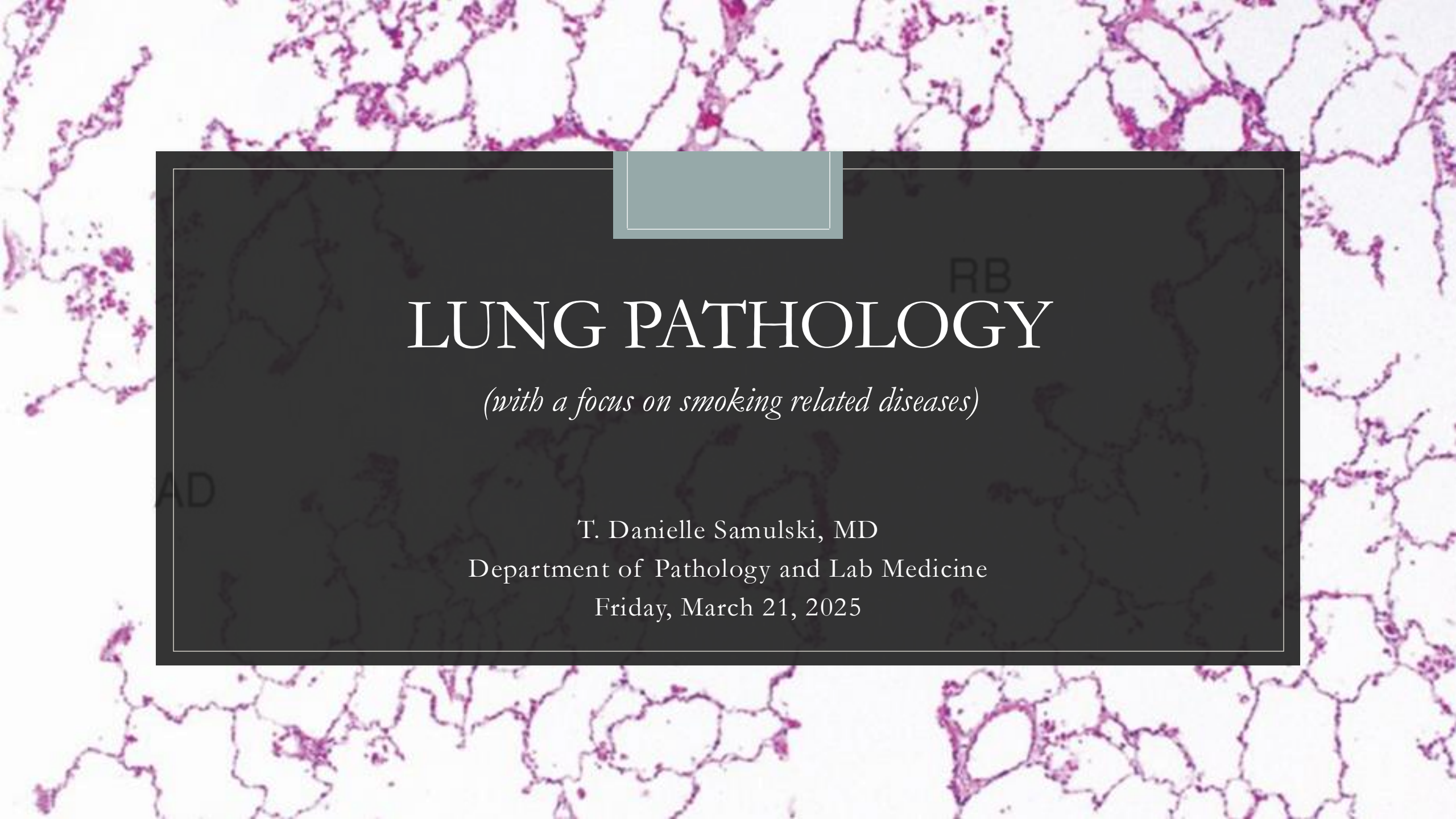

LUNG PATHOLOGY

(with a focus on smoking related diseases)

T. Danielle Samulski, MD
Department of Pathology and Lab Medicine
Friday, March 21, 2025

Outline

- Basic Anatomy and Histology of the Lung
- Impact of Smoking Related Disease
- Emphysema
- Lung Cancer

Outline

- **Basic Anatomy and Histology of the Lung**
- Impact of Smoking Related Disease
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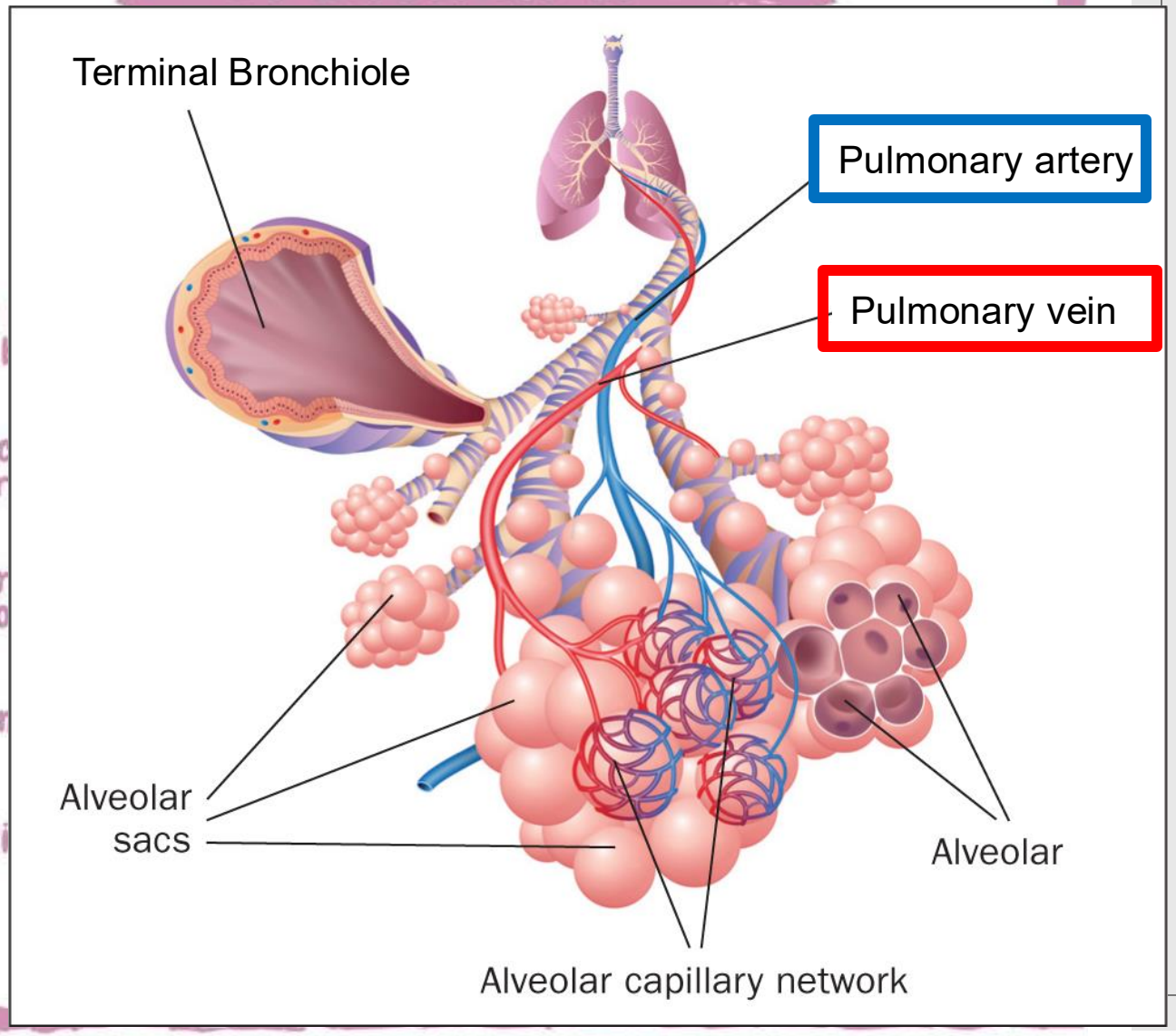
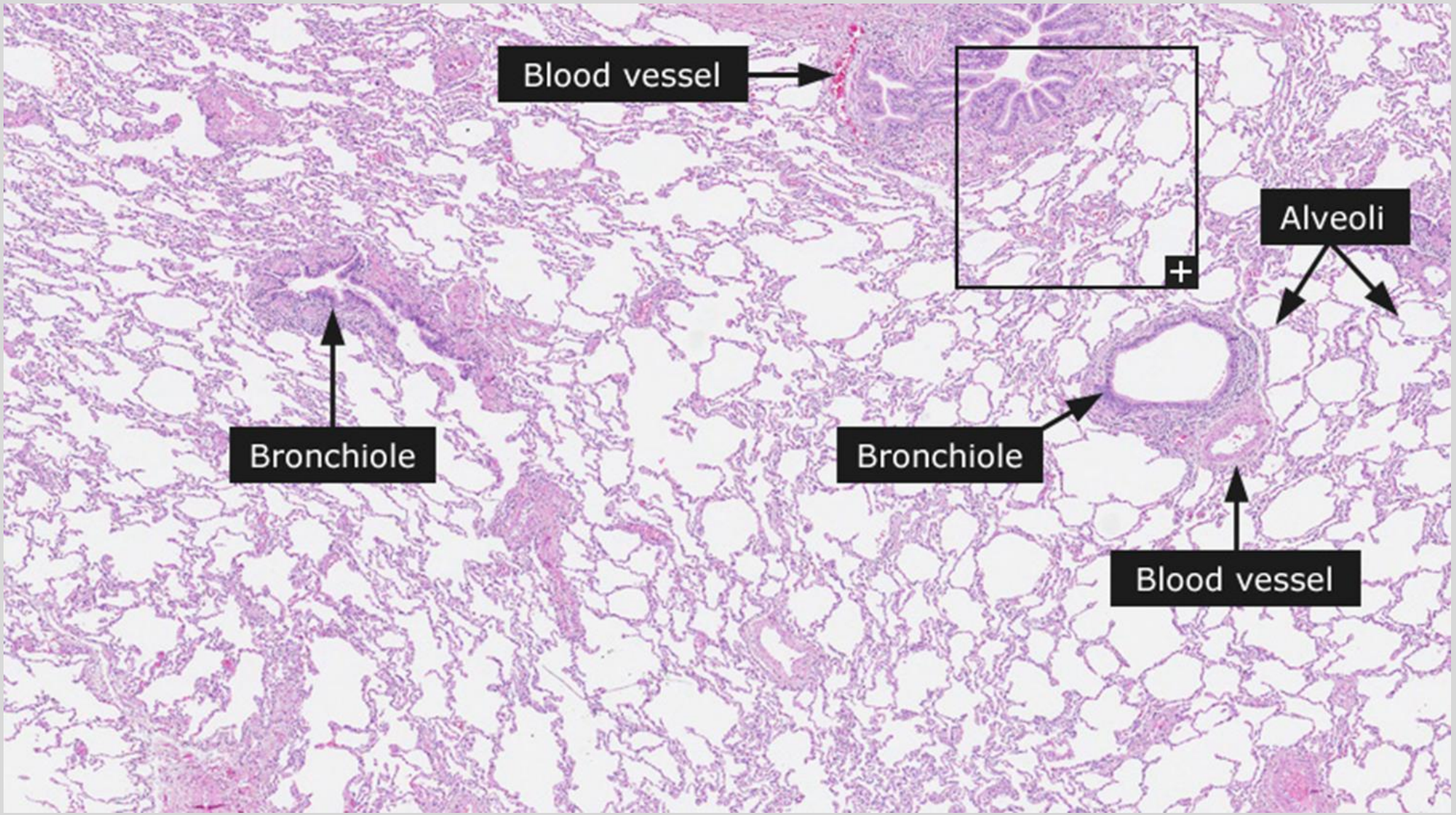
Bronchial Tree



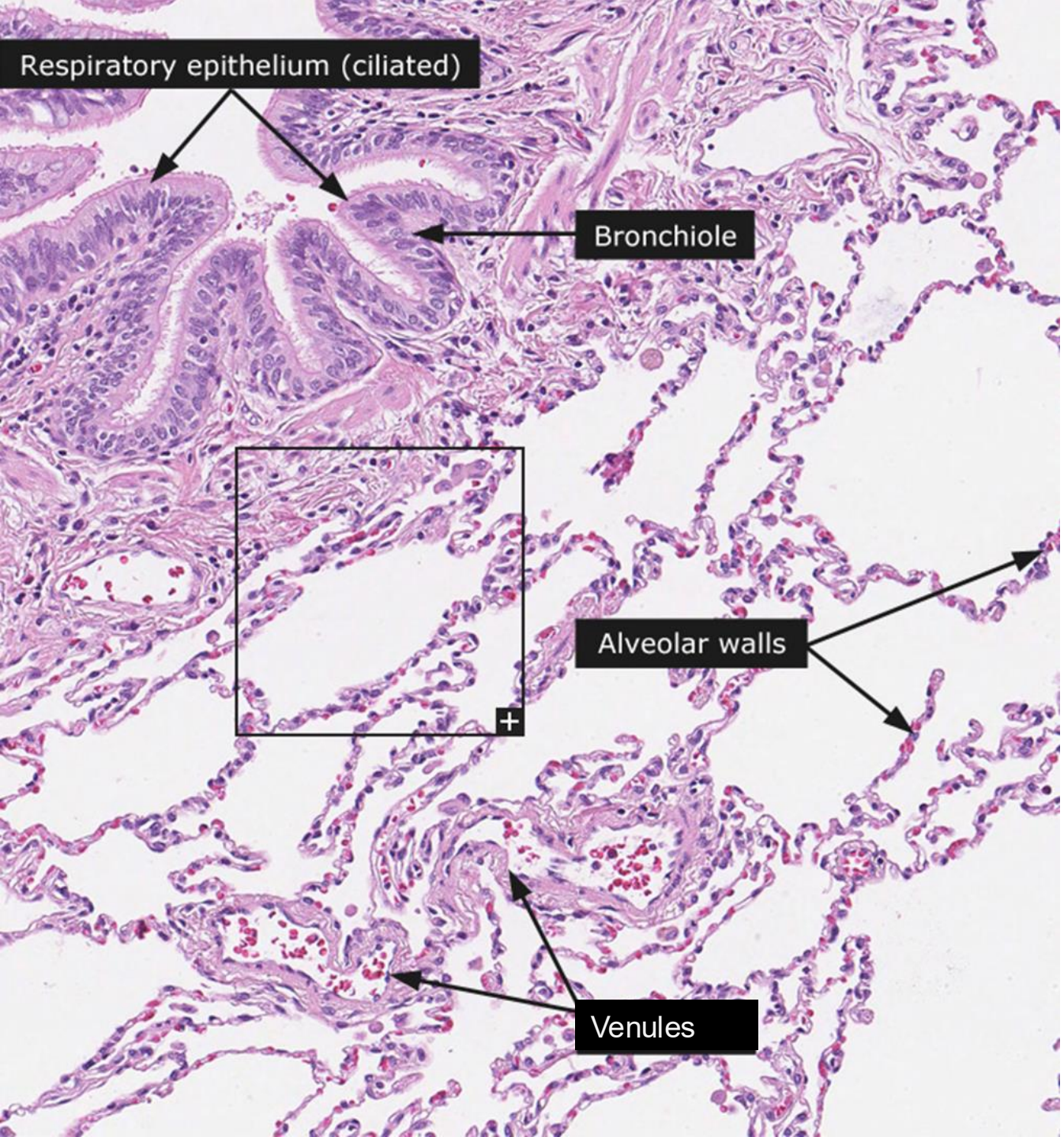
Basic Anatomy

- Branching of the **bronchial tree**
- Transition to **Alveoli**
- Blood from right ventrical --> **pulmonary artery** is DEOXGENATED
- Blood leaving alveolar capillary --> **pulmonary vein** is OXYGENATED

Br J Nurs. 2023 Jul 6;32(13):613-619.

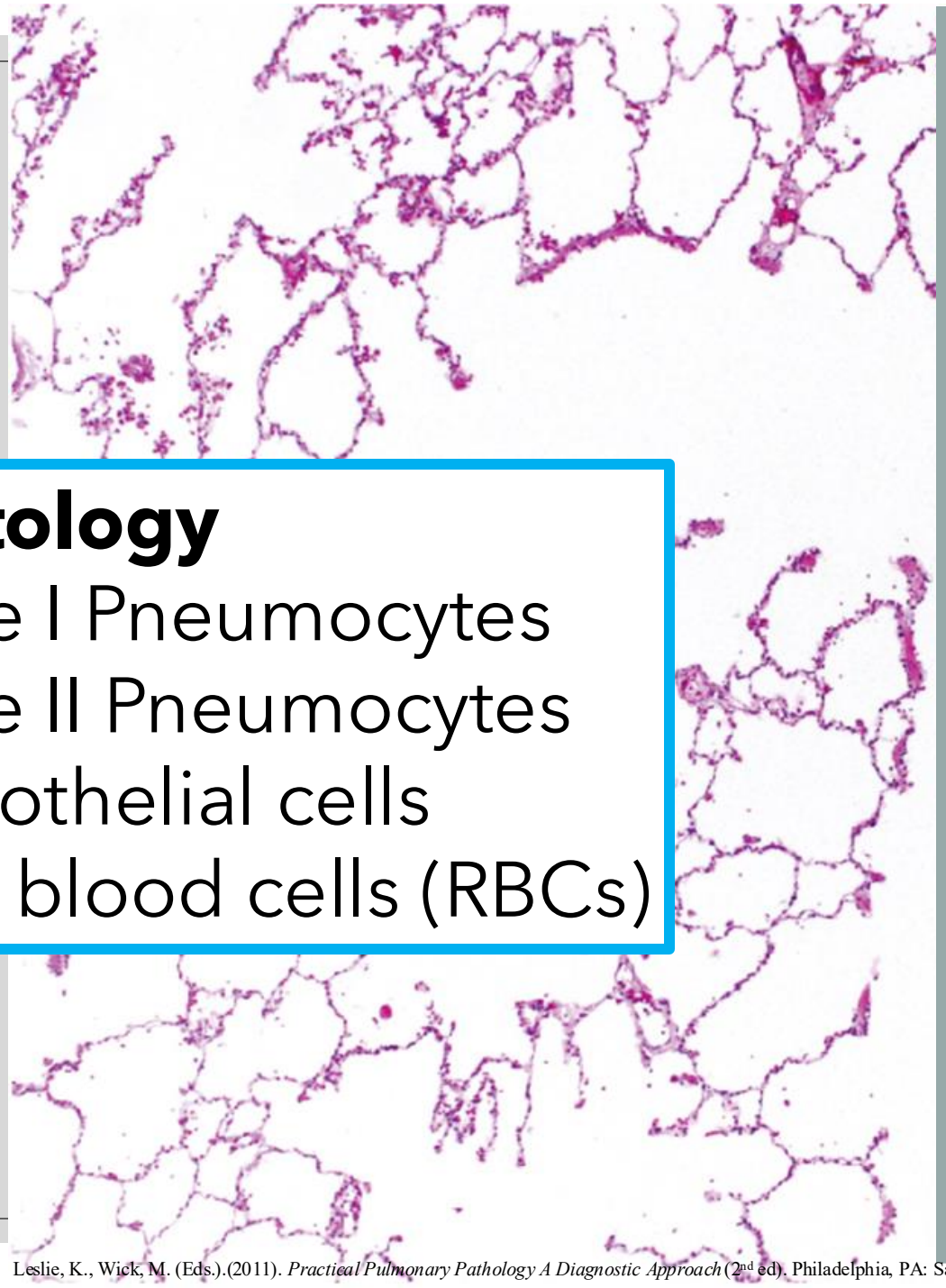


https://www.proteinatlas.org/learn/dictionary/normal/lung

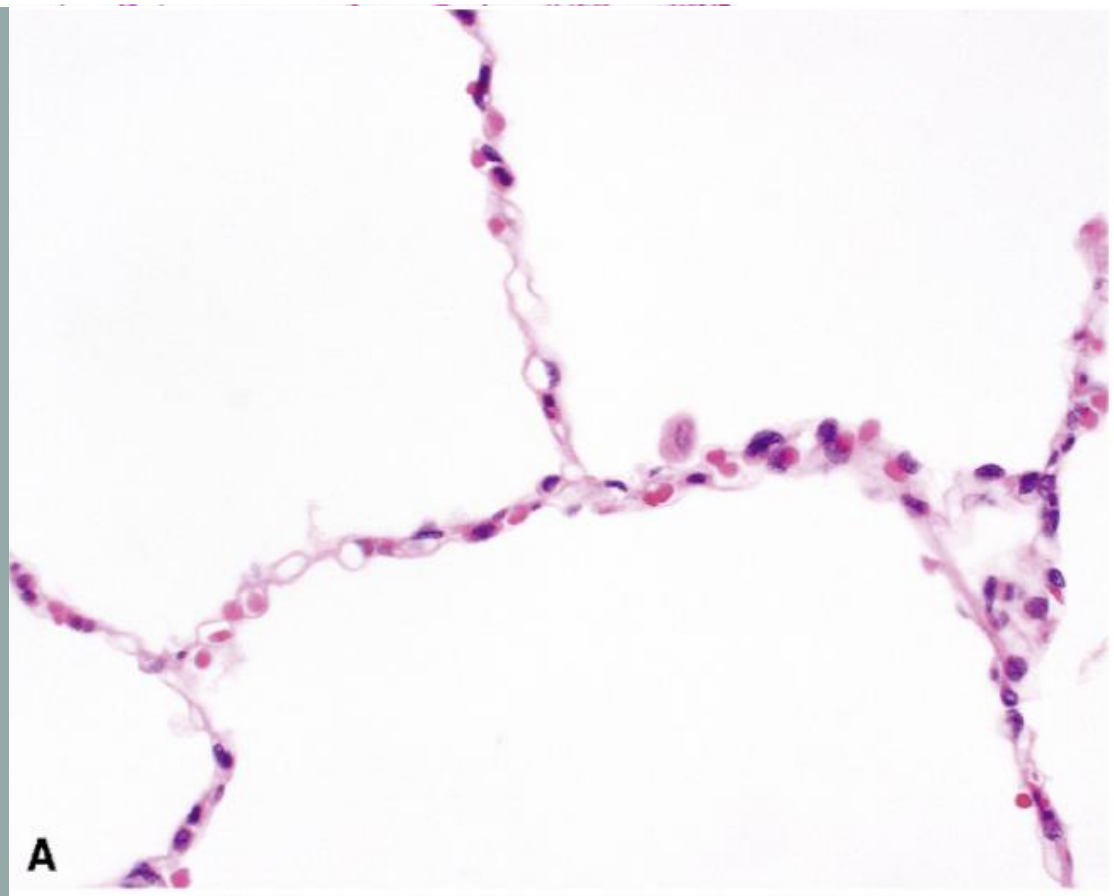


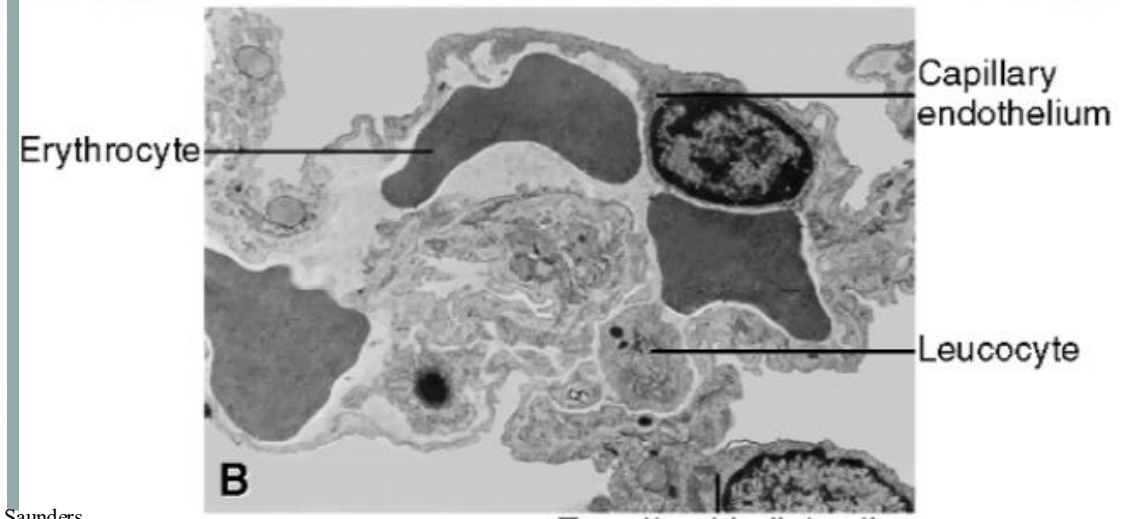
Basic Histology

- **Bronchiole**
- Pseudostratified ciliated respiratory epithelium
- Smooth muscle
- **Alveolar septa (walls)**

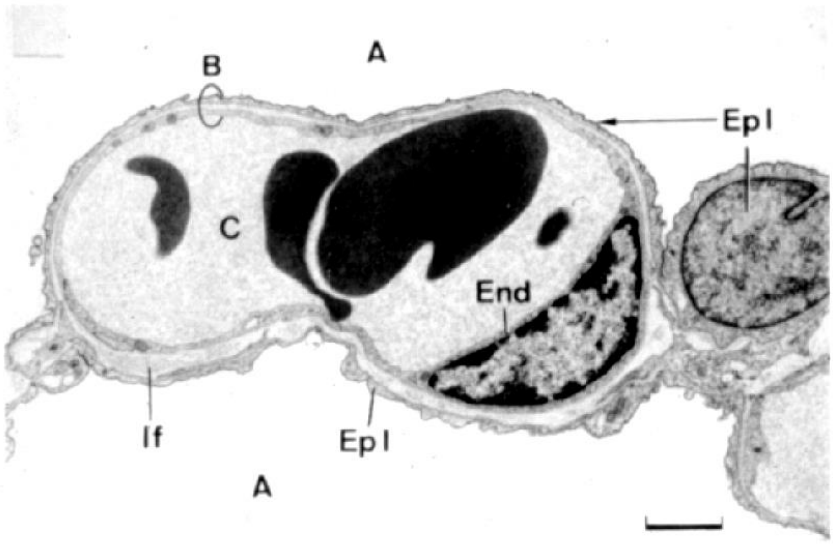


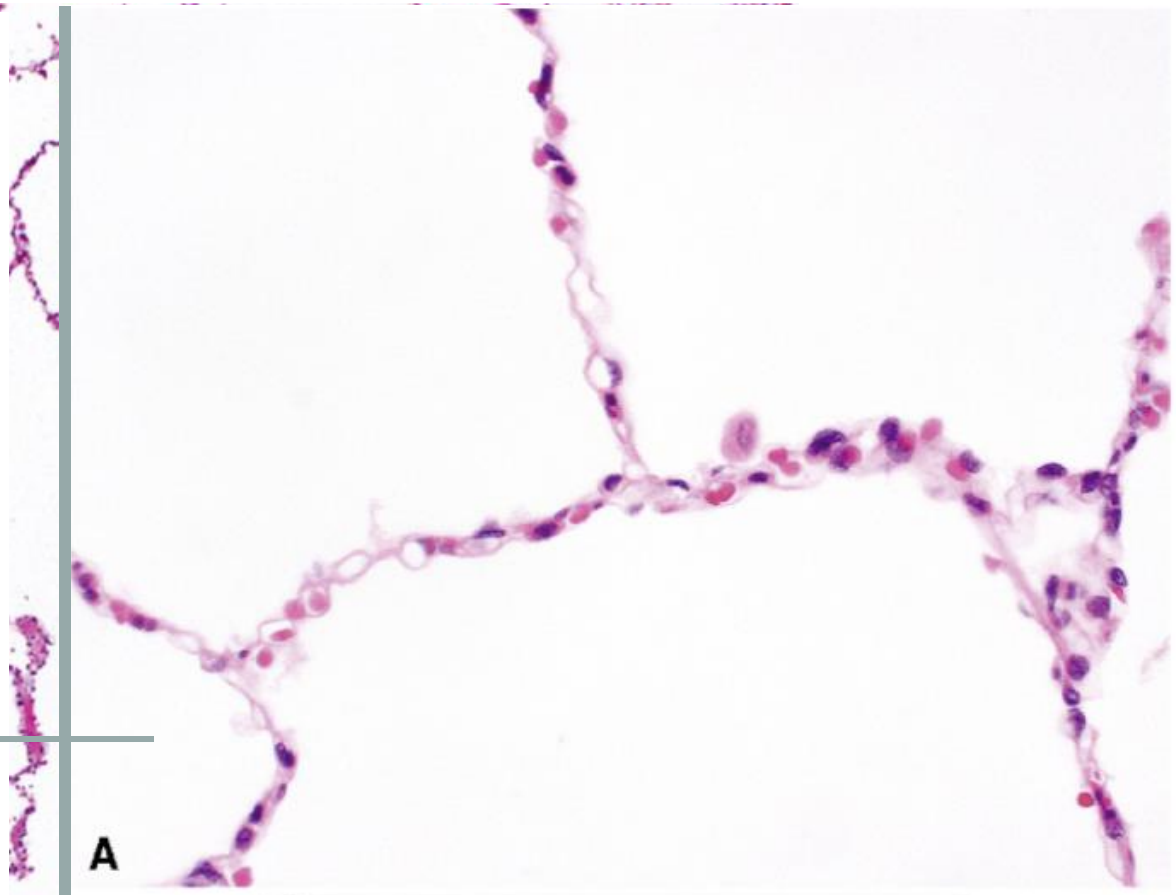
- **Histology**
- Type I Pneumocytes
- Type II Pneumocytes
- Endothelial cells
- Red blood cells (RBCs)

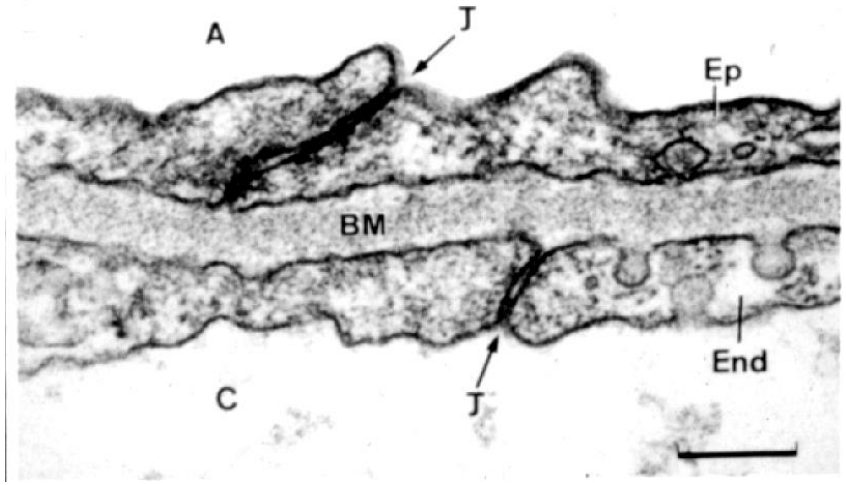


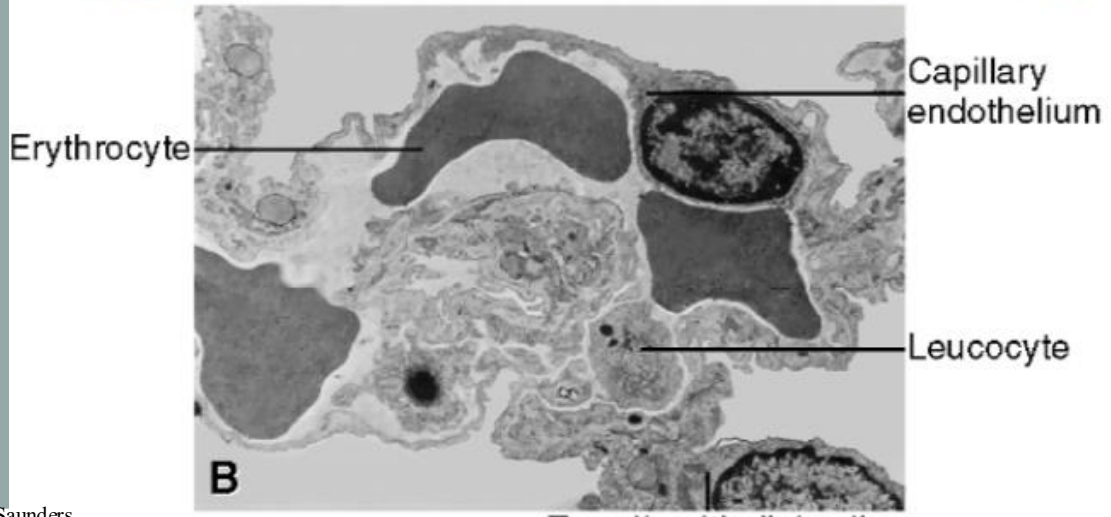


Leslie, K., Wick, M. (Eds.).(2011). *Practical Pulmonary Pathology A Diagnostic Approach* (2nd ed). Philadelphia, PA: Saunders.









Transmission EM of Normal Alveolar Septae

Leslie, K., Wick, M. (Eds.).(2011). *Practical Pulmonary Pathology A Diagnostic Approach* (2nd ed). Philadelphia, PA: Saunders.

Outline

- Basic Anatomy and Histology of the Lung
- **Impact of Smoking Related Disease**
- Emphysema
- Lung Cancer

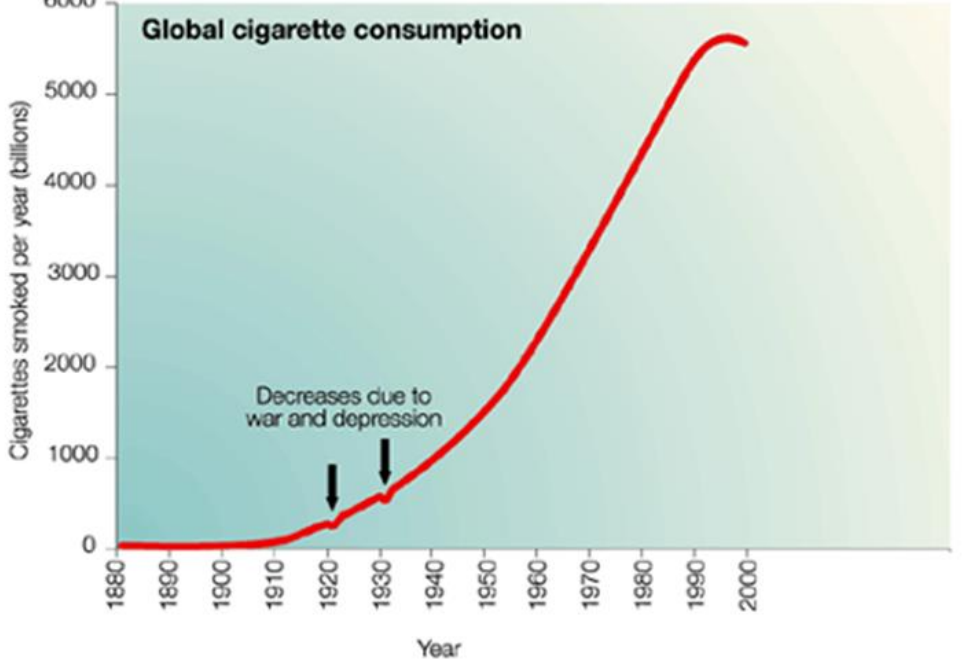
- **Nicotine**: 1% of smoke

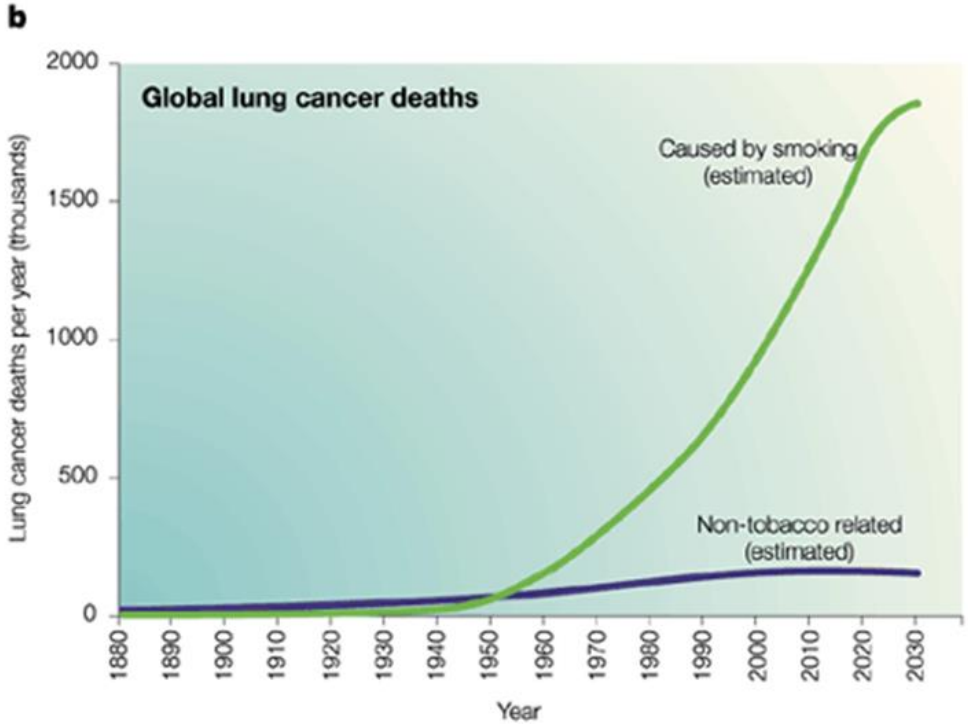
4,000 CHEMICAL COMPOUNDS, OF WHICH 43 ARE CONSIDERED CARCINOGENIC

smoke a cigarette...

- resin cores in 0.3 μM diameter water droplets
  - est. 10^9 particles/ml
  - 50% deposited on and cleared by cilia, remainder by phagocytosis, lymphatic transport

CARCINOGENIC





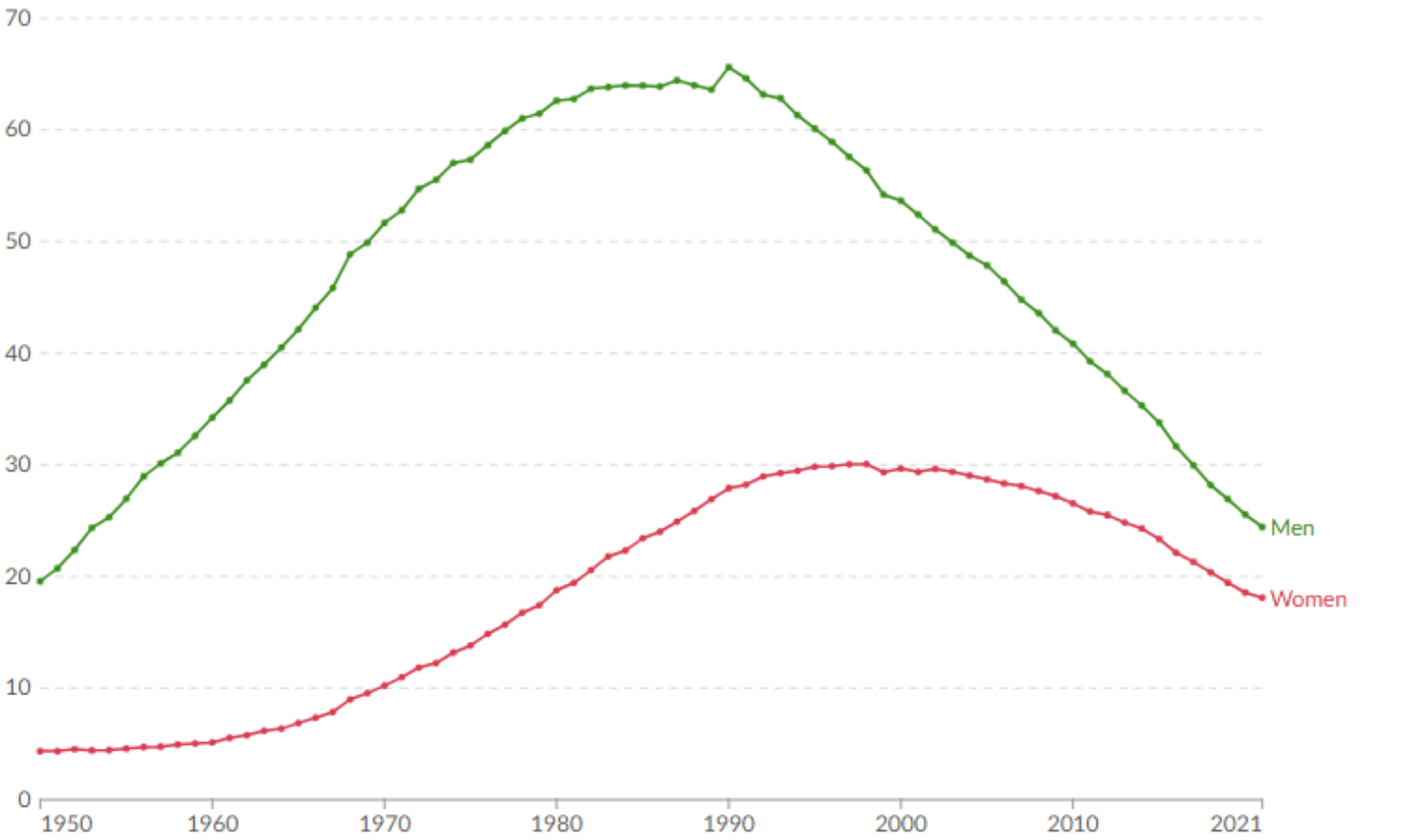
Proctor, Nat Rev Ca (2001); 1:92

Lung cancer death rates, United States

Our World in Data

Reported annual death rate from lung, bronchus or trachea cancers per 100,000 people, based on the underlying cause listed on death certificates.

Table | Chart | Settings



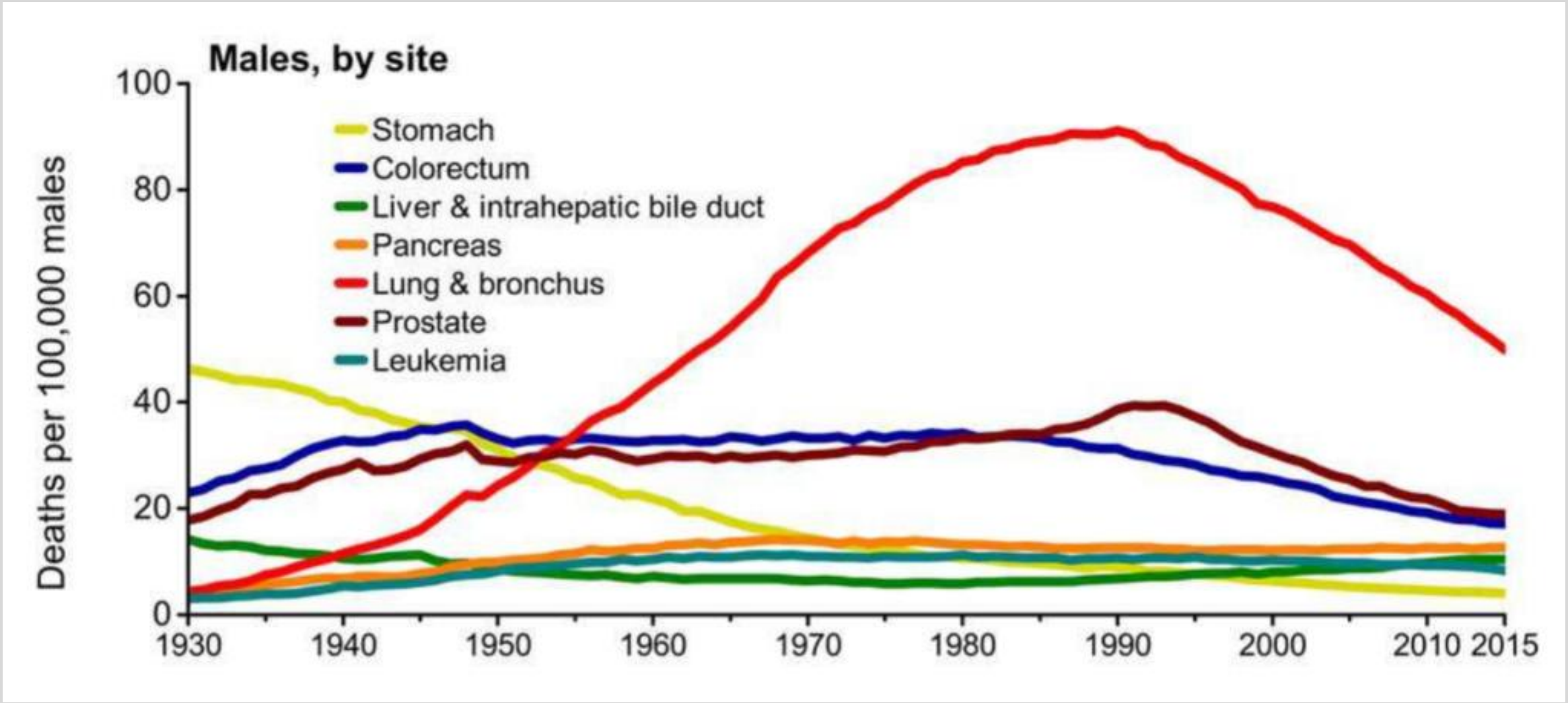
1950 — 2021

Data source: WHO Mortality Database (2024) – Learn more about this data

OurWorldinData.org/smoking | CC BY

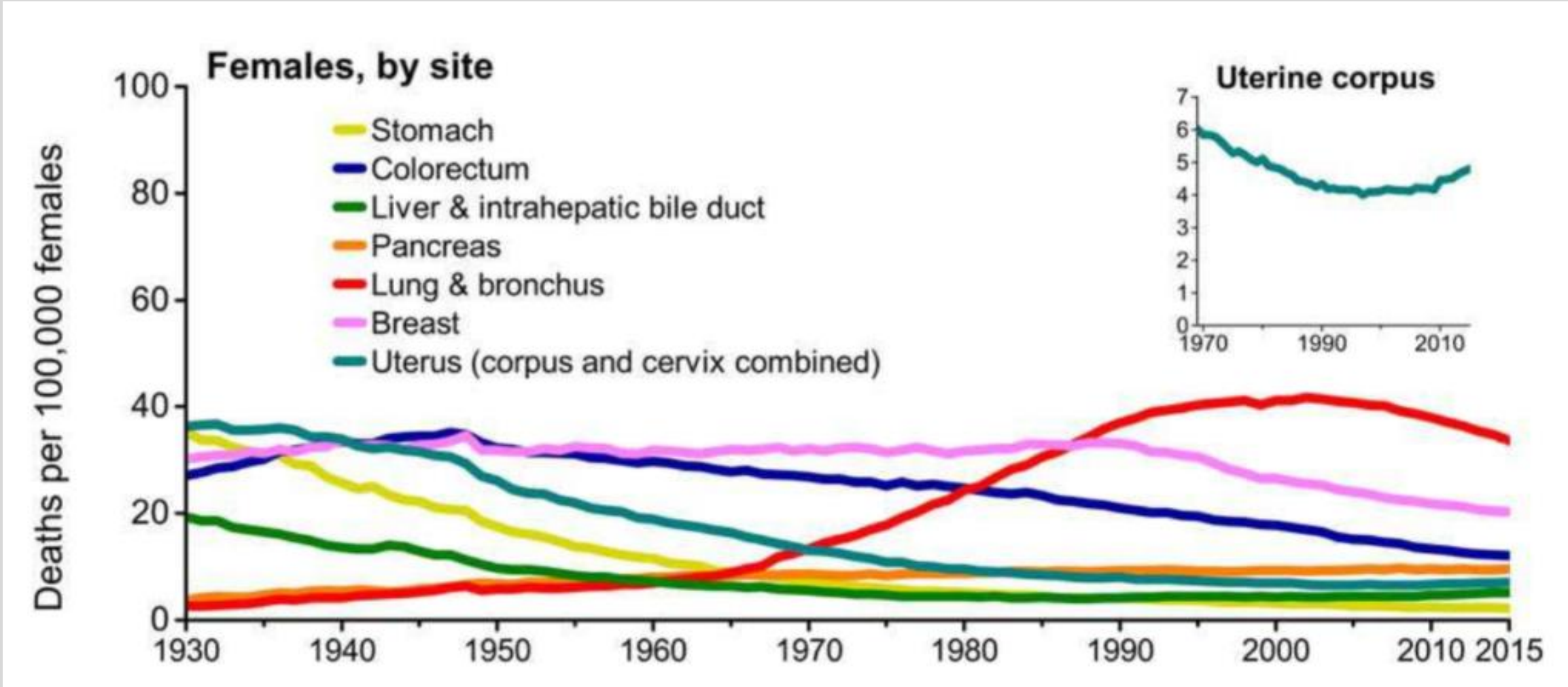
Note: To allow for comparisons between countries and over time, this metric is age-standardized. All deaths in a country may not have been registered with a cause of death.

US Cancer Death Rates, Males, by Primary Site



Siegel, Ca J Clin **2018** Jan;68(1):7-30

US Cancer Death Rates, Females, by Primary Site

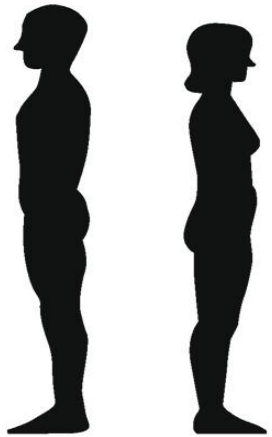


Year of Death

Siegel, Ca J Clin **2018** Jan;68(1):7-30

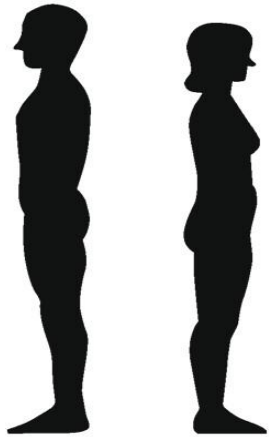
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



Estimated Deaths

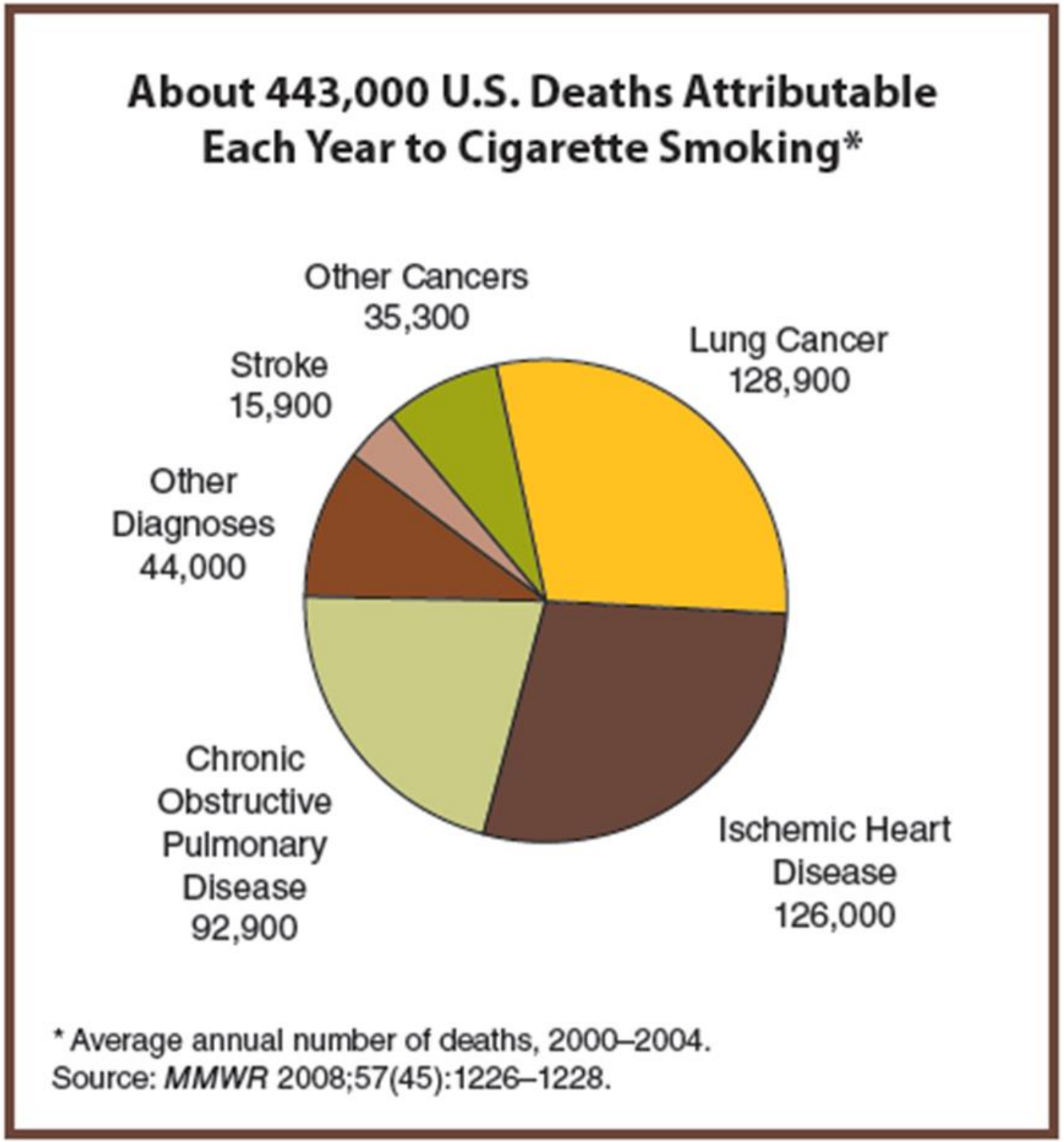
Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Cancer statistics, 2024

CA A Cancer J Clinicians, Volume: 74, Issue: 1, Pages: 12-49, First published: 17 January 2024, DOI: (10.3322/caac.21820)



Impact of Smoking

- **Atherosclerotic Vascular Disease**
- **Hypertension**
- **COPD**
- **Carcinoma-**
  - Oral cavity
  - Larynx
  - Lung
  - Kidney
  - Bladder

Outline

- Basic Anatomy and Histology of the Lung
- Impact of Smoking Related Disease
- **Emphysema**
- Lung Cancer

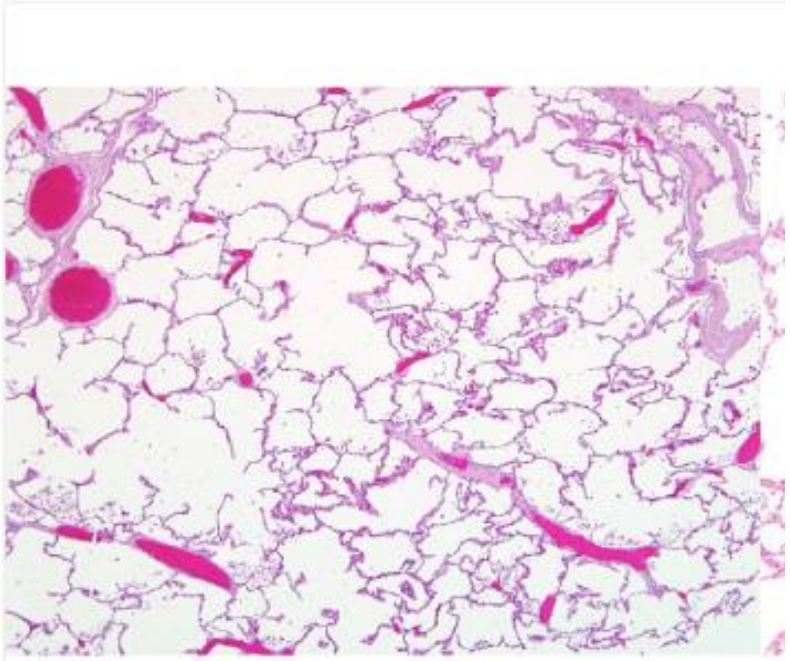
Emphysema

Etiology: *Increased elastase activity*

Dilation of distal airspaces with septal destruction

Elastase destroys elastin in delicate alveolar septa

Alveoli rupture and enlarge



Normal lung

Emphysema

A1AT deficiency: hereditary emphysema, gene mutation causes **α1-antitrypsin** (A1AT) to misfold and prevents A1AT from leaving the hepatocyte ER

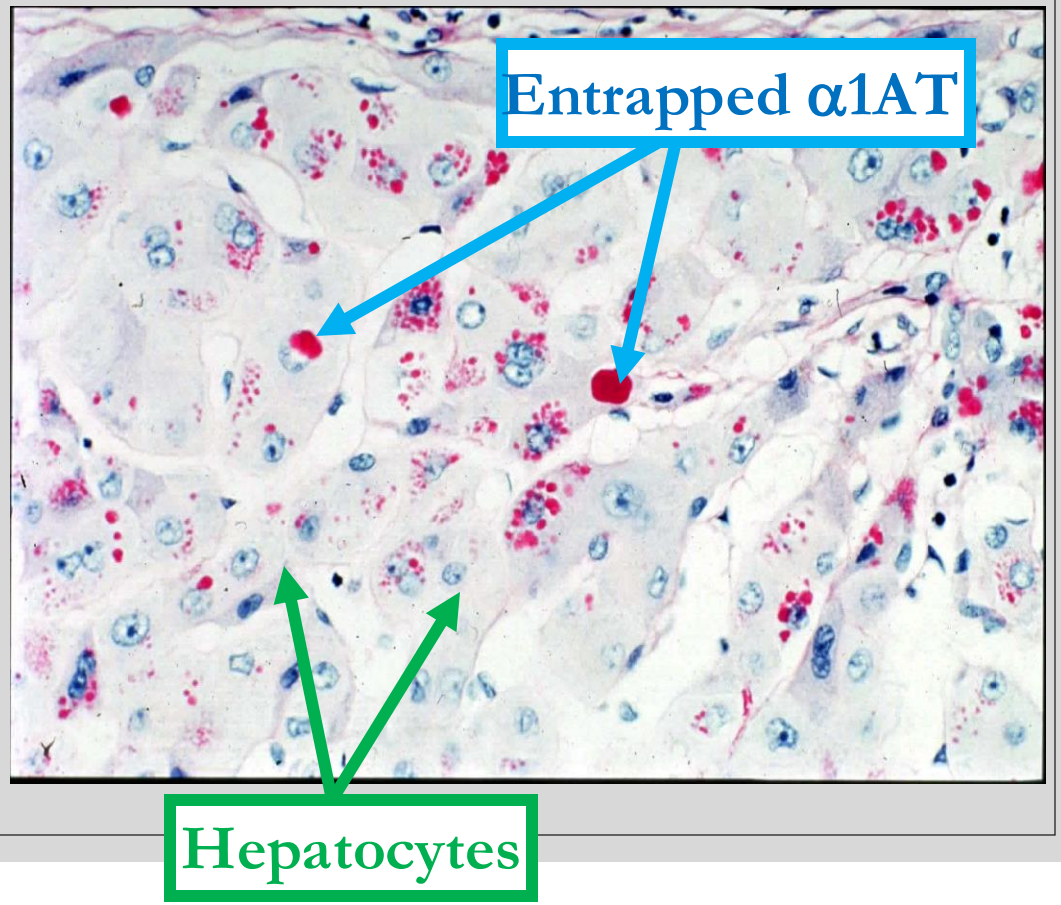
Lung disease 40-50 yrs old, younger if smoker

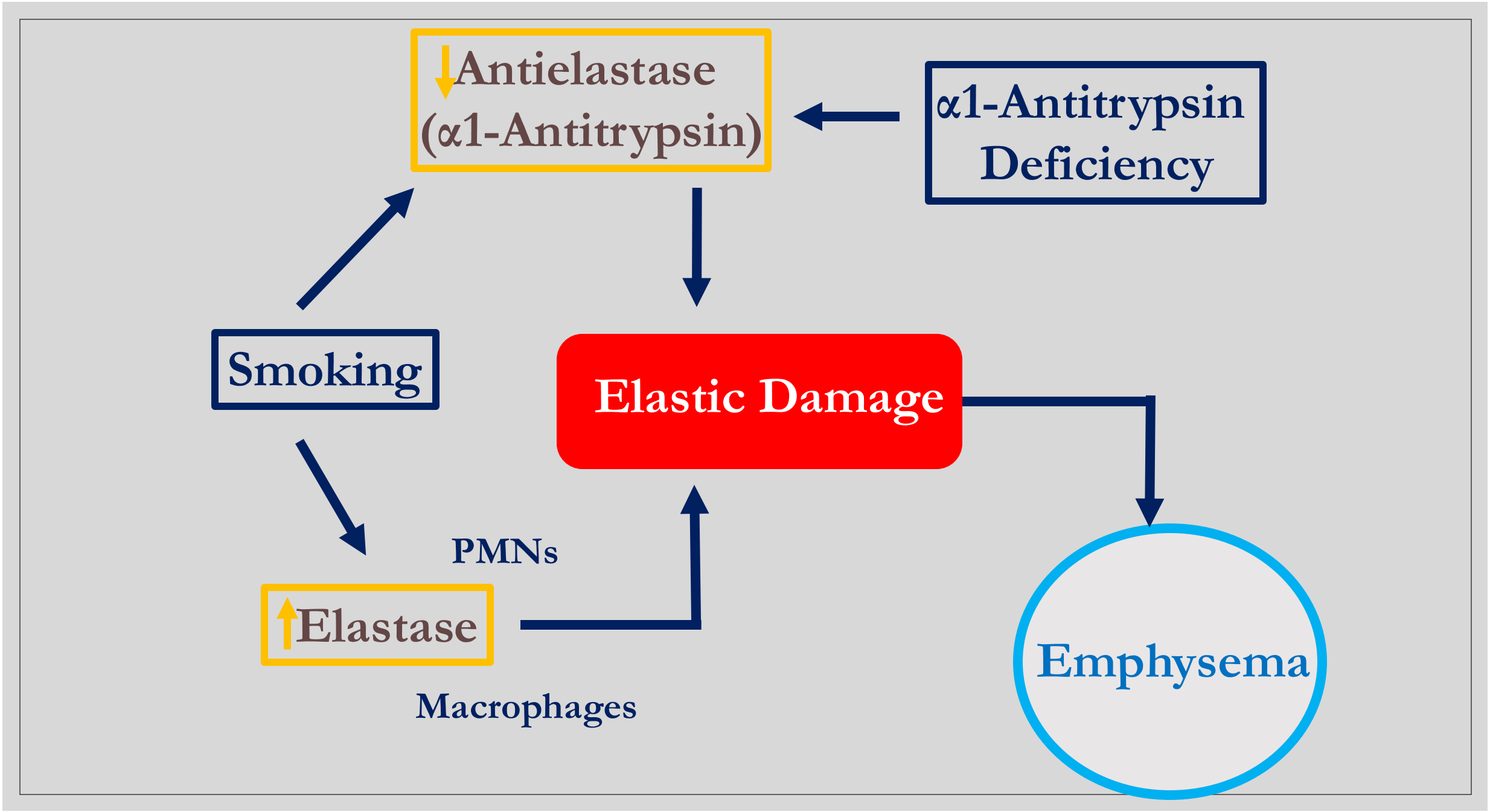
Cigarette smoking --> **centrilobular** destruction

upper lobe > lower lobe

A1AT deficiency --> **panlobular** destruction

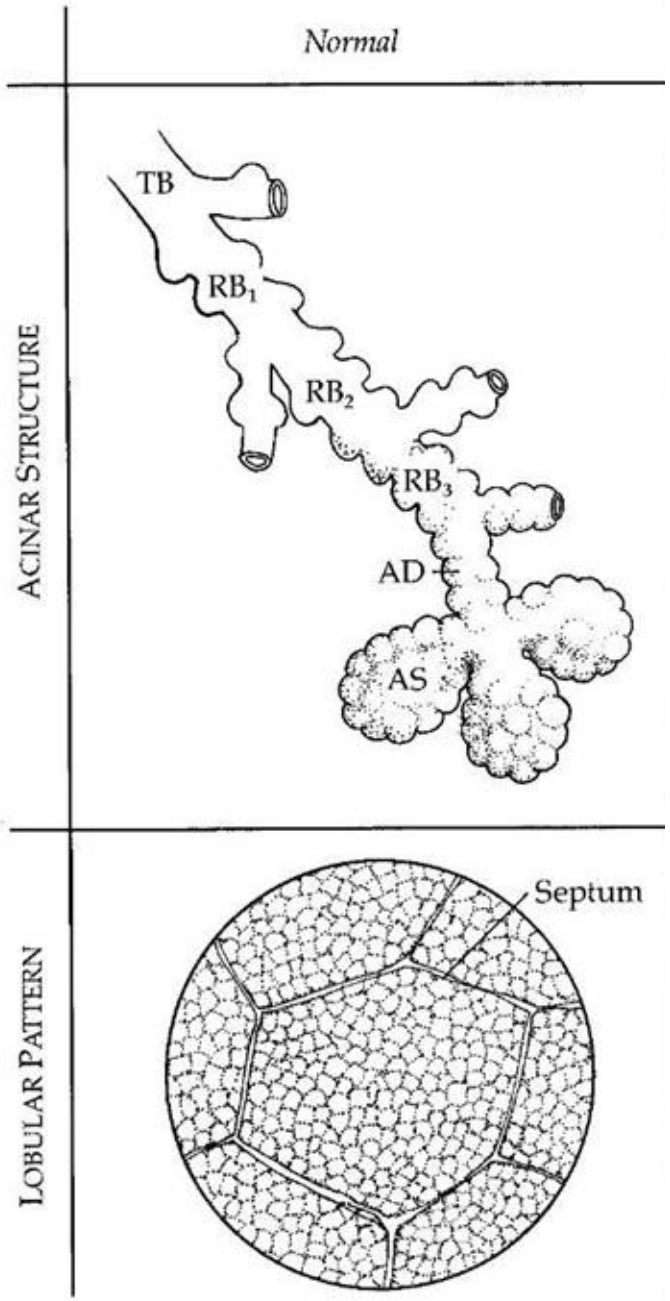
lower lobe > upper lobe



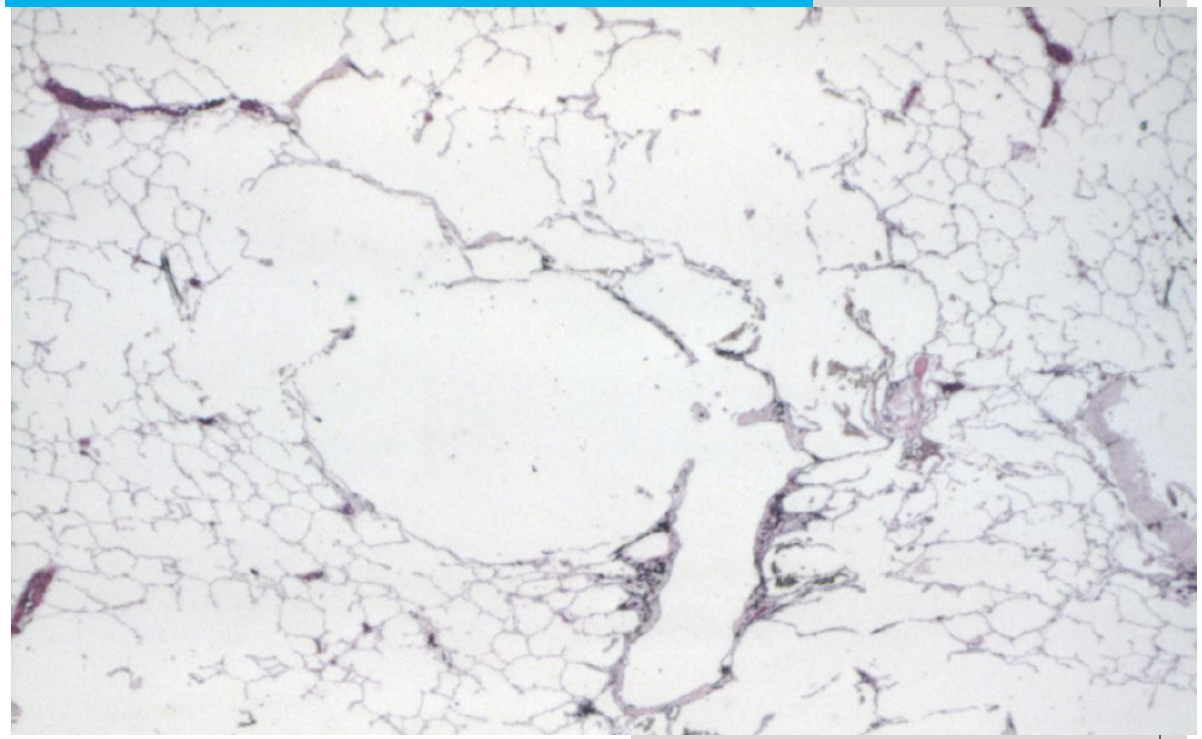


PMN= polymorphonuclear leukocytes

Robbins, Path Basis of Dz, 5th ed.

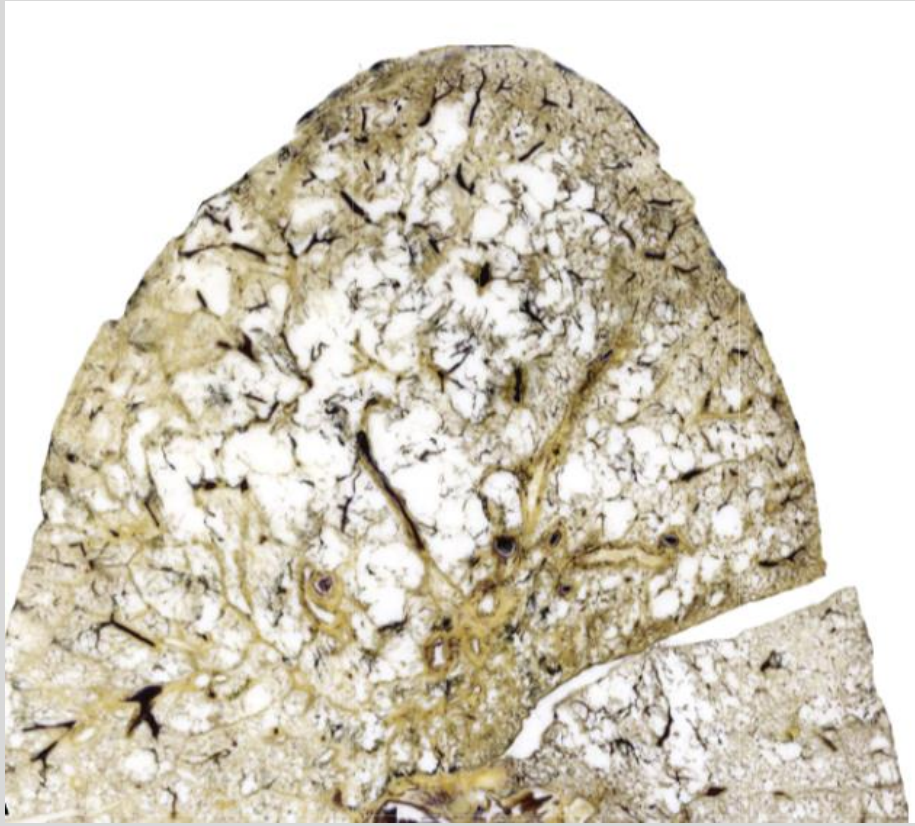


Centrilobular Emphysema



http://what-when-how.com/acp-medicine/chronic-obstructive-diseases-of-the-lung-part-1/

Centrilobular Emphysema in COPD



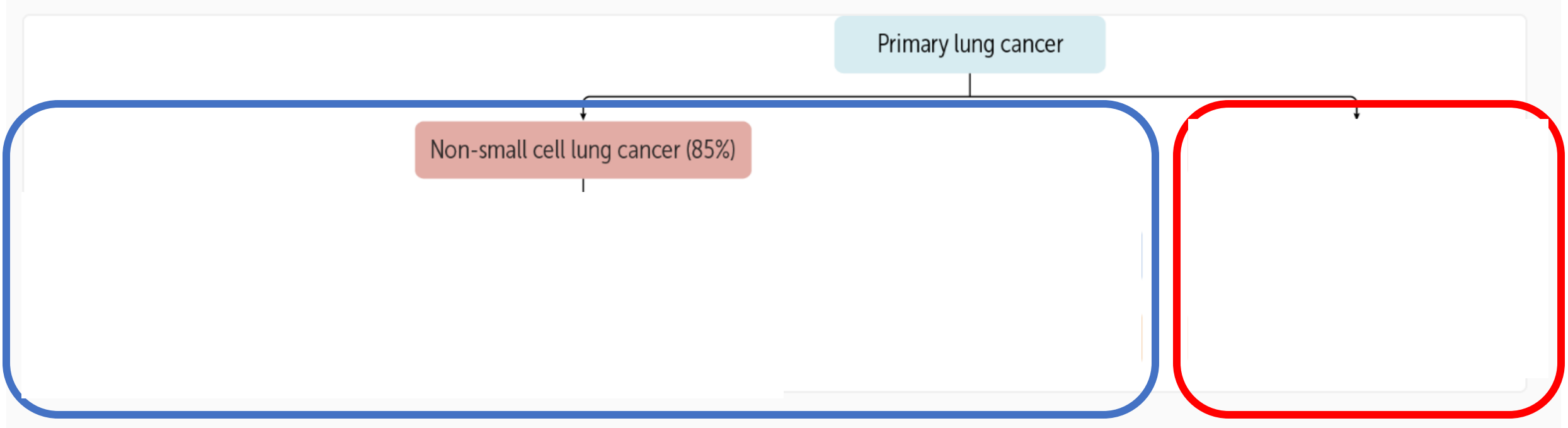
Leslie, K., Wick, M. (Eds.).(2011). *Practical Pulmonary Pathology A Diagnostic Approach* (2nd ed). Philadelphia, PA: Saunders.
Zander, D., Farver, C. (Eds.).(2018). *Pulmonary Pathology: A Volume in the Series Foundations in Diagnostic Pathology* (2nd ed). Philadelphia, PA: Elsevier.

Outline

- Basic Anatomy and Histology of the Lung
- Impact of Smoking Related Disease
- Emphysema
- **Lung Cancer**

Malignant Lung Neoplasms

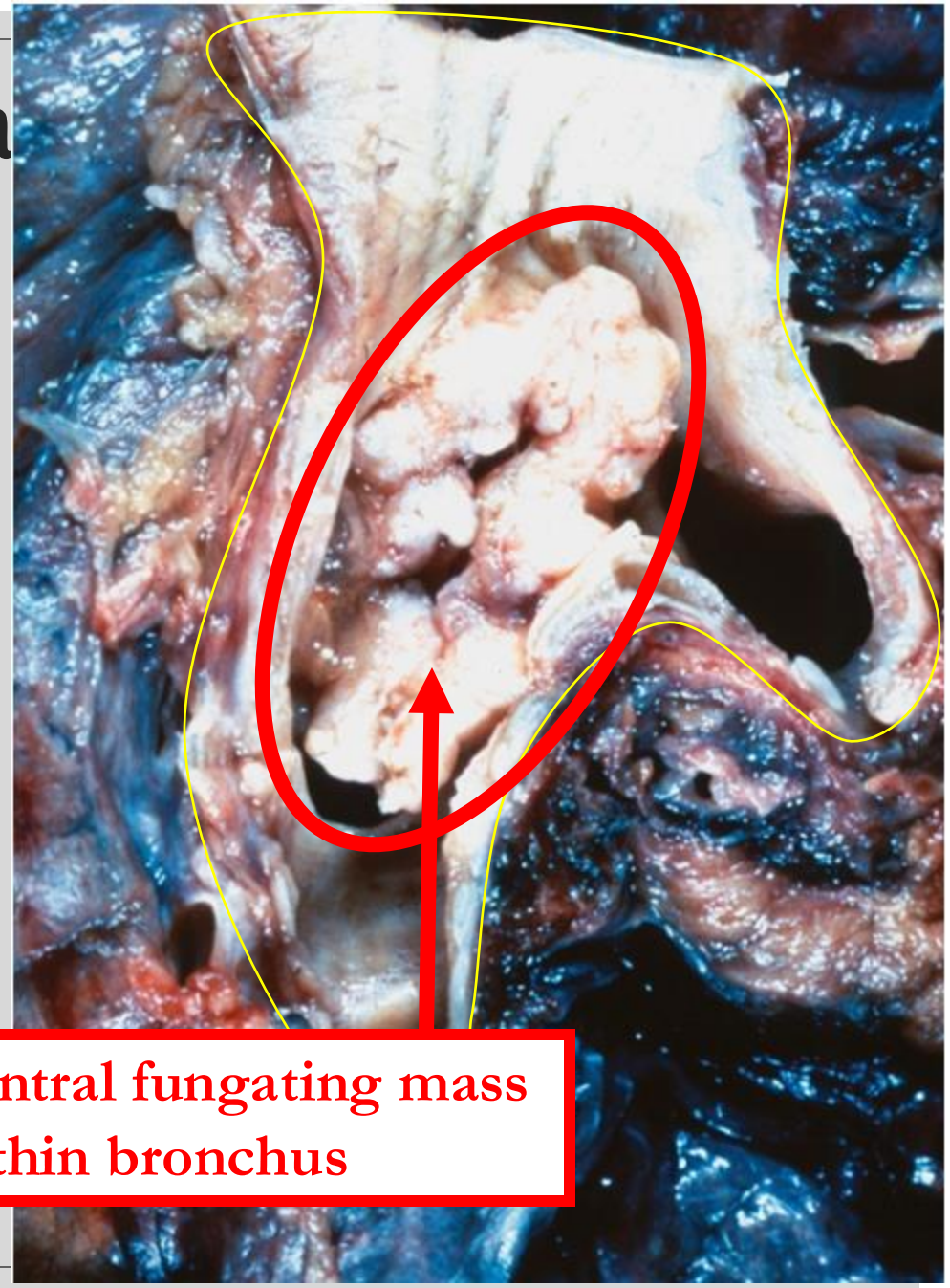
- **Primary** – arises from cells within the lung
- **Secondary**- arises from cells within another organ, metastasized to lung
  - Breast, colorectal, head and neck, urologic, melanoma, gynecologic



Squamous Cell Carcinoma

Strong association with **smoking**
25-30% of common carcinomas

- **Central** >> Peripheral
- Spiculated or cavitating
- **Histology**
  - +/- Desmosomes
    - intercellular bridges
  - +/- Keratin production
    - e.g. keratin pearls



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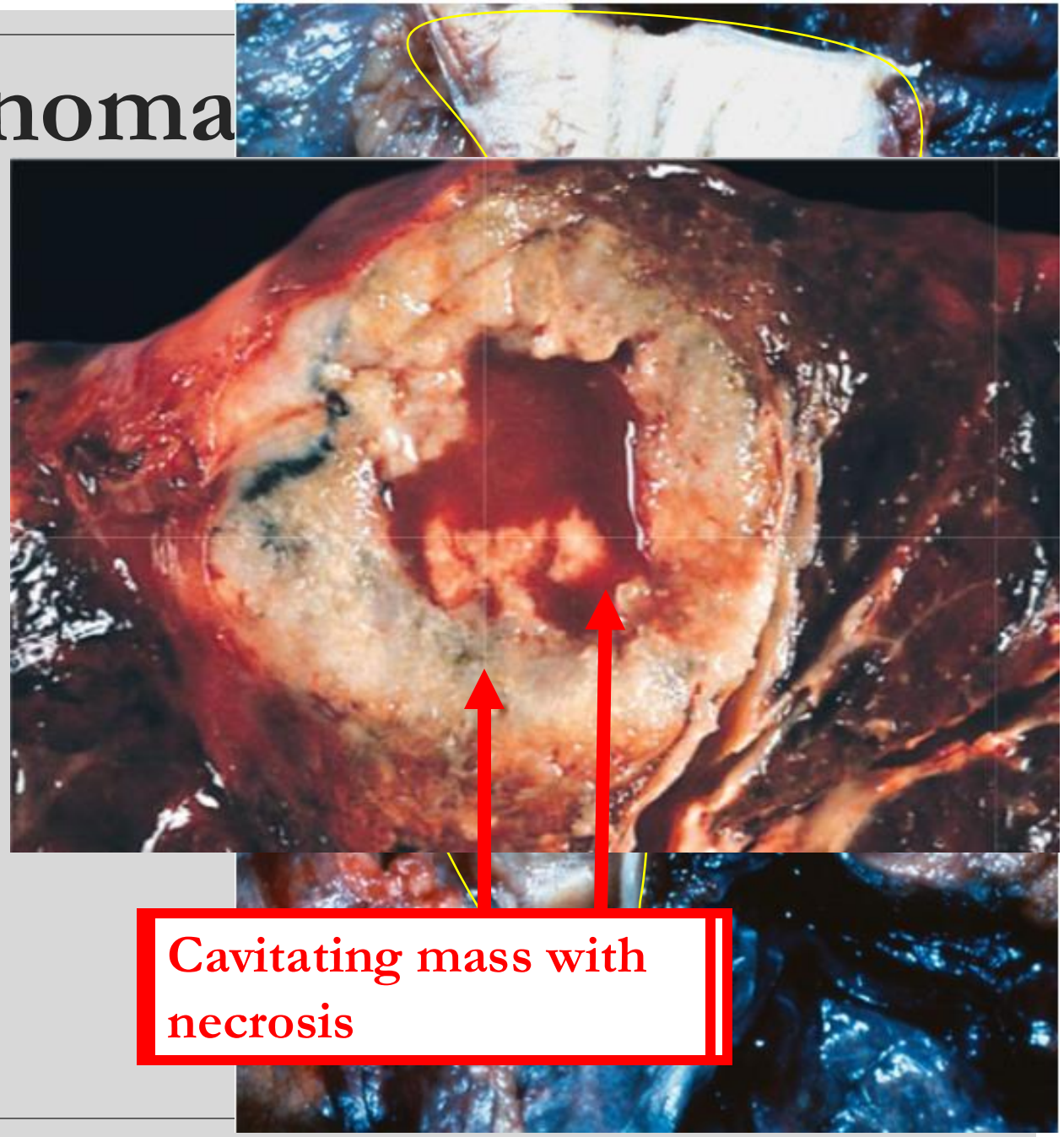
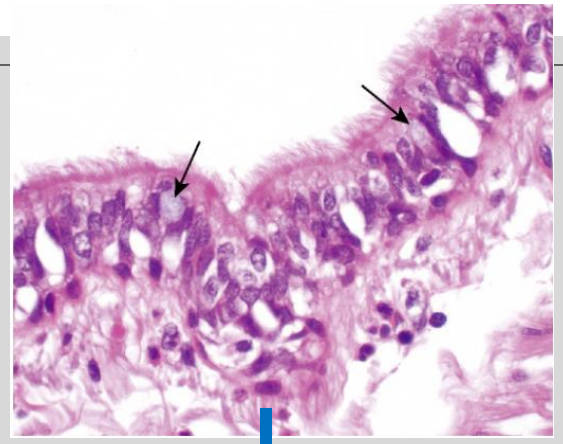
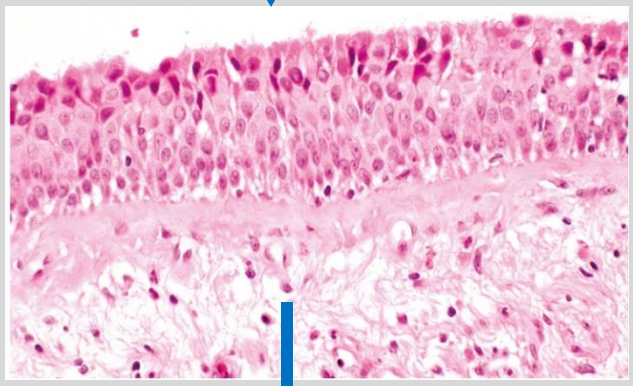
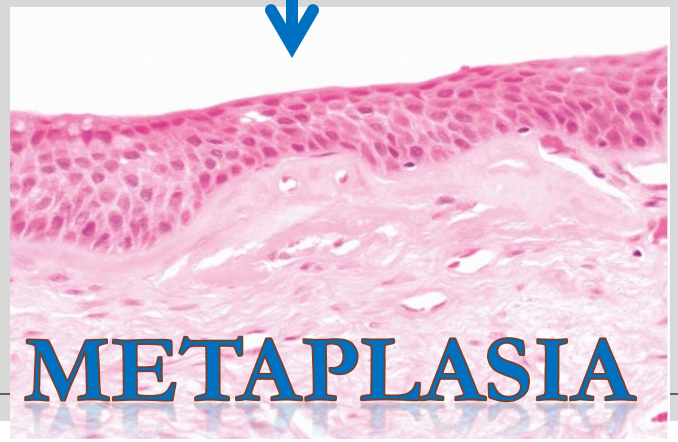
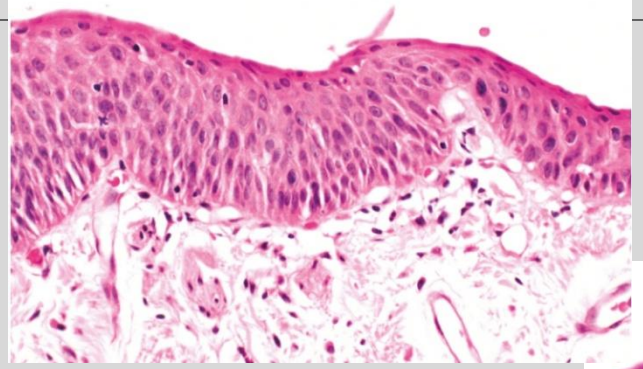




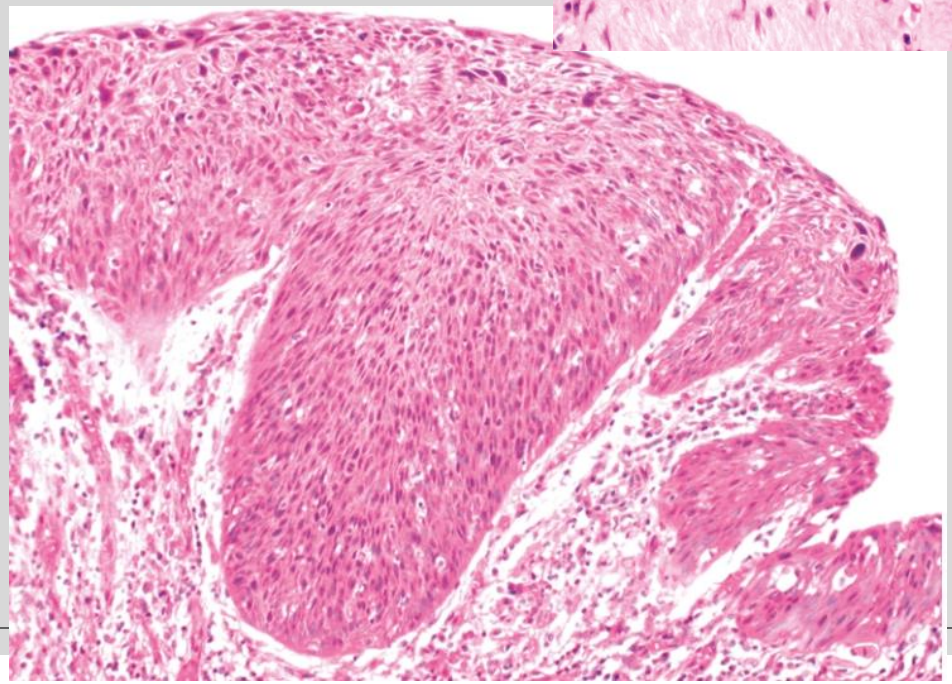


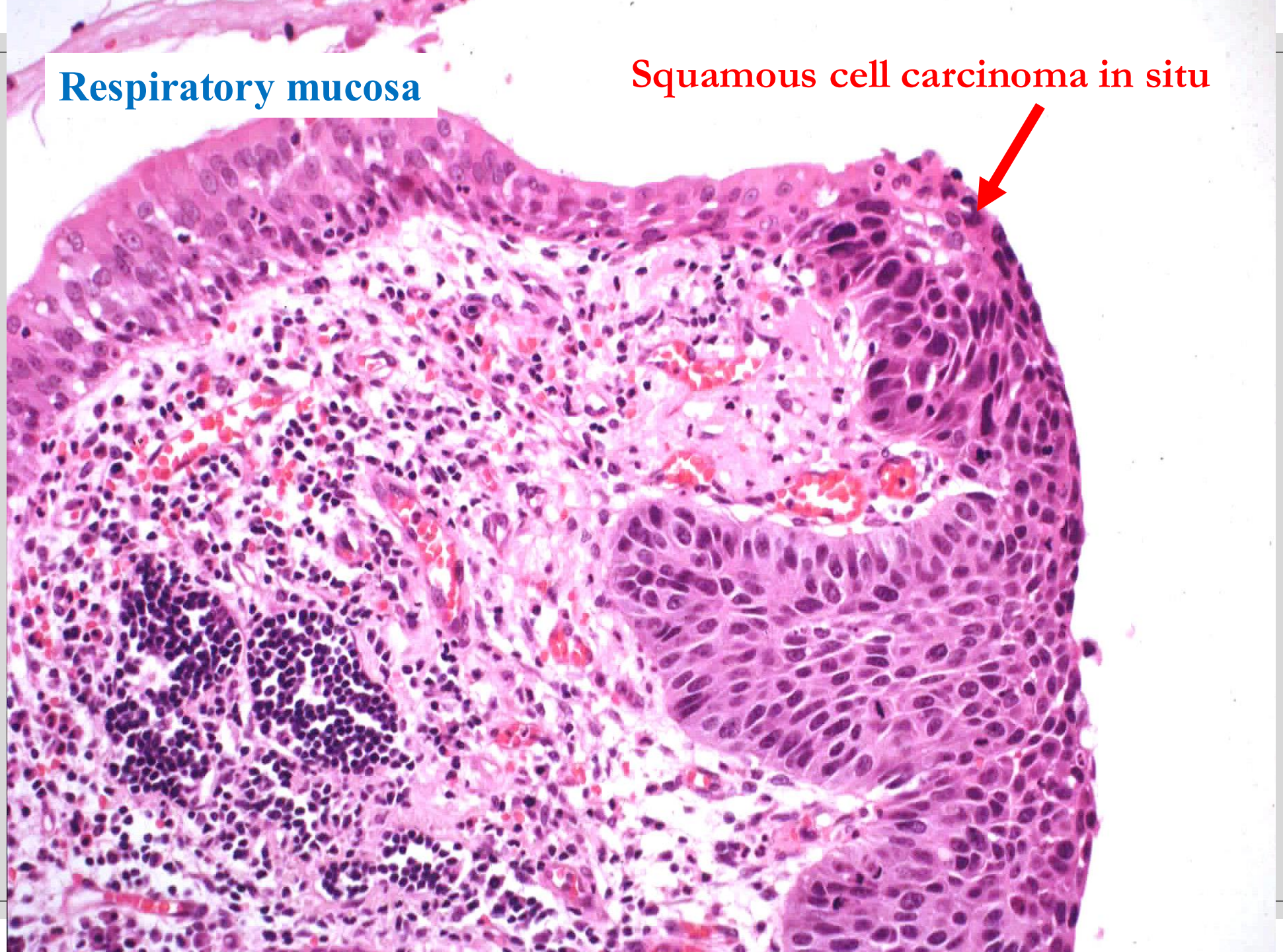


METAPLASIA

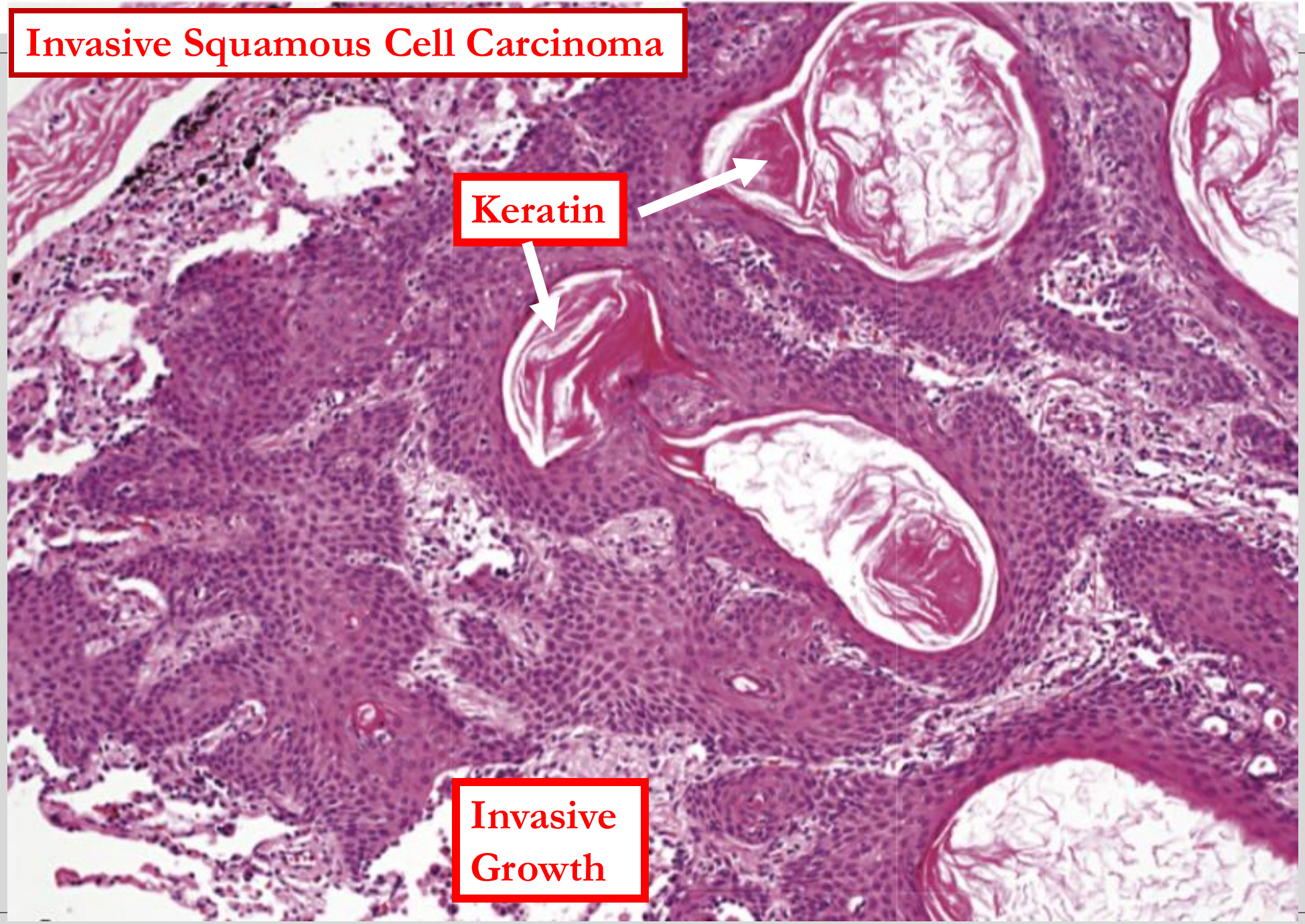


DYSPLASIA



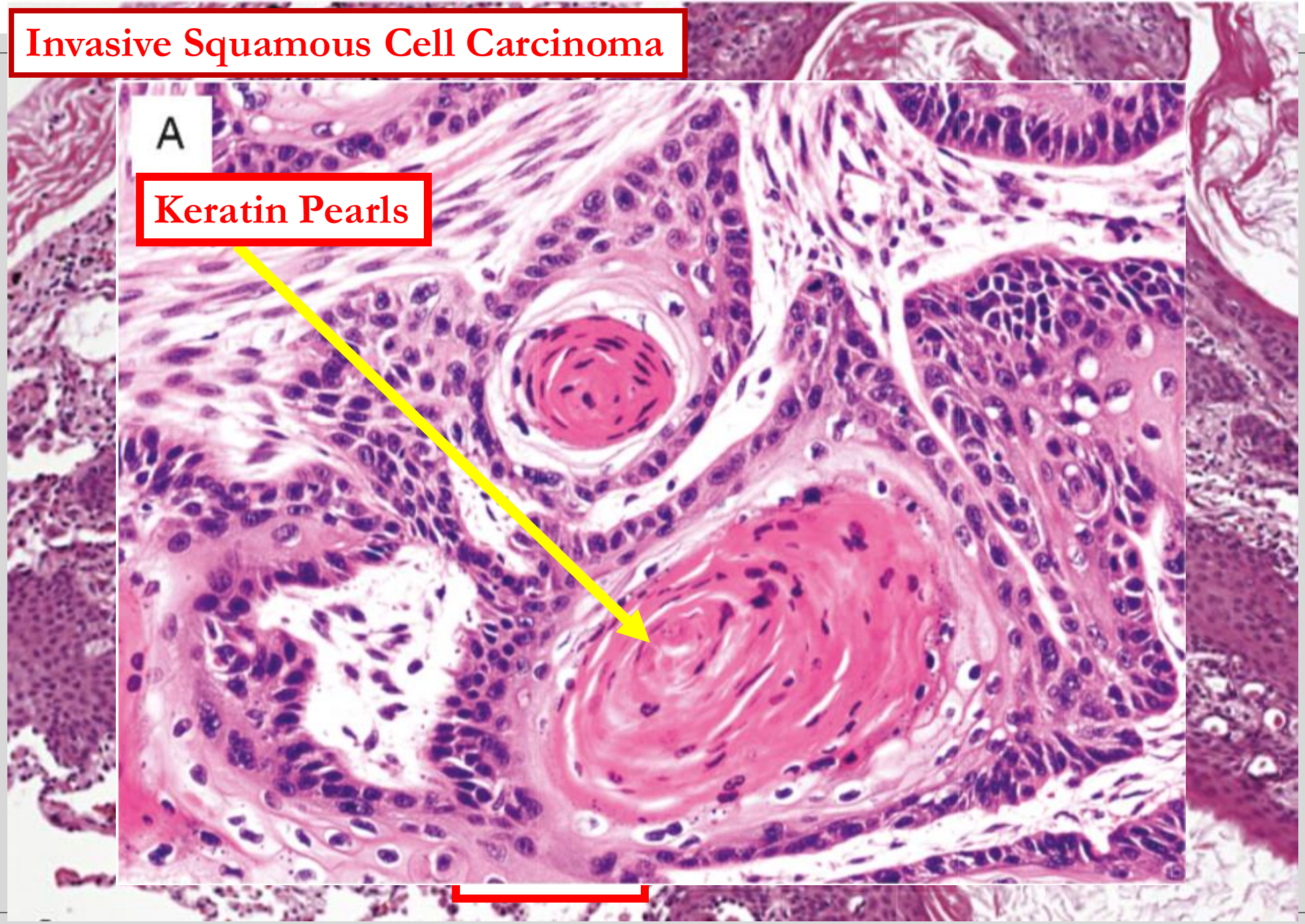

Respiratory mucosa
Squamous cell carcinoma in situ

Invasive Squamous Cell Carcinoma



Leslie, K., Wick, M. (Eds.).(2011). *Practical Pulmonary Pathology A Diagnostic Approach* (2nd ed). Philadelphia, PA: Saunders.c

Invasive Squamous Cell Carcinoma



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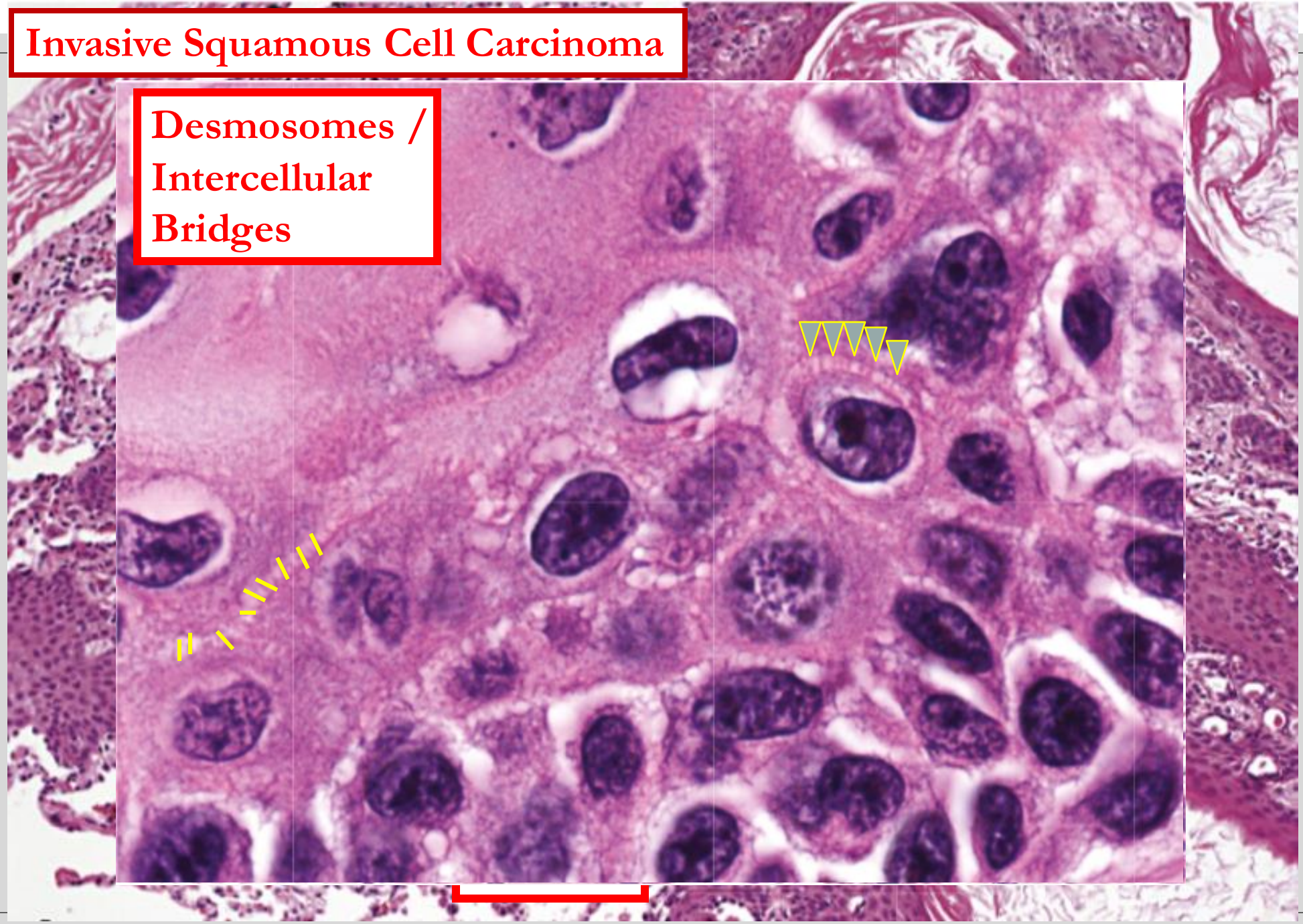
Invasive Squamous Cell Carcinoma



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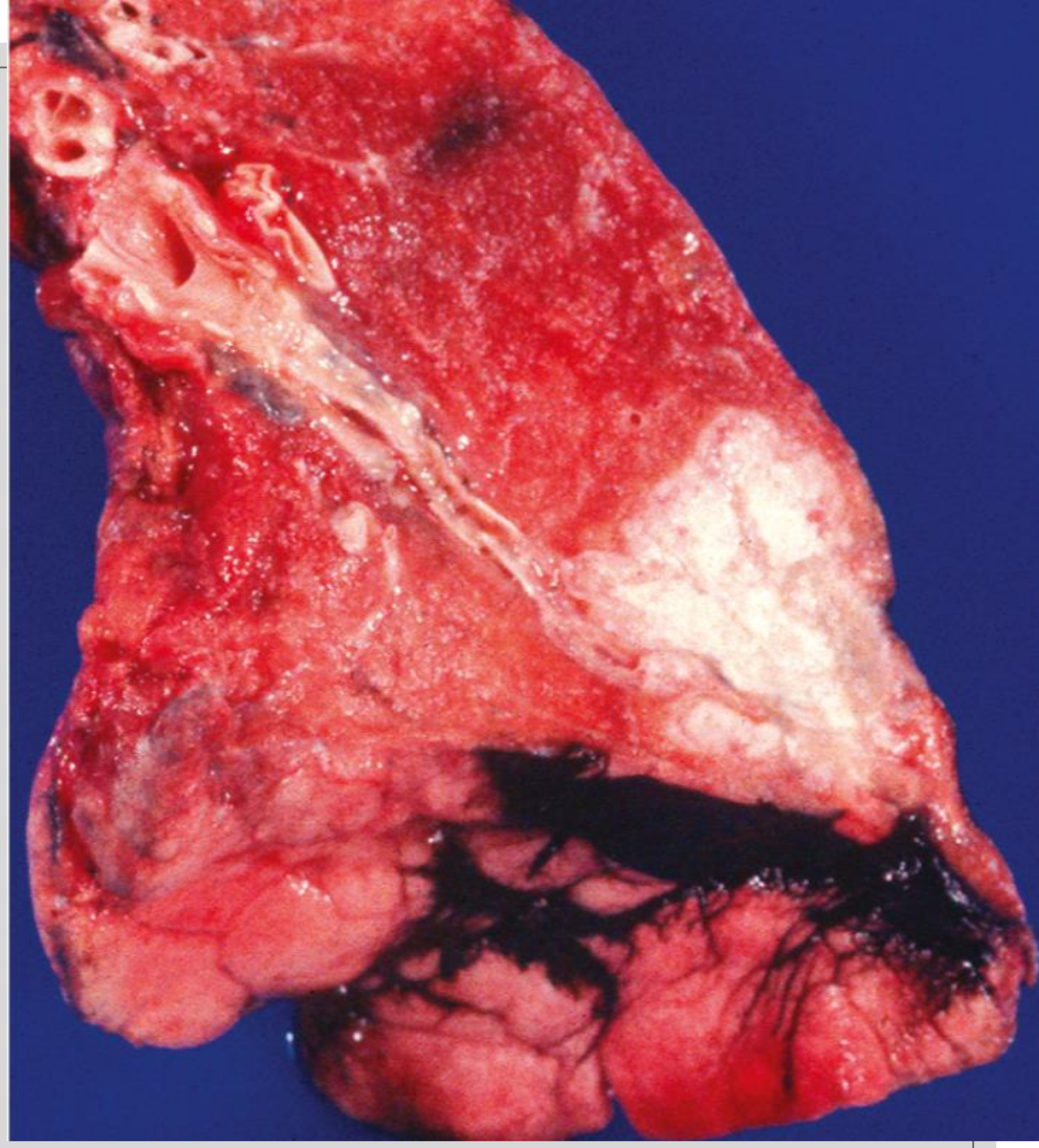
Adenocarcinoma

Most common carcinoma in non-smokers,
smoking still a risk factor 40% of common carcinomas

- Histology
  +/- glands, +/- mucin



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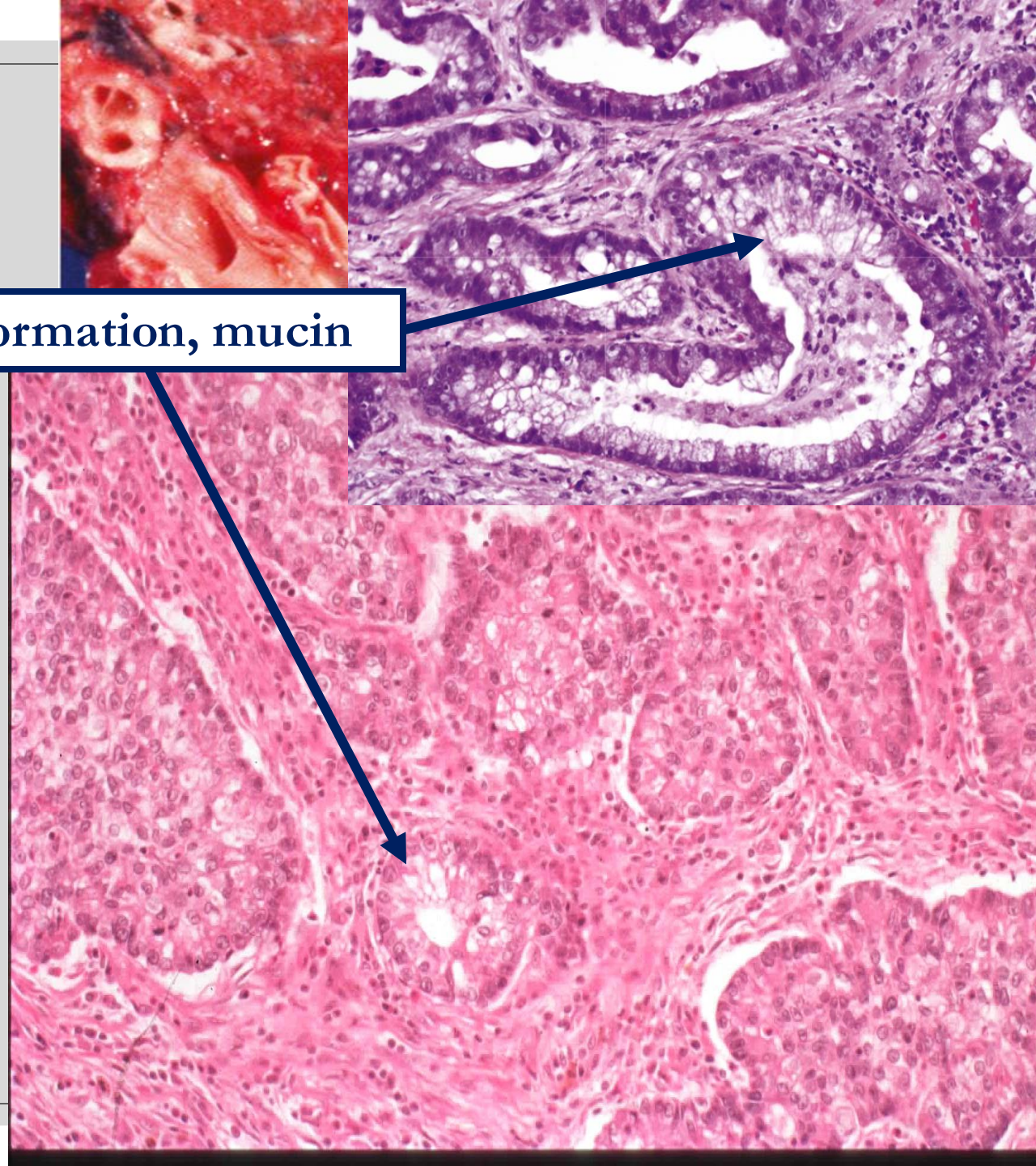


Small Cell Carcinoma

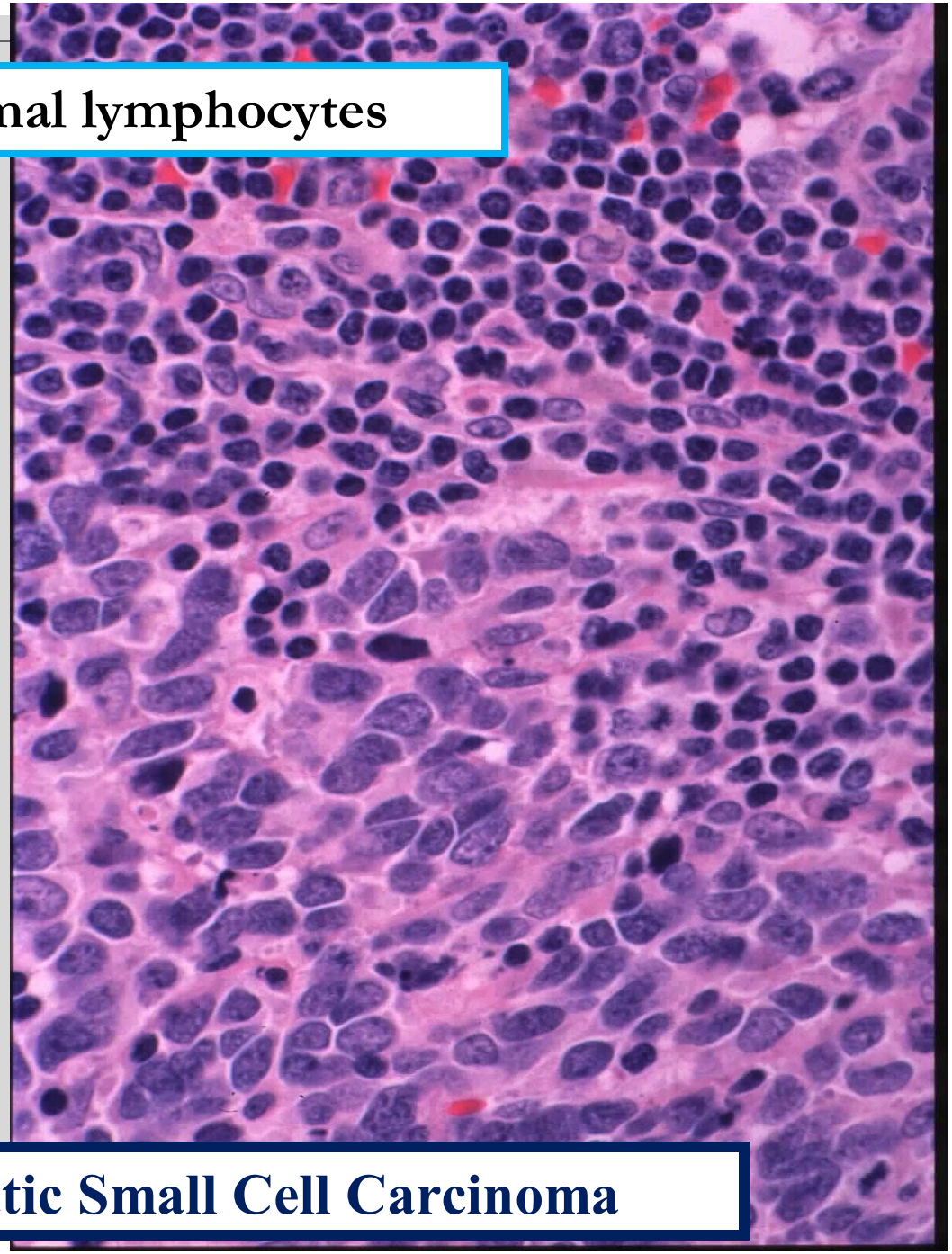
Strongly associated with smoking

15% of common carcinomas

Commonly high stage at presentation

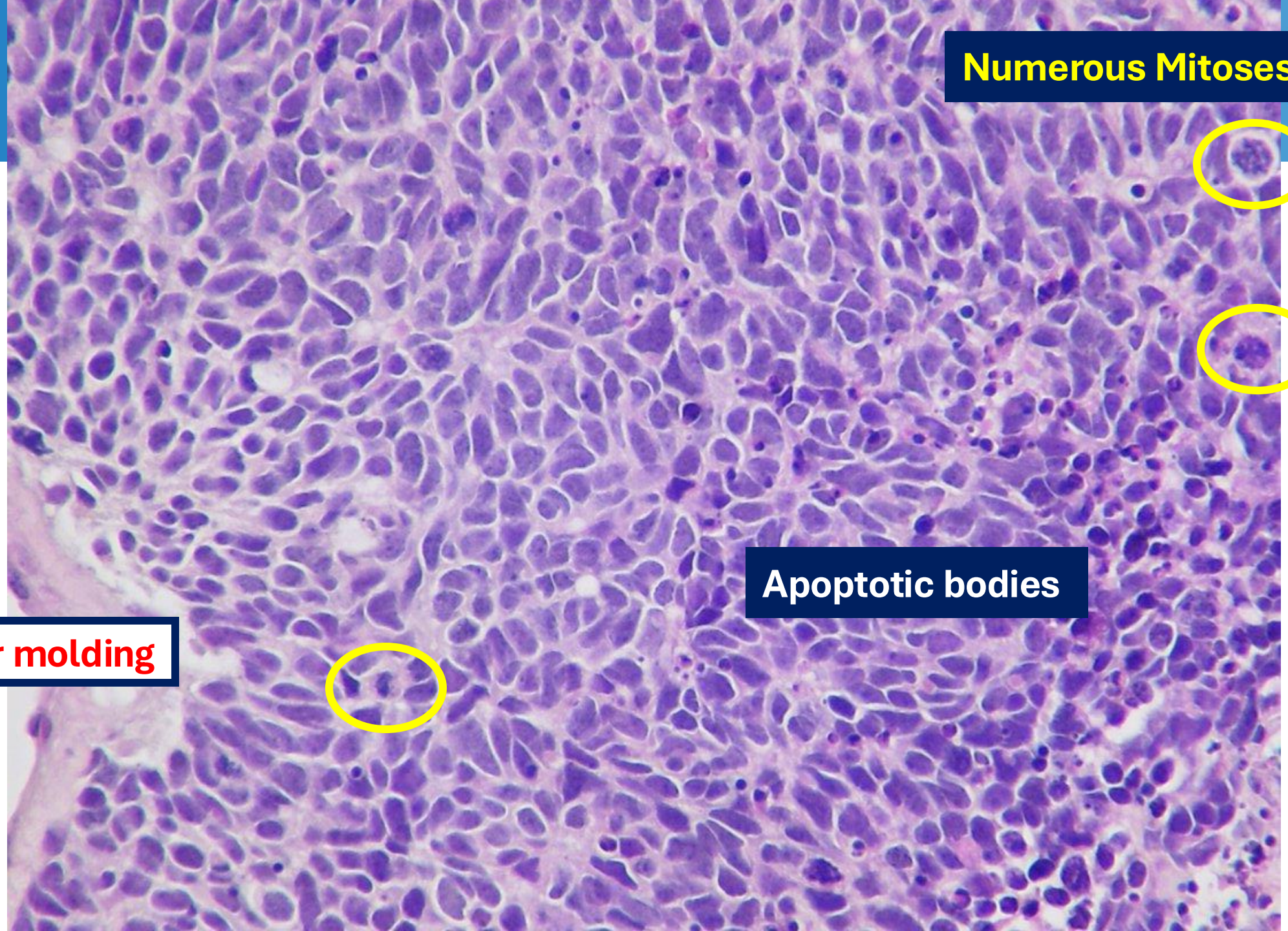
Responsive to chemo/RT, but low 5 yr surv.

- Histology
  - neuroendocrine cytology
  - ↑mitoses, apoptosis, necrosis
  - Nuclear molding



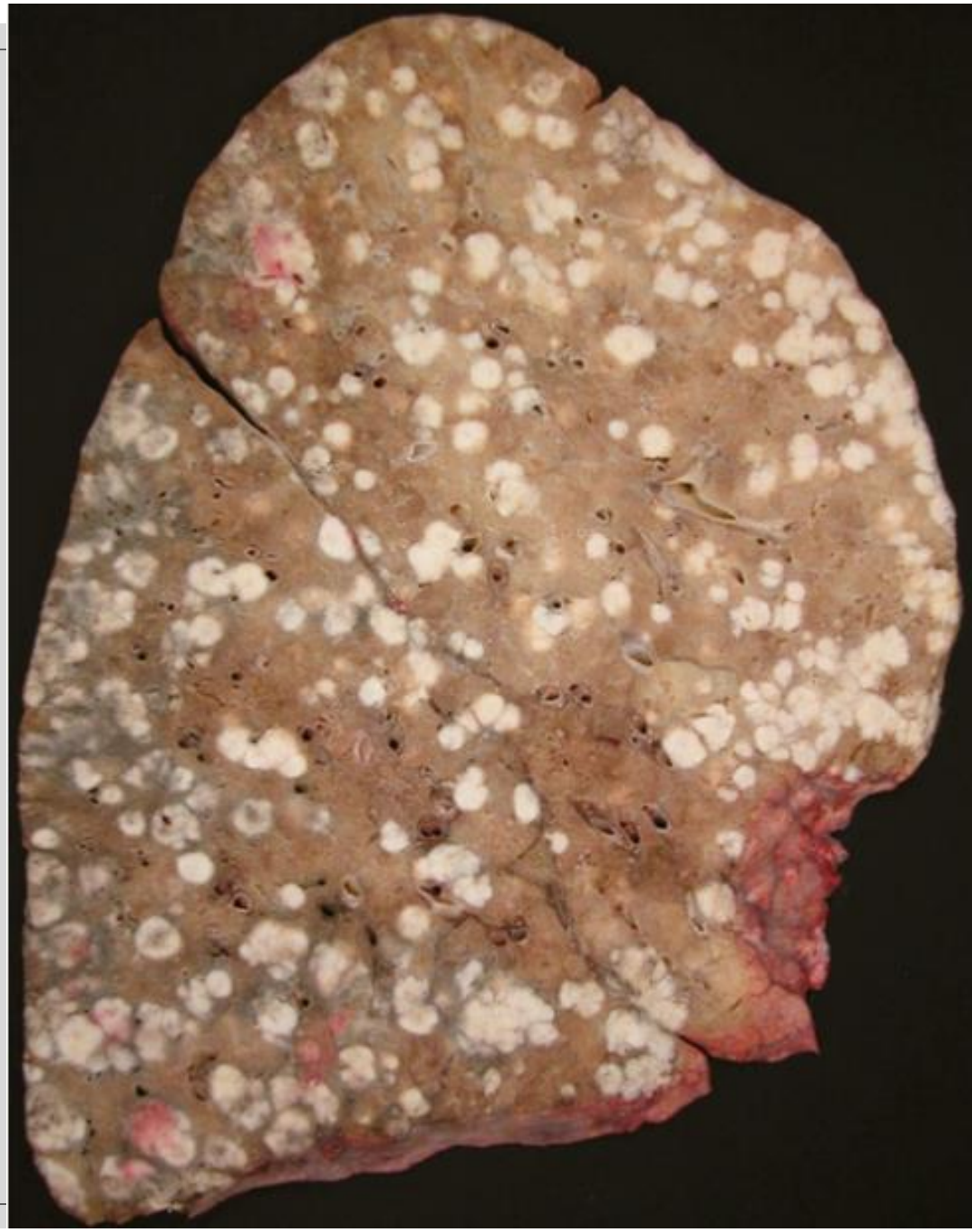
Normal lymphocytes

Metastatic Small Cell Carcinoma


Numerous Mitoses
Apoptotic bodies
Nuclear molding

Metastases

- Lung is a common site for metastasis
- Most common malignancy of the lung
- Multiple well circumscribed nodules favor metastases over 1° neoplasms
  - Breast, colorectal, head and neck, urologic, melanoma, gynecologic



Outline

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- Emphysema
- Lung Cancer

Questions?

UNC SCHOOL OF MEDICINE