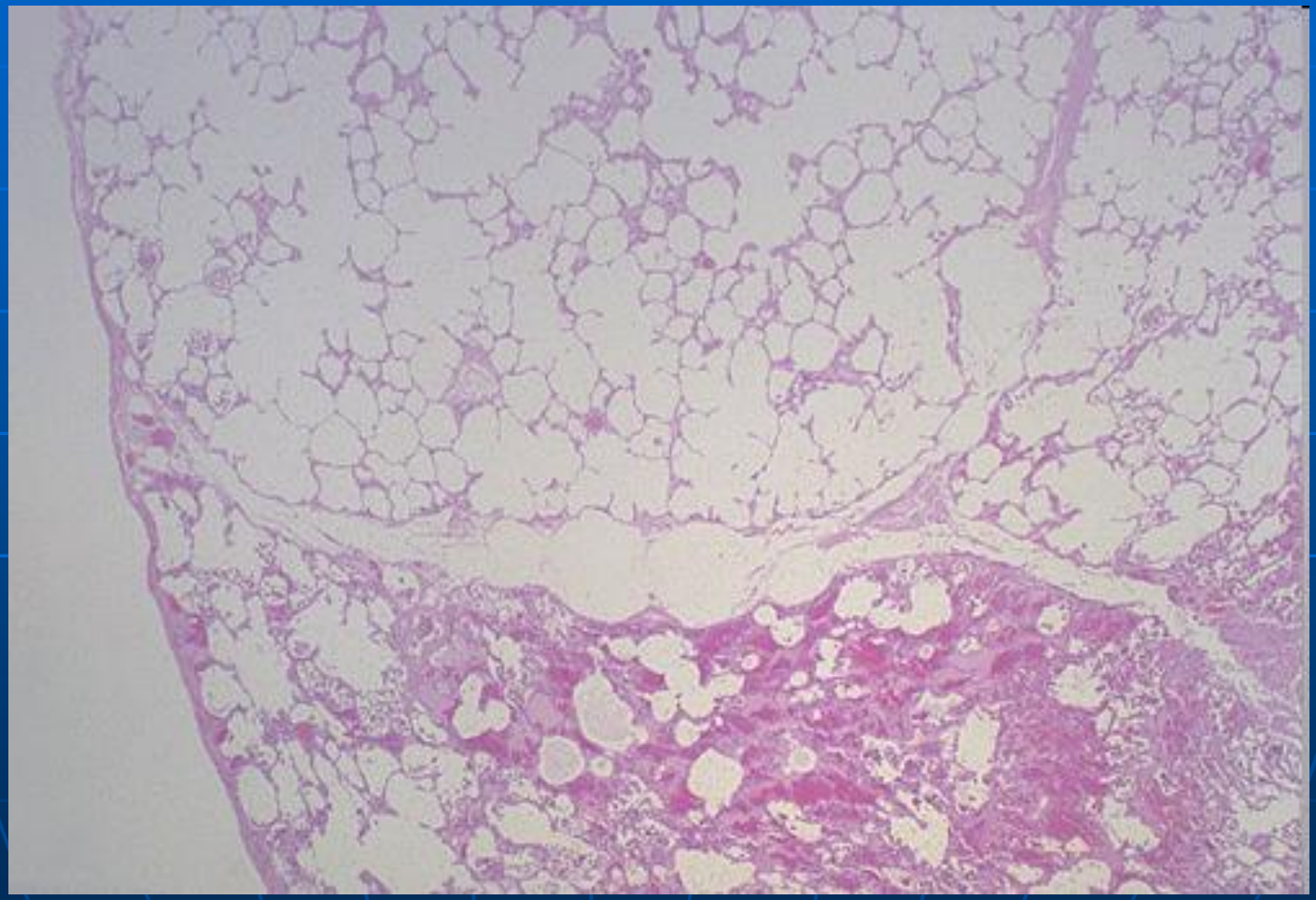
Both restrictive and obstructive lung diseases can affect the pulmonary arterial circulation. The loss of normal lung parenchyma leads to pulmonary hypertension that leads to thickening of the small arteries along with reduplication to form a plexiform lesion, as seen here in a peripheral pulmonary artery.







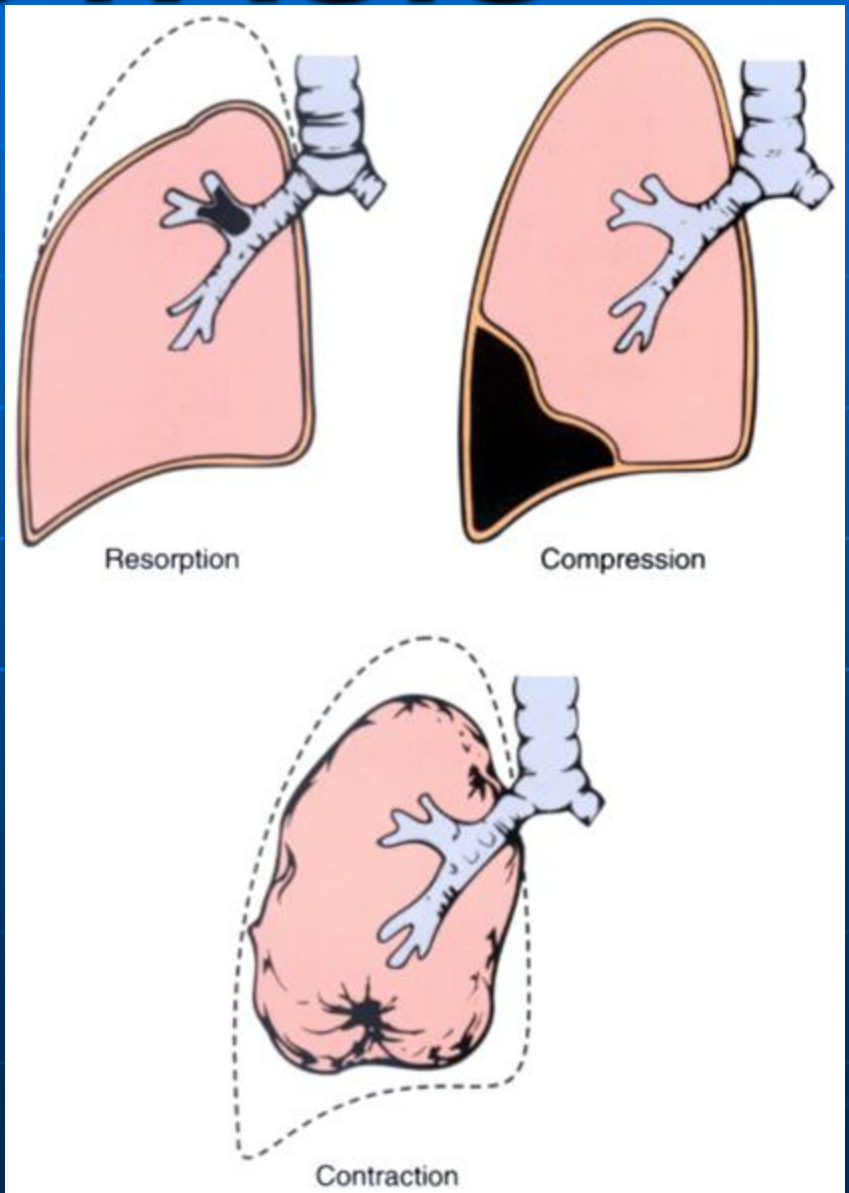
Microscopically at low magnification, the loss of alveolar walls with emphysema is demonstrated. Remaining airspaces are dilated.

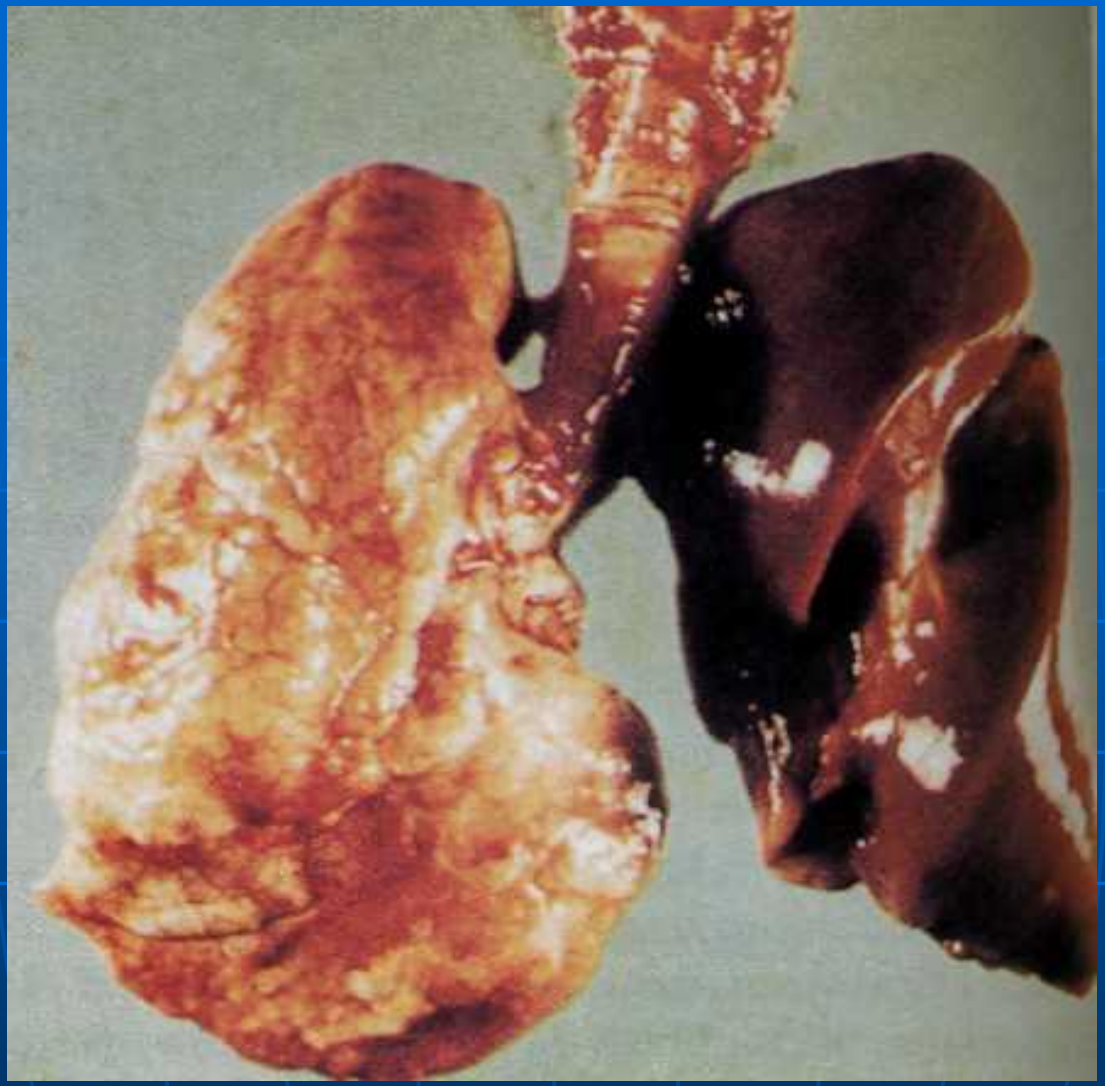


Atelectasis is the collapse of expanded lung tissue. If the supply of air is obstructed, the loss of gas from the alveoli to the blood leads to collapse of the af-fected region. Atelectasis is an important postoperative complication of abdominal surgery, occurring because of mucous obstruction of a bronchus and diminished respiratory movement, which, in turn, occurs because of postoperative pain.

ATALECTASIS

- INCOMPLETE EXPANSION
- COLLAPSE





Atelectasis. The right lung of this infant is pale and expanded by air, whereas the left lung is collapsed.

***Bronchiectasis** is the irreversible dilatation of bronchi as a consequence of destruction of the muscular and elastic elements of their walls.*

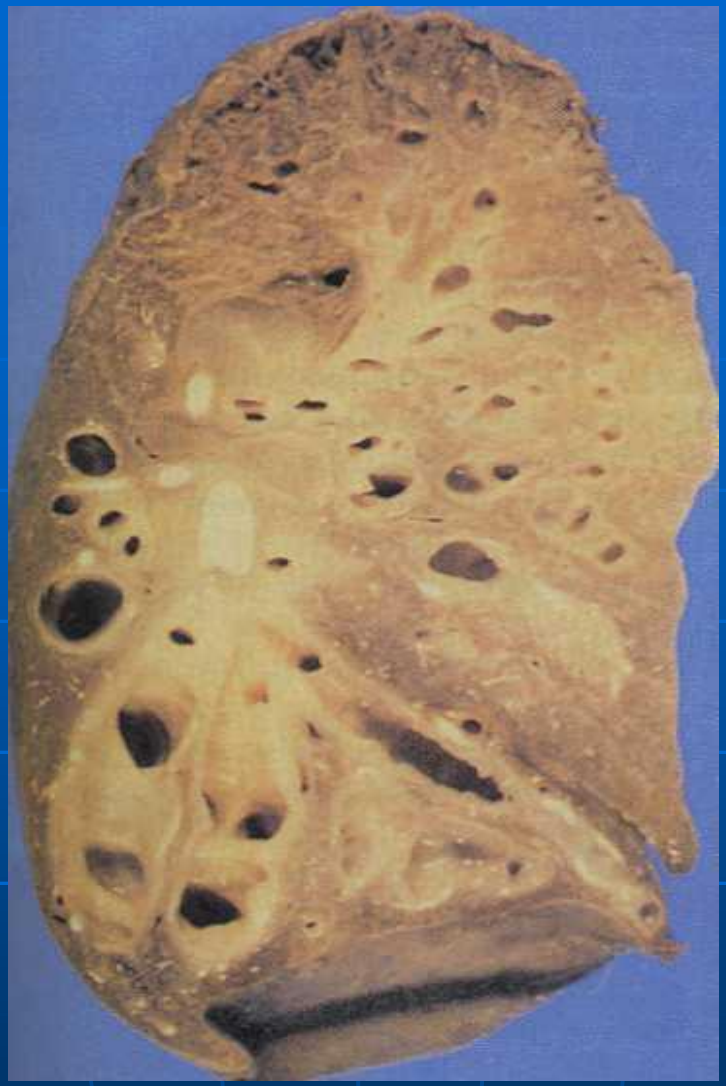
Bronchiectasis may result from mechanical obstruction of central bronchi by inhaled foreign bodies, tumors, mucous plugs in asthma, and compressive lymphadenopathy. More commonly, it is not obstructive in origin but, rather, a complication of respiratory infections or defects in the defense mechanisms that protect the airways from infection.

Localized, nonobstructive bronchiectasis was once a common disease, usually resulting from childhood bronchopulmonary infections such as measles, pertussis, or other bacterial infections. Although vaccines and antibiotics have reduced the frequency of bronchiectasis, one-half to two-thirds of all cases still follow a bronchopulmonary infection.

Generalized bronchiectasis (nonobstructive) is, for the most part, secondary to inherited impairments in host defense mechanisms or acquired conditions that permit introduction of infectious organisms into the airways.

Pathology

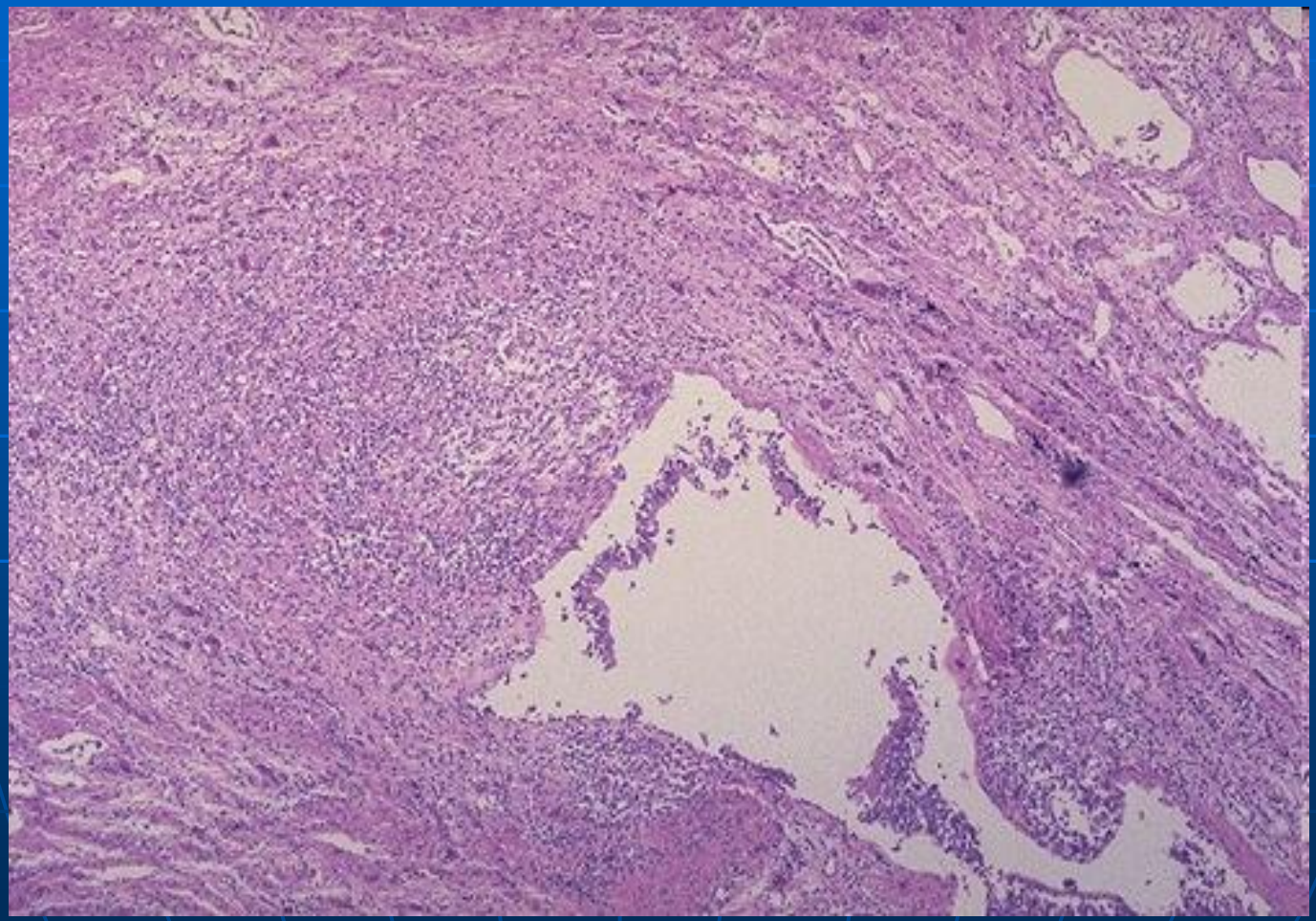
Generalized bronchiectasis is usually bilateral and most common in the lower lobes.
Localized bronchiectasis may be situated wherever the obstruction or infection occurred.



Bronchiectasis. The resected upper lobe shows widely dilated bronchi, with thickening of the bronchial walls and collapse and fibrosis of the pulmonary parenchyma


METRIC 1
2
3

Pathology: The epithelium displays a loss of the normal, pseudostratified appearance and may be denuded, with only the basal cells remaining. The basal cells are hyperplastic, and squamous metaplasia is seen. An increase in the number of goblet cells is also apparent.

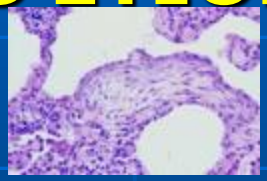


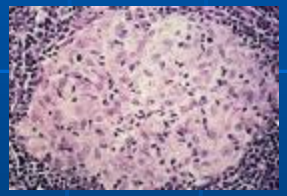
INTERSTITIAL LUNG DISEASES

A large number of pulmonary disorders are grouped as interstitial, infiltrative, or restrictive diseases, because they are characterized by inflammatory infiltrates in the interstitial space and have similar clinical and radiologic presentations.

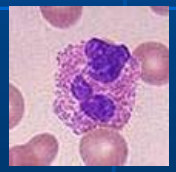
RESTRICTIVE (INFILTRATIVE)

- REDUCED COMPLIANCE, reduced gas exchange)
- Are also DIFFUSE
- HETEROGENEOUS ETIOLOGIES



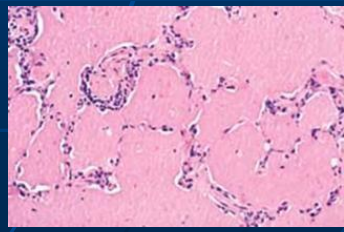


- FIBROSING
- GRANULOMATOUS
- EOSINOPHILIC



- SMOKING RELATED

- PAP (Pulmonary Alveolar Proteinosis



INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis refers to a group of immunologically mediated conditions caused by exposure to organic dusts, in which the alveoli and distal airways are preferentially involved.

INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Pathogenesis: More than 30 environmental antigens are known to produce hypersensitivity pneumonitis. Inhalation of these antigens leads to acute or chronic interstitial inflammation in the lung.

INTERSTITIAL LUNG DISEASES
Hypersensitivity Pneumonitis
Pathogenesis

Most of the responsible antigens are encountered in occupational settings, and the diseases are often labeled according to the specific occupation. For example, farmers exposed to moldy hay suffer from farmer's lung. Sugar cane workers exposed to moldy, pressed sugar cane (bagasse) acquire bagassosis; and bird breeders who come in contact with feathers, serum, and excrement of pigeons have pigeon breeder's disease.

INTERSTITIAL LUNG DISEASES
Hypersensitivity Pneumonitis
Pathogenesis

Hypersensitivity pneumonitis represents a combination of immune complex-mediated (type III) and cell-mediated (type IV) hypersensitivity reactions, although the precise contribution of each is still being debated.

INTERSTITIAL LUNG DISEASES
Hypersensitivity Pneumonitis
Pathogenesis

Whereas acute hypersensitivity pneumonitis is characterized by a neutrophilic infiltrate in the alveoli and respiratory bronchioles, the more chronic lesions display mononuclear cells and granulomas, which are typical of delayed hypersensitivity.

INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Pathology: In the acute phase of hypersensitivity pneumonitis bronchiolar necrosis, an eosinophilic infiltrate, vasculitis and interstitial pneumonia are present. Chronic disease is characterized by extensive interstitial pneumonitis, with a dense infiltrate of lymphocytes and a few plasma cells in the alveolar walls.

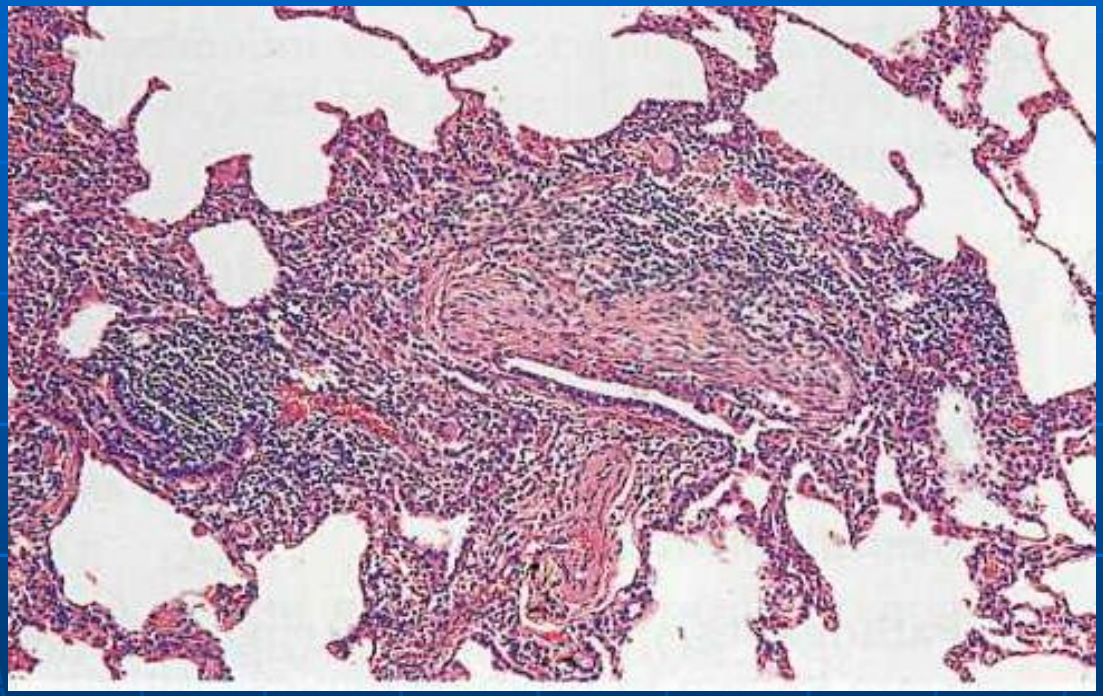
INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Pathology

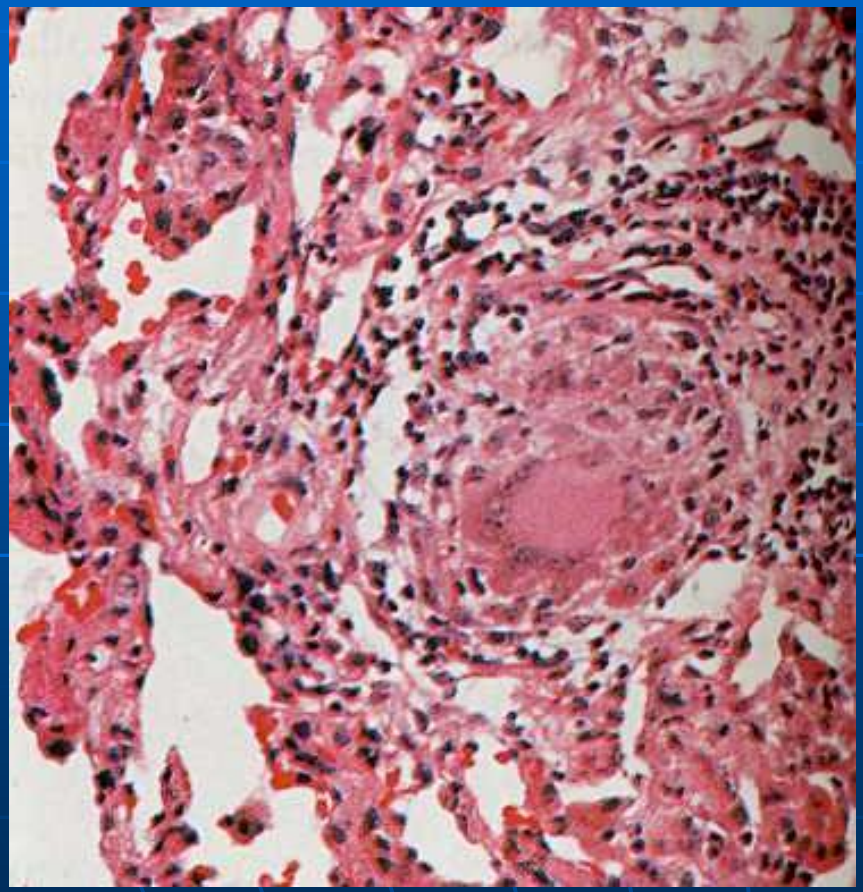
Mild, diffuse alveolar damage is usually present, with hyperplasia of type II pneumocytes. There is also a significant bronchiolar infiltrate, sometimes with bronchiolitis obliterans. Most characteristic is the presence of scattered, poorly formed granulomas that contain foreign body giant cells. In the chronic end stage, the interstitial inflammation recedes. However, fibrosis is more apparent, the lung architecture is distorted, and honeycombing occurs.

INTERSTITIAL LUNG DISEASES
Hypersensitivity Pneumonitis
Pathology



Hypersensitivity pneumonitis. A lung biopsy shows a mild peribronchiolar chronic inflammatory interstitial infiltrate, with a focus of intraluminal organizing fibrosis.

INTERSTITIAL LUNG DISEASES
Hypersensitivity Pneumonitis
Pathology



Focal poorly formed granulomas were scattered in the lung biopsy.

INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Clinical Features: Hypersensitivity pneumonitis may present as acute, subacute, or chronic pulmonary disease, depending on the frequency and intensity of exposure to the offending antigen. The prototype of hypersensitivity pneumonitis is farmer's lung, which is caused by inhalation of thermophilic actinomycetes that grow in moldy hay.

INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Clinical Features

Typically, a farm worker enters a barn where hay has been stored for winter feeding. After a lag period of several hours, the worker rapidly develops dyspnea, cough, and mild fever. The symptoms remit within 24 to 48 hours but return on reexposure and, with time, become chronic.

INTERSTITIAL LUNG DISEASES

Hypersensitivity Pneumonitis

Clinical Features

Pulmonary function studies show a restrictive pattern, which is characterized by decreased compliance, reduced diffusion capacity, and hypoxemia. In the chronic stage of hypersensitivity pneumonitis, airway obstruction may become troublesome.

INTERSTITIAL LUNG DISEASES

Usual interstitial pneumonia (UIP) *is the most common type of idiopathic interstitial pneumonitis and is characterized clinically by progressive respiratory insufficiency and pathologically by interstitial inflammation and fibrosis.* The disease affects persons of all ages, with a mean age at onset of 50 to 60 years.

INTERSTITIAL LUNG DISEASES

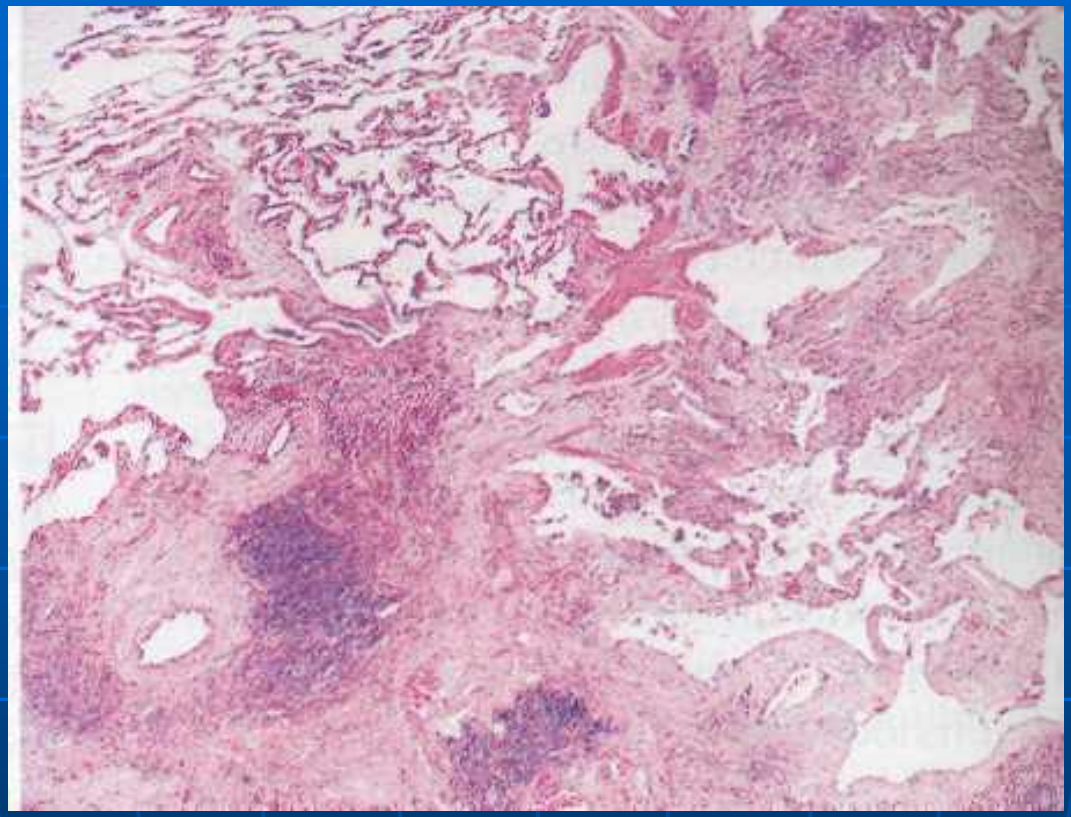
Usual Interstitial Pneumonia

Pathogenesis: It is generally held that UIP has an immunologic basis. Approximately 20% of the cases are associated with collagen vascular diseases, including rheumatoid arthritis, systemic lupus erythematosus, and progressive systemic sclerosis. The disease also occurs in the context of other autoimmune disorders, such as Hashimoto thyroiditis, primary biliary cirrhosis, idiopathic thrombocytopenic purpura, and myasthenia gravis.

INTERSTITIAL LUNG DISEASES
Usual Interstitial Pneumonia
Pathology

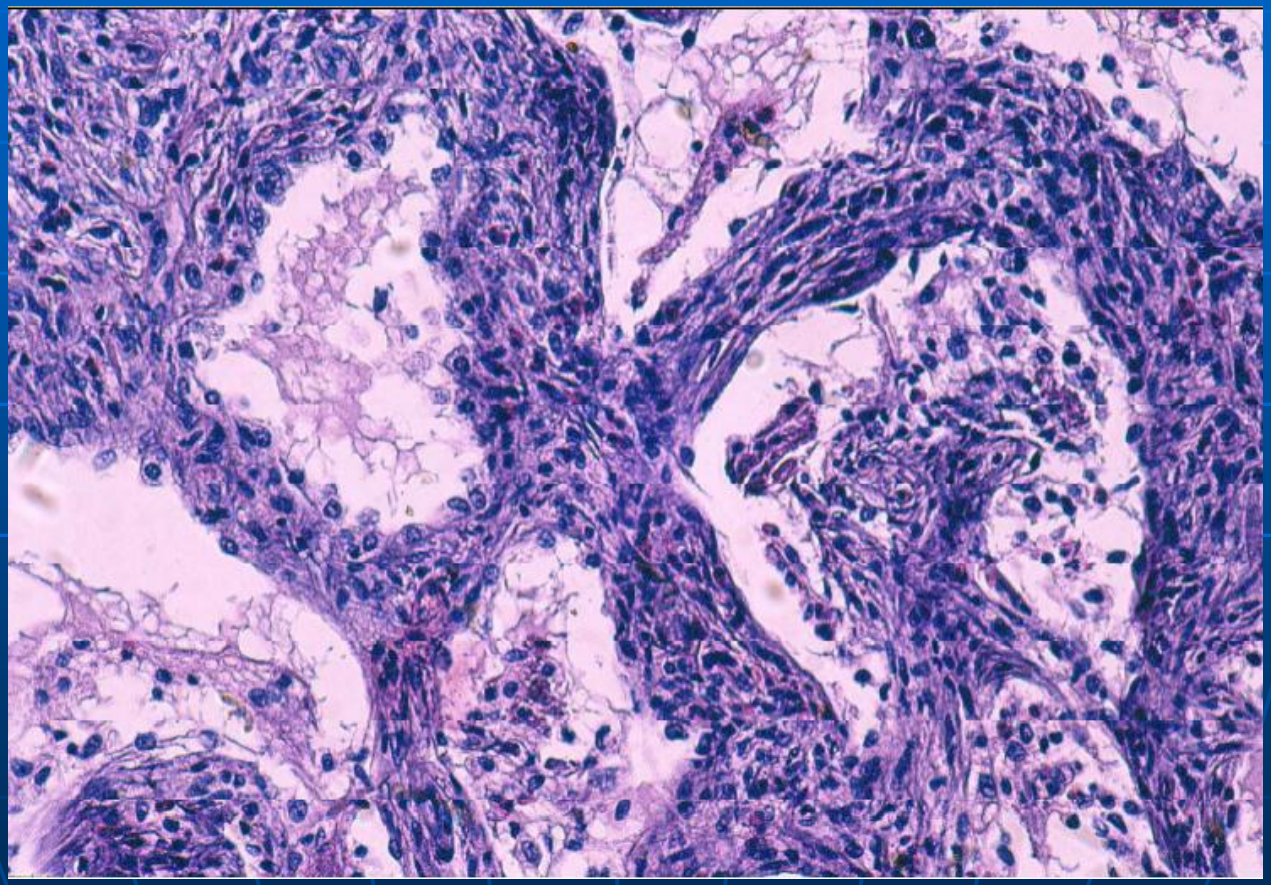
Usual interstitial pneumonitis. A gross specimen of the lung shows patchy dense scarring with extensive areas of honeycomb cystic change.

INTERSTITIAL LUNG DISEASES
Usual Interstitial Pneumonia

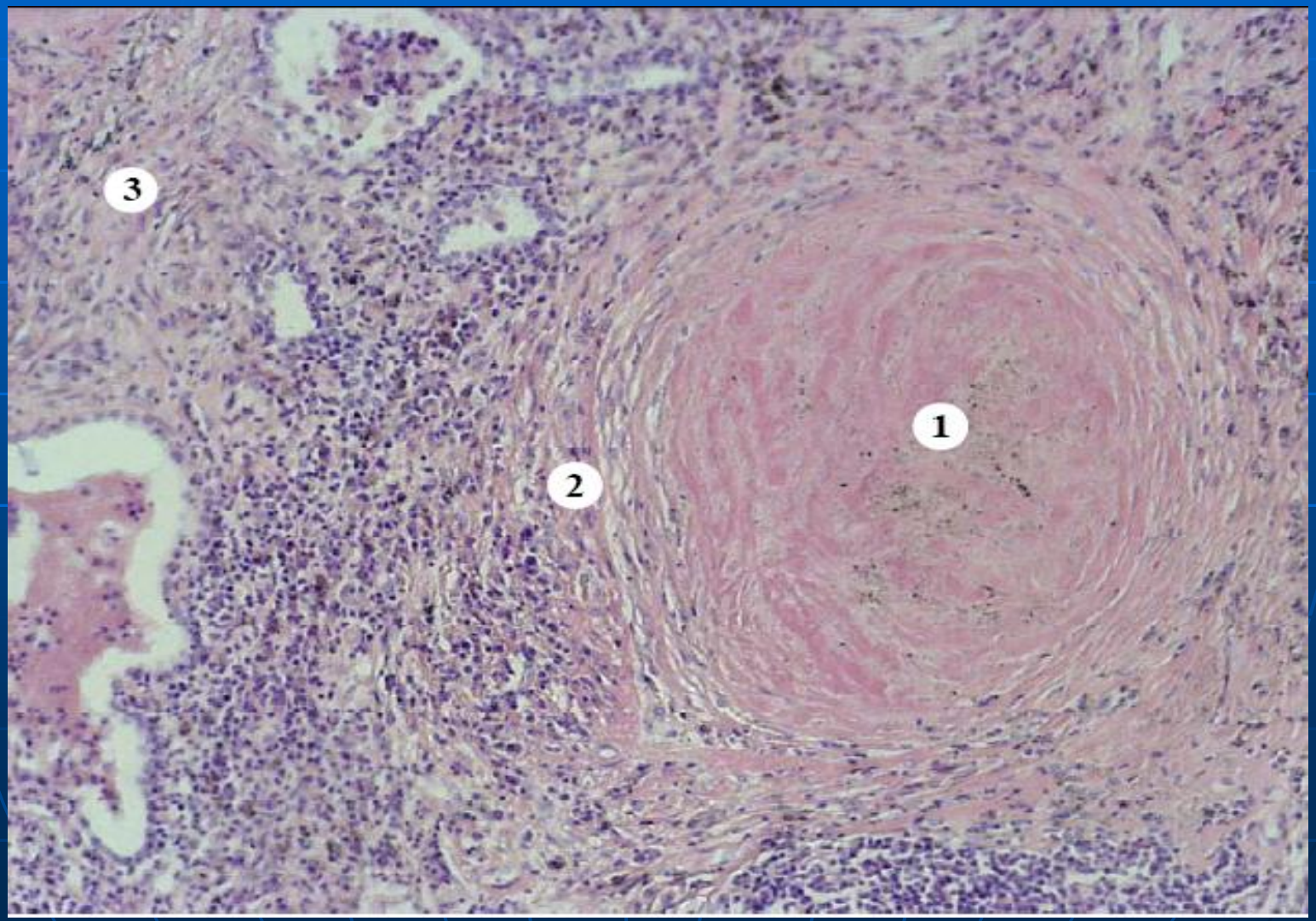


Usual interstitial pneumonitis. A microscopic view discloses patchy interstitial dense fibrosis and interstitial chronic inflammation. The areas of dense fibrosis display remodeling, with loss of the normal lung architecture.

Usual Interstitial Pneumonia



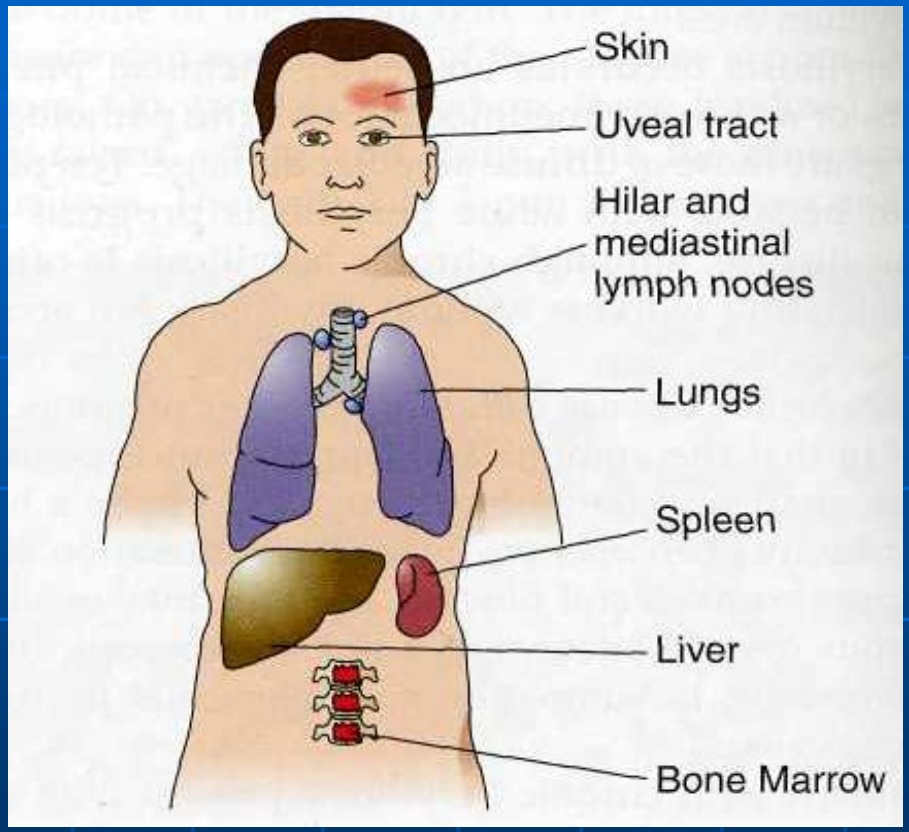
GRANULOMATOUS



INTERSTITIAL LUNG DISEASES
Sarcoidosis

Sarcoidosis is a chronic disease of unknown cause in which noncaseating granulomas occur in almost any organ of the body. The lung is most frequently involved, but the lymph nodes, skin, and eye are also common targets.

INTERSTITIAL LUNG DISEASES
Sarcoidosis



Organs commonly affected by sarcoidosis. Sarcoidosis involves many organs, most commonly the lymph nodes and lung.

INTERSTITIAL LUNG DISEASES

Sarcoidosis

Epidemiology: Sarcoidosis is a worldwide disease affecting all races and both sexes. In North America, sarcoidosis occurs much more frequently in blacks than in whites, with the ratio being approximately 15:1.

INTERSTITIAL LUNG DISEASES

Sarcoidosis

Epidemiology

The disease is often encountered in the Scandinavian countries, where the prevalence is 64 per 100,000 persons(compared with 10 per 100,000 in France and 3 per 100,000 in Poland). It has been reported that the prevalence of sarcoidosis in Irish. Nonspecific polyclonal activation of B cells by T-helper cells leads to hyperglobulinemia, which is characteristic of active sarcoidosis.

INTERSTITIAL LUNG DISEASES

Sarcoidosis

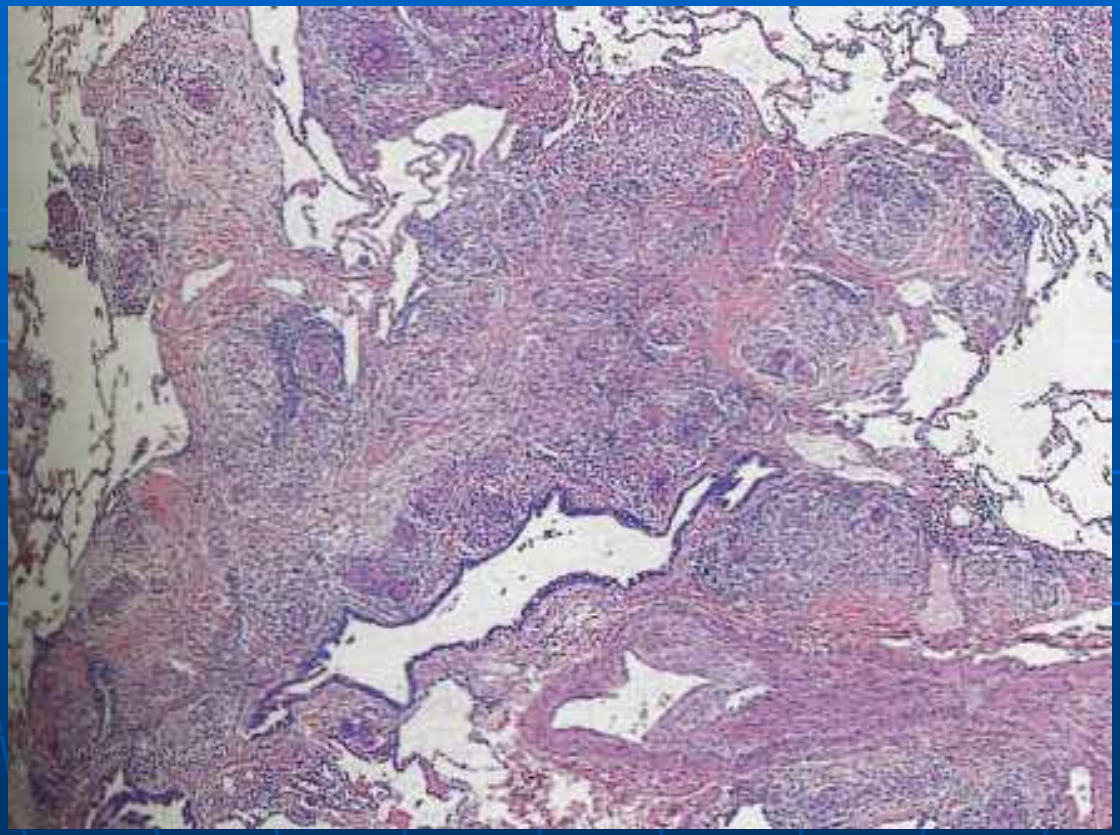
Pathogenesis: There is a consensus that sarcoidosis represents an exaggerated cellular immune response on the part of helper/inducer T lymphocytes to unknown exogenous antigens or autoantigens. These cells accumulate in the affected organs, where they secrete lymphokines and recruit macrophages that participate in formation of noncaseating granulomas.

INTERSTITIAL LUNG DISEASES

Sarcoidosis

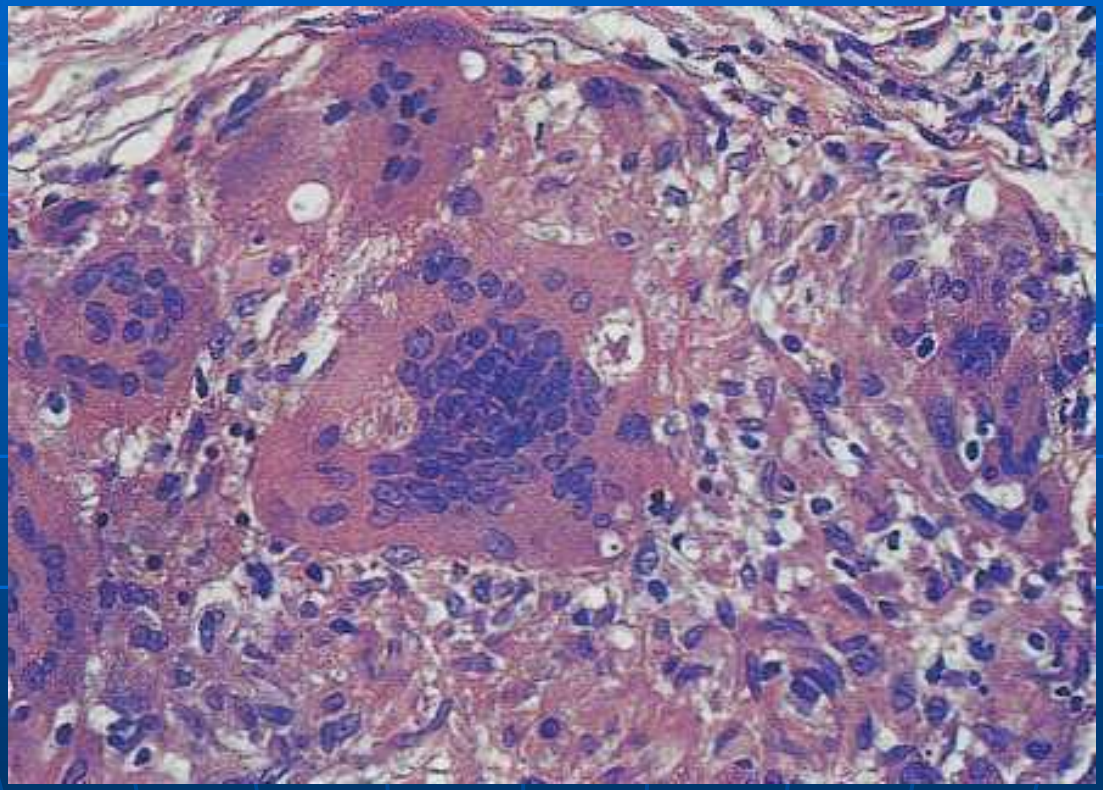
Pathology: Pulmonary sarcoidosis most commonly affects the lung and hilar lymph nodes. Histologically, multiple sarcoid granulomas are scattered in the interstitium of the lung. The central part of the granuloma may be fibrotic and surrounded by palisaded histiocytes.

INTERSTITIAL LUNG DISEASES
Sarcoidosis
Pathology



Sarcoidosis. Multiple noncaseating granulomas are present along the bronchovascular interstitium

INTERSTITIAL LUNG DISEASES
Sarcoidosis
Pathology



Sarcoidosis. Noncaseating granulomas consist of tight clusters of epithelioid macrophages and multinucleated giant cells.

PULMONARY NEOPLASMS

- Lung tumours may be primary or secondary. Both are common.

PULMONARY NEOPLASMS

- Primary carcinoma of the lung
- Most common primary malignant tumour in the world
- Directly related to cigarette smoking
- Associated with occupational exposure to carcinogens
- Overall 5-year survival rate of 4-7%
- Squamous cell, small cell,adenocarcinoma, and large cell undifferentiated types

PULMONARY NEOPLASMS

- Over 90% of primary lung tumours are carcinomas. Lung cancer is the leading cause of death from cancer in the world, with the worst overall prognosis, typically around 5% 5-year survival.This is due to the aggressive natural history of the disease,only about 10% of cases being operable at diagnosis.

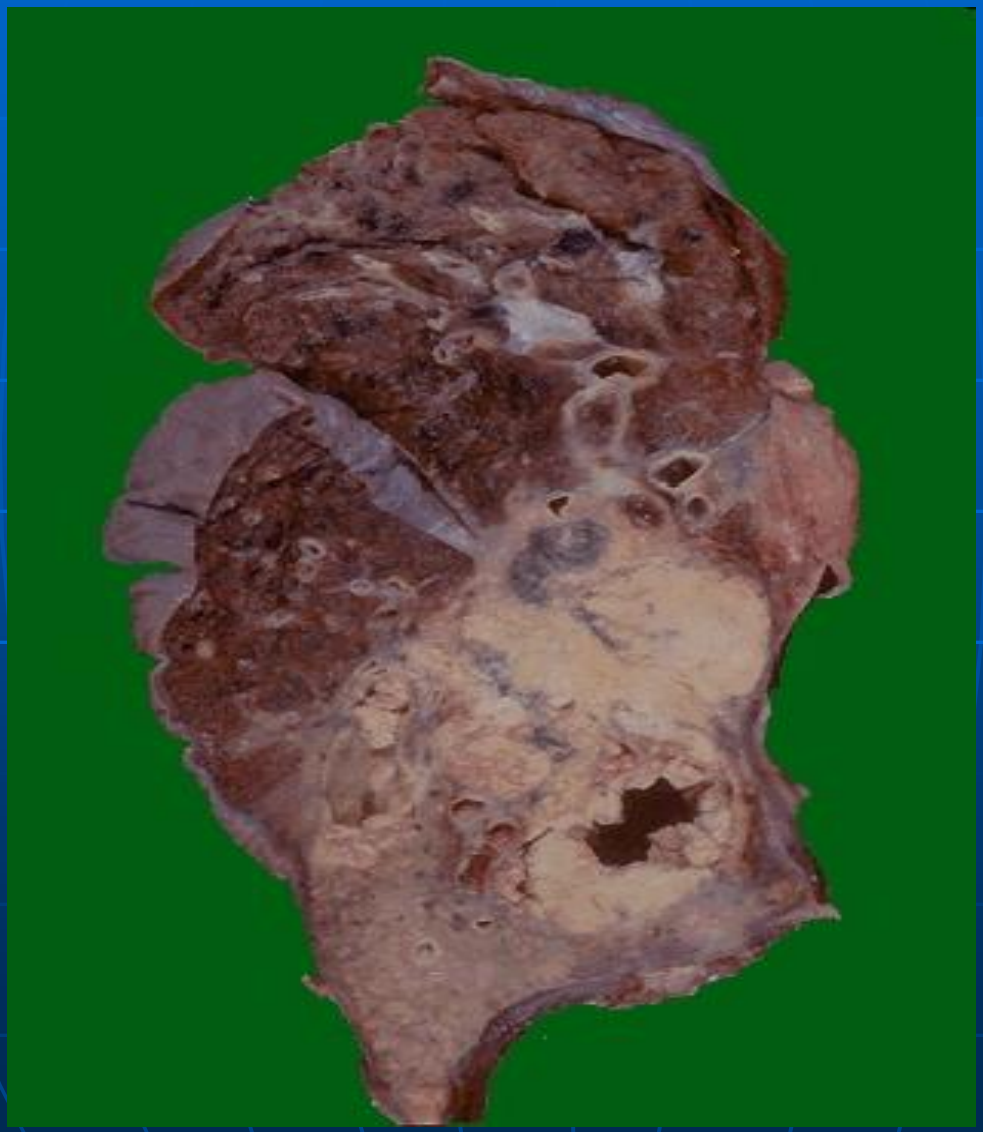
SMALL CELL CARCINOMA
squamous cell carcinoma

- *epidemiology and risk factors:* cigarette smoke; more common in men; occurs on areas of squamous metaplasia (due to irritants)
- *macroscopic features:* typically central and close to carina (frequently presenting with bronchial obstruction)

Carcinoma of the lung

Squamous Cell Carcinoma

Pathology: Most squamous cell carcinomas arise in the central portion of the lung, from the major or segmental bronchi. On gross examination, they tend to be firm, gray-white, and ulcerated lesions that extend through the bronchial wall into the adjacent parenchyma.



clinical presentation: patient may have no signs

- *signs the same as those in metastatic tumours:*
  - *cough* (80% of cases) due to infection distal to airway blocked by tumour
  - *haemoptysis* (70% of cases) due to ulceration of tumour in bronchus
  - *dyspnoea* (60% of cases) due to local extension of tumour
  - *chest pain* (40% of cases) due to involvement of pleura and chest wall
  - *wheeze* (15% of cases) due to narrowing of airway
  - *non-specific systemic signs:* weight loss, anorexia, malaise

staging tumor

- **staging tumor** - gives an indication of severity and prognosis
  - stages are classified from 1 (very good prognosis) to 4 (very bad prognosis)
  - staging is based on:
    - topography (size, direct extension, obstruction)
    - nodal stasis
    - metastasis

Carcinoma of the lung

Squamous Cell Carcinoma

Pathology

Carcinomas of the lung, of all histologic types, metastasize most frequently to the regional lymph nodes, particularly the hilar and mediastinal nodes. The most common site of extranodal metastasis is the adrenal gland, although adrenal insufficiency is distinctly uncommon. Lung cancer not infrequently presents initially as metastatic disease, with the brain, bone, and liver all being common sites.

Carcinoma of the lung

Squamous Cell Carcinoma

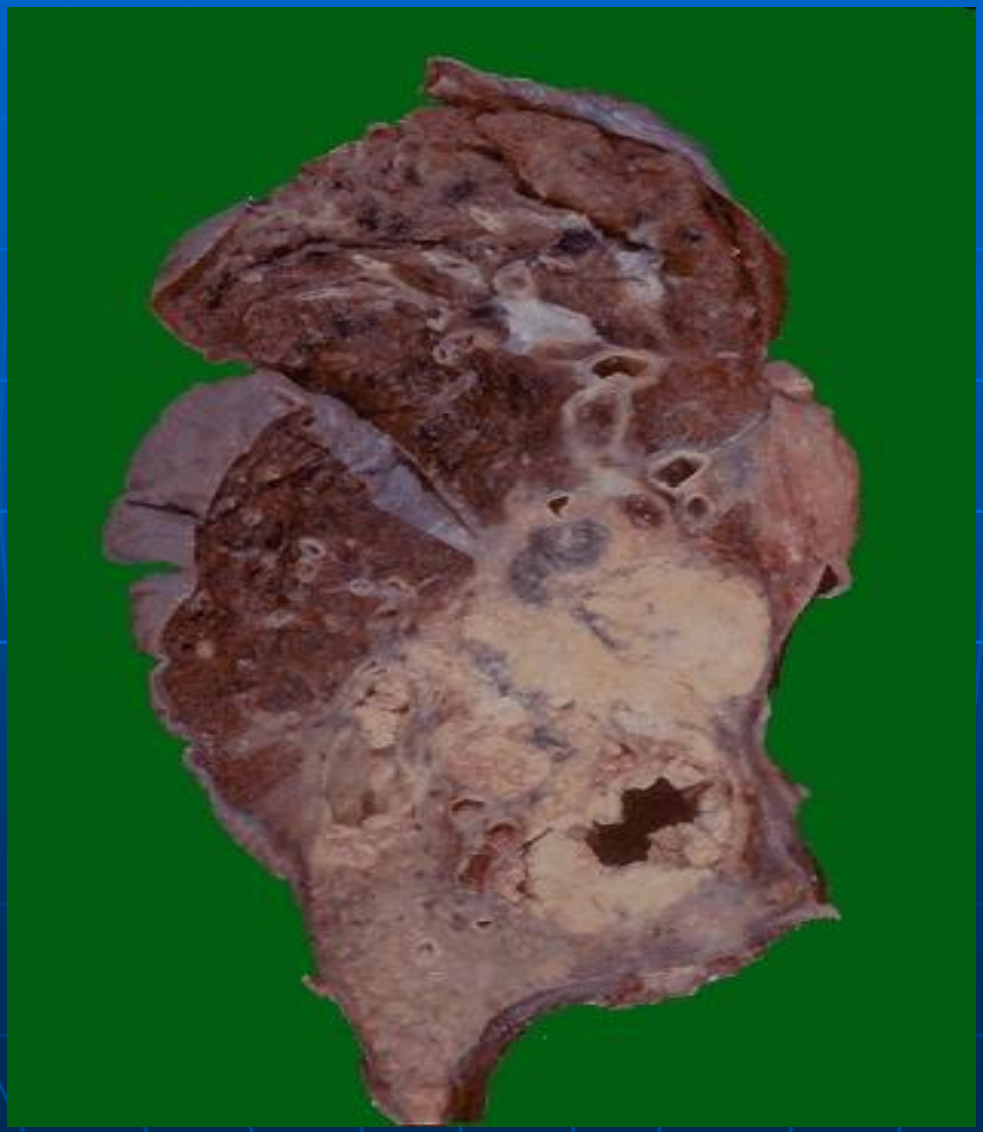
Clinical Features: Most squamous cell carcinomas present with symptoms related to their bronchial origin, including persistent cough, hemoptysis, or bronchial obstruction, with the last being accompanied by pulmonary infections (recurrent pneumonias, lung abscesses) or atelectasis.

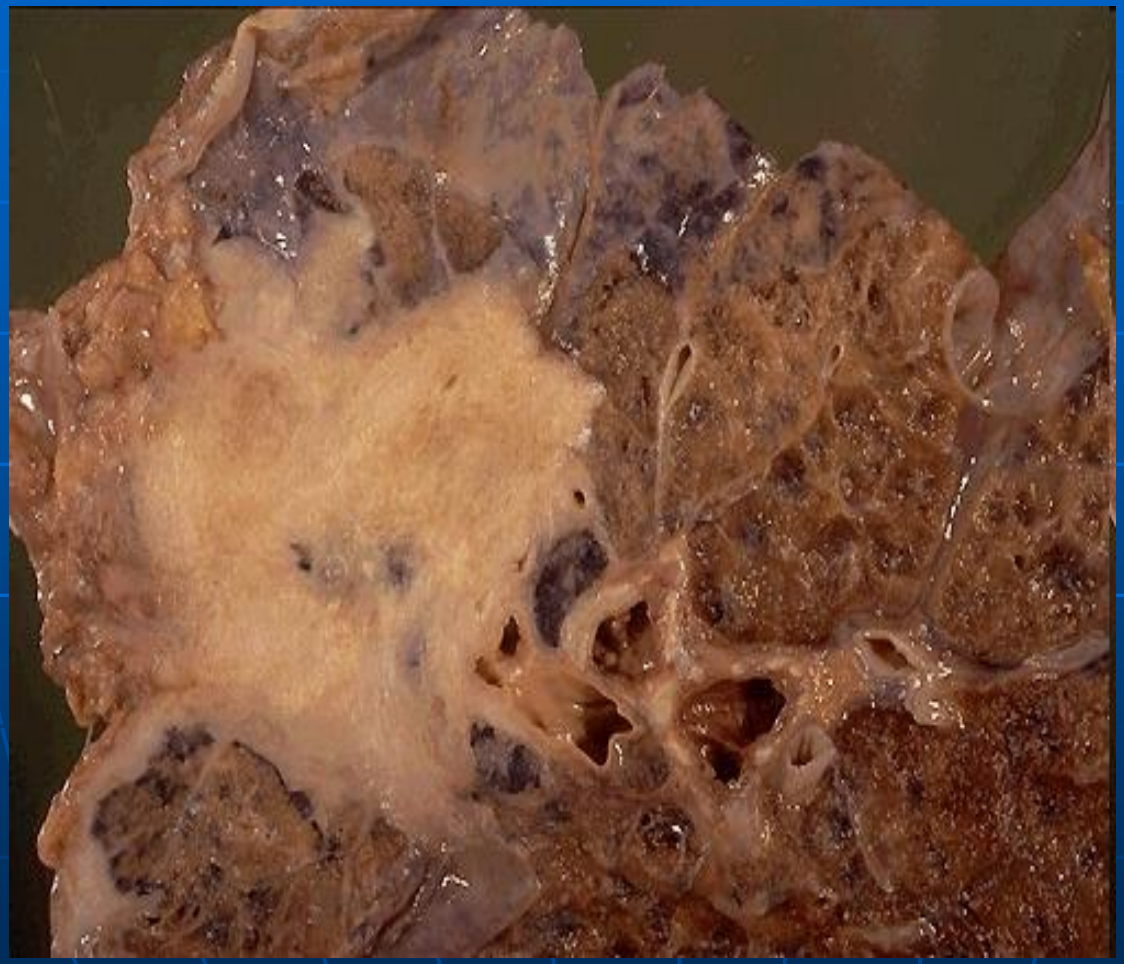
Carcinoma of the lung

Squamous Cell Carcinoma

Clinical Features

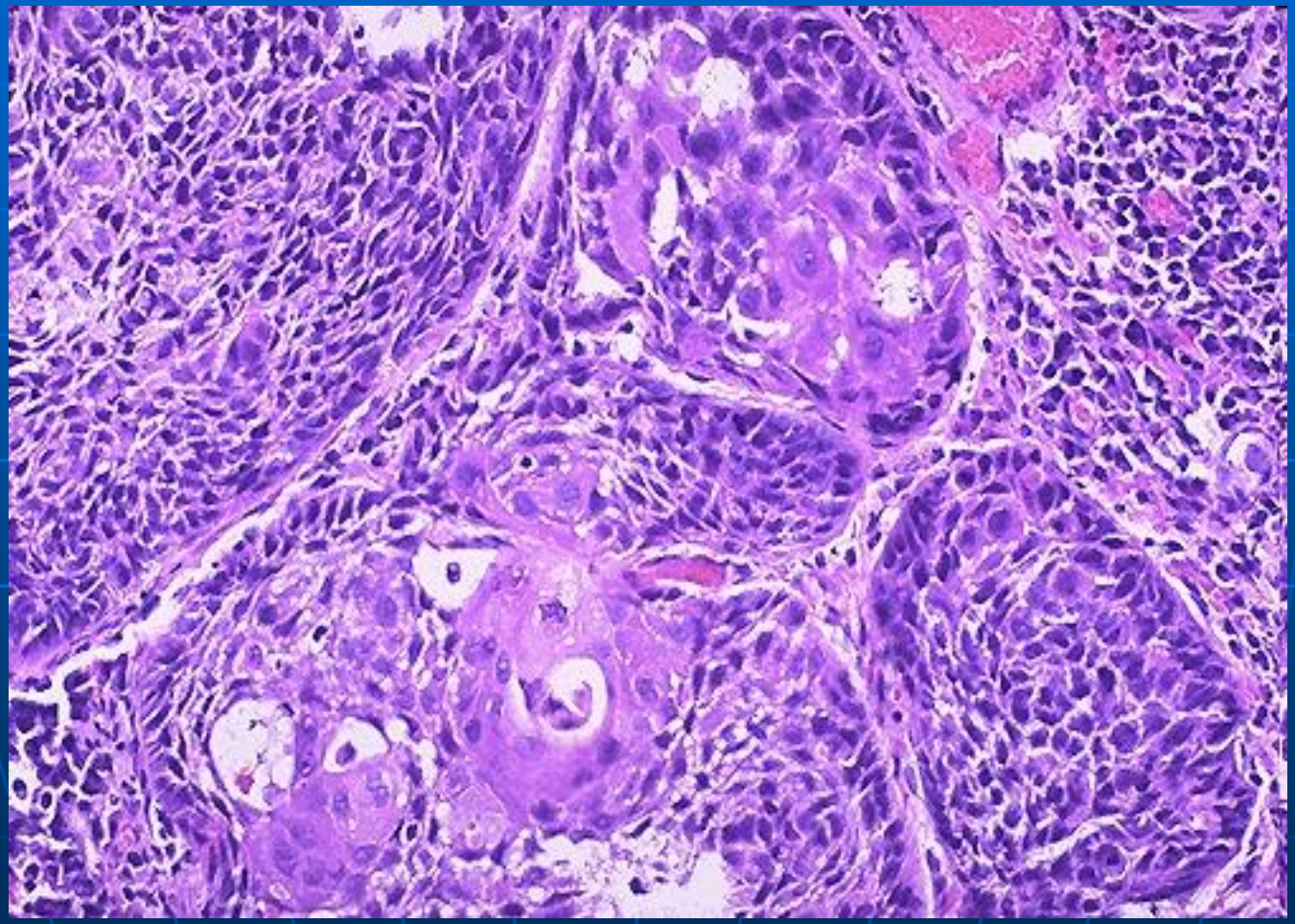
Extension of the tumor may cause compression of the superior vena cava, thereby resulting in severe venous and lymphatic congestion of the upper body (superior vena cava syndrome).

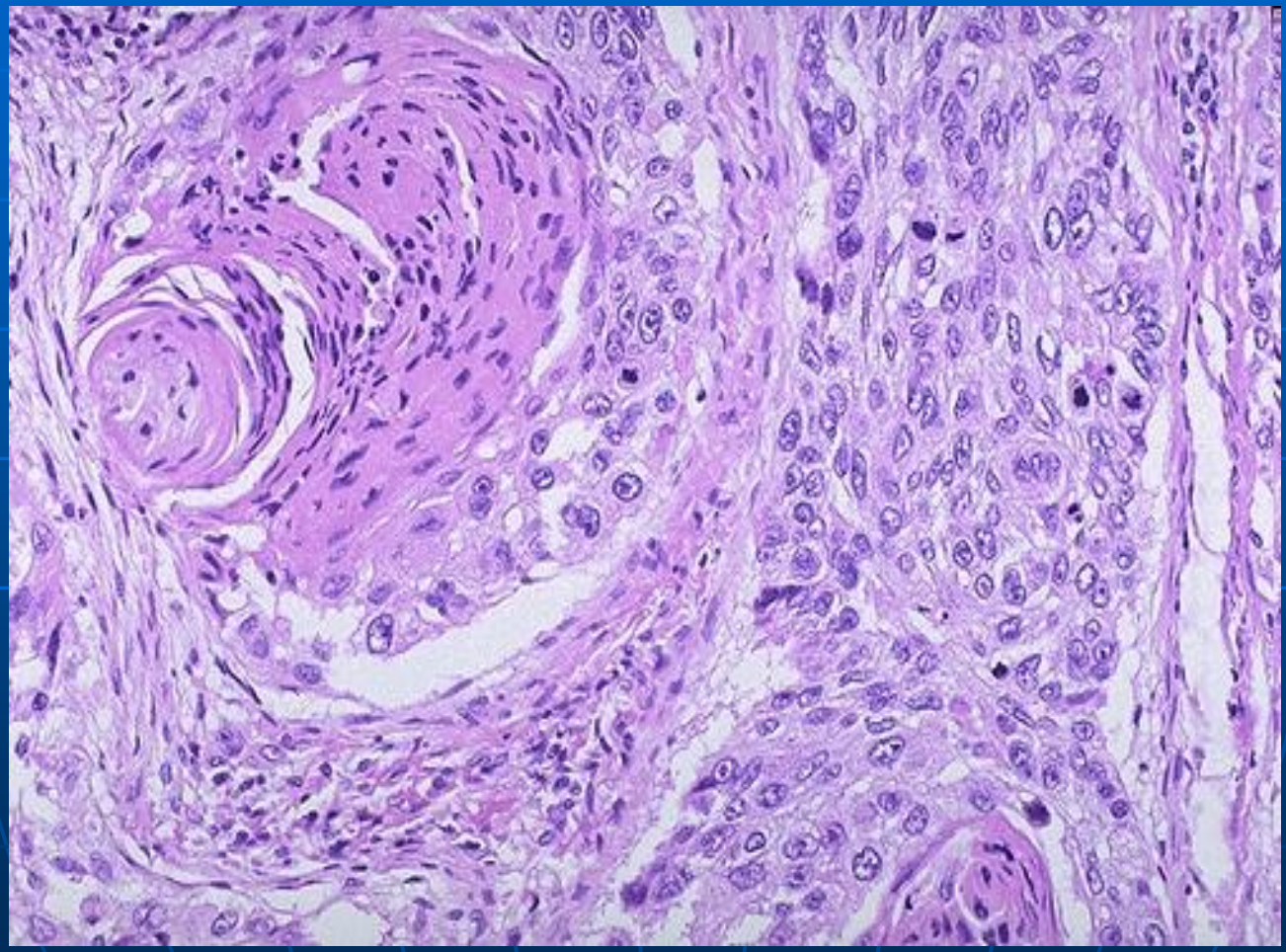


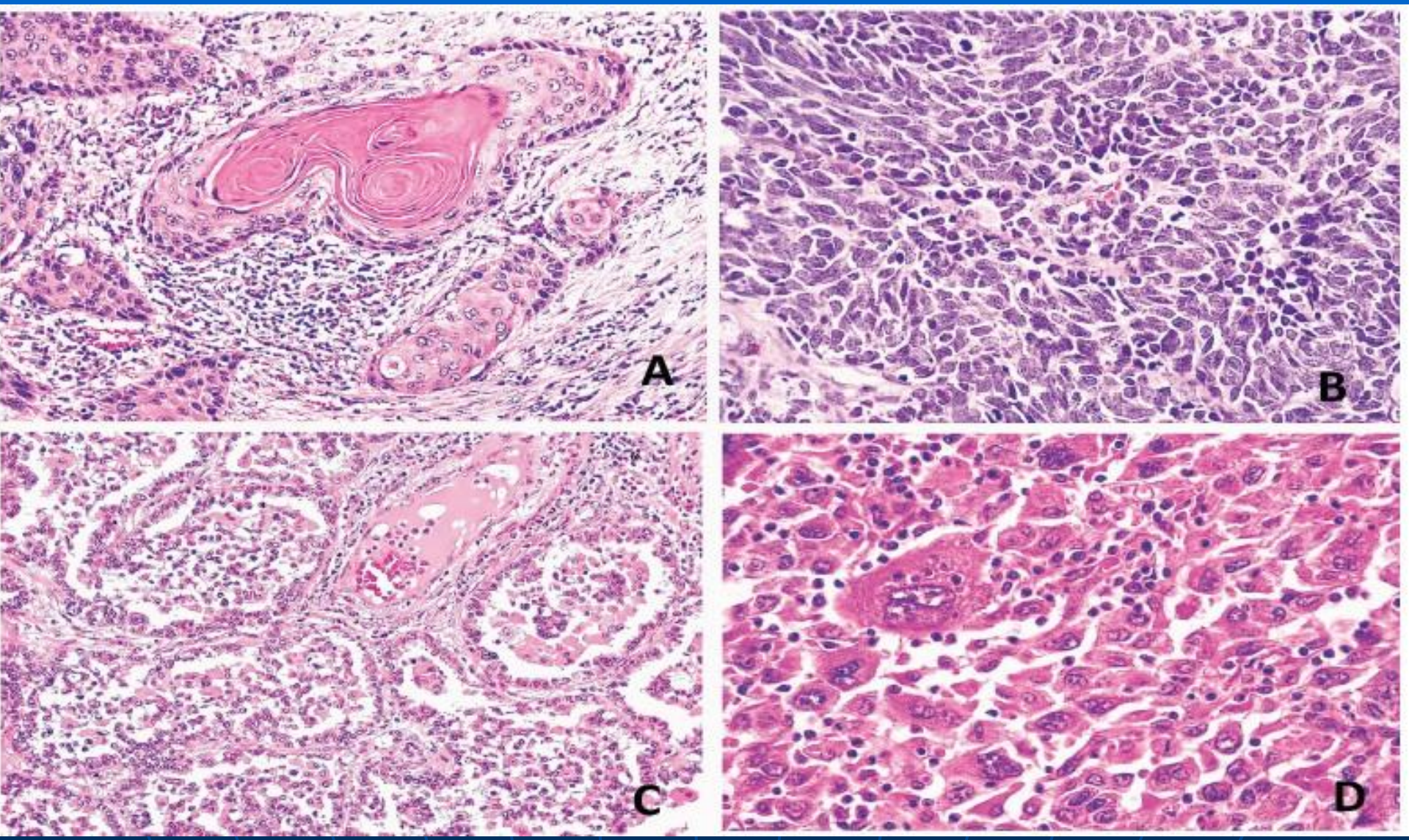


Carcinoma of the lung
Squamous Cell Carcinoma
Pathology

The microscopic appearance of squamous cell carcinoma is highly variable. The range of differentiation extends from mature squamous cells with keratin pearls to an anaplastic lesion recognized as being of squamous cell origin only by electron microscopy and immunohistochemical examination. In well-differentiated tumors, keratin often occurs as "pearls," which appear as central, brightly eosinophilic aggregates of keratin surrounded by "onion skin" layers of squamous cells.



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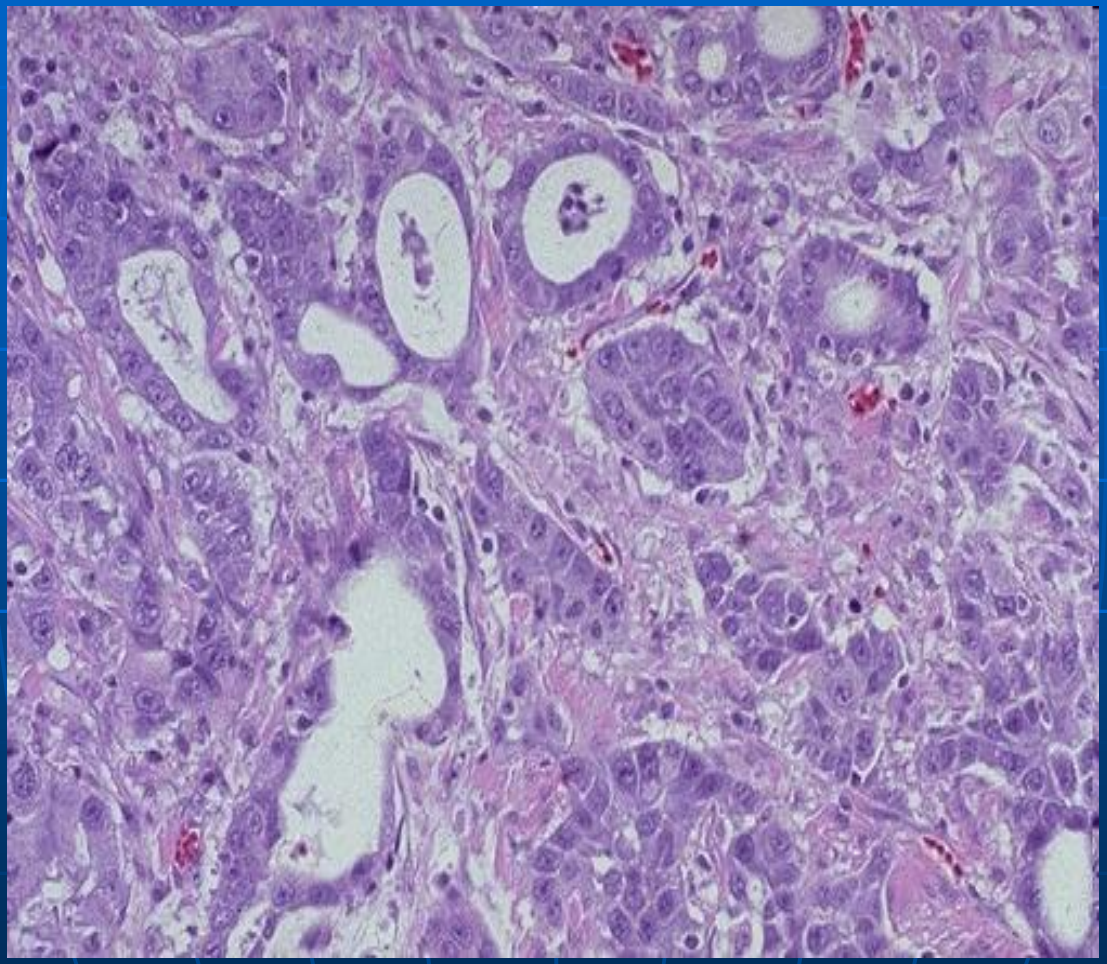
ADENOCARCINOMA

- *epidemiology and risk factors:* not closely linked with cigarette smoke
- *macroscopic features:* typically peripheral, sometimes originating in areas of pre-existing lung scarring
- *prognosis:* poor, because most tumours do not present signs of airway obstruction (because of there peripheral location) and therefore are highly advanced before presentation; bronchioloalveolar carcinoma has a good prognosis

histological features: 4 main histological patterns:

- acinar (gland like spaces)
- papillary (fronds [yes this is a word - according to the Oxford dictionary, it can mean leaf-like] of tumor on thin septa)
- solid carcinoma with mucin production (poorly differentiated)
- bronchioloalveolar carcinoma (arises from Clara cells or type II pneumocytes; distinctive in that it spreads through lungs along alveolar septa; often resembled pneumonic consolidation; cells may secrete mucin; tumor may be diffuse or focal)



MESOTHELIOMA
Pathology

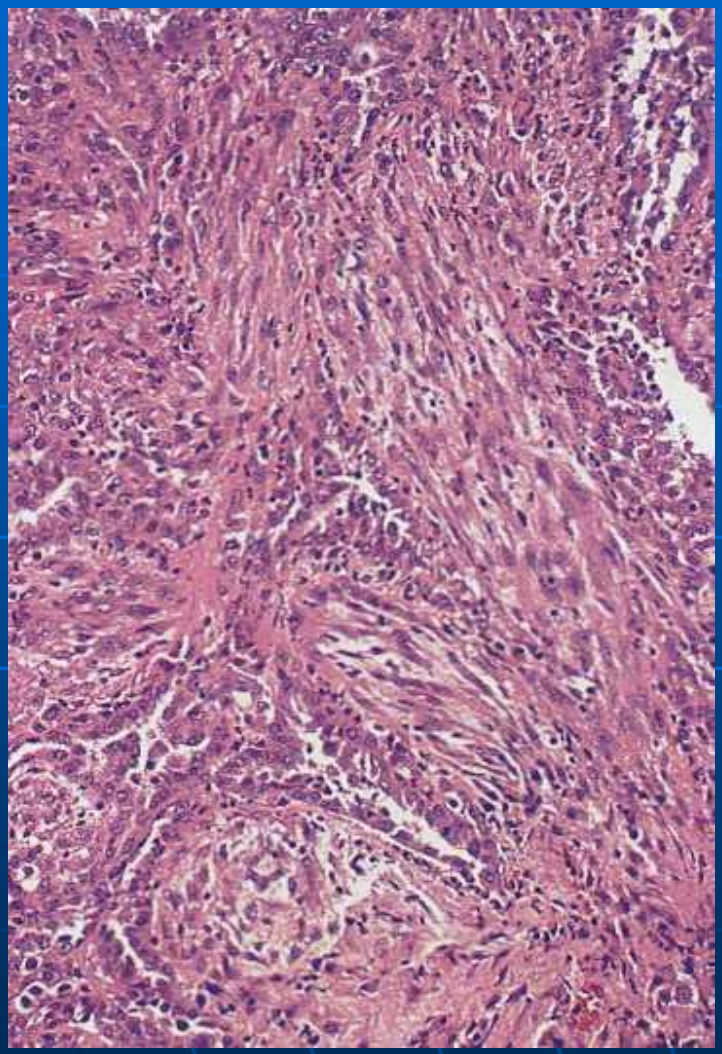
Pleural mesothelioma. Grossly. Pleural mesothelioma characteristically compresses the lungs.

MESOTHELIOMA

Pathology

Microscopically, classic mesothelioma exhibits a biphasic appearance, namely epithelial and sarcomatous patterns. Glands and tubules that resemble adenocarcinoma are admixed with sheets of spindle cells that are similar to a fibrosarcoma.

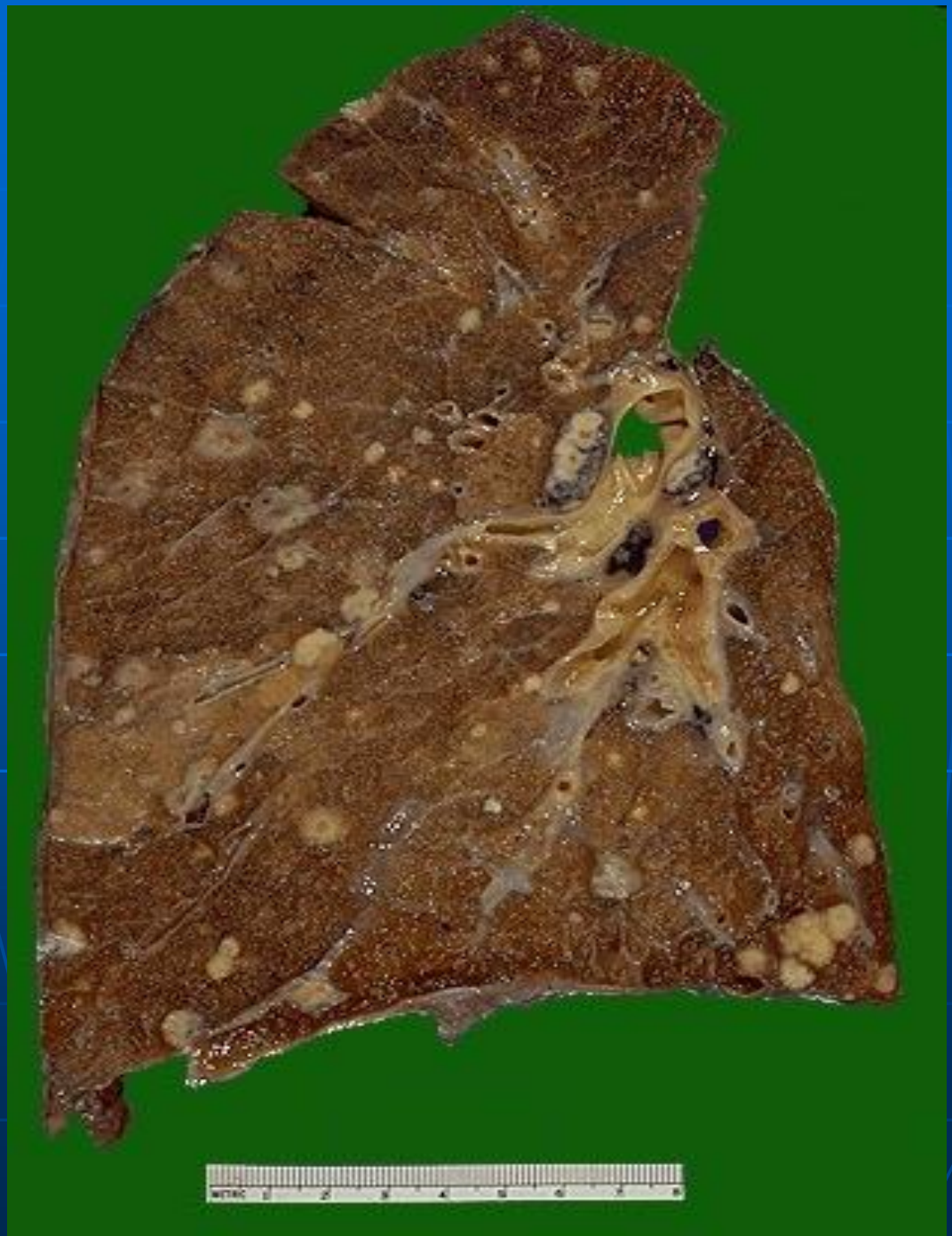
MESOTHELIOMA
Pathology



Pleural mesothelioma.
A microscopic view shows the sarcomatous and epithelial components of the tumor.

secondary tumors of the lung

- *etiology*: any malignancy may reach lung from lymph spread or vascular spread
- *clinical presentation:* is same as primary lesions
- *macroscopic features:*
  - there are 3 common patterns:
    - miliary pattern (many small neoplasms)
    - cannon ball pattern (one large, spherical, well demarcated neoplasm)
    - lymphangitis carcimatosis (spread along lymphatics - white lines through lungs instead of black lines marking lymphatics; usually present with severe dyspnoea because infiltration of lymphatics prevents lymphatics removal of fluid; is rapidly fatal



- usually well circumscribed
- may show features specific to tissue of origin (e.g. bone in lung suggestive of bone metastases, black suggests malignant melanoma)

- *microscopic features*
  - similar to tissue of origin (e.g. melanin suggests melanoma, bile suggests hepatocytes), although most carcinomas look similar (e.g. squamous cell carcinoma primary to lung looks identical to squamous cell carcinoma primary to oesophagus)
- *prognosis:* poor, except if local resection is possible (e.g. renal cell carcinoma often spreads to lung, therefore may only effect one kidney, and cannon ball in lung, hence and operation to remove kidney and part of lung is possible)

- **benign pulmonary lesions**
  - non-neoplastic benign lesions:
    - infectious (e.g. fungal, TB)
    - hamartoma
    - inflammatory pseudotumour
    - malformation
  - neoplastic benign lesions:
    - carcinoid (techniquely this is invasive) (= neuroendocrine tumors (5% of all bronchial lesions); protrude into lumen and often present with early airways obstruction and; histologically cells *may* have no abnormal features; 80% 10 year survival rate)
    - salivary gland type
    - mesenchymal
    - papilloma
    - clear cell carcinoma

THANK YOU