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Original article

A UNIQUE CASE OF ASSOCIATION BETWEEN SILICOSIS, BRONCHIAL ASTHMA AND LUNG CANCER

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ABSTRACT:

Purpose: Silicosis is a specific occupational disease characterized by progressive pulmonary fibrosis. Lung cancer is one of the leading oncological illnesses in incidence and unfavorable prognosis. Bronchial asthma is a chronic allergic inflammation of the airways characterized by reversible bronchial obstruction. These diseases are a great burden for occupational medicine and the financial resource of the healthcare systems. The aim of this article is to prove the correlation between these three important diseases affecting the lungs.

Materials/methods: Discharge summaries, results from imaging and functional lung tests, blood, biochemical, immunohistochemical, microbiological, and serological tests are used to describe the case.

Results: Silicosis represents a risk factor for the occurrence of lung cancer. The presence of a relationship between the duration and intensity of silicon dioxide exposure and the severity and poor prognosis of lung cancer is assumed. In asthma, the mechanical impact of quartz could trigger bronchial obstruction by an irritative mechanism. Endobronchially growing lung cancer could provoke an obstructive ventilatory defect. Bronchial obstruction appears to be a connecting unit in the development of these three diseases. Furthermore, bronchial asthma could additionally complicate the course of silicosis and lung cancer, worsening the prognosis even more.

Conclusions: The case gives an opportunity for strengthening the interdisciplinary collaboration between allergologists, pulmonologists, occupational physicians and oncologists, with the aim for prompter and more accurate diagnose of these diseases. The interdisciplinary approach could improve the control and postpone the complications in patients suffering from these three illnesses, thus improving the quality of their life.

Keywords: silicosis, lung cancer, bronchial asthma, occupational disease,

INTRODUCTION:

Silicosis is a dust lung disease. It is caused by inhaling dust with a high content of free silicon dioxide (quartz). Silicosis is a specific occupational disease and is the most common in practice pneumoconiosis. It is characterized by progressive and irreversible pulmonary fibrosis, which causes fatal outcomes from the developed complications of chronic respiratory failure and chronic pulmonary heart [1, 2, 3, 4]. Besides medical, silicosis is a significant social problem because it requires serious healthcare and economic resource for prevention, early diagnosing, treatment and rehabilitation of the diseased. In 2017, research of the Global Burden of Disease (GBD) identified 23 695 cases of diseased with silicosis, which represents 39% of the total of 60 055 registered patients with pneumoconiosis [5]. It is known that multiple factors participate in inflammatory and fibrotic reactions, such as interleukin-6, interleukin-1 beta, tumor necrosis factor alpha, transforming growth factor beta and insulin-like growth factor 1 [6]. Four clinical forms of the disease are described: simple chronic silicosis, acute silicosis, acute silicoproteinosis and accelerated silicosis [7]. In the initial stage, the patient could be asymptomatic or have complaints of shortness of breath, easy fatigue and chest tightness/shooting pain. Although not pathognomonic, these three symptoms shape the so-called "silicotic triad", which is characteristic of the clinical picture of the initial uncomplicated forms of silicosis. Patients also report night sweats and can also have a low-grade fever [8]. In the beginning, the results from spirometry could also not show deviations from the norm. In the more advanced stages of silicosis, the existing complaints persist and intensify, and a cough with different in quantity expectoration is added to them. The progressing pulmonary fibrosis triggers alterations in the spirometry metrics [3]. When there is an additional bron-

chial obstruction, the restrictive ventilatory defect could become a mixed defect. The symptoms could appear even after suspension of the occupational dust exposure [3, 9]. As primary criteria for setting the diagnosis and labor expert assessment of silicosis are accepted, the following two – the dust-hygiene criteria and the results from lung imaging [1, 2, 3]. The first one requires objectivization of the occupational exposure to excessive levels of quartz in the air of the working environment. The second one should fulfill the radiographic criteria for a given type of pneumoconiosis (after qualitative and quantitative reporting with the help of ILO'1980). In simple chronic silicosis, the chest x-rays show a nodular model of small round shadows, which are distributed symmetrically and are predominant in the upper zones [7]. High-resolution computed tomography (HRCT) has higher sensitivity and is more informative in the detection of lung nodular changes [10]. The currently available therapeutic options are minimal and focus solely on relieving symptoms, prevention further progression of the disease and improving the general condition, as well as reducing the risk of associated disorders [8]. The majority of interventions are maintenance and consist of additional oxygen application in patients with hypoxia, recommended vaccinations, adequate treatment of the infectious complications and pulmonary rehabilitation [11]. Pirfenidone and Nintedanib, approved by the United States Food and Drug Administration for idiopathic pulmonary fibrosis, are well documented in silicotic models [4]. It is considered that the bronchoalveolar lavage improves the control of the illness and the quality of life, especially in the early stages of the disease. Tetrandrine is the only medication approved for the treatment of silicosis in China by the regulatory authorities [9]. Some authors indicate lung transplantation as the first line therapy of silicosis in the advanced stage [11]. In the specialized medical literature, combinations of chronic silicosis with other lung and non-lung diseases are indicated the combinations with lung cancer and rheumatoid arthritis. For the first, association is assumed to be a causative relationship between quartz exposure and lung cancer. On the one hand, it is considered that quartz is among the probable carcinogens in people. On the other hand, chronic silicosis is indicated as a disease most commonly associated with lung cancer [2].

The combination between silicosis and rheumatoid arthritis is more known in the literature as Caplan's syndrome [1, 2, 3]. Other forms are also described, such as combination with scleroderma, systemic lupus erythematosus and dermatomyositis [3]. Lung cancer is one of the most common malignant diseases in the world [12]. The survival rate is one of the worst among all types of tumors, as the 5-year survival rate is 10-20% [13]. The life expectancy is strongly influenced by the stage of the disease. The 5-year survival rate varies from 92% for the earliest to 0% for the latest stages, respectively [14]. Worldwide, most lung cancer cases are attributed to smoking, but they could also be caused by exposure to risk factors from the working environment [15]. The International Agency for Research on Cancer is currently listing 19 substances which are proven to be linked to lung cancer [16]. The classification of lung cancer according to its anatomical localization divides it into central (mostly squamous cell carcinoma and small-cell carcinoma) and peripheral (mostly adenocarcinoma and large-cell carcinoma). According to the histological classification, there could be small-cell lung cancer (small-cell carcinoma) and non-small-cell lung cancer (squamous cell carcinoma, adenocarcinoma, large-cell carcinoma) [17]. Radiotherapy is an important tool used for the treatment of lung cancer. Seventy-seven percents of all patients have evidence-based indication for radiotherapy. It could be used in all stages of the disease [18].

Asthma is a heterogeneous disease characterized by chronic allergic airway inflammation. The criteria for diagnosing and controlling the illness are from the medical history, clinical, functional and laboratory. The most distinguished clinical features of asthma are the attack of expiratory dyspnea and wheezing, as well as some patients experiencing chest tightness and cough. The respiratory symptoms vary in time and in intensity, together with a variable airflow limitation throughout exhalation. The airflow limitation could persist with the disease's progress [19]. Certain diagnosis of asthma requires interpretation of patient-reported symptoms and investigation of lung function. It is essential to exclude asthma-imitating diseases, especially in elderly patients, who are more inclined to have comorbidities. The setting of asthma diagnosis requires the presence of reversible obstruction when performing spirometry [20]. Bronchial obstruction in asthma is reversible spontaneously, or after an appropriate drug treatment, but in case of unsatisfactory therapeutic control, it could progress to airway remodeling, respiratory failure and the patient's disability. An acute worsening of the illness in the form of asthmatic attacks or exacerbations could occur at every moment without warning and could be life-threatening [21]. Inhaled corticosteroids improve the disease control and reduce asthma exacerbations [22].

The aim of this article is to prove the correlation between these three important diseases affecting the lungs.

MATERIALS AND METHODS:

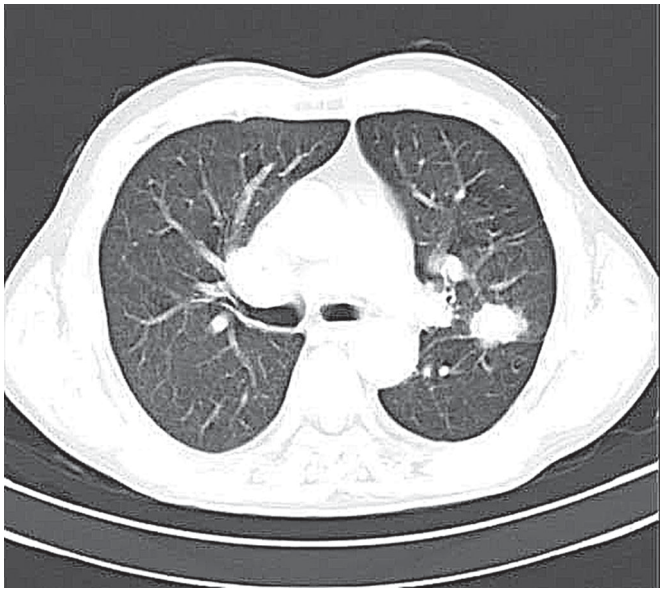
For describing the case, the available medical documentation of the patient is used, including: consultations with specialists and paraclinical investigations in outpatient care, history of the disease from hospitalization of the individual in the Department of Occupational Diseases with Clinical Allergology activity in UMHAT "Saint George" EAD-Plovdiv with applied results from the performed clinical and paraclinical investigations. In other hospitals, discharge summaries are executed with imaging and functional

lung, blood, biochemical, immunohistochemical, microbiological, and serological tests. The lung imaging is performed and deciphered in accordance with the perceived by International Classification of Radiographs of Pneumoconioses (ILO'80) qualitative and quantitative criteria for the description of radiographic findings in silicosis [3]. The patient is discussed by a specialized association with the participation of the working in the clinical structure occupational health physicians, internists, pulmonologists, allergologists, toxicologists and ENT (ear, nose and throat) specialists. The labor-medical expertise of the dust lung disease is performed on the basis of clinical, paraclinical and documentary examination of the individual in accordance with the acting regulatory framework on administering occupational diseases in the Republic of Bulgaria [23]. For describing the case, written consent is received from the patient.

DESCRIPTION OF THE CLINICAL CASE:

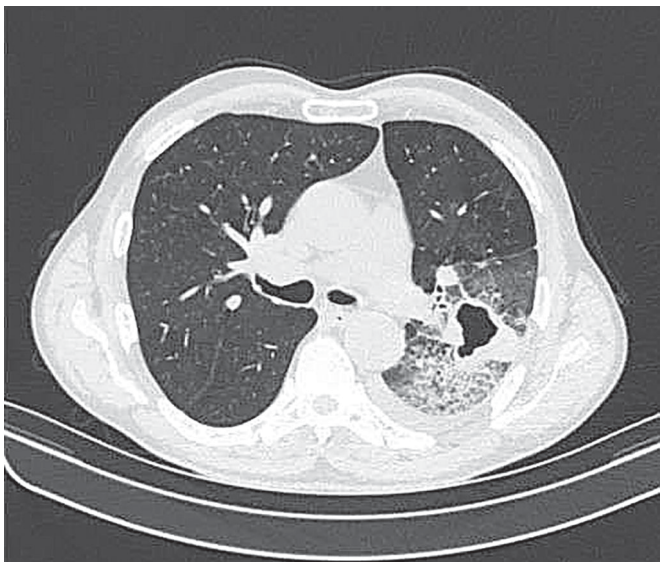
We present a 68-year-old patient, in whom in June 2020, due to complaints of hemoptysis, dyspnea, chest tightness, cough with expectoration of whitish phlegm, episodical wheezing and fatigue, a lung computed tomography is performed. À soft-tissue rounded lesion with spicule-shaped outlines in the area of the third segment of the left lung, sized 28/32/22 mm, is established. A fibrobronchoscopy is performed – without endoscopic data for the endobronchial proliferative process, the formation in the left is peripheral. The histological result is negative for tumor cells. In June 2021, a lung computed tomography is executed again – with data for a soft-tissue lesion in the area of the second segment of the left lung, which is associated with a tumor process; second nodular lesion in the left, dissemination is observed; suspected hilar lymph nodes (fig. 1.).

Fig. 1. Soft-tissue lesion in the area of the second segment of the left lung, which is associated with a tumor process; second nodular lesion in the left



In April 2022, there are computed tomography data for interstitial pneumonia in the left, bronchiectasis in the left, advancing and cavitary disintegration of solid formation in the first and second segments in the left (DD: peripheral lung cancer, aspergilloma, tuberculous cavern), reactive pleural effusion in the left (fig. 2.).

Fig. 2. Interstitial pneumonia in the left, bronchiectasis in the left, advancing and cavitary disintegration of solid formation in the first and second segments in the left lung



The patient is consulted with a phthisiatrician, and tuberculosis is rejected. In May 2022 is performed explorative left thoracotomy with biopsy. A tumor formation is established, deriving out from the upper lobe with a diameter of around 5 cm and central disintegration, growing on a vast base and spreading to the lower lobe. Morphologically, a poorly differentiated squamous cell carcinoma is diagnosed, with lung metastasis in the left perihilarly. Due to the bad results from the functional lung testing (a mixed type ventilatory disorder), it is estimated that a radical surgical intervention (pneumonectomy) could not be executed. An adjuvant chemotherapy is initiated. In January 2023 and August 2023, there are spirometry data for an obstructive ventilatory disorder. In April 2023, stereotactic radiosurgery of the lung metastatic lesion in the left perihilarly is performed.

Occupational route and medical documentation for diseases from health-risk factors of the working environment:

Total work experience of 25 years as a miner. Occupational exposure, preceding the occurrence of diseases, to dust with a high quartz content, unfavorable microclimate, vibrations, noise, dynamic and static overstrain of the limbs. The expert decision of TEMC (territorial expert medical commission) for specific and non-specific lung diseases - Plovdiv is presented, from 2008, with accepted occupational disease: Vibration disease II-III stage for upper limbs from local vibration; Silicosis I stage – mixed form, early, compensated; Respiratory failure 0.

Physical examination:

Poor general condition. Orientated, adequate. Afebrile. Dyspnea and easy fatigue in minimal physical exertion. Spastic cough with expectoration of whitish-yellowish secretions. Pronounced bilateral hypoacusis. Skin and visible mucosae – pale. Tongue – dryish, coated. Peripheral lymph nodes on available for palpation areas – not enlarged. Cardiovascular system: rhythmic heart activity, muffled heart sounds, arterial pressure – 140/90 mmHg, heart rate – 78 bpm. Abdomen: under the level of the thorax, soft, painless on palpation. Liver – on the costal arch. Spleen – not enlarged on palpation. Succussio renalis – negative (-) bilaterally. Musculoskeletal system: without stagnation edema on the lower limbs.

Actual physical lung status:

Emphysematous chest. Operative cicatrix from thoracotomy in the left chest. Hypersonorous percussion sound. Bilaterally weakened vesicular respiration with extended exhalation. Diffusely scattered dry wheezing rales in both lungs. (Tables 1, 2, 3)

Table 1. Blood and biochemical tests

Full blood count	Full blood count	Differential blood count	Biochemistry	Biochemistry
HGB – 102 g/L (140-180 g/L)	(PLT) – 214 x 10^9/l (140-400 x 10^9/l)	Sg – 61.1 % (42-70 %)	GLU – 7.2 mmol/L (2.8-6.1 mmol/L)	ALB – 37.4 g/l (35-52 g/l)
RBC–3.71/l (4.5-6 x 10^{12}/l)	WBC) – 18.25 x 10^9/l (3.5-10.5 x 10^9/l)	Eos – 15.5 % (0-6 %)	CREA– 71 µmol/L (74-134 µmol/L)	CK – 37 U/l (25-200 U/l)
HCT – 0.33 L/L (0.40-0.54 L/L)	MPV – 8 fL (7.2-11.2 fL)	Baso – 0.2% (0-2 %)	URIC ACID – 408 µmol/L (208-428 µmol/L)	CK-MB – 24.4 U/l (0-22 U/l)
MCV – 95.1 fL (82-98 fL)	THROMBOCRIT - 0.172 % (0.109-0.485 %)	Mono – 1.8 % (5.8-11.8 %)	UREA– 6.9 mmol/L (3.2-8.2 mmol/L)	GGT – 24 U/l (0-55 U/l)
MCH – 30.1 pg (27-33 pg)	ESR – 28 mm/h (2-25 mm/h)	Lymph – 8.8 % (22-48 %)	ASAT – 22.3 U/L (0-50 U/L)	ALP – 100 U/l (30-120 U/l)
MCHC–316 g/L (300-360 g/L)	PDW – 7.8 % (8-65 %)		ALAT – 10 U/L (0-50 U/L)	
(RDW) – 22.4 % (11-16%)			T.PROTEIN – 65.6 g/l (60-83 g/l)	

Table 2. Immunological and acid-alkaline tests

Immunology	Indicators of acid-alkaline balance (blood gas analysis)
Total IgE – 410 IU/ml (0-190 IU/ml)	pH – 7.345 (7.350-7.450)
Serum complement C3 – 1.195 g/l (0.811-1.570 g/l)	pCO2 – 45.4 mmHg (35.5-44.7 mmHg)
Serum complement C4 – 0.205 g/l (0.129-0.392 g/l)	pO2 – 68 mmHg (83-108 mmHg)
Serum complement C1-esterase inhibitor /quantity/ - 0.294 g/l (0.220-0.380 g/l)	ctHb – 162 g/l (140-180 g/l)
Serum complement C1-esterase inhibitor /function/ - 90 % (≥68%)	Hct – 49.6 % (40-54 %)
Conclusion from blood gas analysis: Respiratory acidosis, hypoxemia, hypercapnia, hyposaturation.	sO2 – 81 % (≥90 %)
	FO2Hb – 93.3 % (94-98 %)
	FCOHb – 1.3 % (0.5-1.5 %)
	FMetHb – 1.4 % (0-1.5 %)
	cBase(B.ox)c-ABE = -1.6
	cBase(Ecf)c-ABE = -1.7

Table 3. Skin-prick test with panel of allergens

I. GRASSES	20 min.	IV. DUST MITES	20 min.
688 (5 grasses)	10/6	314 (D. farinae)	7/6
671 (Rye)	8/6	315 (D. pteronyssinus)	/-/ neg.
II. TREES		V. ANIMAL ALLERGENS	
632 (Ash tree)	7/5	507 (Cat)	/-/ neg.
615 (Common Birch)	11/6	509 (Dog)	/-/ neg.
716 (Juniper)	5/4		
III.WEEDS		VI. CONTROLS	
604 (Ambrosia)	/-/ neg.	Positive control (Histamine)	35/12
665 (Plantain)	/-/ neg.	Negative control	/-/ neg.
Conclusion: Objectivation of sensitization to pollens from grasses (5 grasses and rye), trees (ash tree, common birch and juniper), and dust mites (D. farinae).			

Therapy:

The therapeutic scheme includes oxygen therapy, inhalation and parenteral application of systemic corticosteroids and bronchodilators in adequate to the state of the patient doses, mucolytics and expectorants.

Hospitalization outcome:

The patient is discharged without essential clinical and physical improvement.

Recommendations given to the general practitioner:

Dynamic clinical and functional lung control. Follow-up by occupational health physician and pulmonologist. Control, treatment and follow-up of the oncological disease in the Complex Oncology Center. Control and therapy of comorbidities – by the respective specialists.

Recommendations for the patient:

To conduct a therapeutic course with the prescribed medications. To comply with the determined hygienic-dietetic regimen.

RESULTS:

• The association between silicosis, bronchial asthma and lung carcinoma in the same person is extremely rare

• The specificity in the etiology, pathogenesis, clinical course and diagnosis of these diseases portend a poor prognosis, regardless of the time of onset and the combination between them

• Bronchial asthma may complicate the already existing combination between silicosis and lung carcinoma and contribute to the worsening of clinical symptoms

• The prognosis is more unfavorable with the combination of these three lung disease entities.

• Despite the availability of officially accepted national and international diagnostic and therapeutic algorithms and guidelines for all three diseases, they remain poorly studied in terms of their relationship with risk factors from the work environment

• Occupational health expertise is an important factor that can prevent the occurrence of pneumoconiosis or slow the progression of pulmonary fibrosis, thereby reducing the risk of subsequent occurrence of lung cancer and asthma

DISCUSSION:

Silicosis is a specific occupational disease, as risk productions for its occurrence are mostly ore mining and coal mining [1-3]. Epidemiological studies show that silica exposure is associated with an increased risk of esophageal, gastric, skin, and especially lung carcinoma. There is unequivocal evidence for a dose-dependent relationship between inhalation of free silica and the risk of lung carcinoma, although the relative risk from exposure to quartz is lower than that from other lung carcinogens, such as tobacco smoke or asbestos [24]. Silica exposure is one of the most important modifiable risk factors for lung carcinoma. The results of a meta-analysis suggest that the risk of developing lung cancer increases with increasing levels of exposure to silica [25]. Another analysis showed that workers in the mining industry had the highest risk of lung cancer [26]. Duration and intensity of quartz exposure determine a more severe course and poor prognosis in patients with silicosis and low-grade lung carcinoma. It is recommended that workers with cumulative exposure to silica greater than 30 years be evaluated with a computed tomography of the chest in order to increase the chances of detecting lung carcinoma as early as possible [24]. Respiratory symptoms in asthma, silicosis, and lung carcinoma largely overlap, contributing to the association between these three disease entities. Bronchial obstruction is a connecting link in the development and progression of all three diseases. Compared to lung cancer, hemoptysis can rarely occur in sili-

cosis - in complications with bronchiectasis, silicotuberculosis and thromboembolism. Regarding functional disorders, restrictive ventilatory failure predominates in silicosis, and at a later stage, after secondary obstruction, the predominant ventilatory defect is of a mixed type [1, 2, 3]. In asthma, unlike silicosis, the ventilatory defect is of an obstructive type. Although perceived as "advanced", current anti-fibrotic treatment of silicosis, including gene therapy, substances directed against growth hormone, cytokines, and antioxidants, is still unproven effective and specific [2, 3]. Most lung cancer patients exhibit symptoms such as hemoptysis, cough, shortness of breath, chest pain, and persistent infections [27]. X-ray and computed tomography are the primary diagnostic methods for detecting a tumor process in the lung. Facial pulmonography is the first test done when lung cancer is suspected [17]. When a suspicious lesion is detected, more detailed information and additional morphological immunogenetic and histochemical studies are required [28]. Lung cancer screening with computed tomography has been shown to reduce mortality in large randomized controlled trials [29]. Lung tumors can present as central or peripheral masses [28]. The clinical symptoms, the physical findings, blood eosinophilia found in the patient, increased levels of total IgE, as well as the positive skin-allergic tests from testing with a panel of indoor and outdoor allergens objectify the diagnosis of bronchial asthma. A number of researchers believe that asthma is a potential risk factor for lung cancer since chronic allergic inflammation, and especially the remodeling of the bronchial tree that occurs in the end stage of the disease, also plays a key role in its pathogenesis [30]. Asthma, lung carcinoma, and silicosis may share some common pathogenetic mechanisms involving proinflammatory mediators. A similar association can be commented on between asthma and silicosis since both diseases have common pathophysiological mechanisms related to the role of cytokines and interleukins, such as IL-1, IL-2, TNFα, γ-interferon and others. Their role as proinflammatory and anti-inflammatory mediators in the pathogenesis of asthma has been proven. In silicosis, they are related to the release of superoxide radicals and cytokines from activated macrophages, which activate T-helpers. Thus, the pathological process in silicosis, which debuted as a mechanical-toxic one, "switches" to a cell-mediated type of immune reaction with the release of IL-2 and γ-interferon from T lymphocytes. Changes in humoral immunity have also been reported, blocking the function of T-suppressor lymphocyte.

CONCLUSION:

The incompletely understood etiology and pathophysiological mechanisms of silicosis and lung cancer, the lack of specific and effective radical treatment, as well as the difficulty in therapeutically controlling bronchial asthma are all factors that are associated with a poor prognosis, especially when the three diseases are combined in the same patient. Nevertheless, the interdisciplinary approach of specialists working in one team - internists, professional pathologists, pulmonologists, allergists, oncologists, enables faster and more accurate diagnosis of diseases, discovers opportunities for prevention of some of them, can improve control and treatment in the same patient and assists in performing an adequate occupational medical examination of the patient to improve the quality of his life.

Abbreviations:

GBD - Global Burden of Disease
ILO·80 - ILO International Radiological Classification of Radiographs of Pneumoconioses, Geneva,1980
HRCT - High-resolution computed tomography
ENT - Ear, Nose and Throat
DD - Differential Diagnosis
TEMC - Territorial Expert Medical Commission
UMHAT - University multiprofile hospital for active treatment

REFERENCES:

1. Kostova V, Petkova V. [Occupational diseases]. [in Bulgarian] Second Amended and Revised Edition, Ralkolobyr, Sofia, 2007: 197,205-209,273

2. Nestorova V, Stoyneva Z, Prakova G, Dermendjiev S, Stoynovska M, Medjidieva D. Occupational diseases. First edition. Varna Medical University Press. 2020; pp.29, 31-34. [Internet]

3. Petrova E. [Guide to dust occupational lung diseases]. [in Bulgarian] First edition, Ministry of Labor and Social Policy, "Working Conditions Fund", 2004: 23, 26-27, 30, 32, 34-35.

4. Li T, Yang X, Xu H, Liu H. Early Identification, Accurate Diagnosis, and Treatment of Silicosis. *Can Respir J.* 2022 Apr 25;2022:3769134. [PubMed]

5. Hoy RF, Jeebhay MF, Cavalin C, Chen W, Cohen RA, Fireman E, et al. Current global perspectives on silicosis-Convergence of old and newly emergent hazards. *Respirology.* 2022 Jun;27(6):387-398. [PubMed]

6. Pang J, Qi X, Luo Y, Li X, Shu T, Li B, et al. Multi-omics study of silicosis reveals the potential therapeutic targets PGD2 and TXA2. *Theranostics.* 2021 Jan 1;11(5):2381-2394. [PubMed]

7. Delgado-García D, Miranda-Astorga P, Delgado-Cano A, Gómez-Salgado J, Ruiz-Frutos C. Workers with Suspected Diagnosis of Silicosis: A Case Study of Sarcoidosis Versus Siderosis. *Healthcare (Basel).* 2023 Jun 16;11(12):1782. [PubMed]

8. Li R, Kang H, Chen S. From Ba-

sic Research to Clinical Practice: Considerations for Treatment Drugs for Silicosis. *Int J Mol Sci.* 2023 May 5;24(9):8333. [PubMed]

9. Martínez-López A, Candel S, Tyrkalska SD. Animal models of silicosis: fishing for new therapeutic targets and treatments. *Eur Respir Rev.* 2023 Aug 9;32(169):230078. [PubMed]

10. Quan H, Wu W, Yang G, Wu Y, Yang W, Min C, et al. Risk Factors of Silicosis Progression: A Retrospective Cohort Study in China. *Front Med (Lausanne).* 2022 Apr 4;9:832052. [PubMed]

11. Baum L, Arnold TC. Silicosis. 2023 Aug 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. [PubMed]

12. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer.* 2013 Apr;49(6):1374-403. [PubMed]

13. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšiæ M, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet.* 2018 Mar 17;391 (10125):1023-1075. [PubMed]

14. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol.* 2016 Jan;11(1): 39-51. [PubMed]

15. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. *Eur Respir J.* 2016 Sep;48(3):889-902. [PubMed]

16. Algranti E, Buschinelli JT, De Capitani EM. Occupational lung cancer. [in English, Portuguese] *J Bras Pneumol.* 2010 Nov-Dec;36(6):784-94. [PubMed]

17. Panunzio A, Sartori P. Lung Cancer and Radiological Imaging. *Curr Radiopharm.* 2020;13(3):238-242. [PubMed]

18. Vinod SK, Hau E. Radiotherapy treatment for lung cancer: Current status and future directions. *Respirology.* 2020 Nov;25 Suppl 2:61-71. [PubMed]

19. 2023 GINA Report, Global Strategy for Asthma Management and Prevention. July 10, 2023. [Internet]

20. Wu TD, Brigham EP, McCormack MC. Asthma in the Primary Care Setting. *Med Clin North Am.* 2019 May;103(3):435-452. [PubMed]

21. Lommatzsch M, Buhl R, Korn S. The Treatment of Mild and Moderate Asthma in Adults. *Dtsch Arztebl Int.* 2020 Jun 19;117(25):434-444. [PubMed]

22. Castillo JR, Peters SP, Busse WW. Asthma Exacerbations: Pathogenesis, Prevention, and Treatment. *J Allergy Clin Immunol Pract.* 2017 Jul-Aug;5(4):918-927. [PubMed]

23. [Normative regulations on the administration of occupational diseases in the Republic of Bulgaria]. [in Bulgarian] Ministry of Labor and Social Policy, Working Conditions Fund, Publishing house"Labor and Law", Sofia, 2008: 2-67

24. Sato T, Shimosato T, Klinman DM. Silicosis and lung cancer: current perspectives. *Lung Cancer (Auckl).* 2018 Oct 26;9:91-101. [PubMed]

25. Shahbazi F, Morsali M, Poorolajal J. The effect of silica exposure on the risk of lung cancer: A dose-response meta-analysis. *Cancer Epidemiol.* 2021 Dec;75:102024. [PubMed]

26. Poinen-Rughooputh S, Rughooputh MS, Guo Y, Rong Y, Chen W. Occupational exposure to silica dust and risk of lung cancer: an updated meta-analysis of epidemiological studies. *BMC Public Health.* 2016 Nov 4; 16(1):1137. [PubMed]

27. Gershman E, Guthrie R, Swiatek K, Shojaee S. Management of hemoptysis in patients with lung cancer. *Ann Transl Med.* 2019 Aug;7(15): 358. [PubMed]

28. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. *J Thorac Oncol.* 2015 Sep;10(9):1243-1260. [PubMed]

29. Revel MP, Abdoul H, Chassagnon G, Canniff E, Durand-Zaleski I, Wislez M. Lung CAncer SCreening in French women using low-dose CT and Artificial intelligence for DEtection: the CASCADE study protocol. *BMJ Open.* 2022 Dec 8;12(12):e067263. [PubMed]

30. Schabath MB, Cote ML. Cancer Progress and Priorities: Lung Cancer. *Cancer Epidemiol Biomarkers Prev.* 2019 Oct;28(10):1563-1579. [PubMed]

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