

Scientific Update on Safe Use of Asbestos

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When We Talk about Asbestos What Do We Mean?

- Anthophyllite Asbestos – Finland was the major producer ends mining 1977.
- Amosite – South Africa was the major producer ends mining in 1992.
- Crocidolite – South Africa was the major producer ends mining in 1997, Western Australia (Wittenoom) closed in 1966 and Bolivia also produced crocidolite.
- Actinolite & Tremolite were never commercially mined to any extent.

Chrysotile was always the predominant asbestos type in commerce recent production of about 2,000,000 metric tons per year.

Legacy and Environmental Exposures to Amphibole Asbestos

- Production of Amosite and Crocidolite ended in 1992 and 1997 respectively.
- With the long latency period for asbestos-related cancer the risk from these exposures could continue into the 2030s.
- Environmental Exposure to Crocidolite and Tremolite-Actinolite Asbestos are known to cause Human Mesothelioma (mainly pleural).
- Exposure to amphibole asbestos in place need to be managed.
- Anthophyllite Asbestos is not a potent inducer of mesothelioma.

United States Continues to Use Chrysotile

- 1,000 metric tons per year
- 57% Chloroalkali Industry, 41% Roofing materials & 2% Unknown

US 5th Circuit Court of Appeal (1991) Vacates EPA's proposed ban on asbestos because the agency had "failed to muster substantial evidence".

Court of Appeals Decision

- Court asks the EPA to muster further evidence in support of their claim that asbestos exposure constitutes an “unreasonable risk”.
- EPA never provided such addition information and many would argue it does not exist.

The Ancient World Knew about the “Magic Mineral”

- But not about the health effects.
- This includes Pliny and Strabo.

Browne and Murray, 1990.
Asbestos and the Romans

What we know about the Health Effects from
Uncontrolled Controlled Exposure to Airborne
Asbestos was learned in the 20th Century

Asbestosis

Excess Lung Cancer Risk

Increased Risk of Pleural and Peritoneal Mesothelioma

Asbestosis: First of Asbestos-Related Diseases Identified

- Fibrosis of the lung from exposure to asbestos was first reported in the France and the United Kingdom in 1906. Dr. Montague Murray had a carder from Barking develop asbestosis. The Patient described how he was the last of 10 men working in the carding room all the other died at ages around 30.
- Cooke (1927) was the first to use the term “asbestosis” and describe the coated asbestos fibers in the lung as “asbestos bodies”.
- These early cases occurred in chrysotile workers and generally among individuals who also had tuberculosis.
- First case of asbestosis without tuberculosis was reported by Seiler (1928).

Asbestos Bodies and Settled Amosite from the Unarco Factory in Paterson, NJ

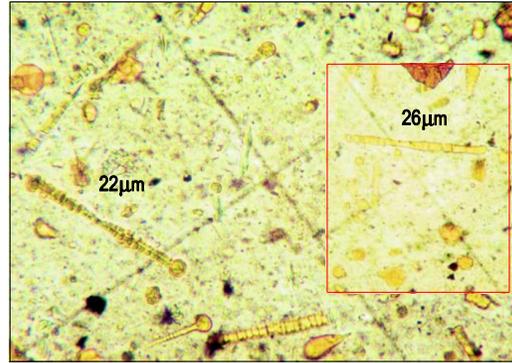


Fig. 1a. Asbestos bodies recovered from the lung parenchyma of an asbestosis case from the Paterson factory. This individual had 13 years of exposure at the factory and died of asbestosis at 50 years of age with 17,500 asbestos bodies per gram of wet lung parenchyma.

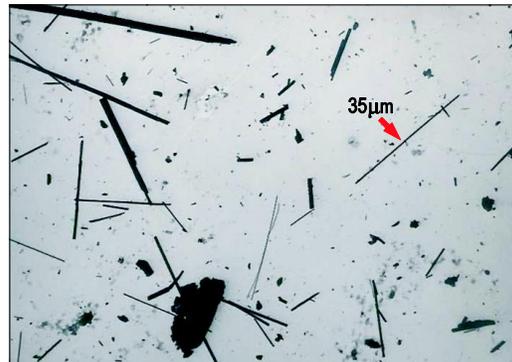


Fig. 1b. Settled grunerite asbestos dust from the Paterson, NJ factory.

Asbestos-Related Lung Cancer

- Case reports of lung cancer in individuals with asbestosis began to appear in the 1930s (Wood and Gloyne 1934, Lynch and Smith 1935).
- The first epidemiological study was Doll (1955) a cohort of chrysotile textile workers with at least 20-years of exposure. Eleven lung cancers occurred where in the general population less than one would be expected.
- All the chrysotile workers with lung cancer also had asbestosis and no mention is made of their smoking history.
- Lung cancers related to chrysotile exposure are bronchogenic carcinomas.

Mesothelioma is a Cancer of the Serosal Membrane.

- There are three anatomical sites where this cancer can occur pleura, peritoneal and pericardium.
- The most common site for mesothelioma in the general population is the pleura; while in amphibole asbestos exposed workers peritoneal can be the most common site.
- Even high cumulative exposures to chrysotile has not cause observable increases in peritoneal mesothelioma.

33 Pleural Mesothelioma cases among asbestos exposed workers was first reported by Wagner et al. (1960)

- About half of the cases had environmental rather than occupational exposure with latencies of 40-years or more; the youngest case was a 21-year old male.
- Asbestos bodies were found in the first case indicating asbestos exposure as the possible etiological agent.
- Careful questioning of the patients and their relatives revealed 32 of the 33 cases were exposed to riebeckite asbestos known commercially as crocidolite (or blue asbestos) in northwest Cape Province Mines in South Africa.

Wagner *et al.*, 1960 establishes Mesothelioma as a type of cancer associated with asbestos exposure.

- South Africa produced chrysotile, amosite, and a second crocidolite producing area in Penge but marked excess mesothelioma cases occurred only among those exposed to crocidolite in the northwest Cape Province.
- Although mesothelioma cases were reported in the medical literature the existence of this type of cancer was still questioned by some.
- The large number of cases collected by Wagner and co-workers over a brief period of time (many with only environmental exposure) to Cape crocidolite attracted the attention of the international medical and scientific community.

State-of-the-Art

Circa 1965

- The NY Academy of Sciences publishes the Proceedings of an International Symposium on “The Biological Effects of Asbestos”.
- Exposure to asbestos can cause asbestosis, excess lung cancer, and mesothelioma.
- A need for further information on the health effects of the various asbestos-types was recognized and additional medical and scientific research is planned.
- It was assumed that we should consider all the asbestos-types are equally hazardous until differences can be shown.

International Agency for Research on Cancer
(IARC), World Health Organization
Lyon, France

- All the Asbestos-Types are known to be Human Carcinogens and are therefore designate by IARC as Group 1.
- IARC lists 116 agents as Group 1 or agents known to be human carcinogens.
- IARC does not address questions of potency of any carcinogen.
- Nor does IARC address the cancer risks from controlled use?
- IARC does not conclude all six asbestos-types equally dangerous?

Epidemiological Studies of Cohorts of Workers Exposed to different Asbestos-Types

- Excess Risk of Lung Cancer was found to follow a Relative Risk Model. Meaning the increased cancer risk from asbestos exposure depends on your underlying lung cancer risk.
- For example lets assume smokers have a 2% lung cancer mortality and non-smokers have 0.5%. A cumulative asbestos exposure sufficient to increase your lung cancer risk 10% would increase the percentage of lung cancer deaths in the smokers for 2% to 2.2% while the non-smoker (with the same asbestos exposure) would increase from 0.5% to 0.55%.
- The excess lung cancer risk from asbestos exposure is relative to the underlying lung cancer risk from smoking.

Lung Cancer: Average Dose-Response for Each Asbestos Exposed Cohort

$$\mathbf{R(L)=100 \times (SMR-1)/X}$$

R(L) is the percentage of excess lung cancer risk multiplied by X
the cumulative exposure given in f/mL x years.

SMR is the ratio of the observed to expected lung cancer deaths
in the cohort of asbestos exposed workers.

$$\text{Relative Risk (RR)} = 2 = 100/R(L) = 1/k$$

(Lash *et al.*, 1997)

Estimate of k (increase in relative risk of lung cancer per fiber/mL x years of exposure) from Chrysotile in different Occupational Settings.

	k	Cumulative Exposure to increase Relative Risk = 2
Mining and Milling	0.00025	4,000
Cement Industry	0.0034	294
Manufacturing and Textiles	0.0077	130
All Cohort	0.0026	385

What Increased Lung Cancer Risk would We Expect at from Controlled Use of Chrysotile?

- Assume controlled use at a Cumulative Exposure of $10\text{f/mL} \times \text{Years}$
- Lash et al. 1997's average cumulative exposure of $385\text{f/mL} \times \text{Years}$ to increase the Relative Risk (RR) of Lung Cancer to 2
- If you were to half this cumulative exposure ($385/2$) your RR would be 1.5
- A cumulative exposure of $10\text{f/mL} \times \text{years}$ RR would be 1.026

Value of R(L) by Asbestos-Type Hodgson and Darnton (2000)

Asbestos-Type	R(L)	Cumulative Exposure to increase RR=2
Crocidolite	4.2	24
Amosite	5.2	19
Mixed (Amphibole and Chrysotile)	0.47	213
Chrysotile	0.62	1613

What would the excess lung be from modern controlled use of Chrysotile?

- Chrysotile Miners and Millers in Quebec had cumulative exposures estimate to be 600 fiber/mL x years with an SMR of 1.36.
- If the exposure response is linear and the cumulative exposure was decreased by half to 300 f/mL x years the SMR would be 1.18.
- If the SMR was decreased to 20 fiber/mL x years the SMR would be 1.01 or 1% excess lung cancer risk.

R(M) is the Mesothelioma Risk expressed as a percentage of all deaths per fiber/mL x years

$$R(M) = 100 \times O(M) / \text{Expect No of Deaths} \times \text{Cumulative Exposure}$$

Where R(M) is the mesothelioma risk and O(M) is the number of deaths from mesothelioma.

Here you calculate the % of mesothelioma deaths among all the deaths (not a Relative Risk like for lung cancer).

Risk of Mesothelioma per fiber/mL x Years Hodgson and Darnton (2000)

Cohorts Exposed to Three Asbestos-Types	% Total Expected Mortality per fiber/mL x Years
Crocidolite	0.51
Amosite	0.10
Chrysotile	0.001

Hodgson and Darnton (2000)

Mesothelioma Potency:

500 Crocidolite:100 Amosite: 1 Chrysotile

Concluded that crocidolite was 500 time more potent for inducing mesothelioma than chrysotile.

It is important to consider if the cohorts predominantly exposed to chrysotile had some crocidolite exposure as well.

Confounding Asbestos Exposures

- After 1965 Investigators were trying to identify cohorts with exposure to single asbestos-type.
- If 99% of the asbestos used was chrysotile and 1% crocidolite, investigator assumed the health effect were predominantly from the chrysotile.
- If the crocidolite is 500x more potent at causing mesothelioma than at 1%, it is still 5-fold more important than the chrysotile exposure for increasing the risk of mesothelioma.

Amosite, Insulation Factory, Paterson, NJ

- Selikoff et al. 1972 publishes in the *Archives of Environmental Health* the evidence for the carcinogenicity of amosite
- Among 105 deaths 13.3% were from Asbestosis, the SMR Lung Cancer not reported and 4.8% from mesothelioma (2 pleural, 3 peritoneal).
- The SMR for lung cancer (last reported in 1986) was 497.
- By 1986, there were 17 mesothelioma cases occurred among 740 deaths in the cohort with 2.3% from mesothelioma (9 were peritoneal).
- Hodgson and Darnton (2000) estimate cumulative exposure at 65f/mL x years.

Anthophyllite Asbestos, Finland

- Epidemiology cohort study of anthophyllite miners reported no mesothelioma case in 248 deaths or less than 0.4% (Meurman et al. 1974).
- By 1994, four cases of mesothelioma were report in anthophyllite miners and millers (one was peritoneal). All four individuals had sufficient anthophyllite exposure to develop asbestosis.
- Meurman et al. 1974 reported excess cases of lung cancer and asbestosis cases.

Crocidolite Exposed Cohorts.

Mining Location	Percentage of Death From Mesothelioma	Cumulative Exposure (f/mL x Years)
South Africa	20/423 (4.75%)	16.4
Australia	231/2549 (9.1%)	23

% of Pleural Mesothelioma Deaths in Cohorts of Four Amphibole Asbestos-Types

Amphibole Asbestos-Type	Cumulative Exposure (f/mL x Years)	% of Deaths from Pleural Mesothelioma
Crocidolite	53	7.1% (252/3,547)
Amosite	44	1.2% (16/1,384)
Tremolite	Unknown	1.8% (14/767)
Anthophyllite	Unknown	0.59% (3/503)

% of Pleural Mesothelioma Deaths in Chrysotile Mining and Manufacturing Cohorts

Industrial Sector	Cumulative Exposure (f/mL x Years)	% of Deaths from Pleural Mesothelioma
Mining and Milling	587	0.44% (35/7,883)
Manufacturing	32	0.26%(10/3,920)

How long have we known about cancers of the serosal membrane?

- Lieutaud (1767) reports two pleural tumors in an autopsy series of 3,000 cases (0.07%). He was a member of the Royal Society of London and the Royal Academy of Sciences in Paris and the personal physician to King Louis XVI of France.
- Laennec (1826) describe how cancer can form in the pleura and compress the lung, and recognizes this is different from tubercles on the pleural surface.
- Rokitansky (1855) Describes primary cancer of the pleura and peritoneal.

Tumors on the Serosal Membrane are Well Describe in the 19th Century Medical Literature

- The term mesothelioma is first used by Minot (1890) to describe the serosal membrane so there are no “mesothelioma” cases prior to this time.
- Adami (1908) describe the first mesotheliomata of the serosal membrane and reports the pleural most common and pericardium least.
- DuBray and Rosson (1920) report the first mesothelioma in the United States and the first called “mesothelioma”. A 40-year old, male physician from California.

Mesothelioma and Asbestos

- Some have claimed that prior to the commercial use of asbestos there were no mesotheliomas and all mesotheliomas are caused by asbestos.
- Primary cancer of the pleura was reported almost two centuries before Wagner *et al.*, 1960 paper.
- The frequency for which mesothelioma occurs (pleura most common and pericardium least) was reported in 1908.
- Modern medicine tells us a cancer can arise in any tissue in the body and there are no single causes of any type of cancer.

South African Experience

Nolan et al. 2006

- Produced the three major commercial types of asbestos.
- Crocidolite, Amosite & Chrysotile.
- Environmental Mesothelioma Cases have been reported.
- What asbestos-type(s) are important risk factors?
- Compensation in South Africa requires an autopsy of the heart and lungs.
- Lung content analysis was done by analytical transmission electron microscopy in a series of 43 consecutive mesothelioma autopsies.

Results of the Lung Content Analysis

- 33 Occupational Cases were Asbestos-Related
- Crocidolite was detected in 31 cases (0.02 to 10.5 million fibers per gram of dried lung tissue).
- Crocidolite was the only asbestos-type in 12 cases.
- Amosite and Tremolite was the only asbestos-type in two cases.
- In four environmental cases all contained crocidolite in three cases it was 100% and in one case 96% of the asbestos was crocidolite.
- In six cases no asbestos of any type was found.