LUNG CANCER

Department of radiation diagnosis, radiotherapy and Oncology

Professor of the Department,

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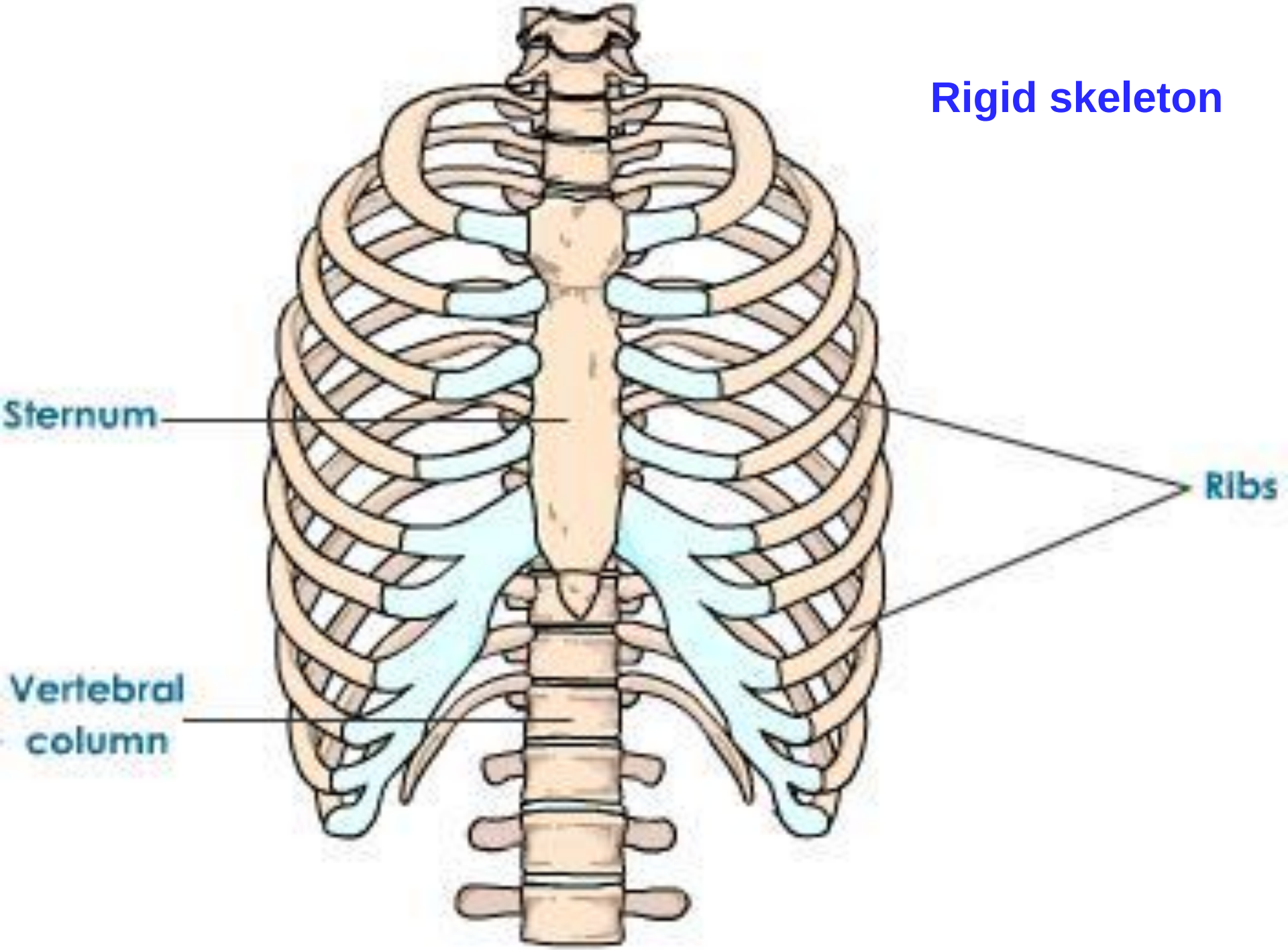
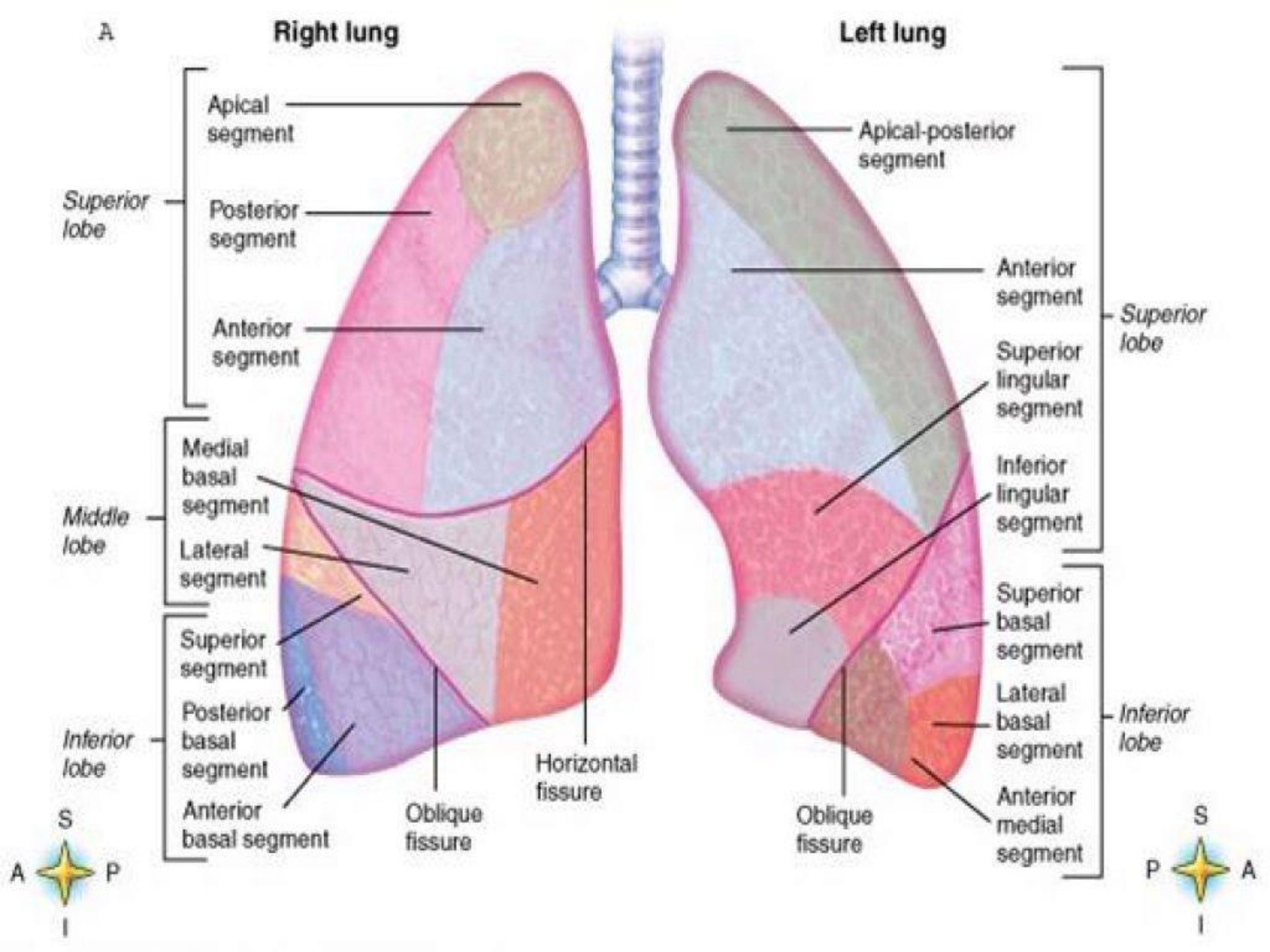
Lung Anatomy

Rigid skeleton




A
Right lung
Left lung
Apical segment
Posterior segment
Anterior segment
Superior lobe
Medial basal segment
Lateral segment
Middle lobe
Superior segment
Posterior basal segment
Anterior basal segment
Inferior lobe
Horizontal fissure
Oblique fissure
Apical-posterior segment
Anterior segment
Superior lingular segment
Inferior lingular segment
Superior lobe
Superior basal segment
Lateral basal segment
Anterior medial segment
Inferior lobe
Oblique fissure
S
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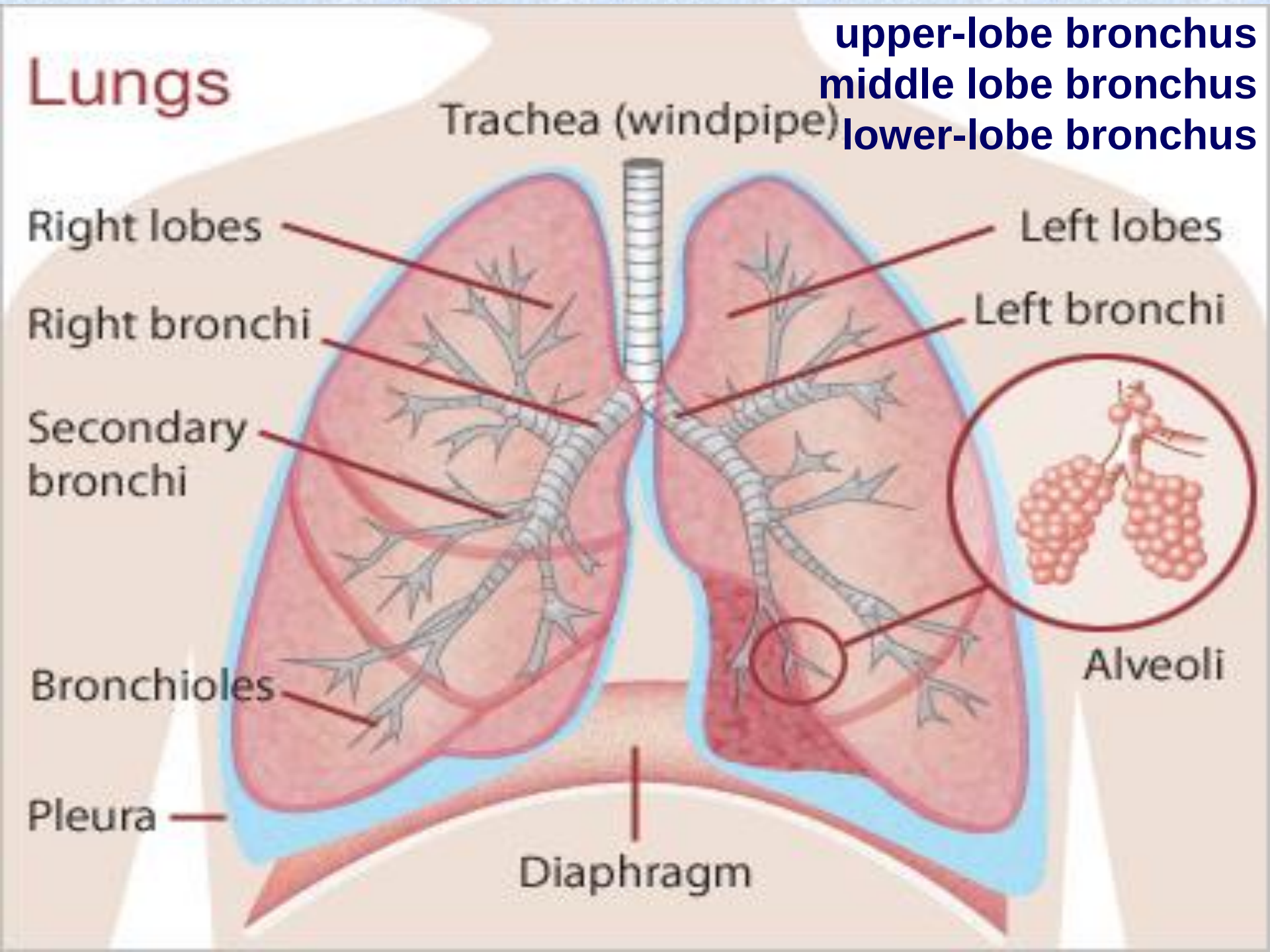
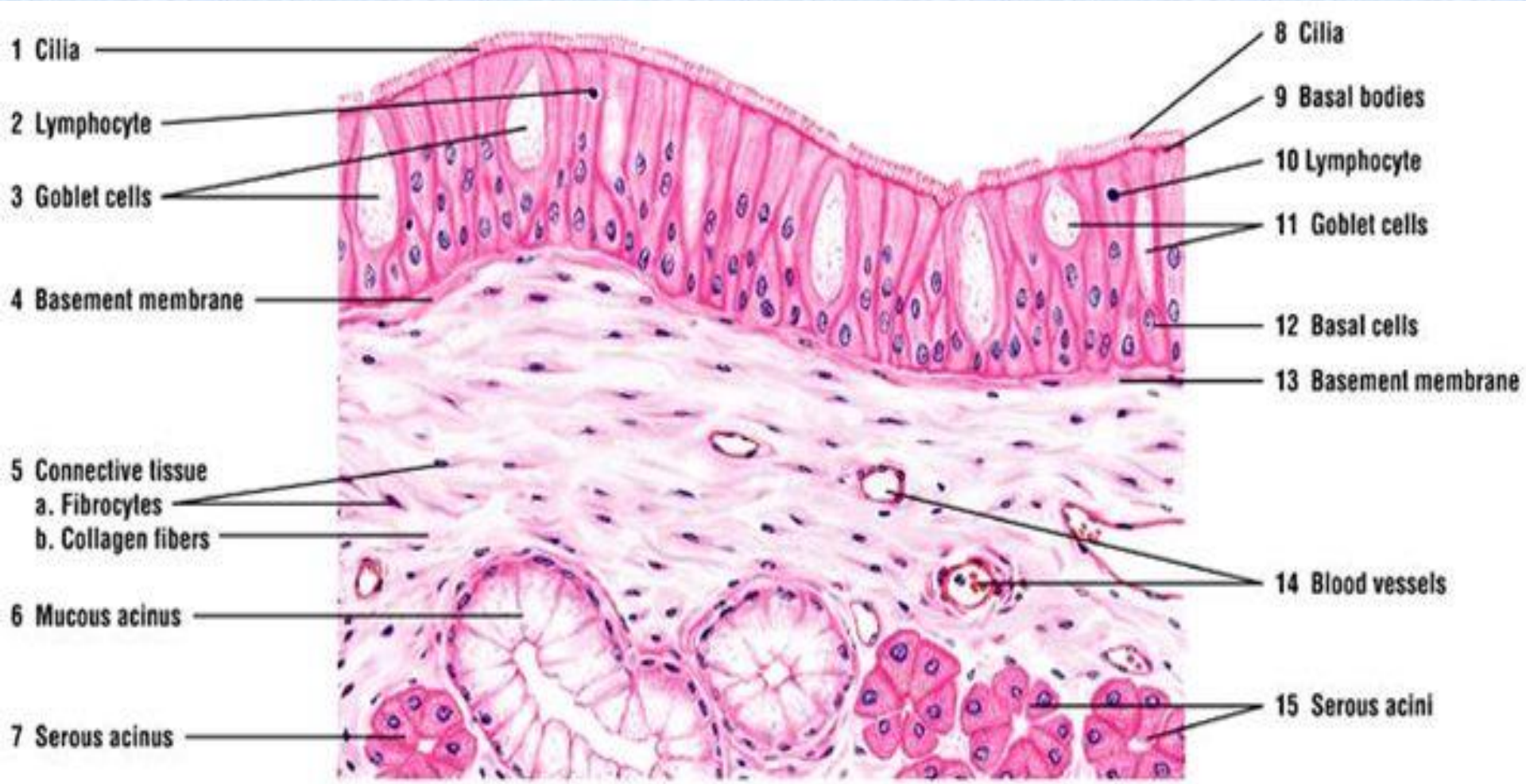
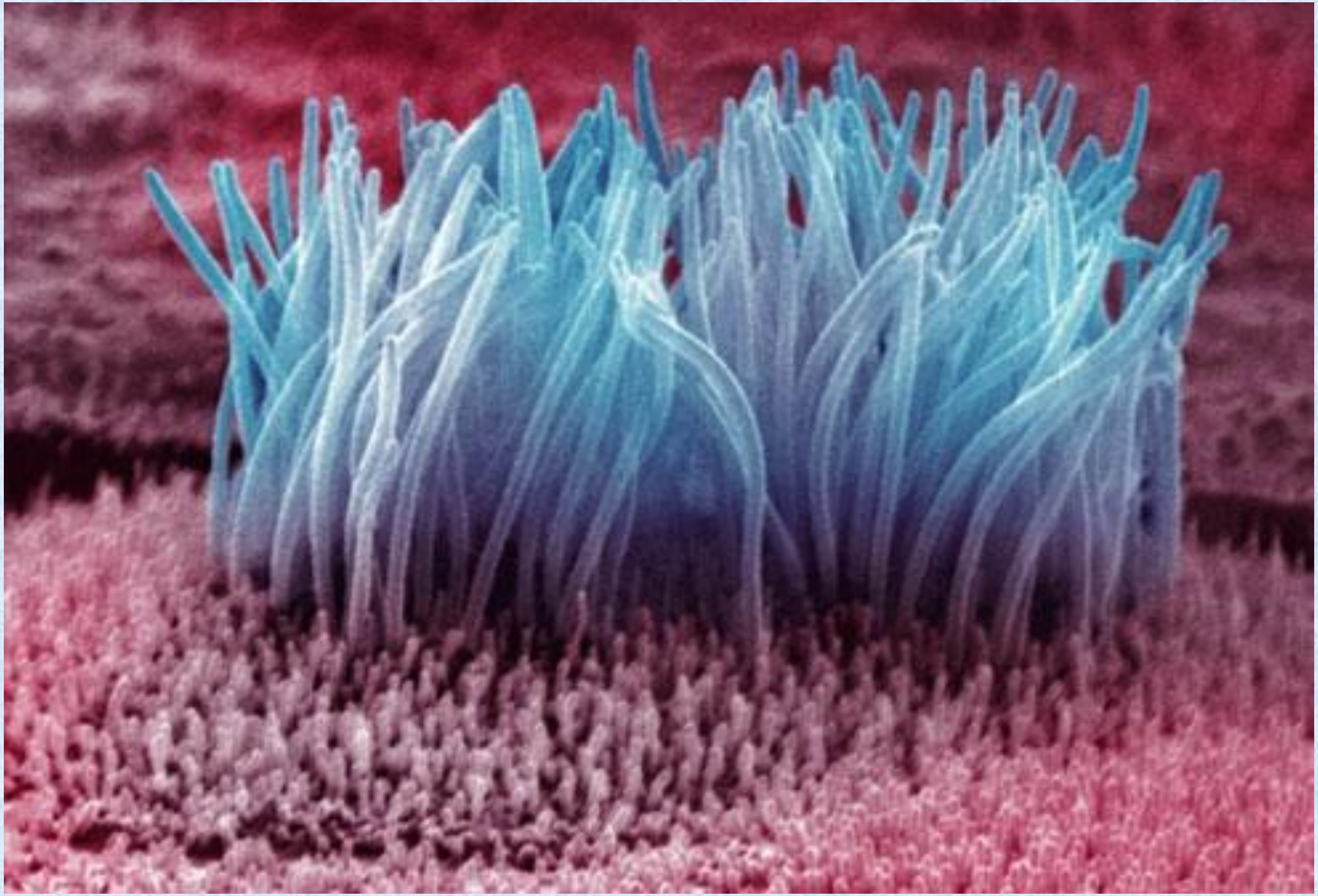

Lungs
upper-lobe bronchus
middle lobe bronchus
lower-lobe bronchus
Trachea (windpipe)
Right lobes
Left lobes
Right bronchi
Left bronchi
Secondary bronchi
Alveoli
Bronchioles
Pleura
Diaphragm

Lung cancer is a tumor of epithelial origin that develops in the mucosa of bronchi, and bronchioles as well as in the alveolus and bronchial glands.

Bronchial mucosa is formed by a pseudostratified columnar ciliated epithelium, with a large number of goblet cells and nerve endings.



Cilia of bronchial epithelium



General Information

Lung cancer is the most frequent cause of major cancer incidence and mortality worldwide.

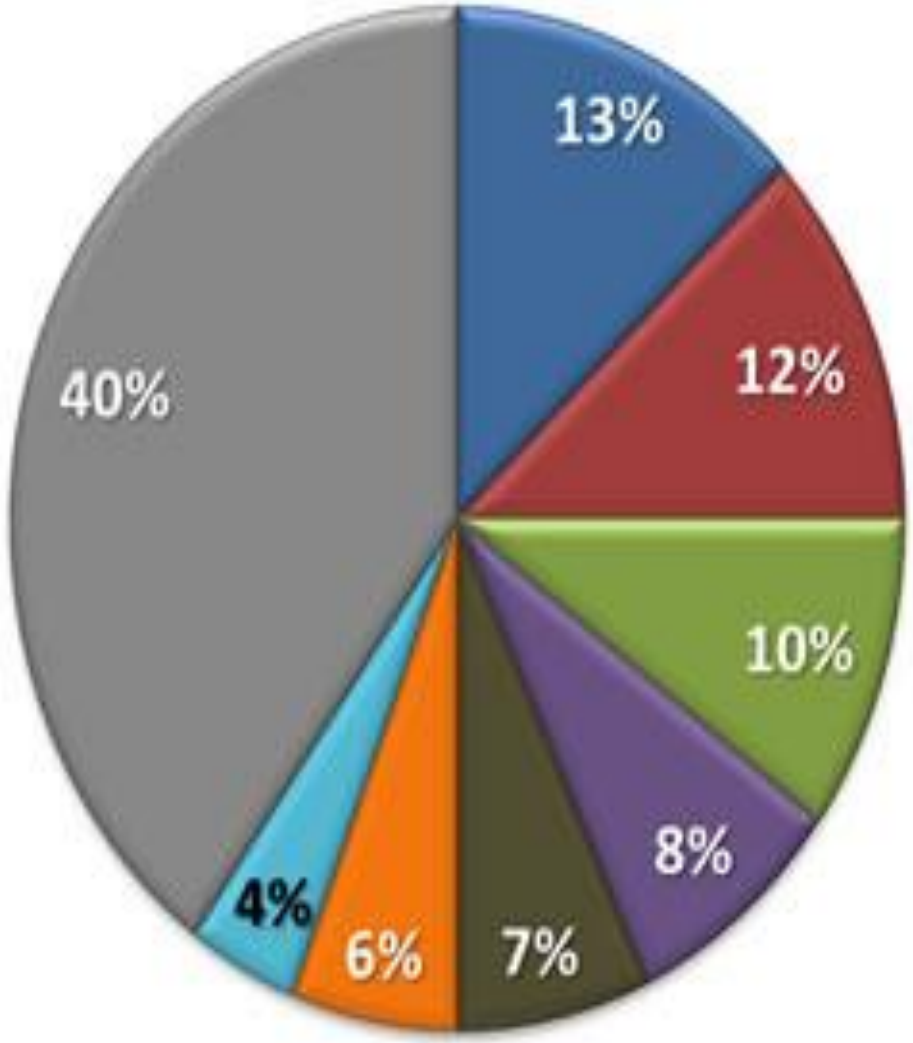
2,094 million new lung cancer cases occurred in 2018.

In 2018 the tracheal, bronchus, and lung cancer was the leading cause for cancer death in men and women, with 1.761 million deaths.

The lung cancer incidence rates is several times higher in more developed countries compared with less developed countries (44,7 vs 3,3 in 100,000 people).

Lung cancer has a poor prognosis. The five-year relative survival rate of lung cancer is 10 – 20 % in worldwide.

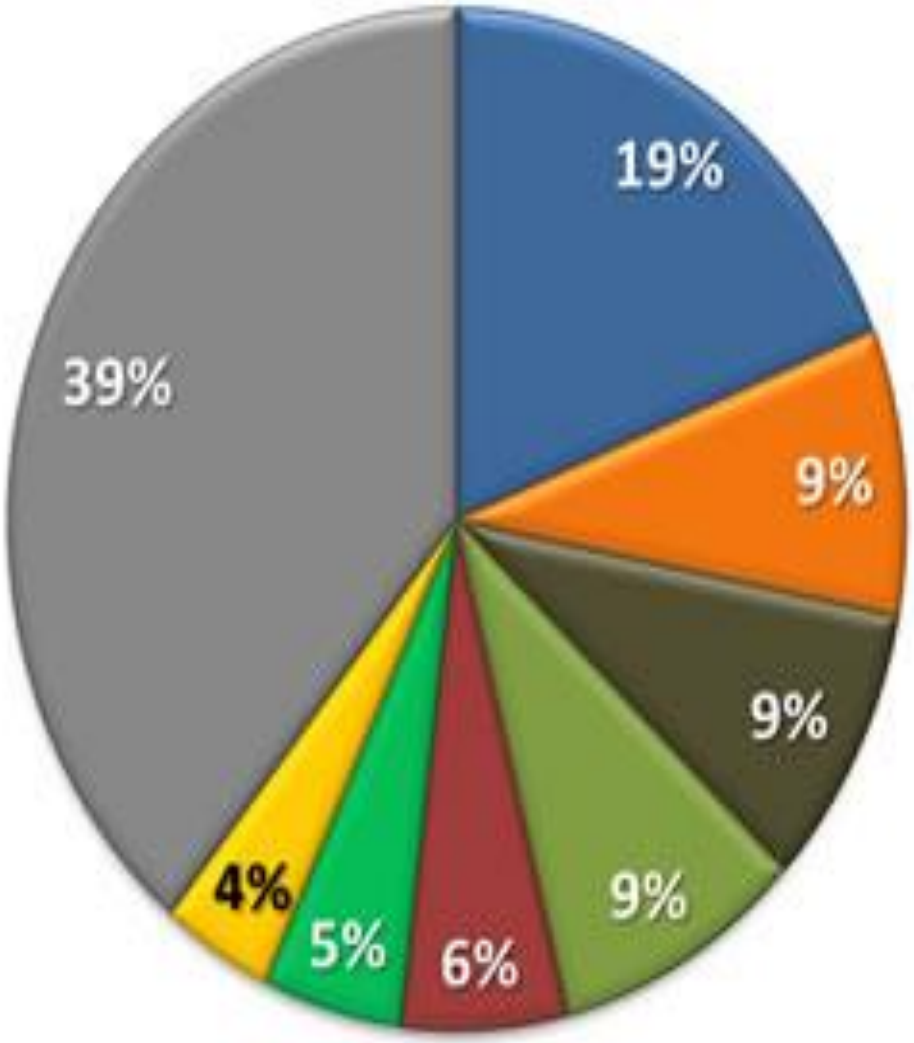
Most Common Cancers Worldwide in 2012



- Lung cancer
- Breast cancer
- Colorectal cancer
- Prostate cancer
- Stomach cancer
- Liver cancer
- Cervical cancer
- Other

Source: GLOBOCAN 2012

Most Common Causes of Cancer Death Worldwide in 2012



- Lung cancer
- Liver cancer
- Stomach cancer
- Colorectal cancer
- Breast cancer
- Esophagus cancer
- Pancreatic cancer
- Other

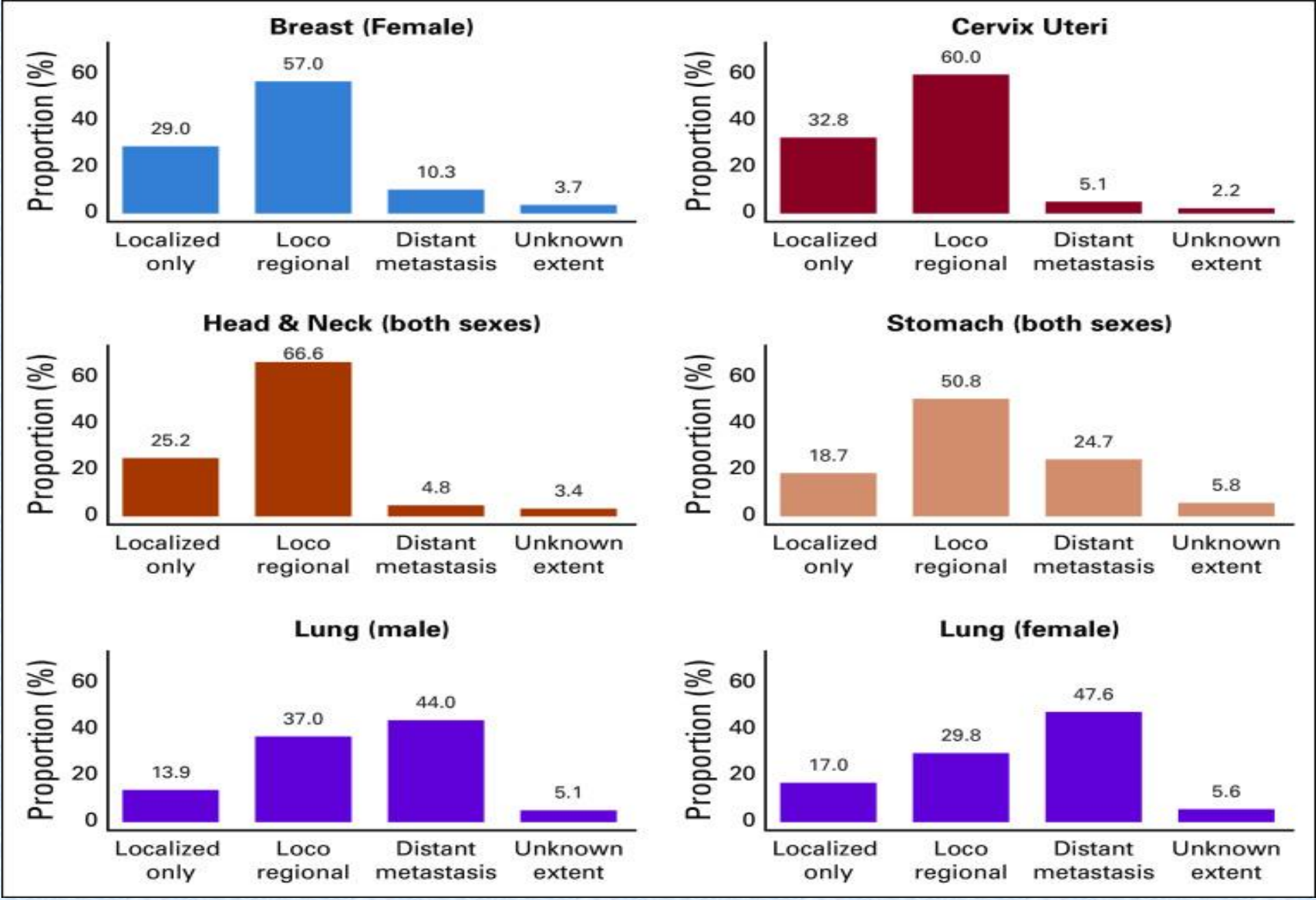
Source: GLOBOCAN 2012

Incidence rates and mortality from lung cancer in the world (2012 г.)

- Lung cancer with standardized incidence rate (ASIR) and standardized mortality rate (ASMR), equal to 23.1 and 19.7 (in 100,000 people).

Incidence rate of lung cancer		Mortality rate
USA	42,1	30,4
Canada	35,9	29,9
Russian Federation	25,5	22,7
China	36,1	32,3
India	6,6	5,9

(in 100,000 people).



Mathur P et al. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. JCO Glob Oncol. 2020 Jul;6:1063-1075.

The etiology of lung cancer
Risk factors

89% (91% in males and 87% in females) of lung cancer cases are linked to major lifestyle and other risk factors.

Main risk factors

- Smoking is the single most important risk factor for lung cancer, which can cause all types of lung cancer but is more strongly linked with squamous-cell carcinoma and small-cell lung carcinoma (SCLC)
- Environmental exposure and occupational exposures
- Precursor lesions of lung
- Genetics factors

Smoking

The probability of occurrence of lung cancer in smokers depends on:

- smoking duration
- the number of smoked cigarettes
- quality cigarette (tar in cigarettes)
- social status
- The presence of comorbidities and occupational exposures

Smoking

The greatest risk of developing lung cancer is observed in the persons:

- who began smoking in childhood and adolescence
- smoking cigarettes. Cigar and pipe tobacco smoking produces relatively large particles that only reach the upper airways. The cigarette smoking produces fine particles that reaches the distal airways.
- smoked more than 25 cigarettes a day

Important!

- Smoking cessation: at all ages smokers can benefit from the cessation of smoking.
- Risk lung cancer in smokers still remains elevated compared to never smokers.
- The secondhand smoke also causes lung cancer.

Environmental exposure and occupational exposures

Occupational exposures:

- Tar and soot
- Production of arsenic, chromium, nickel, aluminum, iron and steel
- Asbestos and Beryllium
- Production of coal/coke and Coal-tar pitch
- Diesel engine exhaust
- Hematite mining

Air pollution

- Lung cancer death risk is higher in people living near major roads

Household coal combustion emissions

- Lung cancer risk is around doubled in people who use coal in the home for cooking or heating

Presence in air the radioactive gas Radon-222

Smoking potentiates the effect of lung carcinogens

Precursor lesions of lung

Squamous dysplasia - precursor lesion for squamous-cell carcinoma.

Adenomatous hyperplasia - precursor lesion for adenocarcinoma.

Idiopathic pulmonary neuroendocrine cell hyperplasia - precursor for pulmonary carcinoids.

These lesions can be caused by:

Chronic bronchitis

Chronic pneumonia

Bronchiectasis

Pulmonary tuberculosis

Asbestosis

Silicosis

Pneumoconiosis

Genetics

Lung cancer risk is 82% higher in people whose sibling has/had lung cancer, and 25-37% higher in people whose parent has/had the disease.

This association is independent of smoking.

Small-cell lung carcinoma (SCLC) often has mutations in MYC, BCL2, c-KIT, p53, and RB

Non-small-cell lung carcinoma (NSCLC) often has mutations in EGFR, KRAS, CD44, and p16.

Other factors increases lung cancer incidence

Previous cancer: Lung cancer risk is higher in patients who had in anamnesis **previous cancer**: Hodgkin and non-Hodgkin lymphoma; breast cancer; testicular cancer; uterine sarcomas; head and neck cancers; lip, oesophagus, bladder cancers and other.

Beta-carotene supplementation in current smokers

Radiation

Prevention of lung cancer

- tobacco control
- reduction of tar in cigarettes
- improvement of ecology and purity of air
- eliminate or reduce of the occupational hazards
- screening in the groups of high risk for lung cancer
- treatment of persons with chronic diseases of bronchial tubes and lungs

Who refer to high-risk group?

- the heavy smokers older than 40 years
- persons with chronic obstructive diseases of the bronchi and lungs
- who had previous cancer of the upper respiratory tract and lungs
- persons who are often ill with influenza and other acute respiratory viral infections
- who having a family history of cancer pathology
- persons, who worked long time with asbestos, arsenic, nickel and chromium

Screening for lung cancer

Low-dose spiral computed tomography reduces lung cancer mortality by 20% in persons aged 55 to 74 years who have cigarette smoking histories of 30 or more pack-years.

98% of all positive low-dose spiral computed tomography screening exams do not result in a lung cancer diagnosis.

NB!

Chest x-ray and/or sputum cytology - No Benefit Associated With Screening

Low-dose helical computed tomography

- allows detection of lesions in lung tissue 2-3 mm in size.
- the radiation dose is only 1.5 times greater than for fluoroscopy
- lesions in the lungs detected in 1-12% of patients at risk
- in 0.5-1.5% of patients, these lesions are bronchogenic cancer
- More than 80% of these tumors can not be seen on X-rays
- in 80-95% of patients CT can detect cancer in stage I

Classification of lung cancer

Clinical and anatomic classification of lung cancer

Russian classification of lung cancer is associated with the tumor localization, the type of tumor growth and the clinical and radiological characteristics of disease.

Central lung cancer

The tumor is located in the main, lobar, segmental and subsegmental bronchi.

Peripheral lung cancer

The tumor is located in the smaller bronchi, bronchioles and alveoli.

Atypical forms of lung cancer.

Types of lung cancer depending on the tumor growth

Central lung cancer

- endobronchial
- exobronchial
- peribronchial branched

Peripheral lung cancer

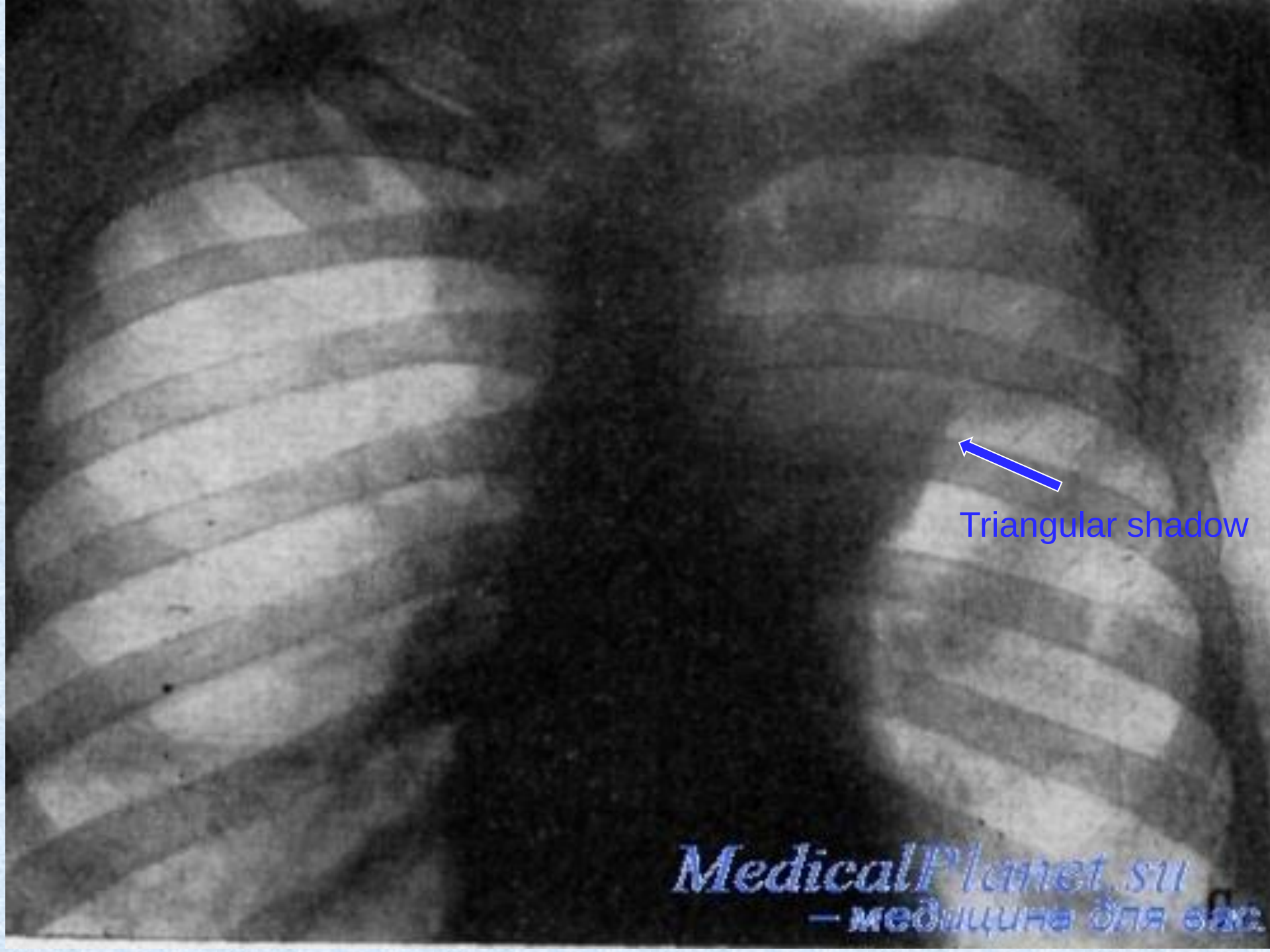
- nodal
- pneumonia-like
- cortico-pleural
- cavitary form
- cancer apex (Pancoast syndrome)

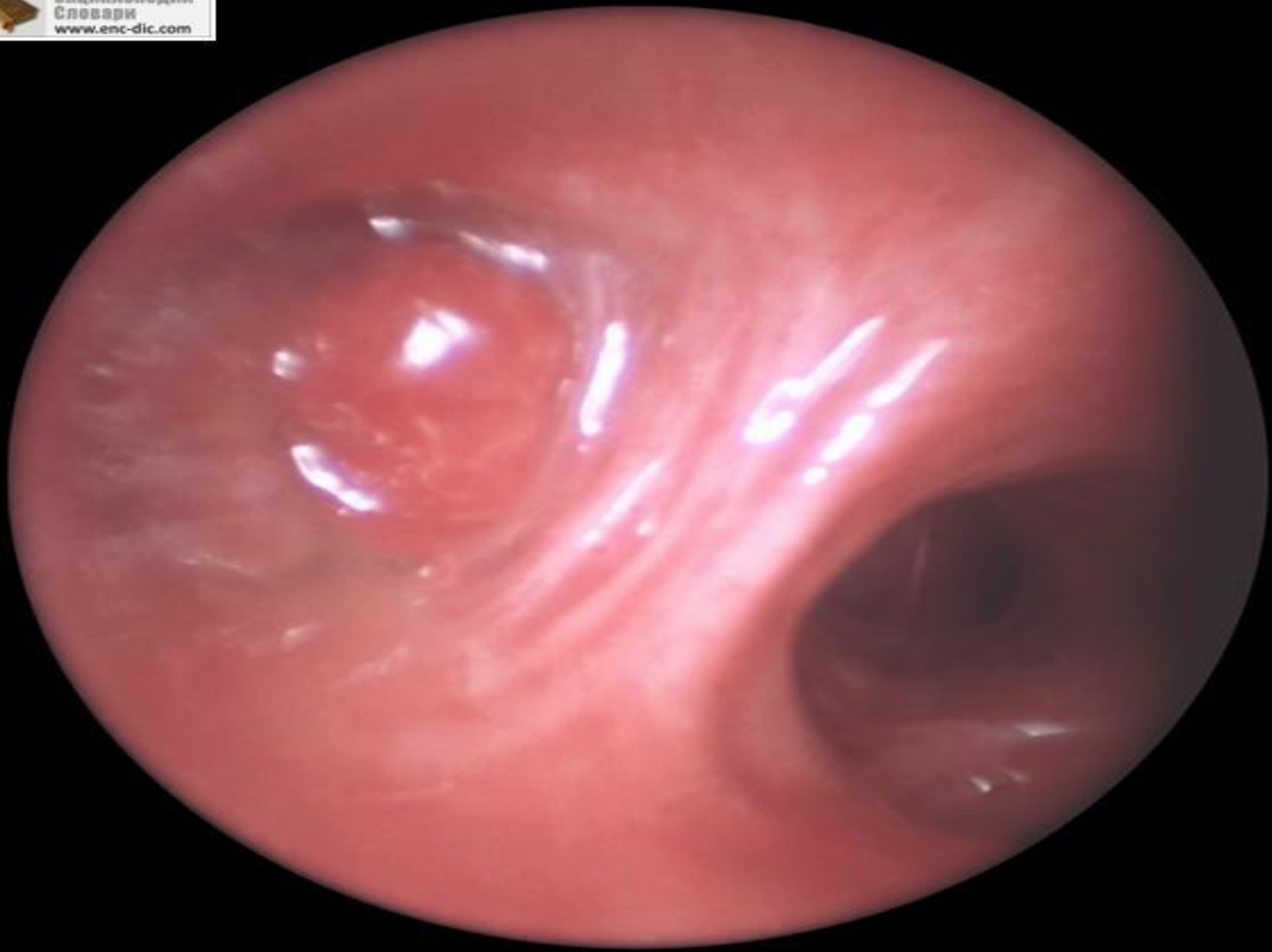
Atypical forms of lung cancer

- miliary form
- carcinomatosis lung
- mediastinal form

Central lung cancer
Endobronchial type of tumor growth

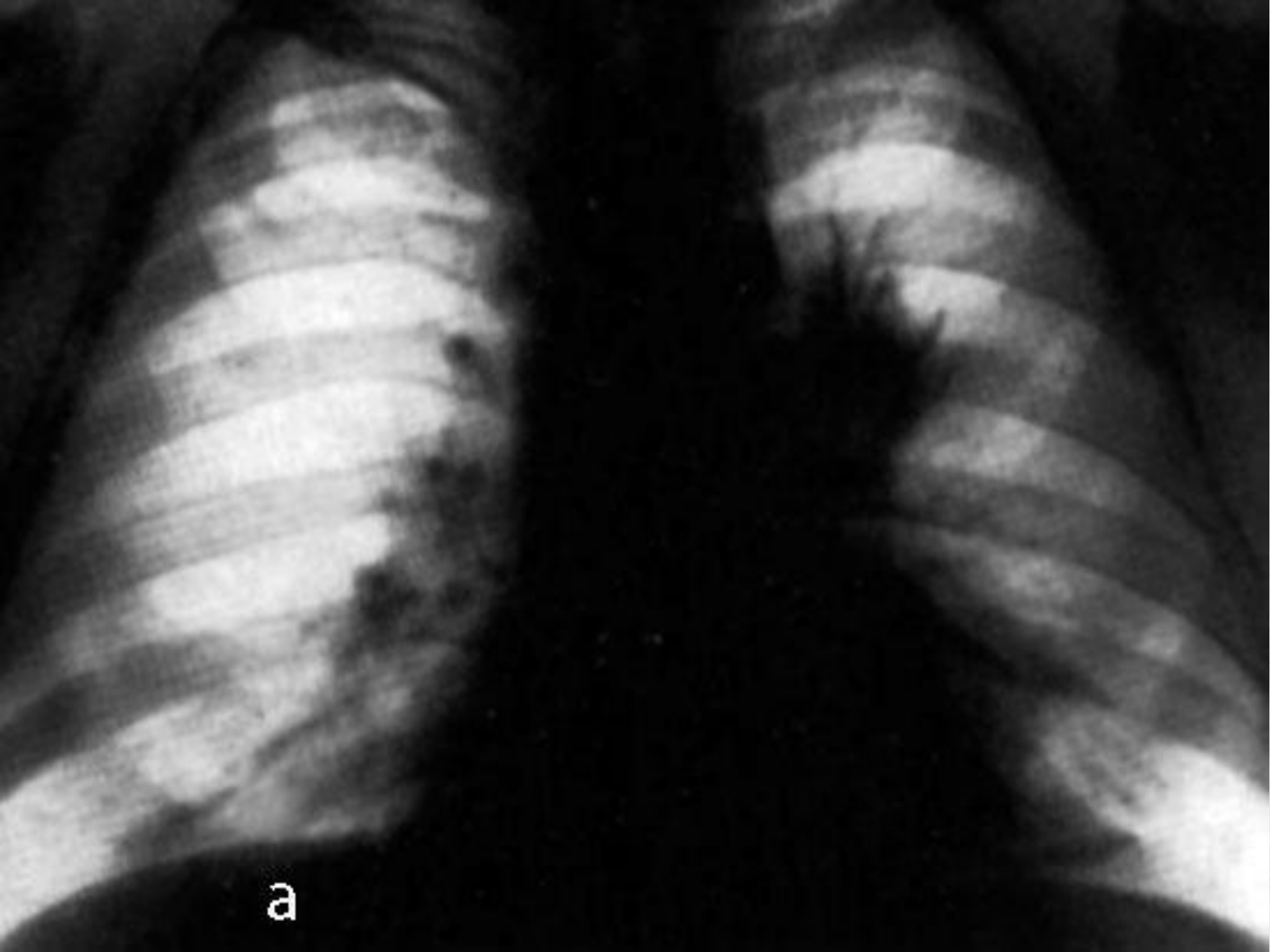
- The tumor growth in the lumen of the bronchus
- Violation of ventilation
- Hypoventilation and atelectasis of the lung tissue
- Compensatory swelling of the adjacent parts of the lung





Central lung cancer
Exobronchial type of tumor growth

- Tumor growth outside from bronchus
- When X-ray - the shade of tumor is visible in the root of the lung
- Long asymptomatic course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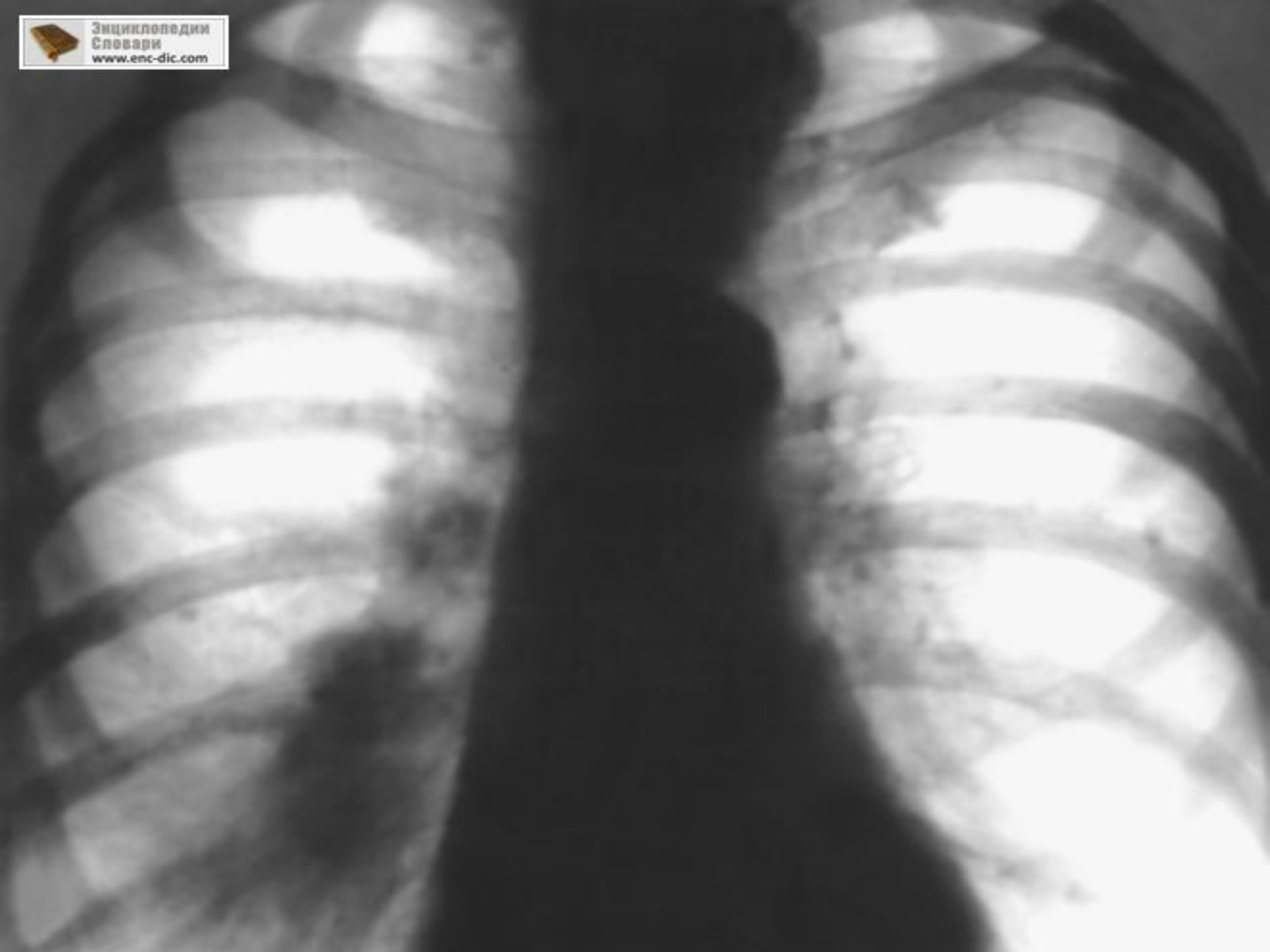


Central lung cancer
Peribronchial branched type of tumor growth

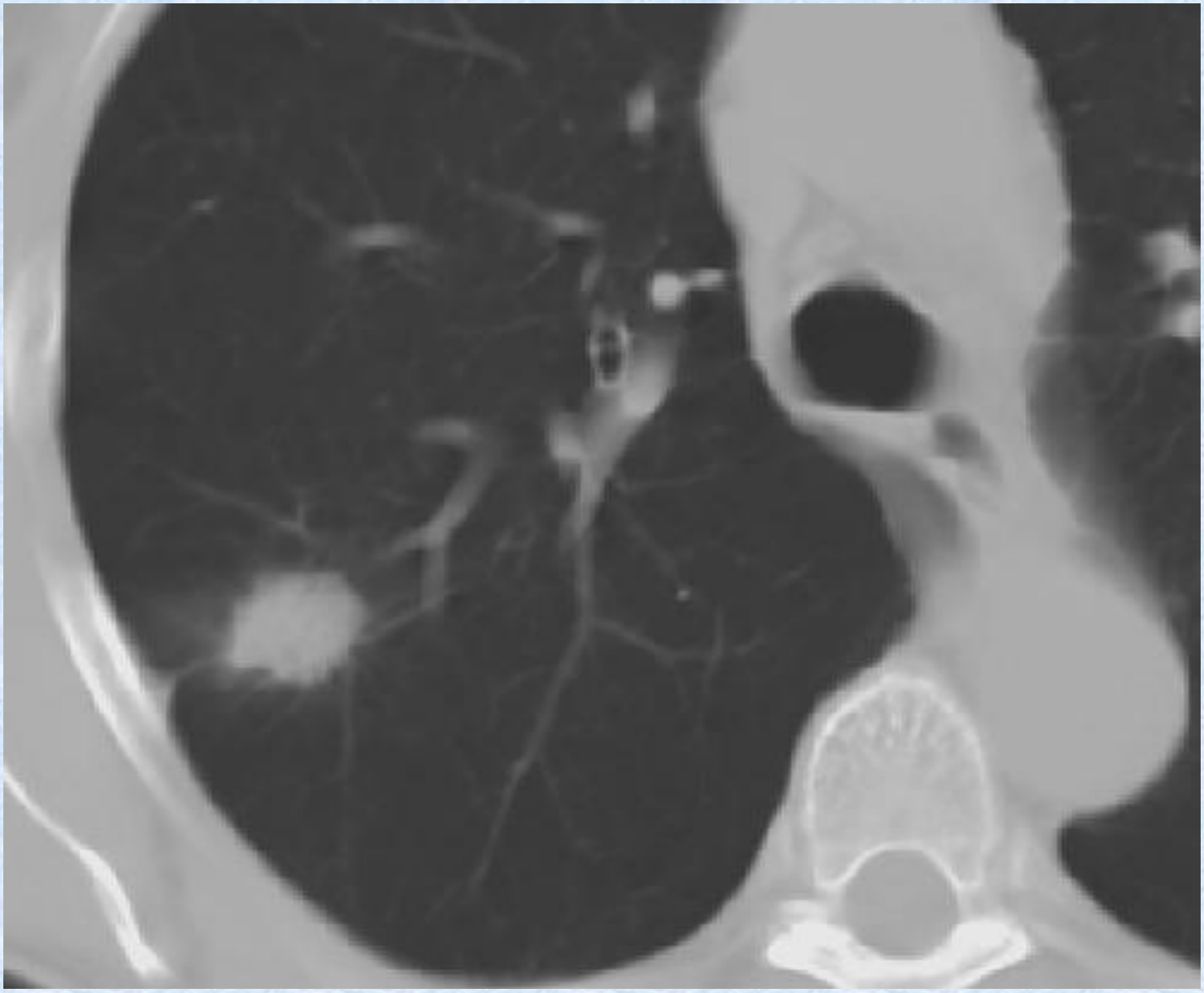
- The tumor grows diffusively under the mucous membrane along the bronchi
- At the X-ray and endoscopy the characteristic features of the tumor may be absent for a long time
- Most often it occurs in undifferentiated tumors
- Late diagnosis. The tumor is often detected in the presence of intrathoracic or distant metastases

Peripheral lung cancer. Nodal form

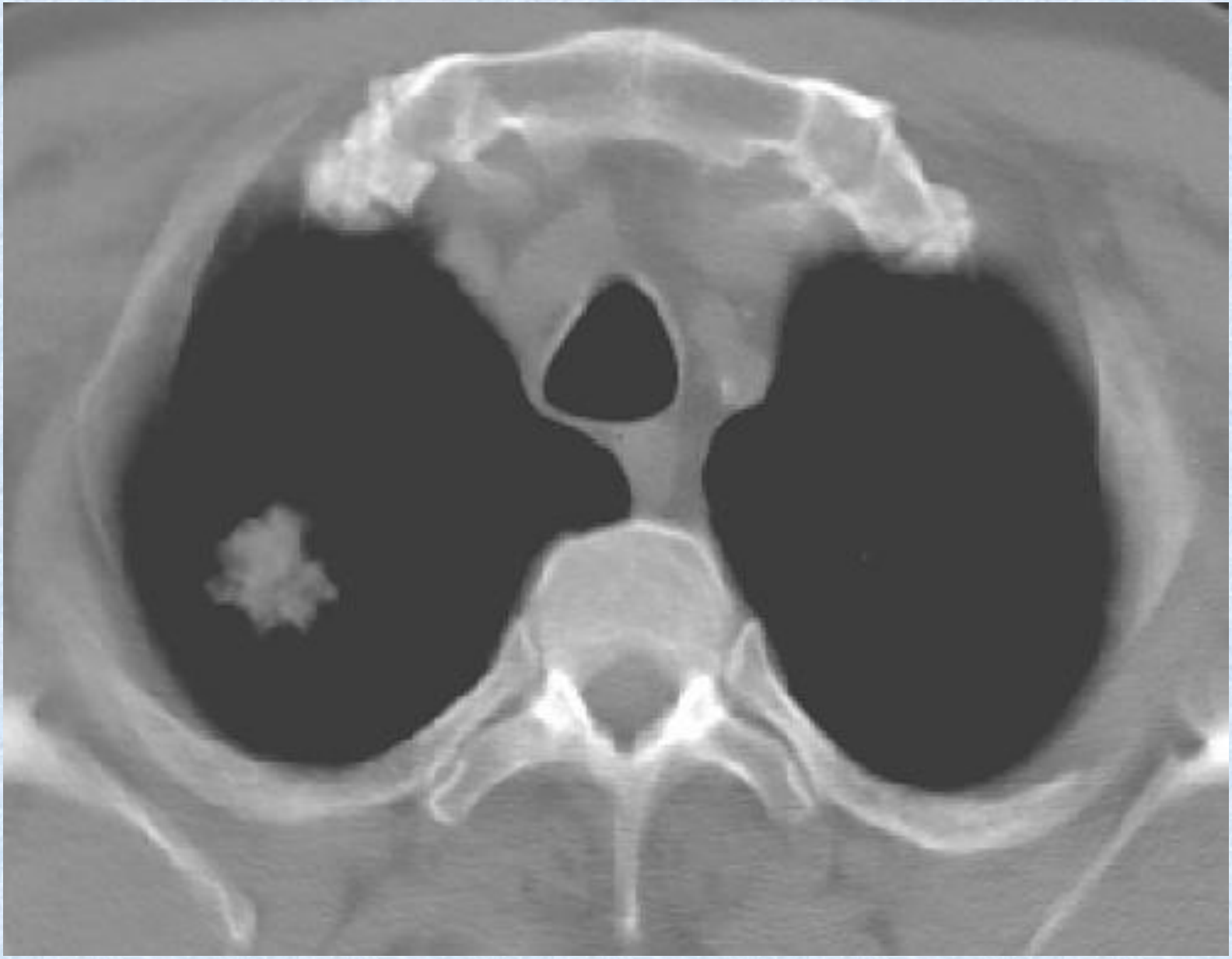
- Most common form of peripheral lung cancer.
- Often located in the second segment of the upper lobe.
- Shape of the tumor is often round.
- The classic radiographic signs include the uneven surface and radiant contours.
- In 7% cases the surface of tumor nodules with smooth clear contours.
- Retraction of the visceral pleura is often observed.
- "Path to the root of lung" is tipical.
- The ingrowth of the tumor in the lumen of the large bronchi or their compression is accompanied by the clinical symptoms of the central lung cancer (atelectasis, pneumonitis). This process is called - the centralization of peripheral lung cancer.

Peripheral lung cancer. Nodal form

Peripheral lung cancer. Nodal form



Peripheral lung cancer. Nodal form

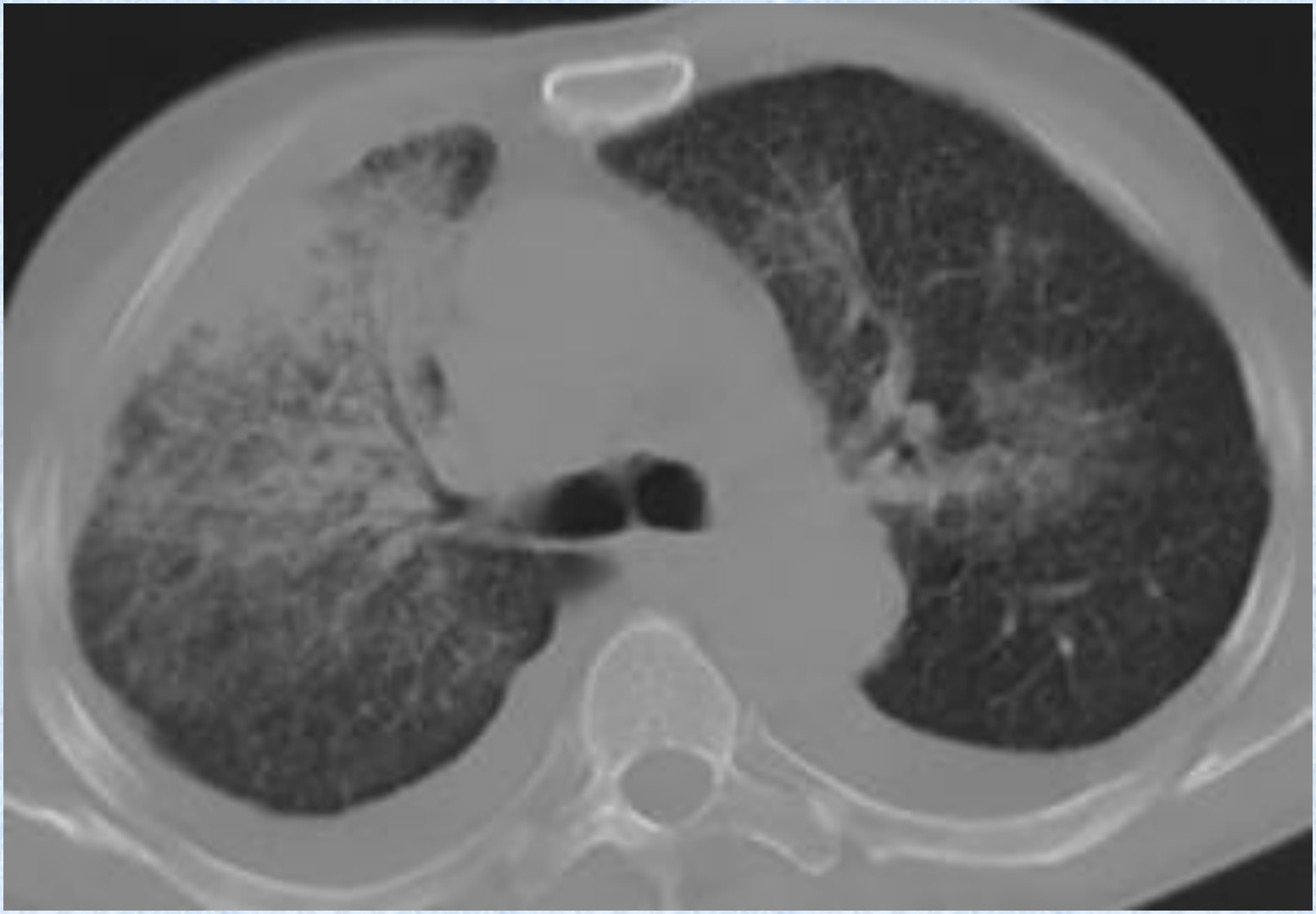


Peripheral lung cancer. Pneumonia-like form

- It is found only in the lung adenocarcinoma
- Histological form is most often the bronchiolo-alveolar carcinoma (in 60% cases)
- Often observed in the middle and lower lobes of the lung
- The X-ray pattern is similar to the inflammatory process.

Peripheral lung cancer. Pneumonia-like form

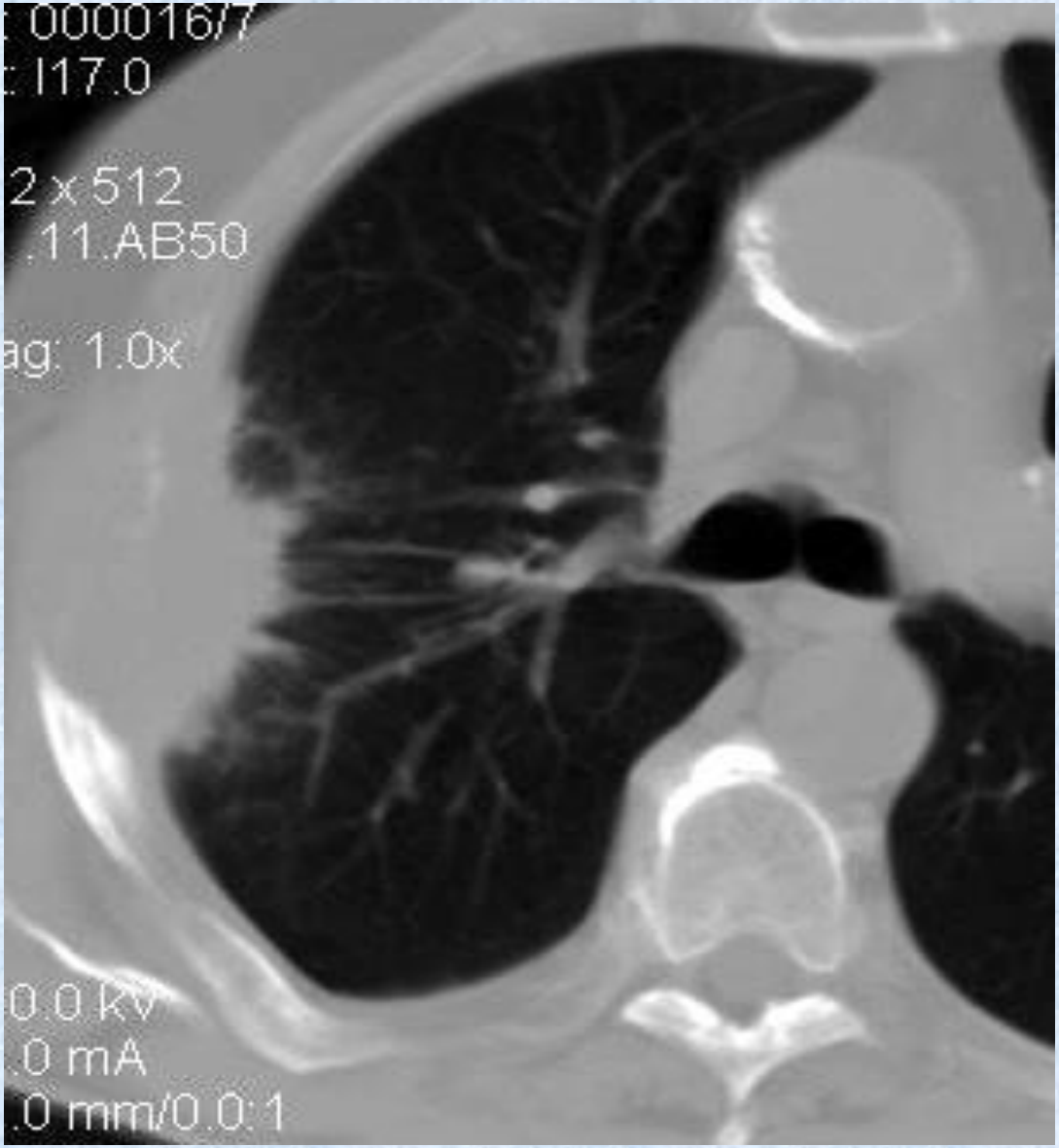
Peripheral lung cancer. Pneumonia-like form



Peripheral lung cancer. Cortico-pleural form

- Located and growing along the pleura
- Tumor often grows into the tissues of the chest wall;
- Usually tumor has an oval shape and a wide base;
- Inner contours are indistinct and radiant

Peripheral lung cancer. Cortico-pleural form

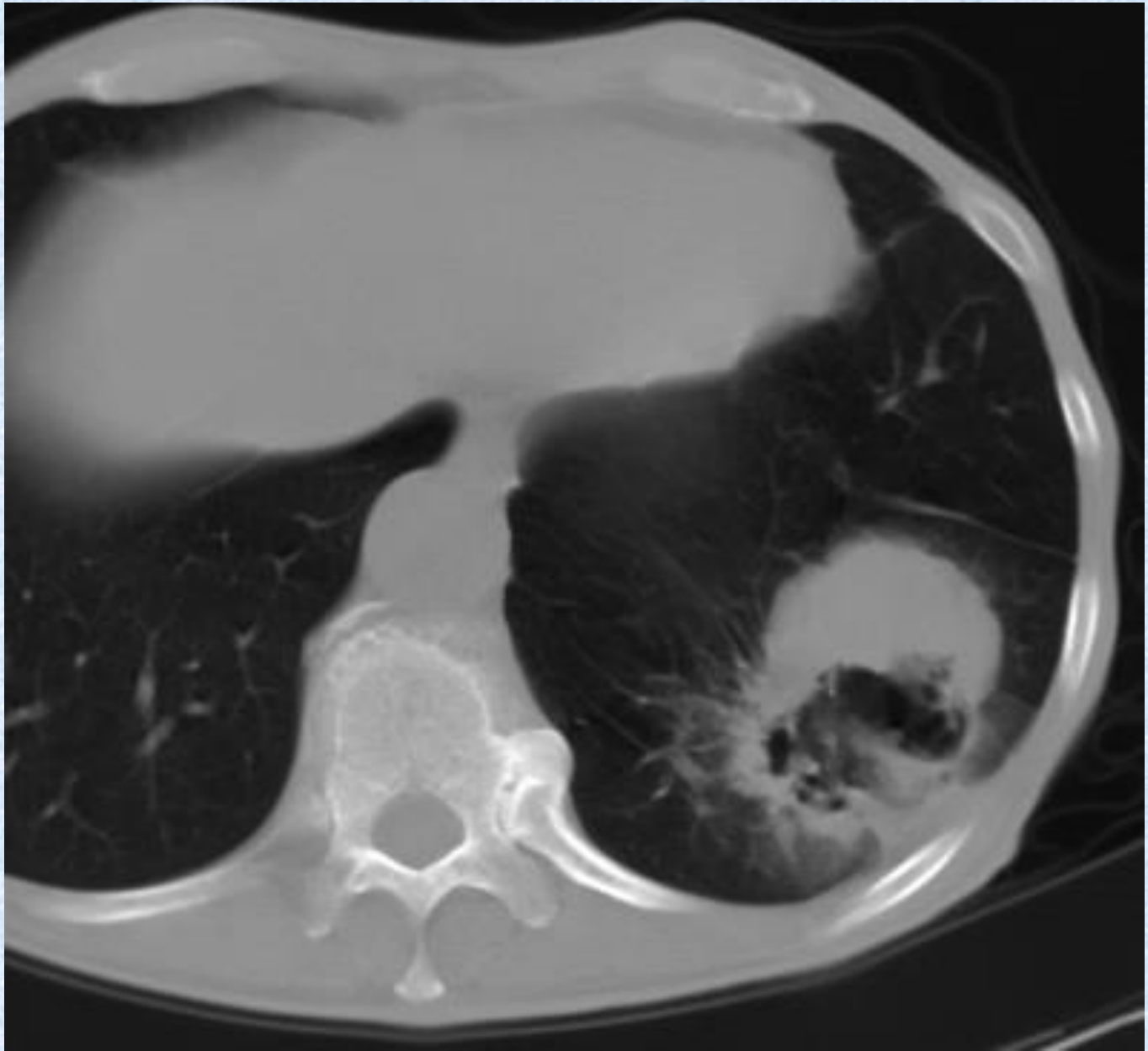


Peripheral lung cancer. Cortico-pleural form

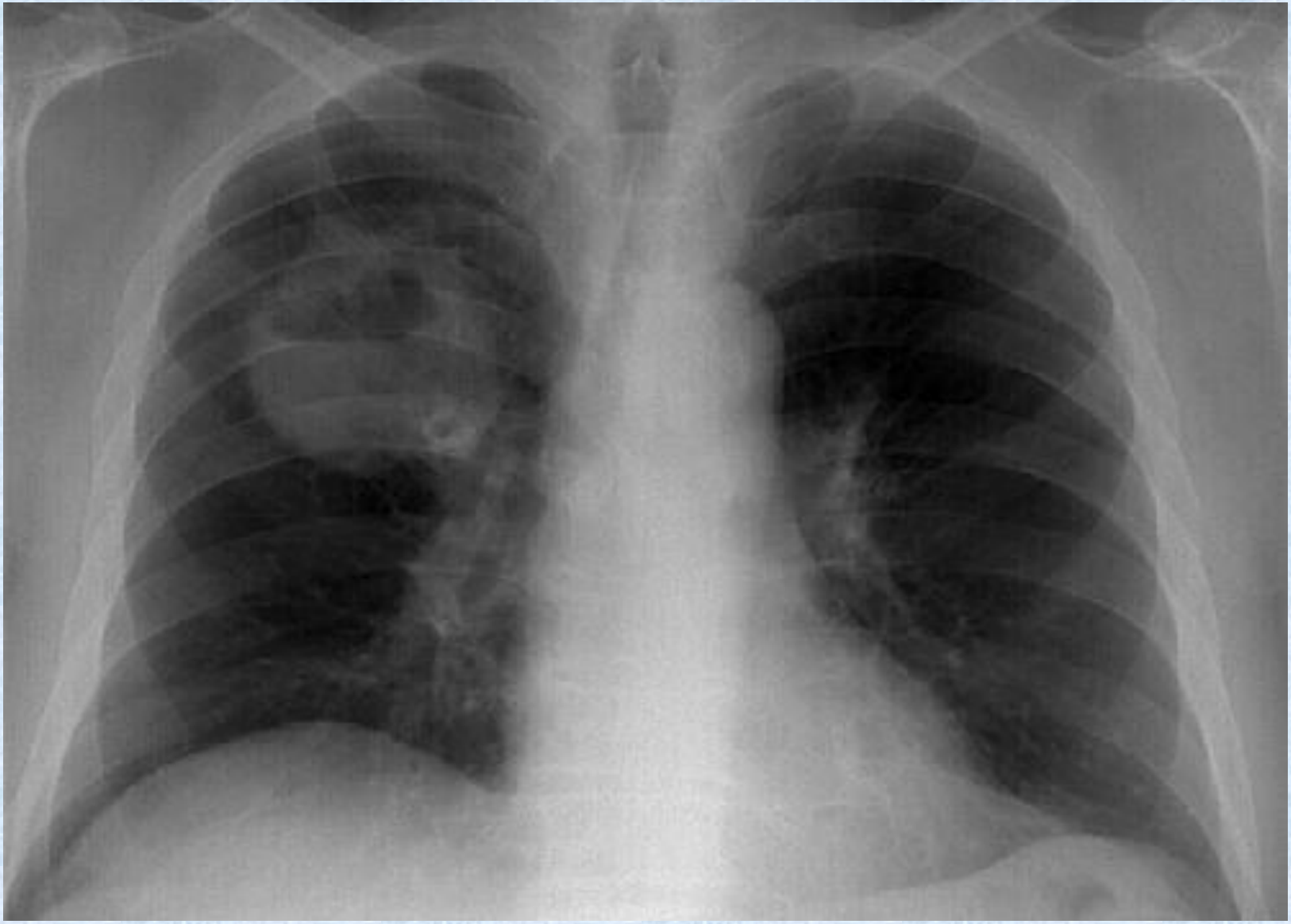
Peripheral lung cancer. Cavitary form

- Observed predominantly in squamous cell lung cancer;
- Usually it presented unicameral, spherical cavity with air
- External contour is indistinct
- Internal contour of cavity is uneven
- Cavernous formation has unevenly thickened wall
- Retraction of visceral pleura
- Asymptomatic course is observed in 60% of cases.
- Acute beginning with hectic rise of body temperature and hemoptysis is noted in 30% of cases

Peripheral lung cancer. Cavitary form



Peripheral lung cancer. Cavitary form



Peripheral lung cancer. Cavitary form

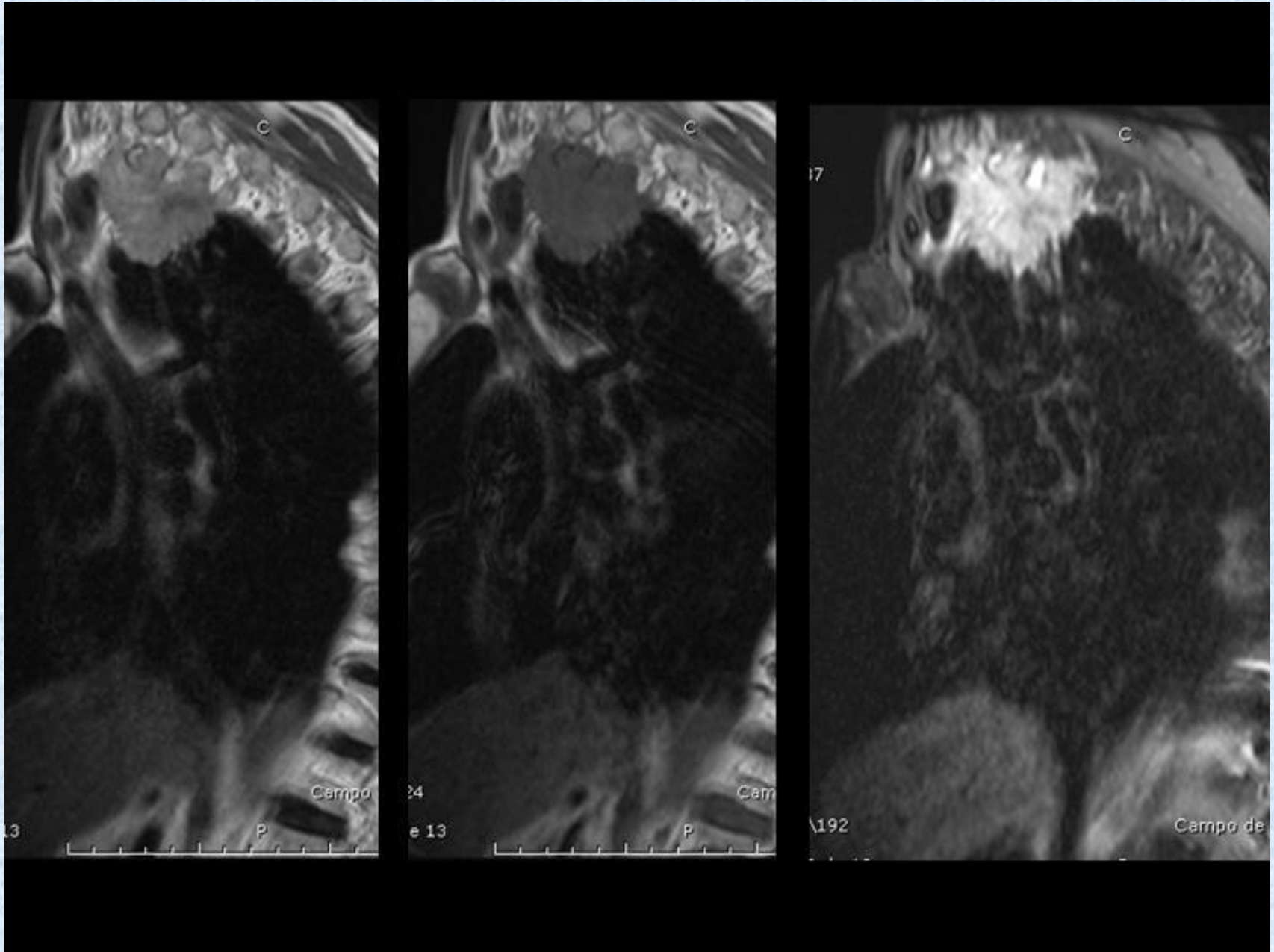
Cancer Pancoast

- For the first time the syndrom was described by H. Pancoast (1924., 1932.)
- Cancer apex of the lung with the involvement of the parietal pleura
- The defeat of the cervical plexus
- Compression of the subclavian vessels
- Destruction of the first rib
- Involvement of the lower cervical sympathetic ganglion (Horner's triad)
- Compression of the recurrent laryngeal nerve (hoarseness)
- The defeat of the spinal cord

Cancer Pancoast

Cancer Pancoast

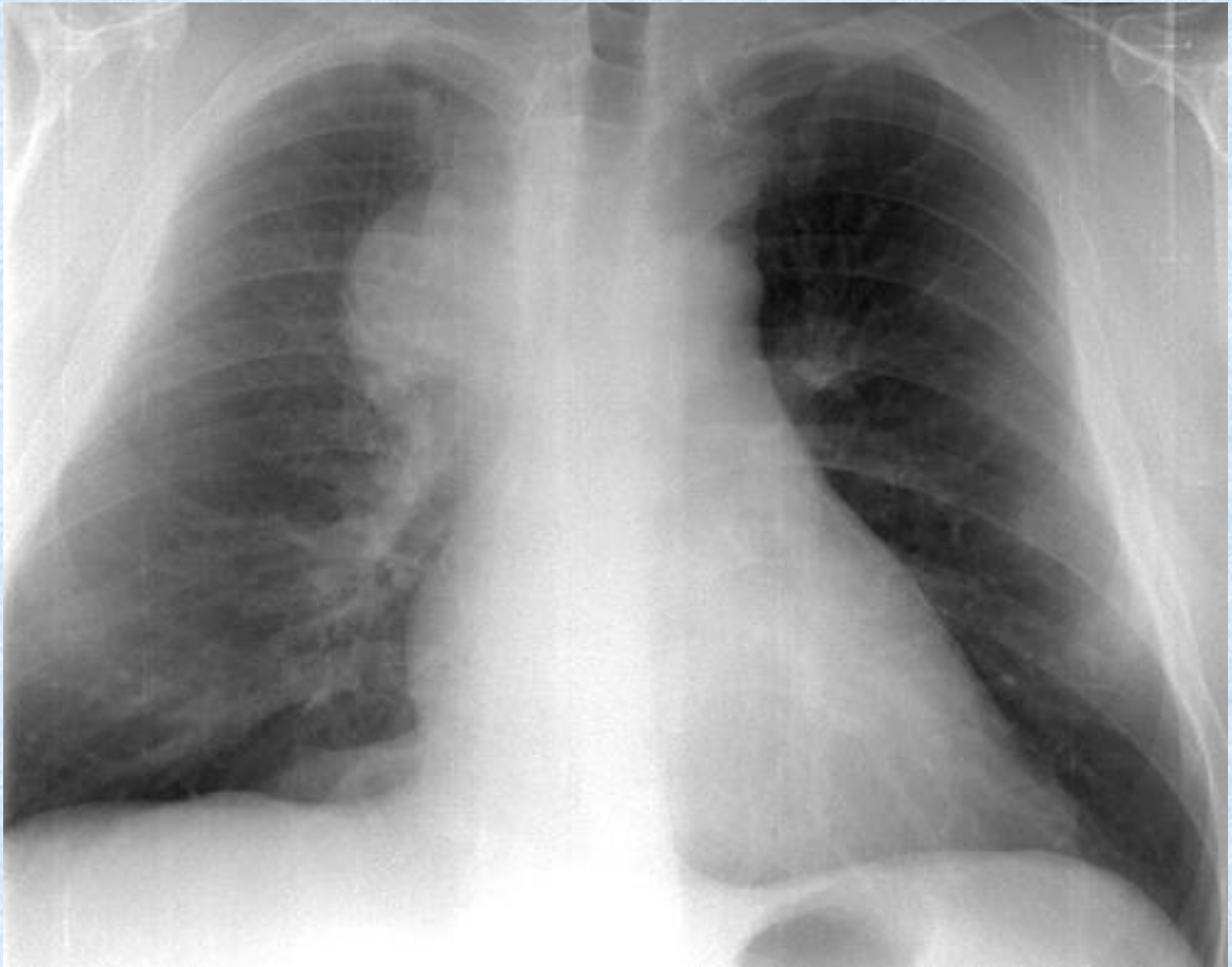
Cancer Pancoast



Mediastinal form of lung cancer

- Enlarged lymph nodes are detected in the upper mediastinum.
- The primary tumor is not determined by X-ray and endoscopic methods of investigation

Mediastinal form of lung cancer



Mediastinal form of lung cancer

The histological classification of lung cancer

Non-small-cell lung cancer (NSCLC, 85%)

squamous-cell carcinoma,

adenocarcinoma,

carcinoid

bronchiolo-alveolar carcinoma

large-cell carcinoma.

Small-cell lung carcinoma (SCLC, 15% of all lung cancer)

In total there are more than 60 different variants of lung cancer

Adenocarcinoma (20 - 38%)

- Always a **peripheral** cancer
- Most common type of lung cancer in **nonsmokers** and more common in **women**
- Arises from small airway epithelial and type II alveolar cells
- Should test for EGFR mutation for possible targeted therapy
- Sometimes appear at site of scarring
- Tend to form glands and secrete mucin

Squamous cell carcinoma (20% - 60%)

- ⅔ central and ⅓ peripheral lung cancer
- Strongly associated with cigarette smoking
- Arises from large (proximal) airway epithelial cells
- Tend to create obstruction of bronchi and cause distal atelectasis
- Intrathoracic lymphogenous spread rather than distant metastasis;
- Best prognosis

Small-cell lung carcinoma (SCLC) (14%)

- Central cancer (peribronchial)
- Strongest smoking association
- Arises from pulmonary neuroendocrine cells, which are responsible for making neurotransmitters, growth factors, and vasoactive substances
- Causes paraneoplastic syndrome: commonly secrete ADH (SIADH) or ACTH (ectopic Cushing syndrome)
- Rapid growth and early distant metastasis (brain, liver, bone)
- Worst prognosis

International classification of lung cancer according to the TNM system

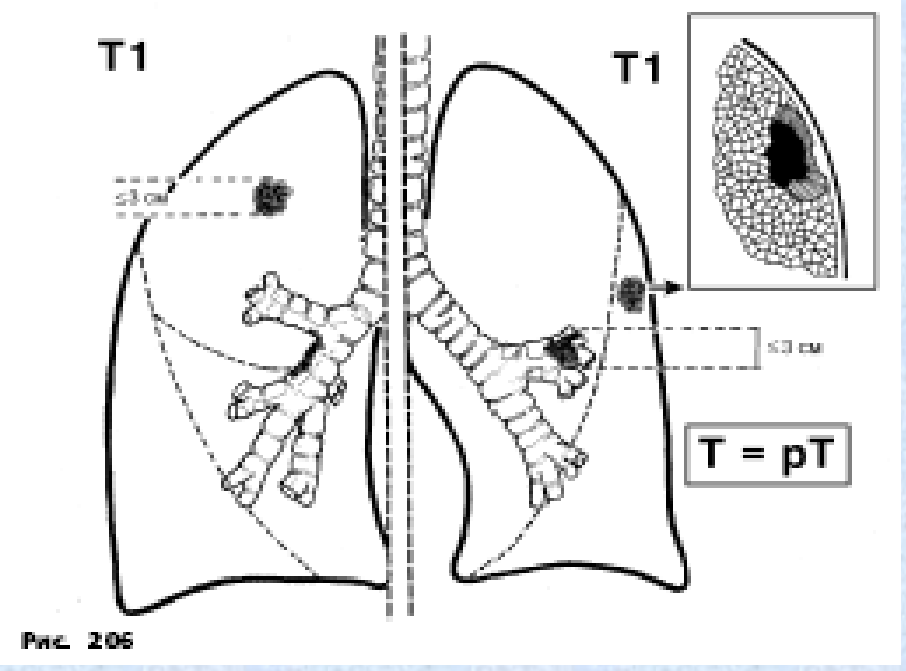
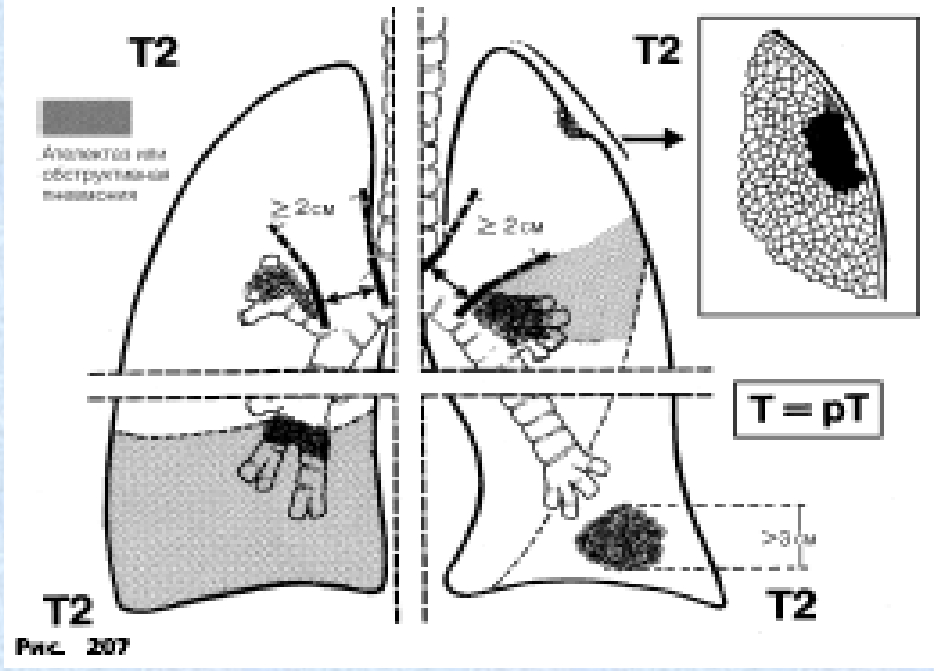


Рис. 206



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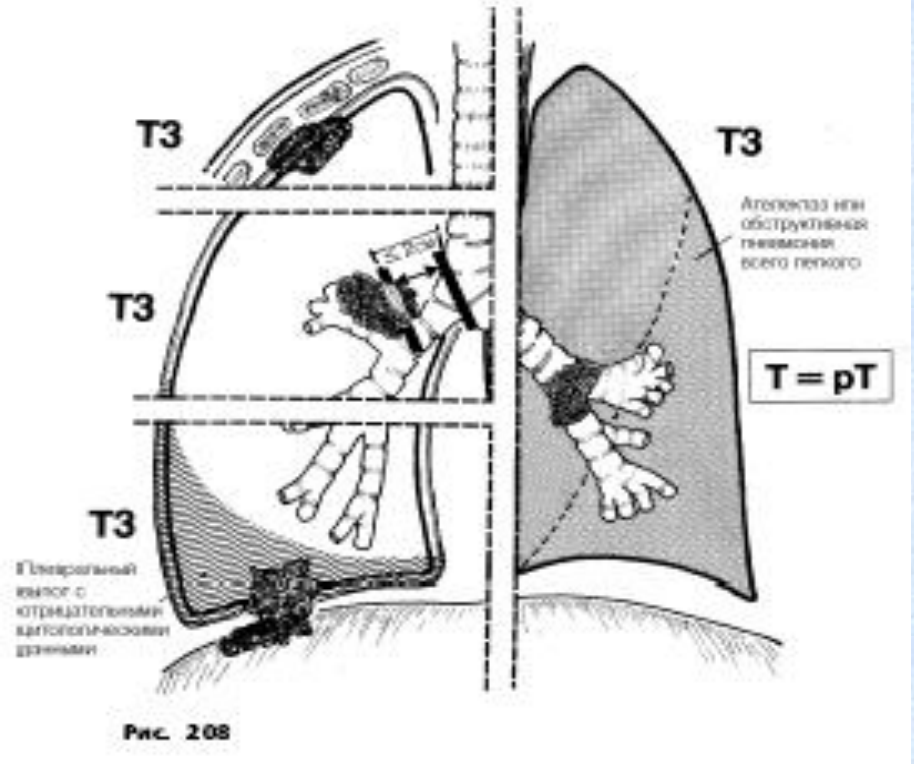

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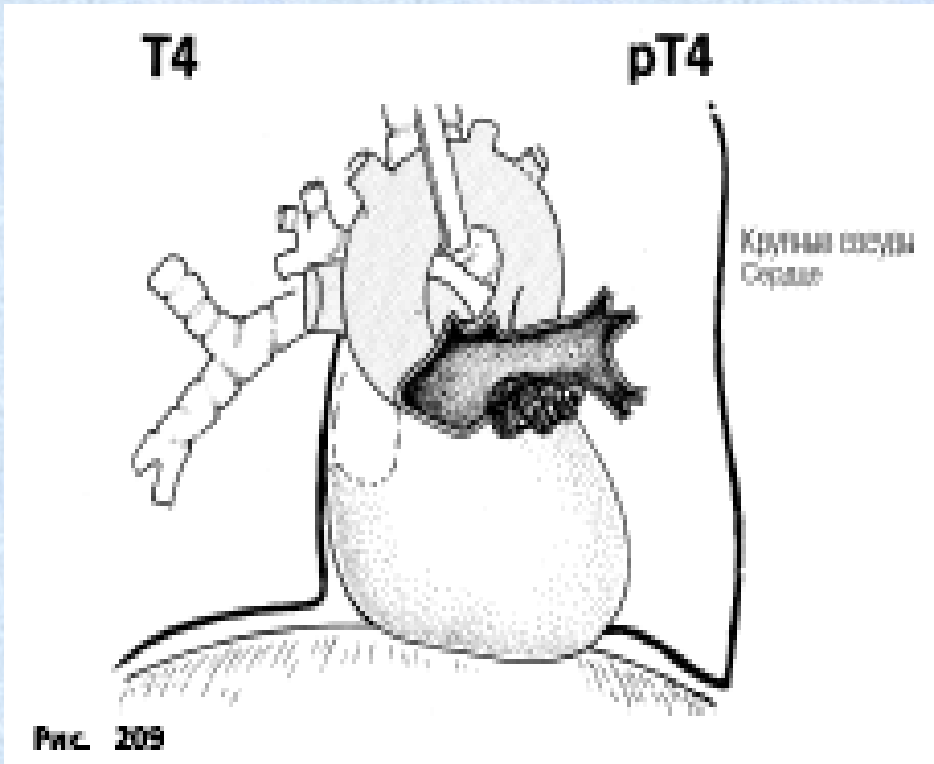

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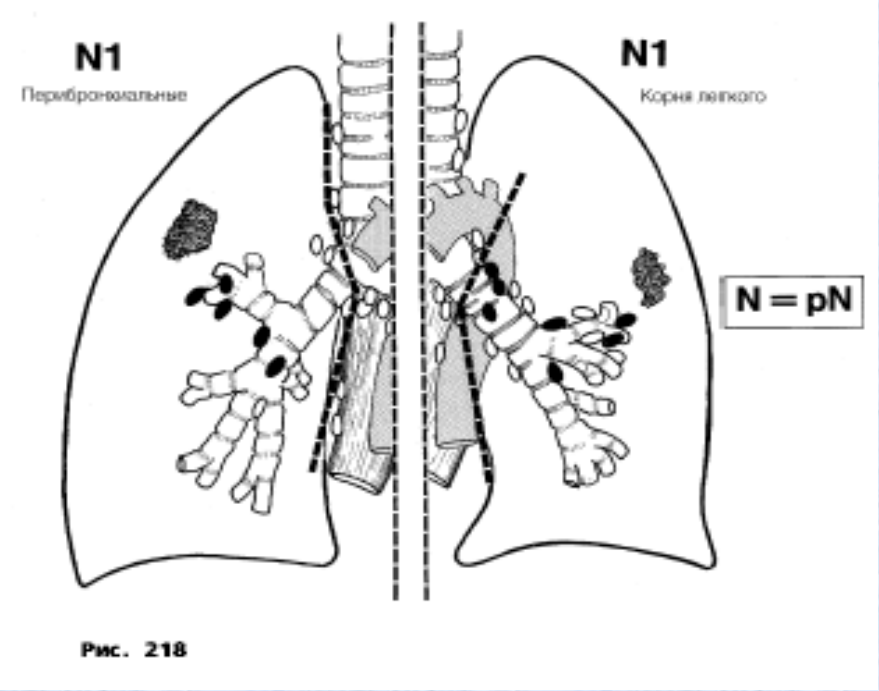

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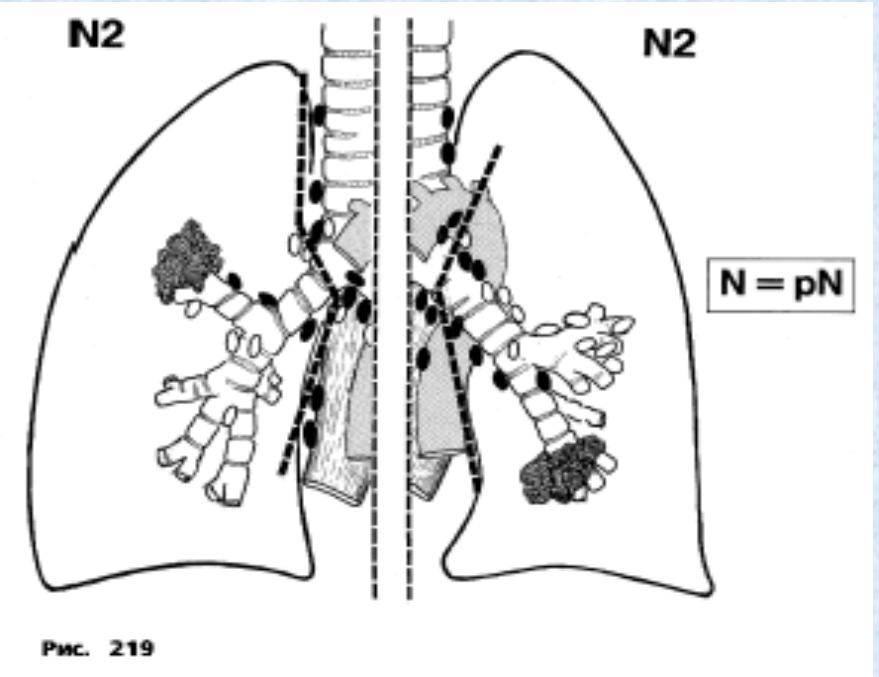

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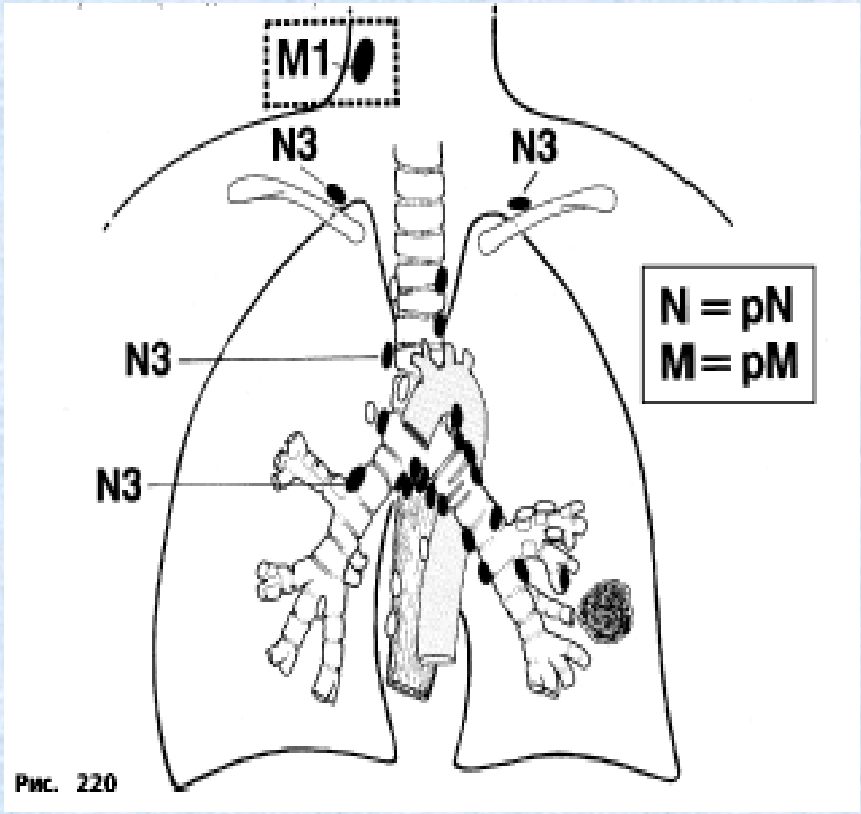


Рис. 220

Stage Grouping

Ia T1 N0 M0

Ib T2 N0 M0

IIa T1 N1 M0

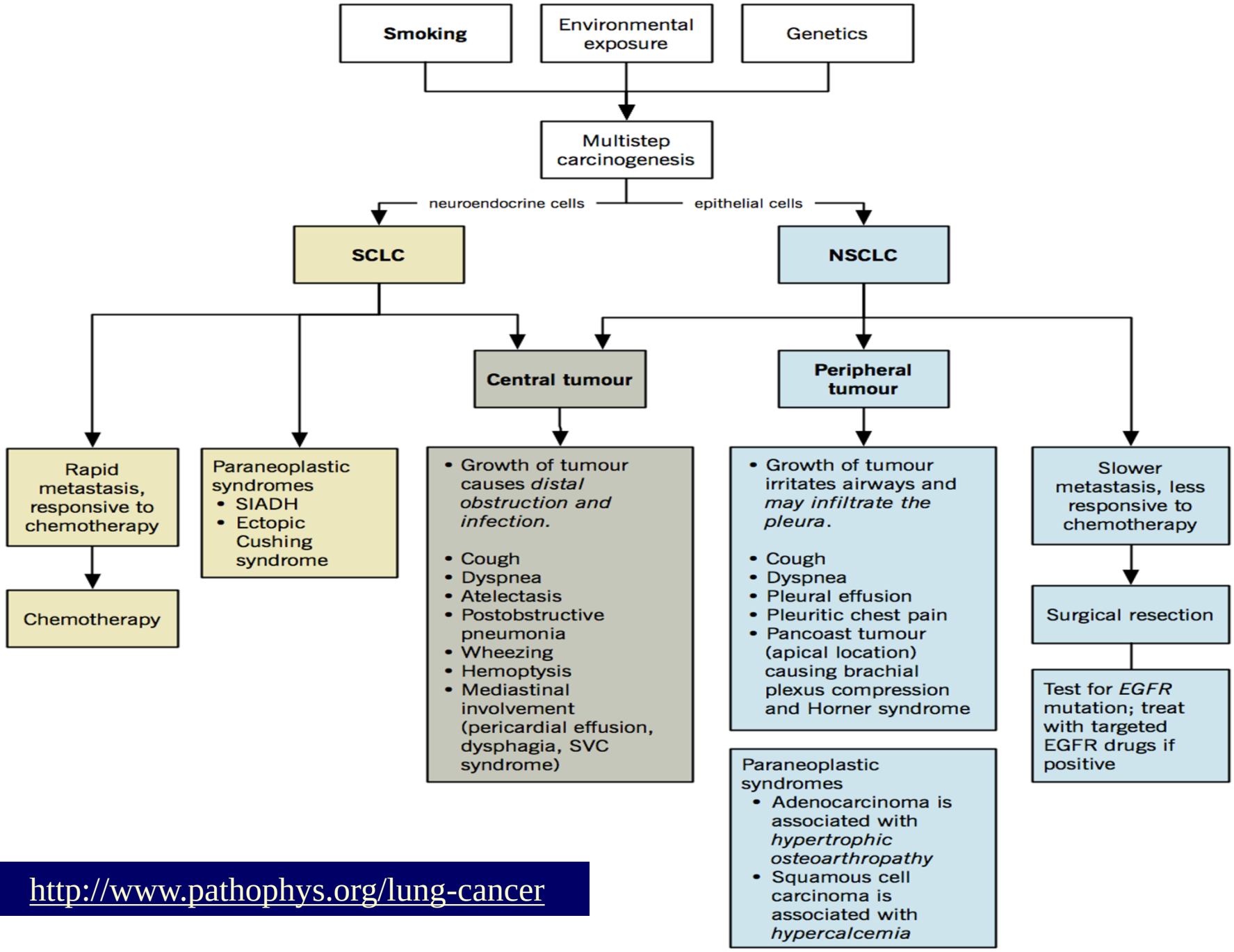
IIb T2 N1 M0; T3 N0 M0

IIIa T3 N1 M0; T1,2,3 N2 M0

IIIb Any T N3 M0; T4, Any N, M0

IV Any T Any N M1

Clinical features of lung cancer



http://www.pathophys.org/lung-cancer

Central lung cancer

Clinical manifestations may be caused by:

Obstruction of the bronchus

Tumor destruction

Compression of vascular and nervous structures as well as the hollow organs of mediastinum by the lymph node with metastasis

Distant tumor metastasis

Paraneoplastic syndromes

Primary lung lesion symptoms

Cough (50-70%)

Hemoptysis (25-50%)

Dyspnea (25%)

Chest pain (20%)

Clinic obstructive pneumonitis (75% in central lung cancer)

Weight loss (46%)

Features of clinical picture of obstructive pneumonia

- Obstructive pneumonia develops within a segment or lobe of the lung. It has clearly defined anatomical boundaries.
- Obstructive pneumonia are often easily treatable, quickly are allowed.
- Obstructive pneumonia usually recurs

Symptoms of mediastinal involvement

- Superior vena cava syndrome
- Pericardial effusion
- Pleural effusion (chest pain and dyspnea)
- Dysphagia
- Hoarseness (recurrent nerve)

Hypertrophic osteoarthropathy and digital clubbing

Symptoms caused by the distant metastasis

- liver - 40% of patients
- brain - 25-40%
- bones - 15-20%
- adrenal glands - at 25-30%
- kidney - 15-20%
- lung - 12%

Diagnosis of lung cancer

Primary diagnosis (all patients)

A. Physical findings

- physical examination should be includes patient examination, lung auscultation and percussion, palpation with the determining of lymph node involvement

B. Instrumental methods

- 1. **Radiographs**
- a. ***Chest radiograph.***
- b. ***Computed tomography*** (CT). Mediastinal lymph nodes are generally considered abnormal when larger than 1.5 cm in diameter and normal when smaller than 1.0 cm; nodes between these two limits are indeterminate. CT scanning provides information
- about the extent of invasion of the primary tumor, the presence of pleural effusion, and lymph node status.
- c) ***Magnetic resonance imaging*** (MRI) rarely adds additional information.

B. Instrumental methods

2. Endoscopic methods

- a. **Flexible fiberoptic bronchoscopy**. Two thirds of all cancers can be directly visualized.

C. Obtaining pathologic proof of lung cancer.

- 1. **Sputum cytology**
- 2. **Biopsy of tumor** or transbronchial biopsy when flexible fiberoptic bronchoscopy
- 3. **Biopsy of suspicious cutaneous nodules**
- 4. **Biopsy of lymph nodes.** Enlarged, hard, peripheral lymph nodes represent another potential site for biopsy.

Subsequent diagnosis to assess the prevalence of lung cancer

1. A bone scan
2. Bone radiograph
3. Spinal MRI
4. Brain CT or MRI
5. Positron emission tomography (PET).
6. Bone marrow aspiration and biopsy.
7. Mediastinoscopy
8. Videothoracoscopy

The current standard of treatment for patients with non-small cell lung cancer

Treatment methods of patients with NSCLC

- surgical
- radiotherapy (for radical and palliative programs)
- drug (neoadjuvant, adjuvant or palliative chemotherapy)

Types of radical surgery for lung cancer

- segmentectomy
- lobectomy
- lobectomy with sleeve resection and plasty of bronchus
- bilobektomiya upper and lower (right lung)
- pneumonectomy

Radiation therapy of NSCLC

- when patients refuse by surgery
- in the presence of contraindications to surgery
- in locally advanced cancers for local control

- **Modes:**
- RT on a radical program
- RT on palliative program
- Postoperative radiation therapy (after surgery)

Chemotherapy of NSCLC

- treatment of patients with advanced process (IIIb-IV stage)
- in combination with radiation therapy for inoperable forms
- as neoadjuvant (preoperative) treatment
- for the adjuvant (post-surgery) treatment

Drugs:

Taxanes
Platinum drugs
Gemzar

General principles of patients treatment with SCLC

- Operation is possible in cases of resectable tumors (T1-2 N0 M0) with followed postoperative combination chemotherapy (4 courses)
- In cases of inoperable tumors (localized form), the combination chemotherapy (4-6 cycles) and then radiation therapy of lung tumor and mediastinum are indicated
- In cases of the presence of distant metastases the combination chemotherapy is indicated. Radiation therapy is carried in the presence of special indications (metastases in the brain and bone, in the adrenal glands)

Thank you for attention!