Original Article

©2022 NRITLD, National Research Institute of Tuberculosis and Lung Disease, Iran ISSN: 1735-0344 Tanaffos 2022; 21(4): 496-502

Frequency of Pulmonary Anthracosis and its Related Factors in Autopsy Specimens in Guilan, Iran, in 2019

Mirsaeed Attarchi ¹, Soheil Soltanipour ², Ali Alavi Foumani ³, Morteza Rahbar-Taramsari ¹, Mehdi Ghorbani Samin ⁴, Mandana Dolati ⁴, Mohamadreza Samie ⁵, Seyed Mohammad Seyedmehdi ⁶

¹ Inflammatory Lung Diseases Research Center, Department of Forensic Medicine, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran, ² GI Cancer Screening and Prevention Research Center, Department of Community Medicine, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran, ³ Inflammatory Lung Diseases Research Center, Department of Internal Medicine, School of Medicine, Razi Hospital, Guilan University of Medical Sciences, Rasht, Iran, ⁴ Guilan Legal Medicine Organization, Rasht, Iran, ⁵ Inflammatory Lung Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran, ⁶ Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences. Tehran. Iran.

Received: 15 December 2021 Accepted: 11 July 2022

Correspondence to: Soltanipour S Address: GI Cancer Screening and Prevention Research Center, Department of Community Medicine, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran Email address: ssoltanipour@yahoo.com **Background:** Anthracosis is caused by several factors and is a risk factor for cancer and tuberculosis. This study investigated the prevalence of anthracosis and the associated factors in autopsy specimens from the Guilan Office of the Iranian Legal Medicine Organization.

TANAFFOS

Materials and Methods: This retrospective study examined the medical records of autopsy specimens (>18 years) in the Guilan Office of the Iranian Legal Medicine Organization in 2019 for pulmonary anthracosis. Data were extracted from the autopsy findings, and demographic characteristics, occupational information, tuberculosis or pulmonary cancer history, and anthracosis were recorded in a checklist. SPSS version 16 was used to analyze the collected data.

Results: The study included 190 autopsy specimens with a 32.1% anthracosis prevalence. Forty-five (23.7%) subjects had anthracofibrosis. Individuals with agricultural carriers or who worked in tobacco fields had the highest prevalence of anthracosis. The frequency of pulmonary cancer and tuberculosis was significantly higher in the specimens with anthracosis (anthracosis group) than in the non-anthracosis group (P<0.05). The use of traditional cooking and heating methods, as well as exposure to carbon and smoke in the workplace, were significantly higher in the anthracosis group than in the non-anthracosis group (P<0.05).

Conclusion: The results of the current study revealed that occupational exposure, tuberculosis, pulmonary cancer, and traditional indoor cooking and heating methods were all associated with anthracosis.

Keywords: Environmental pollutants; Lung diseases; Occupational exposure; Anthracosis

INTRODUCTION

"Anthracosis" refers to coal dust particles and other black pigments derived primarily from carbon (1). Anthracosis can be seen in autopsy specimens as linear (streaky) shadows and an accumulation of anthracotic pigments (2). The estimation of anthracosis prevalence in the general population is relative because a precise diagnosis requires bronchoscopy, which cannot be used for the general population due to ethical considerations. In Iran, the prevalence of anthracosis in the bronchoscopy group has been reported as 3.4%-21% (2). As diagnosed from bronchoscopy, the frequency of anthracosis was lower in Western countries than in other nations. For example, Wynn et al. reported a prevalence of seven per 7,000 bronchoscopy cases (3). Emamhadi et al. (4) examined autopsy specimens from 385 people aged 20 and older who died during 2007-2010, and anthracofibrosis was found in 48 (12.5%) cases.

A range of simple anthracosis in mucus to anthracosis with/without TB has been observed. Anthracosis reduces ciliary mucosa clearance by damaging the bronchial mucosa, which can lead to infections, such as pulmonary TB (5). Many cases of anthracotic pigmentation in bronchoscopy have been diagnosed with TB in examinations (6). A systematic review showed that TB frequency significantly increased in patients with anthracosis under bronchoscopy (7). Anthracosis can be caused by occupational exposure to carbon, silica, and quartz particles (1). Previous studies found a high prevalence of anthracosis among coal miners, while recent studies found it to be common in farmers (40%) (7) and rural populations (55%-65%) (8). Coal deposits can be observed as black plaques in the bronchi of people who work in coal mines or live in urban areas. However, the latter finding is less common (1). In addition to the coal miners, anthracosis is noted in people working in the relevant industries (1).

Inhaling smoke particles can occur as a result of urban air pollution or, more importantly, direct exposure at work (9). Traditional indoor cooking methods using fuels, such as organic fertilizer, wood, and charcoal and their residues, produce dense smoke and massive carbon deposits on the walls and ceiling (10). Moreover, tobacco use is a contributing factor to this disorder. Anthracosis is likely to cause bronchitis cancer. A cross-sectional study investigated patients admitted for bronchoscopy in North Khorasan, Iran, during 2009-2012, demonstrating that anthracosis was diagnosed in 89 of 279 patients (34 men and 55 women) (11).

Most previous studies investigated the frequency and reasons for anthracosis in the bronchoscopy samples, and few investigations assessed the frequency of anthracosis in autopsy specimens. Therefore, the present study evaluated anthracosis frequency in autopsy specimens and determined the associated factors in Guilan province, Iran, in order to take preventative measures in the province population.

MATERIALS AND METHODS

This analytical cross-sectional study assessed the medical records of autopsy specimens (>18 years) in 2019 for the presence of pulmonary anthracosis after obtaining approval from the Guilan Office of the Iranian Legal Medicine Organization. All the provisions of the Helsinki Declaration were followed in this study, and the protocols were approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1398.524).

The samples were selected through the systematic random method using the Guilan Office of Iranian Legal Medicine Organization's list of autopsy records in 2019. Different variables, including age, gender, place of residence, marital status, smoking status, drug addiction, occupational status, type of occupation, history of tuberculosis, lung cancer, and lung autopsy findings (e.g., anthracosis and fibrosis) were collected using a checklist designed specifically for this study. The families of subjects were also contacted by phone to obtain the information missing in their records. If necessary, pathology samples prepared from the autopsy were reviewed by a pathologist. The study excluded records that lacked the necessary data. In this study, 256 records were investigated, and 66 were excluded due to the lack of autopsy reports or other necessary variables or not receiving a response to phone contact.

In this study, TB and pulmonary cancer diagnoses were based on the pathologic reports in their records. Solid fuels, such as organic fertilizer, wood, coal, and their byproducts, are consumed in traditional cooking and heating methods. In addition, jobs that expose workers to carbon or smoke are considered hazardous occupations. Anthracosis was defined as the presence of black pigments similar to carbon in the macrophages of the lung parenchyma or a free black particle in the lymph nodes of the lung or pleura (12). According to Hoseinnia et al. (13), the minimum sample size is calculated by the following formula considering the frequency (P=0.046), the error rate of 5% (z=1.96), and the difference of 3% (d=0.03).

n =
$$\frac{Z^2 P(1 - P)}{d^2} = \frac{(1.96)^2 \times 0.046 \times 0.954}{(0.03)^2} = 188$$

The SPSS software version 16 was used to analyze the collected data. Data distribution was examined utilizing the Kolmogorov-Smirnov test. The Mann-Whitney and Chi-square tests were used to compare the study groups with and without anthracosis. The significance level was considered P \leq 0.05.

RESULTS

In the present study, out of 190 research subjects, 149 (78.4%) were male, and 41 (21.6%) were female. The age of participants ranged from 18 to 96 years, with a mean age of 48.58 (18.7) years. According to the data, 137 (72.1%) and 53 (27.9%) subjects were married and single, respectively. Moreover, 85 (44.7%) and 39 (20.5%) cases were tobacco users and drug addicts, respectively. We found that 13 (6.8%) subjects had lung cancer, and 19 (10%) had TB. It was noted that 34 (17.9%) and 33 (17.4%) individuals had a history of using traditional methods for cooking and heating, respectively, and 61 (32.1%) people had anthracosis. The results of pulmonary histopathology showed that 45 subjects (23.7%) had pulmonary fibrosis, 52 (27.4%) had alveolar macrophages, and 25 (13.25) had pleural thickening.

Table 1 compares the two groups in terms of gender, tobacco smoke status, and history of addiction using the Chi-square test. According to Table 1, there was no significant between-group difference in these factors (P>0.05). However, the marriage rate was significantly higher in the group with anthracosis than without anthracosis (P<0.05). The Kolmogorov-Smirnov test revealed that age distribution in the anthracosis group was not normal. According to the Mann-Whitney test (Table 1), the median age was significantly higher in the anthracosis group than in the non-anthracosis group (P<0.001). Furthermore, the Chi-square test (Table 2) showed that the frequency of lung cancer and TB was significantly higher in the anthracosis group (P<0.05).

The Chi-square test (Table 2) indicated that the frequency of pulmonary fibrosis, alveolar macrophages, and pleural thickening was significantly higher among the anthracosis group than the non-anthracosis group (P<0.001). moreover, the results of the chi-square test (Table 3) showed that the frequency of using traditional methods for cooking and heating and occupational exposure to smoke and carbon (hazardous jobs) was significantly higher in the anthracosis group than in the non-anthracosis group (P<0.05). Table 4 presents the prevalence of pulmonary anthracosis was observed among those working in the agricultural sectors and tobacco fields.

 Table 1. Comparison of demographic data in two groups of with and without lung anthracosis

| Variables | | With anthracosis Number (%) | Without anthracosis Number (%) | OR | 95% CI | P-Value |
|----------------------|------------------|--------------------------------|-----------------------------------|------|------------|---------|
| Sex | Male | 50 (81.97) | 99 (76.74) | 0.70 | 0.33-1.56 | 0.414 |
| | Female | 11 (18.03) | 30 (23.26) | 0.72 | | |
| Age (year) | Median (min-max) | 59 (32-96) | 40 (18-83) | - | - | <0.001 |
| Marital status | Married | 58(95.08) | 79 (61.24) | 10.0 | 3.63-41.17 | 0.001 |
| | Single | 3 (4.92) | 50 (38.76) | 12.2 | | |
| Tobacco use | | 22 (36.10) | 63 (48.89) | 1.59 | 0.31-1.10 | 0.098 |
| History of addiction | | 14 (22.95) | 25 (19.37) | 1.23 | 0.59-2.59 | 0.569 |

Table 2. Investigating clinical and pathologic factors in two groups with and without lung anthracosis

| Variables | | With anthracosis Number (%) | Without anthracosis Number (%) | OR | 95% CI | P-Value |
|--------------|---------------------|--------------------------------|-----------------------------------|------|-------------|---------|
| Tuberculosis | | 12 (19.67) | 7 (5.42) | 4.26 | 1.58-11.47 | 0.002 |
| Lung cancer | | 10 (16.39) | 3 (2.32) | 8.23 | 2.17-31-15 | 0.001 |
| Fibrosis | Pathologic Finding | 32(52.45) | 13 (10.07) | 9.84 | 4.59-21.10 | 0.001 |
| | Alveolar macrophage | 34 (55.73) | 13 (18.95) | 7.76 | 3.82- 15.78 | 0.001 |
| | Pleural thickening | 17 (27.86) | 8 (6.20) | 5.84 | 2.35- 14.49 | 0.001 |

Table 3. Comparison of occupational and environmental factors in two groups with and without lung anthracosis

| Variables | | With anthracosis | Without anthracosis | | 05% 01 | D Value | |
|-------------------------------|-----|------------------|---------------------|------------------|--------------|---------|--|
| | | Number (%) | Number (%) | UK | 95%01 | P-value | |
| lla-andarra iak | Yes | 37 (60.66) | 7 (5.43) | 00.00 | 10.72- 67.34 | 0.001 | |
| Hazardous job | No | 24 (39.34) | 122 (94.57) | 20.80 | | | |
| Tue different en alvie e | Yes | 24 (39.34) | 10 (7.75) | 7 74 | 0.00 47.04 | 0.004 | |
| i raditional cooking | No | 37 (60.66) | 119 (92.25) | 1.11 | 3.38- 17.01 | 0.001 | |
| Tue dition of indexed booting | Yes | 25 (40.98) | 8 (6.20) | 10.50 4.36-25.29 | | 0.001 | |
| i raditional indoor heating | No | 36 (59.02) | 121 (93.80) | | | | |

Table 4. Frequency of pulmonary anthracosis in autopsy specimens based on occupation (n=61)

| Anthracosis - | Job | | | | | | | |
|---------------|--------|----------------------|--------|----------|-------------|-----------|-------|--------|
| | Farmer | Tobacco field worker | Welder | Mechanic | Smoked rice | Tar paper | Guard | Other* |
| Number | 16 | 9 | 8 | 7 | 4 | 3 | 3 | 11 |
| Percent | 26.2 | 14.9 | 13.1 | 11.5 | 6.5 | 4.9 | 4.9 | 18.0 |

*: unemployed - Tea field worker - Freelancer - Tailor - Grocer - Olive seller - Gardener

DISCUSSION

Pulmonary anthracosis occurs following the deposition of carbon, silica, quartz particles, and similar compounds in the mucosa, sub-mucosa, or macrophages of the lungs (1). Anthracosis is characterized by the black discoloration of the tracheobronchial tree caused by deposits of carbon, silica, and other inhaled pollutants. If anthracosis causes bronchial obstruction or obliteration, it is called bronchial anthracofibrosis (14). Anthracofibrosis was found in 23.7% of the participants in the current study. We found a higher frequency of anthracosis than in previous studies because we examined autopsy specimens, whereas previous investigations assessed bronchoscopy results. Two studies in Iran found a prevalence of pulmonary anthracosis ranging from 8.5% to 10.2% (15, 16).

In our study, anthracosis was found to be associated with occupational exposure, TB and lung cancer, and the use of wood and coal for cooking and heating. A study conducted in North Khorasan, Iran, investigated the relationship between anthracosis and comorbidities. The latter cross-sectional study evaluated patients referred to Valiasr Hospital in North Khorasan for bronchoscopy during 2009-2012. In total, 279 patients undergoing bronchoscopy were examined. Eighty-nine patients, comprising 34 men (38.2%) and 55 women (61.79%), were diagnosed with anthracosis. Simple and complicated anthracosis were observed in 42 (48.2%) and 47 (52.8%) patients, respectively. Data showed that 43 subjects (48.3%) had TB, including 28 from the complicated group and 15 from the simple group (P=0.021). This study recommended the precise examination of patients with anthracosis for TB (11).

Emamhadi et al. (4) reported a prevalence of 12.5% for anthracofibrosis among the autopsy specimens. In this study, 385 subjects aged 20 years and above who died during 2007-2010 were included. It was found that 48 specimens had anthracofibrosis. There was no significant between-group difference in mean age, tobacco use, ethnicity, and job. However, the prevalence of anthracofibrosis was significantly higher in women than in men (60.4% vs. 39.6%; P=0.01). There was a significant difference in the prevalence of pulmonary TB between cases with bronchial anthracofibrosis and cases without anthracofibrosis (50% vs. 34.42%; P=0.002). Anthracosis and occupational carbon exposure were found to have a significant relationship (P=0.001).

Occupational exposure to carbon, silica, and quartz particles can cause anthracosis (1). In Iran, industrialization and air pollution have resulted in more deposition of carbon particles in the lungs, resulting in a higher prevalence of anthracosis. In a study, bronchoscopic findings indicated a prevalence of anthracosis among coal miners in different parts of Iran (17). In the present study, there was no significant relationship between anthracosis and tobacco use (P=0.098). Tobacco use and smoking are reported as risk factors for anthracosis in Asian countries, such as Korea, India, Iran, and Turkey (18-19). A study reported a significant relationship between the duration of smoke exposure and anthracosis (OR: 1.05; 95%CI: 1.01-1.09) (20). According to some researchers, tobacco use is not a risk factor for anthracosis because the movement of bronchial ciliates increases in tobacco users (21). Carbon deposition in tobacco smokers declines with augmented mucus and sputum excretion. A higher rate of mucociliary clearance following smoking can reduce the risk of anthracosis (22).

We observed a significant relationship between anthracosis and traditional fuels for cooking and heating (P=0.001). In Iran, particularly in Guilan, coal for cooking causes carbon deposition in the lungs. In an Iranian study, bronchoscopic findings revealed anthracosis in women who had no occupational exposure except for baking bread in traditional ways (16). Indoor exposure to wood smoke from traditional bread cooking ovens increases the risk of anthracosis by 4.3-4.8 times, particularly in women (23, 24). In the present study, anthracosis was significantly related to TB (P=0.002). In the previous investigations, many cases with anthracotic pigmentation (27%-30%), diagnosed by bronchoscopy, were confirmed to have TB (14, 15). It is worth noting that there is some contradictory research on the relationship of TB with anthracosis and anthracofibrosis (25, 26). A meta-analysis showed that the risk of TB is elevated in cases with anthracosis (OR: 3.16, 95% CI: 2.49-6.85) (7). TB causes more deposition and stability of carbon particles in the lungs by impairing mucociliary clearance (12).

A significant relationship was observed between anthracosis and cancer in the present study (P=0.001). Previous studies showed an insignificant relationship between malignant lung lesions and anthracosis (27), the reasons for which are unknown. A study reported the association of anthracosis with lung cancer (12). It has also been suggested in the literature that anthracosis can initiate an inflammatory-fibrotic process in the lungs and contribute to lung cancer (28, 29). In the present study, lung fibrosis, alveolar macrophage, and pleural thickening frequency were higher in the anthracosis group than in the non-anthracosis group (P<0.001).

One of the limitations of our study was its crosssectional design, which made concluding a causal relationship with certainty difficult. Moreover, bias in the data collection of retrospective studies is known. To investigate the causes of anthracosis, a prospective study with a larger sample size is recommended.

In the present study, the frequency of anthracofibrosis was 23.7%. According to the findings of the current research, the risk factors of anthracosis were occupational exposure, TB, lung cancer, traditional cooking methods, and using wood and coal for heating the house. It seems that improving the knowledge of individuals with occupational exposure to carbon and smoke (e.g., people working in the tobacco fields) and providing appropriate ventilation in processes where carbon particles are produced, such as smoked rice and tobacco, can effectively prevent this anthracosis. Furthermore, it is recommended to avoid traditional cooking and heating methods that emit carbon particles and smoke indoors.

Acknowledgments

The authors of the present study would like to thank the Guilan Office of the Iranian Legal Medicine Organization for assisting with this research.

REFERENCES

- Searl A, Nicholl A, Baxter PJ. Assessment of the exposure of islanders to ash from the Soufriere Hills volcano, Montserrat, British West Indies. *Occup Environ Med* 2002;59(8):523-31.
- Sigari N, Mohammadi S. Anthracosis and anthracofibrosis. Saudi Med J 2009;30(8):1063-6.
- Wynn GJ, Turkington PM, O'Driscoll BR. Anthracofibrosis, bronchial stenosis with overlying anthracotic mucosa: possibly a new occupational lung disorder: a series of seven cases From one UK hospital. *Chest* 2008;134(5):1069-73.
- Emamhadi M, Mostafazadeh B, Masjedi MR, Bahadori M, Shafiee G. Relationship between Bronchial Anthracofibrosis and Pulmonary Tuberculosis: Autopsy Findings. *IJOH* 2013;5(1):35-8.
- Castranova V, Porter D, Millecchia L, Ma JY, Hubbs AF, Teass A. Effect of inhaled crystalline silica in a rat model: time course of pulmonary reactions. *Mol Cell Biochem* 2002;234-235(1-2):177-84.
- Samareh Fekri M, Shafahee A, Yazdani R, Hashemi Bajgani M, Naghavi M, Sheykhshoaee Ekhtiarabadi M. A Study on Relationship Between Anthracosis and Pulmonary Tuberculosis. J Adv Med Biomed Res 2020; 28 (126) :11-16.
- Mirsadraee M, Saffari A, Sarafraz Yazdi M, Meshkat M. Frequency of tuberculosis in anthracosis of the lung: a systematic review. *Arch Iran Med* 2013;16(11):661-4.
- Kim YJ, Jung CY, Shin HW, Lee BK. Biomass smoke induced bronchial anthracofibrosis: presenting features and clinical course. *Respir Med* 2009;103(5):757-65.
- Amoli K. Bronchopulmonary disease in Iranian housewives chronically exposed to indoor smoke. *Eur Respir J* 1998;11(3):659-63.

- Martin WJ 2nd, Glass RI, Balbus JM, Collins FS. Public health. A major environmental cause of death. *Science* 2011;334(6053):180-1.
- Mortazavi-Moghaddam SG, Saadatjoo SA. Bronchial anthracotic change in South khorasan province (iran), emphasizing its association with tuberculosis. *Iran J Med Sci* 2014;39(5):418-23.
- Mirsadraee M. Anthracosis of the lungs: etiology, clinical manifestations and diagnosis: a review. *Tanaffos* 2014;13(4):1-13.
- Hosieninia S, Mohammadi-Kebar S, Ghadam-Kheir K. Study the frequency of bronchial anthracosis and its influencing factors in patients undergoing bronchoscopy in Ardabil city hospital, 2013-2015. *Int J Community Med Public Health* 2020;7(10):3843-6.
- Yoon RG, Kim MY, Shim TS, Jang SJ. Anthracofibrosis involving lung parenchyma: CT findings and long-term follow-up. *J Comput Assist Tomogr* 2012;36(6):636-40.
- Tohidi M, Kashmiri M, Attaran D, Ghiasi Moghaddam T, Azarian A. Evaluation of antracofibrosis of the lung and tuberculosis in patients admitted to Ghaem Hospital in Mashhad in 1998-99. *Journal of Mashhad School of Medical Sciences* 2002: 45 (76): 73-6 (Persian).
- Aslani J, Ghanei M, Khosravee L. Relation of bronchial anthracosis with Mycobacterium tuberculosis. *Medical Journal of Tehran University of Medical Science* 2002; 60:460.
- Pazoki M, Moazami Goodarzi H, Hashemi Taheri A, Seifirad S, Nematollahi N, Paknejad O. Prevalence of tuberculosis in patients with anthracosis: study on 150 subjects. *Arch Iran Med* 2012;15(3):128-30.
- Gupta A, Shah A. Bronchial anthracofibrosis: an emerging pulmonary disease due to biomass fuel exposure. *Int J Tuberc Lung Dis* 2011;15(5):602-12.
- Torun T, Gungor G, Ozmen I, Maden E, Bolukbasi Y, Tahaoglu K. Bronchial anthracostenosis in patients exposed to biomass smoke. *Turkish Respir J* 2007;8(2):48-51.
- 20. Qorbani M, Yunesian M. Population attributable fraction of bronchial anthracosis due to smoke exposure while baking

home-made bread in ground oven. *Iranian Journal of Epidemiology* 2012;8(1):31-6.

- Heidarnazhad H. Anthracosis in Iran, un-answered questions. *Arch Iran Med* 2012;15(3):124-7.
- Kala J, Sahay S, Shah A. Bronchial anthracofibrosis and tuberculosis presenting as a middle lobe syndrome. *Prim Care Respir J* 2008;17(1):51-5.
- Qorbani M, Yunesian M, Baradaran HR. Indoor smoke exposure and risk of anthracosis. *Iran J Med Sci* 2014;39(6):571-6.
- Mirsadraee M, Asna-Ashari A, Attaran D, Naghibi S, Mirsadraee S. Bronchial anthracosis: a new diagnosis for benign mass lesions of the lung. *Tanaffos* 2013;12(4): 8-10.
- Long R, Wong E, Barrie J. Bronchial anthracofibrosis and tuberculosis: CT features before and after treatment. *AJR Am J Roentgenol* 2005;184(3 Suppl):S33-6.

- Mirsadraee M, Saeedi P. Anthracosis of lung: evaluation of potential underlying causes. J Bronchology Interv Pulmonol 2005;12(2):84-7.
- Wang D, Minami Y, Shu Y, Konno S, Iijima T, Morishita Y, Noguchi M. The implication of background anthracosis in the development and progression of pulmonary adenocarcinoma. *Cancer Sci* 2003;94(8):707-11.
- Hayes D Jr, Diaz-Guzman E, Davenport DL, Zwischenberger JB, Khosravi M, Absher KJ, et al. Lung transplantation in patients with coal workers' pneumoconiosis. *Clin Transplant* 2012;26(4):629-34.
- Huang C, Li J, Zhang Q, Huang X. Role of bioavailable iron in coal dust-induced activation of activator protein-1 and nuclear factor of activated T cells: difference between Pennsylvania and Utah coal dusts. *Am J Respir Cell Mol Biol* 2002;27(5): 568-74.