

Annual Ramazzini Days 2006

**Epidemiological studies on the effects of asbestos in
Brazil and other developing countries**

**Benedetto Terracini
University of Torino**

**Why do we have so few reports
on asbestos-induced diseases in
developing countries???**

Number of entries in Medline September 2005

	United Kingdom	Brasil	Italy
Asbestos	299	28	296
Chrysotile	30	5	28
Pleural cancer	99	6	174
Mesothelioma	172	4	175

Table 1 | *Number of entries in Medline through some combinations of key words, January 2006.*

	Asbestos	Chrysotile	Pleural Cancer	Mesothelioma	Asbestos + epidemiology
Russia	50	18	9	6	23
China	42	14	23	17	26
Canada	266	104	71	117	157
Brasil	33	7	7	5	9
Kazakhstan	2	1	2	2	0
Zimbabwe	12	5	5	8	7
Japan	104	29	159	74	49
Thailand	3	1	7	2	2
South Korea	8	4	7	2	1
India	37	12	9	9	16
Indonesia	1	1	0	1	1
Mexico	13	1	6	6	6
Italy	301	29	182	179	203
United Kingdom	304	33	115	187	146

Estimate of workers potentially exposed to silica and asbestos in Brazil

Silica	
Mining and prospection	500,000
Industry*	3,400,000
Construction**	?
Asbestos	
Asbestos industry (mining, asbestos-cement, friction materials, textiles and others)	20-22,000
Vehicle brake, clutch and engine repair shops***	223,000
Construction**	?

* Data extrapolated from reference 6, including workers in metallurgy, mineral processing, foundries, machinery, chemical and rubber industries

** Construction workers number 4,300,000. It is not possible to have an accurate estimate of exposure to silica or asbestos.

***Source: SINDIREPA, 1998 (Union of vehicles repair shops)

Some landmarks in occupational data on asbestos exposure in Brazil

Year	Event	Author
1975	First case of asbestosis published	Nogueira et al
1983	Clinical description of 15 cases of asbestosis in Sao Paulo	Costa
1988	Radiological survey on 386 A/C workers from medium-size plants → high prevalence of radiographs compatible with asbestosis in workers with 10 + years of exposure	Amancio et al
1995	Seven out of 10 former A/C workers followed by Ministry of Labour Inspectorate found to have pleural thickening and/or asbestosis	
1998	Exposure in A/C industry fairly well controlled (limit 1 f/ml?)	Amancio et al



Non-malignant consequences of decreasing asbestos exposure in the Brazil chrysotile mines and mills

E Bagatin, J A Neder, L E Nery, M Terra-Filho, J Kavakama, A Castelo, V Capelozzi, A Sette, S Kitamura, M Favero, D C Moreira-Filho, R Tavares, C Peres and M R Becklake

Occup. Environ. Med. 2005;62;381-389
doi:10.1136/oem.2004.016188

The Sociedade Mineradora de Amianto SA Study

Group	Period	Site	Asbestos	Measurements of exposure	Number of workers		
					eligible	dead	complying
I	1940-67	Sao Felix. Bahia	Chrysotile contaminated with tremolite	Subjective	538	148	180
II	1967-76	Canabrava, Goias	No evidence of amphiboles	Subjective	2134	184	1317
III	1977 +			Systematic	3426	10	2137
Total					6098	433	3634

Bagatin E et al Occup Environ Med 2005;62:381-389

The Sociedade Mineradora de Amianto SA Study

Final logistic regression models for radiographic abnormalities Odds ratios and 95% CI

Abnormalities	Group I (reference)	Group II		Group III	
		OR	95% CI	OR	95% CI
Pleural	1	0.49	0.28-0.86	0.33	0.16-0.67
Pleural or parenchymal	1	0.29	0.12-0.69	0.19	0.08-0.45

Bagatin E et al Occup Environ Med 2005;62:381-389

The study on Brazilian asbestos-cement workers

- ❑ 868 former A/C workers enrolled during 1995-99**
- ❑ Exposure scores (1 to 10) on the basis of a job-exposure matrix**
- ❑ 74 with asbestosis**
- ❑ 246 with pleural thickening**
- ❑ Latency time fro first exposure best predictor for both conditions**

Reclassification of 217 death certificates coded as pleural cancer in Rio de Janeiro 1979-2000, on the basis of information contained in death certificates (and hospital records for 73 cases)

	No.	%
Pleural mesothelioma	45	20.7
Pleural neoplasms	90	41.5
Malignant pleural effusion	8	3.7
Metastatic pleural effusion	45	20.7
No pleural disease	29	13.4
Total	217	100.0

**Confirmation of presence of mesothelioma in death certificates
(or in medical records) vs histological diagnosis of mesothelioma in Rio de Janeiro
(only cases whose histology could be re-evaluated)**

		Histopathology		
		Yes	No	total
Death certificate	Yes	11	0	11
	No	20	3	23
	Total	31	3	34

		Histopathology		
		Yes	No	total
Medical record	Yes	17	0	17
	No	14	3	17
	Total	31	3	34

**In the causation of
mesothelioma, is the role of
asbestos surpassed by the
role of genetic susceptibility?**

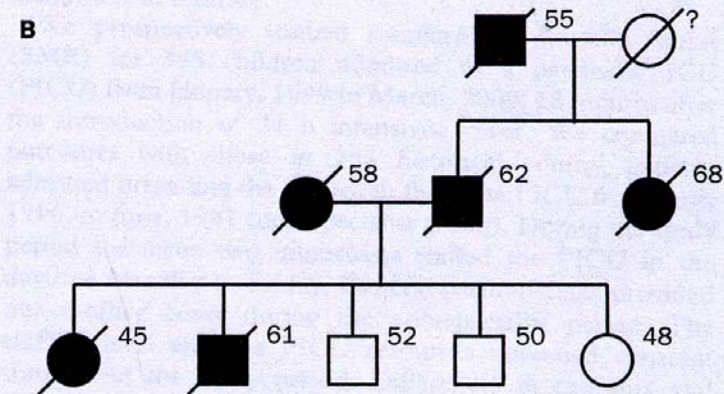
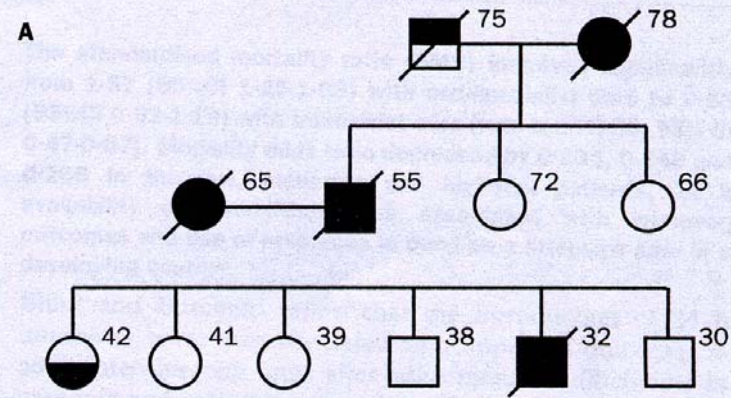
Genetic susceptibility in pleural carcinogenesis induced by asbestos

- ❑ Familial aggregation
- ❑ Genealogical trees in Capadocia
- ❑ Endogenous co-factors
 - Micronuclei in lymphocytes as indicators of genetic instability
 - Genotypes (GSTM1, NAT2, SNPs)

Genetic-susceptibility factor and malignant mesothelioma in the Cappadocian region of Turkey

Roushdy-Hammady I, Siegel J, Emri S, Testa J.R., Carbone M.

THE LANCET Vol 357 Feb 10, 2001



Representative pedigrees of families

A: three-generation pedigree showing vertical transmission of mesothelioma. B: a separate branch of this extended family showing an abridged three-generation pedigree in which vertical transmission of malignant mesothelioma and two generations of affected sibling pairs can be seen. Circles=females; squares=males; clear symbols=unaffected living individuals; solid symbols=malignant mesothelioma; top half-filled symbols=liver cancer; bottom half-filled symbols=pleural thickening; numbers next to the symbols are the ages of individuals or ages at death from malignant mesothelioma; ?=age unknown.

Concerns about the 6-generation study among residents in Karain and Tuzkoy, Cappadocia (Roushdy Hammady et al Lancet 2001;357:444)

- ❑ In each generation, the 50% relative frequency of deaths from mesothelioma corresponds to expectation with no genetic aggregation.**
- ❑ The segregation ratio between affected and non affected offspring is not significantly different from 1:1 (it should have been higher in the case of autosomic transmission).**
- ❑ Half of the cases occurs in the age of reproductive life: this is inconsistent with the hypothesis of a persisting autosomic and lethal gene.**
- ❑ Until 1978, only a minority of mesothelioma cases were identified and diagnosed: reliability of reconstructed genealogical trees over some generations is debatable..**

Saracci R, Simonato L
Lancet 2001;358:1813

Some variables which have been investigated as possible markers of susceptibility to asbestos-induced pleural carcinogenesis in the human species

GSTM1 gene

NAT2

Single nucleotide polymorphisms leading to defective DNA repair

Micronuclei in circulating blood cells

In the etiology of mesothelioma, is the role of asbestos surpassed by the role of genetic susceptibility? (1)

Pros	Cons
<p>“Only” 10% exposed workers develop the disease.</p>	<p>A similar statement could be made for the association tobacco smoke – lung cancer (competitive causes of death are relevant to both circumstances)</p>
<p>The number of reports of familial aggregations is increasing</p>	<p>Editorial trend and publication bias have not been measured. Many clusters are attributable to exposure to asbestos shared by family members.</p>

In the etiology of mesothelioma, is the role of asbestos surpassed by the role of genetic susceptibility? (II)

Pros	Cons
<p>In “highly” polluted areas, more cases are produced by environmental than by occupational exposures, but environmental concentrations have been orders of magnitude lower than in the workplace. Thus, affected persons are hypersusceptible.</p>	<p>We know little about previous asbestos concentrations in the general environment around asbestos plants. Among reliable estimates, cumulative exposure of some residents in Wittenoom exceeded 7 fibre/ml/year.</p>
<p>Contrary to other circumstances, very short exposures are sufficient to produce cancer.</p>	<p>Is the argument relevant to the issue of individual susceptibility?</p>

In the etiology of mesothelioma, is the role of asbestos surpassed by the role of genetic susceptibility? (III)

Pros	Cons
Dose and its proxies are irrelevant to risk	Most studies indicate the opposite. Dose is a component of Peto's and Boffetta's models for risk estimates.
Biological markers of individual susceptibility are cropping up.	Results so far available are either limited or contradictory. Attributable risks cannot be measured. Postulated "low risk" genotypes or phenotypes do not seem to be fully protected.

“Controlled used of asbestos”

All distributors/manufacturers of asbestos will be required to have an import permit, to be withdrawn if following commitments are not met

- ❑ Products to be distributed only to licensed companies, with *ad hoc* trained and licensed workers
- ❑ No resell to third parties and unused materials to be returned to manufacturer
- ❑ List of users to be provided to the responsible government agency
- ❑ Provided products to be cut to specification in equipped centres by trained and licensed workers
- ❑ Monitor and report on the performance of downstream users at regular intervals

Statement filed by Canada in the WTO asbestos case, December 13 1999 (quoted by B. Castleman, IJOEH 2003;9:294-298)

Dr. Peter Infante of the US testified that OSHA, where he worked, had issued 4000 citations in the years 1996-1998 for violations of the 1994 OSHA asbestos standard

A brake manufacturer had been fined \$ 125.000 for exceeding the 0.1 f/ml PEL, not providing respirators, and dry sweeping the floors.

(quoted by B. Castleman, IJOEH 2003;9:294-298)

Hypotheses intended to exculpate opportunities for exposure in asbestos in the workplace

- ❑ Only the first period of exposure is relevant to the induction of mesothelioma.
- ❑ Induction of mesothelioma is dose-independent
- ❑ Genetic (susceptibility) factors play a major role in the origin of mesothelioma
- ❑ Exposure occurred before the moment in which the “scientific community” considered that the evidence of carcinogenicity of asbestos was satisfactory
- ❑ If the “case” is a lung cancer and smoked, given the well known etiological role of tobacco, the disease is attributable to personal behaviour rather than environmental exposures
- ❑ Asbestosis is a *sine qua non* in order to attribute a case of lung cancer to exposure to asbestos
- ❑ Only ultrafine fibres can reach the parietal pleura

