Evidence Suggesting the End of Universal Domestic Asbestos Exposure in Metsovo, NW Greece

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Keywords

Asbestos exposure · Metsovo · Exposure to “luto”

Abstract

Background: Inhabitants of Metsovo, NW Greece, had been domestically exposed to asbestos from a gradually abandoned whitewash (“luto”) that resulted in a declining epidemic of malignant mesothelioma. **Objectives:** We aimed to evaluate whether other sources of asbestos exposure exist following “luto” abandonment. **Methods:** Chest computed tomography (CT) and bronchoalveolar lavage (BAL) were used to evaluate residual asbestos exposure in younger Metsovites through the identification of pleural calcifications and asbestos bodies, respectively. In order to provide a historical universally exposed group for comparison, we used the accumulated chest CTs and chest roentgenograms of our previous studies, performed in Metsovites with confirmed exposure but negative chest roentgenogram. As an additional external comparison group, we also assessed CT scans and chest roentgenograms of Metsovites being older than our target group obtained from the records of the Radiology Department between 2009 and 2011. In order to be able to com-

pare our BAL findings, we sought historical controls among BAL studies performed in Metsovites with known exposure to “luto,” in the 1980s–1990s, mainly to evaluate alveolitis. Those belonging to individuals of the same age range were used for further comparison. **Results:** Twenty-two Metsovites born between 1960 and 1980 consented to undergo a chest CT scan, while another 14 CTs were retrieved from the records of the Radiology Department (among 86 of all ages), thus increasing the number of individuals studied to 36. Five of the 36 Metsovites studied were former “luto” users for a short period of time. Minimal pleural calcifications were present in 2 of them, while all chest CTs of nonusers were negative. All 8 BAL studies were negative for asbestos bodies. **Conclusion:** “Luto” use seems to have been the only source of considerable asbestos exposure in Metsovo.

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Introduction

Asbestos is an established cause of pleural and peritoneal malignant mesotheliomas [1, 2]. Although most cases of mesothelioma are related to occupational exposure

Fig. 1. Chest roentgenogram of an elderly, heavily exposed, Metso-vite with extensive pleural calcifications. This picture is only seen as a result of asbestos exposure, unlike localized calcifications (e.g., calcified pleurisy) seen also after tuberculous pleurisy or hemothorax.

to various types of asbestos [3], not all cases could be ascribed to occupation and it is postulated that one third of all mesotheliomas in the United States could have been due to nonoccupational exposure [4]. These cases could be linked to domestic and neighborhood exposure to asbestos or environmental exposure to naturally occurring asbestos or asbestiform fibers [5–11]. A meta-analysis by Bourdes et al. [11], based on studies available in the early 1990s, estimated relative risks of pleural mesothelioma ranging between 4.0 and 23.7 for household exposure and between 5.1 and 9.3 for neighborhood exposure. Regarding domestic exposure only, a recent evidence synthesis assessing domestic exposure arising from living with and handling the clothing of workers directly exposed to asbestos indicated that available results for domestic exposures are lower than domestic exposures [12]. The risk of mesothelioma from nonoccupational asbestos exposure and sources thereof are of considerable importance for public health and surveillance for asbestos exposure is crucial in the investigation of the exposure-response relationship.

We have previously reported that inhabitants of Metsovo, NW Greece, have been exposed from early childhood [13, 14] to asbestos from the domestic use of a

tremolite-containing whitewash called “luto” that was used by all households until 1940–1950 and was gradually abandoned afterwards [6, 14, 15]. This extreme exposure has resulted in a malignant mesothelioma “epidemic” (almost 300 times more than expected in the first 5 years) [15] and very frequent (almost in half of the population over 30) pleural calcifications (Fig. 1) [16]. Nowadays the “epidemic” is fading [13, 17] in response to the gradual abandonment of “luto,” which was completely abandoned by 1985 [17]. Indeed, the incidence of both pleural calcifications and malignant mesothelioma is declining and we have reported only 2 mesotheliomas after 2000 (2002 and 2005) [17].

During the domestic “luto” use and due to its prevalence and its compelling association with significant asbestos exposure and the subsequent health impact, other, milder, sources of asbestos exposure, should they exist, would be difficult to identify at the time of the endemic peak. Thus, our aim was to investigate whether asbestos exposure is still present in the region of Metsovo, NW Greece, after the documented significant decline of “luto” use and reveal indications, if any, for alternative potential sources of asbestos exposure. Moreover, we aimed to present the evolution in time of the radiographic depiction of this extreme asbestos exposure setting during the peak, decline and abandonment of the “luto” use.

Materials and Methods

Study Population (Fig. 2)

Active Surveillance Group

Between 1960 and 1980, the use of “luto” had declined considerably, giving us for the first time the possibility to evaluate Metsovitites who have lived all their life in a “luto”-free domestic environment. Metsovitites born between 1960 and 1980 were asked to voluntarily undergo chest computed tomography (CT) and bronchoalveolar lavage (BAL). Recruitment lasted from 2007 to 2011. The age range was chosen based upon two facts. First, it takes usually up to 30 years for pleural calcifications to be evident in chest roentgenogram (CXR) [18]. Thus, Metsovitites born after 1980 (aged less than 27 years during the recruitment) were not considered suitable. Second, evaluation of Metsovitites born before 1960 was not considered suitable since, even if they reported “no exposure” at home, “luto” was used by so many households that “background” exposure would have been very difficult to exclude.

Due to the relatively low enrollment rate, we retrospectively reviewed all chest CT scans and respective CXRs performed in Metsovitites falling within the aforementioned age range available in the records of the Roentgenology Department, Ioannina University Hospital between 2009 and 2011, when electronic files became available.

Fig. 2. Linear diagram showing the study design.

Fig. 3. **a** Chest CT of a 47-year-old Metsovite with minimal pleural calcifications (arrow). **b** Area with the calcifications in higher magnification.

Universally Exposed Arm

In order to provide a historical universally exposed group for comparison, the accumulated chest CTs and CXRs reported in our previous studies were retrieved. The CTs were performed in the 1980s, in Metsovitites with confirmed exposure but negative CXR [14].

As an additional external comparison group, we also assessed CT scans and CXRs of Metsovitites being older than our target group obtained from the records of the Radiology Department between 2009 and 2011.

In order to be able to compare our BAL findings, we sought historical controls among BAL studies performed in Metsovitites with known exposure to “luto,” in the 1980s–1990s, mainly to evaluate alveolitis [19]. Those belonging to individuals of the same age range were used for further comparison.

In sum, in agreement with the published literature, control groups (positive controls) were selected based on their document-

ed asbestos exposure when “luto” was used by almost all households (until 1960–1970). Thus, chest CTs and/or BAL obtained for various indications long time ago were used, mainly to stress that both these tools are, if positive, very sensitive indicators of asbestos exposure.

Evaluation of Asbestos Exposure

Asbestos exposure was indicated by the presence of pleural calcifications in chest CT and/or the presence of asbestos bodies in BAL. We have reported in the past that almost all Metsovitites exposed to “luto” had evidence of exposure, pleural calcifications in chest CT, and asbestos bodies in BAL [14, 19]. This high sensitivity of BAL and chest CT in detecting asbestos exposure has also been shown by other investigators [20–25]. Thus, in the absence of pleural calcifications or asbestos bodies, we assumed no clinically significant asbestos exposure.

Table 1. Demographic data, “luto” exposure history, and chest CT/BAL findings

No.	Sex/age, years	Smoking	Luto history	Pleural calcifications in CT	BAL/asbestos bodies
<i>Group A</i>					
1	M/34	no	no	no	no asbestos bodies
2	F/35	no	no	no	not done
3	F/38	no	no	no	no asbestos bodies
4	M/36	ex-	no	no	not done
5	F/30	no	no	no	not done
6	F/39	no	no	no	no asbestos bodies
7	F/37	no	no	no	not done
8	M/34	no	no	no	not done
9	F/48	yes	no	no	not done
10	F/41	ex-	no	no	not done
11	F/37	no	no	no	no asbestos bodies
12	F/39	yes	no	no	not done
13	F/47	no	no	no	not done
14	M/48	ex-	until 13–14 years old	yes	no asbestos bodies
15	F/40	no	no	no	not done
16	M/47	yes	until 5–6 years old	no	no asbestos bodies
17	F/45	no	no	no	not done
18	M/41	no	no	no	not done
19	M/41	no	no	no	not done
20	M/32	no	no	no	no asbestos bodies
21	M/35	no	until 5–6 years old	no	no asbestos bodies
22	M/45	ex-	no	no	not done
<i>Group B</i>					
23	M/43	yes	no	no	
24	F/39	no	no	no	
25	F/47	no	no	no	
26	F/48	no	no	no	
27	F/45	yes	no	no	
28	M/31	yes	no	no	
29	M/30	yes	no	no	
30	F/43	no	UNTIL 5–6 years old	no	
31	M/45	no	no	no	
32	M/46	no	no	no	
33	M/47	yes	until 18 years old	yes	
34	M/45	ex-	no	no	
35	F/33	yes	no	no	
36	F/30	no	no	no	

Group A: Metsovites, 30–49 years old recruited for chest CT and BAL. *Group B:* Metsovites, 30–49 years old with chest CT available from the hospital electronic files. “Luto” history and other information were obtained retrospectively, thus, BAL was not performed.

“Luto” Use

A detailed history of “luto” exposure was obtained in all participants. Questions regarding exposure to “luto” pertained to both childhood and adult life, as in previous studies we have documented that the exposure starts right after birth when “luto” was processed at home [13], as has been the case in some villages of Ana-

tolia, Turkey [26]. The end of “luto” use was confirmed by the testimony of use of modern wall painting materials or rebuilding the individuals’ residing premises. Investigators performing the interviews regarding the use of “luto” were blinded to the results of the chest CT and BAL studies.

Table 2. BAL results in the control group (30–49 years old)

No.	Born/age, years	BAL performed	Pleural calcifications in CXR	Asbestos bodies in BAL	Luto use	Luto use duration, years
1	1941/49	1990	no	yes	yes	20
2	1943/45	1988	yes	yes	yes	NA
3	1939/49	1988	yes	yes	yes	8
4	1944/46	1990	yes	yes	yes	21
5	1956/35	1991	no	no	yes	7
6	1945/47	1992	yes	yes	yes	NA
7	1950/39	1989	no	yes	yes	18

Results

Asbestos Exposure Indicated by Pleural Calcifications in Chest CT

Twenty-two individuals consented to undergo a chest CT scan, while another 14 CTs from Metsovites born between 1960 and 1980 were retrieved from the records of the Radiology Department (among 86 of all ages), thus increasing the number of individuals studied to 36 (Table 1; mean age: 40.0 years, median age: 40.5 years, male: 47%).

Only 5 of these 36 Metsovites (14%) had used “luto” in the past: 2 of them until their adolescence, while the remaining 3 only as toddlers.

No pleural calcifications (or other pleural or parenchymal abnormalities) were observed in the group of individuals with no reported exposure to “luto.” Minimal pleural calcifications (Fig. 3) were present in the 2 Metsovites that had been exposed to “luto” until their adolescence, a finding indicative of the high sensitivity of chest CT. No pleural calcifications (or other abnormalities) were present in the other 3 who reported a very limited “luto” exposure (until 5–6 years of age) (Table 1).

All 18 individuals with a confirmed exposure to “luto” during the time period of universal “luto” use, but with a “negative” CXR, had minimal pleural calcifications in the chest CTs [14].

Asbestos Exposure Indicated by Pleural Calcifications in CXR

CXRs were all “negative” for asbestos exposure in the active surveillance group, including the Metsovites with documented exposure to “luto” only during childhood and minimal pleural calcifications present in chest CTs.

In sharp contrast, evaluation of the 521 CXRs of Metsovites over 30, recruited in our previous studies, born when

“luto” was still widely used 10 and 30 years ago [27], showed that pleural calcifications were very frequent even in those aged 30–49 years in the first study (1978–1982) and 40–49 years in the second study (1998–2002) (Fig. 4). The same was true for CXRs of Metsovites over 50 obtained from our records (89/152 CXRs positive for pleural calcifications).

Asbestos Exposure Documented by Asbestos Bodies in BAL

From the 22 individuals that voluntarily had a chest CT scan, 8 agreed to further undergo BAL. The procedure was performed at the end of a conventional bronchoscopy as previously described [19]. All BAL studies were negative for asbestos bodies, including the 2 with minimal pleural calcifications in chest CT. This is in contrast to the “exposed control group,” where 6 out of the 7 BAL studies in the age group similar to the active surveillance arm (Table 2) and 54/75 (72%) in all age groups revealed asbestos bodies. As shown in the records, CXRs were positive for pleural calcifications in 4/6 30- to 49-year-old Metsovites with asbestos bodies (Table 2).

Evolution over Time of the Radiographic Evidence of Asbestos Exposure

In the process of detecting, quantifying and monitoring the Metsovo mesothelioma “epidemic,” we had the unique opportunity to observe the evolution over time of the radiographic documentation of asbestos exposure and its characteristics. We thus grouped the available radiographic evidence in time windows depending on the dynamics of the exposure. As previously reported [27], the prevalence of pleural calcifications is further decreased, while the age where pleural calcifications in CXRs were first encountered shifted from the 30s in 1980 and 40s in 2000 to the late 50s in 2010 (Fig. 4), thus con-

Fig. 4. Presence of pleural calcifications in chest roentgenograms (vertical axis) in each age group (horizontal axis), in the three studies (1978–1982, 1998–2002 and the present study).

firming that significant exposure to asbestos diminished over time and was present in older Metsovites only. Available CTs of Metsovites over 50 from our records (2009–2011) confirmed an increase by age in the presence of pleural calcifications from 56% (9/16) in the 50- to 59-year-old group to 85% (11/13), 93% (25/27), and 100% (10/10) in the groups aged 60–69, 70–79, and 80 or above, respectively (Fig. 4). They also confirmed that chest CT is more sensitive in uncovering pleural calcifications than CXR. As previously mentioned, 87/152 (57%) CXRs were positive in Metsovites over 50 versus 55/66 chest CTs (83%).

Discussion

In the present study, we provide evidence that asbestos exposure is no longer present in Metsovo. None of the individuals born and raised after “luto” abandonment with no self-reported exposure showed evidence of exposure to asbestos, either as pleural calcifications in CXR and CT or as asbestos bodies in BAL. We are thus in the position to claim that the use of “luto” and more specifically its indoor processing was the only source of asbestos exposure in this setting.

Indications of asbestos exposure can be sought through environmental sampling. Nevertheless, the most

compelling evidence on significant asbestos exposure is the one based on clinical findings. Tremolite-containing whitewash had been used in Metsovo by all households until 1940–1950. Its use declined gradually and was completely abandoned between 1980 and 1985 [14, 27]. We chose to focus on the clinical investigation part of this exposure and recruited young Metsovites, in order to evaluate the presence of two signs of asbestos exposure, i.e., asbestos bodies in BAL and pleural calcifications in chest CT, signs very frequently present among exposed Metsovites in our previous studies, but also in exposed populations studied by other investigators [20–25]. Asbestos bodies can be found in the BAL fluid of more than 95% of patients with asbestosis or just known asbestos exposure [19–23]. Studies of nonoccupationally exposed villagers from Anatolia show BAL to be equally sensitive as in occupational exposure (75%) [24, 26]. The same is true for the sensitivity of chest CT in uncovering pleural calcifications, both in occupational and nonoccupational settings. Among asbestos-exposed subjects in Belgium, chest CT revealed pleural plaques in 70% and none of the controls [25]. Also, in Turkey, chest CT had a sensitivity of 85.7% and specificity of 99.3% in discovering pleural plaques, among nonoccupationally exposed villagers of Anatolia [24, 26].

Given the proven validity of the analytical tools implemented, the choice of the population under study was a pertinent issue. We chose to assess Metsovites who could have been only sporadically or never exposed to “luto” at home. As mentioned before, they had to be at least 30 years old since this is the time required for pleural calcifications to become obvious radiologically [18, 28, 29]. Metsovites aged 30–49 years were born between 1960 and 1980, when “luto” use had dropped (from 68% in 1960 to 15% in 1980) and the majority of the population was never (or very shortly) exposed to it at home. Older Metsovites were considered unsuitable since we could not exclude “background” exposure even if they claimed no “luto” use at home.

The large number of chest CTs (and respective CXRs) obtained from the electronic records of our Radiologic Department drew a broader picture of the situation and gave us the opportunity to document the higher sensitivity of chest CT versus CXR and the opportunity to confirm what we have previously reported, namely that pleural calcifications in CXR are now less frequent and are seen in older age groups than in our previous studies.

Tremolite and erionite whitewash has also been extensively used in vast areas of Anatolia, Turkey, with hun-

dreds of villages built inside asbestos zones and inhabited by millions of people [8, 9, 24, 26]. In most of these villages, “background” asbestos (or erionite) exposure is still possible as fibers are still detected, indoors and outdoors [24, 26, 30], although traditional use of asbestos (or erionite) for whitewashing or other domestic uses has long been abandoned. Interestingly, in a few villages, tremolite (or erionite)-containing soil is still in use, or was at least until 2000 [26].

Unlike Anatolian villages, there is no asbestos inside Metsovo. As mentioned in our previous studies, the material had to be brought, ready for use from nearby hills, at a distance of approximately 10–15 km [31]. Thus, when we evaluated fiber concentrations in Metsovo, our measurements showed >200 fibers/ml while crashing the material, minimal concentrations during various household activities, and 0 fibers/ml in the ambient air of Metsovo [13, 32, 33]. So, unlike Anatolia, there has never been evidence of asbestos fibers in the ambient air of Metsovo. There lies the explanation of our negative findings in terms of ongoing exposure.

Conclusion

There are no signs of asbestos exposure in Metsovites aged under 50 years who have never used “luto.” The domestic use of this tremolite-containing whitewash has been the only source of asbestos exposure in Metsovo. Its abandonment in the 1980s after decades of universal use marks the end of asbestos exposure and predicts the end of the fading mesothelioma epidemic in Metsovo.

Financial Disclosure and Conflicts of Interest

The authors declare no conflicts of interest.

Author Contribution

Concept and design: A.G., E.E.N., C.M.-S., and S.H.C.; analysis and interpretation: A.G., E.E.N., C.M.-S., L.T., S.H.C., and E.L.; drafting the manuscript for important intellectual content: A.G., E.E.N., C.M.-S., S.H.C., A.K., and E.L.

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