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## **Metsovo Lung: History of Population Environmental Exposure to Asbestos**

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### **Abstract**

**Objectives:** Our aim is to review all the literature concerning Metsovo Lung as an emblematic story that demonstrates the strong relationship between non-occupational but environmental and ecological exposure to asbestos and lung diseases. **Materials and Methods:** We searched data from the 1970s when extensive pleural calcifications causing malignant mesothelioma appeared at a high incidence beyond expectation. The most reliable studies

were selected for our research from 2017-2023. **Results:** There wasn't occupational exposure in Epirus. This finding reasonably raised the question of whether it was indeed tuberculous pleurisy or something else. The biopsies carried out confirmed that these were tremolite asbestos fibers. These fibers were derived from 'luto', a water-shielding material containing asbestos. The entire population of Metsovo was exposed to asbestos, without knowing it. This is a global phenomenon, according to which, it is made from a traditional shielding material. The abandonment of 'luto' and its non-use brought about a gradual reduction of the phenomenon, which also marks the reduction of mesothelioma. **Conclusion:** Lessons learned from the history of Metsovo lung showed the importance of the combination of theory and practice in the context of nonoccupational exposure to asbestos. From a public health point of view, it's crucial to know whether exposure to low levels of asbestos is able to induce pleural mesothelioma.

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**Keywords:** Metsovo lung, mesothelioma, asbestos, tremolite

## Introduction

This paper aims to investigate "Metsovo lung" and its impact on the Metsovo population's health. The evolutionary course of the "Metsovo Lung" phenomenon began to be investigated in the 1980s when extensive pleural detritus appeared causing malignant mesothelioma at a high frequency beyond expectation (Navratil M, 1972; Theodoracopoulos P, 1988; Sichletides L, 1989; Constantopoulos SH, 1991; Papiris SA, 1993).

The biopsies carried out confirmed that these were tremolite asbestos fibres. These fibres came from a shielding material containing asbestos. This is a global phenomenon whereby the entire population of Metsovo was exposed to asbestos, without knowing it, from a traditional shielding material. The abandonment of the material and its non-use brought about the gradual reduction of the phenomenon, which also marks the reduction of mesothelioma disease (Bazas T, et al 1981; Constantopoulos SH, Goudevenos JA, 1985; Constantopoulos SH, et al. 1987; Baris YI, et al 1988; Gogali A, et al 2012; Constantopoulos SH 2014; Bouros D 2014; Gogali A, et al 2017).

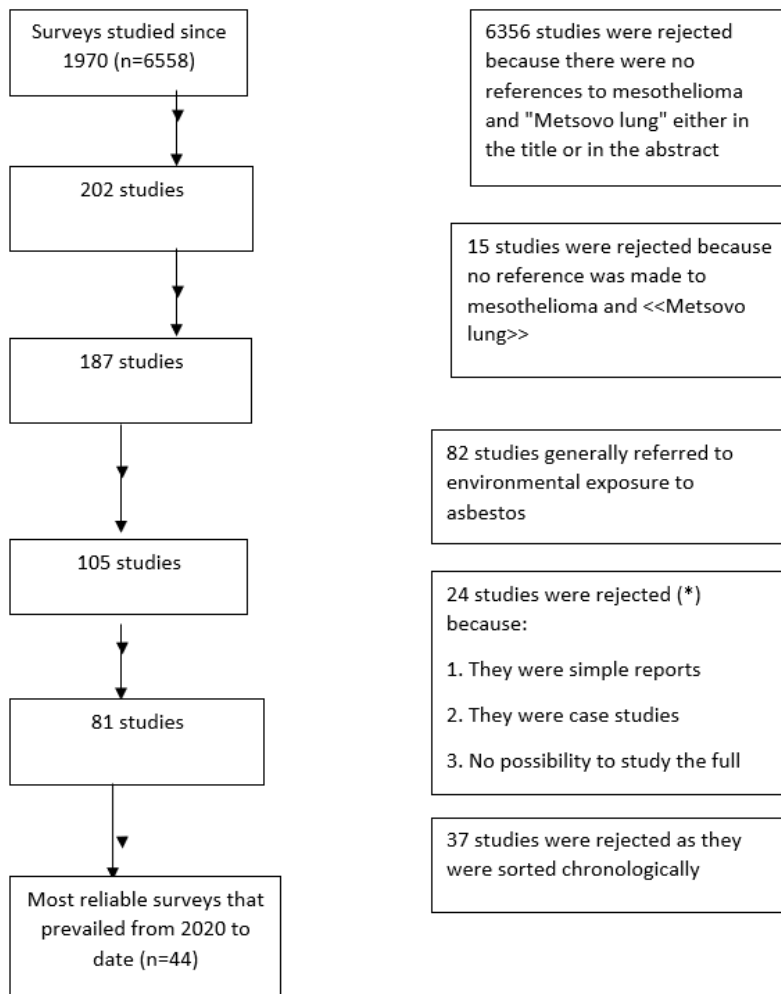
## Methodology

The method used to study "Metsovo lung" was a literature review. Traditional literature reviews often are conducted ad hoc, rather than following a specific methodology. It can be used to create research agendas, identify gaps in research, or simply discuss a particular matter. Therefore, we have the idea to scan the area as a first step to assess the number of research studies. We collected data from all previous studies. The above flowchart describes in enough detail how the literature review was conducted, which

makes it impossible to evaluate both the quality of the review and its contribution to the overall research strategy, the selection and exclusion of articles, and the limitations of the search method.

We searched articles about <<Metsovo Lung>> in various medical literature databases (Scopus, Pubmed, Google Scholar). We used keywords like “Metsovo lung”, “mesothelioma”, “asbestos”, “tremolite” and found articles since 1970. 6356 studies were rejected because there were no references to mesothelioma and Metsovo lung either in the title or in the abstract. Were studied articles on the <<Metsovo Lung>> from 1987 to the present day. In some of them, there were only simple references to the subject of our interest. The remaining were selected for our research as the most reliable (from 2017-2023) [see flowchat].

#### Flowchart of literature research



(\*) relevant simple reports and case studies were rejected because it was not possible to conclude any conclusion in a literature review

## **Chronological History of “Metsovo Lung Disease”**

After the 1970s in a mountainous area of northwestern Greece [Epirus], an increase in pleural calcifications [PCs] was observed in the inhabitants of Metsovo and neighboring villages, Milia, Anilio, and Votonossi, with a total current population of 4,417 inhabitants while in the 1980s the increase was 5% per year (Theodorakopoulos P, 1988; Gogali A, et al 2012).

Besides, after examinations carried out on 688 residents it was confirmed that 46,9 % (i.e. 323 residents) had PCs. For a long time, tuberculosis was thought to be the cause (since 1960), and there was no evidence of occupational exposure to asbestos (Constantopoulos SH, Goudevenos JA, et al 1985).

It was observed that the main source was the domestic use of a traditional mineral material [luto] on a large scale for house whitewashing until 1940-1950 and it was verified that the rate of positive tests was proportional to age. Epidemiological, clinical, and radiological evaluation of inhabitants of the Metsovo area reveals that 47% (329/702) have pleural calcifications. In individuals >70 years the percentage grows to 72%. Also, it was found that the incidence of malignant pleural mesothelioma was very high (313,5 times the predictable). It appears that in this area inhabitants inhaling since childhood a material (luto) used extensively for whitewashing. Transbronchial biopsies showed tremolite fibers in large amounts. The same fibers were found in whitewashed (luto). This indicates that whole Metsovo population over 50 years has been exposed to luto-asbestos (Saratzis N, 1988; Manos E, et al 2019).

The mineral soil contained tremolite fibers which were found to be responsible for the progression of the disease. What was worrying was that exposure to the material started at an early age mainly during the crash and the preparation for whitewashing the walls. In studies carried out it was found that where traditional soil was used for whitewashing, tremolite had caused PCs in all inhabitants of Metsovo before 1940, whereas, where the soil was not used, no PCs were observed (Constantopoulos SH et al, 1987; Constantopoulos SH et al, 1992).

Another study showed that between 1981 and 1985 some patients from the Metsovo area developed malignant pleural mesothelioma. The twist in the investigation occurred when a team led by *Stavros Constantopoulos* sent two x-rays of Metsovites to M. Sinai Hospital in New York for examination and analysis of their findings Tremolite samples were tested in laboratories, their toxicity was measured and it was confirmed that tremolite fibres are responsible for the formation of tumors and the induction of chromosomal mutations. *Selikoff* analyzed the imaged findings and suspected that the mesotheliomas that were imaged had asbestos fibers as their main source of

formation (Constantopoulos SH, ..., Selikoff IJ et al, 1985; Galani V, et al 2002).

After lung biopsies and their analysis at M. Sinai Hospital, asbestos fibers were found. In particular, 1-2 mesotheliomas per year were found in 5,000 inhabitants, while in the entire Greece of 10-11 million, there were 10 mesotheliomas per year (Langer AM, et al 1987; Gogou E, 2019).

Important studies have shown that Mesotheliomas with pleural malignant mesothelioma had no pleural calcifications. Additional proteins in bronchoalveolar lavage fluid [BAL] and lymphocytic alveolitis distinguished two groups with different reactions to asbestos (Constantopoulos SH, 1992; Galani V, et al 2002).

## Results

During the investigation, there were strong concerns and questions such as: Is it possible for asbestos to be found in Metsovo, i.e. in a mountain area [Epirus] where there is no environmental pollution and no occupational exposure to asbestos? However, it was found that inhabitants of Metsovo were using the asbestos soil - 'luto' - to whitewash their houses. The use of this material was universal until 1940-1950, and it was gradually replaced by other materials in the early 1980s and later abandoned altogether.

Usually, the procedure followed was as follows: The material was collected from peripheral hills, compacted by women of Metsovo into balls, and then pulverized, boiled whitewashed, and painted. During the pulverization process, asbestos fibers of more than 200 fibers/ml were suspended in the atmosphere while in occupational settings is 1/ml. The material was applied to the interior walls and especially around the fireplace because "the wall would not become black from the fire" ("amiantos" in Greek = something that does not get dirty). This procedure was repeated once or twice a year. All Metsovo inhabitants from 1940-1950s were used whitewash [asprochoma, luto]. Afterwards, its use was gradually reduced (Gibbs AR, 1990; Sakellariou K, 1996).

Metsovo Lung is of great interest in the research in the public health field, due to its rarity, although similar phenomena have been reported in areas around the world [Turkey, Italy, Spain, New Caledonia]. (Burilkov T, 1970; Davis YI, 1981; Baris YI, et al 1987, Constantopoulos SH. 2008; Velasco-Garcia MI, et al 2017). Other pathologies except lung were associated with asbestos exposure (Shevas AT, 1995; Raptis L, 2007).

It should also be noted that the ignorance of the population of Metsovo about the health impact of the use of a "luto" that existed in the area and used for the whitewashing and beautification of houses was the basis for the creation of the phenomenon (Rabinowitz JG. 1982; Grant DC , Seltzer SE, 1983).

The literature review about " Metsovo lung " was searched and viewed from a public health perspective. The main result of the study showed: a) PCs were observed in Metsovo and in neighboring villages, b) the extensive PCs in 47% of the population were not due to old tuberculosis, c) the cause was asbestos, which contained numerous tremolite fibers causing malignant mesothelioma of the pleura.

After the limited use and then the abandonment of the whitewash (luto) used for painting the walls of the houses of Metsovo was observed gradual reduction of mesothelioma in the Metsovo population (Bouros D, 2014).

## **Discussion**

Some positive elements emerged from the research:

- A. The abandonment of the "luto" marked the decline of mesothelioma, particularly in the 2000-2010s, since the use of the "lutos" was gradually abandoned after 1990.
- B. No asbestos exposure was observed in Metsovo inhabitants under the age of 50 years since the use of "luto" was not practiced.

The positive development of Metsovo Lung disease does not mean that there should be complacency, because new cases of mesothelioma may appear in Metsovo inhabitants in the coming years since mesothelioma can be detected even after 60-70 years. Undeniably, however, it is certain that the cases will be very limited. It is estimated that the Metsovo lung effect will end in the 2020s-2030s. Further research on the evolution of the phenomenon is needed, as well as medical surveillance of the Metsovo population (Manda-Stachouli C 2004; Gourgoulianis KI 2014).

Environment exposure to natural asbestos does not suggest that susceptibility differs according to sex. Solid evidence shows an increased risk of mesothelioma among people whose exposure comes from a nonoccupational or domestic source. The risk of mesothelioma associated with exposure as a result of living near an industrial asbestos source (mines, mills, asbestos processing plants) is clearly confirmed. Nonoccupational exposure to asbestos may explain approximately 20% of the mesotheliomas in industrialized countries (Davis YI, 1981; Baris YI, et al 1988; Zerva LV, 1989; Senyig'it A, 2000; Darcey DJ, 2004; Goldberg M, 2009; Ricchiuti C, 2020; Rey DR, 2022).

Beyond that studying the effects of non-occupational asbestos exposure on mesothelioma risk with molecular biology tests could provide detail information about the nature of the exposure–response relationship. miRNA changes may be sensitive indicators of the effects of acute and chronic environmental exposure and are valuable novel biomarkers for exposure (Tzilias V, et al 2017; Archimandriti DT, et al 2009; Filetti V, 2023).

The decrease and stability of mesothelioma age-standardized mortality rates (ASMRs) in countries that passed asbestos ban laws early indicated the effectiveness of the measures. Greece banned the use of asbestos in 2005. Therefore, ongoing awareness, knowledge, monitoring with a mesothelioma registry, and future epidemiological surveillance of asbestos-related diseases are required (Gogou E, et al 2023).

## Conclusions

Metsovo lung could be considered an emblematic case of extra-occupational environmental domestic exposure to asbestos on human health. Looking at the results, a number of conclusions can be drawn:

- a) below the age of 50, there is no evidence of exposure to asbestos since no use of the "luto" was made.
- b) the main cause of exposure to asbestos in Metsovo was the mineral soil containing tremolite fibres.
- c) once the use of this material was abandoned, asbestos exposure ceased.

We examine "Metsovo lung" history after 40 years. Epidemiologic, ecological, and clinical data confirm the risks of pleural calcifications and malignant pleural mesothelioma associated with non-occupational exposure to asbestos. These pathologies were attributed to household use of asbestos [whitewash (luto) that was found to contain tremolite]. "Metsovo lung" it's been also shown in many other areas in Greece and also in Turkey, Italy, New Caledonia, etc.

"Metsovo lung" study shows a classic example of non-occupational exposure to asbestos. This literature review concerning Metsovo lung intends to demonstrate relationships between environmental exposure to asbestos and lung diseases. Following the gradual abandonment of 'luto', this tremolite-containing whitewash (by 92% of the population in 1950 and only 18% in 1980) has resulted in a drop of mesothelioma incidence to one-half and a drop of mesothelioma relative risk to one-third. The present review has shown that a consistent pattern of decline and final end cannot be accurately predicted in the case of "Metsovo lung". If we take into account a 30–40-year latency period for mesothelioma, we expect that the "Metsovo mesothelioma epidemic" will fade away by the year 2020–2030.

From a public health point of view, it is very important to know whether exposure to low levels of asbestos can induce pleural mesothelioma, certainly Metsovo population is to be tested in the future and further data will be needed from continued follow-up. New specific and sensitive biomarkers [miRNA] for asbestos exposure can be employed, alongside spirometry and X-ray chest analysis, could add further relevant information on subjects who are at a high-risk of developing malignant pleural mesothelioma.



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**Data Availability:** All data are included in the content of the paper.

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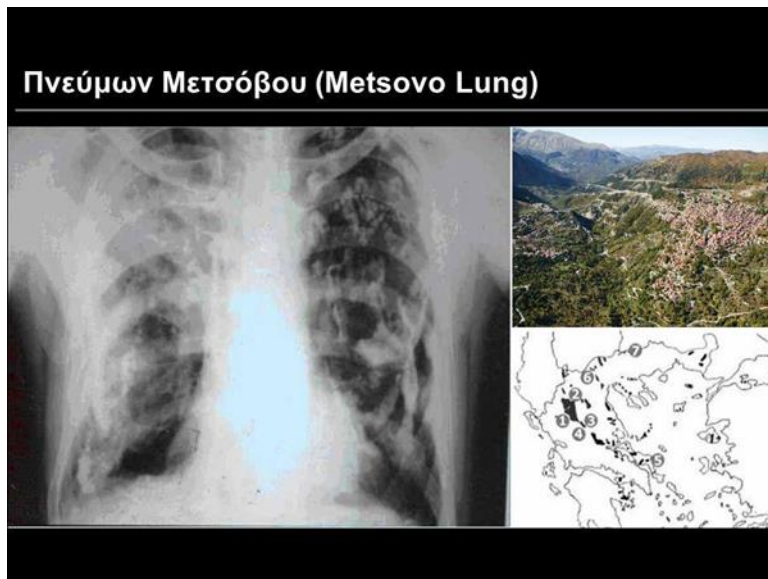
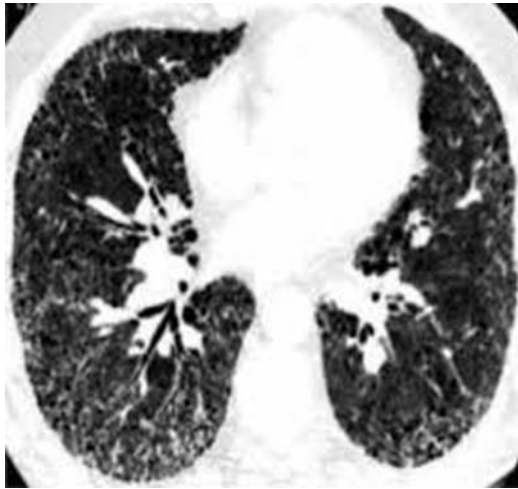


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## Appendix



Grinding Test on Tremolite with Fibrous and Prismatic Habit, *Fibers* 2019, 7(6), 52

