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PROJECTIONS OF ASBESTOS-RELATED DISEASE 1980-2009

FINAL REPORT

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By

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PROJECTIONS OF ASBESTOS-RELATED DISEASE

1980-2009

Overview

It is possible to estimate the amount of asbestos-related disease that will occur in the foreseeable future. One method of projection, together with its assumptions and limitations, will form the subject of this report. The method presented here is distinguished from other possible techniques in that it is tied to events currently being observed.

Projections of future cases of mesothelioma and lung cancer depend on a number of steps, all of them starting with the number of cases of mesothelioma occurring in the United States. We begin with the cases of asbestos-related mesothelioma occurring in the late 1970's and infer the size of the asbestos-exposed populations which would be required to produce that number of cases. Using actuarial techniques and Johns-Manville (J-M) case data to provide some details of exposure timing, we then back-calculate to estimate the size of the original exposed work force from the 1930's on, whose remnants are now alive. Again using actuarial methods and drawing on known exposure-disease incidence curves, we then project the number of cases of mesothelioma and lung cancer which are likely to occur in the future in the exposed worker population.

Since the clinical manifestations of mesothelioma vary according to the intensity of asbestos exposure, we can make a limited refinement of the procedure above by classifying the projected cases as deriving from relatively heavy or relatively light exposures. This is achieved by comparing the distribution of sites of mesothelioma in known relatively heavily exposed cohorts, such as insulation workers, in whom disease is peritoneal at least half the time, with that observed in the U.S. as a whole, in which peritoneal disease occurs only 10% of the time.

Projection of the burden of asbestosis in the United States depends both on the rate of occurrence of new disease and on the prevalence of old disease, which may or may not yet have been medically diagnosed in any given individual. Accounting for prevalent, but, as yet, undiagnosed cases of old disease is necessary for asbestosis, but not for mesothelioma or lung cancer because the latter cancers are either detected or lead to death (usually both) within a period less than two years after clinical onset of disease. Asbestosis sufferers, on the other hand, may live for many years with diagnosable (but undiagnosed) disease, and represent a large pool of potential litigants who can "behave like" new cases at any time, simply by being made aware of the nature and probable origin of their disease.

We have inferred the number of prevalent asbestosis cases in the late 1970's by two principal methods. In the first, we estimate what proportion of mesothelioma cases have diagnosable asbestosis, and we compare this figure to the rate at which people with asbestosis develop mesothelioma. Knowing the approximate number of mesothelioma cases with asbestosis and the rate at which mesothelioma occurs in asbestotics, we can calculate about how many asbestosis sufferers there must be in order to account for the observed number of mesothelioma cases occurring among them. In the second method, we have drawn on another, independent aspect of the asbestosis-mesothelioma relationship. In studies of groups occupationally exposed to asbestos, the death rates from mesothelioma and asbestosis have been found to be nearly identical. Thus, projections of mesothelioma deaths in persons exposed to asbestos can be expected to give a good estimate of the number of asbestosis deaths. Several studies have provided data on the mortality rate in asbestotics, and on what proportion of the mortality is due to asbestos. The number of asbestotics is then inferred from the number of asbestosis deaths and the mortality rates in persons with asbestosis.

At this point the asbestosis projections depend on a scientific judgment which has to be made on the basis of almost no directly relevant data. The question is: do new cases of asbestosis continue to appear many years after the cessation of exposure or, after a certain lag period, does the occurrence of new cases stop? Put another way: does cleaning up the workplace diminsh the risk of those workers who have already been heavily exposed to asbestos but, as yet, have no disease? Preliminary J-M data

suggest that cleaning up the work environment does reduce the risk of those already exposed, although not immediately to zero. Asbestosis prevalence projections have been made on the assumption that new cases actually occur through 1984, and that from 1985 on, any apparent new cases represent new diagnoses of existing disease.

Several other "quick and dirty" asbestosis projections methods are also available. These depend on drawing analogies between the United Kingdom and the United States, on use of relative mortality figures, and on the extrapolation of data from x-ray surveys of exposed workers.

J-M data on women are too scanty to allow any direct estimation of the number of cases of asbestos-related disease on them. (Less than 5% of suits derive from women.) Estimating female disease has to be based on deriving approximate proportionality constants: based on the probable historical timing of female workers exposed to asbestos, the current 5% figure can be expected to decline to nearly zero over the next two decades.

The tasks and subtasks which are involved in disease projection are as follows:

1. Determine the effective number of past asbestos workers.
   a. Determine the number of cases of mesothelioma in the U.S., 1975-1979.
   b. Calculate the fraction of mesothelioma cases with a documentable history of asbestos exposure and what fraction of the exposed are likely to have been heavily exposed.
   c. Estimate the timing of the exposure history for U.S. cases.
   d. Calculate the number of workers now alive and exposed at different times in the past which would be required to account for the current observed mesothelioma incidence.
   e. Using actuarial techniques, calculate the size of the originally exposed worker population which would yield the estimated numbers of currently living, previously exposed workers.
   f. For exposure in the more recent past (which would give rise to no current disease), estimate exposure which could give rise to future disease.
      i. Use survey data to estimate exposure histories.
      ii. Use information on changing workplace environments to adjust crude exposure estimates.
      iii. Adjust all original estimates of the number of exposed workers so that the total number of cases of mesothelioma being observed is consistent with total estimates of the exposed workforce (distant past plus recent past).
2. Project mesothelioma incidence.
   a. Actuarially adjust the size of the exposed population to account for future mortality and calculate the incidence of new cases in the reduced exposed populations.
   b. Examine sensitivity of projections to component assumptions.
3. Project lung cancer incidence.
   a. As above, adjust the size of the at-risk populations to account for future mortality. Calculate the future incidence of lung cancer as a function of future age, future elapsed time from first exposure, and the future size of the population at risk.
   b. Compare projected and observed lung cancer figures.
4. Estimate asbestosis prevalence now and in the future.
   a. i. 1980-1984 prevalence using mesothelioma mortality in asbestotics.
      —How many cases of mesothelioma with asbestosis are occurring?
      —Mesothelioma incidence as in (1a).
      —Proportion of mesothelioma with asbestosis.
      —Estimate frequency of occurrence of mesothelioma in asbestotics.
   ii. Prevalence after 1984.
      —Age the 1980-1984 prevalence group using actuarial techniques.

b. 1980-1984 prevalence based on the equivalence of mesothelioma and asbestosis mortality.
   i. Derive expected number of asbestosis deaths from projected mesothelioma deaths.
   ii. Compare asbestosis deaths to death rates in asbestotics to derive an estimate of the number of asbestotics.

c. "Quick and dirty" projections.
   i. U.K./U.S. equivalence.
   ii. Relative mortality data.
   iii. Extrapolation from x-ray surveys.

d. Derive a general methodology for predicting lawsuits given propensity to sue and disease prevalence.

5. Estimate the amount of asbestos-related disease likely to occur in women.

Task 1a: Determine the number of cases of mesothelioma in the United States, 1975-1979.

The National Cancer Institute (NCI) has sponsored two major cancer incidence surveillance programs since 1969. The first, covering the period 1969-71, coordinated existing regional tumor registries and supported the establishment of new registries, permitting a direct assessment of cancer incidence for about 7% of the U.S. population; this was the Third National Cancer Survey (TNCS). In 1973, the NCI reconstituted the administrative structure of the TNCS to provide for an ongoing system of monitoring cancer incidence. This new program, named the Surveillance, Epidemiology and End Results program (SEER) has been in operation continuously since then. SEER reporting regions are Hawaii, Seattle, San Francisco-Oakland, New Mexico, New Orleans, Utah, Connecticut, Atlanta, Detroit, and Iowa. Collectively these represent about 10% of the population of the United States. In 1980, the NCI (Connelly 1980) released a detailed report of trends in mesothelioma incidence based on TNCS (1969-1971) and the first six years of SEER (1973-1978). The annual age-specific mesothelioma incidence for males in SEER is given in Table 1 below, which also provides an estimate of the total number of men developing mesothelioma in the United States in 1977. The age-specific estimated counts were obtained by multiplying the SEER incidence rates times the Census Bureau's 1977 estimates of the U.S. male population in the various age categories.

TABLE 1

Annual Age-Specific Mesothelioma Incidence for Males

Age Group	Incident Cases Per 100,000 Men Per Year	Implied U.S. Total 1977
0-19	0	0
20-24	0.02	2.0
25-29	0.07	6.1
30-34	0.20	15.2
35-39	0.17	10.2
40-44	0.37	20.2
45-49	1.05	58.9
50-54	1.59	90.8
55-59	2.09	110.1

Age Group	Incident Cases Per 100,000 Men Per Year	Implied U.S. Total 1977
60-64	3.37	147.6
65-69	3.84	143.6
70-74	5.72	148.5
75-79	6.34	100.7
		853.9

The implied total of about 854 new cases of mesothelioma in U.S. men in 1977 is probably inaccurate for a number of reasons and should be adjusted accordingly:

1. Comparison of the TNCS (1969-1971) and SEER (1973-1978) age-standardized male incidence figures shows an overall rise from 0.51 to 0.88 cases per 100,000 men per year, approximately a 10% annual increase from the midpoint of the TNCS to the midpoint of the reported SEER years (1975 ½). To obtain a 1977 incidence figure, a further 15% inflation over the SEER incidence would be appropriate. (The 10% annual increase is virtually identical to the rate of increase in mesothelioma incidence predicted by the incidence model constructed for Task 2. That model predicts annual increases of 11.2% in 1970, declining steadily to 8.4% in 1975.)

2. Since the SEER regions contain proportionately more shipbuilding areas than the U.S. as a whole, the incidence rates are overstated to the extent that mesothelioma occurs more commonly in shipbuilding areas. SEER data suggest that this is indeed the case. The age-standardized white male rates for Seattle and San Francisco are 1.42 and 1.36 cases per 100,000 men annually, while those for Utah and Iowa are 0.82 and 0.54 cases per 100,000 per year. A reasonable estimate as to the overstatement of mesothelioma due to non-representative sampling of the U.S. in SEER overall would be 10-15%, with a best guess of about 12%.

3. Finally, the diagnosis of mesothelioma is by no means easy or clear cut. Selikoff (1980) maintains that a review of all medical evidence in the deaths of U.S. insulation workers from 1967 through 1976 indicates that of 175 mesothelioma deaths, only 104 (59%) had mesothelioma recorded on the death certificate. SEER diagnostic coding is generally felt to be of much higher quality than death certificate information, but since the SEER data are regional, they necessarily derive in part from smaller hospitals with less sophistication in diagnosis than is available in cancer referral centers. A reasonable estimate for the net underreporting in SEER is about 10%.

Combining adjustments for time trends, non-representativeness, and underdiagnosis in the SEER data one arrives at a best guess for the number of mesothelioma cases occurring in U.S. men in 1977, not of 854, but of (853.9) (1.15)/(1.12)/(0.90) = 974 cases. The approximate number occurring in the 1975-1979 quinquennium would be 4870.

Task 1b. Calculate the fraction of mesothelioma cases which have a documented history of asbestos exposure, and estimate what fraction of the exposed are likely to have been heavily exposed.

Not all mesothelioma occurs in men with a documentable asbestos exposure history. Assuming essentially no asbestos exposure in low incidence SEER regions, and that the entire difference in mesothelioma incidence is attributable to asbestos, the differences between the highest and lowest mesothelioma incidence would suggest that 38% of mesothelioma in the high risk areas might be "background" incidence. (The annual incidence per 100,000 white males ranges from 0.54 in Iowa to 1.42 in Seattle; 0.54/1.42 = 38%.) In low incidence areas, the fraction of disease attributable to background would be even higher. Inquiries undertaken among mesothelioma patients have yielded estimates of the percent with an asbestos exposure history running from 16% to 76%, depending principally on whether cases come from areas with heavy asbestos-using industries. Table 2 summarizes the data from a number of sources.

TABLE 2

Proportion of Mesothelioma Cases with Asbestos Exposure History

Reference	Region; Subjects	Source of Data	Proportion of Cases with Asbestos Exposure	(%)
Peto, *et al.*, 1981	Los Angeles 1974-1978; males	Case or close relative interview	69/101 69/91[a]	(68%) (76%)
Vianna, *et al.*, 1981	New York State excluding NY City; males, 1973-1978	Death certificate Occupational record	67/193	(35%)
Vianna, *et al*, 1981	New York State high incidence counties 1968-1978	Patient or first degree relative interview	24/31 17/31[b]	(77%) (55%)
Tagnon, *et al.*, 1980	Coastal Virgina 1972-1978; white males	Patient or next of kin interview	43/56	(77%)
McDonald, *et al.*, 1973	All Canada (emphasis on Quebec) 1968-1970	Relatives and friends interview	11/69[c] 31/69[d]	(16%) (45%)
Newhouse and Thompson 1965	Patients dying at The London Hospital 1964 and earlier	Surviving relatives, medical records	40/76 31/76[b]	(53%) (41%)

a Excludes those for whom interviewee was unsure of work history

b Excludes indirect exposure (e.g. family member of an exposed person)

c "Definite" or "probable" exposures

d Includes "possible" exposure as well

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While much of the variation in Table 2 must result from real differences in the asbestos exposure histories of mesothelioma patients from different regions, there may also be a substantial variation depending on the group interpreting the exposure history. Table 3 (from McDonald and McDonald, 1980) illustrates this phenomenon. Three hundred and forty-four male cases of mesothelioma were paired with cases matched for age, sex, hospital, and year of death. The comparison cases had died with lung metastases from a nonpulmonary malignant tumor. Job histories were obtained from interview of relatives, coded and submitted to four asbestos research centers for interpretation. While there was general agreement on the proportion with "definite" and "unlikely" exposure to asbestos, there was much less concordance in the interpretation of ambiguous exposure histories. One center, the Environmental Sciences Laboratory of the Mount Sinai School of Medicine, was very much more likely than the others to interpret ambiguous histories as "probable" asbestos exposure.

The consensus United States figures (from centers 2, 3 and 4) in Table 3, when averaged, yield an overall figure for the proportion of male mesothelioma cases with a definite or probable history of asbestos exposure of 54%. This number is in the middle of the range of Table 2, and will be used as a best estimate. The proportion with definite exposure appears to be about 20%, averaging the figures from all four centers in Table 3.

A separate line of observation and inference indicates that the proportion of mesothelioma cases attributable to relatively heavy occupational exposure to asbestos is considerably less than the 54% with a definite or probable asbestos exposure history. This is based on the observation of the relative frequencies of involvement of the two major sites of appearance of mesothelioma, the pleura and the peritoneum. As indicated in Table 4, in heavily exposed industrial cohorts, the peritoneum probably accounts for about half of all cases. The most important exception to this pattern arose in a group with what (for an industrial cohort) is an atypical exposure pattern: 75% of the observation time in the group of Australian crocidolite miners reported on by Hobbs *et al* (1980) was in men with a total duration of exposure of less than 12 months. There were no peritoneal tumors documented among these men. In groups less heavily exposed, the peritoneum is less frequently involved, as indicated in Table 5. The least exposed groups are the general population series of incident mesothelioma cases, and those cases determined by direct inquiry to have had no identifiable asbestos exposure. In these groups, the proportion with peritoneal disease is on the order of 10%. See Table 6.

From Tables 4-6, it appears that substantial occupational exposure results in mesotheliomas which are at least 50% peritoneal, and that moderate exposure may result in about 20% peritoneal mesotheliomas. If this is true, then only a small fraction of the total contemporary U.S. mesothelioma incidence (9-13% peritoneal) can be attributable to heavy occupational exposure; at most, about 26% of U.S. cases (the 13% peritoneal and an equal number of pleurals) can be attributable to heavy exposure. In fact, the true proportion of heavily exposed mesothelioma cases must be less than 26%, since peritoneal tumors do arise in persons with little or no known asbestos exposure (see Table 6). The 20% with "definite" exposure in Table 3 may provide a more realistic upper limit to the heavily exposed proportion of persons who develop mesothelioma.

TABLE 3
Distribution (%) of 185 Canadian and 159 U.S. Male Case-Control Pairs According to the Probability of Occupational Asbestos Exposure as Classified in Four Centers*

Center*	Asbestos Exposure								Case-control difference for definite and probable exposures
	Definite		Probable		Possible		Unlikely		
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	
Canada (1960-72)									
1	11.9	1.1	43.8	31.4	4.3	2.7	40.0	64.9	23.2
2	11.9	1.1	20.5	14.6	21.1	15.7	46.5	68.6	16.7
3	13.5	2.7	29.7	21.1	18.9	20.5	37.8	55.7	19.4
4	11.9	1.1	22.7	13.0	22.7	27.6	42.7	58.4	20.5
U.S.A. (1972)									
1	18.2	3.8	51.6	35.2	3.8	1.9	26.4	59.1	30.8
2	18.9	3.8	31.4	18.7	20.8	18.6	28.9	58.9	27.8
3	24.5	6.3	34.0	19.5	16.4	19.5	25.1	54.1	32.7
4	18.9	3.8	33.3	15.1	22.6	27.0	25.2	54.1	33.3

*Centers: (1) Environmental Sciences Laboratory, Mount Sinai School of Medicine, New York

(2) Gesondsheitsorganisatie TNO, den Haag, the Netherlands

(3) Department of Epidemiology & Health, McGill University, Montreal, Canada

(4) TUC Centenary Institute of Occupational Health, London School of Hygiene and Tropical Medicine, London, England

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TABLE 4

Relative Frequencies of Peritoneal and Pleural Mesothelioma in Heavily Asbestos-Exposed Groups

Reference	Source Population	Peritoneal	Pleural	Mixed P-P	Other	% Peritoneal or Mixed P-P
Selikoff 1980	North American Insulation Workers 1/67-12/76	112	63	0	0	64%
Newhouse 1981 ...	English Factory Workers 2 Years Exposure	16	10	0	0	62%
Newhouse 1981 ...	English Female Textile Workers	8	12	0	0	40%
Finkelstein 1981...	Canadian Workers Receiving Asbestos Disability Benefits	4	5	0	0	44%
McDonald & McDonald 1980.	Insulation Workers, Asbestos Production and Manufacture US & Canada 1960-1972	23	29	0	0	44%
Hobbs *et al.* 1980 .	Miners & Millers of Crocidolite W. Australia 1943-1966	0	25	0	0	0%
Elmes & Simpson 1976...	Mesothelioma in UK 1/60-12/69 Classified from Medical Records as "Heavily Exposed to Asbestos"	20	64	6	0	29%

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TABLE 5

Relative Frequencies of Peritoneal and Pleural Mesothelioma in Less Heavily Asbestos-Exposed Groups

Reference	Source Population	Peritoneal	Pleural	Mixed P-P	Other	% Peritoneal or Mixed P-P
Elmes Simpson 1976	Exposed, but not heavily	10	151	13	0	13%
Chovil, *et al.* 1981	"Compensable" mesothelioma in Ontario, including exposure which was "relatively light, of short duration, in the distant past, or all of these"	9	23	0	0	28%
McDonald & McDonald 1980	Heating trades, shipyards, construction (excluding insulation workers), US and Canada 1960-1975	19	117	0	0	16%

TABLE 6

Relative Frequencies of Peritoneal and Pleural Mesothelioma in General Populations and in Cases with No Identifiable Asbestos Exposure

Reference	Source Population	Peritoneal/Pleural/Mixed P-P/Other				% Peritoneal or Mixed P-P
Connelly 1980	SEER 1973-1978 males	43	369	0	55	9%
Breslow 1982	TNCS 1969-1971 males	9	83	0	0	10%
"	U.S. Patients entering comprehensive cancer centers 1978-1980	36	234	0	0	13%
Elmes & Simpson 1970	No known exposure	7	52	4	0	11%
Baris, *et al.* 1979	Turkish villagers in a hyperendemic area	1	20	0	0	5%
McDonald & McDonald 1980	No occupational exposure, US and Canadian cases 1962-1975	37	119	0	0	24%

Task 1c: Estimate the timing of exposure in U.S. cases.

Allegations in J-M mesothelioma case data provide information on the timing of asbestos exposure in those persons who develop mesothelioma. There are 278 J-M mesothelioma cases which give an analyzable asbestos exposure history: a plausible age at first exposure (between 15 and 54 years of age), and a year of first exposure between 1930 and 1954. (See Task 1f for an explanation of the 1954 cutoff.) By five-year age groups we have identified the alleged year of first exposure to asbestos. Applying the percent alleging first exposure at various years in J-M data to the age-specific estimates of asbestos-exposed mesothelioma incidence obtained (after adjustments) from SEER, one can estimate how many cases of mesothelioma occurred among U.S. workers who were first exposed to asbestos at any given age and any given year in the past. This procedure is carried out separately for the 20% of U.S. cases of mesothelioma with presumed heavy exposure, and for the 34% with presumed identifiable light exposure, on the assumption that the relative frequencies of heavy and light exposures did not change greatly until the introduction of dust controls in the work place in the 1960's and the 1970's. Qualitative review of the J-M case data indicates that most current J-M cases are derived from the smaller, more heavily exposed portion of the work force (insulation workers, asbestos factory workers, etc.).

Task 1d: Calculate the number of workers now alive and exposed at different times in the past which would be required to account for the current observed mesothelioma incidence.

How many exposed workers are there? This question can be answered by combining the estimated counts of mesothelioma cases having exposure history with data on the incidence of mesothelioma in exposed workers.

Peto (Peto *et al,* 1982) analyzed Selikoff *et al's* (1980) data on the incidence of mesothelioma in insulation workers and found that incidence could be very closely described by the equation:

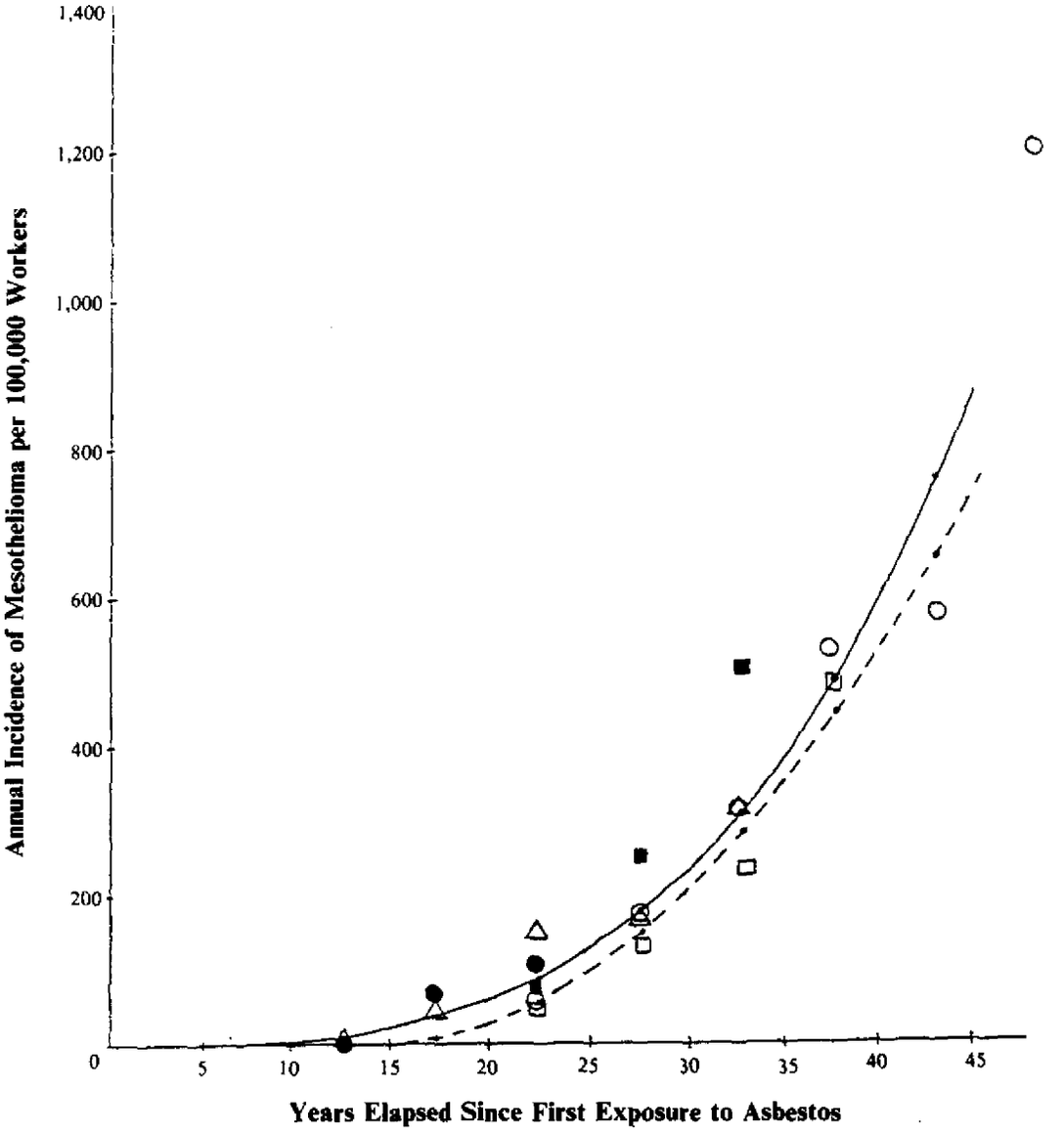
$$I = 4.37 \times 10^{-8} \times t^{(3.2)} \times P_t$$

where I is the number of cases of mesothelioma occurring per year, t is the elapsed time in years since first exposure to asbestos, and P_t is the size of the population of workers with first exposure t years previously. This incidence curve is graphed as a solid line on Figure 1 for a hypothetical population of 100,000 people.

Having derived the above equation on the basis of Selikoff's data, Peto *et al* (1982) examined its generalizability by fitting similar equations, with the same exponent (3.2), to data obtained in a variety of settings. Table 7 provides, for five studies, the Peto estimate of the leading constant term in the above equation, the number of mesotheliomas observed and predicted at five-year intervals from first exposure, and the total number of cases observed. Observed incidence rates from the five studies are plotted on Figure 1, along with Peto's curve (with the constant term calculated from Selikoff's data). All show a sharp increase beginning 15 years from first exposure and continuing—so far as the data tell—indefinitely thereafter.

FIGURE 1

Annual Incidence of Mesothelioma per 100,000 Workers
By Years Elapsed Since First Exposure to Asbestos



Legend:

——— Peto incidence curve (Peto *et al*, 1982)

. . . . . Breslow incidence curve (Breslow, 1982)

Incidence rates reported by Peto *et al* (1982) for five studies (see Table 7):

- ○ Selikoff *et al* (1979)
- △ Newhouse and Berry (1976)
- □ Peto (1980)
- ● Hobbs *et al* (1980)
- ■ Seidman *et al* (1980)

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TABLE 7

Numbers of Pleural (PL) and Peritoneal (Pt) Mesotheliomas, Both Combined (N), and Man-years (MY) of Observation in various studies. Expected Numbers (Exp) are obtained by fitting Death Rate=b (time since first exposure)$^{3.20}$, where b is constant

Study		Years since first exposure 10−	15−	20−	25−	30−	35−	40−	45−	50+	TOTAL
Selikoff et al. (1979)	Pl			2	8	15	20	6	12	2	65
N. American	Pt			1	14	32	26	19	16	7	115
insulation	N			3	22	47	46	25	28	9	180
workers (mixed	Exp			4.58	22.59	44.26	41.64	31.17	23.59	12.17	180.00
exposure;	MY			4939	12815	14711	8756	4391	2328	872	48812
b=4.37 x 10 $^{-8}$)											
Newhouse & Berry	Pl	1	3	7	5	7					23
(1976)	Pt	0	3	8	6	5					22
Factory workers	N	1	6	15	11	12					45
(mixed	Exp	2.59	6.32	10.37	12.84	12.87*					45.00
exposure; b=4.95	MY	16167	3438	9862	6423	3772					49662
x 10^{-8})											
Peto J. (1980)	Pl	0	0	1	2	2	2	0			7
Chrysotile textile	Pt	0	0	0	0	0	0	0			0
factory	N	0	0	1	2	2	2	0			7
(b=2.94 x 10 $^{-8}$)	Exp	0.16	0.52	1.10	1.77	1.69	1.32	0.44			7.00
	MY	1633	1860	1761	1496	837	414	92			8093
Hobbs et al. (1980)	Pl	1	12	13							26
Australian	Pt	0	0	0							0
crocidolite	N	1	12	13							26
miners	Exp	4.53	8.32	13.5†							26.00
(b=5.15 x 10^{-8})	MY	27172	17012	12028							56212
Seidman et al. (1979)	Pl	0	0	1	3	3	0				7
US amosite factory	Pt	0	0	1	2	4	0				7
(b=4.91 x 10^{-8})	N	0	0	2	5	7	0				14
	Exp	0.58	1.48	2.73	4.01	4.68	0.52				14.00
	MY	3628	3174	2618	2026	1383	98				12927

* 30 or more years; 32.5 assumed in calculating expected no.

† 20 or more years; 22.5 assumed in calculating expected no.

Although Peto's equation has the theoretically attractive property that its mathematical form is derivable from current theories of carcinogenesis, it is not the only possible mathematical description of the U.S. insulation worker mesothelioma incidence. Breslow (1982) has used the same data to estimate the components of a second formula which incorporates an estimated latent period as well as the exponential and constant terms used in Peto's formula. The form of this equation was proposed originally by Newhouse and Berry (1976), and in a statistical sense it fits the observations more closely than does the Peto equation. Using the symbols as above, that incidence equation is:

$$I = 1.37 \times 10^{-5} \times (t-15)^{1.846} \times P_t.$$

The better fit of this equation to Selikoff's data derives principally from the fact that it predicts no cases to occur in the first 15 years following first exposure; Peto's equation predicts a small number of cases. In fact, in Selikoff's data none were observed to occur. Breslow's function is plotted as a dashed curve on Figure 1. The two equations give very similar estimates. Throughout the ensuing analysis, Peto's equation has been used because it appears to provide estimates more consistent with the full range of reported values (as opposed to Selikoff's data alone). Nonetheless, projections carried out using the Peto equation have all been verified using the Breslow equation.

Sources reporting to J-M's legal staff indicate that there may be some overstatement in Selikoff's data of the numbers of mesothelioma cases actually occurring. The overstatement certainly appears to be the case for asbestosis, and probably is negligible for lung cancer. For mesothelioma, we have provisionally adopted a correction factor of 0.8 in Peto's and Breslow's equations relating mesothelioma incidence to asbestos exposure. This has the effect of expanding the size of the exposed population required to account for currently observed mesothelioma cases.

Given the number of cases which have occurred and knowing their alleged elapsed interval since first exposure, one can solve the equations above for P_t. We carried out this procedure for all five-year categories of age at diagnosis of mesothelioma in 1975-1979, and for all elapsed times since first exposure, giving a matrix of P_t's which corresponds to the distribution of asbestos workers alive in 1975-1979, which gave rise to mesothelioma, cross-tabulated by age and year of first exposure to asbestos.

The size of the exposed population calculated in this step is an artificial figure corresponding to "insulation worker equivalents", that is, the number of asbestos workers as heavily exposed as the insulation workers studied by Selikoff who would be required to explain the current mesothelioma experience. As outlined in Task 1b, it is likely that only some 37% of exposed mesothelioma cases (20% out of the 54%) actually arise in persons with heavy exposure. The remaining cases derive from larger populations with less intense exposure. For the purposes of mesothelioma incidence projections, there is no need to distinguish between the two situations. A population of 100,000 workers at one exposure level can be expected to give rise to the same number of cases as a population of 200,000 at half the exposure. Therefore the "worker-equivalent" has an interpretation which is independent of the actual distribution of intensities of exposure. For lung cancer, the distinction does make a difference; the larger population will have a larger "background" number of lung cancers to which the asbestos-attributable cancers must be added. In either case, the impression of J-M's legal staff at present is that most lawsuits are coming from heavily exposed plaintiffs, indicating that the distinction may be relevant for a person's propensity to sue. The cancer projections which follow (Tasks 2 and 3) therefore will be divided according to intensity of exposure.

Task 1e: Using actuarial techniques, calculate the size of the originally exposed worker population which would yield the estimated numbers of currently living, previously exposed workers.

Every group of workers now alive with first exposure at some time in the past corresponds to an originally exposed population, some members of which have died with the passage of time. We have used white male actuarial survival tables covering the years 1930-1979 to calculate the originally exposed population as follows: call the population alive in year y, of age a, with time t since first exposure, $P_{y,a,t}$. Call the same population t years previously (when they were a-t years °ld), $P_{y-t,a-t,0}$. If

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the actuarial probability for survival from age a-t to age a, starting in year y-t, is $S_{y-t,a-t,a}$, then:

$$P_{y-t,a-t,0} = P_{y,a,t}/S_{y-t,a-t,a}$$

where $P_{y-t,a-t,0}$ is the number of workers entering the asbestos-exposed work force in year y-t at age a-t who would be required to produce in year y a surviving exposed population of size $P_{y,a,t}$. If that surviving exposed population has already been derived (Task 1d) as one large enough to produce the estimated number of new exposed cases of mesothelioma of age a who report having been first exposed to asbestos t years previously, then $P_{y-t,a-t,0}$ is the size of the new workforce t years earlier which would be required to account for the current mesothelioma experience.

A modification of the actuarial survival figures was necessary before carrying out the above calculations. As noted in Task 1b, some 20/54 (37%) of the insulation worker equivalents estimated here derived from heavily exposed individuals. Selikoff has noted that insulation workers have a 37% higher overall mortality rate than the general population. As a result, a group consisting of 37% heavily exposed workers has approximately a (37%) x (37%) = 14% higher mortality rate than the general population. This correction factor has been introduced into all calculations of the survival of non-diseased, asbestos-exposed groups of insulation-worker equivalents.

Task 1f: For exposure in the more recent past which would give rise to no current disease, estimate the quantity of exposure, since this could still give rise to future disease.

The procedures of Task 1d and 1e begin breaking down when first exposures less than 20 years prior to the 1975-1979 period are considered. Few cases of mesothelioma would have as yet arisen from this period, because of the delayed rise in the mesothelioma incidence curve; thus it is impossible to work backwards to the exposed population with any reliability. Instead, we have used the reported distribution of age at first entry into an asbestos-related industry from a survey of men aged 40 and above, conducted by Elrick and Lavidge. Although that survey does not allow us to calculate the absolute number of heavily exposed asbestos workers entering the workforce each year, it does allow us to calculate the relative number entering. Altogether, the Elrick and Lavidge survey identified 214 individuals who had worked in an asbestos-using industry, of whom 79 were aware of actual exposure to asbestos dust. The results of the survey were as shown in Table 8, from which it is apparent that the distribution of years of entry into asbestos-using industries is essentially identical for men who did recall and those who did not recall direct asbestos exposure. We have based our adjustments on the larger, statistically more stable numbers of all entrants into asbestos-using industries.

TABLE 8
Year of Entry into the Asbestos-Exposed Workforce

	Workers Who Recalled Asbestos Exposure			All Workers In Asbestos-Using Industries		
Year	Number	%	Cumulative %	Number	%	Cumulative %
Before 1930	5	6.3	6.3	16	7.5	7.5
1930-1934	1	1.3	7.6	9	4.2	11.7
1935-1939	6	7.6	15.2	19	8.9	20.6
1940-1944	17	21.5	36.7	45	21.0	41.6
1945-1949	14	17.7	54.4	29	13.6	55.1
1950-1954	5	6.3	60.8	19	8.9	64.0
1955-1959	10	12.7	73.4	29	13.6	77.6
1960-1964	9	11.4	84.8	21	9.8	87.4
1965-1969	7	8.9	93.7	14	6.5	93.9
1970-1974	1	1.3	94.9	5	2.3	96.3
1975-1979	4	5.1	100.0	8	3.7	100.0

The work force was calculated directly from the mesothelioma incidence data through 1954. From 1955 on, we assigned numbers proportional to the annual and special sample number for men in the survey reporting first entry into the asbestos workforce in each quinqennium. Adding the post-1955 workers generally resulted in a small increase in the predicted numbers of mesotheliomas for

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1975-1979. Both pre- and post-1955 figures were then iteratively adjusted until: 1) the pre-1955 figures maintained the year of first exposure distribution implied by the J-M cases, 2) the post-1955 figures stood in the proportion to the pre-1955 that was dictated by the survey, and 3) the 1975-1979 mesothelioma predictions derived from the resulting distribution of exposed workers equalled the numbers actually thought to have occurred.

From 1965 on, it is probable that exposed workers faced diminishing amounts of ambient asbestos fiber. We have accounted for this by recalculating the overall workforce size (as above) but with smaller fractions of the exposed workforce assigned to the post-1955 period. (In effect, this amounts to modeling the health effects of an unchanged number of workers exposed to less and less asbestos by assuming smaller and smaller numbers of workers exposed to essentially the same amount of asbestos.) Workforce discounts used to compensate for recent improvements in the workplace were: 1960-1964, 10%; 1965-1969, 50%; 1970-1974, 75%; and 1975-1979, 100%.

Table 9 gives the number of insulation worker equivalents entering the workforce for each quinquennium 1930-1979, as estimated from J-M data directly, and with adjustment of the post-1955 figures to match the survey data in their calendar year distribution. Of particular interest is the general conformity of the worker distribution for earlier years (as inferred from J-M data, Table 9) to that actually observed in the Elrick and Lavidge survey.

Table 9 also gives the number of insulation worker equivalents entering the workforce in each quinquennium from 1930 to 1979, according to intensity of exposure. For the heavily exposed group, one equivalent can be taken to equal (more or less) one worker. For the less heavily exposed group, there may be as many as five or ten actual workers making up each insulation worker equivalent.

TABLE 9

The Dissemination of Asbestos Exposure In
Insulation Worker Equivalents Entering the U.S. Labor Force

	Heavily Exposed(1)	Lightly Exposed(2)	Total(3)
1930-1934	2,700	3,700	6,400
1935-1939	13,800	18,100	31,900
1940-1944	55,900	74,900	130,800
1945-1949	35,400	49,900	85,300
1950-1954	38,100	59,400	97,500
1955-1959	34,900	49,300	84,200
1960-1964	22,700	32,100	54,800
1965-1969	8,600	12,200	20,800
1970-1974	1,400	2,100	3,500

(1) In the heavily exposed, each insulation worker equivalent corresponds roughly to a single worker.

(2) Many lightly exposed individuals are required to make up a single insulation worker equivalent (listed in the Table).

(3) The total number of insulation worker equivalents, *not* the total of exposed workers.

Task 2a: Adjust exposed population and calculate future incidence of mesothelioma.

For every five year period in the future, we calculated the number of mesothelioma cases that would be expected to arise out of each group of workers we estimated to have entered the workforce at each age-of-entry in each calendar-quinquennium in the past. Using the notation of previous sections, call a the age in 1975-1979, and t the number of years elapsed since first exposure in year y. Call p the number of years into the future for which a projection is being made. Then the age at first exposure is (a−t), age in the projected future year is (a+p), and elapsed time from first exposure in the future is (t+p). The components of the projection equation (Peto *et al,* 1982) are:

$I_{a+p,\,t+p}$—The number of new cases of mesothelioma p years from 1975-1979 among persons then aged (a+p), with time elapsed since first exposure (t+p).

$P_{a-t,0,y}$—The number of persons entering the asbestos workforce t years prior to 1975-1979, at age (a−p), in the year y.

$S_{a-t,\,a+p,\,y}$—Actuarial survival from age (a−t) in year y to age (a+p), taking into account recorded actuarial survival for calender years prior to 1979, and assuming age-specific mortalities after 1979 to be unchanged from their late 1970's values.

K—A constant term derived from Selikoff's observation of insulation workers (Peto et al, 1981), 4.37×10^{-8} for one-year incidence, 2.19 x 10–7 for five-year incidence, multiplied by a correction factor (0.8), for possible excess diagnosis in Selikoff's follow-up.

The projection equation is:

$$I_{a+p,\,t+p} = P_{a-t,\,0,\,y} \times S_{a-t,\,t+p,\,y} \times K \times (t+p)^{3.2}$$

The estimated populations of exposed workers presented at the end of Task 1 in Table 9 yield projections of mesothelioma incidence shown in the first column of Table 10 for the years 1980-2009.

Use of Breslow's projection equation to derive the exposed population and the resultant mesothelioma incidence leads to very similar projected counts, as seen in the second column of Table 10.

Redefining K to equal 1.37×10^{-5} (multiplied again by 0.8), the Breslow projecting equation is:

$$I_{a+p,\,t+p} = P_{a-t,\,0,\,y} \times S_{a-t,\,t+p,\,y} \times K \times (t+p-15)^{1.846}.$$

TABLE 10

Projected Numbers of New Mesothelioma Cases 1980-2009 in Men With Plausible Asbestos Exposure Histories Using Two Models of Incidence

	No Latency Period (Peto)	Latency Period (Breslow)
1980-1984	3,200	3,400
1985-1989	3,500	3,900
1990-1994	3,600	4,200
1995-1999	3,400	4,000
2000-2004	2,900	3,500
2005-2009	2,100	2,500
Total 1980-2009	18,700	21,500

Task 2b: Estimate the sensitivity of mesothelioma projections to the assumptions involved.

Assumptions underlying the mesothelioma analysis fall into two categories, depending on whether they are reflected in the final mesothelioma projections in a linear or non-linear fashion. The linear factors affect the height of the projected curve, whereas the non-linear factors affect its shape.

The linear factors are those of Task 1a (corrections of trend in incidence, non-representativeness of the SEER populations, general underdiagnosis of mesothelioma), and Task 1b (fraction of mesothelioma cases exposed to asbestos). While the net effect of uncertainties in these elements may be as much as 30% either way, it is crucial to bear in mind that the ultimate projections of mesothelioma lawsuits must be tied to the number of suits currently occurring in relation to the number of cases of disease occurring ("propensity to sue"), so that these variations in absolute incidence have no final effect on projections for numbers of lawsuits.

Non-linear effects, because they affect the shape of the future mesothelioma curve, are highly relevant to projections of suits. The shape of the curve is relatively robust to large variations in the non-linear parameters. Assuming that the reported years of first exposure to asbestos in the J-M files were off by five years in either direction gives very distorted year of entry distributions (with peak employment coming before or after the war), and only shifts the incidence peak forward or backward five years, but does not change its broad, relatively flat character. Changing the age distribution of current mesothelioma cases (in the SEER data) by assigning 30% more cases to the 70 and over, or to the under-50 year old age groups shows similar five year shifts in the incidence peak. Assuming that the workplace was entirely cleaned up by 1965 slightly increases the short term projections for mesothelioma and decreased the long term ones, since the effect of recent exposures (or non-exposure) can be expected to be felt only many years in the future. Assigning all worker-equivalents the higher mortality of insulation workers leads to slightly faster decline in the pool of exposed workers, and a 5-10% drop in late (post year 2000) estimated mesothelioma incidence. Assuming that mortality of exposed workers is that of the general population leads to a 5% increase in late mesothelioma incidence.

Task 3a: Adjust the size of the exposed population and calculate future incidence of lung cancer.

The incidence of lung cancer among insulation workers has been reasonably well documented by Selikoff *et al* (1980) and others (Berry 1980, McDonald et al 1980, Henderson and Enterline 1979) to be the product of two terms: the "underlying risk" for lung cancer that would hold in the absence of asbestos exposure, and a multiplication factor resulting from exposure. The underlying

lung cancer risk is a sharply rising function of age. From the 1973-1978 National Cancer Institute report of the Surveillance, Epidemiology, and End Results program the underlying risk for white males is:

TABLE 11

Incidence of Lung Cancer—Underlying Risk

Age (years)	New Cases of Lung Cancer Per 100,000 White Men Per Year
20-24	0.2
25-29	0.6
30-34	2.6
35-39	7.4
40-44	22.8
45-49	58.3
50-54	106.8
55-59	181.7
60-64	284.2
65-69	400.9
70-74	481.5
75-79	519.0

The asbestos-multiplier calculated by Selikoff *et al* varies not with age, but with elapsed time since first exposure. Values for the multiplier are:

TABLE 12

Selikoff Asbestos-Multiplier

Time Since First Exposure (years)	Multiplication Factor
10-14	2.55
15-19	3.40
20-24	3.48
25-29	5.00
30-34	6.08
35-39	5.68
40-44	4.93
45-49	3.89

Although the data which Selikoff has assembled on insulation workers represent the largest, statistically most reliable source of follow-up information, there have been a number of other studies of exposed cohorts. These are summarized on the following page (Table 13). Among all occupational groups, insulators are matched only by factory workers for their levels of lung cancer risks. Miners and, even more so, shipyard workers, have much lower risk multipliers, the former possibly because ambient fiber concentrations are lower in mining than in processing jobs, the latter almost certainly because the category "shipyard worker" includes many people with minimal exposure.

TABLE 13

Risk Multipliers for Lung Cancer from Cohort Studies*

Source	Minimum (years following exposure)		Maximum (years following exposure)	
Insulators				
Selikoff *et al* (1980)	0	(<10)	6.08	(30-34)
Factory workers				
Henderson & Enterline (1979)	1.8	[1]	7.78	[1]
Newhouse & Berry (1979)	2.42	(<2)[2]	5.38	(>2)[2]
Peto *et al* (1977)	1.25	(10-14)	1.71	(≥20)
Cement workers				
Weill *et al* (1979)	0.77	(10-15)	3.33	(30-35)
Shipyard workers (except insulators)				
Kolonel *et al* (1980)	1.1	(<10)	1.3	(≥10)
Miners				
McDonald *et al* (1980)	0.80	(<1)[2]	2.65	(≥20)[2]
Nicholson *et al* (1979)	—	—	4.19	(40-49)
Hobbs *et al* (1980)	2.10	(0-9)	2.46	(≥15)

[1] Time data not given separately from accummulated dust exposure

[2] Time figures are for years of employment

* In each study, if several exposure levels were given, the highest is reproduced here.

The multipliers observed by Selikoff are unlikely to be purely the result of asbestos exposure. To the extent that the asbestos-exposed workers studied by Selikoff differed in their smoking habits from the general population, the multipliers include this effect as well. If part of the purpose of the projections was to estimate what fraction of cases in exposed workers were actually attributable to asbestos exposure, lack of smoking data from Selikoff's workers would represent a serious lack. In fact, the purpose of the projection is to decide how many cases of lung cancer occur *in toto* among exposed workers. For this purpose, it is sufficient to assume that the workers observed by Selikoff have approximately the same fraction of smokers as do asbestos workers in general. This appears to be a reasonable assumption, even for future projections. Although there has been a decrease in adult male smoking in the United States, the trend appears to include blue collar workers to a smaller extent than others (Surgeon General 1978).

Selikoff's multipliers above describe the experience of a cohort of workers with lifetime exposure to asbestos, and may not correctly predict the future experience of workers, after occupational exposure to asbestos has been curtailed. Observations in chrysotile miners (Berry 1980; McDonald *et al* 1980) and asbestos factory workers (Henderson and Enterline 1979) have lent strong support to the idea that relative risk for lung cancer (i.e., the multiplier) may be nearly linearly related to accumulated asbestos exposure over a fairly wide range. Selikoff's multipliers can be interpreted as reflecting a reasonably steady rise through working life, with a decline beginning around the time of retirement, that is, about the time of cessation of asbestos exposure. We have incorporated this phenomenon into the projection equations by constraining the lung cancer multipliers for each exposure cohort to decline from their 1975-1979 value at a rate of 10% per quinquennium. It should be noted that while this discounting of later multipliers fits the Selikoff data most closely, there is no *a priori* reason to expect a decline, and mathematical modeling of other, smaller bodies of data does not suggest a decline. While the values used represent our "best estimate" for projections, experts who disagreed would probably choose somewhat higher multipliers and consequently would project somewhat larger numbers of cases.

The projection equation has the following components:

$I_{a+p,t+p}$—The number of new cases of lung cancer p years from 1975-1979 among persons then aged (a+p) years, with time elapsed since first exposure (t+p).

$P_{a-t,o,y}$—The number of persons entering the asbestos workforce t years prior to 1975-1979, in year y at age (a−t).

$S_{a-t,a+p,y}$—Actuarial survival from age (a−t) to age (a+p), beginning in year y.

L_{a+p}—The underlying risk of lung cancer as determined from NCI tables for white males of age (a+p).

M_t—Lung cancer risk multiplier for elapsed time since first exposure through 1975-1979, reduced by 10% for each subsequent quinquennium.

The projecting equation is:

$$I_{a+p,t+p} = P_{a-t,o,y} \times S_{a-t,a+p,y} \times L_{a+p} \times M_t.$$

The projected incidence is calculated for each worker group entering the workforce at every age in every past year, and the projected number of cases occurring in every five-year period are summed.

The projection procedure described above is, by itself, correct only for a heavily exposed worker cohort (such as insulation workers or factory workers). For a less heavily exposed cohort, such as shipyard workers, the projection predicts only the asbestos-attributable disease, plus the background lung cancers which would be found in a population whose size corresponds to the number of insulation worker equivalents. When the insulation worker equivalent exposures are spread out over a larger number of persons, more background disease needs to be recognized in order to project the total burden of lung cancer (both spontaneous and asbestos-attributable) in asbestos exposed persons. Table 14 presents projections of lung cancer for a worker population, which, on the average, is about one-half as intensely exposed to asbestos as insulation workers. Since our best estimate is that 37% of the "insulation worker equivalents" are indeed heavily exposed, this implies that the remaining 63% of equivalents arise in workers whose exposure intensity is 2.6 times less than that of an insulation worker.

TABLE 14

Projected Numbers of New Lung Cancer Cases 1980-2009
In U.S. Men Plausibly Exposed to Asbestos

Year	Numbers of New Cases
1980-1984	17,800
1985-1989	13,600
1990-1994	10,200
1995-1999	7,000
2000-2004	4,300
2005-2009	2,220

Task 3b: Compare projected and observed lung cancer figures.

Since no part of the model used to predict lung cancer incidence is based on data from lawsuits coming in to J-M, it is possible to test partially the validity of the projections by comparing details of the J-M litigation file against the model's projections. Table 15 displays the distribution of alleged year of first exposure to asbestos among the 349 J-M cases aged 40-79 who filed suit claiming lung cancer in the years 1975-1981, and who further gave a sufficiently detailed exposure history to allow them to be classified. The percent distributions are further cross-classified by the age at which suit was filed. In parallel are the age-specific distributions of years of first exposure to asbestos for the 22,248 male lung cancer cases for the period 1975-1979 predicted by the model developed in Tasks 1 through 3. Lung cancer is less well connected with asbestos exposure than is mesothelioma, both in the medical

and in the legal communities, and so there may be an increased element of serendipity in bringing cases of disease to litigation. Nonetheless, there appears to be a fair correlation between the observed and predicted distribution of years of first exposure, particularly in the overall figures. Although the lawsuits tabulated do not represent the total number coming in to J-M (most do not have detailed asbestos exposure data), their distribution over age categories reflects a plausible pattern of litigiousness when compared to the projected distribution of lung cancers. The highest propensity to sue appears to be in the 40-49 year age group, with a gradual tailing off to age 69, and a precipitous drop thereafter.

TABLE 15

Lung Cancer: Percent Distribution of Year of First Exposure to Asbestos Products Alleged in Lawsuits (1975-1981) and Predicted by Model (1975-1979)

Age at Diagnosis /Lawsuit		1930-34	1935-39	1940-44	1945-49	1950-54	1955-59	1960-64	1965-69	1970-74	Total %	Count
40-49	L(1)	2.7	2.7	13.5	8.1	35.1	18.9	8.1	8.1	2.7	100.0	37
	M(2)	0	0	0	19.7	30.2	29.2	15.5	4.6	0.7	100.0	698
50-59	L	1.6	9.0	30.3	23.0	18.0	9.0	5.7	2.5	0.8	100.0	122
	M	0	2.7	20.3	19.5	20.7	23.0	11.5	2.1	0.1	100.0	3770
60-69	L	4.2	15.5	33.1	22.3	10.1	6.8	4.7	1.4	1.4	100.0	148
	M	3.9	11.0	35.1	16.3	14.5	15.4	3.6	0	0	100.0	8313
70-79	L	7.1	16.7	33.3	14.3	7.1	7.1	7.1	7.1	0	100.0	42
	M	0.8	10.4	56.0	20.3	12.4	0	0	0	0	100.0	9443
Total	L	3.7	12.0	30.1	20.1	15.2	8.9	5.7	3.2	1.1	100.0	349
	M	1.8	9.0	40.3	18.7	15.1	10.6	3.9	0.5	0.0	100.0	22,248

(1)L Lawsuits with analyzable exposure data registered at JM

(2)M Model projections of total number of lung cancer cases arising in asbestos-exposed men in the United States.

Task 4: Predict future asbestosis prevalence.

Unlike persons with mesothelioma or lung cancer, persons with asbestosis are likely to live many years after the onset of their disease. Much or all of that time they may be unaware that their symptoms are due to asbestosis. From the point of view of medical and legal awareness of the disease, then, the key event in the progression of a case of asbestosis is not the date of onset, but rather the date of diagnosis. For predicting the rates of diagnosis (and hence suit) the key underlying figure to examine is the prevalence of potentially diagnosable cases in the general population.

There are no direct measures of the prevalence of diagnosable asbestosis in the United States. There are, however, methods of arriving at educated guesses. One depends on the occurrence of mesothelioma in persons with asbestosis; another depends on an equivalence between asbestosis mortality rates and mesothelioma mortality rates.

Task 4a: Predict asbestosis using mesothelioma mortality rates in asbestotics.

Elmes and Simpson (1976) have reviewed the clinical, pathologic and radiographic records of 327 cases of mesothelioma occurring in the United Kingdom between 1960 and 1969. They found that 70/247 cases with chest radiographs (28%) had clear radiographic evidence of concurrent asbestosis. This figure is not a biological constant; rather it probably reflects the particluar distribution of intensities and durations of exposure to asbestos which U.K. mesothelioma cases had undergone in the 1960's. If the general historical pattern of asbestos exposure in the United States is similar to that in the U.K., then one may estimate that about 28% of the cases of mesothelioma in the U.S. in the late 1970's, or about 273 cases annually, had concurrent diagnosable asbestosis. Put another way, of all the people with diagnosable asbestosis in the United States, about 273 developed mesothelioma each year.

Three studies give rates of occurrence of mesothelioma in persons with asbestosis which are of the same order of magnitude. Berry (1981) provides the most extensive data: 25 cases of mesothelioma

occurred in 665 Englishmen with asbestosis certified for the purpose of disability insurance, followed for 4165 man-years of follow-up between 1952 and 1976. Thus, he found a rate of one case per 166 man-years. A total experience about three-fifths as large was reported by Edge (1979) who observed 7 cases of mesothelioma in 2637 man-years of observation in 429 men who had been identified by chest radiographs showing pleural plaques taken between 1964 and 1971 in an English shipyard community. His observed rate is one case per 377 man-years of observation. Least informative because of its small amount of observation is the report of Finkelstein *et al* (1981) who studied mortality among 172 workers receiving workman's compensation for asbestosis in Ontario between 1942 and 1979 followed for 733 man-years. There were three death certificate records of mesothelioma (one per 244 man-years) and six further cases identified by review of other records (total of one case per 81 man-years of observation). Totalling the experience recorded in the three studies, one obtains reports of 41 cases in 7535 man-years of observation, or one case in 184 man-years of observation. Exclusion of the six Finkelstein cases discovered only after record review would give an overall rate of one case of mesothelioma per 215 man-years. We have chosen a figure of 1 per 200 man-years as a summary figure.

As with the 28% figure for the fraction of mesothelioma cases with asbestosis, the one per 200 man-years estimate for mesothelioma in asbestosis should not be taken to be a biological constant. It too probably reflects the distribution of intensities and durations of exposure to asbestos holding roughly over the three decades ending in 1975.

If, however, we accept the rate of one case of mesothelioma per 200 asbestotics per year, and combine this with the expected number of mesothelioma-asbestosis cases derived before, i.e., 273, we arrive at an overall estimate of about 55,000 persons with diagnosable asbestosis in the United States in the late 1970's.

Expressed algebraically, the line of reasoning above is as follows. Let I be the annual incidence of mesothelioma in asbestotics; let A be the number of asbestotics in the U.S.; let M be the annual number of new mesothelioma cases in the U.S.; and let P be the proportion of those with concurrent asbestosis, then

$$A \times I = M \times P \quad \text{and}$$

$$A = M \times P/I.$$

Substituting known or estimated values:

$$A = (974)(0.28)/(1/200)$$

$$A = 54{,}544 \text{ men with asbestosis.}$$

We have gone through the above calculation separately for each age group in order to derive projected prevalent numbers of asbestosis cases at every age in the period 1975-1979.

At present it is not known for how long new cases of asbestosis will continue to develop among currently healthy workers previously exposed to asbestos, assuming that workplace contamination has been essentially eliminated since 1975, and greatly reduced prior to that. J-M's worker experience indicates that there has been a precipitous decline in new cases of asbestosis over the last decade (Chase 1981). This would argue in favor of not projecting the occurrence of new cases beyond 1985. As a best estimate then, we have based asbestosis prevalence projections on an assumption of continued new occurrence through the first half of this decade. Starting from the projected mesothelioma incidence in 1980-1984, we have projected asbestosis prevalence in each age group for 1980-1984 using the projection equation described above.

For projections beyond 1984, we have aged the populations using modified 1977 white male actuarial survival figures. The modification is based on strong evidence of very much higher mortality rates in men with asbestosis than in the general population. Berry (1981) reports on 283 deaths in asbestotics with only 108.6 expected; Finkelstein *et al* (1981) report 66 deaths in asbestotics with only 16.6 expected. Together these give an overall mortality for asbestotics 2.79 times that which would otherwise be expected. Table 16 provides our projections of annual diagnosable asbestosis prevalence for each quinquennium through the year 2009.

Of particular importance in interpreting Table 16 (and Table 18 in the following task) is that the prevalence figures are for clinically diagnosable (not necessarily diagnosed) asbestosis which would qualify for worker's compensation in the U.K. or Canada. This is inescapable, because the only

detailed survival figures available on men with asbestosis derive from these registered and monitored groups. Depending on the criteria used, very much more "asbestosis" can be diagnosed on the basis of minimal radiologic changes. Table 17 (Selikoff 1976) illustrates the problem. Chest x-rays of 1117 men were graded according to the degree of asbestosis, classified on a four point scale ranging from 0 (no disease) to 3 (severe asbestosis). The readings were cross-classified by time since first exposure to asbestosis. It is very unlikely that workers with Selikoff's minimal (grade 1) asbestosis would qualify for worker's compensation. If such workers were to be included in prevalence estimates, however, the projections of Tables 16 or 18 (Task 4b) would have to be roughly tripled.

TABLE 16

Projections of the Number of Prevalent Cases of Asbestosis In U.S. Males 1980-2009 Based on the Incidence of Mesothelioma in Asbestotics

Years	Number of Men Alive With Asbestosis
1980-1984	65,800
1985-1989	35,400
1990-1994	19,000
1995-1999	9,600
2000-2004	4,400
2005-2009	1,700

TABLE 17

X-ray Changes in Asbestos Insulation Workers

Years Since Onset of Exposure	No.	Percent Distribution by Asbestosis Grade			
		0	1	2	3
40 +	121	5.8	28.9	42.1	23.1
30-39	194	12.9	52.6	25.3	9.3
20-29	77	27.2	45.5	22.1	5.2
10-19	379	55.9	41.7	2.4	0.0
0-9	346	89.6	11.4	0.0	0.0

Task 4b: Estimate asbestosis prevalence using the equivalence between asbestosis and mesothelioma mortality.

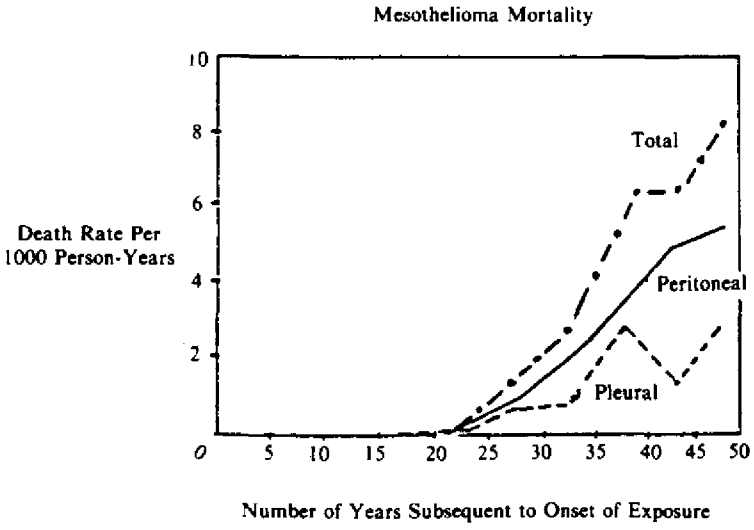
A second line of reasoning about asbestosis prevalence can lead to an independent estimate by which to gauge the results of the previous task. This is based on the near perfect identity of the time course and magnitude of asbestosis mortality and mesothelioma mortality in Selikoff's (1980) insulation worker data, combined with independent estimates of mortality in men with asbestosis.

Selikoff's (1980) observations of mortality from asbestosis and mesothelioma are summarized in Figure 2. It is of particular importance that the asbestosis mortality recorded by Selikoff is not simply an estimate of mortality in men with asbestosis, but rather specifically of mortality due to asbestosis. Berry (1981) found that 56 of 263 deaths (21.3%) in British men with asbestosis were actually attributed to asbestosis. Finkelstein *et al* (1981) found for the more inclusive category "non-malignant respiratory disease" 23 out of 61 deaths (37.7%) in Canadian men receiving workmen's compensation for asbestosis. This figure is consistent with Berry's, which is based on larger numbers and more specific reporting.

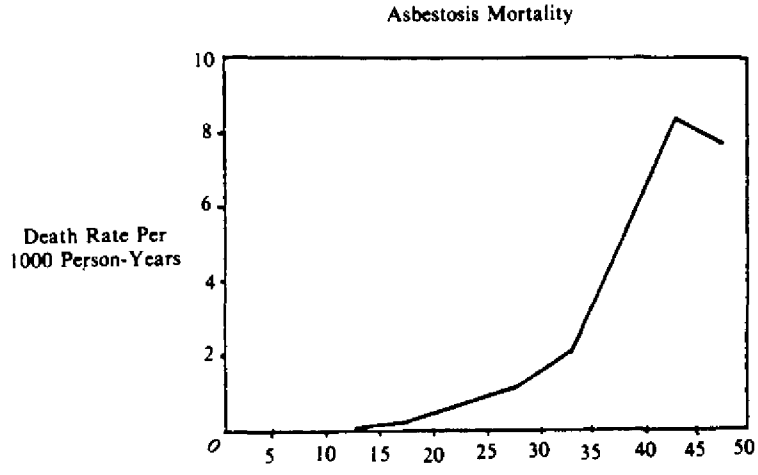
Independent estimates of mortality rates among asbestosis sufferers place them at about 2.8 times the corresponding age-specific rates in the general population (see Task 4a). For any given age group, write the mesothelioma deaths among men exposed to asbestos as M_a, and the corresponding count of all deaths in men with asbestosis as D_a. Then the Selikoff finding of an equality in the numbers of mesothelioma deaths and asbestosis deaths in insulation workers, combined with Berry's finding that 21.3% of all death is due to asbestosis, is

$$M_a = 0.213 \times D_a.$$

FIGURE 2



Deaths per thousand person-years of experience of pleural, peritoneal, and total mesothelioma among 17,800 asbestos insulation workers from 1967-1976, analyzed by duration from onset of employment in five-year periods. Ratios between observed and expected deaths cannot be computed since expected rates are not available for the general population. At least as of 45 years from onset, a decline in rates was not noted. This is consistent with the finding that cigarette smoking did not play a role in the risk of developing mesothelioma, in contrast to lung cancer.



Death rates of asbestosis among 17,800 asbestos insulation workers 1967-1976, analyzed in five-year periods of duration from onset of employment. Some decline is seen after 45 years from onset, possibly related to the added burden of smoking-induced lung disease superimposed upon asbestosis (at least in some cases) with selective survival of nonsmokers.

If the general death rate for men is G, and the number of asbestotics is A, then the total number of deaths in asbestotics is

$$D_a = 2.8 \times G \times A.$$

A is the number of interest. Combining the above equations,

$$A = M_a/(0.213 \times 2.8 \times G).$$

M_a in available for every age and future year from the mesothelioma projections (Task 2) and G is estimable for each age group from current vital statistics data.

Selikoff's data apply to insulation workers exposed to asbestos essentially all their working lives, and cannot, therefore, not be expected to give a reasonable estimate of asbestosis mortality far into the future, after the workplace has been largely cleared of significant asbestos exposure. (Mesothelioma mortality, by contrast, is affected almost entirely by age at first heavy exposure, and is not changed greatly by workplace clean-up, at least as far as concerns already exposed workers.) The problem is that discussed at the end of Task 4a: new asbestosis probably stops occurring (with some lag, perhaps 10 years) after the cessation of asbestos exposure. Thereafter mesothelioma/asbestosis relations observed previously (under conditions of extended exposure) became inapplicable to future projection. As in Task 4a, we have handled this problem by estimating prevalence based on continued new incidence through the 1980-1984 quinquennium, and have estimated subsequent prevalence by aging the 1980-1984 population as described in Task 4a. Table 18 gives the projected asbestosis prevalence figures for U.S. males 1980-2009, using this second projection procedure.

TABLE 18

Projections of the Number of Prevalent Cases of Asbestosis in U.S. Males 1980-2009 Based on the Equivalence of Asbestosis and Mesothelioma Mortality Rates

Years	Number of Men Alive With Asbestosis
1980-1984	64,000
1985-1989	45,300
1990-1994	31,000
1995-1999	19,700
2000-2004	11,400
2005-2009	5,700

Task 4c: Other methods of projecting asbestosis prevalence.

There are several "quick and dirty" estimates of asbestosis prevalence which give estimates of the same order of magnitude as one another.

1. Berry (1981) reports that 133 workers were certified annually by U.K. pneumoconiosis panels in 1973-1976 and that the median survival of the least disabled certified workers was 15 years. This gives a maximum steady-state prevalence of 15 x 133 = 2000 workers in the U.K. with certified pneumoconiosis (essentially all asbestosis). The U.S. is about four times the size of the U.K. Historical exposure patterns being equal, this implies the existence of about 8,000 asbestotic workers or former workers in the U.S. Apart from the looseness of the analogy between the U.K. and the U.S., this projection suffers from its dependence on the number of workers actually certified in the U.K. This is a lower limit to the number actually ill.

2. Burnham (1982) cites an unpublished estimate of the National Center for Health Statistics (NCHS) that there were 427,000 (range 248,000 to 606,000) pneumoconiosis sufferers in the U.S. in 1980. He also points out that the Mortality Statistics Branch of the NCHS noted 1422 deaths ascribed to pneumoconiosis in the U.S., of which 72 were ascribed specifically to asbestos. Applying the death proportionality to the pneumoconiosis prevalence gives an estimate of (72/1422)(427,000) = 21,000 asbestotics (range 12,000 to 30,000). The pneumoconiosis prevalence figure, however, was based on a

questionnaire only and is therefore likely to be an underestimate, and the reporting of asbestosis on death certificates is notoriously low.

3. The prevalence of x-ray changes in workers listed in Table 17 can be multiplied by our estimates of the size of the heavily exposed work force (Table 9), to obtain estimates of asbestosis prevalence ranging from about 18,000 to 150,000 depending on whether radiologic grade 1, 2, or 3 is used as the minimal criterion for a diagnosis of asbestosis. Although the correlation between x-ray changes and symptomatology is imperfect, the low end of this projection (18,000 grade 3 cases) would certainly represent symptomatic individuals in every case. The upper end of the projection (150,000) would include many people with few or no symptoms, whose asbestosis would be detectable by physical or radiologic examination only.

Task 4d: Derive a general methodology for predicting lawsuits as a function of asbestosis prevalence.

Although it is not the purpose of the present work to derive estimates of a person's propensity to bring suit given that he has disease, the difference between asbestosis and the cancers insofar as diagnosability and survival times are concerned calls for some comment.

Mesothelioma and lung cancer come to diagnosis fairly rapidly and reliably, and as a result the propensity to sue can be related directly to disease incidence in order to derive an expected number of lawsuits. Asbestosis is not diagnosed nearly as reliably or as quickly, so that the pathway leading from prevalent disease to a lawsuit involves two probabilistic steps: diagnosis and decision to sue. Men with asbestosis live for decades, and so may be diagnosed for the first time and sue years after the onset of diagnosable disease.

Perhaps the best way to interpret overall propensity to sue for an asbestotic man is to calculate an annual probability of suing. The pool of prevalent, asbestotic men who are potential litigants can then be thought of as being diminished with the passage of time through two effects: first, through their own mortality, and second, through their bringing suit, thus removing themselves from the pool of potential litigants by becoming active litigants. Over years, then, a constant propensity to sue acts on a diminishing pool of potential litigants to produce a declining annual number of lawsuits. By way of illustration, Table 19 gives the expected number of lawsuits by quinquennium, assuming asbestosis prevalence pools as listed in Tables 16 and 18, with cases appearing (and being removed from the pools of potential litigants) at a rate corresponding to suits from 9% of all potential litigants appearing each year.

TABLE 19

Projections of Asbestosis Lawsuits
Assuming 9% of Prevalent Cases (Non-Litigants)
Bring Suit Each Year

	Method Of Projecting Asbestosis	
Years	Meso Incidence in Asbestotics	Meso-Asbestosis Mortality Equivalence
1980-1984	24,800	24,100
1985-1989	8,300	10,600
1990-1994	2,800	4,500
1995-1999	900	1,800
2000-2004	200	700
2005-2009	100	200

The 9% figure was chosen for Table 19 so as to yield current lawsuit rates for the present quinquennium. Bear in mind that the rapid decline of lawsuits in Table 19 is the product of two factors, which hold true only for workers with symptomatic asbestosis. The first is the high mortality rate in these men, discussed in Task 4a; the second is the finite (though large) size of the pool of potential litigants. From Table 17 it should be apparent that the number of workers with minimal disease

(Grade I) is very much larger than the number of seriously affected workers. If in fact a large number of lawsuits derive from the relatively well, exposed population, neither of the conditions on which Table 19 is predicated would hold: mortality in the minimally diseased is not much elevated, and the number of minimally diseased persons is so large that current litigation rates will not result in any meaningful depletion of the pool of potential litigants. Limited J-M data suggest that, in fact, lawsuits from asbestotics do not decline as rapidly after last exposure as one would anticipate from Table 19. In effect, Table 19 represents minimal projection. If only a fraction of current cases are coming from symptomatic cases, then the symptomatic pool is being depleted more slowly than projected in Table 19. Symptomatic cases will come in over a longer period, and the remaining, minimally diseased cases will continue to flow in at a rate (determined by socio-legal factors) which is unlikely to be bounded by purely medical or epidemiological factors such as population mortality rates or depletion of a pool of injured workers. Taking all of these factors into consideration, a reasonable central projection of the number of lawsuits seen from 1982 on is likely to be about 45,000, with a reasonably firm lower bound of 30,000 and a very indefinite upper bound on the order of 120,000.

Task 5: Estimate the amount of asbestos-related disease occurring in women.

Approximately 5% of the lawsuits being filed with J-M derive from women. This number is consistent with an estimate from a variety of sources of about 10% of the asbestos-exposed World War II workforce being female, with a diminished fraction after the war. Exposed female workers still alive can be expected to have an age-at-first-exposure distribution which is even more concentrated in the war years than that of men. The consequence of this is that asbestos-related disease will have reached its peak in women earlier than in men, and is probably past that point already. The number of female cases in J-M is too small to make a direct test of this hypothesis. Probably the most reasonable projection of female cases would involve accepting the current 5% figure and projecting the proportion of female cases to taper off gradually to a negligible number by the year 2000.

REFERENCES

Baris, YI, Artvinli, M and Sahin, AA. (1979) Environmental mesothelioma in Turkey. Annals New York Academy of Sciences *339*:423-432.

Berry, G. (1981) Mortality of workers certified by pneumoconiosis medical panels as having asbestosis. British Journal of Medicine *38*:130-137.

Breslow, N. (1982) Unpublished review of NCI data.

Burnham, CE. (1982) Unpublished letter to Norman Breslow, June 2, 1982.

Chase, G. (1981) Preliminary results from a morbidity study of domestic J-M asbestos-using locations. Johns-Manville Corporation internal document, July 30, 1981.

Chovil, AC, McCracken, WJ, Dowd, EC, *et al.* (1981) Occupational cancer: experience in Ontario. Canadian Medical Association Journal *125*:1237-1241.

Connelly, RR. (1980) Mesothelioma incidence in the United States. Presented at the Workshop on Opportunities for Research and Education in Asbestos-Related Disease, Bethesda, MD, June 17, 1980.

Edge, JR. (1979) Incidence of bronchial carcinoma in shipyard workers with pleural plaques. Annals New York Academy of Science *330*:289-294.

Elmes, PC and Simpson, MJC. (1976) The clinical aspects of mesothelioma. Quarterly Journal of Medicine *XLV*:427-449.

Finkelstein, M, Kusiak, R, and Suranyi, G. (1981) Mortality among workers receiving compensation for asbestosis in Ontario. Canadian Medical Association Journal *125*:259-262.

Henderson, VL and Enterline, P. (1979) Asbestos exposure: Factors associated with excess cancer and respiratory disease mortality. Annals New York Academy of Sciences *330*:117-126.

Hobbs, MST, Woodward, S, Murphy B, *et al.* (1980) The incidence of pneumoconiosis, mesothelioma and other respiratory cancer in men engaged in mining and milling crocidolite in Western Australia. In: *Biological Effects of Mineral Fibres,* J. C. Wagner (ed.), vol. 2, Lyon IARC, pp. 615-625.

Hughes, J. and Weill, H. (1980) Lung cancer risk associated with manufacture of asbestos-cement products. In: *Biological Effects of Mineral Fibres,* J. C. Wagner (ed.), IARC Scientific Publication No. 30, IARC, Lyon.

Kolonel, LN, Hirohata, T, Chappell, BV, *et al.* (1980) Cancer mortality in a cohort of naval shipyard workers in Hawaii: Early findings. Journal of the National Cancer Institute *64*:739-743.

McDonald, AD and McDonald, JC. (1973) Epidemiologic surveillance of mesothelioma in Canada. Canadian Medical Association Journal *109*:359-362.

McDonald, AD and McDonald, JC. (1980) Malignant mesothelioma in North America. Cancer *46*:1650-1656.

McDonald, JC, Liddell, FDK, Gibbs, GW, *et al* (1980) Dust exposure and mortality in chrysotile mining, 1910-1975. British Journal of Industrial Medicine *37*:11-24.

Newhouse, M. (1981) Epidemiology of asbestos-related tumors. Seminars in Oncology *8*:250-257.

Newhouse, ML and Berry, G. (1976) Predictions of mortality from mesothelial tumors in asbestos factory workers. British Journal of Industrial Medicine *33*:147-151.

Newhouse, ML and Berry, G. (1979) Patterns of mortality in asbestos factory workers in London. Annals New York Academy of Sciences *330*:53-60.

Newhouse, ML and Thompson, H. (1965) Mesothelioma of the pleura and peritoneum following exposure to asbestos in the London area. British Journal of Industrial Medicine *22*:261-269.

Peto, J, Doll, R, Howard, SV, *et al.* (1977) A mortality study among workers in an English asbestos factory. British Journal of Industrial Medicine *34*:169-173.

Peto, J, Henderson, BE and Pike, MC. (1981) Trends in mesothelioma incidence in the United States and the forecast epidemic due to asbestos exposure during World War II. In: *Quantification of Occupational Cancer*, R. Peto and M. Schneiderman (eds.), Banbury Report 9, Cold Spring Harbor Laboratory, pp. 51-69.

Peto, J, Seidman, H and Selikoff IJ. (1982) Mesothelioma mortality in asbestos workers: Implications for models of carcinogenesis and risk assessment. British Journal of Cancer *44*.

Selikoff, IJ, Hammond, EC and Seidman, H. (1980) Latency of asbestos disease among insultation workers in the United States and Canada. Cancer *46*:2736-2740.

Surgeon General (1978) *Smoking and Health*. U.S. Dept. of Health Education and Welfare.

Tagnon, I, Blot, WJ, Stroube, RB, *et al.* (1980) Mesothelioma associated with the shipbuilding industry in coastal Virginia. Cancer Research *40*:3875-3879.

Vianna, NJ, Maslowsky, J, Roberts, S, *et al.* (April 1981) Malignant mesothelioma: Epidemiologic patterns in New York State. New York State Journal of Medicine pp. 735-738.

Scientist says chemical make-up not to blame

Asbestos-fibre size 'cancer-causing'

By HARRY NELSON

Asbestos causes cancer because the fibres are of a certain microscopic size, not because of the chemical composition of the asbestos, a National Cancer Institute scientist has reported.

Very fine fibres of asbestos, glass or sapphire caused a high incidence of cancers in experimental rats, but coarse fibres or powdered material of the same composition rarely caused cancer, according to Dr. Mearl F. Stanton.

Dr. Stanton reported that cancer-causing fibres were about one-hundredth as thick as an eyelash and less than one-tenth as long (between one-half and five microns in diameter and 80 microns long).

Asbestos fibres have been strongly linked with a type of human cancer called mesothelioma which affects the membranes lining the lungs and abdomen. This type of cancer is rare in the general population but very common among asbestos workers.

Asbestos is second only to cigarette smoke as a cause of lung cancer, according to the National Cancer Institute.

Stanton, whose research was done at NIC's laboratory of pathology, presented results of his rat studies at a conference on the biological effects of asbestos held in Lyon, France. His coworkers were Mrs. Constance Wrench and Miss Eliza Miller.

Several months ago Stanton reported on studies in which asbestos-covered glass mesh pads were implanted directly against the membrane lining of rats. The membranes later were examined for cancer at the site of asbestos exposure.

The three chemically distinct types of asbestos (crocidulite, chrysotile and amosite) were used in the experiments. Also tested separately were two metals which commonly contaminate asbestos and fine particles of silica, the major constituent of asbestos.

The rats exposed to the asbestos-fibre-coated glass had high rates of mesothelioma — 58 to 75 per cent of the 450 rodents in the study.

The rate of cancer production by various asbestos samples did not depend on the presence or absence of impurities. Nether of the two metals which commonly contaminate asbestos produced any cancers, and the fine particles of silica produced only one mesothelioma among 48 rats.

Stanton concluded that neither the chemical composition of asbestos nor the presence of impurities could account for the cancer-causing potential.

When asbestos fibres were ground to very short submicroscopic lengths, the cancer rate was less than half that in rats exposed to natural-length fibres.

The glass-mesh pads without asbestos did not cause cancer, but when the glass was treated to reduce it to small fibres about the size of asbestos fibres mesothelioma did occur.

None of 150 rats exposed to two samples of fully pulverized asbestos, non-fibrous aluminum oxide or two samples of glass with large fibres have so far developed any cancer, Stanton said.

"We know that asbestos fibres cause cancer in man," he said. "We have no evidence on whether other kinds of fibres will also prove hazardous (in man)."

References

[1] Ramazzini, B. quoted in ref. 3
[2] Fowling, G., 'Cement eczema and chromium allergy'. Thesis, Univ. of Bergen, School of Medicine, 1970
[3] Calnan, C. D., *J. occup. Med.*, 1960, 2, 15
[4] Fregert, S. & Gruvberger, B., *Berufsderm.*, 1972, 20, 238
[5] Kanan, M. W., *Brit. J. Derm.*, 1972, 86, 155
[6] 'Technical report on admixtures for concrete'. *London: The Concrete Society*
[7] Meneghini, C. L., personal communication
[8] Burrows, D. & Calnan, C. D., *Trans. St. John's Hosp. Derm. Soc.*, 1965, 51, 27
[9] Meneghini, C. L., Rantuccio, F. & Riboldi, A., *Berufsderm.*, 1963, 11, 131
[10] Miescher, G., Amrein, H. P. & Leder, M., *Dermatologica*, 1955, 110, 266
[11] Wahlberg, J., *Berufsderm.*, 1969, 17, 184
[12] Samitz, M. H., Gross, S. & Katz, S., *J. invest. Derm.*, 1962, 38, 5
[13] Cronin, personal communication
[14] Fregert, S., personal communication
[15] Fregert, S., Gruvberger, B. & Heijer, A., *Berufsderm.*, 1970, 18, 254

Occupational disease in road and building industry

Respiratory disease

Peter C Elmes

That part of the human lung where oxygen passes through into the blood stream in exchange for carbon dioxide is made up of tiny chambers called alveoli. These are lined by a layer of cells so thin that it took the electron microscope to prove that they actually existed. To preserve these cells from drying and breaking, a layer of moisture lies between them and the air in the lung, moisture whose surface tension is reduced by a surfactant to prevent the alveoli from emptying completely when you breathe out.

This delicate arrangement is protected from damage from dust by the extremely efficient filtration, moistening and warming system provided by the nose, the trachea and bronchial tubes. Coarse particles of dust are removed by the hairs at the entrance to the nose. From there on down the airways are lined by cells coated with a layer of watery jelly known as mucus. This mucus layer is kept moving by cilia, tiny hairs which wave in a coordinated manner so as to propel the mucus both from the lung and the nose into the back of the throat where it is swallowed. As air is drawn into the lungs it passes down tubes which branch repeatedly into smaller and smaller tubes. At each branching the airflow is thrown into a vortex which spins out the heavier dust particles until they touch the mucus lining in the tubes and become caught. The dust particles caught by the mucus are cleared from the tubes of the normal lung within 20 minutes of inhalation and end up in the stomach.

Size and shape of dust particles

The system of filtration is so efficient that only a small range of particles reach that part of the lung where gas exchange occurs. If deposited there particles can do harm. The vortex clearance of the particles from the air stream is proportional to the sedimentation rate of the particles in moist air. For approximately round particles anything larger than 5μm is filtered off. Particles between 5 and 0·5μm tend to be retained in the alveolar part of the lung because they land beyond the mucus escalator. Particles below 0·5μm tend to remain suspended in air and be breathed out again without doing any harm. Elongated particles such as vegetable and mineral (asbestos) fibres sediment in air at a rate proportional to their transverse diameter. This means that fibres at 100μm or more long could get down into the lung provided they were thin enough. Furthermore, a long particle may get caught at one of the places where the tubes divide and be driven through the wall into the underlaying tissue when the person breathes out. Fortunately most vegetable fibres (cotton and so on) and wool or hair are too coarse to get very far down the airway. Almost all commercial glass fibre is also too coarse. The molecular structure of asbestos is such that it readily splits lengthways into very fine fibres. Chrysotile, the most widely used commercial asbestos readily breaks up into bundles of fibres only 200–300Å in diameter, amosite and crocidolite easily form fibres in the 600 to 1200Å range. Bundles of this thickness, and from 1 to say 150μm in length, would be retained in the lung provided they were straight. In practice dust particles of amosite and crocidolite are straight and a large proportion of inhaled particles of this size range are retained in the lung. Because they are curved the fine fibres of chrysotile are more readily caught by the filter system and are less likely to be forced through the bronchial walls into the tissue. It is probably for this reason that chrysotile dust is less likely to cause lung damage than similar dust derived from amosite or crocidolite.

In general, the size of the dust particle generated by any process depends on the speed of impact. Hand-driven tools produce very little respirable dust but high-speed drills, crushers, saws, and so on produce a high proportion of fine dust which, unless it is accompanied by larger particles, is invisible to the naked eye. In time dust particles tend to aggregate with each other and especially with particles of moisture to form larger particles which are removed by the respiratory filter. Therefore dust is most dangerous close to the point at which it is formed.

Chemical nature of dust

A dust particle, irrespective of its chemical nature, will create a disturbance when it lands on the lining of the airway and therefore most people cough and wheeze when they

Professor Elmes of Queen's University, Belfast delivered this paper at a meeting of the Road & Building Materials Group of the SCI in London on 23 November 1972.

part inhaling even inert dust. The particles which get through the filter to be retained in the alveolar or gas exchange part of the lung cause no immediate disturbance. If they are inert, like the iron particles retained by an arc welder, they will be packed away in special cells in the lung and remain there for the rest of the individual's life. Silica dust is not inert and as long as it remains in the lung it dissolves to give an acid which destroys cells while the lung tries to imprison the particles in a scar. The process of cell death and scar formation makes the lung stiff so that it becomes more and more difficult to use because of the work required getting the air in and out.

Although all asbestos minerals are silicates they do not behave like pure silica particles. They cause damage to the lung apparently because of their needle-like shape rather than because of the release of a toxic chemical. Asbestos fibres become coated with brown material and may be identified in the lung 30 or more years after they were inhaled. From the occupational health point of view, asbestos differs from silica in two important ways. Firstly, particles of respirable size may be released from prepared asbestos by simple handling, high-speed impacts are not necessary. Secondly, although chemically inert, a heavy load of dust particles continues to damage the lung for many years after exposure has ceased.

History of asbestos usage

Asbestos was used by prehistoric man in Finland to reinforce clay cooking pots, and by the Greeks and Romans to make wicks for altar lamps and shrouds for emperors. Its special properties were not fully appreciated until the middle of the nineteenth century when fireproof insulation became essential in the manufacture of ships and locomotives, anywhere where high pressure steam was generated from a furnace and boiler. Old mines in Northern Italy and Finland were enlarged and then large deposits in eastern Canada, South Africa and Siberia were discovered. Very large quantities of cheap fibre became available by the end of the first world war. Until that time asbestos cloth quilts and boiler compound (a mixture of magnesia and fibrous asbestos) were the main end product, both being used for insulation.

Between the wars and following the second war, the strength, durability and cheapness of the material was appreciated increasingly. Asbestos is now mainly used to strengthen cement products such as corrugated roofing and cladding boards, pipes and heat-resistant cladding of the steel framework of buildings. This consumes over 90 per cent of the world production of asbestos. Reinforcement of plastic tiles and so on and pure insulation comes next, and then very small quantities in certain special filters and other uses. The main technical problem at the present time is whether asbestos is really essential in the asbestos cement products or whether a cheap safe substitute can be found.

Occupational hazards of asbestos

Asbestosis

Because of its chemically inert nature, manufacturers and workers handled asbestos like wool without fear of the consequences until 1930. Cases of lung damage in asbestos workers had been reported by doctors from 1900 onwards, but were usually attributed to a modified form of tuberculosis. It was not until a survey of asbestos factory workers was carried out by the factory inspectorate that it was realised that many workers were dying of lung fibrosis within 15 years of first exposure.[1] Death was due to a progressive replacement of the lung by scar tissue resulting from its destruction by very large numbers of asbestos fibres – perhaps a million fibres in every millilitre of lung.

Regulations were introduced in the asbestos textile and parts of the asbestos cement factories to control the dust levels. As a result asbestosis among factory workers entering the industry since 1933 has almost disappeared. Studies with chrysotile dust indicate that if the dust level is kept below 2 fibres per millilitre of air, less than 1 per cent of workers develop asbestosis before they retire after 50 years' work. This is a cumulative limit of 100 fibre years/ml, and appears to hold good irrespective of the age at which the worker is first exposed.[2] Similar standards have been applied to the use of amosite and crocidolite but are probably not satisfactory for reasons which will appear later. This standard of less than 2 fibres per millilitre in the breathing zone of workers in asbestos factories has been achieved in most factories in Britain. It was not applied to the handling of asbestos in the user industries such as shipbuilding, civil engineering and the manufacture of cars and so on.

The incidence of new cases of asbestosis among asbestos factory workers began to fall soon after the introduction of the new regulations in 1933. By the early 1950s it was already apparent that the only serious new cases were derived from the diminishing population of workers who had been employed before 1933. However, new cases of asbestosis were being reported from insulation workers in factories and shipyards and by the middle 1960s these cases exceeded the cases arising from the asbestos factories and the total number of cases certified each year continued to rise. The new regulations, if applied to all the user industries, should see a change for the better in the number of cases of asbestosis certified in the next few years.

Lung cancer

Lung cancer, especially in men who smoke, has become increasingly common during the last 30-40 years so that the first few reports of cancer in asbestos workers were regarded as chance occurrences. However, the Medical Inspector of Factories in his report for 1947 noted that 17 per cent of men dying after certification for asbestosis had lung cancers as well.[3] This was beyond the realms of chance and provoked an investigation in one particular factory population[4] which confirmed an increased risk of lung cancer in workers with asbestosis. However, this, and a follow-up study published in 1968,[5] suggested that the risk was only serious in factory workers who had been exposed before the introduction of the 1933 regulations. There remained the problem of men being exposed to asbestos in the user industries. By 1965 Buchanan had shown[6] that over 50 per cent of men certified as suffering from asbestosis in Britain died with lung cancer and this proportion may now be about 70 per cent. Reports from America indicate that this lung cancer risk may only affect cigarette smokers and that asbestos does not cause a serious increase in lung cancer in non-smokers.[7] If it proves possible to apply the current dust regulations to the construction industry then the risk of lung cancer may be avoided, but men who have already been exposed to large amounts of dust are likely to develop their lung cancer at about the age of 55 or 60 if they continue to smoke irrespective of their future dust exposure. The withdrawal of men from work because on X-ray or other medical testing they show evidence of heavy dust exposure does not reduce the risk of cancer as far as we know.

Mesothelioma

In the late 1950s a number of cases of a rare cancer of the lining of the chest wall occurred in South Africa, a number far in excess of any previously reported. These patients had asbestos dust in their lungs and had at some time or other lived near (but not necessarily worked in) the blue asbestos (crocidolite) mines in the North West Cape province.[8] Fifteen such cases of mesothelioma had already been reported from Belfast and subsequent studies there, in London, in other shipyard cities and in New York have confirmed the relationship between this tumour and asbestos exposure. The worrying aspects of this work have been the slight degree of exposure to the dust (3-6 months handling asbestos filter pads for gas masks *with* local exhaust ventilation) and the very long latent period between exposure and the development of the tumours. The average age of death from this tumour in Belfast is about 60 years and the mean interval between first exposure to asbestos and the development of the tumour is 43 years.[9]

Much work has been done on this tumour during the last 15 years. It now seems likely that crocidolite is responsible for the majority of cases but that amosite may be responsible for some. It is possible that chrysotile does not produce this tumour at levels of exposure which have existed up to the present time, although it can cause the tumour in experimental animals. It seems wise not to allow any exposure to crocidolite dust in any industry and to restrict amosite to essential uses. But restrictions applied at the present time are not likely to affect the rising incidence of this tumour for many years to come. There must be many thousands of individuals who have already received their dose of dust and who will develop this tumour when they reach the age of 60 (give or take 15 years either way). Stopping further exposure to dust and stopping smoking are both unlikely to influence the outcome.

The tumour may be present for weeks or months before the patient is aware of it. It usually starts in the chest but can start in the abdomen. The patient is usually still in good general health when he first consults his doctor because of a dull ache or heaviness in one side of his chest. Unproductive cough and breathlessness soon follow. At this stage the patient is sent to hospital and investigations reveal the presence of fluid (which may contain blood) or scarring around one lung. It can be difficult to establish the diagnosis for certain without an operation and even then the diagnosis may remain doubtful. There is no satisfactory treatment and patients usually die about a year to eighteen months after the onset of symptoms. Increasing breathlessness is the main difficulty and this can sometimes be relieved by the periodic withdrawal of fluid from the chest. Towards the end the patients may develop difficulty in swallowing and lose weight rapidly. Pain often becomes severe and is difficult to control with drugs. This may persuade doctors to try various forms of treatment including operations which are of little value. In some cases these patients may survive for two to three years after the onset of pain and one can but admire the fortitude with which many cope with this situation.

From being a rare disease this kind of cancer is now occurring at a rate of 100 to 150 new cases each year and this incidence is likely to continue to rise.

Specific industrial risks

The general description of the hazards to health which may result from exposure to asbestos is alarming and is difficult to interpret in relation to specific occupations or industries. The studies which led to the regulation of the dust concentrations in asbestos factories were only done on textile workers. For the next 20 years attention was focused on these workers and men doing similar work in asbestos cement factories. Even in these situations dust analysis was not done regularly and it is difficult to estimate the cumulative dust exposure of older men who have been in the industry since boyhood. In most user industries, especially those like construction work which moves from site to site, information on dust levels does not exist. Changing materials, changing techniques and the use of high-speed tools all alter dust conditions so that the prediction of the health hazard in a working population from the records of past exposure is impossible. The only way to determine the hazard is to study the health of the workers. No relevant study has yet been made in the construction industry. Such studies are urgently needed and a study done on insulation workers in Belfast illustrates the way in which studies can be carried out.

The conventional way of investigating an industrial health hazard is to examine a representative sample of working men and see whether they show any signs of disease when compared with a sample of the general population. This kind of survey is effective in revealing disease which develops relatively early in a man's working career provided he is able to remain at work after the disease has become apparent. It was effective in demonstrating the presence of asbestosis in textile workers in 1930[1] only because conditions were very bad. In Belfast 50 insulation workers were selected and compared with 50 men from the municipal transport department who were matching them for age, height and smoking habits. There was no difference between the two groups of men, either from the point of view of their general health, or as a result of X-rays and detailed tests on their lungs. Both groups contained some older men and heavy smokers who had shortness of breath, a cough and the other features associated with chronic bronchitis.[10]

This preliminary study was followed by a thorough examination of all the insulation workers in Northern Ireland who were willing to spend half a day with us. 93 Per cent of the men came and they appeared normal for their age. As in the first sample the older men tended to have the symptoms of bronchitis and the X-rays showed a high proportion of abnormalities in these older men. In a very few it was possible to say for certain that they were suffering from asbestosis, but even in these it was hard to say whether their asbestosis was causing them as much trouble as their chronic bronchitis. There were no cases of lung cancer or mesothelioma picked up in this survey of men at work.[12]

The third part of the investigation consisted of going over the records of the trades union branch to which these insulation workers belong and the records of the contractors who employ them to find out who was doing insulation work in 1940.[11] One sinister piece of information which came from the union was that there were no insulation workers drawing their old age pension from their contributory pension scheme. It was possible to identify 165 men at work in 1940 and Mrs Simpson had the task of finding out what had happened to them. If they had died we then found out both from the Registrar General and the hospital records the cause of death. Wherever possible this diagnosis was confirmed by re-examination of preserved tissues removed at operations or post-mortem. This was necessary because in the early part of the period (1940-55) most pathologists were

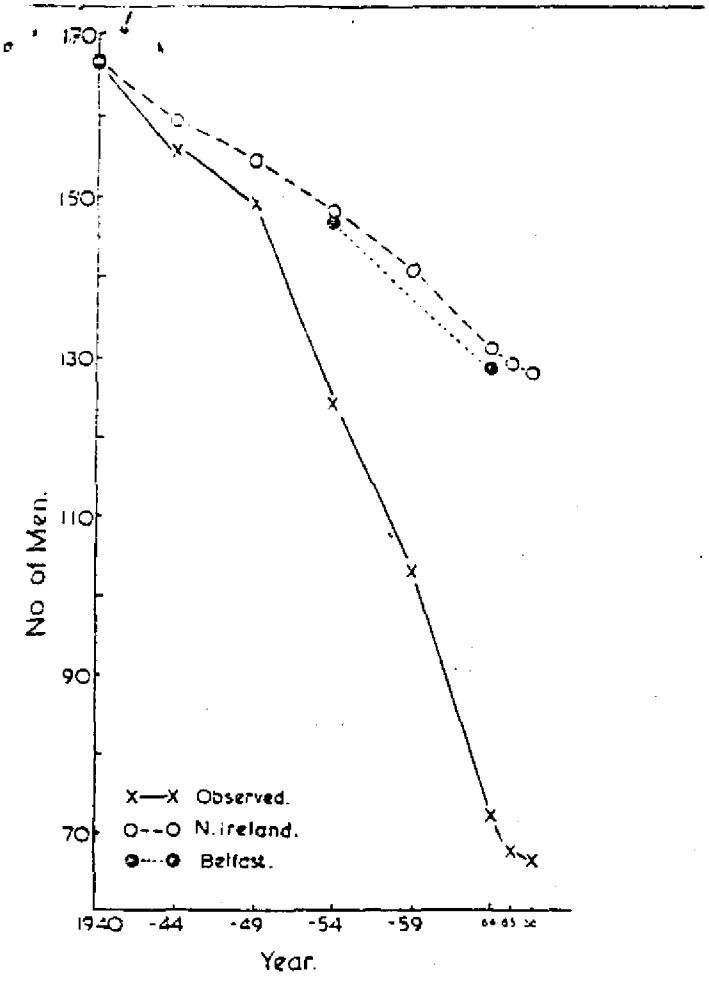


Fig 1 [illegible]

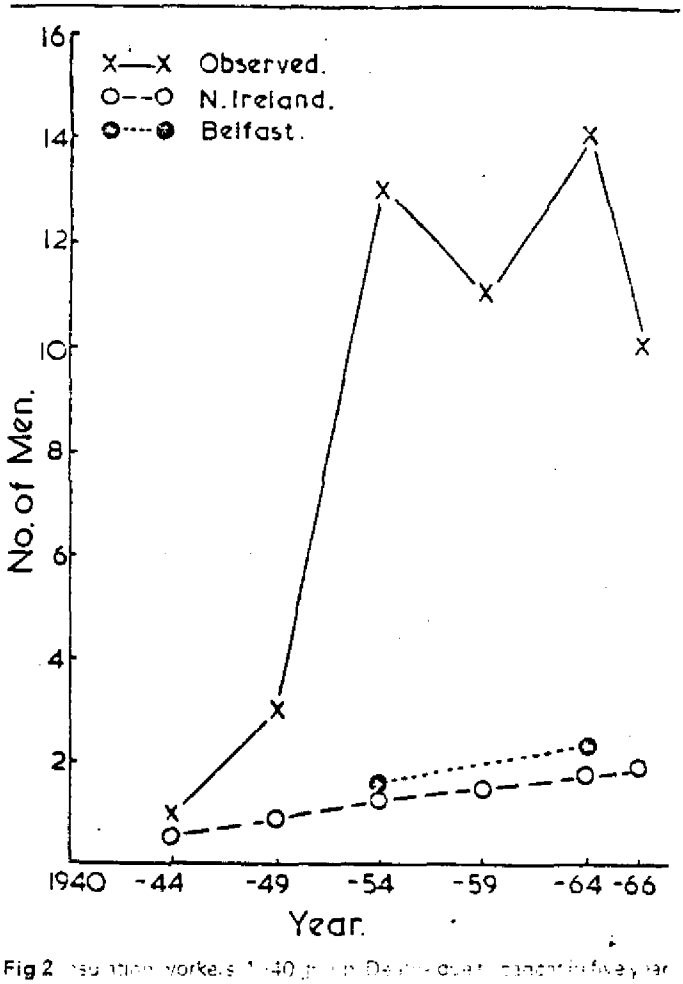


Fig 2 [illegible]

unlikely to differentiate between a mesothelioma and a lung cancer. The experience of these men was compared with the Registrar General's analysis of causes of death in Northern Ireland for men of the same age as our insulation workers over the same period (1940-66). The results of this complex investigation are shown in three graphs. In the first (Fig 1) the survival is compared with the survival of equivalent men in the general population of both Northern Ireland as a whole and more specifically of Belfast where these figures were available. The lines start to diverge in 1950 and by 1966 only 65 men survived of the 168 when about 100 should have survived. There had been 35 more deaths than expected.

In the second and third graphs (Figs 2 and 3) the number of men dying in each five-year period is compared with the number expected. In Fig 2 deaths due to all kinds of cancer are shown. In Fig 3 deaths from lung cancer and mesothelioma are shown together. Both graphs show that from 1950 onwards the number of men dying from cancer, in particular cancer of the lung and pleura, are many times the number expected. This investigation revealed an obviously unacceptable occupational hazard which was not even hinted at by the results of studies on men still at work.

The reason for different results from the two methods of study is the delay between exposure and the development of these to cancers (25 to 30 years for the lung cancer and perhaps 40 years for the mesotheliomas) so that the illness may not develop until after the man has left the industry. In any case a man does not continue to work for many years after a cancer has reached the stage at which it would be revealed by X-ray or clinical examination.

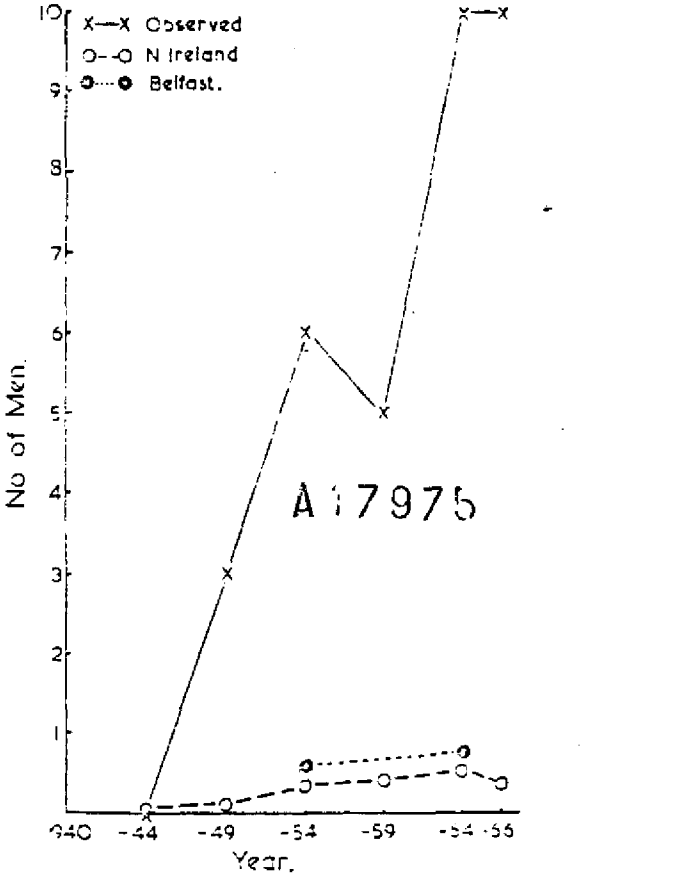


Fig 3 [illegible]

Selection of groups for study

It would be a monumental task to set up this sort of investigation for all construction workers who handle asbestos at some time during their working lives. However, there is a method of finding out which workers are likely to be at hazard. The mesothelioma is a rare tumour and in Britain about 80 per cent of cases are thought to be due to exposure to asbestos at work. Therefore if an investigation is made of the work history of all people dying of mesothelioma then it is possible to show what occupations are responsible and consequently need further investigation. In Belfast the cases can be divided into two main categories, those working most of their lives in the shipyards and those who were mainly employed elsewhere. Of 62 cases recently investigated, the occupations are as shown in Tables 1 and 2. In Table 1 it is seen that the shipyard has given rise to 45 out of the 62 cases, but that only 10 of these occurred in insulation workers. The majority of the shipyard cases arose in men whose exposure was an incidental result of the work mainly because of working in confined spaces near men handling insulation material. It is understandable that pipe and engine fitters should be exposed especially during repair work because their concern is with equipment normally covered by insulation. But platers and so on and electricians were less expected and the extent and circumstances of their past and present exposure manifestly needs investigation. Outside the shipyard there were 17 cases and of obvious concern to the construction industry are the eight cases arising in builder's labourers, joiners, sawyers and timber workers. In the latter group, retrospective questioning did not reveal the source of asbestos.

This was a relatively small study in one city heavily biassed by the presence of a large shipyard. To be of real value this kind of investigation should be carried out on a nationwide basis. It has the major disadvantage of revealing the consequences of working conditions many years before. But it is the only method of pinpointing hazardous occupations with respect to asbestos at the present time. Once identified the extent of the hazard requires detailed investigation along the lines used in the Belfast insulation study. This work takes time and awareness of the possible risk should be the reason for the introduction of preventive measures rather than waiting for the results of detailed studies.

Table 1 **Mesotheliomas in shipyard workers in Belfast – 45 of a group of 62 cases**

Insulators:		
Full-time	5	10
Transient	5	
Other occupations (helpers and labourers included):		
Plumbers, pipefitters and boiler makers		17
Engine fitters		4
Platers, riveters and welders		4
Electricians		8
Other		2

Table 2 **Mesotheliomas in non-shipyard workers in Belfast – 17 of a group of 62 cases**

Known exposure:	
Heating engineers and boilerman	2
Builders' labourers and joiners	6
Dockers	1
No known exposure:	
Linen workers (women)	2
Sawyers and timber workers	2
Baker	1
Postman	1

References

1. Merewether, E. R. A. & Price, C. W., 'Report on the effects of asbestos dust on the lungs and dust suppression in the asbestos industry', 1930, *London: HMSO*
2. 'Hygiene standards for chrysotile asbestos dust', British Occupation Hygiene Society, 1968. *Pergamon Press*
3. Merewether, E. R. A. Annual report of the Chief Inspector of Factories for the year 1947, 1949, p79. *London: HMSO*
4. Doll, R., *Brit. J. Ind. Med.*, 1955, **12**, 81
5. Knox, J. F., Holmes, S., Doll, R. & Hill, I. D., *ibid*, 1960, **25**, 243
6. Buchanan, W. W., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 1, 507
7. Hammond, E. C. & Selikoff, I. J., 'Relation of cigarette smoking to risk of death of asbestos associated disease among insulation workers in the United States'. Meeting of a Working Group to review the Biological Effects of Asbestos. Lyon, 2-5 October 1972, in press
8. Wagner, J. C., Sleggs, C. A. & Marchand, P., *Brit. J. ind. Med.*, 1960, **17**, 26
9. Elmes, P. C., *Journal Ir. Coll. Physic. Sur.*, 1972, **1**, 117
10. Wallace, W. F. M. & Langlands, J. H. M., *Brit. J. ind. Med.*, 1971, **28**, 211
11. Elmes, P. C. & Simpson, M. J. C., *ibid*, 1971, **28**, 226
12. Langlands, J. H. M., Wallace, W. F. M. & Simpson, M. J. C., *ibid*, 1971, **28**, 217

Letters to the editor

Gelatin emulsions in the formation of microcapsules

Sir,—Dr A. Courts in his lecture on 'Gelatin emulsions in the formation of microcapsules' before the SCI Food Symposium in March 1972 and reprinted in *Chemistry and Industry*[1] states that the most profitable application for microcapsule technology is to be found in the carbonless copy paper manufacture.

We are convinced that the readers of *Chemistry and Industry* will find Dr Court's lecture extremely valuable because it presents a fair picture of the present knowledge on gelatin based micro encapsulation technique.

There are, however, some errors which we would like to correct. Dr Courts states 'The capsules are coated onto the underside of a sheet of paper and this is then contacted with a surface coat of attapulgus clay on the following sheet. When the capsules are broken by the pressure from a typewriter key, or a pen, the dye is released and reacts with the clay surface, which induces oxidation leaving a blue coloured print. One dye is oxidised immediately and the second dye provides the more lasting effect'.

In actual fact[2,3] the primary mark on breaking the capsules is brought about by the immediate ring opening of crystal violet lactone in contact with the clay surface. No other chemical reaction is involved and a blue image of limited light stability is produced. The lasting blue-green image occurs slowly through the decomposition of benzoyl leuco methylene blue in a complex mechanism[4] involving oxidation as well as the action of light.

Yours faithfully

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References

1. Courts, A., *Chem. & Ind.*, 1973, 943
2. Abrahart, E. N., *Chem. & Ind.*, 1962, 1512
3. 'Recent advances in the progress of applied chemistry', vol XVI, 1971, p139 and vol XVII, 1972, p135
4. Potts, H. A., Wood, A. H. & Cook, C. C., *J. appl. Chem. Biotechnol.*, 1972, **22**, 651

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