RESPIRATORY TRACT PATHOLOGY

Dian yuliartha lestari

Poin penting

- Saluran pernafasan atas menghantarkan, menghangatkan, melembabkan, dan menyaring udara
- Mekanisme transpor mukosiliaris memerangkap organisme dan bahan partikel
- Saluran pernafasan bawah berperan pada pertukaran gas

Penyakit saluran nafas atas : Hidung

- *Polip nasal dan Paranasal (inflammatory polyp)*
  - Most common type of nasal polyp
  - Due to recurrent attacks of rhinitis (allergic, inflammatory)
  - Most people with polyps are NOT atopic; only 0.5% with atopy develop polyps
  - Usually ages 30 years or older (rarely < age 20 years)
  - Often recurs after surgery
  - Often associated with asthma, chronic rhinitis, aspirin intolerance (14%)

- Gross description :
  - Usually multiple and bilateral and involve nasal cavity and paranasal sinuses
  - Have translucent, moist or edematous cut surface (opaque areas may represent papilloma)
  - Broad base of attachment is present
  - Usually not destructive
- Microscopic description
  - Respiratory epithelium, often with squamous metaplasia, edematous and loose stroma with hyperplastic mucous glands, inflammatory infiltrate (lymphocytes, plasma cells, eosinophils, neutrophils, mast cells)
  - Mucosa may be ulcerated or infected
  - Basal membrane may be thickened
  - May have bizarre stromal cells (large and pleomorphic) due to reactive changes
  - May have prominent glandular component

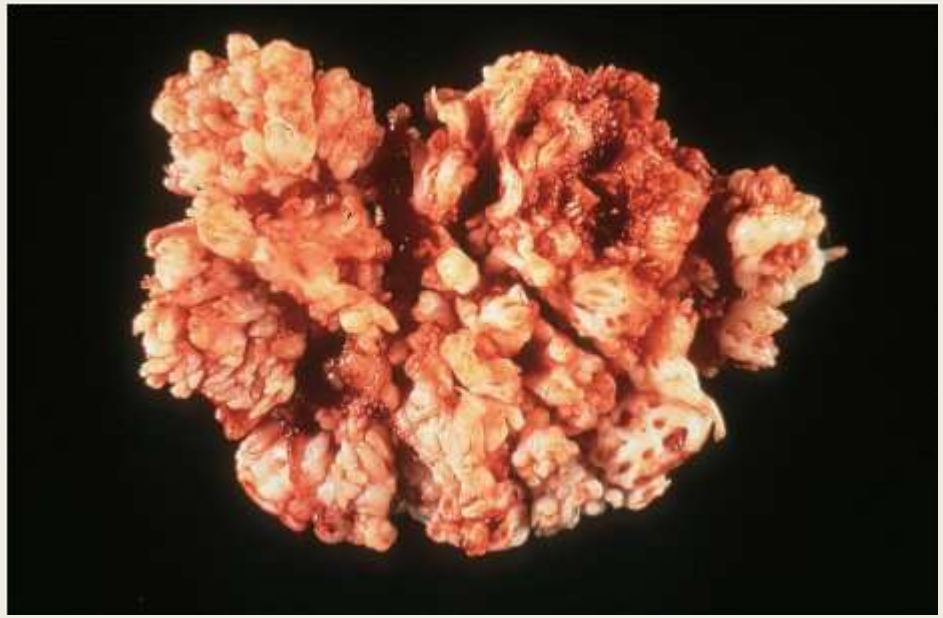
- *Schenedirian papiloma*
  - Sinonasal papilloma is a benign epithelial neoplasm of sinonasal tract
  - WHO has divided sinonasal papilloma into 3 distinct types
    - Inverted papilloma
    - Exophytic papilloma
    - Oncocytic papilloma
- Other terminologies that have been used in the literature and previous versions of WHO classification include:All types: Schneiderian papilloma and epithelial papilloma
- Exophytic type: transitional cell papilloma, fungiform papilloma, Ringertz papilloma and septal papilloma
- Oncocytic type: cylindrical cell papilloma and columnar cell papilloma

- **Epidemiology**
  - Annual incidence is 0.74 - 2.3 per 100,000 population
  - Inverted papilloma is the most common subtype, followed by exophytic papilloma; oncocytic papilloma is the least common
  - Inverted and oncocytic papilloma most commonly affect patients in their 5th to 6th decades, while exophytic papilloma occurs in 3rd to 5th decades
  - Inverted and exophytic papilloma occur more frequently in males, with a male to female ratio of 2 - 3:1 and 10:1, respectively; oncocytic papilloma affects both genders equally
- **Sites**
  - Sinonasal papilloma commonly affects nasal cavity or paranasal sinuses
  - Exophytic papilloma is typically located in the nasal septum, while the inverted and oncocytic types predominantly affect lateral nasal wall or paranasal sinuses
  - Inverted papilloma may secondarily extend to nonsinonasal sites, e.g. pharynx, ear, cranial cavity
  - Sinonasal papilloma is usually unilateral; bilateral involvement is rare

- **Etiology**
  - Role of high risk human papillomavirus (HPV) in inverted papilloma remains controversial
    - Reported rate of high risk HPV in inverted papilloma and carcinoma ex inverted papilloma ranges from 0 - 100%
    - WHO gives a frequency of 38.5% in inverted papilloma
  - Low risk HPV, especially types 6 and 11, has also been detected in inverted papilloma and is more common than high risk HPV
  - Other etiologic factors implicated in inverted papilloma include exposure to welding, organic solvents and smoking
  - Exophytic papilloma may be related to low risk HPV, especially types 6 and 11
  - No significant association between oncocytic papilloma and HPV

- **Clinical features**
  - *Symptoms are usually nonspecific, including nasal congestion, nasal obstruction, nasal discharge or epistaxis*
- **Prognostic factors**
  - Increased risk of recurrence if involvement of sphenoid sinus, frontal sinus or maxillary sinus walls other than medial or extrasinus extension
  - Major cause of recurrence is incomplete resection
  - Risk of malignant transformation is ~9% in inverted papilloma (range: 5 - 15%)
  - 4 - 17% of oncocytic papilloma undergo malignant transformation
  - Exophytic papilloma is not associated with an increased incidence of carcinoma

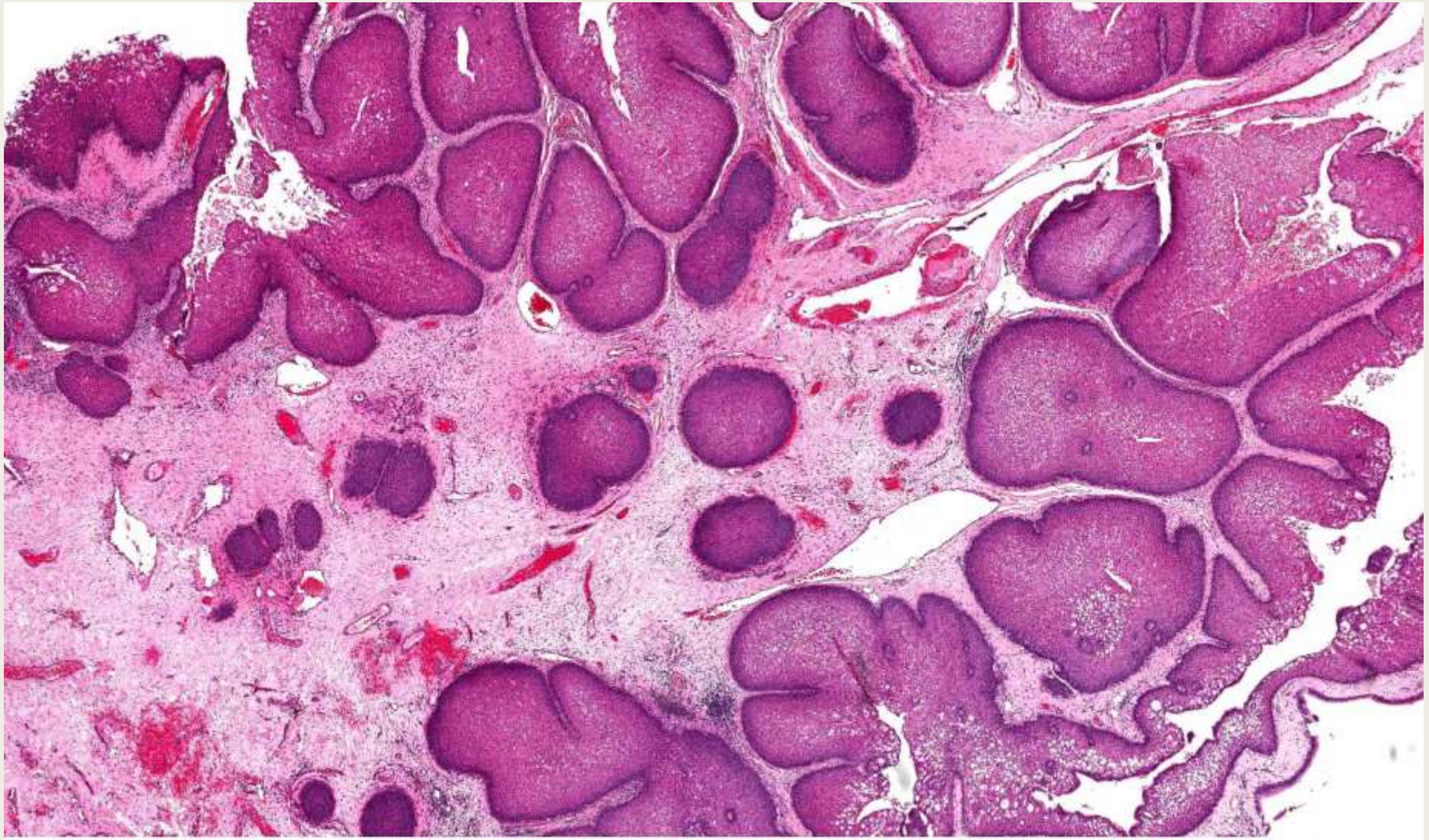
- **Gross description**
  - Inverted papilloma: pink-tan-gray, soft to moderately firm polypoid growth with convoluted or wrinkled surface
  - Exophytic papilloma: usually mushroom shaped and exophytic with papillary appearance
  - Oncocytic papilloma: fleshy polypoid growth of variable color
  - Generous or complete sampling is advised to search for focus of malignant transformation



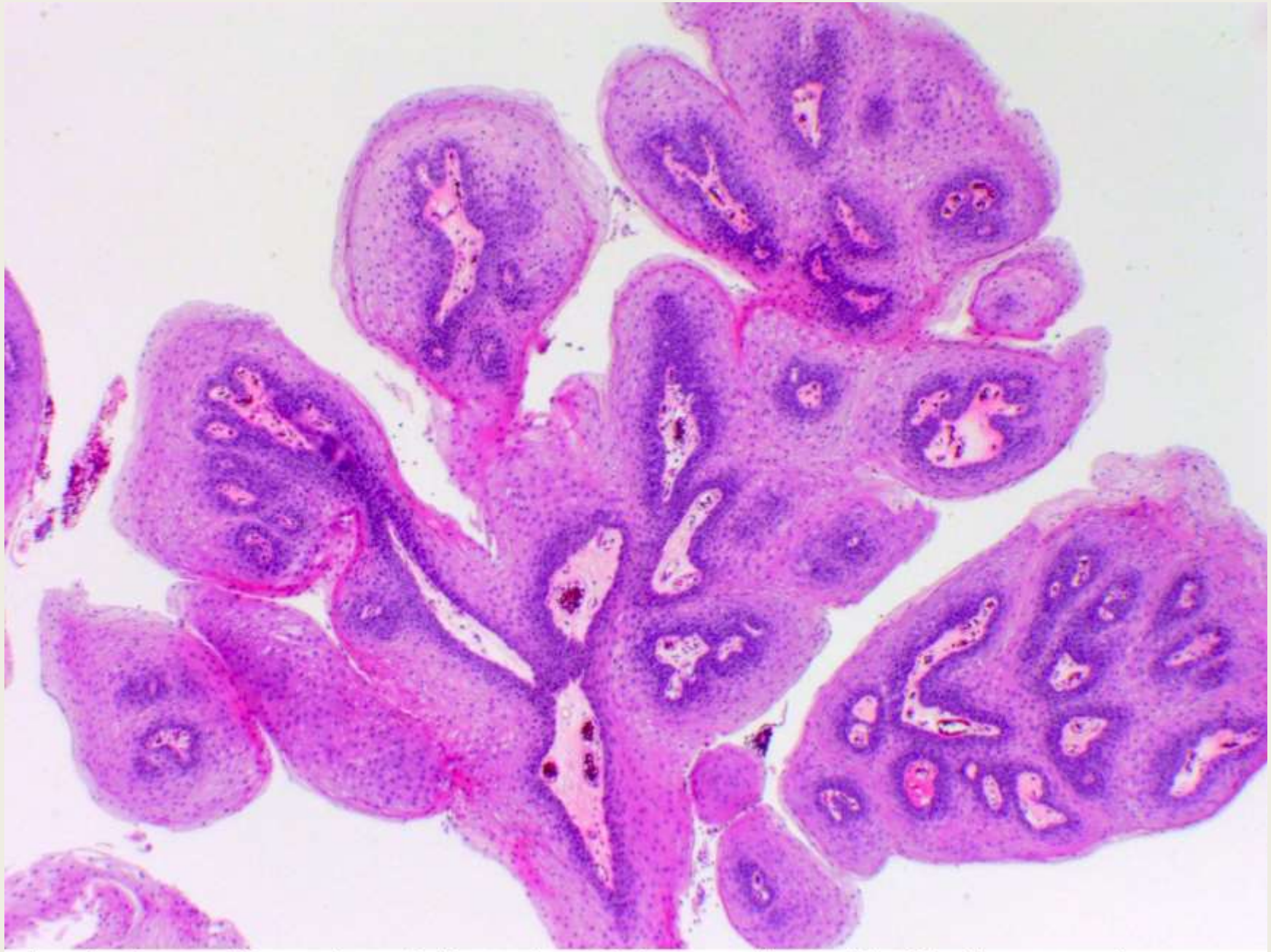
Microscopic (histologic) description

- **Inverted papilloma**: Architecture: prominent downward endophytic growth of round to elongated interconnected epithelial nests with smooth outer contour
  - Epithelium is hyperplastic (5 - 30 cell layers in thickness) and may be of squamous, transitional or respiratory type
  - Transmigrating neutrophils and neutrophilic microabscesses may be seen
  - Stroma may have edema or chronic inflammation
  - Seromucinous gland in the lamina propria is commonly decreased or absent
- **Oncocytic papilloma**:Architecture: may have endophytic (inverted) or exophytic growth patterns
  - Epithelial lining is pseudostratified and columnar with abundant eosinophilic granular cytoplasm and hyperchromatic uniform nuclei
  - Intraepithelial mucin filled cysts with neutrophilic microabscesses may be seen

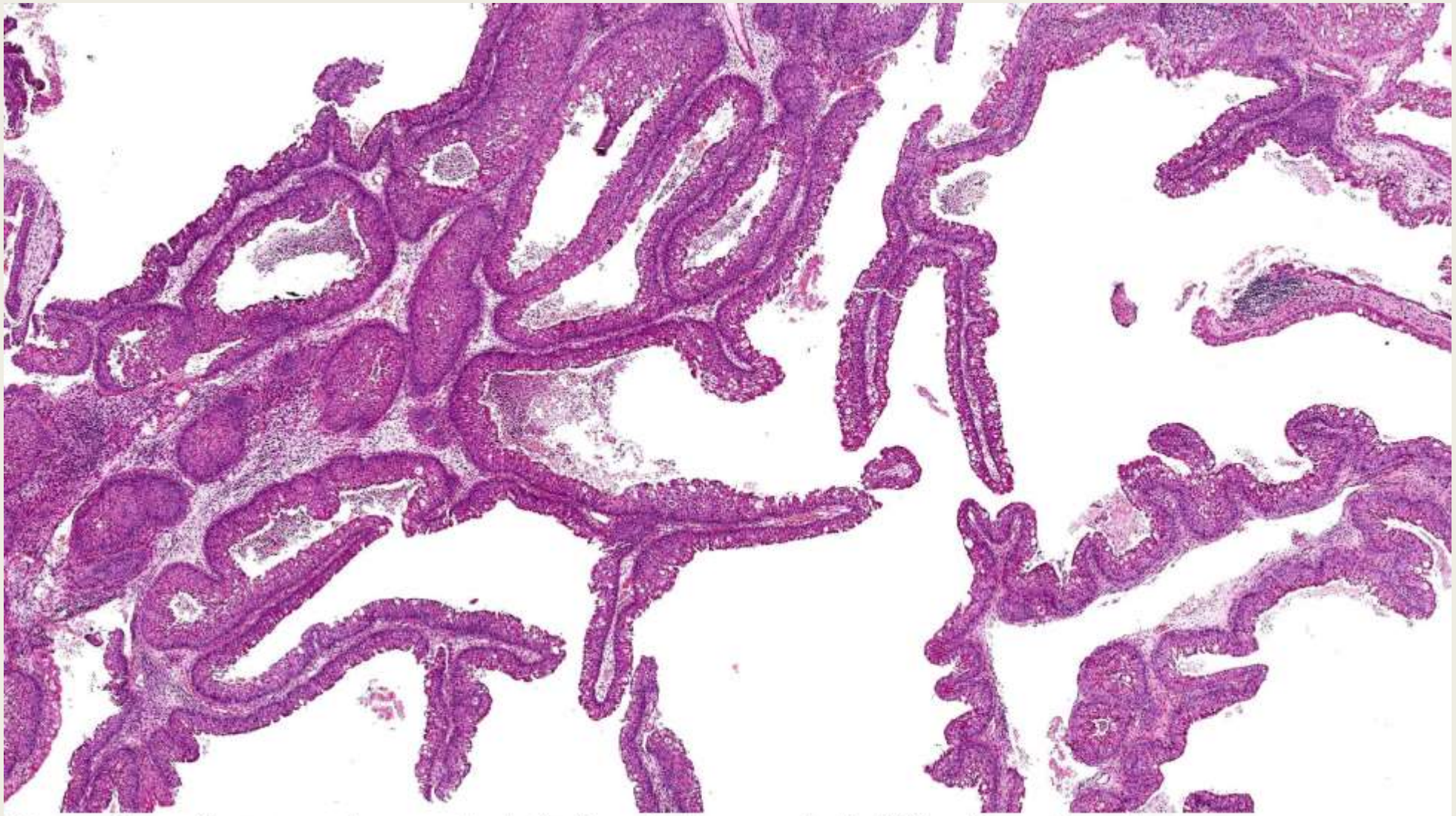
- **Exophytic papilloma**: Architecture: filiform or papillary arrangement with delicate fibrovascular core
  - Epithelial lining can be either squamous, respiratory or transitional; it may contain mucus secreting cells and goblet cells
  - Variable koilocytosis may be present
  - Usually no / scant surface keratinization
  - Mitotic figures are absent or limited to the basal layer
  - Minimal inflammatory cells
- **Malignant transformation (carcinoma ex sinonasal papilloma)**:Most common type of carcinoma arising in sinonasal papilloma is squamous cell carcinoma
  - Other types of carcinoma that have been reported include verrucous carcinoma, mucoepidermoid carcinoma, small cell carcinoma and sinonasal undifferentiated carcinoma
  - Carcinoma is characterized by marked nuclear pleomorphism and hyperchromasia, frequent mitotic figures beyond basal layer including the atypical forms, tumor necrosis and frank invasion with infiltrative irregular nests and desmoplastic stromal reaction



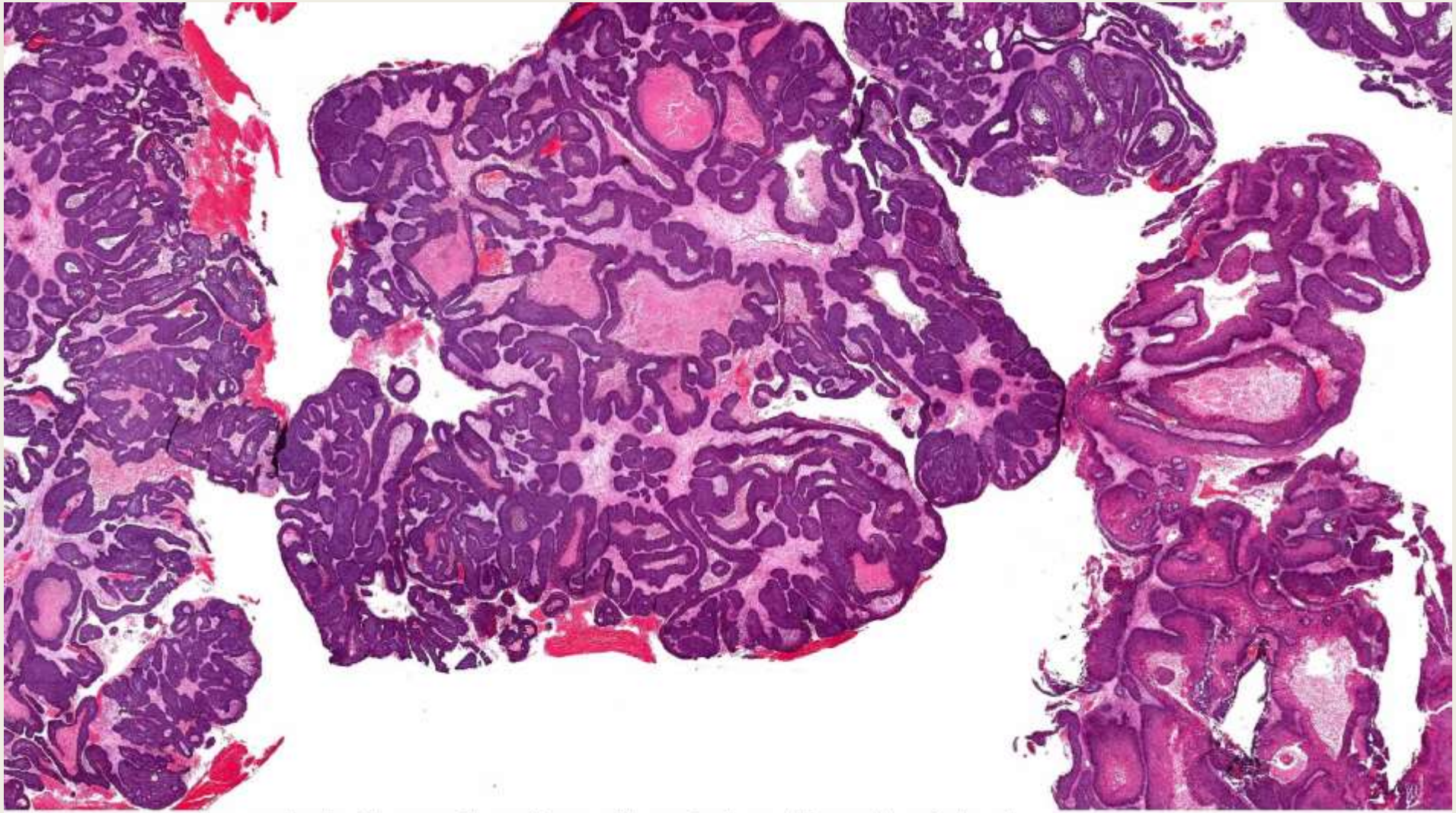
Inverted papilloma is characterized by endophytic growth of epithelial nests with smooth outer contour



Exophytic papilloma has delicate branching papillae with thin fibrovascular core



Oncocytic papilloma may have endophytic (inverted) or exophytic (filiform) growth pattern



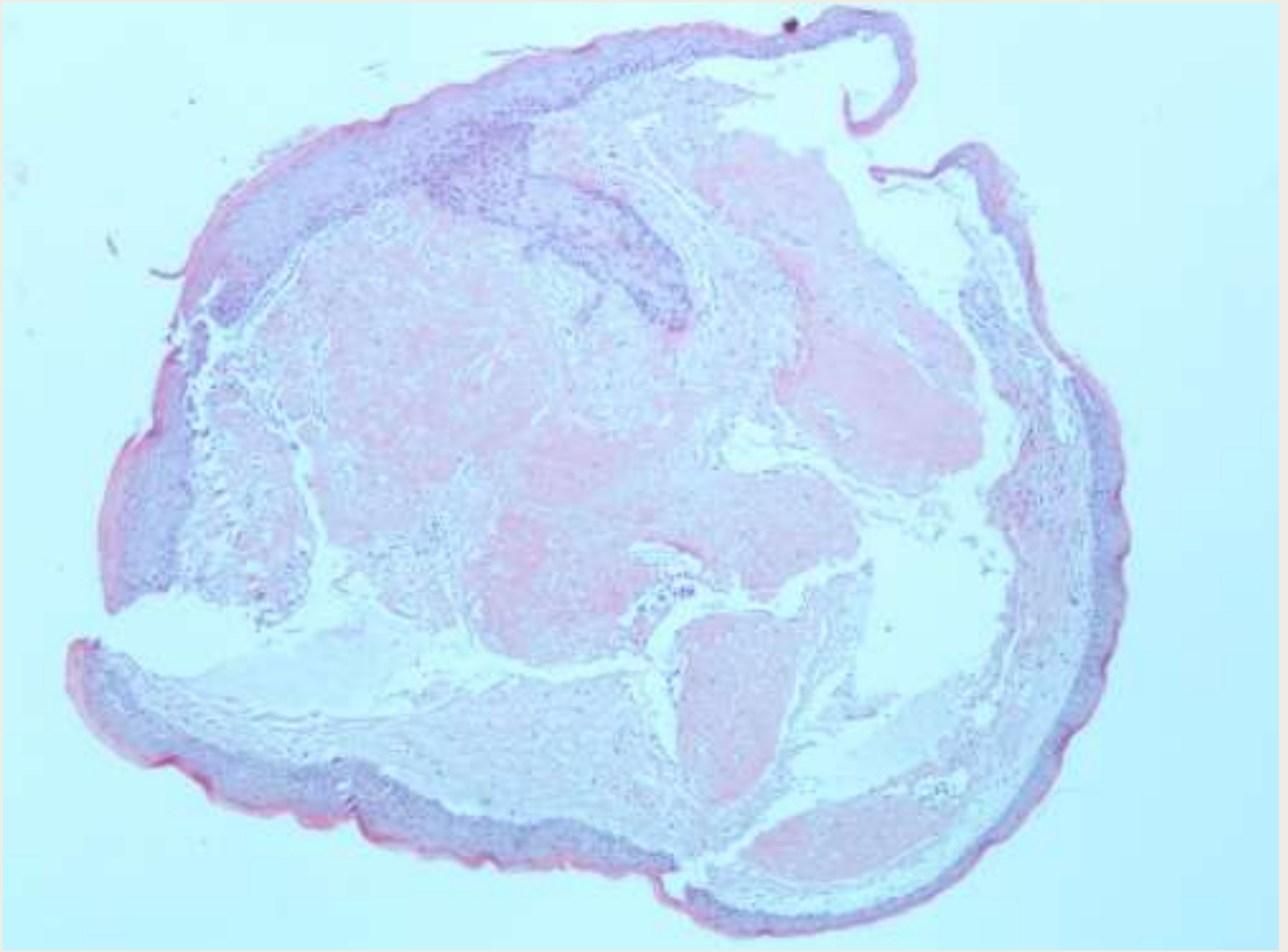
At low power, the endophytic growth pattern of inverted papilloma is retained

Laring dan hipolaring

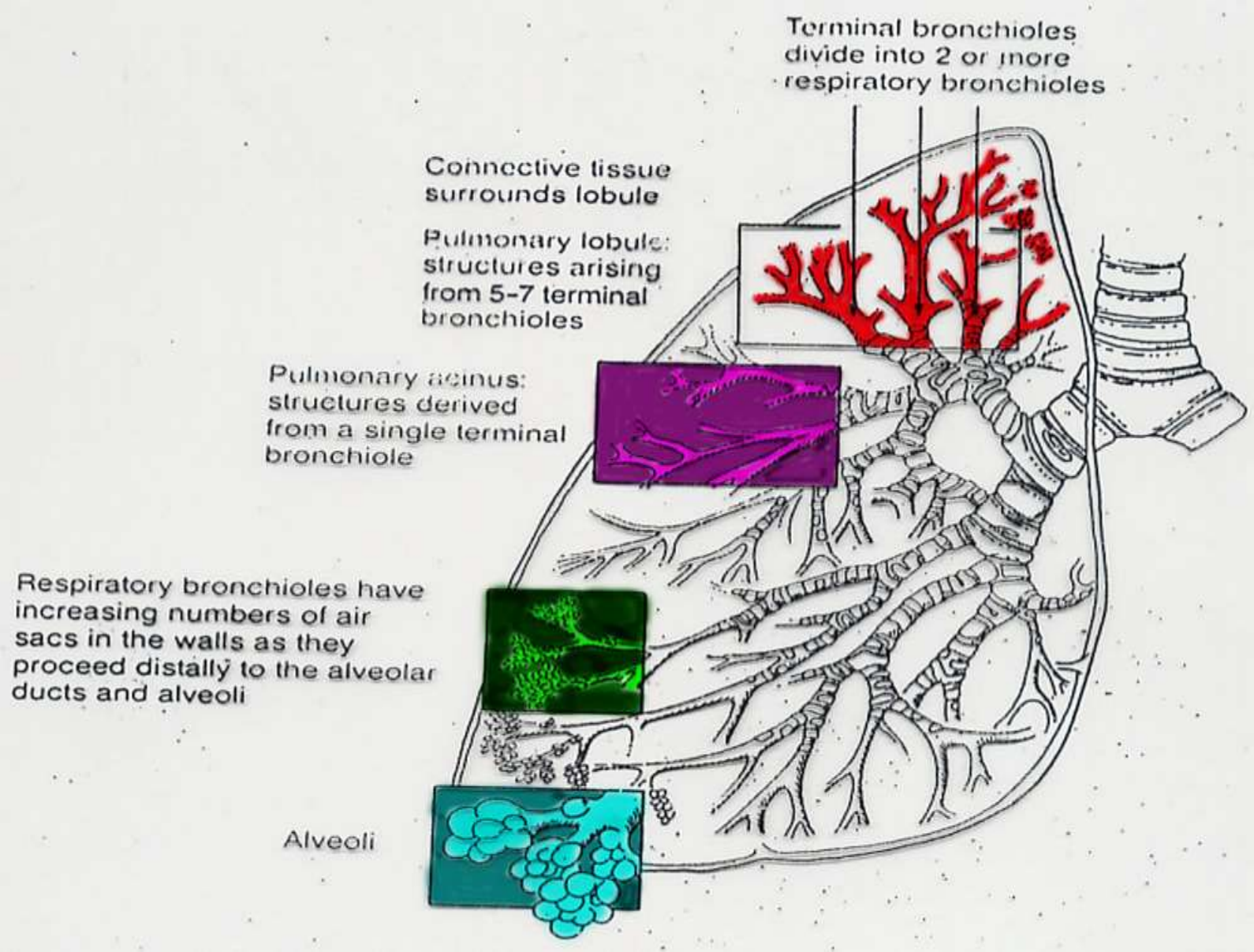
- Vocal cord polyp
  - Also called laryngeal nodule or singer's nodule
  - Noninflammatory response to injury causing hoarseness
  - More common in heavy smokers or singers due to inflammation, allergic or immunologic causes, possibly secondary to hemorrhage
  - Almost never transforms to malignancy

  Gross description
  - *Smooth, round, 1 - 3 mm growths on true vocal cords, often on anterior third*

  Microscopic (histologic) description
  - *(a) Telangiectatic polyps with stratified squamous epithelium overlying numerous thin walled dilated vessels and fibrinous exudates in edematous mucosa, variable chronic inflammatory infiltrate or (b) gelatinous polyps with stratified squamous epithelium, edematous submucosa containing fibrin and proliferating fibroblasts, thin walled vessels present but less than telangiectatic subtype*
  - *Vessels may resemble thrombosed varices*
- Malignancy → **SQUAMOUS CELL CARCINOMA**

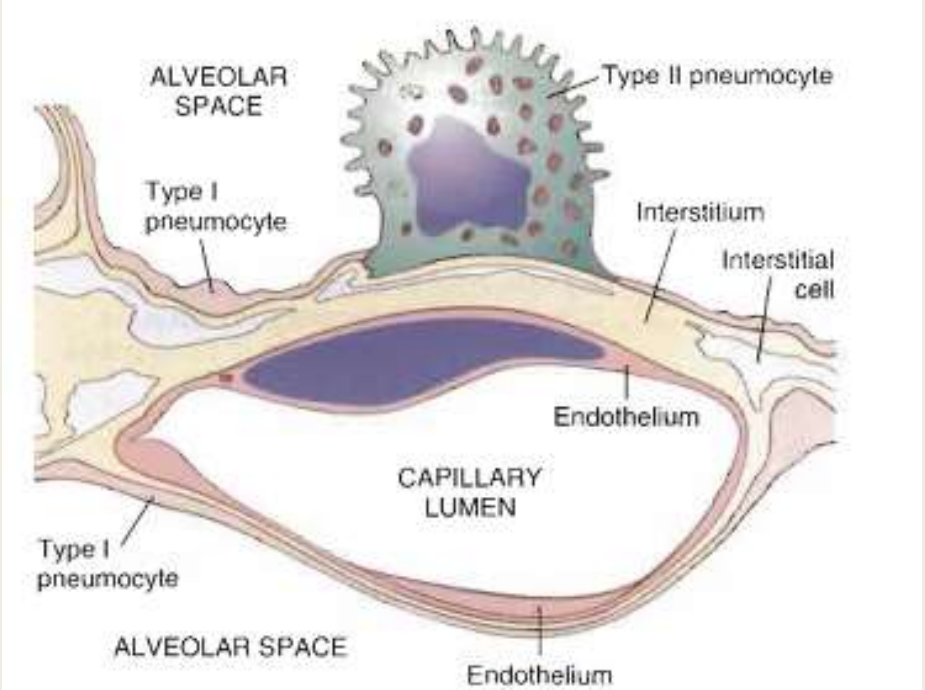


PULMO


Terminal bronchioles divide into 2 or more respiratory bronchioles
Connective tissue surrounds lobule
Pulmonary lobule: structures arising from 5-7 terminal bronchioles
Pulmonary acinus: structures derived from a single terminal bronchiole
Respiratory bronchioles have increasing numbers of air sacs in the walls as they proceed distally to the alveolar ducts and alveoli
Alveoli

Alveolar walls (alveolar septa)

- Capillary endothelium
- Basement membrane
- Alveolar epithelium
  - *Pneumocyte type 1*
  - *Penumocyte type 2*
- Alveolar macrophage



ATELECTASIS (COLLAPSE)

- Pengembangan paru tidak sempurna
- Akibat adanya oksigenasi inadekuat dari arteri pulmonalis ke vena
- Reversible → dapat mengembang lagi jika penyebab dihilangkan
- Jenis :
  - *Resorption → obstruksi pada bagian distal → absorbsi O2 → alveolus kolaps*
  - *Compression → penekanan dari luar (cairan, darah, udara, tumor)*
  - *Contraction → local/diffuse fibrosis*

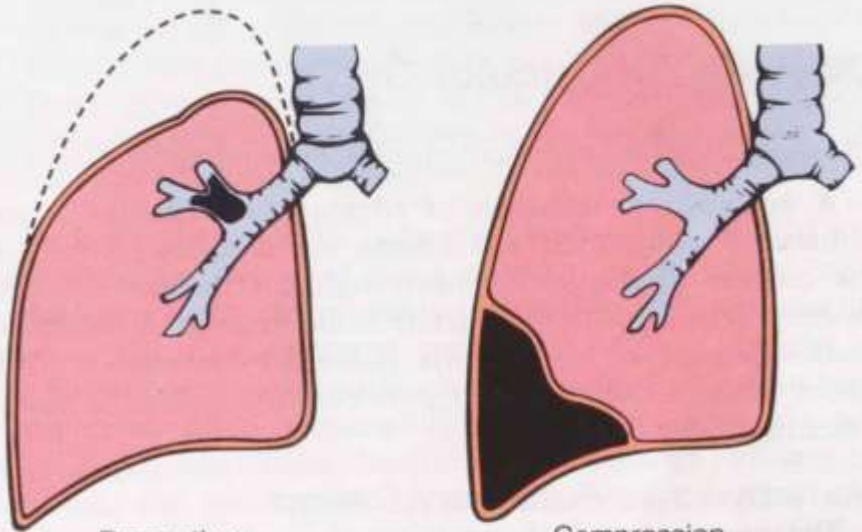


Figure 16–2

Various forms of atelectasis in adults.

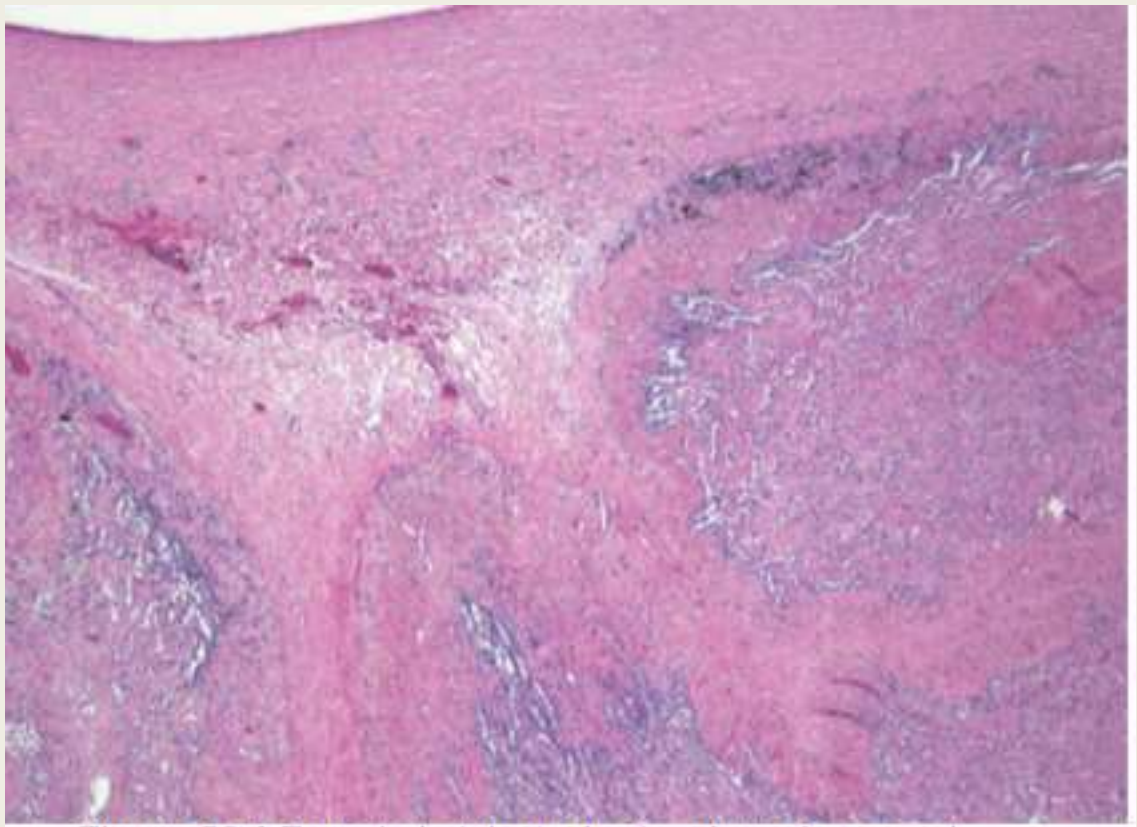


Figure 58.1 Rounded atelectasis: the pleura is scarred resulting in atelectatic change secondary to contraction. Note the infolding of scarred pleural tissue.

ARDS (ACUTE RESPIRATORY DISTRESS SYNDROME)

- Bentuk ekstrem dari cedera paru akut yang terjadi akibat berbagai gangguan pulmonal dan ekstrapulmonal (sepsis, trauma, luka bakar, akut intersitial pneumonia)
- Kerusakan yang terjadi : Diffuse alveolar Damage (DAD)
- **Klinis** : dispnea berat, hipoksemia, sianosis, takipnea
- Sindroma ini diperantarai oleh sel-sel PMN dan dapat memiliki komplikasi fibrosis
- Patologi memperlihatkan membran hialin serta trombus fibrin yang berkembang menjadi fibrosis intra-alveolus dan intersitial
- ARDS ditandai dengan aktivasi mediator inflamasi yang tidak terkontrol → TNF, IL-1, -6,-8

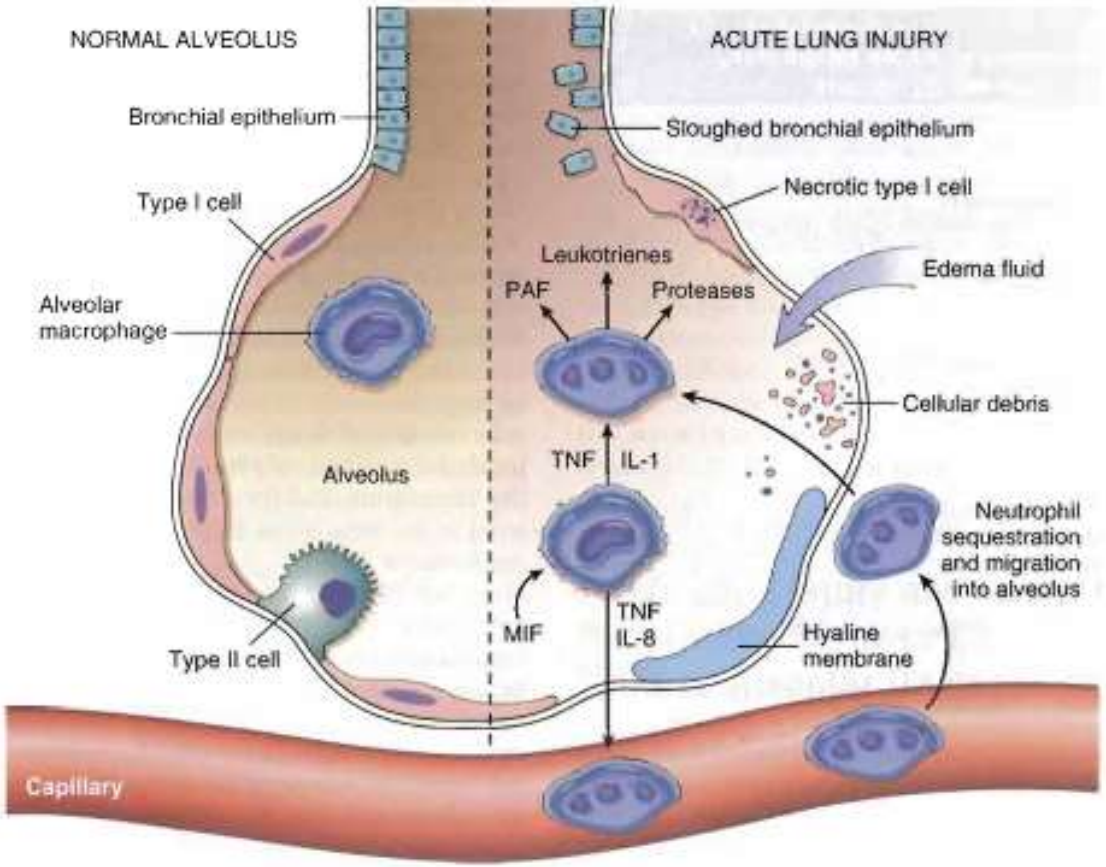


FIGURE 15–4 The normal alveolus *(left side)* compared with the injured alveolus in the early phase of acute lung injury and acute respiratory distress syndrome. Pro-inflammatory cytokines such as interleukin 8 (IL-8), interleukin 1 (IL-1), and tumor necrosis factor (TNF) (released by macrophages), cause neutrophils to adhere to pulmonary capillaries and extravasate into the alveolar space, where they undergo activation. Activated neutrophils release a variety of factors, such as leukotrienes, oxidants, proteases, and platelet-activating factor (PAF), which contribute to local tissue damage, accumulation of edema fluid in the airspaces, surfactant inactivation, and hyaline membrane formation. Macrophage migration inhibitory factor (MIF) released into the local milieu sustains the ongoing pro-inflammatory response. Subsequently, the release of macrophage-derived fibrogenic cytokines such as transforming growth factor β (TGF-β) and platelet-derived growth factor (PDGF) stimulate fibroblast growth and collagen deposition associated with the healing phase of injury. (Modified with permission from Ware LB, Matthay MA: The acute respiratory distress syndrome. N Engl J Med 342:1334, 2000.)

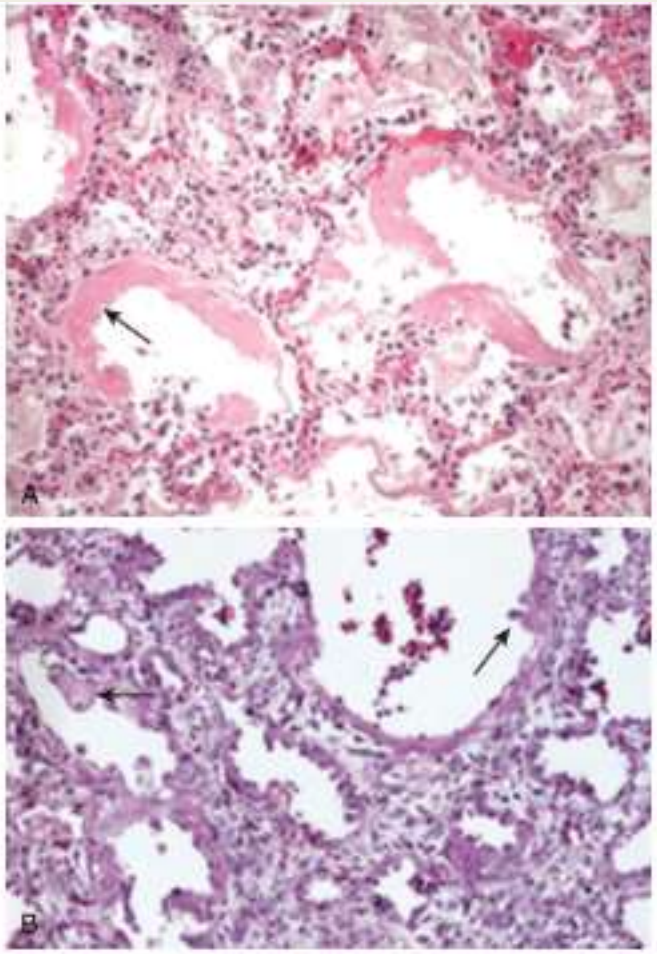


Fig. 13.3 Acute lung injury and acute respiratory distress syndrome. (A) Diffuse alveolar damage in the acute phase. Some alveoli are collapsed, while others are distended; many are lined by bright pink hyaline membranes *(arrow)*. (B) The healing stage is marked by resorption of hyaline membranes and thickening of alveolar septa by inflammatory cells, fibroblasts, and collagen. Numerous reactive type II pneumocytes also are seen at this stage *(arrows)*, associated with regeneration and repair.

Diffuse pulmonary disease → **Obstructive** dan **Restrictive**

- **Obstructive** → peningkatan resistensi aliran udara akibat adanya obstruksi
  - *Penyebab tersering : emfisema, bronchitis kronik, bronchiectasis, asma*
- Restrictive → terdapat 2 kondisi :
  - *Kelainan pada dinding dada (obese, kelainan pada pleura)*
  - *Acute (ARDS) dan kronik intersitial lung disease (pneumoconiasis, intersitial fibrosis, sarcoidosis)*

Table 13.1 Disorders Associated With Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucous gland hypertrophy and hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hypertrophy and hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Small airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

*Can be present in all forms of obstructive lung disease or by itself.

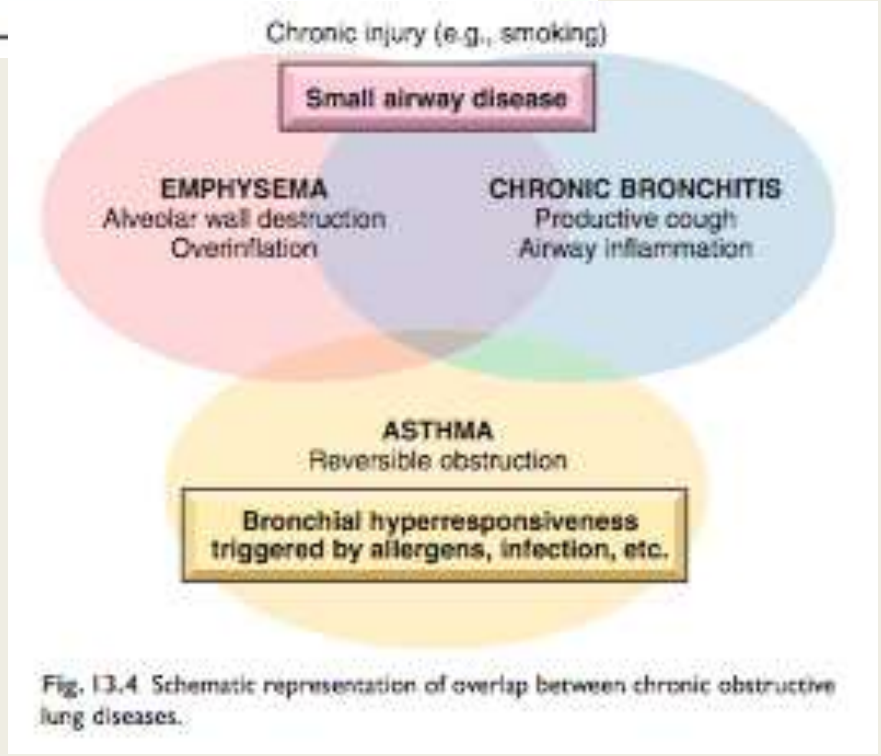


Fig. 13.4 Schematic representation of overlap between chronic obstructive lung diseases.

Emfisema

- Pembesaran / pelebaran abnormal yang permanent dari rongga udara distal bronchiolus terminalis disertai *kerusakan* dinding alveolus
- Jenis :
  - *Centriaciner (sentrilobular)*
    - Dari proksimal acinus
    - Penyebab : bronchitis kronis
  - *Panacinar (panlobular)*
    - Seluruh acinus terkena
    - Penyebab : defisiensi alfa-1 antitripsis
  - *Distal acinar (paraseptal)*
    - Bagian distal yang terkena
    - Bullous emfisema
  - *irreguler*

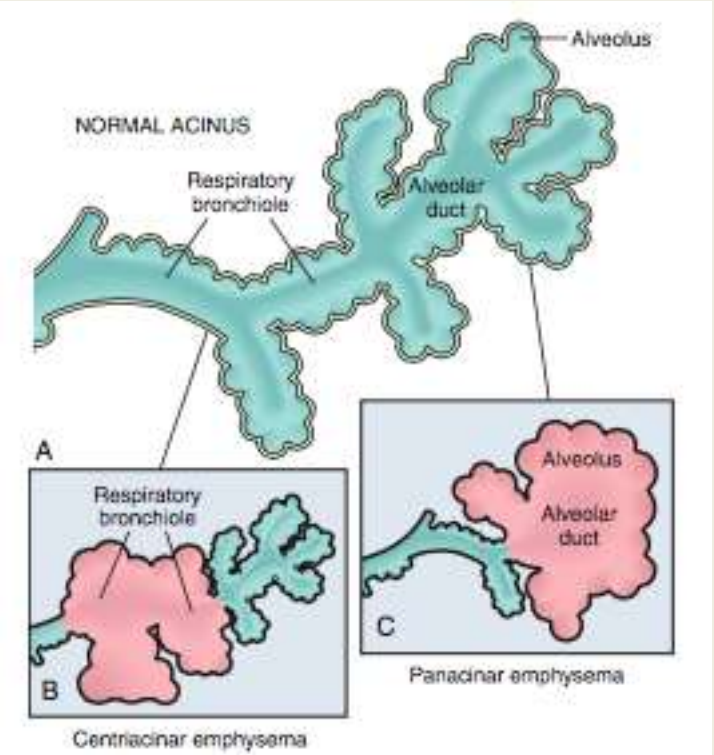


Fig. 13.5 Major patterns of emphysema. (A) Diagram of normal structure of the acinus, the fundamental unit of the lung. (B) Centriacinar emphysema with dilation that initially affects the respiratory bronchioles. (C) Panacinar emphysema with initial distention of all the peripheral structures (i.e., the alveolus and alveolar duct); the disease later extends to affect the respiratory bronchioles.

- **Sites**
  - Centriacinar emphysema
    - Upper lobe predominant
    - Respiratory bronchioles and surrounding lung parenchyma
  - Panacinar emphysema
    - Lower lobe predominant
    - Entire acinus
  - Paraseptal emphysema
    - Upper lung
    - Distal part of acinus in subpleural area
- **Etiology**
  - *Inhalation*
    - Cigarette smoking and environmental pollutants, especially for centriacinar emphysema
    - However, there is individual susceptibility
  - *Infections*
  - *Genetic factors*
    - Alpha-1-antitrypsin deficiency is well known risk factor, especially for panacinar
    - Telomerase mutations, especially for CPFE
    - Serpin mutation

Clinical features

- Dyspnea; chronic, progressive and usually irreversible
- Chest inflation
- CPFE → Coexistence of interstitial fibrosis and emphysema of unknown causes
  - Patients with CPFE have different pulmonary function tests and outcomes than patients with pure emphysema or pure fibrosis
- Interstitial emphysema → Air gains access to the pulmonary interstitium to cause air leak and pneumothorax
  - Common in premature infants
  - Adults: commonly in usual interstitial pneumonia, but can occur in any interstitial lung diseases
- Bullous emphysema → Formation of multiple bullae > 1 cm with thin wall
  - Can cause bullae inflation and pneumothorax
- Senile emphysema → Due to age related alteration of acini
- Irregular emphysema → Occurs in relation to scars
- Congenital lobar emphysema →Hyperinflation of one or more lobes due to malformation of bronchioles
  - Causes respiratory distress
  - Can be sporadic or caused by autosomal dominant inheritance

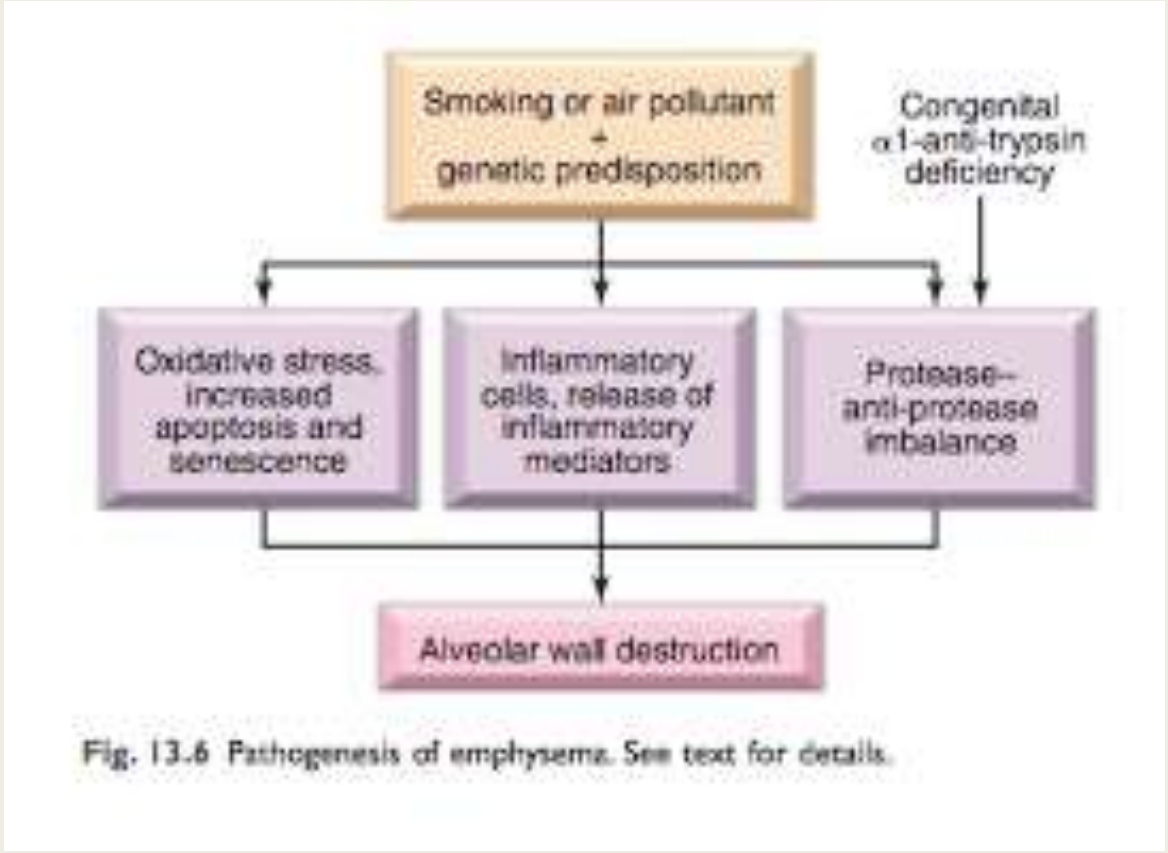


Fig. 13.6 Pathogenesis of emphysema. See text for details.

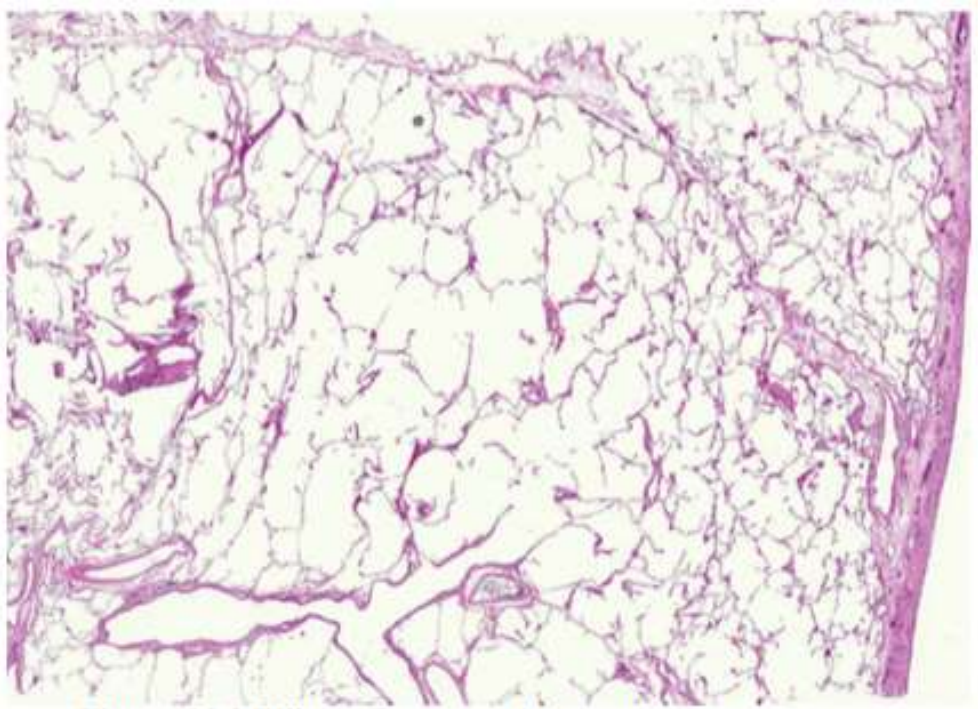


Figure 99.3 Diffuse airspace enlargement throughout the pulmonary lobule in a smoker with centrilobular and panacinar emphysema. Panacinar emphysema is associated with alpha-1-antitrypsin deficiency, but may be observed in some smokers without known deficiency of this enzyme.

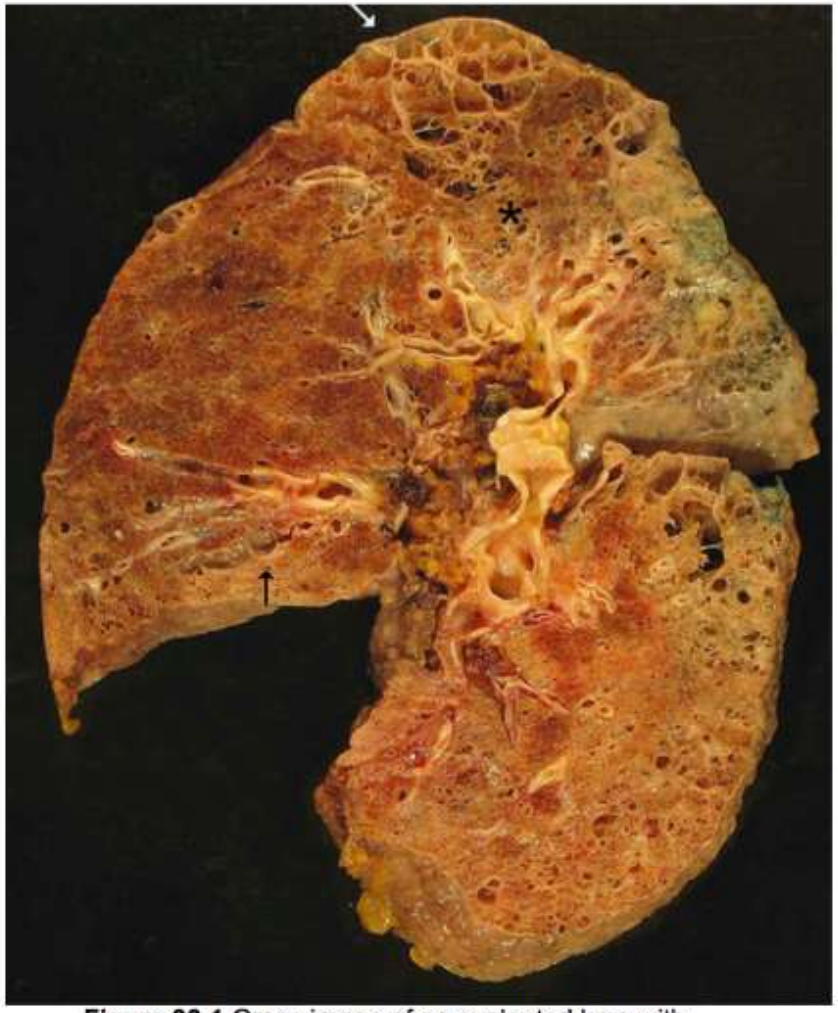


Figure 99.1 Gross image of an explanted lung with combined emphysema and pulmonary fibrosis. Emphysematous changes are most pronounced in the apex of the upper lobe *(white arrow)* and superior segment of the lower lobe; small subpleural bullae are evident at both sites. The centrilobular distribution of emphysematous destruction is most evident in the upper lobe *(asterisk)*. The lower lobe and inferior aspect of the upper lobe both show increased tissue density and traction bronchiectasis *(black arrow)* due to excess collagen deposition consistent with a concomitant fibrosing process.

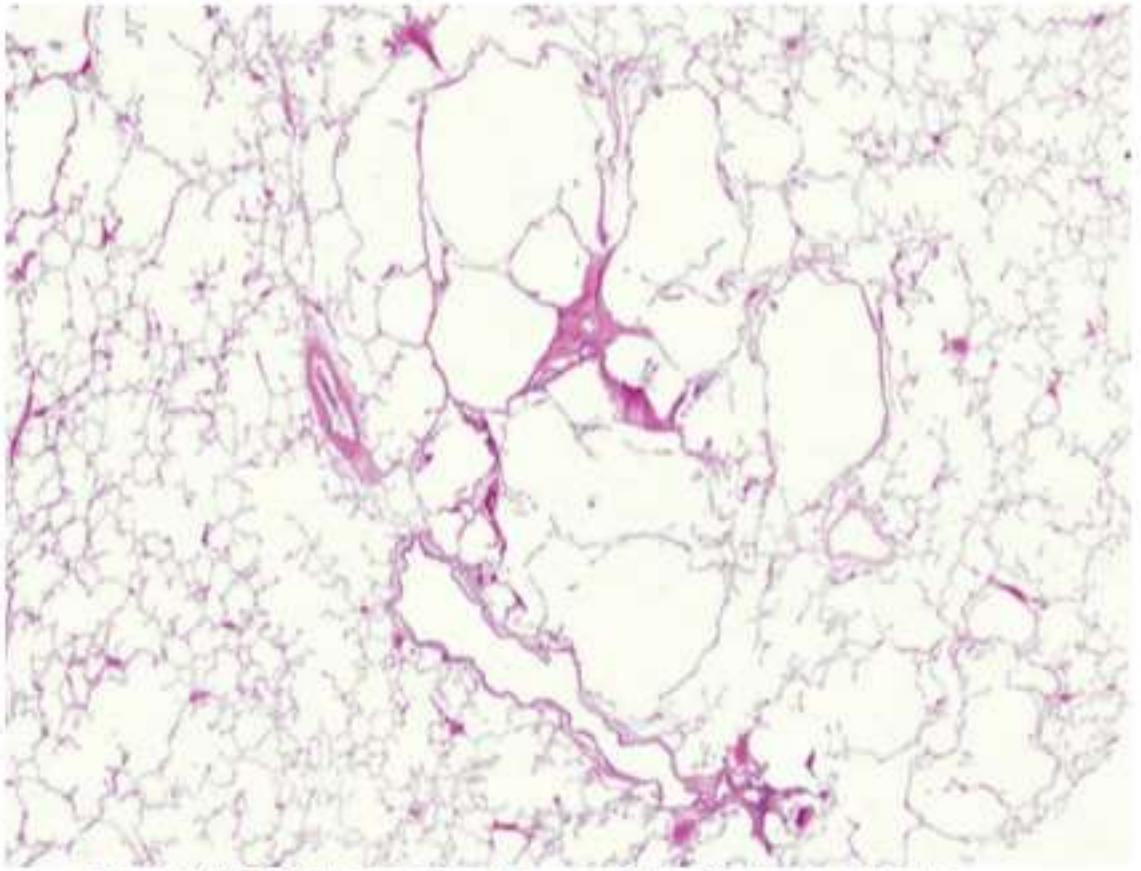


Figure 99.2 Enlarged peribronchiolar airspaces due to tissue destruction in a patient with smoking-related centrilobular emphysema. There is mildly increased collagen deposition in the residual airway structure. Areas of relatively preserved acinar structures can be seen in the tissue surrounding the emphysema.

BRONCHITIS KRONIK

- Keadaan dimana penderita mengalami batuk persisten yg produktif selama 3 bulan dalam 2 th terakhir
- Incidence : Laki dan Wanita Segala umur

  Perokok meningkat 4 – 10 x
- Patogenesa : 1. Irritasi Kronik

  2. Infeksi Bakteri
- **Macros**: hiperemi, swelling, edema pada membrane mucosa
- **Micros**: chronic inflammation, goblet cell increase, hyperplasia, reid index increasing, kadang didapatkan squamous metaplasia dan dysplasia, berat → bronchiolitis obliterans

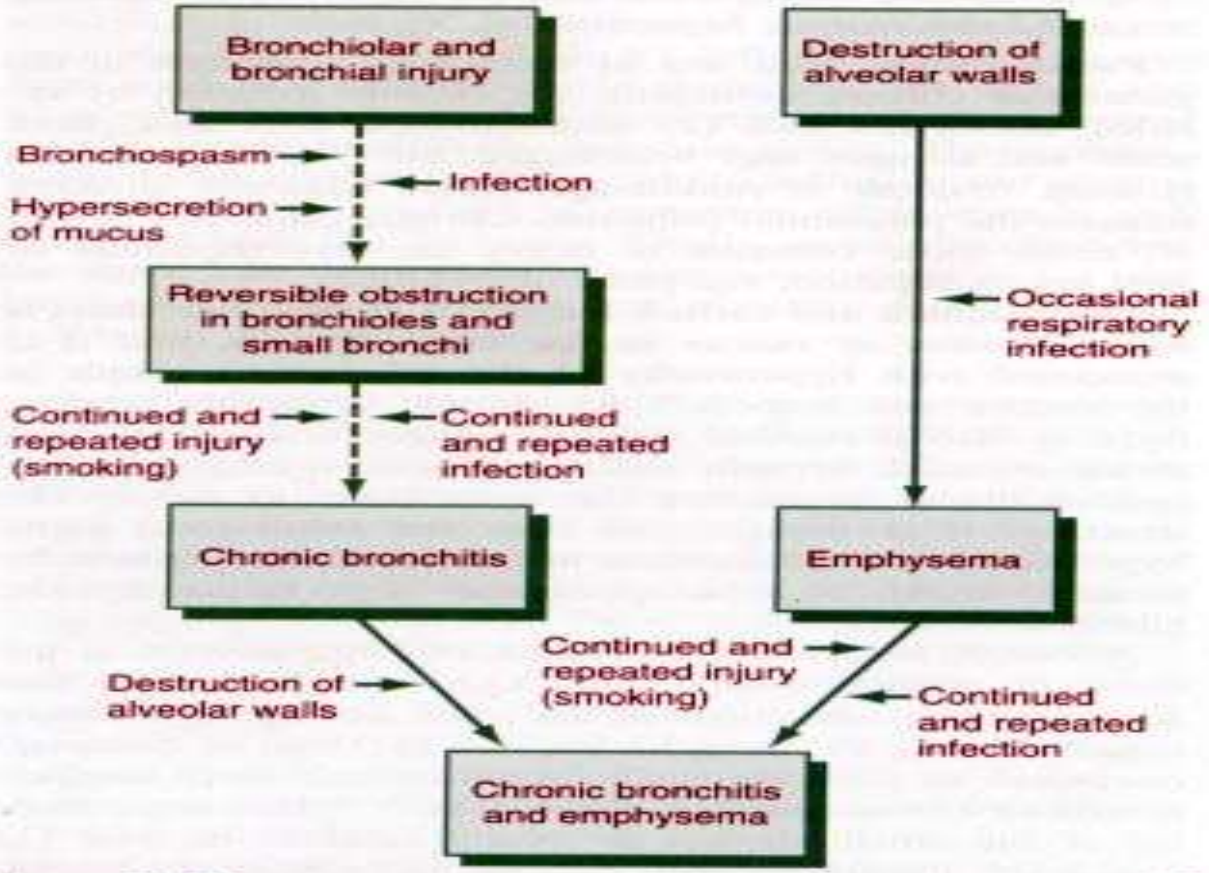


Figure 16–12

Schematic representation of evolution of chronic bronchitis *(left)* and emphysema *(right)*. Although both can culminate in chronic bronchitis and emphysema, the pathways are different, and either one may predominate. The dashed arrows on the left indicate that, in the natural history of chronic bronchitis, it is not known whether there is a predictable progression from obstruction in small airways to chronic (obstructive) bronchitis. (Redrawn from Fishman AP: The spectrum of chronic obstructive disease of the airways. In Fishman AP (ed): Pulmonary Diseases and Disorders, 2nd ed. New York, McGraw-Hill, 1988, p 1164.)

Clinical features

- Simple chronic bronchitis: cough but no physiologic evidence of airway obstruction
- Chronic asthmatic bronchitis: hyperreactive airways with intermittent bronchospasm and wheezing
- Obstructive bronchitis: often have associated emphysema, small airway disease
- Causes: 4× - 10× more common in smokers, chronic irritation and infections may contribute
- Other causes and contributors are air pollution including passive cigarette smoke, marijuana smoke and occupational dust exposure
- Tobacco interferes with ciliary action, directly damages airway epithelium and inhibits ability of white blood cells to clear bacteria; infections maintain but do not initiate chronic bronchitis
- Often diagnosed at time of acute respiratory illness More infections, purulent sputum, hypercapnia, hypoxia than emphysema; clinically called "blue bloaters"
- May cause secondary pulmonary vascular hypertension, cor pulmonale, congestive heart failure, death due to respiratory acidosis and coma, congestive heart failure and pneumothorax
- **Reid index**: ratio of thickness of mucus gland layer to thickness of wall between epithelium and cartilage; normal is 0.4, increased in chronic bronchitis

Microscopic (histologic) description

- ***Early***: hypersecretion of mucus in large airways with hypertrophy of submucosal glands in tracheobronchial tree
- ***Later***: increase in goblet cells in small airways contributes to excessive mucus production and airway obstruction
- Increased percentage of bronchial wall is occupied by submucosal mucous glands, as measured by Reid index; this directly correlates with sputum production, variable dysplasia, squamous metaplasia, bronchiolitis obliterans
- Chronic inflammatory infiltrates range from absent to prominent

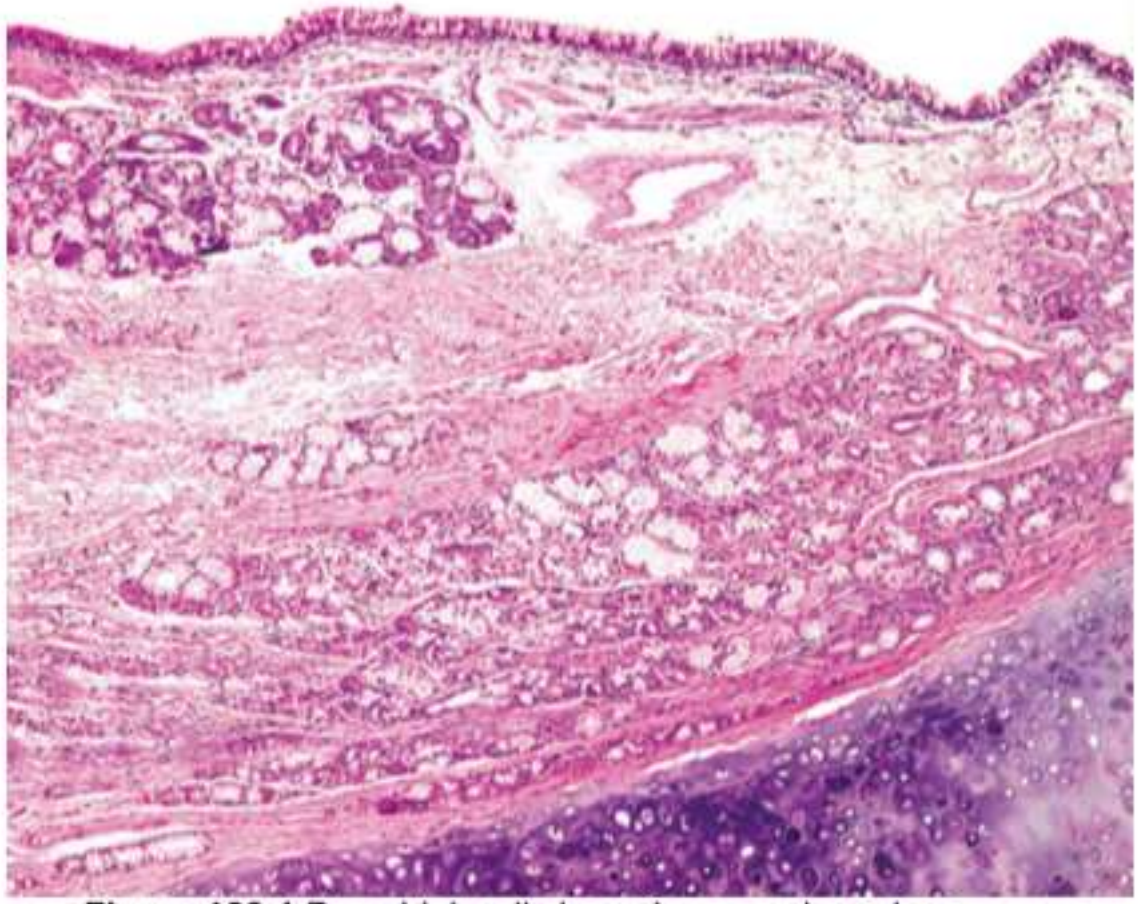


Figure 100.1 Bronchial wall shows increased numbers of bronchial glands characteristic of chronic bronchitis.

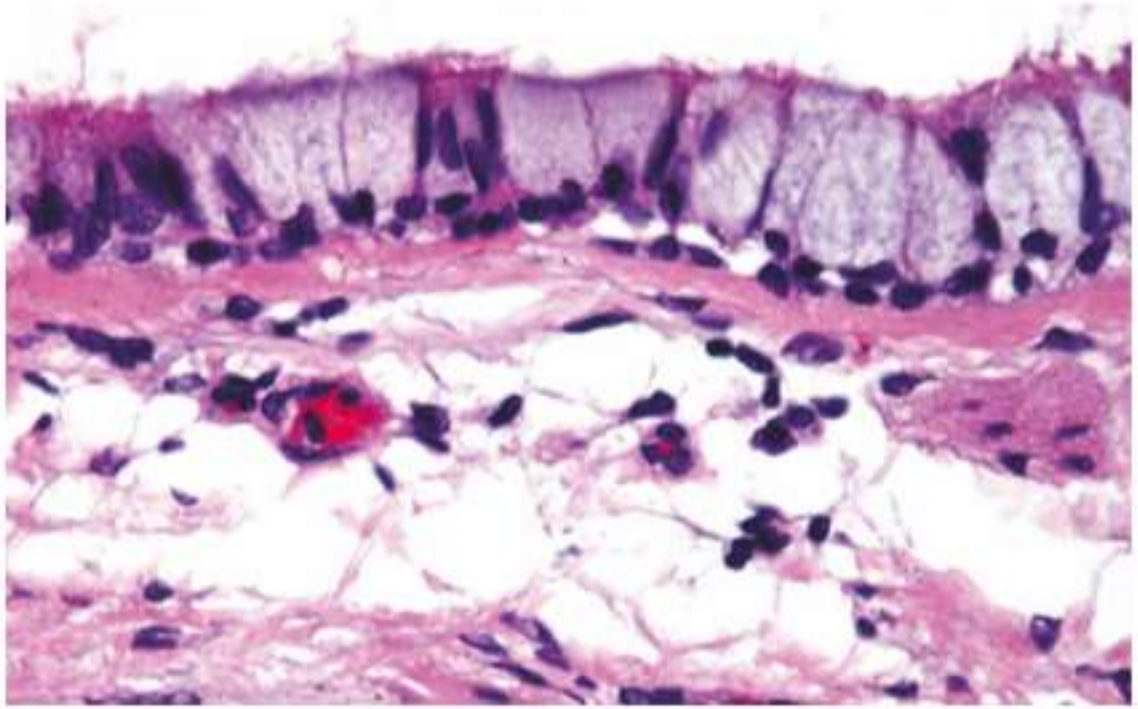


Figure 100.2 Chronic bronchitis shows bronchial surface epithelium with goblet-cell metaplasia.

ASMA

Cytologic Features

- Findings are not specific for asthma; however, abundant mucus, eosinophils and Charcot–Leyden crystals, Creola bodies, and Curschmann's spirals can be seen.

Histologic Features

- Bronchial and bronchiolar smooth muscle hyperplasia.
- Bronchial mucus gland hyperplasia.
- Goblet-cell metaplasia.
- Mixed inflammation of the bronchial wall typically with abundant eosinophils can be seen.
- Basement membrane thickening and abundant mucous or mucin plugs in bronchi.

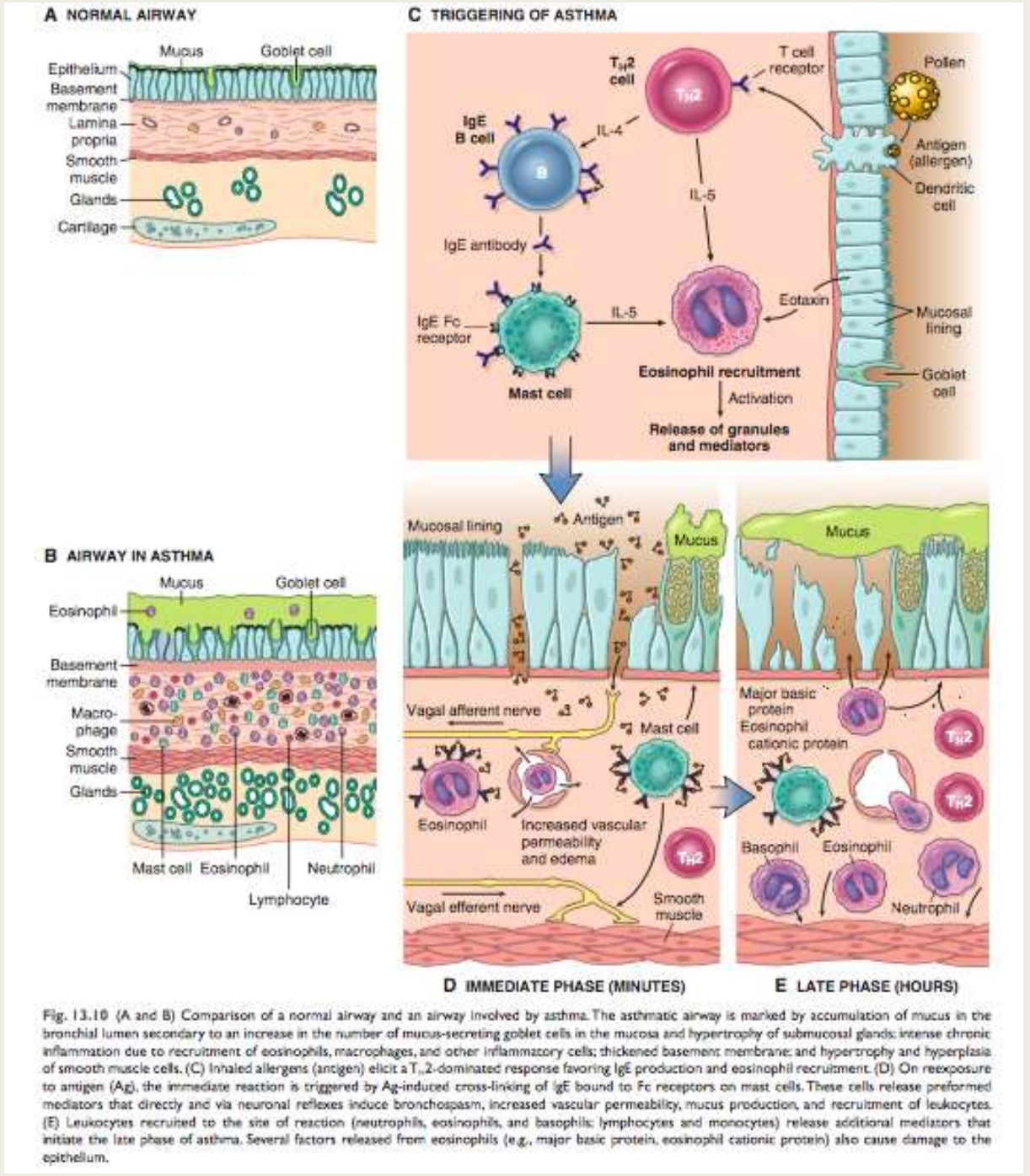


Fig. 13.10 (A and B) Comparison of a normal airway and an airway involved by asthma. The asthmatic airway is marked by accumulation of mucus in the bronchial lumen secondary to an increase in the number of mucus-secreting goblet cells in the mucosa and hypertrophy of submucosal glands; intense chronic inflammation due to recruitment of eosinophils, macrophages, and other inflammatory cells; thickened basement membrane; and hypertrophy and hyperplasia of smooth muscle cells. (C) Inhaled allergens (antigen) elicit a T_H2-dominated response favoring IgE production and eosinophil recruitment. (D) On reexposure to antigen (Ag), the immediate reaction is triggered by Ag-induced cross-linking of IgE bound to Fc receptors on mast cells. These cells release preformed mediators that directly and via neuronal reflexes induce bronchospasm, increased vascular permeability, mucus production, and recruitment of leukocytes. (E) Leukocytes recruited to the site of reaction (neutrophils, eosinophils, and basophils; lymphocytes and monocytes) release additional mediators that initiate the late phase of asthma. Several factors released from eosinophils (e.g., major basic protein, eosinophil cationic protein) also cause damage to the epithelium.

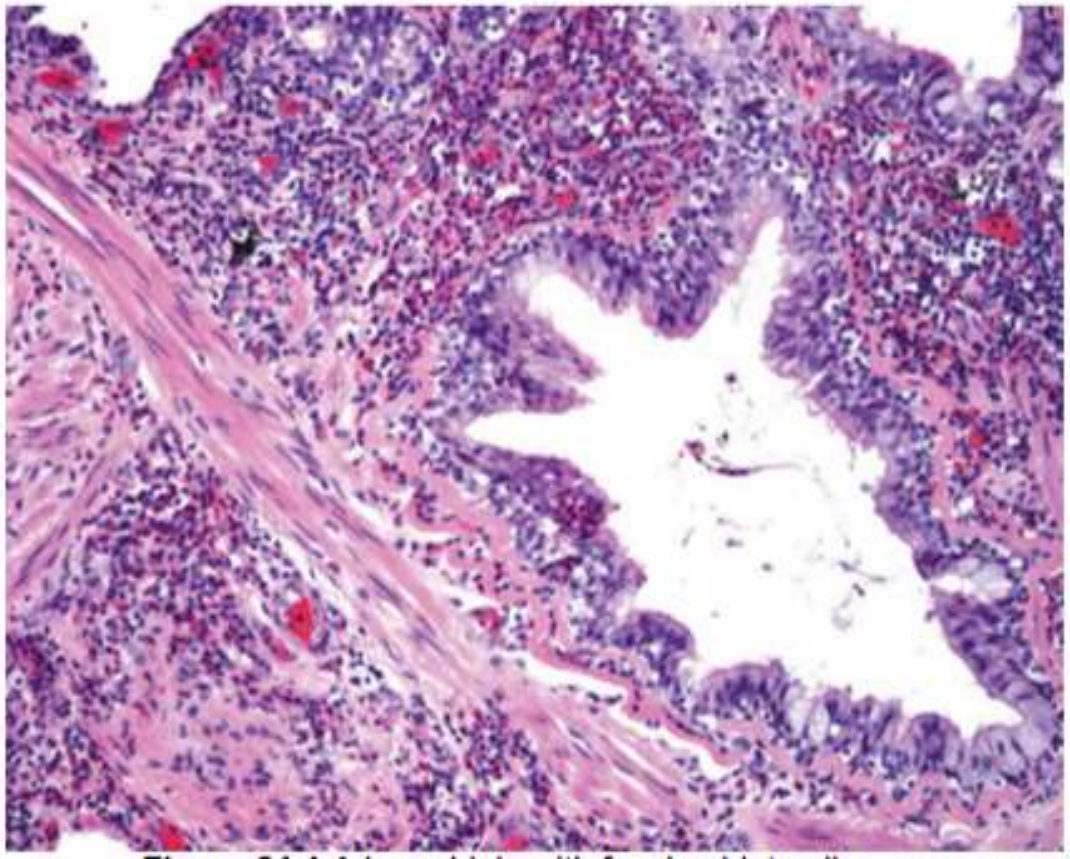


Figure 81.1 A bronchiole with focal goblet-cell metaplasia and surrounding smooth muscle hyperplasia. A mixed inflammatory infiltrate is seen within the wall, and numerous eosinophils are present.

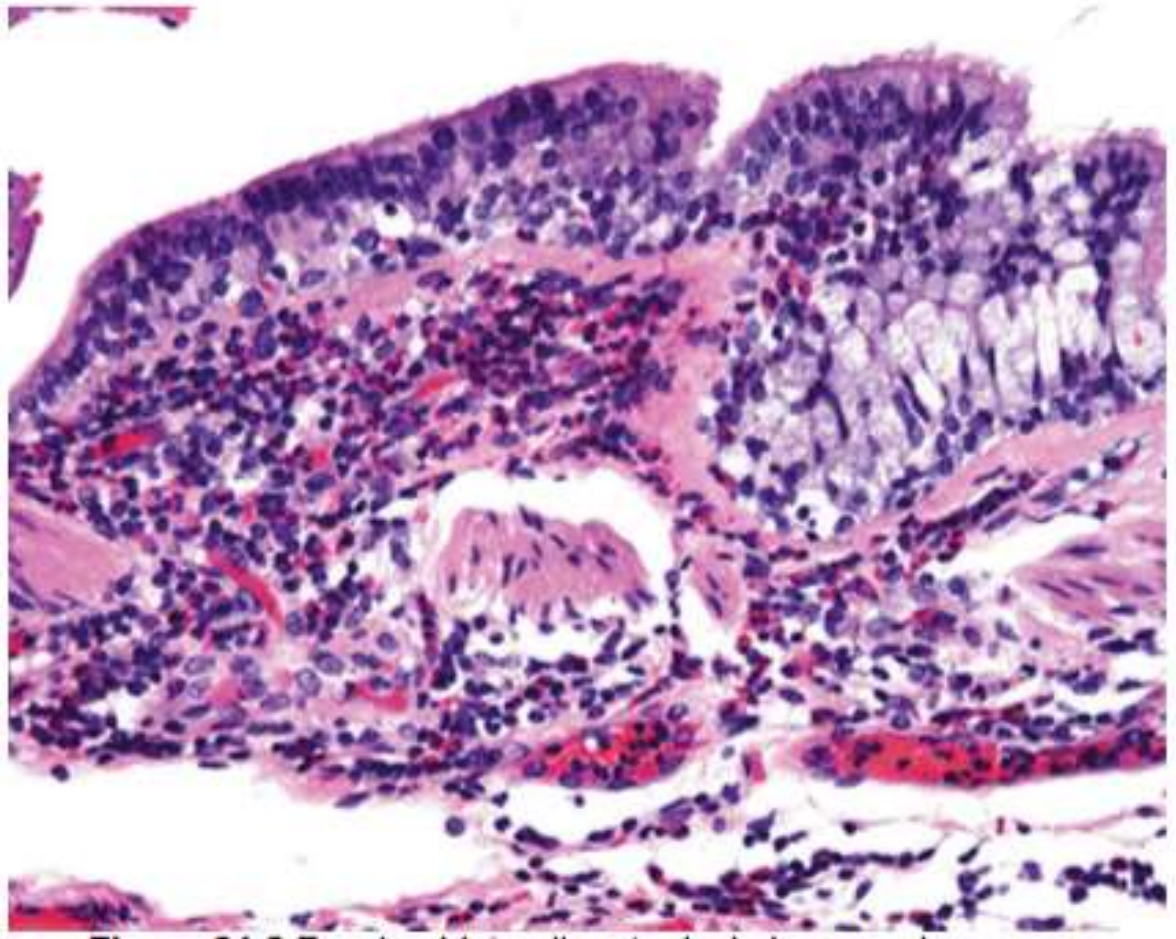


Figure 81.2 Focal goblet-cell metaplasia is seen along with numerous eosinophils.

BRONCHIECTASIS

- " Infeksi kronik *(nekrosis)* pd Bronchus dan Bronchiolus yang menyebabkan atau disertai dilatasi abnormal jalan nafas"
- *Incidence* : Pria dan Wanita

  Sering pd anak – anak

  Gx timbul < 20 th
- Etiologi : 1. Obstruksi Bronchus

  2. Kelainan Congenital

  3. Pneumonia Necrotizing

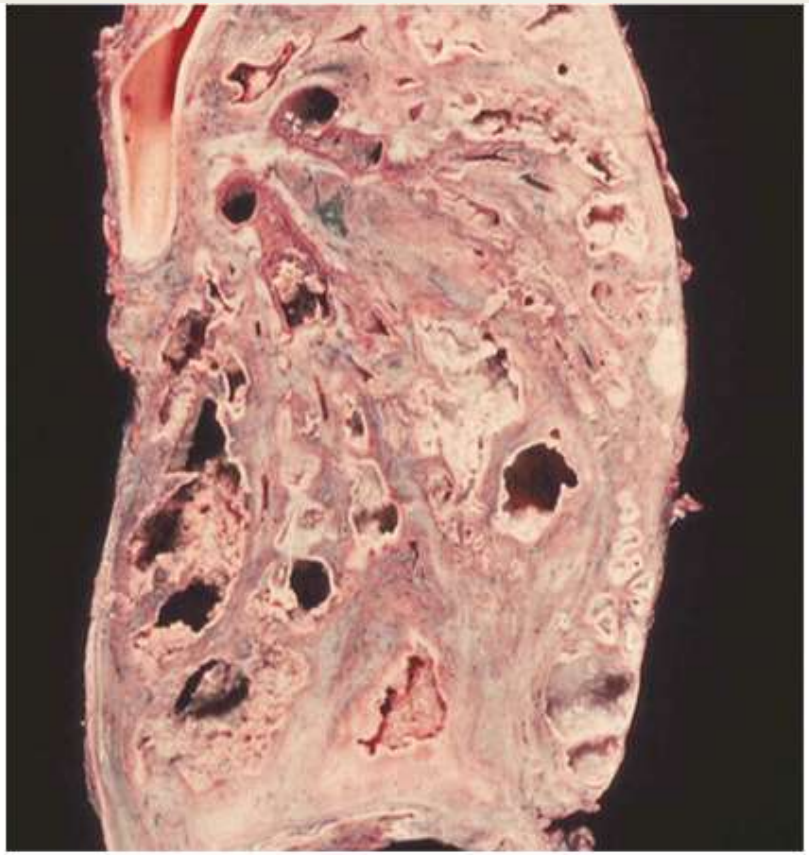


Figure 78.1 Gross image of bronchiectasis showing dilated segmental bronchi and surrounding parenchymal fibrosis.

Histologic Features

- Dilated bronchi; often variable amounts of inflammation, erosion/ulceration, and squamous metaplasia of the bronchiolar epithelium can be seen.
- Lymphoid follicles may be present in the bronchial walls.
- Fibrosis of the bronchial wall and surrounding tissues; destruction of bronchial wall structures.
- Similar changes often seen in downstream bronchioles (bronchiolectasis).
- Often associated with other pathologic processes (e.g., acute and chronic pneumonia, organizing pneumonia, and fibrosing conditions).

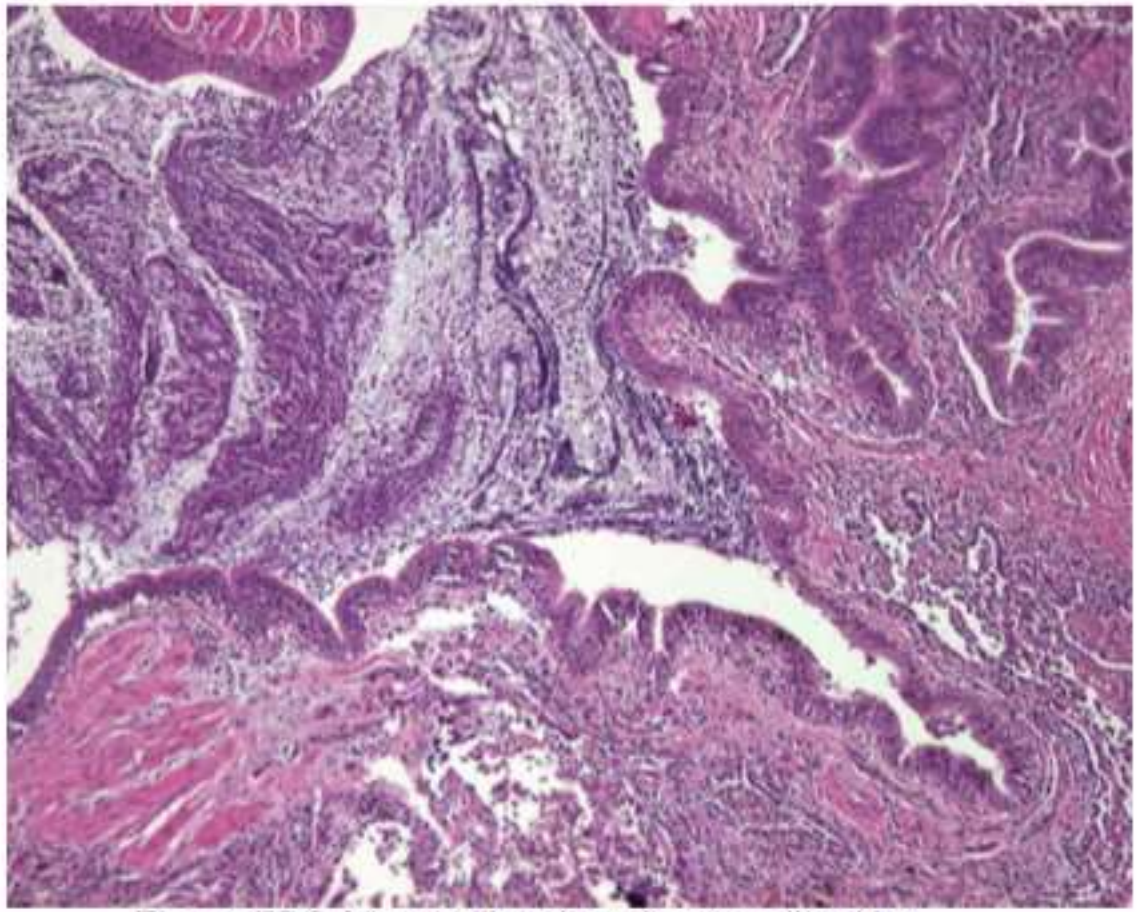


Figure 78.2 A large dilated cystic space lined by ciliated respiratory epithelium and containing mucin with admixed acute inflammatory cells. Surrounding fibrosis can be seen.

Clinical features

- Diagnosis is based on presence of infection (stasis occurs in dilated bronchi) and obstruction
- Patients have significant morbidity
- 9% prevalence in Korean study; associated with TB
- **Symptoms**: cough, fever and copious amounts of foul smelling, purulent sputum
- **Causes**: bronchial obstruction (localized bronchiectasis), congenital bronchiectasis, cystic fibrosis, intralobar sequestration of lung, immunodeficiency, immotile cilia / Kartegener syndrome, Young syndrome, necrotizing pneumonia (staphylococcus, tuberculosis)
- ***Cystic fibrosis***: obstruction due to mucus plugs, infection due to decreased ciliary clearance of bacteria
- ***Kartegener syndrome***: autosomal recessive condition with variable penetrance; due to absent or irregular dynein arms of cilia, which causes defective bacterial clearance (bronchiectasis, sinusitis), defective cell motility during embryogenesis (situs inversus) and immotile sperm (infertility)
- ***Young syndrome***: infertility caused by azoospermia, but without ultrastructural ciliary abnormalities

RESTRICTIVE INTERSITIAL LUNG DISEASE

- Idiopatic fibrosing disease
- Pneumoconiasis
- Granulomatous disease → Sarcoidosis

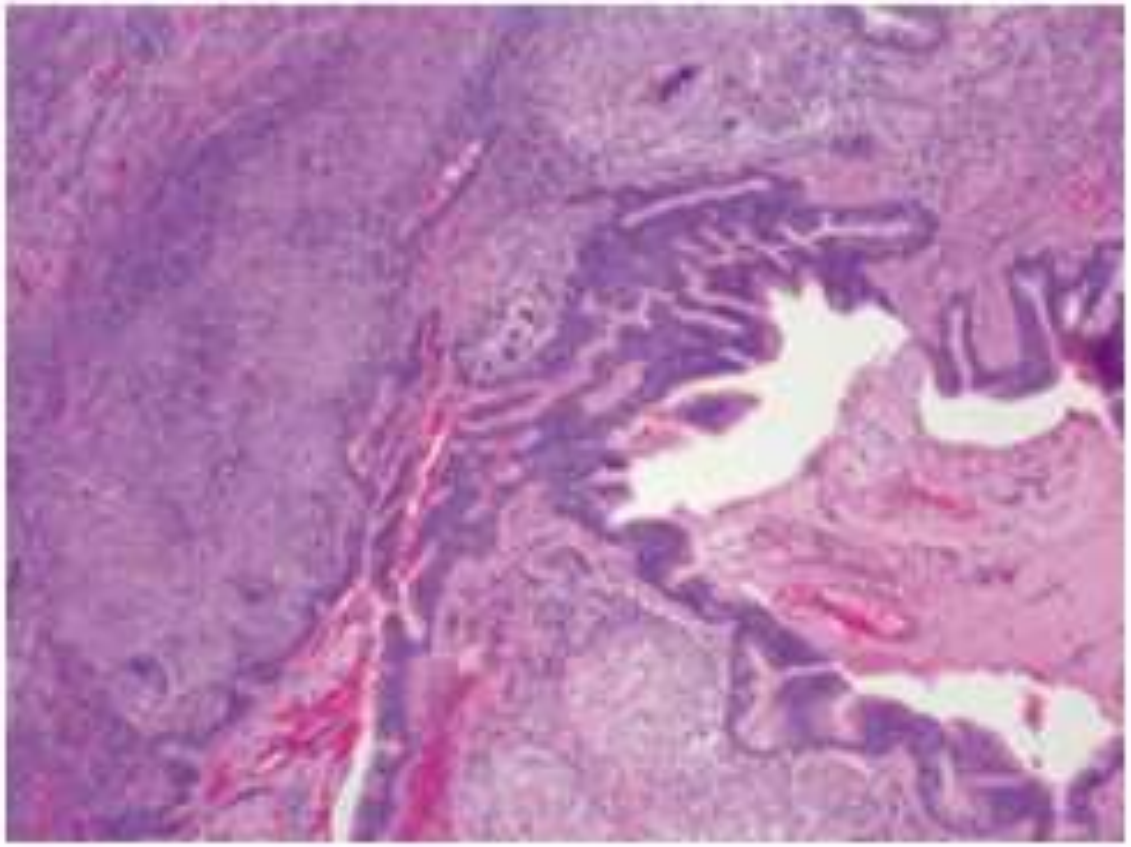


Fig. 13.21 Sarcoid. Characteristic peribronchial noncaseating granulomas with many giant cells are present.

INFECTION :
1. PNEUMONIA

- Infeksi bakterial yang sering fatal dan multiple yang biasanya berasal dari infeksi bronchus dan bronchioli yang meluas ke alveoli
- Incidence : anak dan lansia

Pathogenesa : ~ primer

~ Sbg Komplikasi

- Jenis :
  - *Lobar pneumonia*
  - *bronchopneumonia*

Table 13.5 The Pneumonia Syndromes and Implicated Pathogens

Community-Acquired Bacterial Pneumonia
Streptococcus pneumoniae *Haemophilus influenzae* *Moraxella catarrhalis* *Staphylococcus aureus* *Legionella pneumophila* Enterobacteriaceae (*Klebsiella pneumoniae*) and *Pseudomonas* spp. *Mycoplasma pneumoniae* *Chlamydia pneumoniae* *Coxiella burnetii* (Q fever)
Community-Acquired Viral Pneumonia
Respiratory syncytial virus, human metapneumovirus, parainfluenza virus (children); influenza A and B (adults); adenovirus (military recruits)
Nosocomial Pneumonia
Gram-negative rods belonging to Enterobacteriaceae (*Klebsiella* spp., *Serratia marcescens*, *Escherichia coli*) and *Pseudomonas* spp. *S. aureus* (usually methicillin-resistant)
Aspiration Pneumonia
Anaerobic oral flora (*Bacteroides*, *Prevotella*, *Fusobacterium*, *Peptostreptococcus*), admixed with aerobic bacteria (*S. pneumoniae*, *S. aureus*, *H. influenzae*, and *Pseudomonas aeruginosa*)
Chronic Pneumonia
Nocardia Actinomyces Granulomatous: Mycobacterium tuberculosis and atypical mycobacteria, *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*
Necrotizing Pneumonia and Lung Abscess
Anaerobic bacteria (extremely common), with or without mixed aerobic infection *S. aureus*, *K. pneumoniae*, *Streptococcus pyogenes*, and type 3 pneumococcus (uncommon)
Pneumonia in the Immunocompromised Host
Cytomegalovirus *Pneumocystis jiroveci* Mycobacterium avium complex (MAC) Invasive aspergillosis Invasive candidiasis "Usual" bacterial, viral, and fungal organisms (listed above)

Manifestasi klinis :

- Often divided into community acquired, hospital acquired and aspiration pneumonia
- Common agents: *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Legionella pneumophila, Pseudomonas aeruginosa*, coliforms
- Complications: abscess, empyema, organization, sepsis, meningitis
- Consolidation: exudative solidification of lung
- Signs and symptoms of pneumonia: shortness of breath, fever, productive cough, malaise, friction rub (if fibrinous pleuritis)
- Bronchopneumonia: patchy consolidation of lung centered on bronchi; may progress to lobar pneumonia; patterns of bronco- and lobar pneumonia may overlap
- Lobar pneumonia: affects entire lung but now rare due to antibiotics; associated with increased virulence of organism or increased host vulnerability (infants, elderly); may be due to extension of existing bronchiolitis or bronchitis

LOBAR PNEUMONIA

- **radang akut paru yang mengenai sebagian besar / seluruh paru**
- Incidence : Orang Dewasa

  Pria : Wanita = 3-4 : 1
- Etiologi : 90 –95 % Pneumococcus
- Pathogenesa : virulensi kuman host
- Predisposisi → Daya tahan menurun – kuman TR – menuju TR bagian bawah – alveoli – pores of kohn – tersebar

Fase patologis lobar pneumonia

- KONGESTI
  - *Edema inflamasi yang meluas, jarang timbul dan mengindikasikan adanya edema paru*
- HEPATISASI MERAH
  - *Lobus yang terserang menjadi padat dan berwarna merah seperti hepar, bronchi kecil tersumbat fibrin, alveoli terisi sel darah serta fibrin, PMN sedikit*
- HEPATISASI KELABU
  - *Paru-paru menjadi padat, berwarna abu-abu atau kuning, alveoli terisi fibrin, PMN >>, sel darah merah sedikit, arteriol paru dapat mengalami trombosis*
- RESOLUSI
  - *Macrofag menyingkirkan eksudat dari alveoli, arsitektur normal kembali, paru pulih kembali*

Fig. 13.30 Lobar pneumonia with gray hepatization. The lower lobe is uniformly consolidated.

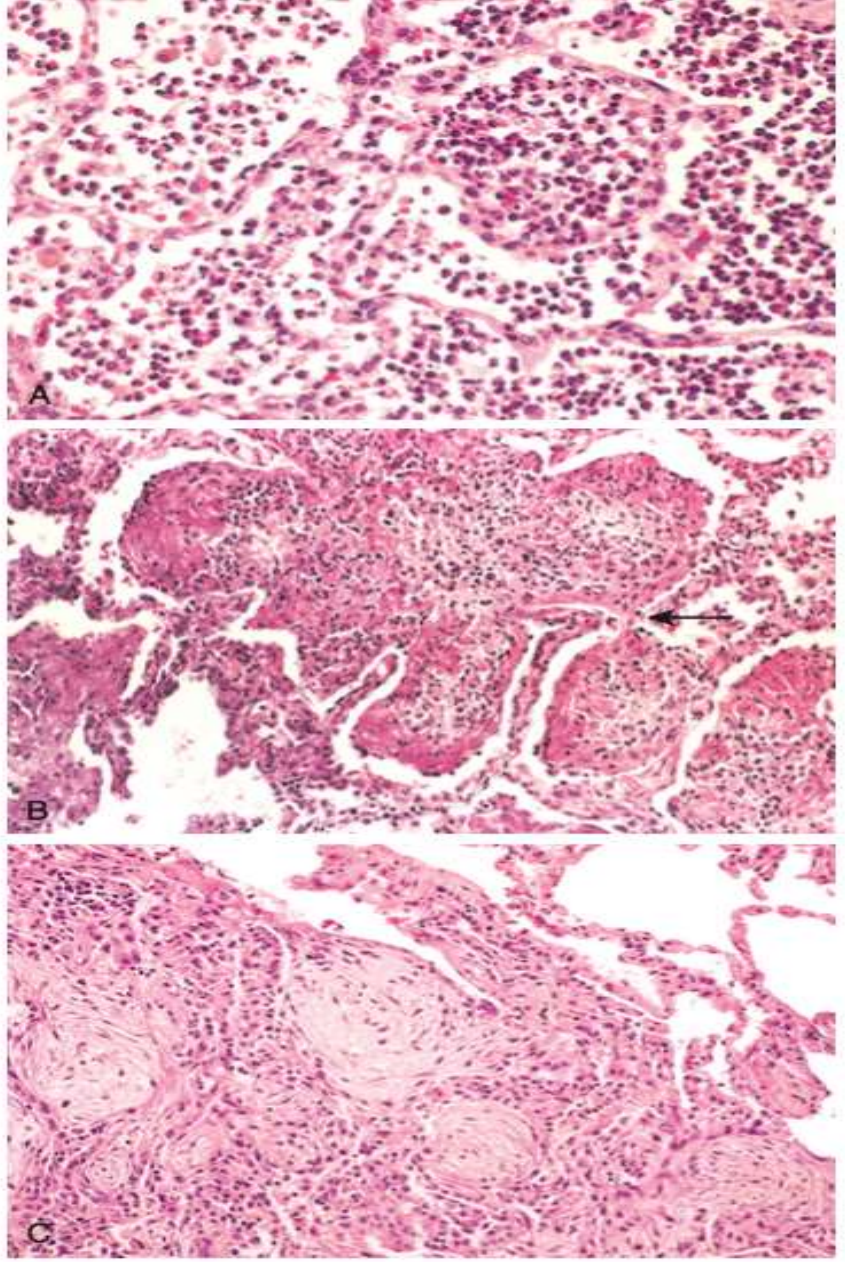


Fig. 13.31 (A) Acute pneumonia. The congested septal capillaries and extensive neutrophil exudation into alveoli correspond to early red hepatization. Fibrin nets have not yet formed. (B) Early organization of intraalveolar exudates, seen in areas to be streaming through the pores of Kohn *(arrow)*. (C) Advanced organizing pneumonia, featuring transformation of exudates to fibromyxoid masses richly infiltrated by macrophages and fibroblasts.

BRONCHOPNEUMONIA

- Bronchopneumonia: neutrophils in bronchi, bronchioles and adjacent alveolar spaces; lipid pneumonia, if marked, has lipid laden macrophages

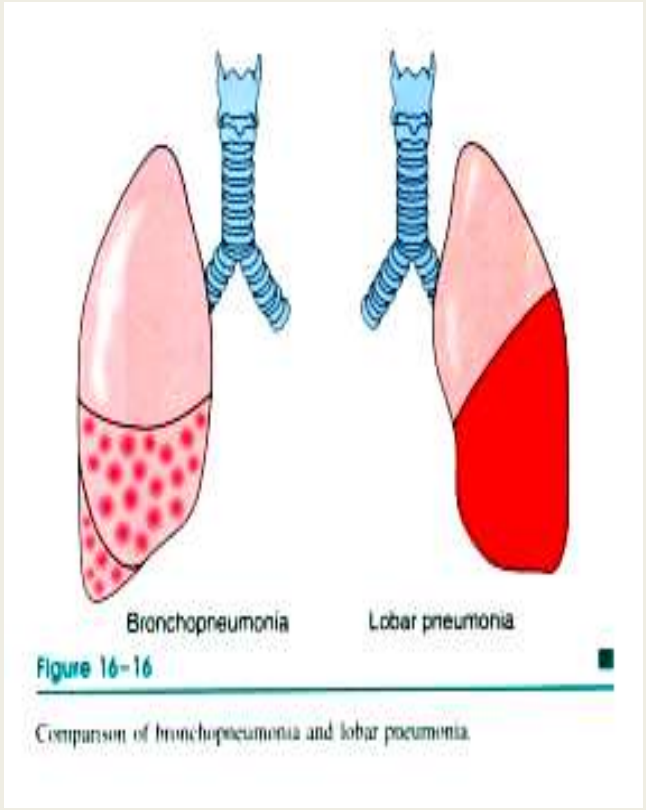
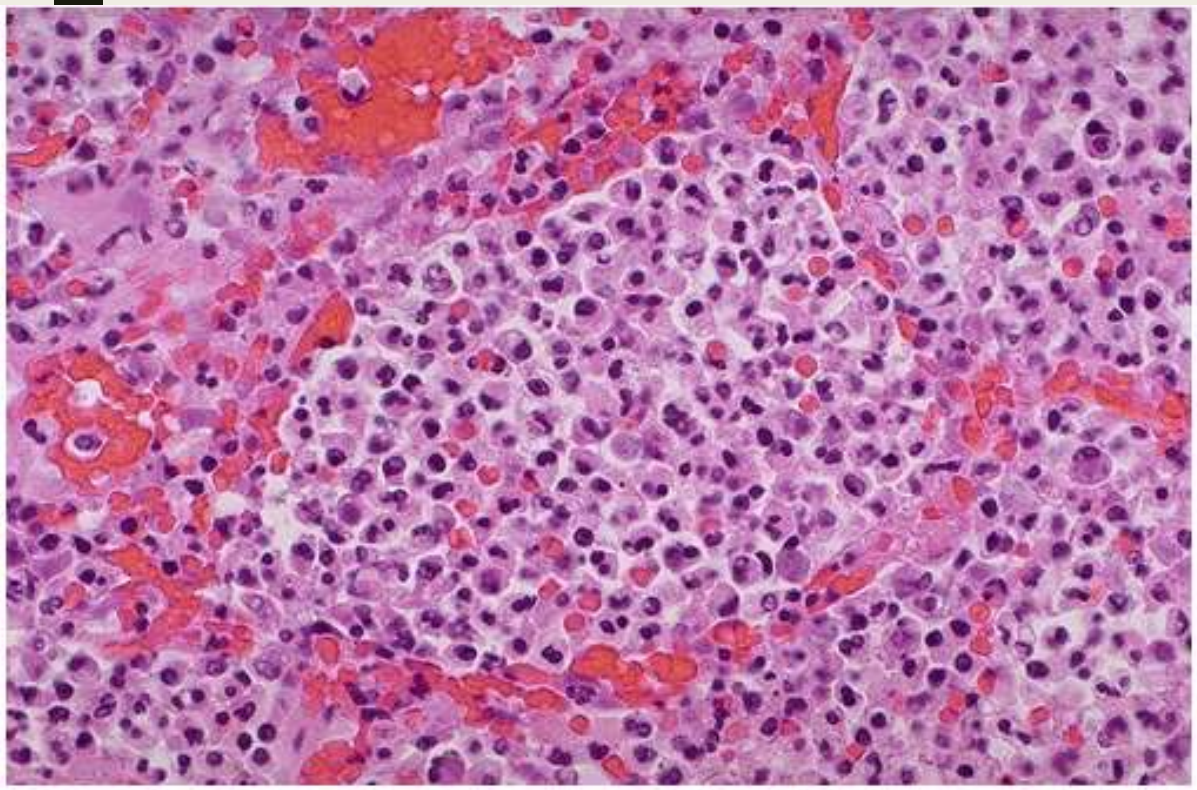


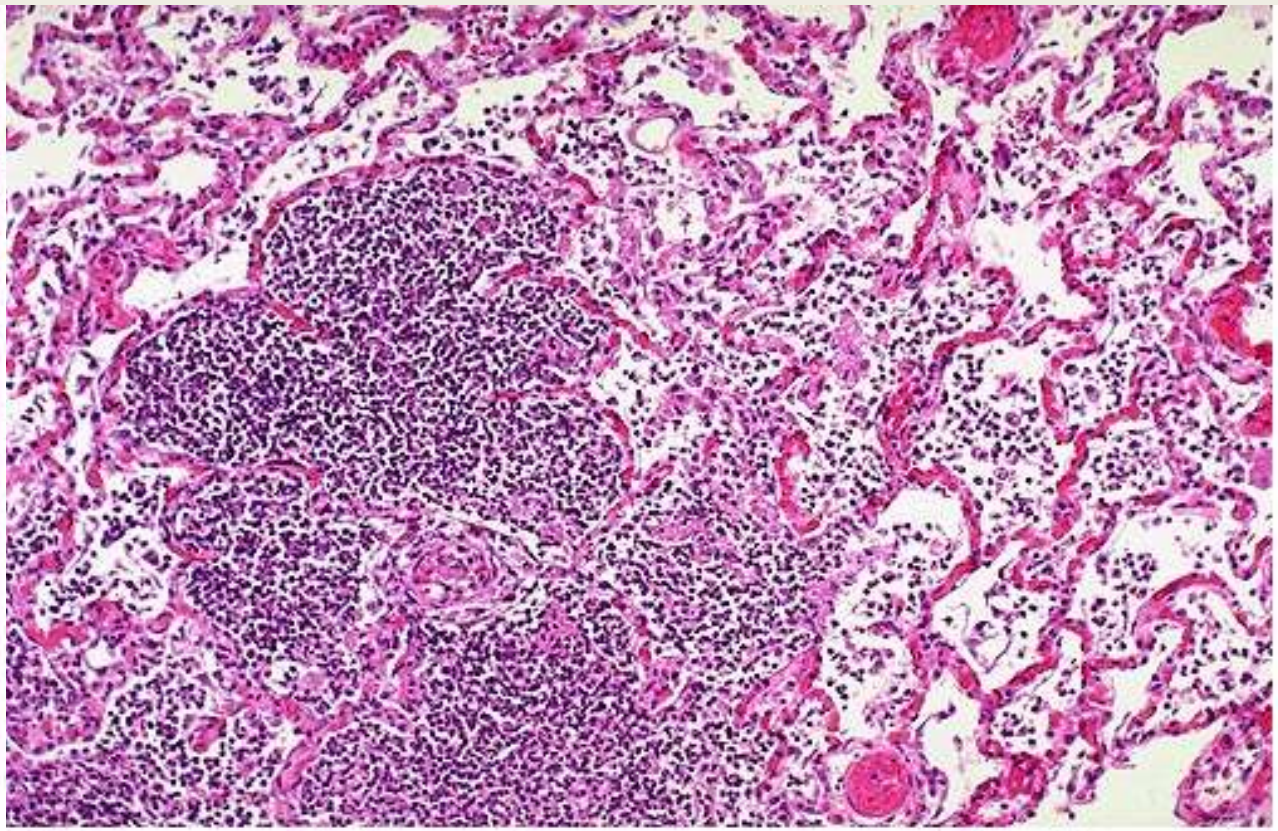
Figure 16-16

Comparison of bronchopneumonia and lobar pneumonia.

Here is another example of a bronchopneumonia. The lighter areas that appear to be raised on cut surface from the surrounding lung are the areas of consolidation of the lung.



At high magnification, the alveolar exudate of mainly neutrophils is seen. The surrounding alveolar walls have capillaries that are dilated and filled with RBC's. Such an exudative process is typical for bacterial infection. This exudate gives rise to the productive cough of purulent yellow sputum seen with bacterial pneumonias.



At higher magnification can be seen a patchy area of alveoli that are filled with inflammatory cells. The alveolar structure is still maintained, which is why a pneumonia often resolves with minimal residual destruction or damage to the lung.

ABSES PARU

KERADANGAN DGN PEMBENTUKAN SUPP LOKAL DLM PARU. DITANDAI DGN NEKROSIS DARI JARINGAN PARU.

Incidence : Dewasa muda, pria > wanita

Etiologi : Streptococcus
Staphylococcus
Pneumococcus

Patogenesa : Aspirasi
Sudah ada infeksi
Emboli septic
Neoplasma
Trauma tembus

Makros : Beberapa milimeter – 5-6 cm

Jumlah tergantung penyebab

Fokus hyperemi ~> sentral nekrosis ~> isi pus ~> dinding fibrosis

Mikros : Parenchym paru nekrosis

Serbukan PMN,MN

Dinding nekrosis

Komplikasi : Abscess otak

Meningitis

TBC

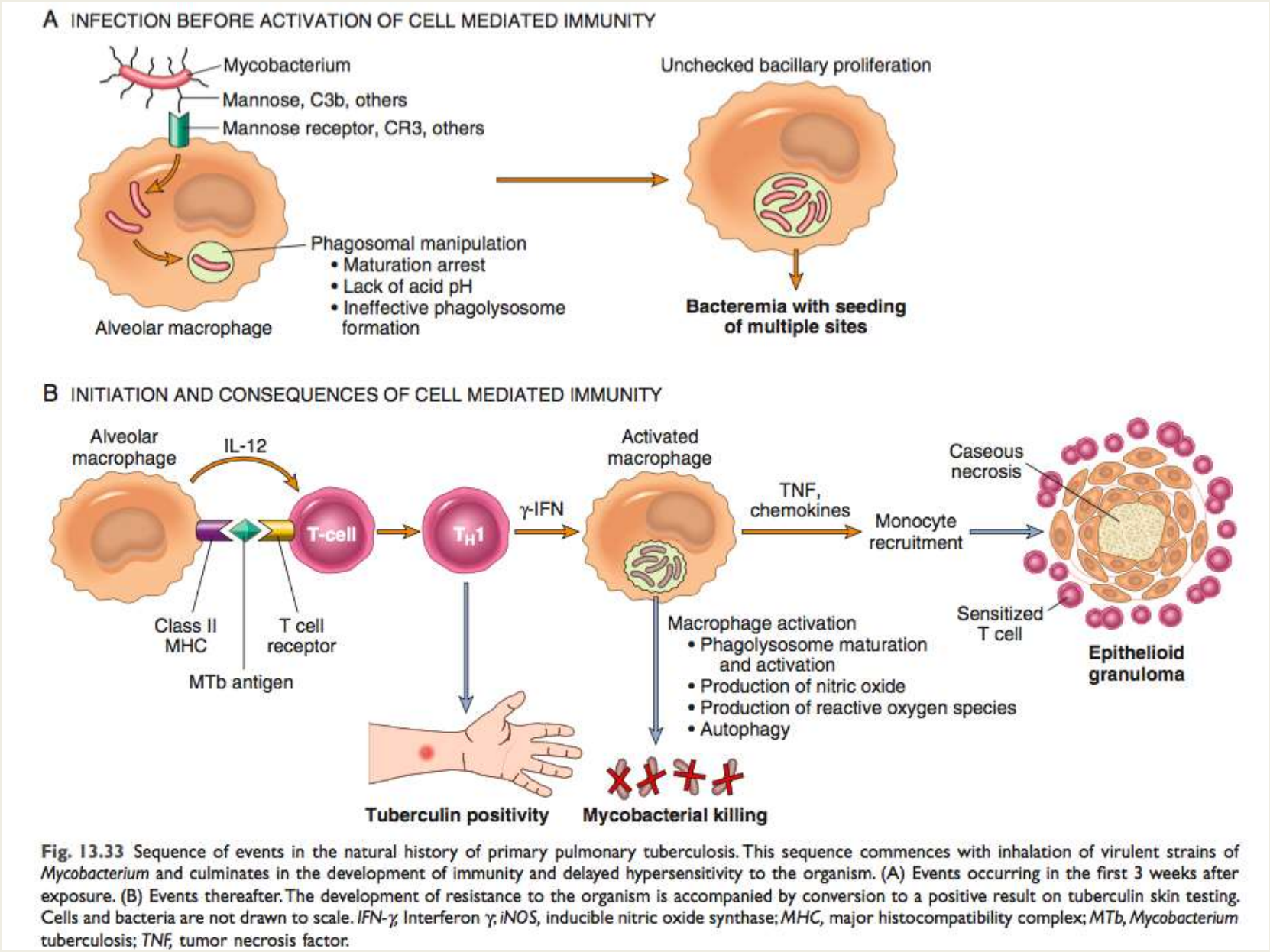


Fig. 13.33 Sequence of events in the natural history of primary pulmonary tuberculosis. This sequence commences with inhalation of virulent strains of *Mycobacterium* and culminates in the development of immunity and delayed hypersensitivity to the organism. (A) Events occurring in the first 3 weeks after exposure. (B) Events thereafter. The development of resistance to the organism is accompanied by conversion to a positive result on tuberculin skin testing. Cells and bacteria are not drawn to scale. *IFN-γ*, Interferon γ; *iNOS*, inducible nitric oxide synthase; *MHC*, major histocompatibility complex; *MTb*, *Mycobacterium* tuberculosis; *TNF*, tumor necrosis factor.

TB PRIMER

- Kuman Exogen 10 – 14 hr → Sensitisasi
- Fokus Pertama :

gohn kompleks →

- Lesi parenchymal Subpleural → Ghon Fokus
- KGB membesar dengan fokus caseosa tracheobroncial

Mikros :

- Hard Tubercle →
- Soft Tubercle

- Histiosit → epiteloid
- Giant cell Langhans
- Fibroblas & Limfosit

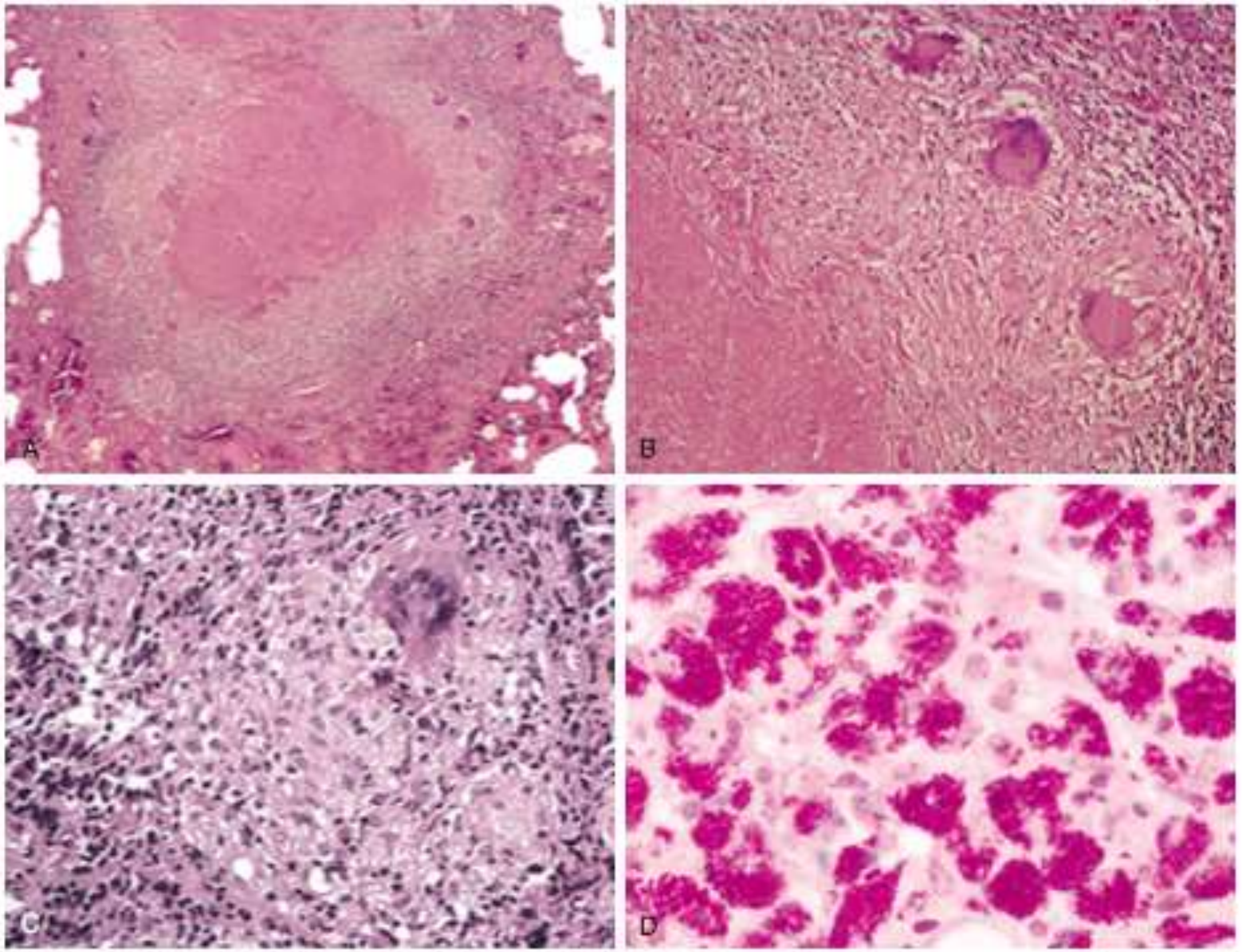


Fig. 13.35 The morphologic spectrum of tuberculosis. A characteristic tubercle at low magnification (A) and at higher power (B) shows central granular caseation surrounded by epithelioid and multinucleate giant cells. This is the usual response in individuals who develop cell-mediated immunity to the organism. (C) Occasionally, even in immunocompetent patients, tubercular granulomas may not show central caseation; hence, irrespective of the presence or absence of caseous necrosis, use of special stains for acid-fast organisms is indicated when granulomas are present. (D) In this specimen from an immunosuppressed patient, sheets of macrophages packed with mycobacteria are seen (acid-fast stain).

TB SEKUNDER

5 – 10% Reaktivasi

Di apex – high oxygen tension

Fokus diameter < 3 cm

Pada reinfeksi selalu kelenjar regional mengalami aktivitas yg sama

Kerusakan sekunder >> primer

Late progressive pulmonary TBC

Beberapa bulan/ tahun, biasanya disertai kerusakan bronchus / bronchiolus ~> Fibrocaseus TBC + cavitasi

Penyebaran : Lymphohematogenous

Lymphe ~>...~> Jantung kanan~> seluruh paru

Arteri ~> Paru

Vena ~> seluruh tubuh

- Gambaran Makros : 1 mm, putih kekuning-kuningan, padat.
- Mikros : bbrp tubercle dgn sentral nekrosis caseosa

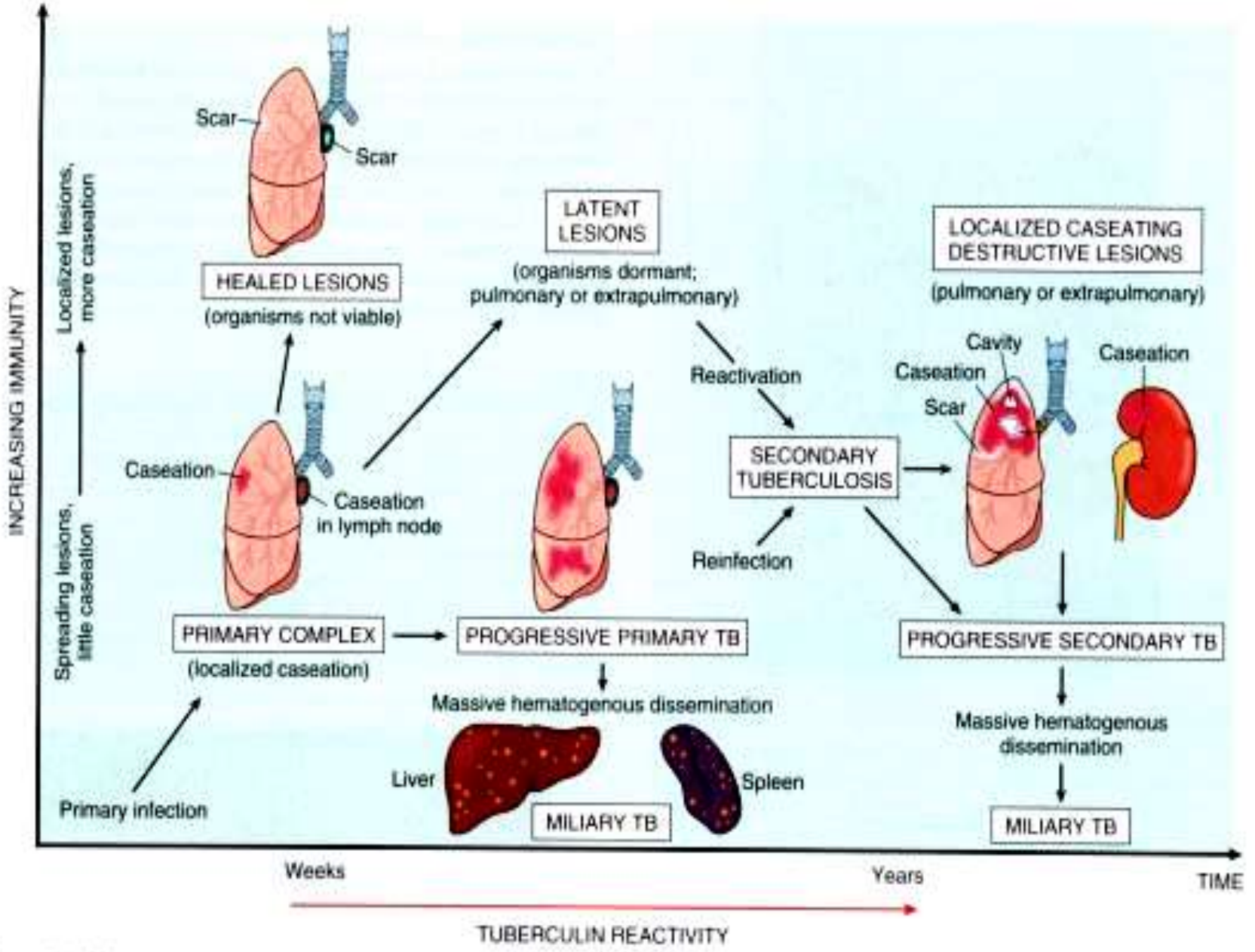


Figure 16-23

Natural history and spectrum of tuberculosis (TB). (Adapted from a sketch provided by Dr. R. K. Komar, The University of New South Wales, School of Pathology, Sydney, Australia.)

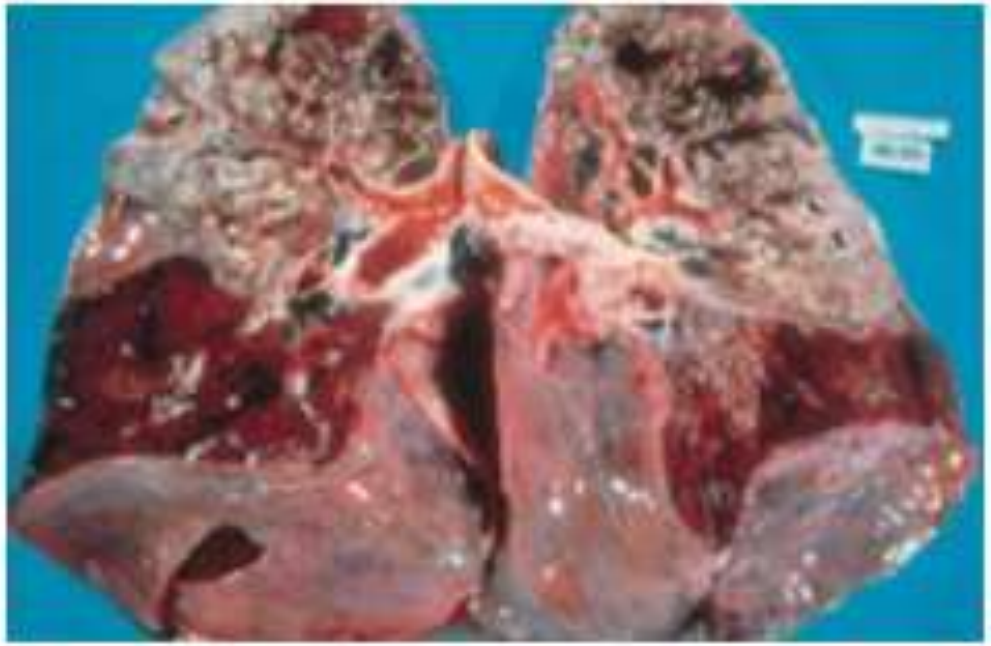


Fig. 13.36 Secondary pulmonary tuberculosis. The upper parts of both lungs are riddled with gray-white areas of caseation and multiple areas of softening and cavitation.

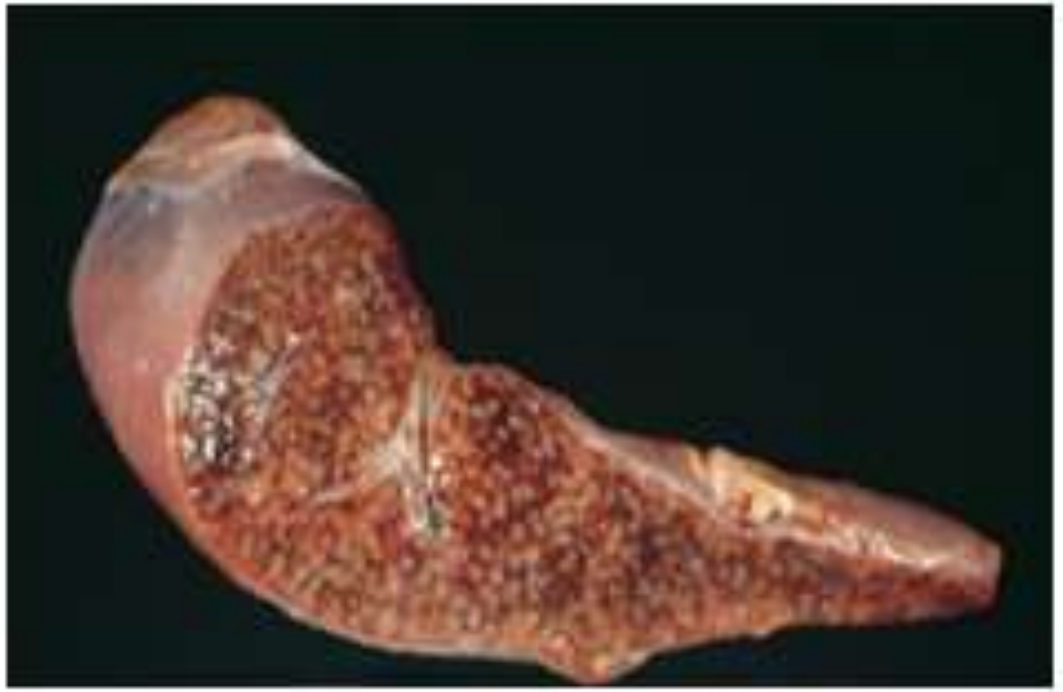


Fig. 13.37 Miliary tuberculosis of the spleen. The cut surface shows numerous gray-white granulomas.

SARS-COV-2

- Etiologi : coronavirus
  - *Nonsegmented*
  - *Enveloped*
  - *ssRNA*
- 4 protein
  - *Spike surface glycoprotein* —berikatan→ *ACE-2*
  - *Small envelope protein*
  - *Matrix protein*
  - *Nucleocapside protein*

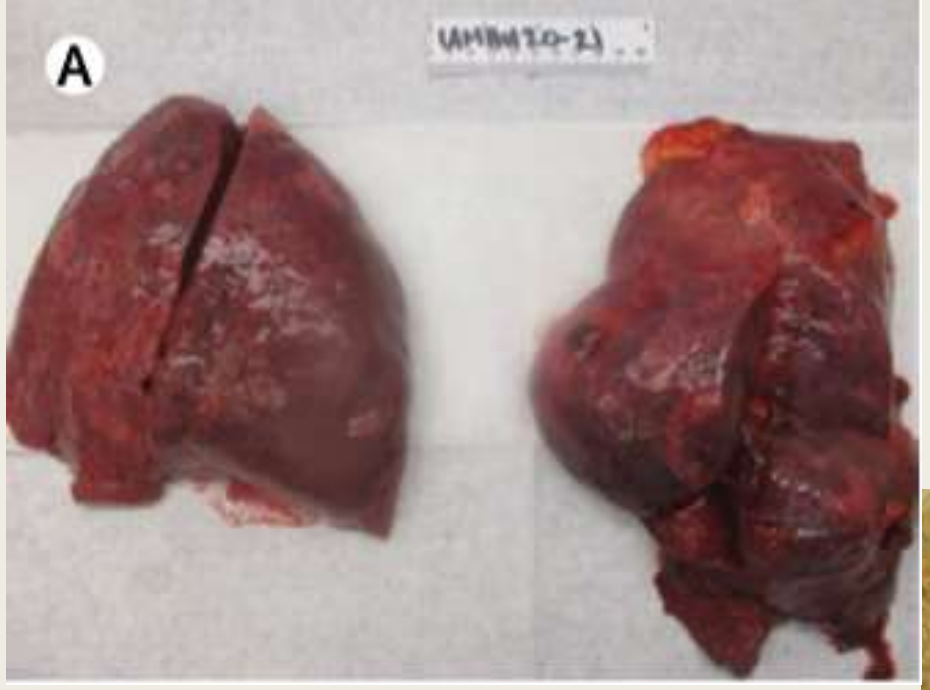
- Gejala klinis → asymptomatic
  - *Fever*
  - *Dry cough*
  - *Dypsneu*
  - *Confusion*
  - *Muscle pain*
  - *Headache*
  - *Sore throat*
  - *Rhinorrea*
  - *Chest pain*
  - *Diarrhea*
  - *Naussea*
  - *vomiting*

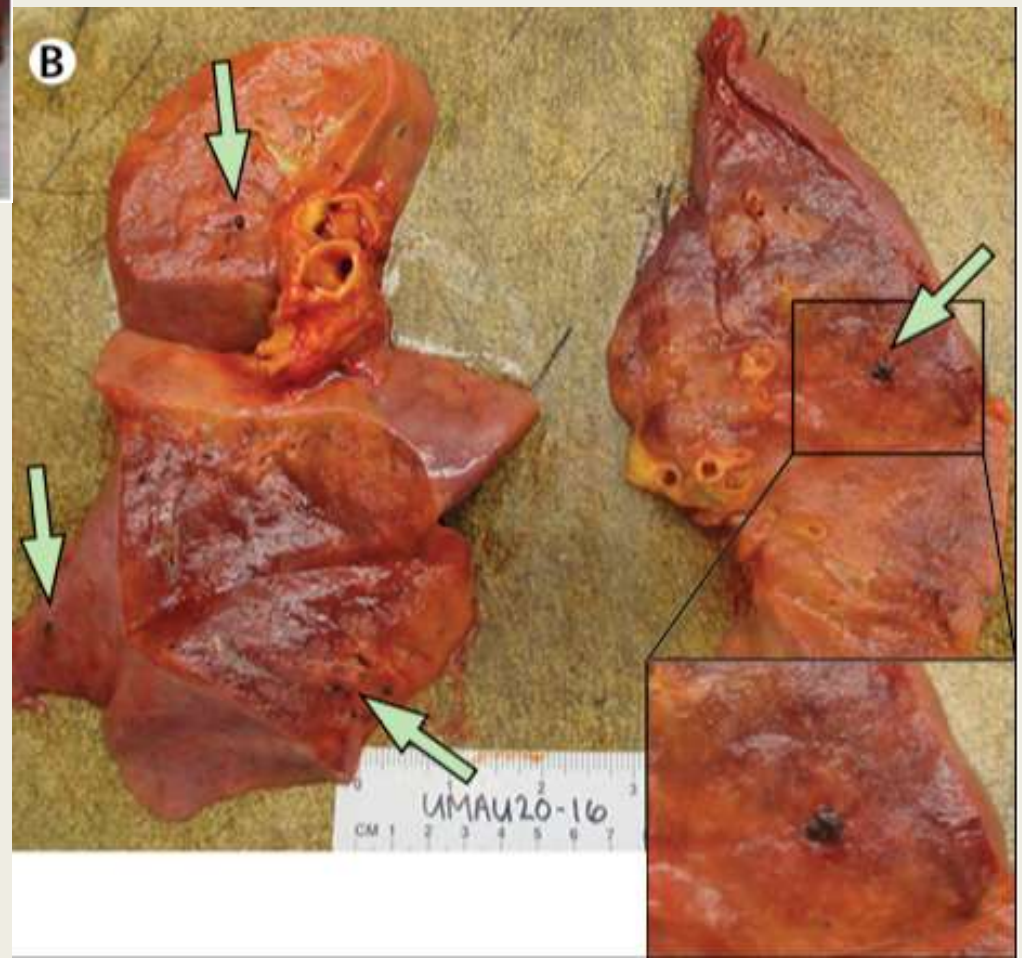
Gross findings

= ARDS

- Diffuse edematous
- Padat kenyal
- perdarahan pada perifer
- Cut section :
  - *Bercak perdarahan (luas 3-6cm)*
  - *Perdarahan pada permukaan luar*
  - *Tampak trombi pada small vessel*

Fox et al, 2020





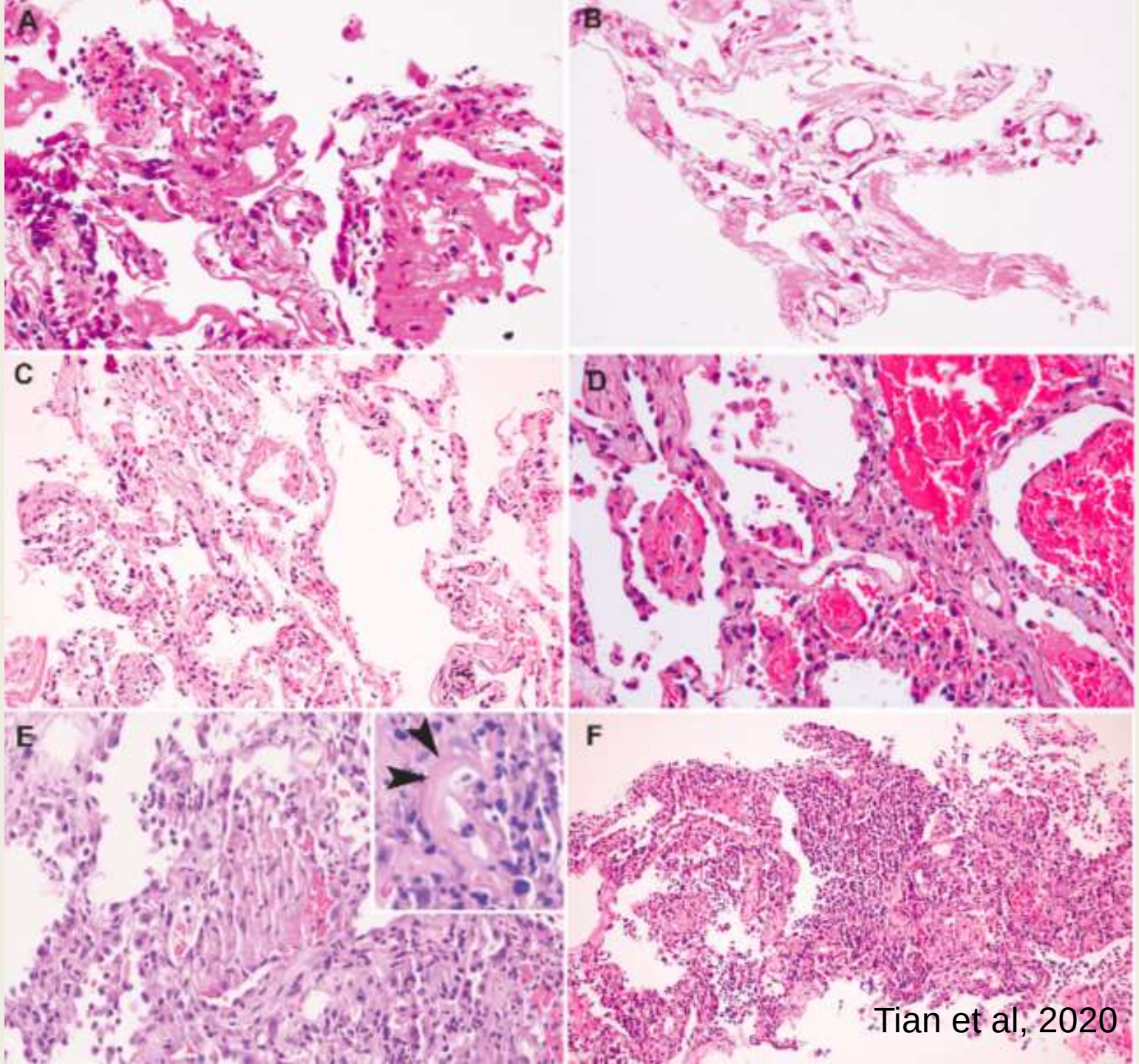
Fox et al, 2020

Microcopic findings

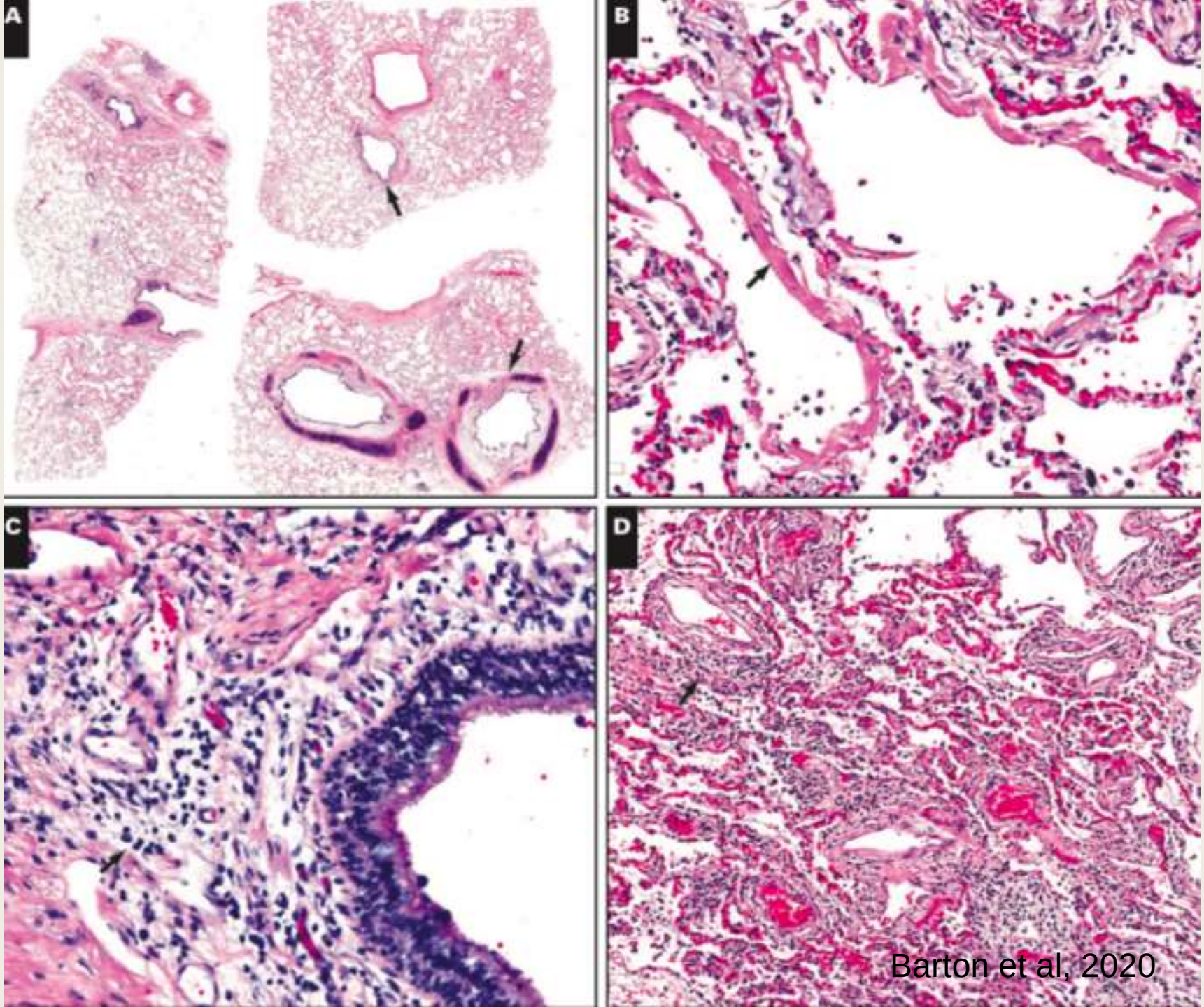
= Diffuse Alveolar Damage

- Hyaline membrane
- Infiltrasi sel radang MN
- Pneumocyte type II hyperplasia
- Alveolar space → blood exudate

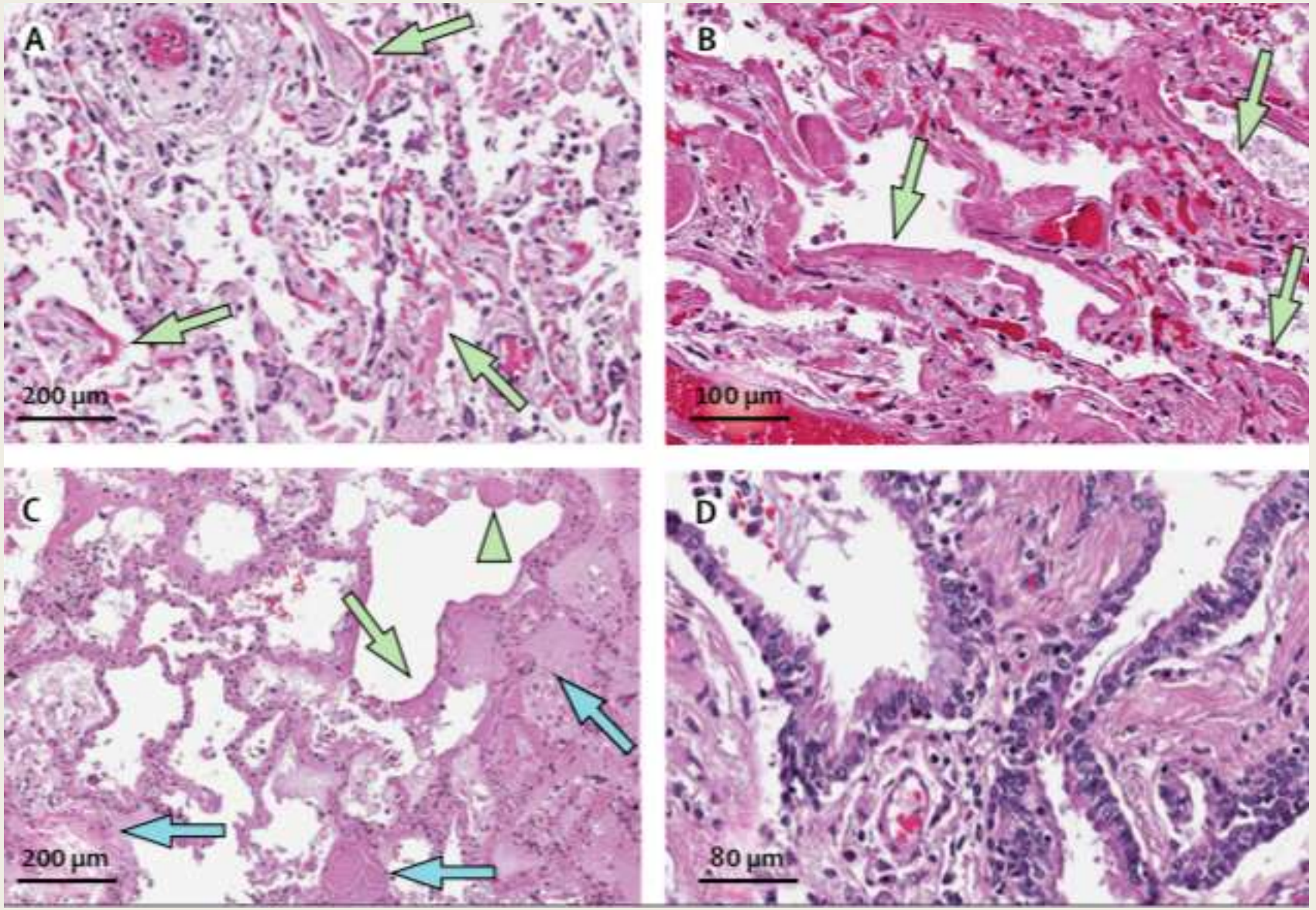
Tian et al, 2020



Tian et al, 2020



Barton et al, 2020



Fox et al, 2020

CA PARU

- Sekunder > primer
- Primer 90 – 95% Bronchogenic Carcinoma
- Bronchogenic Carcinoma

Squamous cell 35 – 50 %
Adeno Ca 25 – 35 %
Small cell 20 – 25 %
Large cell 10 – 15 %
Alveolar carcinoma
Bronchial carcinoid 5 – 10 %

Bronchogenic Ca.

Incidence : 40 – 70 tahun
Pria : Wanita = 7 : 1 (1960)
Pria : Wanita = 3 : 1 (1984)

Etiologi + Patogenesis

Perokok :

- Statistik – cara, lamanya
- Klinis – cilia (-); epithelia hyperplasia, nucleus abnormal
- Experimental – Beberapa carcinogen

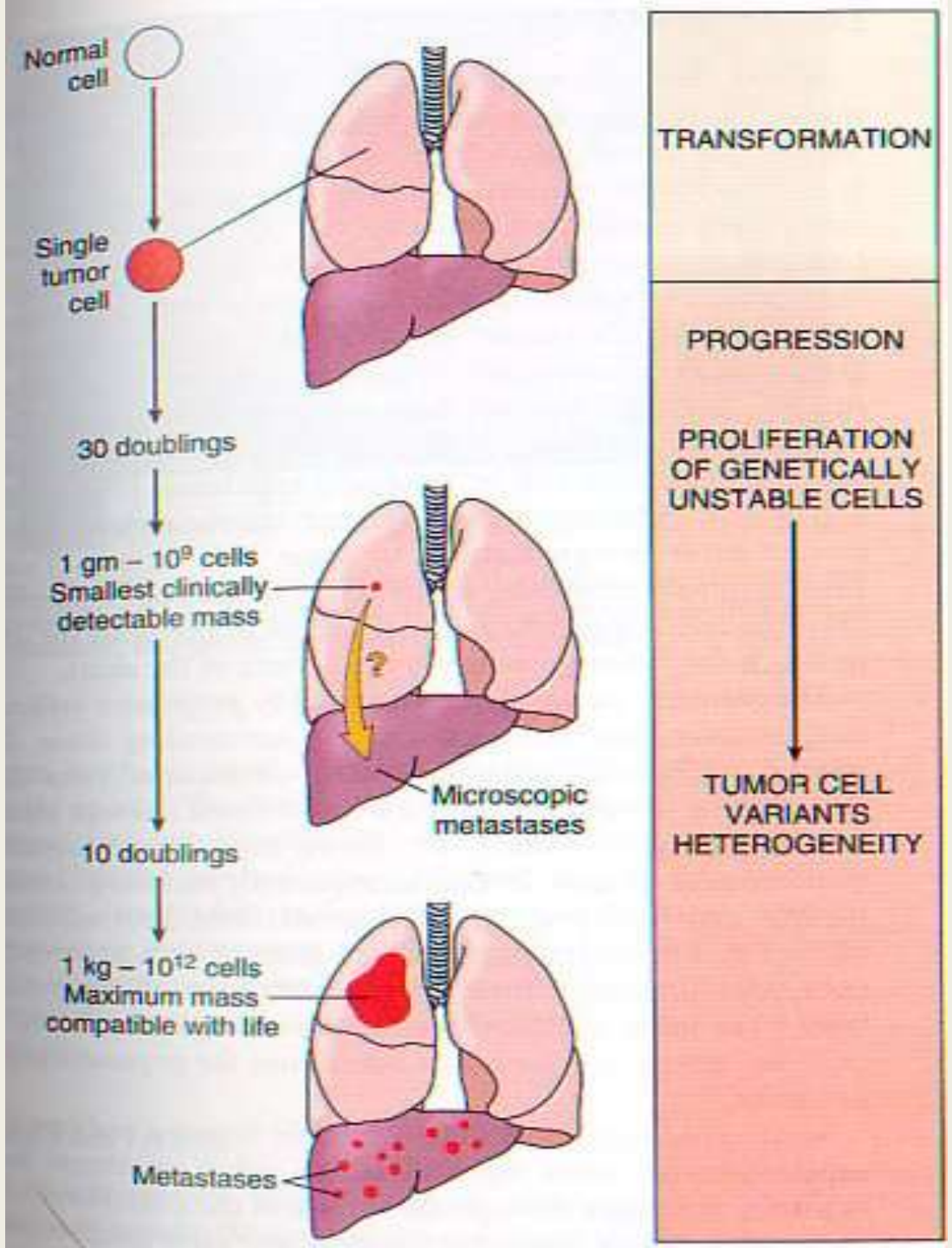
Industri – Radiasi – Radon – Uranium, asbestos + perokok 92 X

Polusi udara

Genetik AHH meningkat

Enzym Arylhydrocarbon Hydrolase

Scarring – “ Scar Cancer”


Normal cell
Single tumor cell
30 doublings
1 gm – 10^9 cells
Smallest clinically detectable mass
?
Microscopic metastases
10 doublings
1 kg – 10^{12} cells
Maximum mass compatible with life
Metastases
TRANSFORMATION
PROGRESSION
PROLIFERATION OF GENETICALLY UNSTABLE CELLS
TUMOR CELL VARIANTS HETEROGENEITY

IGURE 15–47 Numerous metastases from a renal cell carc
ioma. (Courtesy of Dr. Michelle Mantel, Brigham and Women'
lospital, Boston, MA.)

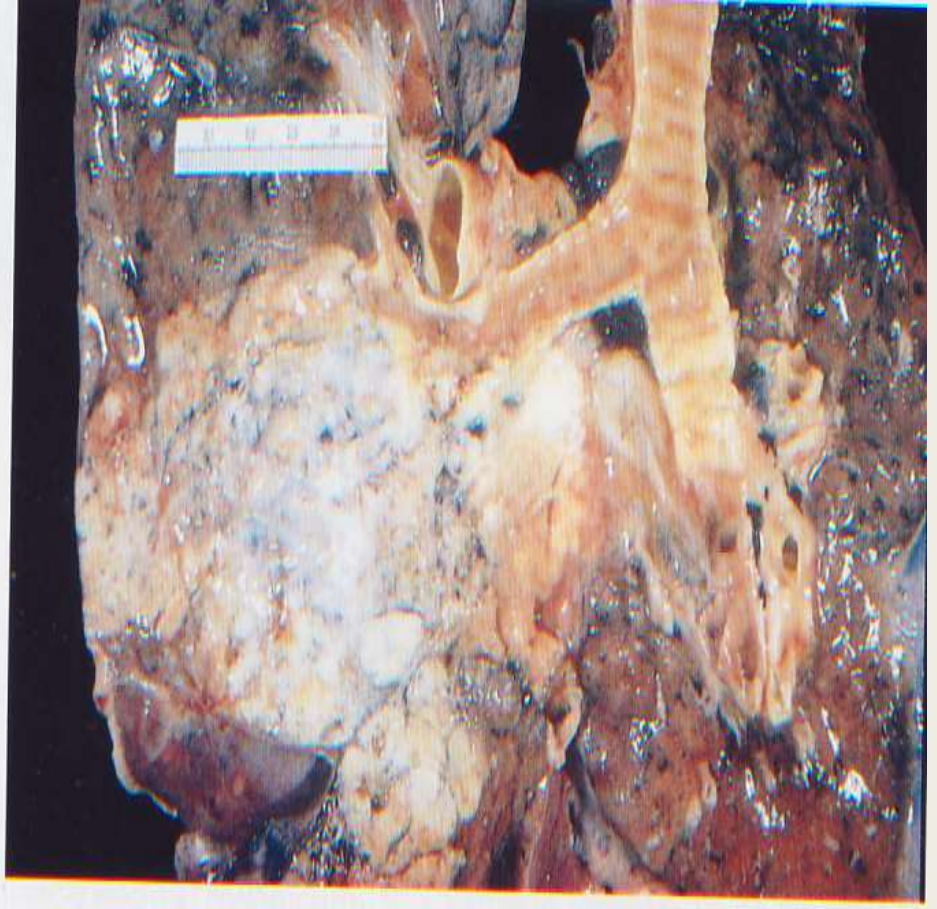


FIGURE 15–42 Lung carcinoma. The gray-white tumor tissue is
seen infiltrating the lung substance. Histologically, this large
tumor mass was identified as a squamous cell carcinoma.

SQUAMUS CELL CA

Tumor (pria) – hubungan erat dengan merokok. Tumbuh > cepat,

Metastase lambat
Dimulai dengan squamous metaplasia ~> dysplasia – Carcinoma insitu ~> Carcinoma

Mikros : sama dengan di tempat lain

Gambaran PA :

Tumor di daerah hilus

75 % pd cabang Bronchus I, II, III

Cara tumbuh : Mula-mula epitel berubah atypik ~>

menonjol / menebal kedalam lumen

Fungating

Infiltratif

Seperti bloomkol

Jarang tumor menembus paru

Makroskopik : abu – abu putih, padat kenyal, bila besar terdapat fokal nekrosis + pendarahan

Penyebaran : regional, scalenous, organ jauh

ADENO CARCINOMA

- Asal epitel bronchial
- Asal TB / Alveolar

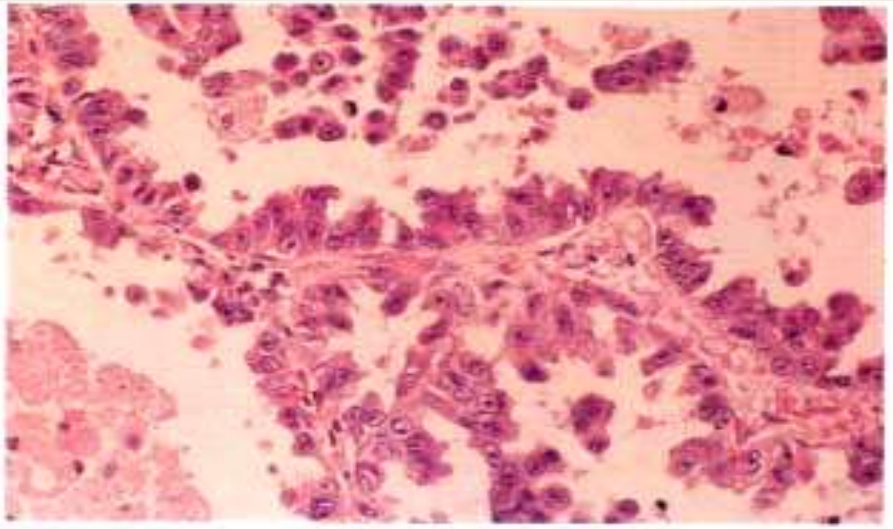


Figure 16–43

Terminal bronchioloalveolar carcinoma with characteristic tall columnar cell papillary growth. Note the loose tumor cells in the alveoli, which may account for the "aerogenous" spread of tumor often observed.

- ✓ Lokalisasi > perifer
- ✓ Mencapai diameter 2 cm +/- 25 th
- ✓ Kadang disertai scarring
- ✓ Hubungan dengan rokok tidak jelas
- ✓ 80 % mengandung mucin

LARGE CELL CA

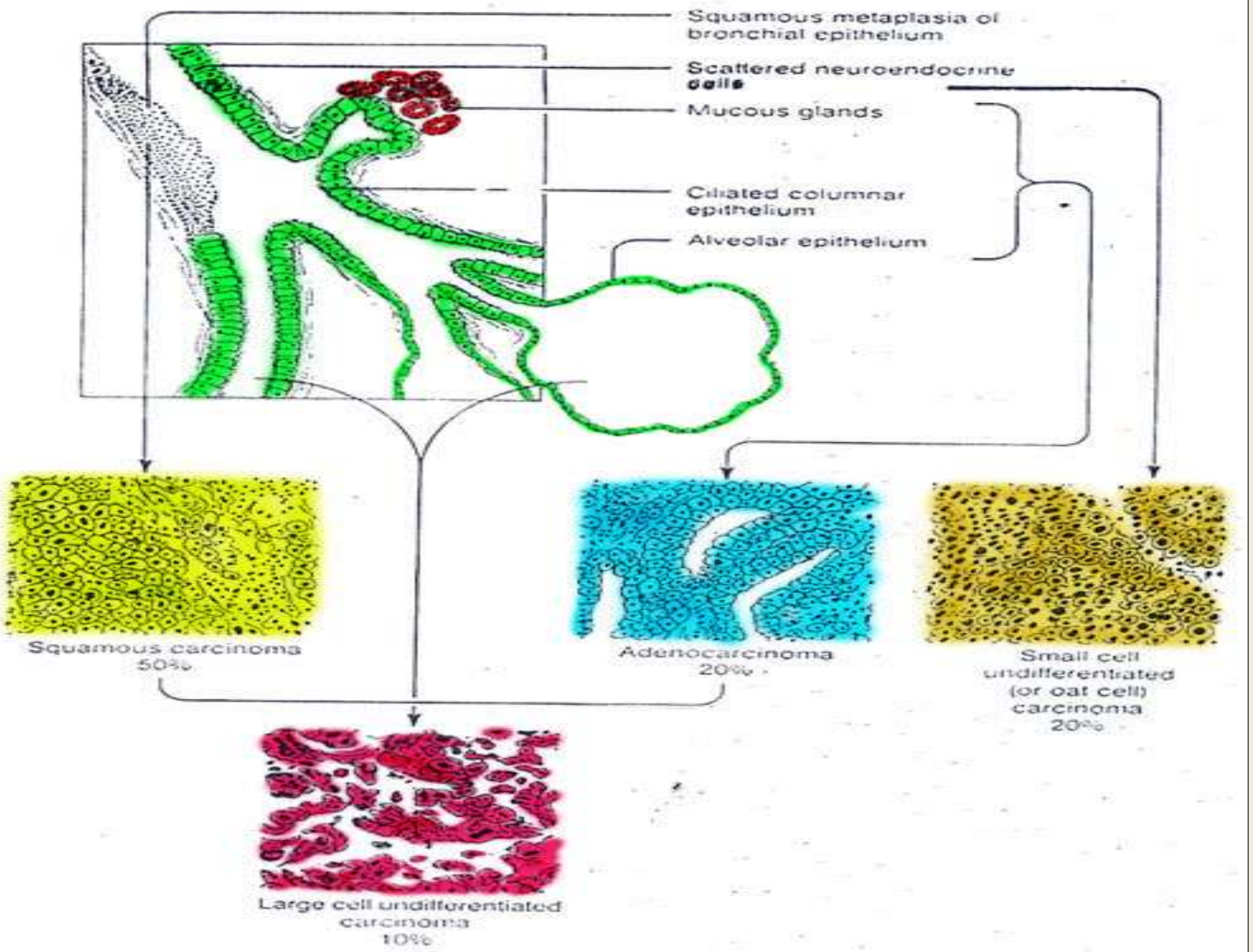
Sering disebut sebagai Anaplastic Carcinoma dengan bentuk sel – sel yang poligonal dan inti yang vesicular. Large cell Ca ini sering tampak sebagai squamous cell Ca dan Adeno Ca.

Pada beberapa large cell Ca terdapat bahan mucinous dan juga multinucleat cell (giant cell)

SMALL CELL CA

Sangat ganas
Erat hubungannya dengan merokok
Metastase jauh
Produksi hormon

Mikros :
Sel ganas kecil – kecil, bulat – oval
(Kulchitsky cell)
Sitoplasma sedikit / tidak ada
Bisa sebesar 2x lymphocyt
Tidak mirip squamous / adeno


Squamous metaplasia of bronchial epithelium
Scattered neuroendocrine cells
Mucous glands
Ciliated columnar epithelium
Alveolar epithelium
Squamous carcinoma 50%
Adenocarcinoma 20%
Small cell undifferentiated (or oat cell) carcinoma 20%
Large cell undifferentiated carcinoma 10%

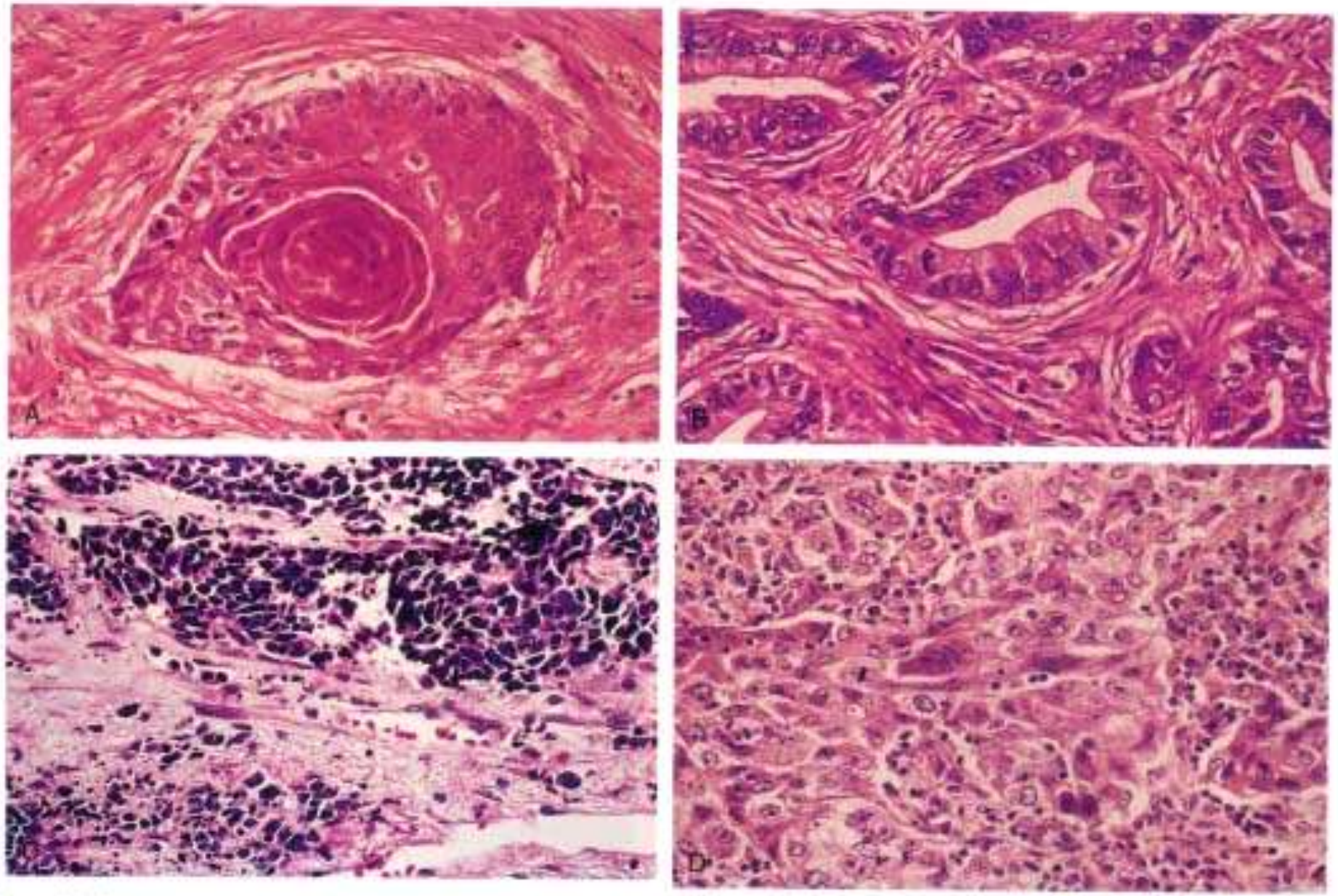


Figure 16–41

Histologic appearance of bronchogenic carcinoma. *A*, Well-differentiated squamous cell carcinoma showing keratinization. *B*, Gland-forming adenocarcinoma. *C*, Small cell carcinoma with islands of small deeply basophilic cells and areas of necrosis. *D*, Large cell carcinoma, featuring pleomorphic, anaplastic tumor cells and absence of squamous or glandular differentiation.

TRIMS