Pleuropulmonary Neoplasia

APPROVED

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Robbins Questions w/ tumors/cancers:
#14, 18, 23, 24, 25, 29,33, 37, 40, 47, 49, 57,

Common Cancers and Cancer Deaths

Three Most Common Cancers among Men

- **Prostate: (157/100,00)**
- **Lung/Bronchus: (80/100,00)**
- **Colorectal: (53/100,00)**

Three Most Common Cancers among Women

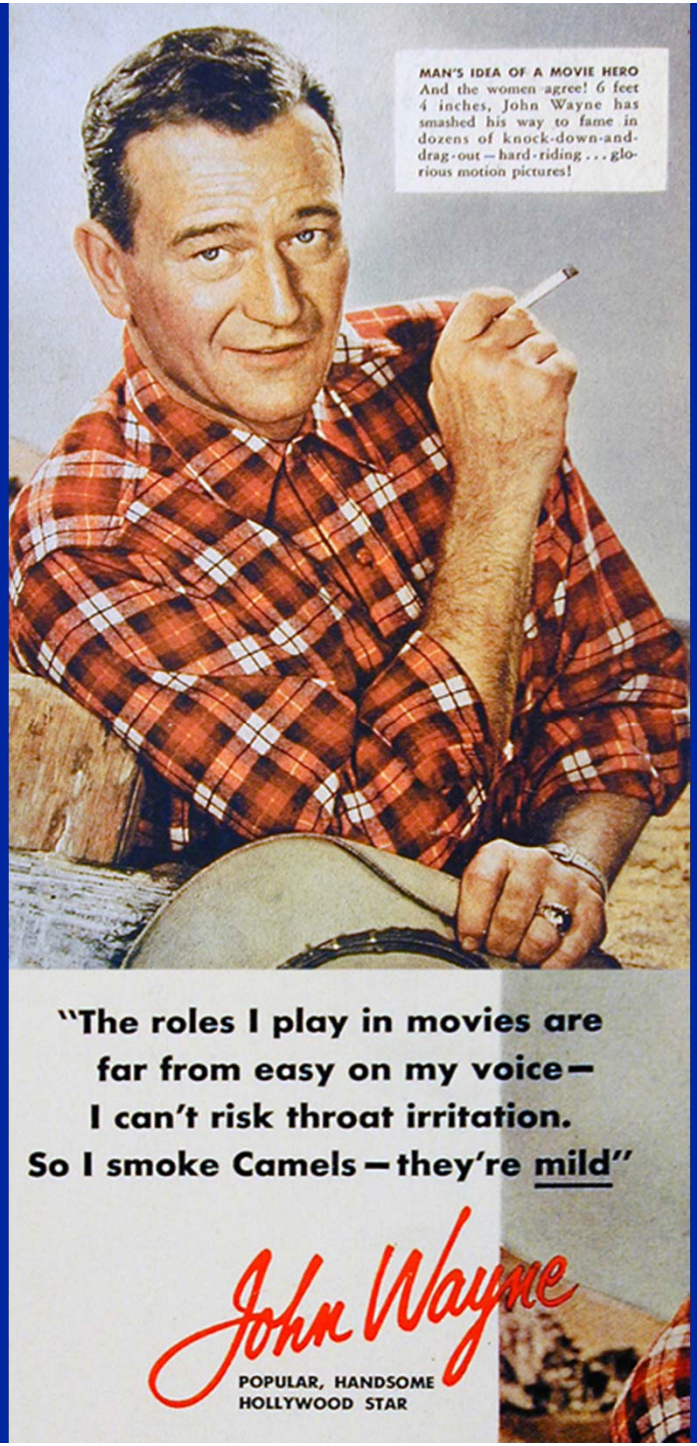
- **Breast: (120/100,00)**
- **Lung/Bronchus: (55/100,00)**
- **Colorectal: (41/100,00)**

Lung Cancer and Women

- Estimated 72,000 lung cancer deaths among women in the USA in 2010
- Leading cause of cancer death in both sexes, more deaths from lung ca than all the other most common solid tumors combined, women achieved equity with men in 2005

Carcinoma of the Lung

- **Leading cause of cancer death IN THE WORLD- 1990 data 1million cases worldwide, 1 million deaths, accounts for nearly 13% all cancers globally.**
- **Most who develop lung cancer DIE FROM IT**



John Wayne, an American icon, unfortunately died from lung cancer

Many other celebrities have died from lung cancer, and he thinks there is not enough publicity for lung cancer

Lung Cancer killed them too

Paul Newman, Joe Dimaggio, Walt Disney, Duke Ellington, George Harrison, Nat King Cole, Yul Brynner, Suzanne Pleshette, Vincent Price, Desi Arnaz, John Updike, Ayn Rand as well as 90,139 and 69,078 less famous men and women in 2005 alone

Lung cancer- risk factors

-Tobacco usage, esp. **cigarette smoking** accounts for up to **90%** of all lung cancer deaths, fewer than **20% of smokers** get ca

environmental tobacco smoke

- ETS/ cigars
- Radon
- Asbestos

Who painted this? Van Gogh, late 1870s. Surgeon General warning came out in 1960s. Van Gogh painted this just to annoy his instructor.

Lung cancer risk-gender

- 1950-1990, **600%** rise in lung cancer mortality in women
- ? Increased biologic susceptibility suggested in case control studies
- Female smokers have 2-3 x risk of developing **small cell carcinoma**

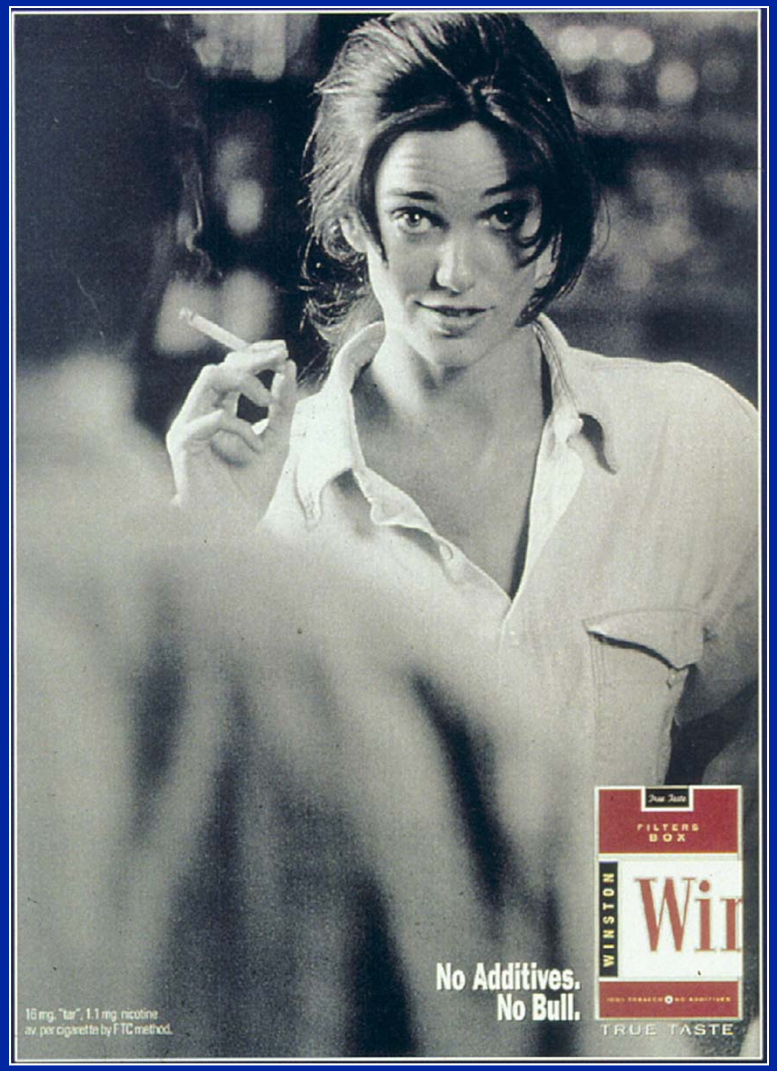
huge increase

we don't know why this is true

this is a particularly dire form

increase in lung cancer in women is due to their increase in smoking in the 1960s which was due to new cigarettes such as Virginia Slims that were advertised to women

these days, cigarette companies still target young women and he says there should be more public outcry on this, I agree



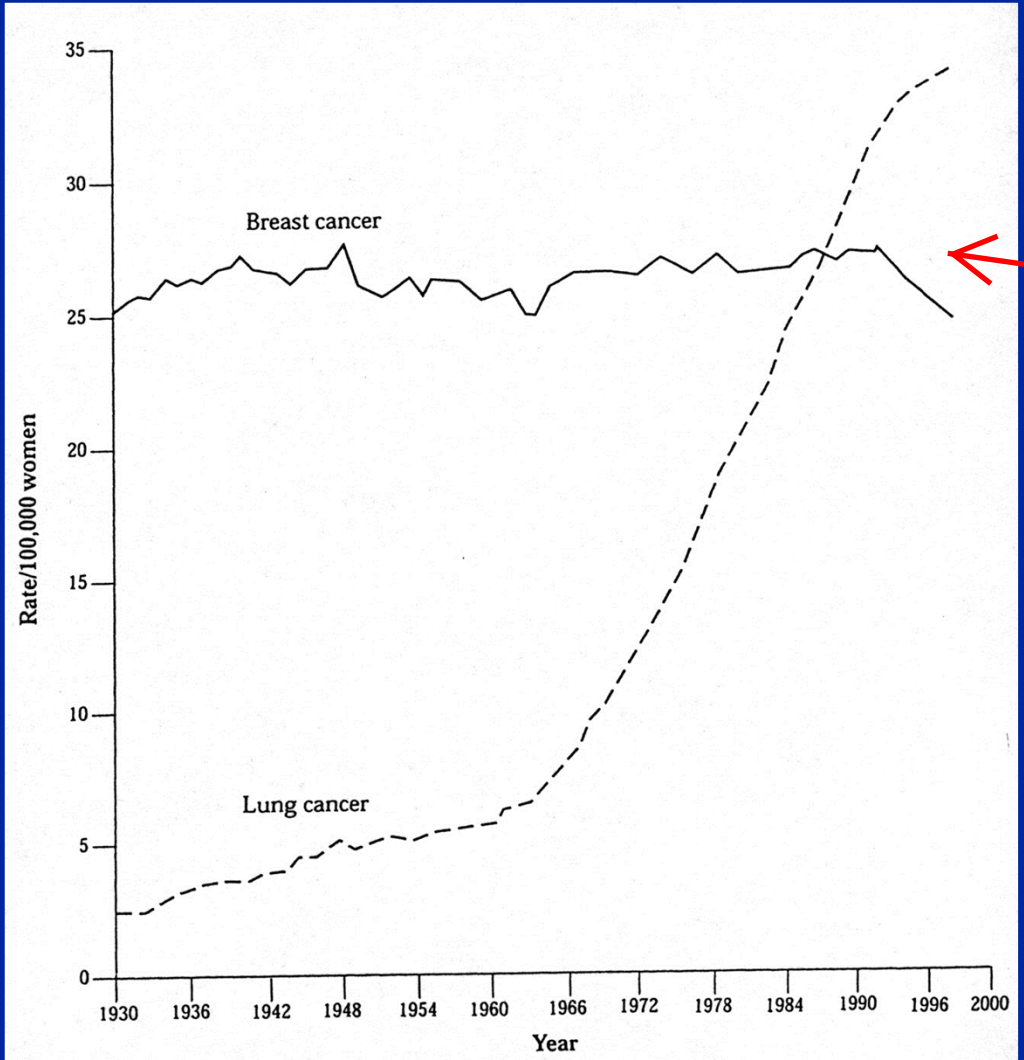


Figure 2. Age-adjusted death rates for lung cancer and breast cancer among women, United States, 1930–1997. Death rates are adjusted to 1970 population. (*From* USDHHS: Women and Smoking. A Report of the Surgeon General. pp 193–209, 2001; with permission.)

these has been decrease in death rate for breast cancer in the last couple decades but this is not true for lung cancer

Lung cancer mortality by state (1992-1996)

- **Highest: Kentucky>Arkansas>W. Va**
- **New England: ME #8, RI#22, NH# 23, VT # 29,**
- **North Carolina #16**
- **Lowest= Utah. Mortality patterns generally reflect prevalence of smoking**

there are more people smoking in certain states

It is always better to quit smoking. The earlier the better. However, even if you quit, your risk will not come back down to normal.

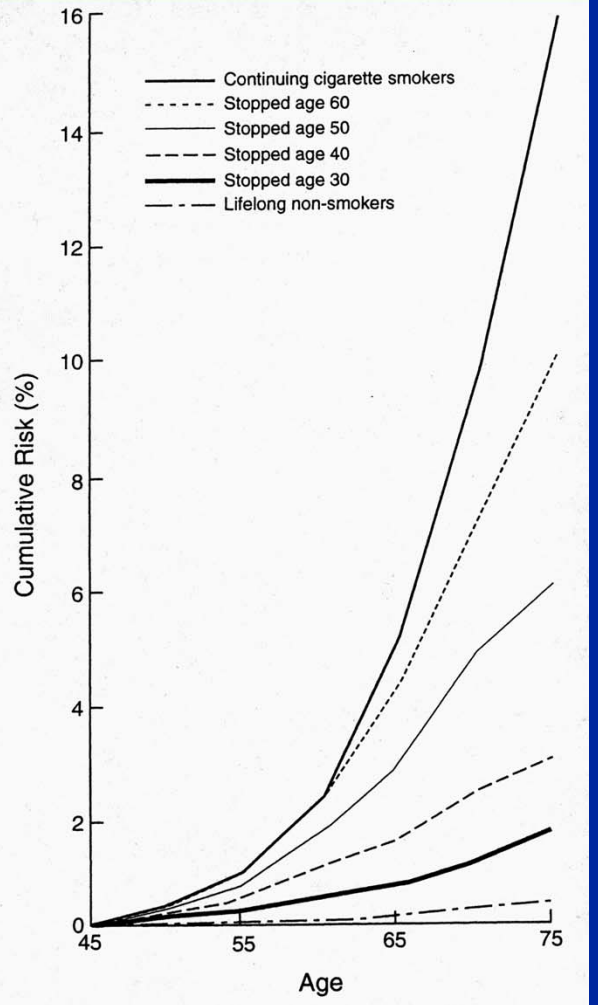


Figure 8. Effects of stopping smoking at various ages on the cumulative risk for death from lung cancer up to age 75 at death rates for men in the United Kingdom in 1990. Nonsmoker risks are taken from a US prospective study of mortality. (*From* Peto R, Darby S, Deo H, et al: Smoking, smoking cessation, and lung cancer in the UK since 1950: Combination of national statistics with two case-control studies. BMJ 321:323–329, 2000; with permission.)

Classification

- Small cell vs Non-small cell carcinoma (bronchogenic ca)
- Bronchial tumors, salivary gland-like tumors
- Malignancies of the pleura

bronchogenic carcinoma is synonymous with cancer of the lung, strictly speaking this term is for cancer arising from within the bronchi, but it is a little bit of a misnomer

W.H.O. CLASSIFICATION OF LUNG CANCER

4 basic types

- Adenocarcinoma
- Squamous cell carcinoma
- Large cell carcinoma
- Small cell carcinoma

BRONCHOGENIC CARCINOMA

- SMALL CELL 20-25%
- NON-SMALL CELL
  - SQUAMOUS CELL - 25-40%
  - ADENOCARCINOMA - 25-40%
  - LARGE CELL - 10-15%

this is the most common lung cancer of the non-small cell cancers

most of these cancers have strong association with smoking

Subtype by smoker status

- Squamous cell: 98% vs 2%
- Adenocarcinoma: 82% vs 18%
- BAC: 70% vs 30%
- Small cell: 99% vs 1%
- Large cell: 93% vs 7%

Biology of lung cancer

- Local growth, local invasion of bronchi, vasculature and pleura
- Spread via **lymphatics:** peribronchial, hilar and mediastinal lymph node groups
- Distant hematogeneous metastases- **bone, liver, adrenal glands and CNS**

spreads first via the lymphatics

it is very bad once it gets into the mediastinum

these are the common sites of metastases

all solid tumors regardless of body topography are staged this way

Staging: TNM system

- T= features of primary tumor: size, relationship to carina, mediastinal structures, chest wall
- N=nodes: peribronchial, hilar, mediastinal
- M=metastases: lung, adrenals, bones, brain.

Non-small cell carcinomas

- Squamous
- Large cell
- Adenocarcinoma
- Mixed
- Behavior primarily a function of clinical stage, more than type.
- Surgical approach

there are some with mixed histologies

behavior depends on the stage of the cancer

usually with non-small cell carcinoma.

Signs and Symptoms

- Local direct effects from endobronchial growth, obstruction
- Direct extension into mediastinum and chest wall, nerve entrapment syndromes, superior vena cava syndrome
- Paraneoplastic/endocrine syndromes

beneath the bronchi or in the mucosa itself

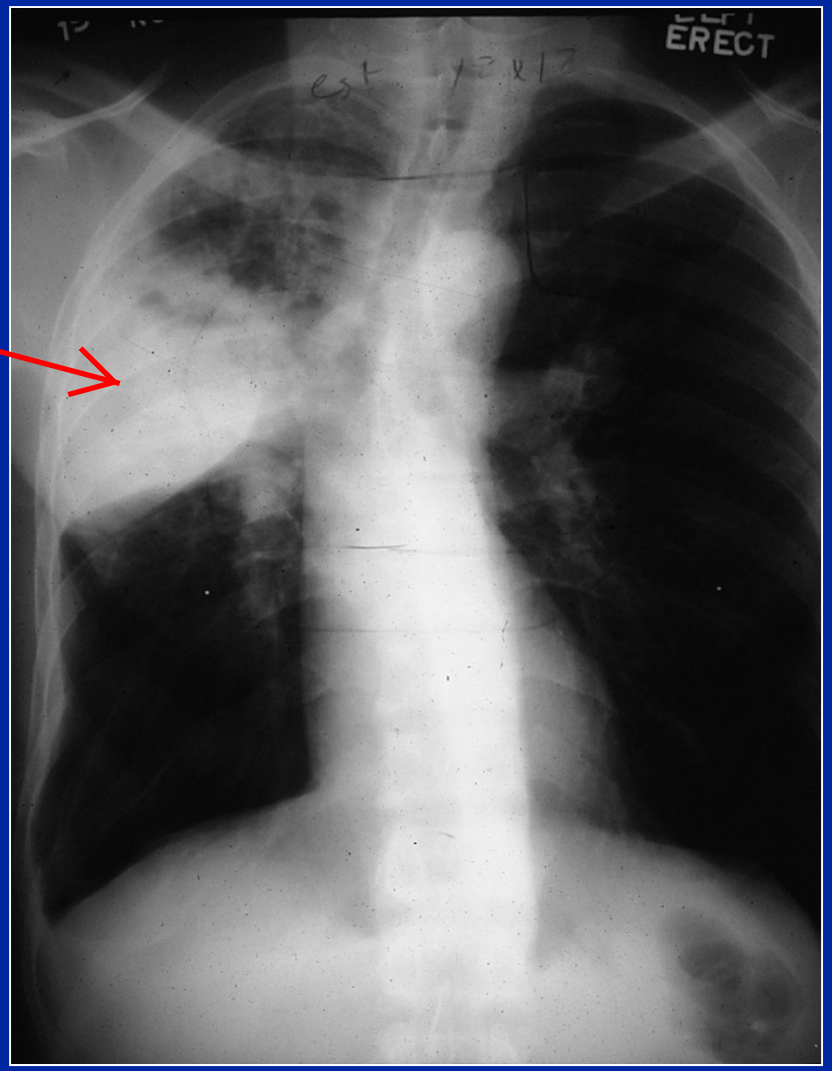
may see recurrent pneumonias, cough, spitting up blood (hemoptyisis)

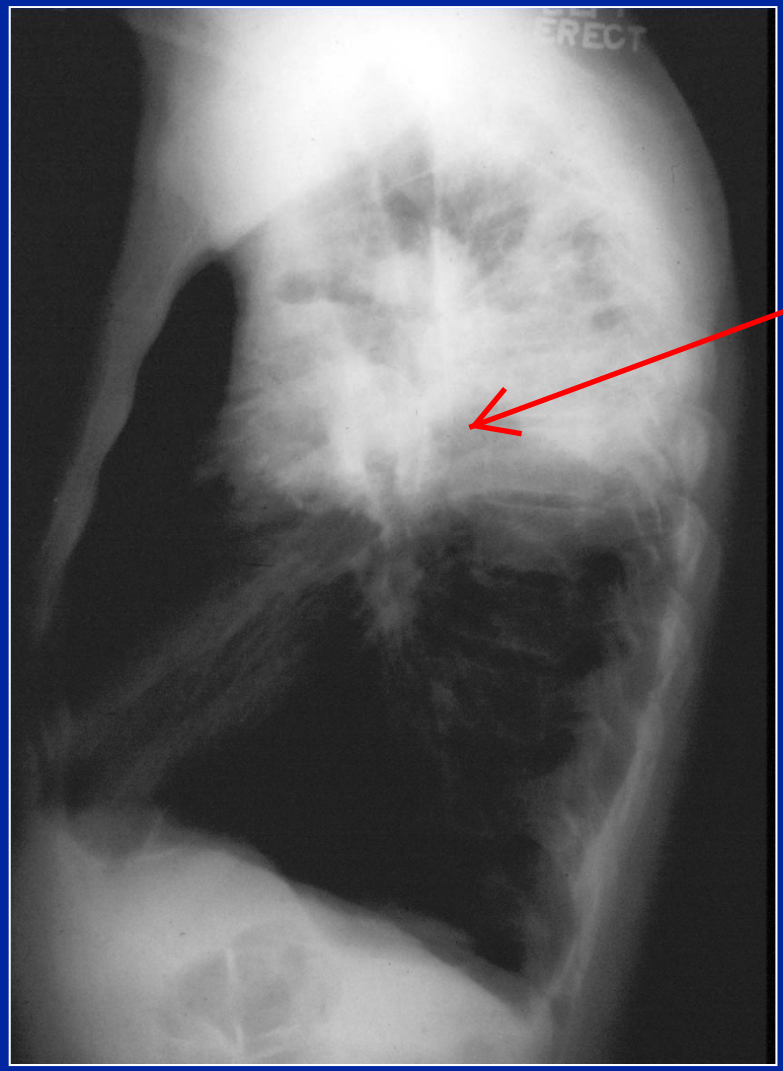
may see chest pain

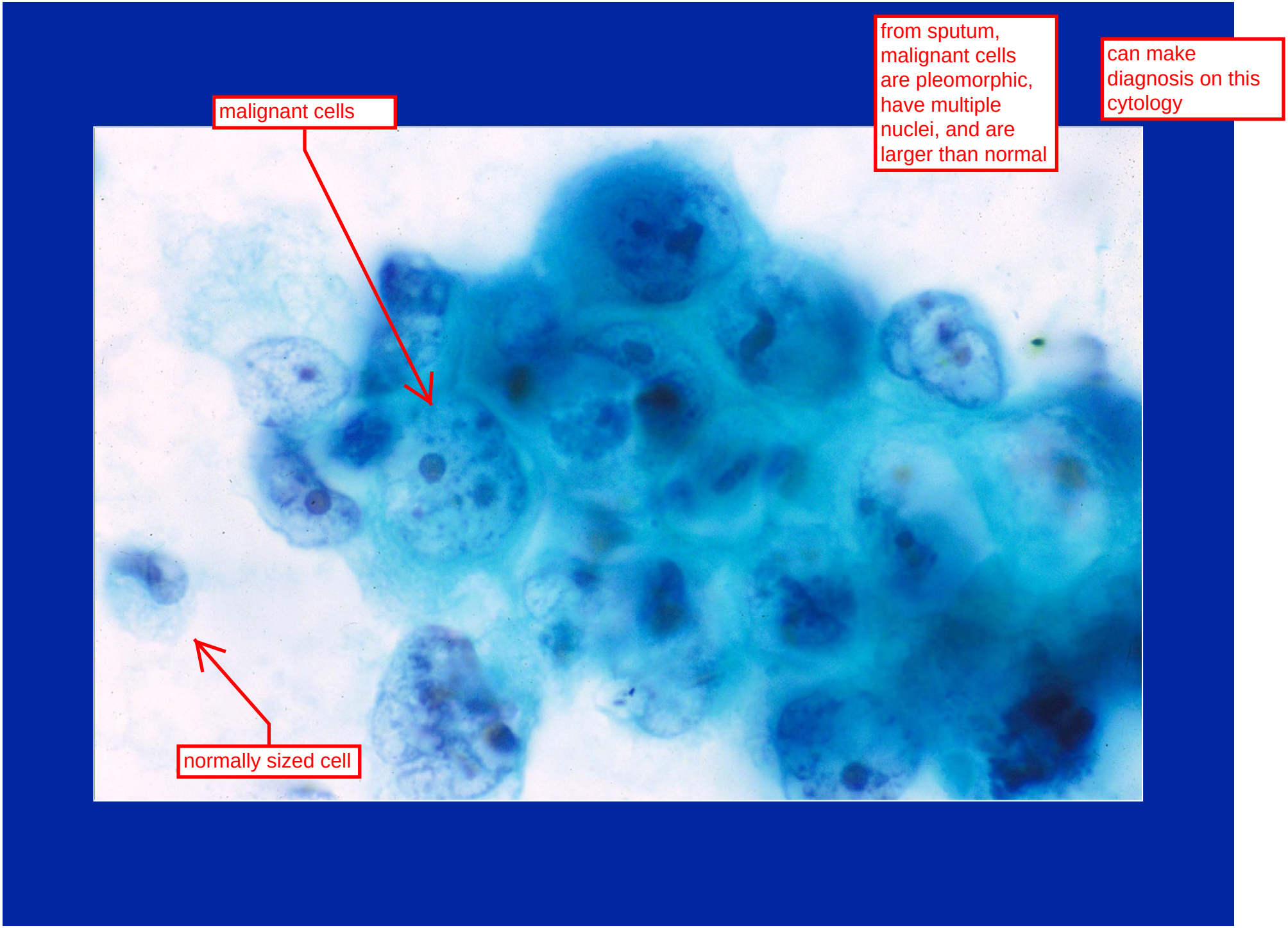
congestion of the upper extremeties

a lot of these cancers may secrete hormones

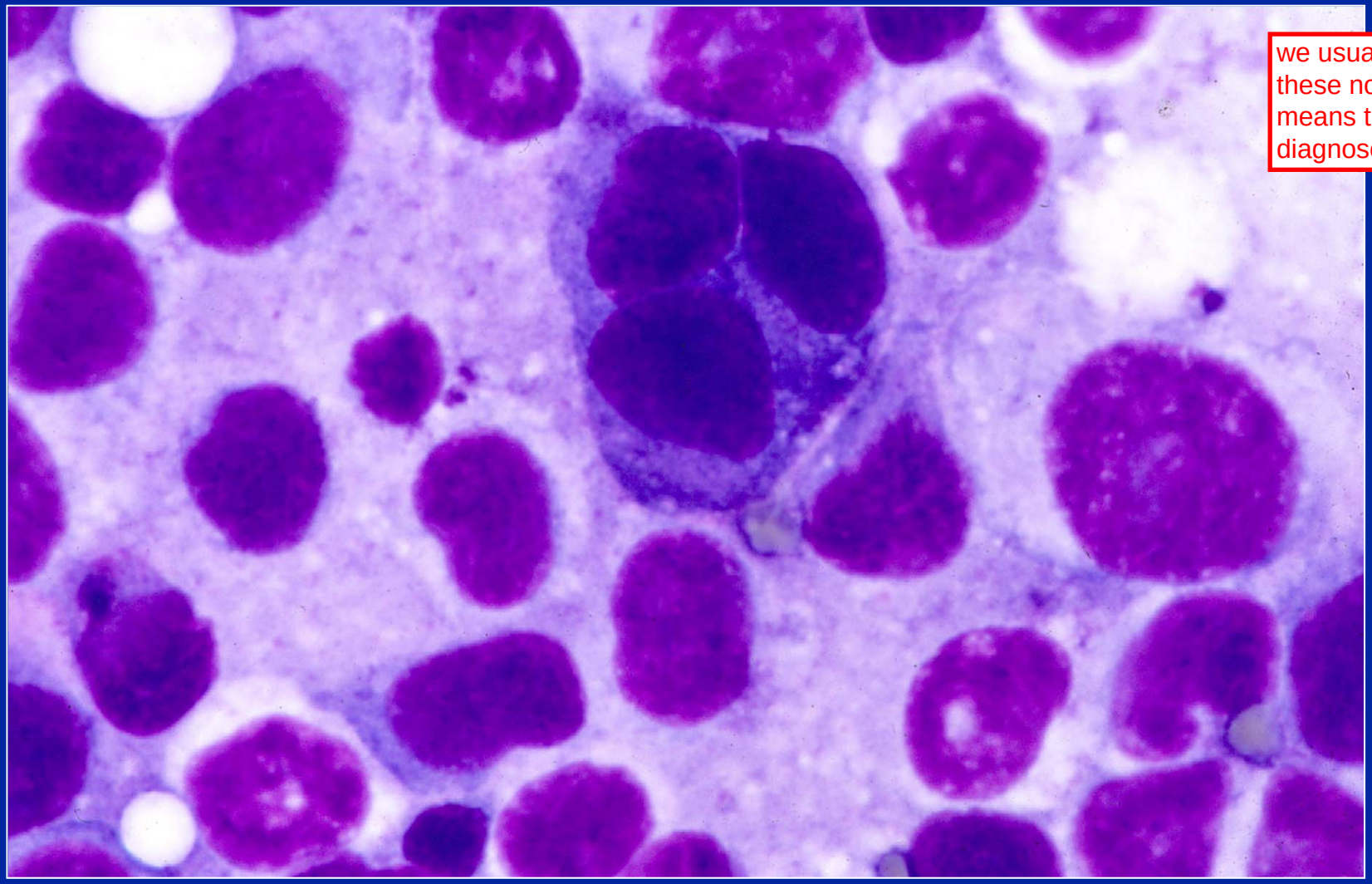
see a mass that is not aerated




see it in this view,
this is a typical
local lung cancer


malignant cells
from sputum, malignant cells are pleomorphic, have multiple nuclei, and are larger than normal
can make diagnosis on this cytology
normally sized cell

can do needle aspiration and do stain



we usually use these noninvasive means to diagnose

Squamous Cell Ca

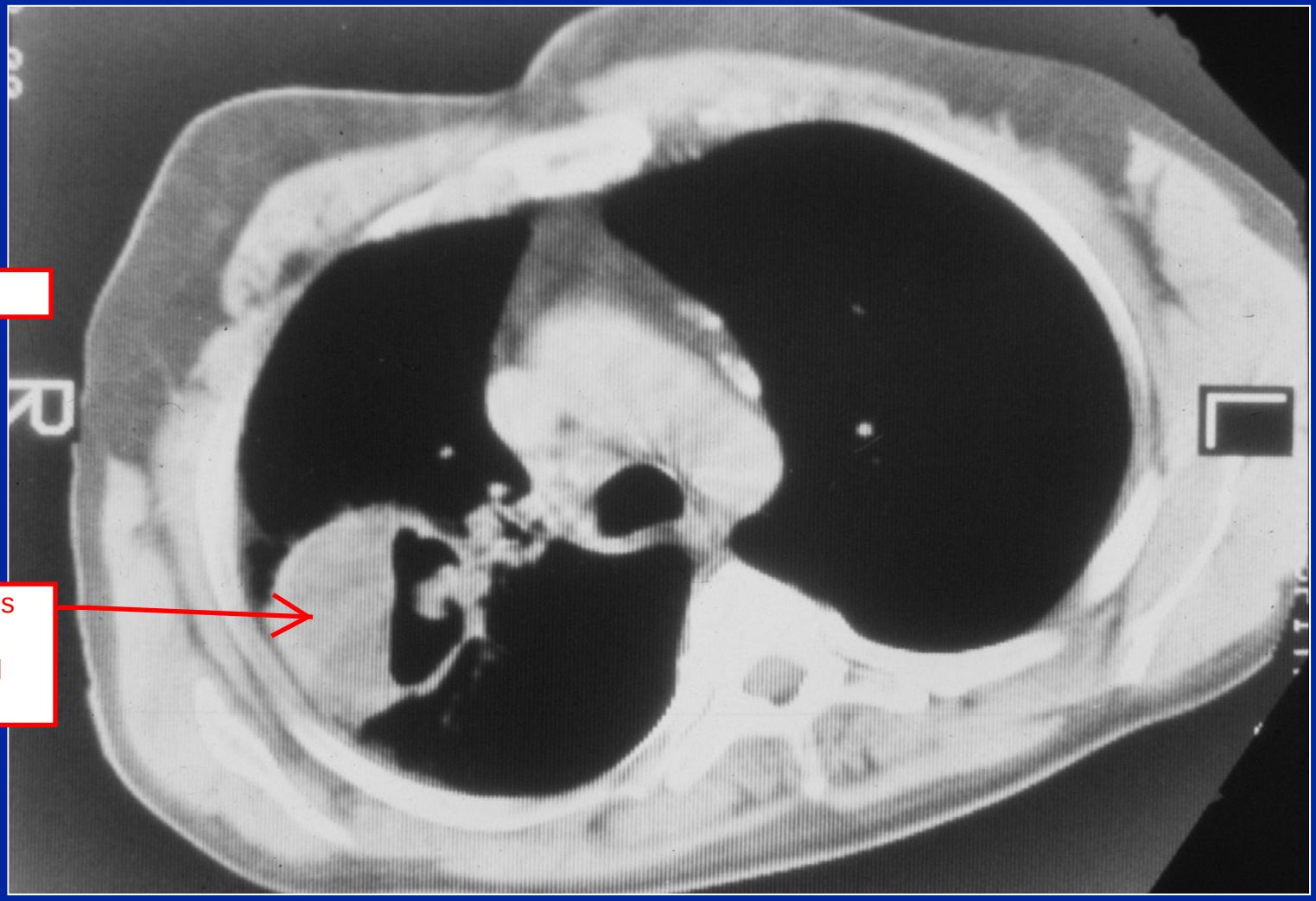
- 30% of all primary lung malignancies
- Central, involve large airways, endobronchial growth
- Strong association with cigarette smoking

Squamous cell ca: morphology

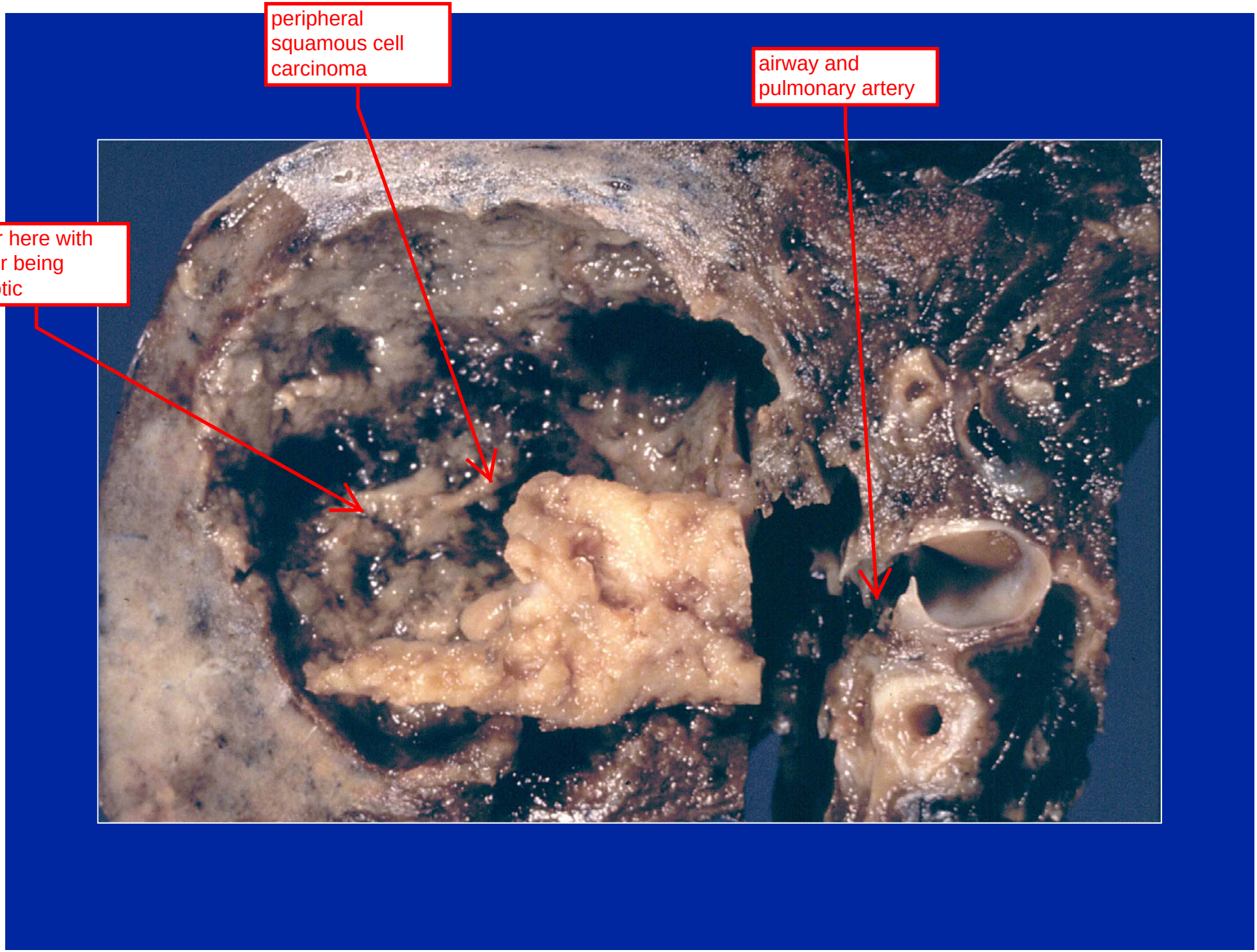
kind of looks like skin histologically

- Differentiating features of squamous epithelium; keratinization (pearls) and intercellular bridges
- likely to cavitate: 70% cavitary lung ca are squamous

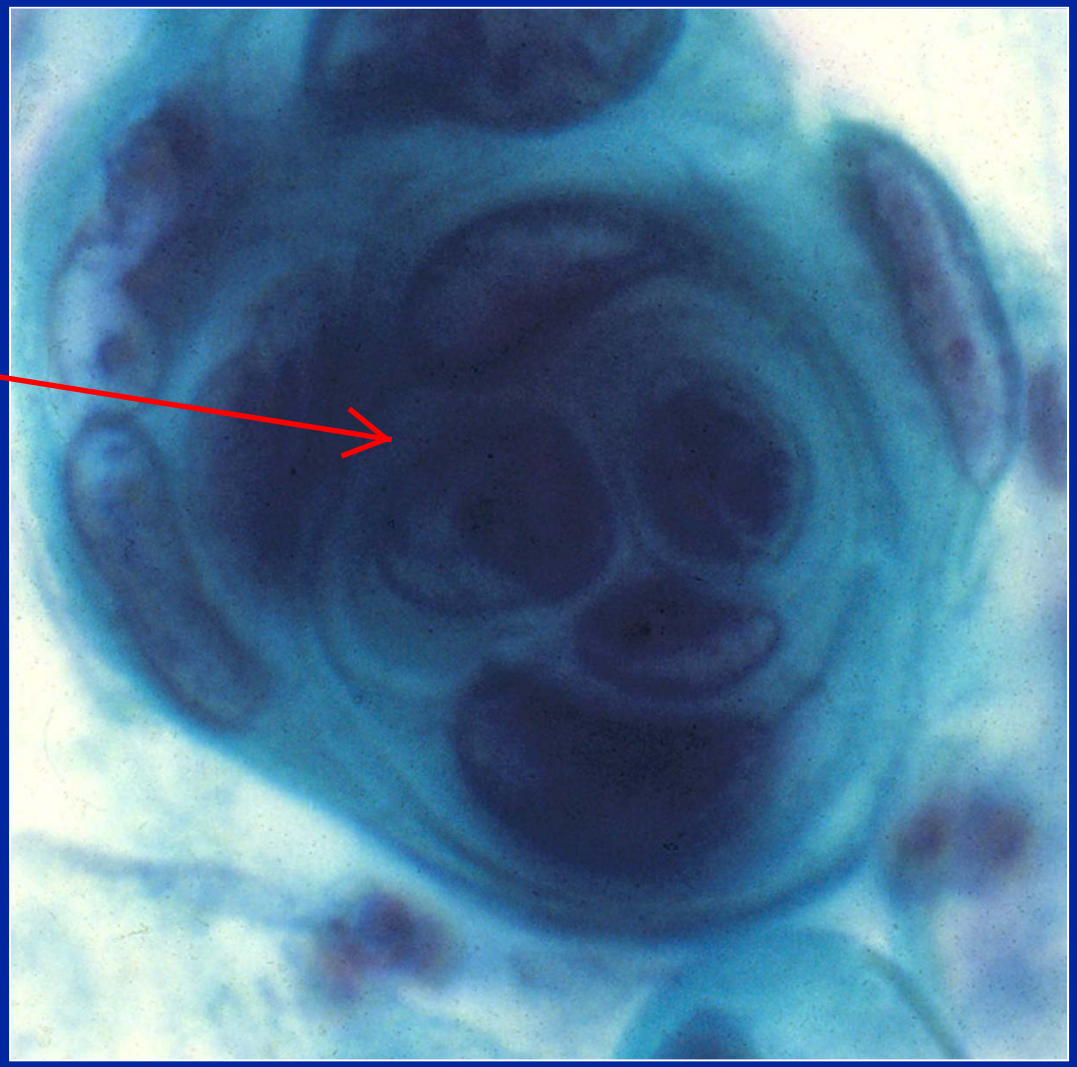
CT scan



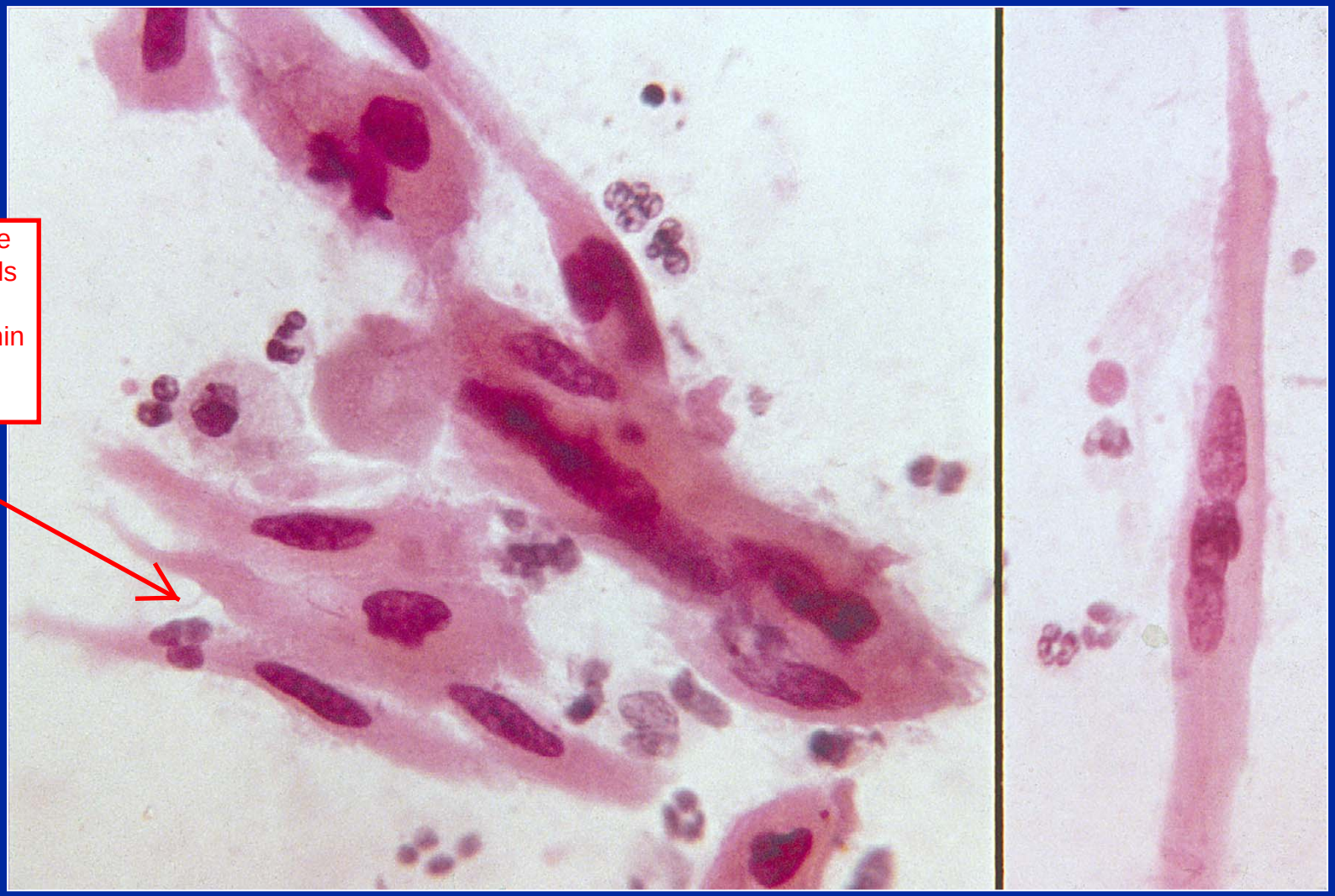
large squamous cell carcinoma with an air fluid level in it

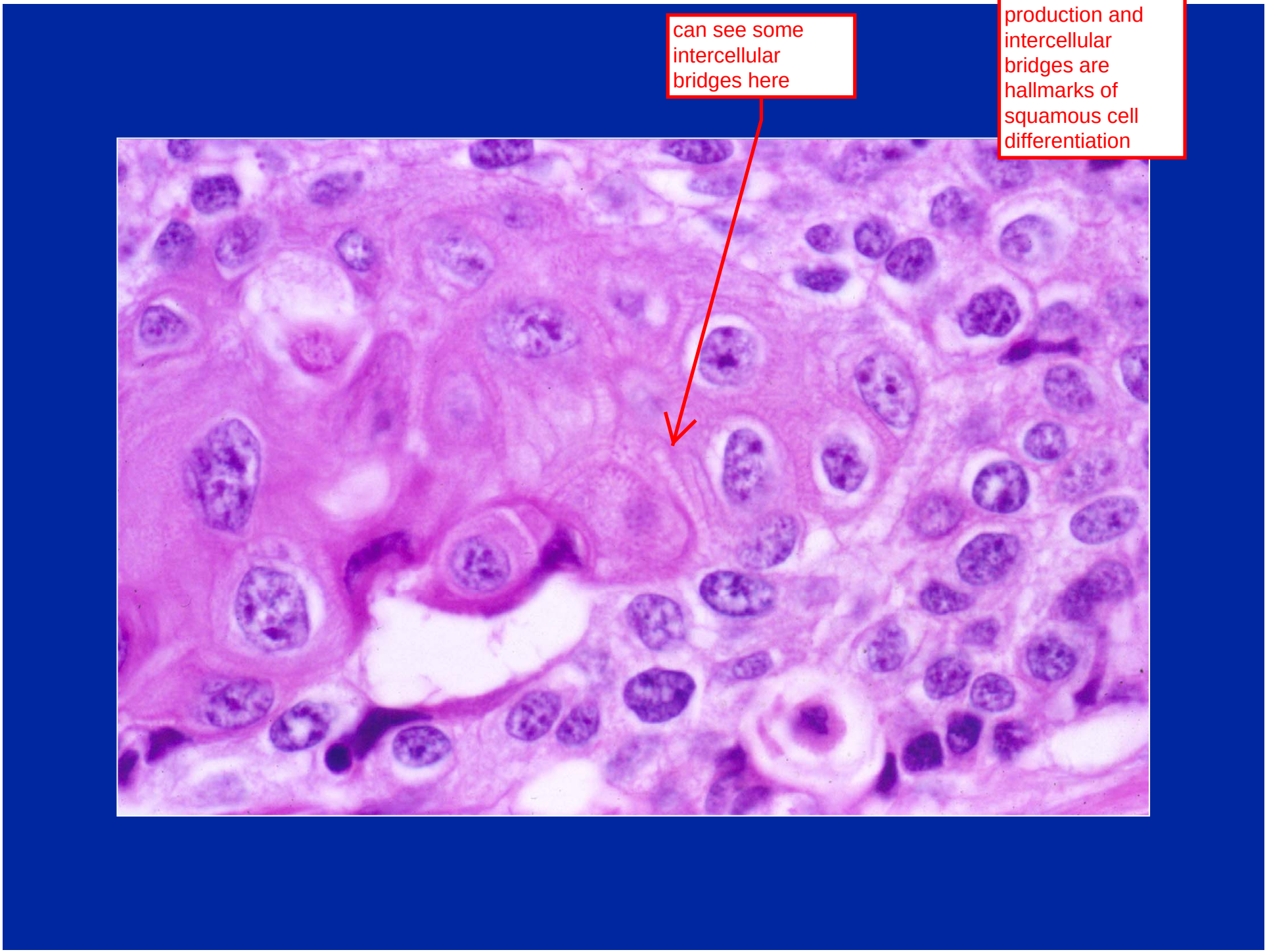

peripheral squamous cell carcinoma
airway and pulmonary artery
tumor here with center being necrotic

cytologically, squamous cell carcinoma cells like to wrap around each other

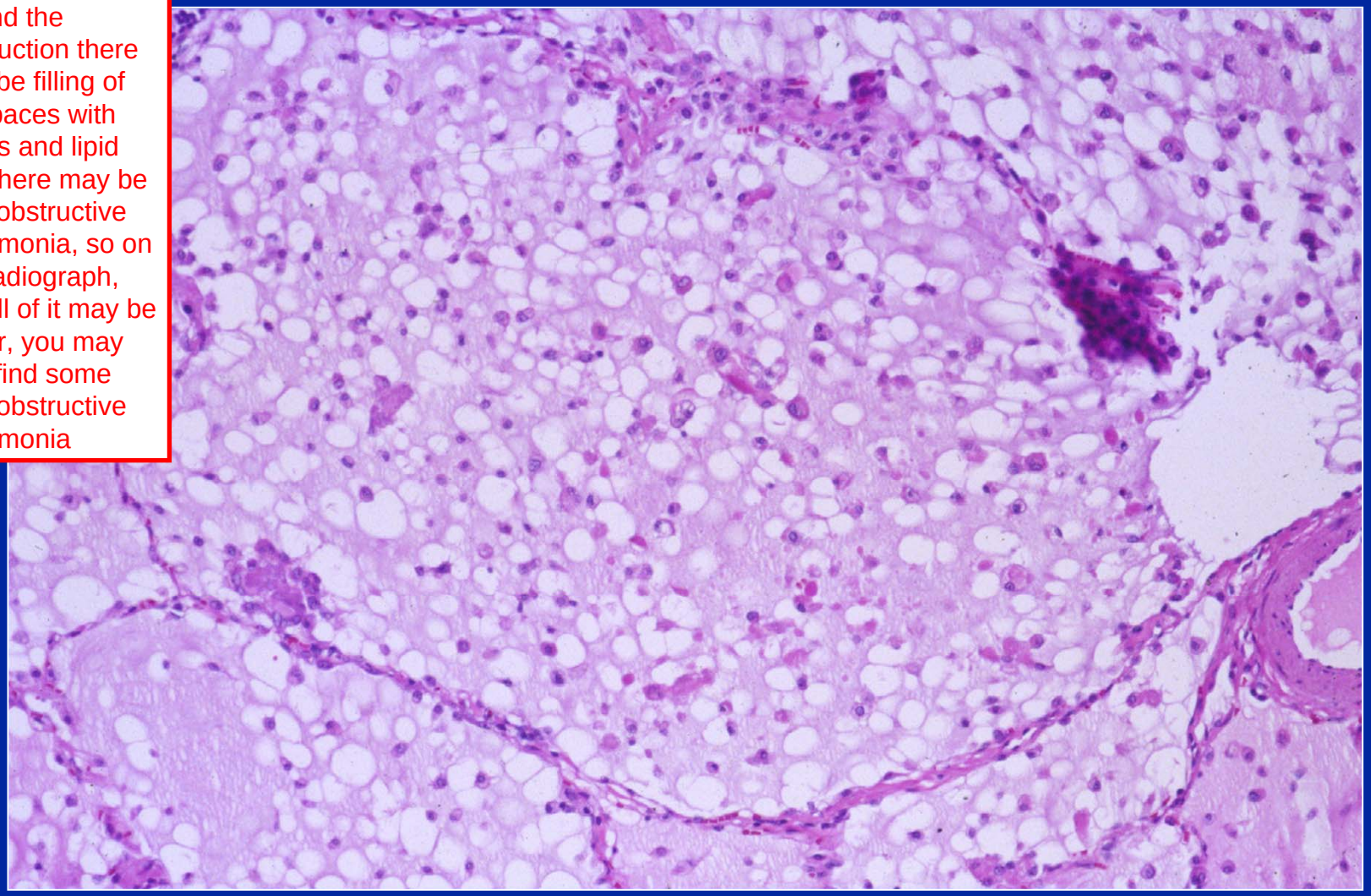


in sputum can see the elongated cells and also see keratin (pink) within the cytoplasm of the cells




can see some intercellular bridges here
so, keratin production and intercellular bridges are hallmarks of squamous cell differentiation

because these tumors grow endobronchially, behind the obstruction there may be filling of air spaces with debris and lipid and there may be post obstructive pneumonia, so on the radiograph, not all of it may be tumor, you may also find some post obstructive pneumonia



Bronchogenic ca: small cell carcinoma

- 20-25% all lung cancers
- aggressive, responsive to chemo
- central tumor, staged as limited (30%) vs extensive (70%)
- Distinctive clinical manifestations : Eaton-Lambert syndrome, SIADH, ACTH

most lethal form of lung cancer

cures are generally less than 10%

may be quizzed about these on the wards

inappropriate ACTH

small cell ca is most likely to have paraneoplastic syndromes

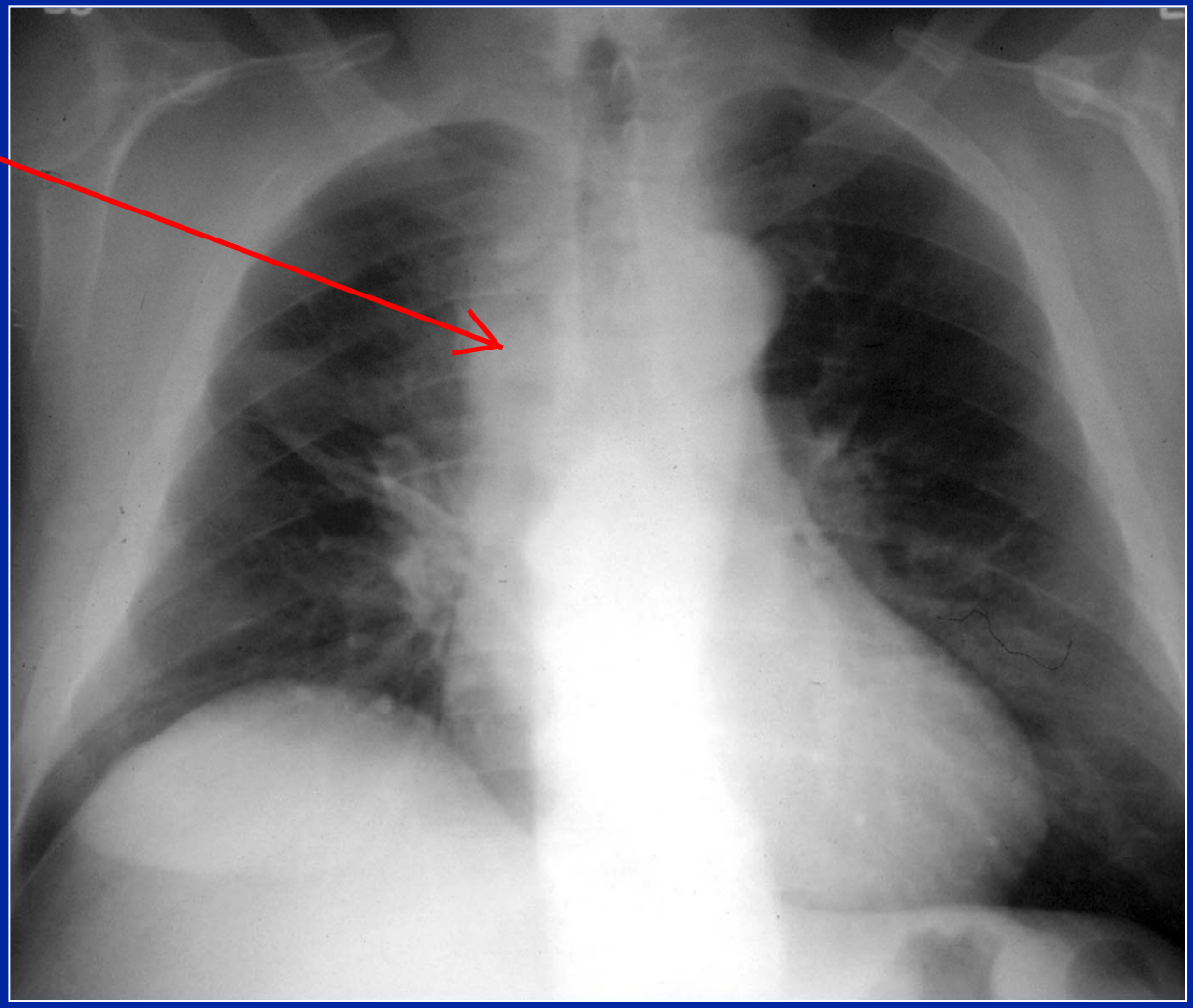
inappropriate ADH

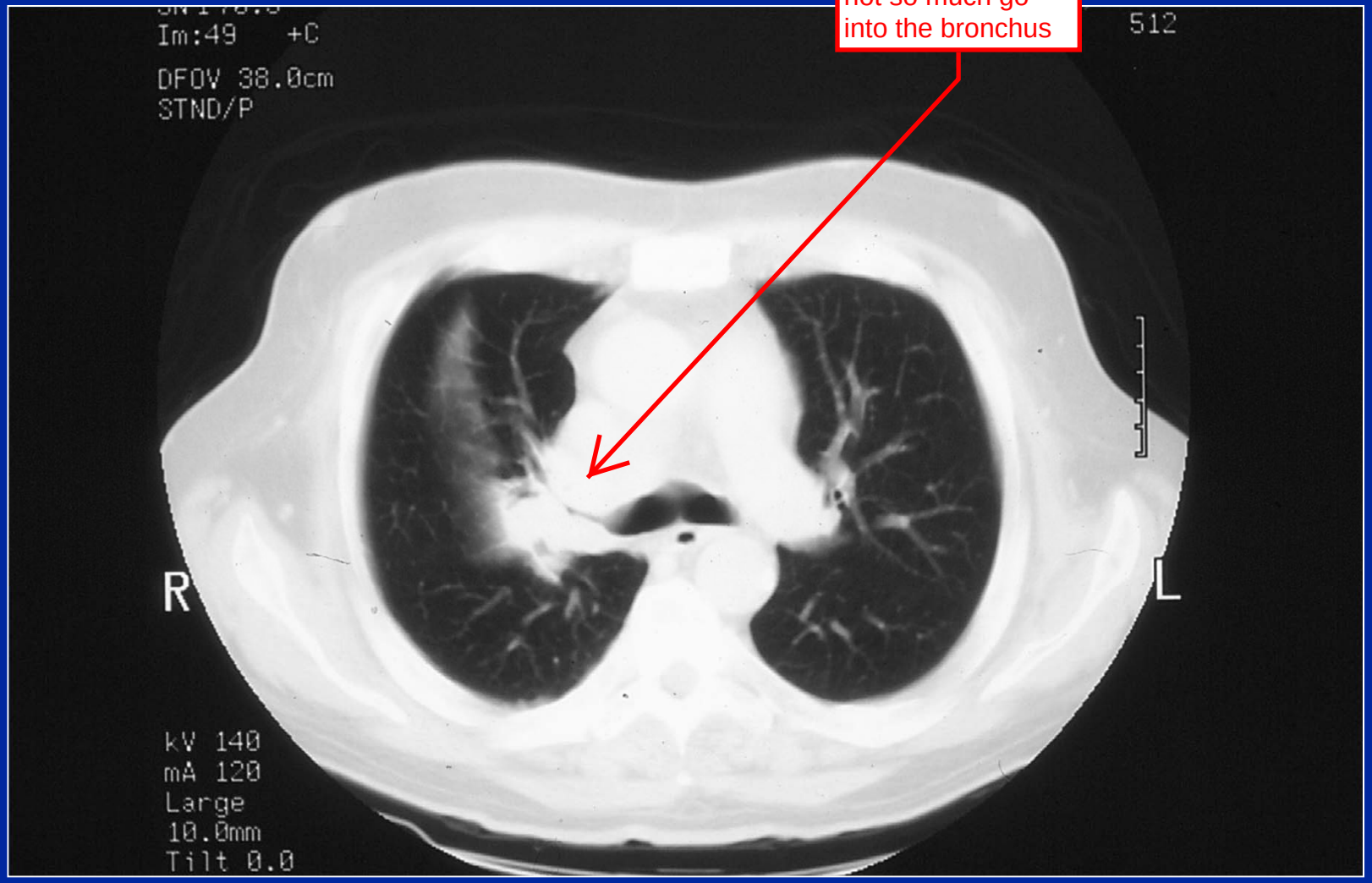
proximal muscle weakness

SYMPTOM COMPLEXES

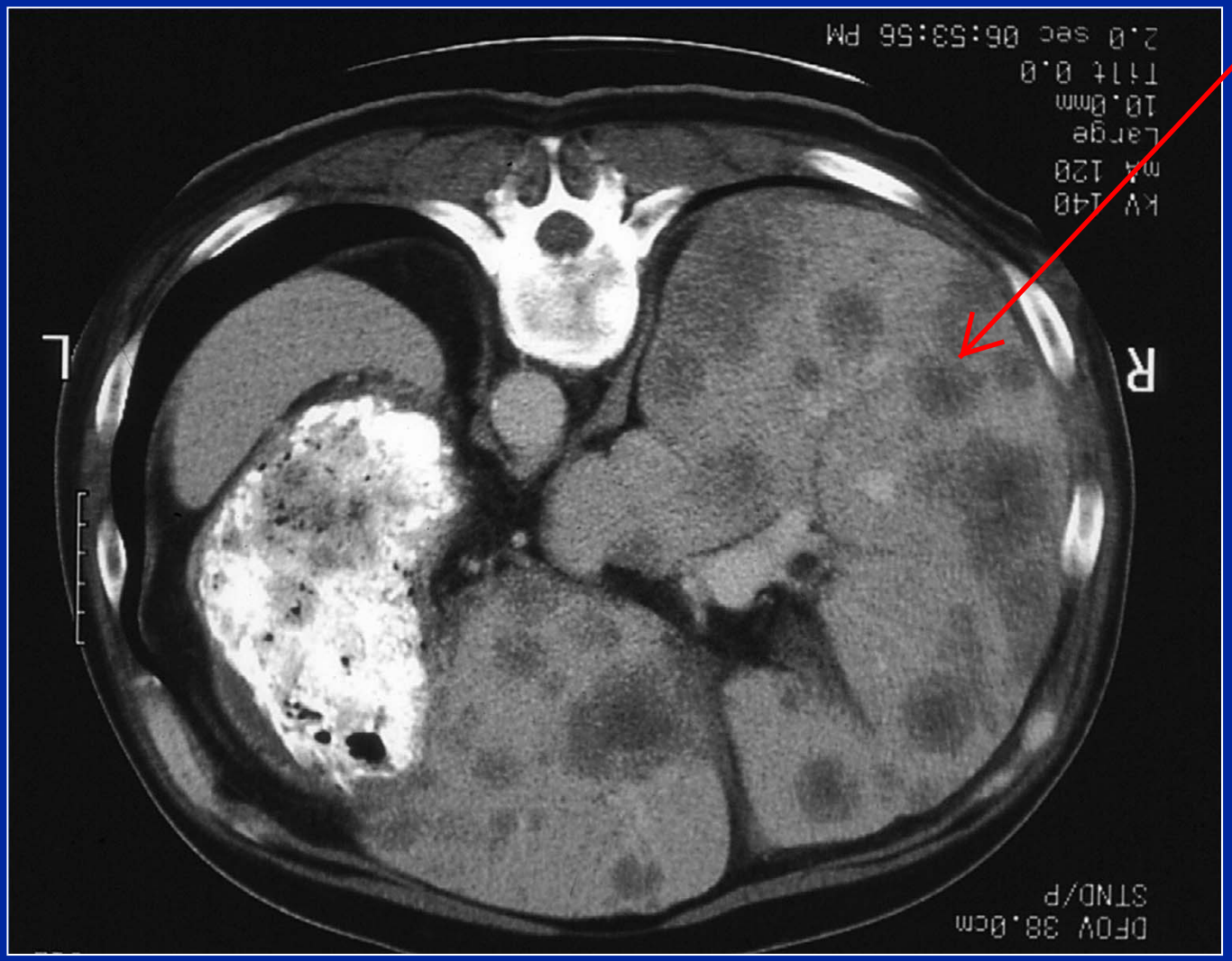
- CENTRAL/ENDOBRONCHIAL GROWTH
- PERIPHERAL GROWTH
- REGIONAL SPREAD
- PARANEOPLASTIC SYNDROMES

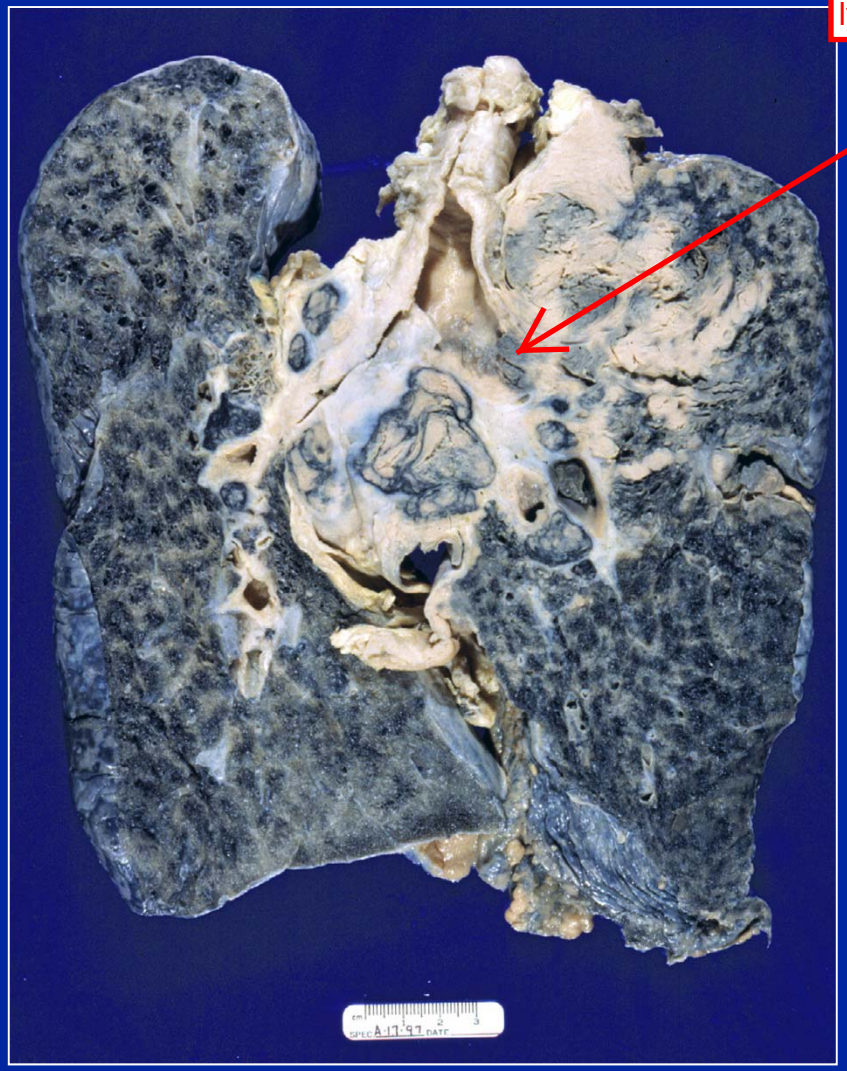
small cell ca tends to be central tumor, you can see that it is central




small cell ca tends to compress bronchus from the outside, and does not so much go into the bronchus
Im:49 +C
DFOV 38.0cm
STND/P
512
R
L
kV 140
mA 120
Large
10.0mm
Tilt 0.0

small cell ca often metastasizes to the liver as can be seen here

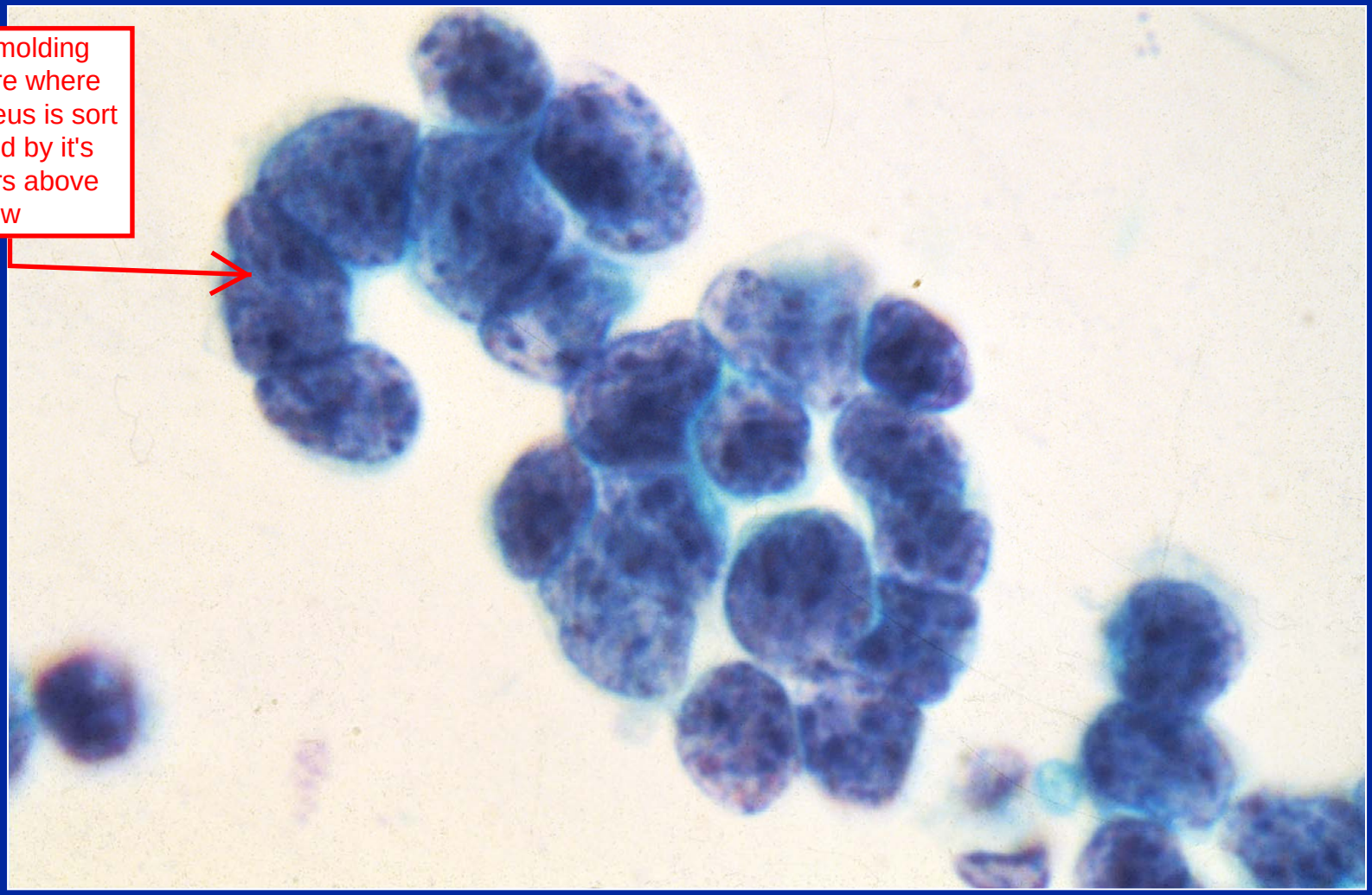


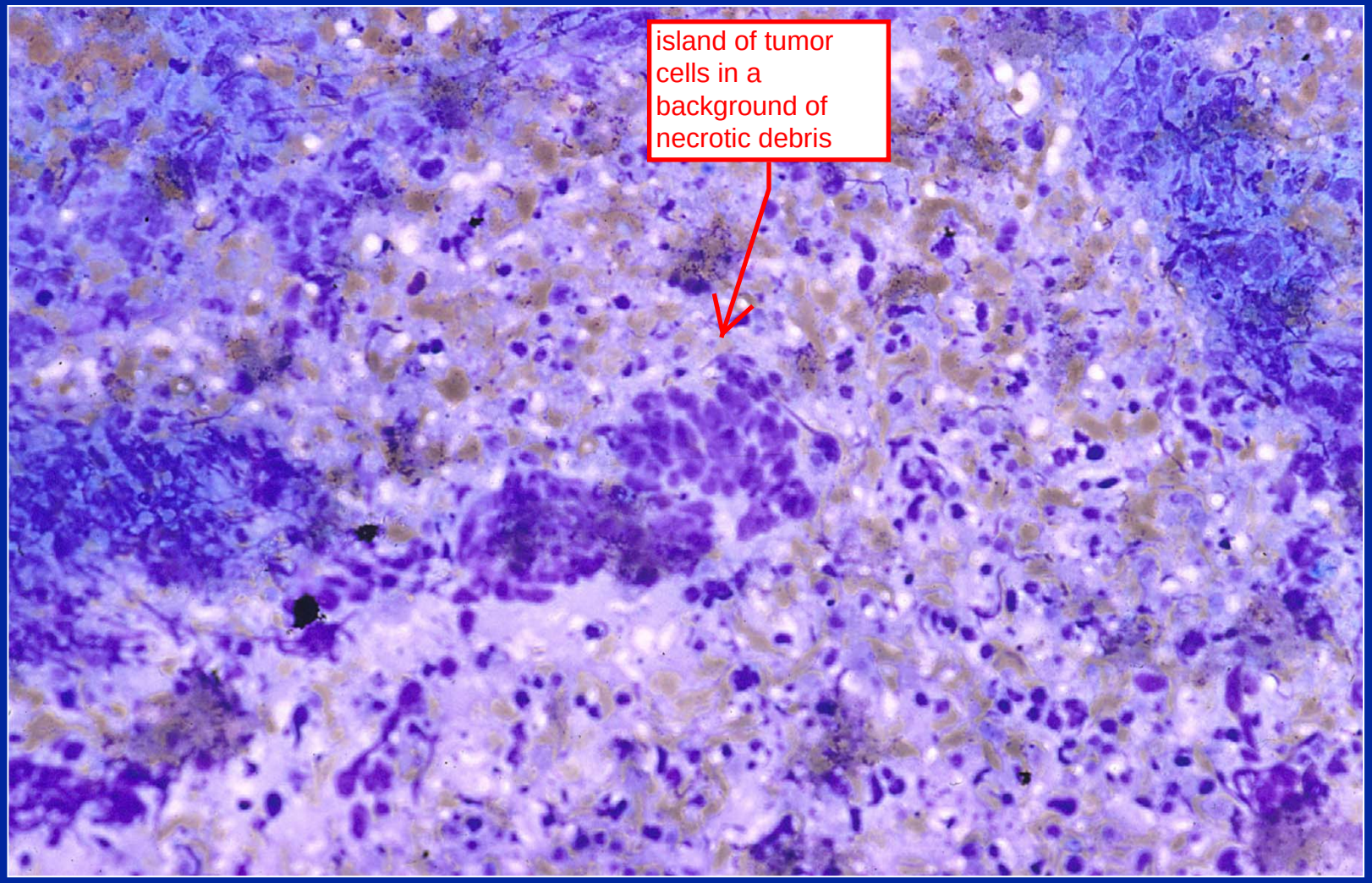

both lungs, see tumor in the central part and it is in the upper lobe and into the lymph nodes

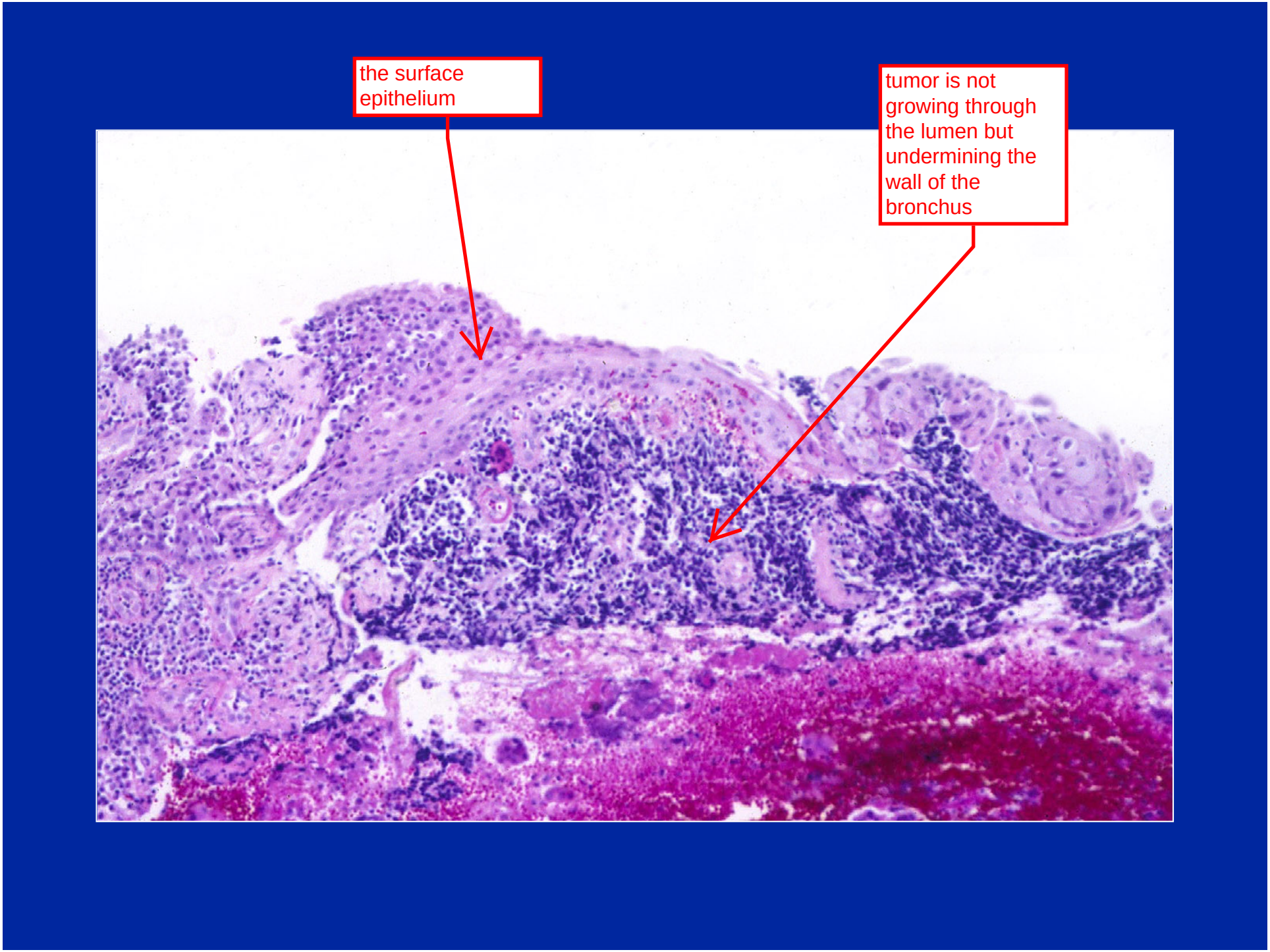
small cell ca tends not to grow discrete masses but grows out via the airways into the periphery

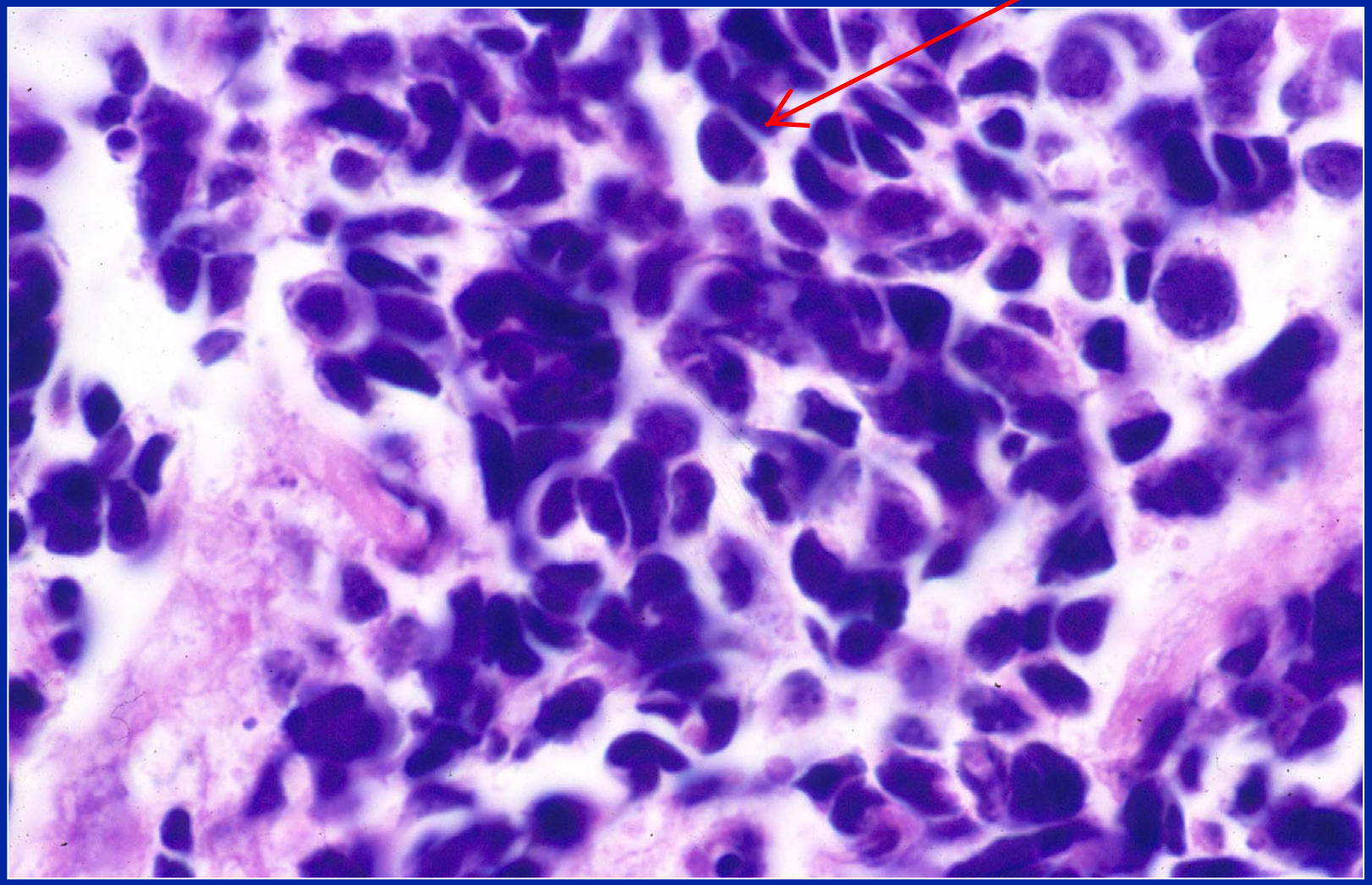
Small cell carcinoma: morphology

- Small cells,(1-1.5 x lymphocyte)
- Hyperchromatic nuclei, molding and crush
- necrosis


nuclear molding seen here where the nucleus is sort of molded by it's neighbors above and below


island of tumor cells in a background of necrotic debris


the surface epithelium
tumor is not growing through the lumen but undermining the wall of the bronchus


small angulated hyperchromatic nuclei with almost no cytoplasm

most common form of primary lung cancer

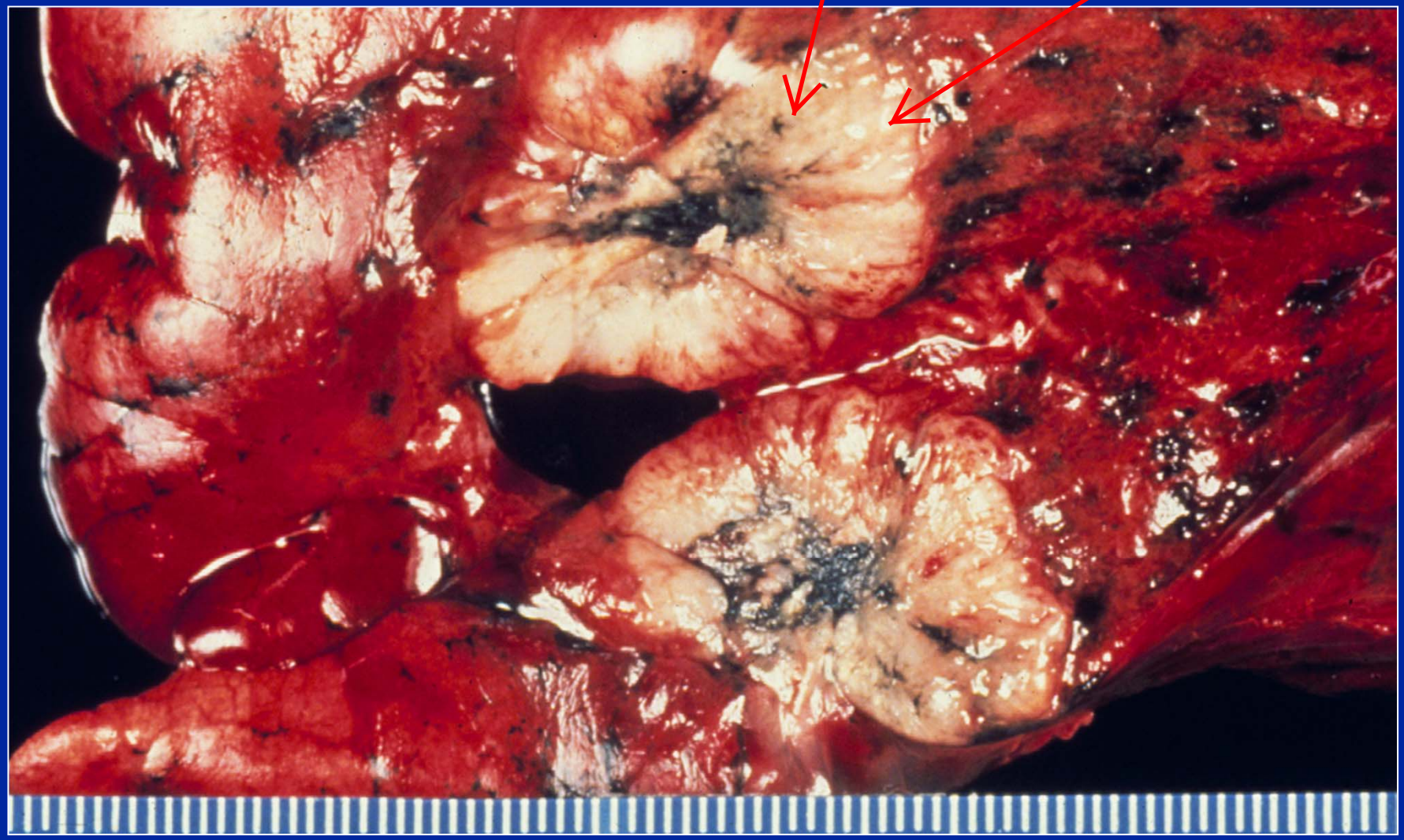
not central but tend to be in periphery

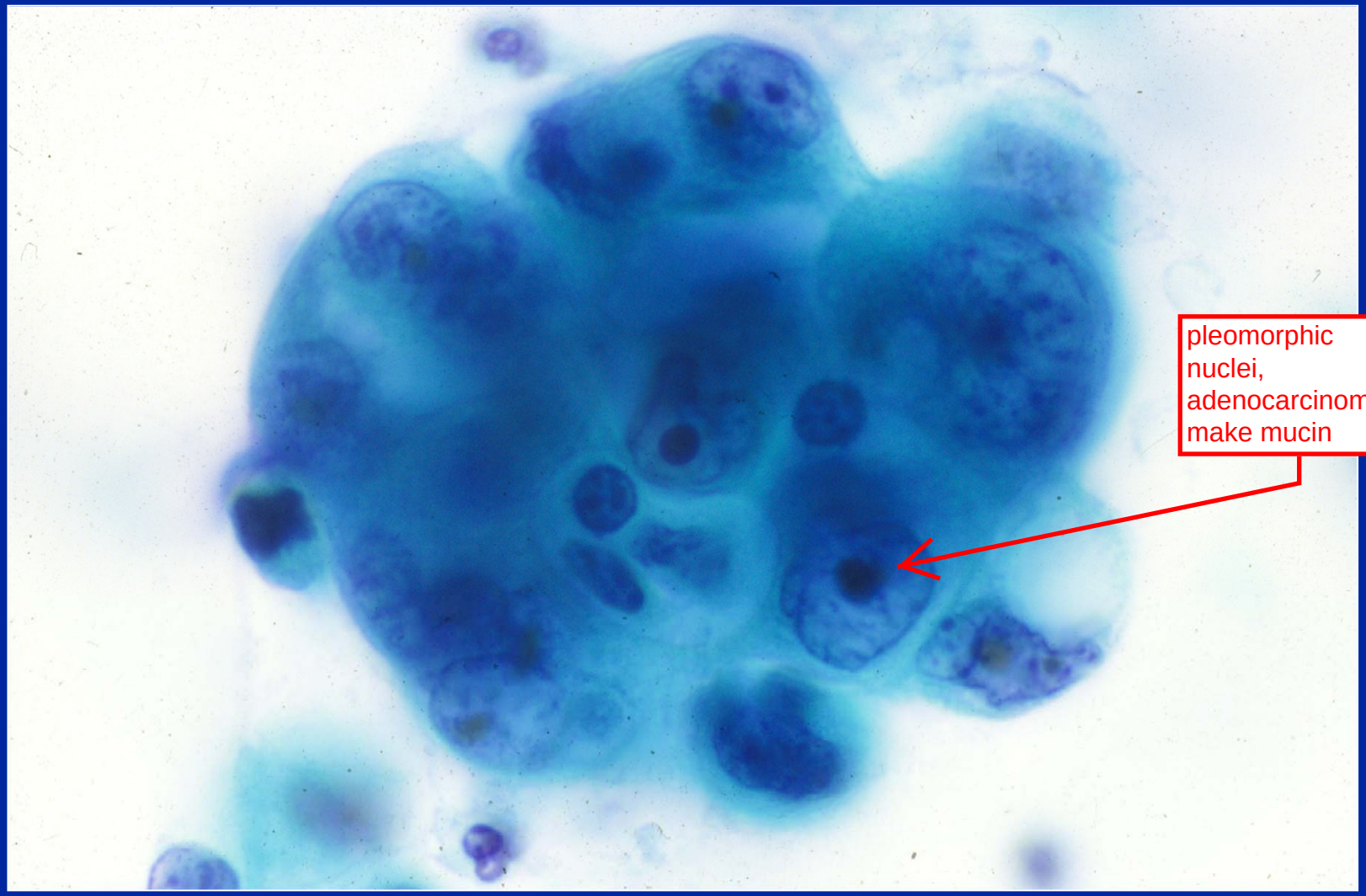
Adenocarcinoma

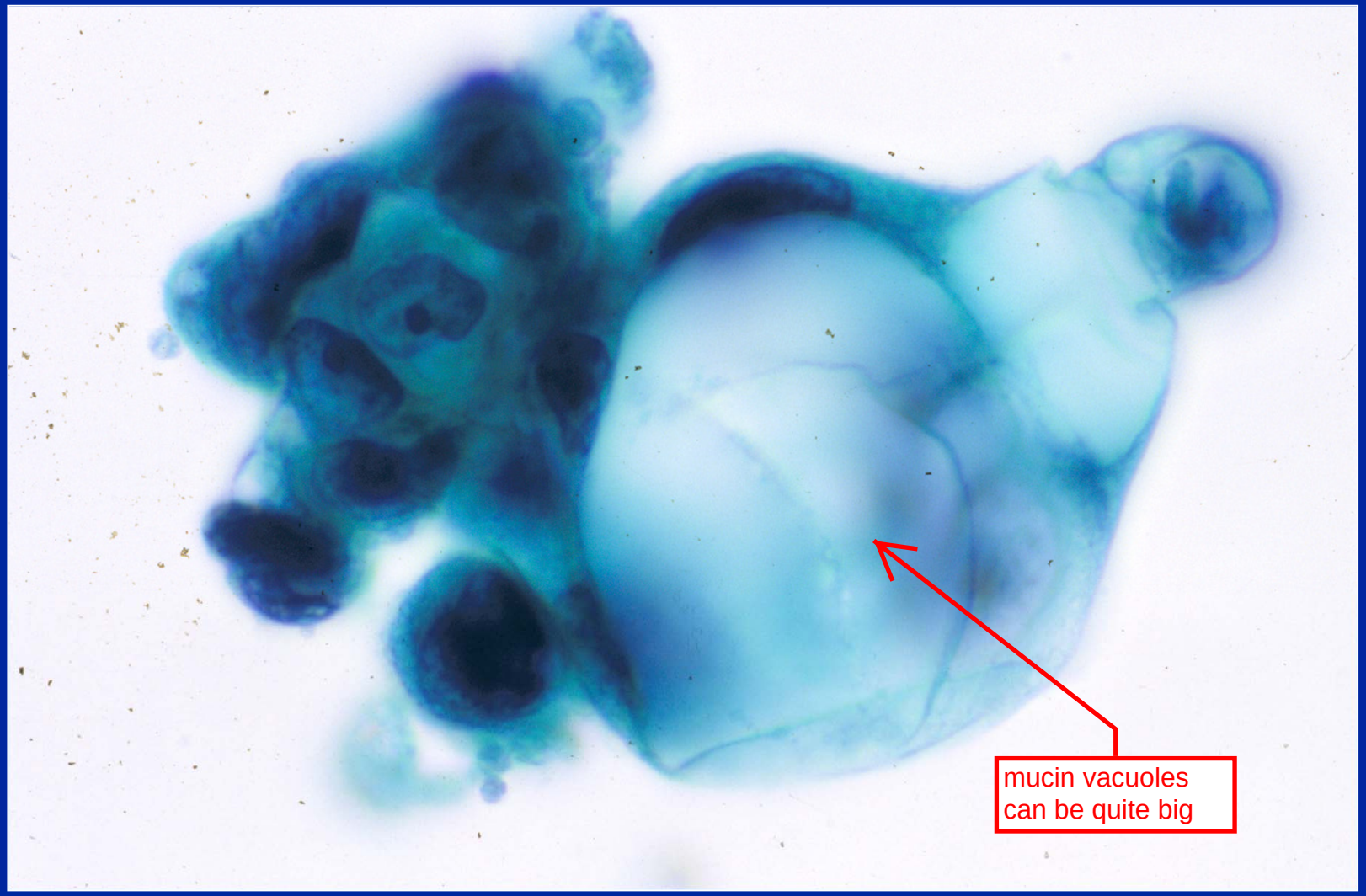
- 35% primary lung malignancies
- most common type involving the nonsmoker
- typically peripheral, subpleural
- heterogenous morphology; acinar, papillary, solid, bronchiolo-alveolar cell (BAC) types

Adenocarcinoma, morphology:

- Acinar/glandular
- papillary
- solid with mucin production
- BAC

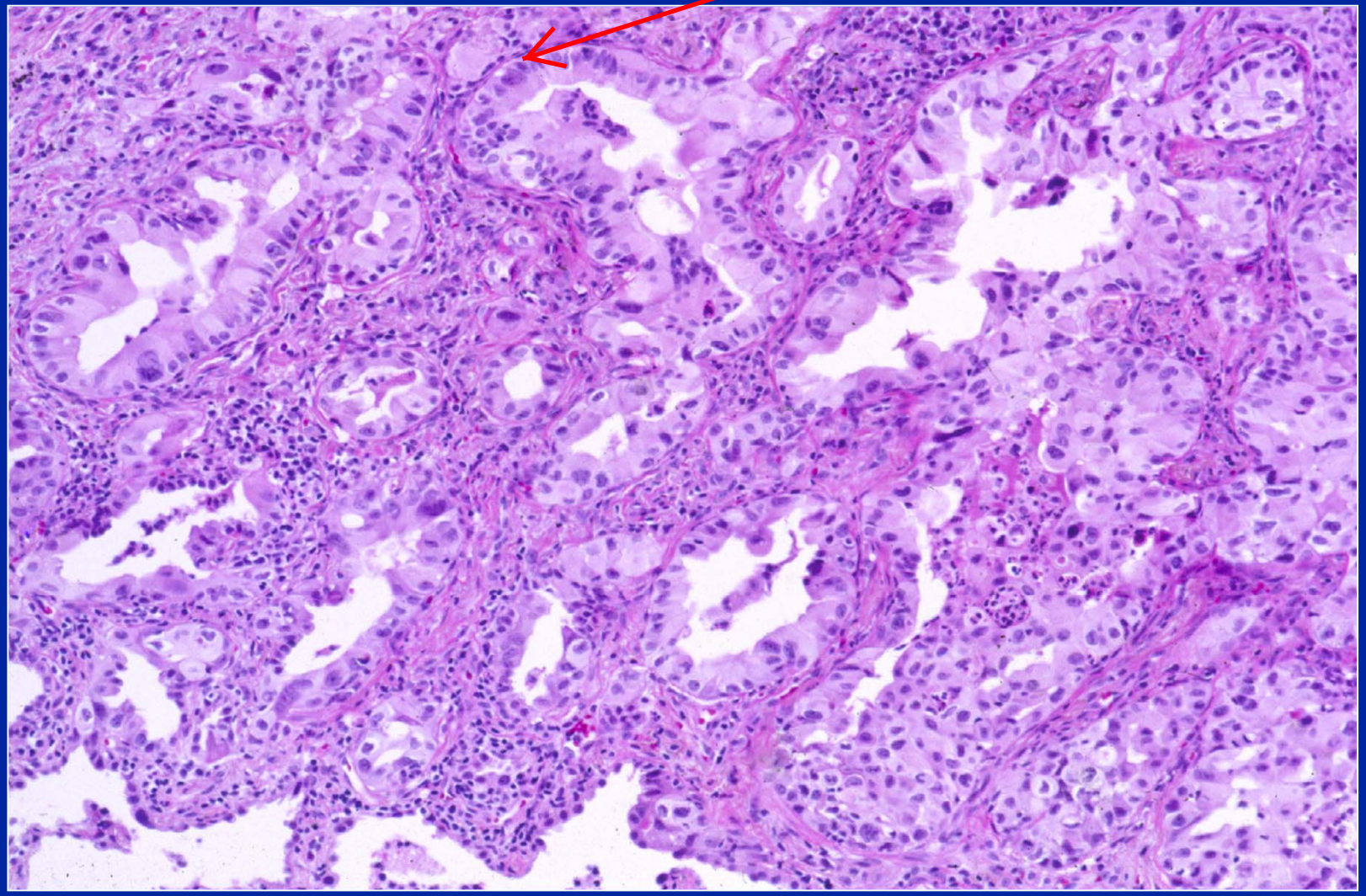

example of peripheral adenocarcinoma
cut in half, cancer is tucked right under the pleura


pleomorphic
nuclei,
adenocarcinomas
make mucin


mucin vacuoles
can be quite big

tumor cells form glands

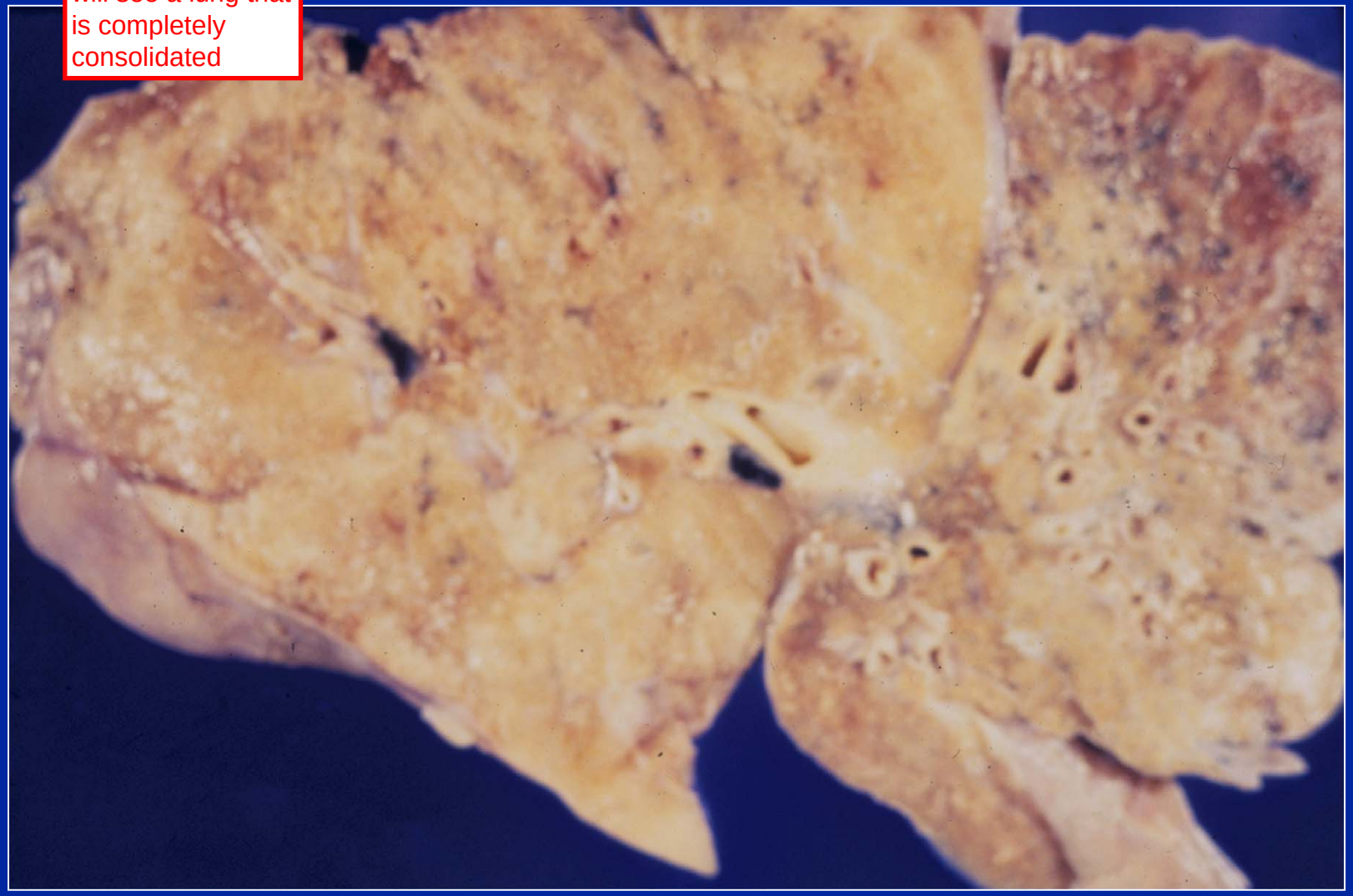
so know that adenocarcinomas form glands and make mucin

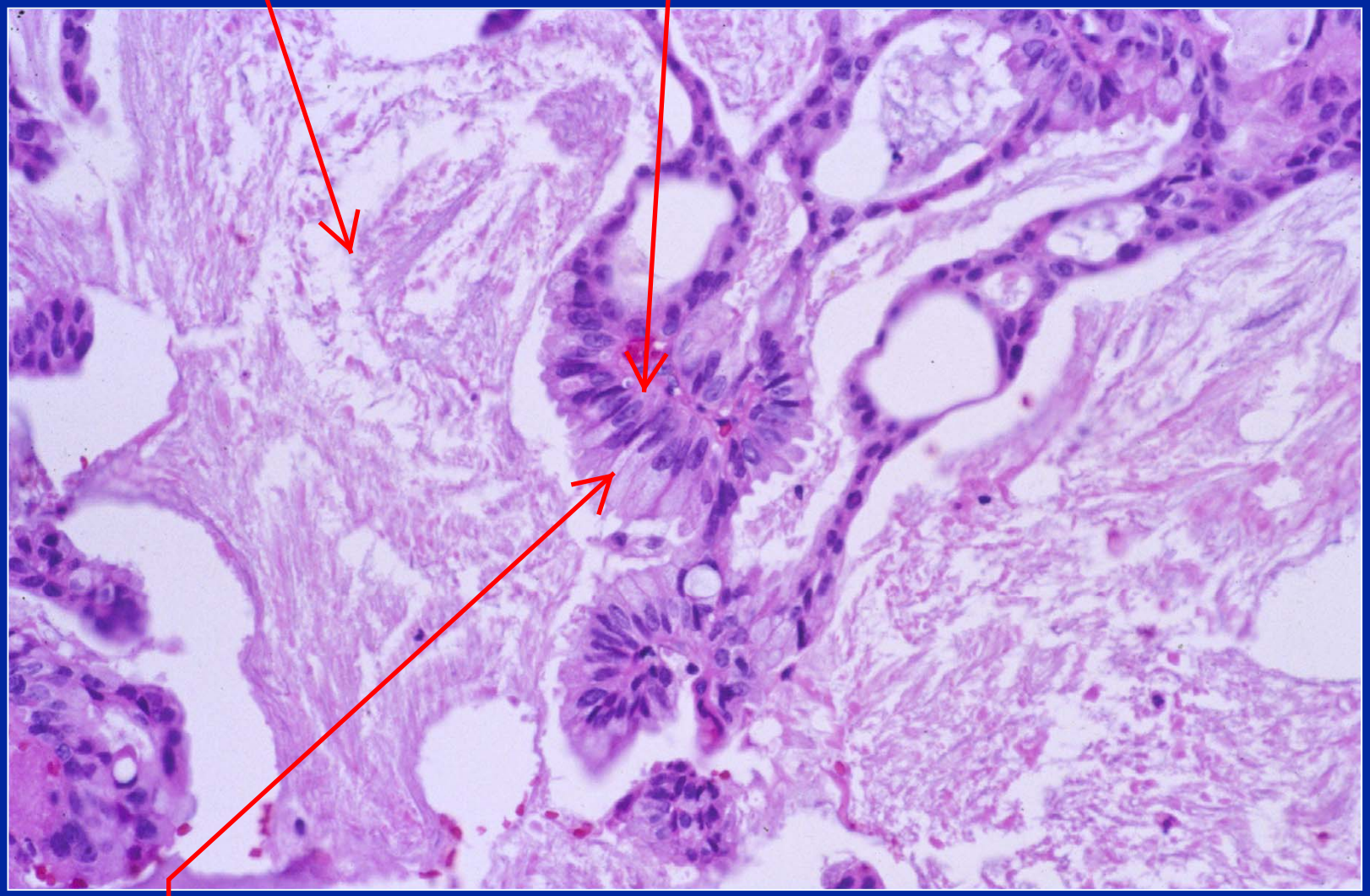


Bronchiolo-alveolar cell carcinoma

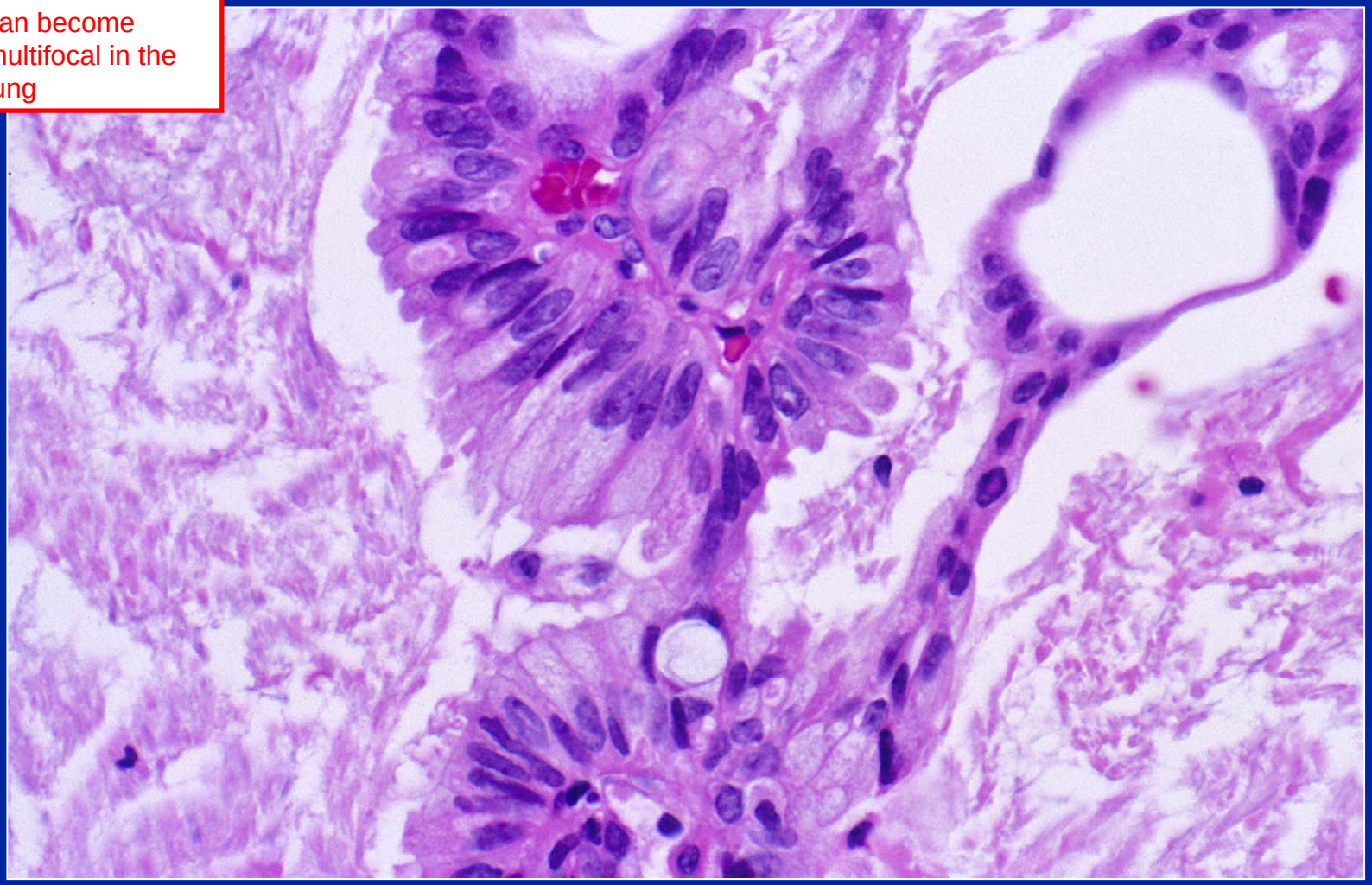
- Unusual and by definition non-invasive variant of adenocarcinoma, least strong association with smoking or extrapulmonary manifestations
- Non-invasive, but *aerogenous* spread in the lung makes them frequently inoperable owing to multifocality
- Mucinous and non-mucinous variants

at late stage you will see a lung that is completely consolidated




mucin
BAC cells, basally oriented nuclei, mucin in the cytoplasm
BAC cell can become detached from other cells and spread to other parts of the lung

BAC does not metastasize but it can become multifocal in the lung



Large cell carcinoma

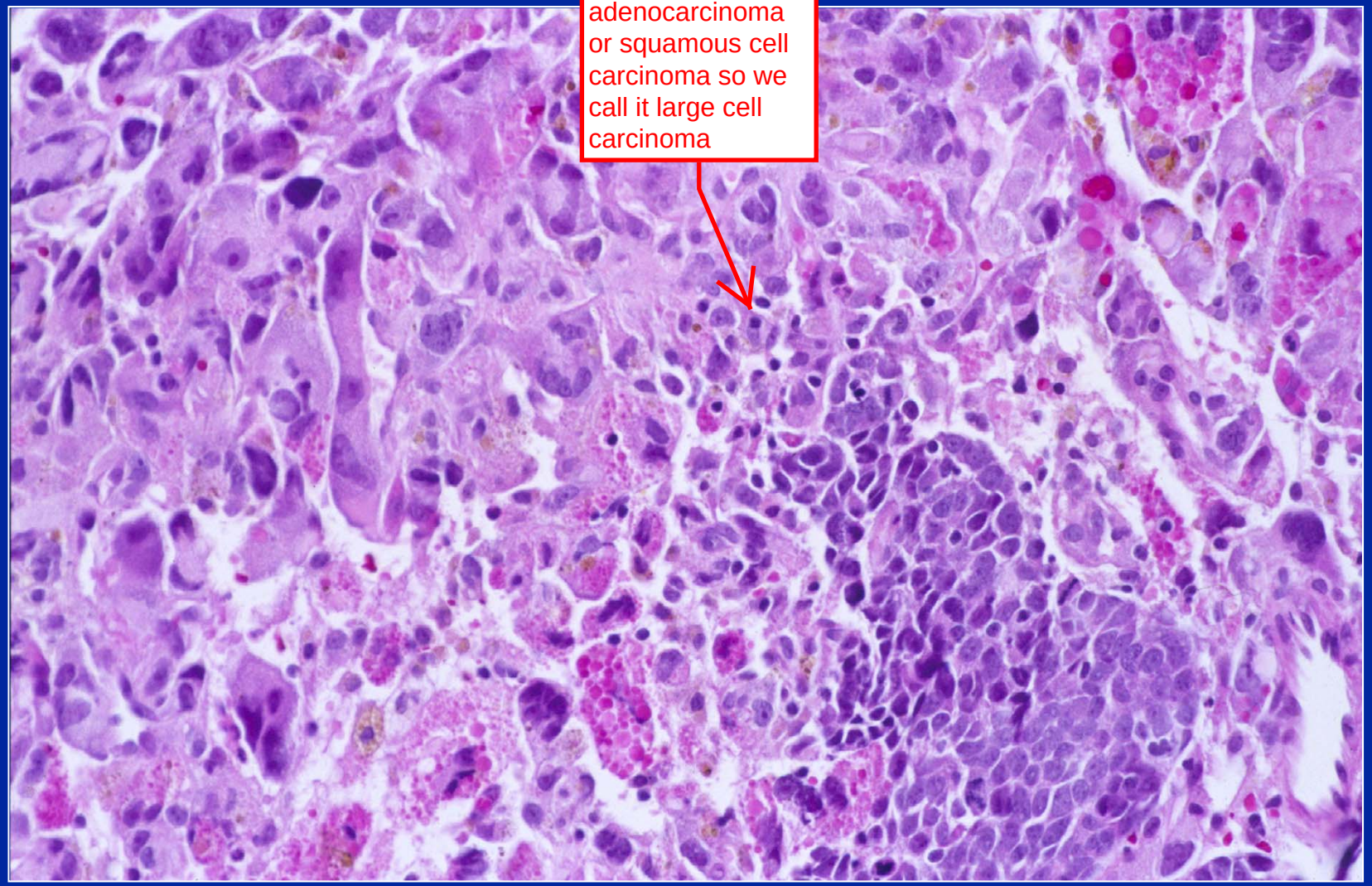
so are not called adenocarcinoma or squamous cell carcinoma because lacks these characteristics

- Lacks glandular differentiation or mucin production (adenocarcinoma)
- Lacks intercellular bridges or cytoplasmic keratinization (squamous cell)
- May have neuroendocrine features

large cell carcinoma, cannot tell by gross exam that this is large cell carcinoma, need to do microscopic exam

if see peripheral nodules more likely to be adenocarcinoma but do not know for sure

histologically we see that the cells are pleomorphic but do not have characteristics of adenocarcinoma or squamous cell carcinoma so we call it large cell carcinoma

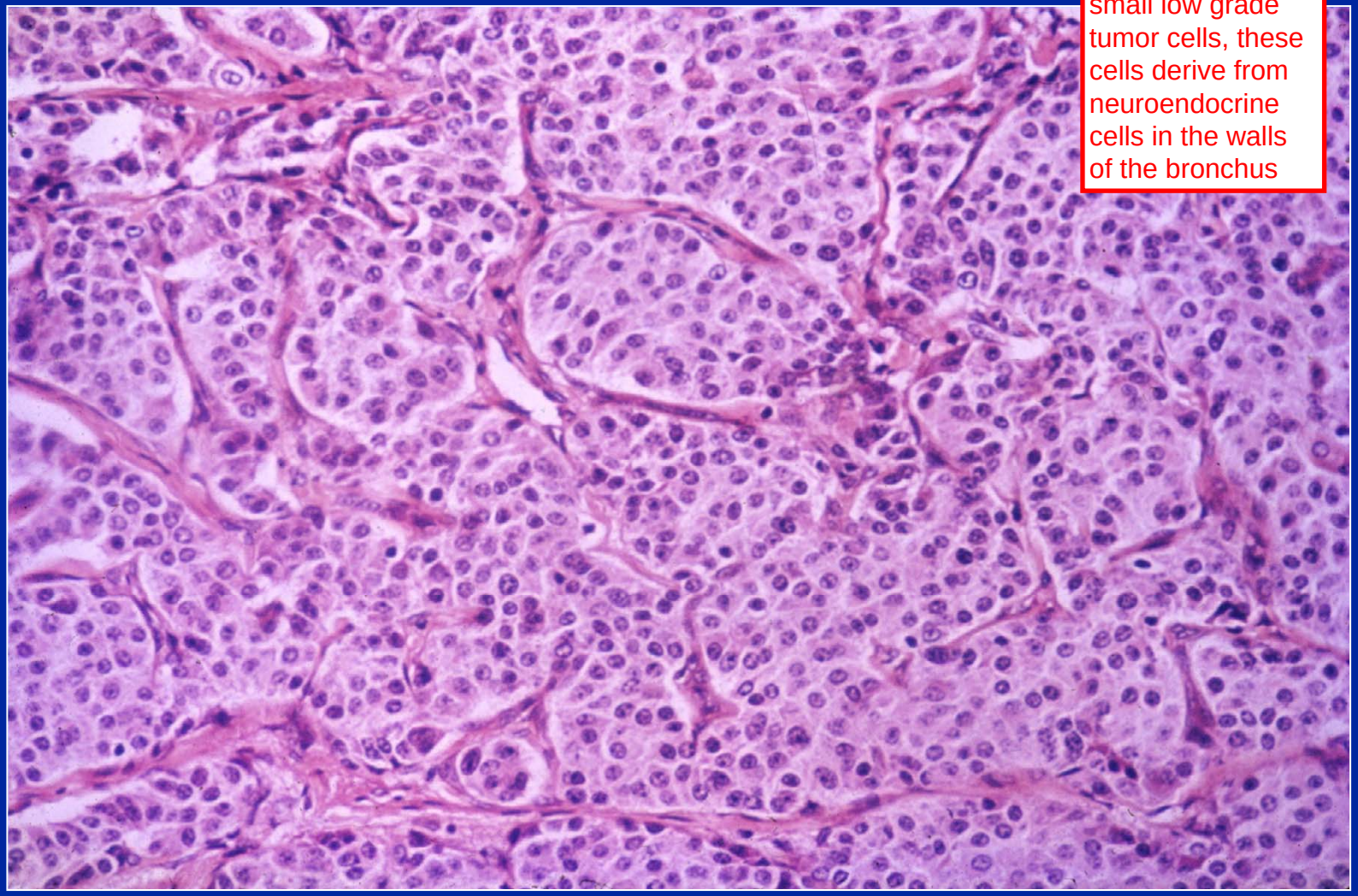


Pulmonary carcinoid tumors

- Generally low grade neuroendocrine malignancies classically presenting in the airways, often in younger patient population and unrelated to smoking
- Unlike gastrointestinal carcinoid tumors unlikely to result in the carcinoid syndrome

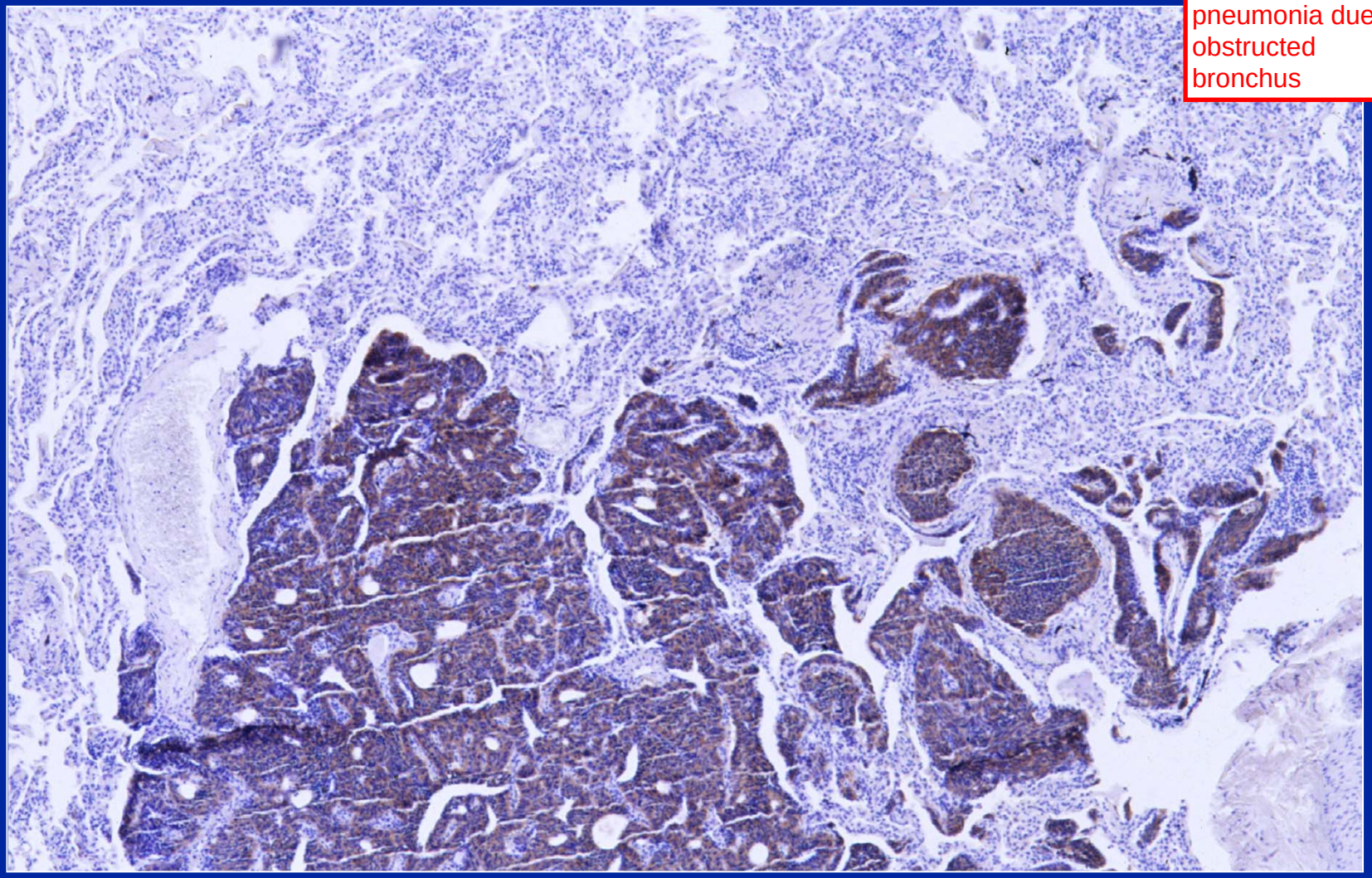
which has to do with catecholamine production and flushing in the patients


carcinoid tumor occluding the airway lumen
MASS. GENERAL HOSPITAL
METRIC 1 2 3 4
R 751



tend to have nested pattern of small low grade tumor cells, these cells derive from neuroendocrine cells in the walls of the bronchus

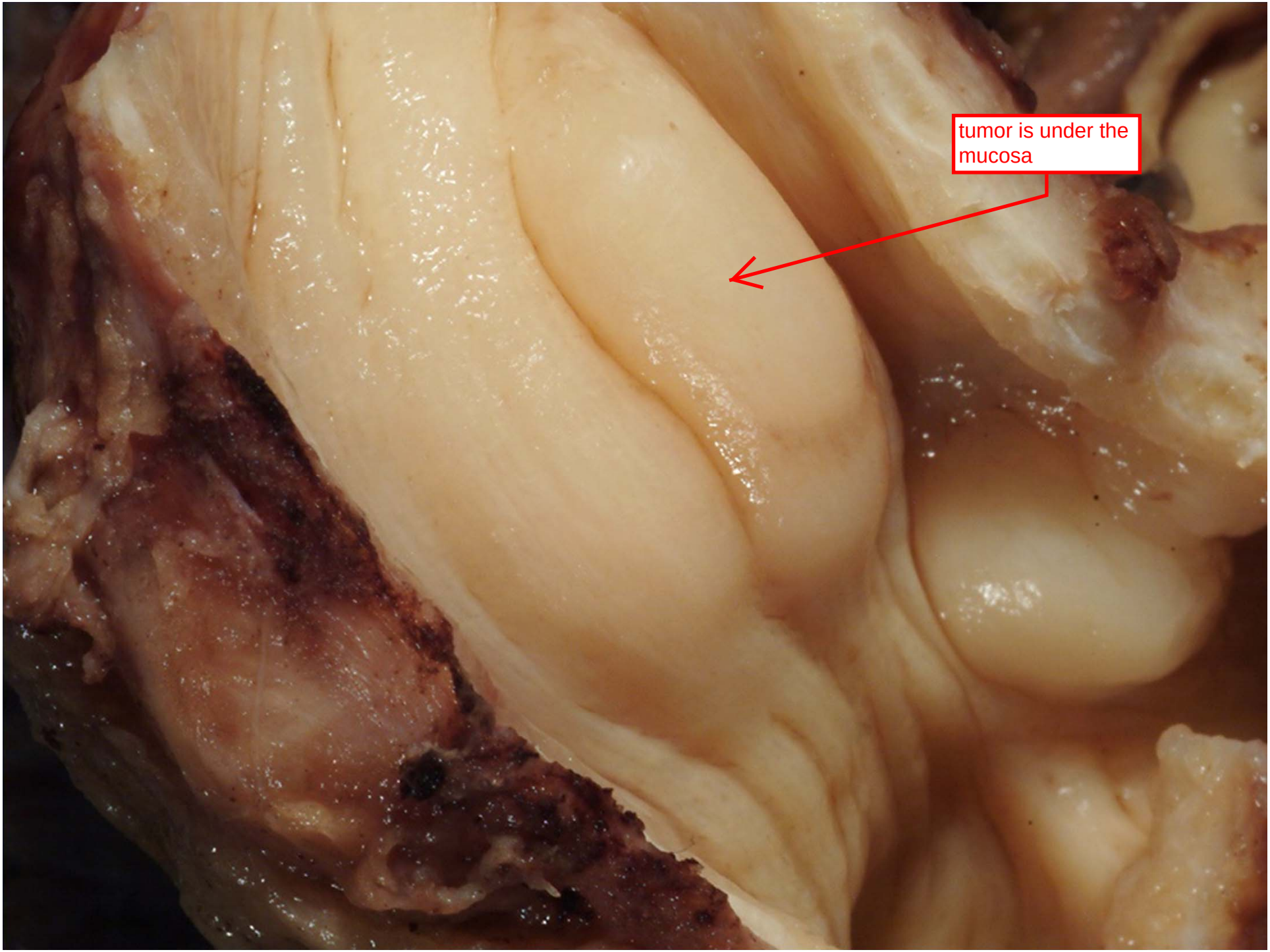
patients may develop cough or wheeze or pneumonia due to obstructed bronchus

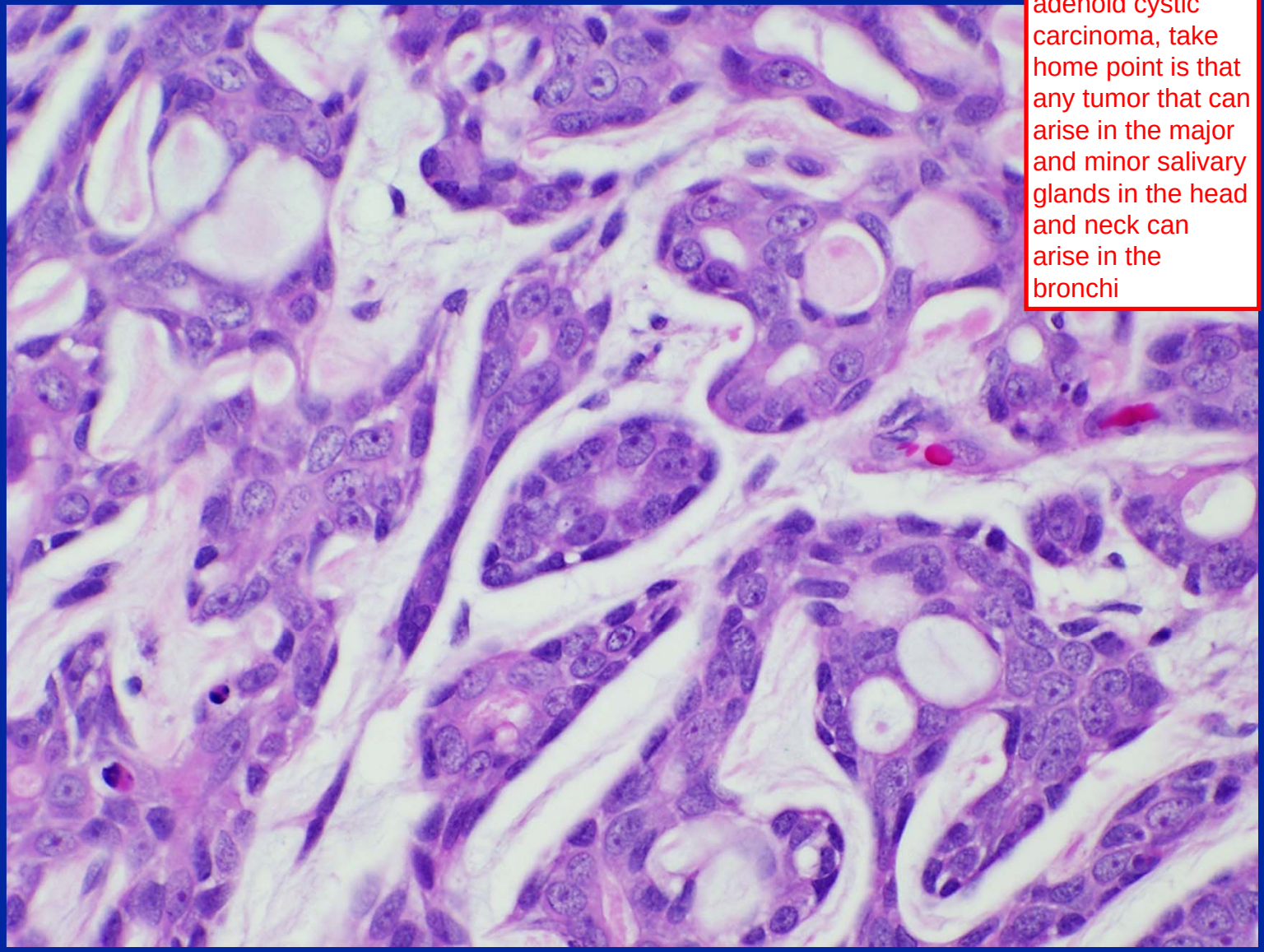


BRONCHIAL TUMORS

- Same histologic classification as tumors of major and minor salivary glands, but are arising in bronchi
- Adenoid cystic carcinoma
- Mucoepidermoid carcinoma
- Acinic cell carcinoma
- Younger patient population with symptoms relating to endobronchial obstruction


bronchial tumor of
salivary gland type


tumor is under the mucosa



example of adenoid cystic carcinoma, take home point is that any tumor that can arise in the major and minor salivary glands in the head and neck can arise in the bronchi

Asbestos-associated diseases

- benign pleural disease: effusions, plaques, fibrosis
- pulmonary fibrosis (asbestosis)
- mesotheliomas
- cocarcinogen with cigarette smoke in the development of bronchogenic carcinoma

no role of smoking in mesothelioma

asbestos and smoking work synergistically to produce cancer, 55 fold increase in risk

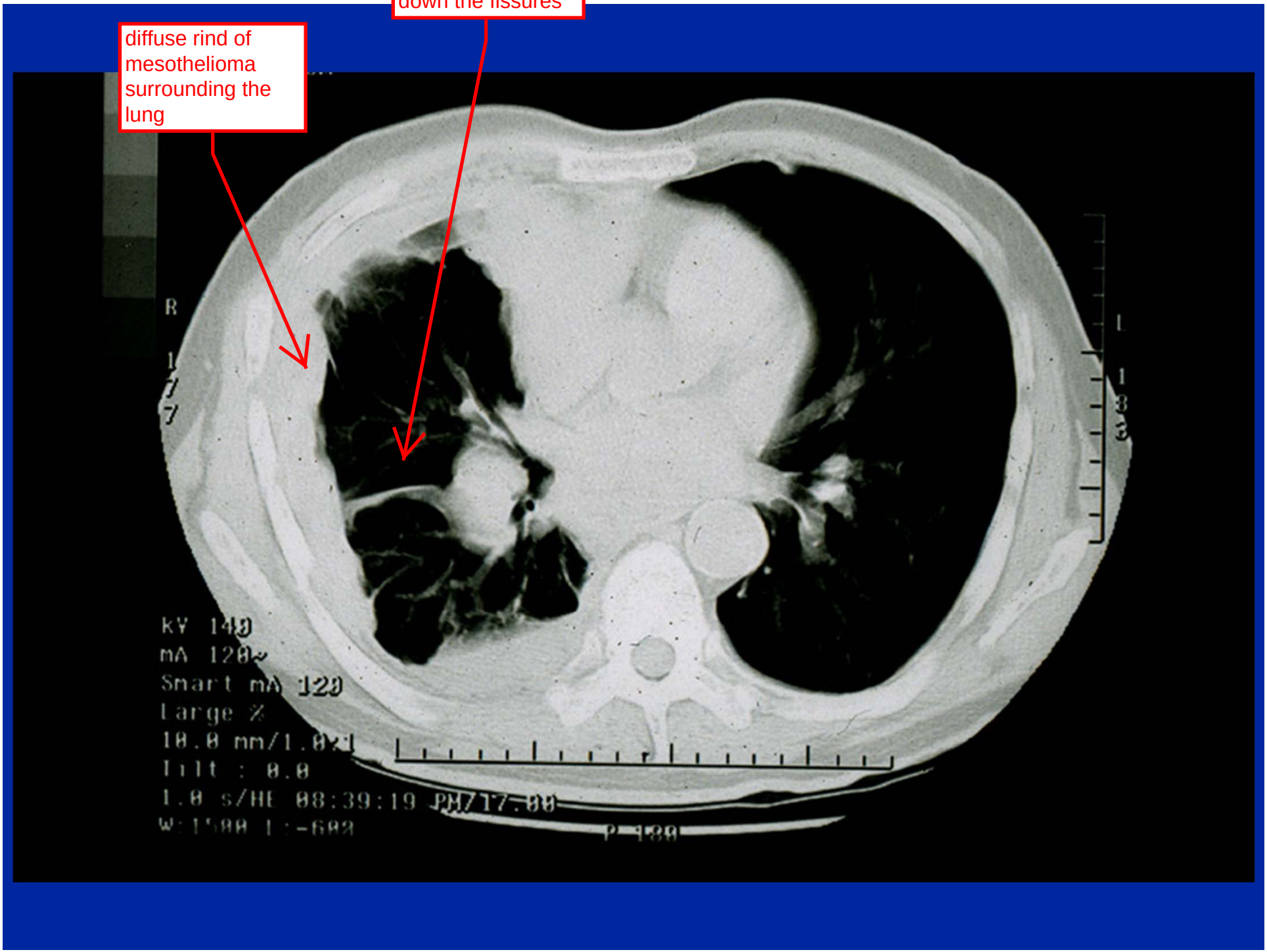
Malignant Mesothelioma

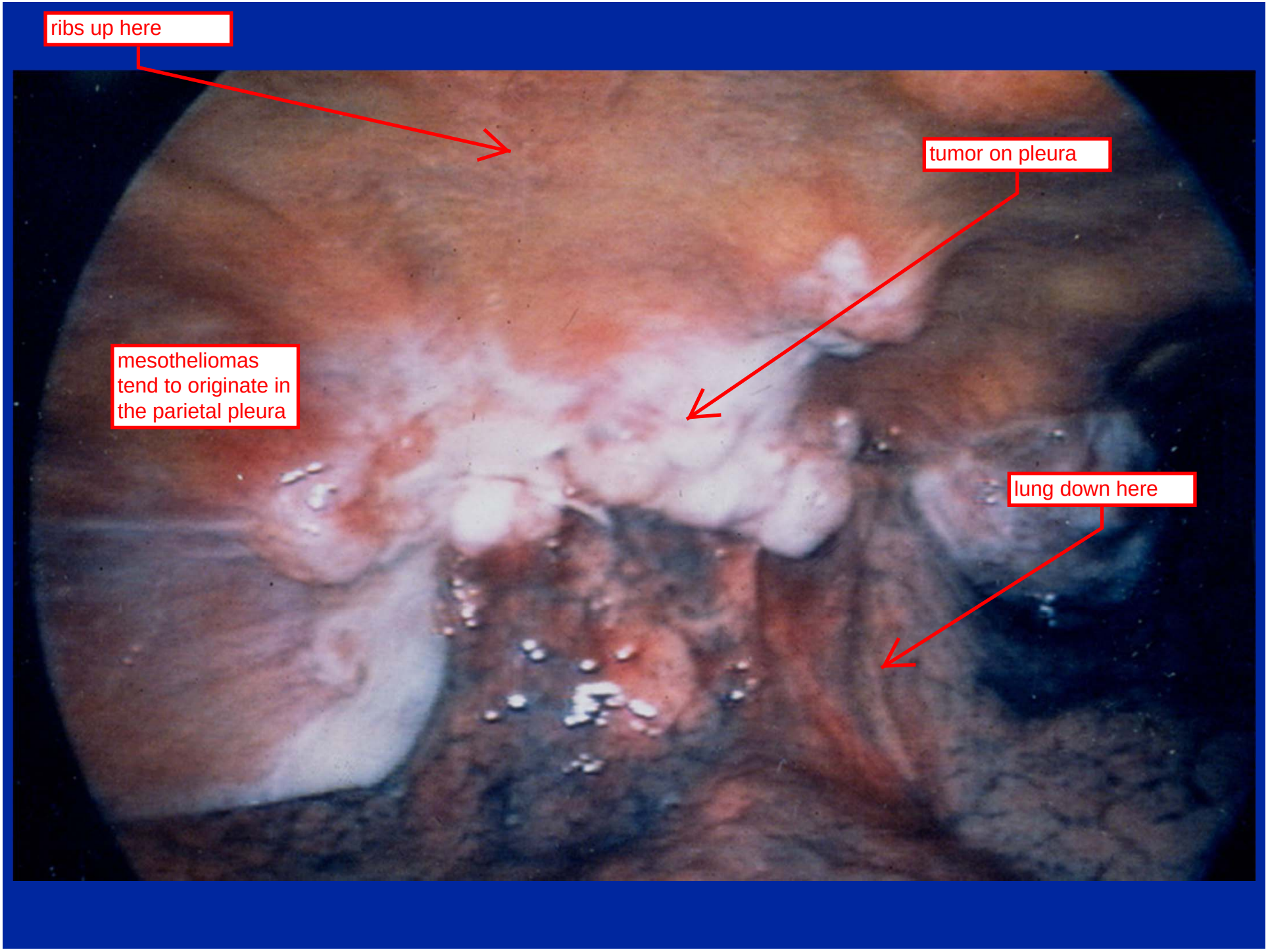
- Rare tumor, increasing incidence 3000-4000 new cases/year
- tumor grows along serosal surfaces- pleura, pericardium , peritoneum, tunica vaginalis testis
- Strong association with asbestos exposure, NOT tobacco

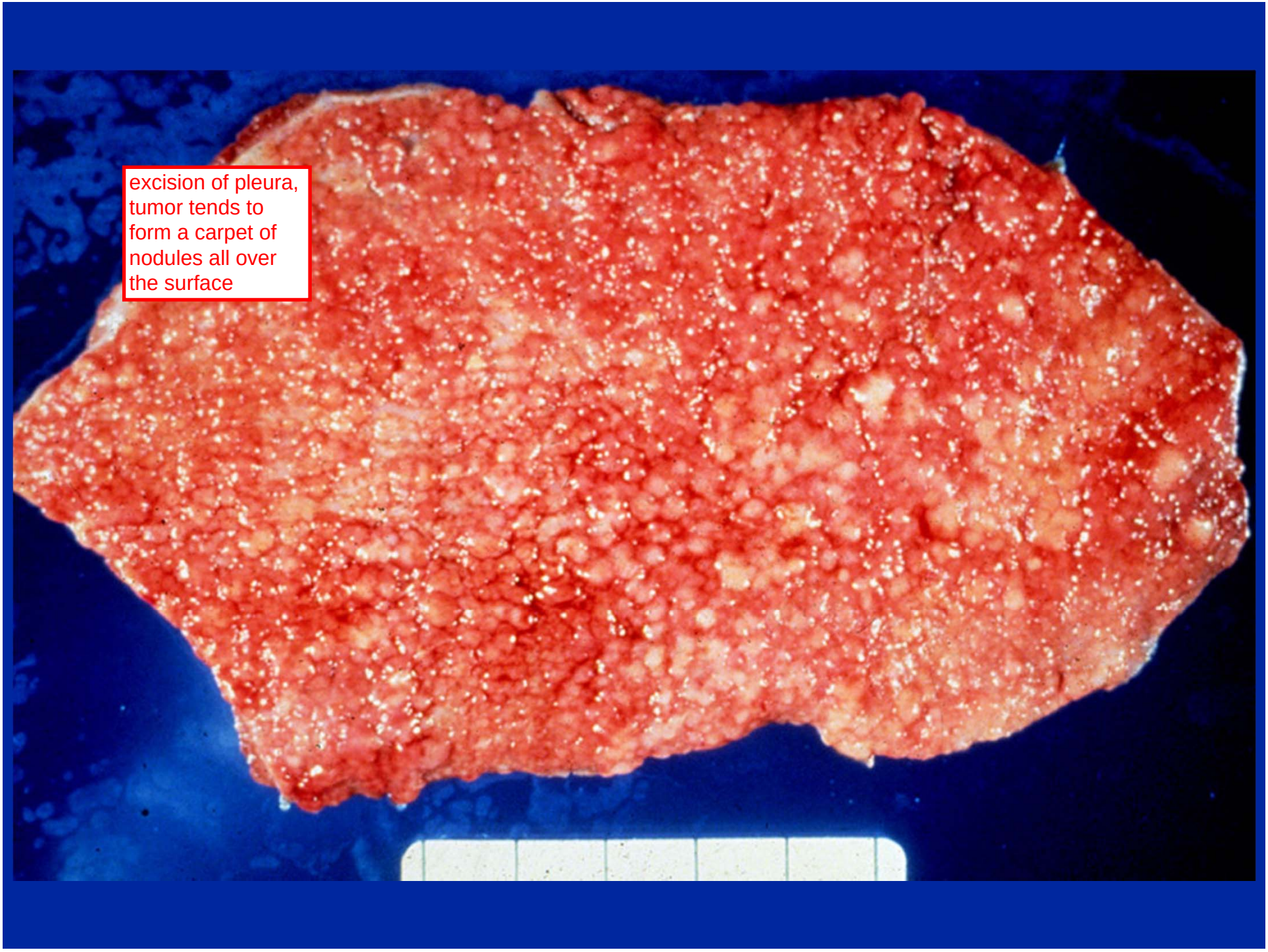
Pleural Mesothelioma

- Grows as rind around lung along fissures, invades chest wall and mediastinum
- approach is surgical, Rad Extrapleural pneumonectomy, poor response to therapy.

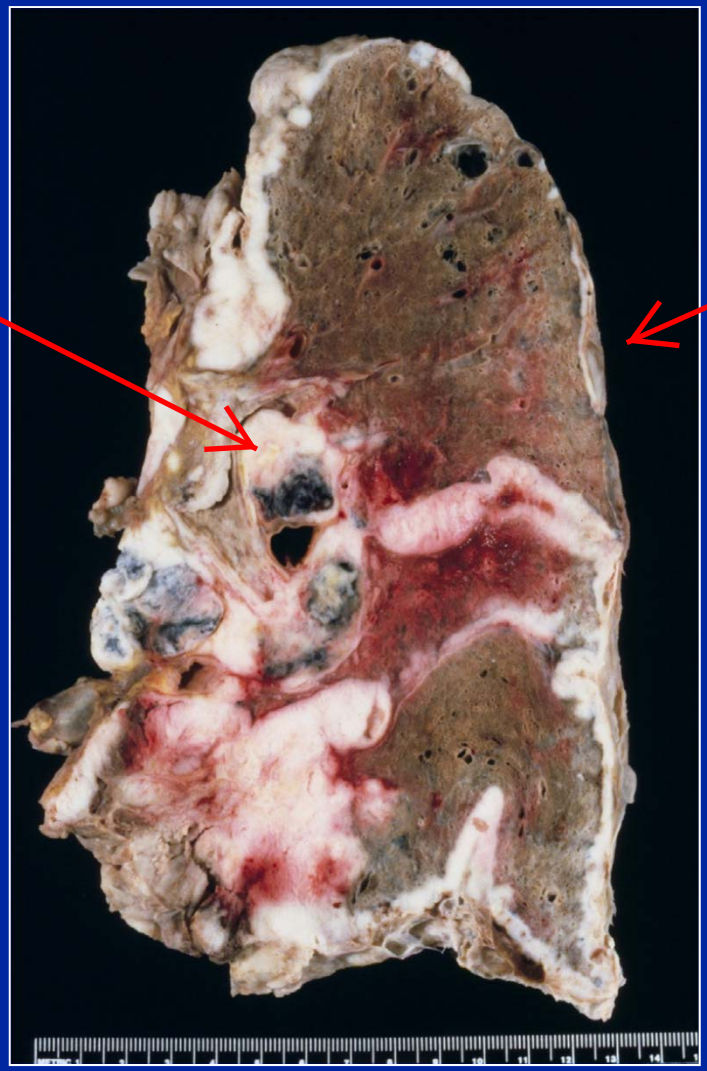
can look this up on google if interested, unfortunately most ppl with this cancer succumb to the disease


cancer growing down the fissures
diffuse rind of mesothelioma surrounding the lung
R
kV 140
mA 120~
Smart mA 120
Large %
Tilt : 0.0
1.0 s/HE 08:39:19 PM/17-08


ribs up here
tumor on pleura
mesotheliomas tend to originate in the parietal pleura
lung down here


excision of pleura, tumor tends to form a carpet of nodules all over the surface

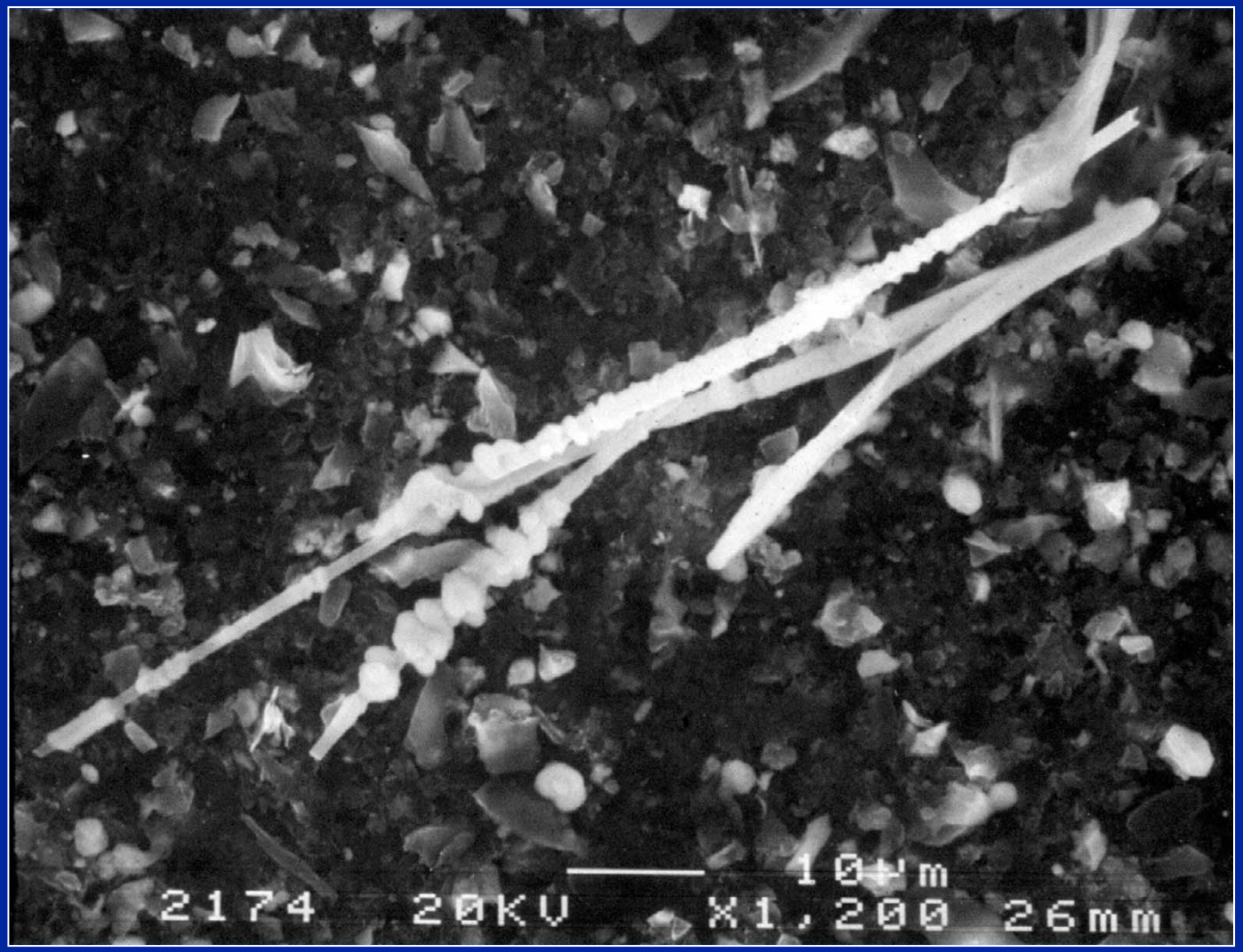
metastases into lymph nodes

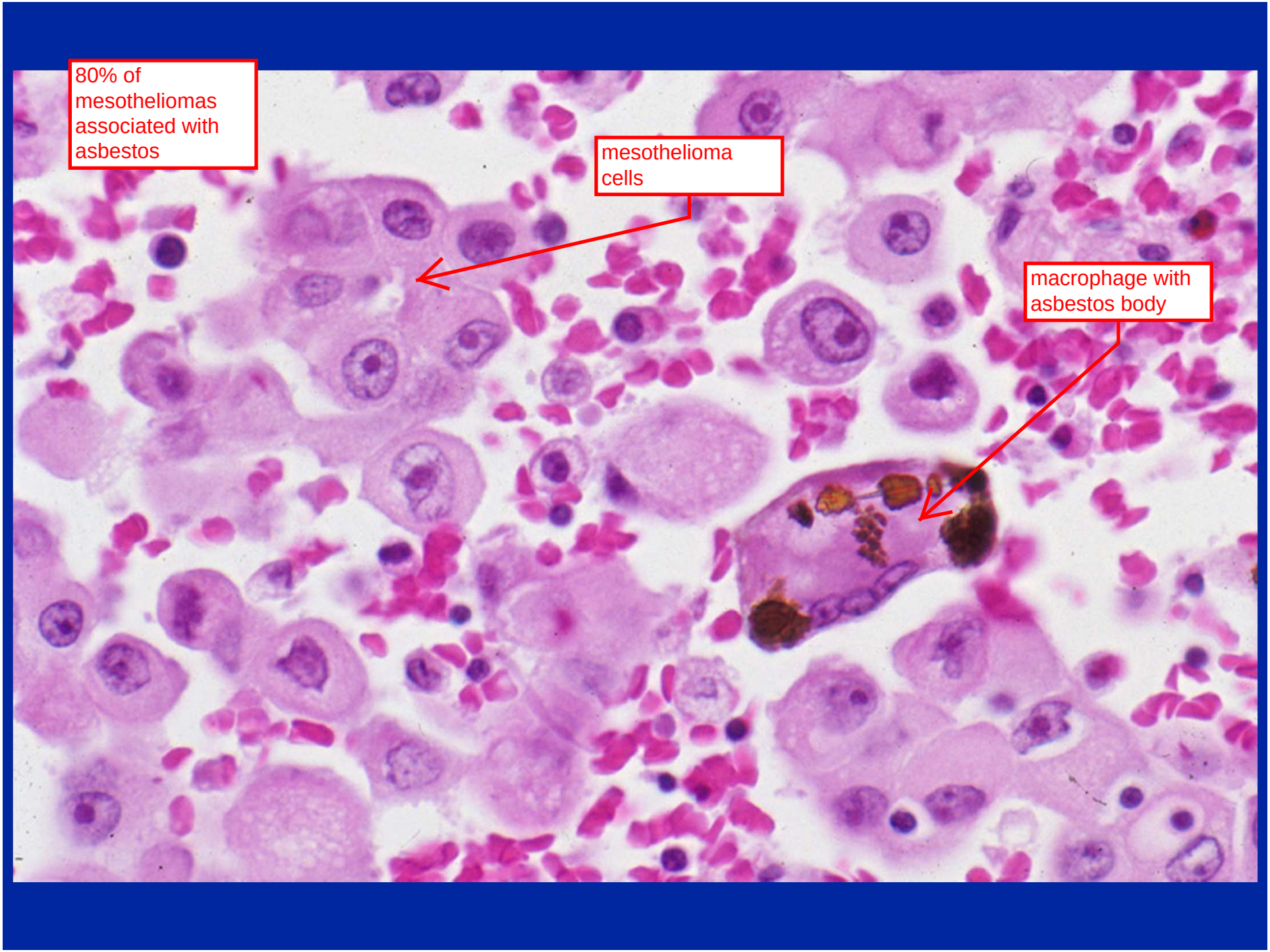


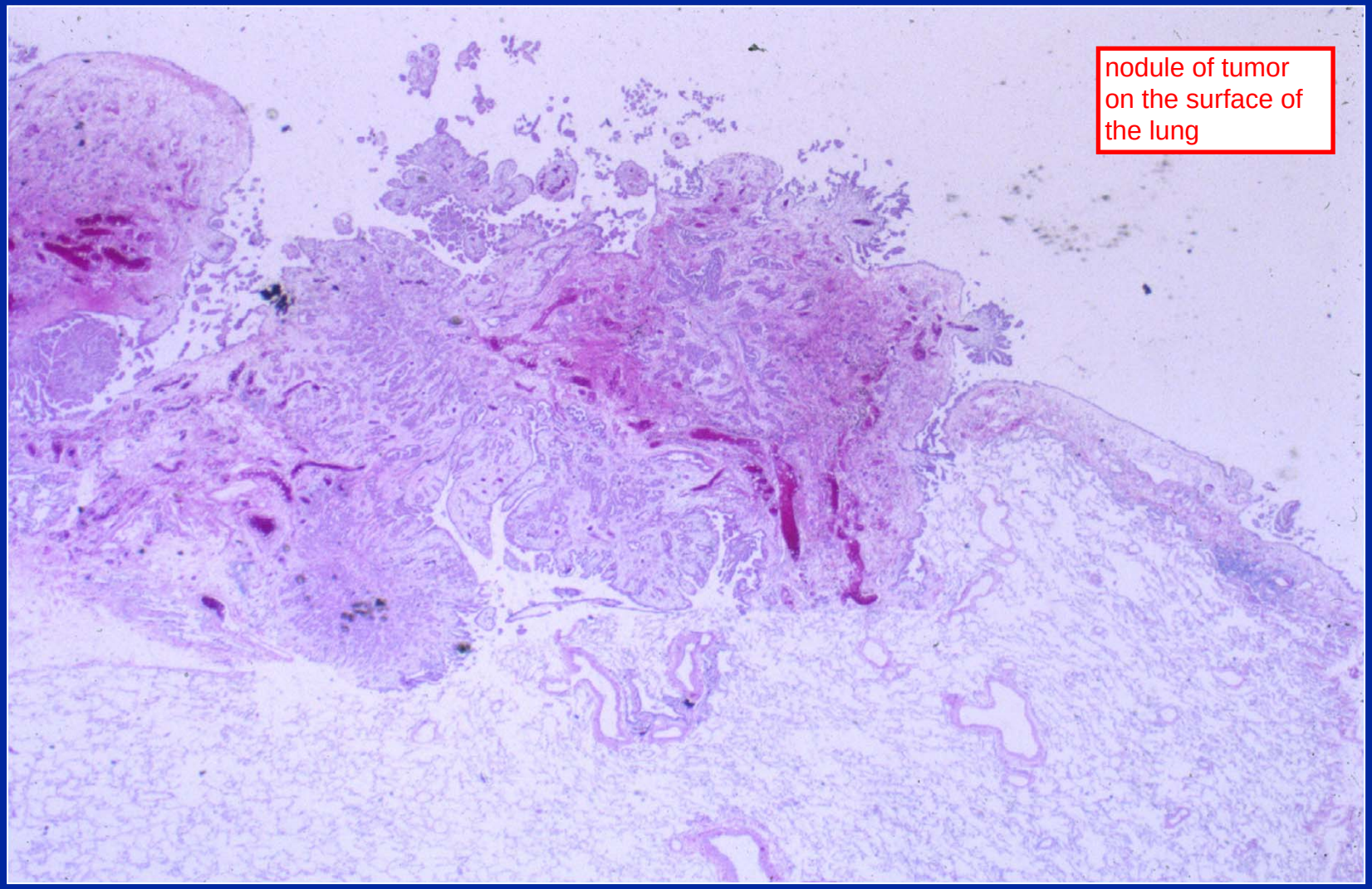
rind of tumor around the lung

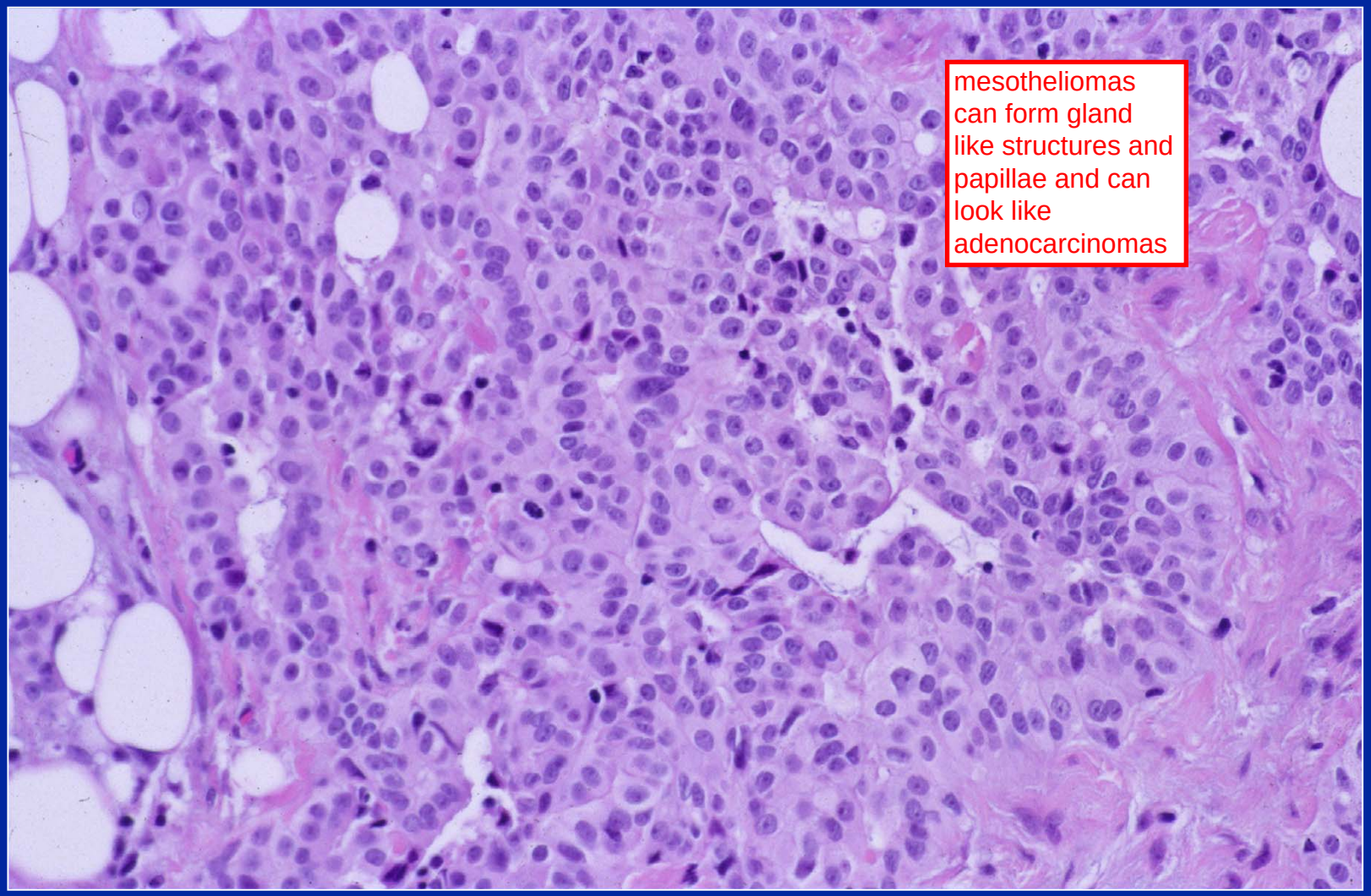
Mesothelioma, role of asbestos:

- Plaques: hallmark of asbestos exposure in over 70%
- asbestosis in 20 % (increased tissues asbestos levels with associated interstitial fibrosis)


10μm
2174 20KV X1,200 26mm

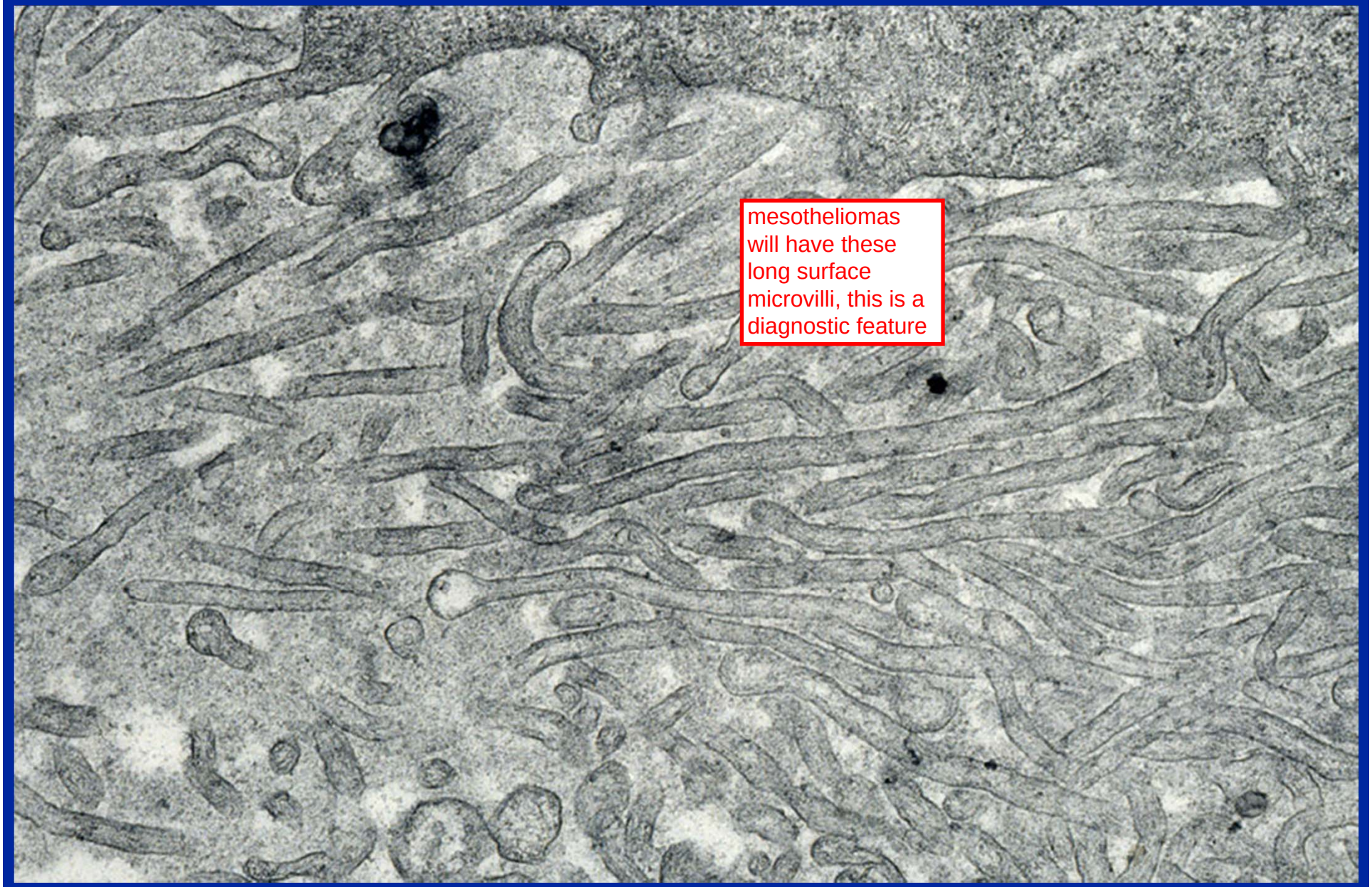

80% of mesotheliomas associated with asbestos
mesothelioma cells
macrophage with asbestos body

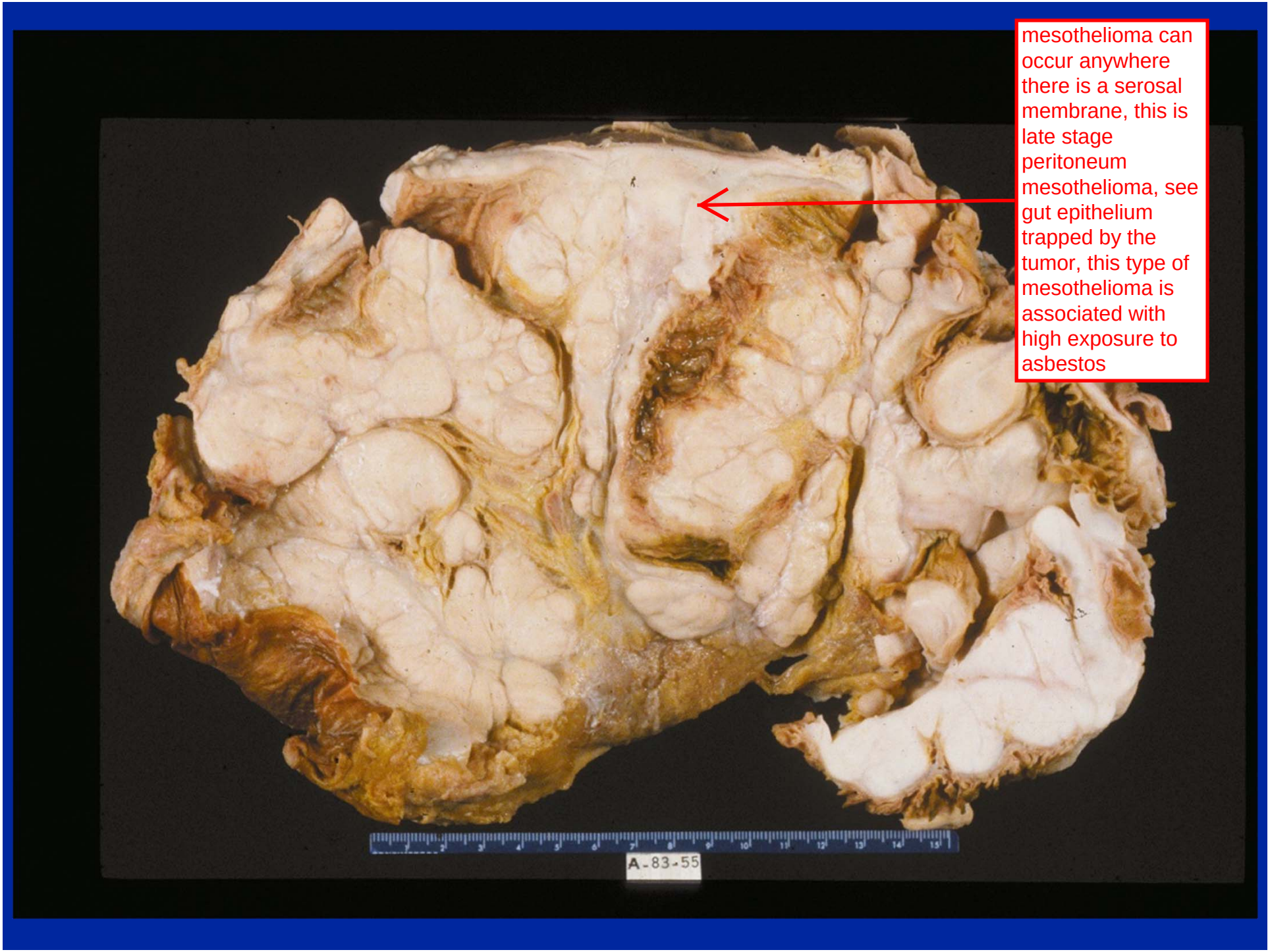

nodule of tumor
on the surface of
the lung


mesotheliomas
can form gland
like structures and
papillae and can
look like
adenocarcinomas

Diagnostic Elements in Malignant Mesothelioma

- Gross distribution of tumor
- H&E
- Histochemistry: mucins and glycoproteins
- Immunohistochemistry
- Electron microscopy

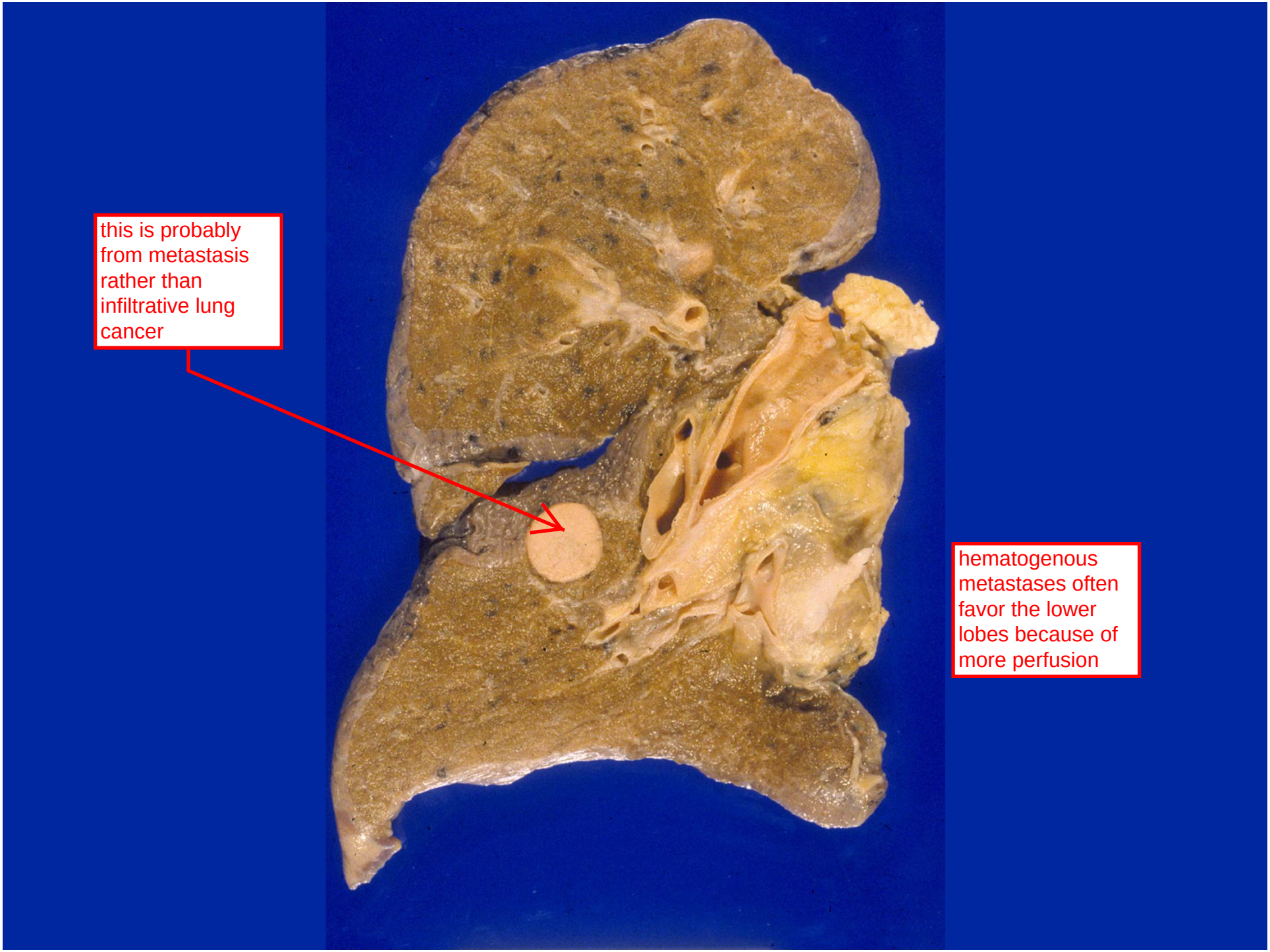

mesotheliomas will have these long surface microvilli, this is a diagnostic feature


mesothelioma can occur anywhere there is a serosal membrane, this is late stage peritoneum mesothelioma, see gut epithelium trapped by the tumor, this type of mesothelioma is associated with high exposure to asbestos
A-83-55


pericardium
mesothelioma

The lung and metastatic disease

- Metastasizes to: lung, regional nodes, sbones, brain, liver, adrenals
- Receives hematogenous and lymphatic metastases from breast, GI, sarcomas, H/N melanoma
- Mucinous lung primaries also spread aerogenously within lung


this is probably from metastasis rather than infiltrative lung cancer
hematogenous metastases often favor the lower lobes because of more perfusion

late stage metastases from the colon

breast, melanoma, and gastrointestinal metastases are most common seen at Duke

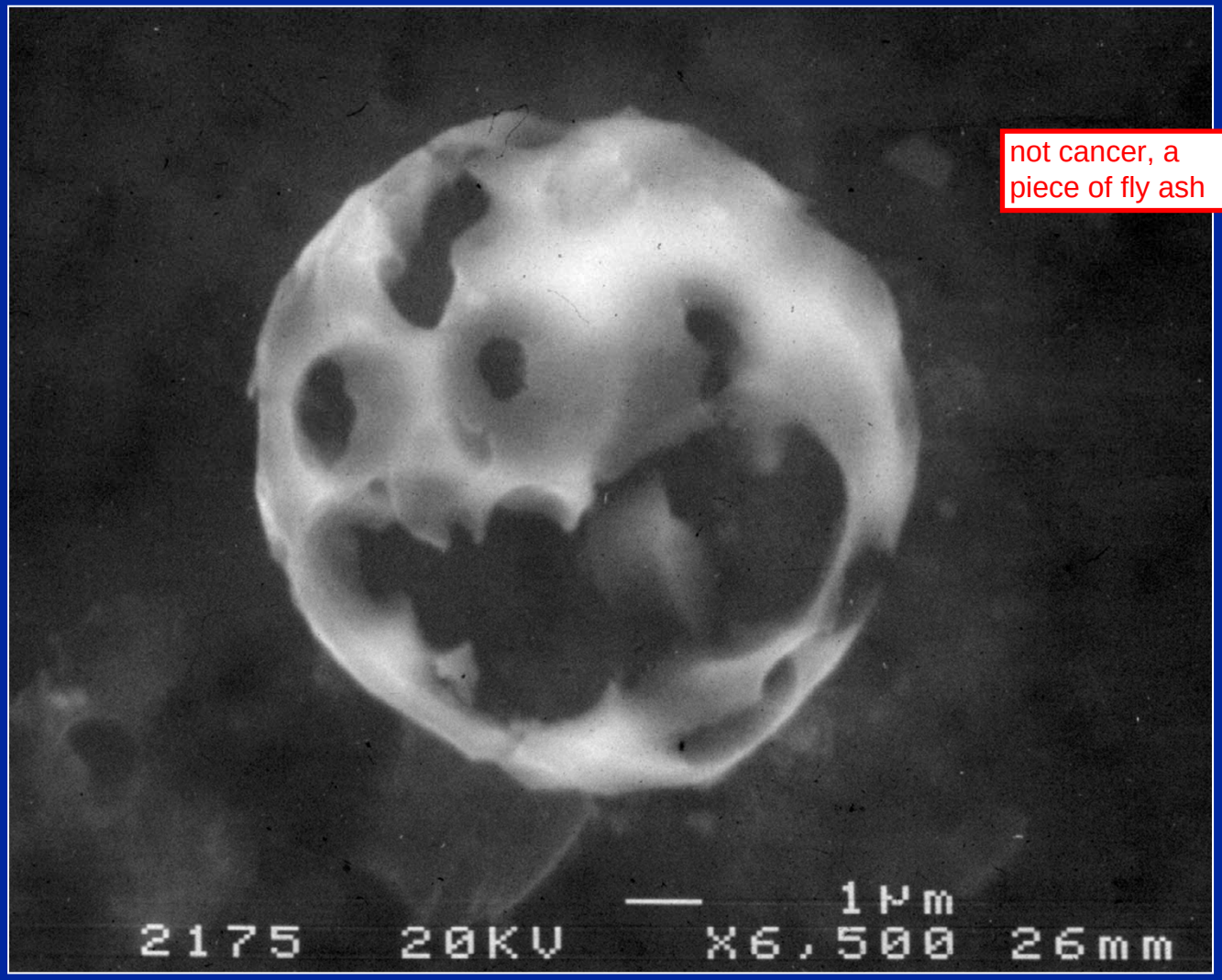
Benign tumors

tend to be quite rare

- Most common in the lung is the **hamartoma;** a benign but abnormal proliferation of mesenchymal elements (cartilage, connective tissue and fat) normally present within that particular site


see islands of cartilage and connective tissue
METRIC 1


completely
benign, just
abnormal growth


not cancer, a
piece of fly ash
1μm
2175 20KV X6,500 26mm