PATHOLOGY & NEOPLASMA OF THE RESPIRATORY TRACT

UPPER AND LOWER RESPIRATORY TRACT

UPPER RESPIRATORY TRACT

Nose

Sinuses

Nasopharynx

Epiglottis

Larynx

NOSE

Inflammation

- Acute :

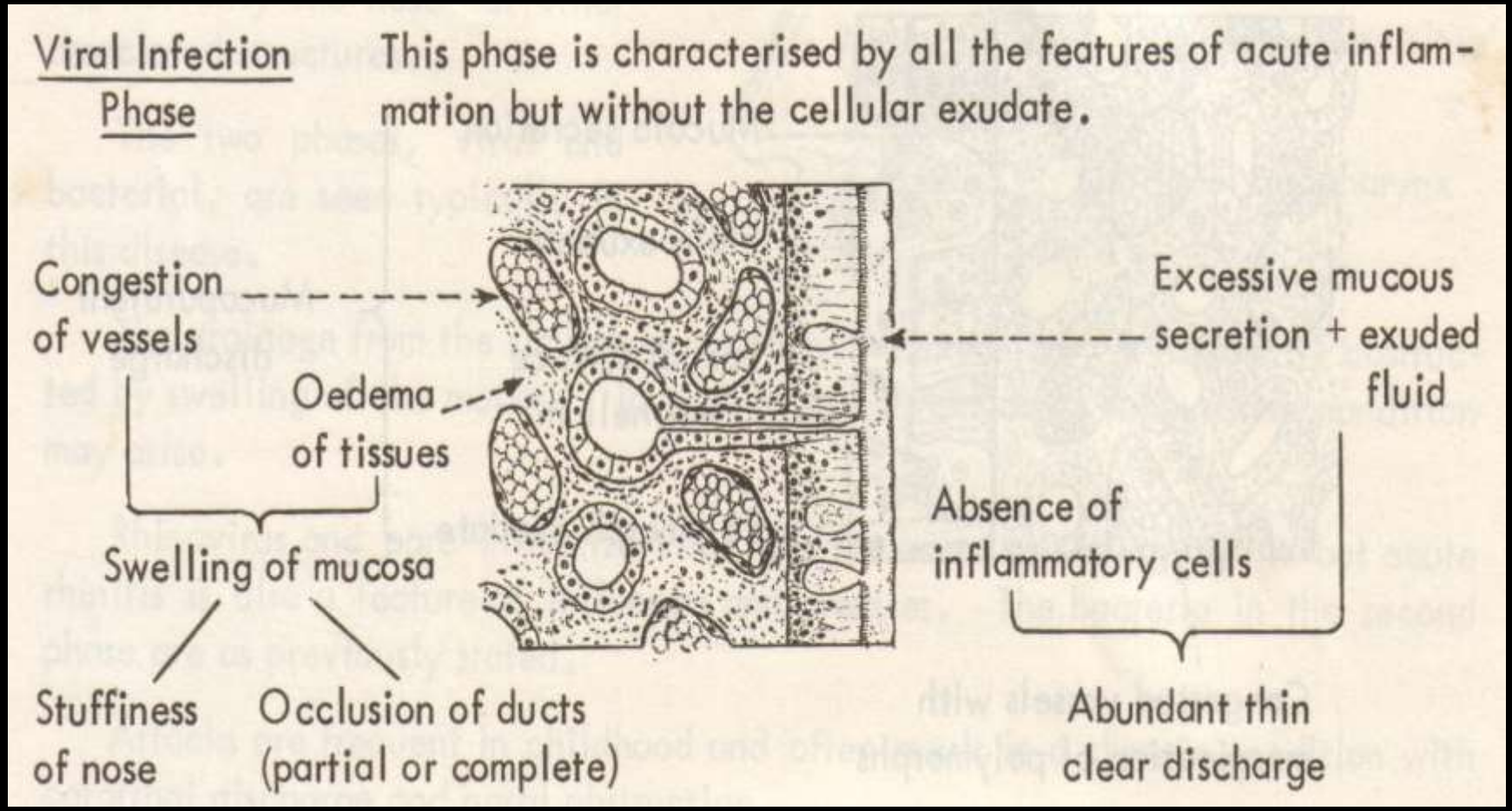
- acute rhinitis
- allergic rhinitis
- vasomotor rhinitis

- Chronic rhinitis

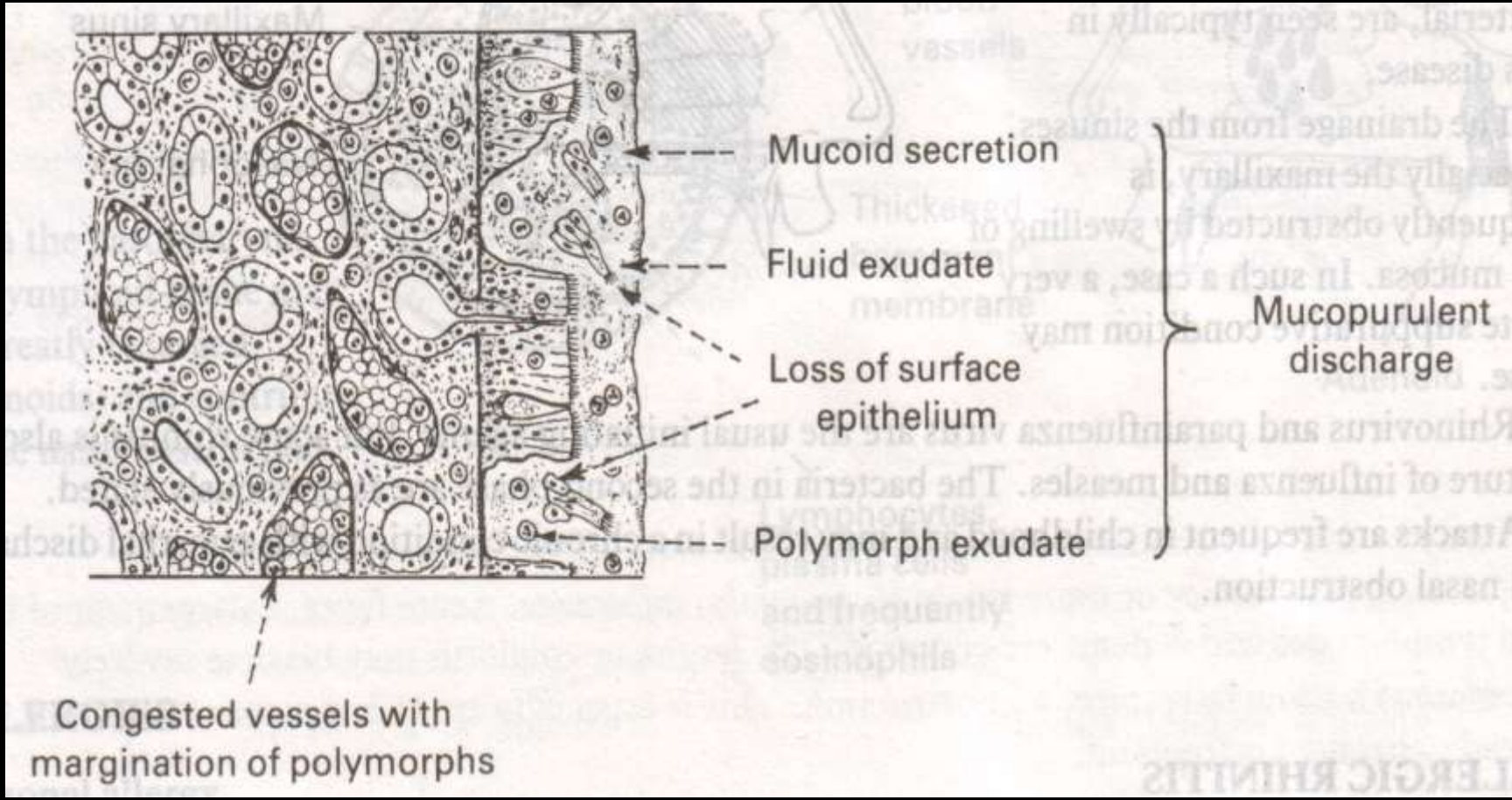
Neoplasma

- Angiofibroma
- Nasal polyp
- Extranodal NK/T-Cell Lymphoma, Nasal-Type
- Squamous cell papilloma
- Inverted papilloma
- Squamous cell Ca

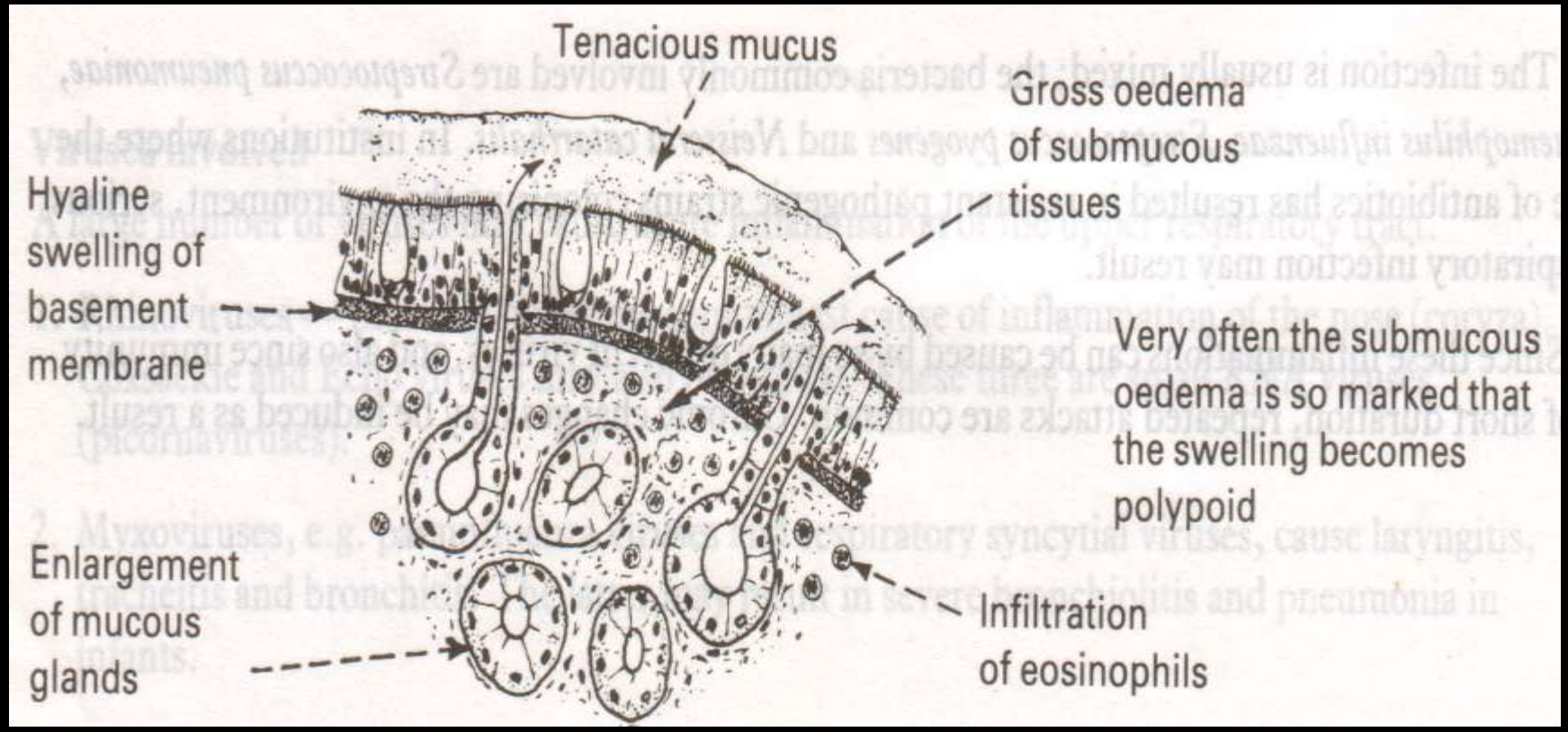
ACUTE RHINITIS: VIRAL PHASE



ACUTE RHINITIS: BACTERIAL PHASE

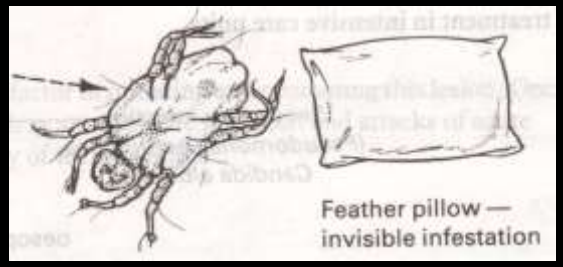


ALLERGIC RHINITIS

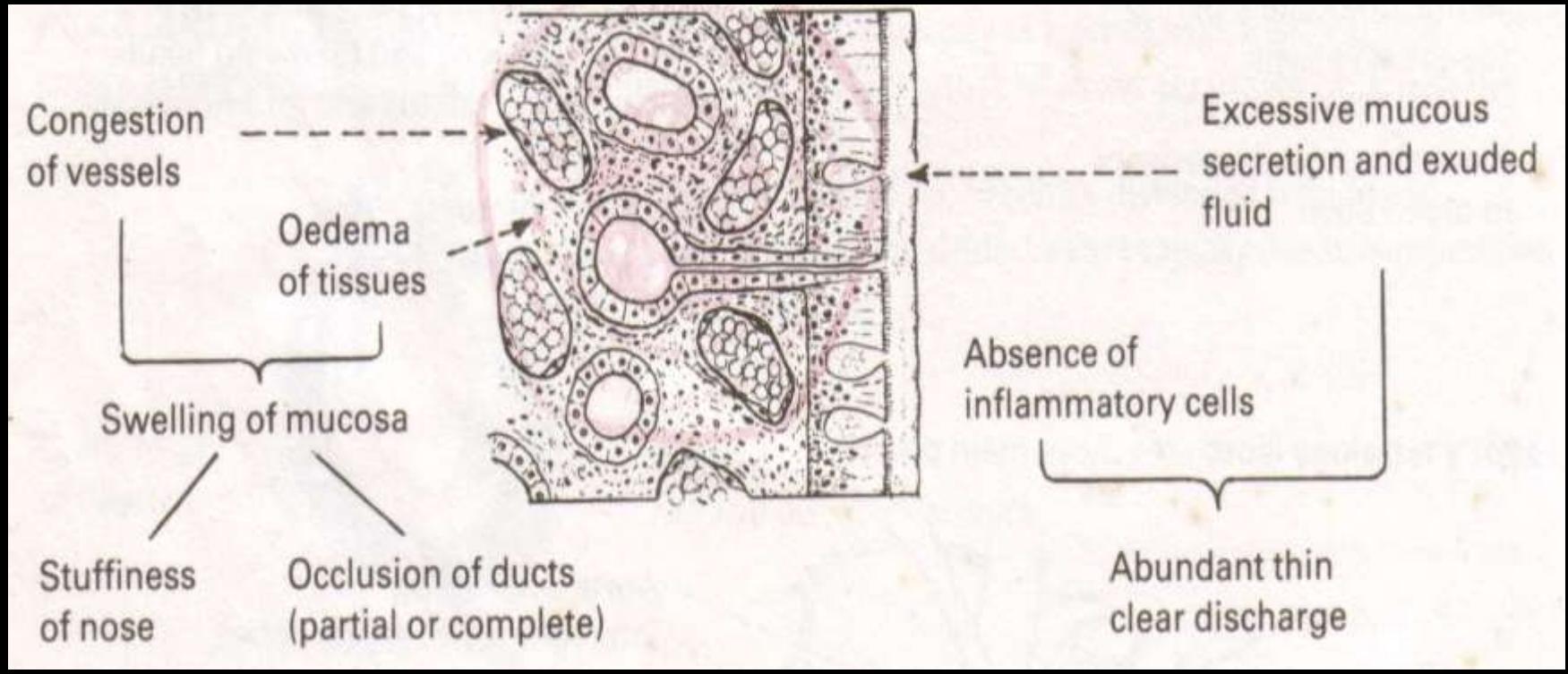


ETIOLOGY

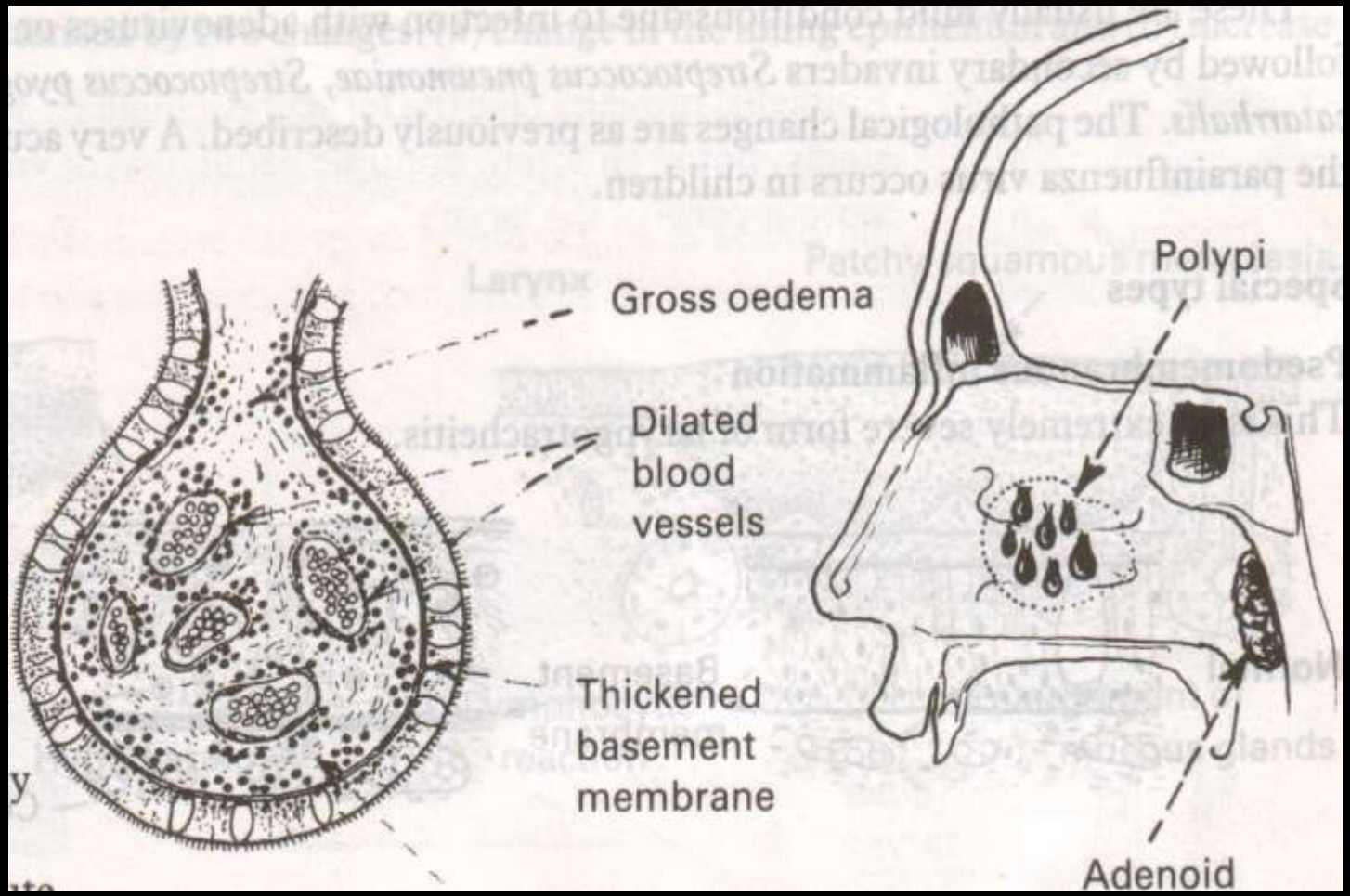
- Seasonal allergy
- Non-seasonal allergy

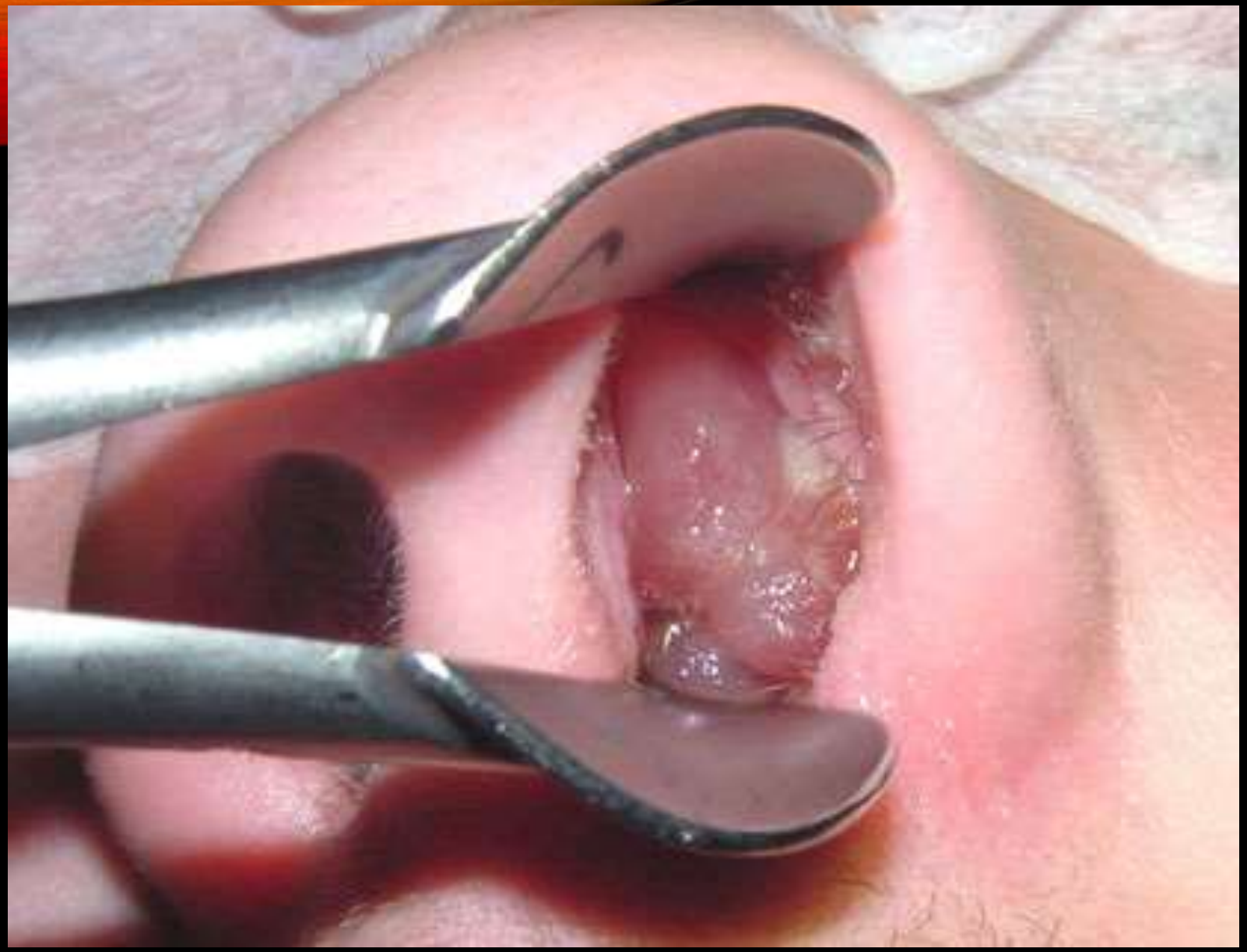


VASOMOTOR RHINITIS



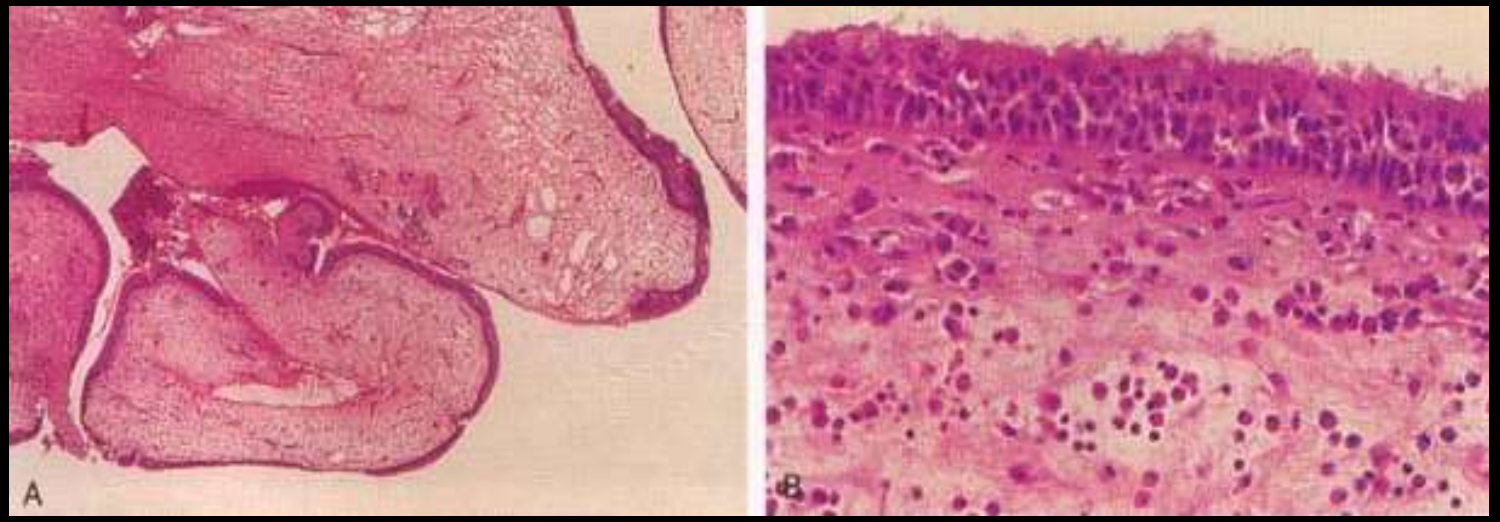
COMPLICATION OF CHRONIC RHINITIS





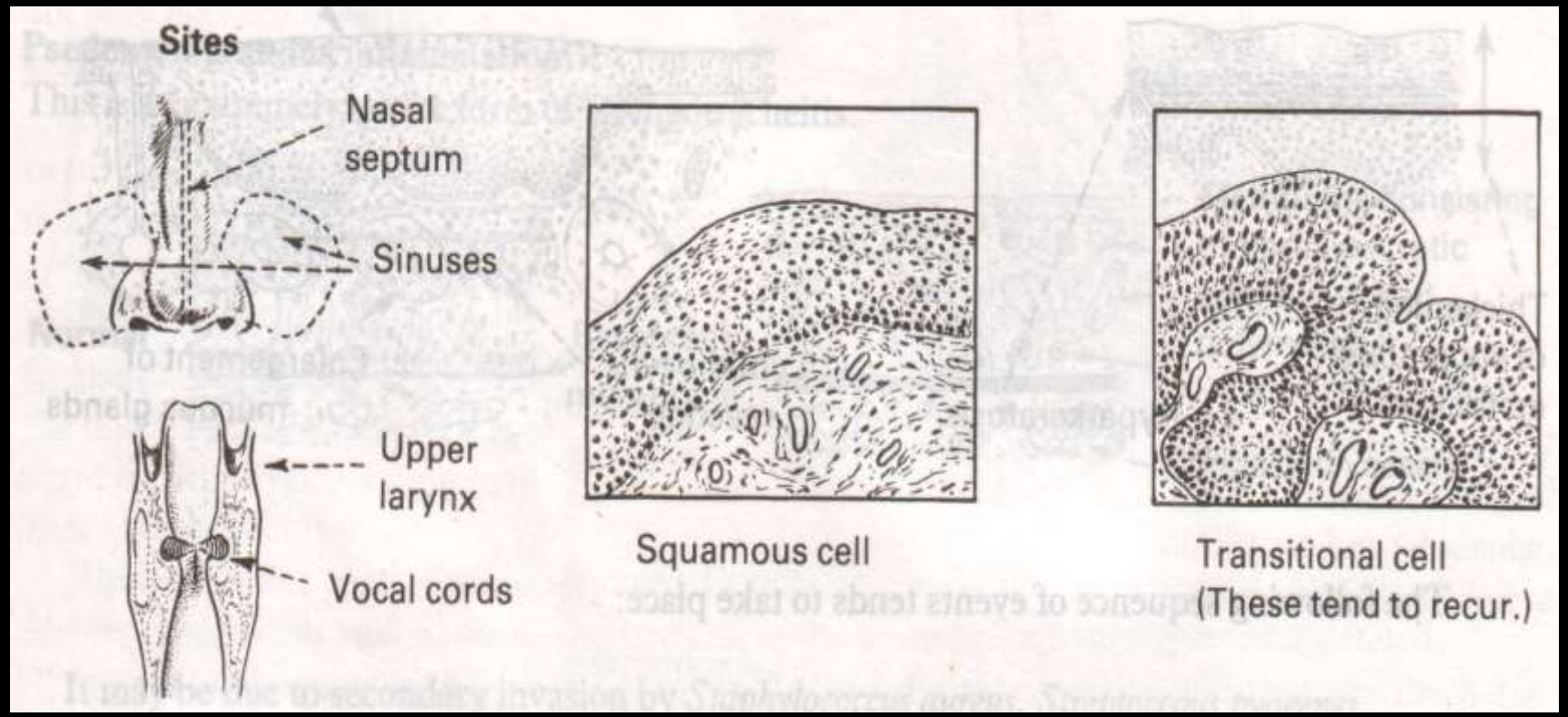
NASAL POLYP

NASAL POLYP

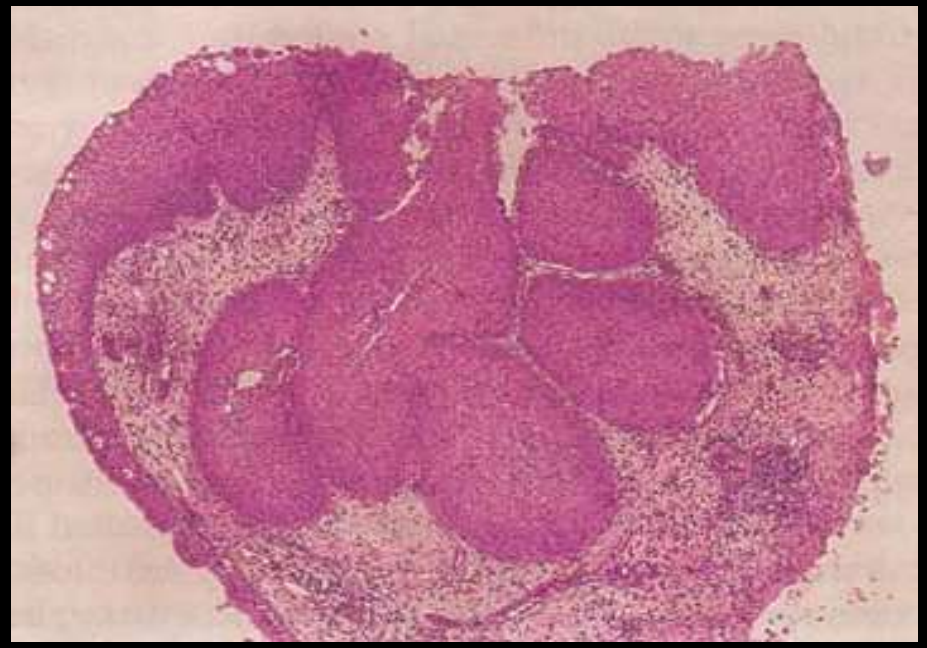


Low power	High power

NEOPLASMA

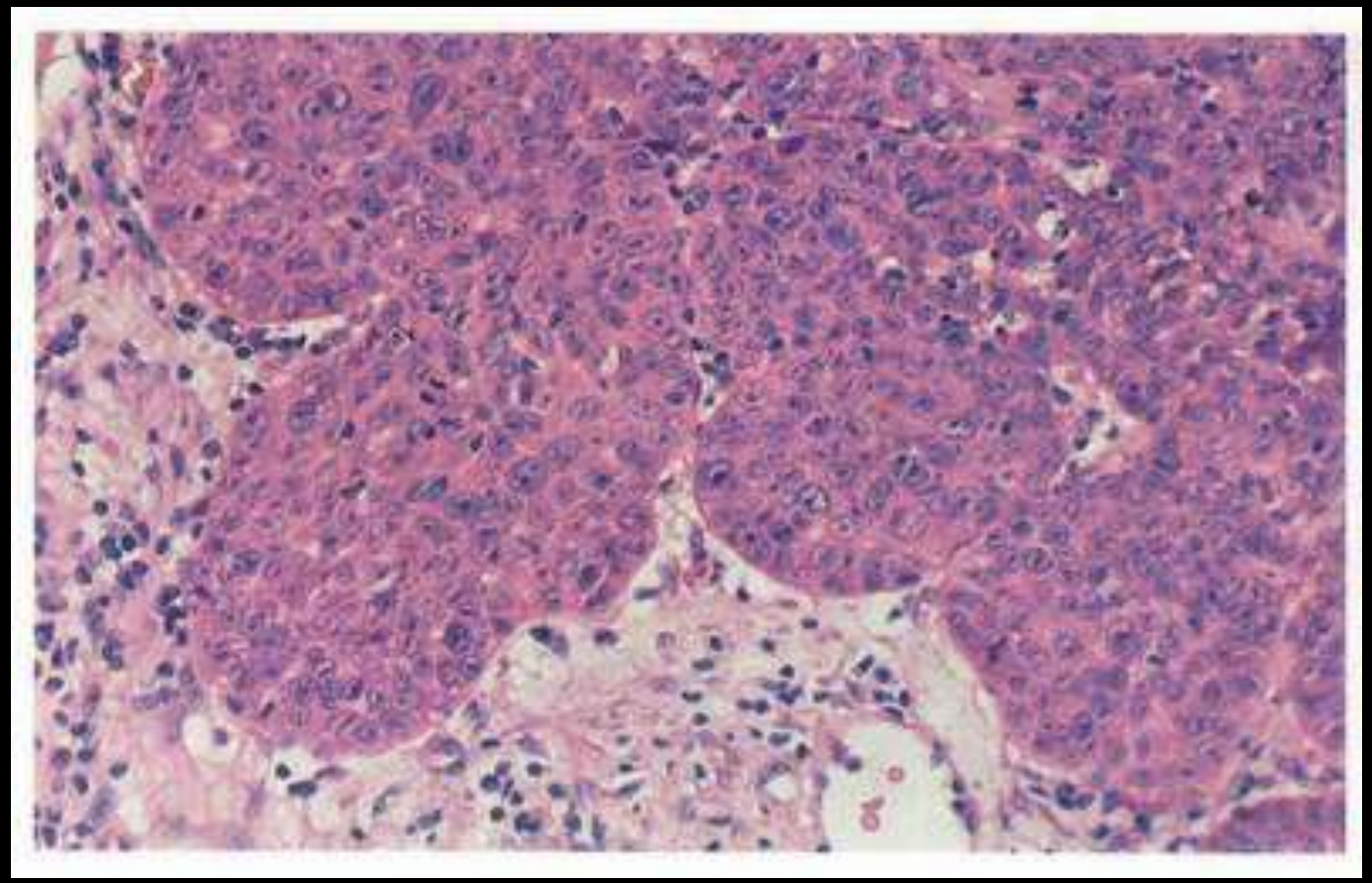

Sites
Nasal septum
Sinuses
Upper larynx
Vocal cords
Squamous cell
Transitional cell
(These tend to recur.)

INVERTED PAPILLOMA

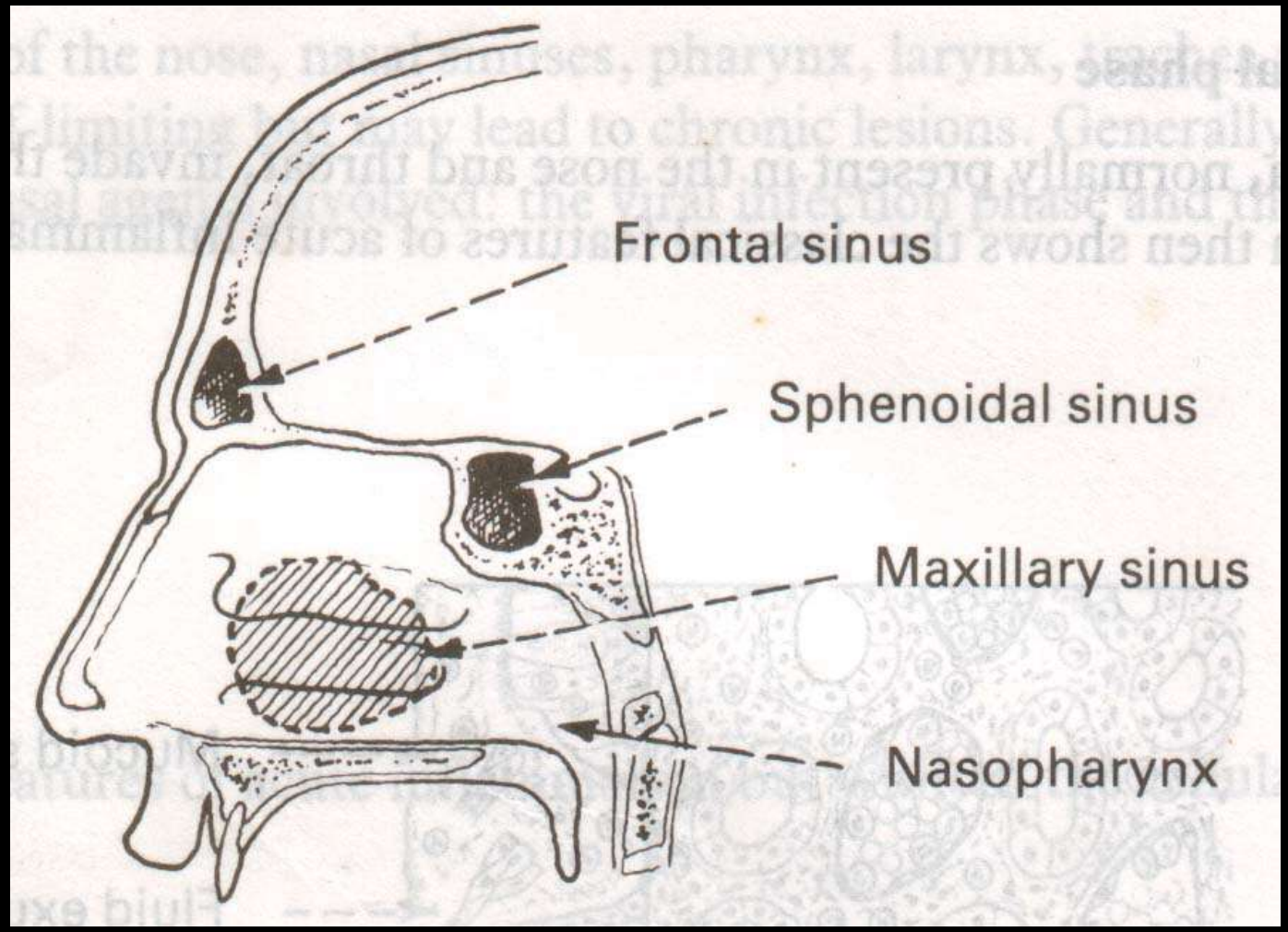


The tumor mass is growing inward (inverted)

SQUAMOUS CELL CA, NON-KERATINIZING

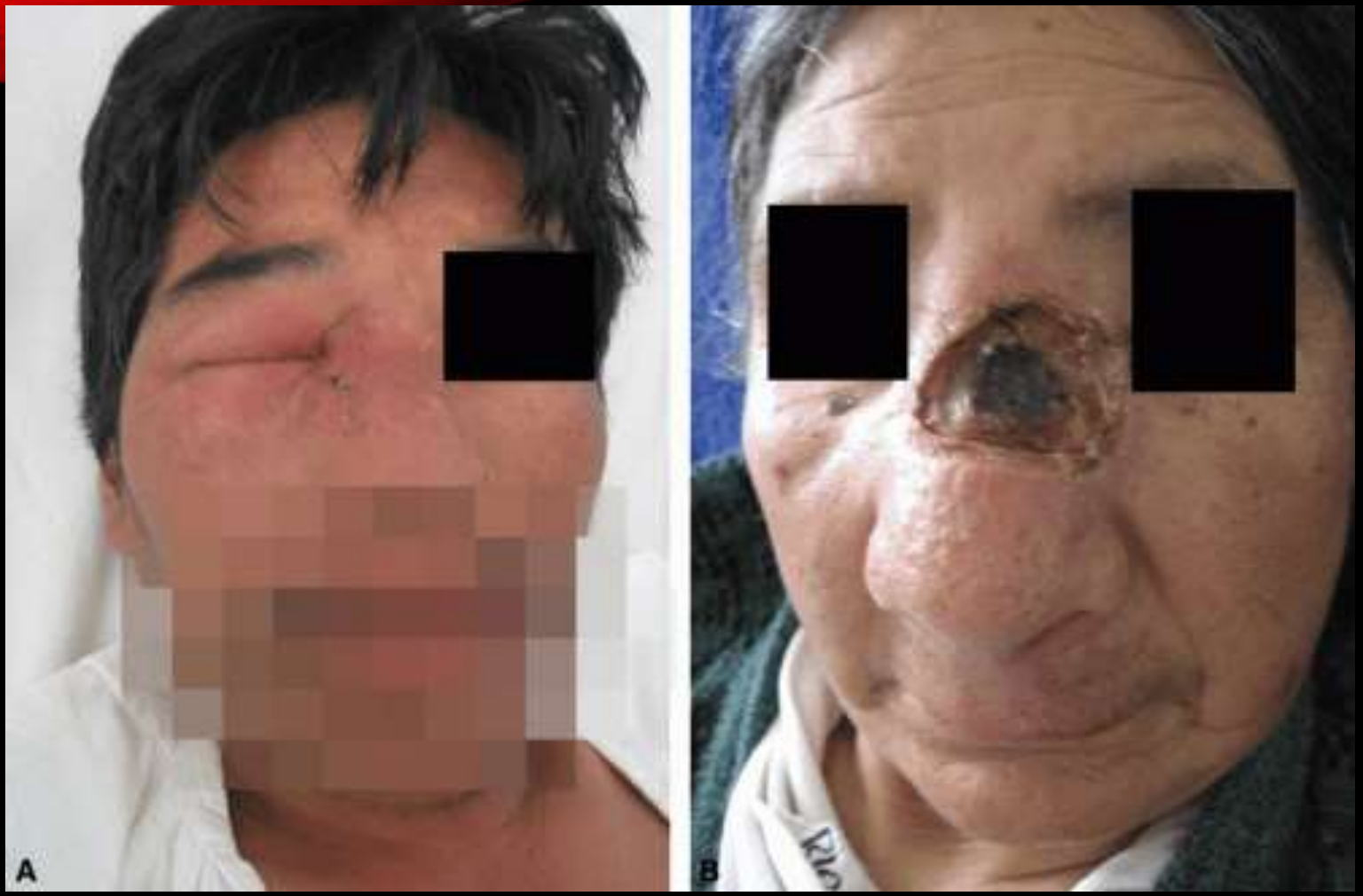


SINUSITIS


Frontal sinus
Sphenoidal sinus
Maxillary sinus
Nasopharynx

EXTRANODAL NK/T-CELL LYMPHOMA, NASAL-TYPE

CD3 & CD56



http://www.pathologyoutlines.com/topic/lymphomanonBnasal.html

EXTRANODAL NK/T-CELL LYMPHOMA, NASAL-TYPE

- Extranodal NK/T-cell lymphoma, nasal-type (ENKTL) is an aggressive, extranodal necrotizing tumor associated with Epstein–Barr virus (EBV) infection. ENKTL invariably presents in the nasal cavity. Cutaneous involvement, including the skin of the nasal cavity,1,2,3 may present either as a primary phenomenon (cutaneous NK/T-cell lymphoma [CNKTL]) or as a secondary manifestation of the disease.4
- ENKTL is characterized by an infiltrate of small to large lymphoid cells usually arranged in an angiocentric and angiodestructive pattern. ENKTL can have either an NK-cell or a cytotoxic T-cell phenotype.

NASOPHARYNX

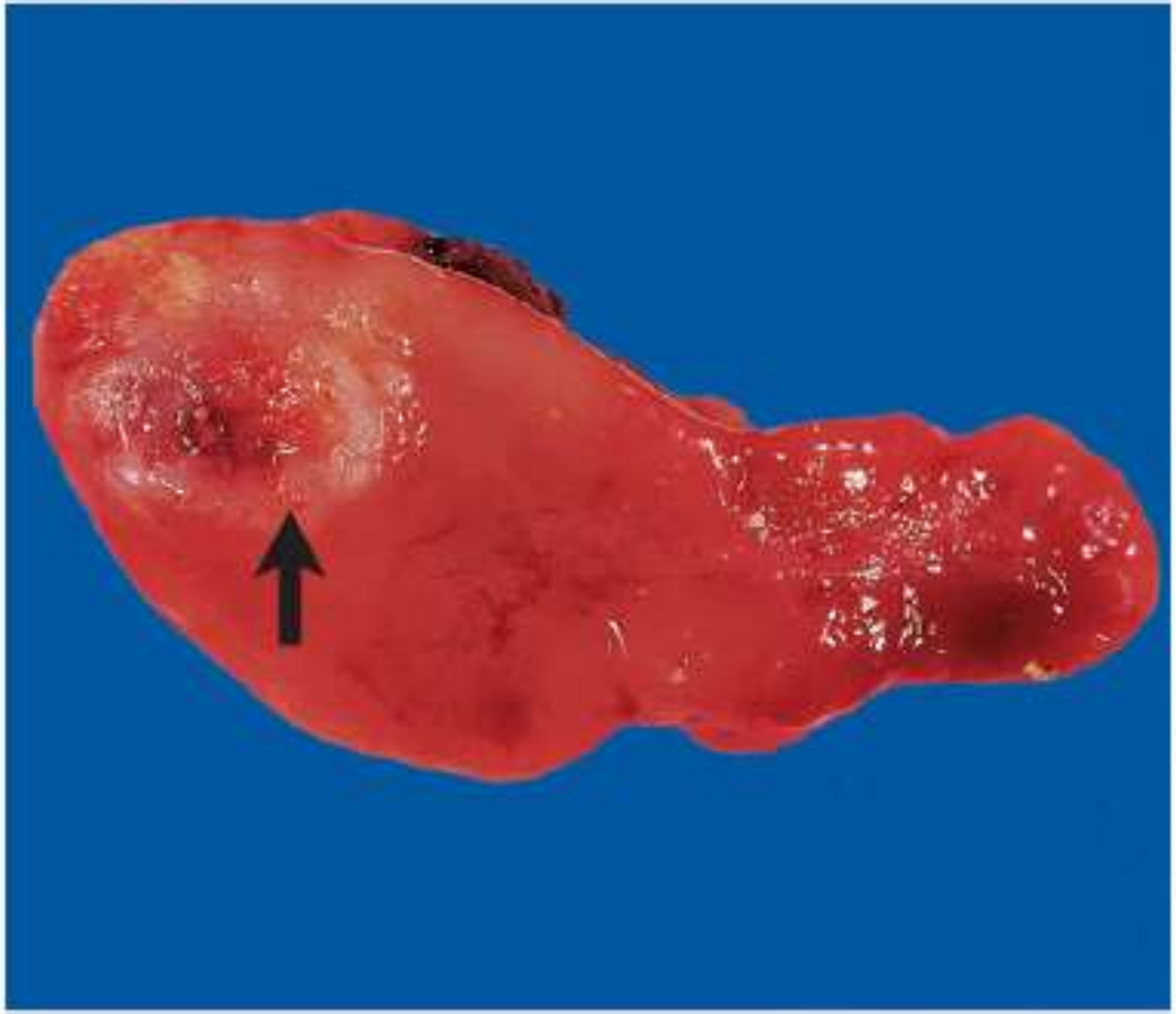
Inflammation

- Acute
- Chronic

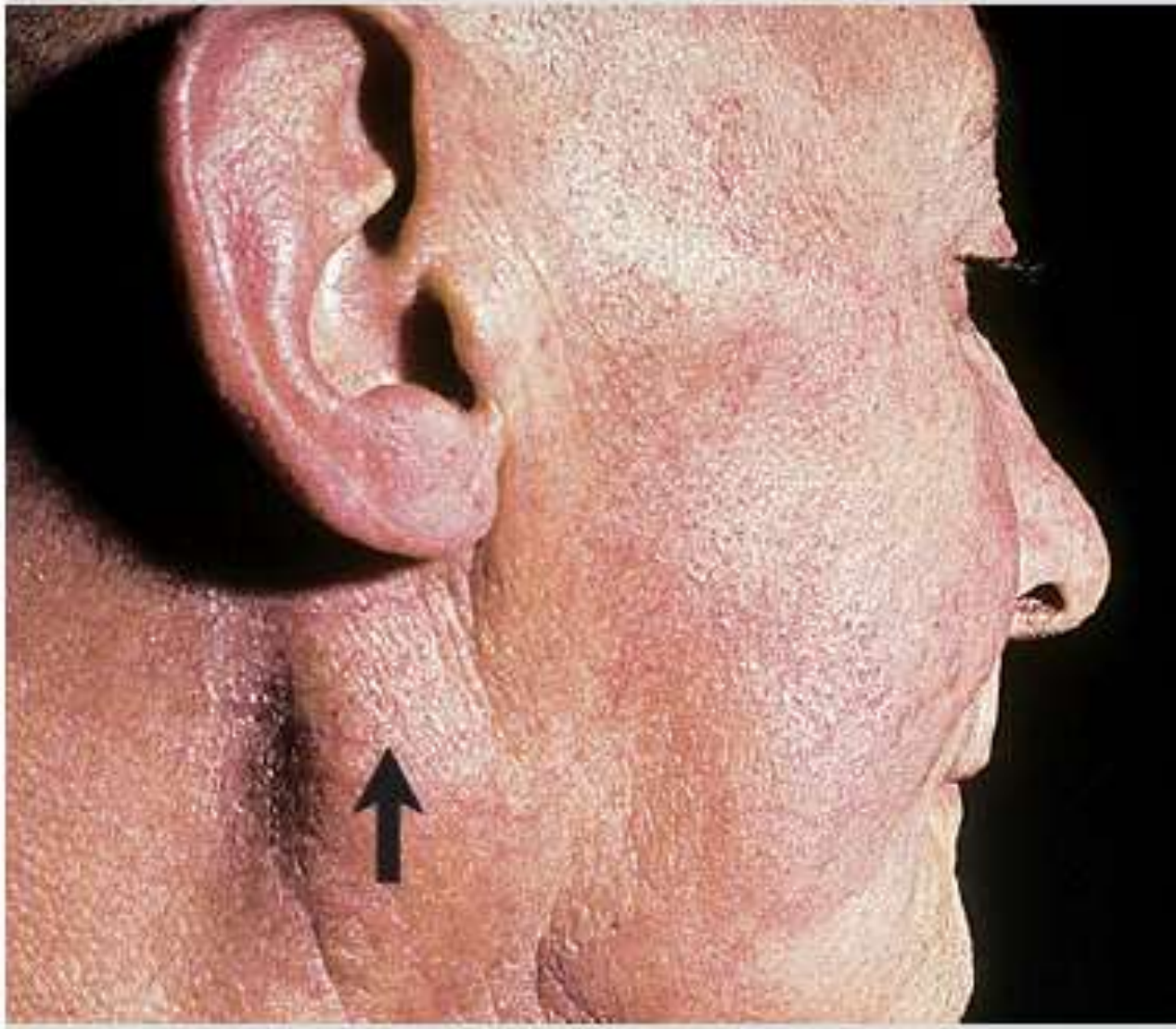
Neoplasm

- Juvenile angiofbroma
- Undifferentiated carcinoma

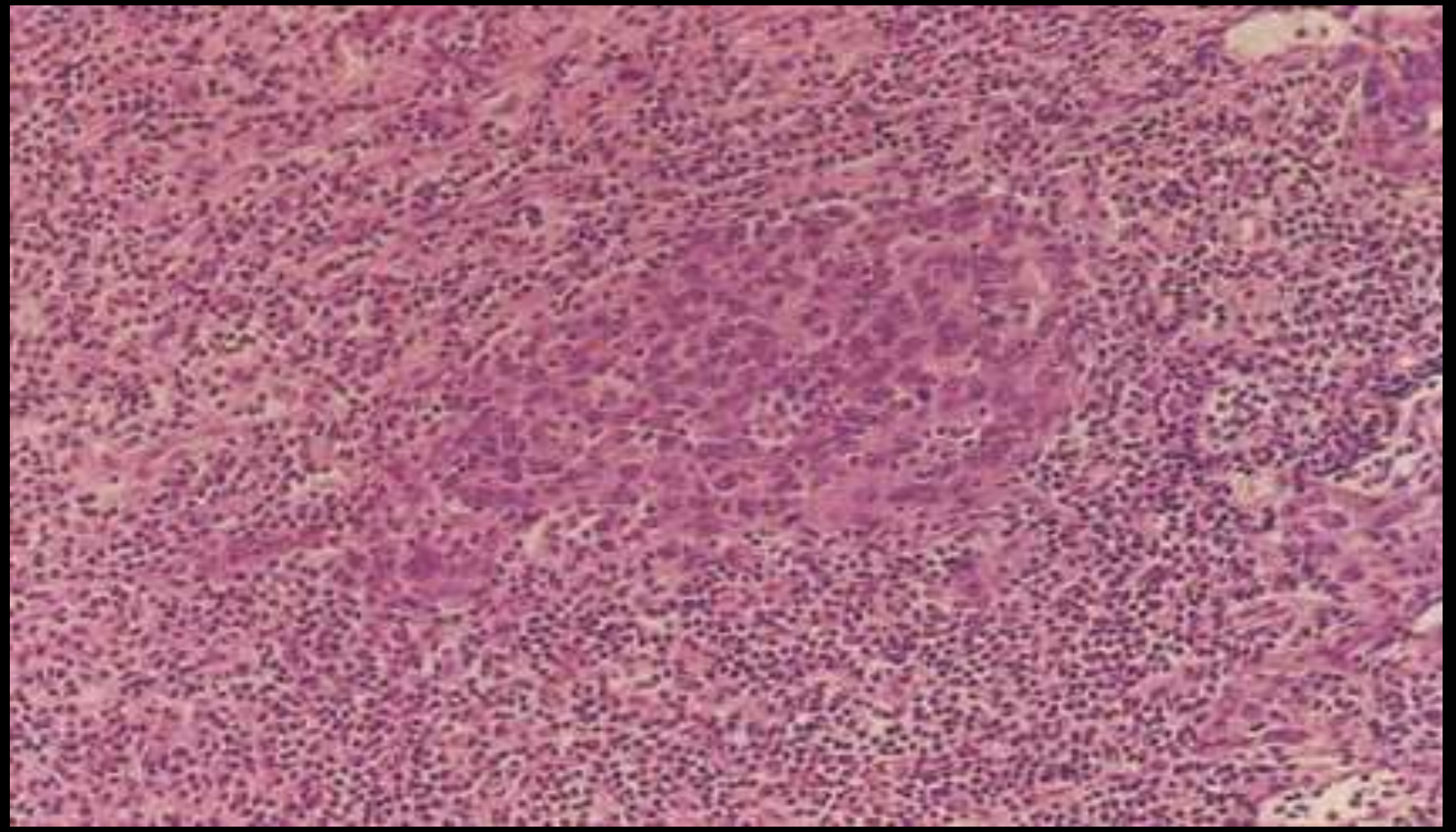
E **Lymph node metastasis**

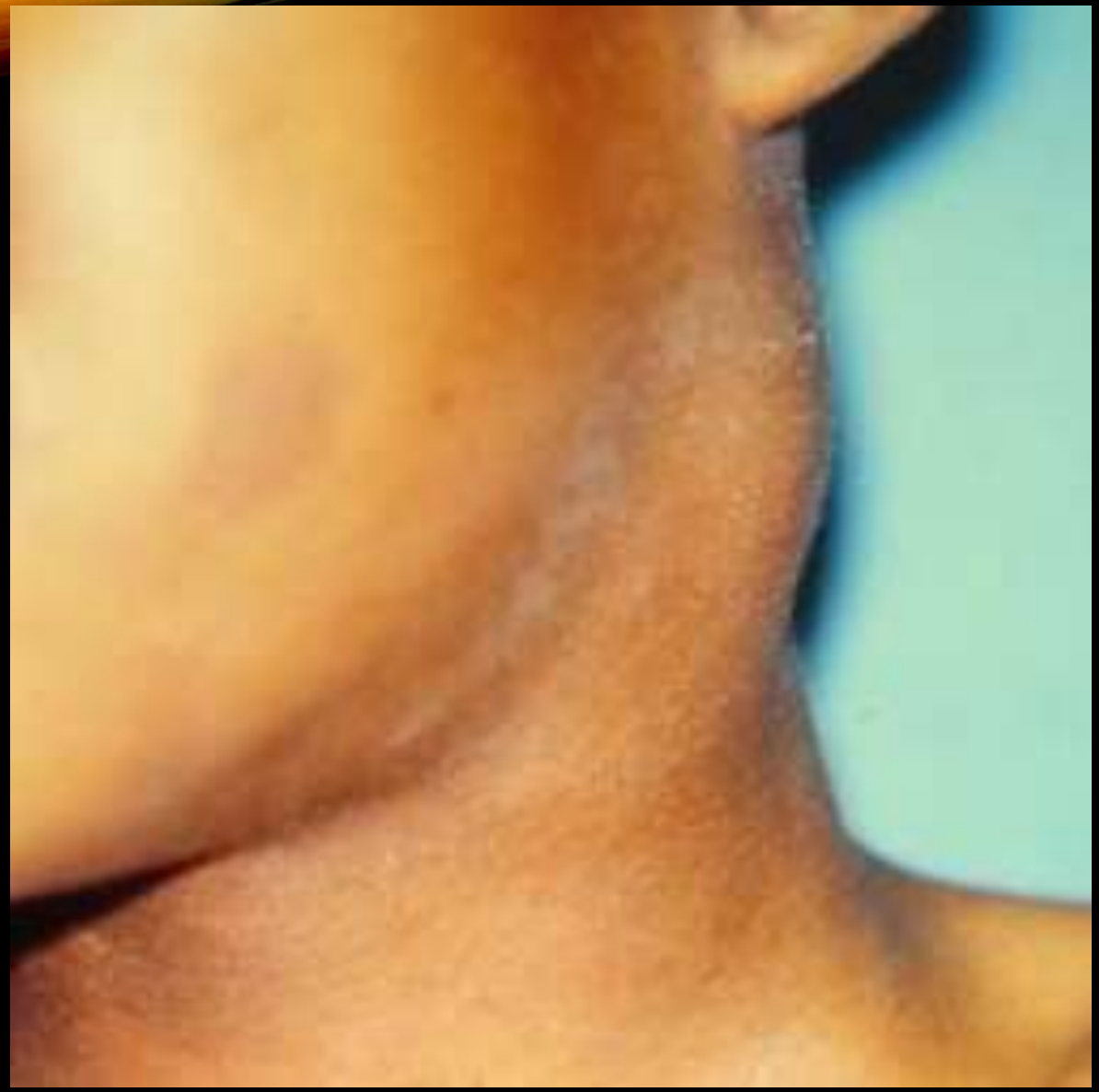


F **Metastasis:** cervical lymph node

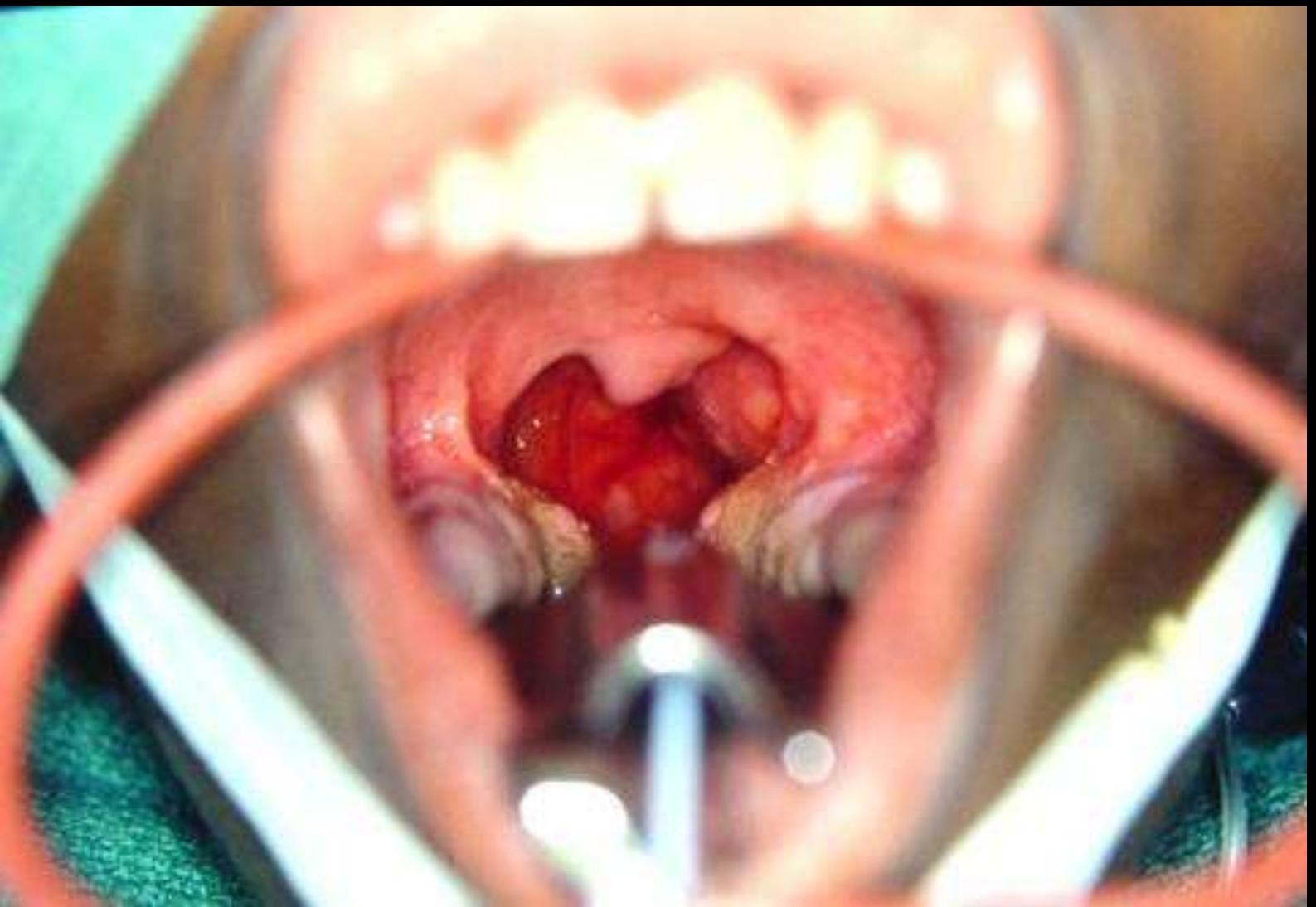


METASTASIS
ANAPLASTIC (UNDIFFERENTIATED) CARCINOMA





ALAT MCIVOR DIPASANG, NAMPAK MASSA NASOFARING KIRI MELUAS SAMPAI DI PALATUM MOLE (LUNAK) DAN PILAR POSTERIOR KIRI. DIAGNOSIS AKHIR ADALAH LIMFOEPITHELIOMA



NASOPHARINGEAL CA, NON-KERATINIZING, DIFF.

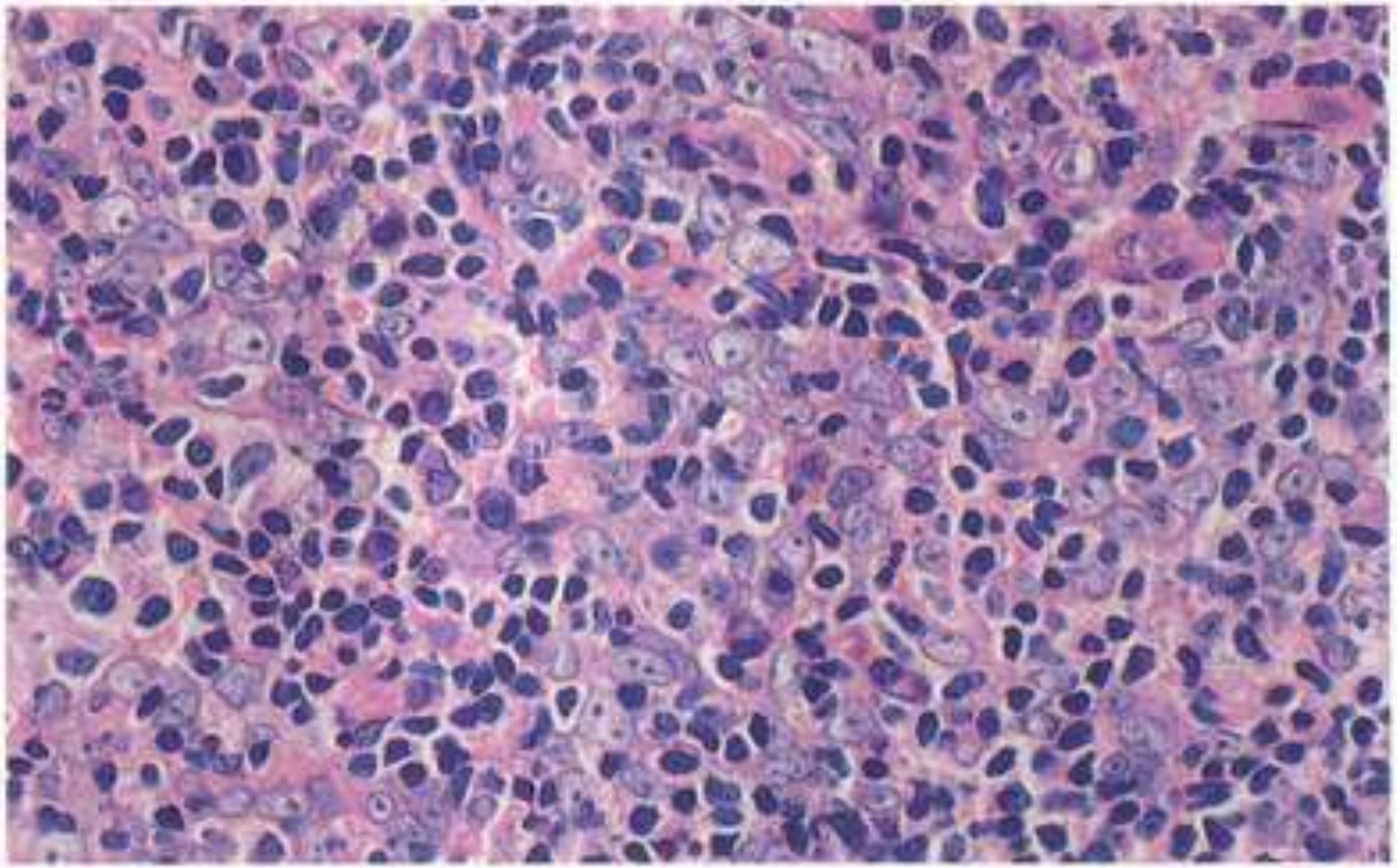


Fig. 53. *Nasopharyngeal carcinoma, non-keratinizing, undifferentiated.* Undifferentiated carcinoma heavily admixed with lymphocytes and plasma cells – lymphoepithelial carcinoma

NASOPHARINGEAL CA, NON-KERATINIZING, UNDIFF.

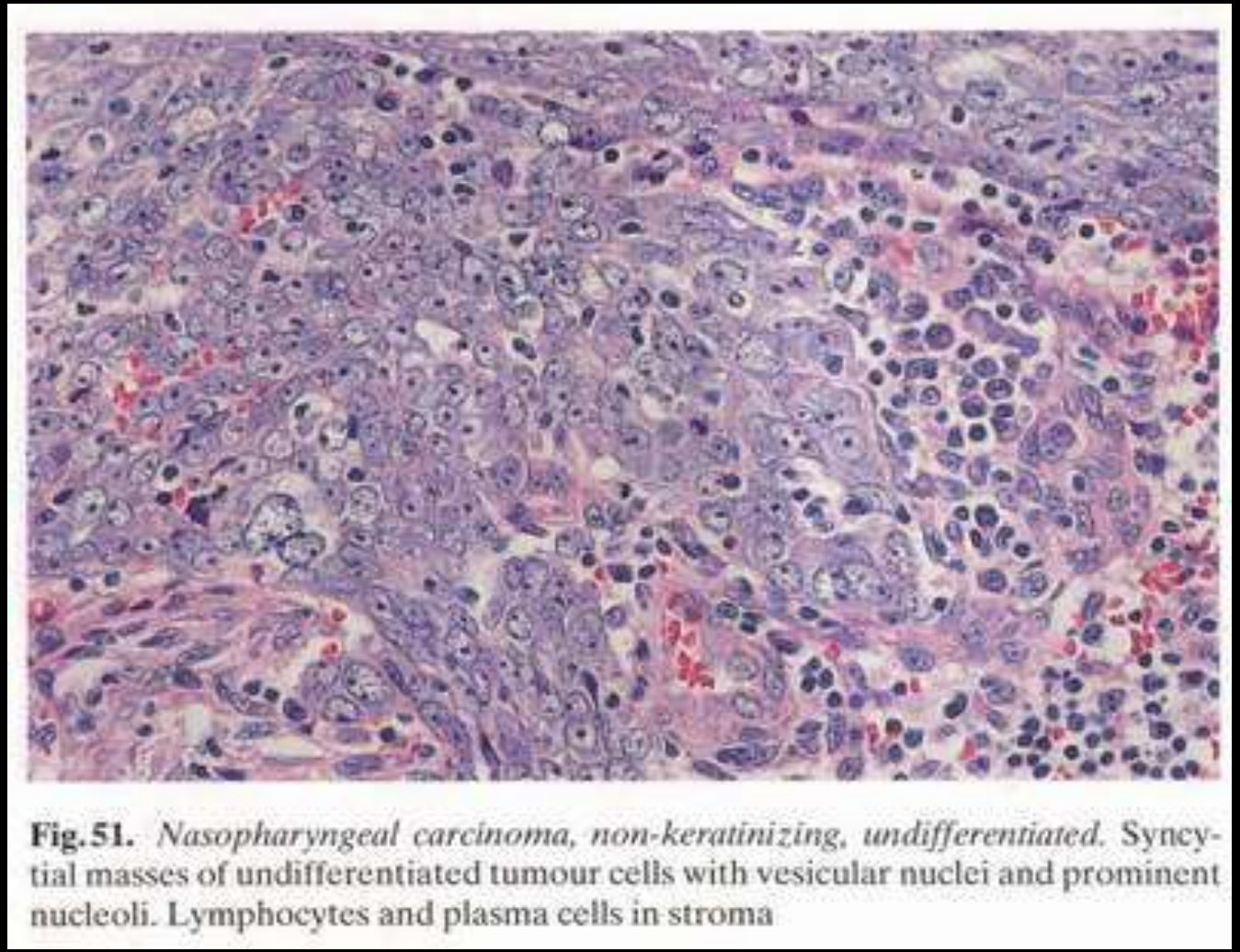
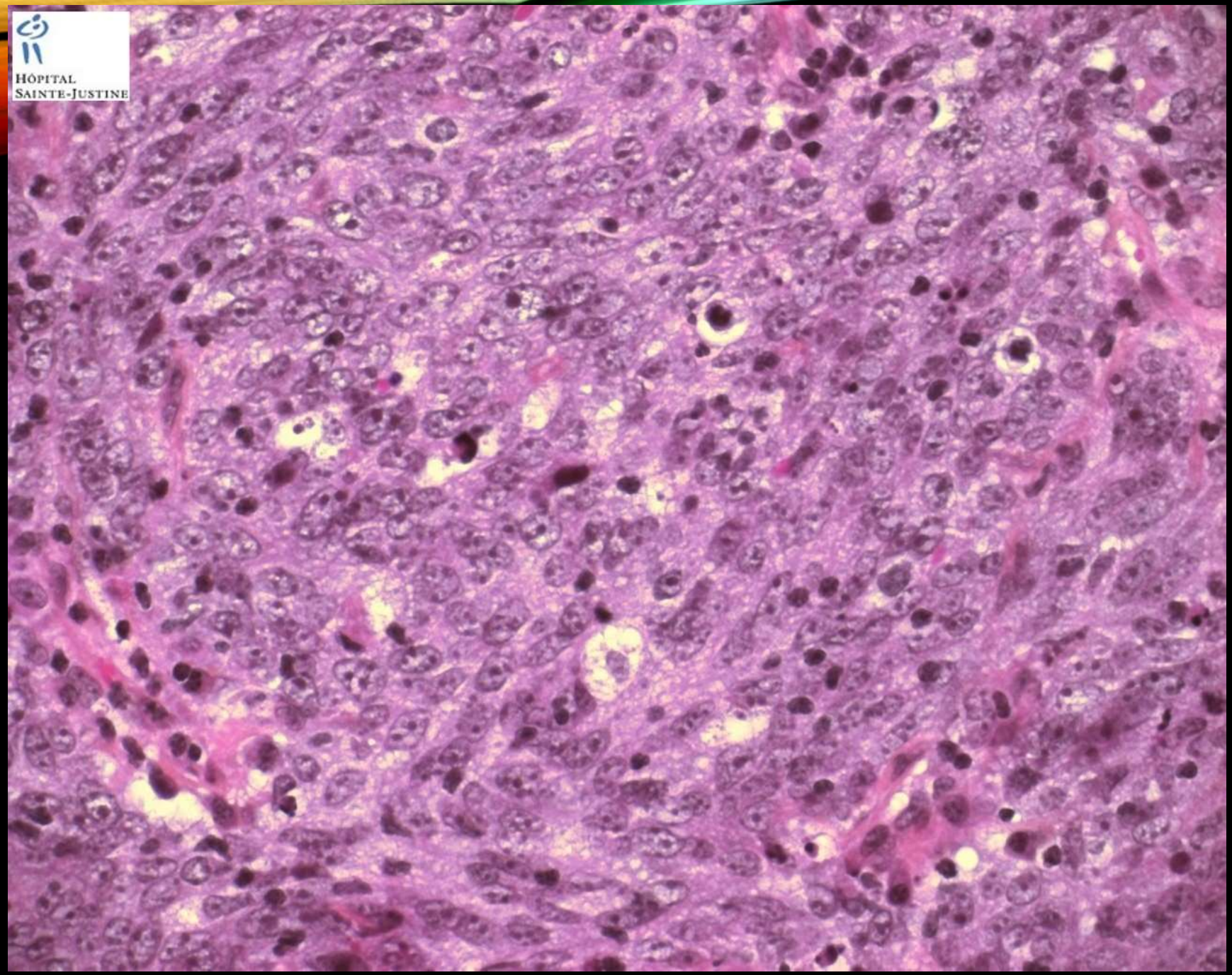
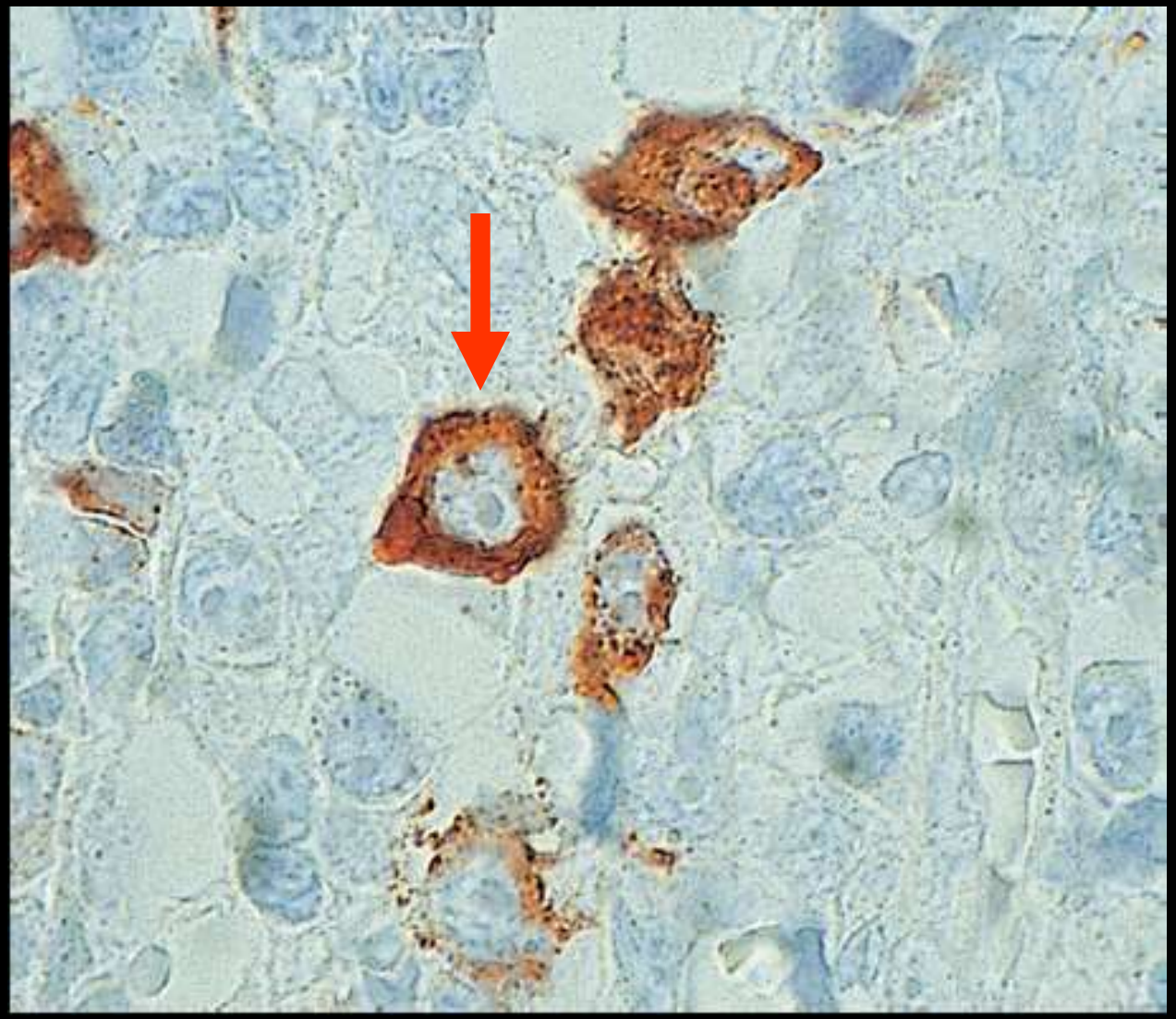


Fig. 51. *Nasopharyngeal carcinoma, non-keratinizing, undifferentiated.* Syncytial masses of undifferentiated tumour cells with vesicular nuclei and prominent nucleoli. Lymphocytes and plasma cells in stroma


HÔPITAL
SAINTE-JUSTINE

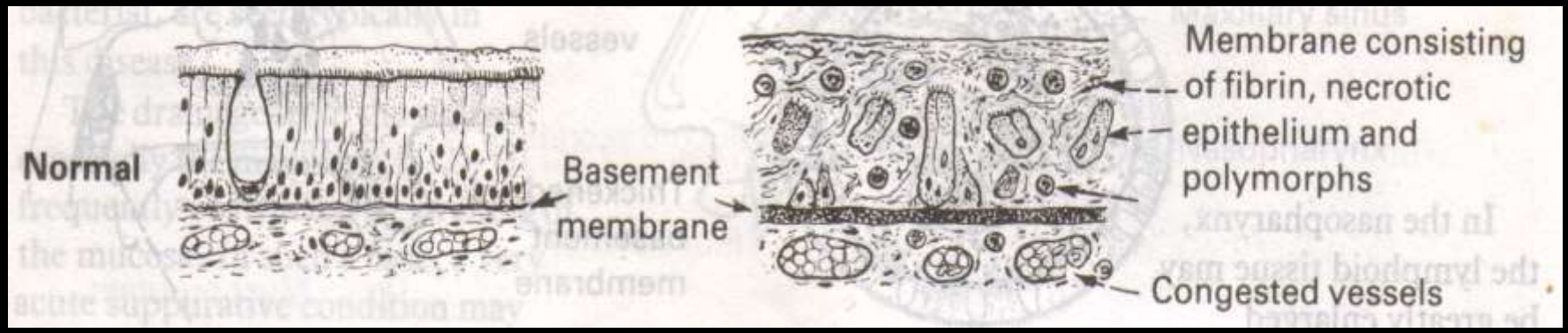
EBV

(IH; LMP-1) X 600



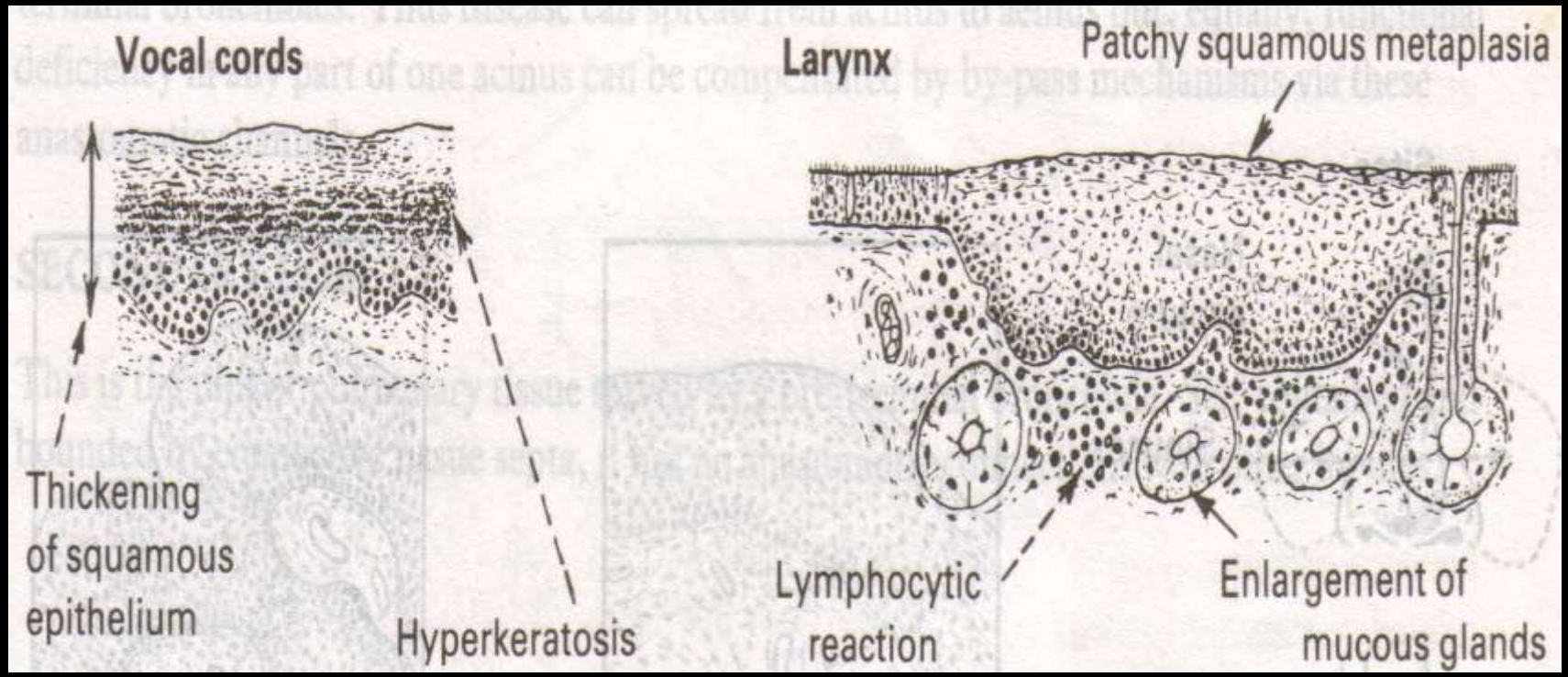
ACUTE LARYNGITIS AND TRACHEITIS

- Mild: parainfluenza and adenovirus → Strept.pneumoniae and pyogenes, and Neisseria catarrhalis
- Severe laryngotracheitis: pseudomembranous inflammation → Staph. Aureus. Strept. pyogenes



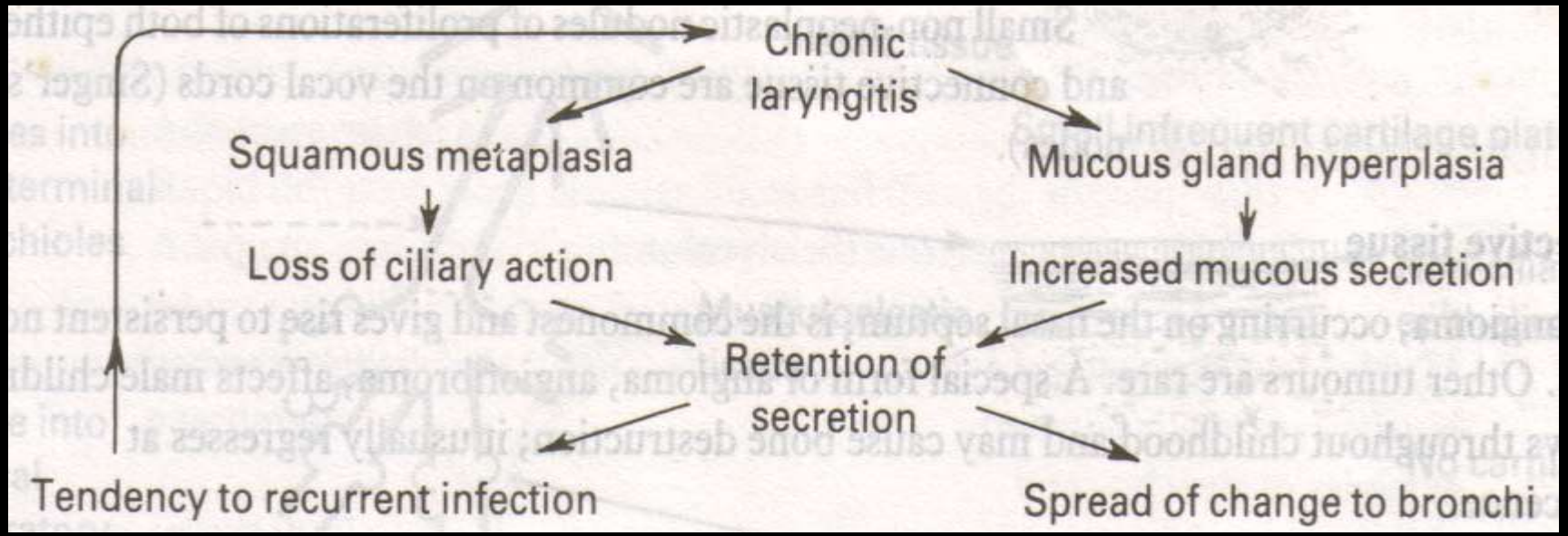
Special form of pseudomembranous inflammation: Diphtheria

CHRONIC LAYNGITIS AND TRACHEITIS

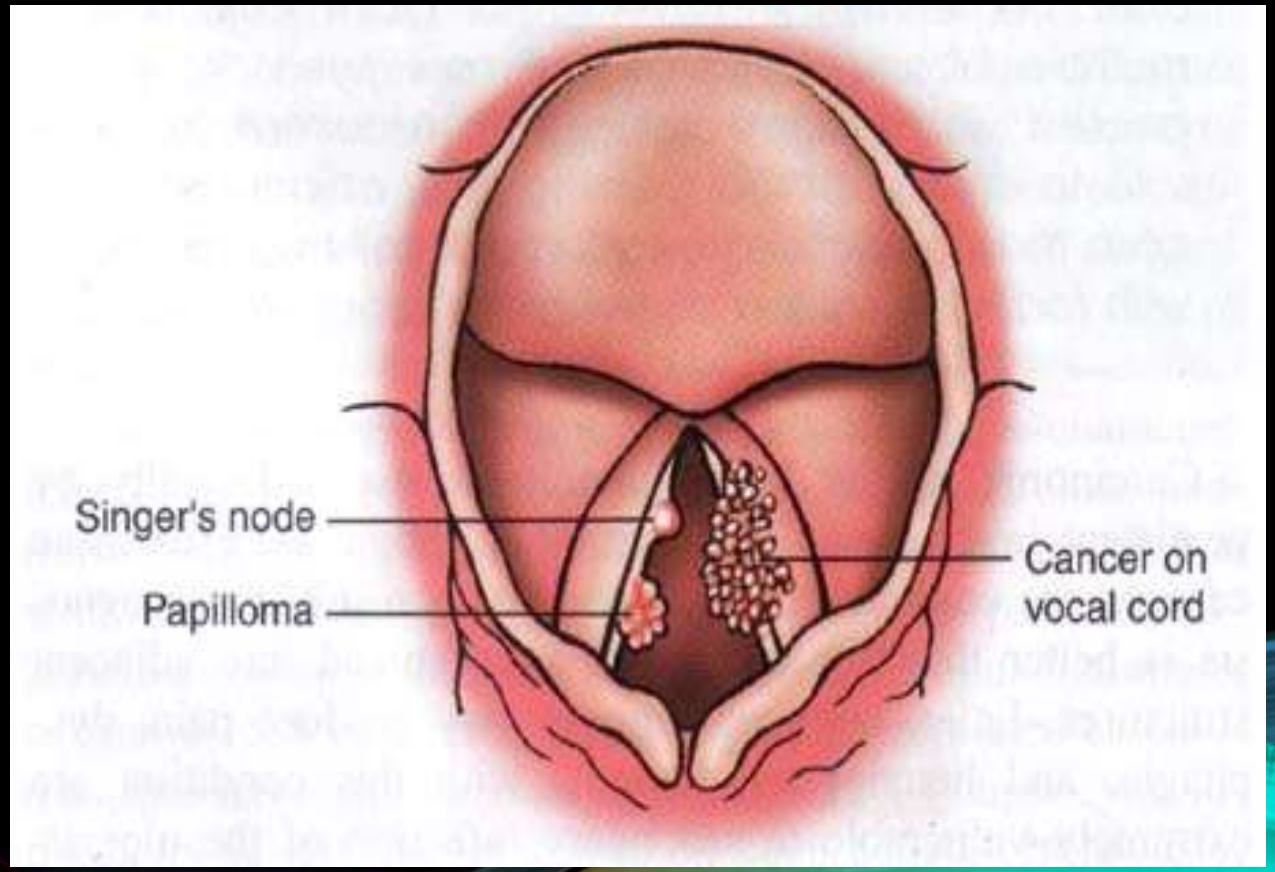


Specific: Tbc and Syphilis

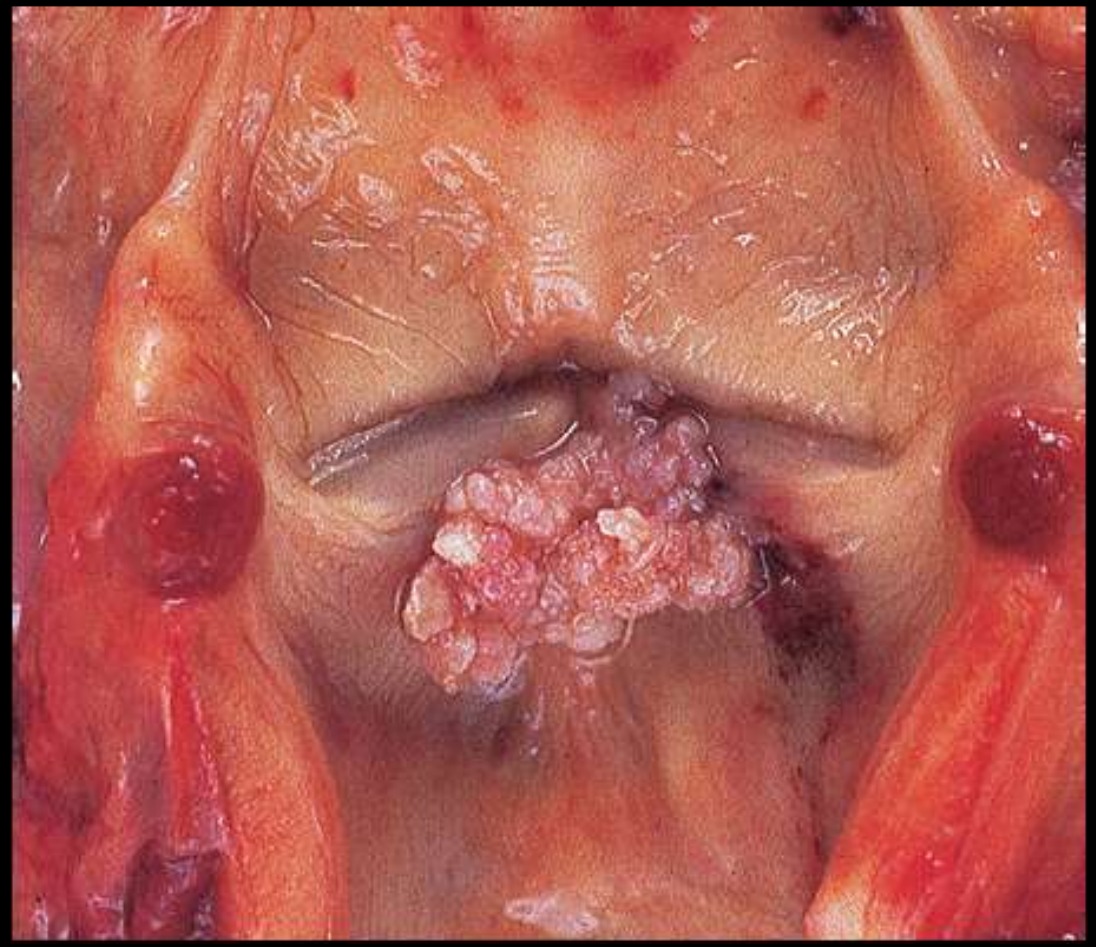
CHRONIC LARYNGITIS



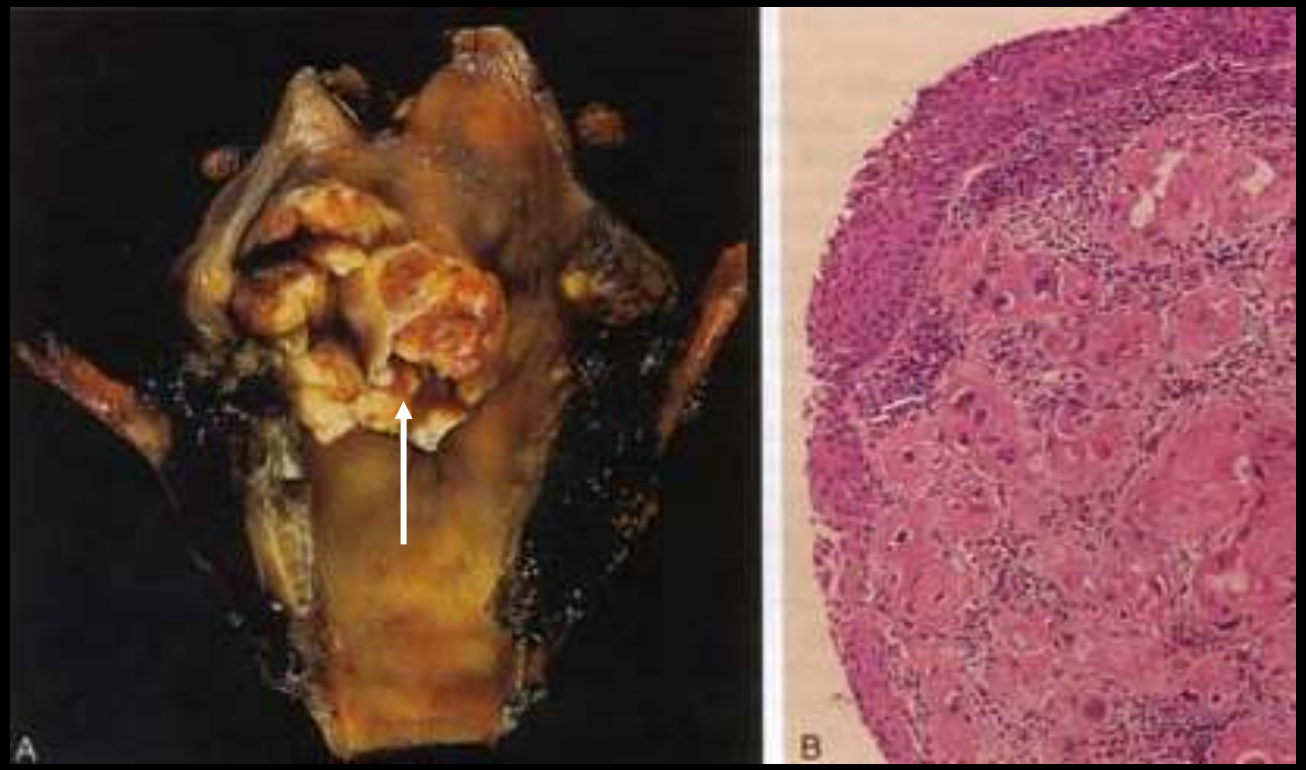
LARYNX: BENIGN VS MALIGNANT



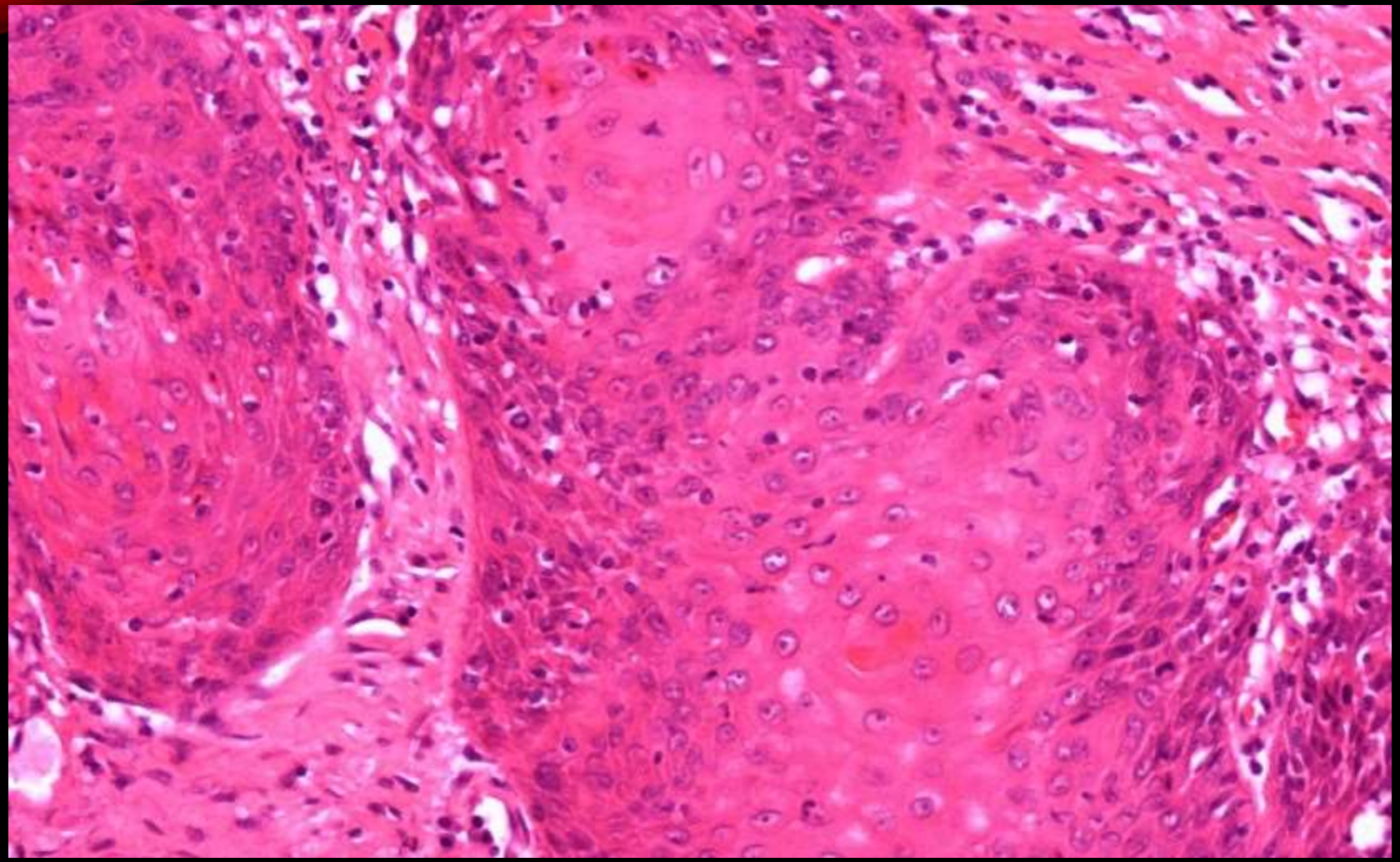
LARYNGEAL PAPILLOMATOSIS



LARYNGEAL CARCINOMA



Gross: fungating/papillary	Microscopical: well.diff. SCC



WELL DIFFERENTIATED SQUAMOUS CELL CARCINOMA

PATOLOGI PARU

- Kelainan bawaan
- Atelektasis
- Hyaline membrane disease (RDS Type I)
- Gangguan sirkulasi
- Radang / infeksi
- Penyakit Pulmonar Obstruktif Kronis (COPD)
- Penyakit Paru Restriktif
- Neoplasma

PATHOLOGY OF THE LUNG

I. Congenital Anomalies

II. Atelectasis

III. Hyaline membrane disease (RDS Type I)

IV. Circulation disorders

V. Inflammatory disorders / infection

VI. Chronic Obstructive Pulmonary Diseases (COPD)

VII. Restrictive Pulmonary Diseases (RPD)

VIII. Neoplasms

Table 14.1 Major aetiological factors in respiratory disease

Aetiological factor	Disease
Genetic	Cystic fibrosis α_1-Antitrypsin deficiency Some asthma
Environmental	
Smoking	Lung cancer Chronic bronchitis and emphysema Susceptibility to infection
Air pollution	Chronic bronchitis Susceptibility to infection
Occupation	Pneumoconiosis Asbestosis, mesothelioma and lung cancer
Infection	Influenza Measles Bacterial pneumonias Tuberculosis

Table 2-1

PHASES OF LUNG DEVELOPMENT*

Phase	Gestation	Major Events
Embryonic	26 days to 6 weeks	Development of major airways
Pseudoglandular	6 to 16 weeks	Development of airways to terminal bronchioles
Canalicular	16 to 28 weeks	Development of the acinus and its vascularization
Saccular	28 to 36 weeks	Subdivision of saccules by secondary crests
Alveolar	36 weeks to term (and up to 4 years of age)	Acquisition of alveoli

*Modified from reference 2.

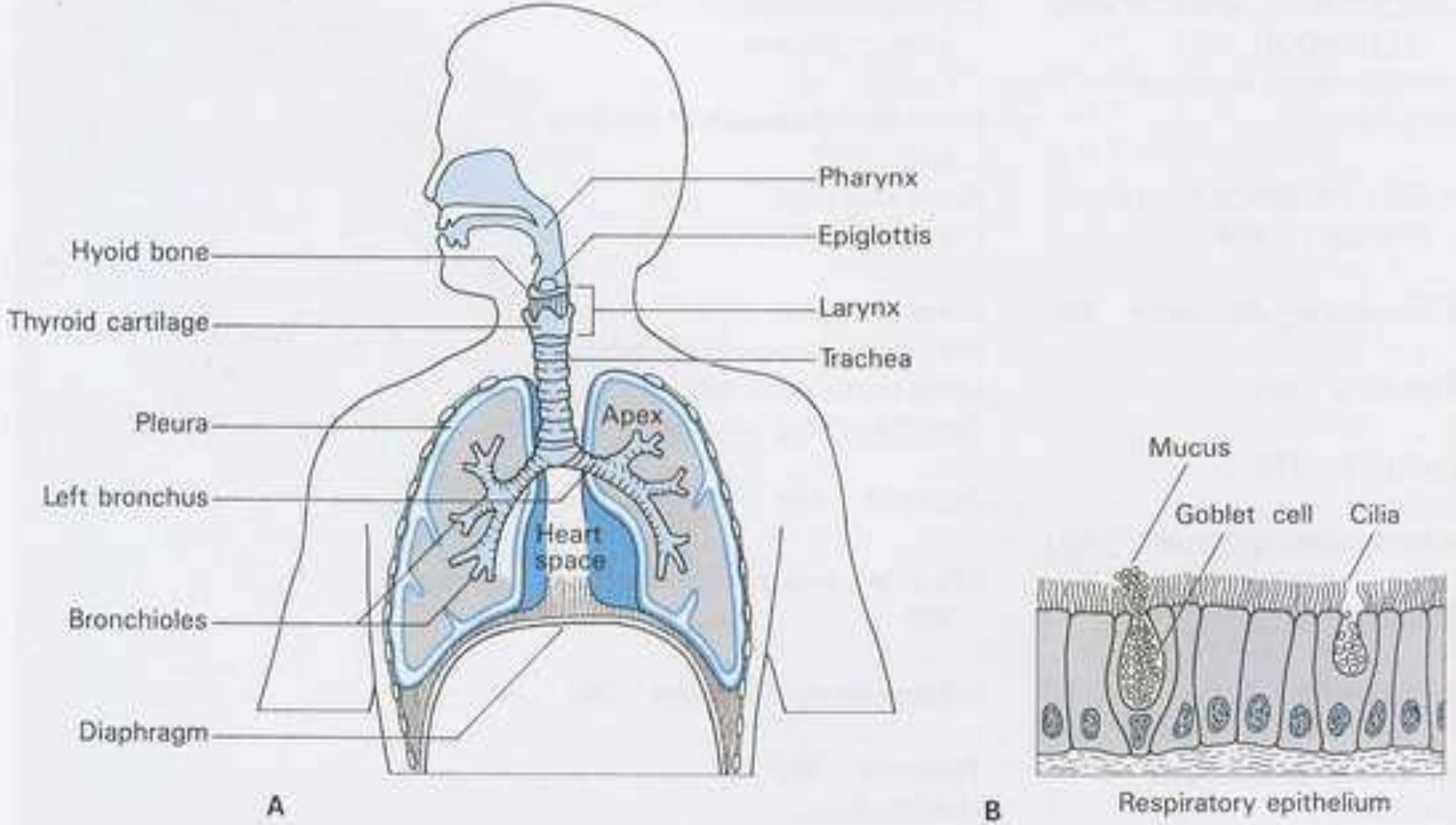
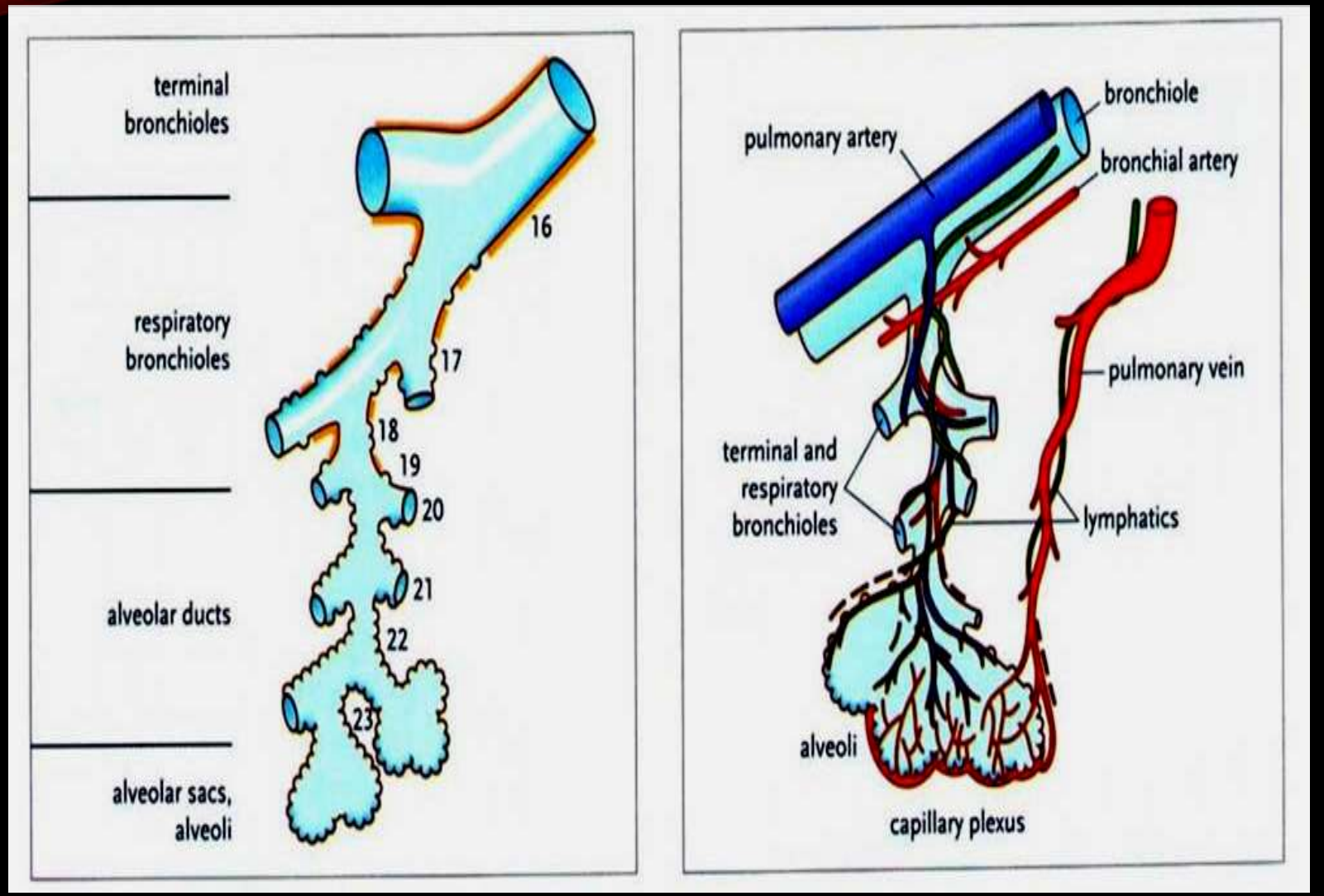
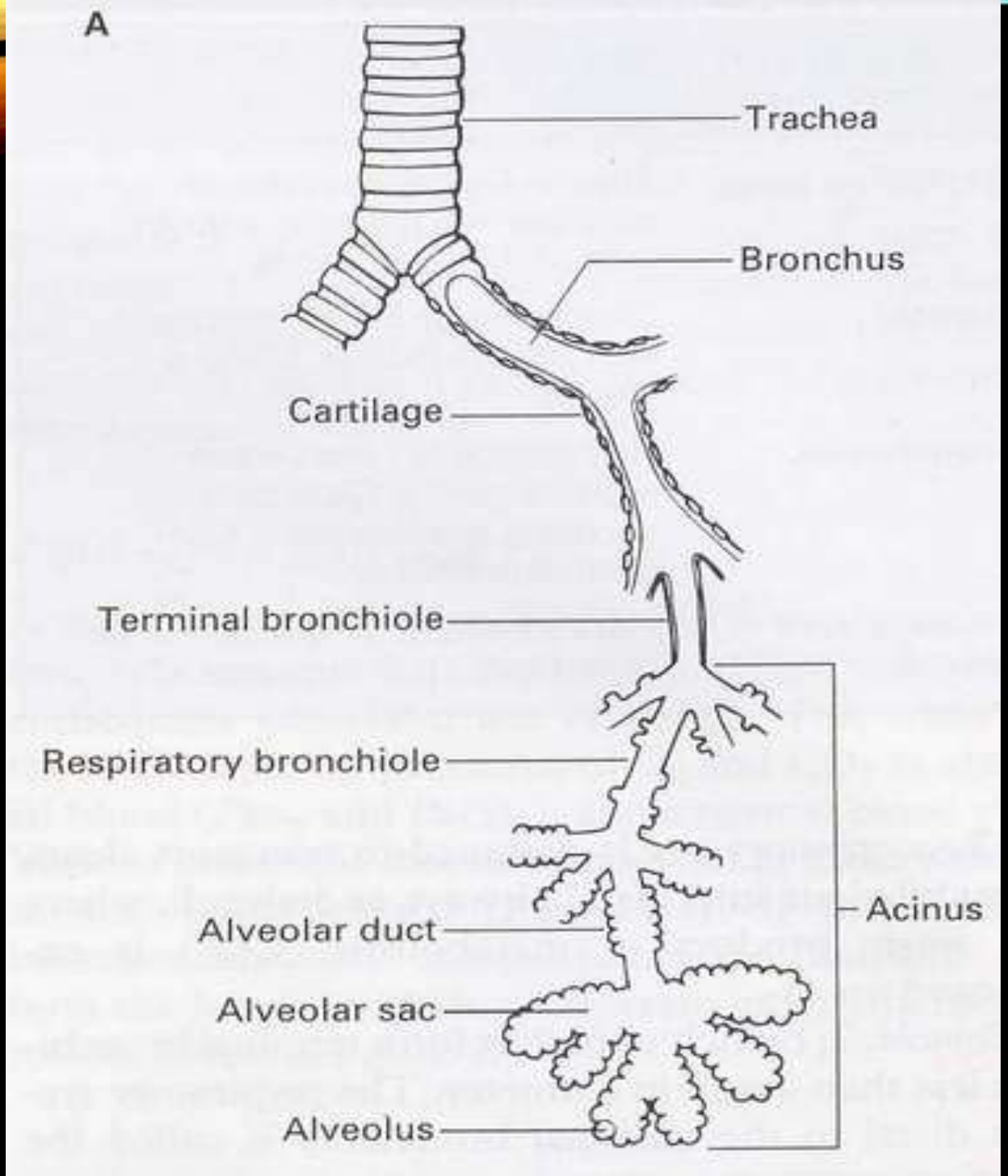


Fig. 14.1 The respiratory system

A. Anatomy of the respiratory tract. **B.** Histology of respiratory epithelium. With the exception of the pharynx, epiglottis and vocal cords, the respiratory tract is lined by specialised ciliated mucus-secreting epithelium.

PARU


terminal bronchioles
respiratory bronchioles
alveolar ducts
alveolar sacs, alveoli
16
17
18
19
20
21
22
23
pulmonary artery
bronchiole
bronchial artery
pulmonary vein
terminal and respiratory bronchioles
lymphatics
alveoli
capillary plexus


A
Trachea
Bronchus
Cartilage
Terminal bronchiole
Respiratory bronchiole
Alveolar duct
Alveolar sac
Alveolus
Acinus

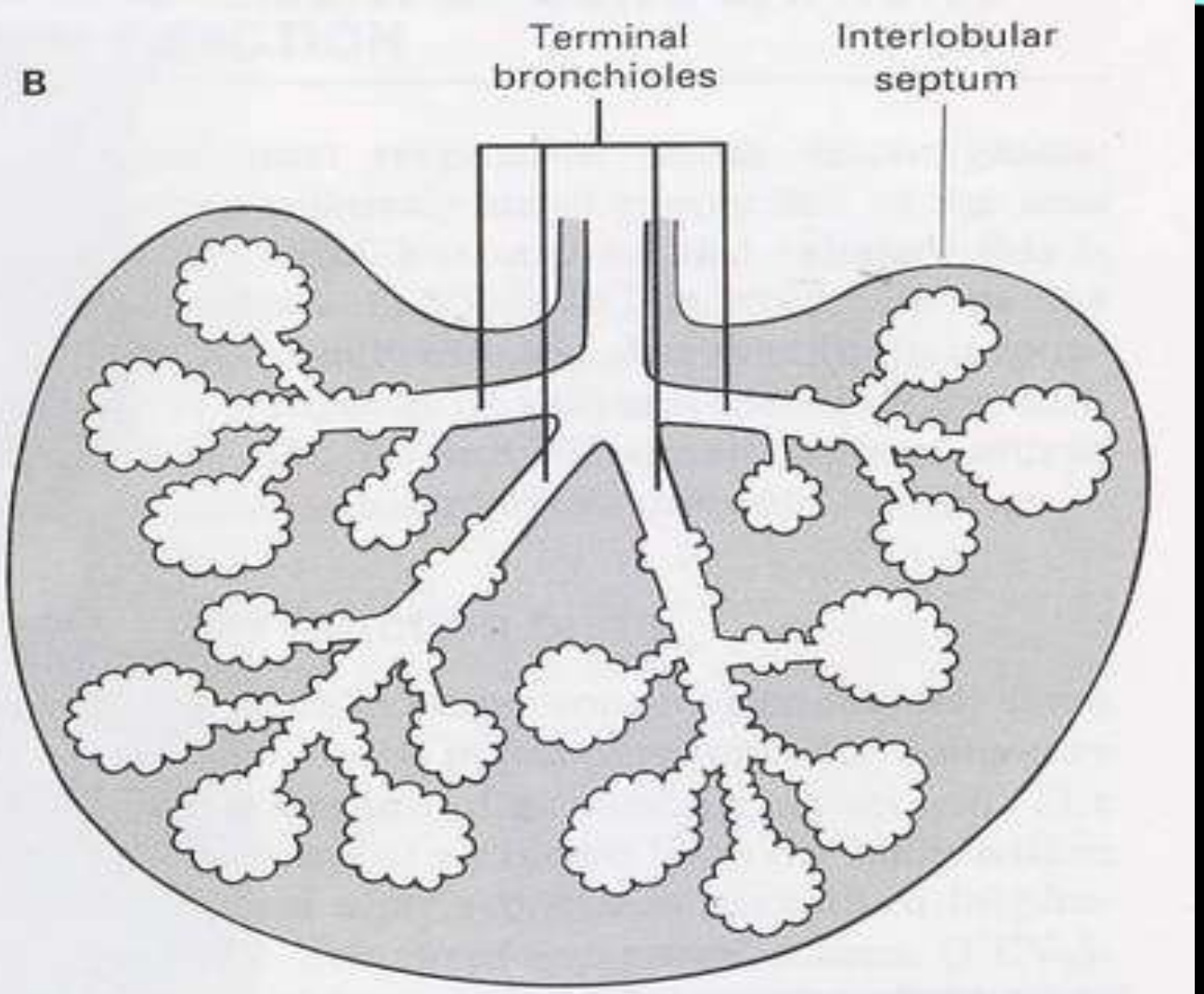
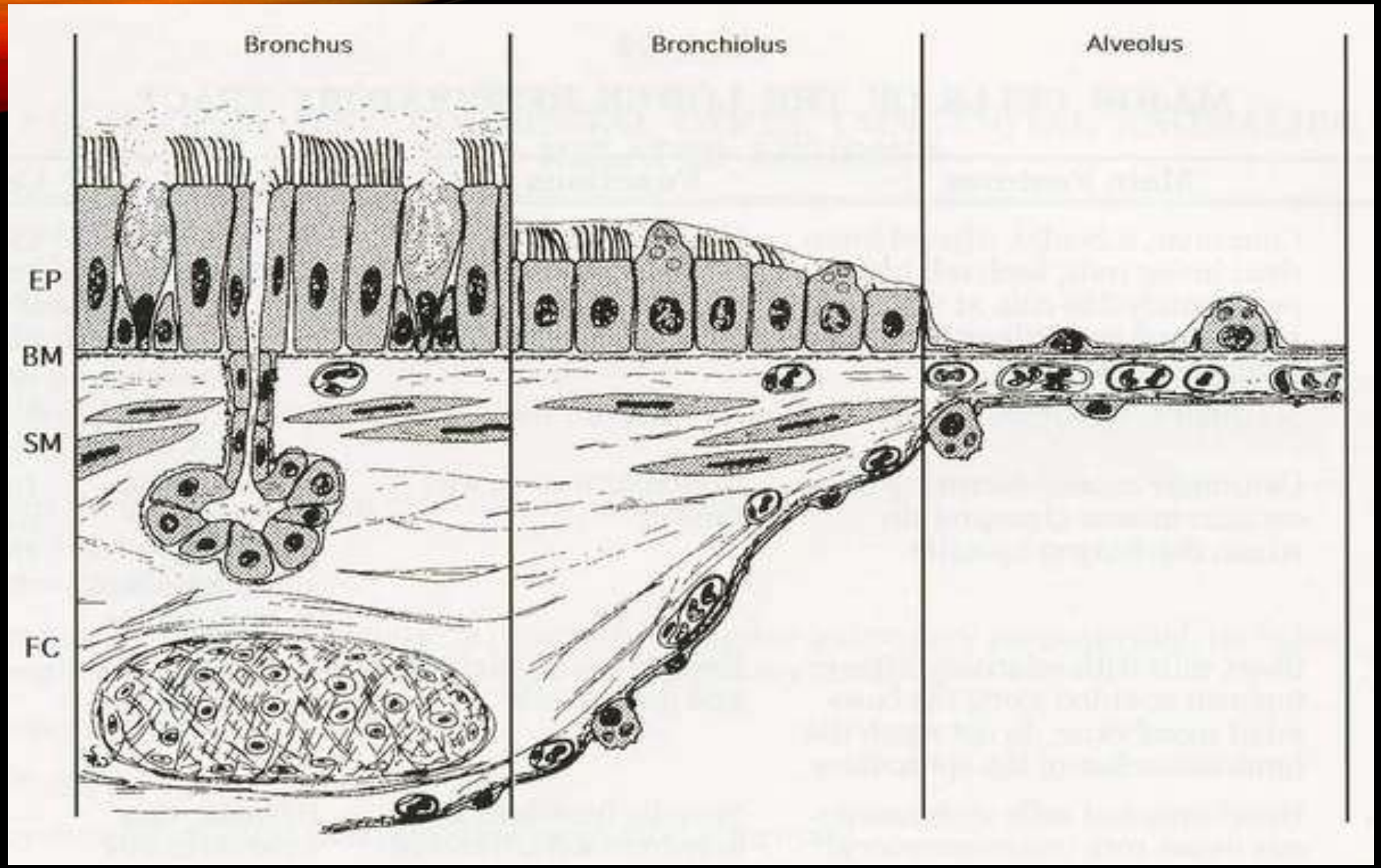
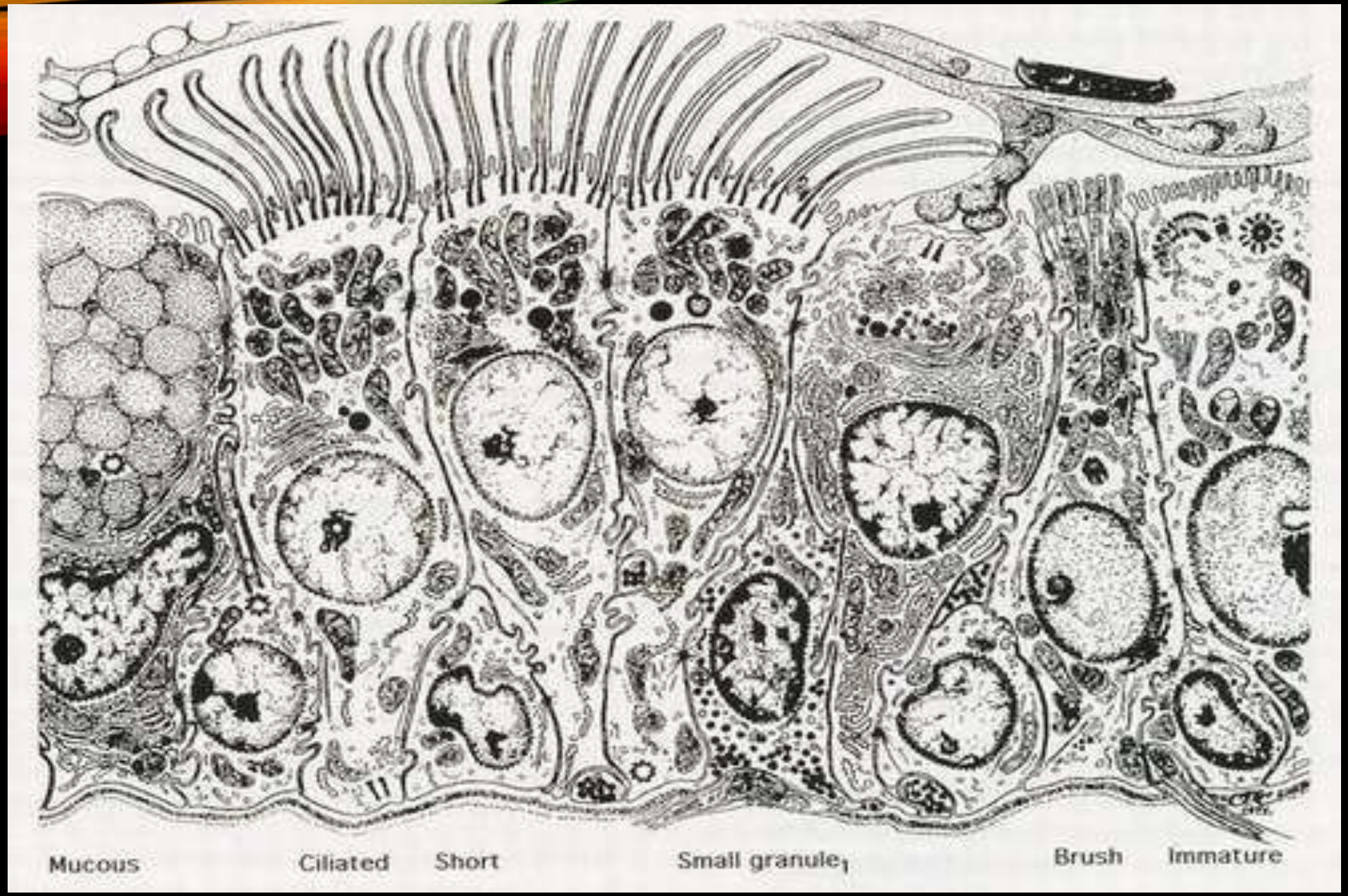


Fig. 14.2 The lower respiratory tract

A. Structure and nomenclature of the lower respiratory tract.
B. Schematic detail of a lobule. Different diseases affect different parts of the tract.


Bronchus
Bronchiolus
Alveolus
EP
BM
SM
FC


Mucous
Ciliated
Short
Small granule
Brush
Immature

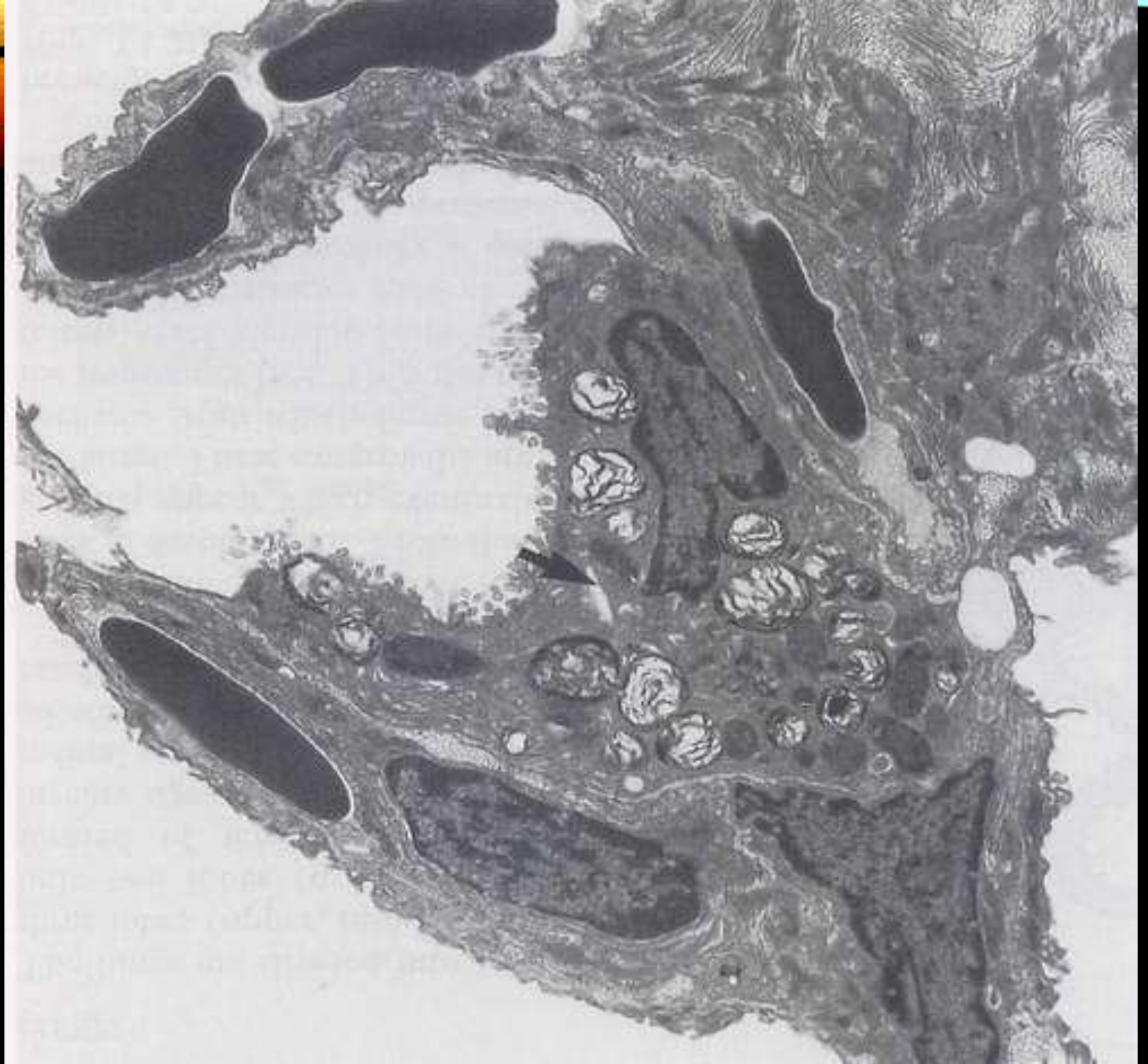
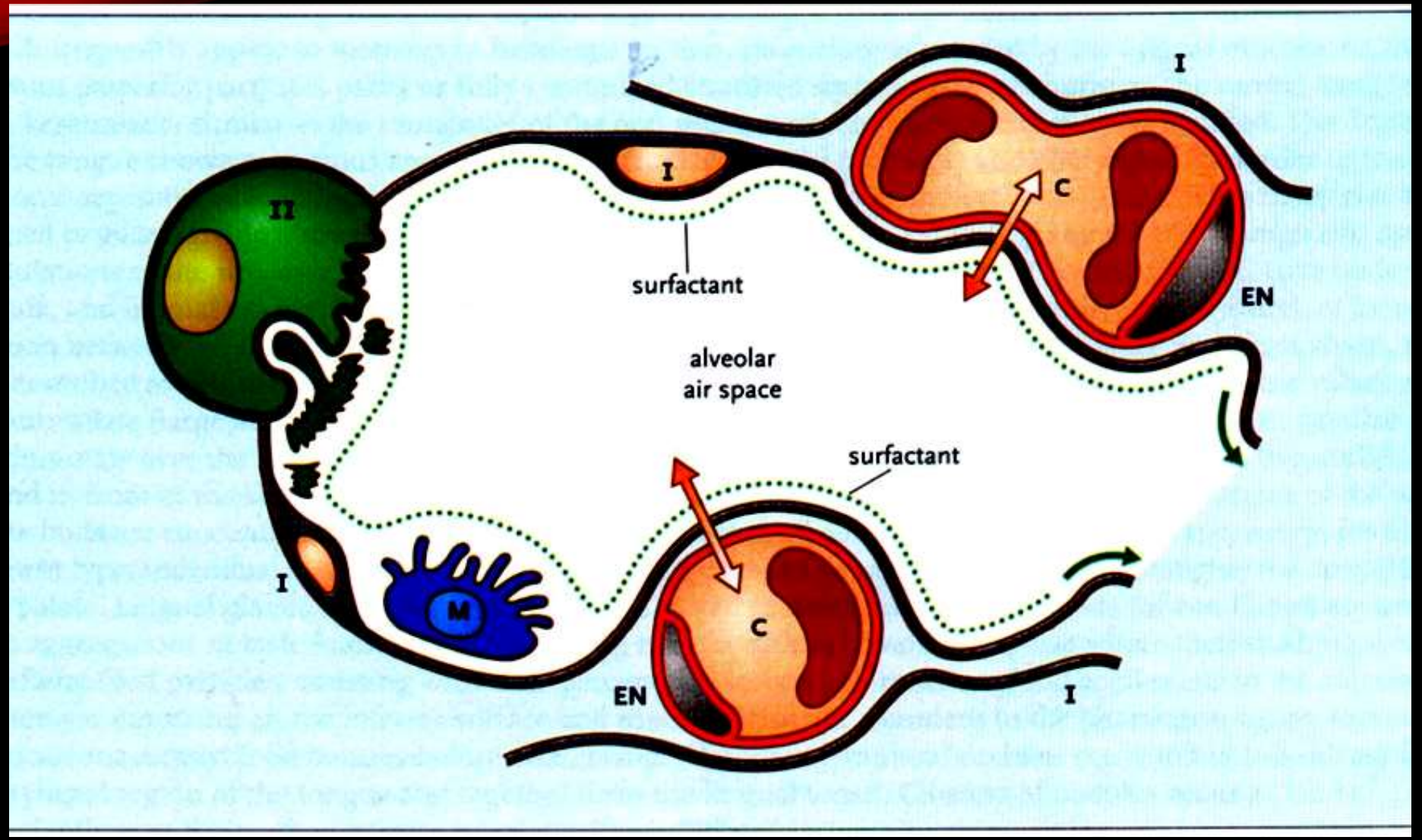


Table 14.2 Structure of the respiratory tree

Part of respiratory tract	Structure
Trachea	Anterior C-shaped plates of cartilage with posterior smooth muscle. Mucous glands
Bronchi	Discontinuous foci of cartilage with smooth muscle. Mucous glands
Bronchioles	No cartilage or submucosal mucous glands. Clara cells secreting proteinaceous fluid. Ciliated epithelium
Alveolar duct Alveoli	Flat epithelium. No glands. No cilia Type I and II pneumocytes

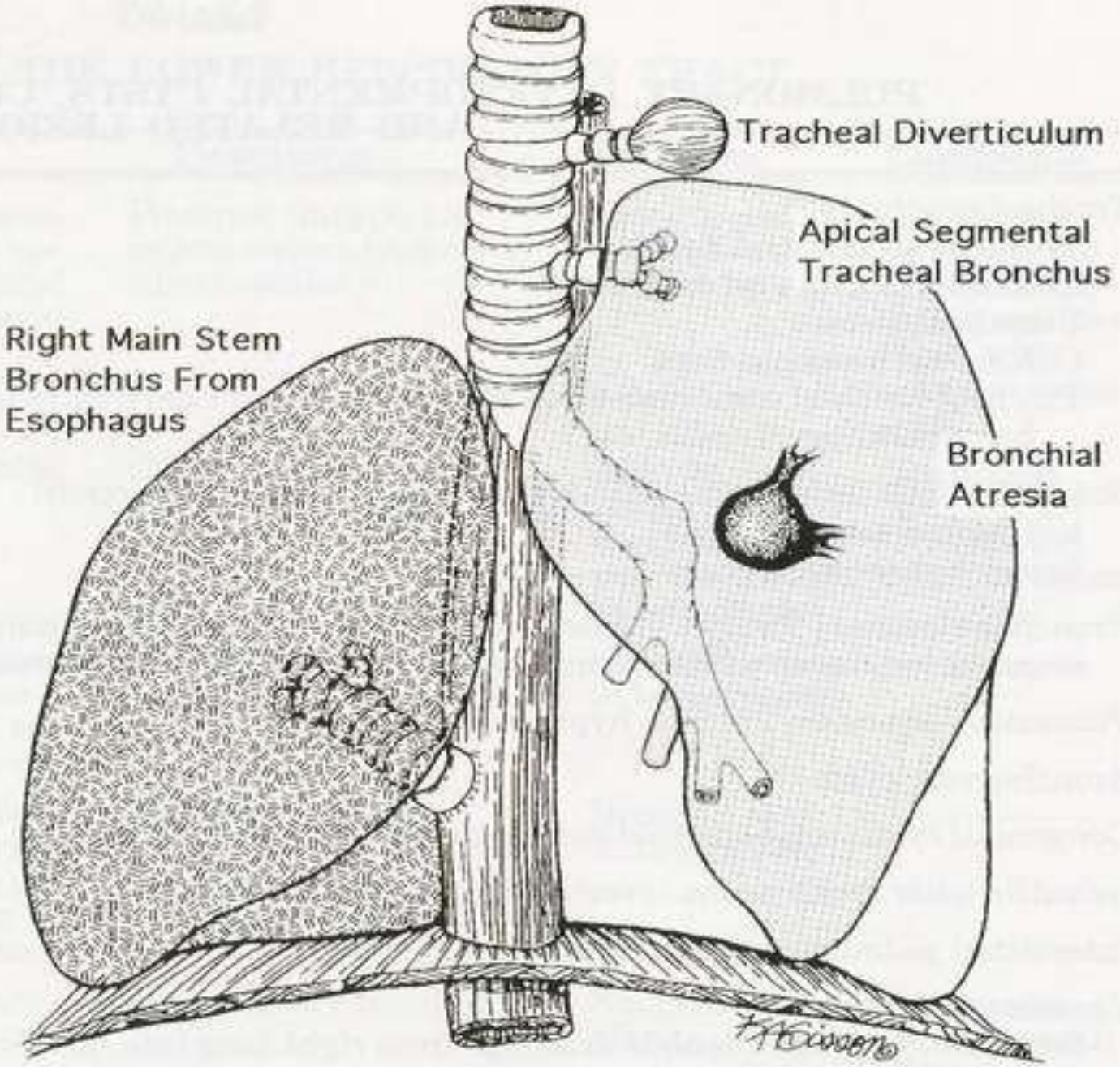
ALVEOLI



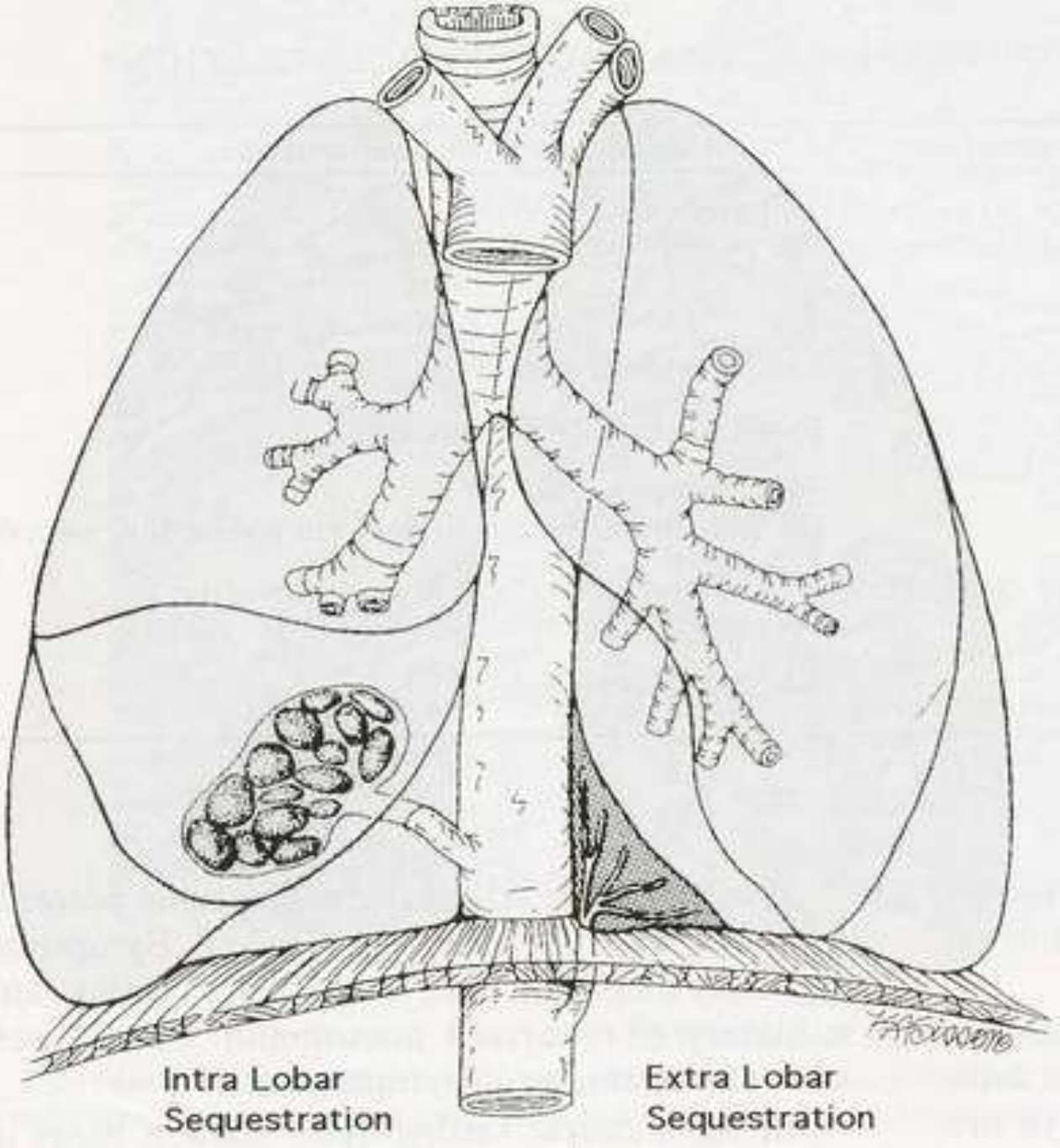
KELAINAN BAWAAN

- **Hipoplasia** (akibat dari pengecilan volume thorax waktu pertumbuhan)
  - kompresi (hernia diafragmatika, penyakit ginjal polikistik)
  - defisiensi cairan amnion → penurunan gerakan respirasi fetal
- **Hernia diafragmatika**
  - sebagian atau seluruh diafragma hilang → isi abdomen mendesak ke atas
- **Kista bronkogenik**
  - kista dilapisi epitel bronkus, kadang dengan tulang rawan, di dalam atau di luar paru (mediastinum sekitar bifurkatio trakealis), berisi mukus → abses
- **Sequestrasi bronkopulmonar**
  - potongan jaringan paru tanpa hubungan dengan percabangan trakeo- bronkial, menerima darah biasanya dari aorta
  - lokasi: intralobar dan ekstralobar

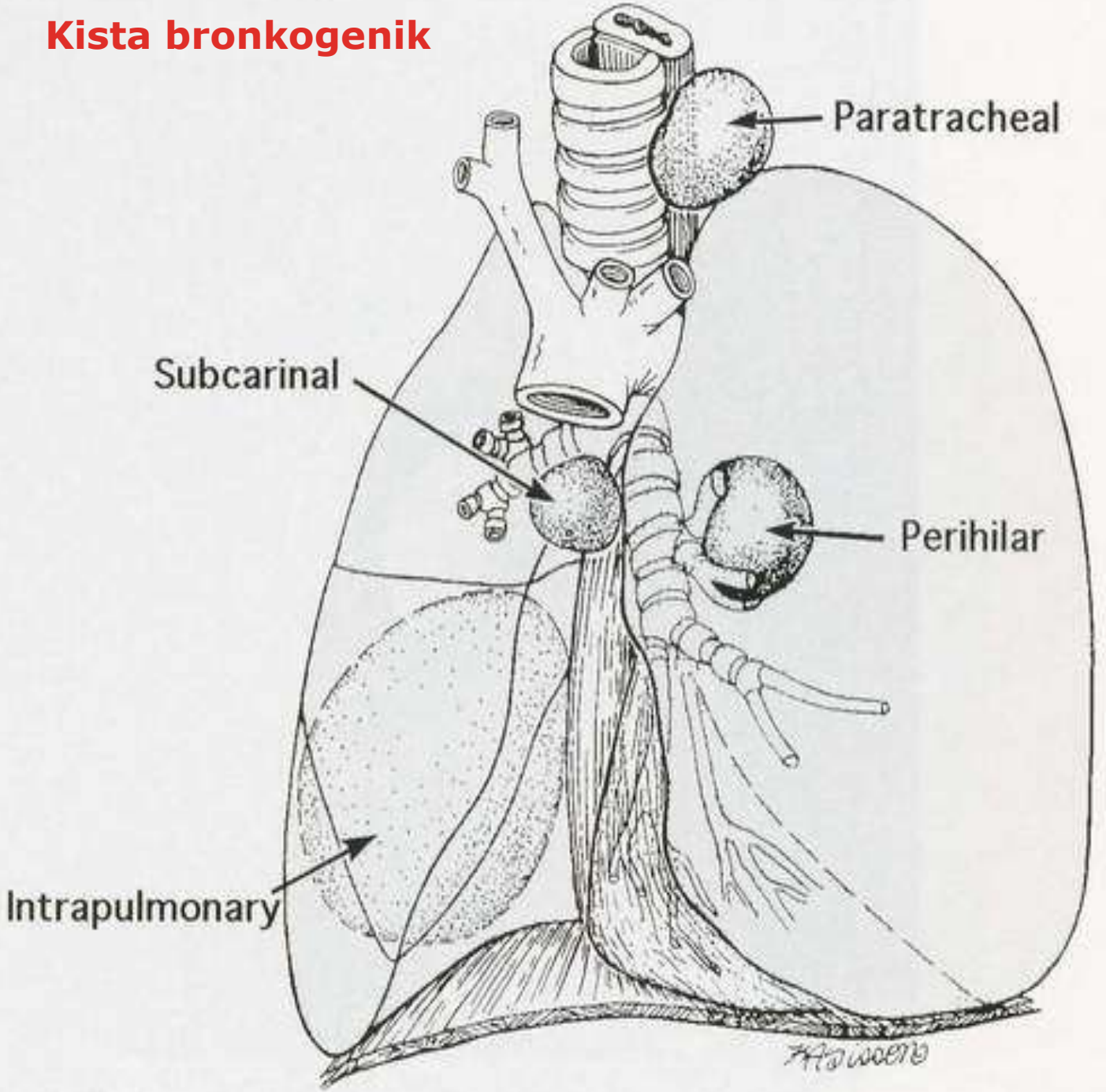
Malformasi jalan napas



Sequestrasi bronkopulmonar



Kista bronkogenik



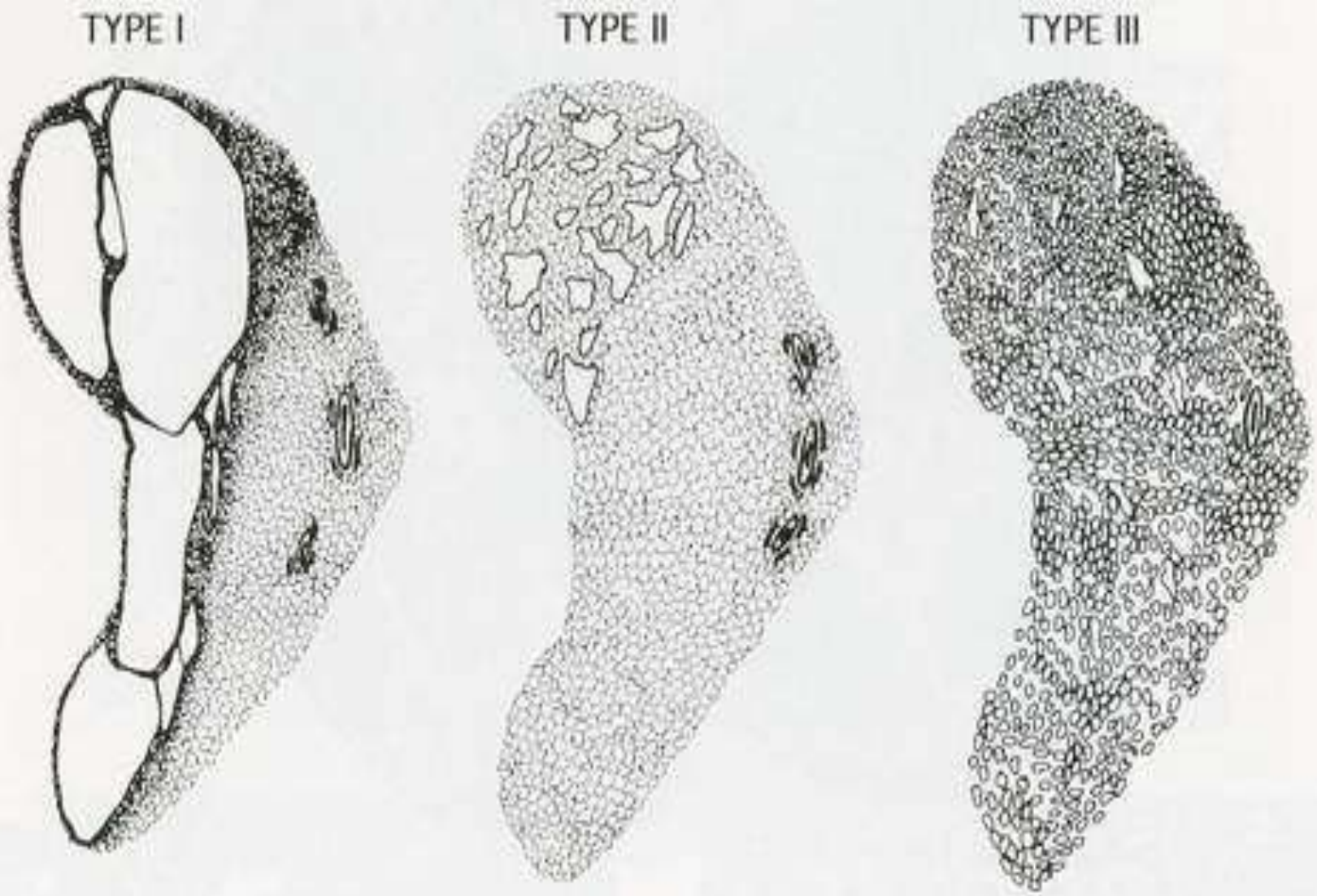
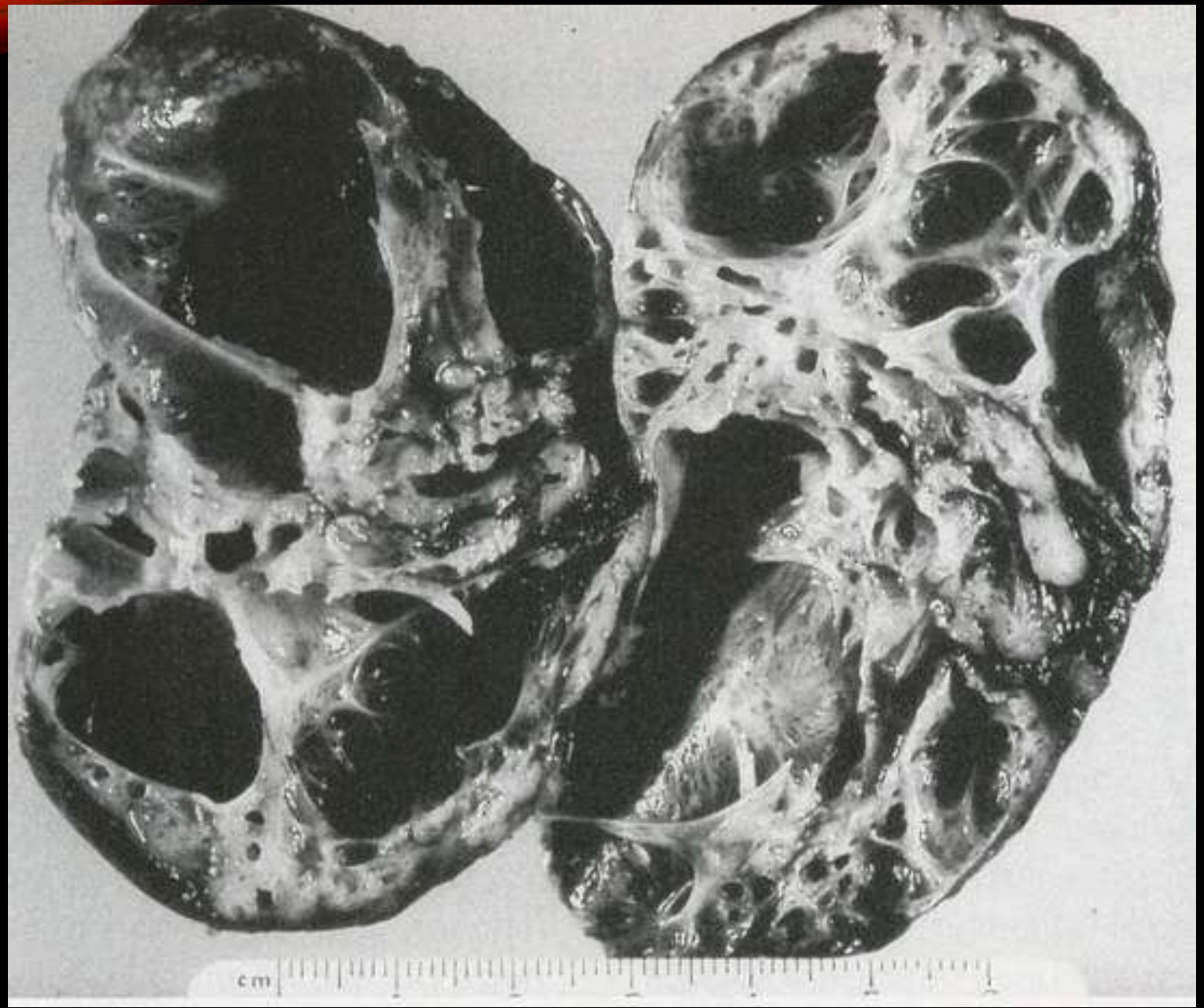


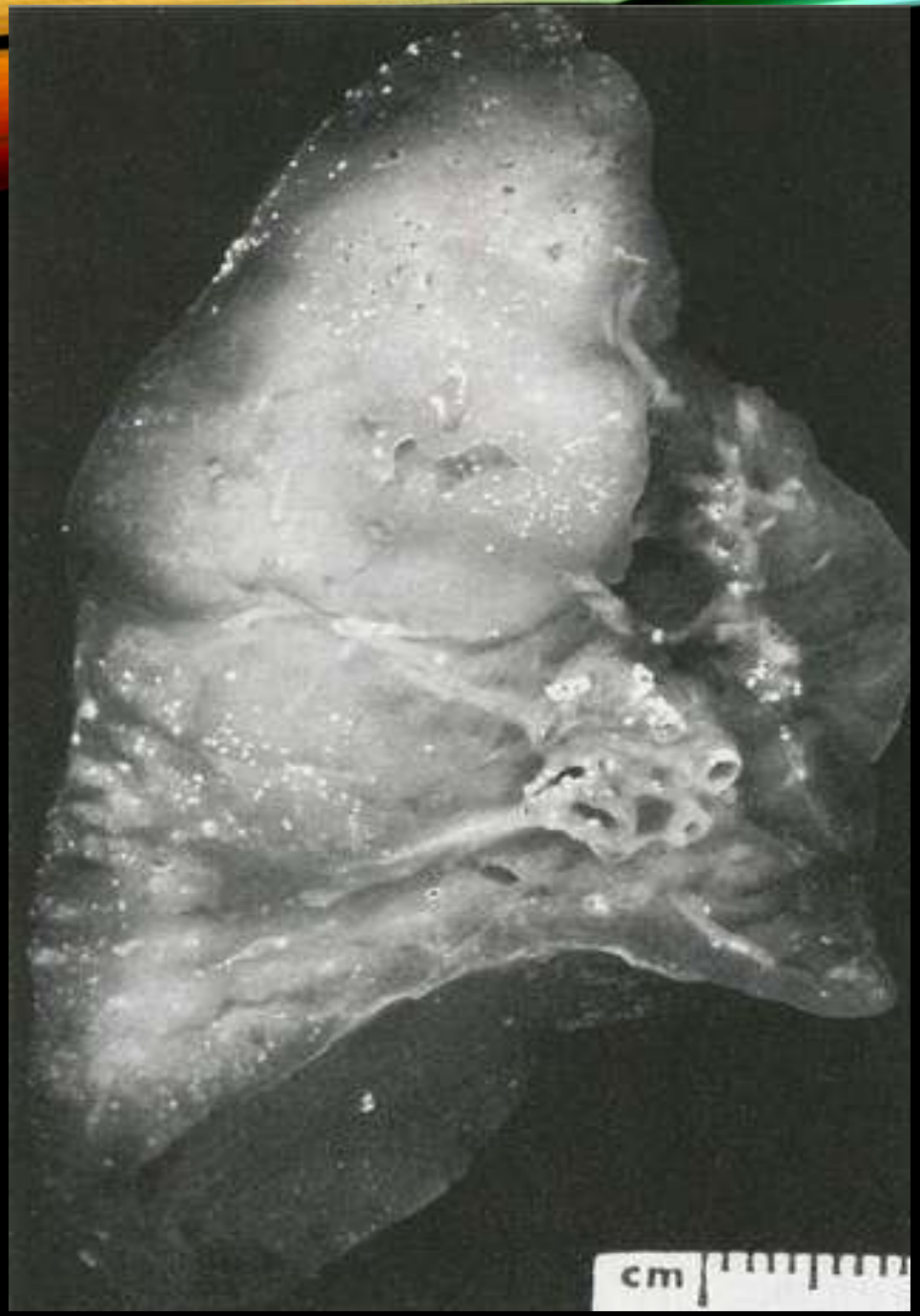
Figure 2-17
CONGENITAL CYSTIC ADENOMATOID MALFORMATION

Diagramatic representation of the three types of congenital cystic adenomatoid malformation. (Fig. 1 from Stocker JT, Madewell JE, Drake RM. Congenital cystic adenomatoid malformation of the lung: classification and morphologic spectrum. Hum Pathol 1977;8:155–72.)

KISTA PARU



CONGENITAL HYPOPLASIA



II. ATELEKTASIS

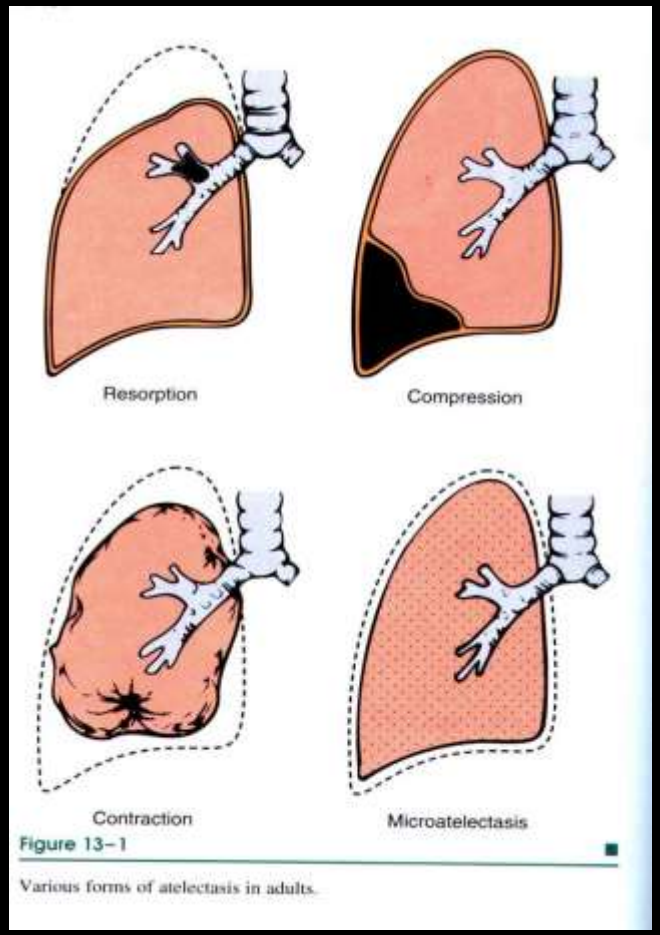


Figure 13–1

Various forms of atelectasis in adults.

Atelektasis primer (neonatorum)

- Akibat gagal bernapas pada saat lahir: trauma, obstruksi bronkial, obat, imaturitas, dll.
- Tidak terapung dalam air (tidak berisi udara)

Atelektasis sekunder (dapatan)

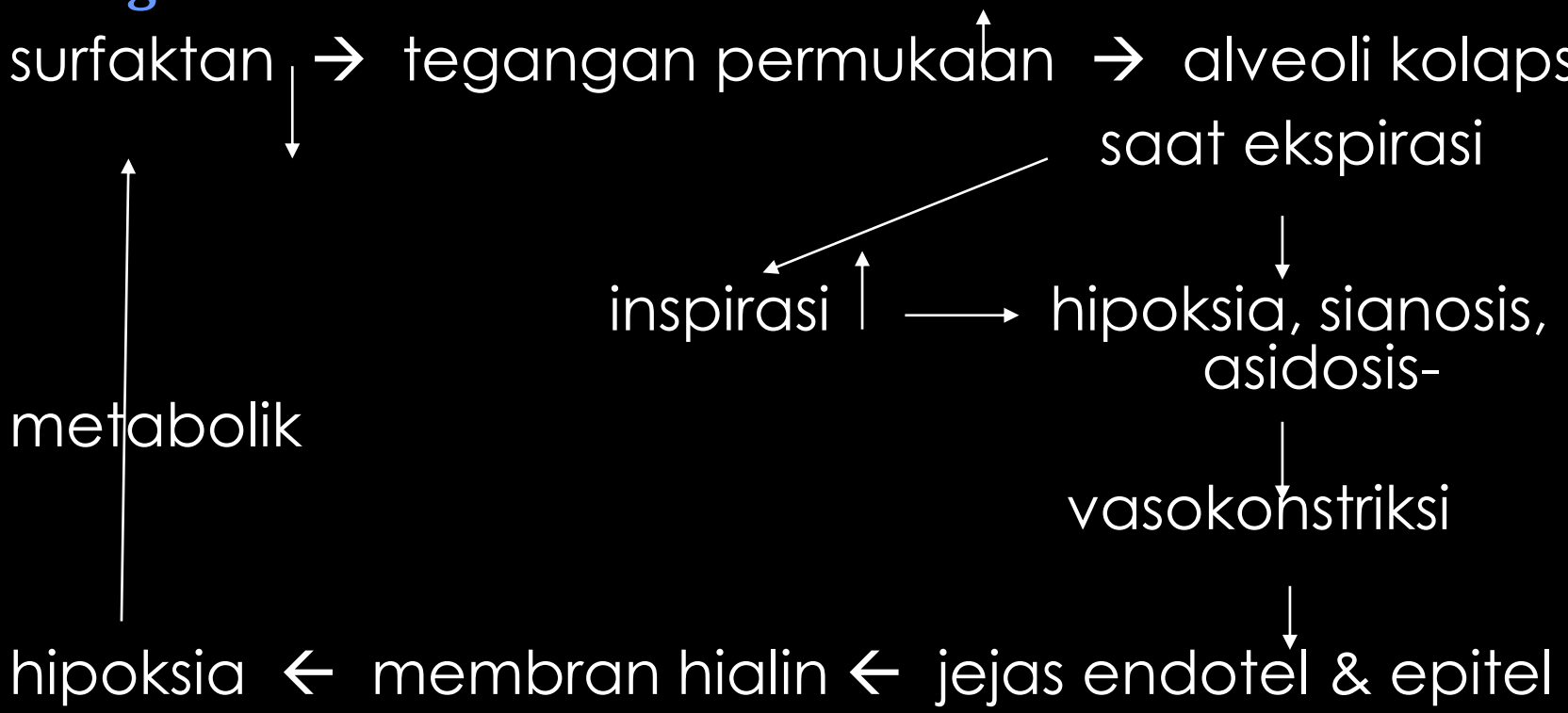
- Resorpsi
- Kompresi
- Kontraksi
- Mikroatelektasis

III. HYALINE MEMBRANE DISEASE (RDS TIPE I)

- **Etiologi**

  defisiensi surfaktan (material lipid yang diproduksi oleh pneumosit tipe II untuk menurunkan tegangan permukaan alveoli → menjaga alveoli tetap terbuka): prematuritas, SC, Ibu DM

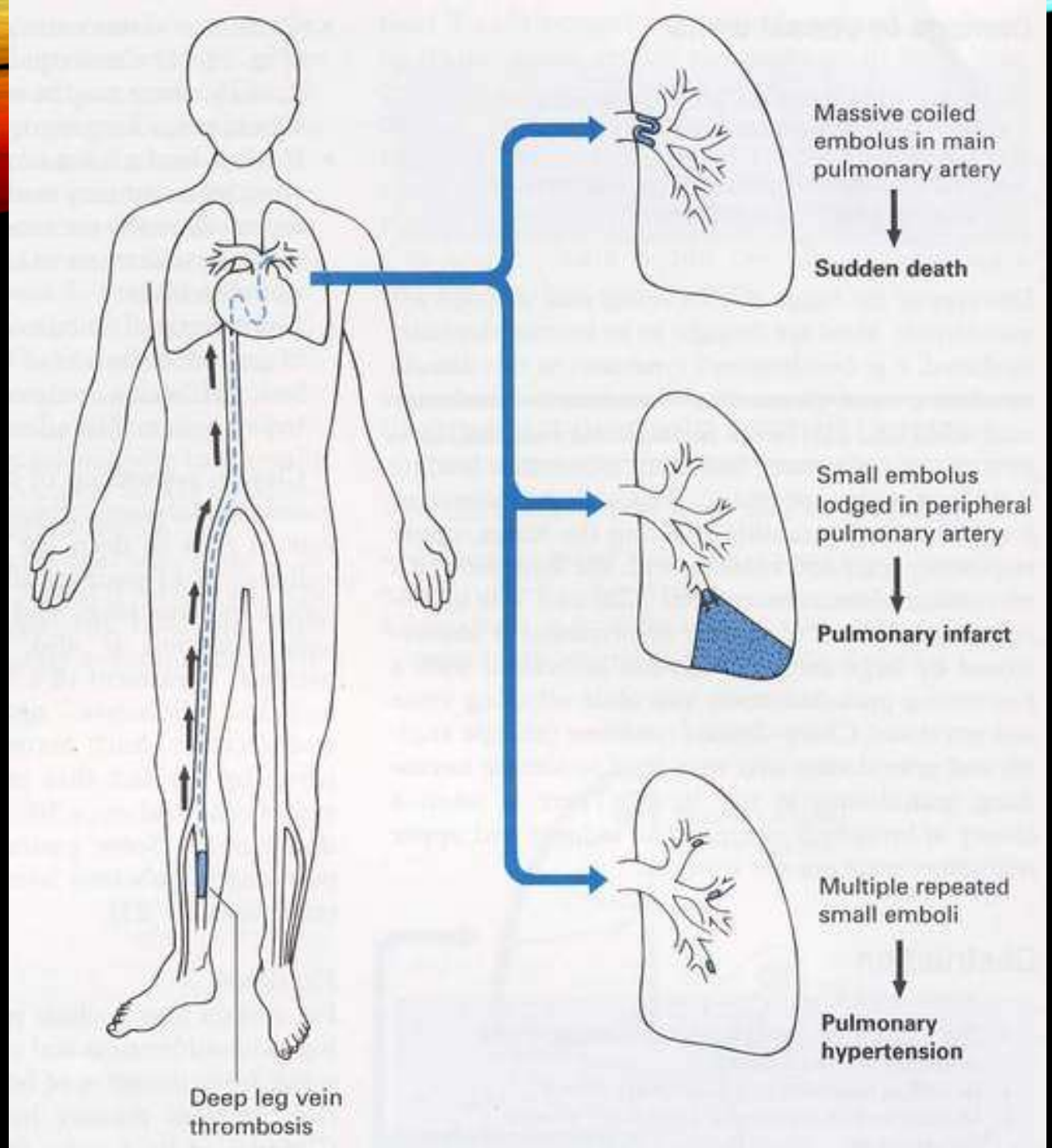
- **Patogenesis**

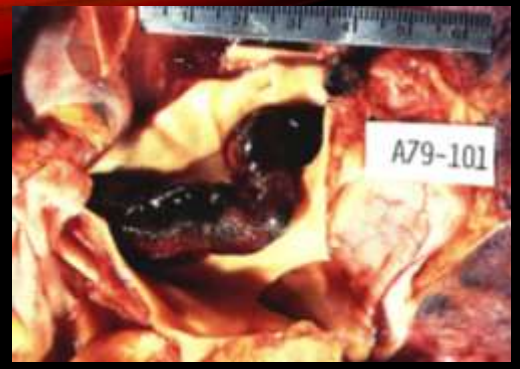


IV. GANGGUAN SIRKULASI

- Edema paru:
  - gagal jantung kongestif (gagal jantung kiri / kanan) infark miokard, penyakit jantung hipertensif, stenosis mitralis
- Emboli paru
  - biasanya berasal dari trombus vena profunda tungkai bawah
- Infark paru
- Hipertensi paru
  - obstruksi, konstriksi, obliterasi, aliran meningkat → resistensi vaskular paru meningkat → tekanan vaskular meningkat (hipertensi)

INFARK PARU


Massive coiled embolus in main pulmonary artery
Sudden death
Small embolus lodged in peripheral pulmonary artery
Pulmonary infarct
Multiple repeated small emboli
Pulmonary hypertension
Deep leg vein thrombosis



Emboli IV.

- emboli besar → emboli pelana
- emboli sedang
- emboli kecil

Emboli → sumbatan → penurunan aliran darah pada jaringan paru (vascular bed) → hipertensi pulmonar → gejala klinis: dispneu pada kerja fisik, nyeri anginal, pelebaran vena leher, → syncope

Infark

Akibat dari emboli → sumbatan → trias: dispneu – hemoptisis – nyeri dada pleuritik (dengan / tanpa bising gesek pleura)

V. RADANG

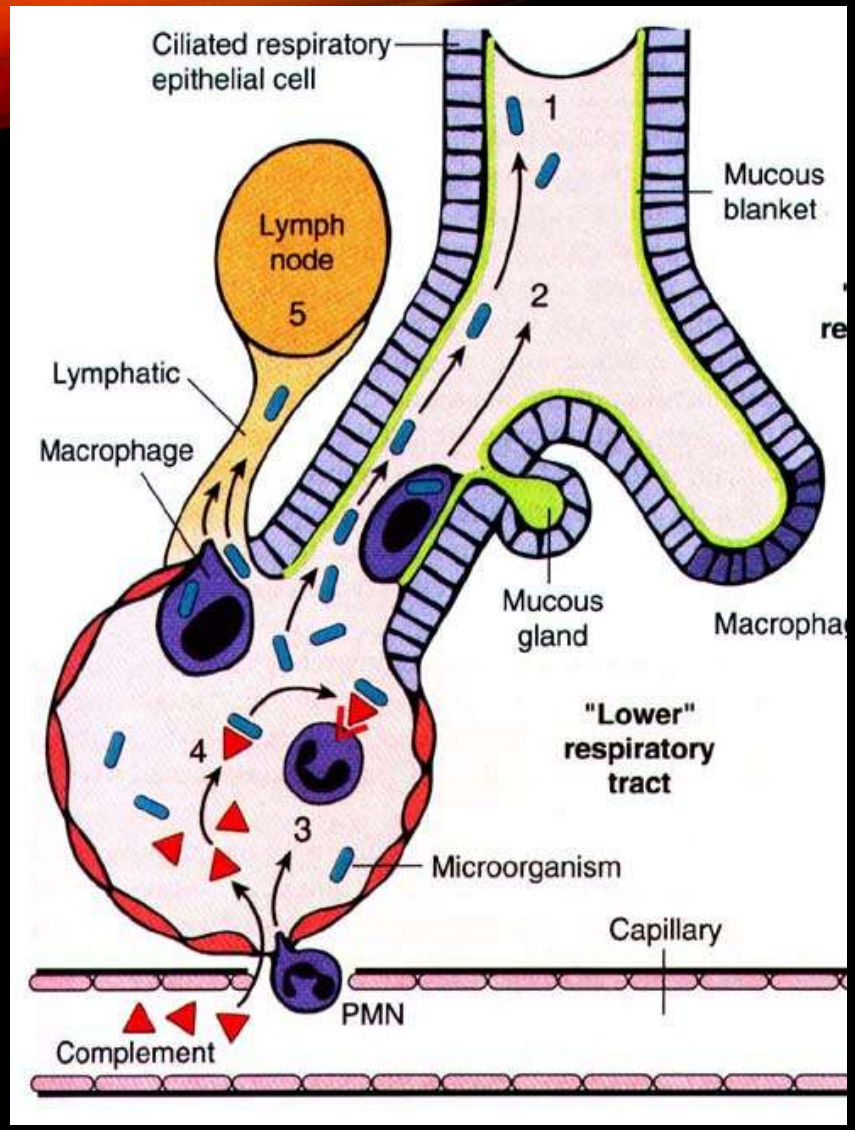
- Sebagai lanjutan infeksi saluran napas bagian atas
- Epitel permukaan terbuka → polusi udara / kontaminasi
- Aspirasi flora nasofaring selama tidur
- Penyakit paru umum → rentan terhadap bakteri virulen

V. RADANG

NON-SPESIFIK:

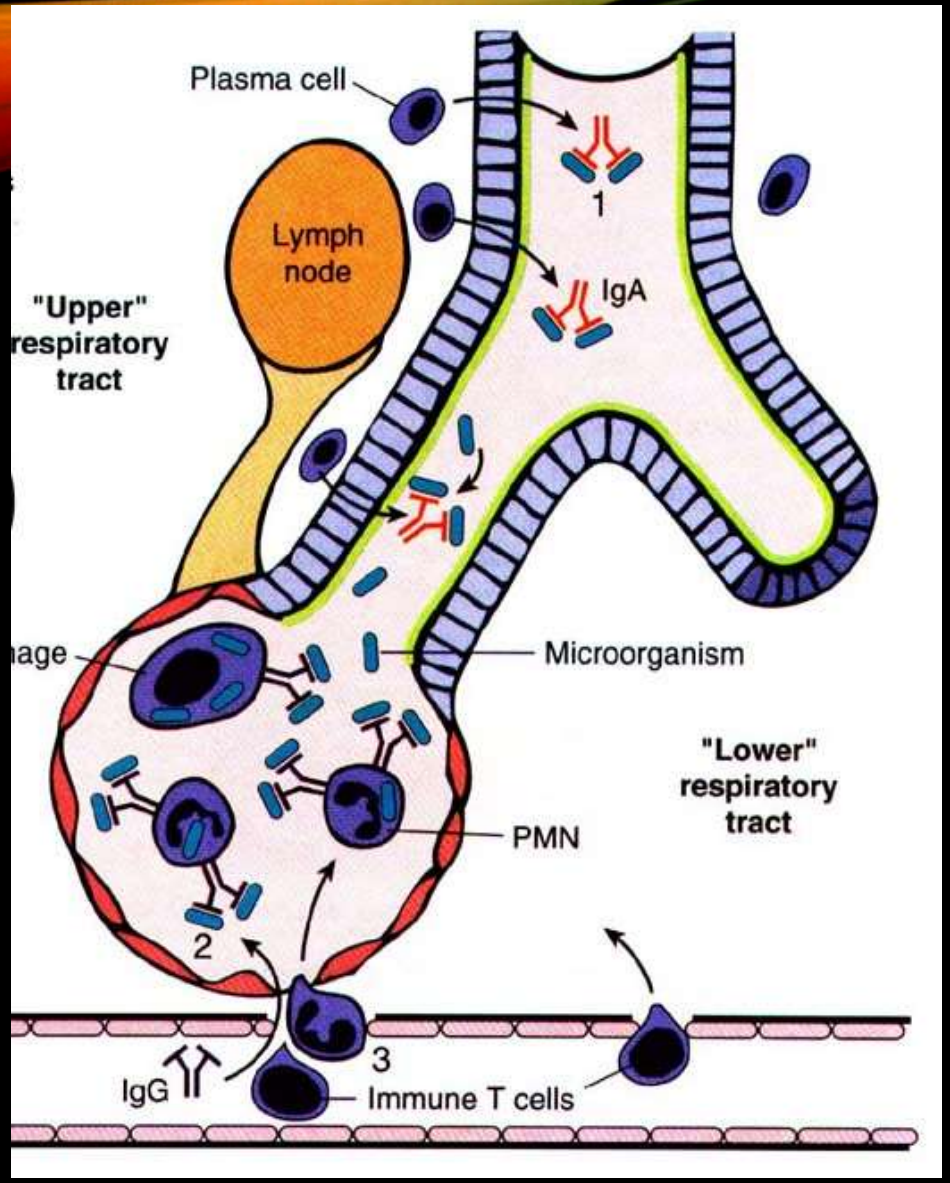
- Bronkitis akut
- Pneumonia mikoplasma / viral
- Pneumonia bakterial
  - morfologi: pneumonia lobaris & bronkopneumonia
  - etiologik: stafilokok, gram negatif (Klebsiella pneumoniae, Hemophilus influenzae, Pseudomonas aeruginosa, gram negatif enterik)
- Pneumonia mikotik
- Pneumonia kimiawi
- Abses paru

SPESIFIK: Tbc paru



PARU NON-IMUN

1. Perangkap mukus → elevator mukosilier (bronkioli →)
2. Fagositosis & pembunuhan oleh makrofag alveolar → mukosilier
3. Fagositosis & pembunuhan oleh netrofil (sistem komplemen)
4. Komplemen serum → opsonisasi → fagositosis
5. Mikroorganisme → inisiasi respon imun



PARU IMUN

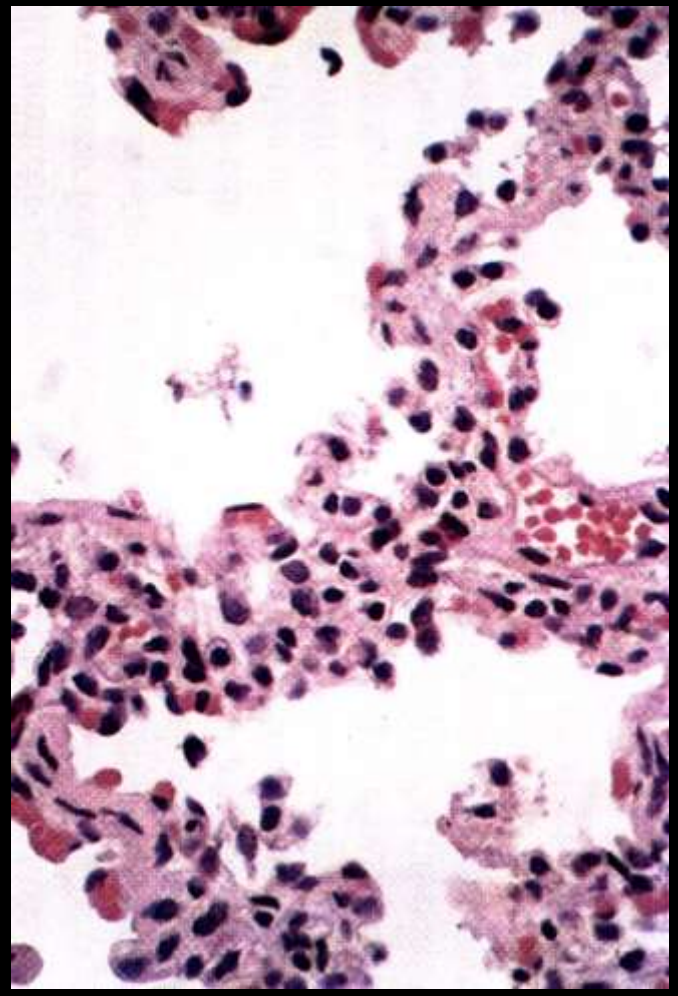
1. Sekresi IgA mencegah melekatnya mikro-organisme ke epitel (bronkioli ke atas)
2. Distal bronkioli: IgM & IgG (antibodi) → humoral-mediated imunity
3. Akumulasi sel T → cell-mediated immunity

V. RADANG

A. Bronkitis akut

- sebagai lanjutan dari infeksi saluran napas atas
- gas iritan: asap, amonia, sulfur dioksida, gas panas, dll.

V. RADANG



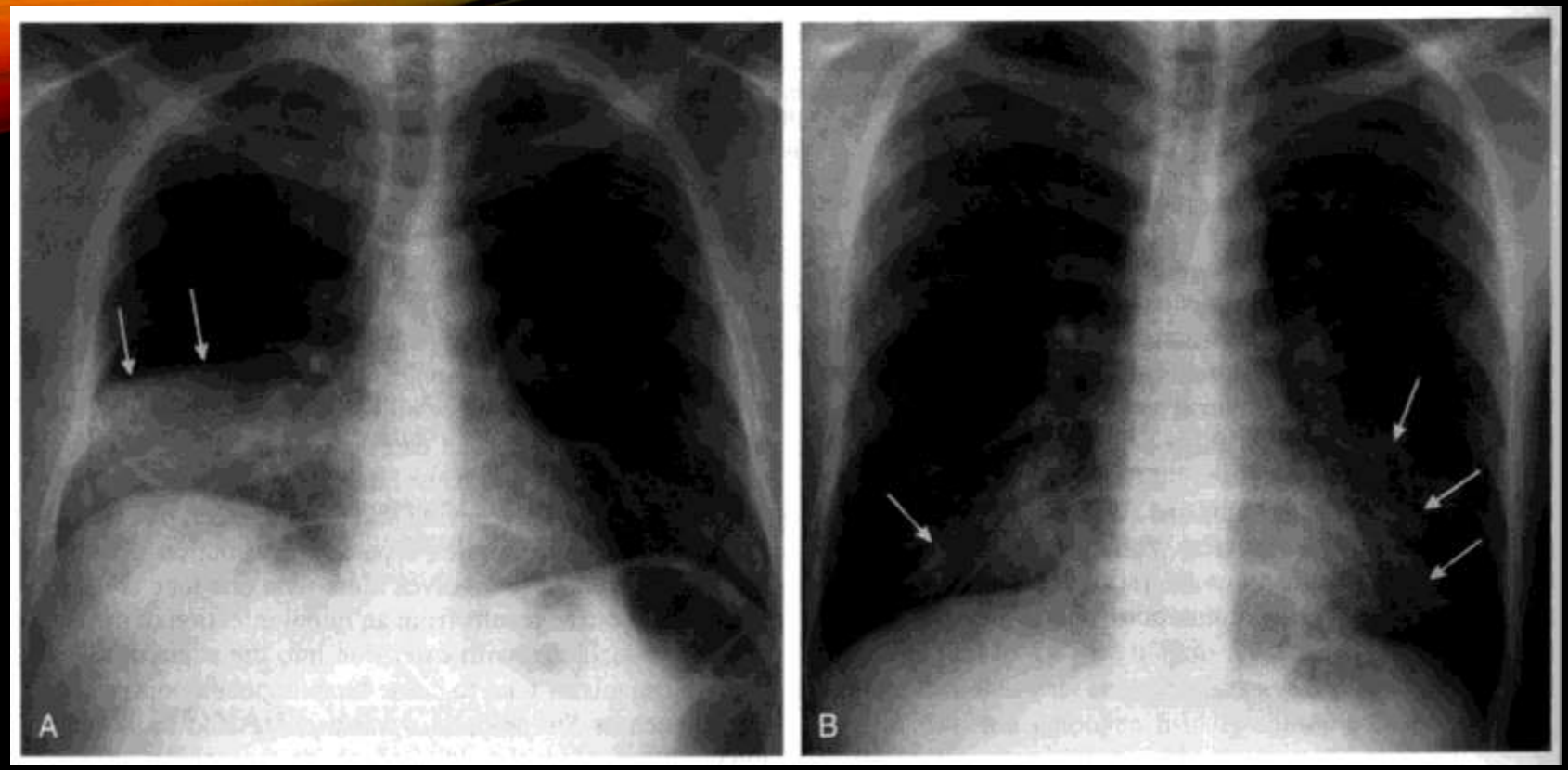
B. Pneumonia Viral / Mikoplasma

-Mycoplasma pneumoniae, dan virus

- Lesi peribronkiolar dan interstisial
- Edema dinding alveoli
- Sebukan mononuklear

-Biasanya tidak ada eksudat dalam rongga alveoli

PNEUMONIA



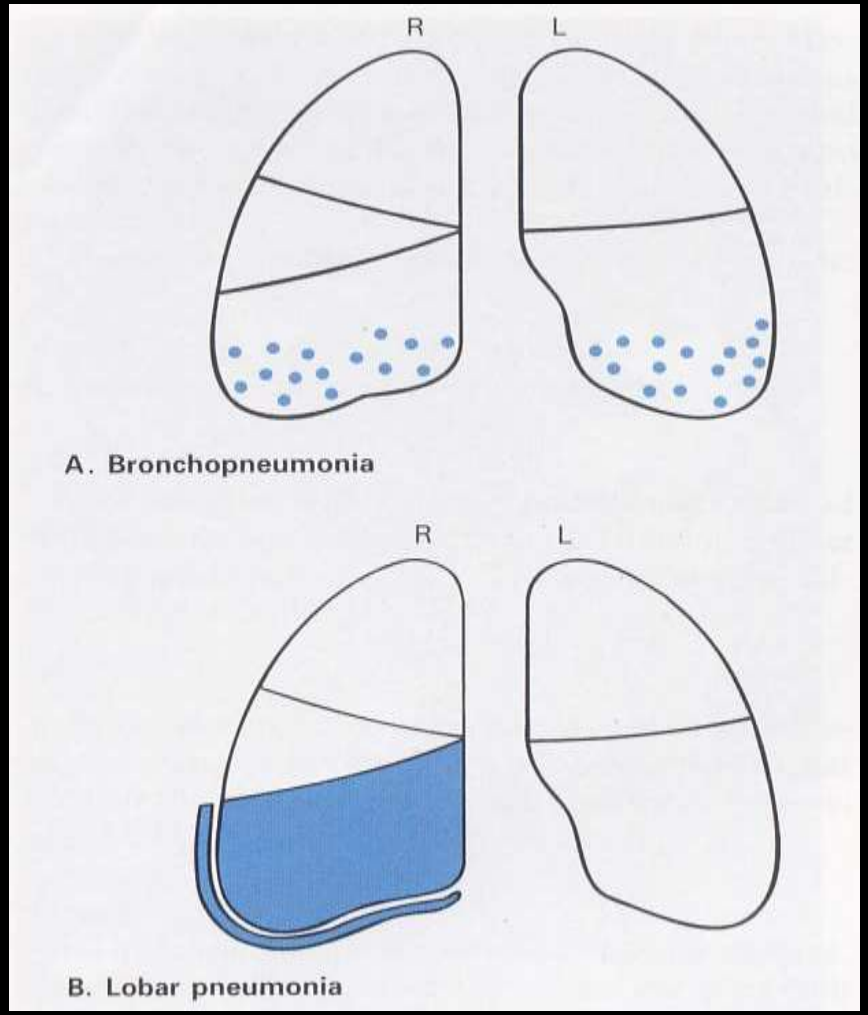
Pneumonia lobaris

- Radang parenkim paru yang melibatkan seluruh lobus atau lebih
- Distribusi lobar menunjukkan virulensi organisme dan / atau rendahnya pertahanan tubuh

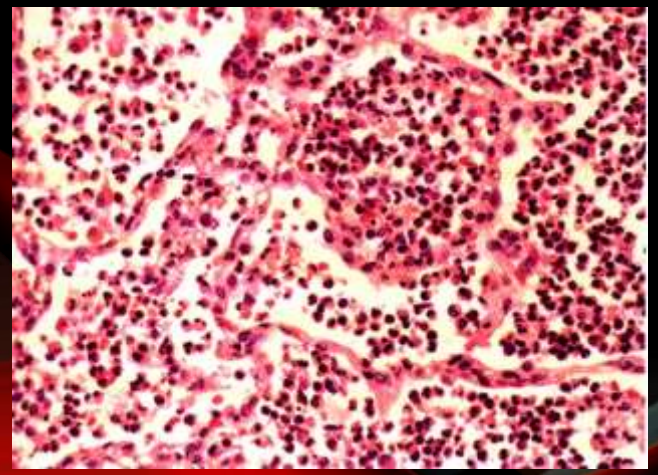
Bronkopneumonia

- Radang paru kurang ekstensif, lebih destruktif daripada pneumonia lobaris
- Konsolidasi bentuk bercak di seluruh lobus terutama lobus inf.
- Trakeobronkial → bronki/oli

PNEUMONIA



PNEUMONIA LOBARIS



Stadium

1. Kongesti

- proliferasi bakteri cepat → respon radang stadium awal (hiperemia & eksudasi ke rongga alveoli)

2. Hepatisasi merah

- ekstravasasi eritrosit & netrofil, fibrin → konsistensi dan warna mirip hati
- pelebaran vaskular nyata → merah

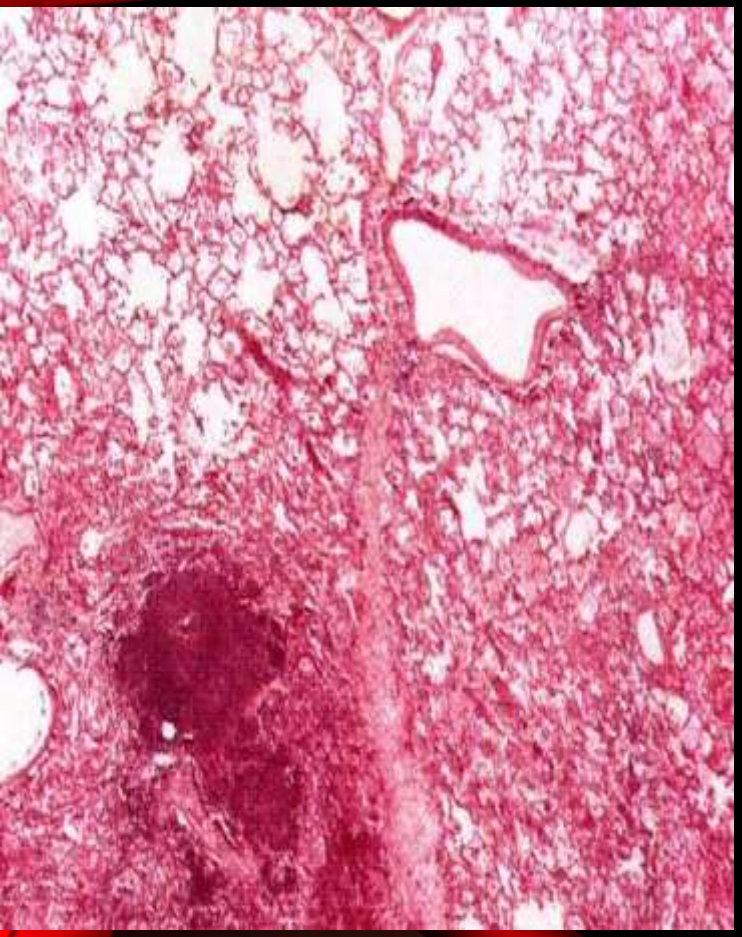
3. Hepatisasi kelabu

- Disintegrasi eritrosit dan netrofil, akumulasi fibrin melanjut → parenkim padat dan abu-abu
- vasa mengecil kembali

4. Resolusi

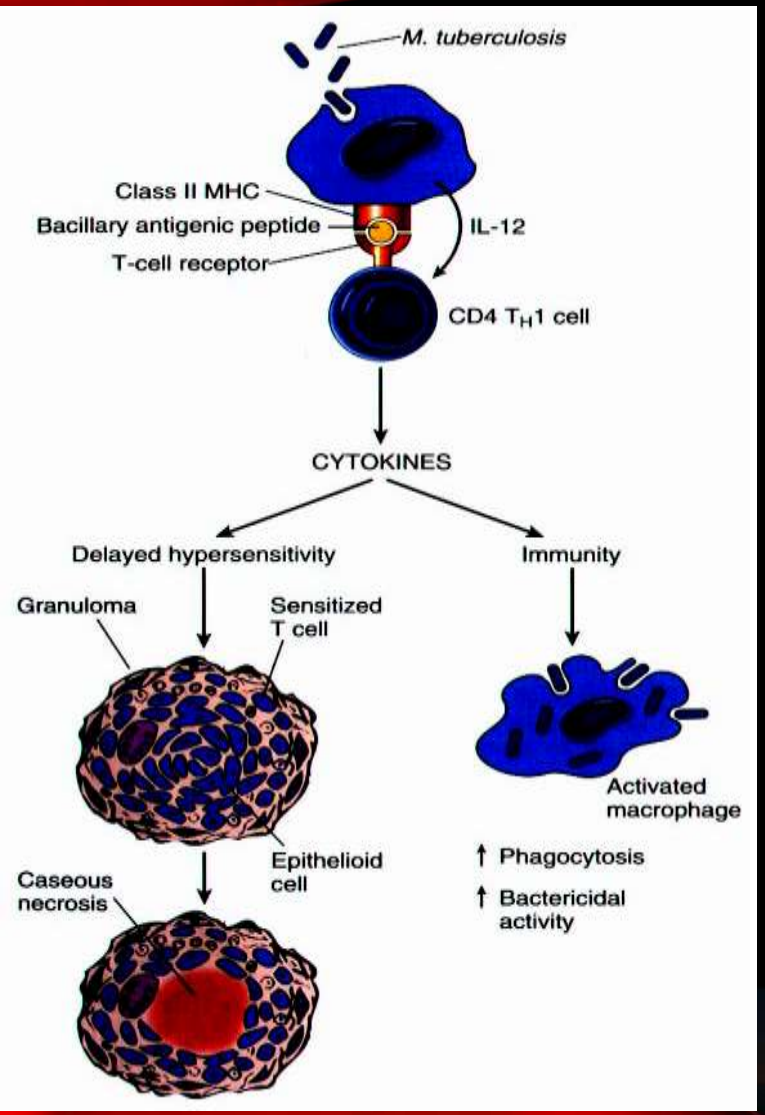
- semua debris dan isi alveoli didigesti → dibuang

BRONKOPNEUMONIA



- Radang paru sebagai lanjutan dari trakeobronkial → bronki / bronkioli,
- atau karena sistemik: malnutrisi, alkoholisme, gagal jantung kongestif dengan edema paru
- radang terpusat di jalan napas → meluas ke parenkim sekitarnya → merusak jaringan, mikroabses → jaringan parut

TUBERKULOSIS PARU V.

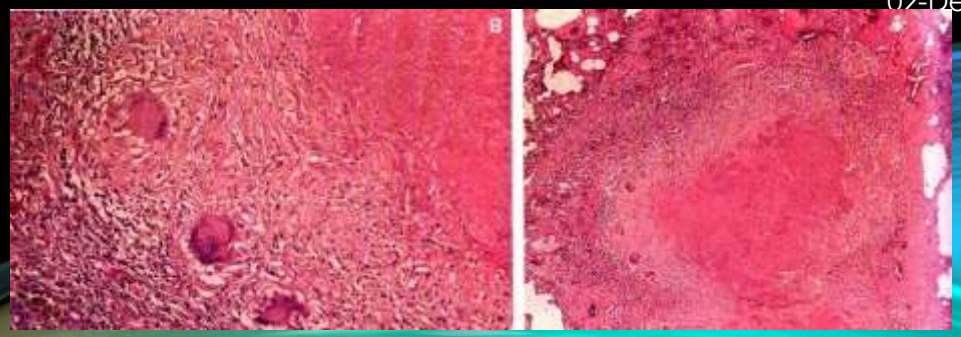


Etiologi: (terutama)

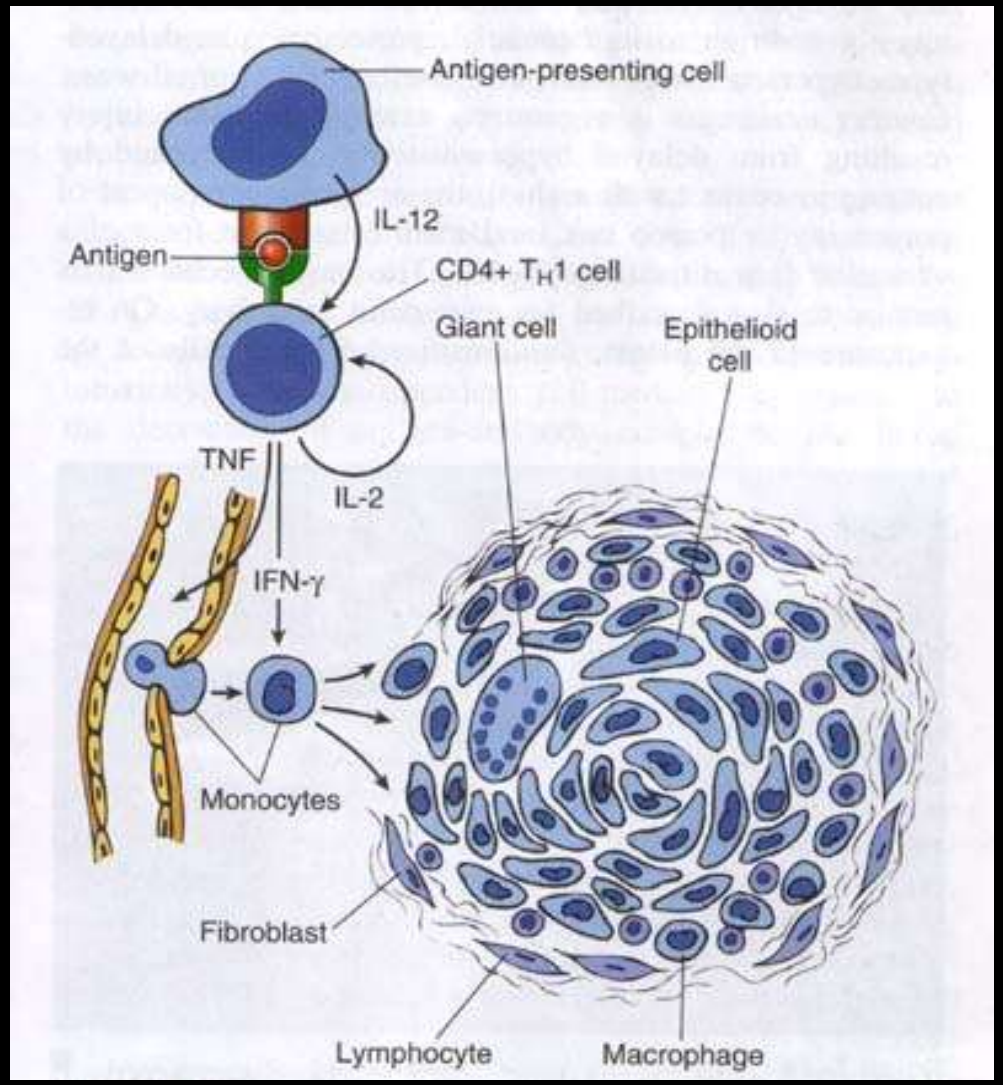
Mycobacterium tb. Hominis

Patogenesis:

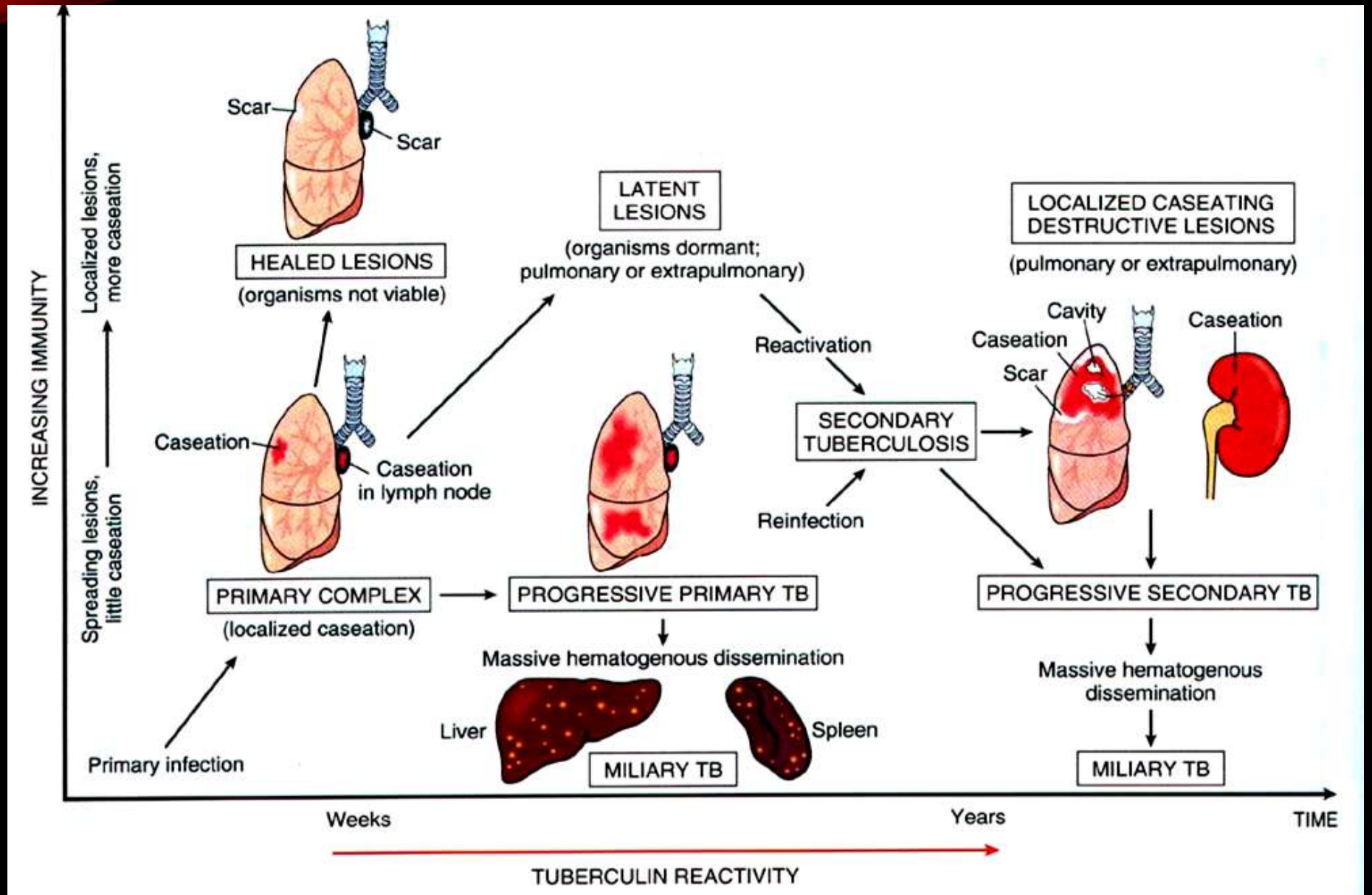
Sekarang dipercaya karena proses: hipersensitivitas tipe IV



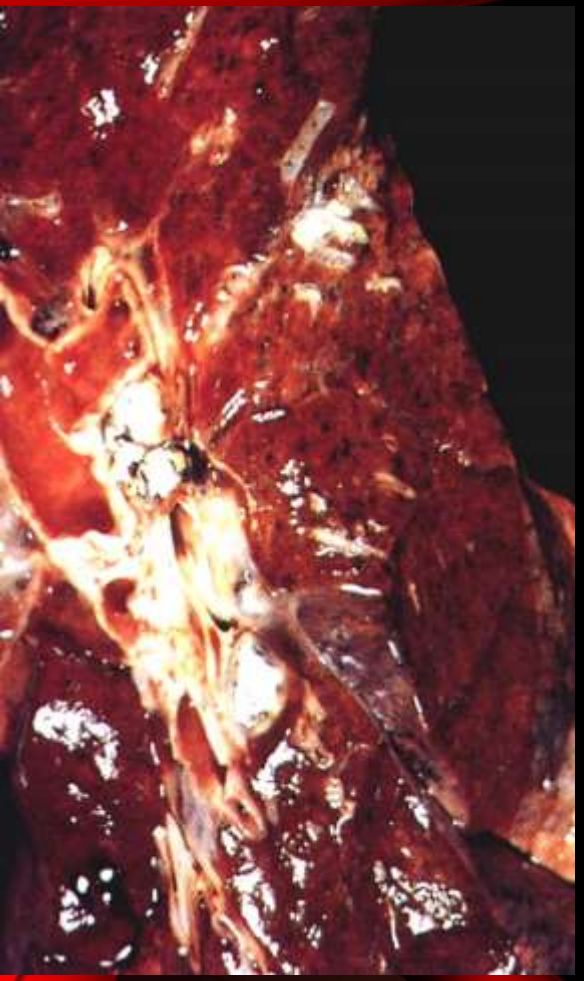
PATHOGENESIS



V. Perjalanan penyakit TUBERKULOSIS



TBC PRIMER



Bentuk Tbc pada individu yang belum tersensitisasi (belum pernah kontak)

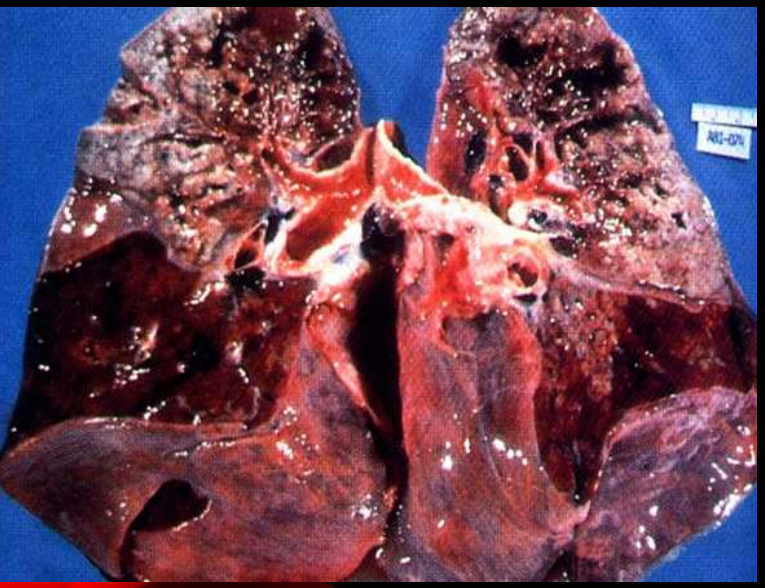
Ada 2 bentuk:

1. Afek primer → fokus Gohn (lesi sub-pleural,1-1,5 cm, tuberkel epiteloid, sel raksasa Langhans, dan nekrosis kaseosa), di bagian bawah lobus superior.

2. Komplek primer → fokus Gohn plus penyebaran di hilus → menyebar: pneumonia tbc, atau disseminasi bronkogenik, limfogen, hematogen →

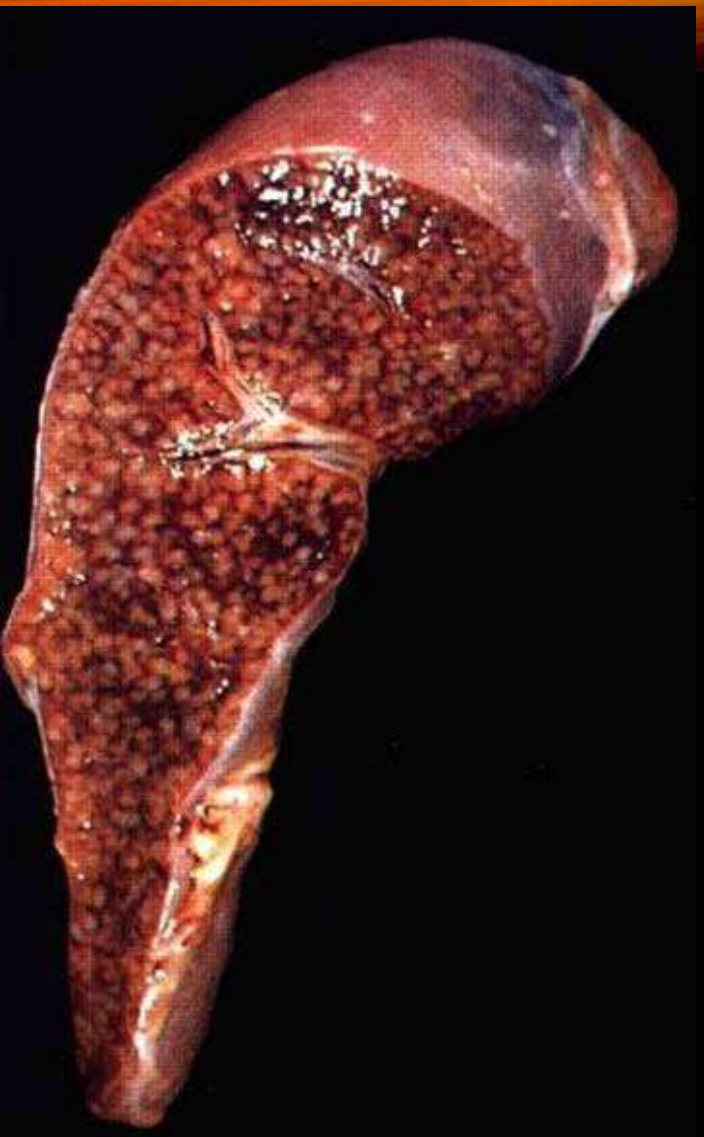
   tbc miliaris → mengitis tbc

TBC SEKUNDER



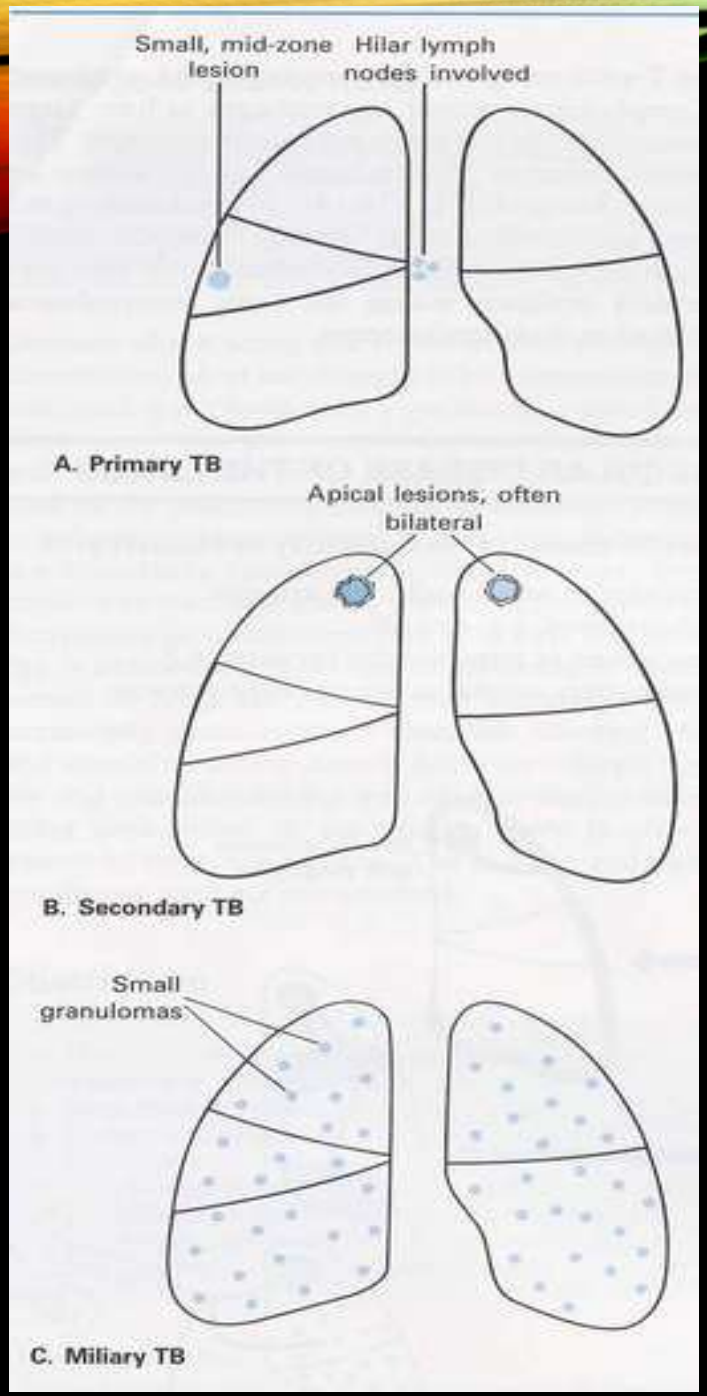
- Pada orang dewasa (reaktivasi, reinfeksi)
- Nama lain: Tbc postprimer
- Terutama di apex paru (daerah kaya oksgen)
- Tuberkel epiteloid dengan perkejuan → konglomerasi → kaverne → hemoptisis
- Kaverne dianggap sebagai tanda utama tbc sekunder
- Kaverne → dapat sembuh dengan fibrosis → diseminasi melalui percabangan trakeobronkial saluran limfe, atau saluran darah → milier

TBC MILIER

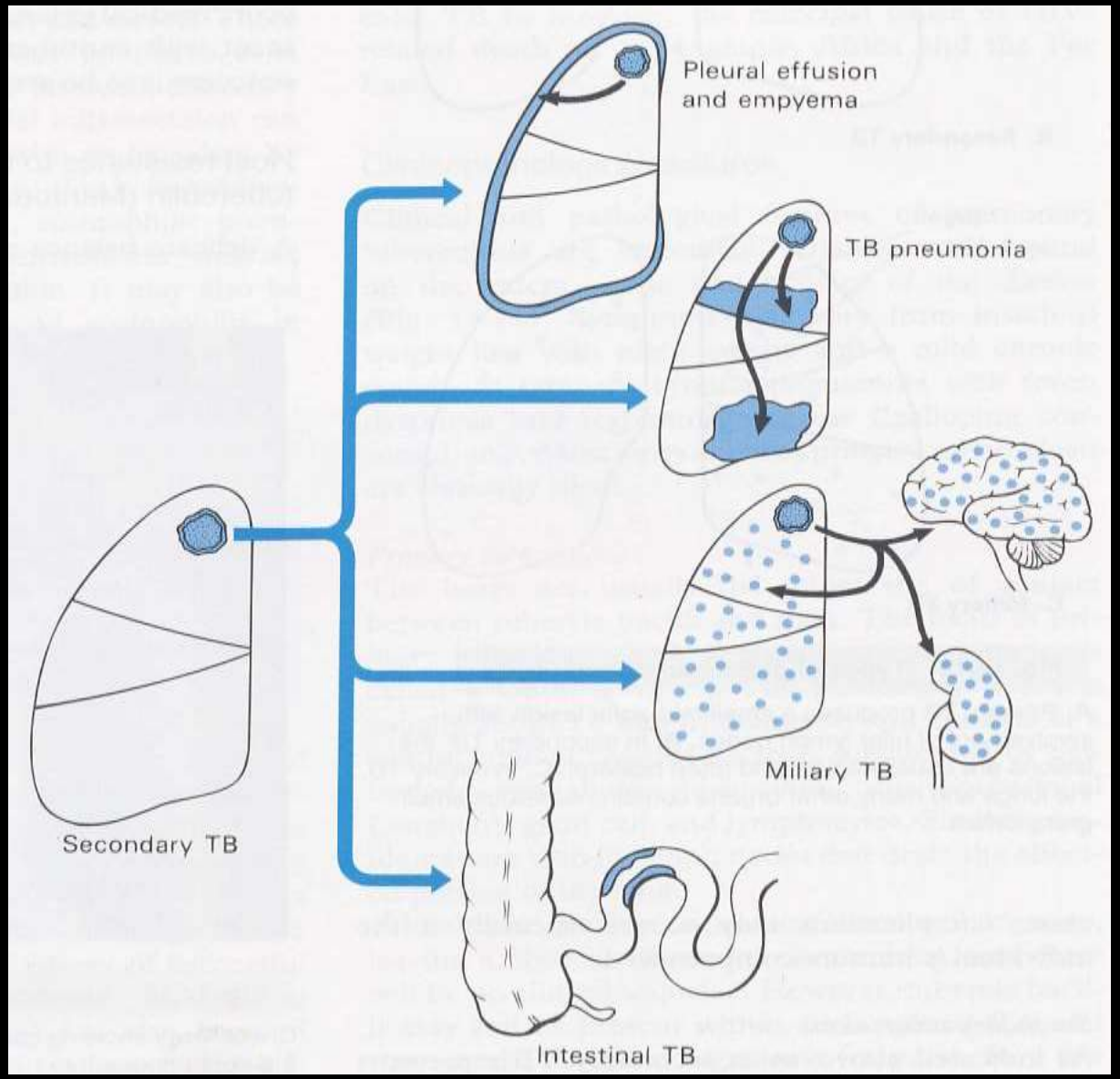


- Penyebaran dari tbc paru, baik limfogen maupun hematogen
- Menyebar ke organ dan jaringan: hati dan limpa, tuba Falopii (infertil sekunder, otak, ginjal, dll)

JENIS TUBERKULOSIS



PENYEBARAN TBC



KLINIS

- Maleise, anorexia, BB turun, demam ringan kumat-kumatan (biasanya sore hari → sembuh tanpa obat
- Hemoptisis: separoh kasus
- Kadang ada nyeri pleuritik

DIAGNOSIS

- Reaksi tuberkulin
- Identifikasi kuman
- Polymerase Chain Reaction (PCR) → DNA kuman tbc

V. PNEUMONIA KIMIAWI

Pneumonia aspirasi

- pada penderita yang tidak sadar dengan episoda batuk berulang, pada penekanan reflek batuk karena alkohol, gangguan fungsi CNS, intoksikasi obat akut

- aspirasi cairan lambung → reaksi radang → edema paru & kerusakan epitel luas dengan perdarahan & membran hialin ----→ parenkim paru rusak

- klinis 2-5 jam sesudah aspirasi:sianosis, dispneu, takipneu, takikardia → syok, sputum berdarah, kongesti pulmonum

Pneumonia lipid

- Endogen: komplikasi dari lesi obstruktif percabangan bronkial → mikroskopik timbunan makrofag berisi surfaktan dan lipid dari sel-sel degeneratif

- Eksogen: aspirasi obat tetes hidung dengan pelarut lemak, jarang memberikan gejala klinis: batuk produktif. X-ray: kadang tampak seperti masa Ca / granuloma

ABSES PARU

- Etiologi
  - aspirasi (mikroorganisme anerobik) dari rongga mulut
  - komplikasi dari pneumonia bakterial
  - obstruksi bronkial
  - emboli septik
  - luka tusuk
- Patologi
  - terjadi karena nekrosis lekuefaksi parenkim
  - bisa tunggal atau multipel, ukuran mm s/d 5-15 cm
  - nyeri dada disertai napas bau busuk, sering dengan demam
  - yang multipel mortalitasnya sampai 50%

V. INFEKSI LAIN-LAIN

- **Infeksi CMV**

  - Transmisi: transplasental, sekresi vagina (persalinan), saliva (pra-sekolah), dewasa: paling banyak seksual, sekresi respirasi, fekal-oral, iatrogenik

  - Cytoplasmic inclusion dalam parenkim paru

  - Owl'eye pada epitel traktus urinarius

- **Infeksi jamur:**

  - Histoplasmosis, Coccidiomycosis, Candidiasis, Blastomycosis, Cryptococcosis, Mucormycosis

- **Infeksi oportunistik**

  - infeksi oleh Pneumocystis carinii → Pneumonia pneumocystis, pada penderita AIDS

VI. PENY. PARU OBSTRUKTIF KRONIS

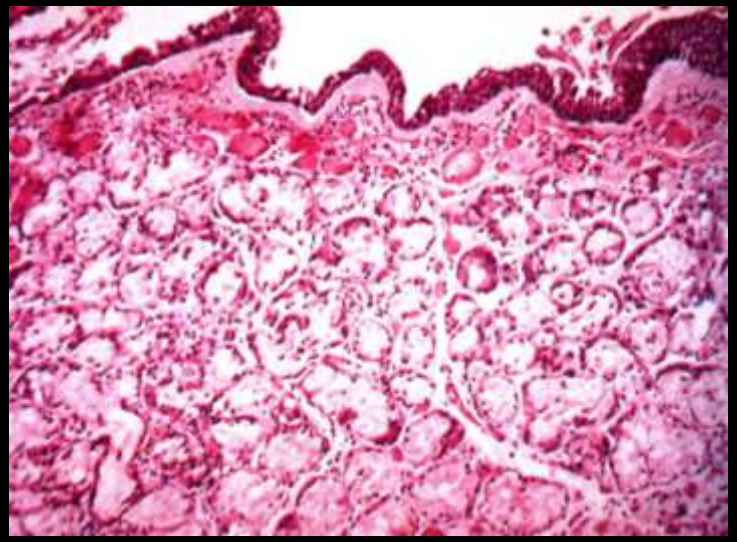
- BRONKITIS KRONIS
- EMFISEMA

  - Sentrilobular, Panasinar, Paraseptal, iregular
- ASMA BRONKIALE

  - Ekstrinsik (atopik → hipersensitivitas tipe I)
  - Intrinsik (non-atopik)
- BRONKIEKTASIS

  - silindrikal, sakular

BRONKITIS KRONIS
(UMUR 40 – 65 TH)



- ***Radang bronkus*** *dengan batuk kronis dan produksi sputum, selama paling tidak 3 bulan dalam setahun, dalam 2 tahun berturut-turut*
- **Patogenesis:**

  - sebagai mekaniseme pertahanan terhadap iritasi pada mukosa trakeobronkial oleh asap rokok atau polusi yang lain
- Polusi/rokok → iritasi kronis → hipertrofi dan hiperplasi kelenjar (sel goblet)→ hipersekresi mukus → fokus infeksi → iritasi kronis → infeksi berulang
- **Bentuk:**

  - bronkitis kronis biasa: jalan napas belum tertutup
  - bronkitis mukopurulen kronis
  - bronkitis asmatis kronis
  - bronkitis obstruktif kronis

ASMA BRONKIALE

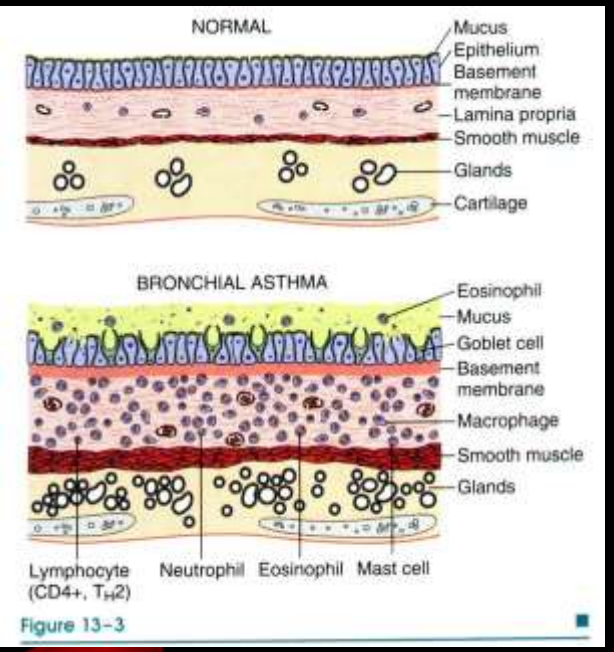


Figure 13–3

Bronkospasme berkala akibat respon bronko-

Konstriktor berlebihan terhadap berbagai Stimuli.

Mikros:

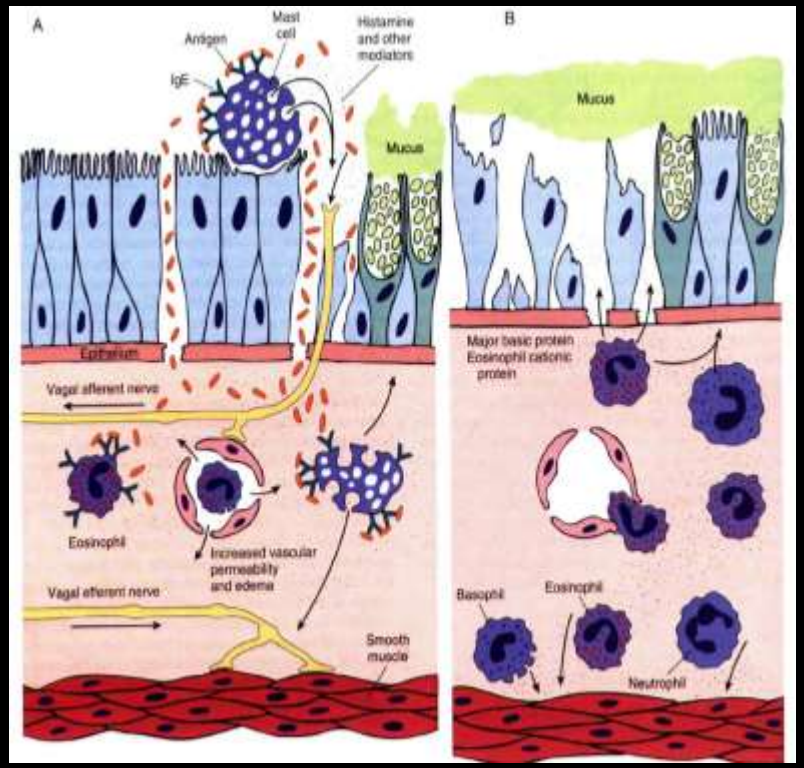
- lumen bronkus berisi mukus pekat dengan lepas dan rusak, eosinofil
- submukosa edema & kongestif
- membrana basalis menebal & hialinisasi
- hipertrofi otot polos
- hiperplasi & hipersekresi kelenjar
- → akibat: lumen obstruksi

Dalam sputum ditemukan:

1. Spiral Curschmann
2. Kristal Charcot-Leyden, dikelilingi sel-sel eosinofil

PATOGENESIS

ASMA BRONKIALE



Fasa awal **Fasa akhir**

Bronkospasme berkala akibat respon bronkokonstriktor berlebihan terhadap berbagai stimuli.

Patogenesis

1. Ektrinsik

- reaksi hipersensitif tipe I terhadap antigen ekstrinsik
- IgE meningkat, eosinofil bertambah
- ada riwayat keluarga
- onset pada dekade 1 – 2

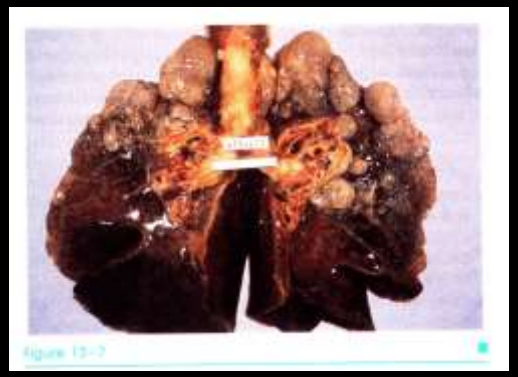
2. Intrinsik

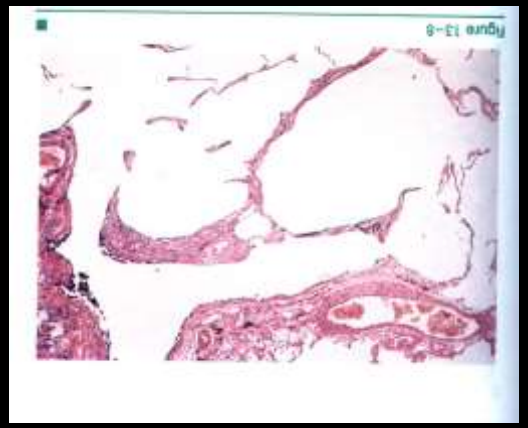
- mekanisme pemicu non-imun: aspirin, infeksi paru (virus), suhu dingin, psikologik, gas tertentu: sulfur oksida
- hipersensitivitas trakeobronkial

MEDIATOR (DILEPASKAN OLEH MASTOSIT)

- Leukotriene C_4, D_4, dan E_4 :
  - bronkokonstriksi berkepanjangan
  - peningkatan permeabilitas vaskular
  - sekresi musin bertambah
- Prostaglandin D_2 (PGD_2) :
  - bronkokonstriks & vasodilatasi
- Eosinophilic & neutrophilic chemotactic factor, dan leukotriene B_4 :
  - mengaktivasi eosinofil dan netrofil
- PAF + IL_5 :
  - agregasi trombosit
  - lepasnya histamin dari granula mastosit
  - kemotaktik untuk eosinofil

EMFISEMA





Pelebaran permanen dari ruang udara di sebelah distal bronkiolus terminalis disertai dengan kerusakan dindingnya.

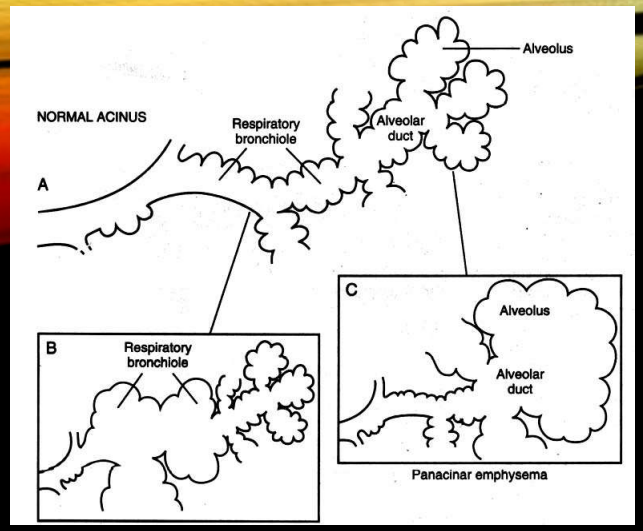
Ditemukan pada 50% kasus otopsi

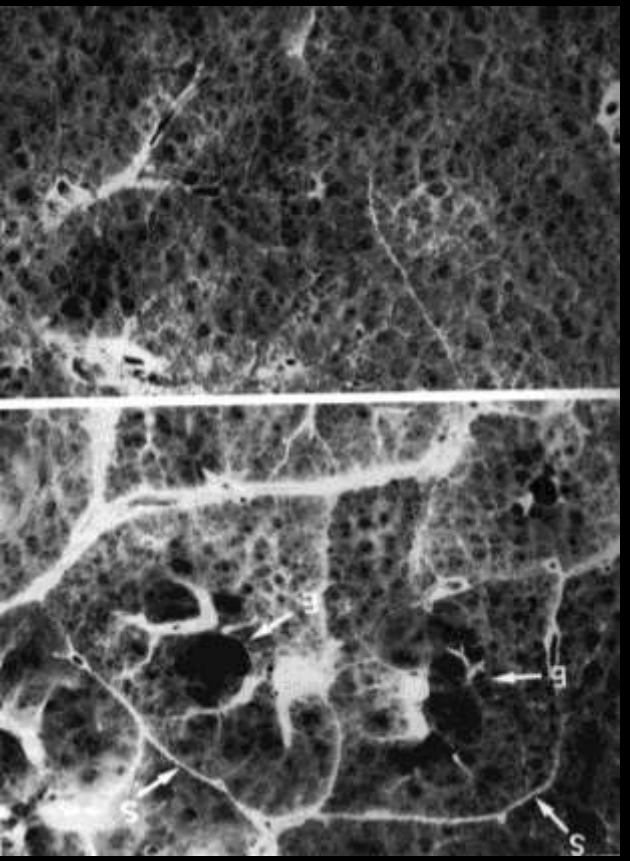
ANTIELASTASE (a_1-antitripsin) ↓ (a_1-antitripsin) menurun

Merokok → ELASTASE (dari netrofil)
- Makrofag
- PMN

ELASTASE → Kerusakan Serabut elastis → EMFISEMA

Emfisema VI.





- SENTRILOBULAR (sentriasinar)
  - pelebaran pada bronkiolus respiratorius
  - kebanyakan di lobus superior → apikal
- PAN-ASINAR (panlobular)
  - pelebaran pada duktus alveolaris dan alveoli
  - biasanya berhubungan dengan defisiensi antitripsin alfa-1

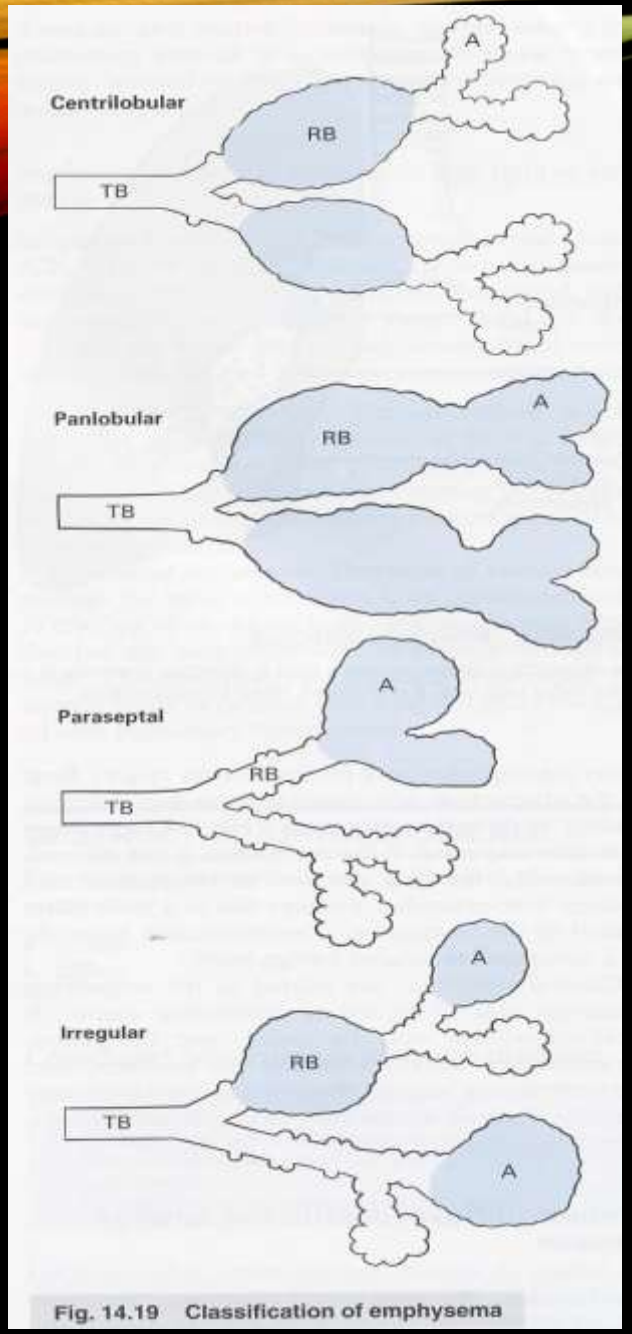
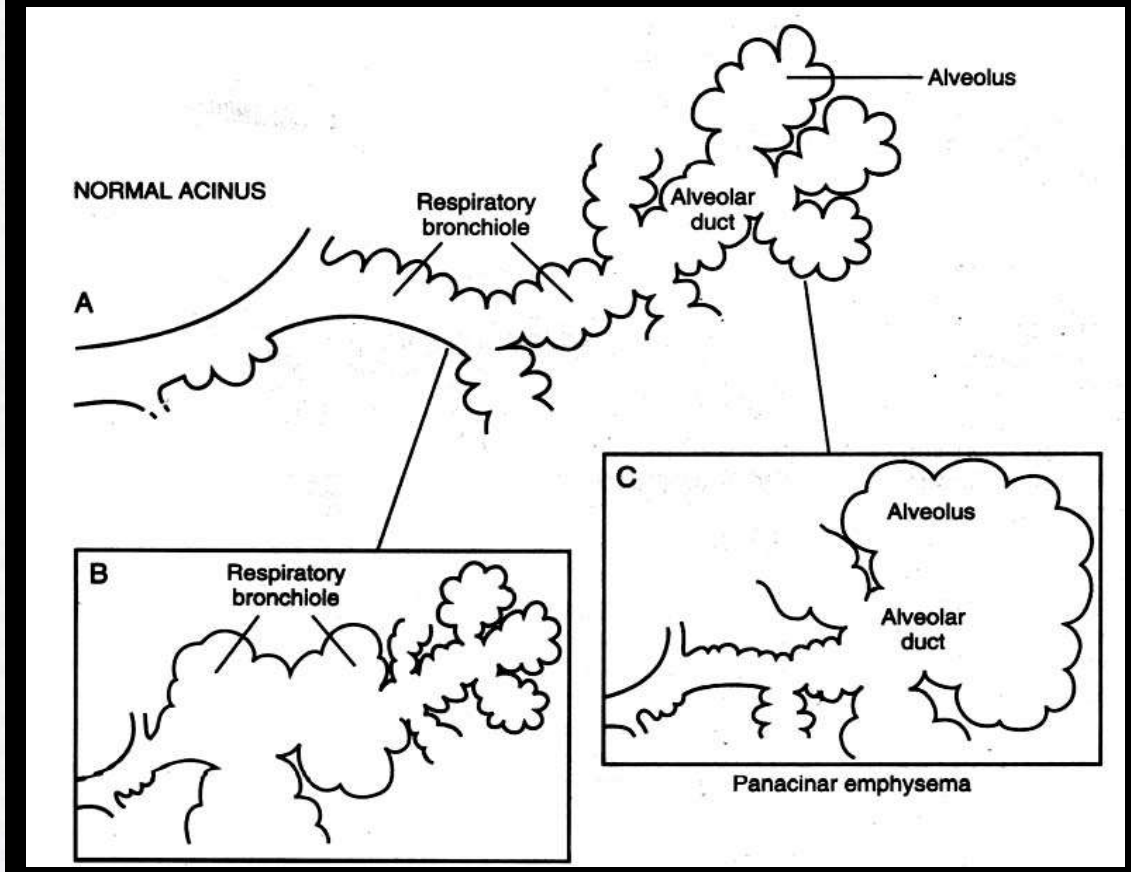
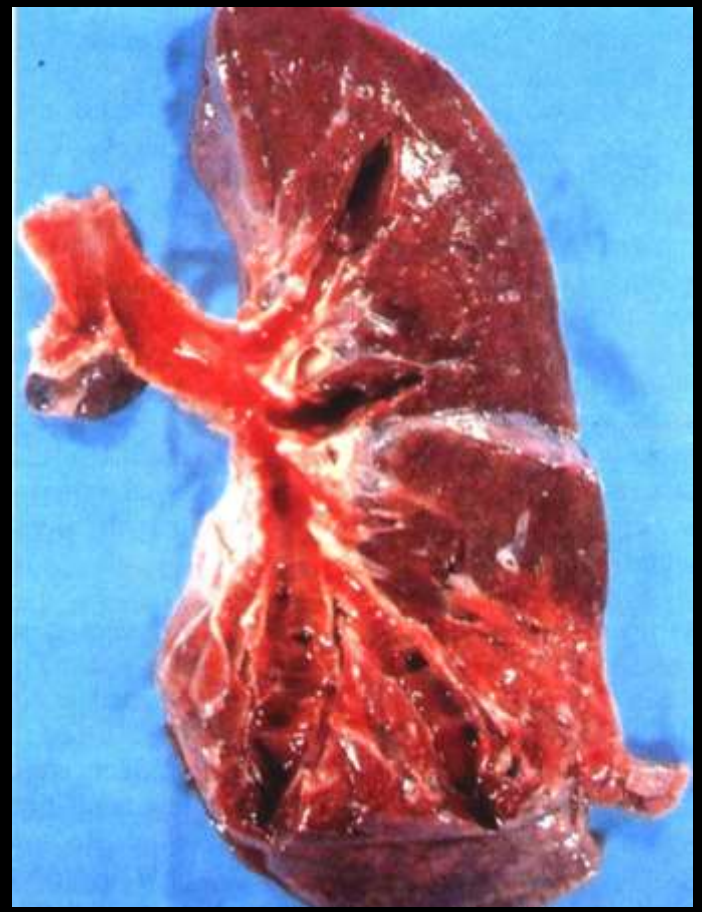


Fig. 14.19 Classification of emphysema



VI. BRONKIEKTASIS



- Dilatasi permanen satu bronkus atau lebih, disertai bau yang istimewa
- Bentuk anatomik:
  - Sakular
    - dilatasi seluruh panjang bronki
    - biasanya di lobus inferior
  - Silindrikal
    - dilatasi lokal (sakular)
- Predisposisi:
  - Obstruksi bronkial (tumor, benda asing, mukus → karena radang)
  - Kerusakan dinding bronki karena radang supuratif dan nekrotik
  - Kelainan bawaan

BRONKIEKTASIS

VII. PENYAKIT PARU RESTRIKTIF

Akibat berkurangnya kapasitas total paru, kapasitas difusi oksigen, dan elastisitas paru

PNEUMOKONIOSIS
- antrakosis, silikosis, asbestosis

PNEUMONIA INTERSTISIAL KRONIS (non-infeksius)
- Fibrosis paru idiopatik (sindroma Hamman-Rich)
- Pneumonitis interstisialis deskuamatif
- Pneumonia interstisialis limfoid
- Proteinosis alveolar paru
- Pneumonitis hipersensitif (alveolitis alergika ekstrinsik)
- Bronkiolitis obliterans

SARKOIDOSIS

PNEUMOKONIOSIS

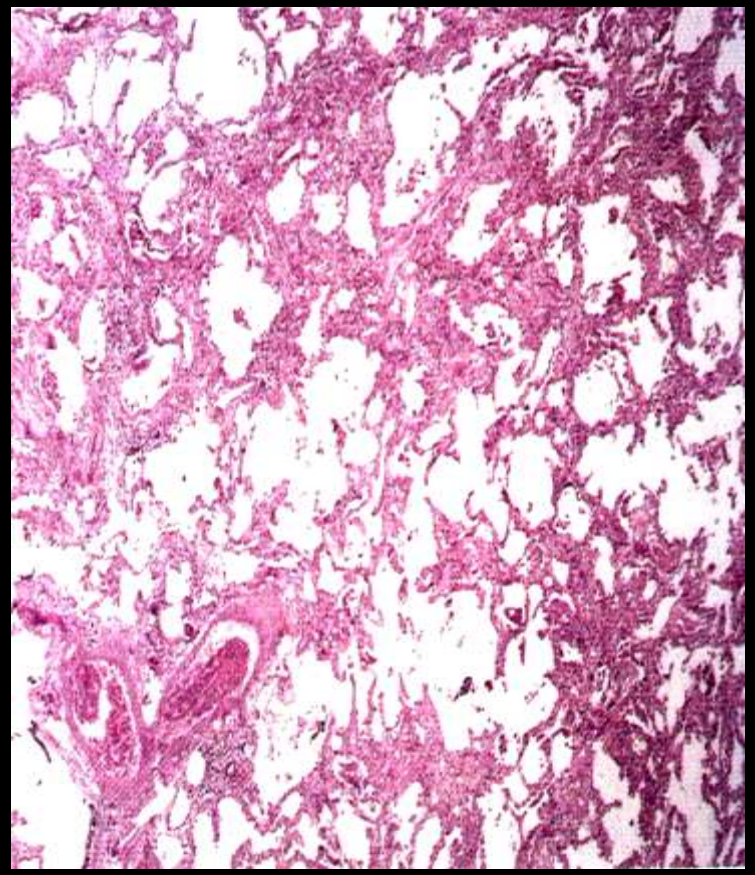
Anthracosis: karena debu karbon (tambang arang batu)

Silicosis: karena debu silika (tambang silika, pemecah batu, pekerja keramik, dll.) → silkosis akut & kronis

Asbestosis: tambang asbes → efusi pleura, fibrosis difus, mesotelioma, Ca (paru, laring, lambung, kolon)

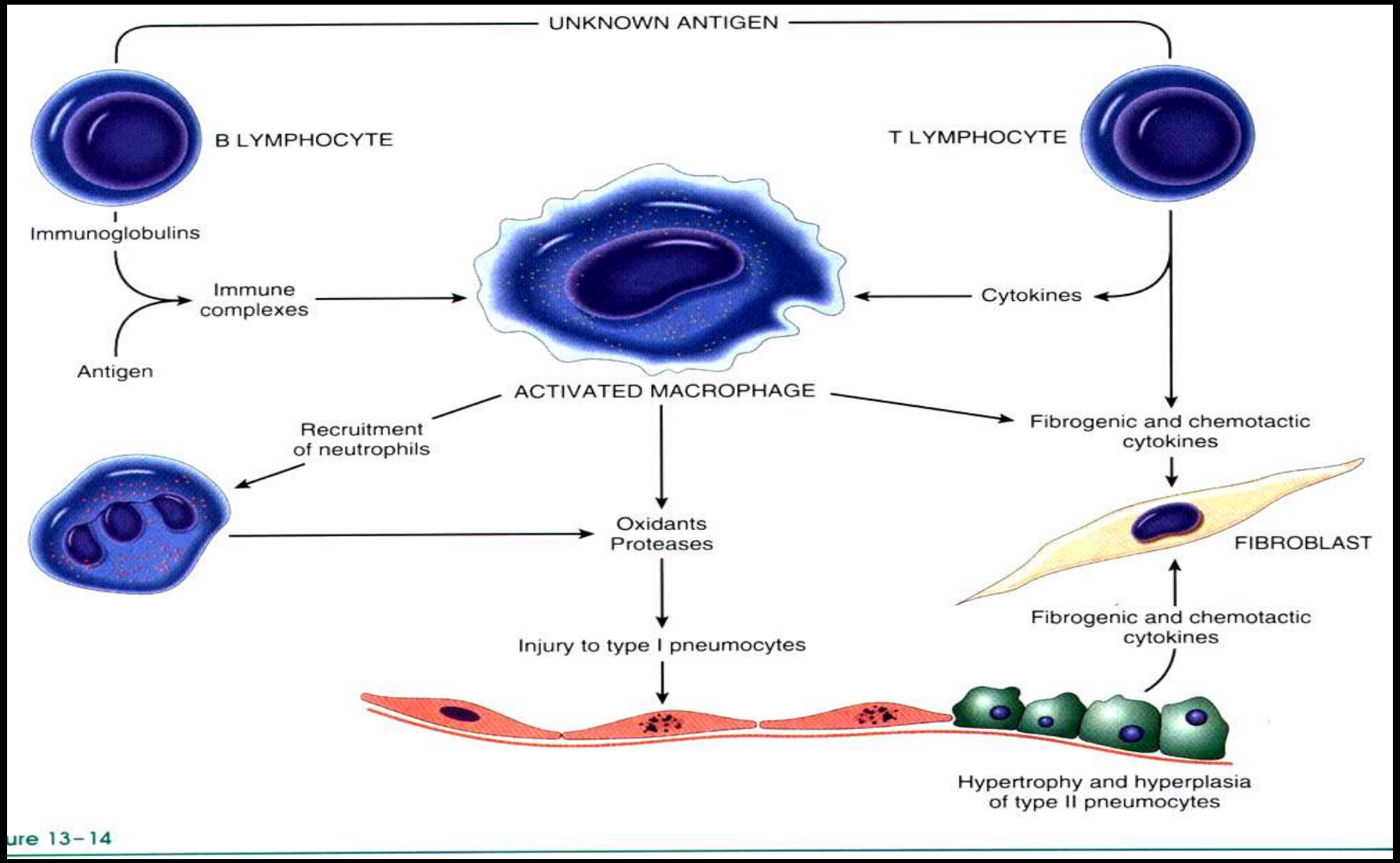
Berylliosis: energi nuklir, industri pesawat → beryllium granulomatosis

VI.3 FIBROSIS PULMONAR IDIOPATIK



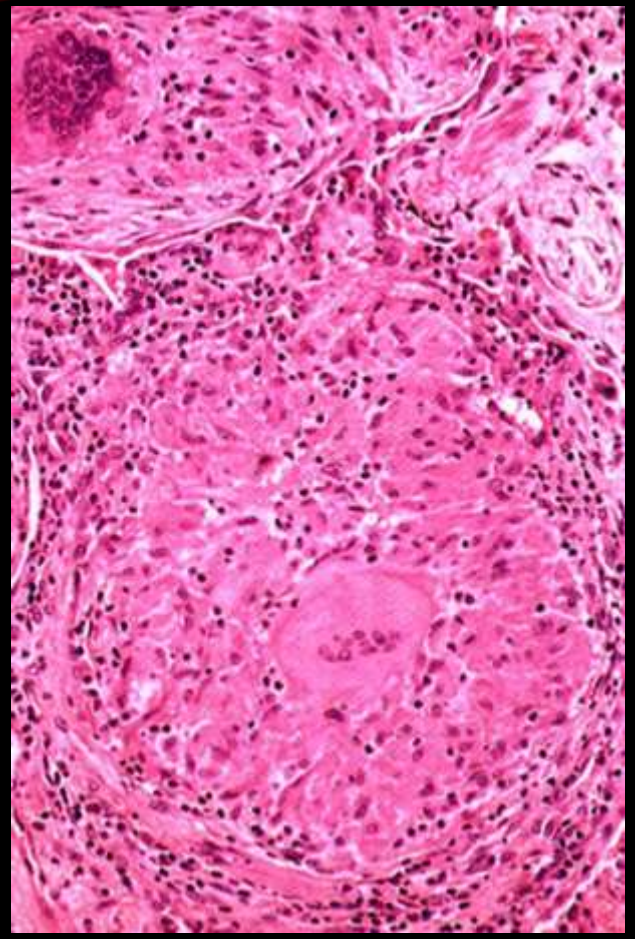
- Kausa tidak diketahui
- Mikroskopik:
  - fibrosis → penebalan dinding alveoli
  - hiperplasia pneumosit tipe II
- Makroskopik
  - Daerah fibrosis berselang
  -seling dengan daerah dilatasi → gambaran honey-comb
- Klinis dapat berakibat cor pulmonale → gagal jantung

FIBROSIS PULMONAR IDIOPATIK



ure 13–14

SARKOIDOSIS VII.



- Penyakit multisistem dengan penyebab yang tidak diketahui dan tanda khas adanya granuloma non-kaseasi pada berbagai jaringan dan organ
- Paru merupakan organ paling banyak terkena
- Organ lain: mata (kel.lakrimal), kel. Ludah
- Sindroma mikulicz → + parotis bilateral, sub maksilaris, sub-lingualis
- Limpa, hati

ARDS (RDS TIPE II): KERUSAKAN ALVEOLAR DIFUS

PATOGENESIS-ENDOTOKSINEMIA

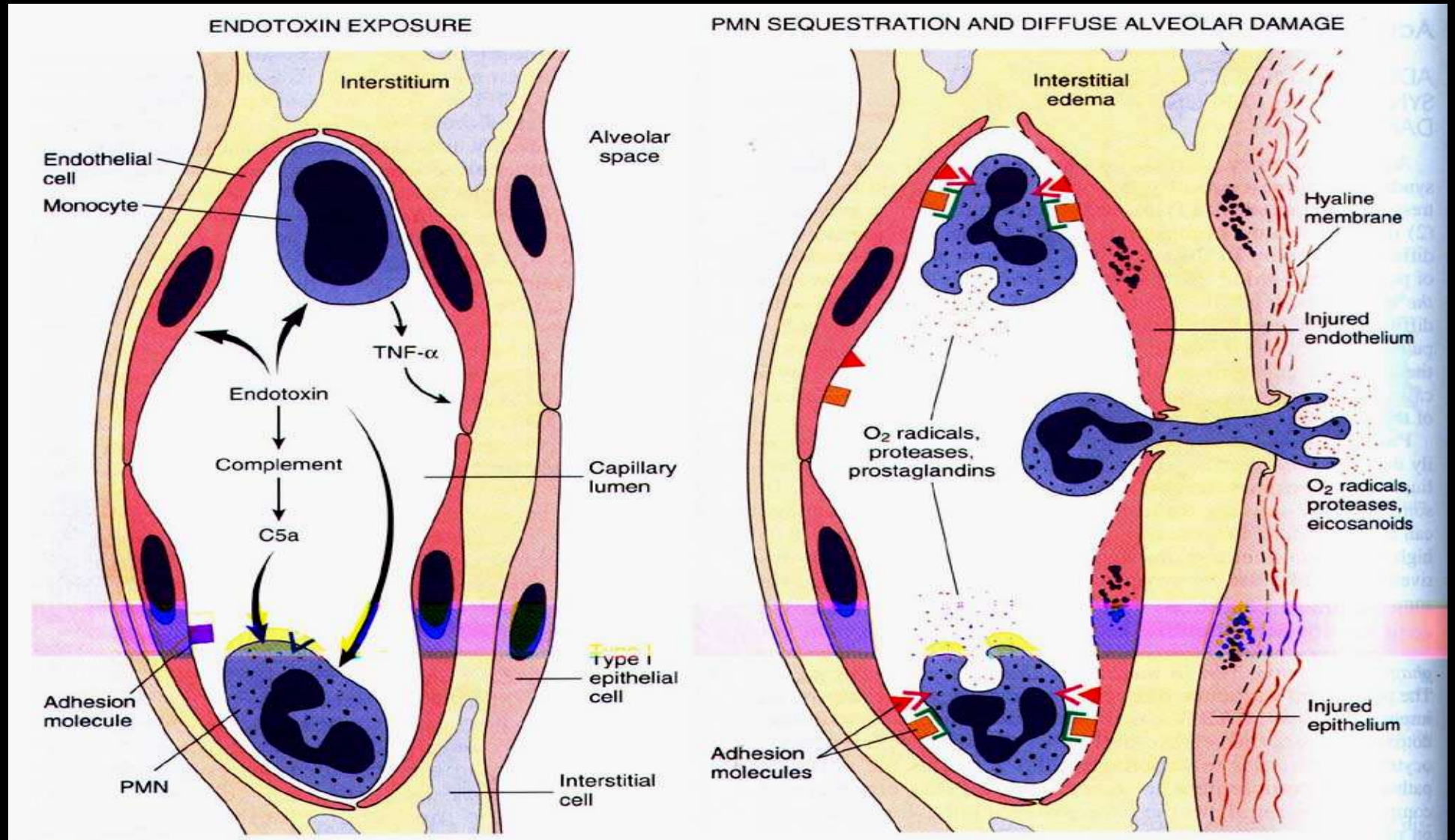
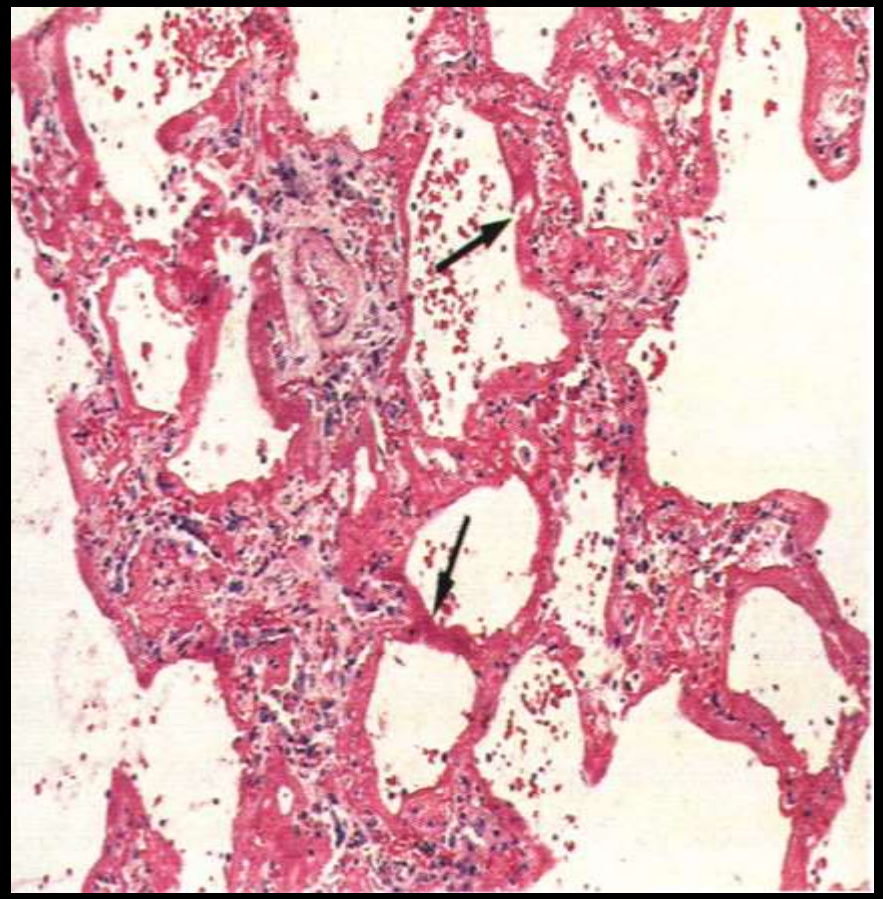


Figure 13–12

ARDS (RDS TIPE II)



- Beberapa alveoli kolaps
- Yang lain melebar
- Banyak yang dibatasi membran hialin merah terang

KATEGORI UTAMA PENYAKIT PARU RESTRIKTIF

Etiologi diketahui	Etiologi tak diketahui
A. Respon paru: alveolitis, radang interstisial, & fibrosis difus	
Lingkungan: asbes, asap, gas	Penyakit vaskular kolagen:
Radiasi ionisasi	skleroderma, artritis reumatika,
Lanjutan ARDS	SLE, dermatomiositis,
Obat: busulfan, bleomycin	Fibrosis pulmonar idiopatik
	Sindroma Goodpasture
	Hemosiderosis pulm. idiopatik
B. Respon paru: sama dengan A, tetapi dengan granuloma	
Beryllium	Sarcoidosis
Pneumonitis hipersensitif	Granuloma eosinofilik
	Granulomatosis Wegener

LUNG TUMOR

https://www.pathologyoutlines.com/lungtumor.html

https://www.pathologyoutlines.com/topic/lungtumorcarcinomageneral.html

TUMORS OF THE LUNG

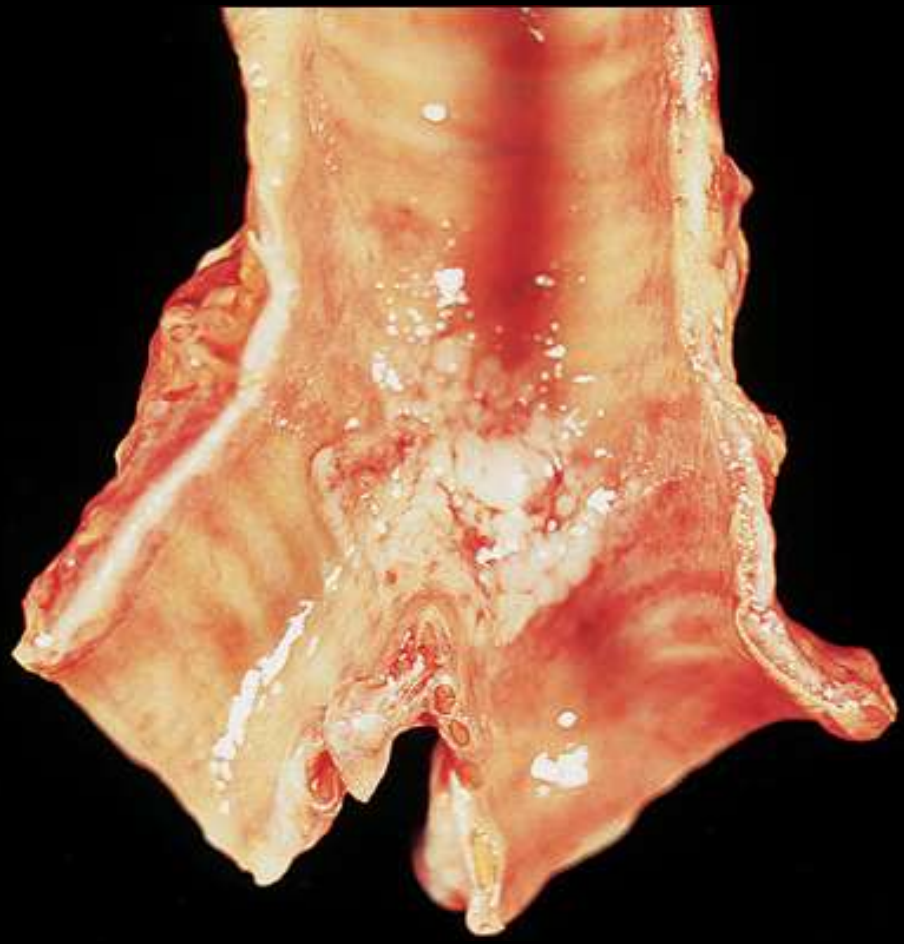
Histological classification

Primary tumors

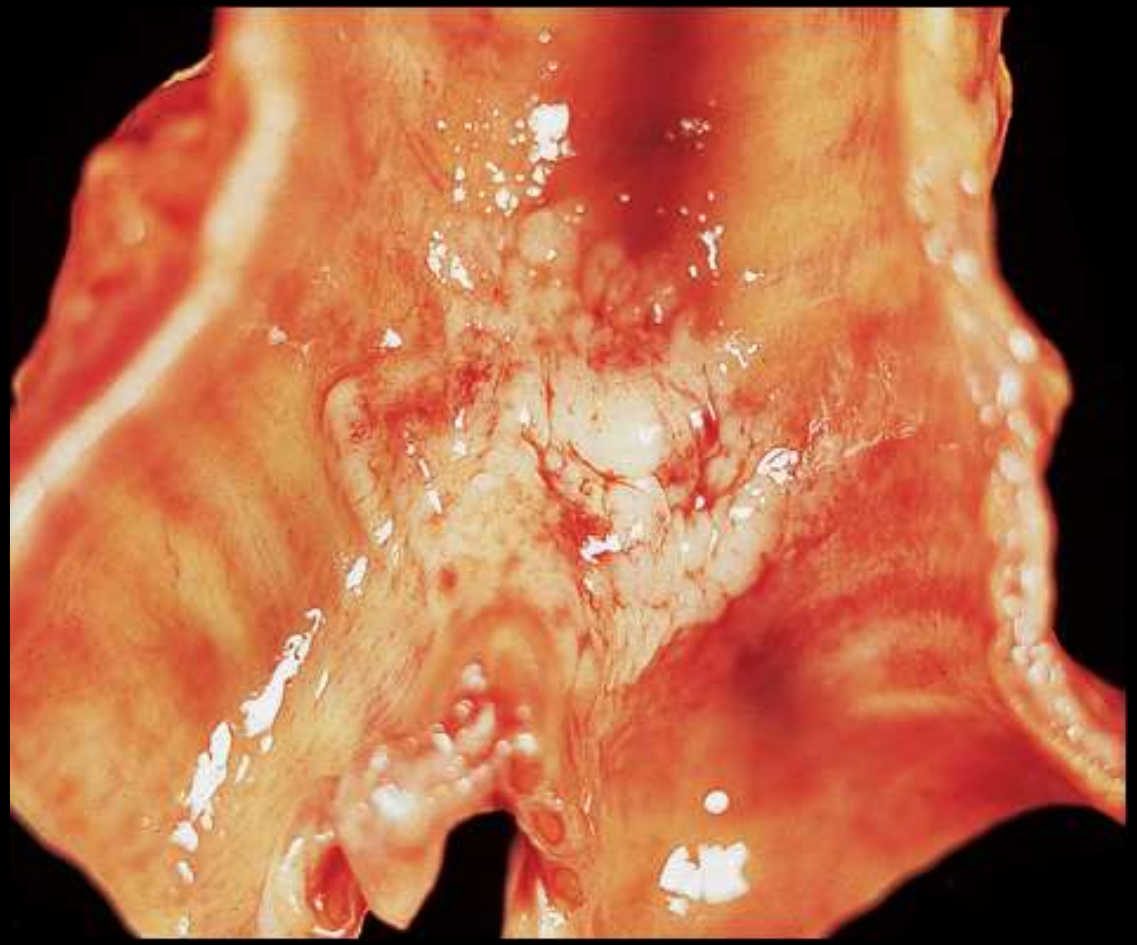
- Bronchogenic tumors
- Non-bronchogenic tumor

Secondary tumors (metastasis)

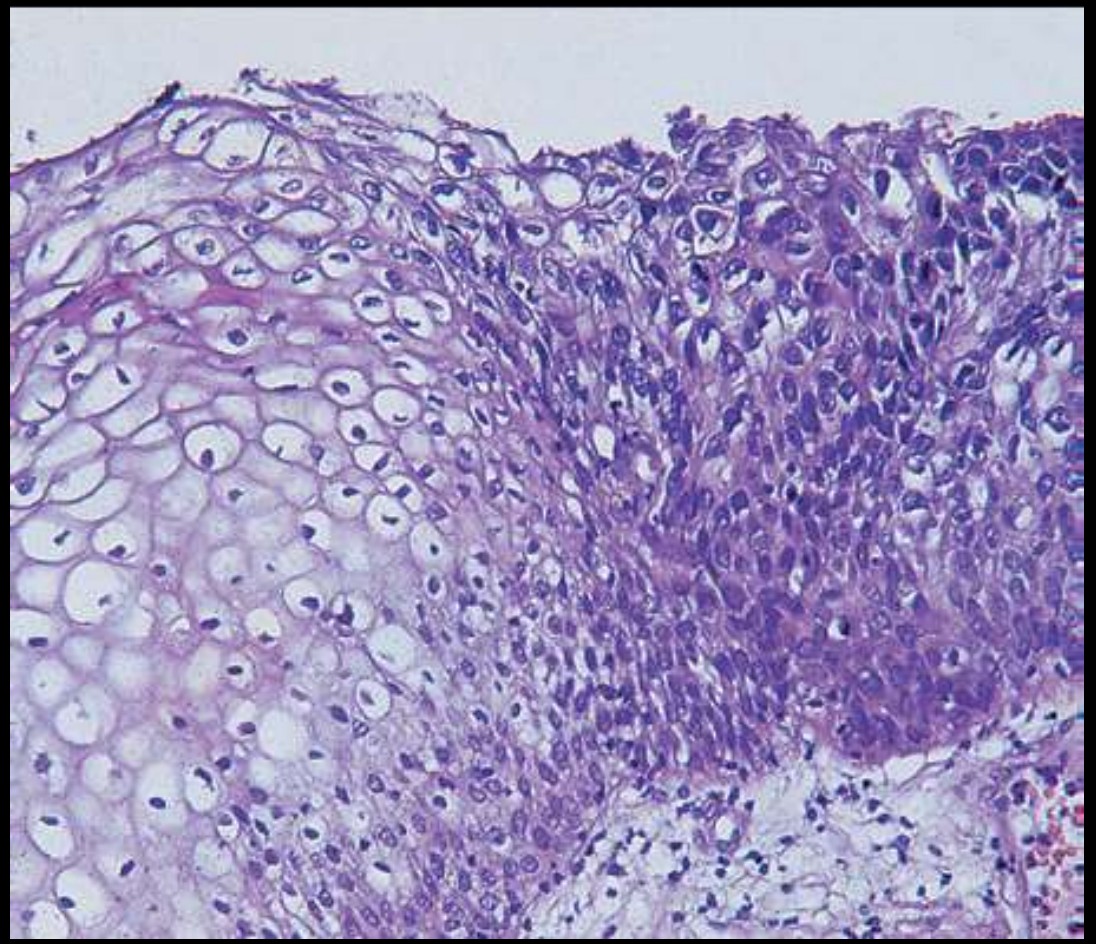
CARCINOMA IN SITU: BRONCHUS



CARCINOMA IN SITU: BRONCHUS



CARCINOMA IN SITU: BRONCHUS



THE INCIDENCE OF THE BRONCHOGENIC TUMORS

1. Non-small cell lung Ca (NSCLC): 70-75%
   a. SCC : 25 – 30 %
   b. AdenoCa,
      including bronchioloalveolar carcinoma
      : 30 – 35 %
   c. Large cell Ca : 10 – 15 %
2. Small Cell Lung Ca (SCLC) : 20 – 25 %
3. Combined : 5 – 10 %
   - SCC + adenoCa
   - SCC + SCLC

WHO CLASSIFICATION LUNG

https://www.pathologyoutlines.com/topic/lungtumorWHO.html

WHO (2015)

WHO classification of tumors of the lung (Travis: WHO Classification of Tumours of the Lung, Pleura, Thymus and H

Epithelial tumorsICD-O codes

- Adenocarcinoma8140/3
  - Lepidic adenocarcinoma8250/3
  - Acinar adenocarcinoma8551/3
  - Papillary adenocarcinoma8260/3
  - Micropapillary adenocarcinoma8265/3
  - Solid adenocarcinoma8230/3
  - Invasive mucinous adenocarcinoma8253/3
    - Mixed invasive mucinous and nonmucinous adenocarcinoma8254/3
  - Colloid adenocarcinoma8480/3
  - Fetal adenocarcinoma8333/3
  - Enteric adenocarcinoma8144/3
  - Minimally invasive adenocarcinoma
    - Nonmucinous8256/3
    - Mucinous8257/3
  - Preinvasive lesions
    - Atypical adenomatous hyperplasia8250/0
    - Adenocarcinoma in situ8140/2
      - Nonmucinous8250/2
      - Mucinous8253/2

SQUAMOUS CELL CARCINOMA 8070/3

- Keratinizing squamous cell carcinoma 8071/3
- Nonkeratinizing squamous cell carcinoma 8072/3

- Basaloid squamous cell carcinoma 8083/3
- Preinvasive lesion
  - Squamous cell carcinoma in situ 8070/2

- Neuroendocrine tumors
  - Small cell carcinoma 8041/3
    - Combined small cell carcinoma 8045/3
  - Large cell neuroendocrine carcinoma 8013/3
    - Combined large cell neuroendocrine carcinoma 8013/3
  - Carcinoid tumors
    - Typical carcinoid 8240/3
    - Atypical carcinoid 8249/3
  - Preinvasive lesion
    - Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia 8040/0

- Large cell carcinoma 8012/3
- Adenosquamous carcinoma 8560/3
- Pleomorphic carcinoma 8022/3
- Spindle cell carcinoma 8032/3
- Giant cell carcinoma 8031/3
- Carcinosarcoma 8980/3
- Pulmonary blastoma 8972/3
- Other and unclassified carcinomas
  - Lymphoepithelioma-like carcinoma 8082/3
  - NUT carcinoma 8023/3
- Salivary gland type tumors
  - Mucoepidermoid carcinoma 8430/3
  - Adenoid cystic carcinoma 8200/3
  - Epithelial myoepithelial carcinoma 8562/3
  - Pleomorphic adenoma

- PapillomasSquamous cell papilloma8052/0
  - Exophytic8052/0
  - Inverted8053/0
- Glandular papilloma8260/0
- Mixed squamous and glandular papilloma8560/0

ADENOMAS

- Sclerosing pneumocytoma8832/0
- Alveolar adenoma8251/0
- Papillary adenoma8260/0
- Mucinous cystadenoma8470/0
- Mucous gland adenoma8480/0

Mesenchymal tumors

- Pulmonary hamartoma 8992/0
- Chondroma 9220/0
- PEComatous tumors
  - Lymphangioleiomyomatosis 9174/1
  - PEComa, benign 8714/0
    - Clear cell tumor 8005/0
  - PEComa, malignant 8714/3
- Congenital peribronchial myofibroblastic tumor 8827/1
- Diffuse pulmonary lymphangiomatosis
- Inflammatory myofibroblastic tumor 8825/1
- Epithelioid hemangioendothelioma 9133/3
- Pleuropulmonary blastoma 8973/3
- Synovial sarcoma 9040/3
- Pulmonary artery intimal sarcoma 9137/3
- Pulmonary myxoid sarcoma with *EWSR1-CREB1* translocation 8842/3
- Myoepithelial tumors
  - Myoepithelioma 8982/0
  - Myoepithelial carcinoma 8982/3

Lymphohistiocytic tumors

• Extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT lymphoma)	9699/3
• Diffuse large B cell lymphoma	9680/3
• Lymphomatoid granulomatosis	9766/1
• Intravascular large B cell lymphoma	9712/3
• Pulmonary Langerhans cell histiocytosis	9751/1
• Erdheim-Chester disease	9750/1

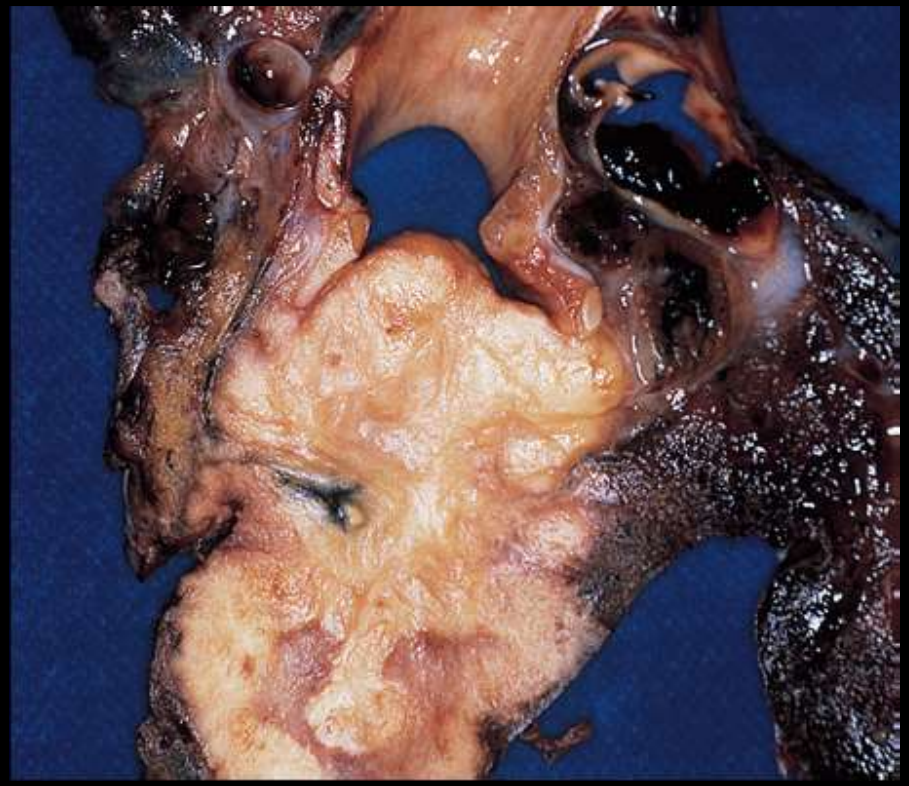
Tumors of ectopic origin

• Germ cell tumors	
◦ Teratoma, mature	9080/0
◦ Teratoma, immature	9080/1
• Intrapulmonary thymoma	8580/3
• Melanoma	8720/3
• Meningioma, NOS	9530/0

Metastatic tumors

- **ICD-O note**: behavior is coded: /0 for benign tumors; /1 for unspecified, borderline, or uncertain behavior; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumors

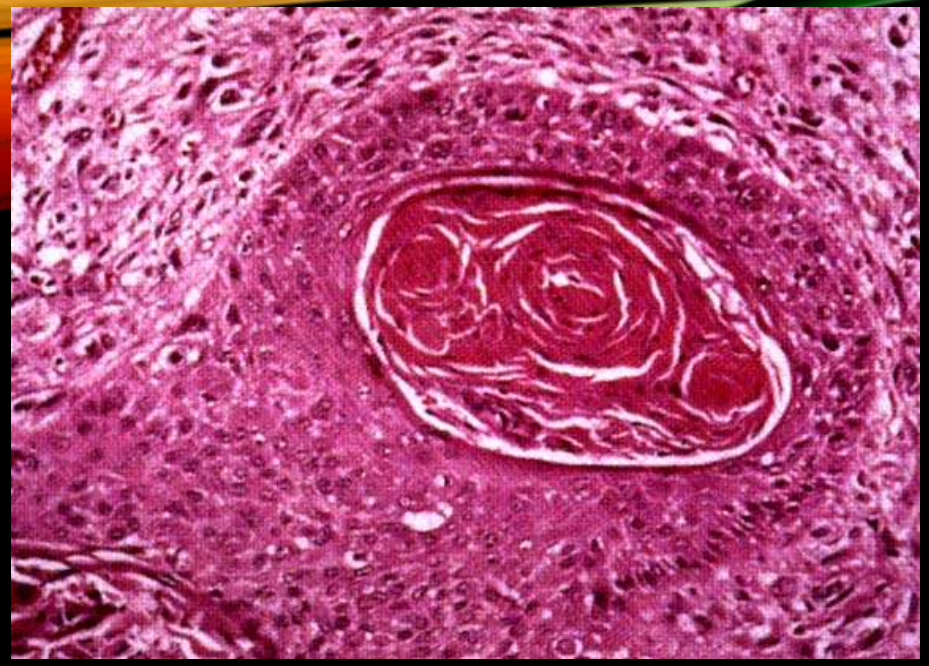
LUNG CARCINOMA

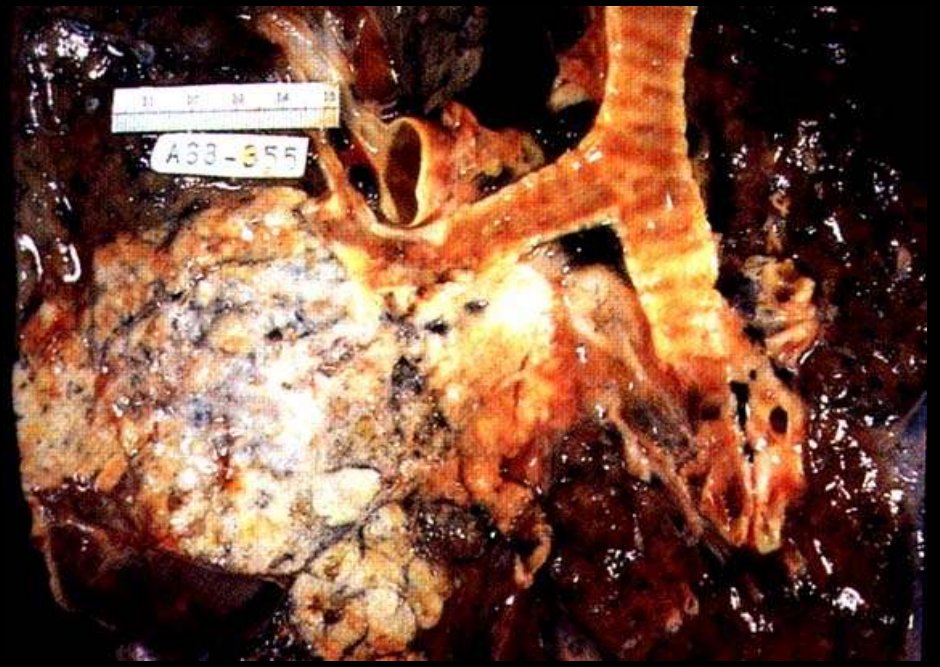


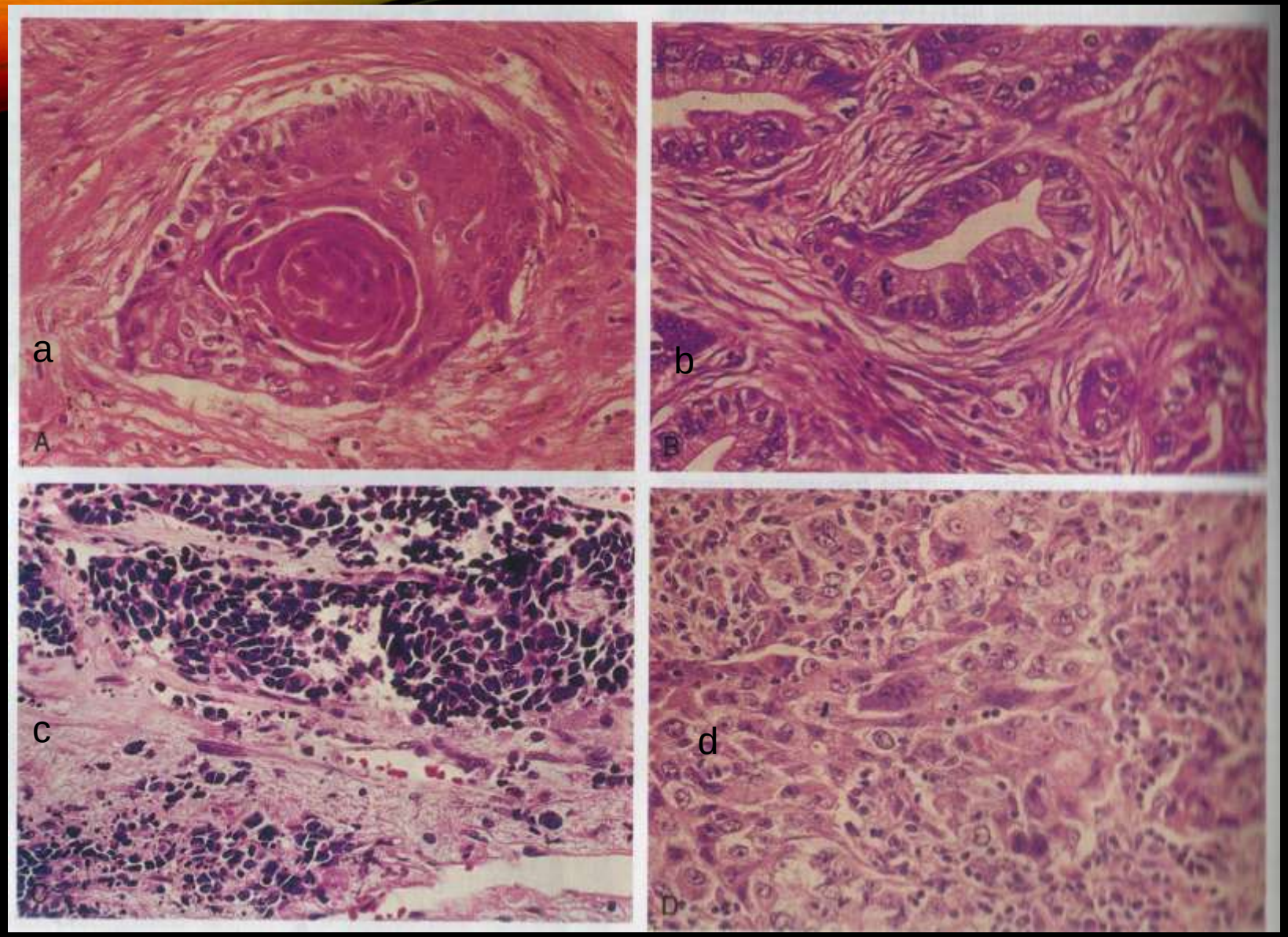
central lung carcinoma

Peripheral lung carcinoma

BRONCHOGENIC CARCINOMA






a
A
b
B
c
d
D

a. Squamous cell ca.: men >> women, smoking history
central bronchus
squamous metaplasia-displasia-Ca

b. **Adenocarcinoma** : bronchial/ bronchioloalveolar type
Women >> men, non smokers & smoker (filter)
pheripherally location
grow more slowly than SCC

c. **Small cell ca** : Highly malignant tumor
smokers, Hilar/ central
EM: neurosecretory granules
high response to chemotherapy

d. **Large cell ca** : Undifferentiated ca

AGE SPECIFIC RATE BY HISTOLOGIC TYPE (1983-1987)

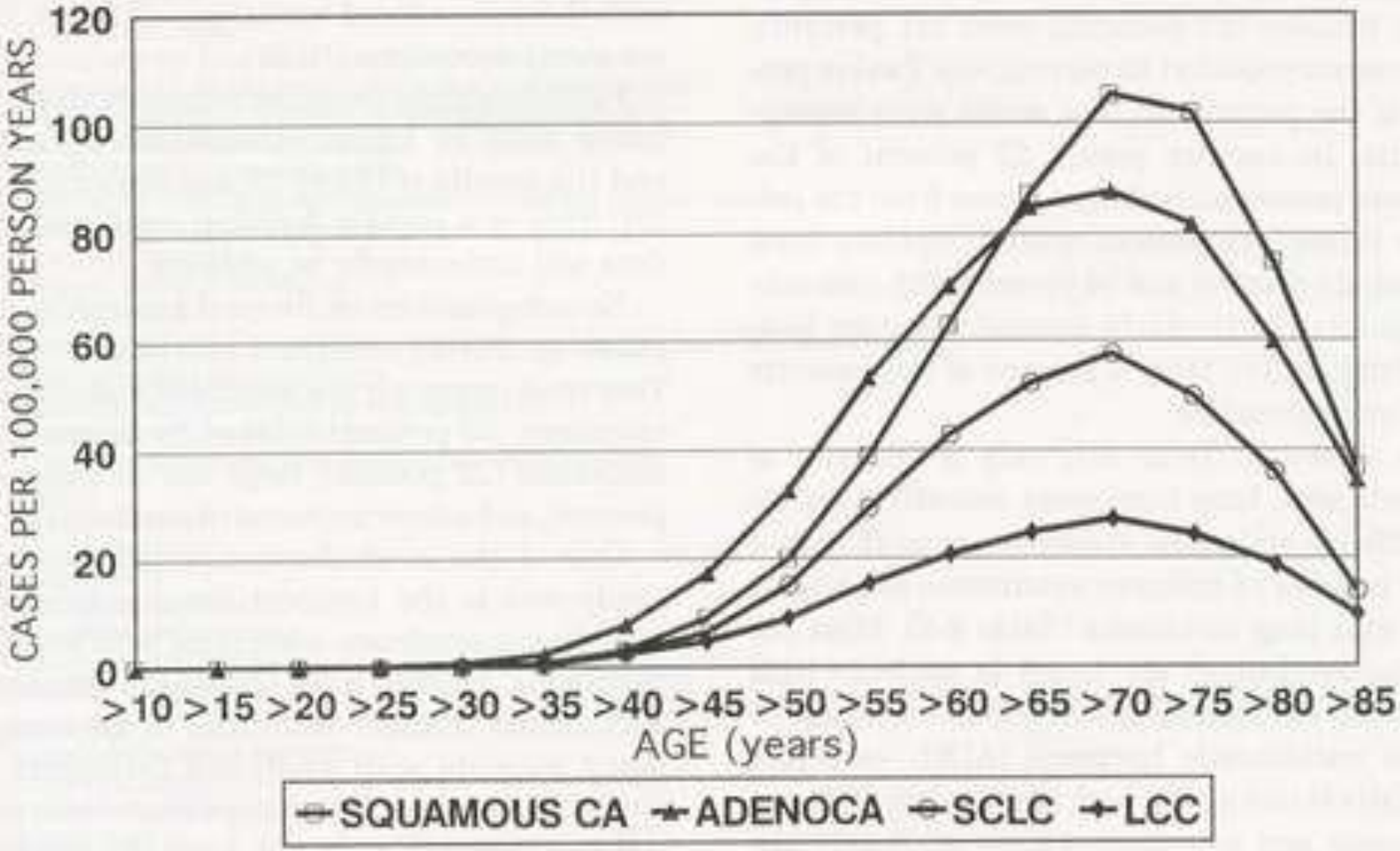


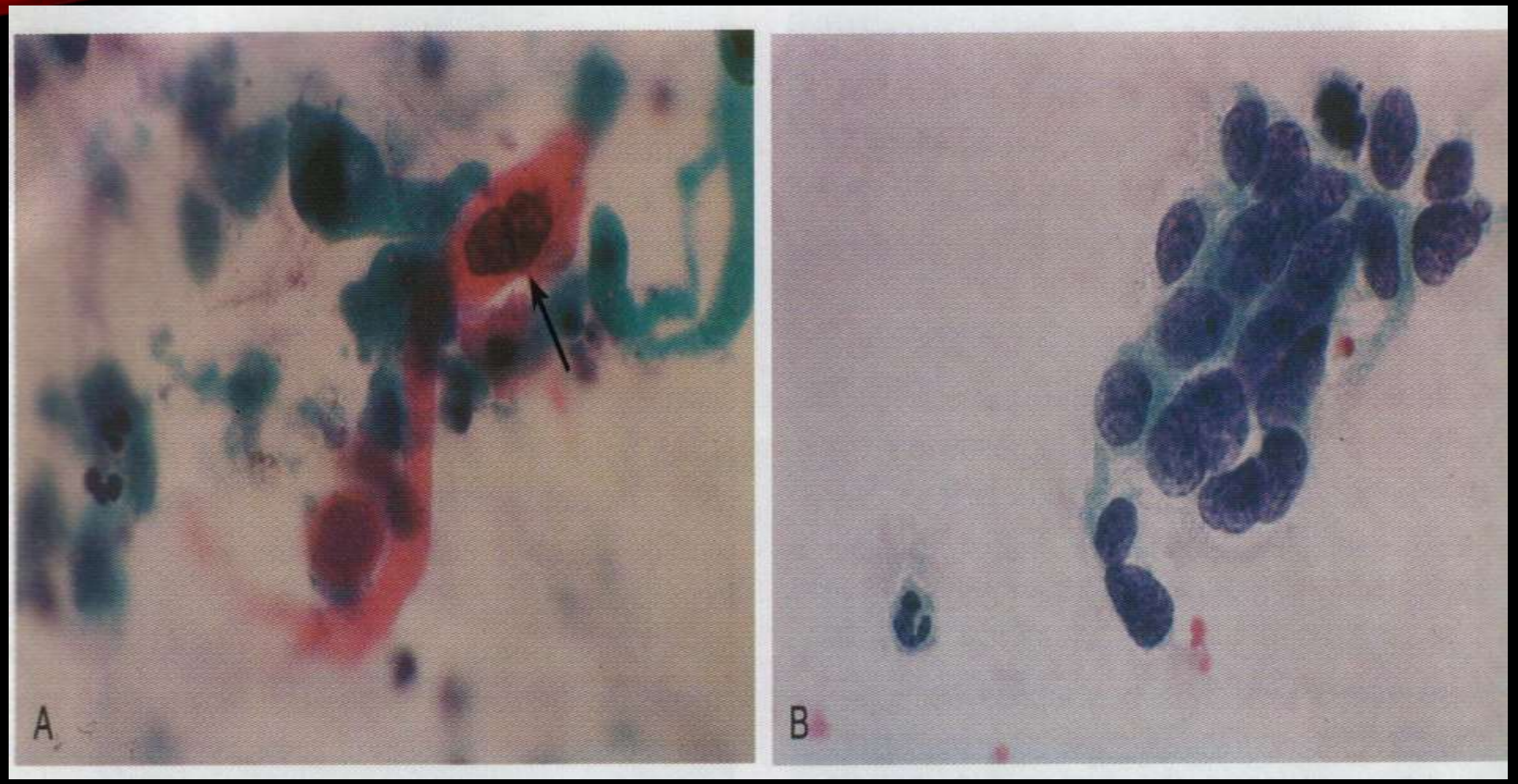
Figure 8-1
AGE-SPECIFIC RATE OF LUNG CANCER
The age-specific rate of lung cancer by histologic type is shown from the SEER data for 1983-1987 (74).

SQUAMOUS CELL CARCINOMA

https://www.pathologyoutlines.com/topic/lungtumorSCC.html

Cytologic diagnoses of lung cancer

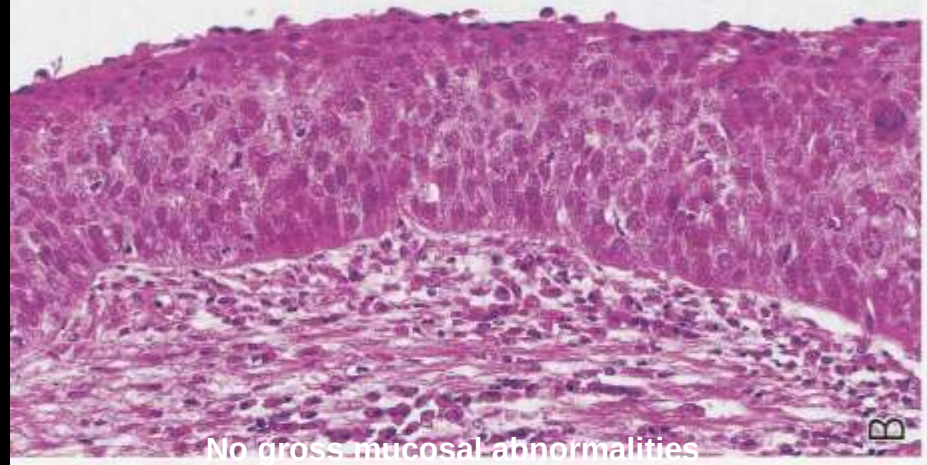
https://www.pathologyoutlines.com/topic/lungtumorcytology.html



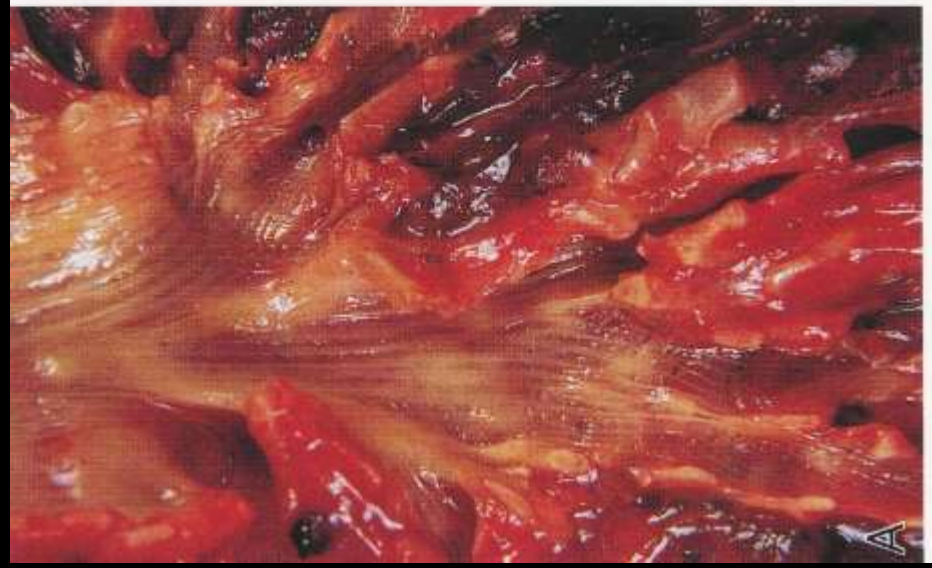
a. Sputum specimen
b. FNA of Lnn : small cell ca

S C CARCINOMA IN SITU

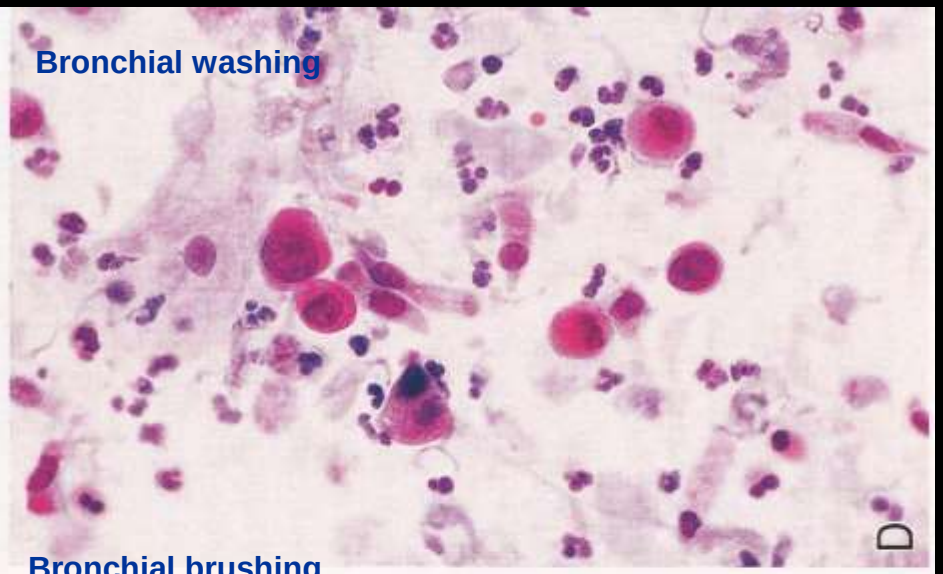
SCC in situ



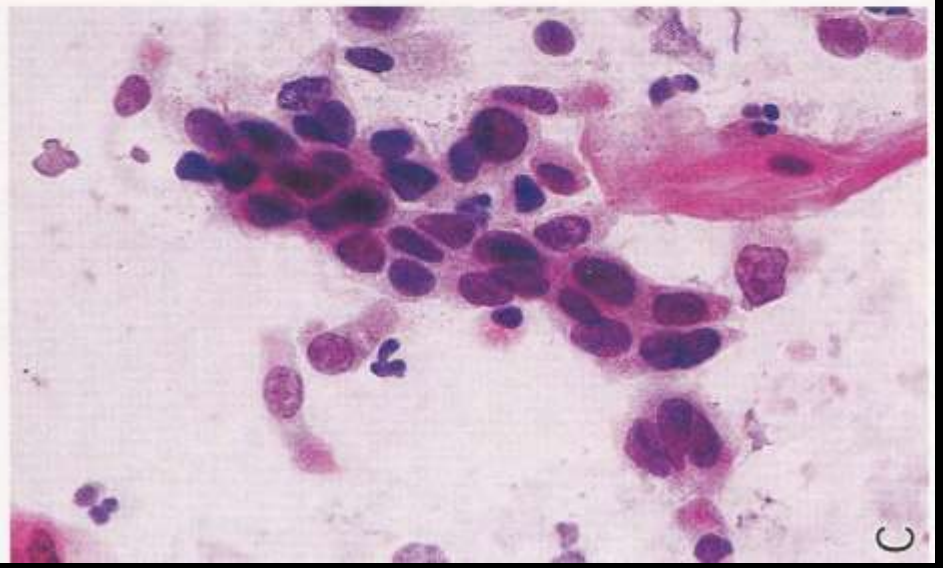
No gross mucosal abnormalities



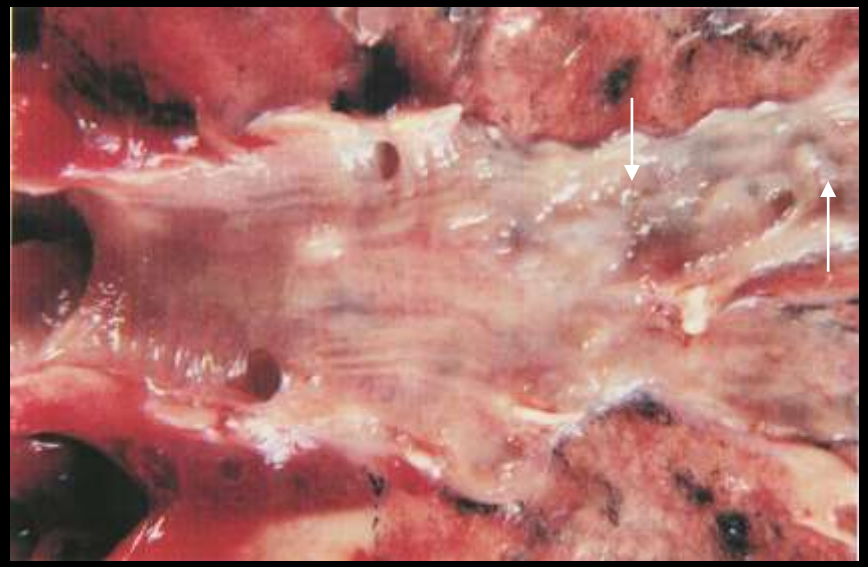
Bronchial washing



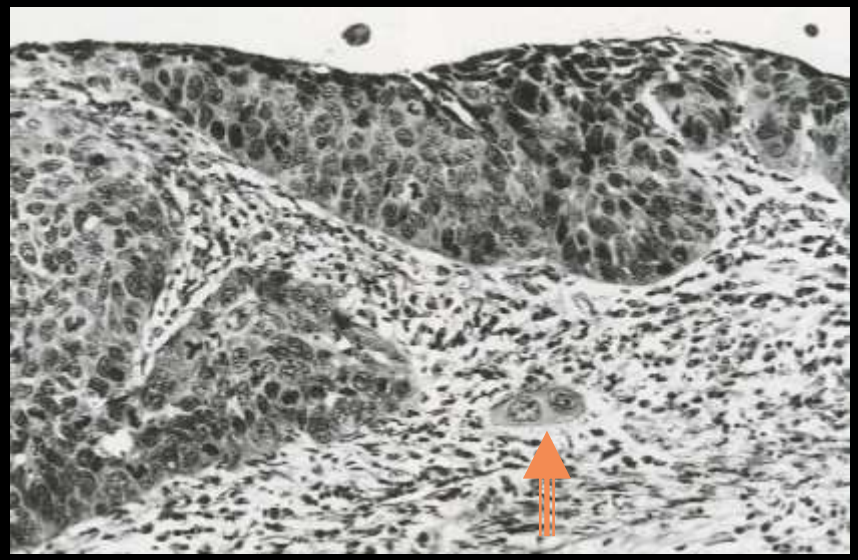
Bronchial brushing



EARLY INVASIVE SCC

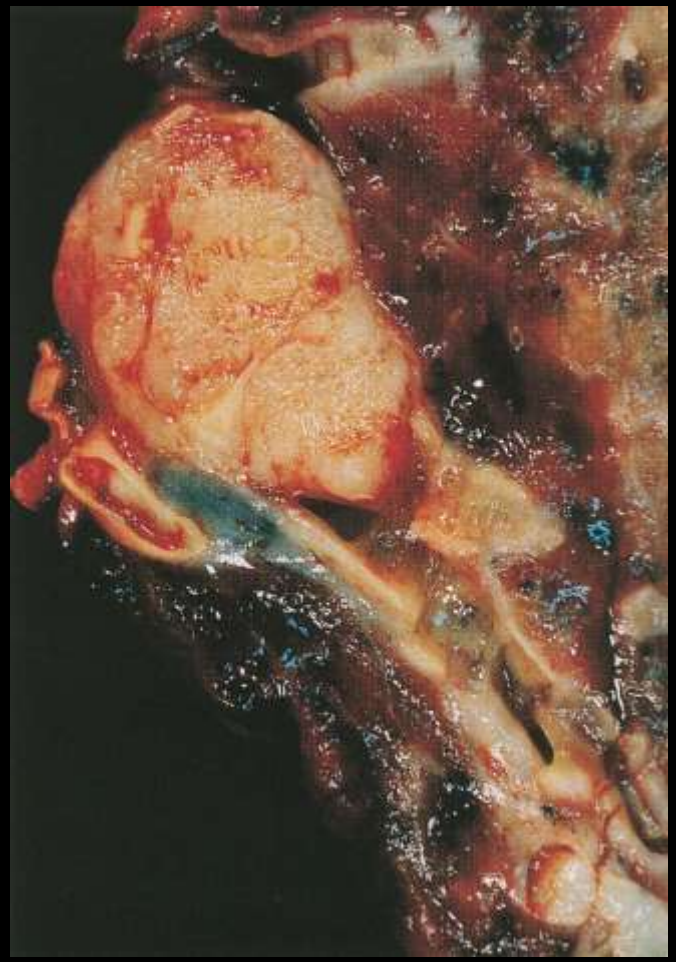


SCC in situ with foci of early invasion (nodular thickening)



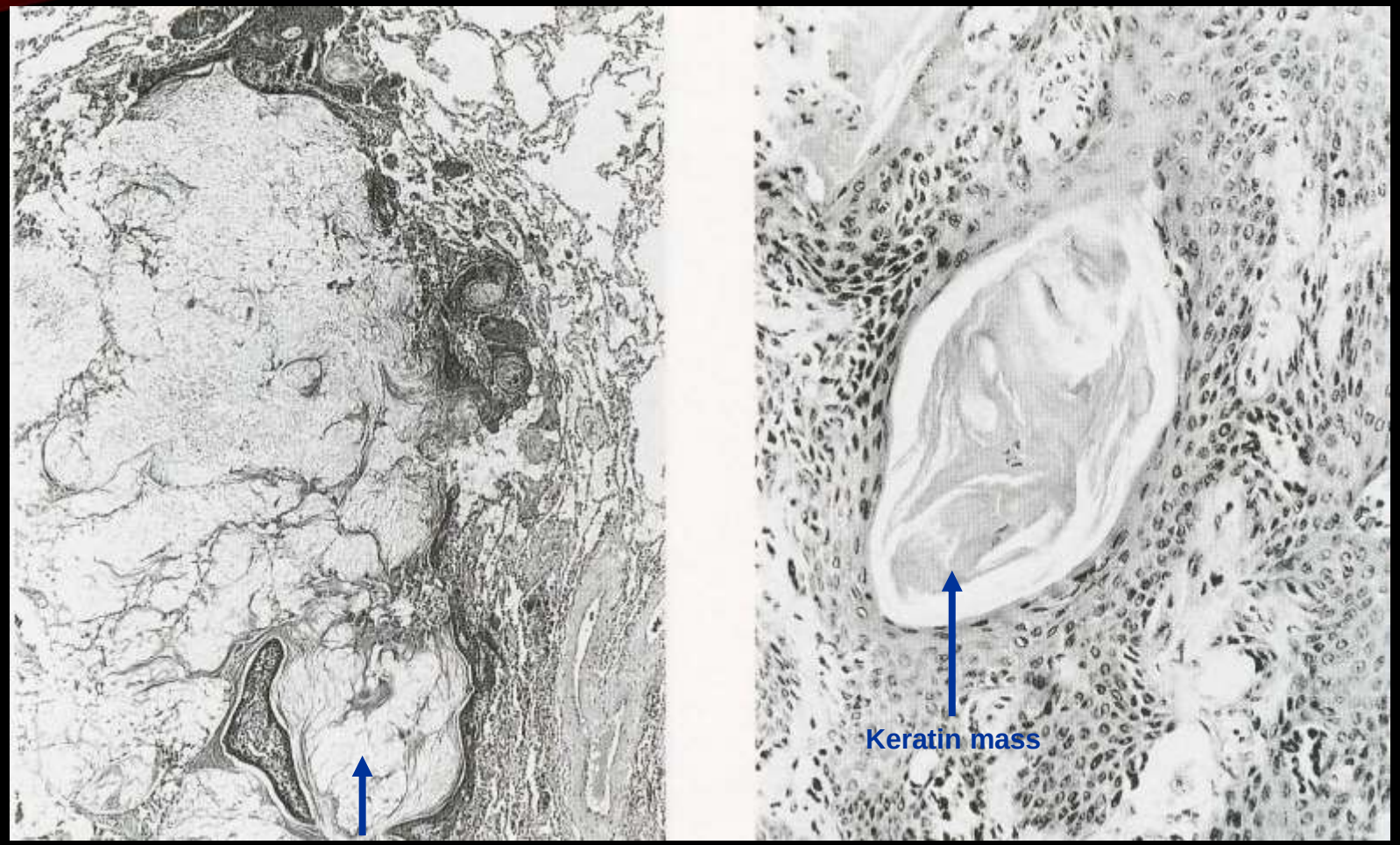
Early invasive scc

SCC

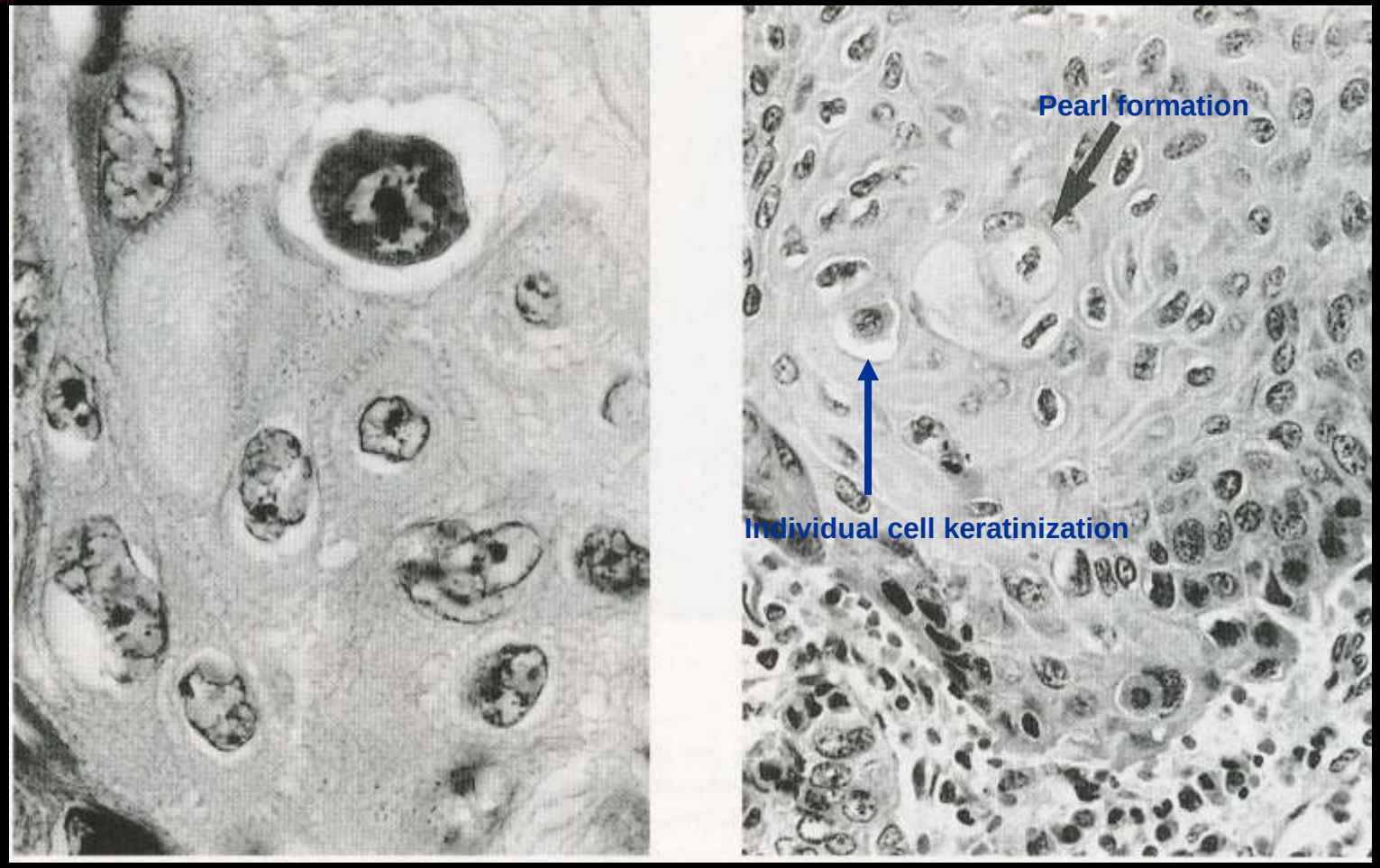


Endobronchial SCC

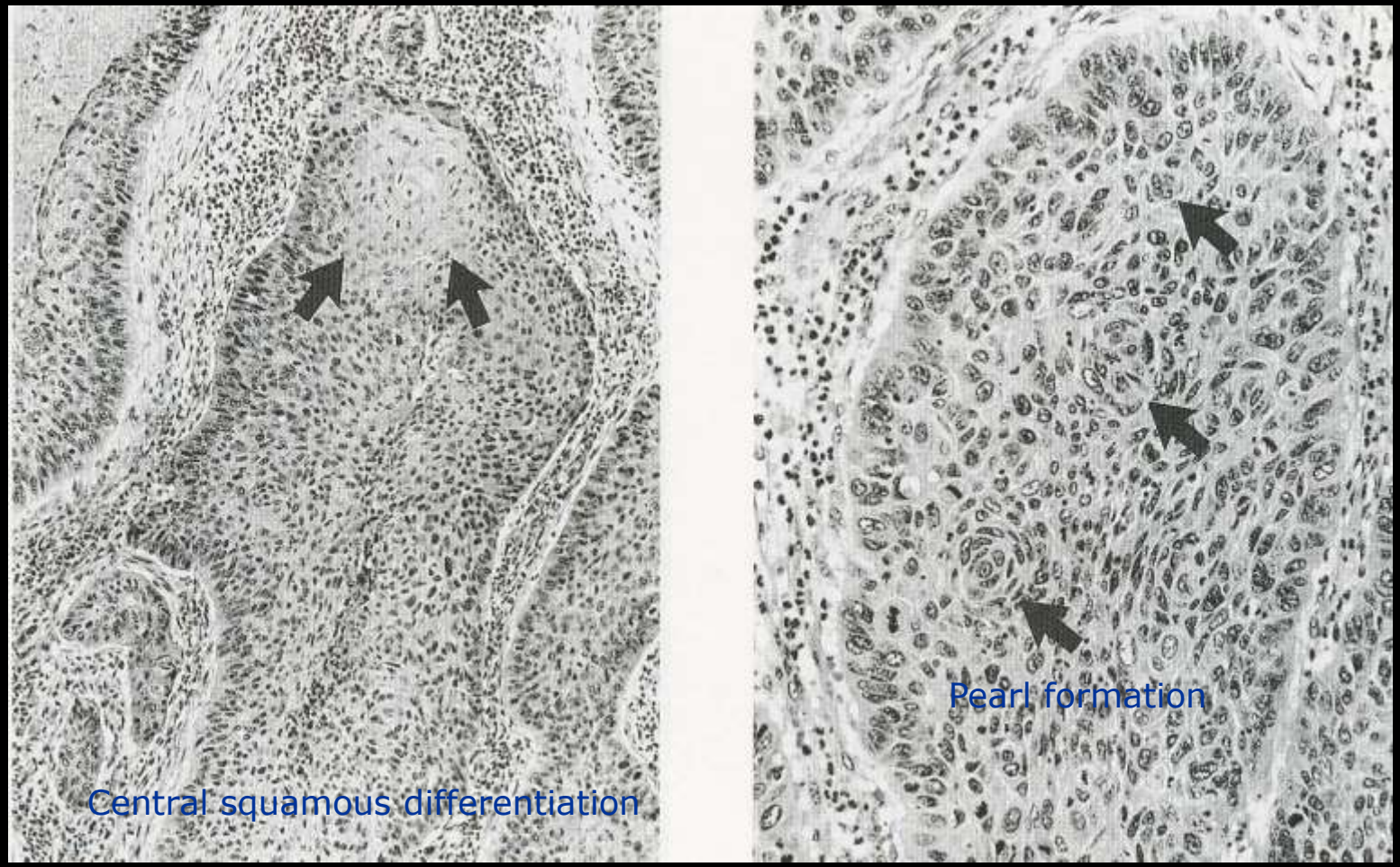
WELL DIFFERENTIATED SCC



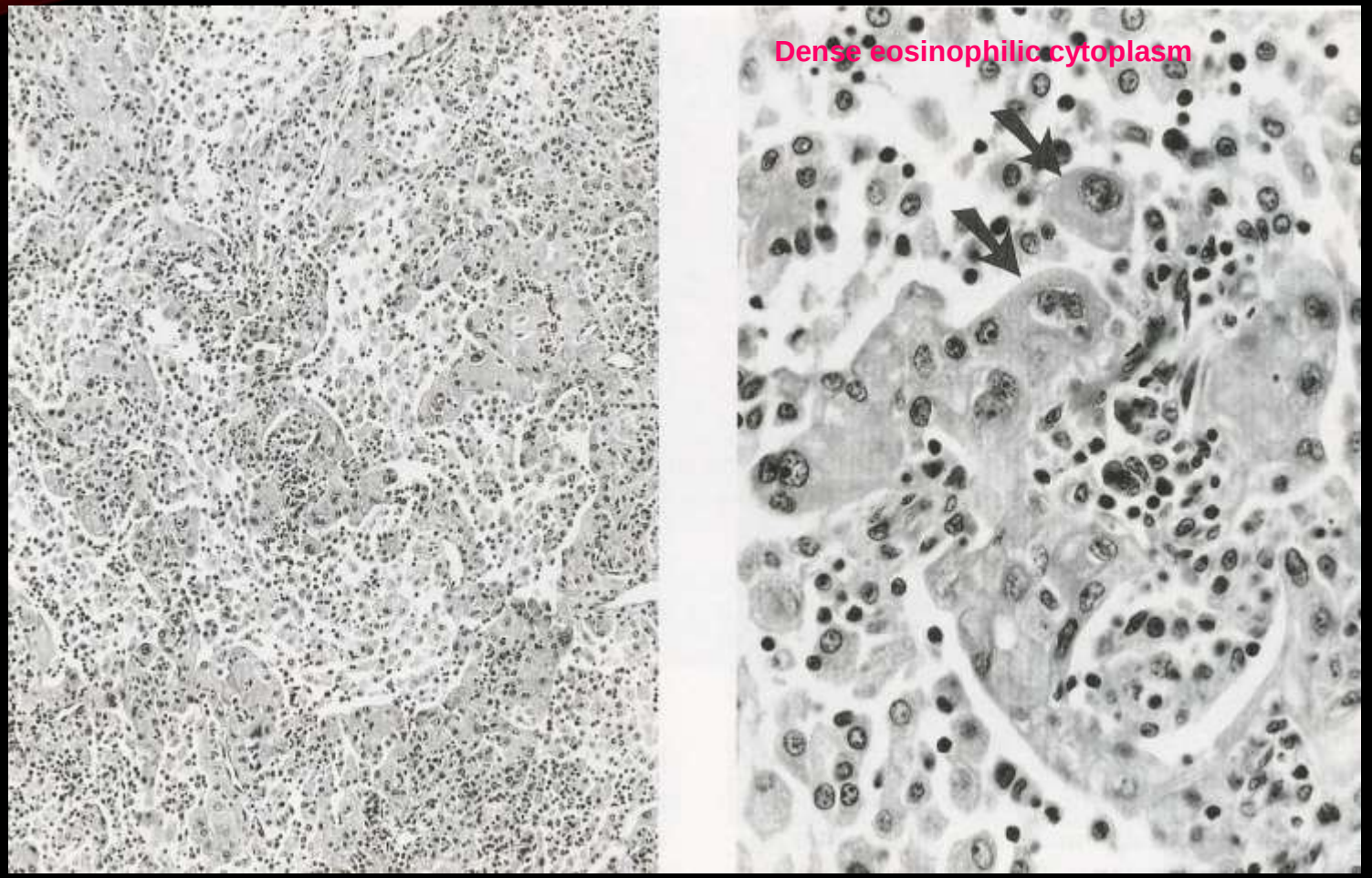
SCC MODERATELY DIFFERENTIATED



SCC MODERATELY DIFFERENTIATED



SCC POORLY DIFFERENTIATED

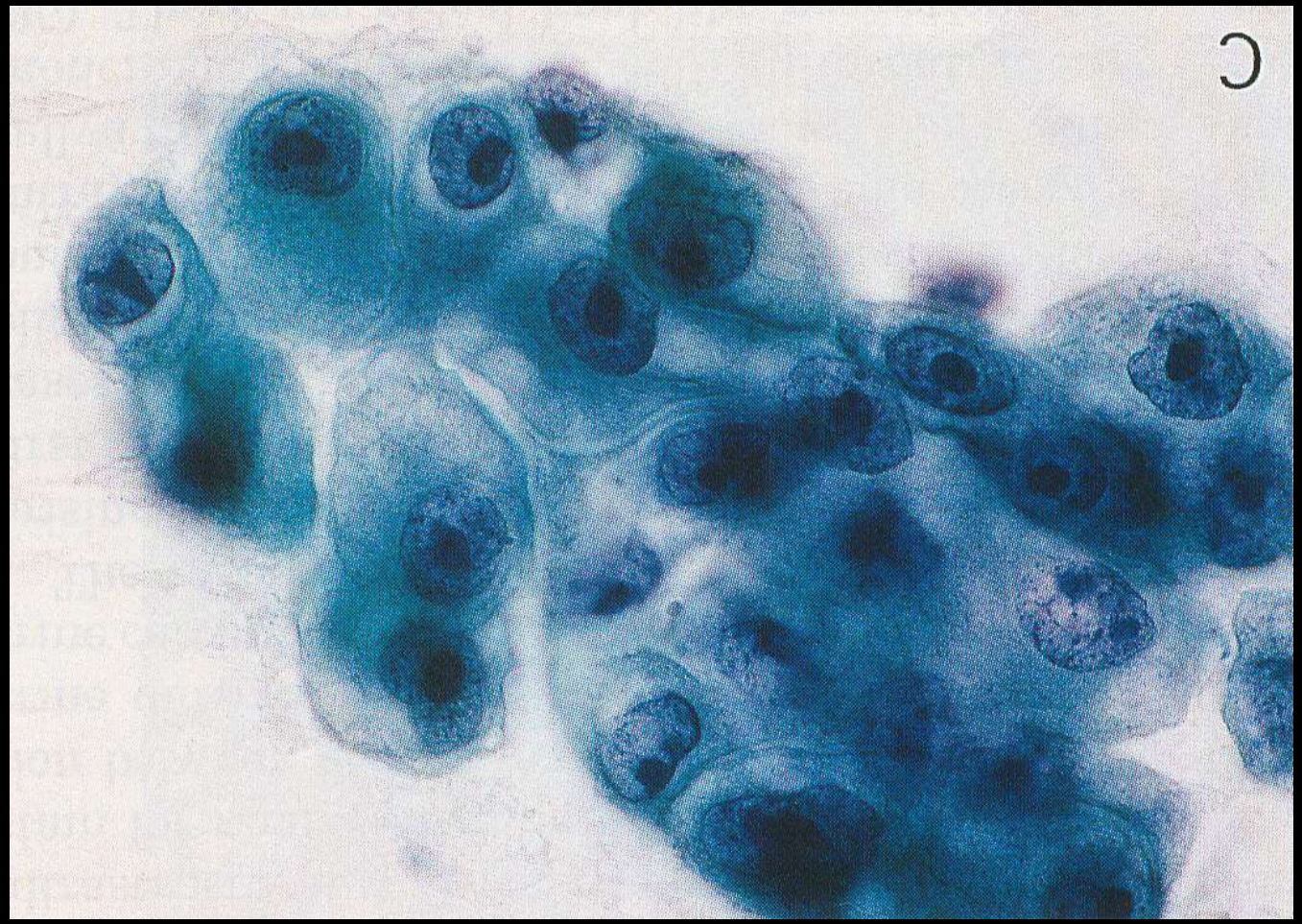


ADENOCARCINOMA

http://www.pathologyoutlines.com/topic/lungtumoradenocarcinoma.html

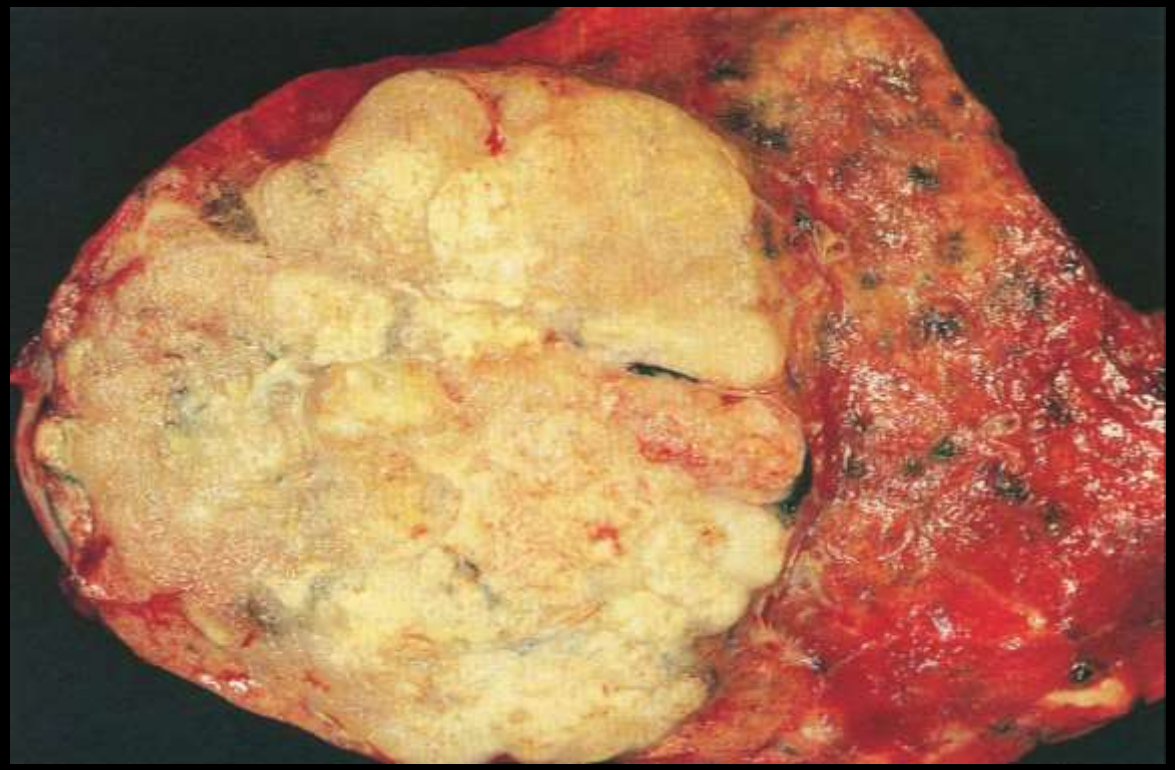
ADENOCARCINOMA

CYTOLOGY



3 dimension cell group, vacuolization

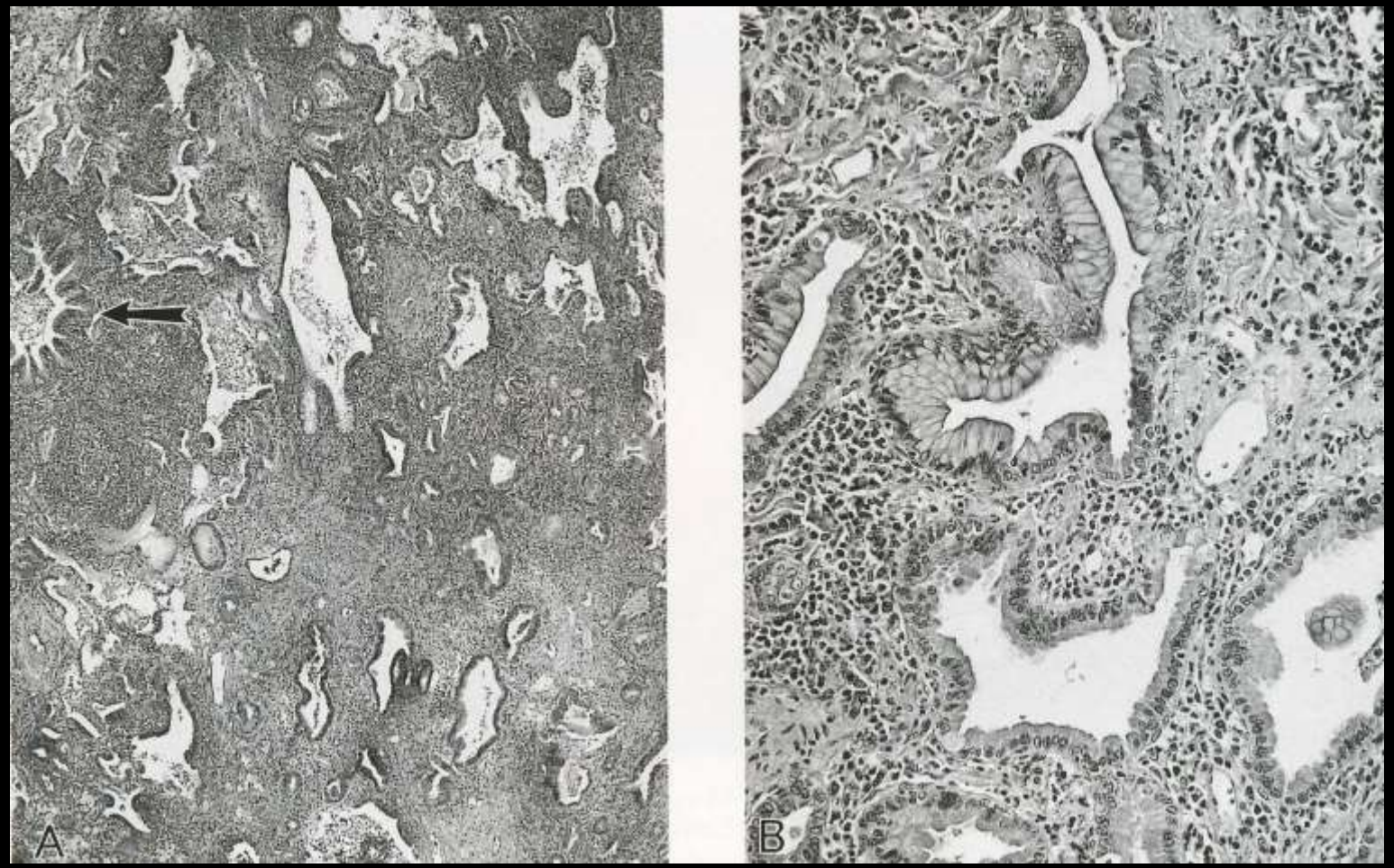
ADENOCARCINOMA



This lobectomy specimen shows a lobulated, somewhat glistening mass

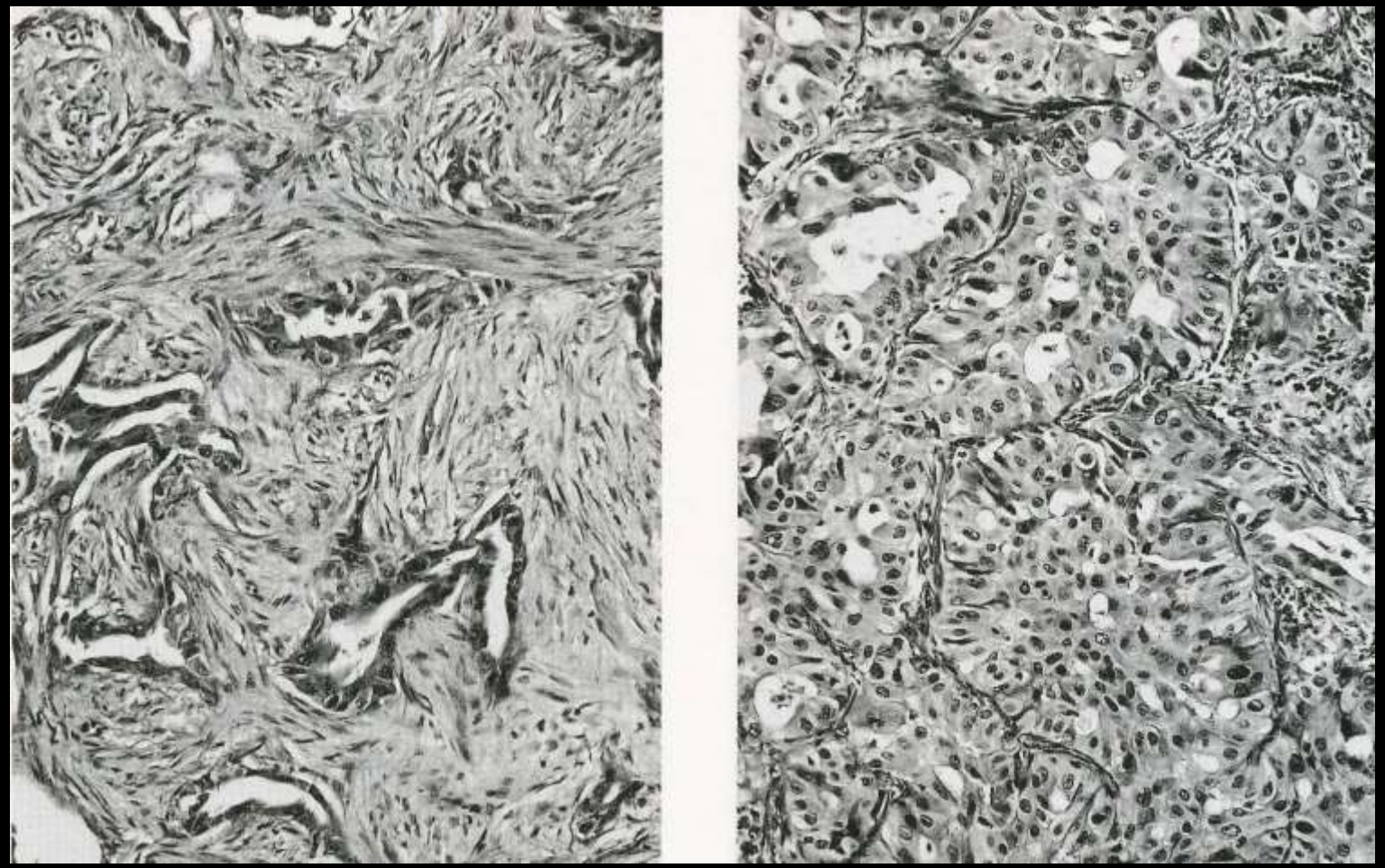
ADENOCARCINOMA

WELL DIFFERENTIATED



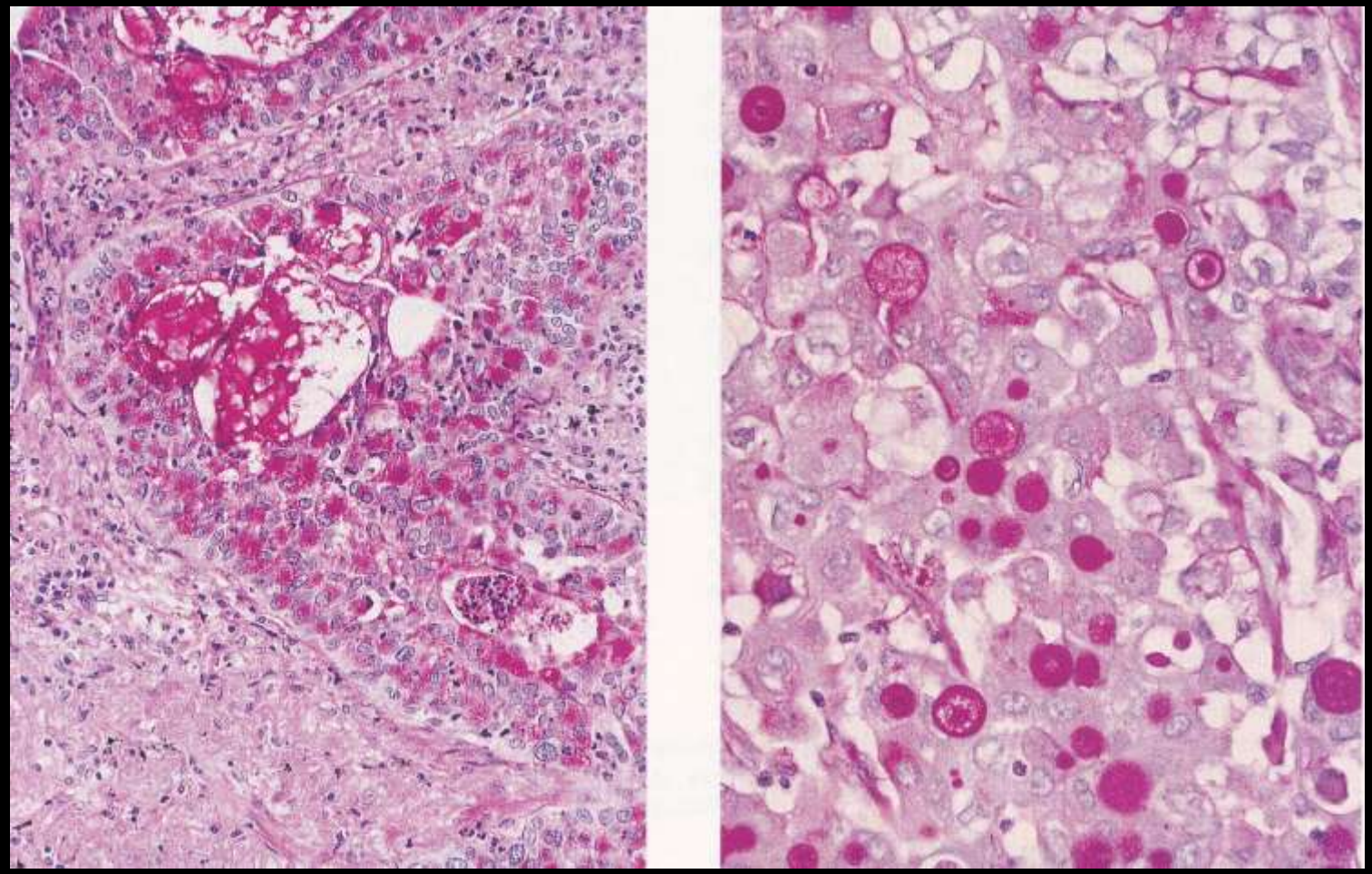
ADENOCARCINOMA

MODERATELY DIFFERENTIATED



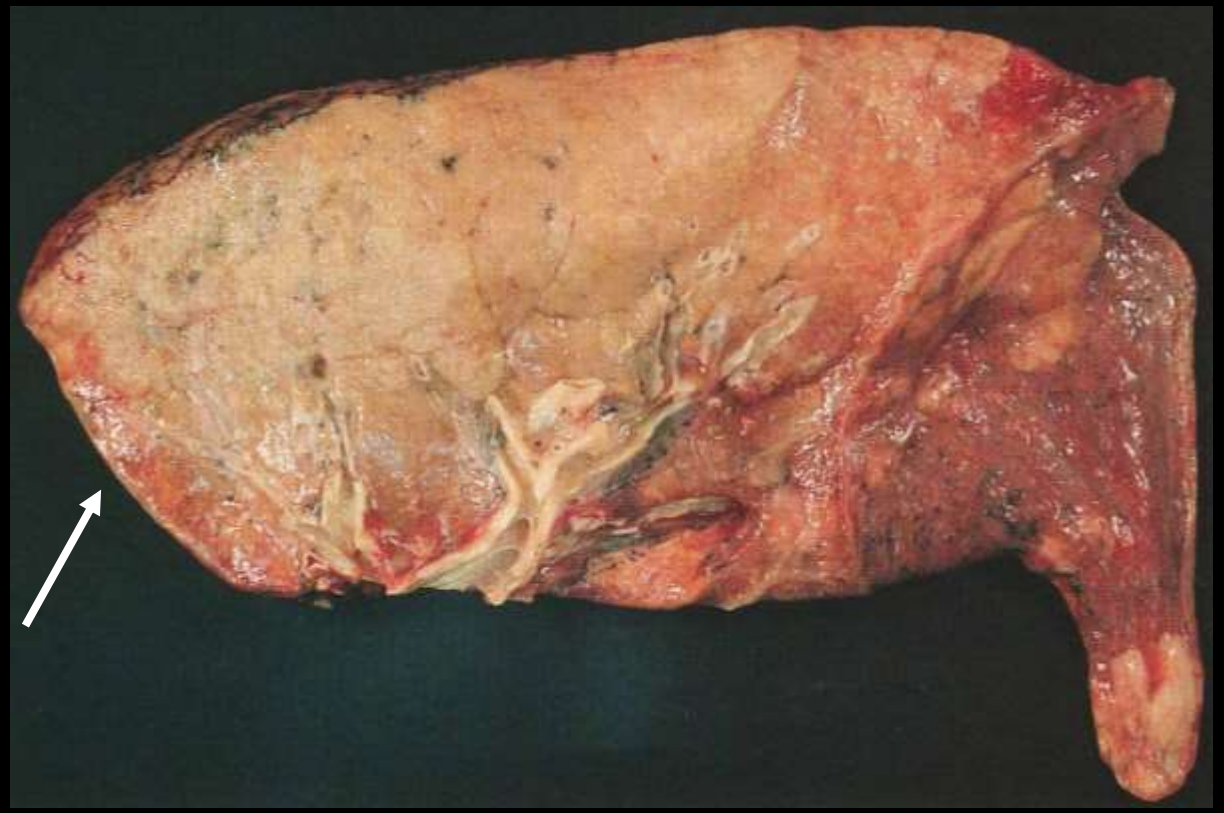
ADENOCARCINOMA

POORLY DIFFERENTIATED



BRONCHIOLOALVEOLAR CARCINOMA (BAC)

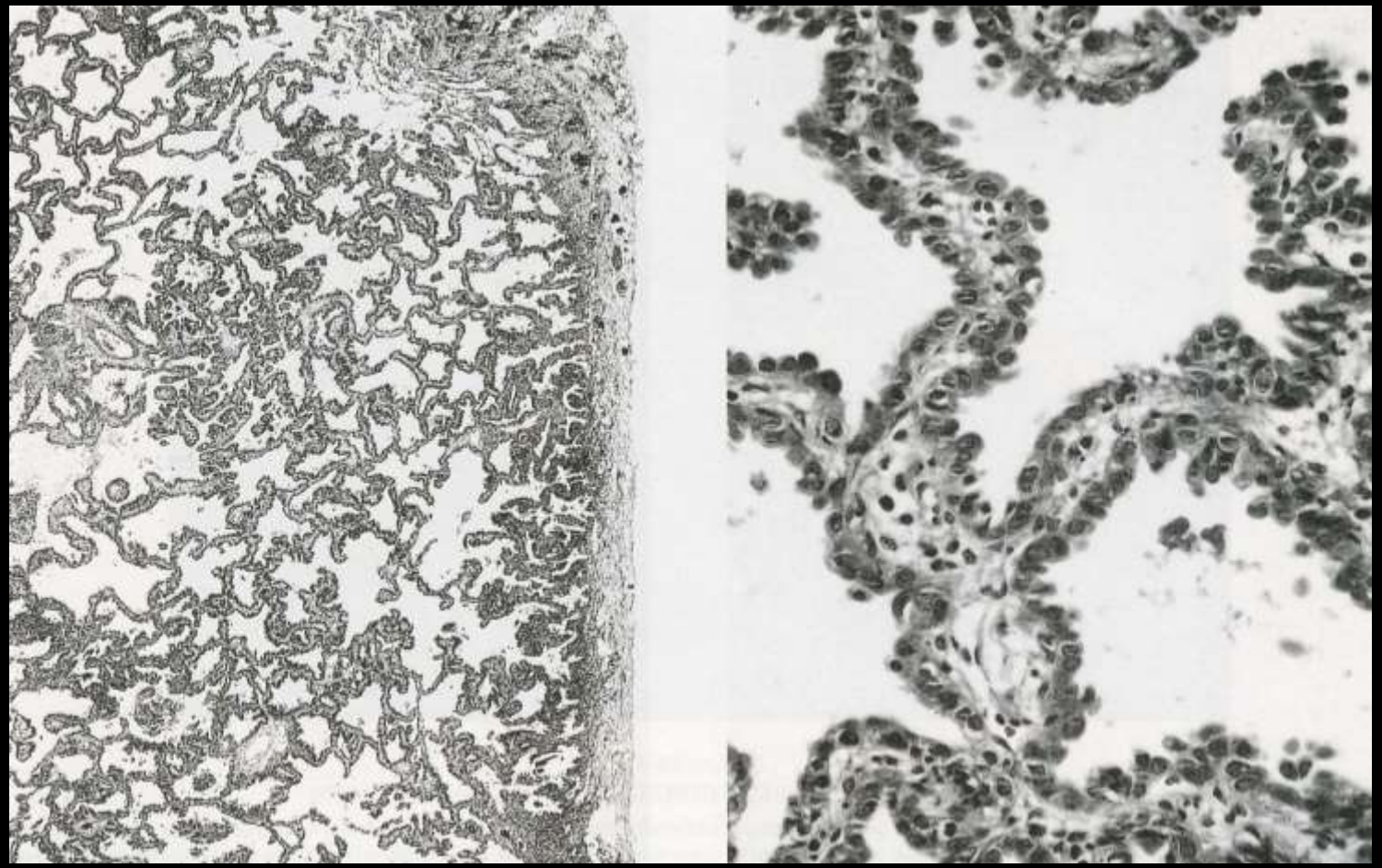
NONMUCINOUS TYPE



Upper lobe is almost entirely consolidated by mucinous BAC, architecture is maintained, and there is an absence of necrosis and hemorrhage

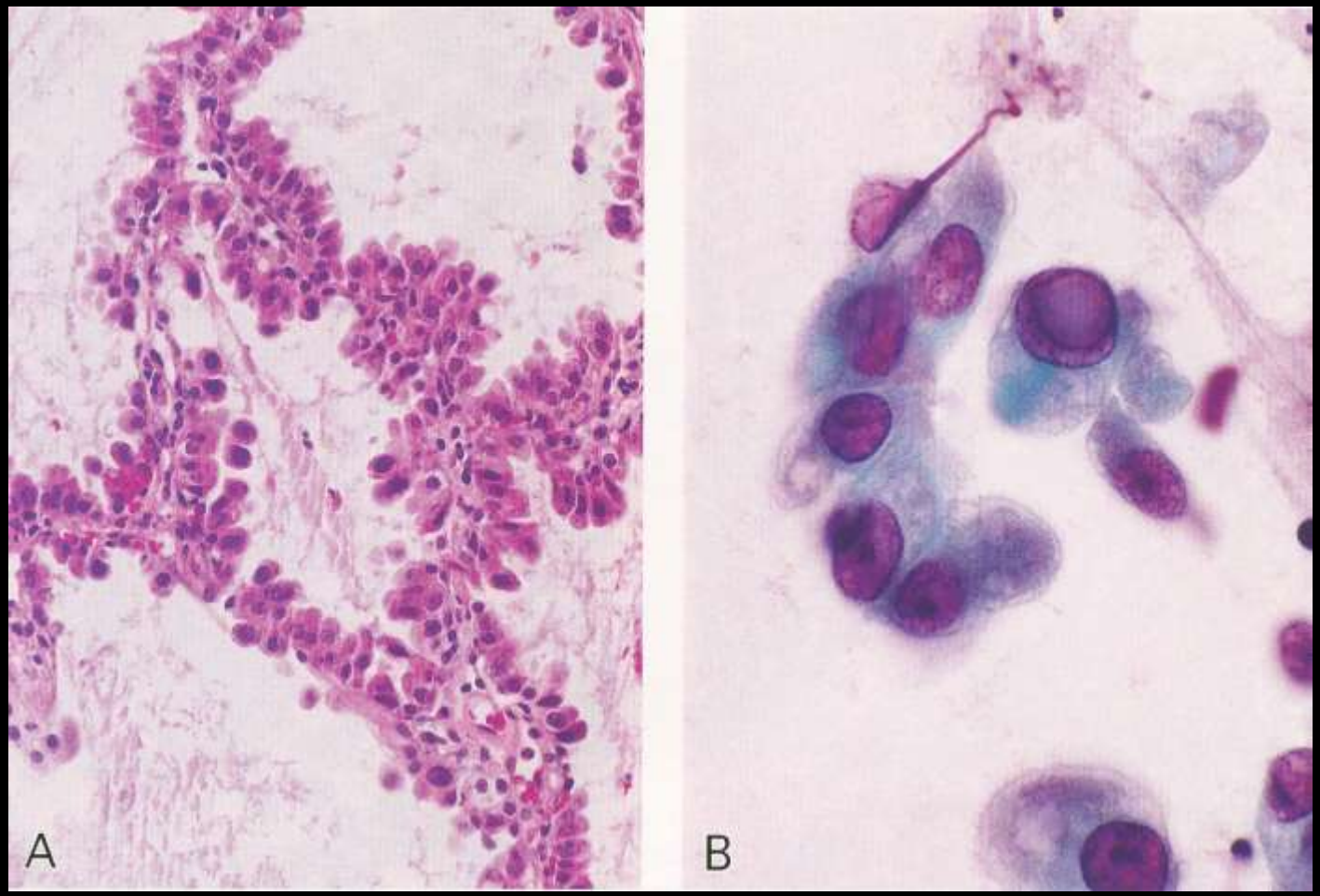
BRONCHIOLOALVEOLAR CARCINOMA (BAC)

NONMUCINOUS TYPE



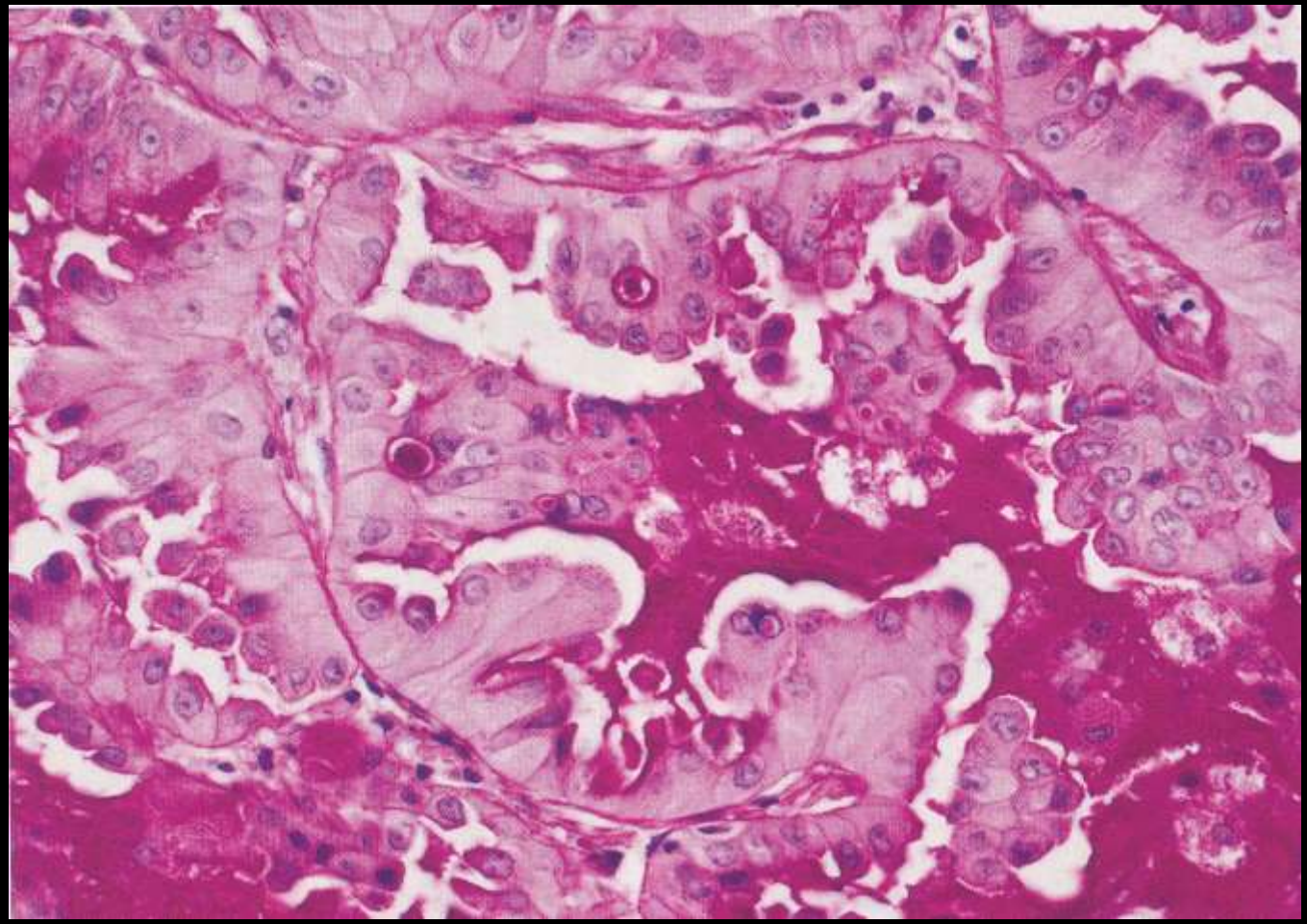
BRONCHIOLOALVEOLAR CARCINOMA (BAC)

NONMUCINOUS TYPE



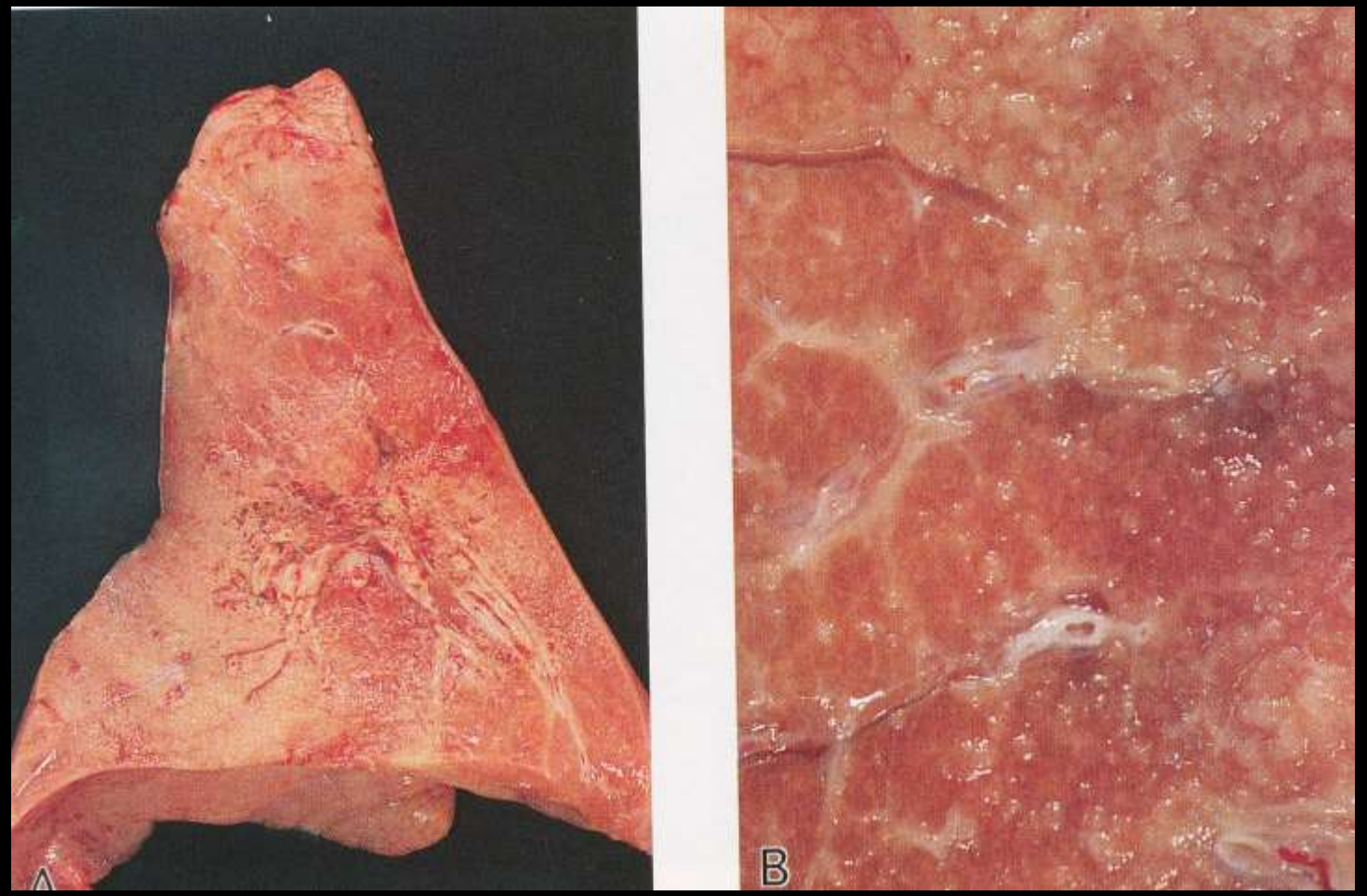
BRONCHIOLOALVEOLAR CARCINOMA (BAC)

NONMUCINOUS TYPE



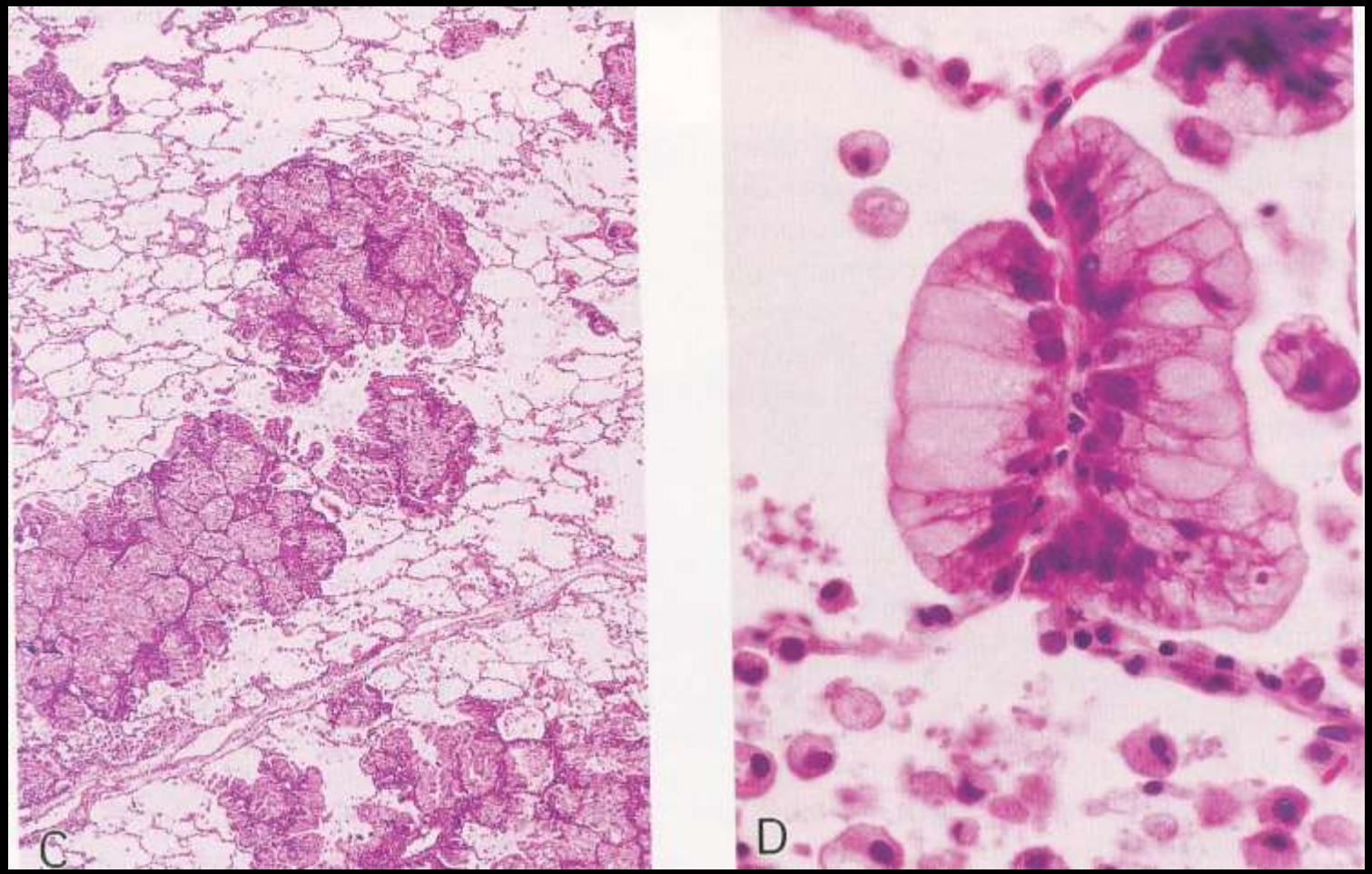
BRONCHIOLOALVEOLAR CARCINOMA (BAC)

MUCINOUS TYPE

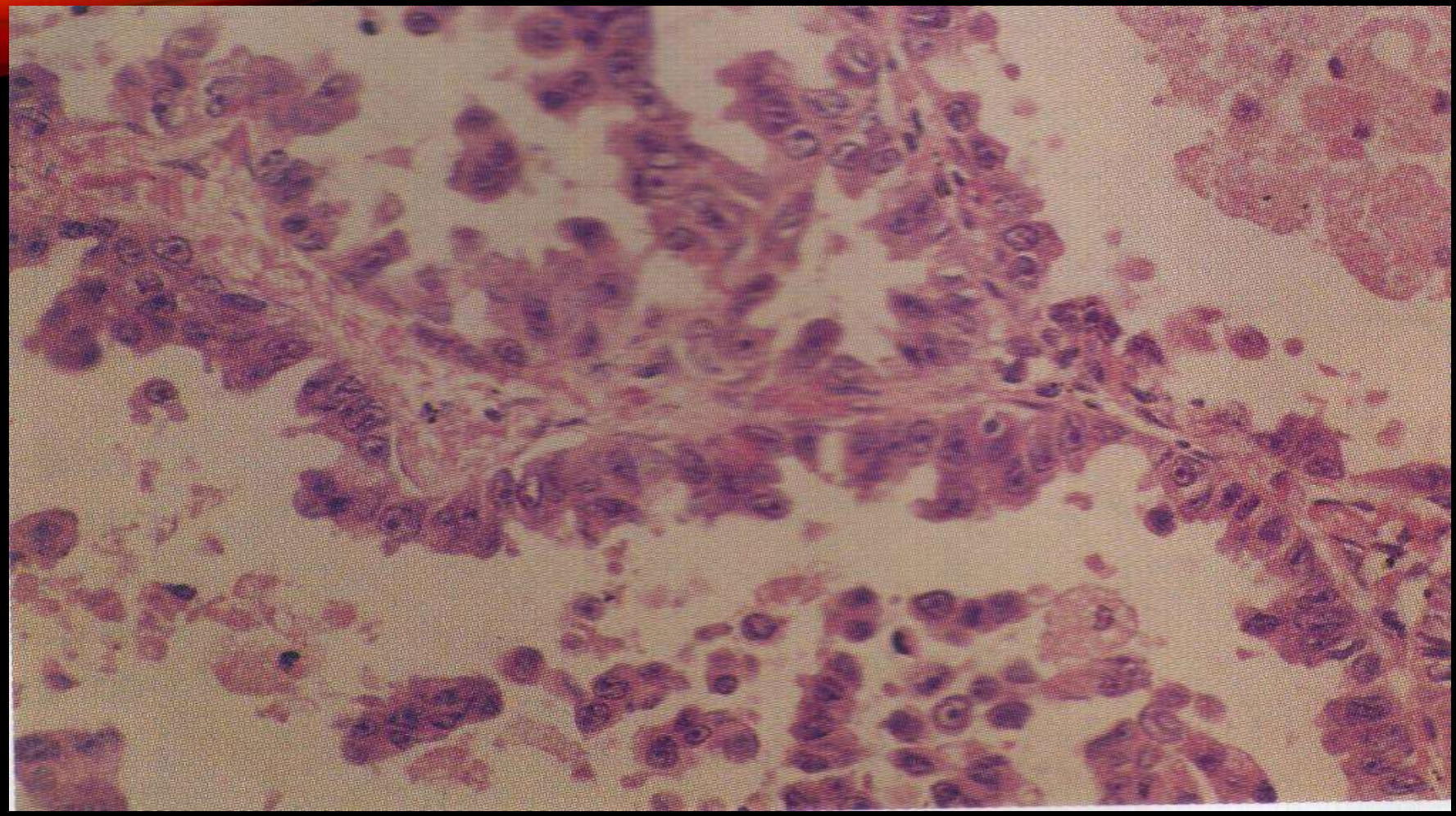


BRONCHIOLOALVEOLAR CARCINOMA (BAC)

MUCINOUS TYPE



Bronchioloalveolar carcinoma



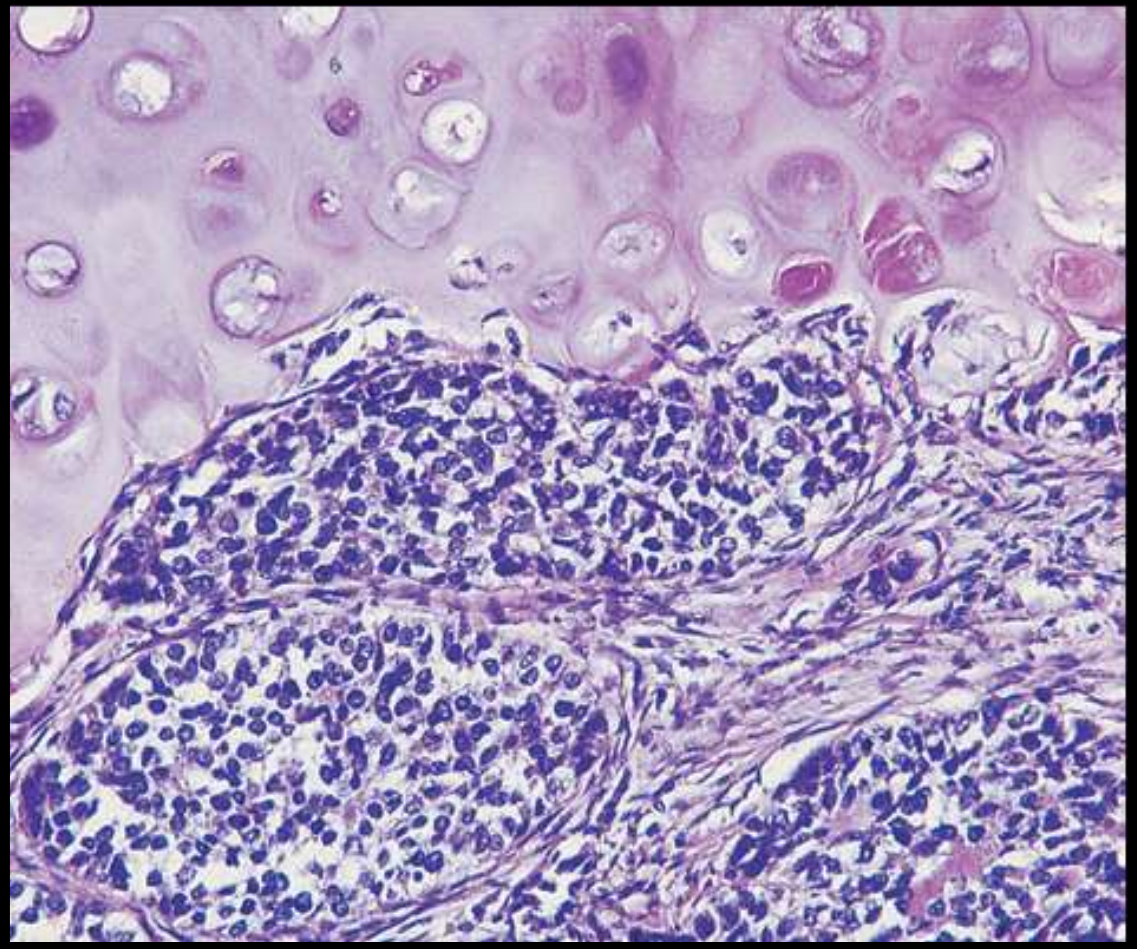
Terminal bronchoalveolar region
Peripheral portion of the lung
Males = females, all ages(3rd decade- advanced years)

SMALL CELL (LUNG) CARCINOMA

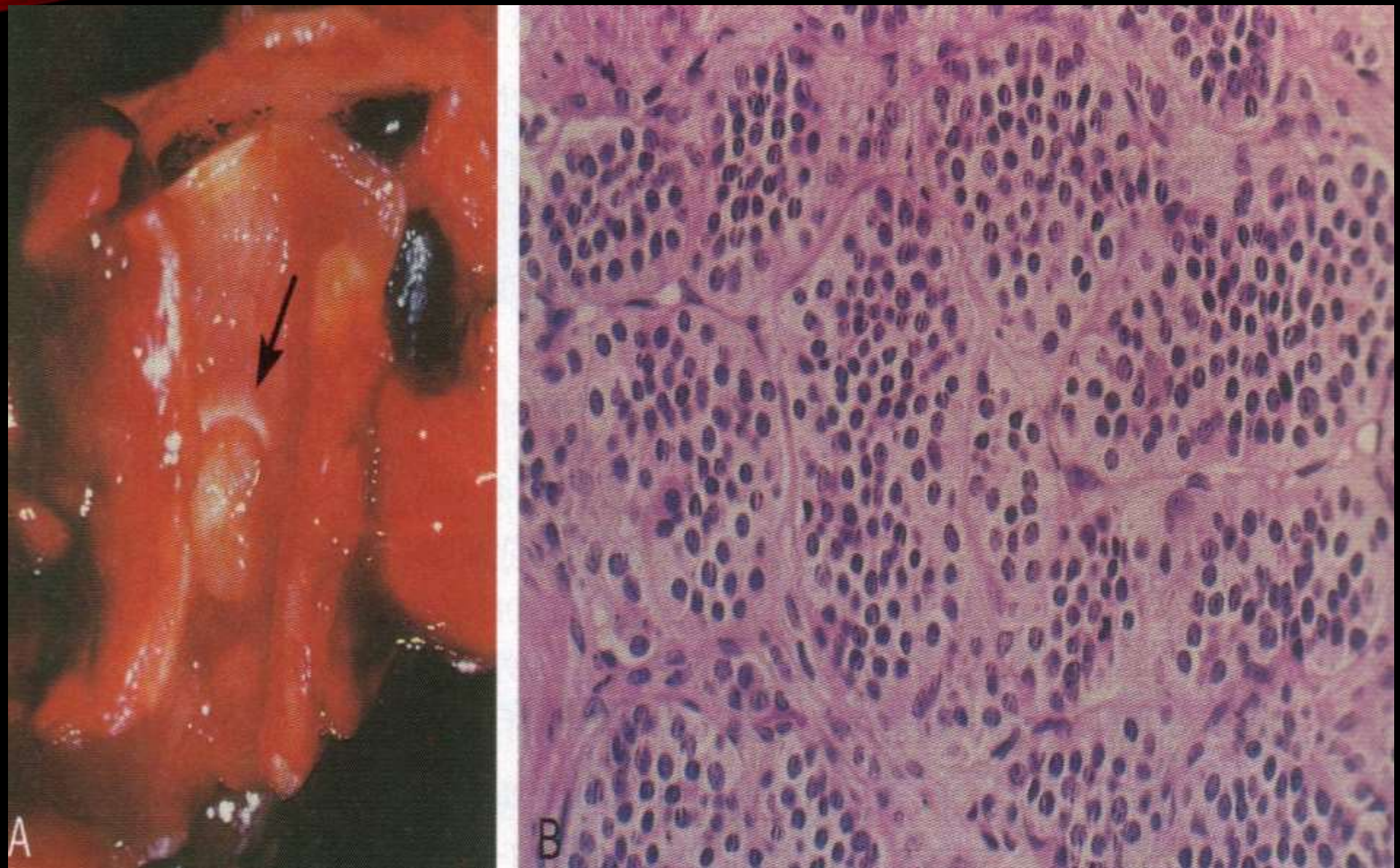
http://www.pathologyoutlines.com/topic/lungtumorsmallcell.html

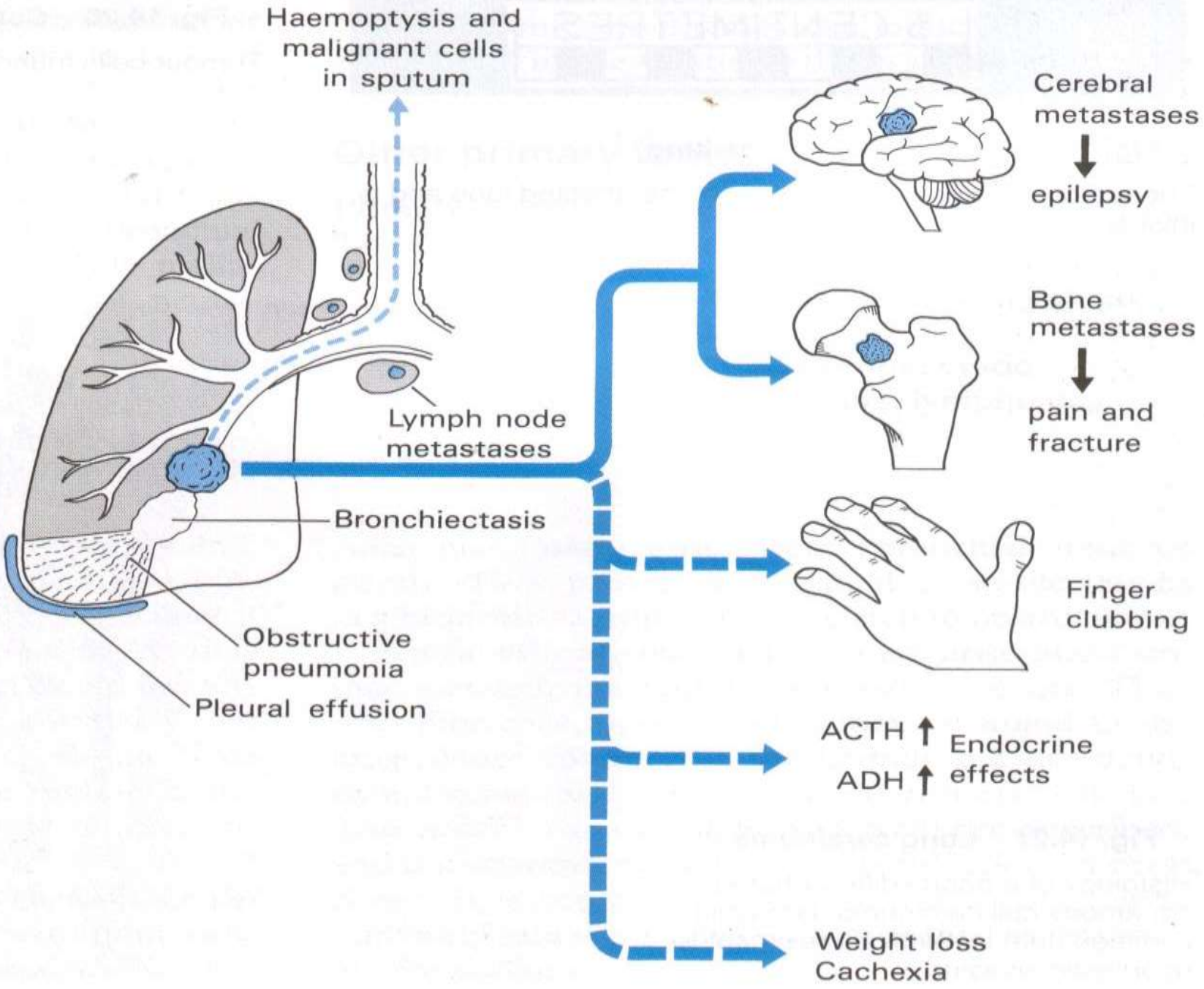
SMALL CELL (LUNG) CARCINOMA

(HE) X 50

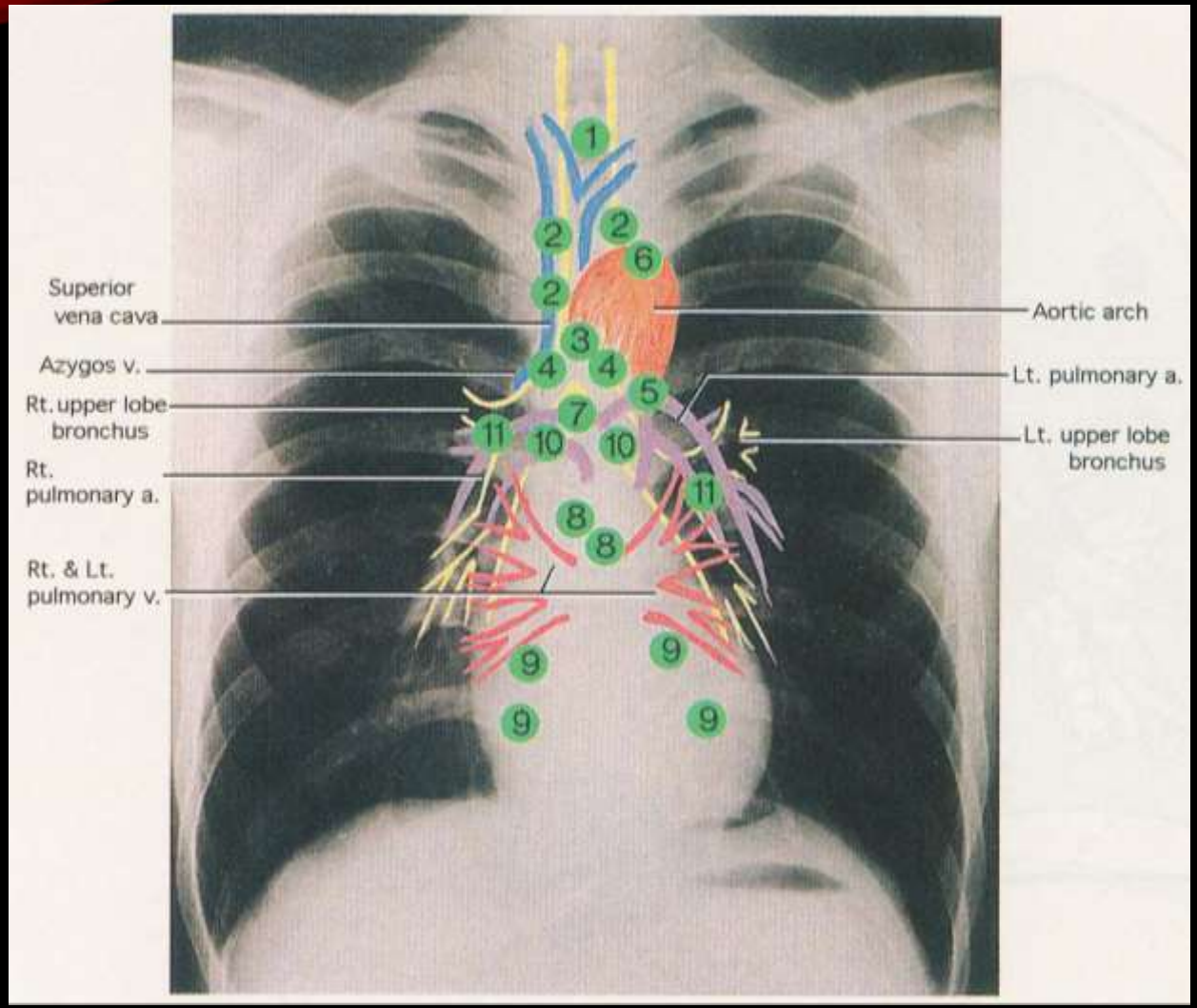


BRONCHIAL CARCINOID




Haemoptysis and malignant cells in sputum
Cerebral metastases
epilepsy
Bone metastases
pain and fracture
Lymph node metastases
Bronchiectasis
Obstructive pneumonia
Pleural effusion
Finger clubbing
ACTH ↑
ADH ↑
Endocrine effects
Weight loss
Cachexia

LYMPHNODE STATIONS



Lymphnode stations are shown projected onto a chest-roentgenogram

PATTERN OF SPREAD

1. Direct extention to adjecent structure
2. Aerogenous spread
3. Lymphatic spread
4. Hematogenous dissemination
5. Pleural seeding

STAGING SYSTEM FOR LUNG CANCER

https://www.pathologyoutlines.com/topic/lungtumorstaging.html

NEW INTERNATIONAL STAGING SYSTEM FOR LUNG CANCER

	Stage Grouping		
Stage Ia	T1	N0	M0
Stage Ib	T2	N0	M0
Stage IIa	T1	N1	M0
Stage IIb	T2 T3	N1 N0	M0 M0
Stage IIIa	T1-3 T3	N2 N1	M0 M0
Stage IIIb	Any T T3 T4	N3 N2 Any N	M0 M0 M0
Stage IV	Any T	Any N	M1

STAGING SYSTEM FOR LUNG CANCER

T1	Tumor<3cm without pleural or main stem bronkhus involvement
T2	Tumor>3cm or involvement main stem bronkhus 2cm from carina, visceral pleural involvement, or lobar atelectasis
T3	Tumor witht involvement of chest wall (including superior sulcus tumor), diaphragma, mediastinal pleura, pericardium, main stem bronkhus 2 cm from carina, or entire lung atelectasis
T4	Tumor with invasion of mediastinum, heart, grat vessels, trachea, esophagus, vertebral body, or carina or with a malignant pleural effusion
No	No demonstrable metastasis to regional lymph nodes
N1	Ipsilateral hilar or peribronchial nodal involvement
N2	Metastasis to ipsilateral mediastinal or subcarinal lymph nodes
N3	Metastasis to contralateral mediastinal or hilar lymph nodes, ipsilateral or contralateral scalene, or supraclavicular lymph nodes
M0	Tumor<3cm without pleural or main stem bronkhus involvement
M1	Tumor<3cm without pleural or main stem bronkhus involvement

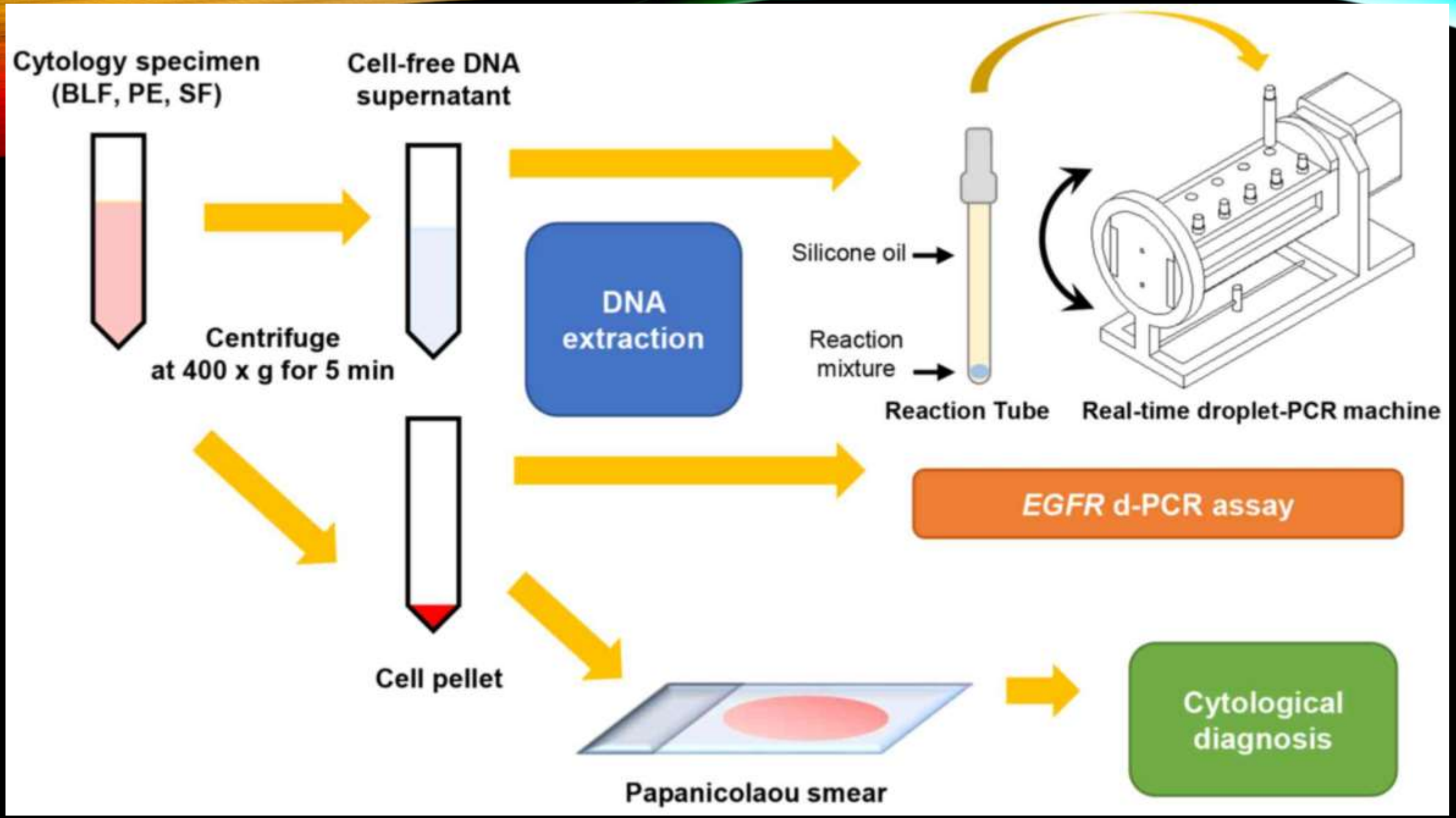
DIAGNOSIS & THERAPY LUNG CANCER

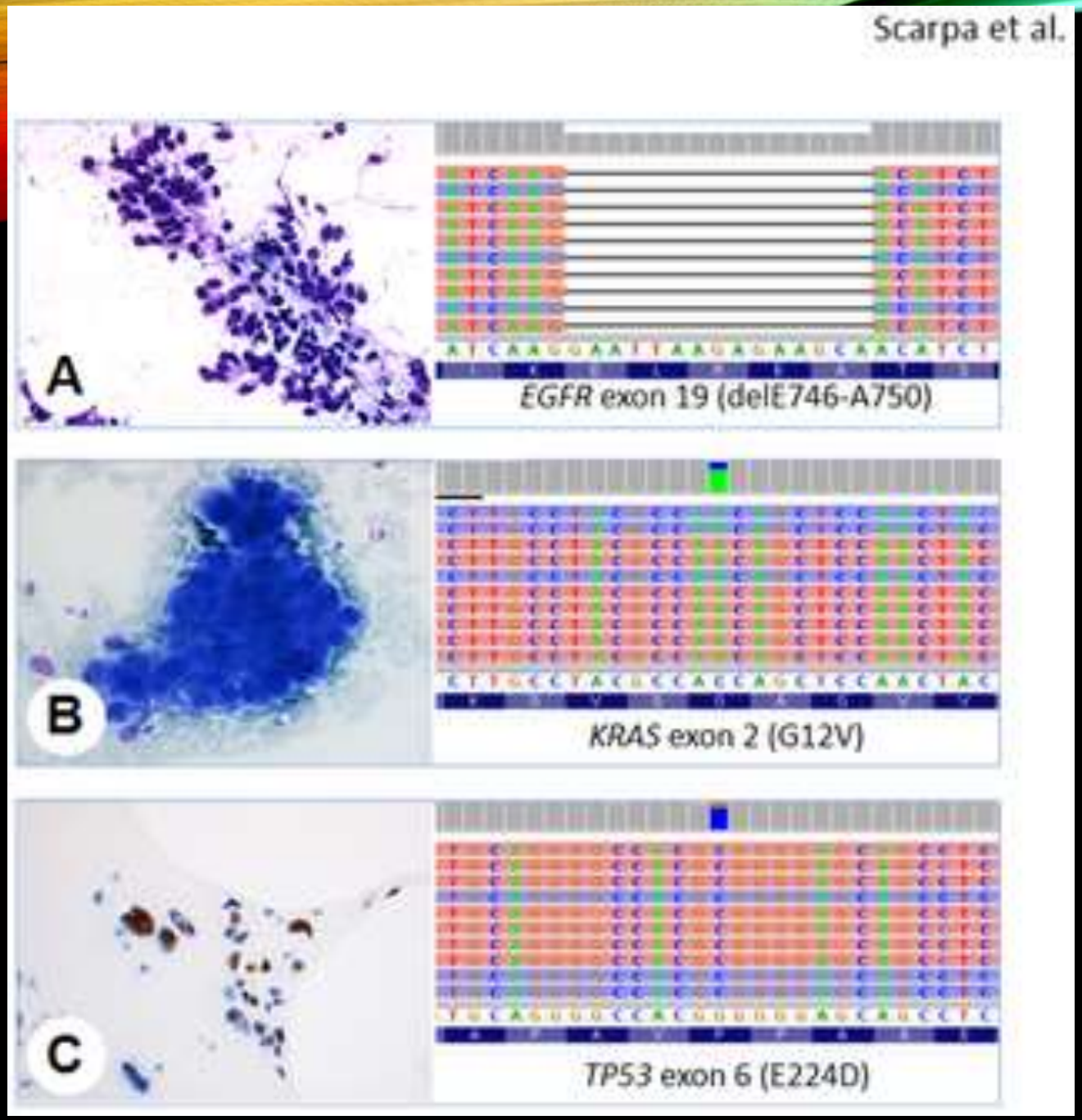
Biomarkers *allow physicians to classify patients by their probable disease risk, prognosis and/or response to treatment*

Insights into biomarkers analysis have resulted in scientists being able to understand **the diversity of lung cancer** better than ever before

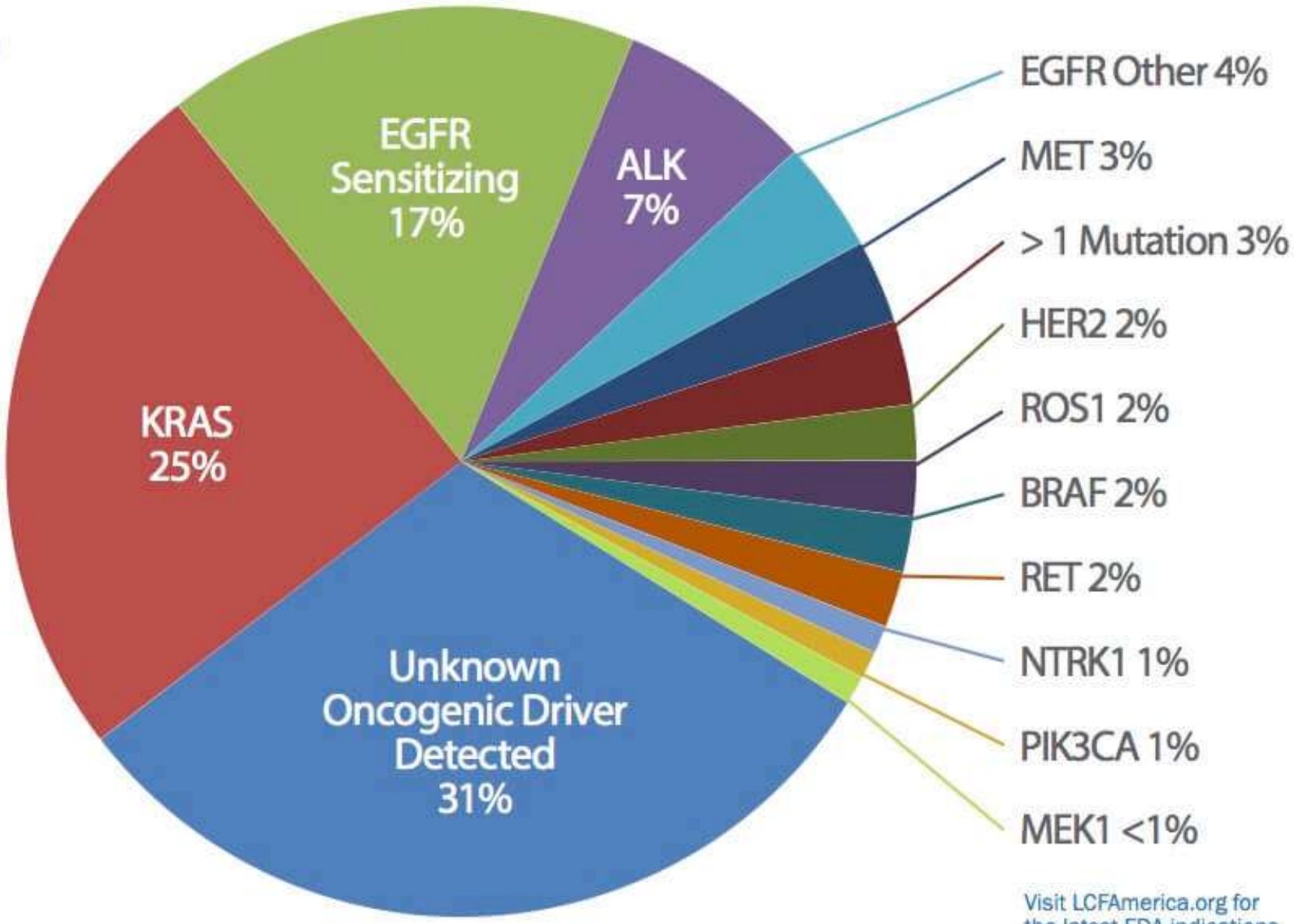
References: Vargas AJ & Harris CC. Biomarker development in the precision medicine era: lung cancer as a case study. Nature Reviews Cancer. 2016:16:525-537 **Document ID: Z4-9122 Date of preparation: February 2018 Date of expiry: February 2020**

MedImmune AstraZeneca


Cytology specimen
(BLF, PE, SF)
Cell-free DNA
supernatant
Centrifuge
at 400 x g for 5 min
DNA
extraction
Silicone oil
Reaction
mixture
Reaction Tube
Real-time droplet-PCR machine
EGFR d-PCR assay
Cell pellet
Papanicolaou smear
Cytological
diagnosis



MOLECULAR TYPING OF LUNG ADENOCARCINOMA ON CYTOLOGICAL SAMPLES USING A MULTIGENE NEXT GENERATION SEQUENCING PANEL


EGFR Sensitizing 17%
ALK 7%
KRAS 25%
Unknown Oncogenic Driver Detected 31%
EGFR Other 4%
MET 3%
> 1 Mutation 3%
HER2 2%
ROS1 2%
BRAF 2%
RET 2%
NTRK1 1%
PIK3CA 1%
MEK1 <1%
Visit LCFAmerica.org for the latest FDA indications.

MOLECULAR / CYTOGENETICS DESCRIPTION

- Due to targeted therapy, molecular testing is routine
- Epidermal growth factor receptor (EGFR) mutations:
  - 10-15% of lung adenocarcinoma
  - More common in never smokers, females
- Tumors with EGFR mutation are responsive to treatment with tyrosine kinase inhibitors (Science 2004;304:1497)

MOLECULAR / CYTOGENETICS DESCRIPTION

- Kras mutation found in 15-25%
- More common in smokers
- Patients with Kras mutation have a poorer prognosis and are resistant to EGFR-tyrosine kinase inhibitors (Proc Am Thorac Soc 2009;6:201)

MOLECULAR / CYTOGENETICS DESCRIPTION

- Fusion between echinoderm microtubule-associated protein like 4 (EML4) and ALK:
- Present in 2-7%
- More common in nonsmokers or light smokers
- Patients with ALK rearrangement benefit from treatment with ALK inhibitors

EGFR, KRAS AND ALK MUTATIONS ARE MUTUALLY EXCLUSIVE

MOLECULAR / CYTOGENETICS DESCRIPTION

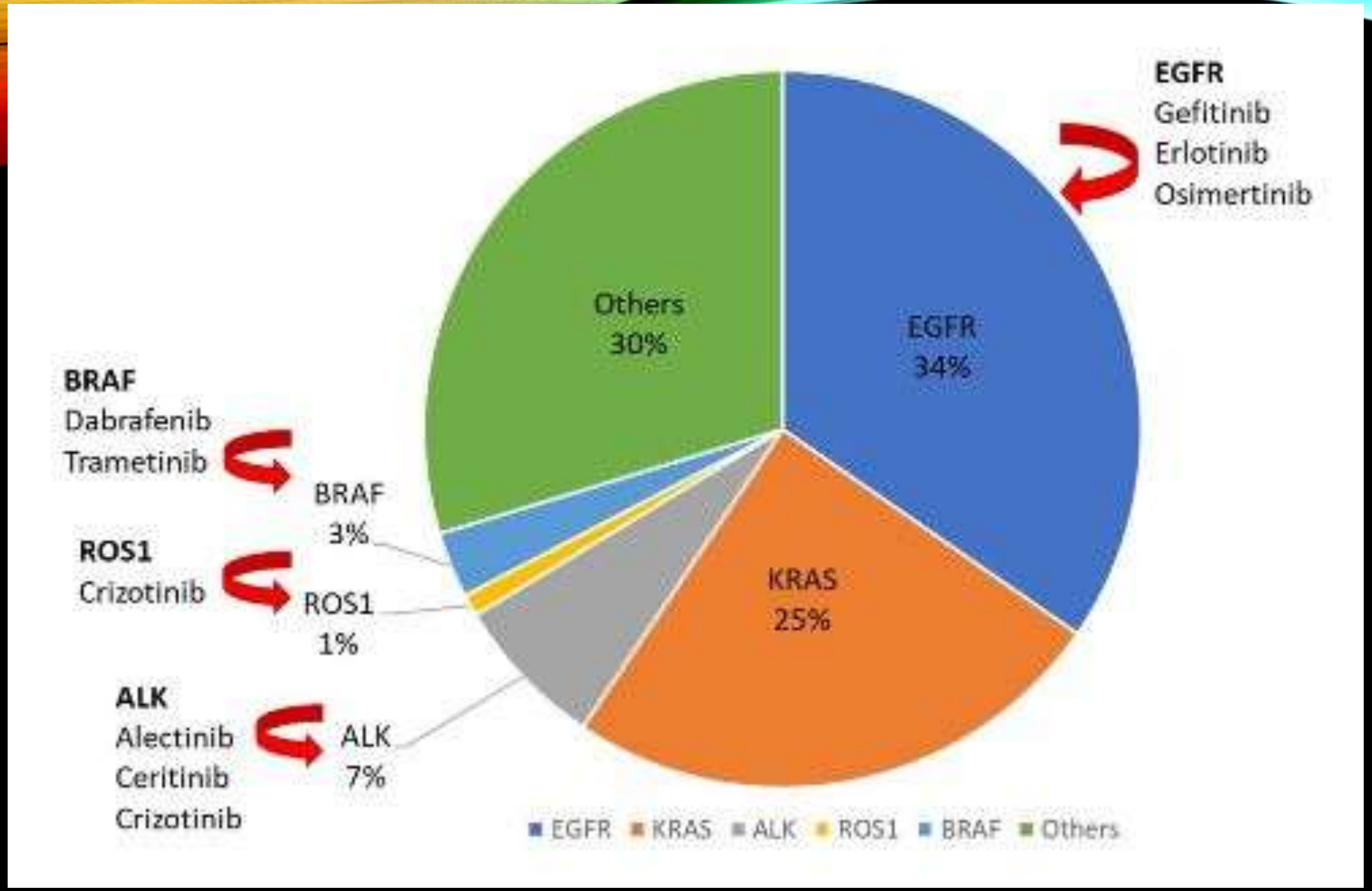
- Met is a heterodimere receptor tyrosine kinase involved in organogenesis
- Met amplification is associated with poor prognosis and EGFR acquired resistance
- Several Met inhibitors have demonstrated beneficial effect in treatment of NSCLC (Transl Lung Cancer Res 2013;2(1))

TARGETED THERAPIES

HTTPS://LCFAMERICA.ORG/RESEARCH-GRANTS/THERAPIES/AVAILABLE-TARGETED-THERAPIES
HTTPS://WWW.CANCER.ORG/CANCER/LUNG-CANCER/TREATING-NON-SMALL-CELL/TARGETED-THERAPIES.HTML

- EGFR (EPIDERMAL GROWTH FACTOR RECEPTOR)
- ALK (ANAPLASTIC LYMPHOMA KINASE)
- KRAS
- ROS1

- VEGF
- HER2 –
- MET –
- RET
- IGF1R –
- BRAF
- PIK3CA –
- ERBB2 –
- PD-L1


EGFR
Gefitinib
Erlotinib
Osimertinib
Others
30%
EGFR
34%
BRAF
Dabrafenib
Trametinib
BRAF
3%
ROS1
Crizotinib
ROS1
1%
KRAS
25%
ALK
Alectinib
Ceritinib
Crizotinib
ALK
7%
EGFR KRAS ALK ROS1 BRAF Others

Successful treatment of non-small-cell lung cancer with afatinib and a glucocorticoid following gefitinib- and erlotinib-induced interstitial lung disease: A case report

TETSUO TANI[1], KATSUHIKO NAOKI[2], TAKANOBU ASAKURA[1], TOSHIYUKI HIRANO[2], SHOJI SUZUKI[1], KEITA MASUZAWA[1], HANAKO HASEGAWA[1], AOI KUBODA[1], HIROYUKI YASUDA[1], MAKOTO ISHII[1], KENZO SOEJIMA[1] and TOMOKO BETSUYAKU[1]

[1]Division of Pulmonary Medicine, Department of Medicine, [2]Cancer Center, Keio University School of Medicine, Shinjuku, Tokyo 160-8582, Japan

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DOI: 10.3892/mco.2016.981

Abstract. Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI)-induced interstitial lung disease (ILD) may be a life-threatening condition that may develop during treatment of lung cancer patients harboring EGFR mutations. We herein present the case of a 41-year-old female patient diagnosed with lung adenocarcinoma with an EGFR mutation (exon 19 deletion). The patient was treated with gefitinib followed by erlotinib and developed ILD induced by both EGFR-TKIs; furthermore, the patient acquired resistance to EGFR-TKI treatment. A repeat biopsy revealed a T790M mutation, which is associated with resistance to first-generation EGFR-TKIs, along with an exon 19 deletion identified by cytology of the pleural fluid. Treatment with afatinib and prednisolone resulted in tumor shrinkage, without worsening of the ILD. The present case demonstrated that combination treatment with afatinib and a glucocorticoid may be effective for the treatment of lung cancer patients who develop EGFR-TKI-induced ILD.

Introduction

Detection of epidermal growth factor receptor (EGFR) mutations in lung cancer patients is vital in order to predict the therapeutic response to EGFR-tyrosine kinase

the major mechanism underlying the development of resistance to first-generation EGFR-TKIs. Approximately half of EGFR-TKI-resistant cases are due to the EGFR-T790M mutation. Recent advances in drug research have led to the development of several novel EGFR-TKIs, including the pan-HER inhibitor afatinib and the EGFR mutation-specific inhibitor osimertinib (2). However, even with the emergence of these novel drugs, tumor heterogeneity remains an important issue when treating EGFR-TKI-resistant patients. Although the tumor characteristics are similar between the primary site and metastatic lesions (3), tumor heterogeneity has been reported even within the original tumor, or between primary and metastatic sites. Therefore, the same patient may develop EGFR-TKI resistance through different mechanisms at different sites (4).

EGFR-TKI-induced interstitial lung disease (ILD) represents a major issue with this type of treatment, and its incidence among Japanese patients is higher compared with that in other ethnicities (5). There is currently no established treatment for lung cancer patients with EGFR-TKI-induced ILD and EGFR-TKI resistance.

The present study reports a case of a lung cancer patient with an EGFR mutation conferring sensitivity to EGFR-TKIs, who was treated with gefitinib followed by erlotinib, resulting

https://www.spandidos-publications.com/10.3892/mco.2016.981

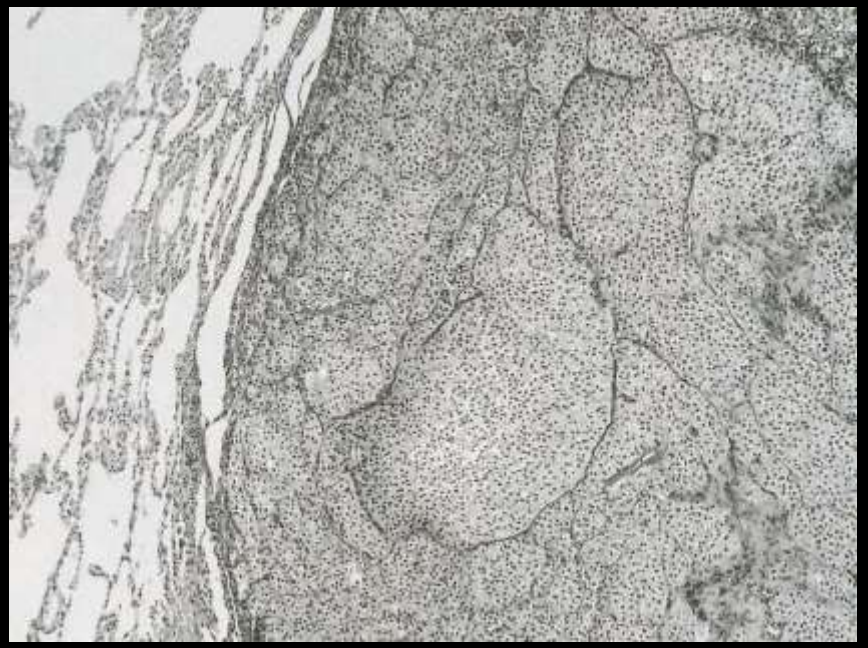
TUMOR METASTASIS TO LUNG

Table 25-1

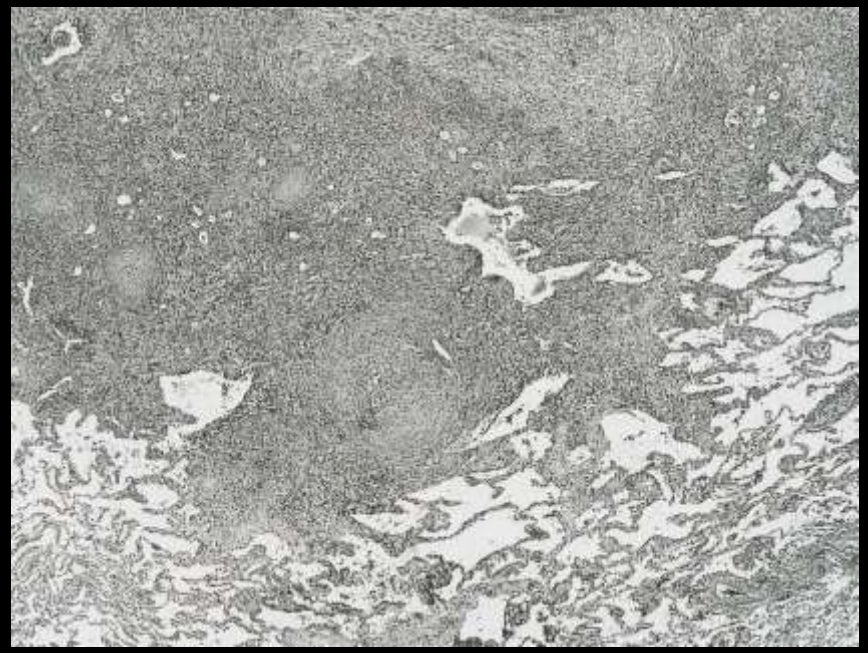
FREQUENCY OF METASTASES TO LUNG FOR SELECTED PRIMARY TUMORS*

Primary Tumor	Found at Autopsy (%)	Clinically Recognized Premortem (%)
Malignant melanoma	80	5 (2-5)**
Ewing sarcoma	77	18
Osteosarcoma	75	15
Germ cell tumors (testicular)	70-80	12
Choriocarcinoma (women)	70-100	60
Thyroid carcinoma	65	5-10
Breast carcinoma	60	5 (1-2)
Prostatic carcinoma	53	5
Rhabdomyosarcoma	55	21
Renal cell carcinoma	50-75	5-30
Colorectal carcinoma	40	5 (2)
Head and neck carcinoma†	40	5
Bladder carcinoma	30	5-10

THE BORDER OF THE METASTASIS TUMOR MASS



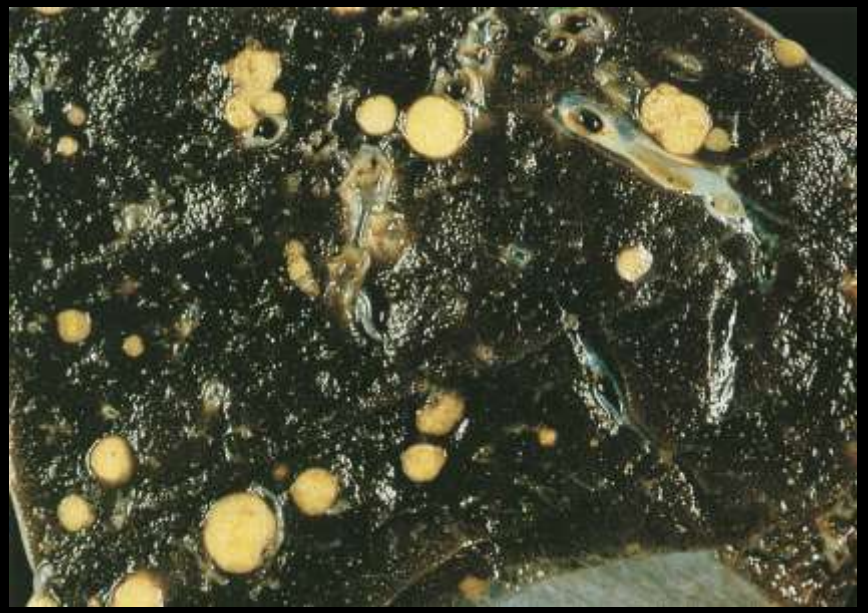
Alveolar soft part sarcoma, **well circumscribed with pushing border**. Metastases often have this appearance.



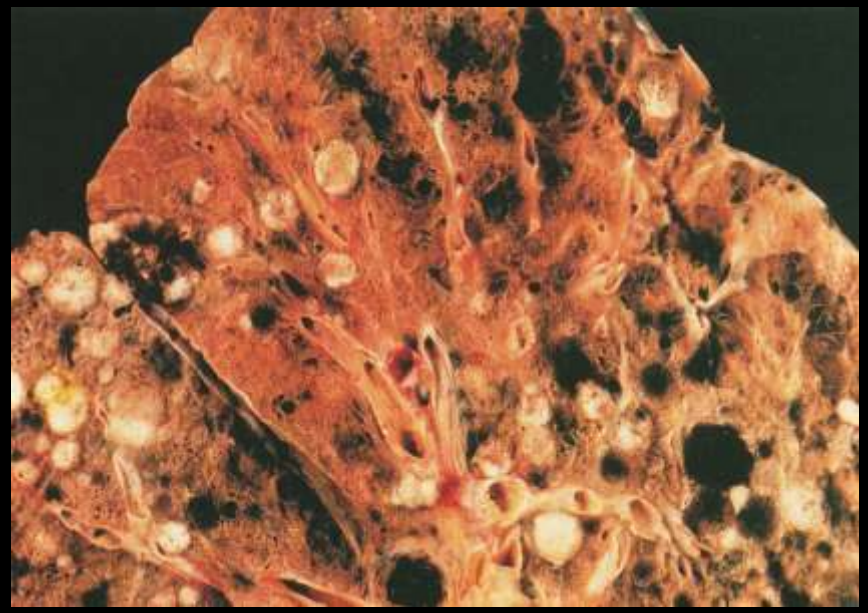
Irregular border: a nodule of metastatic leio-myosarcoma extends into the interstitium of the surrounding lung

PATTERN OF METASTASIS

MULTINODULAR METASTASIS



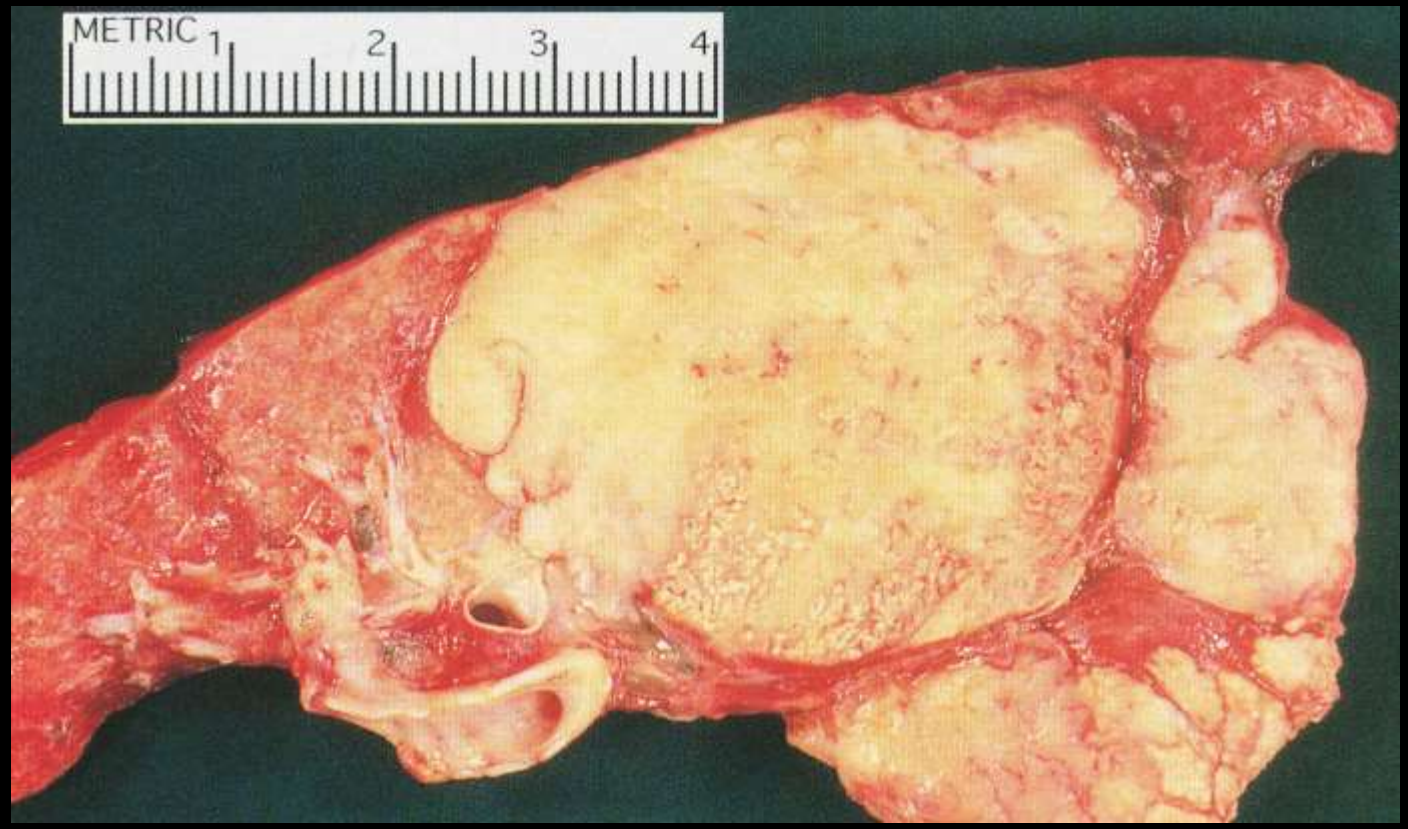
Yellow appearance to the metastatic nodules: abundant fat content of primary tumor: renal-cell carcinoma



Black appearance in some nodules: primary Tumor is malignant melanoma

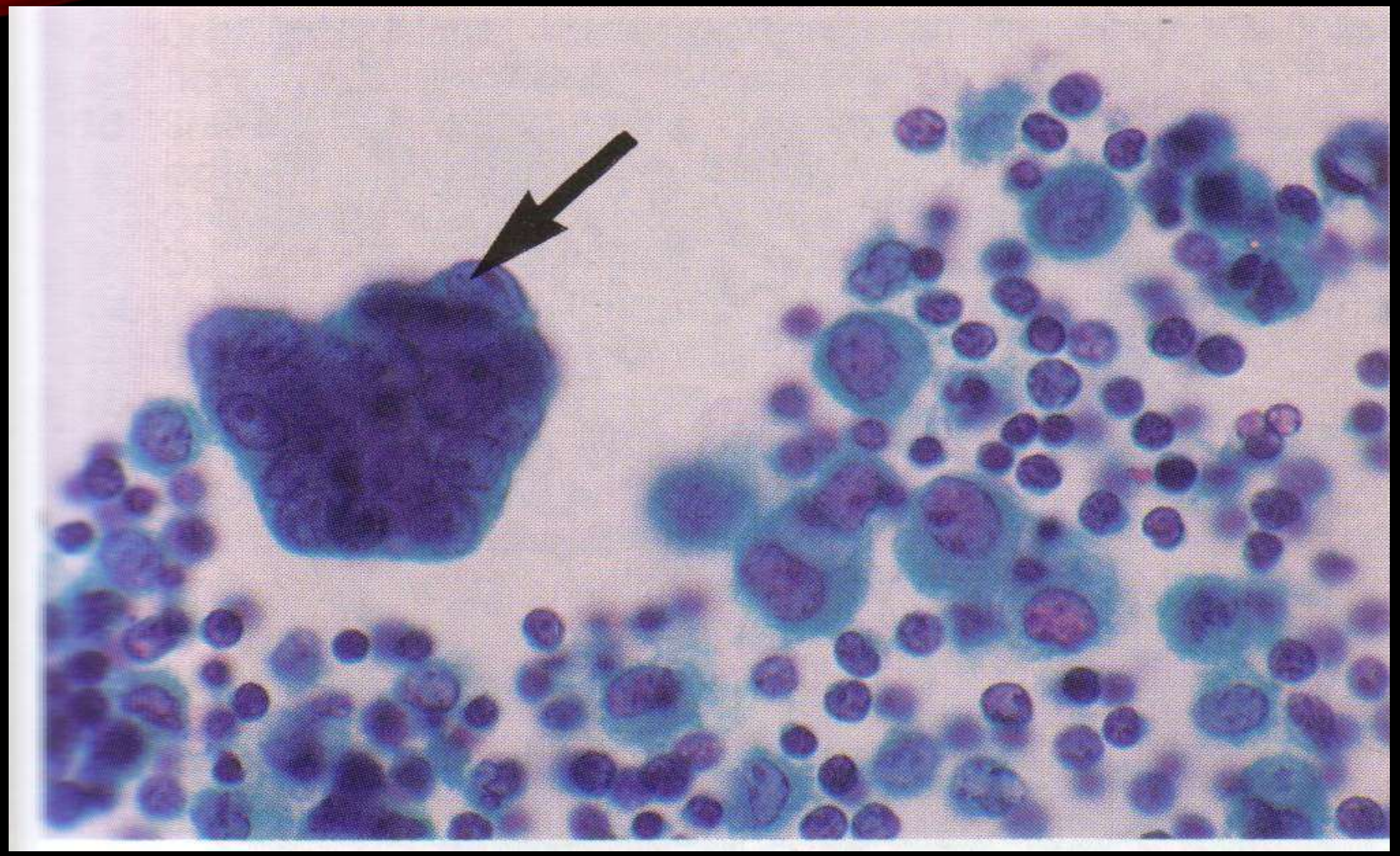
PATTERN OF METASTASIS

"CANNONBALL" METASTASIS



Primary tumor: osteogenic sarcoma. A variety of tumors: sarcoma, renal cell Ca, malignant melanoma, colorectal Ca, may produce this appearance

SECONDARY TUMORS (METASTASIS)



PARANEOPLASTIC SYNDROMES

Product	Syndromes
ADH	Hyponatremia owing to inappropriate ADH secretion
ACTH	Cushing syndrome
Parathormone, parathyroid hormone-related peptide, PGE, some cytokines	Hypercalcemia
Calcitonin	Hypocalcemia
Gonadotropins	Gynecomastia
Serotonin & bradikinin	Carcinoid syndrome
Autoantibodies	Lambert-Eaton myasthenic syndrome, peripheral neuropathy, acanthosis nigricans, leukemoid reactions, hypertnesive pulmonary arthropathy

LOCAL EFFECTS OF LUNG TUMOR SPREAD

Clinical Feature	Pathologic Basis
Pneumonia, abscess, lobar collaps	Tumor obstruction of airway
Lipid pneumonia	Tumor obstruction; accumulation of cellular lipid in foamy macrophages
Pleural effusion	Tumor spread to pleura
Hoarseness	Recurrent laryngeal nerve invasion
Dysphagia	Esophageal invasion
Diaphragm paralysis	Phrenic nerve invasion
Rib destruction	Chest wall invasion
SVC syndrome	SVC compression by tumor
Horner syndrome	Sympathetic ganglia invasion
Pericarditis tamponade	Pericardial involvement

PLEURA

http://www.pathologyoutlines.com/topic/testismesotheliomamalignant.html

PLEURA

Pneumotorak: - tertutup
- terbuka
- tension pneumothorax

Efusi pleura

- keadaan umum yang berhubungan dengan ketidakseimbangan sodium dan protein (gagal jantung kongestif, sindroma nefrotik)
- peningkatan tekanan kapilar pulmonar (gagal jantung kiri akut, trombosis paru venosa)
- peningkatan permeabilitas kapilar pleura (radang)
- penurunan drainage limfatik pleural (radang pleura parietalis, infiltrasi tumor pada aluran limfe)

Neoplasma

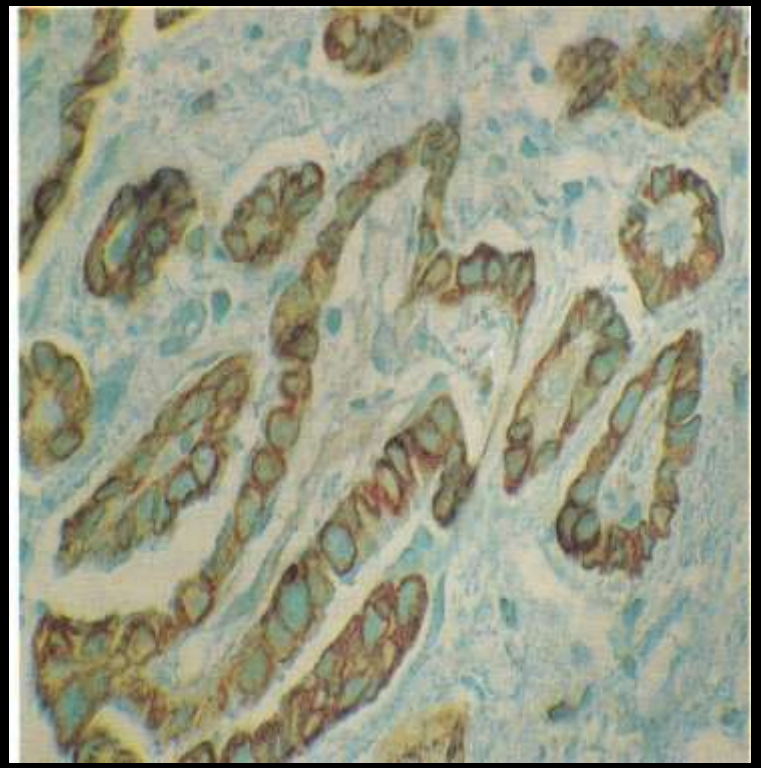
Mesotelioma

PLEURAL SPACE FLUID ACCUMULATION

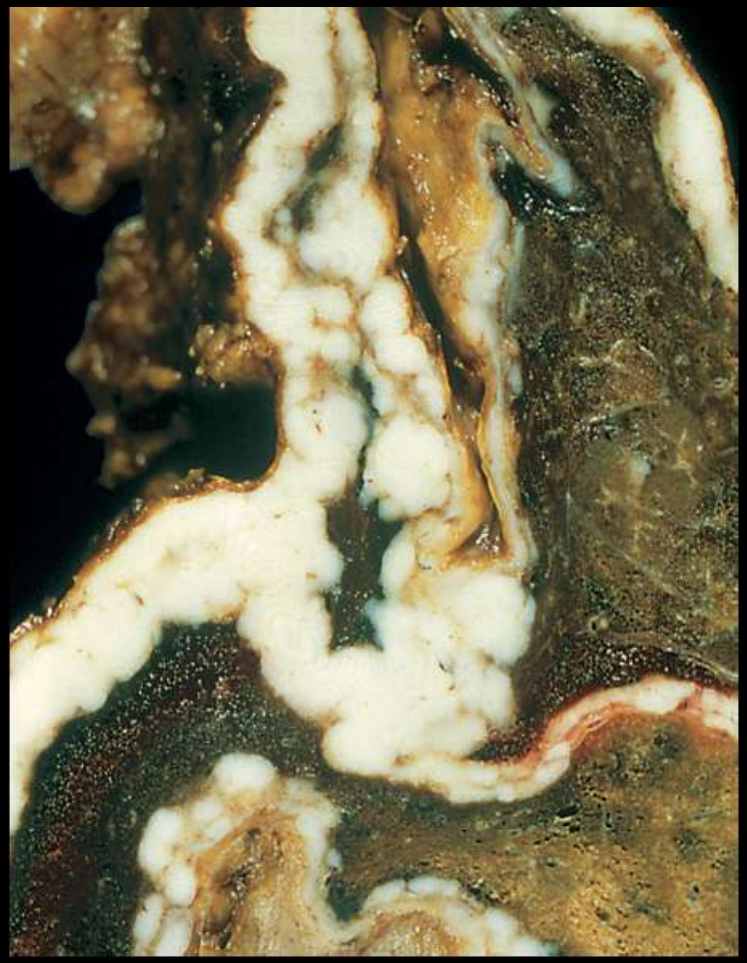
Condition	Type of Fluid	Common Association
Inflammatory		
Serofibrinous pleuritis	Serofibrinous exudate	Inflammatory in adjacent lung Collagen vascular disease
Suppurative pleuritis (empyema)	Pus	Suppurative infection in adjacent lung
Hemorrhagic pleuritis	Bloody exudate	Tumor
Non-inflammatory		
Hydrothorax	Transudate	Congestive heart failure
Hemothorax	Blood	Ruptured aortic aneuryasm, trauma
Chylothorax	Chyle (lymph)	Tumor obstruction of normal lymphatics

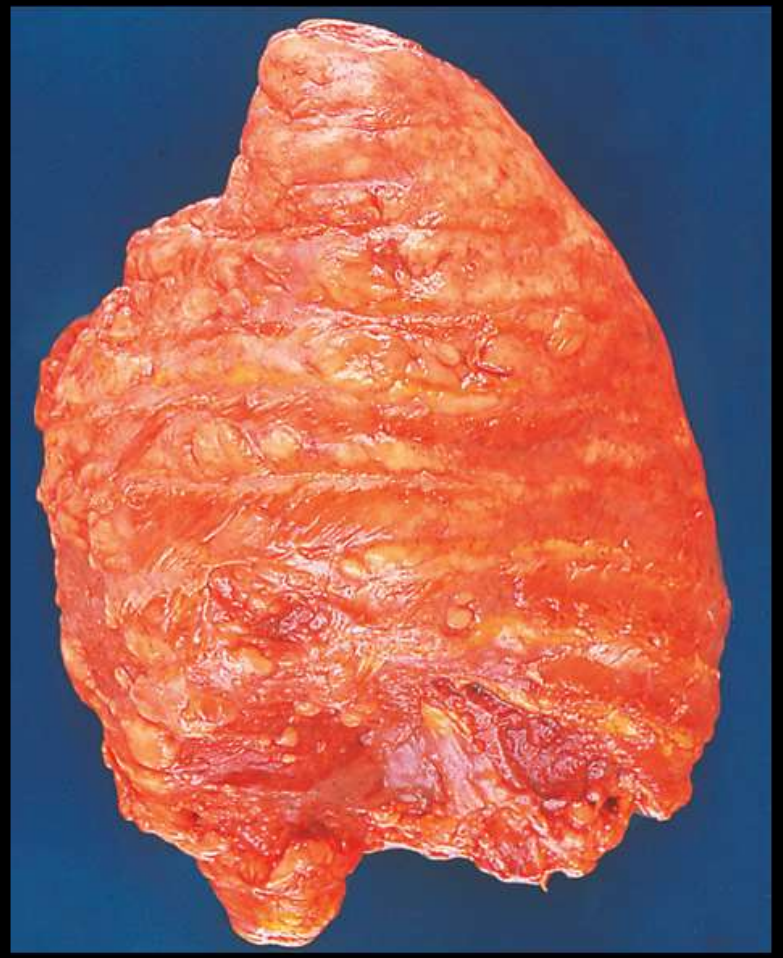
PLEURAL TUMORS

Mesothelioma

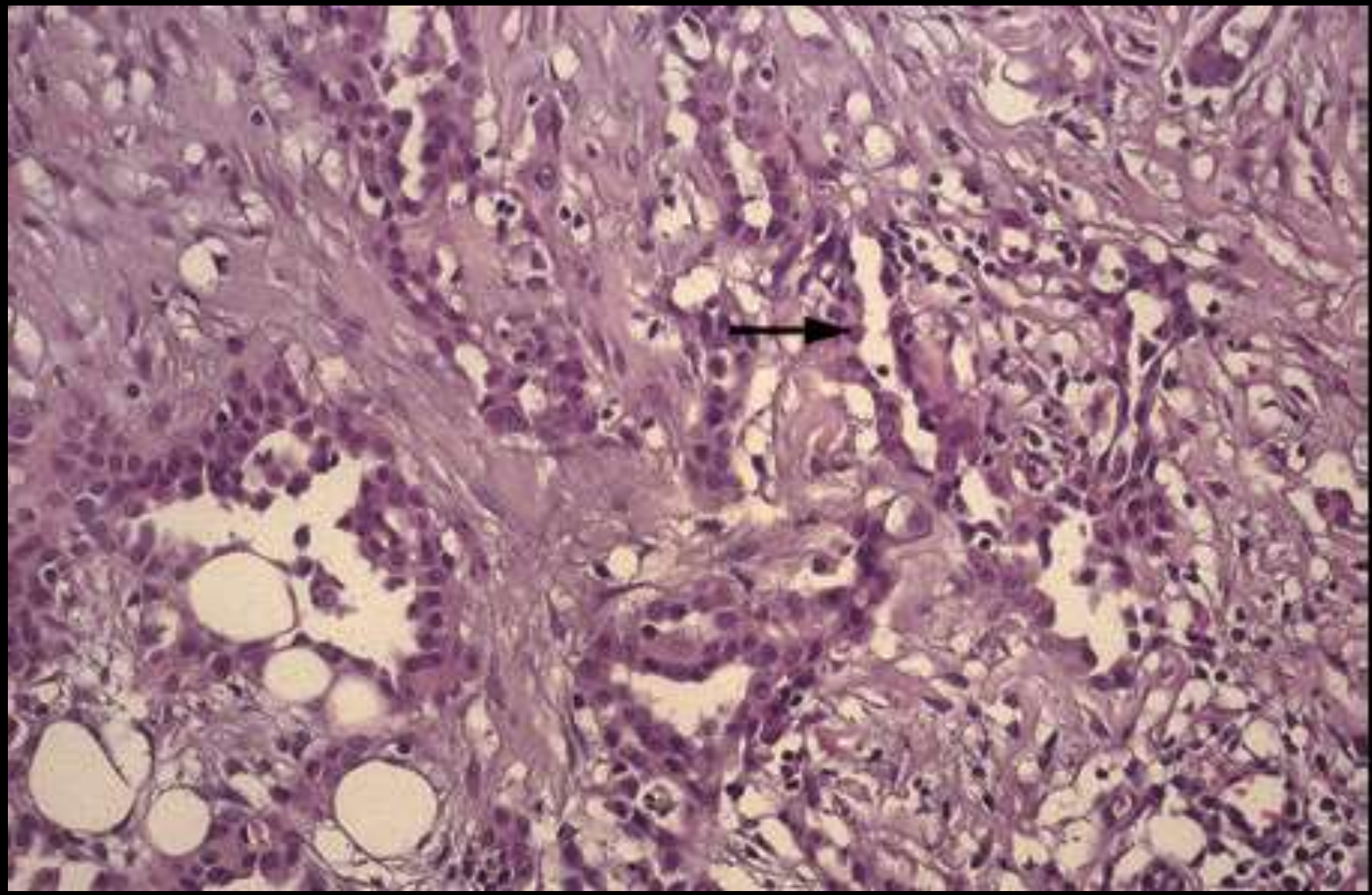


PLEURAL MESOTHELIOMA

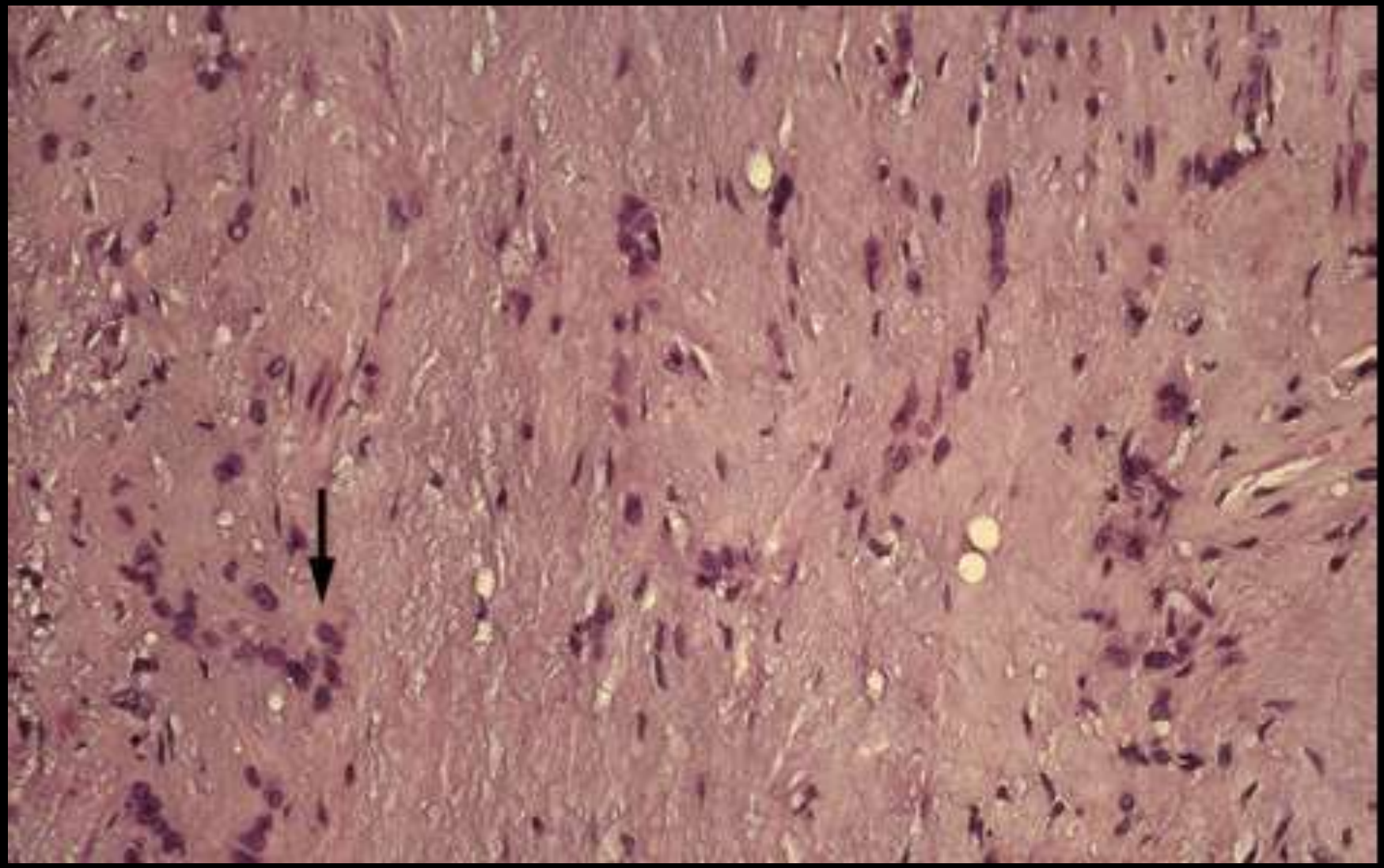




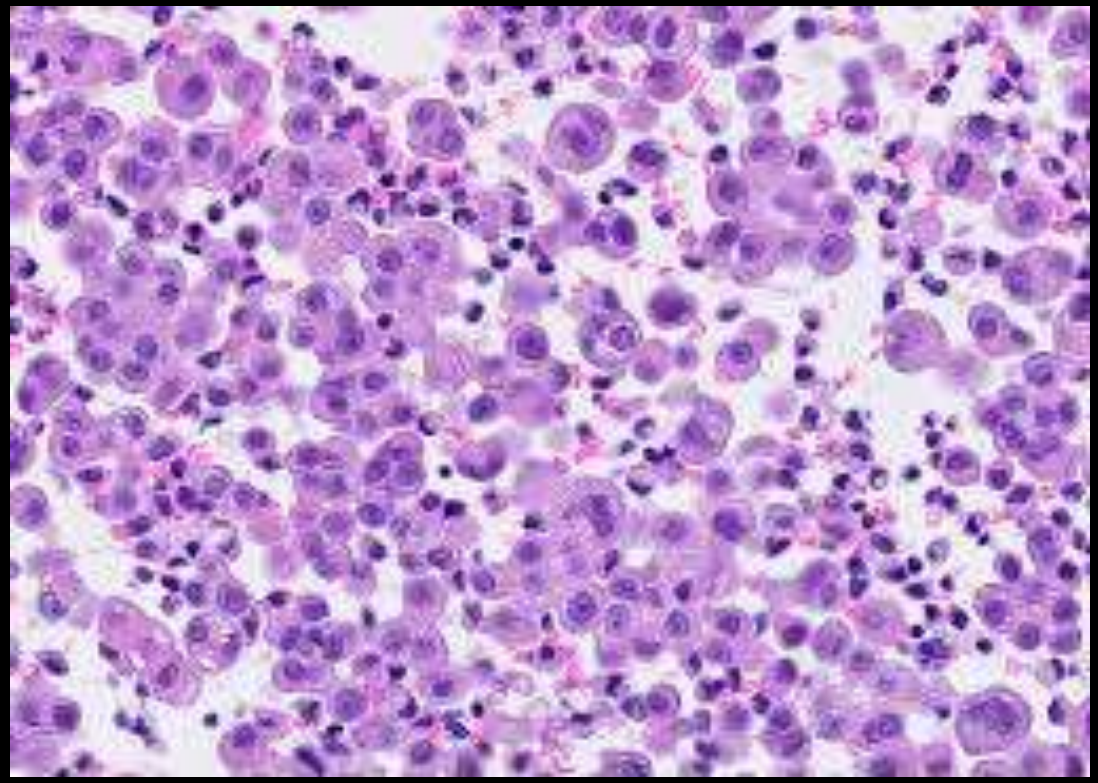
EPITHELIAL MESOTHELIOMA

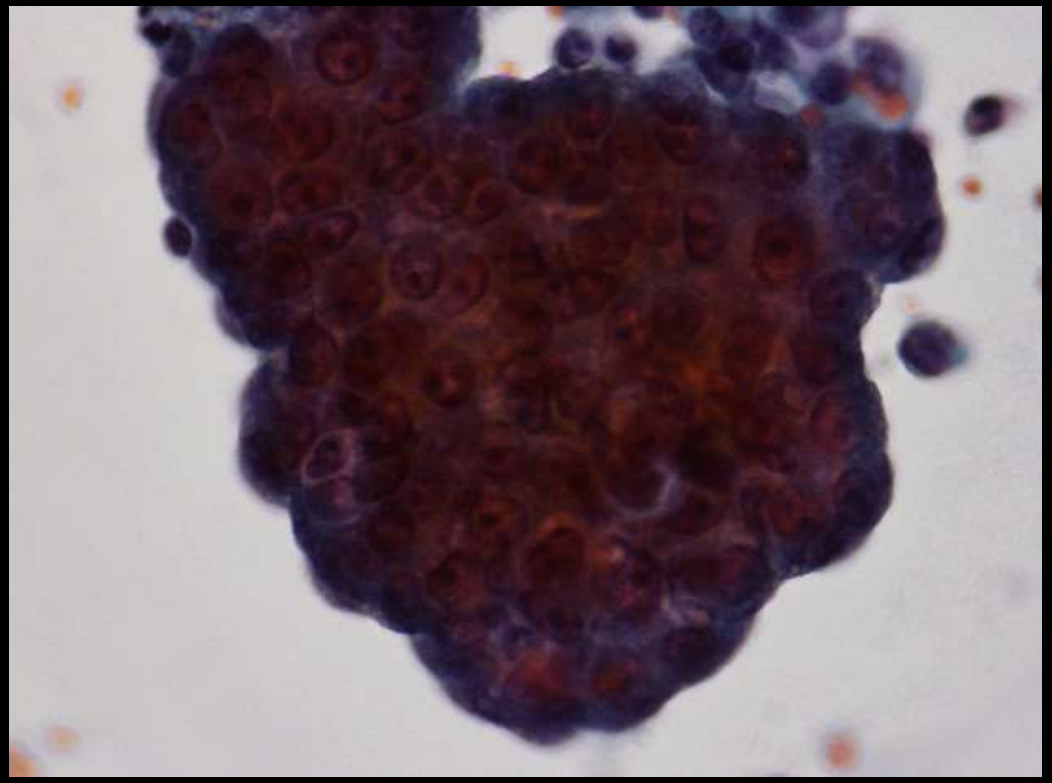


SARCOMATOUS MESOTHELIOMA



SITOLOGI CAIRAN PLEURA





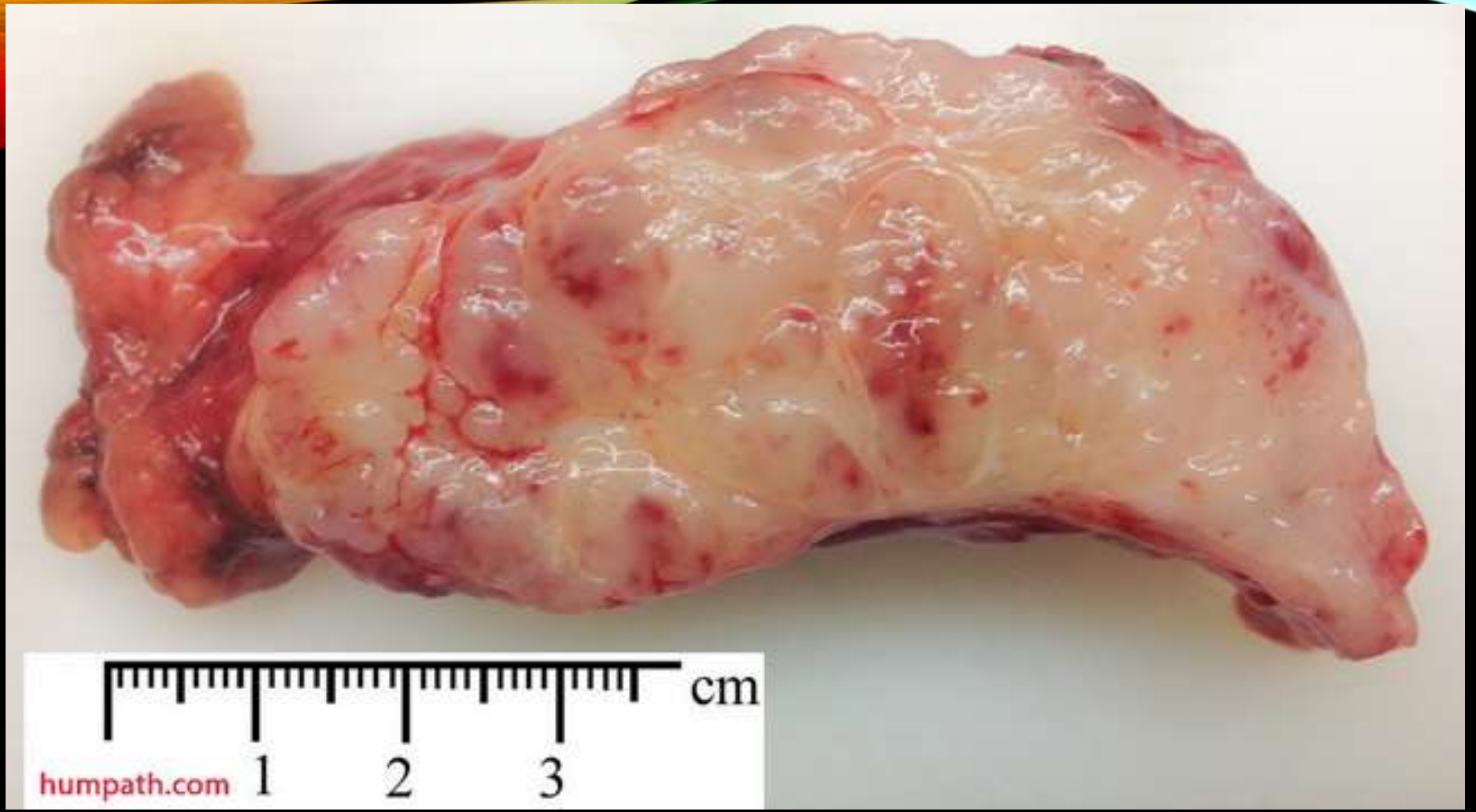
Mikroskopis sitologi cairan pleura mesothelioma dengan pulasan HE dan calretinin

MEDIASTINAL TUMORS & OTHER MASSES

Superior Mediastinum	Posterior Mediastinum
•Lymphoma •Thymoma •Thyroid lesions •Metastatic carcinoma •Parathyroid tumors	•Neurogenic tumors (schwannoma, neurofibroma) •Lymphoma •Gastroenteric hernia
Anterior Mediastinum	**Middle mediastinum**
•Thymoma •Teratoma •Lymphoma •Thyroid lesions •Parathyroid tumors	•Bronchogenic cyst •Pericard cyst •Lymphoma

THYMOMA

http://www.pathologyoutlines.com/topic/mediastinumthymoma.html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humpath.com
1
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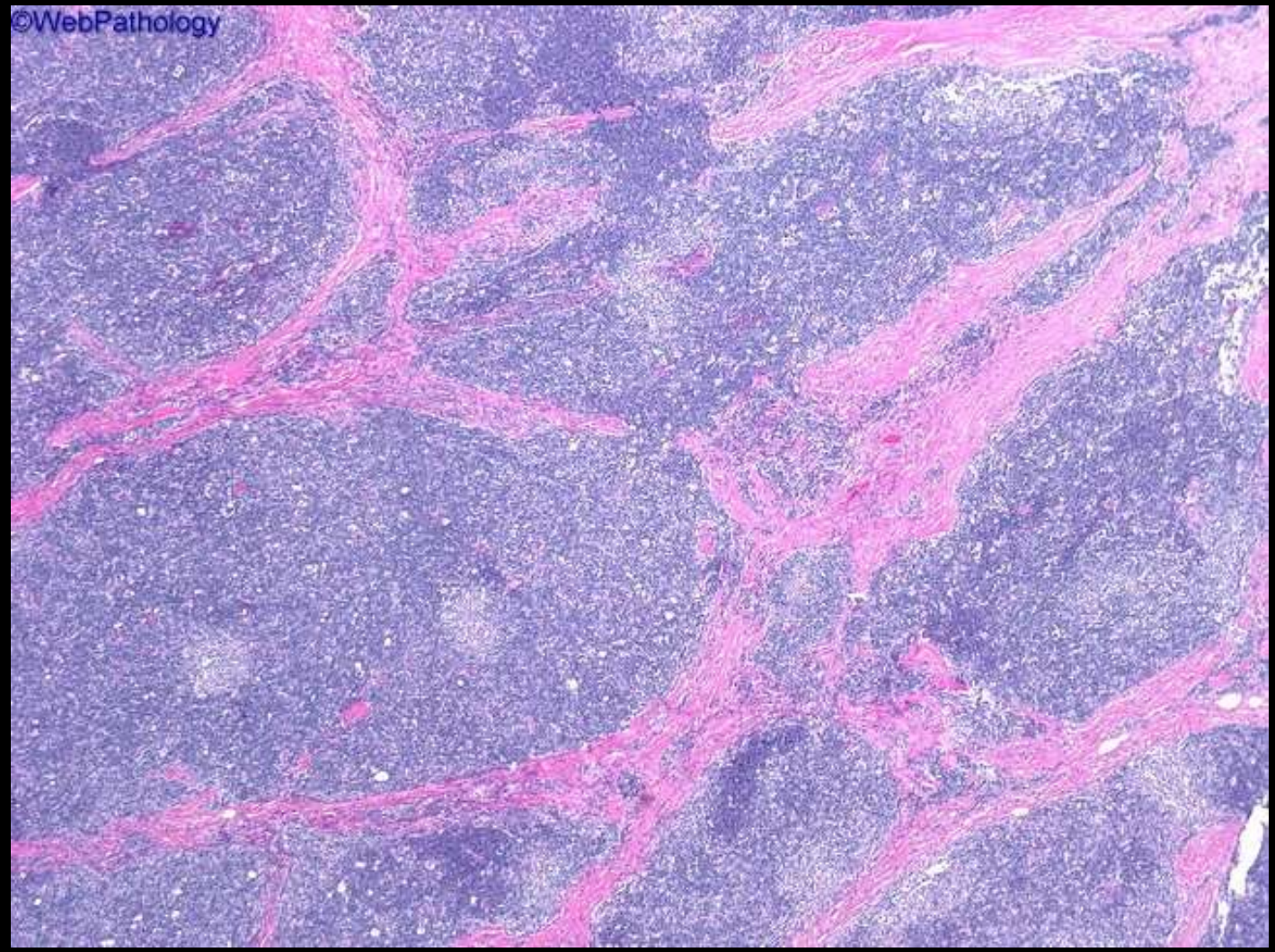
THYMOMAS

Thymomas have lobulated architecture with fibrous bands separating individual lobules as seen in this low power view. Some lobules may have angulated contours. The lobules are composed of neoplastic epithelial cells and non-neoplastic lymphocytes in varying proportions. The lymphocytes of thymoma are of T-cell derivation and have the phenotype of immature thymocytes, including positivity for TdT, CD99, and CD1a.



CLINICAL FEATURES

- Associated with myasthenia gravis (MG) (10% with MG have thymoma, 30 - 45% with thymoma develop MG, higher risk for MG if lymphoid follicles are present in thymoma or adjacent thymus)
- Associated with other immune mediated disorders: acquired hypogammaglobulinemia (12%), aplastic anemia, pure anerythrogenesis, dermatomyositis, leukemia, lymphoma, lymphopenia, motor neuropathy, mucocutaneous candidiasis, myeloma, myocarditis, myositis, relapsing polychondritis, rheumatoid arthritis, scleroderma, Sjögren disease, syndrome of inappropriate antidiuretic hormone secretion, systemic lupus erythematosus
- Patients with thymomas have increased risk of developing additional malignancies, especially thymomas with predominantly cortical component (Histopathology 2012;60:437)
- All thymic tumors, regardless of histology, are associated with invasion and metastases (Mod Pathol 2012;25:370)
- Although much emphasis in recent years has been placed on the histological classification of thymoma, the bulk of the evidence continues to point to clinical staging as the most important parameter for prognostication (J Clin Pathol 2006;59:1238)

MICROSCOPIC (HISTOLOGIC) DESCRIPTION

- Spindle cell histologic patterns have indolent behavior, may be associated with hematologic malignancies
- Non spindle cell thymomas are also called cortical thymomas
- Cytologically bland epithelial cells and nonneoplastic lymphocytes
- Capsule may be thick and calcified
- May have prominent vasculature, microcystic and pseudopapillary patterns, extensive sclerosis
- Rarely has marked plasma cell infiltrate, amyloid, rosettes without central lumina
- Usually no well formed Hassall corpuscles
- Thymoma with pseudosarcomatous stroma: highly cellular spindle cell proliferation without nuclear atypia (Am J Surg Pathol 1997;21:1316)

A: EPITHELIAL,
AB: MIXED THYMOMA
B1: LYMPHOCYTE RICH;
B2: CORTICAL
B3: EPITHELIAL CELLS
C: THYMIC CARCINOMA

A: also called epithelial, spindle cell, medullary; atrophic, mimics adult thymus; homogenous population of neoplastic epithelial cells with spindle / oval shape, no nuclear atypia and accompanied by few or no nonneoplastic lymphocytes

AB: mixed thymoma; tumor in which foci having the features of type A thymoma are mixed with foci rich in lymphocytes; the segregation of the two patterns can be sharp or indistinct (Am J Surg Pathol 1999;23:955)

B: bioreactive, resembles thymus in fetus and infant

B1: lymphocyte rich; resembles normal functional thymus by combining large expanses having normal thymic cortical areas with those resembling thymic medulla

B2: cortical; neoplastic epithelial component appears as scattered plump cells with vesicular nuclei, distinct nucleoli; heavy population of lymphocytes, perivascular spaces are common

B3: epithelial cells with round / polygonal shape and mild atypia, mixed with minor component of lymphocytes; foci of squamous metaplasia and perivascular spaces common

C: thymic carcinoma