David Egilman MD, MPH
Clinical Professor
Department of Family Medicine
Alpert School of Medicine, Brown University
President of GHETS.ORG

Disclosure: I serve, or have served, as a consultant to workers, spouses, and consumers who have been injured as a result of inhaling asbestos fibers, and to asbestos product manufacturing and mining companies – including Turner & Newall -- who have been sued by workers, spouses, and consumers who have been injured as a result of inhaling asbestos fibers.
Framing is key

“Values are always with us. There can be no view except from a viewpoint. Prior to answers there must be questions. In the question raised the viewpoint has already been chosen and the valuations implied.”

- Gunnar Myrdal
Agreements

Chrysotile causes mesothelioma

Chrysotile causes lung cancer

Debate on these things
Why do we care?

Compensation

Utilitarian question related to removal
The question reframed

How much chrysotile does it take to cause mesothelioma?
Science is the art of disproving hypotheses

Sir Karl Popper (1902-1994)
Hypothesis:
All Swan are white

High exposure are required to cause mesothelioma
(what’s low) 7-10f/cc-yrs

Is disproved by finding black swans.
"If you think that by hanging us you can stamp out the labour movement... the movement from which the downtrodden millions, the millions who toil in misery and want, expect salvation - if this is your opinion, then hang us!

Here you will tread on a spark, but there and there, behind you - and in front of you, and everywhere, flames blaze up. It is a subterranean fire. You cannot put it out."
<table>
<thead>
<tr>
<th>Applicable evidence</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traditional</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lung fiber levels</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Molecular understanding &amp; genetics</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td>Animal Studies – Mega Mouse</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td>Case Reports</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Traditional epidemiology

- Doses are guesses
- No data at low doses
- Cases are outliers
- No control group

Physiologic function does not follow math models
Asbestosis and Cancer have different causal mechanisms

More fibers = more scars
FEW asbestos fibers → genetic change → cancer cell → doubling → malignant tumour

Dose Response Curve

HIGHER DOSE = MORE SCARING

Cancer Development

Asbestos → Lung
“…chrysotile is quickly eliminated from the lung parenchyma but remains in the pleura, while amphiboles are present in very much lower concentrations in the pleura than in the lung.”
THE HYGIENE STANDARD FOR CHRYSOTILE ASBESTOS*

JULIAN PETO

D.H.S.S. Cancer Epidemiology and Clinical Trials Unit,
9 Keble Road, Oxford
Assuming lung fiber method is reliable

Linear dose-response
“Linear dose–response …is expected if mesothelioma were initiated by a single asbestos fibre in a single cell…”
Molecular factors

Genetic susceptibility is obvious and proven

**BAP1**

Mesothelioma attack rate low: 10/1,000,000 = huge increase

People are not mice
Humpty Dumpty sat on a wall,
Humpty Dumpty had a great fall.
All the king’s horses and all the king’s men
Couldn’t put Humpty together again.

He was susceptible
Molecular understanding
Mesothelioma genetic and epi genetic factors

Mesothelioma confounders

Linearity is not expected
Mega Mouse – linear dose response

½’ing Dose

2x # of mice

= No threshold

Low dose cases

Greenberg and Davies (1974)

Duration of exposure

1 day
Raise your hand if you have seen a black swan

Get a form from Tess
Have you seen a patient with brief low dose exposure to asbestos?

Your Name

Address:

City:_____ State:_______Country_____Mailcode______________

Email:___________________

Exposure description:

Please return to Dr. David Egilman: degilman@egilman.com
Main presentation
<table>
<thead>
<tr>
<th>Applicable evidence</th>
<th>YES</th>
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</tr>
<tr>
<td>Case Reports</td>
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<td></td>
</tr>
</tbody>
</table>
Traditional epidemiology/case reports

Black swans
Low dose cases
Gilham, et al. (J.Peto) (2016)

handling sealed asbestos waste

office worker in company handling building materials

using asbestos ironing boards at work
No asbestos fibres detected in 4 of the 14 male mesotheliomas …

Worked in high risk or construction jobs with short or occasional asbestos exposure in their work.

## Low dose cases

<table>
<thead>
<tr>
<th>Author</th>
<th>Exposure Duration</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lieben &amp; Pistawka</td>
<td>Hours</td>
<td>1967</td>
</tr>
<tr>
<td>Greenberg</td>
<td>1 day</td>
<td>1974</td>
</tr>
<tr>
<td>NIOSH Recommended Asbestos Standard</td>
<td>Single Day’s exposure to chrysotile (animal and human)</td>
<td>1976</td>
</tr>
<tr>
<td>Skammeritz, et al</td>
<td>Days</td>
<td>2011</td>
</tr>
<tr>
<td>Andrion et al</td>
<td>17 year old talc exposure</td>
<td>1994</td>
</tr>
<tr>
<td>Gordon</td>
<td>Cosmetic talc</td>
<td>2014</td>
</tr>
</tbody>
</table>
# Mesothelioma: One Day Of Asbestos Exposure

**STUDIES OF HUMAN POPULATION CARCINOGENICITY**

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Finding</th>
<th>Group and Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mixed Types of Fibers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delajarte et al (France)</td>
<td>1973</td>
<td>Evidence of association between mesotheliomas and past exposure to asbestos</td>
<td></td>
</tr>
<tr>
<td>Gobbato and Ferri (Italy)</td>
<td>1973</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Webster (South Africa)</td>
<td>1973</td>
<td></td>
<td></td>
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<tr>
<td>Greenburg and Lloyd</td>
<td>1974</td>
<td></td>
<td></td>
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<tr>
<td>Davies (UK)</td>
<td>1974</td>
<td></td>
<td></td>
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<tr>
<td>Nurminen (Finland)</td>
<td>1975</td>
<td></td>
<td></td>
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<tr>
<td>Stunn (Ger. Dem. Rep.)</td>
<td>1975</td>
<td></td>
<td></td>
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<tr>
<td>Zielhuis (The Netherlands)</td>
<td>1975</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newhouse et al</td>
<td>1973</td>
<td>Peritoneal tumors associated to heavy exposures</td>
<td></td>
</tr>
<tr>
<td>Gilson</td>
<td>1973</td>
<td>5% to 7% asbestos workers’ deaths due to mesotheliomas</td>
<td></td>
</tr>
<tr>
<td>Hammond and Selikoff</td>
<td>1973</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selikoff</td>
<td>1976</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newhouse and Berry</td>
<td>1975</td>
<td>11% asbestos workers deaths due to mesotheliomas</td>
<td></td>
</tr>
</tbody>
</table>

*Occupational exposures in some cases as brief as one day*

---

U.S. Department of Health, Education, and Welfare
December 1976
Low dose cases

Greenberg and Davies (1974)

<table>
<thead>
<tr>
<th>Case number</th>
<th>Duration of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>EW 67/70</td>
<td>14 years</td>
</tr>
<tr>
<td>EW 68/174</td>
<td>3 years</td>
</tr>
<tr>
<td>EW 68/38</td>
<td>22 years</td>
</tr>
<tr>
<td>EW 68/86</td>
<td>Unknown</td>
</tr>
<tr>
<td>S 68/71</td>
<td>15 years</td>
</tr>
<tr>
<td>S 68/31</td>
<td>30 years</td>
</tr>
<tr>
<td>S 68/23</td>
<td>Unknown</td>
</tr>
<tr>
<td>EW 68/82</td>
<td>14 years</td>
</tr>
<tr>
<td>EW 67/115</td>
<td>Unknown</td>
</tr>
<tr>
<td>EW 68/19</td>
<td>17 years</td>
</tr>
<tr>
<td>EW 68/88</td>
<td>40 years</td>
</tr>
<tr>
<td>EW 68/190</td>
<td>2 years</td>
</tr>
<tr>
<td>EW 68/186</td>
<td>Unknown</td>
</tr>
<tr>
<td>EW 68/80</td>
<td>4 years</td>
</tr>
<tr>
<td>EW 68/186</td>
<td>3 years</td>
</tr>
<tr>
<td>EW 68/80</td>
<td>1 year</td>
</tr>
</tbody>
</table>

Resident within yards of an asbestos factory; at school nearby
Resident close to an asbestos factory; probably went to school nearby;
Both parents worked in a asbestos factory
Resident worked in an asbestos factory
Resident worked in asbestos factory
Resident worked in an asbestos factory
Husband worked in an asbestos factory
Lived in a house largely composed of asbestos cement sheeting
Worked on and lived adjacent to chicken farm composed of asbestos cement buildings
Intermittent exposure to brother’s overalls contaminated with asbestos
Sawing up asbestos cement sheets to construct two sheds
## Low dose cases

<table>
<thead>
<tr>
<th>Job</th>
<th>Time</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welder</td>
<td>35 years</td>
<td>Welding rods</td>
</tr>
<tr>
<td>Salesman</td>
<td>hours</td>
<td>Applying asbestos cement to boiler</td>
</tr>
</tbody>
</table>

---

Lieben & Pistawka 1967: Mesothelioma and asbestos exposure, Arch Env. Health Vol 14 pg 559-566
...approximately 50% of the [122] patients had a cumulative exposure of <10 fibers/cm³-year.

<table>
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<tr>
<th>Applicable evidence</th>
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<td><strong>Animal Studies – Mega Mouse</strong></td>
<td></td>
<td>±</td>
</tr>
<tr>
<td><strong>Case Reports</strong></td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>
Traditional epidemiology

- No control group
- Doses are guesses
- No data at low doses
- Cases are outliers

Physiologic function does not follow math models
No control group

Churg and Warnock, Asbestos Fibers in the general population, American Review Of Respiratory Disease, Volume 122, 669-779, 1980
Traditional epidemiology

If you do not know the dose, you cannot construct a dose-response curve or a “safe” exposure level
Traditional epidemiology

Dose data is unreliable
Dose definition

Particles are a mixture of asbestos (fibers) and dust
Midget impinger cannot tell the difference between asbestos (fibers) and dust.
Asbestos and Dust...counted as the same
Particle to fiber conversion

“Fibre/dust ratio - ranging from 0.3 to 30 (fibres per ml)/mppcf ...”

with midget impinger:

Fibre exposure and mortality from pneumoconiosis, respiratory and abdominal malignancies in chrysotile production in Quebec, 1926-75 by Liddell, F D Annals of the Academy of Medicine, Singapore 0304-4602 1984-04 Vol. 13 Issue 2 suppl Page 340 - 344
McDonald QAMA/McGill

J.C. McDonald asks: “Can an inaccurate instrument like the midget impinger (MI), give an accurate result?”

Rendall responds: “..the MI is the wrong instrument on which to base standards.”
Of course, even a broken watch is right twice a day!
McDonald et al. prove that there is no fiber-particle count relationship - 13% better than blind darts.

Asbestos fibers per cc

Where wasn’t dust measured?

“No measurements were made in the open pit and maintenance departments, and only a limited number measurements were made in underground mines.”

Problem 2: How many samples?

- 4,152 samples 1948-1966 = 231 samples/year
- $1.4/5,783$ different jobs = samples per job
- Study period from 1904-1988
No simple or consistent relationship exists between particle counts taken in the past with different instruments, or between particles and fibres. Comparisons of measurements with different instruments have revealed inconsistencies in the ratio of particle to fibre counts between instruments, between personal and static samples, between different sectors of the industry, and even between different areas within a single factory. In view of these inconsistencies, the ratio of particle to fibre counts observed in parallel studies provides a very unreliable basis for converting earlier (and often much higher) particle counts to fibre counts.
Dose data problems

Effects Results

MODEL CALCULATIONS
"Garbage In-garbage Out" Paradigm

GARBAGE DATA → PERFECT MODEL → GARBAGE RESULTS

PERFECT DATA → GARBAGE MODEL → GARBAGE RESULTS
How bad is the data? (Really Bad)

McDonald studies ... The pre-manipulation results:

"In all the conditional regression analyses of the full model, i.e. with 13 exposure measures there was at least one negative regression coefficient, which taken at face value would imply a protective effect of exposure."

The Fix: Throw out the bad data, re-calculate, repeat…

“Years in the highest relevant dust category were pooled with those in the adjacent category and the analysis was repeated. This process was iterated until either all coefficients had become positive, when it was terminated, or until the only negative coefficient was for category 1; in that circumstance category 1 was eliminated from the model, which was equivalent to setting the coefficient to zero and the odds ratio to unity …” [Liddell et al., 1998]

“The Fix: Throw out the bad data, re-calculate, repeat…”

“Admittedly, there was a degree of arbitrariness in some of the pooling carried out but every effort was made to retain any ‘significant’ effects.”

MODEL CALCULATIONS
"Garbage In-garbage Out" Paradigm

GARBAGE DATA -> PERFECT MODEL -> GARBAGE RESULTS

PERFECT DATA -> GARBAGE MODEL -> GARBAGE RESULTS
Low dose, no data
all dose data is bad
Additional examples
In fact, a study done on five Canadian mines and their associated mills gave average fibres/ml/mpcf ratios varying from 1.7 to 21.8, with an overall mean of 9.1. Our own work on this subject would also confirm a major degree of uncertainty in any attempted correlation of mcpf with fibres/ml.
Surely the fact that exposure is only a guess should be emphasised and made clear. I think it is very wrong of him to say that it is inevitable that pre-war dust levels have been grossly underestimated. Harries, et-al on measurements recently of laggers who were fully protected in a space suit, recorded levels of up to 1000 f/cc in their working environment.”
Mr. Peto makes unjustified assumptions in his estimates of dose …before 1951….reasonable to assume 1936-46 were twice those in 1952 (i.e 50f/cc, with a range of possibly 20-200.)

Unpublished letter to Lancet
"..I am reluctant to accept any of the three sets of exposure data produced in the last ten years without seeing the exposure data."

— Julian Peto
Risk Assessments = “Guesstimates”

Update of Potency Factors for Asbestos-Related Lung Cancer and Mesothelioma

D. Wayne Berman
Asbestos, Inc., Albany, California, USA
Kenny S. Crump
Louisiana Tech University, Ruston, Louisiana, USA

“may not have been as quantitative as originally envisioned”

were developed from 20 studies from 18 locations, compared to 12 locations covered in the EPA 1990 update. Mesothelioma potency factors (Kq) were derived for 12 locations compared to 14 locations in the EPA 1990 update. Although the Houston area used to calculate Kq in the EPA 1990 update include one location with exposures to asbestos and three with exposures to another type, the 14 Kq’s derive in the present analyses also include 6 locations in which exposures were predominantly to chrysotile and 1 where exposures were only to crocidolite.

Address correspondence to D. Wayne Berman, Asbestos, Inc., 741 Taft St., Albany, CA 94706-1026, USA. E-mail: heman@comcast.net

Letters to the Editor

The Quantitative Risks of Mesothelioma and Lung Cancer in Relation to Asbestos Exposure: The Wittenoom Data

Received 16 February 2001

“exposure values . . . should be recognized as ‘guesstimates’ made by people who have not been trained in occupational hygiene.”

face with the general particulate (non-fibre) standards of the day. Many hundreds of such measurements were recorded for the early 1950s until 1966. The vast majority of the results were recorded as 1000+ particles per cc, indicating overflowing of the instrument, and research has found consequently that these data were never suitable for estimating airborne fibre concentrations.


## Other studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Area samples</th>
<th>Method</th>
<th>Years measured</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>South Carolina textile workers</strong>&lt;br&gt;Dement et al. (2012)**</td>
<td>X</td>
<td>Midget impinger (MI) <em>(in 1968 and 1971, both MI and PCM samples collected)</em></td>
<td>1930-1975</td>
</tr>
<tr>
<td><strong>Balangero Mine</strong>&lt;br&gt;Piolatto et al. (1990)**</td>
<td>X</td>
<td>PCM</td>
<td>1969</td>
</tr>
<tr>
<td><strong>New Orleans cement</strong>&lt;br&gt;Hughes et al. (1987)**</td>
<td>X</td>
<td>Midget impinger</td>
<td>early 1950s</td>
</tr>
<tr>
<td><strong>Connecticut brake manufacturing</strong>&lt;br&gt;McDonald et al. (1984)**</td>
<td>X</td>
<td>Midget impinger</td>
<td>1930, 1935, 1936, and 1939</td>
</tr>
</tbody>
</table>
Hodgson & Darnton respond to Criticisms:

Letters to the editor


We thank Drs. Liddell and Browne for their interest in our paper (Hodgson and Darnton, 2001), and their generally supportive comments. Between them they make a number of points which we would like to respond to. We will not deal with the comments from Drs. Liddell and Browne, (unpublished) for reasons which we have already stated.

CAROLINA COHORT

Both correspondents challenge the view that our Carolina cohort is at risk for cancer. They also question the validity of the estimates we have made for the cohort. We do not deny that the Carolina cohort is at risk for cancer. However, our estimate of the risk is based on a much larger database than was available to us. The database includes information on all residents of the county who have had medical care at the University of North Carolina Medical Center, and who have been diagnosed with cancer.

We have also been able to obtain information on cancer incidence in the county from the North Carolina Cancer Registry. This registry is based on reports from all hospitals in the county, and includes information on all cancer cases diagnosed in the county.

We believe that the database we have used is the best available for estimating the risk of cancer in the Carolina cohort.

COHORT AVERAGES

Another general criticism focuses on our use of what we have called "cohort average." We agree that this is not a perfect measure of risk, but it is the best available given the limitations of our data. We have used this measure to make our point that the Carolina cohort is at risk for cancer, and that this risk is higher than the risk in the general population.

Certainly these estimates are much less soundly based than one would wish. Some view does however need to be taken, and in presenting both range and point estimates we have sought to convey both a reasoned best estimate and the degree of uncertainty (which, of course, increases as doses fall below epidemiologically observed levels). It is difficult to convey the balance between what is reasonably arguable in the way of risk estimation, and the associated uncertainties. That is why we chose in table 11 to give...
Don’t Just do something – stand there
"Statistics are human beings with the tears wiped away."

- Irving J. Selikoff, M.D.
Wrong view ≠ need to be taken

Asbestos ban

Available since 1890
Threshold over time

Using bad data
1938 TLV 200,000 mpcf-yrs

20% asbestosis at 1/4 TLV
50% asbestosis at 1/2 TLV

Using bad data is a tradition
Doing the wrong thing is worse than standing there

1962 TLV meeting:

“Vermont …slate had thirty-five percent quartz content… and the existing feeling was [that a] threshold limit of twenty million dust particles per cubic foot of air was acceptable, and that industry accepted that, and they fought like hell to reduce it even to twenty. And we have a sanitorium that has many men who have died of silica tuberculosis because of an M.A.C. that was too high.”

New silica standard 2016
“Other evidence shows that chrysotile causes a much lower mesothelioma risk than amosite or crocidolite.\textsuperscript{12, 13}”

Citation 12

Hodgson and Darnton (2000)
“The risk of mesothelioma derived from these new data is higher by a factor of 10 than that which emerged from our meta-analysis.”
Is there a threshold? Hodgson and Darnton (2000)

- “Several lines of argument also suggest that any threshold for mesothelioma is at a very low level.”
- Some cohorts have produced mesotheliomas and no excess lung cancers.
- Occupational PMRS for British men suggest wide range of jobs for which mesothelioma rates are above background.

“All of these observations suggest that relatively brief exposures may carry a low, but non-zero, risk of causing mesothelioma.”

## How much asbestos is needed?

<table>
<thead>
<tr>
<th>Author</th>
<th>Dose</th>
<th>Result</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>LaCourt, et al</td>
<td>0 - 0.1 f/cc/years</td>
<td>OR = 4.0 (99% CI, 1.9 - 8.3)</td>
<td>2014</td>
</tr>
<tr>
<td>Rodelsperger, et al</td>
<td>0.0 - 0.15 f/cc/years</td>
<td>OR = 7.9 (95% CI, 2.1 - 30.0)</td>
<td>2001</td>
</tr>
<tr>
<td>Offermans, et al</td>
<td>0.2 f/cc/years</td>
<td>HI = 2.69 (95% CI, 1.60 - 4.53)</td>
<td>2014</td>
</tr>
<tr>
<td>Iwatsubo et al</td>
<td>0.5 - 0.99 f/cc/years</td>
<td>OR = 4.0 (95% CI, 2.0 - 8.8)</td>
<td>1998</td>
</tr>
</tbody>
</table>
Chrysotile as amphibole
“Owing to their straight splinter form harsh fibres tend to behave more like amphibole asbestos fibres when aerosolized…”

Inhalation of respirable straight fibres is associated with greater penetration to the terminal bronchioles as compared to curly fibres.”
Shape of curve at low doses unknown
Shape of low dose curve unknown
Chrysotile and Mesothelioma Mechanisms

C) Array of chrysotile fibers with bound pSV2-neo DNA. In several places DNA can be detected on the surface of ordinarily smooth fibers. The arrows point to places at which this DNA extends from the fibers.

Chrysotile carries plasmid to nucleus and induces p53 oncogene.

Lung fiber epidemiology
<table>
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<td>±</td>
<td></td>
</tr>
<tr>
<td><strong>Case Reports</strong></td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
If the only tool you have is a hammer, every problem looks like a nail

Epidemiology cannot answer every question
Does fiber counting count?
Issues - lung fiber epidemiology
J. Peto (2016)

Chrysotile
(Short fibers)
(Cancer found here)

Lung
(Amphiboles found here)
(No cancer found here)
Size cut off changes results

![Fiber Size Distribution by Fiber Type](image)

Churg and Warnock, Asbestos Fibers in the general population, American Review Of Respiratory Disease, Volume 122, 669-779, 1980
Location sampled changes results

PU = peripheral upper lobe;
CU = central upper lobe,
PL= peripheral lower lobe
CL= central lower

Churg and Warnock, Asbestos Fibers in the general population, American Review Of Respiratory Disease, Volume 122, 669-779, 1980
Location sampled changes results

Upper lobes >

Lower lobes

Lobe differences
10 fold

Most fibers in the pleura are chrysotile.

Predominant fibers in lung

Predominant fibers in pleura
Only 23 (of 151) had amphiboles


Should fiber counting count?
“This study has demonstrated that the retention of asbestos dusts in parietal pleura was related to type and size: most of the fibres were short chrysotile fibres.

The finding of only chrysotile-type fibres within the parietal pleural tissue suggests two possible explanations: fibres of all types are transported to the pleural area, but only chrysotile fibres are retained in pleural tissue; or only chrysotile fibres can migrate to the pleura.
Bad Assumptions
A building constructed on false and/or unsupported assumptions

**Assumes** Fibers <5 um do not cause mesothelioma.

- Stanton found risk at fiber lengths > 4 um

Assumes: 5 micron = causation
4.99 ≠ causation

- Short chrysotile fibers predominate in the pleura of mesothelioma cases.

Fiber size and location

**Figure 6.** Size distribution: (--) lung; (—) mesothelioma.

Lung fiber epidemiology

- Lung cancer controls creates potential for selection bias.
- **Assumes**: “only a small proportion of all lung cancers are caused by asbestos”
- Per J. Peto and Boffetta 2012 Ratio of lung cancer from meso mortality

UK approximately 2 LCs per Meso (mixed 1.9)

UK meso deaths males  2200 x 2 = 5000
Male LC deaths 20,000
Proportion is 25% NOT SMALL

Latency Not Accounted For

Half-life
Chr 1/6 yr
Croc 6 yrs
Amo 10 yrs

Exposure

- Chrysotile
- Asbestos Type
- Crocidolite
“The half-life of amphiboles in the lung has been estimated as about 6–10 years for crocidolite and perhaps 20 years for amosite. However, we have not attempted to adjust our data for elimination, for two reasons.”
Assumption 1.

- Exposures ended when imports ended

Not so: carpenters, painters, electricians, plumbers all exposed to in-place asbestos
Assumption 2.

- Fibers are 100% bio-persistent citing Tossavainen
Latency ignored

But Tossavainen did not test this; he assumed this!!

“In those calculations, the clearance of amphibole asbestos was assumed to be negligible, i.e., the effect of varying time from the exposure to the date of tissue sampling was not taken into account.”

The cumulative equation, … depends on many parameters that are subject to considerable and unquantifiable uncertainty. Although the original levels were not known, no clearance of long amphibole fibers from the non-ciliated alveolar region of the respiratory tract was demonstrable by kinetic calculations. Recent exposures to amphibole asbestos, therefore, could not be distinguished from earlier exposures since the fibers deposited in the lungs retain their initial level for decades as well as their chemical and physical properties, except for the formation of asbestos bodies.

Lung fiber count epidemiology

- Assumes exposures were equal and occurred at the same time in the same year for all occupations from 1960 > 1980

- Carpenters, painters, electricians, plumbers all exposed to varying doses and dose rates
- Work practice changes and regulations
Lung fiber epidemiology

**Technique issues**

- The authors dried lung specimens overnight in a vacuum dessicator and then ashed the specimens. Freeze drying results in less fiber loss.

- The authors do not report the use of positive or negative controls (inter-laboratory variability makes it difficult to compare results).

---


A building constructed on false and/or unsupported assumptions

- **Assumes** no difference in reliability of primary vs secondary (relative) interviewees. No data on % of secondary interviews provided

- History form not provided – Did not ask about talc exposure (Personal communication Gilham)
Assumes no synergy

Balangero Ch mine
Amosite Factory
Insulators Am+Ch

PMM

0.5 Chry
4.6 Amosite
8.6 Both

50f/cc
15f/cc
A building constructed on false and/or unsupported assumptions

When you have 6 data points you can draw a line.

Biology ≠ Math
Case reports
Why the “conversation”?  

The von Paelleske family vs
Asbestos companies argue that asbestos remediation is not cost effective.

If I hit your car and cause $1000 damage from a public health perspective, it's more cost-effective if I donate the money to feed poor children rather than compensate you.
Owns the majority of asbestos liability in US

$7.1 billion in cash and securities from Lloyd's of London
$2 billion from CNA Financial Corp.
$3.5 billion from AIG

Corporate money for research to prove chrysotile is safe - $150 million US

Money to develop a cure $0.00 - transaction costs billions per yr.

http://www.wsj.com/articles/SB10001424052748704658704576274662791668194
- Re-doing Vietnam’s Health System with $130 million from the World Bank
- Developed Women’s Health Curriculum used worldwide
- Over 20 New Family Medicine Programs in Africa
- Crowdfunding platform connecting funders to grassroots projects
THIS AND OTHER RELATED PPTS & PUBLICALLY AVAILABLE CITATIONS

Downloadable at:

WWW.IMIGEGILMANREFERENCES.COM
Supplemental slides
Chrysotile causes mesothelioma
Chrysotile causes mesothelioma

- Human epidemiology
- Fiber size and location
- Animal data
- Mechanism
- Synergy
- Analogy
<table>
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## Chrysotile causes mesothelioma – Human studies

<table>
<thead>
<tr>
<th>AUTHOR, YEAR</th>
<th>Observed / Expected</th>
<th>Relative Risk / Odds Ratio</th>
<th>P-Value (95% CI)</th>
<th>Alleged Contaminant</th>
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<tr>
<td><strong>COHORT STUDIES</strong></td>
<td></td>
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<tr>
<td>Piolatto (1990)</td>
<td>2 v. 0.20</td>
<td>10.0</td>
<td>1.21 – 36.12</td>
<td>Balangeroite</td>
</tr>
<tr>
<td></td>
<td>5 v. 0.45</td>
<td>11.1</td>
<td>3.61 - 25.93</td>
<td></td>
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<tr>
<td>Silvestri (2001)</td>
<td>2 v. 0.03</td>
<td>66.7</td>
<td>8.07 – 240.82</td>
<td>Tremolite</td>
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<tr>
<td></td>
<td>4 v. 0.04</td>
<td>100.0</td>
<td>27.25 – 256.04</td>
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<tr>
<td>Yano (2001)</td>
<td>2 v. 0.015</td>
<td>133</td>
<td>16.15 - 481</td>
<td>Anthophyllite</td>
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<tr>
<td></td>
<td>4 v. 0.015</td>
<td>267</td>
<td>72 – 682</td>
<td></td>
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<tr>
<td>Xiaorong (2005)</td>
<td>7 v. 1.167</td>
<td>6</td>
<td>2.41-12.36</td>
<td>None</td>
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<tr>
<td><strong>CASE CONTROL STUDIES</strong></td>
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<td>Rogers (1991)</td>
<td>12</td>
<td>8.67</td>
<td>1.77-48.14</td>
<td>None</td>
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<tr>
<td></td>
<td>24</td>
<td>15.7</td>
<td>6.1-40</td>
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<tr>
<td>Camus (1998)</td>
<td>Women Thetford Mining Area</td>
<td>7 v. 0.92</td>
<td>7.63</td>
<td>3.06 – 15.73</td>
</tr>
<tr>
<td>Robinson (1979)</td>
<td>Textile, Friction &amp; Packing Workers</td>
<td>17 (males) 4 (females)</td>
<td>19.46 (SMR) 27.03 (SMR)</td>
<td>10.36 – 33.28 7.36 – 69.20</td>
</tr>
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Chrysotile causes mesothelioma
Chrysotile causes mesothelioma

Human epidemiology

Fiber size and location

Animal data

Mechanism

Synergy

Analogy
Chrysotile causes mesothelioma – Animal Data

Chrysotile causes mesothelioma

Human epidemiology

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Chrysotile causes mesothelioma

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Chrysotile causes mesothelioma - Synergy

Exposure to mixtures of asbestos fibres is more dangerous than exposure to a single type. … Mixed-fibre populations were associated with 22 of the 33 mesotheliomas…

Asbestos in the lungs of persons exposed in the USA

A.M. Langer, J.P. Nolan

Studied in: occupational hygienists in the USA.

Introduction

Asbestos exposure may be associated with mesothelioma. However, when mesothelioma is found without asbestos exposure, it is generally associated with other types of commercial amphibole asbestos. Chrysotile contamination of asbestos needs to be considered as well as other sources of mesothelioma containing chrysotile.

Exposure to mixtures of asbestos fibres is more dangerous than exposure to a single type. There is a synergistic interaction between exposure to mixed-fibres as compared with the risk following exposure to either commercial amphibole asbestos alone. Mesothelioma occurred in four cases where chrysotile was the only asbestos fibre found, compared to seven cases where only a single amphibole asbestos fibre type was found. Mixed-fibre populations were associated with 22 of the 33 mesotheliomas. These numbers only slightly approximate the multiplicative model proposed by Asbestos and Cancer [15] (82–7–4).

Mixed-fibre populations were associated with 22 of the 33 mesotheliomas…

Product type and work environment control the nature of exposure, dose and disease. The majority of the mesotheliomas (22) occurred in persons whose work environments provided opportunities for asbestos as well as mixed-fibre exposure. An exposure which mitigates against dose as a controlling factor, e.g., insulation workers are exposed to high chrysotile concentrations as well as to asbestos. The data indicate that chrysotile would not cause mesothelioma, but the fibre exposure required to cause such a disease is much higher than that associated with exposure to amphibole asbestos. Exposure to a mixture of chrysotile and amphibole fibres may account for some mesotheliomas not more common. The question is not so much whether or not chrysotile is mesotheliogenic but rather how much. The data indicate that it is not as potent an agent as, for instance, chrysotile on a fibre-size basis.

Conclusion

The pulmonary tissues of a group of amphibole-exposed persons in the USA, who died of mesothelioma, contained asbestos fibres in the lungs at the greatest frequency, followed by chrysotile. The two asbestos fibres differed in their occurrence in the lung tissue. Asbestos in the lung tissue was associated with mesothelioma, even if it was not the main fibre found. The frequency of occurrence and concentration data are so derived from USA consumption data, that the surface of the latter is sparging exposure is questionable. For example, excessive asbestos consumption in the USA induced an average of 25
d of the mesothelioma deaths at age 50 and over in many states. However, it is assumed to be present in the lungs of 20% of all workers aged 50 and over of exposed workers. A similar distribution holds for asbestosis. Asbestos exposure among shipyard and insulation workers has been found previously to be associated with increased risk for mesothelioma thought to be especially associated with shipyard workers.

Mixed-fibre populations were associated with 22 of the 33 mesotheliomas. Mixed-fibre populations were associated with 22 of the 33 mesotheliomas…

Mesothelioma Risk Different fiber types synergy (Churg 1995)
Chrysotile causes mesothelioma

Human epidemiology

Fiber size and location

Animal data

Mechanism

Synergy

Analogy
Chrysotile causes lung cancer—Animal Data

Mesothelioma risk
Different occupations (Churg 1995)
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Other populations of chrysotile-exposed workers with mesothelioma

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<td>McDonald</td>
</tr>
<tr>
<td>Plasterers using Chrysotile Joint Compound</td>
<td>Stern</td>
</tr>
<tr>
<td>Wives of Canadian Chrysotile Miners</td>
<td>Camus</td>
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<tr>
<td>Australian Chrysotile Workers</td>
<td>Leigh</td>
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<td>American Plastic Factory Workers using Chrysotile</td>
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<td>East German Chrysotile Workers</td>
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<td>Danish Chrysotile Cement Workers</td>
<td>Raffn</td>
</tr>
<tr>
<td>U.S. Textile Workers</td>
<td>Dement</td>
</tr>
<tr>
<td>U.S. Railroad Workers using Chrysotile</td>
<td>Mancuso</td>
</tr>
</tbody>
</table>
Balangero

….the data suggest that exposure to chrysotile asbestos (or to the fibre balangeroite that accounts for 0-2-0.5% of total mass in the mine) is associated with some, however moderate, excess risk of laryngeal cancer and pleural mesothelioma.”

Scientific & regulatory bodies agree: chrysotile causes mesothelioma
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Garbage in ➔ Gospel out