

Environmental pleural plaques in an asbestos exposed population of northeast Corsica

F. Rey*, C. Boutin*, J. Steinbauer*, J.R. Viallat**, P. Alessandrini+,
P. Jutisz+, D. Di Giambattista+, M.A. Billon-Galland#, P. Hereng##,
P. Dumortier##, P. De Vuyst**

Environmental pleural plaques in an asbestos exposed population of northeast Corsica. F. Rey, C. Boutin, J. Steinbauer, J.R. Viallat, P. Alessandrini, P. Jutisz, D. Di Giambattista, M.A. Billon-Galland, P. Hereng, P. Dumortier, P. De Vuyst. ©ERS Journals Ltd 1993.

ABSTRACT: The purpose of this study was to determine whether the inhabitants of villages environmentally exposed to asbestos, in northeast Corsica, had a higher incidence of pleural plaques.

X-rays were obtained from subjects aged over 50 yrs, with no occupational exposure to asbestos or history of pleural disease, in one village exposed to asbestos, Murato, and a nonexposed, control village, Vezzani. In addition, the mineral content of the air and parietal pleura of animals in the exposed zone was studied, using transmission electron microscopy.

The incidence of bilateral pleural plaques in the exposed population was 41%, as compared to 7.5% in the nonexposed population ($p < 0.00001$). The levels of airborne tremolite were higher in Murato ($6-72 \text{ ng}\cdot\text{m}^{-3}$) than in Vezzani ($< 1 \text{ ng}\cdot\text{m}^{-3}$), but chrysotile levels were similar. Significant numbers of chrysotile and tremolite fibres were identified in the parietal pleura of animals from the exposed village.

This study confirms the well-known correlation between bilateral pleural plaques and environmental exposure to low levels of asbestos.

Eur Respir J., 1993, 6, 0978-982.

* Hôpital de la Conception, Marseille, France. ** Institut Paoli-Calmettes, Marseille, France. + Private Medical Practice, Murato, Corsica. ++ Private Medical Practice, Vezzani, Corsica. # Laboratoire des particules inhalées, DASS, Paris. ## Hôpital Erasme, Bruxelles, Belgium.

Correspondence: C. Boutin
Hôpital de la Conception
147 Bd. Baille
13385 Marseille
Cedex 5, France.

Keywords: Airborne pollution measurement; asbestos; Corsica; environmental pleural plaques; pleural mineralogy; pleural plaques

This work was supported by INSERM, grant no. 921002.

Received: May 29 1992

Accepted after revision April 27 1993

The relationship between bilateral pleural plaques and asbestos exposure has been recognized since the initial report by LYNCH and CANNON [1] in 1948. In 1960, KIVILUOTO [2] described an endemic occurrence of pleural calcifications in subjects, without occupational exposure, living near anthophyllite mines in Finland. Since that time, environmental pleural plaques have been reported in Bulgaria [3], Czechoslovakia [4, 5], Austria [6], Turkey [7, 8], Greece [9], Cyprus [10], and Russia [11].

The asbestos mine at Canari in the Cape of Corsica was closed in June 1965. We were in charge of the medical surveillance of the ex-miners who extracted chrysotile from this mine [12]. This experience drew our attention to two findings. The first was that radiologically detectable pleural plaques developed in some miners shortly after entering the mine, whereas it generally takes from 15-20 yrs for pleural plaques to appear on chest X-rays. The second finding was that the prevalence rate of bilateral pleural plaques was high (3.8%) in control subjects, who had never worked in the mine. These findings suggested environmental exposure due to the geology of the island. Unlike the northwest coast that is made of granite, the northeast coast of Corsica is composed of shiny schists, with surface deposits of chrysotile and tremolite-rich amphiboles.

In order to study this possibility, a retrospective survey was conducted of the chest X-rays of 1,721 patients born in northern Corsica, with no occupational exposure to asbestos [13, 14]. The prevalence of pleural plaques was 3.8% in subjects from the northeast versus 1.1% in subjects from the northwest ($p < 0.05$). Measurement of airborne asbestos levels in four exposed villages and four control villages in northeast Corsica confirmed high levels of chrysotile and even higher levels of tremolite [15].

The purpose of this study was to determine the prevalence of environmental pleural plaques in northeast Corsica. To achieve this goal, chest X-rays were performed on inhabitants of Murato, a village in an area with surface deposits of asbestos, and Vezzani, a village in a nonexposed area.

Material and methods

Villages

After studying a geological map, a number of villages were preselected in the exposed and unexposed regions of northeast Corsica. Murato and Vezzani (fig. 1) were

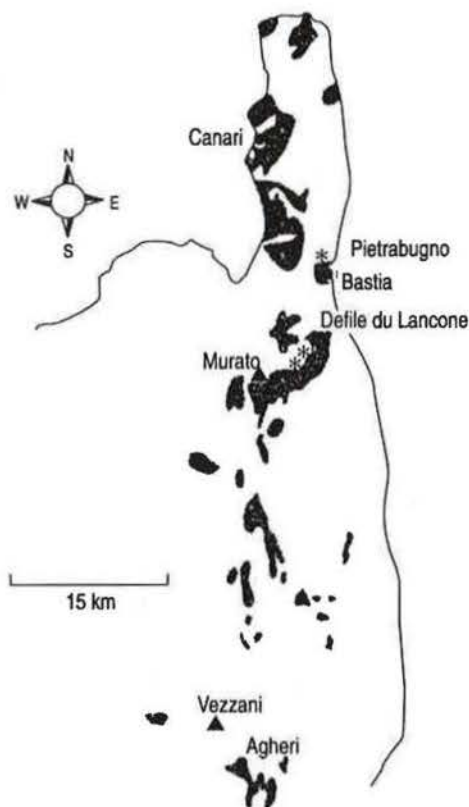


Fig. 1. - Geological map of Northeast Corsica. ■: zones with surface deposits of asbestos; ▲: villages studied; *: regions from which autopsied animals were taken. ●: villages/towns not studied.

finally chosen because the necessary X-ray equipment was available, and the radiologists agreed to participate in the study. The village of Murato was built on one of the largest surface deposits of asbestos in Northeast Corsica. Vezzani is located outside the surface deposit, but some peasants from Vezzani occasionally worked in fields in Agheri, an exposed hamlet located 7 km away. Both villages were in a rural mountain area (altitude 600 m) free of industrial pollution.

Population

This study was designed to include a maximum number of native inhabitants over the age of 50 yrs, who lived in the village more than 6 months a year. Each candidate was asked to complete a questionnaire, detailing his or her personal background, places of residence, medical and surgical history, tobacco use, and job experience. Special attention was given to uncovering possible previous occupational exposure to asbestos. Subjects with a history of occupational exposure to asbestos or of pleural disease were excluded.

Chest roentgenograms

Each subject had a 35×35 high-voltage anteroposterior chest X-ray. Images were interpreted independently by

two specialists, who did not know the geographical origin of patients, using the 1980 International Labour Office (ILO) International Classification of Pneumoconioses. In the case of disagreement, the X-ray was interpreted by a third specialist, and the opinion of the majority was retained. Only bilateral pleural plaques, with or without calcification, were considered to be related to environmental asbestos exposure.

Metrological assessment

Atmospheric samples. The concentration of airborne chrysotile and tremolite was measured in each village. Samples were taken in four different locations, *i.e.* outside, at three different altitudes in each village (lower, medium and highest part), and inside the town hall which was constructed of the same materials as the other houses in the villages. Air was filtered at a flow rate of 16 l·min⁻¹ for 11 h (overnight from 8 p.m. to 7 a.m.). The filter diameter was 47 mm and pore size was 0.45 μ. Specimens were analysed with transmission electron microscope (TEM) by the Laboratoire des Particules Inhalées (LEPI), according to the technique described of SEBASTIEN *et al.* [16]. Results were expressed in ng·m⁻³ for each type of fibre.

Pleural samples. To confirm the existence of airborne environmental pollution in this area, a study was undertaken of the pleural asbestos levels of animals living in exposed areas. One dog and two goats, 5, 9 and 10 yrs respectively, were included. Pleural specimens were taken at autopsy from the median part of the costovertebral gutter and were analysed with TEM by one of us (PDV). Samples were first washed at low temperature for 6 h, and the mineral content was filtered through 0.45 μ Millipore® filters and then transferred onto TEM grids. TEM analysis was made at a magnification of ×22,000.

Statistical analysis

Results were given as mean±SEM. Comparison of the exposed and nonexposed population was achieved using the Chi-squared test. Mineralogic data were compared using the mean variance method.

Results

Population

Birth records showed 150 eligible inhabitants in Vezzani and 120 in Murato. In Vezzani, 131 (87%) of the eligible subjects were examined. One subject with occupational exposure to asbestos, and 22 subjects born in neighbouring exposed villages, were excluded. The final study population was 108 (48 men and 60 women, mean age 66±1 yr); 38% were smokers (75% of men versus 9% of women).

In Murato, 12 subjects were excluded because they lived in the village for less than 6 months a year and 90 (83%) were examined. Seven subjects with occupational exposure to asbestos were excluded. The final study

Table 1. - Characteristics of the populations studied

		Murato exposed	Vezzani control
Subjects	n	83	108
Sex	M/F	34/49	48/60
Sex ratio		0.7	0.8
Mean age	yrs	68±1	66±1
Smokers	M/F	26/4	36/5
Age groups	n (%)		
	50-59 yrs	22 (26.5)	32 (29.5)
	60-69 yrs	21 (25.5)	36 (33.5)
	70-79 yrs	28 (33.5)	31 (28.5)
	> 80 yrs	12 (14.5)	9 (8.5)

population was 83 (34 men and 49 women, mean age 68±1 yr); 37% were smokers, including 77% of men and 8% of women.

The characteristics of the patients studied are given in table 1. The Chi-squared test confirmed that these two populations were comparable.

Prevalence of pleural plaques

In Vezzani, pleural plaques were documented in eight subjects, *i.e.* 7.5% of the population. This unusually high incidence was probably due to the proximity of surface asbestos deposits in nearby (7 km) Agheri, where some inhabitants occasionally worked in the fields. The plaques were calcified in seven of the eight subjects.

In Murato, bilateral pleural plaques were documented in 34 subjects, *i.e.* 41% of the population ($p < 0.00001$, odds ratio=8.67, relative risk=5.53). Bilateral plaques were calcified in 32 of the 34 subjects (94%) (table 2). In the remaining two subjects, one had calcifications on one side

and fibrohyaline plaques on the other, whilst the second had only fibrohyaline plaques.

Characteristics of subjects with pleural plaques in Murato

Several risk factors for pleural plaques were observed in Murato: male sex, interval since first exposure (age), and duration of exposure. Indeed the prevalence of pleural plaques was significantly higher in men (65%) than in women (25%) ($p < 0.0002$). Sixty one percent of smokers had plaques, *versus* 36% of nonsmokers, but this difference was not statistically significant. The prevalence of pleural plaques increased with age, which indicates the interval since first exposure. Thus, it varied from 14% between 50-60 yrs to 67% between 80-90 yrs. More than 60% of the inhabitants over 70 yrs presented radiologically visible bilateral pleural plaques. The mean age in subjects with pleural plaques (73±1.3 yrs) was significantly higher than the mean age of subjects without pleural plaques (64±1.3 yrs) ($p < 0.05$). The duration of exposure, which takes into account the time spent outside the village (military service, work on the mainland, *etc.*), did not differ significantly between the group with pleural plaques (60±3.5 yrs) and the group without plaques (54±2.5 yrs).

Measurements of asbestos pollution in airborne samples

The concentrations of chrysotile and tremolite observed in the two villages are shown in table 3. Unlike chrysotile which was detected at low levels indoors and outdoors in both villages, tremolite concentrations were high in Murato (6-72 ng·m⁻³) and very low (<1 ng·m⁻³) in Vezzani ($p < 0.05$).

Table 2. - Location and extent of pleural calcifications observed in Murato, according to the 1980 ILO International Classification

Extent	Location					
	Diaphragm		Chest wall		Pericardium/mediastinum	
	Right	Left	Right	Left	Right	Left
1	3	8	12	6	1	3
2	12	13	13	15	6	4
3	0	0	7	7	3	0
Total	15	21	32	28	10	7
%	47	66	100	88	31	22

ILO: International Labour Office.

Table 3. - Airborne asbestos pollution as assessed using transmission electron microscopy ($\times 10^{-9}$ g·m⁻³)

	Murato				Vezzani				
	I	H	M	L	I	H	M	L	
Chrysotile	0.6	1	0.4	0.3	0.3	-	0.2	0.1	ns
Tremolite	44	34	6	72	1	-	-	0.4	$p < 0.05^*$

I: indoors; H, M, L: outdoors at different levels in the village (high, medium, low); ns: not significant. *: Murato values *versus* Vezzani.

Table 4. - Pleural asbestos levels in three animals from the exposed region of northeast Corsica by transmission electron microscopy

	Dog	Goat 1	Goat 2
Age yrs	5	9	10
Number of fibres*	4.5	82	52
Mean length (μ)	1.21 \pm 0.01	1.14 \pm 0.1	0.9 \pm 0.06
Mean diameter (μ)	0.1 \pm 0.02	0.09 \pm 0.01	0.09 \pm 0.01
Ratio tremolite/ chrysotile	9/91	5/95	5.95

*: $\times 10^6$ fibres-g⁻¹ of dried pleura.

Asbestos content in the parietal pleura of animals from the exposed area

As indicated in table 4, the levels of chrysotile and tremolite fibres in the parietal pleura of the three animals were remarkably high (mean counts: $46 \pm 27 \times 10^6$ fibres-g⁻¹ of dried tissue). Fibres were short, with mean lengths ranging from 0.9–1.2 μ . Tremolite accounted for 5–9% of the total fibres.

Discussion

Because of its geological features, the northeastern region of Corsica provides an excellent opportunity to document the role of environmental exposure to asbestos deposits in inducing pleural plaques. The risk of developing plaques was much higher in Murato, the exposed village, where pleural plaques were observed in 41% of subjects over 50 yrs than in Vezzani, the nonexposed village where pleural plaques were observed in only 7.5% of the corresponding population.

Since none of these subjects had occupational exposure to asbestos, it is suggested that the presence of plaques resulted from environmental exposure. Our asbestos pollution data, which showed high airborne fibre levels (table 3) in all samples taken indoors, and outdoors, support this contention. It is likely that pollution was even greater in the past, when roads, streets and squares, were not paved. Some patients told us that during childhood they would look for long asbestos fibres in order to make wicks for lighters and oil lamps.

Findings similar to ours have previously been reported in other geographical areas. The incidence of pleural plaques induced by environmental exposure to mineral fibres ranges from 3.3–5.3% in Eastern Europe [3, 6, 11], and in 8% in Finland [2]. In Turkey [7, 8, 17, 18], and Greece [19, 20], incidences ranging from 14–47% have been observed in exposed adults. In comparison, according to the review by HILLERDAL [21], the incidence of radiologically detectable pleural plaques ranges from 0–1.3% in the general population, and from 0.1–13% in workers exposed to asbestos.

In this study, the prevalence of plaques is higher in men than in women (64.5% versus 24.5%). Although this discrepancy has been observed in most previously reported series, it has usually been lower [19, 22]. Whether or not smoking plays a role in these observed differences can-

not be answered from our data. However, BAZAS *et al.* [22] concluded that there was a lack of correlation between smoking habits and pleural plaques.

BOHLIG and ORTO [23] documented the link between pleural plaques and exposure to low levels of asbestos fibres. The concentration of airborne fibres in Turkey [18] or Corsica [15] is 2–3 fold lower than occupational dust levels [24]. In the present report, the levels of airborne asbestos measured in Murato were similar to those observed in other villages in northeast Corsica in a previous study [13].

The presence of pleural plaques indicates previous exposure to asbestos only, but not disease. The interval since first exposure is a more determinant factor than the duration of exposure for development of environmental pleural plaques. Formation of fibrohyaline plaques requires 15–20 yrs, and calcification requires 20–30 yrs. In our study, as well as in other series [17, 19, 22], the incidence of pleural plaques increased with age. That development of pleural plaques does not depend on the cumulative dose of inhaled fibres [25] is supported by the observation that migrant workers from Metsovo, an exposed village in Greece, had the same chest X-ray abnormalities as lifelong inhabitants of Metsovo [26]. Dose-dependent asbestos-induced parenchymal fibrosis is rare in environmental exposure [10, 22, 25].

The pathogenesis of pleural plaques is unclear. Amphiboles are supposedly more likely to induce pleural plaques than chrysotile, since they remain in the lungs longer [25]. Mineralogical data based on autopsy findings [27–29] have confirmed a correlation between the presence of pleural plaques and asbestos levels in the lung. It has been hypothesized that early exposure to long, thin amphibole fibres (crocidolite, amosite), or zeolite (erionite) causes mesothelioma, whilst early exposure to short, thick amphiboles (tremolite) induces pleural plaques [25, 30, 31]. However, regardless of the type of exposure, only small fibres reach the parietal pleura in men [32, 33] as well as in animals [34]. In Corsica, tremolite is the main pollutant in air samples and lung specimens from patients presenting with environmental diseases [35, 36]. However, in this preliminary study, chrysotile was the major component of pleural fibres in animals living in the same exposed area.

In Corsica, we have recorded 13 cases of environmental mesothelioma since 1980 [37], and another case was reported by MAGEE *et al.* [36]. There is no evidence, however, that pleural plaques are precancerous lesions, or that they are a risk factor for pleural mesothelioma [25]. Conceivably, the finding of concomitant pleural plaques in 43% of cases of environmental mesothelioma [37] results from a parallel evolution of the two conditions [25], as observed in Greece and Turkey [18, 38].

References

1. Lynch KM, Cannon WM. - Asbestosis. VI. Analysis of 40 necropsy cases. *Dis Chest* 1948; 14: 874–889.
2. Kiviluoto R. - Pleural calcification as a roentgenologic sign of non-occupational endemic anthophyllite asbestosis. *Acta Radiol* 1960; 194: 15–66.

3. Burilkov T, Michailova L. - Asbestos content in the soil and endemic pleural asbestosis. *Environ Res* 1970; 3: 443-451.
4. Rous V, Studeny J. - Etiology of pleural plaques. *Thorax* 1970; 25: 270-284.
5. Navratil M, Moravkova K, Trippe F. - Follow-up study of pleural hyalinosis in individuals not exposed to asbestos dust. *Environ Res* 1975; 114: 1433-1438.
6. Neuberger M, Grundorfer W, Haider M, et al. - Endemic pleural plaques and environmental factors. *Zentralbl Bakteriol* 1978; 167: 391-404.
7. Yazicioglu S. - Pleural calcification associated with exposure to chrysotile asbestos in southeast Turkey. *Chest* 1976; 70: 43-47.
8. Baris YI, Simonato L, Artvintli M, et al. - Epidemiological and environmental evidence of the health effects of exposure to erionite fibers; a four year study in the Capadocian region of Turkey. *Int J Cancer* 1987; 39: 10-17.
9. Constantopoulos SH, Saratzis NA, Kontagiannis D, Karantanis A, Goudevenos JA, Katsiotis P. - Tremolite white-washing and pleural calcifications. *Chest* 1987; 92: 709-712.
10. MacConnochie K, Simonato L, Mavrides P, Pooley FD, Wagner JC. - Mesothelioma in Cyprus: the role of tremolite. *Thorax* 1987; 42: 342-347.
11. Kogan FM. - Research on asbestos health problems in the USSR. In: Peters GA, Peters BJ, eds. *Asbestos Medical Research*. New York, Garland Law Publishing, 1989; pp. 527-547.
12. Viallat JR, Boutin C. - Radiographic changes in chrysotile mine and mill ex-workers in Corsica. (A survey 14 years after cessation of exposure). *Lung* 1980; 157: 155-163.
13. Boutin C, Viallat JR, Steinbauer J, Dufour G, Gaudichet A. - Bilateral pleural plaques in Corsica: a marker of nonoccupational asbestos exposure. In: Bignon J, Peto J, Saracci R, eds. *Non-occupational Exposure to Mineral Fibres*. Lyon: IARC Scientific Publications, 1989; 90: pp. 406-410.
14. Steinbauer J, Boutin C, Viallat JR, et al. - Plaques pleurales et environnement asbestosique en Corse du Nord. *Rev Mal Respir* 1987; 4: 23-27.
15. Billon-Galland MA, Dufour G, Gaudichet A, Boutin C, Viallat JR. - Environmental airborne asbestos pollution and pleural plaques in Corsica. *Ann Occup Hyg* 1988; 32: 497-504.
16. Sebastien P, Billon MA, Janson X, Bonnaud G, Bignon J. - Utilisation du microscope électronique à transmission (MET) pour la mesure des contaminants par l'amiante. *Arch Mal Prof* 1978; 39: 229-248.
17. Yazicioglu S, Ilcayto R, Balci K, Sayli BS, Yorulmal B. - Pleural calcification, pleural mesotheliomas, and bronchial cancers caused by tremolite dust. *Thorax* 1980; 35: 564-569.
18. Baris YI, Saracci R, Simonato L, Skidmore JW, Art-Vinli M. - Malignant Mesothelioma and radiological chest abnormalities in two villages in central Turkey. An epidemiological and environmental investigation. *Lancet* 1981; ii: 984-987.
19. Constantopoulos SH, Goudevenos JA, Saratzis N, Langer AM, Selikoff IJ, Mousopoulos HM. - Metsovo lung: pleural calcification and restrictive lung function in northwestern Greece. Environmental exposure to mineral fiber as etiology. *Environ Res* 1985; 38: 319-331.
20. Constantopoulos SH, Theodoropoulos P, Dascalopoulos G, Saratzis N, Sideris K. - Metsovo lung outside Metsovo. Endemic pleural calcifications in the ophiolite belts of Greece. *Chest* 1991; 99: 1158-1161.
21. Hillerdal G. - Pleural plaques: occurrence, exposure to asbestos, and clinical importance. Thèse Docteur en Médecine, Uppsala, 1980.
22. Bazas T, Oakes D, Gilson JC, Bazas B, McDonald JC. - Pleural calcification in northwest Greece. *Lancet* 1985; 38: 239-247.
23. Bohlig H, Otto H. - Asbest und Mesothelion. Arbeit und Gesundheit. In: Goetz E, Wagner R, eds. *Med Schriftenreihe des BM für Arbeit und Sozialordnung Hrsg. Stuttgart: Heft 89. Georg Thieme Verlag, 1975.*
24. Bignon J. - Mineral fibres in the non-occupational environment. In: Bignon J, Peto J, Saracci R, eds. *Non-occupational Exposure to Mineral Fibres*. Lyon: IARC, Scientific Publication, 1989; 90: pp. 3-29.
25. Neuberger M. - Pleural plaques from low levels of asbestos. In: Peters GA, Peters BJ, eds. *Asbestos Medical Research*. New York: Garland Law Publishing, 1989; pp. 231-275.
26. Constantopoulos SH, Langer AM, Saratzis N, Nolan LP. - Regional findings in Metsovo lung. *Lancet* 1987; ii: 452-453.
27. Andron A, Bellis D, Bertoldo E, Mollo F. - Coated and uncoated lung mineral fibres in subjects with and without pleural plaques at autopsy. *Path Res Pract* 1984; 178: 611-616.
28. Churg A. - Asbestos fibers and pleural plaques in a general autopsy population. *Am J Pathol* 1982; 109: 88-96.
29. Warnock ML, Prescott BT, Kuwahara TH. - Numbers and types of asbestos fibers in subjects with pleural plaques. *Am J Pathol* 1982; 109: 37-46.
30. Wagner JC, Chamberlain M, Brown RC, et al. - Biological effects of tremolite. *Br J Cancer* 1982; 45: 352-360.
31. WHO. - Asbestos and other natural mineral fibres. *Environmental Health Criteria 53*, World Health Organization, Geneva, 1986.
32. Boutin C, Sebastien P, Janson X, Viallat JR. - Métrologie des fibres minérales dans les biopsies thoroscopiques pulmonaires et pleurales. Résultats préliminaires. *Poumon-coeur* 1981; 37: 253-257.
33. Dodson RE, Williams MG, Corn CJ, Brollo A, Bianchi C. - Asbestos content of lung tissue, lymph nodes, and pleural plaques from former shipyard workers. *Am Rev Respir Dis* 1990; 42: 843-847.
34. Rey F, Viallat JR, Fariisse P, Boutin C. - Pleural migration of asbestos fibres after intratracheal injection in rats. *Eur Respir Rev* 1992; (in press).
35. Viallat JR, Boutin C, Steinbauer J, Gaudichet A, Dufour G. - Pleural effects of environmental asbestos pollution in Corsica. *Ann NY Acad Sci* 1991; 643: 438-446.
36. Magee F, Wright JL, Chan N, Lawson L, Churg A. - Malignant mesothelioma caused by childhood exposure to long-fiber low aspect ratio tremolite. *Am J Ind Med* 1986; 9: 529-533.
37. Rey F, Viallat JR, Boutin C, et al. - Les mésothéliomes environnementaux en Corse du nord-est. *Rev Mal Respir* 1992; 9 (S3): R151.
38. Constantopoulos SH, Malamou-Mitsi V, Goudevenos J, Papathanasiou M, Pavlidis N, Papadimitriou C. - High incidence of malignant pleural mesothelioma in neighbouring village of northwestern Greece. *Respiration* 1987; 51: 266-271.